
# STREAMLINING THE ACCESS TO METAL CARBENES THROUGH AROMATIVE DECARBENATIONS

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UNIVERSITAT ROVIRA i VIRGILI

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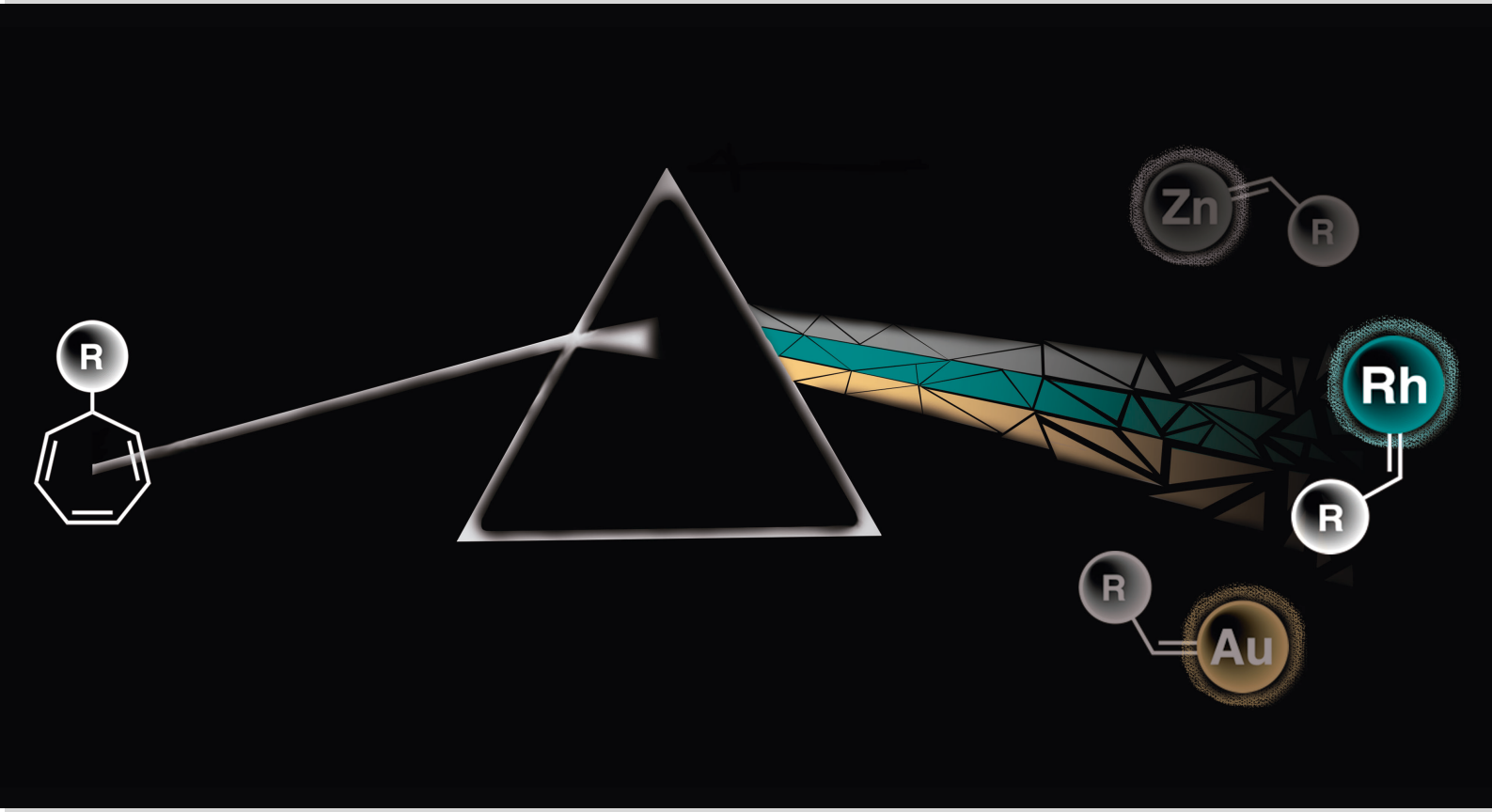



**DOCTORAL THESIS**
**2021**

*Mauro Mato Gómez*

# Streamlining the Access to Metal Carbenes through Aromative Decarbenations

DOCTORAL THESIS

Supervised by Prof. Antonio M. Echavarren

Institut Català d´Investigació Química (ICIQ)


UNIVERSITAT ROVIRA i VIRGILI

Tarragona 2021

I STATE that the present study, entitled "Streamlining the Access to Metal Carbenes through Aromative Decarbenations", presented by Mauro Mato Gómez to award the degree of Doctor, has been carried out under my supervision at the Institut Català d´Investigació Química (ICIQ).

Tarragona, July 5th, 2021

Doctoral Thesis Supervisor

Prof. Antonio M. Echavarren Pablos

*A mis padres y mi hermana*

*"Do not demand events to turn out the way you want,*

*welcome them in whichever way they happen: this is the path to peace"*

Epictetus (*Discourses*, 108 AD)

## *Acknowledgements*

La aventura que inicié en Tarragona durante mi *Summer Fellowship* y que culmina con la defensa de este trabajo no hubiera sido posible sin el inconmensurable apoyo del Prof. Antonio M. Echavarren. Su confianza desde el primer momento en que me permitió empezar a trabajar en su grupo hasta el día de hoy ha derivado en la mejor formación como investigador que uno puede desear. El excelente ambiente —tanto a nivel científico como humano— generado en el que ha sido mi segundo hogar durante los últimos años, y la libertad para perseguir cualquier meta científica, me han hecho vivir unos de los mejores años de mi vida. Gracias, Antonio.

Por supuesto, parte del mérito de que todo esto sea posible se debe al impecable trabajo y buen trato por parte de Sònia Gavaldà y la Dra. Imma Escofet. Quiero agradecer cada gestión que hacen, que por muy desapercibida que pueda pasar, forma los cimientos para que los demás podamos dedicarnos libremente a investigar.

También quiero transmitir mis más sinceras palabras de agradecimiento a los miembros del grupo de Metodología Sintética y Catalítica de la Universidade da Coruña, especialmente al Prof. José Pérez-Sestelo y al Prof. Luis A. Sarandeses, por despertar mi interés por la química orgánica, la investigación, y por iniciarme en el camino que me ha llevado hasta aquí. También quiero agradecer a la Dra. Cristina Pérez-Caaveiro por su paciencia, entusiasmo y dedicación, y por enseñarme prácticamente todo lo que sé sobre química experimental. También quiero extender mi agradecimiento a mis compañeros y amigos durante la carrera, especialmente a Mario Andrade, Adriana Mañana y Javier Orosa.

Huge thanks also to Prof. Phil S. Baran! Not only he allowed me to join his group for an awesome short stay at Scripps California during my PhD, but his fascinating research was also a key inspiration and motivation for me to pursue a career in chemistry research, from my very early stages as an undergraduate student. Also, thanks to the rest of the Baran Lab for making me feel at home, especially to Dr. Natalia M. Padial (the best lab buddy I could have hoped for!) and Dr. Julien C. Vantourout, for bringing a small portion of Europe to San Diego.

I would like to continue by thanking all my collaborators over the years at the Echavarren group, starting for my co-supervisor during my *Summer Fellowship*, Dr. Beatrice Ranieri, who taught me everything I needed to know to do research at ICIQ. Also, thanks to Dr. Bart Herlé and Dr. Xiang Yin, who introduced me to the amazing world of metal carbenes and to the mighty retro-Buchner reaction! In the same manner, I would like to thank Dr. Marc Montesinos-Magraner and Arnau R. Sugranyes, for becoming magnificent heirs of this chemistry. I am certain that I leave it in great hands.

I would also like to thank all the past and present members of the group, for fantastic moments inside and outside the lab. A special shot-out to Dr. Juan M. Sarria Toro, Dr. Fedor Miloserdov, Dr. Xiao-Li Pei, Dr. Miguel Peña López, Dr. Margherita Zanini (and our time well spent looking at graphical abstracts), Dr. Leonardo Nannini, and my collaborator and companion throughout both my Master's and my PhD, Helena Armengol-Relats.

Un segundo hogar no es un hogar sin una familia. Por ello me gustaría dar las gracias a la gente que no solo ha hecho de Tarragona un lugar increíble, sino que me ha hecho evolucionar durante estos años. Gracias Inma Martín, por ser una luz tan brillante como un relámpago que atraviesa una ventana, tanto durante el día como en los momentos de oscuridad. Gracias Ana Arroyo —la mejor compañera para salir de una *habitación*— por acompañarme en este

camino, desde el día en que nos declaramos oficialmente como amigos, hasta donde nos deparen nuestras aventuras en tierras germanoparlantes. Gracias Dra. Otty Stoica, la mejor amiga española que uno puede pedir. Gracias Alba Helena Pérez —un resquicio que permite acordarse del *norte de verdad* desde Tarragona— por sacar siempre una sonrisa, incluso cuando está nublado. Gracias Dra. Cristina García, no solo por ser una buena amiga, sino también por enseñarme a apreciar tanto el lado práctico como el lado *teórico* de la vida. Gracias Gala Ogalla, por intentar prepararme galletas y mejorar en tu toma de decisiones. Gracias Dr. Ángel Mudarra —la incorporación oficial no oficial al grupo— por las conversaciones filosóficas, y las no tan filosóficas. Gracias a mis catalanes favoritos, Bruna Sánchez y Dr. Adirán de Aguirre. Gracias a la Dra. Antonia Rinaldi (*come si dice 'grazie'?*), la Dra. Ruth Dorel y la Dra. Pilar Calleja por compartir buenos momentos. Gracias también a las nuevas incorporaciones, Tania Medina, y la Dra. Anna Sadurní. Por último, quiero dar las gracias al Dr. Joan Guillem Mayans, por ser siempre un recuerdo viviente de que mientras seas feliz y lo compartas con los tuyos, todo va a ir bien. And of course, for introducing a life-changing new hobby in my life!

This brings me to saying thanks to all the climbing team, for unforgettable moments both in the *roco* and in the mountains. Thanks Jake, Anna, Jan, Anna, Cris, Jana and Jessica! It has been a pleasure to grow and send alongside all of you. Gracias al Dr. Pablo Bonilla, un modelo a seguir tanto a nivel escalador como organizativo. Y gracias a Patri, por recordarme el valor de la empatía y el humanitarismo, por insistirme en que use los pies, por no dejar que me vuelva (más) loco durante la escritura, y por sonsacarme todos mis secretos.

Para terminar, quiero dar las gracias a toda mi familia, especialmente a mis padres. Las páginas que escribo a continuación no son solo obra mía, sino también vuestra. Gracias por darme la mejor educación posible, por apoyarme, y por transmitirme vuestro cariño y confianza. Muchas gracias también a mi hermana, Sabela, por acompañarme por la vida desde que tenía cuatro años, y por recordarme que la ciencia, sin arte, no tiene sentido. ¡Y por el diseño de la portada de la tesis!

Gracias a todos.

This work was carried out with the support of the Ministerio de Ciencia e Innovación (projects CTQ2016-75960-P and PID2019-104815GB-I00, and FPI predoctoral fellowship to M.M.), the Severo Ochoa Excellence Accreditation 2014-2018 and 2020–2023 (SEV-2013-0319, CEX2019-000925-S), the European Research Council (Advanced Grants No. 321066 and 835080), the AGAUR (2017 SGR 1257), the CERCA Program/Generalitat de Catalunya and the Institute of Chemical Research of Catalonia (ICIQ).

## *List of Publications*

At the time of writing this thesis, the research summarized herein has resulted in the following articles:

***"Rh(II)-Catalyzed Alkynylcyclopropanation of Alkenes by Decarbenation of Alkynylcycloheptatrienes"***

Mato, M.; Montesinos-Magraner, M.; Sugranyes, A. R.; Echavarren, A. M.

*J. Am. Chem. Soc.* **2021**, doi: 10.1021/jacs.1c05422 *(In Press).*

**"*Assembling Complex Structures through Cascade and Cycloaddition Processes via Non-Acceptor Gold or Rhodium Carbenes*"**

Armengol-Relats, H.; Mato, M.; Escofet, I.; Echavarren, A. M.

*Synthesis* **2021**, doi: 10.1055/a-1535-3215 *(Invited Review)*.

**"*Metal-Catalyzed Decarbenations by Retro-Cyclopropanation*"**

Mato, M.; Echavarren, A. M.

Book Chapter for "Transition Metal-Catalyzed Carbene Transformations" (Wiley VHC).

*(In Press).*

**"*Assembly of Complex 1,4-Cycloheptadienes by (4+3) Cycloaddition of Rhodium(II) and Gold(I) Non-Acceptor Carbenes*"**

Mato, M.;[*] Armengol-Relats, H.;[*] Echavarren, A. M. *Angew. Chem. Int. Ed.* **2021**, *60*, 1916–1922. [*] *These authors contributed equally to this work.*

**"*Gold-Catalyzed Synthesis of Small Rings*"**

Mato, M.; Franchino, A.; García-Morales, C.; Echavarren, A. M. *Chem. Rev.* **2020**.

doi: 10.1021/acs.chemrev.0c00697.

**"*Synthesis of Trienes by Rhodium-Catalyzed Assembly and Disassembly of Non-Acceptor Cyclopropanes*"**

Mato, M.; García-Morales, C.; Echavarren, A. M. *ACS Catal.* **2020**, *10*, 3564–3570.

**"*Cyclopropane-Alkene Metathesis by Gold(I)-Catalyzed Decarbenation of Persistent Cyclopropanes*"**

Mato, M.; Martín-Torres, I.; Herlé, B.; Echavarren, A. M. *Org. Biomol. Chem.* **2019**, *17*, 4216–4219.

*Invited submission as a part of the themed collection "Carbenes in Organic Synthesis".*

**"*Donor Rhodium Carbenes by Retro-Buchner Reaction*"**

Mato, M.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2019**, *58*, 2088–2092.

*Highlighted as Very Important Paper (VIP).*

**"*Generation of Gold Carbenes by Retro-Buchner Reaction: From Cyclopropanes to Natural Products Synthesis*"**

Mato, M.; García-Morales, C.; Echavarren, A. M. *ChemCatChem* **2019**, *11*, 53–72.

Special Issue: 10th Anniversary of *ChemCatChem*

*Highlighted as Very Important Paper (VIP).*

**"*Cyclopropanation by Gold- or Zinc-Catalyzed Retro-Buchner Reaction at Room Temperature*"**

Mato, M.; Herlé, B.; Echavarren, A. M. *Org. Lett.* **2018**, *20*, 4341–4345.

**"*Gold(I)-Catalyzed Synthesis of Indenes and Cyclopentadienes: Access to (±)-Laurokamurene B and the Skeletons of the Cycloaurenones and Dysiherbols*"**

Yin, X.; Mato, M.; Echavarren, A. M. *Angew. Chem. Int. Ed.* **2017**, *56*, 14591–14595.

## Table of Contents

## *Prologue*

This PhD Thesis has been divided into three parts: a general introduction about metal carbenes and two main research chapters covering the obtained experimental results. These sections are preceded by the abstract and general objectives and are followed by the overall conclusions of the work. For clarity, each of the two main research chapters has been subdivided into parts, covering the different research projects that have been carried out during this PhD thesis. A specific introduction to each topic is provided when appropriate, and a methods section is located at the end of each main research chapter, describing the experimental or theoretical methods employed. For the sake of clarity, in general, the work described in each chapter is organized chronologically. Characterization data for compounds that were unknown at the time of performing the corresponding experiments are also provided. In case of collaborative projects, experimental and computational details are included only for the experiments/calculations performed by the author of this thesis, unless stated otherwise. When presenting DFT energy profiles, intermediates and transition states are numbered independently within each Section. References are given as footnotes and have a continuous numeration throughout the thesis—some of them are intentionally duplicated instead of cross-referenced in order to facilitate reading. Generally, nucleophilic components (e.g., alkenes) are color-coded in ***green*** and electrophilic ones (e.g., carbenes) in ***blue***.

**Chapter I**, ***"General Introduction"***, provides an overview of the bonding model in metal carbenes and reviews the main reactivity trends and methods of generation of these reactive intermediates. The discovery and development of the gold(I)-catalyzed retro-Buchner reaction for accessing non-acceptor gold(I) carbenes is also presented.

- These topics have been reviewed by us in (a) *ChemCatChem* **2019**, *11*, 53–72; (b) *Chem. Rev.* **2020** doi: 10.1021/acs.chemrev.0c00697; (c) "*Metal-Catalyzed Decarbenations by Retro-Cyclopropanation*" **(**Book Chapter, for "Transition Metal-Catalyzed Carbene Transformations, Wiley VHC).

**Chapter II**, ***"Design and Development of New Non-Acceptor Metal Carbene Precursors"***, describes our efforts towards expanding the use of aromative decarbenation processes for accessing a wide range of non-acceptor carbenes of different metals. The application of new carbene precursors in the development of new cyclopropanation reactions is also discussed.

- Thus far, this work has been published in (a) *Org. Lett.* **2018**, *20*, 4341–4345; (b) *Angew. Chem. Int. Ed.* **2019**, *58*, 2088–2092; (c) *Org. Biomol. Chem.* **2019**, *17*, 4216–4219.

**Chapter III**, ***"New Cycloheptatriene Derivatives as Tools for Reaction Discovery"***, summarizes the discovery and development of new synthetic methodologies based on the use of cycloheptatrienes as carbene precursors. These new reactions, which involve cycloadditions, oxidations, insertions or cascade ring-opening processes, have been applied to the synthesis of natural products and other biologically relevant structures.

- Thus far, this work has been published in (a) *Angew. Chem. Int. Ed.* **2017**, *56*, 14591–14595; (b) *Angew. Chem. Int. Ed.* **2019**, *58*, 2088–2092; (c) *ACS Catal.* **2020**, *10*, 3564–3570; (d) *Angew. Chem. Int. Ed.* **2021**, *60*, 1916–1922.

## *Abbreviations and Acronyms*

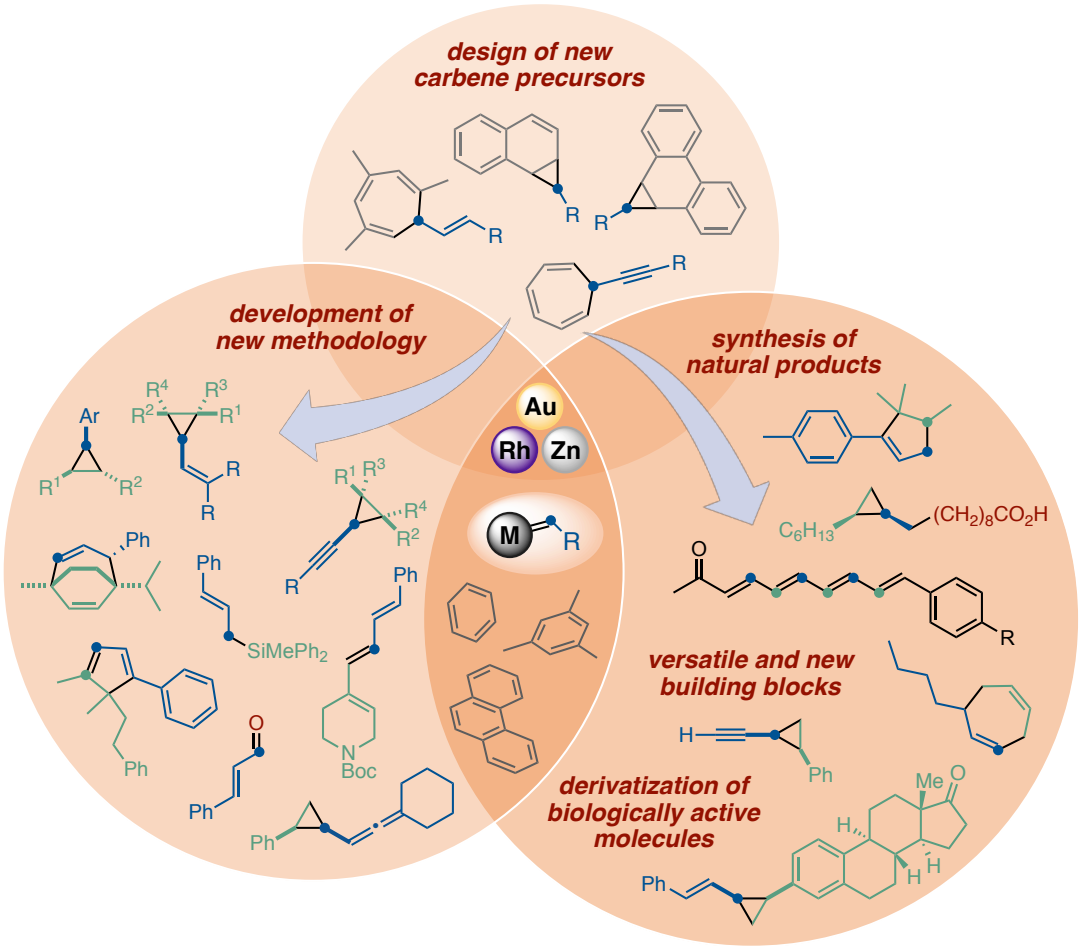
In this manuscript, the abbreviations and acronyms most commonly used in organic and organometallic chemistry have been used following the recommendations of "Guidelines of Authors" of the Journal of Organic Chemistry.

Additional abbreviations and acronyms used in this manuscript are listed below:

| | |
|---|---|
| APCI | atmospheric pressure chemical ionization |
| $BAr_4^{F-}$ | tetrakis[3,5-bis(trifluoromethyl)phenylborate] |
| CHT | cycloheptatriene |
| DCE | 1,2-dichloroethane |
| DFT | density-functional theory |
| dr | diastereomeric ratio |
| ee | enantiomeric excess |
| er | enantiomeric ratio |
| rr | regioisomeric ratio |
| ESI | electrospray ionization |
| EDA | ethyl diazoacetate |
| Fc | ferrocenyl |
| JohnPhos | (2-biphenyl)di-*tert*-butylphosphine |
| n/d | not detected |
| *t*BuXPhos | 2-(di-*tert*-butylphosphino)-2′,4′,6′-triisopropyl-1,1′-biphenyl |
| RuPhos | 2-dicyclohexylphosphino-2′,6′-diisopropoxybiphenyl |
| IPr | 1,3-bis(2,4,6-trimethylphenyl)imidazole-2-ylidene |
| L | ligand |
| M | metal |
| MALDI | matrix assisted laser desorption ionization |
| NPhthal | *N*-phthalimide |
| HRMS | high resolution mass spectrometry |
| MW | microwave irradiation |
| NCD | norcaradiene |
| TFA | trifluoroacetate |
| TS | transition state |

## *Abstract*

Modern synthetic organic chemistry relies significantly in metal catalysis, a discipline that often involves the study of reactive organometallic intermediates. One of the fundamental intermediates in organometallic chemistry are metal carbenes. Metal carbenes display very unique reactivity patterns, which makes them invaluable for the construction of certain structures, such as cyclopropanes. Diazo compounds are the most widely studied metal-carbene precursors. However, they present many limitations: for instance, they are generally toxic and not easy to prepare. Particularly if not stabilized by acceptor groups, diazo compounds can be explosive and difficult to handle and store. For these reasons, we propose the use of alternative precursors based on the concept of aromative decarbenation, or retro-Buchner reaction.




In the presence of cationic gold(I) complexes, 7-subtituted cycloheptatrienes can undergo a decarbenation via retro-Buchner reaction, generating gold(I) carbenes upon release of a molecule of benzene. In this PhD thesis, we have extended this concept for the development

of new and more reactive carbene precursors, based on the release of different aromatic and polyaromatic molecules.

These findings not only allowed the generation of a wider range of carbene fragments (such as rare alkynyl carbenes), but also led to the discovery of new metal-based catalytic systems that are able to promote this type of decarbenation process. Thus, through the gold(I)-, rhodium(II)- and zinc(II)-catalyzed decarbenation of cycloheptatrienes (and related substrates), we developed new and improved cyclopropanation protocols, which allowed the assembly of more than 150 di- to pentasubstituted cyclopropanes (often with high *cis*-diastereoselectivity), bearing aryl, alkenyl, alkyl, allenyl, alkynyl, amino or alkoxy substituents.

We also found that, besides cyclopropanations, these types of carbene intermediates can take part in processes such as higher formal cycloadditions, insertions, oxidations and cascade ring-opening reactions. Thus, we exploited the same strategy to develop a variety of methodologies which allowed the assembly of synthetically challenging structures. For instance, we prepared a variety of cyclopentadienes, 1,4-cycloheptadienes, allylsilanes, conjugated aldehydes, cyclopropyl ethers and polyenes, among others. When considered appropriate, we studied the mechanism of the new transformations through a combination of experiments and DFT calculations.

Finally, we illustrated the potential of the new methodologies through the total synthesis of different natural products and other relevant compounds, such as versatile synthetic intermediates or derivatives of drug-like molecules.

### *General Objectives*

The general aim of this doctoral thesis was the development of new precursors of metal carbenes and the application of these intermediates in the discovery of new chemical reactions. In particular, the objectives of the work described herein were:

- The design and development of new and more reactive gold-carbene precursors based on the concept of aromative decarbenation by retro-Buchner reaction.
- The extension of this chemistry to the generation of carbenes of metals other than gold(I), such as rhodium(II) or zinc(II), and the evaluation of their chemical orthogonality.
- The increase of the scope and variety of carbene units that can be transferred using this strategy, such as alkynyl carbenes.
- The development of new or improved cyclopropanation reactions derived from the decarbenation of the aforementioned precursors.
- The discovery of new cycloadditions, insertions, and cascade processes based on the use of the aforementioned carbene intermediates, and the study of their mechanism by combining both experiments and theory.
- The application of the new methodologies in the synthesis of natural products and derivatives of biologically relevant complex molecules.

Each chapter of this PhD thesis contains a more detailed description of the objectives of the corresponding chapter.

# *Chapter I: General Introduction*

## I.1. Metal Carbenes: Key Intermediates in Chemical Synthesis

### *Prologue*

Around 420 BC, Greek pre-Socratic philosopher Empedocles stated that all matter is made up of four elemental substances: fire, water, air and earth. Contrastingly, Democritus later argued that matter is composed of indestructible and indivisible units called atoms (from Greek ατομον, *atomon*, i.e., "uncuttable"). Since ancient times, the study of the nature of matter has fascinated humankind. However, it was not until the 17th century that our knowledge on the subject started to rapidly develop, when Robert Boyle (regarded by many as the first modern chemist) refined the scientific method and distilled chemistry from alchemy.[1]

Similarly to most scientific disciplines, our understanding of matter and its changes has experienced an exponential growth during modern times. Today, chemistry is not only a window to comprehending Nature, but also the most powerful tool to modify matter at our will, much like ancient alchemists had imagined.

In 1828, Friedrich Wöhler reported the first synthetic preparation of a naturally occurring substance: urea.[2] From that point, chemists began to design synthetic strategies that, starting from simple building blocks, allowed them to assemble molecules of increasing structural complexity which had required millions of years of natural evolution to emerge in the first place.[3] With the development of new reaction methodologies throughout the 20th and 21st centuries, synthetic chemists have been continuously proving the possibility of breaking and making new types of chemical bonds in manners that were previously thought impossible. In a way that often resembles art almost as much as science, modern synthetic chemistry allows the execution of surgically precise modifications in molecules, granting access to new chemical compounds that can drastically impact the progress of humanity.[4]

A cornerstone addition to the modern synthetic-organic-chemistry toolbox is metal catalysis. Over the past few decades, the use of metal salts or complexes as reaction catalysts has unlocked a vast array of novel reactivity paradigms which would have been inaccessible otherwise. For instance, nowadays, metal-catalyzed cross-coupling reactions are the most used

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1 Asimov, I. *A Short History of Chemistry* (1st Ed, 1965). Anchor Books (Garden City, New York, USA).

2 Wöhler, F. Über künstliche Bildung des Harnstoffs. *Annalen der Physik und Chemie* **1828**, *88*, 253–256.

3 Baran, P. S. Natural Product Total Synthesis: As Exciting as Ever and Here to Stay. *J. Am. Chem. Soc.* **2018**, *140*, 4751–4755.

4 (a) Noyori, R. Synthesizing our future. *Nat. Chem.* **2009**, *1*, 5–9. (b) Bostöm, J.; Brown, D. G.; Young, R. J.; Keserü, G. M. Expanding the medicinal chemistry synthetic toolbox. *Nat. Rev. Drug Discov.* **2018**, *17*, 709–727.

processes to forge C–C bonds in medicinal chemistry but were virtually unknown until the 1980s.[5] In this type of metal-catalyzed transformations, chemical entities containing C–M bonds are often involved as intermediates. The study of such species evolved into a whole different field, which is known as organometallic chemistry.

One of the most important types of intermediates in organometallic chemistry are metal carbenes: species containing a carbon atom bonded only to two substituents and to one metal center. This doctoral thesis focuses on the study of the reactivity of metal carbenes and aims to streamline the in-situ generation of a broad range of these versatile synthetic intermediates.

***Carbenes and Metal Carbenes: Classification and Bonding Models***

Carbenes are electrically neutral species $R_2C$: in which the carbon C is covalently bonded to two univalent groups of any kind (generally organic fragments or H) or to one divalent group (e.g., in vinylidenes) and has two nonbonding electrons.[6]

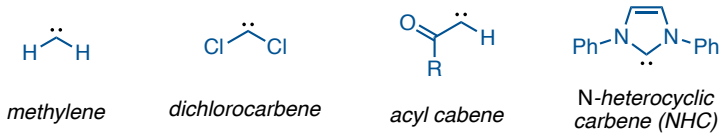


**Figure 1**. Examples of historically relevant free carbenes.

The first courageous proposal of the formation of carbene fragments dates as back as 1855, more than 150 years ago, even before free radicals were assumed to exist.[7] After the work of E. Buchner with acyl carbenes,[8] H. Staudinger proposed methylene as intermediate in the cyclopropanation of alkenes with diazomethane in 1912.[9] Later, von Doering illustrated the synthetic utility of dihalocarbenes (first explored by Hermann and Geuther),[7] which can be straightforwardly generated by the reaction of haloforms with a base.[10]

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5 *Metal-Catalyzed Cross-Coupling Reactions* (2nd Ed, 2004). Ed.: de Meijere, A.; Diederich, F. Wiley-VCH.

6 IUPAC. *Compendium of Chemical Terminology, the "Gold Book"* (2nd Ed, 1997). Compiled by McNaught, A. D. and Wilkinson, A. Blackwell Scientific Publications, Oxford

7 (a) Hermann, M. Ueber die bei der technischen Gewinnung des Broms beobachtete flüchtige Bromverbindung. *Justus Liebigs Ann. Chem.*, **1855**, *95*, 211–225. (b) Geuther, A. Ueber die Zersetzung des Chloroforms durch alkoholische Kalilösung. *Justus Liebigs Ann. Chem.*, **1862**, *123*, 121–122.

8 Buchner, E.; Feldmann, L. Diazoessigester und Toluol. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 3509.

9 Staudinger, H.; Kufer, O. Über Reaktioneen des Methylens. III. Diazomethan. *Ber. Dtsch. Chem. Ges.* **1912**, *45*, 501–509.

10 Von E. Doering, W.; Koffmann, A. K. The Addition of Dichlorocarbene to Olefins. *J. Am. Chem. Soc.* **1954**, *76*, 6162–6165.

The two non-bonding electrons in the carbene carbon (C) can be spin-paired (singlet carbene, Figure 2A) or non-spin-paired (triplet carbene, Figure 2B).[11]

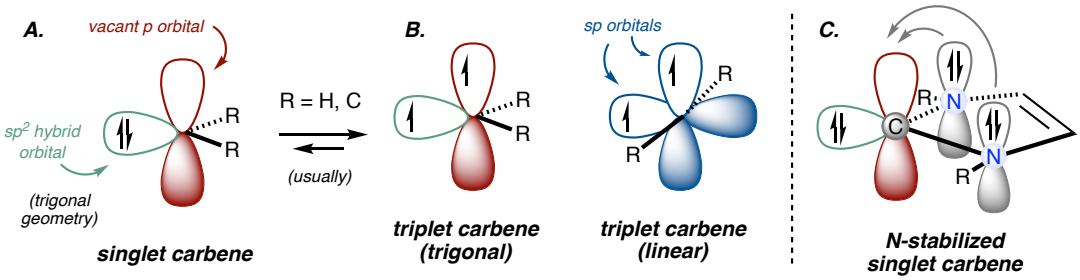


**Figure 2**. Bonding model for singlet (A), triplet (B) and stabilized singlet (C) carbenes.

The R–C–R bond angle in singlet carbenes usually ranges between 105º and 115º. This can be roughly rationalized by an $sp^2$ hybridization model (trigonal geometry, Figure 2A) in which there is a fully occupied $sp^2$ orbital, two bonding $sp^2$ orbitals, and a vacant p orbital. In contrast, triplet carbenes can exist in either a trigonal ($sp^2$) or a linear (sp) geometry (Figure 2B). The former display R–C–R angles between 120º and 135º, while the latter are very close to 180º. In simple hydrocarbons such as methylene, triplet carbenes are often more stable than their singlet counterparts.[12] This fact can be rationalized by Hund's rule of maximum multiplicity. However, the presence of heteroatoms capable of donating electrons to an empty p orbital can drastically stabilize the singlet state. This is the case in *N*-heterocyclic carbenes (NHC), an important class of persistent singlet carbenes first reported by Arduengo and coworkers in 1991,[13] in which the non-bonding pairs of nitrogen stabilize the empty p orbital of the singlet carbene carbon (Figure 2C).

In terms of reactivity, singlet and triplet carbenes behave differently. Singlet carbenes, with a vacant p orbital, are generally electrophilic, and engage in concerted reactions, such as the stereospecific cyclopropanation of alkenes through a 3-carbon/4-electron system. On the other hand, triplet carbenes, which can be considered diradicals, participate in stepwise radical additions, and have to go through intermediates with two unpaired electrons, resulting in non-stereospecific, but rather stereoselective processes.

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11 Hoffmann, R. *Molecular Orbitals of Transition Metal Complexes* (2005). Oxford.

12 (a) Mueller, P. H.; Rondan, N. G.; Houk, K. N.; Harrison, J. F.; Hooper, D.; Willen, B. H.; Liebman, J. F. Carbene Singlet–Triplet Gaps. Linear Correlations with Substituent π Donation. *J. Am. Chem. Soc.* **1981**, *103*, 5049–5052. (b) Nemirowski, A.; Schreiner, P. R. Electronic Stabilization of Ground State Triplet Carbenes. *J. Org. Chem.* **2007**, *72*, 9533–9540.

13 Arduengo III, A. J.; Harlow, R. L.; Kline, M. A stable crystalline carbene. *J. Am. Chem. Soc.* **1991**, *113*, 361–363.

IUPAC defines metal-carbene complexes as coordination compounds $R_2CML_n$ (M = metal, L = ligand) in which a carbene is formally coordinated to a metal center.[6,14] In contrast to singlet/triplet free carbenes, metal-stabilized carbenes are usually classified in two main types: Schrock and Fischer carbenes (Figures 3 and 4). Schrock carbenes, named after Richard R. Schrock,[15] are nucleophilic (and basic) in nature and present short C–M bonds to metals usually in high oxidation state. Fischer carbenes, named after Ernst Otto Fischer,[16] are electrophilic and have longer C–M bonds, often with metals in low oxidation state.

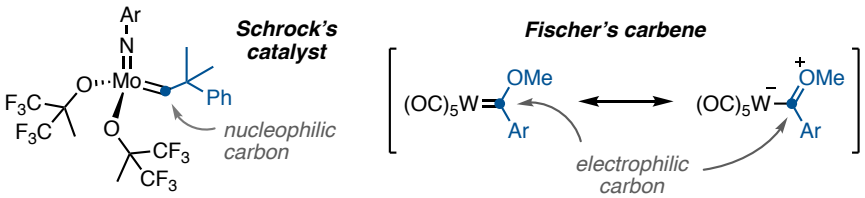


**Figure 3**. Representative examples of each type of metal carbene.

A bonding model for Schrock-type carbenes can resemble that of a triplet-state carbene bonded to a triplet-state metal. These bonds are polarized towards the carbon atom (which is more electronegative than metals) and therefore, the carbene can act as a nucleophile (Figure 4A).

The bonding in Fischer carbenes can be rationalized by the σ-donation from a filled $sp^2$ orbital of a singlet-state carbene carbon to an empty d-orbital of the metal, together with the π-backdonation of a filled d-orbital of the metal to the empty p-orbital of the carbon (Figure 4B). This has the overall effect of generating a positive charge on the carbon atom, and as a result, making the carbene fragment electrophilic in nature.

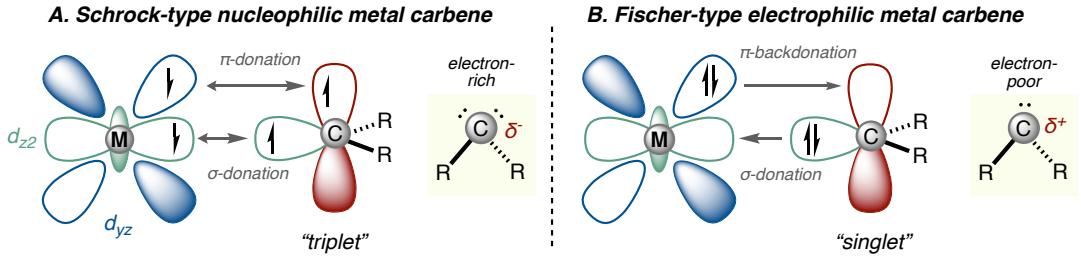


**Figure 4**. A bonding model for Schrock-type (A) and Fischer-type (B) metal carbenes.

14 Crabtree, R. H. in *The Organometallic Chemistry of the Transition Metals* (2005). John Wiley & Sons, Inc. 309–341.

15 Schrock, R. R. Alkylcarbene complex of tantalum by intramolecular α-hydrogen abstraction. *J. Am. Chem. Soc.* **1974**, *96*, 6796–6797.

16 Fischer, E. O.; Maasböl, A. On the Existence of a Tungsten Carbonyl Carbene Complex. *Angw. Chem. Int. Ed. Engl.* **1964**, *3*, 580–581.

### *Stability and Characterization of Metal Carbenes*

As already mentioned above (Figure 2C), some carbenes such as NHCs are indefinitely stable at room temperature in the absence of oxygen and moisture. However, most free carbenes and many metal-stabilized carbenes are very short-lived. Fischer carbenes, which have found diverse applications in synthesis,[17] are usually characterized for having donor substituents (e.g., MeO) on the carbene carbon, contributing to their stability.[18]

Accordingly, some classical Fischer-type carbenes such as **1** are stable at room temperature, even under air. If the substituents are exchanged for electron-rich aryl units, the resulting carbenes (**2** and **3**) are stable enough to be kept in solution at -20 ºC for several hours and to be characterized in the solid state, as demonstrated by Fürstner and coworkers in 2015.[19] On the other end of the spectrum, electron-neutral monosubstituted aryl carbenes such as **4** can only be observed and characterized by NMR at cryogenic temperatures, as shown by our group in 2019 (Figure 5).[20]

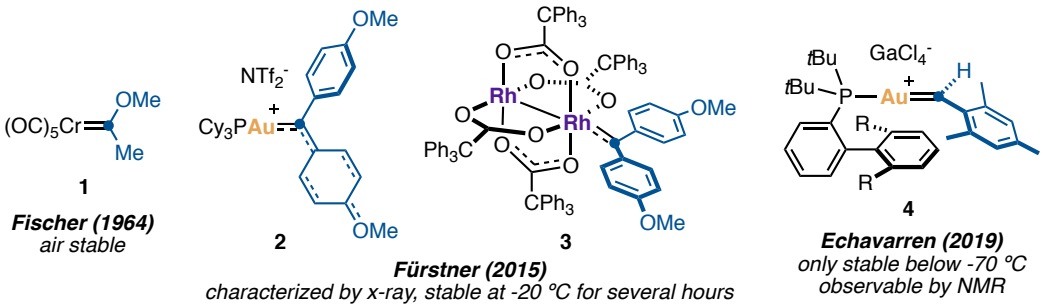


**Figure 5**. Relative stability of different metal carbenes. The further away from the Fischer-type heteroatom stabilization, the lower the stability of the complexes.

In the presence of external nucleophiles, these metal-stabilized carbenes readily undergo an ample range of transformations even at low temperatures, which highlights the synthetic potential of this type of intermediates.

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17 de Meijere, A.; Schrimer, H.; Duetsch, M. Fischer Carbene Complexes as Chemical Multitalents: The Incredible Range of Products from Carbenepentacarbonylmetal α,β-Unsaturated Complexes. *Angew. Chem. Int. Ed.* **2000**, *39*, 3964–4002.

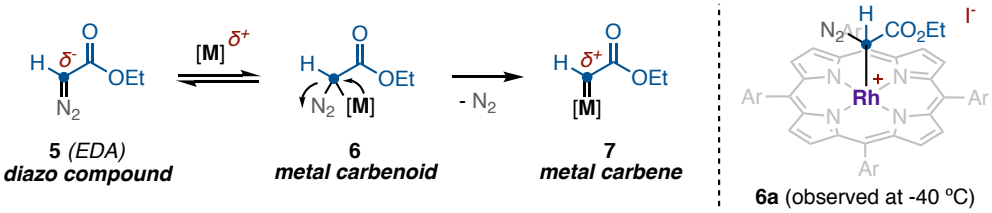
18 Santamaría, J.; Aguilar, E. Beyond Fischer and Schrock carbenes: non-heteroatom-stabilized group 6 metal carbene complexes – a general overview. *Org. Chem. Front.* **2016**, *3*, 1561–1588.

19 Werlé, C.; Goddard, R.; Fürstner, A. The First Crystal Structure of a Reactive Dirhodium Carbene Complex and a Versatile Method for the Preparation of Gold Carbenes by Rhodium-to-Gold Transmetalation. *Angew. Chem. Int. Ed.* **2015**, *54*, 15452–15456.

20 García-Morales, C.; Pei, X.-L.; Sarria Toro, J. M.; Echavarren, A. M. Direct Observation of Aryl Gold(I) Carbenes that Undergo Cyclopropanation, C–H Insertion, and Dimerization Reactions. *Angew. Chem. Int. Ed.* **2019**, *58*, 3957–3961.

### *Carbenes, Carbenoids and Diazo compounds*

The work described in this Thesis aims at streamlining the in-situ generation of non-stabilized metal carbenes, such as **4**. The first and most studied strategy for accessing this type of carbenes is the decomposition of diazo compounds through the release of a nitrogen molecule, which may occur promoted by light, heat,[21] or a metal complex.[22] In the latter case, the reaction is proposed to occur by nucleophilic attack of the diazo compound to the electrophilic metal center, giving rise to $N_2$-containing metal-carbenoid intermediate **6**, that readily evolves into electrophilic metal carbene **7** by releasing nitrogen gas irreversibly (Scheme 1).[23]




**Scheme 1**. Metal-catalyzed generation of carbenes from diazo compounds.

It is important to note the difference between metal-carbene species and metal carbenoids. Metal carbenoids are organometallic species of the type (X)(M)C($R^1$)($R^2$) (such as **6** in Scheme 1), in which an $sp^3$ carbon atom C (for which $R^1$ and $R^2$ are H or organic substituents) is bonded both to a metal M and to a leaving group X. These species can evolve or be in equilibrium with the corresponding carbenes (M)=C$R^1R^2$ (**7**), upon release of the leaving group X, and can display similar reactivity than the latter.[24] Besides possible discussions about the bonding situation, a reason why these two terms are often used interchangeably in the context of metal-catalyzed carbene-transfer processes from diazo compounds may be the fact that these reactions actually pass through both types of intermediates **6** and **7** (Scheme 1). As inferred by the electrophilic nature of intermediates such as **7** (which react with a broad range of nucleophiles, such as alkenes to give cyclopropanes), it is reasonable to simply classify them as a less stable type of Fischer carbene complexes, and not as carbenoids.

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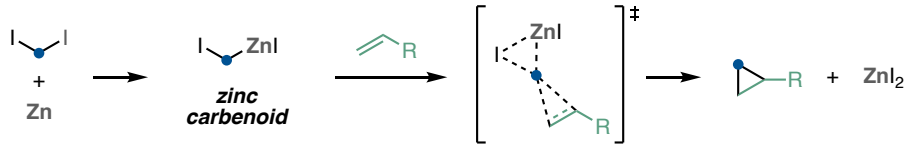
21 Silberrad, O.; Roy, C. S. Gradual decomposition of ethyl diazoacetate. *J. Chem. Soc., Trans.* **1906**, *86*, 179.

22 Yates, P. The Copper-catalyzed Decomposition of Diazoketones. *J. Am. Chem. Soc.* **1952**, *74*, 5376–5381.

23 Wong, F. M.; Wang, J.; Hengge, A. C.; Wu, W. Mechanism of Rhodium-Catalyzed Carbene Formation from Diazo Compounds. *Org. Lett.* **2007**, *9*, 1663–1665.

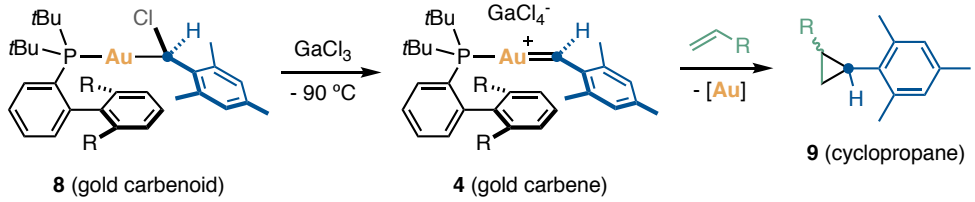
24 (a) Wang, Y.; Muratore, M. E.; Echavarren, A. M. Gold Carbene or Carbenoid: Is There a Difference? *Chem. Eur. J.* **2015**, *21*, 7332–7339. (b) Caballero, A.; Pérez, P. J. Dimensioning the Term Carbenoid. *Chem. Eur. J.* **2017**, *23*, 14389–14393.

It is also worth noting that there are certain chemical processes for which only metal carbenoids (and not metal carbenes) are proposed to be involved as intermediates. For instance, in the Simmons–Smith reaction, $CH_2I_2$ reacts with Zn to form zinc carbenoid $IZnCH_2I$, which in the presence of an alkene engages in a direct concerted cyclopropanation, through a "butterfly-like" transition state, releasing $ZnI_2$ and the corresponding cyclopropane product (Scheme 2).[25] As previously stated, even though the reaction does not go through a carbene intermediate, carbenoid $IZnCH_2I$ displays a reactivity that is analogous to that of metal carbenes (the cyclopropanation of alkenes).




**Scheme 2**. Simmons-Smith cyclopropanation through a Zn(II)-carbenoid intermediate.

There are very few cases in which $N_2$-containing metal-carbenoid intermediates can be observed and characterized, and such is the case of **6a** in Scheme 1.[26] However, if the $N_2$ leaving group is substituted by a halide, the resulting carbenoids can be much more stable, and easily characterized by NMR or X-ray diffraction.[27] This is the case of aryl gold(I) chlorocarbenoids such as **8**, which are unreactive towards alkenes, but can be activated by a chloride scavenger ($GaCl_3$) generating gold(I) carbenes (**4**). These carbenes can be characterized under cryogenic conditions and display the typical reactivity of this type of intermediates. For instance, in the presence of an alkene, carbene **4** reacts to give the corresponding mesityl cyclopropane **9** (Scheme 3).[20]




**Scheme 3**. Activation of thermally stable gold(I) chlorocarbenoids to generate carbenes.

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25 Simmons, H. E.; Smith, R. D. A New Synthesis of Cyclopropanes from Olefins. *J. Am. Chem. Soc.* **1958**, *80*, 5323–5324.

26 Maxwell, J. L.; Brown, K. C.; Bartley, D. W.; Kodadek, T. Mechanism of the Rhodium Porphyrin-Catalyzed Cyclopropanation of Alkenes. *Science* **1992**, *256*, 1544–1547.

27 Sarria Toro, J. M.; García-Morales, C.; Raducan, M.; Smirnova, E. S.; Echavarren, A. M. Gold(I) Carbenoids: On-Demand Access to Gold(I) Carbenes in Solution. *Angew. Chem. Int. Ed.* **2017**, *56*, 1859–1863.

### *Refining the Bonding Model in Non-Acceptor Metal Carbenes*

Besides being considered a special type of non-stabilized Fischer-type complexes, the most appropriate bonding model to describe metal carbenes such as **2**, **3** or **4** (Figure 5, page 31) is highly dependent on the metal center, the ligand, and the substituents of the carbene carbon. The nature of these intermediates ranges from more carbene-like species to metal-stabilized carbocations. The fundamental idea behind the research presented in this Thesis is the study of the generation and reactivity of gold(I) and rhodium(II) carbenes without stabilizing functional groups, but rather with simple aryl or alkenyl substituents. The bonding model that fits best this specific type of organometallic complexes has been a subject of discussion.[28]

For gold(I) in particular, the most widely accepted description for this type of complexes was proposed by Toste and Goddard in 2009: *"The reactivity in gold(I)-coordinated carbenes is best accounted for by a continuum ranging from a metal-stabilized singlet carbene to a metal-coordinated carbocation. The position of a given gold species on this continuum is largely determined by the carbene substituents and the ancillary ligand"*.[29] Thus, factors that decrease the σ-donation from the carbene carbon to gold (such as strong σ-donating ancillary ligands, e.g., L = IPr), or that increase the π-backbonding from gold to the carbene carbon (such as weakly π-acidic ligands, also L = IPr) will lead to structures with more carbene-like character (Figure 6A).

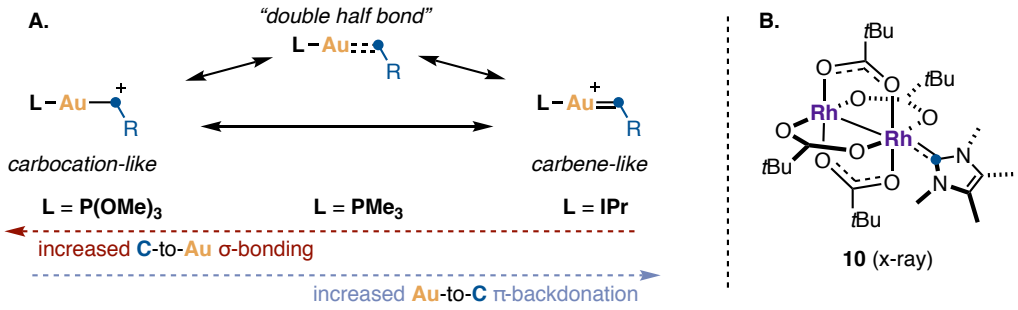



**Figure 6**. Gold(I) carbenes vs gold(I)-stabilized carbocations (A) and solid-state structure of a rhodium(II) carbene fitting the *double half-bond* model (B).

A similarly broad range of scenarios can be envisioned when discussing the bonding situation in carbenes stabilized by dirhodium(II) tetracarboxylate complexes. A *double half-bond* model has been used to describe complexes such as **10** (Figure 6B), in which half of the Rh–C bonding electrons come from the σ-donation of the carbene fragment lone pair to the Rh, and

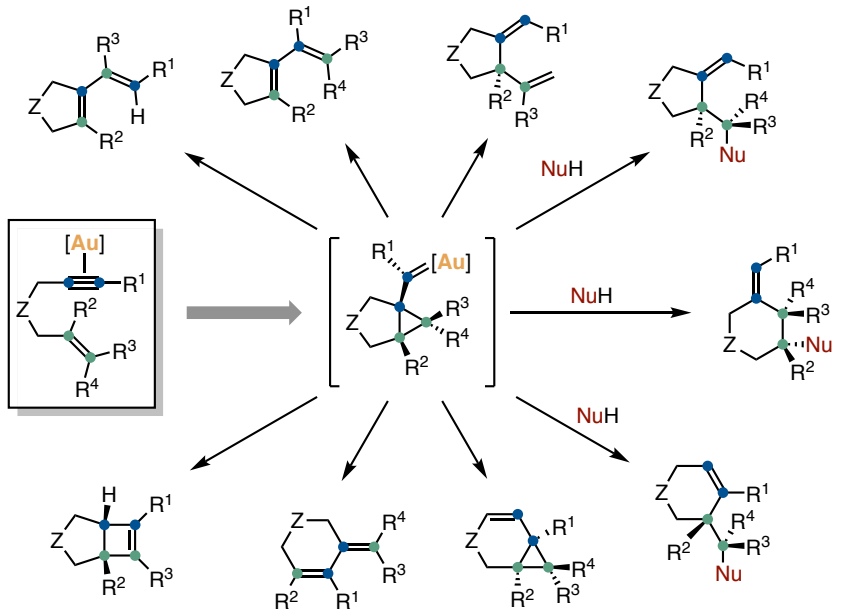
28 Harris, R. J.; Widenhoefer, R. A. Gold carbenes, gold-stabilized carbocations, and cationic intermediates relevant to gold-catalysed enyne cycloaddition. *Chem. Soc. Rev.* **2016**, *45*, 4533–4551.

29 Benitez, D.; Shapiro, N. D.; Tkatchouk, E.; Wang, Y.; Goddard III, W. A.; Toste, F. D. A bonding model for gold(I) carbene complexes. *Nat. Chem.* **2009**, *1*, 482–486.

the other half from the π-back-donation at Rh to the empty carbon p-orbital (see Figure 4B).[19,30] Importantly, in the case of both gold(I) and rhodium(II) carbenes, the depiction of a metal–carbon double bond should not be taken as an indication of a bond order of two, but rather as a way of illustrating that both σ and π components are present in the bond. This can lead to misconceptions, since the overall bond order in these complexes is usually less than or equal to one.[29]

### *Gold(I)-Carbene Intermediates in Catalysis*

Gold(I) catalysis has recently emerged as one of the most powerful tools for the rapid construction of molecular complexity in a single reaction flask. This comes as a result of the ability of gold(I) complexes to activate C–C multiple bonds in a very selective manner.[31] This uniqueness is often attributed to relativistic effects, which reach a maximum for gold in the periodic table, resulting in features such as an abnormally high electronegativity and its characteristic color in its metallic form.[32] The power of gold in the quick assembly of varied complex structures is illustrated by the multiple mechanistic pathways arising from the cycloisomerization of 1,6-enynes (Scheme 4).



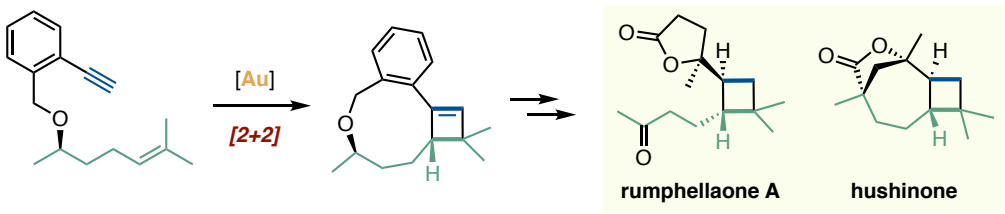

**Scheme 4**. Generation and fate of cyclopropyl gold(I) carbenes from 1,6-enynes.

30 Snyder, J. P.; Padwa, A.; Stengel, T.; Arduengo III, A. J.; Jockisch, A.; Kim, H.-J. A Stable Dirhodium Tetracarboxylate Carbenoid: Crystal Structure, Bonding Analysis, and Catalysis. *J. Am. Chem. Soc.* **2001**, *123*, 11318–11319.

31 Dorel, R.; Echavarren, A. M. Gold(I)-Catalyzed Activation of Alkynes for the Construction of Molecular Complexity. *Chem. Rev.* **2015**, *115*, 9028–9072.

32 Gorin, D. J.; Toste, D. Relativistic effects in homogeneous gold catalysis. *Nature* **2007**, *446*, 395–403.

Based on these complex mechanistic scenarios, many methodologies for the assembly of synthetically complex structures, such as 3- and 4-membered rings, have been developed using gold(I) catalysis.[33] These strategies have been extensively applied in the context of total synthesis of natural products.[34] For instance, we could construct the core of rumphellaone A and hushinone in a straightforward manner by a gold-catalyzed [2+2] cycloaddition process that invokes gold(I) carbenes as intermediates (Scheme 5).[35]




**Scheme 5**. Total synthesis through a gold(I)-catalyzed [2+2] macrocyclization.

All in all, gold(I) complexes have recently emerged as one of the most powerful catalysts for carbene-transfer reactions.

***Metal Carbenes in Catalysis***

The starting point of the work described in this PhD dissertation was the study of the generation and reactivity of non-stabilized gold(I) carbenes. These species are proposed as intermediates in many fundamental gold(I)-catalyzed transformations, such as the cycloisomerization of enynes described in the previous section (Scheme 4).

As described throughout this first part of the "General Introduction", metal carbenes are a fundamental type of organometallic species which displays very particular reactivity patterns. For instance, they are arguably the most powerful tool for the synthesis of cyclopropanes.[33] In practical terms, their intrinsically low stability translates into a high and versatile reactivity, which allows metal carbenes to engage in a huge variety of downhill cycloadditions or complex cascade processes. Overall, this makes the study of metal carbenes one of the most attractive fields in modern organometallic chemistry.[36]

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33 Mato, M.; Franchino, A.; García-Morales, C.; Echavarren, A. M. Gold-Catalyzed Synthesis of Small Rings. *Chem. Rev.* **2020**, doi: 10.1021/acs.chemrev.0c00697.

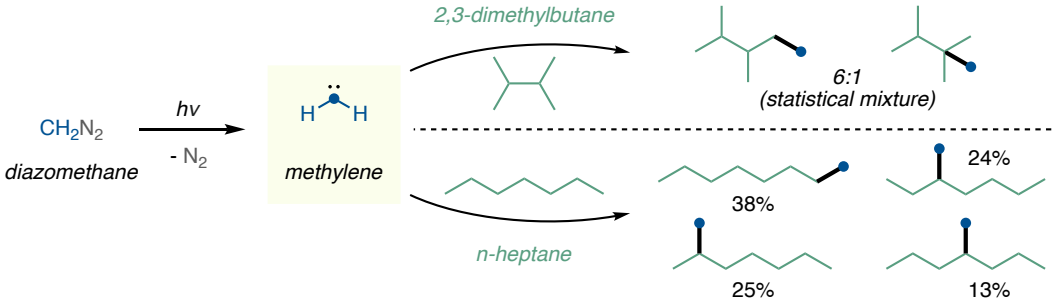
34 Pflästerer, D.; Hashmi, A. S. K. Gold catalysis in total synthesis – recent achievements. *Chem. Soc. Rev.* **2016**, *45*, 1331–1367.

35 Ranieri, B.; Obradors, C.; Mato, M.; Echavarren, A. M. Synthesis of Rumphellaone A and Hushinone by a Gold-Catalyzed [2 + 2] Cycloaddition. *Org. Lett.* **2016**, *18*, 1614–1617.

36 *Metal Carbenes in Organic Synthesis* (in Topics in Organometallic Chemistry, 2004). Ed.: Dötz, K. H. Springer-Verlag Berlin Heidelberg.

## I.2. Reactivity Patterns of Metal Carbenes

At the early stages of the development of carbene chemistry, free carbenes such as methylene were *"classified as the most indiscriminate reagents known in organic chemistry"*.[37] This was indeed well founded, as evidenced by the exact statistical mixture of C–H insertion products that was obtained when decomposing diazomethane upon light irradiation in the presence of 2,3-dimethylbutane (Scheme 6). As other groups showed later, this trend was consistent across a variety of hydrocarbons. For instance, the same reaction performed in *n*-heptane led also to an almost statistical mixture of products.[38]




**Scheme 6**. Indiscriminate reactivity of free methylene with alkanes.

Fortunately, based on the use of metal catalysts that can bias the stereoelectronic properties of these intermediates, chemists are now able to tame the reactivity of carbenes and engage them in highly regio- and stereoselective processes (Figure 7).[39]

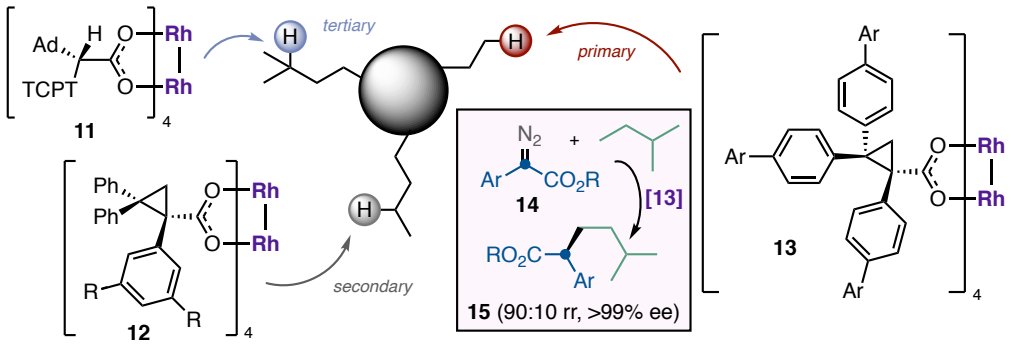



**Figure 7**. Rh(II) carbene-based systems for highly selective C–H insertion reactions. TCPT = Tetrachlorophthalimide.

37 Von E. Doering, W.; Buttery, R. G.; Laughlin, R. G.; Chaudhuri, N. Indiscriminate Reaction of Methylene with the Carbon–Hydrogen Bond. *J. Am. Chem. Soc.* **1956**, *78*, 3224.

38 Richardson, D. B.; Simmons, M. C.; Dvoretzky, I. The Reactivity of Methylene from Photolysis of Diazomethane. *J. Am. Chem. Soc.* **1961**, *83*, 1934–1937.

39 Davies, H. M. L.; Liao, K. Dirhodium tetracarboxylates as catalysts for selective intermolecular C–H functionalization. *Nat. Chem. Rev.* **2019**, *3*, 347–360.

As an illustrative example, Davies and coworkers developed several systems based on dirhodium(II) carboxylate dimers which allow targeting carbene fragments towards very specific C–H bonds of electronically unbiased hydrocarbons. Thus, chiral complex **13** allows to perform a regioselective carbene transfer process from diazo compound **14** to isopentane, to give **15** in a 9:1 ratio of regioisomers and perfect enantioselectivity (Figure 7).[40]

Together with insertion processes, the benchmark reaction of free carbenes and metal carbenes is the cyclopropanation of alkenes. This is the most powerful and studied approach for the construction of 3-membered carbocycles, motifs that cannot be usually assembled through classical cyclization pathways, due to energetic considerations.[33,41] Analogously to free singlet carbenes, or to "ideal" Fischer carbenes, metal carbenes generated from diazo compounds usually react with alkenes through a stereospecific concerted pathway to give cyclopropanes (Figure 8).

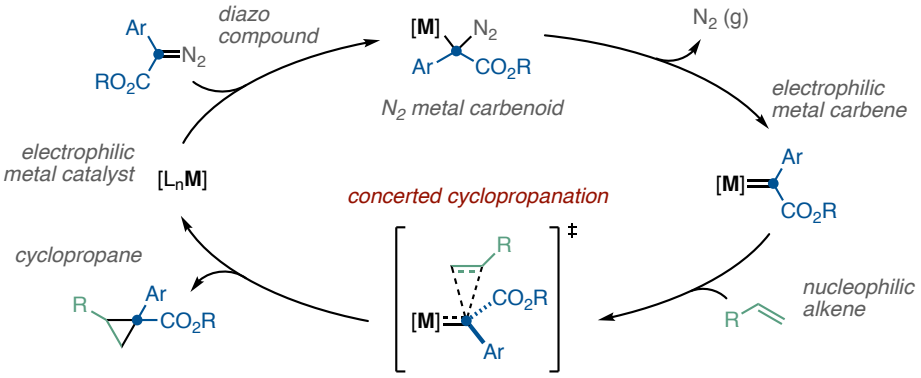



**Figure 8**. Metal-catalyzed cyclopropanation of alkenes with diazo compounds.

Besides X–H (X = C, Si, O, S, N, etc.) insertions or simple (2+1) cyclopropanations, this type of metal carbenes can engage in a variety of higher formal cycloaddition processes,[42] give rise to ylides which undergo further reactivity,[43] and take part in migratory-insertion sequences[44] among other types of reactivity.[36]

40 Liao, K.; Yang, Y.-F.; Li, Y.; Sanders, J. N.; Houk, K. N.; Gusaev, D. G.; Davies, H. M. L. Design of catalysts for site-selective and enantioselective functionalization of non-activated primary C–H bonds. *Nat. Chem.* **2018**, *10*, 1048–1055.

41 Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. Stereoselective Cyclopropanation Reactions. *Chem. Rev.* **2003**, *103*, 977–1050.

42 Frühauf, H.-W. Metal-Assisted Cycloaddition Reactions in Organotransition Metal Chemistry. *Chem. Rev.* **1997**, *97*, 523–596.

43 Zhang, Y.; Wang, J. Catalytic [2,3]-sigmatropic rearrangement of sulfur ylide derived from metal carbene. *Coord. Chem. Rev.* **2010**, *254*, 941–953.

44 Xia, Y.; Qiu, D.; Wang, J. Transition-Metal-Catalyzed Cross-Couplings through Carbene Migratory Insertion. *Chem. Rev.* **2017**, *117*, 13810–13889.

## I.3. New Methods for the Generation of Metal Carbenes

Metal carbenes are highly energetic molecules and, therefore, highly energetic precursors have to be employed for its downhill generation. As discussed above, the most widely known method to access metal carbenes is through decomposition of diazo compounds. However, there are safety concerns to consider while handling these compounds.[45]

Besides their toxicity,[46] diazo compounds can explode if handled incorrectly. As Silberrad and Roy stated in their 1906 publication about ethyl diazoacetate (a stabilized diazo compound, often considered harmless in solution): *"When the diazoacetate is added to copper dust, no reaction appears to take place below 80° C, but above that temperature the addition of the first drop of ester is accompanied by an explosion of sufficient violence to shatter the flask"*.[21]

This problem is accentuated when diazo compounds are not stabilized by acceptor groups: non-acceptor diazo compounds are usually challenging to prepare, inherently unstable, explosive in pure form, cannot be stored for long periods of time and are prone to dimerization.[47] This limits drastically the scope of carbene fragments that can be accessed by this means.

For all these reasons, many groups have turned their attention towards the identification and development of new and safe types of carbene precursors. Many of the most studied carbene precursors that have been developed during the last few decades are shown in Figure 9. First, hydrazone derivatives have been extensively studied as surrogates of diazo compounds. These are considered as a safer alternative, since the diazo compound can be generated in situ upon treatment with base.[47] A similar scenario arises when treating primary amines with sodium nitrite under aqueous conditions.[48]

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45 Green, P.; Wheelhouse, K. M.; Payne, A. D.; Hallett, J. P.; Miller, P. W.; Bull, J. A. Thermal Stability and Explosive Hazard Assessment of Diazo Compounds and Diazo Transfer Reagents. *Org. Process Res. Dev.* **2020**, *24*, 67–84.

46 LeWinn, E. B. Diazomethane Poisoning: Report of a fatal case with autopsy. *Am. J. Med. Sci.* **1949**, *218*, 556–562.

47 Fulton, J. R.; Aggarwal, V. K.; de Vicente, J. The Use of Tosylhydrazone Salts as a Safe Alternative for Handling Diazo Compounds and Their Applications in Organic Synthesis. *Eur. J. Org. Chem.* **2005**, 1489.

48 Barrett, A. G. M.; Braddock, D. C.; Lenoir, I.; Tone, H. 5,10,15,20-Tetraphenylporphyrinatorhodium(III) Iodide Catalyzed Cyclopropanation Reactions of Alkenes Using Glycine Ester Hydrochloride. *J. Org. Chem.* **2001**, *66*, 8260–8263.

Some diazo-free approaches include the use of phenyliodonium ylides,[49] sulfoxonium and sulfonium ylides,[50] or 1,2,3-triazoles (which exist in equilibrium with their diazoimine tautomers and are precursors of α-iminyl metal carbenes).[51] Furthermore, in the presence of metal catalysts and upon treatment with O- or N- transfer reagents (of the type $X^+$–$O^-$ or $X^+$–$N^-$, generally with X = N, S), alkynes give rise to α-oxo metal carbenes and α-imino metal carbenes, respectively. These last processes have been studied mostly under gold catalysis.[52]

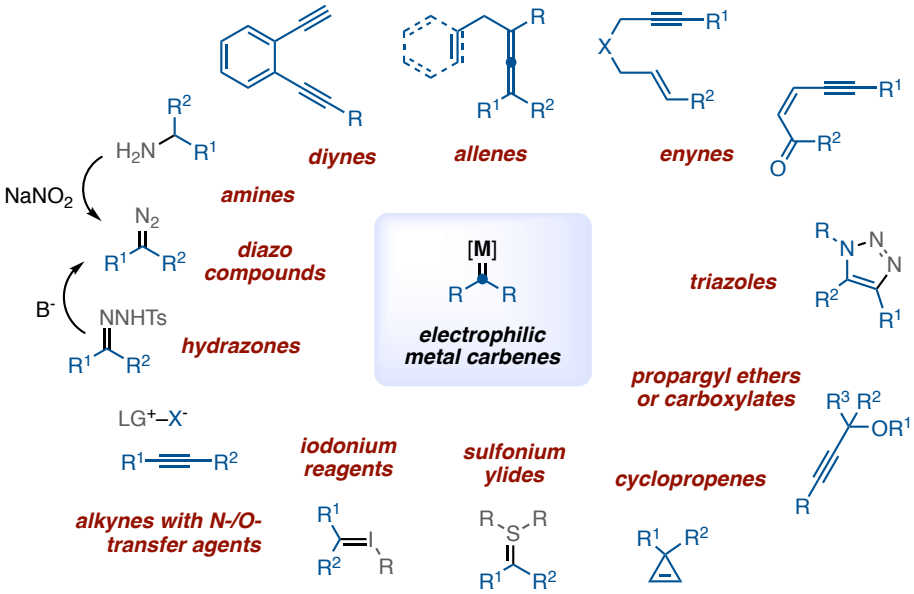


**Figure 9**. Representative examples of metal carbene precursors.

A common trend for diazo compounds, their surrogates, and other precursors mentioned in the last paragraph is that they are often only suitable for the generation of metal carbenes with acceptor groups (such as esters or ketones) attached to the carbene carbon. Practical methods that allow the easy and safe generation of donor (i.e., non-acceptor) metal carbenes are scarcer.[53]

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49 Müller, P. Asymmetric Transfer of Carbenes with Phenyliodonium Ylides. *Acc. Chem. Res.* **2004**, *37*, 243–251.

50 Burtoloso, A. C. B.; Dias, R. M. P.; Leonarczyk, I. A. Sulfoxonium and Sulfonium Ylides as Diazocarbonyl Equivalents in Metal-Catalyzed Insertion Reactions. *Eur. J. Org. Chem.* **2013**, 5005–5016.

51 Davies, H. M. L.; Alford, J. S. Reactions of metallocarbenes derived from N-sulfonyl-1,2,3-triazoles. *Chem. Soc. Rev.* **2014**, *43*, 5151–5162.

52 Ye, L.-W.; Zhu, X.-Q.; Sahani, R. L.; Xu, Y.; Qian, P.-C.; Liu, R.-S. Nitrene Transfer and Carbene Transfer in Gold Catalysis. *Chem. Rev.* **2020**, doi: 10.1021/acs.chemrev.0c00348.

53 Zhu, D.; Chen, L.; Fan, H.; Yao, Q.; Zhu, S. Recent progress on donor and donor–donor carbenes. *Chem. Soc. Rev.* **2020**, *49*, 908–950.

Throughout this discussion, we refer as acceptor carbenes to those containing one or two electron-withdrawing groups directly attached to the carbene carbon. We define donor carbenes as those containing only non-acceptor groups, such as alkyl, alkynyl or most aryl fragments. Ideal Fischer-type carbenes containing heteroatom-substituents would also fall into the classification of donor metal carbenes. In the middle ground are donor–acceptor carbenes, with one substituent of each type (Figure 10).

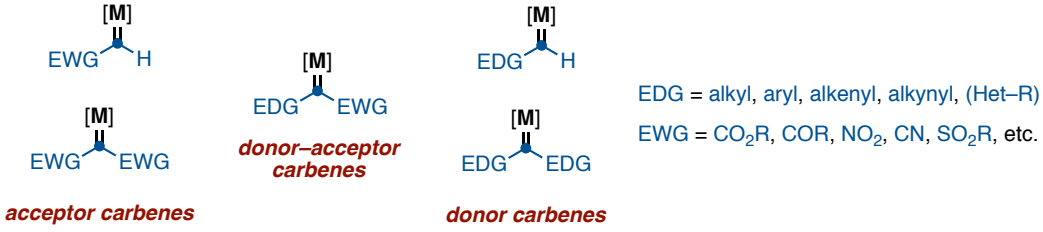


**Figure 10**. A classification of metal carbenes according to their electronic properties.

The metal-catalyzed cyclizations of diynes,[54] polyunsaturated allenes,[55] or enynes (as illustrated by the examples in Scheme 4)[31] often derive in the formation of donor carbenes, which then can be trapped by nucleophiles and/or undergo further rearrangements.[53] Other precursors are propargylic esters (via 1,2-migration or Rautenstrauch rearrangement),[56] and cyclopropenes,[57] both resulting in the generation of non-acceptor alkenyl carbene intermediates (Figure 9).

All the methods mentioned in this section have been successfully developed and applied in the synthesis of relevant structures, but they often suffer from drawbacks, such as safety issues or lack of generality. In this regard, metal-catalyzed aromative decarbenations as the gold(I)-catalyzed retro-Buchner reaction have emerged as powerful alternatives for the in-situ generation of simple donor carbenes. These processes reach an interesting compromise between reactivity, generality, versatility, and relative simplicity of the corresponding carbene precursors.[58]

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54 Asiri, A. M.; Hashmi, A. S. K. Gold-catalysed reactions of diynes. *Chem. Soc. Rev.* **2016**, *45*, 4471–4503.

55 Cañeque, T.; Truscott, F. M.; Rodriguez, R.; Maestri, G.; Malacria, M. Electrophilic activation of allenenes and allenynes: analogies and differences between Brønsted and Lewis acid activation. *Chem. Soc. Rev.* **2014**, *43*, 2916–2926.

56 Shiroodi, R. K.; Gevorgyan, V. Metal-catalyzed double migratory cascade reactions of propargylic esters and phosphates. *Chem. Soc. Rev.* **2013**, *42*, 4991–5001.

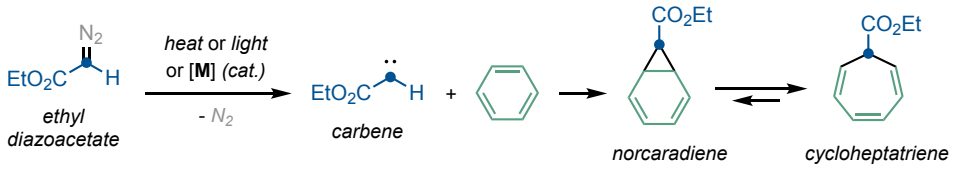
57 Miege, F.; Meyer, C.; Cossy, J. When Cyclopropenes Meet Gold Catalysts. *Beilstein J. Org. Chem.* **2011**, *7*, 717–734.

58 Mato, M.; García-Morales, C.; Echavarren, A. M. Generation of Gold(I) Carbenes by Retro-Buchner Reaction: From Cyclopropanes to Natural Products Synthesis. *ChemCatChem* **2019**, *11*, 53–72.

## I.4. The Gold(I)-Catalyzed Retro-Buchner Reaction

### *Prologue*

In 1885, E. Buchner and T. Curtius reported the reactivity of ethyl diazoacetate with aromatic compounds.[59] Promoted by either heat, light or a metal catalyst, diazo compounds generate carbenes that can cyclopropanate arenes, giving rise to norcaradienes, which are in equilibrium with the corresponding cycloheptatrienes through a thermally allowed disrotatory electrocyclic ring opening (Scheme 7).[60]




**Scheme 7.** The Buchner ring expansion.

More than 100 years later, our group reported the first example of the opposite process: the gold(I)-catalyzed retro-Buchner reaction, one of the first examples of an aromative decarbenation process.[61]

### *Decarbenation Reactions: General Process and Definition*

We define *decarbenation* as a process involving the fragmentation of a molecular entity to release a carbene fragment, upon generation of a stable molecule as the driving force.

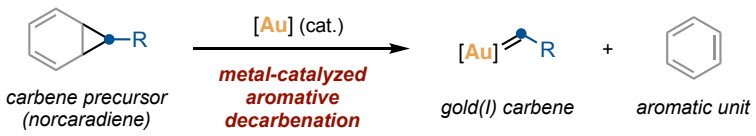
In the context of this thesis, the term *metal-catalyzed aromative decarbenation* is employed to define any process in which a metal carbene is generated catalytically, by cleavage of two C–C sigma bonds, upon release of an aromatic fragment, through a formal *retro-Buchner* or *retro-cyclopropanation* reaction. The driving force of these decarbenations is the opening of a strained three-membered ring while releasing a much more stable aromatic unit, such as benzene. The most studied decarbenation process by retro-cyclopropanation is the metal-catalyzed retro-Buchner reaction of 7-subsituted 1,3,5-cycloheptatrienes, through cleavage of

59 Buchner, E.; Curtius, T. Ueber die Einwirkung von Diazoessigäther auf aromatische Kohlenwasserstoffe. *Ber. Dtsch. Chem. Ges.* **1885**, *18*, 2377–2379.

60 McNamara, O. A.; Maguire, A. R. The norcaradiene-cycloheptatriene equilibrium. *Tetrahedron*, **2011**, *67*, 9–40.

61 Solorio-Alvarado, C. R.; Wang, Y.; Echavarren, A. M. Cyclopropanation with Gold(I) Carbenes by Retro-Buchner Reaction from Cycloheptatrienes. *J. Am. Chem. Soc.* **2011**, *133*, 11952–11955.

their norcaradiene tautomer, which generates a metal carbene upon release of an aromatic molecule (Scheme 8).[58]

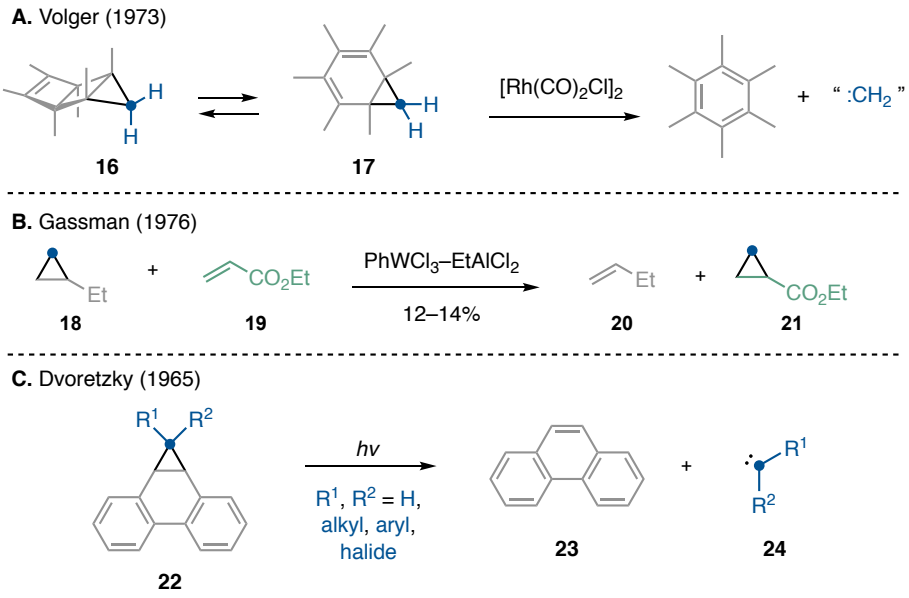



**Scheme 8**. The gold(I)-catalyzed retro-Buchner reaction

Some other processes leading to carbene intermediates, such as the decomposition of diazo compounds (see previous sections) or alkene metathesis cycles,[62] would also fall under the wide definition of *decarbenation* reactions. However, since they involve the cleavage of double C–C or C–heteroatom bonds and do not involve the release of an aromatic unit, they will not be discussed in this section of the General Introduction.

### *A Historical Walkthrough*

From the 1970s, 100 years after the Buchner reaction was first disclosed, some isolated examples of the opposite process were reported (Scheme 9). However, the possibility of using the formally released carbene fragments in a synthetically useful manner was not clear at the time. It was not until gold(I) catalysis came into play that aromative decarbenations emerged as a powerful synthetic tool.[58]

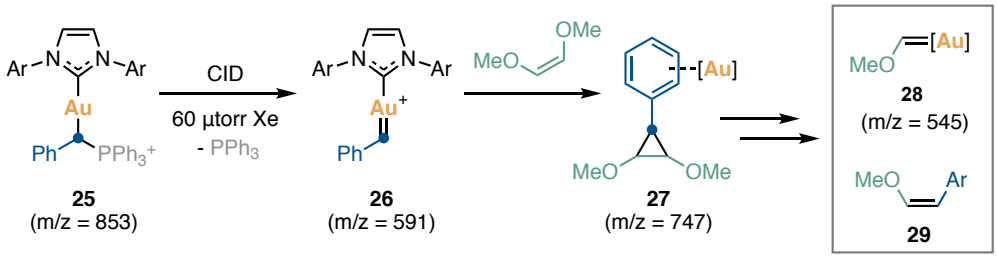



**Scheme 9**. Early examples of retro-cyclopropanations.

62 Ogba, O. M.; Warner, N. C.; O'Leary, D. J.; Grubbs, R. H. Recent advances in ruthenium-based olefin metathesis. *Chem. Soc. Rev.* **2018**, *47*, 4510–4544.

To the best of our knowledge, the first example of a metal-catalyzed retro-cyclopropanation process was reported by Volger and coworkers in 1973. This transformation involved the Rh(I)-catalyzed formal extrusion of a methylene carbene unit from hexamethylnorcaradiene **17**, to produce hexamethylbenzene quantitatively (Scheme 9A).[63] Gassman and Johnson showed that, in the presence of the highly-electrophilic $PhWCl_3$–$EtAlCl_2$ pair, simple ethylcyclopropane **18** reacted with ethyl acrylate to give some amount of cyclopropyl ester **21**, resulting in an overall cyclopropane–alkene-metathesis process (Scheme 9B).[64] Dvoretzky and coworkers showed that phenanthrene derivatives **22** could undergo a retro-cyclopropanation process under photochemical conditions, releasing phenanthrene without the aid of a metal catalyst.[65]

Besides other secluded examples,[66] the concept of metal-promoted retro-cyclopropanation was not revisited in detail until 2008, when Chen and coworkers reported the generation and detection of gold(I)-carbene complexes by gas-phase decarbenation of gold(I) phosphonium ylides such as **25**, upon collision-induced dissociation (CID). This procedure allowed the detection of intermediates **26**, which display the typical reactivity of metal carbenes: cyclopropanation of alkenes to give **27**. Furthermore, the resulting cyclopropanes were found to undergo retro-cyclopropanations under the same conditions. Thus, both an alternative carbene fragment **28** and the formal carbene–alkene metathesis product **29** were detected, confirming the reversibility of the cyclopropanation steps (Scheme 10).[67]




**Scheme 10**. Generation and fate of gold carbenes in the gas phase.

63 Volger, H. C.; Hogeveen, H.; Roobeek, C. F. Transition-metal-catalysed cheletropic elimination of carbene and oxygen from seven-membered ring systems. *Recl. Trav. Chim. Pays-Bas* **1973**, *92*, 1223–1231.

64 Gassman, P. G.; Johnson, T. H. Cyclopropane-olefin cross metathesis. *J. Am. Chem. Soc.* **1976**, *98*, 6058–6059.

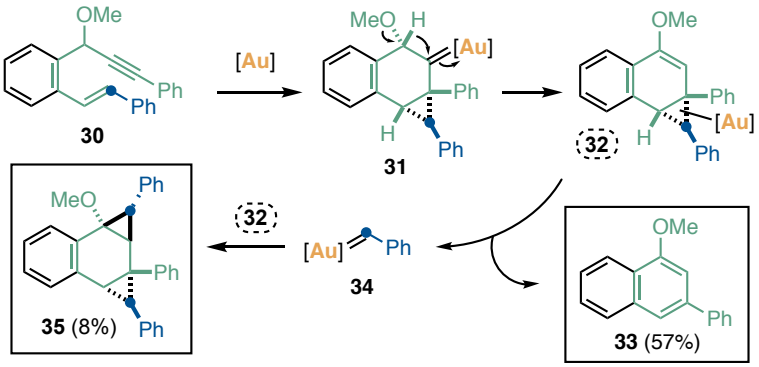
65 Richardson, D. B.; Durrett, L. R.; Martin, J. M.; Putnam, W. E.; Slaymaker, S. C.; Dvoretzky, I. Generation of Methylene by Photolysis of Hydrocarbons. *J. Am. Chem. Soc.* **1965**, *87*, 2763–2765.

66 Saito, K.; Kozaki, M.; Takahashi, K. Aromatization and Hydrogen-Shift of 7-Substituted 1,3,5-Cycloheptatrienes in the Presence of Palladium(II) Acetate. *Chem. Pharm. Bull.* **1993**, *41*, 2187–2189

67 Fedorov, A.; Moret, M.-E.; Chen, P. Gas-Phase Synthesis and Reactivity of a Gold Carbene Complex. *J. Am. Chem. Soc.* **2008**, *130*, 8880–8881.

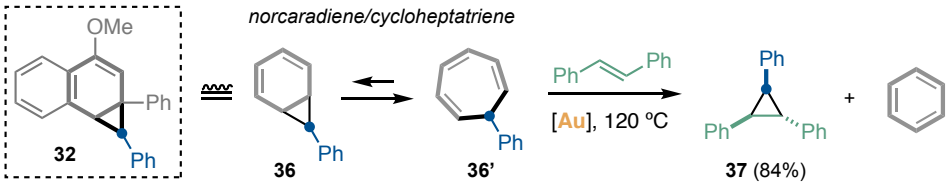
***The Discovery of the Gold(I)-Catalyzed Retro-Buchner Reaction***

In 2010, while studying the gold(I)-catalyzed cycloisomerization of aryl-linked 1,6-enynes **30**, the generation of free aryl gold carbenes by retro-cyclopropanation of electron-rich benzo-fused norcaradienes **32** was observed (Scheme 11). In the presence of cationic gold(I) complexes, **30** evolves at room temperature into a mixture of naphthalene **33** and biscyclopropane **35**. Naphthalene **33** was proposed to arise from the retro-cyclopropanation of intermediate **32**, and the resulting free aryl gold(I) carbene **34** would be trapped by another unit of dihydronaphthatlene **32**, giving biscyclopropane **35**. The mechanistic proposal was supported by the independent synthesis of gold-free **32**. Treatment of this dihydronaphthalene with a cationic gold(I) complex led to a similar distribution of products.[68]




**Scheme 11**. Gold(I)-catalyzed annulation/fragmentation of phenyl-linked 1,6-enynes.

The structural resemblance of carbene precursor **32** to the norcaradiene tautomer of 7-phenyl-1,3,5-cycloheptatriene **36'** paved the way for the discovery and implementation of 7-substituted cycloheptatrienes as practical alternatives for the generation of gold(I) carbenes. Thus, it was found that the reaction of **36** with (*E*)-stilbene in the presence of a cationic gold(I) complex at 120 ºC affords 1,2,3-triphenylcyclopropane **37** as a single diastereoisomer, upon release of benzene instead of a naphthalene (Scheme 12).[61]



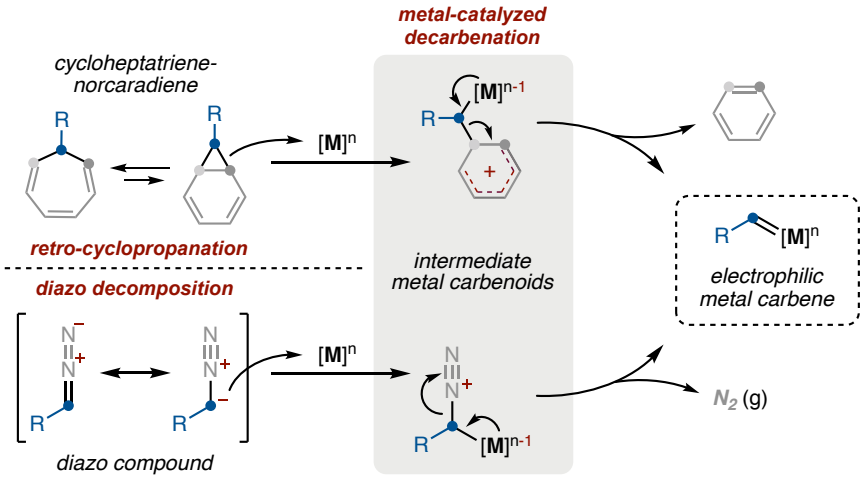

**Scheme 12**. Gold(I)-catalyzed decarbenation by retro-Buchner reaction followed by cyclopropanation.

68 Solorio-Alvarado, C. R.; Echavarren, A. M. Gold-Catalyzed Annulation/Fragmentation: Formation of Free Gold Carbenes by Retro-Cyclopropanation. *J. Am. Chem. Soc.* **2010**, *132*, 11881–11883.

A similar scenario to the one shown in Scheme 11 was later proposed by Hashmi and coworkers in the context of the gold-catalyzed cycloisomerization of diynols, in which a benzo-fused norcaradiene would release ethylene (as evidenced by MS) to give rise to a naphthalene, through a formal retro-cyclopropanation process.[69]

***Overview of the Mechanism behind the Retro-Buchner Reaction***

As described in the previous sections of the General Introduction, the generation of metal carbenes from diazo compounds has been extensively studied in the past: nucleophilic diazo compounds react with electrophilic metal centers, forming carbenoid adducts which evolve to metal carbenes upon downhill release of molecular nitrogen (Scheme 13, bottom).




**Scheme 13**. Overall mechanistic idea behind decarbenations. Analogy between retro-cyclopropanations and diazo decomposition.

Overall, the mechanistic proposal for metal-catalyzed decarbenations via retro-cyclopropanation or retro-Buchner reaction is analogous to that for the decomposition of diazo compounds (Scheme 13, top). First, the norcaradiene tautomer reacts with the electrophilic metal complex, in a process in which the first C–C bond of the three-membered ring is cleaved. This is often the rate-limiting step of the process (with barriers in the range of 15–25 kcal/mol) and it leads to a Wheland-type carbenoid intermediate (Scheme 13, grey box, top). The latter is usually a shallow minimum that evolves smoothly to generate a metal carbene, upon cleavage of the second C–C bond, while releasing an aromatic molecule.[70]

69 Lauterbach, T.; Higuchi, T.; Hussong, M. W.; Rudolph, M.; Rominger, F.; Mashima, K.; Hashmi, A. S. K. Gold-Catalyzed Carbenoid Transfer Reactions of Diynes – Pinacol Rearrangement versus Retro-Buchner Reaction. *Adv. Synth. Catal.* **2015**, *357*, 775–781.

70 Wang, Y.; McGonigal, P. R.; Herlé, B.; Besora, M.; Echavarren, A. M. Gold(I) Carbenes by Retro-Buchner Reaction: Generation and Fate. *J. Am. Chem. Soc.* **2014**, *136*, 801–809.

# *Chapter II: "Design and Development of New Non-Acceptor Metal Carbene Precursors"*

*Part of the work described in this chapter was carried out in collaboration with* ***Dr. Bart Herlé***, ***Inmaculada Martín-Torres***, ***Dr. Marc Montesinos-Magraner*** *and* ***Arnau R. Sugranyes***.

## II.1. Background: From Cyclopropanes to Carbenes

### *Cyclopropanes*

Cyclopropane was first synthesized by August Freund in 1882 (via Wurtz coupling of 1,3-dibromopropane), who already proposed its correct structure.[71] The structure and properties of this highly strained 3-membered carbocycle have fascinated chemists ever since.[72] Cyclopropanes are not only considered interesting for purely academic reasons: the appeal of these structures to the scientific community goes far beyond that, since the cyclopropane unit is a privileged motif in medicinal chemistry. This does not come as a surprise, since 3-membered rings appear in many naturally occurring and biologically active molecules.[73]

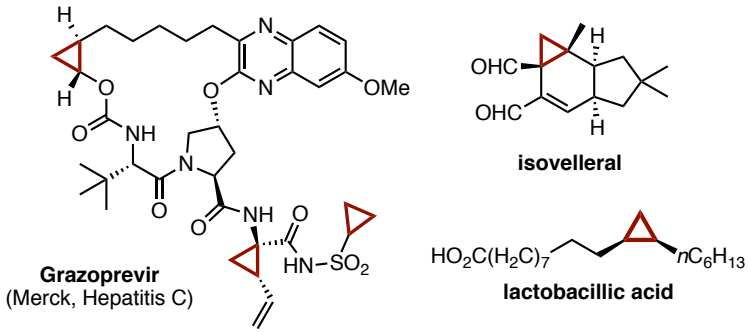
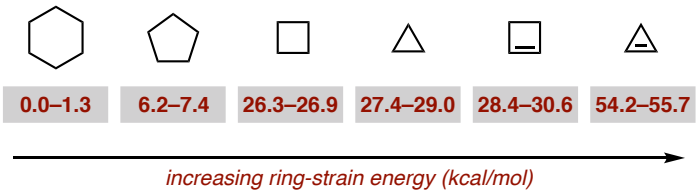



**Figure 11**. The cyclopropane ring in natural products and drugs.

Due to their inherent strain (60° C–C bond angles compared to 109° for typical $C_{sp3}$–$C_{sp3}$ bonds), the reactivity of cyclopropanes often resembles more closely that of alkenes than that of alkanes. Strikingly, the strain energy of cyclobutane and cyclopropane is rather similar (Scheme 14). [74]




**Scheme 14**. Strain energy of different carbocycles.

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71 Freund, A. Ueber Trimethylen. *J. Prakt. Chem.* **1882**, *26*, 367–377.

72 Faust, R. Fascinating Natural and Artificial Cyclopropane Architectures. *Angew. Chem. Int. Ed.* **2001**, *40*, 2251–2253.

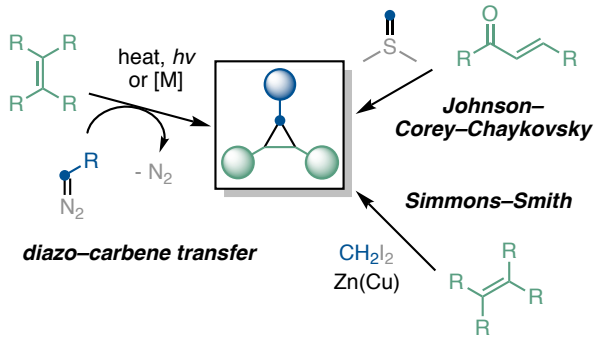
73 (a) Pauling, L. The Nature of the Chemical Bond. *J. Am. Chem. Soc.* **1931**, *53*, 1367–1400. (b) de Meijere, A. Bonding Properties of Cyclopropane and Their Chemical Consequences. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 809–826.

74 Wiberg, K. The Concept of Strain in Organic Chemistry. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 312–322.

This has been rationalized by taking both C–C and C–H bond energy components into consideration: the total C–C bond strain of cyclopropane is 10 kcal/mol higher than for cyclobutane, but this is largely compensated by the stronger C–H bonds of cyclopropane (8 kcal/mol).[75]

### *Synthesis of Cyclopropanes*

As a consequence of the uphill thermodynamics, methods for the assembly of strained small rings differ significantly from those employed to build medium or large rings. For instance, many classical methods to obtain cyclopropanes rely on passing through highly energetic intermediates, such as metal carbenes (already discussed in the *General Introduction*).[33]




**Scheme 15**. Traditional approaches towards cyclopropanes.

Besides classical diazo–carbene transfer processes[76] and the use of free dihalocarbenes,[77] the synthesis of cyclopropanes has been approached by named methodologies such as the Simmons–Smith reaction (through metal carbenoids),[78] the Johnson–Corey–Chaykovsky reaction (Scheme 15),[79] or the Kulinkovich reaction.[80]

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75 (a) Exner, K.; Schleyer, P. v. R. Theoretical Bond Energies: A Critical Evaluation. *J. Phys. Chem. A* **2001**, *105*, 3407–3416. (b) Bach, R. D.; Dmitrenko, O. Strain Energy of Small Ring Hydrocarbons. Influence of C−H Bond Dissociation Energies. *J. Am. Chem. Soc.* **2004**, *126*, 4444–4452.

76 Davies, H. M. L.; Antoulinakis, E. G. Intermolecular Metal-Catalyzed Carbenoid Cyclopropanations. *Organic Reactions* **2001**, 1–326.

77 Fedoryński, M. Syntheses of *gem*-Dihalocyclopropanes and Their Use in Organic Synthesis. *Chem. Rev.* **2003**, *103*, 1099–1132.

78 Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoiness, C. M. Cyclopropanes from Unsaturated Compounds, Methylene Iodide, and Zinc-Copper Couple. *Org. React.* **1973**, *20*, 1–133.

79 Corey, E. J.; Chaykovsky, M. Dimethyloxosulfonium Methylide ($(CH_3)_2SOCH_2$) and Dimethylsulfonium Methylide ($(CH_3)_2SCH_2$). Formation and Application to Organic Synthesis. *J. Am. Chem. Soc.* **1965**, *87*, 1353–1364.

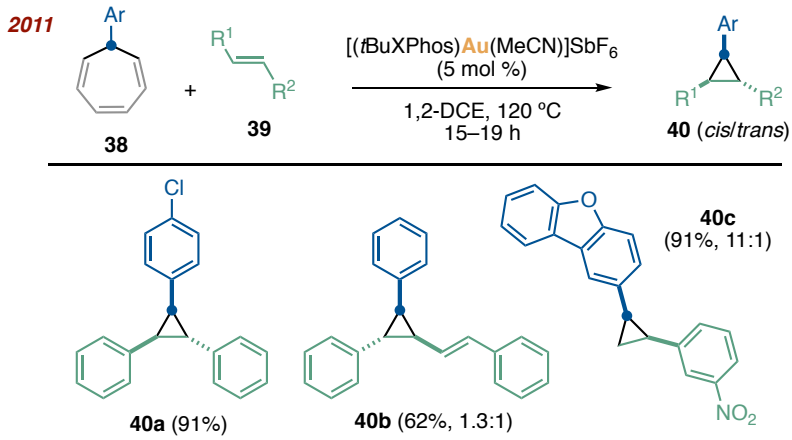
80 Kulinkovich, O. G.; de Meijere, A. 1,*n*-Dicarbanionic Titanium Intermediates from Monocarbanionic Organometallics and Their Application in Organic Synthesis. *Chem. Rev.* **2000**, *100*, 2789–2834.

Some alternative ways for the synthesis of cyclopropanes involve the use of different types of ylides,[81] direct cyclizations,[82] ring contractions[83] and radical pathways,[84] among others.[85]

***Generation of Carbenes to Build Non-Acceptor Cyclopropanes***

Arguably, the most studied method to obtain cyclopropanes is the use of metal carbenes and alkenes. However, as stated in the *General Introduction*, most methods for the generation of non-acceptor carbenes suffer from different drawbacks, creating huge scope limitations.

In our group, the gold(I)-catalyzed retro-Buchner reaction was developed as a way of generating non-acceptor carbenes, which react smoothly with styrenes to afford cyclopropanes, without the need of transferring potentially undesired stabilizing acceptor groups (Scheme 16).[61]




**Scheme 16**. Gold(I)-catalyzed arylcyclopropanation of styrenes.

This method unlocked the access to synthetically challenging 1,2,3-trisubstituted cyclopropanes. When asymmetrical styrenes are employed, diastereomeric ratios ranging from 1:1 to >20:1 were obtained depending on the substituents of the aryl groups. Most likely, this

81 Aggarwal, V. K.; Alonso, E.; Fang, G.; Ferrara, M.; Hynd, G.; Porcelloni, M. Catalytic Asymmetric Synthesis of Epoxides from Aldehydes Using Sulfur Ylides with In Situ Generation of Diazocompounds. *Angew. Chem. Int. Ed.* **2001**, *40*, 1433–1436.

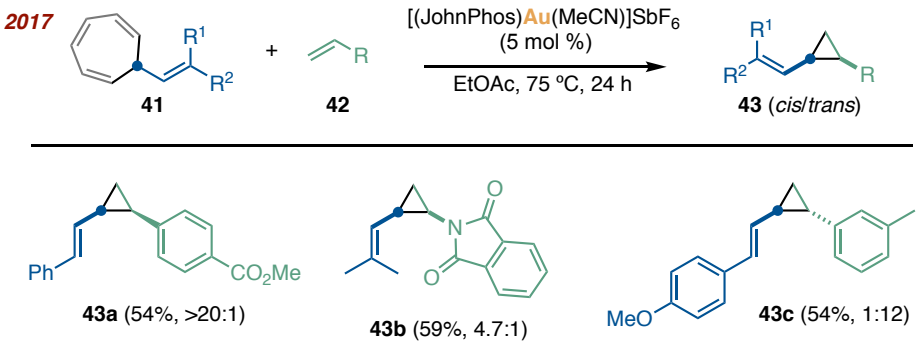
82 Hartog, T. d.; Rudolph, A.; Maciá, B.; Minnaaed, A. J.; Feringa, B. L. Copper-Catalyzed Enantioselective Synthesis of *trans*-1-Alkyl-2-substituted Cyclopropanes via Tandem Conjugate Addition−Intramolecular Enolate Trapping. *J. Am. Chem. Soc.* **2010**, *132*, 14349–14352.

83 Conia, J. M.; Salaun, J. R. Cyclobutane Ring Contractions not Involving Carbonium Ions. *Acc. Chem. Res.* **1972**, *5*, 33–40.

84 del Hoyo, A. M.; Herraiz, A. G.; Suero, M. G. A Stereoconvergent Cyclopropanation Reaction of Styrenes. *Angew. Chem. Int. Ed.* **2017**, *56*, 1610–1613.

85 Lautens, M.; Klute, W.; Tam, W. Transition Metal-Mediated Cycloaddition Reactions. *Chem. Rev.* **1996**, *96*, 49–92.

comes as a consequence of the harsh conditions (120 ºC) required for the retro-Buchner reaction to proceed. A significant step forward was made years later, when this methodology was extended to the alkenylcyclopropanation of styrenes and related activated alkenes (Scheme 17).[86]




**Scheme 17**. Gold(I)-catalyzed alkenylcyclopropanation of activated alkenes.

This allowed the synthesis of a broad scope of vinyl cyclopropanes, mostly with good diastereomeric ratio, favoring the *cis* isomer. However, in some cases in which electron-rich styryl carbene fragments were employed, lower ratios, or even the *trans* diastereoisomers (**43c**, 1:12 *cis*/*trans*) were obtained. In this study, it was found that the same cationic gold(I) complex used to catalyze the cyclopropanation reaction could also promote a *cis* to *trans* cyclopropane isomerization that for some substrates occurred at a significant rate under the required reaction temperature (75 ºC).

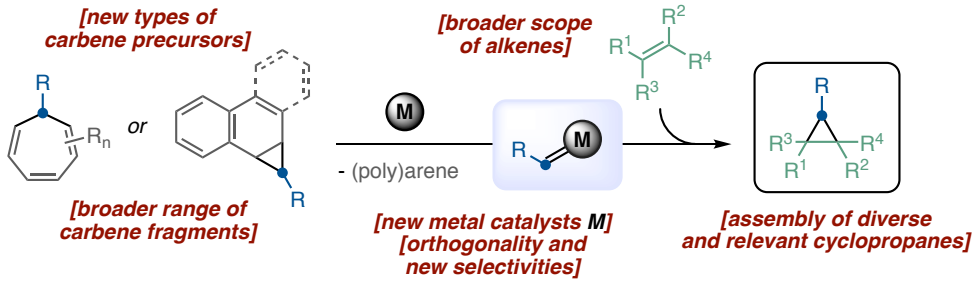
Considering these precedents, we embarked in the design and development of new carbene precursors that would allow us to carry out cyclopropanations under milder conditions, with improved stereoselectivity, under catalysis of other metals, and with a wider scope of both alkenes and non-acceptor carbene fragments.

86 Herlé, B.; Holstein, P. M.; Echavarren, A. M. Stereoselective *cis*-Vinylcyclopropanation via a Gold(I)-Catalyzed Retro-Buchner Reaction under Mild Conditions. *ACS Catal.* **2017**, *7*, 3668–3675.

## II.2. Objectives

The global objective of the projects discussed within this chapter was the design and development of new metal-carbene precursors based on the gold(I)-catalyzed retro-Buchner reaction, with the aim of streamlining the use of aromative decarbenations for the synthesis of a wide range of cyclopropanes. In particular, we wanted to:

- Develop a new generation of cycloheptatrienes or analogous substrates (such as benzo-fused norcaradienes) which would be more reactive towards metal-catalyzed decarbenations.
- Ideally, these new precursors would allow us to carry out retro-Buchner/cyclopropanation sequences at lower temperatures, with higher stereocontrol, and under catalysis of metals other than gold.
- The generalization of aromative decarbenations for the generation of carbenes of different metals would allow us to evaluate their orthogonality, and potentially expand the range of both alkenes and carbene fragments that can be transferred.
- When appropriate, mechanistic investigations would be performed in order to shed light into how these processes take place.
- The improved or newly developed transformations would be applied for the assembly of relevant cyclopropane-containing molecules, such as natural products or derivatives of bioactive molecules.




**Scheme 18.** Decarbenation processes as a general method for accessing new metal carbenes and cyclopropanes.

## II.3. Development of a New Generation of More Reactive Cycloheptatrienes

### *Working Hypothesis*

In 2014, our group developed the first theoretical model to rationalize the mechanism of the gold(I)-catalyzed retro-Buchner reaction of 7-aryl-1,3,5-cycloheptatrienes (Figure 12).[87]

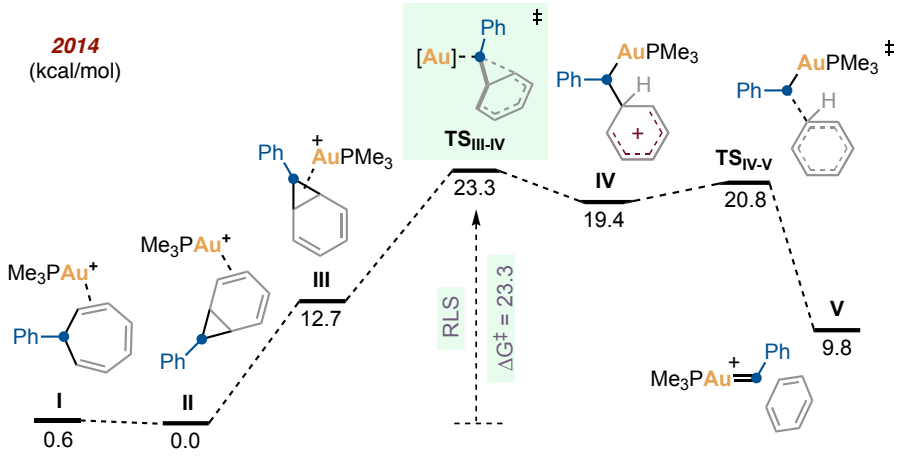



**Figure 12**. DFT model for the retro-Buchner reaction of **I**.

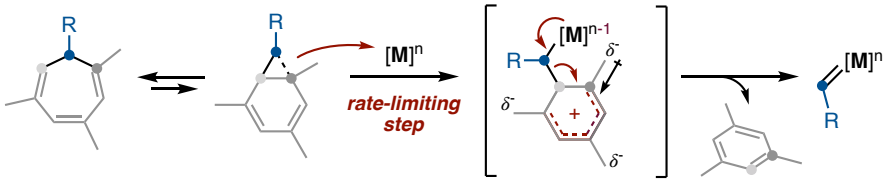
According to the calculations, the first C–C bond in **III** is cleaved through $\mathbf{TS_{III\text{-}IV}}$, giving Wheland carbenoid-type intermediate **IV**. This is the rate-limiting step of the entire process, with an activation barrier of 23.3 kcal/mol from **II**. The actual limiting barrier in the arylcyclopropanations of styrenes, for example, would most likely be higher if an styrene–Au resting state was considered, correlating with the experimentally required temperatures of 100–120 ºC. From that point, intermediate **IV** is a shallow minimum that evolves smoothly through $\mathbf{TS_{IV\text{-}V}}$ to give benzene-coordinated gold(I) carbene **V**. A similar scenario was observed when studying the styrylcyclopropanation of alkenes.[88]

According to the state-of-the-art limitations presented in the introduction and objectives of this chapter, we wanted to develop a new generation of more reactive cycloheptatrienes. In this regard, our working hypothesis was based in the previously developed mechanistic pictures (Figure 12). We aimed for the stabilization of the transitions states and intermediates leading to the formation of metal carbenes such as **V**. In particular, the transition state leading to Wheland-type intermediate **IV** would be stabilized by the introduction of electron-donating

87 Wang, Y.; McGonigal, P. R.; Herlé, B.; Besora, M.; Echavarren, A. M. Gold(I) Carbenes by Retro-Buchner Reaction: Generation and Fate. *J. Am. Chem. Soc.* **2014**, *136*, 801–809.

88 Herlé, B.; Holstein, P. M.; Echavarren, A. M. Stereoselective *cis*-Vinylcyclopropanation via a Gold(I)-Catalyzed Retro-Buchner Reaction under Mild Conditions. *ACS Catal.* **2017**, *7*, 3668–3675.

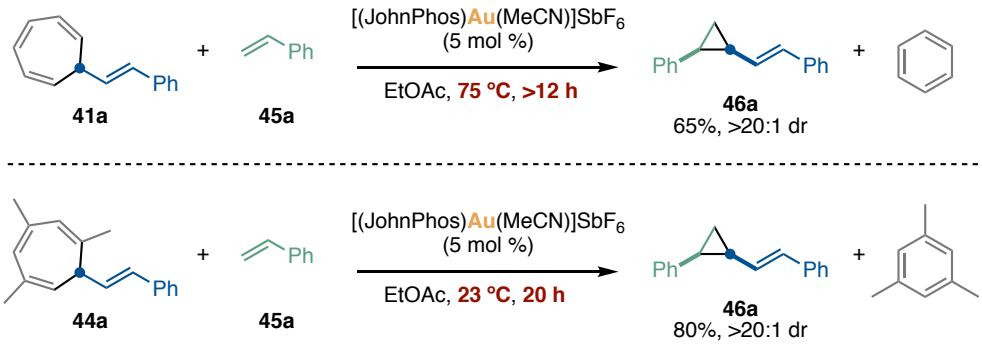
substituents in the cycloheptatriene ring, lowering the activation barrier of the proposed rate-limiting step of the decarbenation process.




**Scheme 19**. Working hypothesis for the design of more reactive cycloheptatrienes.

To prove this concept, we selected 7-alkenyl substituted cycloheptatrienes, since they are already more reactive than their aryl counterparts (75 ºC vs 120 ºC for the retro-Buchner/cyclopropanation sequence to take place at a synthetically useful rate).

After an initial survey of several electron-rich substituents in the cycloheptatriene ring of 7-styryl-1,3,5-cycloheptatriene,[89] we found that 7-styryl-1,3,5-trimethyl-1,3,5-cycloheptatrienes **44** are significantly more reactive than the non-methylated original analogs **41** (room temperature vs 75 ºC, respectively, Scheme 20).[90]




**Scheme 20**. First vs second generation of styrylcyclohepatrienes.

Methyl substituents were found to be the ideal compromise between a significant increase in reactivity, and a relatively straightforward synthesis. Apart from a more challenging preparation, more electron-donating elements such as MeO- can lead to much more stable resting states, translating into higher overall activation barriers.[91]

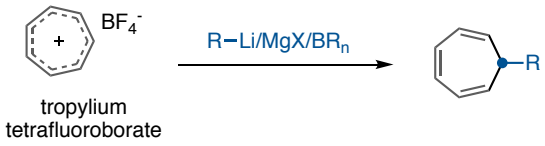
89 Herlé, B. Doctoral Thesis, "Stereoselective Cyclopropanations via Gold(I)-Catalyzed Retro-Buchner Reactions" (2017).

90 Mato, M.; Herlé, B.; Echavarren, A. M. Cyclopropanation by Gold- or Zinc-Catalyzed Retro-Buchner Reaction at Room Temperature. *Org. Lett.* **2018**, *20*, 4341–4345.

91 Our studies on the synthesis of MeO-substituted analogs and an initial evaluation of their reactivity are described at the end of this section.

### *General Approach to Make Monosubstituted Cycloheptatrienes*

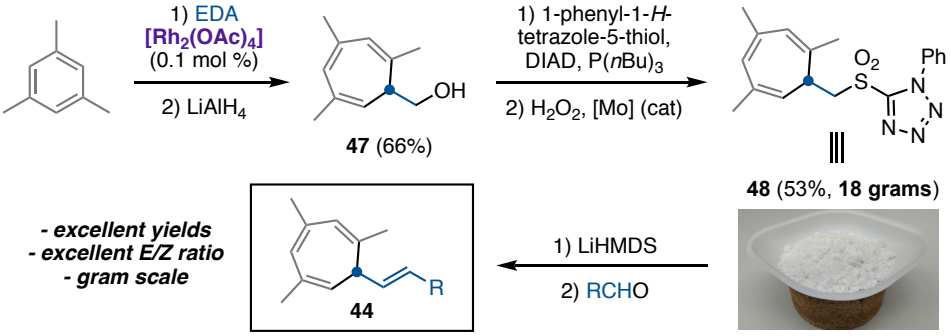
The more widespread approach for the synthesis of 7-substituted cycloheptatrienes consists in the reaction of a nucleophilic species (such as an organolithium, Grignard or organoboron reagent) and an electrophilic tropylium salt. The tropylium cation is an aromatic 7-membered ring derived from the hydride abstraction of cycloheptatriene, and different salts of this cation are bench stable, and easy to prepare.[92] Specifically, tropylium tetrafluoroborate is a practical, commercially available reagent to make simple 7-substituted cycloheptatrienes in only one step (Scheme 21).[93]




**Scheme 21**. General approach to monosubstituted cycloheptatrienes.

### *Development of A New Generation of Cycloheptatrienes*

However, there are no general methods reported in the literature for the regioselective preparation of polysubstituted cycloheptatrienes. For this reason, we optimized the decagram-scale synthesis of sulfone **48**, a bench-stable white solid which can be used to prepare a wide range of 7-alkenyl-1,3,5-trimethyl-1,3,5-cyclohepatatrienes **44**.



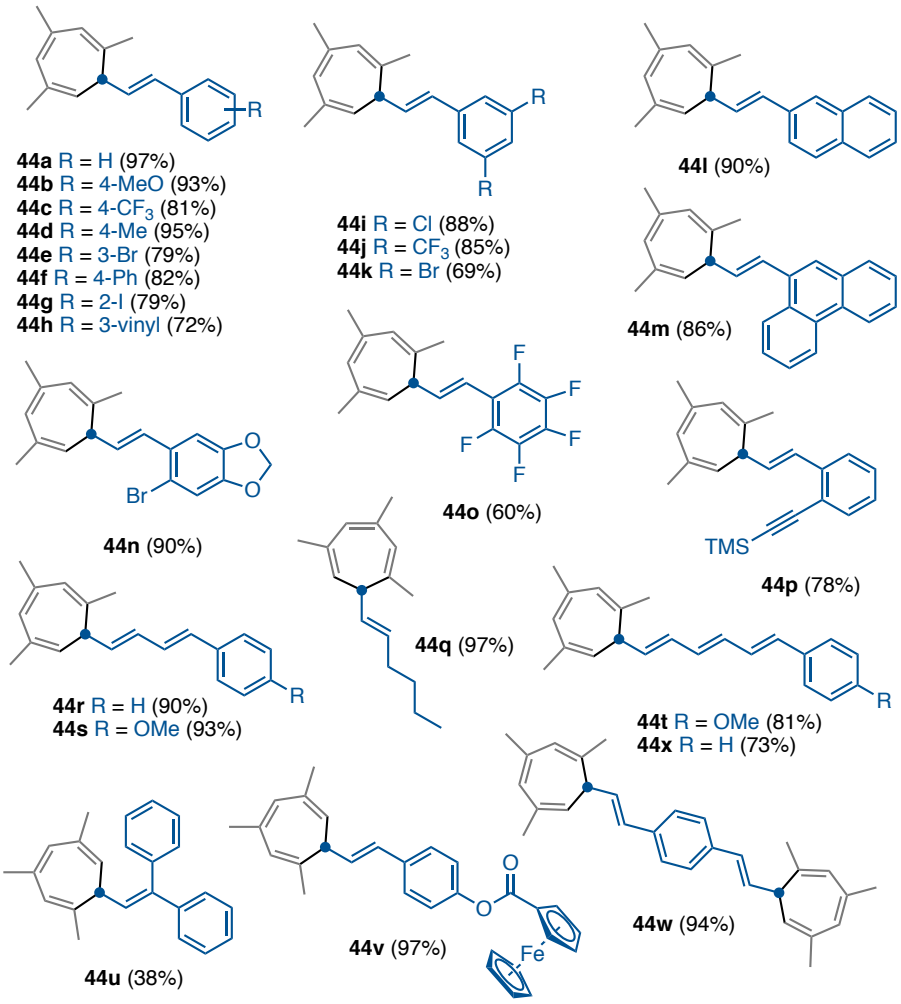

**Scheme 22**. Synthesis and reactivity of sulfone **48**.

Buchner reaction of mesitylene with ethyl diazoacetate (EDA), using only 0.1 mol % of rhodium(II) acetate dimer, followed by $LiAlH_4$ reduction affords alcohol **47** in *ca.* 50 g-scale. This compound was then submitted to Mitsunobu reaction with 1-phenyl-1-*H*-tetrazole-5-

92 Conrow, K. Tropylium Tetrafluoroborate. *Org. Synth.* **1963**, *43*, 101.

93 Kane, J. L.; Danheiser, R. L. "Tropylium Tetrafluoroborate" in *Encyclopedia of Reagents for Organic Synthesis* (2001).

thiol, and subsequent oxidation with hydrogen peroxide using ammonium heptamolybdate tetrahydrate as catalyst afforded Julia–Kocienski reagent **48** in batches of almost 20 g. Deprotonation of sulfone **48** in THF at -78 ºC using LiHMDS, followed by the addition of a carbonyl compound (usually an aldehyde) gives 7-alkenyl trimethylcycloheptatrienes **44** generally as the single *E* diastereoisomer. According to this strategy, a library of more reactive alkenyl carbene precursors was successfully accessed (Scheme 23).[94]

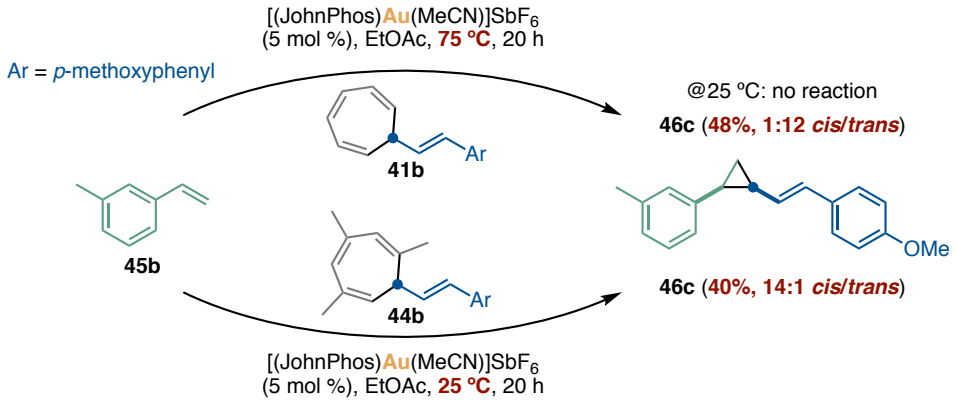



**Scheme 23**. New family of more reactive trimethylcycloheptatrienes.

94 All the new 7-alkenyl-1,3,5-trimethyl-1,3,5-cycloheptatrienes **44** prepared during this Doctoral Thesis are included on this page. Some of them were not used in the early cyclopropanation stages, but in other projects which will be discussed in a different section or chapter.

### *Gold(I)-Catalyzed Styrylcyclopropanations at Room Temperature*

After proving the concept and with gram-quantities of an ample range of substrates in hand, we proceeded to evaluate the potential benefits of being able to perform a retro-Buchner/alkenylcyclopropanation sequence at room temperature. We tested some of the substrates that were giving *trans* cyclopropanes at high temperature, due to a potentially undesired gold(I)-catalyzed *cis* to *trans* isomerization. This process only takes place significantly at 75 ºC with electron-rich substrates that can stabilize the allyl cation intermediate proposed for the isomerization.[88] Gratifyingly, when we performed the same reaction at room temperature with more reactive substrate **44b**, we obtained the *cis* diastereoisomer almost exclusively. This allows accessing either one of the two isomers just by adjusting the reaction temperature (Scheme 24).

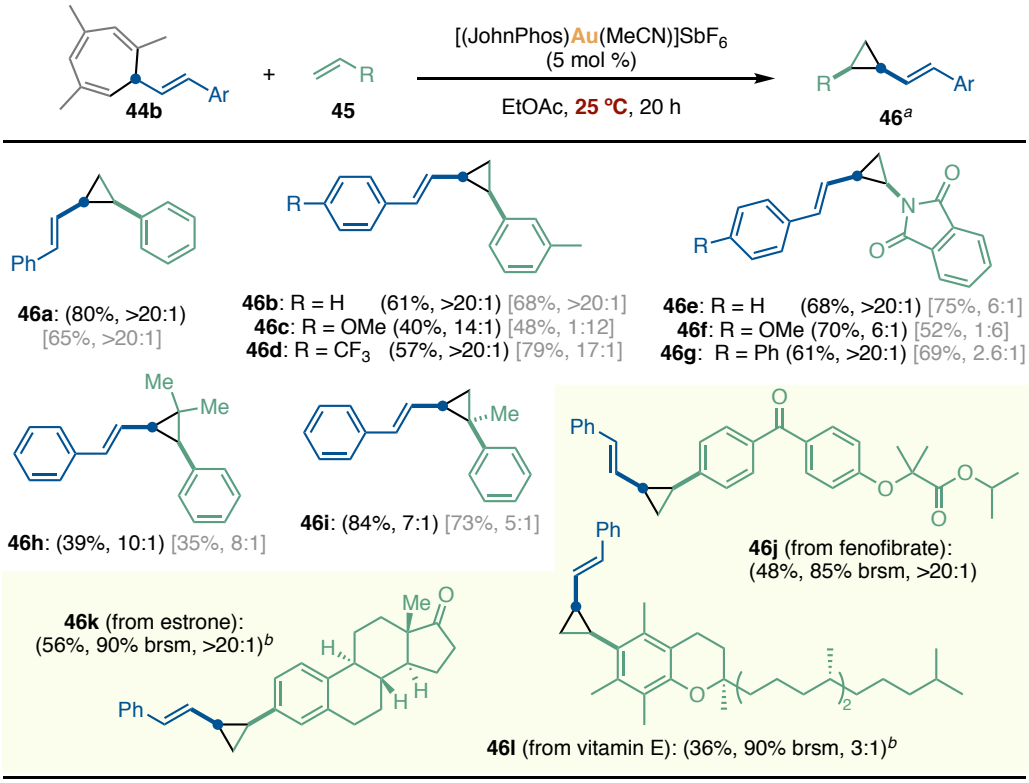



**Scheme 24**. Selectivity inversion at lower temperature.

Then we proceeded to evaluate the scope of the new room-temperature version of the cyclopropanation reaction, focusing on substrates that performed worse in the original procedure at 75 ºC (Scheme 25).

Simple 1-styryl-2-phenylcyclopropane **46a** could be obtained in high yield and perfect *cis*-diastereoselectivity. Both electron-rich and electron-poor carbene fragments could be transferred successfully with excellent *cis* selectivity, improving the result obtained at higher temperatures (e.g., 14:1 vs 1:12 for R = MeO and >20:1 vs 17:1 for R = $CF_3$). A particularly problematic alkene substrate at higher temperatures is *N*-vinylphthalimide, giving cyclopropylamines **46e–g** in *cis*/*trans* ratios ranging between 6:1 and 1:6. We found that, at room temperature, these products could be obtained in good to excellent (>20:1) *cis* diastereoselectivities, even when using electron-rich styryl cycloheptatrienes as substrates (**46f**).

Styrenes with different substitution patterns were also tested (**46h**, **46i**), giving the corresponding cyclopropanes in slightly better yield and dr than when the reaction is performed at high temperature.




**Scheme 25**. Scope of the room-temperature cyclopropanation and comparison with the previous version. [a] Isolated yield and *cis*/*trans* ratio of diastereoisomers in parenthesis. Yield and dr obtained with the previous generation of cycloheptatrienes (75 °C)[88] in brackets. [b] Obtained as a 1:1 mixture of the two-possible *cis*-cyclopropane products.

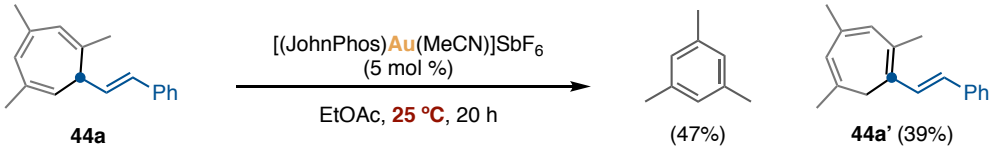
Finally, we illustrated the versatility of this improved protocol through the late-stage functionalization of several biologically relevant complex structures (Scheme 25, bottom). Thus, we prepared *cis*-cyclopropane derivatives of fenofibrate (**46j**, used in hypercholesterolemia treatment), estrone (**46k**, a steroid) and α-tocopherol (**46l**, one of the components of vitamin E).

*Overall, an improved version of the gold(I)-catalyzed alkenylcyclopropanation reaction was developed. The milder conditions required allow carrying out more stereoselective carbene transfer processes. Furthermore, a clear avenue for developing enantioselective variants of these transformations has been established.*[95]

95 See section II.5 for our initial explorations using different catalytic systems.

### *Kinetic and Control Experiments*

When the reaction was run in the absence of an external nucleophilic partner, mesitylene was still formed in 47% yield. The fate of the resulting carbene units is presumed to be the cyclopropanation of other molecules of **44a**, resulting in oligomerization processes. This is evidenced by the detection of several molecules with *m/z* of one unit of **44a** plus one unit of styryl carbene by GC-MS analysis. The other main side product of these reactions is the product of 1,5-H shift of the starting cycloheptatriene, to form fully conjugated structures such as **44a'** irreversibly (Scheme 26).




**Scheme 26**. Control experiment without external alkene.

We followed the cyclopropanation reaction of styrene by $^{1}H$ NMR in $CDCl_3$ at room temperature, with varying amounts of the different components of the system (the cycloheptatriene, styrene and the gold catalyst). According to the initial rates method (for which we assume that during the first half hour of reaction there are no significant changes in the concentration of the components), we plotted the initial reaction rates against the initial concentration of each reagent in a logarithmic scale (Figure 13).

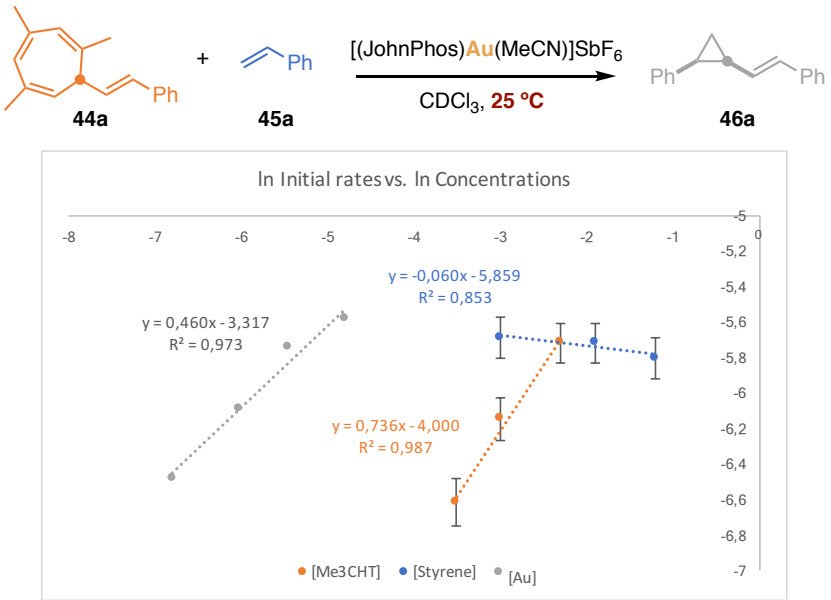



**Figure 13**. Initial rates method logarithmic plot.

A positive slope was found for both cycloheptatriene **44a** and the gold catalyst, although with fractional slopes (which is consistent with the fact that other process such as the isomerization presented in Scheme 26 is taking place at the same time). The horizontal line observed for styrene indicates zero order for the alkene. Although this kinetic model is not ideal to study this system, these observations are consistent with the hypothesis of the gold(I)-catalyzed retro-Buchner process being the rate-limiting step.

The influence of the substituents at the *para* position in the aromatic ring of the styryl carbene fragment was also studied (Figure 14).

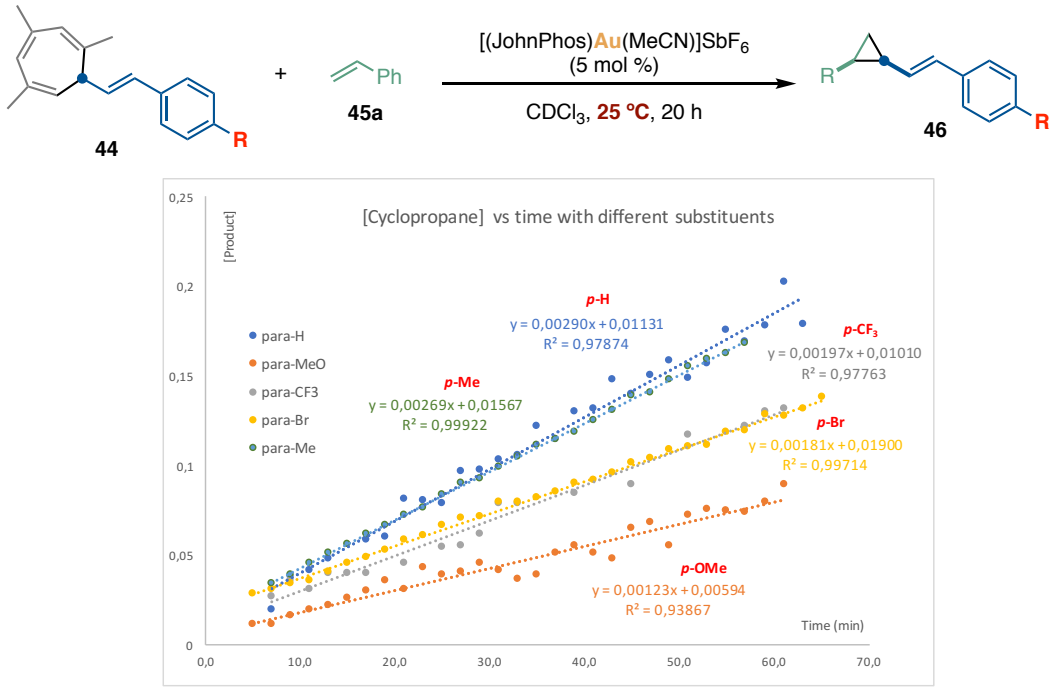



**Figure 14**. Effect of the *para* substituents in the transferred styryl carbene fragment.

When plotting the logarithmic rates against the $\sigma^+$ Hammett values for each *para* substituent,[96] no clear linearity is observed (Figure 15). Similar values are obtained for R = Me and R = H, and lower rates observed for electron-withdrawing R = Br and R= $CF_3$. This might suggest that electron-withdrawing groups can destabilize the positive charge that builds up in the transition state leading to Wheland intermediates **IV** (the proposed rate-limiting step, see Figure 12 in page 54).

96 (a) Brown, H. C.; Okamoto, Y. Electrophilic Substituent Constants. *J. Am. Chem. Soc.* **1958**, *80*, 4979–4987. (b) Hansch, C.; Leo, A.; Taft, R. W. A survey of Hammett substituent constants and resonance and field parameters. *Chem. Rev.* **1991**, *91*, 165–195.

On the other hand, R = OMe leads to an abnormally lower rate. Presumably, this could be due to the fact that the corresponding electron-rich *p*-MeO-styrene units in both **44** and **46** form more stable adducts with the gold(I) complex, and this factor outweighs the rate acceleration caused by the presence of an electron-donating group in transition states such as $\mathbf{TS_{III\text{-}IV}}$ (Figure 12, page 54).

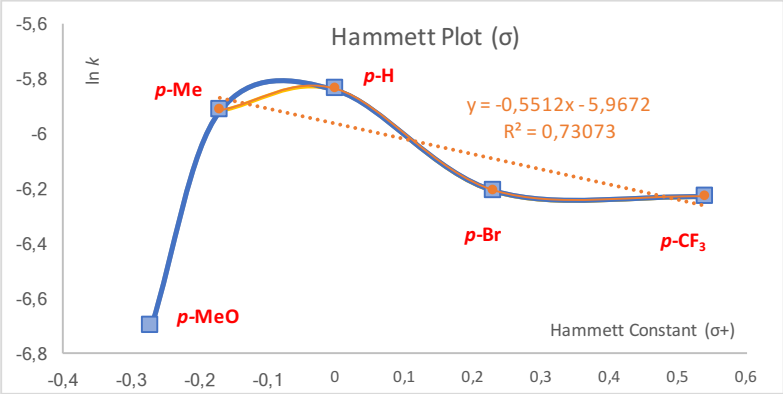
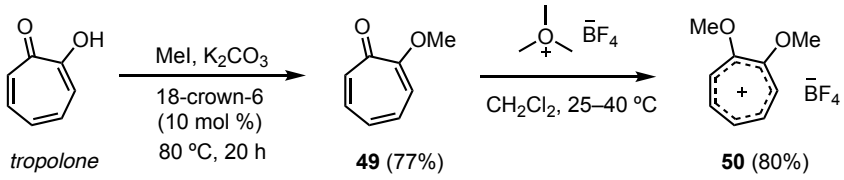



**Figure 15**. Logarithmic reaction rates vs Hammett constants $\sigma^+$.

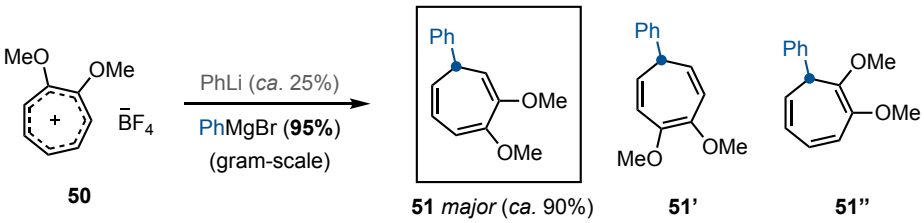
***Synthesis and Testing of Other Electron-Rich Substrates***

In an attempt to unlock an entry point to potentially more reactive cycloheptatrienes, we designed a route for the synthesis of polysubstituted versions of the tropylium tetrafluoroborate aromatic salt. Thus, methylation of tropolone with MeI afforded methyltropolone **49**, which could be further methylated using a Meerwein-type salt to give **50** as a crystalline solid,[97] which could be fully characterized and appears to be a bench-stable salt (Scheme 27).




**Scheme 27**. Synthesis of dimethoxytropylium tetrafluoroborate.

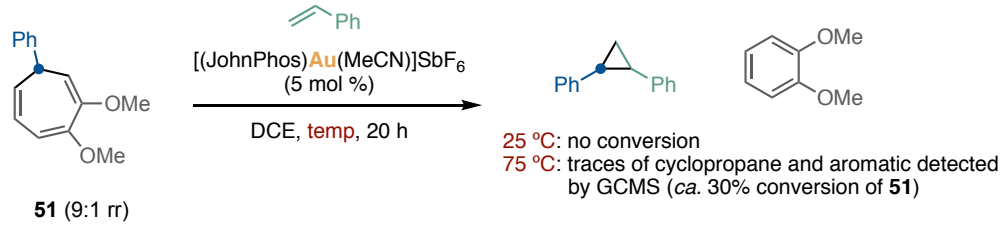
The reaction of salt **50** with phenyl magnesium bromide gave a good yield of a mixture of 7-phenyl trimethoxycycloheptatrienes regioisomers. By NMR analysis, the major one appears to be 2,3-dimethoxy-7-phenyl-1,3,5-cycloheptatriene **51** (Scheme 28).




**Scheme 28**. Addition of nucleophiles to electron-rich tropylium salt **50**.

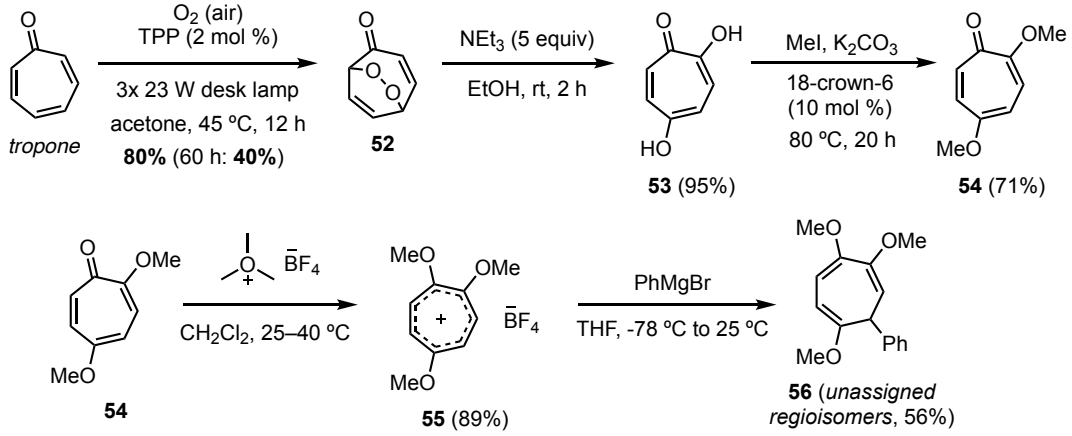
When submitting the mixture of regioisomers to the gold-catalyzed cyclopropanation of styrene, no conversion was observed at room temperature. At 75 ºC, 30% conversion of the starting material was obtained, and both 1,2-diphenylcyclopropane and 1,2-dimethoxybenzene were detected by GC-MS. Unfortunately, the NMR yield was found to be lower than 5% (Scheme 29). The starting cycloheptatrienes are most likely evolving through 1,5-H shift to afford fully conjugated isomers irreversibly (see Scheme 31).

97 Olekhnovich, L. P.; Budarina, Z. N.; Borodkin, G. S.; Kurbatov, S. V.; Vaslyaeva, G. S.; Zhdanov, Yu. A. Acylotropic Tautomerism: XXXV. R–L-Inversion of Configuration of Dipolar Spyrocyclic and Open-Chain 2-Arylaminotropone Isomers. *Russ. J. Org. Chem.* **2002**, *38*, 713–722.



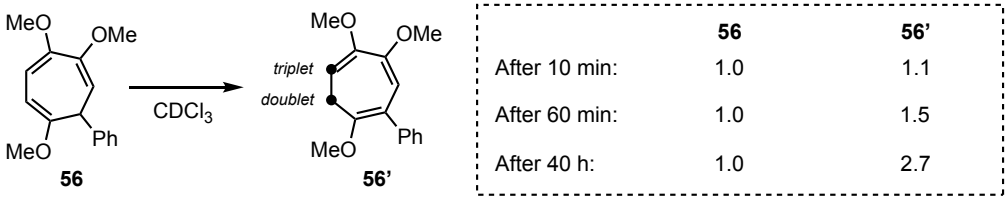

**Scheme 29**. Preliminary evaluation of the reactivity of cycloheptatriene **51**.

We decided to use an analogous strategy to obtain a more electron-rich version of the same tropylium salt. Thus, we submitted tropone to a photocycloaddition with singlet oxygen, produced by using air and tetraphenylporphyrin (TPP) as photosensitizer, to give peroxide **52**.[98] Under basic conditions, **52** opens up to afford dihydroxytropone **53**, which can then be methylated twice with MeI, and once more with Meerwein's salt to afford 1,2,5-trimethoxytropylium tetrafluoroborate **55**.




**Scheme 30**. Synthesis of trimethoxycycloheptatrienes.

Addition of phenylmagnesium bromide to salt **55** afforded **56** as a *ca.* 1:1 mixture of two isomers (according to $^1$H NMR in $CDCl_3$), which were assigned to be one of the two possible products of 7-addition of the nucleophilic phenyl group (**56**), and the corresponding fully-conjugated product of 1,5-H shift (**56'**).

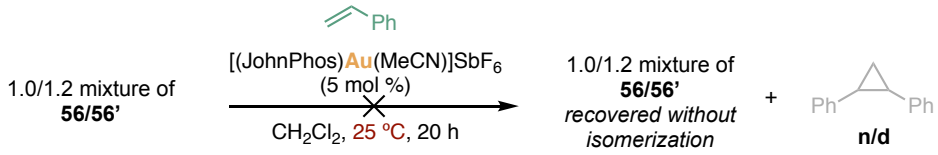



| | 56 | 56' |
|---|---|---|
| After 10 min: | 1.0 | 1.1 |
| After 60 min: | 1.0 | 1.5 |
| After 40 h: | 1.0 | 2.7 |

**Scheme 31**. High tendency of cycloheptatrienes **56** to undergo 1,5-H shift in solution.

98 Oda, M.; Kitahara, Y. Photo-oxygenation of tropone. A convenient synthesis of 5-hydroxytropolone and tropolone. *Tetrahedron Lett.* **1969**, 3295–3296.

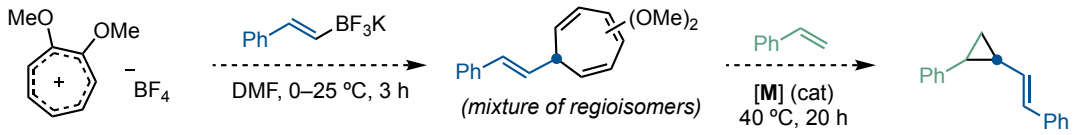
We found that just by being dissolved in deuterated chloroform, **56** was slowly shifting towards **56'** over time (Scheme 31). Most likely, **56** was initially obtained as the only product of nucleophilic addition but started to isomerize immediately in the reaction mixture and/or during workup/purification. Then, it continued to further decompose slowly in $CDCl_3$. After 40 h, not only **56** and **56'** were observed, but also other products of background decomposition. This type of 1,5-H shift is known to be the main side pathway in most metal-catalyzed retro-Buchner reactions (a thermodynamic dead-end, due to the full conjugation of the triene with the aromatic system), and it is apparently facilitated by the presence of methoxy groups. When this 1:1.2 mixture was submitted to the gold(I)-catalyzed reaction conditions at room temperature in dichloromethane, no conversion was observed and the mixture of isomers **56**/**56'** was recovered (Scheme 32).




**Scheme 32**. Unsuccessful arylcyclopropanation attempt at room temperature.

Unfortunately, due to time constraints, these new tropylium salts and carbene precursors were not explored further. However, even though this strategy presents drawbacks (e.g., having to deal with mixtures of regioisomers or a more favorable 1,5-H shift pathway), it is probably worth exploring further, perhaps using different transition metals as catalysts (see next section).

An interesting possibility to continue this study would be the preparation of 7-styryl analogs and directly compare their performance with 7-styryl-1,3,5-trimethyl-1,3,5-cycloheptatrienes **44** presented in the previous section (Scheme 33).



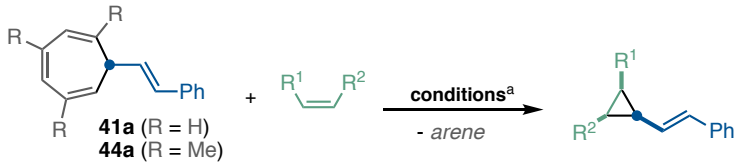

**Scheme 33**. Proposed synthesis of more reactive styryl cycloheptatrienes for cyclopropanation reactions.

## II.4. Beyond Gold Carbenes: Other Metals as Decarbenation Catalysts

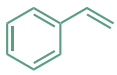
During the first 8 years of development of the retro-Buchner reaction, one of the main drawbacks was the fact that it only allowed the access to gold(I) carbenes. This limited the strategy to the use of gold complexes and blocked the development of transformations that cannot be carried out under gold(I) catalysis.

### *The Zinc(II)-Catalyzed Retro-Buchner Reaction*

With the new generation of more reactive cycloheptatrienes **44** in hand, we embarked on the journey towards the discovery of new aromative decarbenation catalysts. During our initial explorations using high throughput screening techniques, we observed that most of the commercially available transition-metal catalysts that we tested resulted in either no conversion of the starting cycloheptatriene **44**, or in its conversion to the corresponding conjugated isomers through 1,5-H shift (Scheme 26, page 60). The latter was usually the case for harder Lewis acids such as copper(I), silver(I), or gold(III) salts. Fortunately, we eventually identified simple zinc(II) halide salts as active catalysts in the retro-Buchner reaction of 7-styryl-1,3,5-trimethyl-1,3,5-cycloheptatrienes **44**, and in the subsequent cyclopropanation of alkenes.




**Conditions A**: 1.5 equiv of alkene, 0.1 M in EtOAc, **[Au]**[b] (5 mol %), 25 ºC, 24 h
**Conditions B**: 4.0 equiv of alkene, 0.1 M in DCE, **$ZnBr_2$** (10 mol %), 65 ºC, 40 h

| entry | deviations from **A** or **B** | yield/% (dr) | alkene |
|---|---|---|---|
| 1 | **A** | **80 (>20:1)** |  |
| 2 | **B** | 51 (>20:1) | |
| 3 | **A** with R = H (**41a**) | n/d | **styrene** |
| 4 | **B** | **55 (5:1)** | |
| 5 | **A** | 12 (n/d) |  |
| 6 | **B** with R = H (**41a**) | traces | |
| 7 | **B** with $ZnCl_2$, 90 ºC | 34 (4:1) | **cyclohexene** |
| 8 | **B** with $ZnI_2$, 90 ºC | 15 (3:1) | |

**Scheme 34**. Discovery of the zinc(II)-catalyzed retro-Buchner reaction. [a] Unless otherwise stated, **44a** (R = Me) is used as substrate. [b] [Au] = [(JohnPhos)Au(MeCN)]$SbF_6$.

Initially, we studied the cyclopropanation system using styrene as substrate, obtaining 51% yield of the corresponding cyclopropane by using 10 mol % of $ZnBr_2$ as catalyst at 65 ºC (Scheme 34, entry 2). Although the yield obtained with a cationic gold(I) complex is slightly

higher, the zinc(II)-based system is around 1000-fold cheaper than the gold(I)-based one (according to the current price per gram in Sigma-Aldrich).

In order to illustrate the complementarity of the two methods, we used zinc(II) catalysis to explore substrates with which the gold(I) system does not perform well. For instance, when using the gold(I)-based system to cyclopropanate cyclohexene, only 12% of product was obtained (Scheme 34, entry 5). This might come as a consequence of the high affinity of gold(I) to form stable adducts with this type of alkenes.[99] On the other hand, $ZnBr_2$ as catalyst afforded the product of styrylcyclopropanation of cyclohexene in 55% yield and 5:1 *endo*/*exo* ratio (Scheme 34, entry 4). We observed that using less reactive non-methylated cycloheptatriene **41a** only traces of product were obtained (Scheme 34, entry 6), and that other zinc(II) salts such as $ZnCl_2$ (34%) or $ZnI_2$ (15%) performed worse (Scheme 34, entries 7–8). Non-halide zinc(II) compounds with anions such as $OTf^-$ and $NTf_2^-$ are unactive in the transformation. The higher temperature required might be because of the low solubility of these salts in the reaction solvent (unfortunately, more coordinating solvents such as THF lead to no reactivity).

Even after finding opposing reactivity trends between gold(I) and zinc(II), we performed several control experiments with all-new material and with >99.999% quality $ZnBr_2$, obtaining the same results. Moreover, we found that anhydrous >99.999% $ZnBr_2$ purchased from ACROS Organics™ performed slightly better (*ca*. 10% higher yields) than manually dried 98% $ZnBr_2$. We also observed that the zinc(II)-catalyzed reaction was significantly more sensitive to moisture and the presence of coordinating entities than the gold(I)-catalyzed process (which can be successfully carried out under air using non-dry solvents).

At this point, we moved on to explore the scope of the new zinc(II)-catalyzed styrylcyclopropanation of non-activated alkenes (Scheme 35). As evidenced by both X-ray diffraction and nOe NMR studies,[100] the major isomer obtained was the *cis*- or *endo*- one in all the studied cases. First, we examined the transfer of carbene fragments with different electronic properties. All electron-rich or electron-neutral substrates performed very well. However, we found worse results in terms of both rate and *cis*-selectivity for electron-poor fragments (**58a–f**). Nevertheless, with longer reaction times, it was also possible to transfer $CF_3$- or Br-containing styryl carbenes in moderate yields.

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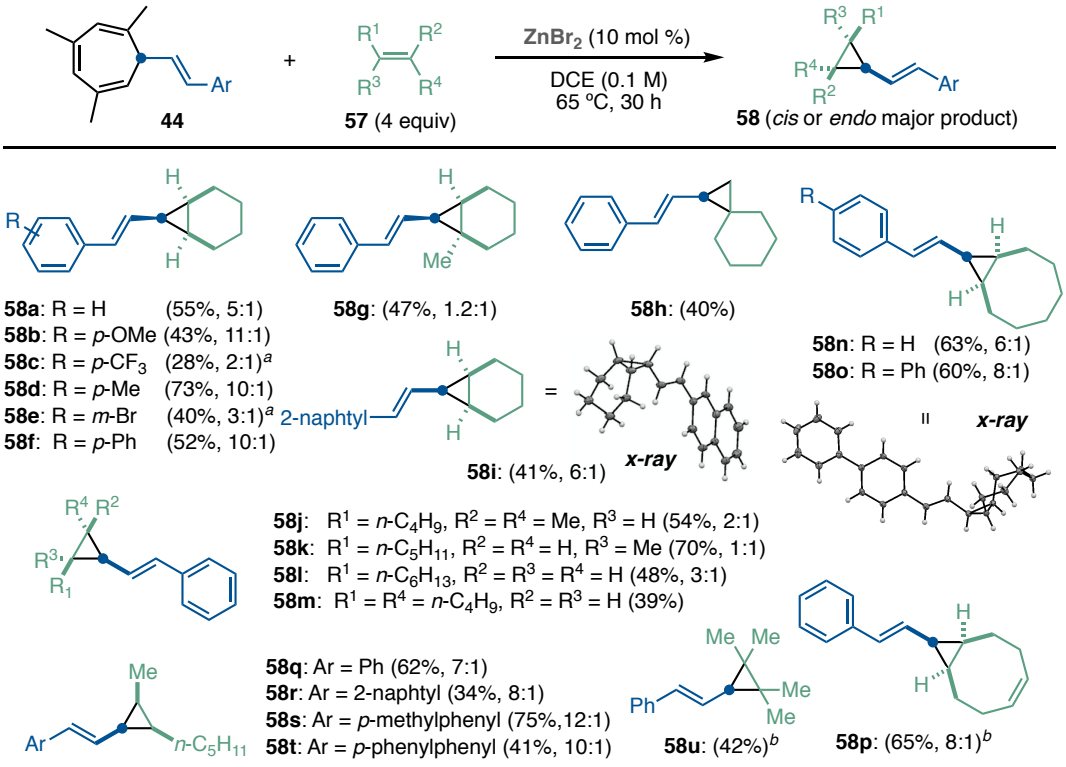
99 Brooner, R. E. M.; Widenhoefer, R. A. Synthesis and Structure of Dicationic, Bis(gold) π-Alkene Complexes Containing a 2,2′-Bis(phosphino)biphenyl Ligand. *Organometallics* **2012**, *31*, 768–771.

100 For details, see experimental section.

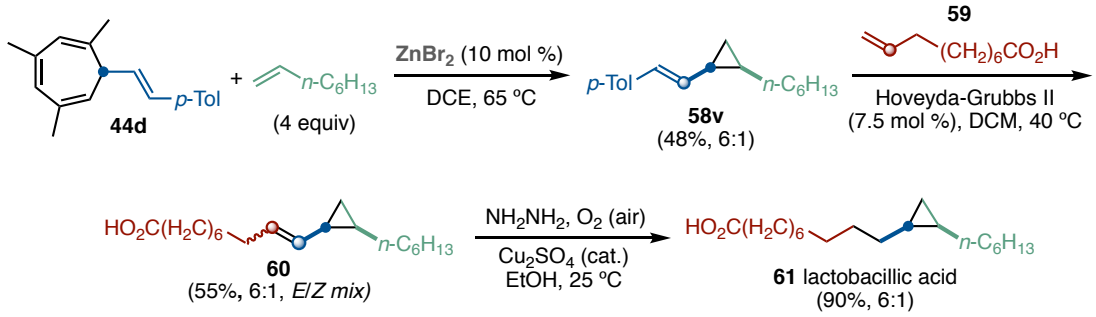



**Scheme 35**. Scope of the Zn(II)-catalyzed cyclopropanation of non-activated alkenes. [a] At 80 ºC for 60 h. [b] 10 equiv of alkene employed to minimize volatility or selectivity issues.

Then, we examined the scope of non-activated simple alkenes that could be cyclopropanated with this methodology. Besides cyclohexene, bicyclic systems of different sizes such as **58n** and **58o** were accessed. We found that aliphatic alkenes with different substitution patterns were suitable for this transformation. Thus, di-, tri-, tetra-, or pentasubstituted alkenyl cyclopropanes could be synthesized in moderate to good yields and with varying levels of *cis*-selectivity (**58j–m**, **58q–u**). As expected, trisubstituted alkenes were the worst performing ones in terms of diastereoselectivity (**58g**, **58j–k**), and *Z*-disubstituted alkenes the best ones (**58q–t**). Furthermore, interesting spirocyclic structures such as **58h** could be assembled, and by using an excess of nucleophile, 1,5-cyclooctadiene could be selectively monocyclopropanated in good yield and dr (**58p**).

Finally, we observed that whereas this methodology behaves satisfactorily for the functionalization of simple, non-activated alkenes, the presence of heteroatoms in the substrates is highly detrimental for the reaction. For these cases, the previously developed gold(I)-based system (see previous section), or the one that we developed next based on rhodium(II) catalysis (see next section) are much better alternatives.

To illustrate the utility of this transformation, we applied it to the total synthesis of lactobacillic acid, a cyclopropane-containing natural fatty acid.[101] Thus, the reaction of cycloheptatriene **44d** with 1-octene in the presence of $ZnBr_2$ as catalyst afforded *cis*-vinylcyclopropane **58v** in 6:1 dr. This intermediate was then submitted to cross-metathesis with 9-decenoic acid (**59**) using the 2nd generation Hoveyda–Grubbs catalyst. The obtained *E*/*Z* mixture of **60** was finally reduced with diimide to afford lactobacillic acid in 90% yield (**61**, Scheme 36).




**Scheme 36**. Total synthesis of lactobacillic acid.

The main advantage of this route is its versatility, since it could potentially be used to obtain a variety of natural or non-natural cyclopropane-containing fatty acids simply by tuning the number of carbon atoms in the aliphatic chains of the alkene that gets cyclopropanated and the carboxylic acid **59**.

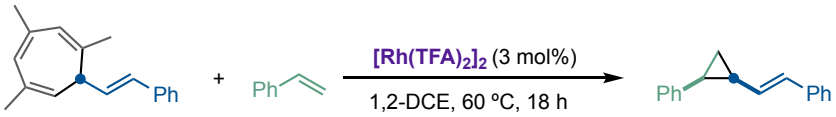
101 (a) Craven, B.; Jeffrey, G. A. The Structure of Lactobacillic Acid. *J. Am. Chem. Soc.* **1960**, *82*, 3858–3860. (b) Coxon, G. D.; Al-Dulayymi, J. R.; Baird, M. S.; Knobl, S.; Roberts, E.; Minnikin, D. E. The Synthesis of (11*R*,12*S*)-Lactobacillic Acid and its Enantiomer. *Tetrahedron Asymmetry* **2003**, *14*, 1211–1222.

### *The Rhodium(II)-Catalyzed Retro-Buchner Reaction*

After identifying zinc(II) halides as competent, cheap and complementary catalysts for the retro-Buchner/cyclopropanation sequence, we wanted to look for a new metal which could potentially allow us to find new reactions that are inaccessible under gold(I) or zinc(II) catalysis. Rh(II) dimers were probably the best candidates, since they are arguably the most studied and versatile catalysts for carbene-transfer processes from diazo compounds. Besides classical cyclopropanation and Buchner reactions, a vast variety of insertions and cycloadditions have been developed using rhodium(II) catalysis.[102] For these reasons, after screening a range of Rh(II) complexes, we found that highly electrophilic rhodium(II) trifluoroacetate dimer is a very active catalyst for the decarbenation of cycloheptatrienes **44**.[103]

To prove the concept, we explored first the activity of rhodium(II) catalysts in the retro-Buchner/cyclopropanation sequence. This system was found to be highly versatile and complementary to gold(I) or zinc(II), allowing the development of several new methodologies which occur exclusively under rhodium(II) catalysis. These methodologies are later discussed in Section II.7 and in different sections of Chapter III.

We established the use of 3 mol % of $[Rh_2(TFA)_4]$ and 1,2-DCE (0.1 M) at 60 ºC as the standard set of conditions for the cyclopropanation of styrene (4 equiv) using carbene precursor **44a** (Scheme 37, entry 1). In all cases, the *cis* cyclopropane was obtained as the major one.




**44a** **46a**

| *entry* | *deviation from standard conditions* | *yield of 46a* |
|---|---|---|
| 1 | none | 72% |
| 2 | $[Rh(OAc)_2]_2$ (5 mol%) instead | 30% |
| 3 | $[Rh(esp)_2]_2$ (5 mol%) instead | 45% |
| 4 | 25 ºC for 18 h | 30% |
| 5 | 25 ºC for 60 h | 60% |
| 6 | non-methylated styrylcycloheptatriene **41a** | n/d |
| 7 | no catalyst | n/d |

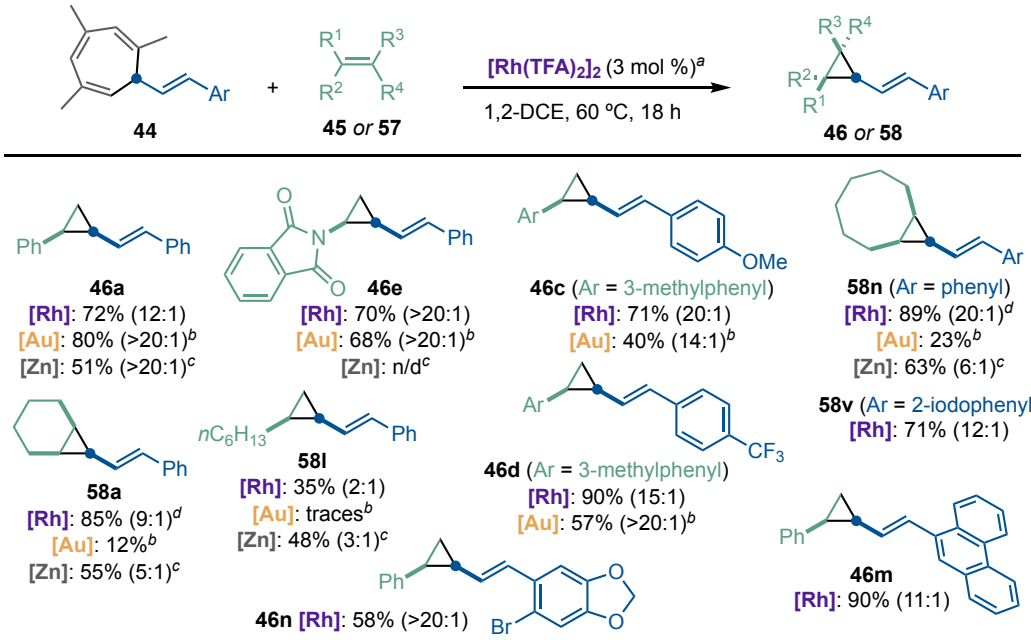
**Scheme 37**. Discovery and development of the Rh(II)-catalyzed cyclopropanation.

102 Davies, H. M. L.; Parr, B. T. *Rhodium Carbenes* in *Contemporary Carbene Chemistry* (2013). Ed.: Moss, R. A.; Doyle, M. P. John Wiley & Sons, Inc.

103 Mato, M.; Echavarren, A. M. Donor Rhodium Carbenes by Retro-Buchner Reaction. *Angew. Chem. Int. Ed.* **2018**, *58*, 2088–2092.

We found that the use of less electrophilic dimers such as $[Rh_2(OAc)_4]$ or $[Rh_2(esp)_2]$ leads to slower reactivity and lower overall yield (Scheme 37, entries 2 and 3). The Rh(II)-catalyzed cyclopropanation can also be carried out at room temperature, though it takes more than two days to reach full conversion. Finally, the importance of the use of the new generation of more reactive 1,3,5-trimethyl cycloheptatrienes is clearly highlighted by the fact that the use of non-methylated analog **41a** leads to no productive reactivity in the evaluated range of temperatures (25–80 ºC). 7-Aryl-1,3,5-cycloheptatrienes **38** were also unreactive under these conditions.

We evaluated the performance of the Rh(II)-based system versus the ones developed with gold(I) and zinc(II) catalysts. Although for some specific cases the latter behave slightly better, the general trend is that rhodium(II) outperforms the other two metals, and gives better yields and selectivities over a broader range of alkenes (Scheme 38).




**Scheme 38**. Comparison and scope of the Rh(II)-catalyzed cyclopropanation. [a] New conditions with 1 equiv of **44**, 4 equiv of **45**/**57**, 3 mol % of $[Rh_2(TFA)_4]$ and 1,2-DCE (0.1 M) at 60 ºC for 18 h. [b] 1 equiv of **44**, 1.5 equiv of **45**/**57**, 5 mol % of [(JohnPhos)Au(MeCN)]$SbF_6$ and EtOAc (0.1 M) at 25 ºC for 20 h. [c] 1 equiv of **44**, 4 equiv of **45**/**57**, 10 mol % of $ZnCl_2$ and 1,2-DCE (0.1 M) at 65 ºC for 30 h

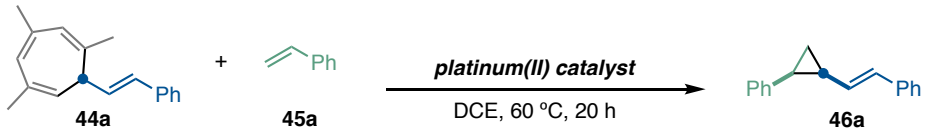
Gold(I) generally outperforms the other catalysts in the cyclopropanation of styrenes, giving the best result for the synthesis of simple 1,2-phenylstyrylcyclopropane **46a**. When varying the electronics of the styryl group, rhodium was found to work generally better (**46c**, **46d**). In the case of enamines such as *N*-vinylphthalimide, both gold(I) and zinc(II) deliver product **46e** in the same level of efficiency and selectivity, whereas the zinc(II) system is not active. For the cyclopropanation of non-activated olefins such as cyclohexene, gold(I) usually performed poorly, while zinc halides were very competent catalysts. We found that not only rhodium(II)

is active when using this type of alkenes, but it often outperforms zinc(II) in both terms of yield and diastereoselectivity (**58a**, **58n**). Finally, we expanded the scope of the rhodium(II)-catalyzed cyclopropanation to show that different aryl-halide (**46n** Br, **58v** I) or polyaromatic units (**46m**) could be transferred successfully.

*Overall, we unlocked the access to simple rhodium(II) alkenyl metal carbenes. This led to the development of the best method for the synthesis of non-acceptor alkenylcyclopropanes, as it was found to be more general than the previous systems based on zinc(II) and gold(I) catalysis. As it will be illustrated in the different sections throughout this Doctoral Thesis, this discovery also enabled the development of several new methodologies based in the use of rhodium(II) carbenes that do not proceed under gold(I) or zinc(II) catalysis.*

***Further Exploration: Other Metals as Retro Buchner-Reaction Catalysts***

Before chemists came across with the higher activity and selectivity of gold(I) complexes, platinum(II) catalysis was one of main tools for the cycloisomerization of enynes.[104] The advances in gold(I) catalysis led our group to the discovery of the retro-Buchner reaction. Thus, besides opening new opportunities in terms of developing selective carbene-transfer reactions, the possibility of unlocking the use of platinum(II) catalysts for the decarbenation of cycloheptatrienes would close this cycle of discovery.




**44a** **45a** **46a**

| *entry* | *platinum(II) catalyst* | *46a NMR yield* |
|---|---|---|
| 1 | $PtCl_2$ (10 mol %) | 11% |
| 2 | $PtCl_2(PPh_3)_2$ (10 mol %) | n/d |
| 3 | $PtCl_2$(bpy) (10 mol %) | n/d |
| 4 | $PtCl_2(MeCN)_2$ (10 mol %) | 8% |
| 5 | $PtCl_2(PhCN)_2$ (10 mol %) | 9% |

**Scheme 39**. Preliminary work on the Pt(II)-catalyzed decarbenation of cycloheptatrienes.

Preliminary exploration of several platinum(II) complexes shows that, albeit in poor yield, it is indeed possible to carry out a retro-Buchner/cyclopropanation sequence promoted by this metal (Scheme 39). These results are currently being studied further in our group, using different platinum(II)-based systems, and other metal complexes.

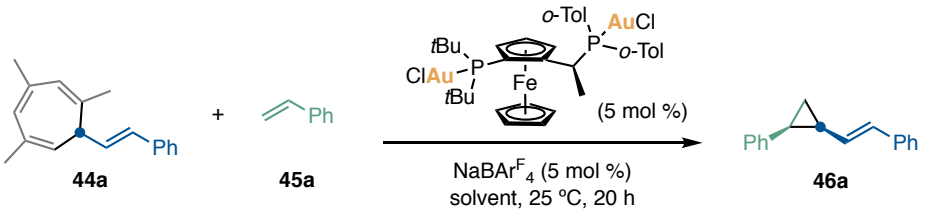
104 Fürstner, A.; Stelzer, F.; Szillat, H. Platinum-Catalyzed Cycloisomerization Reactions of Enynes. *J. Am. Chem. Soc.* **2001**, *123*, 11863–11869.

## II.5. En Route Towards an Enantioselective Cyclopropanation with Non-Acceptor Carbenes

The discovery of a new generation of cycloheptatrienes that can react at room temperature clears the way for proving the possibility of developing asymmetric versions of the retro-Buchner/cyclopropanation sequences. Furthermore, the possibility of using different metals broadens the chances of success. This is an important challenge: to the best of our knowledge, general asymmetric versions of simple cyclopropanations with non-acceptor carbenes have not yet been developed. In this section, an initial exploration with different metals of the enantioselective version of our styryl cyclopropanation is presented.

### *Chiral Gold(I) Systems*

We started by the evaluation of several combinations of monodentate and bidentate phosphine ligands with gold(I). A preliminary exploration of ligands was performed by high throughput screening. This allowed us to identify that Josiphos-type ligands (previously successful in our group to develop gold(I)-catalyzed enantioselective [2+2] cycloadditions)[105] were giving promising amounts of efficiency and some asymmetric induction.



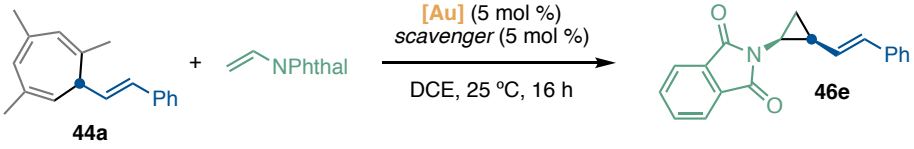

| *entry* | *conditions* | *NMR yield* | *er* |
|---|---|---|---|
| 1 | DCE (0.1 M) | 53% | 57:33 |
| 2 | $PhCF_3$ (0.1 M) | 31% | 64:36 |
| 3 | $PhCF_3$ (0.05 M) | 30% | 64:36 |
| 4 | $PhCF_3$ (0.5 M) | 22% | 64:36 |
| 5 | $PhCF_3$ (0.1 M), 2.5 mol % [Au]/$NaBAr^F_4$ | 27% | 64:36 |
| 6 | $PhCF_3$ (0.1 M), $AgSbF_6$ (5 mol %) | - | - |
| 7 | $PhCF_3$ (0.1 M), 7 °C instead of 25 °C | 18% | 66:34 |

**Scheme 40**. Chiral Josiphos-digold complex in asymmetric cyclopropanations.

105 García-Morales, C.; Ranieri, B.; Escofet, I.; López-Suárez, L.; Obradors, C.; Konovalov, A. I.; Echavarren, A. M. Enantioselective Synthesis of Cyclobutenes by Intermolecular [2+2] Cycloaddition with Non-C2 Symmetric Digold Catalysts. *J. Am. Chem. Soc.* **2017**, *139*, 13628–13631.

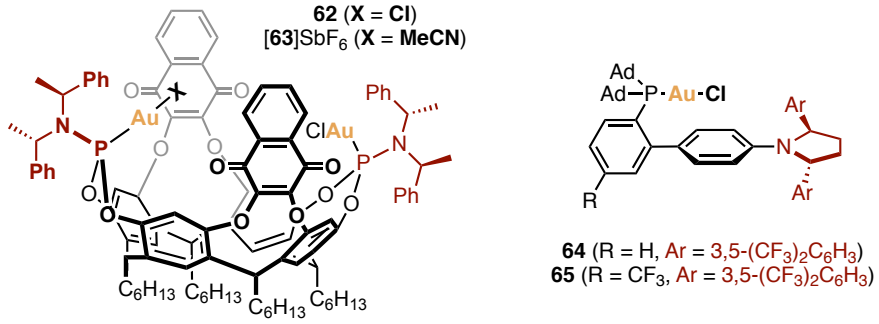
Unfortunately, enantiomeric excesses higher than 28% could not be achieved with the best performing Josiphos ligand (Scheme 40). Experimental variables such as solvent, concentration (Scheme 40, entries 1–4) or amount of chloride scavenger (Scheme 40, entry 5) only had an influence in efficiency, but not in enantioselectivity. Lowering the temperature to 7 ºC had almost no effect in stereoselectivity but slowed down the reaction significantly.

We also performed an initial exploration with two new types of ligands recently developed in our group, which have demonstrated an exceptional enantiocontrol in the context of the cycloisomerization of enynes: JohnPhos-type chiral pyrrolidine ligands (**64**–**65**)[106] and chiral gold(I) cavitands (**62**–**63**).[107] In this case, we used the cyclopropanation of *N*-vinylphthalimide (which often performs well in terms of diastereoselectivity, presumably due to strong attractive non-covalent interactions) as model system (Scheme 41).




**44a** **46e**

| *entry* | [Au] (5 mol %) + *scavenger (5 mol %)* | *conversion*[a] | *er* |
|---|---|---|---|
| 1 | **62** + $NaSbF_6$ | <5% | n/d |
| 2 | **62** + $AgSbF_6$ | >95% | 59:41 |
| 3 | [**63**]$SbF_6$ | >95% | 60:40 |
| 4 | **64** + $AgSbF_6$ | >95% | 36:64 |
| 5 | **65** + $AgSbF_6$ | >95% | 35:65 |



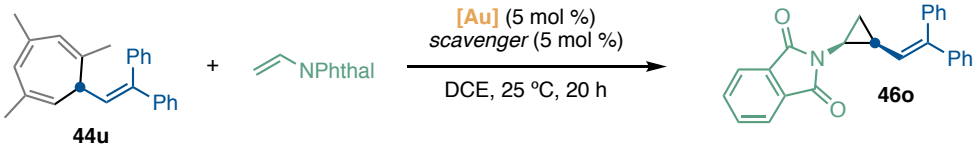

**Scheme 41**. Initial explorations on the enantioselective cyclopropanation with gold(I) non-acceptor carbenes. [a] Yield was not determined.

106 Zuccarello, G.; Mayans, J. G.; Escofet, I.; Scharnagel, D.; Kirillova, M. S.; Pérez-Jimeno, A. H.; Calleja, P.; Boothe, J. R.; Echavarren, A. M. Enantioselective Folding of Enynes by Gold(I) Catalysts with a Remote $C_2$-Chiral Element. *J. Am. Chem. Soc.* **2019**, *141*, 11858–11863.

107 Martín-Torres, I.; Ogalla, G.; Yang, J.-M.; Rinaldi, A.; Echavarren, A. M. Enantioselective Alkoxycyclization of 1,6-Enynes with Gold(I)-Cavitands: Total Synthesis of Mafaicheenamine C. *Angew. Chem. Int. Ed.* **2021**, *60*, 9339–9344.

While testing gold(I)-chloride cavitand **62**, we observed that $NaSbF_6$ was not enough to activate the complex and promote the transformation. When $AgSbF_6$ was used as chloride scavenger, cyclopropane **46e** was obtained in a 59:41 ratio of enantiomers. Similarly, the use of cationic gold complex [**63**]$SbF_6$ afforded, without activation, the same product with a similar level of enantioinduction (Scheme 41, entries 1–3). On the other hand, both chiral JohnPhos-type ligands in complexes **64** and **65** afforded the product in 36:64 and 35:65 er, respectively, upon activation with $AgSbF_6$. In all cases we observed significant conversion of the starting material to the corresponding isomerized cycloheptatrienes (see Scheme 26, page 60). In principle, this could be minimized by using non-silver chloride scavengers, but those were found to be not strong enough to activate these gold(I) chloride complexes.

A bulkier carbene precursor (**44u**) was prepared and tested with the same three complexes. Cationic gold cavitand [**63**]$SbF_6$ gave a reasonable yield of the product of cyclopropanation in a 58:42 ratio of enantiomers. On the other hand, chiral JohnPhos-type complexes afforded only trace amounts of product. These systems gave a high conversion to the product of 1,5-H shift of cycloheptatriene **44u**.



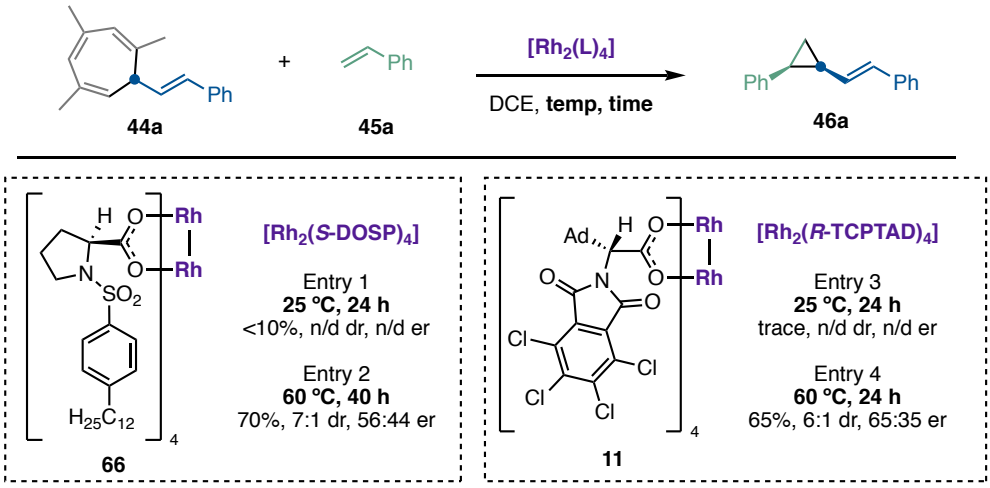

| *entry* | [Au] (5 mol %) + *scavenger (5 mol %)* | *er* |
|---|---|---|
| 1 | [**63**]$SbF_6$ | 58:42 |
| 2 | **64** + $AgSbF_6$ | n/d (<5% yield) |
| 3 | **65** + $AgSbF_6$ | n/d (<5% yield) |

**Scheme 42**. Asymmetric attempts with a bulkier carbene precursor.

*Overall, the possibility of inducing enantioselectivity in an intermolecular cyclopropanation reaction using simple styryl non-acceptor gold(I) carbenes as intermediates was demonstrated for the first time. The results obtained thus far are only preliminary, and further exploration of new gold(I)-based systems will be necessary to improve the enantioselectivity of the reaction.*

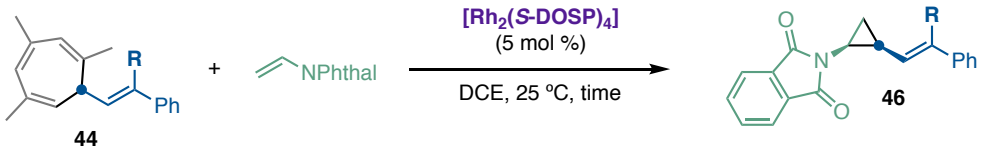
### *Chiral Rh(II) Systems*

Chiral rhodium(II) carboxylate complexes proved to be less reactive than more elctrophilic rhodium(II) trifluoroacetate. Two commercially available chiral Rh(II) complexes were tested, [$Rh_2$(*S*-DOSP)$_4$] and [$Rh_2$(*R*-TCPTAD)$_4$], and in both cases, temperatures above 25 ºC were required to reach a significant conversion. At 60 ºC, both catalysts gave the product in good yield and diastereoselectivity but failed to give the major isomer in an enantiomeric excess higher than 30% (Scheme 43, entries 2 and 4).




**Scheme 43**. Styrylcyclopropanation using chiral Rh(II) complexes.

The cyclopropanation of *N*-vinylphthalimide was also evaluated using [$Rh_2$(*S*-DOSP)$_4$] with two different alkenyl carbene precursors. Even though both reactions were very clean (almost no side-product formation), monosubstituted styryl-carbene precursor **44a** reacted very slowly, taking 3 days to reach 40% conversion to give the cyclopropane with 20% ee (Scheme 44, entry 1). On the other hand, bulkier disubstituted precursor **44u** reacted faster, giving good yield of cyclopropane **46o** in a higher 30% ee.

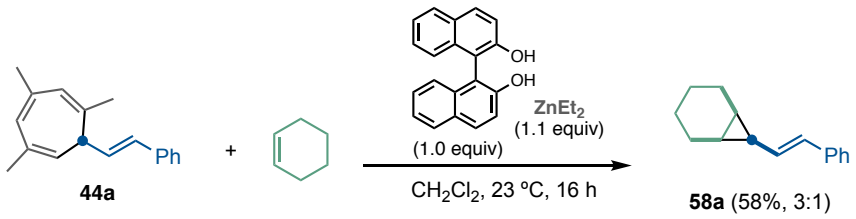



| *entry* | *cycloheptatriene* | *time* | *conversion 44* | *er* |
|---|---|---|---|---|
| 1 | **R = H** | 72 h | 40% | 60:40 |
| 2 | **R = Ph** | 16 h | >90% | 65:35 |

**Scheme 44**. Cyclopropanation of *N*-vinylphthalimide with a chiral Rh(II) complex.

### *Chiral Zn(II) Systems*

After the discovery of zinc(II) halides as catalysts for the retro-Buchner reaction, we evaluated the activity of several chiral zinc-based systems. However, the addition of any N- or P-based ligands to $ZnBr_2$ shot down the reactivity. The only system we found to be active in our reaction involved the use of binaphthols and diethyl zinc. The Lewis acid formed in situ by the combination of 1 equiv of BINOL and 1.1 equiv of $ZnEt_2$ promoted cleanly a retro-Buchner/cyclopropanation sequence at room temperature (Scheme 45).




**Scheme 45**. Retro-Buchner/cyclopropanation sequence promoted by a BINOL–Zn system.

This type of system has been employed by different groups, using several metals such as Ti or Zr to promote enantioselective Lewis acid-catalyzed transformations.[108] An analogous well-known system is the one based on the combination of ProPhenol Trost ligands with diethyl zinc.[109]

The specific system that is formed by the combination of BINOLs with $Et_2Zn$ has also been employed in asymmetric catalysis but it is not easy to establish the actual structure of the active species.[110] Deprotonation of the phenol groups in BINOL leads to the formation of Zn–O bonds upon evolution of ethane (which can be clearly observed experimentally). This can potentially give rise to a variety of oligomeric species.[111]

With the new retro-Buchner system in hand, we decided to evaluate the level of asymmetric induction that could be achieved in the styrylcyclopropanation of styrene.

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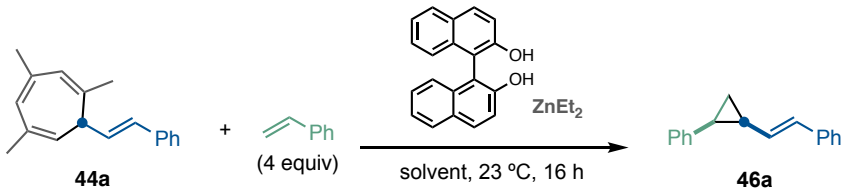
108 Ishitani, H.; Ueno, M.; Kobayashi, S. Enantioselective Mannich-Type Reactions Using a Novel Chiral Zirconium Catalyst for the Synthesis of Optically Active β-Amino Acid Derivatives. *J. Am. Chem. Soc.* **2000**, *122*, 8180–8186.

109 Trost, B. M.; Hung, C.; Guillaume, M. Dinuclear Metal-ProPhenol Catalysts: Development and Synthetic Applications. *Angew. Chem. Int. Ed.* **2020**, *59*, 4240–4261.

110 Du, H.; Long, J.; Hu, J.; Li, X.; Ding, K. 3,3'-$Br_2$-BINOL-Zn Complex: A Highly Efficient Catalyst for the Enantioselective Hetero-Diels-Alder Reaction. *Org. Lett.* **2002**, *4*, 4349–4352.

111 Hu, Q.-S.; Huang, W.-S.; Vitharana, D.; Zheng, X.-F.; Pu, L. Functionalized Major-Groove and Minor-Groove Chiral Polybinaphthyls: Application in the Asymmetric Reaction of Aldehydes with Diethylzinc. *J. Am. Chem. Soc.* **1997**, *119*, 12454–12464.

Selected entries of the optimization process are shown in Scheme 46. Unfotunately, we found that for this reaction to proceed at a significant level of efficiency, stoichiometric amounts of BINOL (1 equiv) and $ZnEt_2$ (1.1 equiv) were required (Scheme 46, entry 1). Also, the use of both 2:1 or 1:2 BINOL/$ZnEt_2$ ratios (or the use of only either one of the two components of the catalytic system) led to no conversion at all. The reaction outcome was dependant on the used solvent, and even though highly heterogeneous mixtures were obtained, the best performing ones were benzene (in terms of efficiency, Scheme 46, entry 5) and toluene (in terms of enantioselectivity, Scheme 46, entry 3).

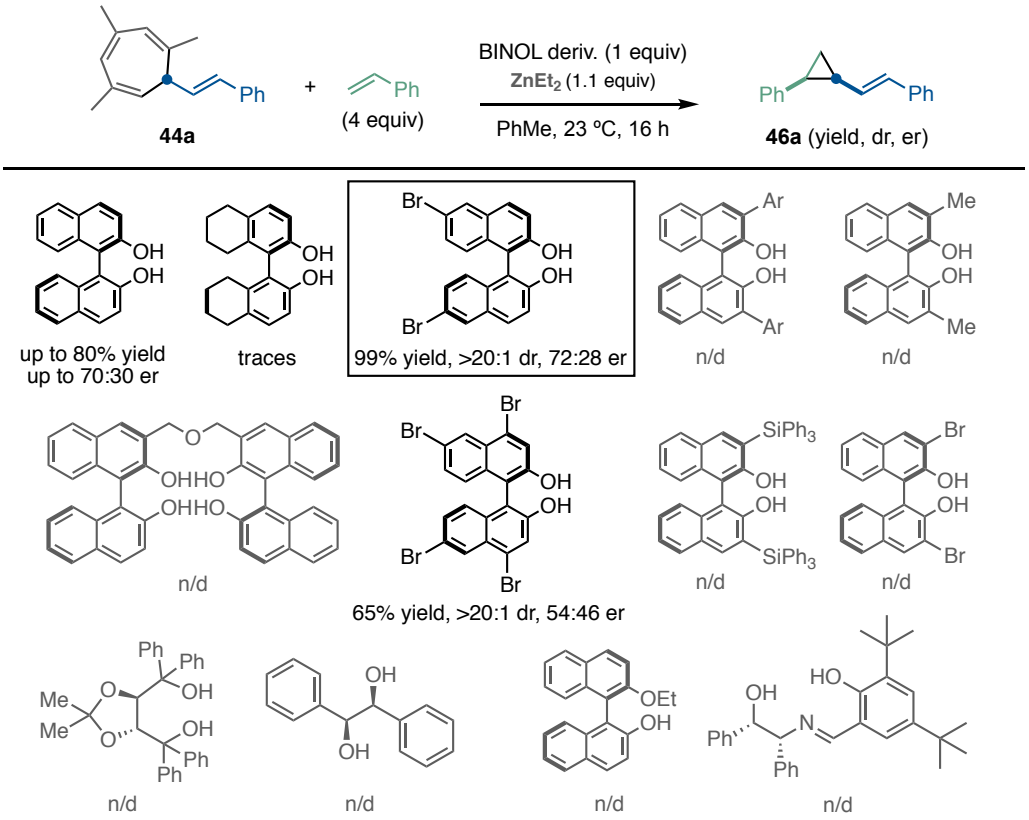



| *entry* | *conditions* | *NMR yield, dr, er* |
|---|---|---|
| 1 | 1 equiv BINOL, 1 equiv $ZnEt_2$, $CH_2Cl_2$ (0.15 M) | 61%, >20:1, 53:47 |
| 2 | 0.5 equiv BINOL, 0.5 equiv $ZnEt_2$, $CH_2Cl_2$ (0.1 M) | 15%, n/d, n/d |
| 3 | 1 equiv BINOL, 1 equiv $ZnEt_2$, **PhMe** (0.15 M) | 46%, >20:1, **70:30** |
| 4 | 1 equiv BINOL, 1 equiv $ZnEt_2$, DCE (0.15 M) | 58%, >20:1, 54:46 |
| 5 | 1 equiv BINOL, 1 equiv $ZnEt_2$, **PhH** (0.15 M) | **80%**, 11:1, 64:46 |

**Scheme 46**. Selected examples of the optimization process.

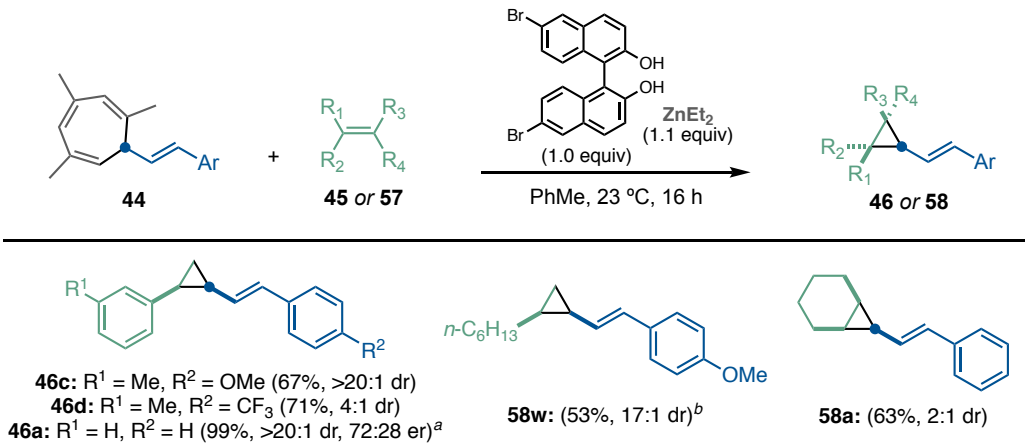
With these conditions in hand we synthesized and tested a significant variety of enantiopure BINOL derivatives (Scheme 47). In this type of asymmetric chemistry, 2,2'-substituted BINOL derivatives are often the ones leading to higher enantioninductions, due to obvious steric considerations. Unfortunately, we found that locating substituents in the 2,2'-positions of BINOL leads to a system unable to promote our reaction. Therefore, we studied the effect of several substituents in other positions of the chiral scaffold. More electron rich h8-BINOL afforded only traces os product. Thus, we decided to introduce electron-withdrawing bromide groups in different positions of the BINOL. This led us to identify 6,6'-$Br_2$BINOL as the most active and selective ligand for the transformation, giving cyclopropane **46a** in quantitative yield, excellent diastereoselectvity and 44% enantiomeric excess.

Besides BINOLs, we tested the reactivity of different simple alcohols or phenols (such as ethanol or phenol) in combination with $ZnEt_2$, but none led to the formation of an active catalyst. Other hydroxy-based ligands such as TADDOL, benzoin or BINOL-monoethyl ether also led to inactive species.




**Scheme 47**. Screening of different BINOL derivatives and related ligands.

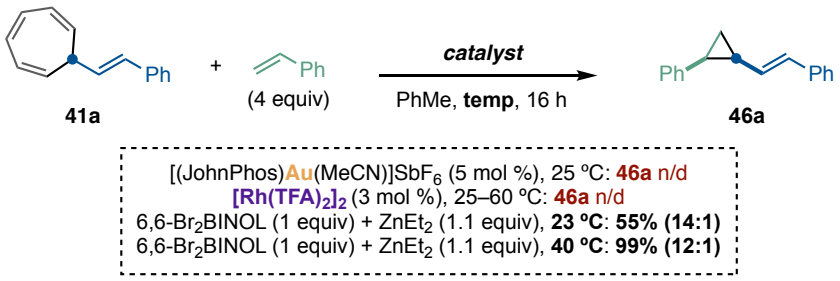
Finally, we tested a small range of alkenes and cycloheptatrienes with racemic 6,6'-$Br_2$BINOL to confirm the versatility of the system and to identify any selectivity differences (Scheme 48). Both styrenes and conjugated olefins could be cyclopropanated successfully. Interestingly, this system gave an excellent result in terms of *cis*-diastereoselectivity in the cyclopropanation of *n*-octene, 17:1, comparing favorably to the 2:1 and 3:1 ratios obtained under [$Rh_2$(TFA)$_4$] and $ZnBr_2$ catalysis, respectively.




**Scheme 48**. Scope of the BINOL–Zn-promoted cyclopropanation. [a] Reaction performed with (*R*)-6,6'-$Br_2$BINOL. [b] Isolatd yield at 1.5 mmol scale using BINOL.

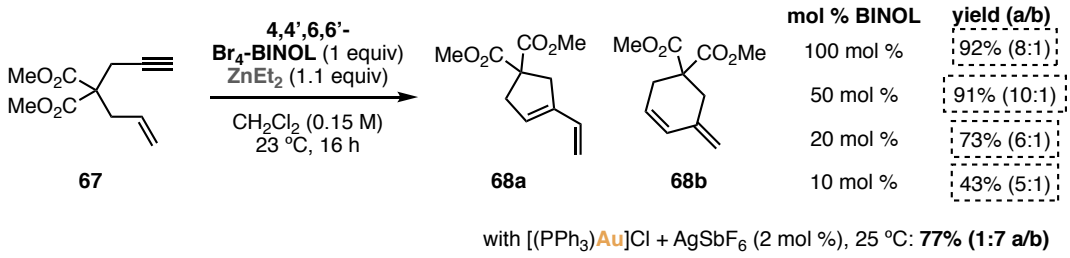
### *The BINOL–Zn System in Other Gold(I)-Catalyzed Transformations*

We found that the combination of (*R*)-6,6'-$Br_2$BINOL with $ZnEt_2$ forms a species electrophilic enough to promote decarbenation/cyclopropanation sequences at room temperature, even when using less reactive non-methylated 7-styryl-1,3,5-cycloheptatriene **41a**, outperforming both gold(I) and rhodium(II) in this particular case (Scheme 49).




**Scheme 49**. Decarbenation of a non-methylated cycloheptatriene at room temperature.

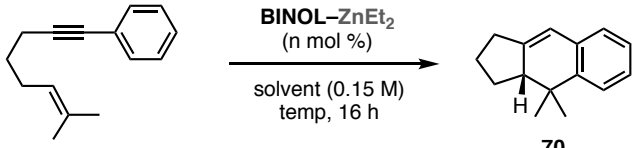
Encouraged by this fact, we wondered whether it would be possible to extend the use of this zinc(II)-based system to promote other chemical reactions often catalyzed by gold(I) complexes. Satisfactorily, we found that our electrophilic system was active in the cycloisomerization of enynes such as **67**. Contrarily to the reaction with cycloheptatrienes, in this case, it was possible to lower the loading of BINOL/$ZnEt_2$ down to 10–20 mol % and still get synthetically useful yields, proving that the active species can indeed act catalytically. Interestingly, the major product of the reaction was cyclopentene **68a**, arising from the 5-*exo*-dig cyclization of **67**, whereas the use of cationic gold(I) complexes leads to the product of 6-*endo*-dig **68b** as the major one (Scheme 50).[112]




**Scheme 50**. Zn(II)-catalyzed cycloisomerization of enyne **67**.

112 Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jiménez-Núñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M.; Echavarren, A. M. Gold(I)-Catalyzed Cyclizations of 1,6-Enynes: Alkoxycyclizations and *exo*/*endo* Skeletal Rearrangements. *Chem. Eur. J.* **2006**, *12*, 1677–1693.

The cycloisomerization of enyne **67** is pretty straightforward and has been reported with different metals as catalysts. On the other hand, the cyclization of more challenging enynes such as **69**, which can undergo formal [4+2] cycloadditions, has been studied almost exclusively under gold(I) catalysis.[113] In the presence 1 equiv of enantiopure (*R*)-BINOL and 1.1 equiv of $ZnEt_2$, **69** underwent such cycloaddition at 23 ºC, affording **70** in 35% yield and in 30% ee (Scheme 51, entry 1). A more electrophilic system using (*R*)-6,6'-$Br_2$BINOL was reactive enough to drive the reaction to full conversion, giving **70** in quantitative yield, but as a racemic mixture (entry 5).




**69** **70**

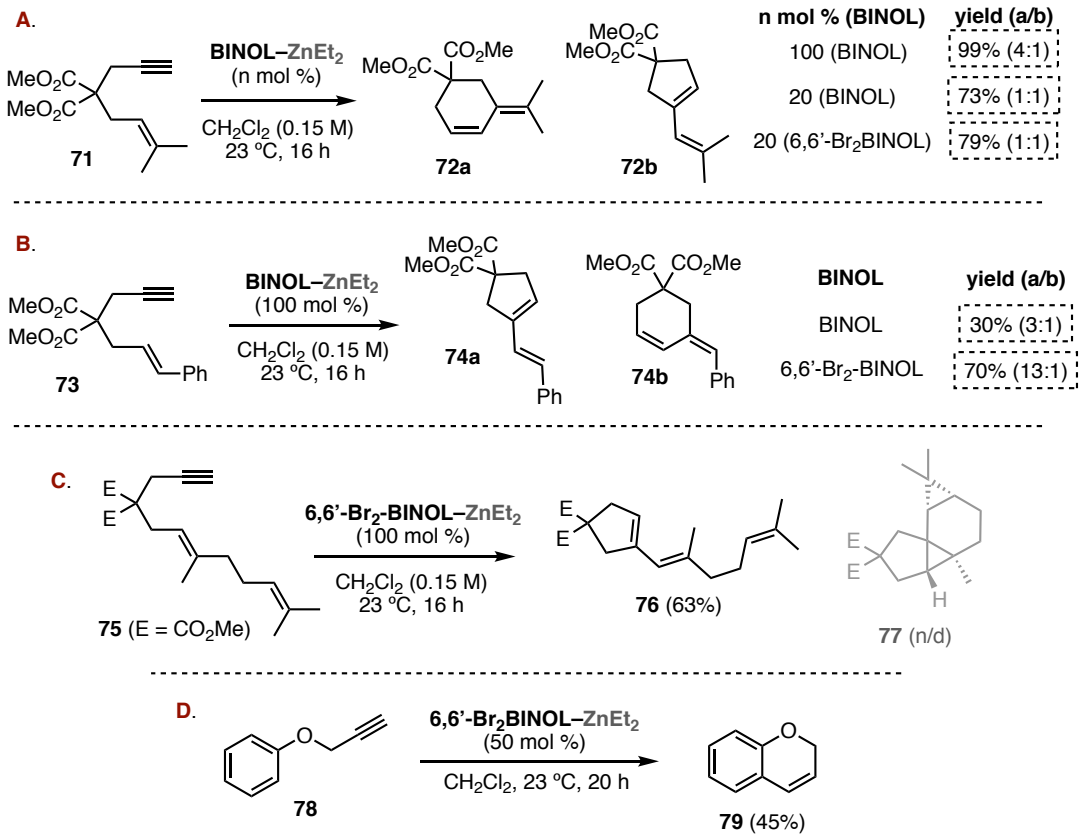
| *entry* | *conditions* | *yield (er)* | *conversion* |
|---|---|---|---|
| 1 | 1.0 equiv BINOL–Zn, $CH_2Cl_2$, 23 ºC | 35% **(65:35 er)** | 38% |
| 2 | 1.0 equiv BINOL–Zn, $CH_2Cl_2$, 40 ºC | 51% (60:40 er) | 52% |
| 3 | 0.5 equiv BINOL–Zn, $CH_2Cl_2$, 40 ºC | 14% | 15% |
| 4 | 1.0 equiv 6,6'-$Br_2$BINOL–Zn, $CH_2Cl_2$, 25 ºC | 82% (54:46 er) | 100% |
| 5 | 1.0 equiv 6,6'-$Br_2$BINOL–Zn, PhMe, 25 ºC | **99%** (49:51 er) | 100% |

**Scheme 51**. Zinc(II)-catalyzed [4+2] cycloaddition of 1,6-enynes.

At this point, we wanted to explore further the range of cyclizations traditionally catalyzed by gold(I) in which this system is active. First, we explored 1,6-enynes with different substituents in the alkene. Enyne **71** gave good yields of the cycloisomerization product even using 20 mol % of zinc Lewis acid, although erosion of the 6-*endo*/5-*exo* selectivity was observed when lowering the catalyst loading (Scheme 52A). On the other hand, phenyl-substituted enyne **73** gave the product of 5-*exo*-dig cyclization as the major one. Using simple BINOL, **74** was obtained as a 3:1 mixture in 30% yield. However, the use of more electron-poor ligand 6,6'-$Br_2$BINOL led to a 70% yield and a 13:1 **74a**/**74b** ratio (Scheme 52B). Dienyine **75** gave the product of simple 5-*exo*-dig cyclization and rearrangement exclusively. The product of 5-*exo*-dig followed by intramolecular trapping of the cyclopropyl metal carbene by the distal alkene, often obtained under gold(I) catalysis, was not observed (Scheme 52C). Finally, the intramolecular hydroarylation of phenyl propargyl ether **78**, often promoted by Lewis acids

113 Nieto-Oberhuber, C.; Pérez-Galán, P.; Herrero-Gómez, E.; Lauterbach, T.; Rodríguez, C.; López, S.; Bour, C.; Rosellón, A.; Cárdenas, D. J.; Echavarren, A. M. Gold(I)-Catalyzed Intramolecular [4+2] Cycloadditions of Arylalkynes or 1,3-Enynes with Alkenes: Scope and Mechanism. *J. Am. Chem. Soc.* **2008**, *130*, 269–279.

such as gold(I), indium(III) or even zinc(II) complexes,[114] was also carried out to give 2*H*-chromene (**79**, Scheme 52D).




**Scheme 52**. Exploring the activity of the BINOL–$ZnEt_2$ system in a variety of typically gold(I)-catalyzed transformations.

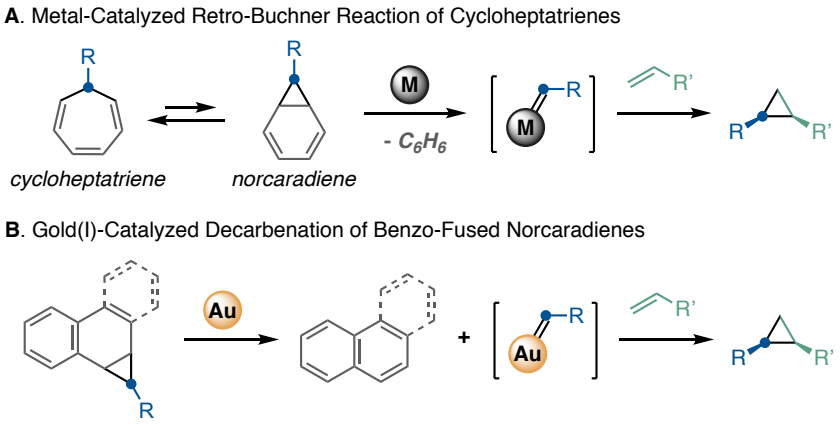
*In summary, we discovered that an electrophilic system based on the combination of BINOL derivatives and diethyl zinc is able to promote a retro-Buchner/cyclopropanation sequence. Furthermore, we showed how the same system is active in other processes typically catalyzed by gold(I) complexes such as the cycloisomerization of enynes. The possibility of inducing enantioselectivity in these transformations was also proved. Together with the initial screenings performed with gold(I) and rhodium(II), these exploratory results could potentially lead to the development of new asymmetric transformations.*

114 (a) Alonso-Marañón, L.; Sarandeses, L. A.; Martínez, M. M.; Sestelo, J. P. Sequential In-catalyzed intramolecular hydroarylation and Pd-catalyzed cross-coupling reactions using bromopropargyl aryl ethers and amines. *Org. Chem. Front.* **2017**, *4*, 500–505. (b) Li, G.; Wang, C.; Li, Y.; Shao, K.; Yu, G.; Wang, S.; Guo, X.; Zhao, W.; Nakamura, H. Zinc(II)-catalyzed intramolecular hydroarylationredox cross-dehydrogenative coupling of *N*-propargylanilines with diverse carbon pronucleophiles: facile access to functionalized tetrahydroquinolines. *Chem. Commun.* **2020**, *56*, 7333–7336.

## II.6. Release of Polyaromatic Units from Persistent Cyclopropanes

As previously mentioned, 7-substituted cycloheptatrienes exist in a tautomeric equilibrium with its corresponding norcaradienes,[60] which are the productive intermediates in the corresponding metal-catalyzed retro-Buchner reaction. This results in the release of a highly stable benzene molecule (or other arenes) as the driving force to generate carbene units.

We wondered whether it would be possible to translate this concept to the release of extended aromatic molecules, expanding the range of available carbene precursors at our disposal.[115] As a matter of fact, this hypothesis was backed up by the early experiments that led to the development of the gold(I)-catalyzed retro-Buchner reaction. In these experiments, it was indeed a benzo-fused norcaradiene that led to the generation of free gold(I) carbenes upon release of a naphthalene derivative (Scheme 11, page 45).[116] Therefore, we embarked on the design and development of a new family of carbene precursors which would release polyaromatic units as driving force. The decarbenation of these persistent cyclopropanes in the presence of external alkenes would result in an overall cyclopropane–alkene metathesis process (Scheme 53).[117]



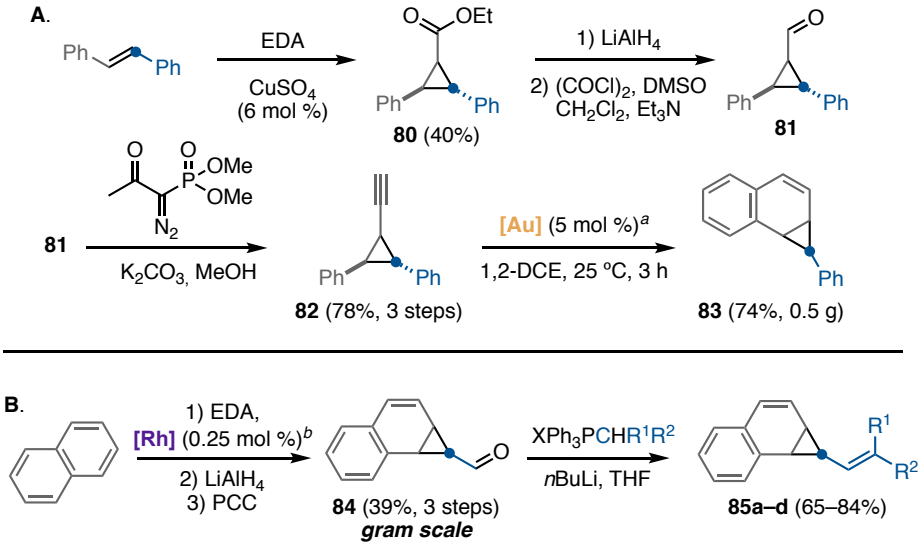

**Scheme 53**. Decarbenation of cycloheptatrienes (A) or persistent cyclopropanes (B).

115 All experiments described in this section were performed jointly with Inmaculada Martín-Torres and were based upon preliminary work by Dr. Bart Herlé.

116 Solorio-Alvarado, C. R.; Echavarren, A. M. Gold-Catalyzed Annulation/Fragmentation: Formation of Free Gold Carbenes by Retro-Cyclopropanation. *J. Am. Chem. Soc.* **2010**, *132*, 11881–11883.

117 Mato, M.; Martín-Torres, I.; Herlé, B.; Echavarren, A. M. Cyclopropane–alkene metathesis by gold(i)-catalyzed decarbenation of persistent cyclopropanes. *Org. Biomol. Chem.* **2019**, *17*, 4216–4219.

In order to prove this concept, we commenced by the synthesis of simple benzo-fused norcaradiene **83**, which would act as phenyl carbene equivalent upon release of naphthalene. The copper(II)-catalyzed cyclopropanation of *E*-stilbene with ethyl diazoacetate delivered **80** in gram quantities. Donor–acceptor cyclopropane **80** was then submitted to a sequence involving a reduction of the ester to a primary alcohol, Swern oxidation to afford the corresponding aldehyde, and finally Seyferth–Gilbert homologation with the Bestmann–Ohira reagent to afford alkyne **82** in three steps, after a single chromatographic purification. Finally, **83** was submitted to a gold(I)-catalyzed hydroarylation which takes place smoothly at room temperature over 3 h (Scheme 54A)

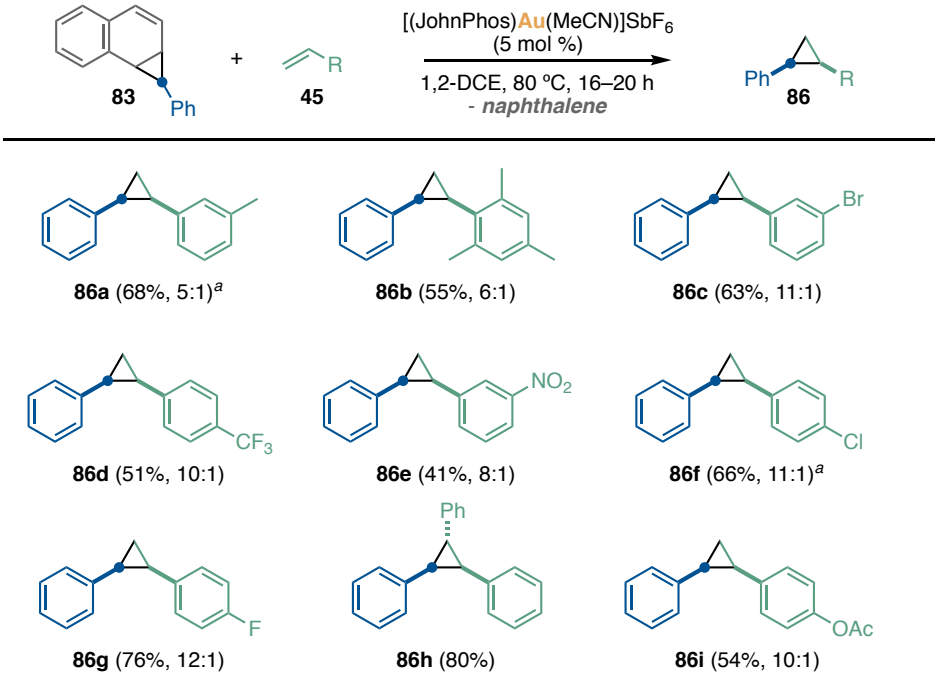



**Scheme 54**. Synthesis of benzo-fused norcaradienes. [a] [Au] = [(JohnPhos)Au(MeCN)]$SbF_6$. [b] [Rh] = [$Rh_2(TFA)_4$].

We followed a different strategy in order to access alkenyl benzo-fused norcaradienes **85a–d**. We performed the cyclopropanation of naphthalene with ethyl diazoacetate, using only 0.25 mol % [$Rh_2(TFA)_4$] as catalyst.[118] Redox manipulation of the resulting ester afforded aldehyde **84**, which was then submitted to different Wittig olefinations to afford several alkenyl carbene precursors. Noteworthily, when an asymmetric Wittig ylide was employed ($R^1 \neq R^2$), both the *E* and *Z* alkenes could be isolated separately by column chromatography (Scheme 54B).

118 (a) Müller, P.; Toujas, J.-L.; Bernardinelli, G. A Stereospecific '2-Aza-divinylcyclopropane' Rearrangement. *Helv. Chim. Acta* **2000**, *83*, 1525–1534. (b) Pérez, P. J.; Díaz-Requejo, M. M.; Revilla, I. Gold-catalyzed naphthalene functionalization. *Beilstein J. Org. Chem.* **2011**, *7*, 653–657.

We were glad to find that the reaction of benzo-fused norcaradiene **83** with 3-methylstyrene in the presence of 5 mol % of a cationic gold(I) complex at 80 ºC provided, after 16 h, the corresponding product of phenylcyclopropanation **86a** in good yield, giving the *cis* diastereoisomer preferentially. The generality of this phenyl carbene-transfer process was demonstrated across a range of styrenes, with both electron-rich and electron-withdrawing substituents, giving in all cases the corresponding *cis*-diarylcyclopropanes in good yield and diastereoselectivity (Scheme 55). It is worth highlighting that this arylcyclopropanation reaction proceeds smoothly at 80 ºC, comparing favorably to the previously required 120 ºC to transfer aryl carbene groups from 7-aryl-1,3,5-cycloheptatrienes.

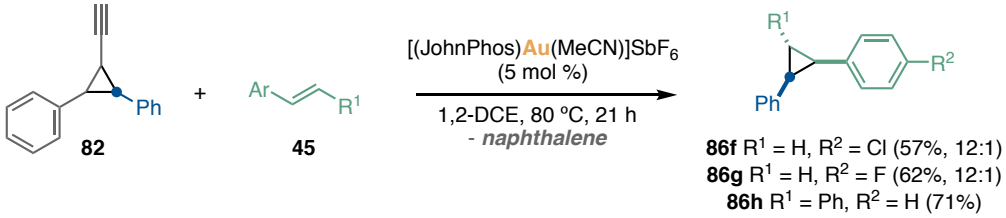



**Scheme 55**. Gold(I)-catalyzed phenylcyclopropanation upon release of naphthalene.
[a] Stirred at 100 ºC for 20 h.

As expected, the main side-product of the reaction was found to be the product of phenylcyclopropanation of the styrene double bond in **83** (see Methods Section II.9 for details). This was further confirmed by treatment of **83** with the same catalyst, without external nucleophile. This gave quantitative conversion of **83** to naphthalene and the biscyclopropane product. Fortunately, this side-pathway could be minimized statistically by the use of an excess (4 equiv) of external styrenes.

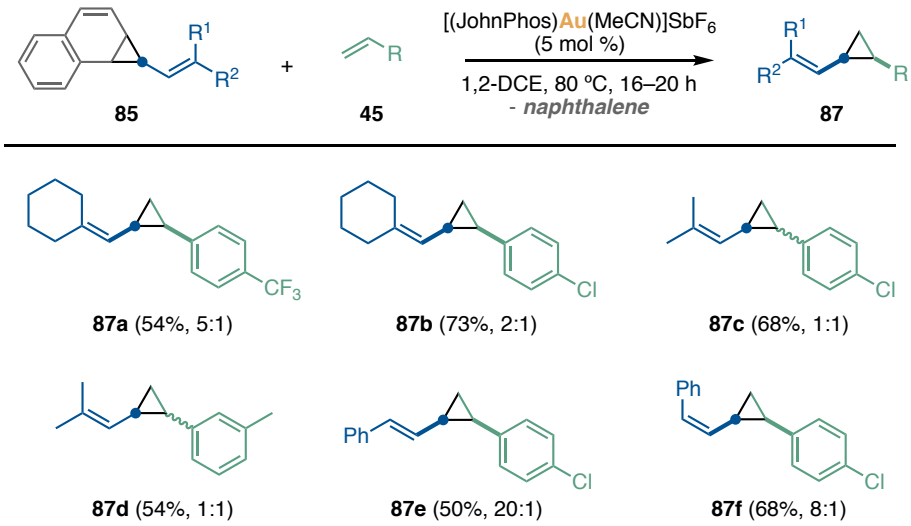
Furthermore, we exploited the fact that benzo-fused norcaradiene **83** can be prepared by gold(I)-catalyzed hydroarylation of alkynylcyclopropane **82** (Scheme 54A) in order to design a one-pot procedure for the entire sequence.

Thus, the same cationic gold(I) complex was used to promote, in a sequential manner, the hydroarylation of **82** to give **83** in situ, and its decarbenation to generate phenyl gold carbenes, which could be trapped in good yields by styrenes (Scheme 56). This afforded *cis*-diarylcyclopropanes **86f**, **86g** and **86h** in equal or better levels of efficiency and selectivity than for the stepwise procedure (Scheme 56). This method allows the use of **82** as a rather unprecedented type of metal-carbene precursor.




**Scheme 56**. One-pot gold(I)-catalyzed hydroarylation/decarbenation/cyclopropanation sequence.

Similarly, alkenyl derivatives **85** underwent the same type of decarbenation process, releasing naphthalene and generating in situ vinyl or styryl gold(I) carbenes, which could be trapped with styrenes to afford a variety of alkenylcyclopropanes (Scheme 57).



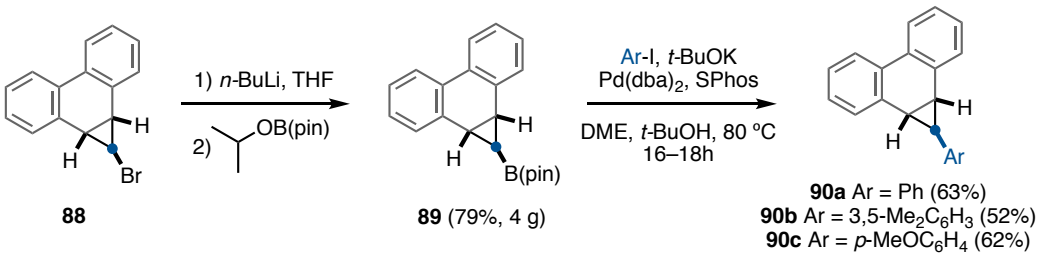

**Scheme 57**. Alkenylcyclopropanation of styrenes upon release of naphthalene.

Alkenyl-carbene fragments containing both aliphatic and aromatic substituents could be transferred successfully. Simple vinyl carbene units afforded the corresponding vinylcyclopropanes generally with low diastereoselectivity, presumably due to less efficient non-covalent interactions between the two organic fragments during the cyclopropanation event. On the other hand, styryl carbenes gave the products of styrylcyclopropanation in good to excellent diastereomeric ratios. Interestingly, since both *E* and *Z* isomers of precursor **85d**

were accessible, both *E* and *Z* styrylcyclopropanes **87e** and **87f** could be assembled (Scheme 57).

Subsequently, we wanted to prove if the release of extended polyaromatic units such as phenanthrene would be a strong-enough driving force for the generation of highly reactive aryl gold(I) carbenes. Furthermore, this type of precursor, lacking the reactive styrene-type double bond in **83** or **85**, would lead to the desired cyclopropanes more cleanly.

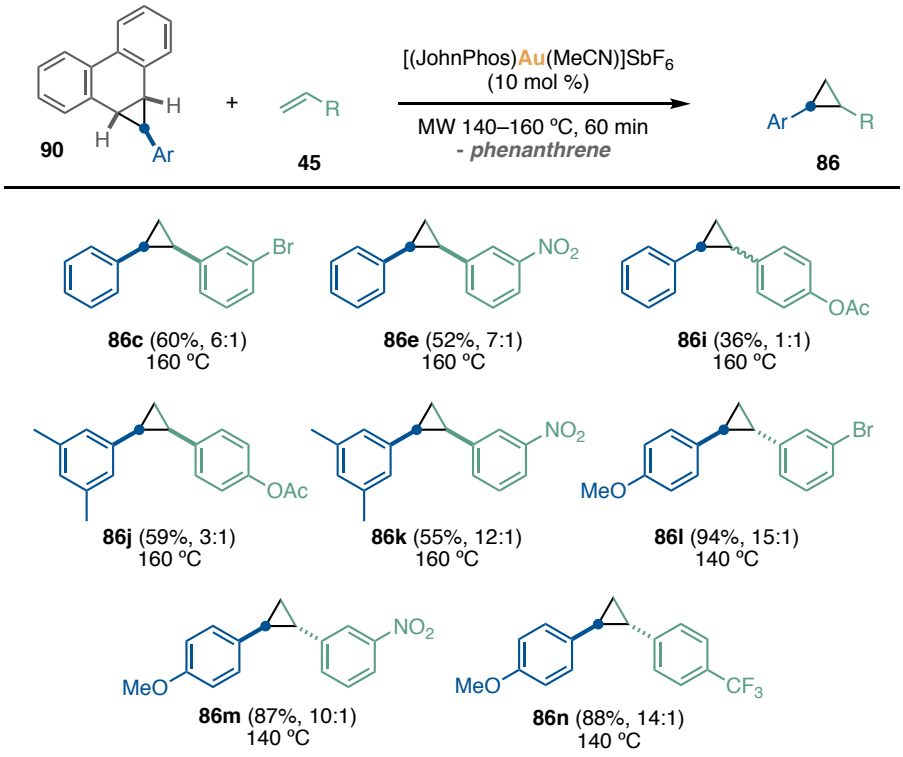
We prepared *exo*-bromocyclopropane **88** through a reported procedure involving the dibromocyclopropantion of phenanthrene, and a selective mono lithium–halogen exchange followed by protonation.[119] Treatment of this compound with *n*-BuLi and isopropoxy pinacolborane afforded multi-gram amounts of **89**. Finally, **89** could be used as nucleophilic partner in palladium-catalyzed Suzuki couplings with aryl iodides, to give phenanthrene derivatives **90a–c** in good yields (Scheme 58).




**Scheme 58**. Preparation of dibenzo-fused norcaradienes.

Analogous reaction conditions than those for the decarbenation of **83** or **85** afforded conversions lower than 20% in temperature ranges from 50 to 120 ºC. Fortunately, the problem of lower reactivity could be solved by the use of microwave heating. Thus, the reaction of **90a** with only 2 equiv of 3-bromostyrene in the presence of 10 mol % of [(JohnPhos)Au(MeCN)]$SbF_6$ upon 60 min of microwave irradiation in 1,2-dichloroethane at 160 °C led to the clean formation of cyclopropane **86c** in 60% yield, upon release of phenanthrene. Different *cis* cyclopropanes could be obtained by this method, bearing different substituents in both aromatic rings (Scheme 59). Interestingly, increasing the electron density on the aromatic ring of the carbene unit speeds up the reaction, allowing to reach full conversion and excellent yields at a lower temperature (**86l–n**). Regarding the diastereoselectivity, cyclopropanes bearing only electron-withdrawing groups were obtained preferentially as the *cis* isomers.

119 Graves, K. S.; Thamattoor, D. M.; Rablen, P. R. Experimental and Theoretical Study of the 2-Alkoxyethylidene Rearrangement. *J. Org. Chem.* **2011**, *76*, 1584–1591.




**Scheme 59**. Arylcyclopropanation of styrenes upon release of phenanthrene.

On the other hand, electron-rich cyclopropanes bearing *p*-methoxy substituents were obtained almost exclusively as the *trans* isomers (**86l**–**n**). This trend was already observed in the context of cyclopropanation by retro-Buchner reaction of 7-aryl 1,3,5-cycloheptatrienes,[120] and can be rationalized by a *cis* to *trans* isomerization catalyzed by gold(I).[88] Since there are reports of the generation of free carbenes from certain dihydrophenanthrene derivatives without the need of transition metals,[121] the reaction was also tested without catalyst, giving no conversion, which confirms the need of the gold(I) complex for the decarbenation reaction to proceed. Besides, it is worth highlighting the cleanness of this transformation, since no byproducts other than phenanthrene were detected in the reaction mixtures.

*In conclusion, the possibility of carrying out a cyclopropane–alkene metathesis though the decarbenation of persistent cyclopropanes was demonstrated. This adds new alternatives to the carbene-precursors toolbox, which release polyaromatic units as driving force.*

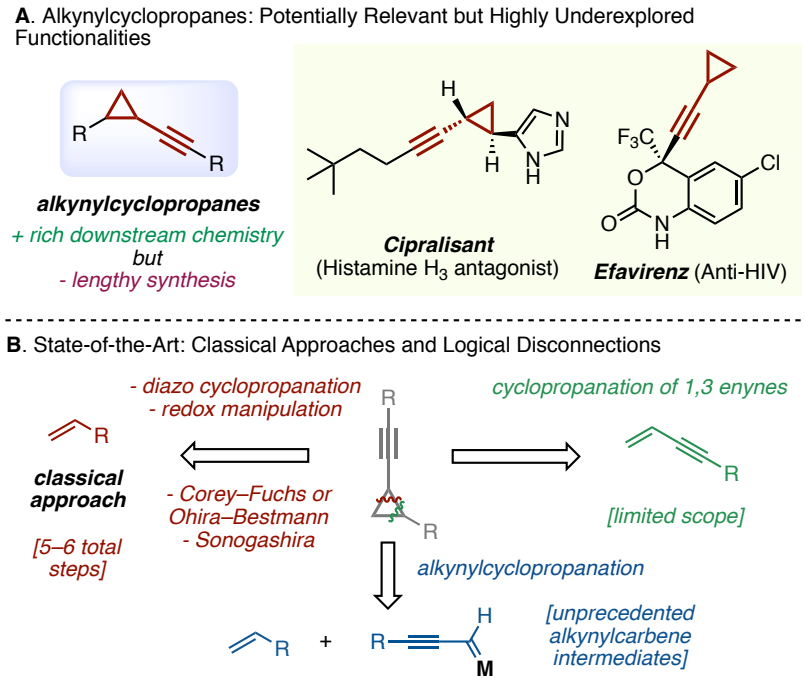
120 Solorio-Alvarado, C. R.; Wang, Y.; Echavarren, A. M. Cyclopropanation with Gold(I) Carbenes by Retro-Buchner Reaction from Cycloheptatrienes. *J. Am. Chem. Soc.* **2010**, *132*, 11881–11883. Correction of the relative configuration of some of the products: *J. Am. Chem. Soc.* **2017**, *139*, 2529.

121 Nigam, M.; Platz, M. S.; Showalter, B. M.; Toscano, J. P.; Johnson, R.; Abbot, S. C.; Kirchhoff, M. M. Generation and Study of Benzylchlorocarbene from a Phenanthrene Precursor. *J. Am. Chem. Soc.* **1998**, *120*, 8055–8059.

## II.7. Rhodium(II)-Catalyzed Alkynylcyclopropanation of Alkenes

One of the least explored types of non-acceptor-carbene transfer processes is the one that involves the generation and trapping of simple alkynylcarbene intermediates. The few methodologies featuring this strategy lack of generality or of ready availability of starting materials,[122] relying often in the use of donor–acceptor alkynyl diazo compounds.[123]

Alkynylcyclopropanes display a diverse downstream chemistry,[124] and can be found in the structure of natural products[125] or drugs (Scheme 60A).[126] However, due to the lack of availability of alkynylcarbene precursors, the short synthesis of alkynylcyclopropanes is significantly challenging, making them rather underexplored functionalities.




**Scheme 60**. Relevancy and synthetic approaches towards alkynylcyclopropanes.

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122 Barluenga, J.; Fernández-Rodríguez, M. A.; Andina, F.; Aguilar, E. A Novel [2 + 2 + 1]/[2 + 1] Tandem Cycloaddition Reaction of Fischer Alkynyl Carbenes with Strained Bicyclic Olefins. *J. Am. Chem. Soc.* **2002**, *124*, 10978–10979.

123 Davies, H. M. L.; Boebel, T. A. Asymmetric synthesis of 1-alkynylcyclopropane-1-carboxylates. *Tetrahedron Lett.* **2000**, *41*, 8189–8192.

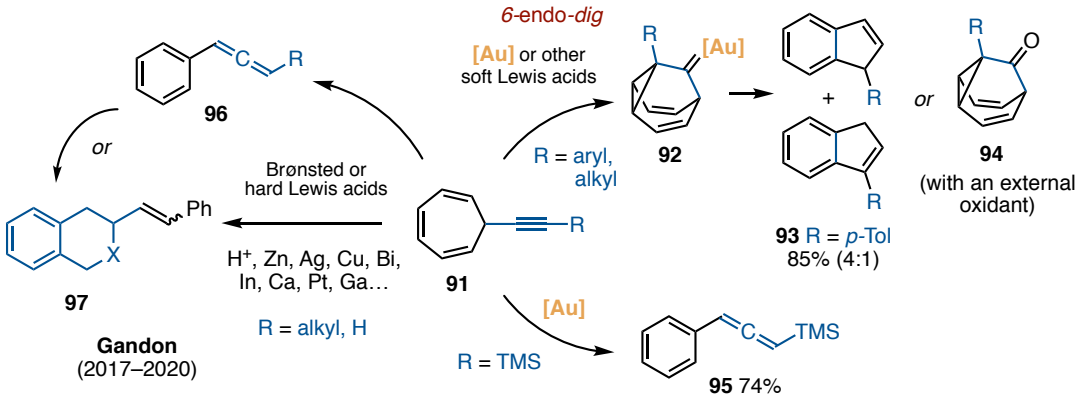
124 Trost, B. M.; Xie, J.; Maulide, N. Stereoselective, Dual-Mode Ruthenium-Catalyzed Ring Expansion of Alkynylcyclopropanols. *J. Am. Chem. Soc.* **2008**, *130*, 17258–17259.

125 Evans, D. A.; Hu, E.; Burch, J. D.; Jaeschke, G. Enantioselective Total Synthesis of Callipeltoside A. *J. Am. Chem. Soc.* **2002**, *124*, 5654–5655.

126 Rakhmanina, N. Y.; van den Anker, J. Efavirenz in the therapy of HIV infection. *Expert Opin. Drug Metab. Toxicol.* **2010**, *6*, 95–103.

Despite the recent development of several strategies for the synthesis of alkynylcyclopropanes, such as the cyclopropanation of 1,3-enynes[127] or the hydroalkynylation of cyclopropenes,[128] in most cases, more than 4 synthetic steps are required to arrive to the desired product (Scheme 60B). For this reason, even today, most methodologies that use alkynylcyclopropanes as starting materials simply rely on a classical approach for their synthesis: the cyclopropanation of an alkene with ethyl diazoacetate, redox manipulation to get the corresponding aldehyde, and finally an alkynylation such as the Seyferth–Gilbert or the Corey–Fuchs reaction, followed by functionalization if a disubstituted alkyne is required (i.e., 5–6 steps, Scheme 60B, left).[129] Thus, a short method for the in-situ generation of simple alkynylcarbene intermediates would be highly desirable (Scheme 60B, bottom).

Therefore, we envisioned that 7-alkynyl-1,3,5-cycloheptarienes **91** (which can be prepared in one step from terminal alkynes and commercially available tropylium tetrafluoroborate) would be an almost ideal precursor of alkynyl metal carbenes and, consequently, alkynylcyclopropanes. However, previous studies on these substrates show that they can evolve through an extensive variety of reaction pathways in the presence of many transition metals and other Lewis acids (Scheme 61).




**Scheme 61**. Known reactivity of 7-alkynylcycloheptatrienes in the presence of a variety of metals.

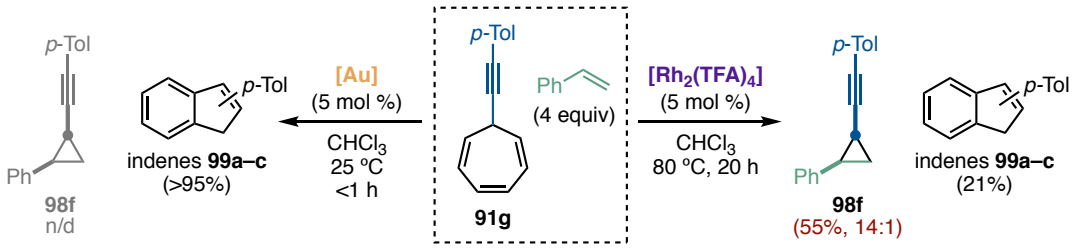
127 Morandi, B.; Carreira, E. M. Iron-Catalyzed Cyclopropanation in 6 M KOH with in Situ Generation of Diazomethane. *Science* **2012**, *335*, 1471–1474.

128 Teng, H.-L.; Ma, Y.; Zhan, G.; Nishiura, M.; Hou, Z. Asymmetric C(sp)−H Addition of Terminal Alkynes to Cyclopropenes by a Chiral Gadolinium Catalyst. *ACS Catal.* **2018**, *8*, 4705–4709.

129 Li, C.-W.; Pati, K.; Lin, G.-Y.; Sohel, S. M. A.; Hung, H.-H.; Liu, R.-S. Gold-Catalyzed Oxidative Ring Expansions and Ring Cleavages of Alkynylcyclopropanes by Intermolecular Reactions Oxidized by Diphenylsulfoxide. *Angew. Chem. Int. Ed.* **2010**, *49*, 9891–9894.

One should bear in mind that 7-alkynyl-1,3,5-cycloheptatrienes are actually 1,6-enynes, compounds that can be easily activated by gold and many other transition metals.[130] Particularly, gold(I) complexes have been found to excel in the performance of this task. In 2012, our group showed that in the presence of gold complexes, **91** readily evolves through a 6-*endo*-dig cyclization to generate cyclopropyl gold carbenes **92** (i.e., barbaralyl cations), which further rearrange to afford indenes **93** under very mild conditions.[131] Alternatively, in the presence of an external oxidant such as diphenyl sulfoxide, these intermediates can be trapped as barbaralones **94** (Scheme 61, right).[132] Furthermore, Gandon and coworkers found that this type of cycloheptatrienes react in the presence of a variety of Lewis acids, giving allenes or products of further reactivity.[133]

Fortunately, we found that the unique activity of rhodium(II) complexes (described in Section II.4 as catalysts for the retro-Buchner reaction) allowed the minimization or suppression of the cyclization/rearrangement side-pathways, promoting the decarbenation of alkynylcycloheptatrienes **91** instead. Thus, whereas the reaction of **91g** and styrene in the presence of [(JohnPhos)Au(MeCN)]$SbF_6$ gives very fast quantitative conversion to a mixture of indenes **99a** and **99b** (at 25 ºC or 80 ºC), the use of [$Rh_2$(TFA)$_4$] as catalyst leads mainly to the formation of the product of decarbenation/cyclopropanation **98f** in a 14:1 *cis*/*trans* ratio (Scheme 62).




**Scheme 62**. Gold(I) vs rhodium(II) in the reactivity of 7-alkynylcycloheptatrienes.

130 Hu, Y.; Bai, M.; Yang, Y.; Zhou, Q. Metal-catalyzed enyne cycloisomerization in natural product total synthesis. *Org. Chem. Front.* **2017**, *4*, 2256–2275.

131 McGonigal, P. R.; de León, C.; Wang,Y.; Homs, A.; Solorio-Alvarado, C. R.; Echavarren, A. M. Gold for the Generation and Control of Fluxional Barbaralyl Cations. *Angew. Chem. Int. Ed.* **2012**, *51*, 13093–13096.

132 Ferrer, S.; Echavarren, A. M. Synthesis of Barbaralones and Bullvalenes Made Easy by Gold Catalysis. *Angew. Chem. Int. Ed.* **2016**, *55*, 11178–11182.

133 (a) Vayer, M.; Guillot, R.; Bour, C.; Gandon, V. Revealing the Activity of π-Acid Catalysts using a 7-Alkynyl Cycloheptatriene. *Chem. Eur. J.* **2017**, *23*, 13901–13905. (b) Vayer, M.; Bour, C.; Gandon, V. Exploring the Versatility of 7-Alkynylcycloheptatriene Scaffolds Under π-Acid Catalysis. *Eur. J. Org. Chem.* **2020**, 5350–5357.

Similarly, the rhodium(II)-catalyzed reaction of 7-phenylethynyl-1,3,5-cycloheptatriene **91a** led to the distribution of products shown in Figure 16, which could be easily followed by $^{1}$H NMR at 50 ºC observing the main alkynylcyclopropanation pathway (blue) and the competing irreversible cycloisomerization side-pathways (green).

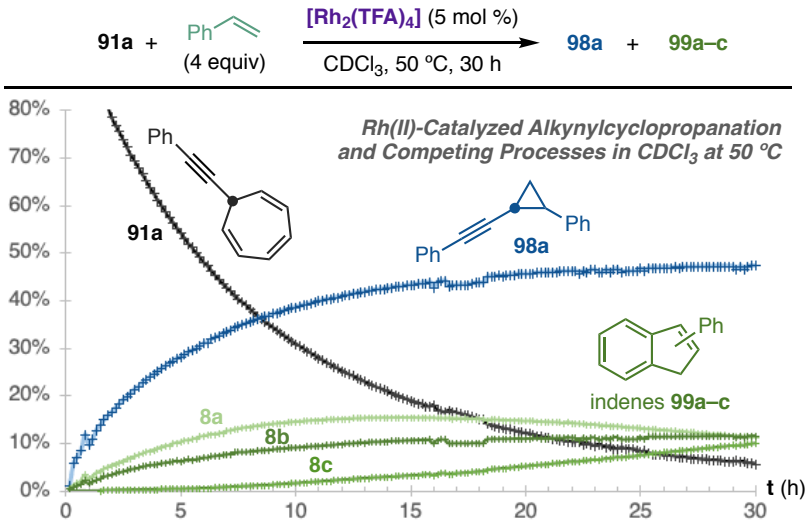
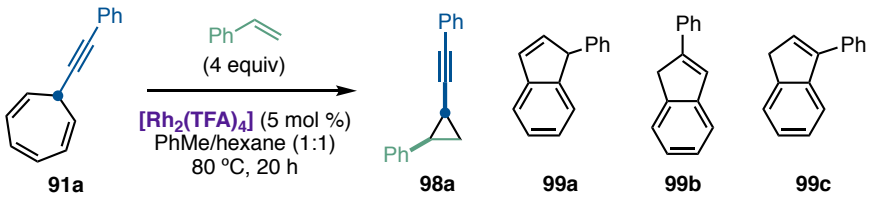



**Figure 16**. Kinetic profile of the Rh(II)-catalyzed alkynylcyclopropanation.

After the initial discovery, we started the optimization process of the aryl-alkynylcyclopropanation reaction, using **91a** and styrene as the model substrates (Scheme 63). Eventually, we found that the use of 4 equiv of styrene and 5 mol % of $[Rh_2(TFA)_4]$ as catalyst in a 1:1 toluene/hexane mixture at 80 ºC for 20 h, afforded **98a** in 70% yield (and 10:1 *cis*/*trans* ratio), with only 15% of indene side products (Scheme 63, entry 1). Again, the reaction under gold(I) catalysis provided quantitative conversion to the indenes, without any traces of cyclopropane (Scheme 63, entries 2 and 3). Zinc(II) halides did not promote either of the two pathways significantly at 80 ºC (Scheme 63, entry 7). Less electrophilic rhodium(II) catalysts performed much worse (Scheme 63, entries 4 and 5). The solvent choice is also critical for the reaction: highly coordinating solvents deactivated the catalyst (Scheme 63, entry 11), and among all the tested combinations, a 1:1 mixture of toluene and hexane gave the best result in terms of efficiency (Scheme 63, entry 1). Hexane alone gave slightly better diastereoselectivity (12:1, Scheme 63, entry 10), but due to solubility issues with some substrates, the toluene/hexane mixture was selected as standard choice. The reaction was significantly slower at 40 ºC (Scheme 63, entry 13), and at 110 ºC both the yield and the *cis*/*trans* ratio of diastereoisomers dropped (Scheme 63, entry 15).

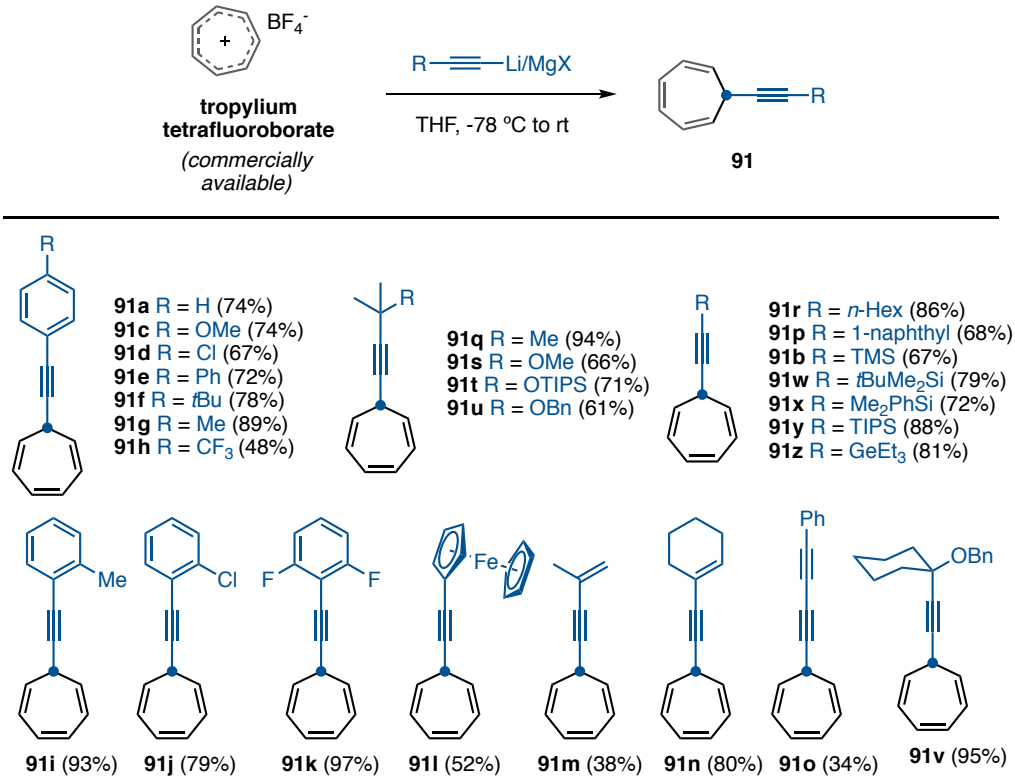



| *entry* | *deviations from standard conditions* | **98a** (*cis*/*trans*)[a] | **99a** | **99b** | **99c** |
|---|---|---|---|---|---|
| **1** | **none** | **70% (10:1)** | **-** | **7%** | **8%** |
| **2** | [Au][d] (5 mol %) at 25 °C[c] | - | 75% | 21% | - |
| **3** | [Au][d] (5 mol %) at 80 °C[c] | - | 68% | 17% | - |
| **4** | $[Rh_2(OAc)_4]$ (5 mol %)[c] | trace (n/d) | - | - | - |
| **5** | $[Rh_2(esp)_4]$ (5 mol %)[c] | 17% (n/d) | - | - | - |
| **6** | 1.7% of $[Rh_2(TFA)_4]$[b] | 61% (6:1) | 8% | 4% | - |
| **7** | $ZnCl_2$ (10 mol %) at 80 °C[c] | - | - | 2% | 2% |
| **8** | PhMe as solvent | 57% (9:1) | - | 12% | 12% |
| **9** | $CHCl_3$ as solvent | 54% (8:1) | - | 16% | 13% |
| **10** | hexane as solvent | 65% (12:1) | - | 7% | 8% |
| **11** | THF, MeCN, DMF, or EtOAc as solvent | - | - | - | - |
| **12** | 0.05 M in hexane | 64% (12:1) | 12% | 5% | - |
| **13** | PhMe at 40 °C (66% conversion) | 36% (10:1) | 9% | 14% | - |
| **14** | hexane at 40 °C (17% conversion) | 17% (n/d) | - | 2% | 3% |
| **15** | PhMe at 110 °C | 27% (2.3:1) | - | 9% | 7% |

**Scheme 63**. Optimization and control experiments. [a] Yields and dr determined by $^1$H NMR using $Ph_2CH_2$ as internal standard. [b] Hexane used as solvent. [c] $CHCl_3$ used as solvent. [d] [Au] = [(JohnPhos)Au(MeCN)$SbF_6$.

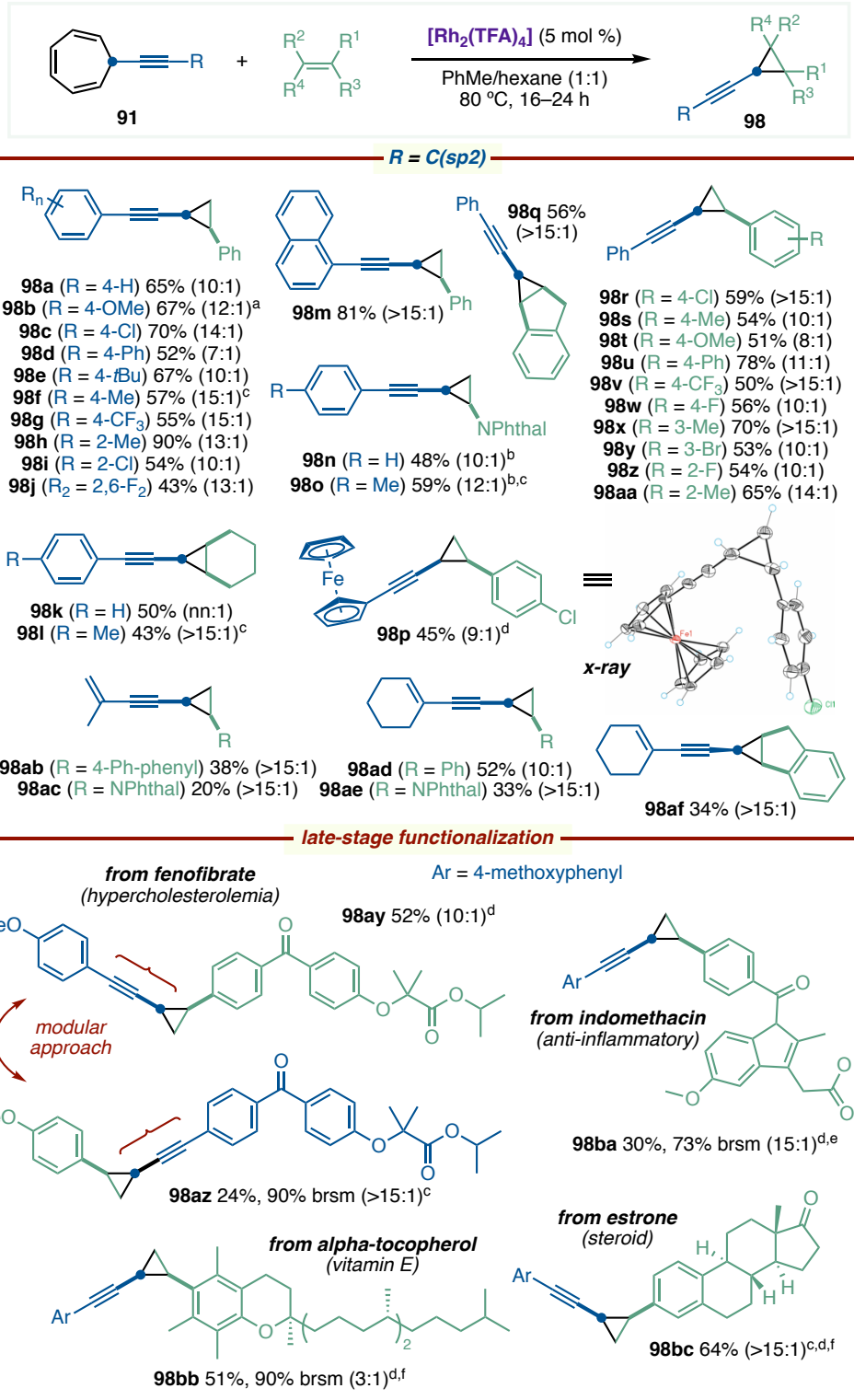
With the optimized conditions in hand, we set forth to evaluate the scope of this alkynylcyclopropanation.[134] The practicality of the reaction relies on how easy it is to access 7-alkynyl cycloheptatrienes **91**. Nucleophilic attack of alkynyl organometallic compounds (which are prepared in situ by deprotonation of terminal alkynes) to commercially available tropylium tetrafluoroborate directly gives the desired substrates. The synthesis of some of them was already reported by us, but all the ones used in this work are shown in Scheme 64.[131,132]

134 The scope and optimization of this transformation were developed in collaboration with Dr. Marc Montesinos-Magraner and Arnau R. Sugranyes. To illustrate the range of products that can be accessed with this chemistry, all examples are included in the tables, but only the characterization data of the products synthesized by the author of this Doctoral Thesis are included in the methods section. This work has been recently accepted for publication: Mato, M.; Montesinos-Magraner, M.; Sugranyes, A. R.; Echavarren, A. M. *J. Am. Chem. Soc.* **2021**, doi: 10.1021/jacs.1c05422.



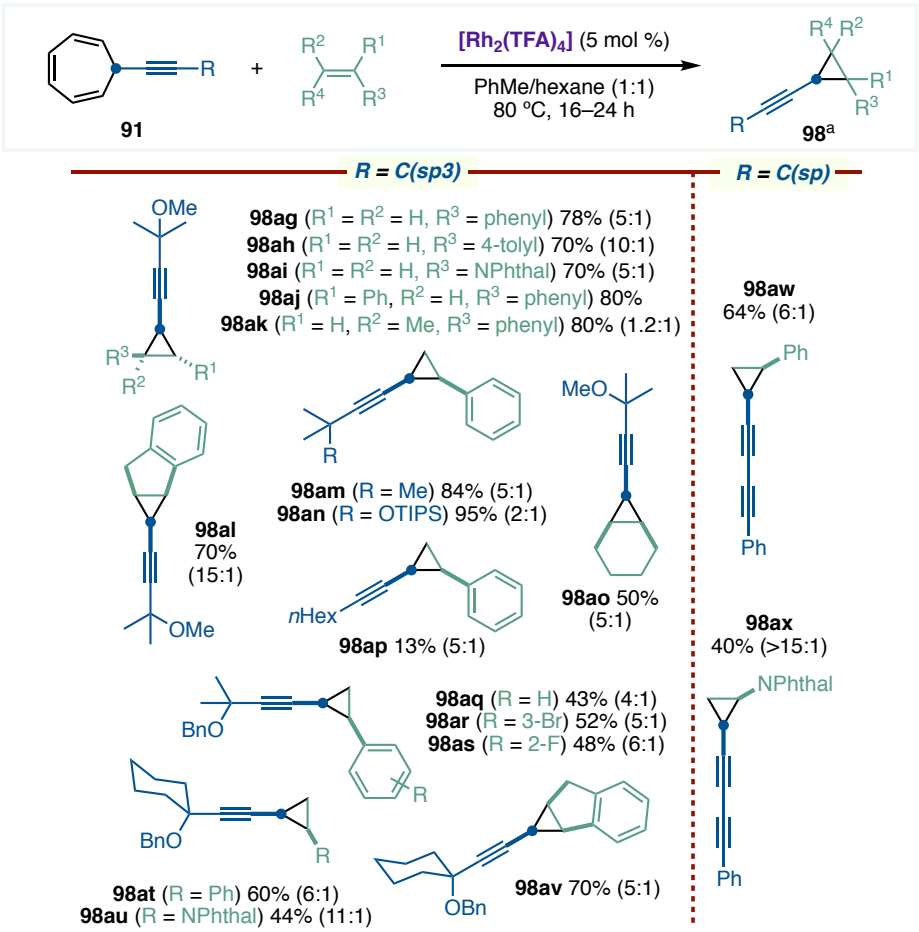

**Scheme 64**. Synthesis of 7-alkynyl-1,3,5-cycloheptatrienes **91**.

With a varied range of cycloheptatrienes in hand, we started by evaluating the scope of the alkynylcyclopropanation with aromatic substituents in the alkyne terminus (Scheme 65). First off, we studied the effect of the substituents in the aryl fragment of the carbene, using simple styrene as model alkene. Functional groups of a variety of electronic and steric properties were perfectly tolerated, giving the corresponding alkynylcyclopropanes in good yield and *cis*/*trans* ratio (**98a–98j**). Other aromatic units, such as 1-naphthyl (**98m**) or ferrocenyl (**98p**) could be transferred along with the alkyne. Ferrocene-derivative **98p** could be used to confirm the *cis* configuration of the major products, which can often also be correlated with nOe-NMR experiments. Then, we examined the scope of alkene partners that could be employed, finding that a wide range of styrenes (**98r–aa**) would trap the alkynyl carbenes successfully. As usual with this chemistry, different aryl halide groups are tolerated (**98c**, **98i**, **98r**, **98w**, **98y**, **98z**), allowing for an easy further functionalization. Indenes (**98q**), enamines (**98n**, **98o**), and non-activated alkenes such as cyclohexene (**98k–l**) were also employed. Finally, we found that apart from aryl substituents in the alkyne terminus, simple alkene groups could be transferred as well (**98ab–98af**).




**Scheme 65**. Scope of the arylalkynylcyclopropanation reaction. [a] 60 ºC instead of 80 ºC. [b] 2 equiv of alkene instead of 4. [c] $CHCl_3$ as solvent. [d] 1 equiv of alkene and 1.5 equiv of **91**. [e] PhMe/$CHCl_3$ (2:1) as solvent. [f] Obtained as a 1:1 mixture of the two possible *cis* products.

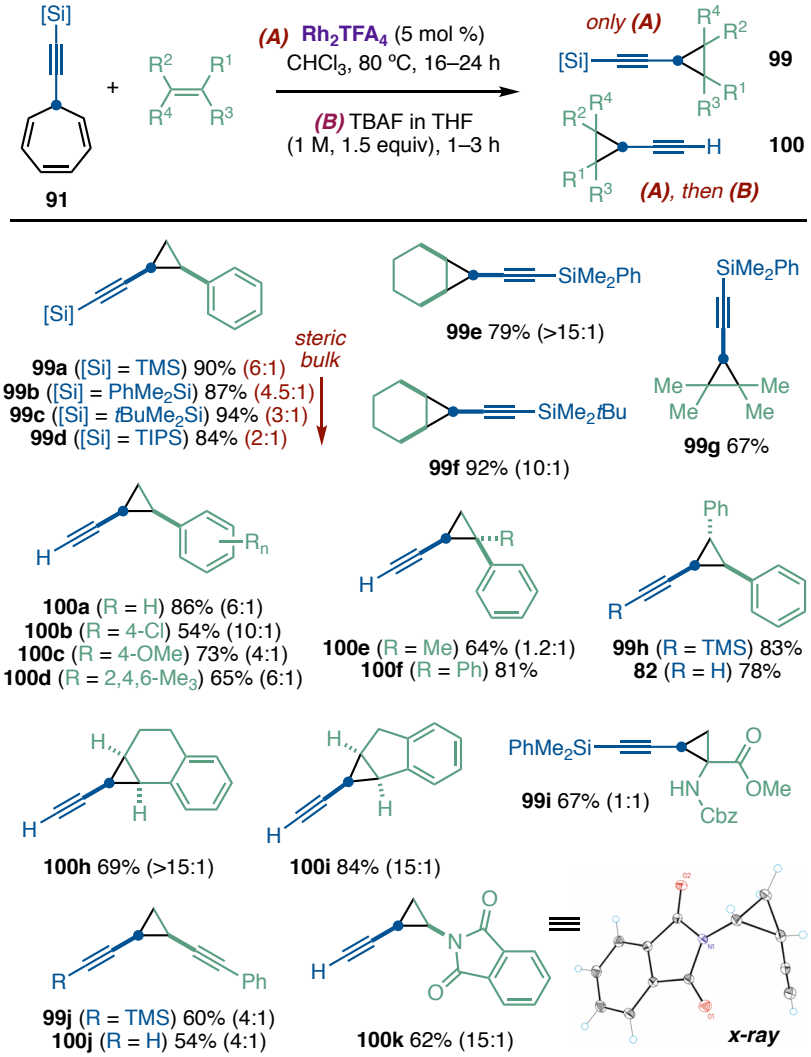
In order to illustrate the versatility of the transformation, we prepared several derivatives of biologically relevant molecules (Scheme 65, bottom). Thus, *cis*-alkynylcyclopropane derivatives of indomethacin (an anti-inflammatory drug, **98ba**), α-tocopherol (from vitamin E, **98bb**) and estrone (a steroid, **98bc**) were prepared from the corresponding styrenes. We also showed how the same approach can be applied in a modular manner: transferring the complex drug-like fragment as either the nucleophilic (alkene) or electrophilic (carbene) component of the reaction. In this fashion, we prepared two regioisomeric derivatives of fenofibrate (**98ay** and **98az**), a drug widely used to treat hypercholesterolemia.




**Scheme 66**. Scope of the alkynylcyclopropanation with $C_{sp3}$ and $C_{sp}$ substituents.

Then, we showed how it is also possible to transfer both $C_{sp3}$ and $C_{sp}$ substituents in the alkyne terminus (Scheme 66). Whereas primary and secondary alkyl substituents led to low yields of cyclopropanes (e.g., **98ap**), due to a much faster cycloisomerization to give indenes, tertiary alkyl groups were well tolerated, giving a range of propargylether-substitued cyclopropanes. Similarly, 1,3-diynylcyclopropopanes **98aw** and **98ax** could be obtained.

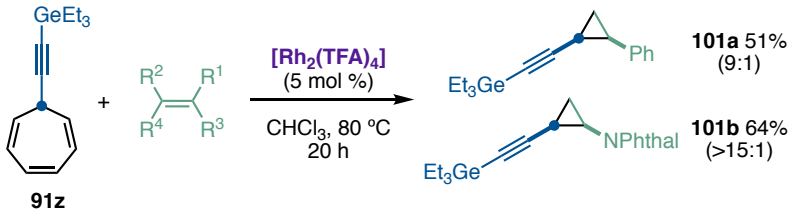
Unfortunately, when attempting the alkynylcyclopropanation reaction with simple terminal 7-ethynyl-1,3,5-cycloheptatriene, rapid decomposition was observed, and the desired product was not detected. To circumvent this problem, we envisioned a strategy in which a silylalkynyl carbene group would be transferred to the corresponding alkene, and deprotected afterwards in a one-pot procedure. For this purpose, we tested several substrates **91** with different silyl group at the alkyne terminus and, gratifyingly, we obtained the corresponding cyclopropanes in almost quantitative yield in all cases (**99a–d**). This reaction is exceedingly clean by both TLC and NMR, as no side products could be detected, suppressing any competing cycloisomerization pathway. It is worth noting that when the reaction with these substrates was attempted under gold(I) catalysis, phenyl allene **95** was obtained as the only product, resulting from the ring contraction of **91a** (Scheme 61, page 90).




**Scheme 67**. Synthesis of silyl-protected and terminal alkynylcyclopropanes.

We observed that the steric bulkiness of the silyl group correlated inversely with the obtained *cis*/*trans* ratio of cyclopropanes (Scheme 67, **99a–99d**). Considering that TMS-acetylene is the cheapest precursor for a silyl-protected cycloheptatriene **91**, and that it led to the best diastereoselectivity outcomes, we conveniently selected it as the best candidate for the one-pot cyclopropanation/deprotection sequence. Thus, we treated a mixture of 7-(TMS-ethynyl)-1,3,5-cycloheptatriene **91b** and styrene with 5 mol % of $[Rh_2(TFA)_4]$ in chloroform at 80 ºC. After **91b** was consumed, we added a commercial solution of TBAF (1.5 equiv) in THF at room temperature and stirred the mixture for 1–3 h. After removal of the solvent and purification, terminal alkynylcyclopropane **100a** was isolated in excellent yield and 6:1 dr.

Then, we evaluated the scope of the transformation. For practical reasons, some alkynylcyclopropanes **99** were isolated without deprotection (usually due to its volatility), and others (**100**) after one-pot removal of the silyl group (for these, the TMS-ethynyl fragment was always used). Some were isolated both before and after deprotection, in order to confirm that the two versions of the procedure gave similar results (e.g., **99a**/**100a** or **99h**/**82**). First, we cyclopropanated several styrenes (**100a–f**), indene (**100h**) or 1,2-dihydronaphthalene (**100i**) in high yield and moderate to good *cis*-diastereoselectivity. Less activated alkenes such as cyclohexene (**99e** and **99f**) and even tetrasubstituted ones such as tetramethylethylene (**99g**) could be cyclopropanated efficiently. More electron-rich alkenes as *N*-vinylphthalimide also performed well (**100k**). We could also cyclopropanate a dehydroalanine derivative, to obtain interesting α-amino-acid cyclopropane derivatives, though as a *cis*/*trans* 1:1 mixture. The cyclopropanation of a 1,3-enyne gave bisalkynylcyclopropanes **99j** and **100j**, which cannot be obtained by classical 1,3-enyne cyclopropanations. As an illustrative example of the practicality of this method, we prepared 1-ethynyl-2,3-diphenylcyclopropane **82** in just two steps from TMS-acetylene, which is one of the carbene precursors that we described in the previous section of this chapter (Scheme 56, page 86) and required 4 steps when that project was being developed (Scheme 54, page 84).

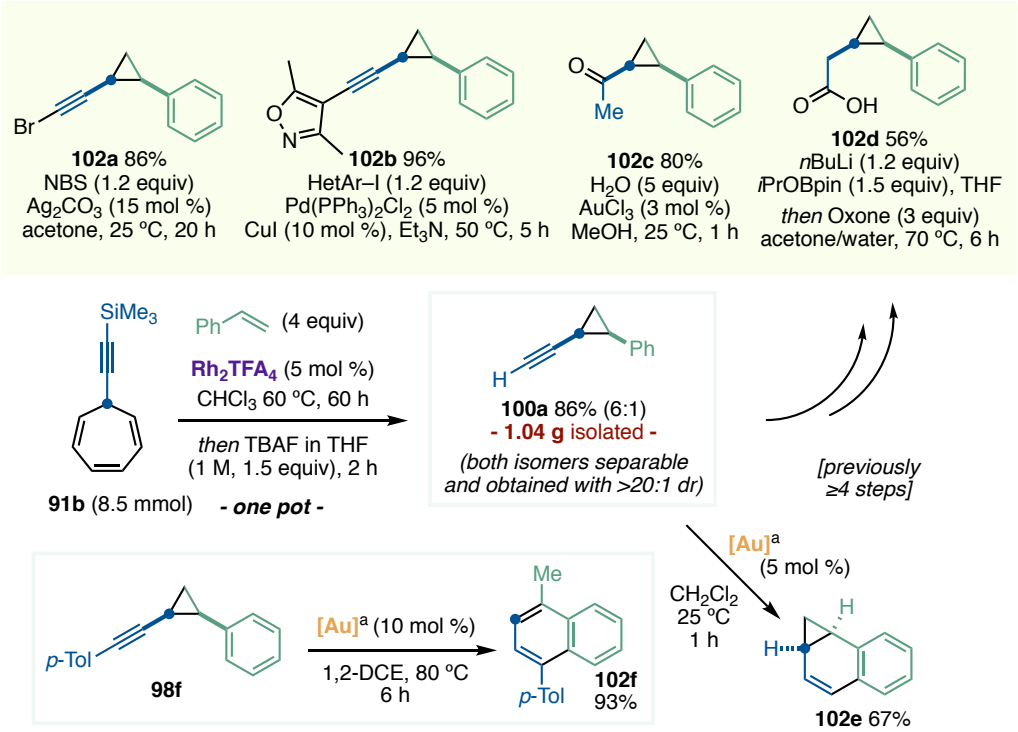



**Scheme 68**. Synthesis of germanylalkynylcyclopropanes.

Finally, we wanted to know if a germanyl group would be compatible with the same rhodium(II)-catalyzed process. Thus, we prepared **91z** and submitted it to the same reaction

conditions (Scheme 68). This allowed us to unlock the access to a new type of cyclopropane-containing organogermane compounds.

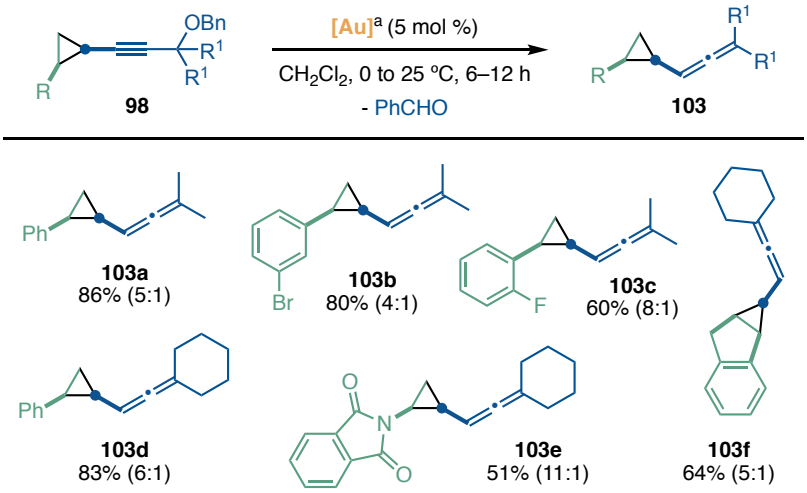
When exploring the scope of substituents in the alkyne terminus, we found that some heteroatoms such as halogens or nitrogen were not tolerated. However, the synthesis of these and many other compounds can be tackled by the use of versatile intermediates such as **100a**. This simple substrate could also be used as potential starting substrate to explore new alkynylcyclopropane downstream reactivity. Thus, we scaled up the synthesis of terminal alkynylcyclopropane **100a**, obtaining it in gram quantities with a 6:1 *cis*/*trans* ratio. Both diastereoisomers could be isolated separately in >20:1 dr by simple flash-chromatography purification. To illustrate its versatility, we submitted the major isomer to several reaction conditions. Treatment with NBS and $Ag_2CO_3$ led to bromoalkyne **102a** in high yield. Simple Sonogashira conditions allowed the introduction of a heterocyclic ring in the alkyne terminus. The gold(III)-catalyzed hydration of **100a** gave cyclopropylketone **102c**, a typical structure obtained when performing acceptor carbene-transfer processes with stabilized diazo compounds (which usually lead to poor diastereoselectivities with this type of simple substrates). Finally, sequential lithiation, borylation and oxidation of **100a** gave carboxylic acid **102d** in 56% yield over two steps (Scheme 69).




**Scheme 69**. Gram-scale synthesis and diversification of intermediate **100a**.
[Au] = [(JohnPhos)Au(MeCN)]$SbF_6$.

Furthermore, we treated **100a** with a cationic gold(I) complex at room temperature and obtained cleanly the corresponding product of hydroarylation, giving tricyclic structure **102e** in good yield and as a single diastereoisomer (Scheme 69). On the other hand, when disubstituted alkyne **98f** was submitted to the same reaction conditions, the product of hydroarylation was not observed. However, if the reaction is performed at 80 ºC, naphthalene **102f** is obtained in almost quantitative yield. This might form as a result of a sequence involving a gold(I)-catalyzed cyclopropane opening to give a methylallene intermediate, which evolves via Friedel–Crafts cyclization to give the corresponding methylnaphthalene (Scheme 69).[135]

Finally, we also found that benzyloxy-substituted products **98aq–av** can be transformed into allenyl cyclopropanes **103a–f** (Scheme 70). We used a modified version of a reported protocol based on a gold(I)-catalyzed retro-ene reaction, which releases benzaldehyde as byproduct.[136] This results in a two-step formal transfer of an allenylcarbene unit, a challenging transformation that has not been explored thus far. This grants an easy access to another type of versatile synthetic intermediates, avoiding the use of synthetically challenging 7-allenyl-1,3,5-cyclohepatrienes, which have not yet been described in the literature.




**Scheme 70**. Isomerization of cyclopropylpropargyl ethers for the assembly of allenylcyclopropanes. [a] [Au] = [(JohnPhos)Au(MeCN)]$SbF_6$.

135 Velegraki, G.; Stratakis, M. Aryl-Substituted Cyclopropyl Acetylenes as Sensitive Mechanistic Probes in the Gold-Catalyzed Hydration of Alkynes. Comparison to the Ag(I)-, Hg(II)-, and Fe(III)-Catalyzed Processes. *J. Org. Chem.* **2013**, *78*, 8880–8884.

136 Bolte, B.; Odabachian, Y.; Gagosz, F. Gold(I)-Catalyzed Rearrangement of Propargyl Benzyl Ethers: A Practical Method for the Generation and in Situ Transformation of Substituted Allenes. *J. Am. Chem. Soc.* **2010**, *132*, 7294–7296.

In order to rationalize the observed differences in chemoselectivity while using rhodium(II) or gold(I) catalysis in the reaction of 7-alkynyl-1,3,5-cycloheptatrienes, we modelled both the decarbenation/cyclopropanation sequence and the cycloisomerization pathway.[137] We used **91a** and styrene as model substrates, and $[Rh_2(TFA)_4]$ or $[(PMe_3)Au]^+$ as model catalysts, with DFT at the B3LYP-D3/6-311G(2d,2p)(H, C, O, F, P) + LANL2TZ(Rh, Au) (single point)//6-31G(d,p)(H, C, O, F, P) + LANL2DZ(Rh, Au) (optimization) level of theory (Figure 17).[138]

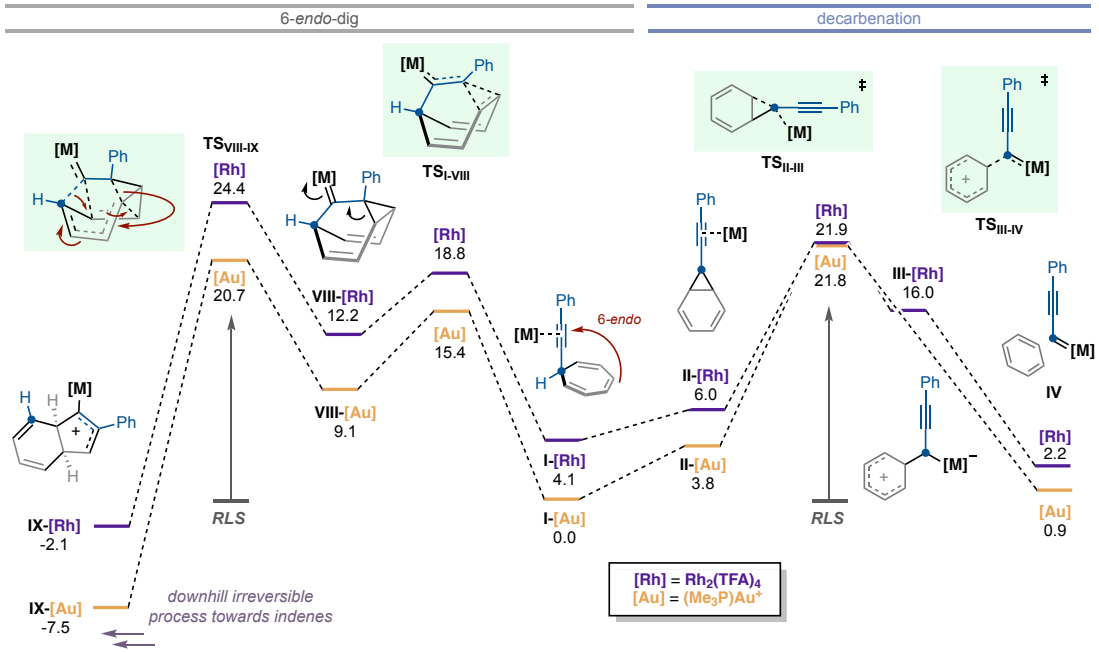



**Figure 17**. Free-energy profile of the divergent cycloisomerization (left) or decarbenation (right) of alkynyl cycloheptatrienes calculated by DFT (kcal/mol).

For gold, alkynylcycloheptatriene **91a** coordinated to the $[(PMe_3)Au]^+$ was found to be the resting state of the catalytic cycle. In the case of rhodium, after examining different structures, we established dimer $[Rh_2(TFA)_4]$ coordinated to two cycloheptatrienes **91a** (through each of the two metal centers of the dimeric complex) as the resting state. Both complexes **91**–M (**I**) can evolve directly through a 6-*endo*-dig cyclization (Figure 17, left pathway) to form metal-

137 The full model for the metal-catalyzed cycloisomerization of **91a** was based on previous calculations performed by our group and the group of Gandon, see: (a) McGonigal, P. R.; de León, C.; Wang, Y.; Homs, A.; Solorio-Alvarado, C. R.; Echavarren, A. M. Gold for the Generation and Control of Fluxional Barbaralyl Cations. *Angew. Chem. Int. Ed.* **2012**, *51*, 13093–13096. (b) Vayer, M.; Guillot, R.; Bour, C.; Gandon, V. Revealing the Activity of π-Acid Catalysts using a 7-Alkynyl Cycloheptatriene. *Chem. Eur. J.* **2017**, *23*, 13901–13905.

138 The DFT calculations presented in this section were performed in collaboration with Dr. Marc Montesinos-Magraner, who developed the model for the 6-*endo*-dig cyclization and refined the entire mechanistic proposal.

stabilized barbaralyl carbocations (or cyclopropylgold(I) carbenes) such as **VIII**.[139] These species can undergo rearrangement to give indene precursors such as **IX**, through transition states $\mathbf{TS_{VIII\text{-}IX}}$, which are the rate-limiting step of the entire cycloisomerization process. From this point, as previously demonstrated by Gandon and coworkers, intermediates **IX** evolve through small energy barriers, to afford indenes **99a–c** irreversibly.[137] Correlating with the experimental observations, the cycloisomerization pathway is significantly more favored for gold(I) compared to rhodium(II). On the other hand, norcaradiene-metal complexes **II** can undergo cleavage of the first C–C bond of the three-membered ring, through $\mathbf{TS_{II–III}}$. This was found to be the rate-limiting step of the decarbenation by retro-Buchner reaction. Considering the barriers of the two rate-limiting steps, we found the cycloisomerization to be preferred with gold, and the decarbenation pathway to be more favored under Rh(II)-catalysis. Finally, $\mathbf{TS_{II–III}}$ leads to the formation of carbenoid Wheland-type intermediate **III**, which is a shallow minimum that evolves smoothly to give alkynyl carbene **IV** upon release of benzene.

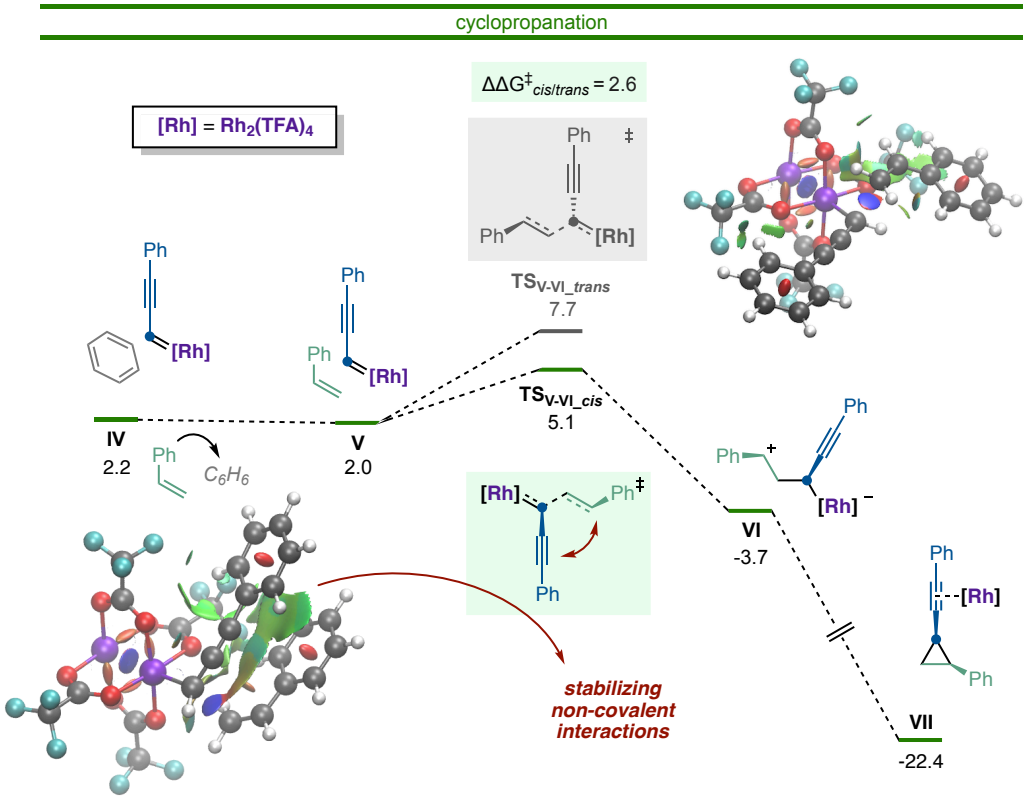



**Figure 18**. Free-energy profile of the alkynyl cyclopropanation of styrene (kcal/mol) and NCI plots for both $TS_{V–VI}$. In the NCI plots, strong attractive interactions are blue (C–C bond formation), weak attractive interactions are green (non-covalent interactions), and strong repulsive interactions are red. Color code: Rh, violet; O, red; F, cyan; C, gray; H, white.

139 We found different tautomeric structures which can rapidly interconvert connecting the different intermediates of the cycloisomerization process, through barriers always lower than that for $\mathbf{TS_{VIII–IX}}$.

Subsequently, we modeled the cyclopropanation process (Figure 18). After ligand exchange, nucleophilic attack of styrene in **V** leads to the formation of cationic intermediate **VI**,[140] which is a shallow minima and rapidly closes up to give the corresponding alkynylcyclopropane–Rh(II) complex **VII**. In order to understand the diastereoselectivity of the transformation we compared the energies of $\mathbf{TS_{V–VI\_trans}}$ and $\mathbf{TS_{V–VI\_cis}}$, which were separated by 2.6 kcal/mol favoring the *cis* cyclopropanation, correlating with the good *cis*-selectivities observed experimentally (Scheme 65, page 95). Furthermore, we carried out a NCI (non-covalent interactions) analysis using the NCIPLOT software.[141] NCI representation of both the *cis* and *trans* versions of the transition state of the diastereodetermining step ($\mathbf{TS_{V–VI}}$) revealed very significant non-covalent attractive interactions between the two organic fragments (the phenyl of styrene and the ethynylphenyl of the carbene) in the *cis* transition state, whereas these are absent in the more energetic *trans* transition state (Figure 18, green surfaces in the NCI plots).

This model based on non-covalent attraction to favor the *cis*-cyclopropanation can also be used to rationalize how trialkylsilyl groups in the alkyne terminus often led to cyclopropanes with lower *cis*/*trans* ratio than aryl groups, due to the absence of π–π stacking. Moreover, the inverse correlation between *cis*-diastereoselectivity and bulkiness of the silyl groups employed, can also be explained by a reduction of this stabilizing component upon increase of steric hindrance (R = Ph, 10:1 dr, R = TMS, 6:1 dr; R = $PhMe_2Si$, 4.5:1 dr; R = TBDMS, 3:1 dr; R = TIPS, 2:1 dr; Scheme 67, page 97).

*Overall, a simple, practical alkynylcyclopropanation reaction has been developed which allows, for the first time, a general assembly alkynylcyclopropanes in just two steps from terminal alkynes and alkenes. The method is based on the rhodium(II)-catalyzed decarbenation of 7-alkynylcyclohepatrienes. The unique performance of this system solves a fundamental problem in cycloheptatriene chemistry, since these substrates usually evolve preferentially through cycloisomerization or ring-contraction pathways under catalysis of gold(I), or many other metals.*

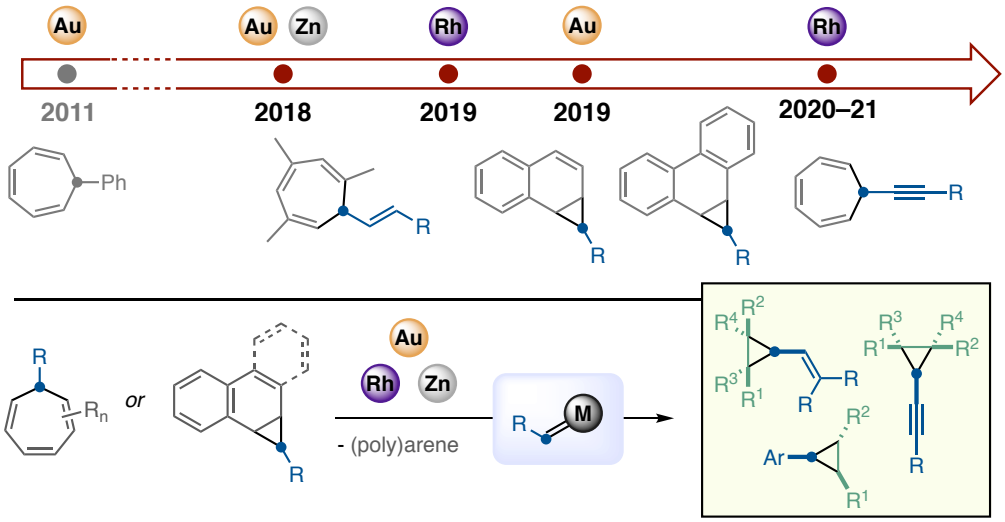
140 A concerted cyclopropanation pathway which did not involve the intermediacy of carbocations **VI** could not be located.

141 Johnson, E. R.; Keinan, S.; Mori-Sánchez, P.; Contreras-García, J.; Cohen, A. J.; Yang, W. Revealing Noncovalent Interactions. *J. Am. Chem. Soc.* **2010**, *132*, 6498–6506.

## II.8. Conclusions

Based upon the concept of metal-catalyzed aromative decarbenation by retro-Buchner reaction of 7-substituted cyclohepatrienes, we have developed new types of non-acceptor carbene precursors. We found that besides benzene, other aromatic units such as mesitylene or polyaromatics can be released as driving force for the generation highly reactive carbenes. Through the design of more reactive precursors, such as trimethylcycloheptatriene derivatives, we discovered that this process can be promoted not only by gold(I) under milder conditions, but also under catalysis of cheaper zinc(II) salts, or more versatile rhodium(II) complexes.

This led to the development of new selective cyclopropanation strategies. An illustrative example is the divergent reactivity of alkynylcycloheptatrienes, which undergo cycloisomerizations under gold(I) catalysis, but undergo retro-Buchner reactions under rhodium(II) catalysis. These findings were applied for the development of not only improved, but also new methods for the synthesis of vast range of non-acceptor cyclopropanes, allowing the transfer of the most general types of non-acceptor-carbene fragments: aryl, alkenyl and alkynyl carbenes.




**Scheme 71**. Discovery of new carbene precursors and application to the development of cyclopropanation reactions.

The results summarized in Chapter II pave the way for the discovery of new chemical transformations based upon these now readily accessible metal carbene intermediates (see Chapter III). This work also lays the ground for the design of an even wider variety of carbene precursors, the identification of new catalytic systems, and the development of enantioselective transformations.

## II.9. Methods Section

### *General Experimental Methods*

Unless otherwise stated, the all the reactions reported herein were carried out under argon atmosphere in solvents dried by passing through an activated alumina column on a PureSolv™ Solvent Purification System (SPS, Innovative Technologies, Inc., MA), or in commercially available anhydrous solvents purchased from ACROS Organics. Some reactions were performed at temperatures higher than the boiling point of the employed solvents, in sealed microwave vials using an aluminum heating block; the appropriate precautions for working in such set up must be taken. Yields refer to chromatographically and spectroscopically pure ($^1$H NMR) homogeneous material, unless otherwise stated. Thin layer chromatography was carried out using TLC aluminum sheets coated with 0.2 mm of silica gel (Merck Gf234) using short-wave UV light as visualizing agent and phosphomolybdic acid, $KMnO_4$ or acidic vanillin followed by heat as developing agents. Chromatographic purifications were carried out using flash grade silica gel (SDS Chromatogel 60 ACC, 40-60 μm) as the stationary phase manually, or using a CombiFlash®$R_f$ instrument with normal phase disposable columns of different sizes (Teledyne Isco). Preparative TLC was performed on 20 cm x 20 cm silica gel plates (2.0 mm thick, catalogue number 02015, Analtech or 1.0 mm thick, catalogue number P02013 Analtech). NMR spectra were recorded at 23 ºC (unless stated otherwise) on a Bruker Avance 300, 400 Ultrashield or Bruker Avance 500 Ultrashield apparatus. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane, using residual solvent ($CHCl_3$ at 7.28 ppm $^1$H NMR, 77.00 ppm $^{13}$C NMR) or tetramethylsilane as reference. Coupling constants are reported in hertz (*Hz*). The following abbreviations were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintuplet, m = multiplet, br = broad. Mass spectra were recorded in a Waters LCT Premier Spectrometer (ESI and APCI) or in an Autoflex Bruker Daltonics (MALDI and LDI). LCMS was performed in an Agilent 1290 Infinity II coupled with an Agilent Infinity Lab LC/MSD XT (APCI). GCMS was performed in an Agilent 6890N GC System coupled with an Agilent 5975B inert XL MSD. Melting points were determined using a MP70 Melting Point System (Mettler Toledo). Single-crystal X-ray-diffraction data were recorded on a Bruker Kappa APEX II DUO diffractometer equipped with an APPEX 2 4K CCD area detector, a Microsource with $Mo_{ka}$ radiation and an Oxford Cryostream 700 low temperature device (T = -173 ºC). Unless otherwise stated, all reagents were purchased from commercial sources and used without further purification.

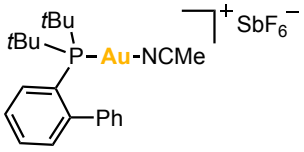
### *Handling and Sources of Metal Catalysts*

#### Rhodium(II) Catalysts

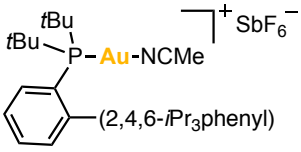
Rhodium(II) trifluoroacetate dimer (min. 95% purity) was purchased from STREM Chemicals (45-1960) and used as received. For reproducibility reasons, it was stored in an argon-filled glovebox and all rhodium(II)-catalyzed reactions of the different scopes were set up inside the glovebox under inert atmosphere. However, most of them are not significantly sensitive to air and can be carried out without a protective inert atmosphere, using rhodium(II) complexes stored in a desiccator. Other Rh(II) sources used, such as $[Rh(OAc)_2]_2$, $[Rh(esp)_2]_2$, and chiral rhodium(II) catalysts were also purchased from commercial sources, used as received, and stored in a desiccator or in the glovebox.

#### Gold(I) Catalysts

All gold complexes, such as (acetonitrile)[(2-biphenyl)di-*tert*-butyl-phosphine]gold(I) hexafluoroantimonate (**A**) and (acetonitrile)[2-di-*tert*-butyl(2′,4′,6′-triisopropylbiphenyl)-phosphine]gold(I) hexafluoroantimonate (**B**), were purchased from Sigma-Aldrich. The bottles were not stored under inert atmosphere, and thus, unless otherwise stated, the gold(I)-catalyzed reactions were carried out under air in HPLC-grade solvents.




**A**




**B**

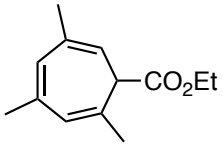
#### Zinc(II) Catalysts

$ZnBr_2$ 99.999% (trace metal basis) was purchased from ACROS Organics™ and stored in a nitrogen-filled glovebox. Most of the Zn(II)-catalyzed reactions were carried out using this salt, for both efficiency and reproducibility reasons. $ZnBr_2$ of other qualities (down to 98%) or even stored under air, could also be used in the zinc(II)-catalyzed transformations, although the presence of moisture proved to be detrimental to the chemical yields. The rest of the zinc(II) salts used on the optimization were also >98% pure and stored in a nitrogen-filled glovebox. Diethylzinc (1.0 M) was purchased as a solution in hexane from Sigma-Aldrich and used as received.

***Synthetic Procedures and Analytical Data***

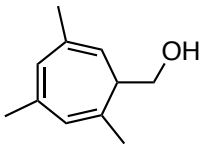
**Gram-Scale Synthesis of Julia-Kocienski Sulfone Reagent (48)**

**Ethyl 2,4,6-trimethylcyclohepta-2,4,6-triene-1-carboxylate**




A dry two-necked 1 L round-bottomed flask equipped with a Teflon-coated magnetic stirring bar was charged with $Rh_2(OAc)_4$ (140 mg, 0.316 mmol, 0.10 mol %) and then evacuated and refilled with argon three times. Mesitylene (53 mL, 0.379 mol, 1.2 equiv) was added via syringe, dissolved in dichloromethane (210 mL, 1.5 M), and the mixture was degassed by bubbling argon through, while stirring, for 30–60 min. Ethyl 2-diazoacetate (40 mL, 0.316 mol, 1.0 equiv) was then added via automatic syringe to the stirring solution over 60 hours (*ca.* 0.5 mL/h) at room-temperature, before dichloromethane was removed in vacuum. Crude product was filtered through a big plug of silica gel, which was eluted with cyclohexane/EtOAc 9:1, until no more product came out. The solvent was removed in a rotatory evaporator and then, the product was dried in high vacuum overnight in order to remove excess mesitylene, leaving ethyl 2,4,6-trimethylcyclohepta-2,4,6-triene-1-carboxylate (50.1 g, 0.243 mol, 77%) with enough purity for the next step (>90%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.25 (s, 1H), 5.84 (s, 1H), 5.38 (d, *J* = 6.5 Hz, 1H), 4.29-4.19 (m, 2H), 2.86 (d, *J* = 6.5 Hz, 1H), 2.01 (s, 3H), 1.93 (d, *J* = 1.2 Hz, 3H), 1.90 (t, *J* = 1.1 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 172.8, 138.1, 133.6, 129.6, 128.5, 125.3, 114.3, 60.6, 48.2, 24.3, 21.5, 20.3, 14.3 ppm. **HRMS** (ESI Positive): calculated for $C_{14}H_{19}O_2$ $[M-H]^+$: 219.1380; found: 219.1379.

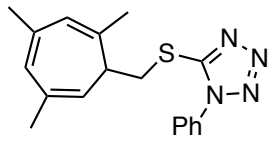
**(2,4,6-Trimethylcyclohepta-2,4,6-trien-1-yl)methanol (47)**




A dry three-necked 3 L round-bottomed flask equipped with a Teflon-coated magnetic stirring bar was charged with ethyl 2,4,6-trimethylcyclohepta-2,4,6-triene-1-carboxylate (45 g, 0.218 mol, 1.0 equiv) and after evacuating and refilling the flask with argon, it was dissolved in dry ethyl ether (1.1 L, 0.2 M). The flask was cooled down to 0 ºC with an ice bath, and then lithium aluminum hydride (10.76 g, 0.284 mol, 1.2 equiv) was carefully added in portions of 1 g, one every 3–5 minutes. The resulting suspension was stirred for 16 h whilst warming to room-temperature, and after confirming the disappearance of all the starting material by TLC (a new more polar spot appears, corresponding to the alcohol, which reveals clearly with acidic vanillin stain followed by heat), the mixture is cooled back down to 0 ºC before water is slowly added, up to 300 mL. Then, HCl 10% aqueous solution was added, while the mixture is stirred vigorously until completely dissolving all solids (*ca.* 300 mL) in the aqueous phase (which becomes a white suspension; mechanical stirring may be necessary in large-scale). The

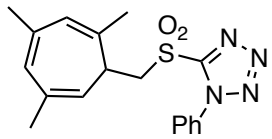
ethereal phase (upper layer) was decanted, and the aqueous phase extracted 2 times with diethyl ether (3x300 mL). The three organic fractions combined were washed with water (1x400 mL) and brine (1x400 mL), and after drying over anhydrous $Na_2SO_4$, the solvent was removed to give (2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)methanol **47** (29 g, 0.177 mol, 86% yield), after filtration through a $SiO_2$ plug, as a pale-yellow oil with enough purity for the next step (>90%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 6.16 (s, 1H), 5.85 (s, 1H), 5.02 (d, *J* = 7.3 Hz, 1H), 3.73 – 3.67 (m, 2H), 2.53 (q, *J* = 7.7 Hz, 1H), 2.00 (d, *J* = 1.6 Hz, 3H), 1.99 (d, *J* = 1.4 Hz, 3H), 1.89 (d, *J* = 1.3 Hz, 3H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 137.6, 135.0, 134.5, 129.0, 125.3, 117.4, 61.1, 45.4, 24.8, 22.6, 22.3 ppm. **HRMS** (APCI Positive): calculated for $C_{11}H_{17}O$ $[M+H]^+$: 165.1274; found: 165.1281.

**1-Phenyl-5-(((2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)methyl)thio)-1*H*-tetrazole**



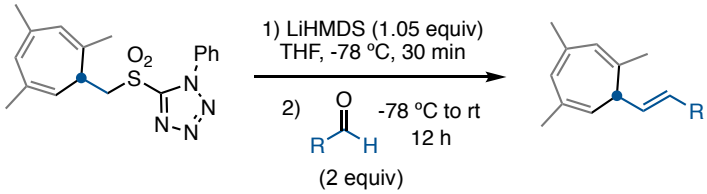

A dry two-necked 2 L round-bottomed flask equipped with a Teflon-coated magnetic stirring bar was charged with 2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)methanol **47** (18 g, 110 mmol, 1.0 equiv) and 1-phenyl-1*H*-tetrazole-5-thiol (19.9 g, 112 mmol, 1.02 equiv) before the atmosphere was evacuated and refilled with argon three times. Everything was dissolved in anhydrous THF (600 mL, *ca*. 0.2 M) before it was cooled down to 0 ºC in an ice bath, and tri(*n*-butyl)phosphine (28.4 ml, 115 mmol, 1.05 equiv) was added via syringe in a single portion. To the resulting solution was added diisopropyl (*E*)-diazene-1,2-dicarboxylate, DIAD (23.1 ml, 115 mmol, 1.05 equiv) via syringe, steadily, in a single portion (over less than 1 min) while stirring vigorously (the orange color of DIAD disappears within seconds during the addition, until >1 equiv is added, then the orange color persists). The mixture was allowed to stir whilst coming to room-temperature over 12 h. 500 mL of water were added, and the aqueous phase was extracted 3 times with diethyl ether (3x400 mL). Combined organic fractions were washed with water once (1x300 mL) and with brine once (1x300 mL), solvent was removed, and the crude product was purified by CombiFlash column chromatography in $SiO_2$ (2x330 g, purified in two separate flash chromatography runs), using a gradient of [cyclohexane with 5% $CH_2Cl_2$] and [EtOAc] 9:1 to 8:2 as eluent giving 1-phenyl-5-(((2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)methyl)thio)-1*H*-tetrazole (25 g, 77 mmol, 70% yield) as a pale yellow oil. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.59 – 7.51 (m, 5H), 6.13 (d, *J* = 2.0 Hz, 1H), 5.84 (t, *J* = 1.5 Hz, 1H), 5.12 (d, *J* = 7.9 Hz, 1H), 3.46 – 3.36 (m, 2H), 2.92 (q, *J* = 8.0 Hz, 1H), 1.97 (d, *J* = 1.4 Hz, 3H), 1.96 (d, *J* = 1.4 Hz, 3H), 1.84 (d, *J* = 1.3 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 155.00, 137.83, 135.87, 135.13, 134.16, 130.40, 130.12, 129.45, 125.69, 124.24, 118.73, 42.16, 32.34, 25.19, 22.89, 14.42. **GC-MS** (EI): calc. for $C_{18}H_{20}N_4S$ $[M]^+$: 324.1; found: 324.1.

**1-Phenyl-5-(((2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)methyl)sulfonyl)-1*H*-tetrazole, Julia-Kocienski Reagent (48)**



Under air, a two neck 2 L round-bottomed flask equipped with a magnetic stirring bar was charged 1-phenyl-5-(((2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)methyl)thio)-1*H*-tetrazole (22 g, 68 mmol, 1 equiv) and it was dissolved in HPLC grade ethanol (600 mL, *ca.* 0.1 M) and the solution was cooled in an ice bath. A solution of ammonium molybdate tetrahydrate (8.1 g, 6.8 mmol, 10 mol %) in hydrogen peroxide (30% in water) (104 ml, 1.02 mol, 15 equiv) (prepared with only glass material) was added dropwise using a dropping funnel over 1 h, and the resulting mixture was further stirred for 20 h while coming to room temperature. After confirming complete conversion of the stating thioether, water (500 mL) was added, and the mixture was extracted three times with dichloromethane (3x400 mL) (if the two phases do not split, addition of 50 mL of brine can be helpful). Combined organic fractions were washed with water once (1x400 mL) and with brine once (1x400 mL), dried over $Na_2SO_4$ and concentrated under vacuum. Flash chromatography with CombiFlash in $SiO_2$ (220 g), using a gradient of [cyclohexane with 5% $CH_2Cl_2$] and [EtOAc] 9:1 to 8:2 as eluent gave 1-phenyl-5-(((2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)methyl)-sulfonyl)-1*H*-tetrazole **48** (18.0 g, 50 mmol, 74 % yield) as a white solid, after sonicating with pentane. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.69-7.59 (m, 5H), 6.21 (s, 1H), 5.88 (s, 1H), 5.16 (d, $J$ = 8.4 Hz, 1H), 3.74 (t, $J$ = 8.4 Hz, 2H), 3.42-3.32 (m, 1H), 2.03-2.02 (m, 6H), 1.84 (d, $J$ = 1.3 Hz, 3H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 153.9, 138.2, 135.7, 133.1, 132.2, 131.4, 129.6, 129.5, 126.1, 125.2, 115.2, 54.3, 36.4, 24.7, 24.3 ppm. **HRMS** (ESI Pos): calc. for $C_{18}H_{20}N_4NaO_2S$ $[M+Na]^+$: 379.1199; found: 379.1196. **MP** 90–93 ºC. **FTIR (ATR)** 3060, 3023, 2980, 2916, 2854, 1594, 1497, 1457, 1327, 1313, 1135, 1041, 786, 761, 690, 528 $cm^{-1}$.

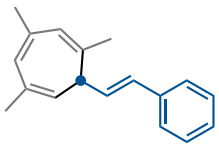
**General Procedure A for the Synthesis of 7-Styryl-1,3,5-trimethyl-1,3,5-cycloheptatrienes (44) by Julia–Kocienski Olefination**




A dry screw-cap culture tube or microwave vial (small scale) or a round-bottom flask (gram scale) equipped with a Teflon-coated stirring bar was charged with 1-phenyl-5-(((2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)methyl)sulfonyl)-1*H*-tetrazole **48** (1 equiv), which was dissolved, under argon, in anhydrous THF (0.1–0.2 M). The mixture was cooled down to -78 ºC using a cryocooler bath, and then a freshly prepared solution of lithium bis(trimethylsilyl)amide (1.05 equiv) in anhydrous THF (*ca*. 0.5 M) was added dropwise. After stirring for 30 minutes at -78 ºC, to the resulting yellow solution was added the corresponding aldehyde (1.0 equiv), either neat via syringe (liquid substrates) or dissolved in anhydrous THF (solid substrates or small amounts, *ca.* 0.5 M) in a single portion (the mixture usually evolves from intense yellow to pale yellow-colorless). After 15 minutes, the cryocooler was turned off or the flask/tube was taken out of the bath and stirred for 8–12 h whilst coming to room temperature. Water was added, and the mixture was extracted 3 times with diethyl ether. Combined organic fractions were washed twice with water and once with brine and concentrated under vacuum. Crude product was purified by flash column chromatography in $SiO_2$ using pentane or gradients of pentane/$Et_2O$ as eluent (or CombiFlash chromatography using cyclohexane/EtOAc gradients) to give the corresponding 7-styryl-1,3,5-trimethyl-1,3,5-cycloheptatriene **44**.

**Characterization Data of Cycloheptatrienes (44)**

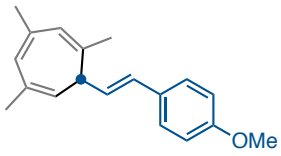
**(*E*)-1,3,5-Trimethyl-7-styrylcyclohepta-1,3,5-triene (44a)**



The title compound (pale yellow oil, 1.29 g, 97% yield) was obtained following General Procedure A from reagent **48** (2.00 g, 5.61 mmol) and benzaldehyde (1.19 g, 11.2 mmol, 2 equiv) using LiHMDS (0.99 g, 5.89 mmol, 1.05 equiv) after purification by flash column chromatography on $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.40 (d, *J* = 7.0 Hz, 2H), 7.33 (t, *J* = 7.6 Hz, 2H), 7.27 – 7.22 (m, 1H), 6.46 (d, *J* = 2.3 Hz, 2H), 6.25 (s, 1H), 5.84 (s, 1H), 5.11 (d, *J* = 6.7 Hz, 1H), 2.89 – 2.81 (m, 1H), 2.06 – 2.04 (m, 3H), 2.00 (d, *J* = 1.2 Hz, 3H), 1.92 (s, 3H).**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 137.95, 137.70, 135.04, 132.90, 130.33, 129.43, 129.30, 128.63, 128.48, 128.06, 127.06, 126.19, 124.14, 118.40, 77.34, 77.02, 76.71, 45.93,

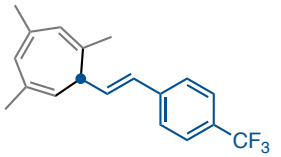
24.65, 21.93, 21.84.**HRMS** (APCI Positive): calculated for $C_{18}H_{20}$ $[M+H]^+$: 237.1638; found: 237.1637.

**(*E*)-7-(4-Methoxystyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (44b)**



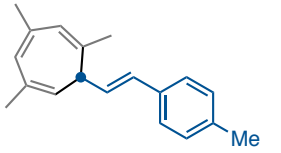

The title compound (pale yellow oil, 0.51 g, 93% yield) was obtained following General Procedure A from reagent **48** (0.70 g, 1.96 mmol) and 4-methoxybenzaldehyde (0.54 g, 3.93 mmol, 2 equiv) using LiHMDS (0.35 mg, 2.06 mmol, 1.05 equiv) after purification by flash column chromatography on $SiO_2$ using pentane/$Et_2O$ 99:1 to 97:3 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.37 – 7.31 (m, 2H), 6.91 – 6.86 (m, 2H), 6.43 – 6.29 (m, 2H), 6.26 (s, 1H), 5.84 (s, 1H), 5.13 – 5.09 (m, 1H), 3.84 (s, 3H), 2.81 (t, *J* = 7.3 Hz, 1H), 2.08 – 2.04 (m, 3H), 2.00 (d, *J* = 1.1 Hz, 3H), 1.92 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.87, 137.94, 135.40, 132.73, 130.53, 129.78, 129.31, 127.29, 124.02, 118.76, 113.93, 55.29, 45.98, 24.66, 21.92, 21.76. **HRMS** (APCI Positive): calculated for $C_{19}H_{21}O$ $[M–H]^+$: 265.1587; found: 265.1585.

**(*E*)-1,3,5-Trimethyl-7-(4-(trifluoromethyl)styryl)cyclohepta-1,3,5-triene (44c)**




The title compound (pale yellow oil, 52 mg, 81% yield) was obtained following General Procedure A from reagent **48** (75 mg, 0.210 mmol) and 4-(trifluoromethyl)-benzaldehyde (74 mg, 0.42 mmol, 2 equiv) using LiHMDS (37 mg, 0.22 mmol, 1.05 equiv) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 99:1 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.57 (d, *J* = 8.2 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 6.56 – 6.43 (m, 2H), 6.24 (s, 1H), 5.86 (s, 1H), 5.11 (d, *J* = 6.9 Hz, 1H), 2.91 (t, *J* = 7.2 Hz, 1H), 2.06 – 2.03 (m, 3H), 2.00 (s, 3H), 1.92 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.17, 137.95, 134.21, 133.34, 132.08, 129.35, 129.27, 129.03, 128.91, 128.71, 128.39, 128.32, 126.28, 125.63, 125.49, 125.45, 125.41, 125.37, 124.44, 122.92, 120.22, 117.57, 45.85, 24.62, 22.10, 22.00. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -62.52. **HRMS** (APCI Positive): calculated for $C_{19}H_{20}F_3$ $[M+H]^+$: 305.1512; found: 305.1517.

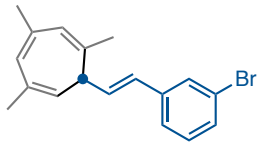
**(*E*)-1,3,5-Trimethyl-7-(4-methylstyryl)cyclohepta-1,3,5-triene (44d)**




The title compound (pale yellow oil, 1.2 g, 95% yield) was obtained following General Procedure A from reagent **48** (1.8 g, 5.1 mmol) and 4-methylbenzaldehyde (1.21 g, 10 mmol, 2 equiv) using LiHMDS (0.89 g, 5.3 mmol, 1.05 equiv) after purification by flash column chromatography on $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz,

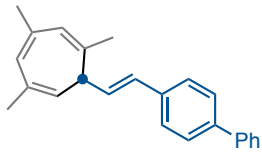
Chloroform-*d*) δ 7.30 (dd, *J* = 8.0, 1.8 Hz, 2H), 7.18 – 7.12 (m, 2H), 6.43 – 6.40 (m, 2H), 6.28 – 6.21 (m, 1H), 5.84 (t, *J* = 1.4 Hz, 1H), 5.11 (dt, *J* = 6.6, 1.5 Hz, 1H), 2.82 (dt, *J* = 7.2, 3.5 Hz, 1H), 2.37 (s, 3H), 2.05 (s, 3H), 1.92 (t, *J* = 1.1 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 137.97, 136.82, 134.93, 132.80, 130.25, 129.37, 129.32, 129.19, 128.47, 126.10, 124.06, 118.62, 45.95, 24.65, 21.91, 21.74, 21.17. **HRMS** (APCI Positive): calculated for $C_{19}H_{23}$ $[M+H]^+$: 251.1794; found: 251.1795.

**(*E*)-7-(3-Bromostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (44e)**



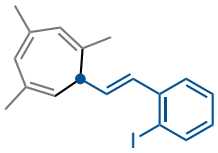

The title compound (pale yellow oil, 140 mg, 79% yield) was obtained following General Procedure A from reagent **48** (200 mg, 0.56 mmol) and 3-bromobenzaldehyde (208 mg, 1.12 mmol, 2 equiv) using LiHMDS (99 mg, 0.59 mmol, 1.05 equiv) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 99:1 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.54 (t, *J* = 1.8 Hz, 1H), 7.36 (ddd, *J* = 7.9, 2.0, 1.1 Hz, 1H), 7.28 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.22 – 7.17 (m, 1H), 6.47 – 6.36 (m, 2H), 6.24 (d, *J* = 1.8 Hz, 1H), 5.85 (t, *J* = 1.4 Hz, 1H), 5.10 (dt, *J* = 6.9, 1.4 Hz, 1H), 2.87 (t, *J* = 7.3 Hz, 1H), 2.04 (d, *J* = 1.3 Hz, 3H), 1.99 (d, *J* = 1.5 Hz, 4H), 1.92 (t, *J* = 1.1 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 139.90, 137.95, 133.21, 130.99, 130.00, 129.91, 129.30, 128.98, 128.96, 128.85, 124.93, 124.37, 122.73, 117.89, 45.86, 24.67, 22.06, 22.00. **HRMS** (APCI Pos): calculated for $C_{18}H_{20}{}^{79}Br$ $[M+H]^+$: 315.0743; found: 315.0744.

**(*E*)-4-(2-(2,4,6-Trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)-1,1'-biphenyl (44f)**



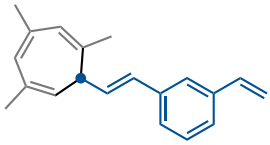

The title compound (white solid, 180 mg, 82% yield) was obtained following General Procedure A from reagent **48** (250 mg, 0.70 mmol) and 4-phenylbenzaldehyde (256 mg, 1.40 mmol, 2 equiv) using LiHMDS (123 mg, 0.74 mmol, 1.05 equiv) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 97:3 as eluent. **$^1$H NMR** (300 MHz, Chloroform-*d*) δ 7.65 – 7.56 (m, 4H), 7.46 (ddd, *J* = 7.8, 4.4, 1.9 Hz, 4H), 7.39 – 7.33 (m, 1H), 6.53 – 6.45 (m, 2H), 6.25 (s, 1H), 5.85 (t, *J* = 1.4 Hz, 1H), 5.12 (d, *J* = 6.7 Hz, 1H), 2.95 – 2.81 (m, 1H), 2.05 (d, *J* = 1.3 Hz, 3H), 2.01 (d, *J* = 1.4 Hz, 3H), 1.92 (t, *J* = 1.0 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 140.85, 139.87, 137.99, 136.76, 135.02, 132.97, 129.89, 129.62, 129.33, 128.78, 127.22, 126.93, 126.61, 126.43, 124.19, 118.35, 45.99, 24.68, 21.97, 21.89. **HRMS** (APCI Positive): calculated for $C_{24}H_{25}$ $[M+H]^+$: 313.1951; found: 313.1947. **MP** 49–52 ºC.

**(*E*)-1,3,5-Trimethyl-7-(2-iodostyryl)cyclohepta-1,3,5-triene (44g)**



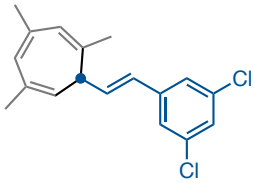
The title compound (pale yellow oil, 0.65 g, 79% yield) was obtained following General Procedure A from reagent **48** (0.75 g, 2.10 mmol) and 2-iodobenzaldehyde (0.98 g, 4.21 mmol, 2 equiv) using LiHMDS (0.37 g, 2.21 mmol, 1.05 equiv) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane to cyclohexane/EtOAc 98:2 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.81 (d, *J* = 9.0 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 1H), 6.92 – 6.87 (m, 1H), 6.57 (d, *J* = 15.6 Hz, 1H), 6.28 – 6.18 (m, 2H), 5.82 (s, 1H), 5.09 (d, *J* = 6.8 Hz, 1H), 2.92 (t, *J* = 7.5 Hz, 1H), 2.01 (s, 3H), 1.97 (s, 3H), 1.89 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.21, 139.77, 138.25, 134.29, 133.61, 132.87, 129.69, 128.93, 128.63, 126.93, 124.80, 118.31, 100.01, 46.06, 27.30, 25.09, 22.44. **HRMS** (APCI Positive): calculated for $C_{18}H_{20}I$ $[M+H]^+$: 363.0604; found: 363.0607.

**(*E*)-1,3,5-Trimethyl-7-(3-vinylstyryl)cyclohepta-1,3,5-triene (44h)**



The title compound (160 mg, 72% yield) was obtained following General Procedure A from reagent **48** (300 mg, 0.84 mmol) and 3-vinylbenzaldehyde (222 mg, 1.68 mmol, 2 equiv) using LiHMDS (148 mg, 0.88 mmol, 1.05 equiv) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane to cyclohexane as eluent. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.41 (q, *J* = 1.4 Hz, 1H), 7.30 (d, *J* = 1.3 Hz, 3H), 6.75 (dd, *J* = 17.6, 10.9 Hz, 1H), 6.51 – 6.41 (m, 2H), 6.25 (d, *J* = 1.8 Hz, 1H), 5.85 (t, *J* = 1.4 Hz, 1H), 5.79 (dd, *J* = 17.6, 1.0 Hz, 1H), 5.29 (dd, *J* = 10.9, 1.0 Hz, 1H), 5.12 (d, *J* = 6.7 Hz, 1H), 2.86 (t, *J* = 6.3 Hz, 1H), 2.05 (d, *J* = 1.2 Hz, 3H), 2.00 (d, *J* = 1.5 Hz, 3H), 1.92 (d, *J* = 1.1 Hz, 3H). **GCMS** (EI Positive): calculated for $C_{20}H_{20}$ $[M]^+$: 262.2; found: 262.2.

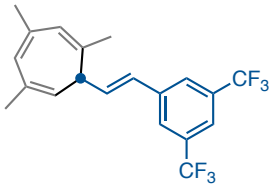
**(*E*)-1,3,5-Trimethyl-7-(3,5-dichlorostyryl)cyclohepta-1,3,5-triene (44i)**



The title compound (colorless oil, 188 mg, 88% yield, 5:1 *E*/*Z*) was obtained following General Procedure A from reagent **48** (250 mg, 0.70 mmol) and 3,5-dichlorobenzaldehyde (245 mg, 1.40 mmol, 2 equiv) using LiHMDS (123 mg, 0.74 mmol, 1.05 equiv) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 99:1 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.20 – 7.16 (m, 3H), 6.38 (dd, *J* = 15.8, 8.2 Hz, 1H), 6.25 (d, *J* = 15.9 Hz, 1H), 6.19 (s, 1H), 5.81 (s, 1H), 5.04 (d, *J* = 6.9 Hz, 1H), 2.85 (t, *J* = 7.5 Hz, 1H), 1.99 (s, 3H), 1.94 (s, 3H), 1.87 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.12, 138.28, 135.36, 133.85, 132.74, 129.63, 128.05, 127.35, 127.13, 124.91, 124.89, 117.73,

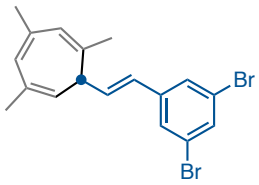
46.12, 25.02, 22.61, 22.40. **HRMS** (APCI Positive): calculated for $C_{18}H_{19}Cl_2$ $[M+H]^+$: 305.0858; found: 305.0863.

**(*E*)-7-(3,5-Bis(trifluoromethyl)styryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (44j)**



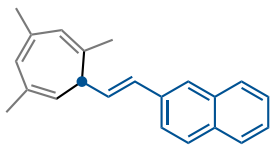
The title compound (colorless oil, 0.41 g, 85% yield) was obtained following General Procedure A from reagent **48** (0.46 g, 1.21 mmol) and 3,5-bis(trifluoromethyl)benzaldehyde (0.63 g, 2.41 mmol, 2 equiv) using LiHMDS (0.23 g, 1.36 mmol, 1.05 equiv) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane to cyclohexane to cyclohexane/EtOAc 99:1 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 1.7 Hz, 2H), 7.72 (s, 1H), 6.52 – 6.48 (m, 1H), 6.24 (s, 1H), 5.87 (t, *J* = 1.5 Hz, 1H), 5.12 (d, *J* = 7.1 Hz, 1H), 2.98 (t, *J* = 7.1 Hz, 1H), 2.04 (t, *J* = 1.8 Hz, 3H), 2.01 (d, *J* = 1.4 Hz, 3H), 1.93 (d, *J* = 1.3 Hz, 3H). **$^{13}$C NMR** (126 MHz, Chloroform-*d*) δ 140.10, 138.29, 134.11 (d, *J* = 5.3 Hz), 129.62, 127.76, 126.30, 125.11, 124.83 (q, *J* = 5.0 Hz), 120.75 (q, *J* = 4.0 Hz), 121.6 (q, *J* = 273 Hz),117.38, 46.11, 24.99, 22.79, 22.43. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -63.10. **HRMS** (APCI Positive): calculated for $C_{20}H_{18}F_6$ $[M+H]^+$: 373.1313; found: 373.1313.

**(*E*)-7-(3,5-Dibromostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (44k)**



The title compound (amorphous white foam, 0.42 g, 69% yield) was obtained following General Procedure A from reagent **48** (0.55 g, 1.54 mmol) and phenanthrene-9-carbaldehyde (0.50 g, 2.41 mmol, 2 equiv) using LiHMDS (0.21 g, 1.27 mmol, 1.05 equiv) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane to cyclohexane to cyclohexane/EtOAc 99:1 as eluent. The product was obtained in a purity of around 60% by NMR. Since the reagent worked on the decarbenation, further purification was not attempted. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.38 (d, *J* = 1.7 Hz, 2H), 7.24 (d, *J* = 2.2 Hz, 1H), 6.36 (dd, *J* = 15.8, 8.1 Hz, 1H), 6.18 (d, *J* = 1.8 Hz, 1H), 5.80 (t, *J* = 1.4 Hz, 1H), 5.03 (d, *J* = 7.0 Hz, 1H), 2.85 (t, *J* = 7.6 Hz, 1H), 1.99 (d, *J* = 1.3 Hz, 3H), 1.94 (d, *J* = 1.4 Hz, 3H), 1.87 (t, *J* = 1.0 Hz, 3H). **GC-MS** (EI): calculated for $C_{18}H_{18}{}^{79}Br_2$ $[M+]^+$: 392.0; found: 392.0.

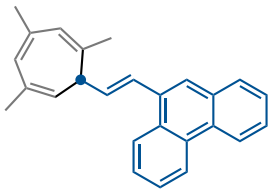
**(*E*)-2-(2-(2,4,6-Trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)naphthalene (44l)**



The title compound (pale yellow oil, 144 mg, 90% yield) was obtained following General Procedure A from reagent **48** (200 mg, 0.56 mmol) and 2-naphtaldehyde (175 mg, 1.12 mmol, 2 equiv) using LiHMDS (99 mg, 0.59 mmol, 1.05 equiv) after purification by flash column

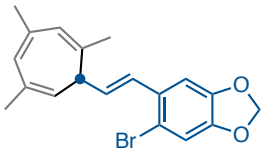
chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 98:2 as eluent. **$^1$H NMR** (300 MHz, Chloroform-*d*) δ 7.84 – 7.76 (m, 4H), 7.71 (d, *J* = 1.7 Hz, 1H), 7.62 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.45 (ddd, *J* = 6.9, 4.2, 2.1 Hz, 2H), 6.65 – 6.46 (m, 2H), 6.26 (s, 1H), 5.86 (t, *J* = 1.5 Hz, 1H), 5.14 (d, *J* = 6.7 Hz, 1H), 2.90 (t, *J* = 6.3 Hz, 1H), 2.06 (d, *J* = 1.2 Hz, 3H), 2.02 (d, *J* = 1.4 Hz, 3H), 1.93 (d, *J* = 1.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 137.99, 135.16, 135.01, 133.69, 133.00, 132.79, 130.45, 129.87, 129.34, 128.07, 127.87, 127.65, 126.17, 125.74, 125.58, 124.22, 123.71, 118.35, 46.06, 24.69, 21.98, 21.95. **HRMS** (APCI Positive): calculated for $C_{22}H_{23}$ $[M+H]^+$: 287.1794; found: 287.1800.

**(*E*)-9-(2-(2,4,6-Trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)phenanthrene (44m)**



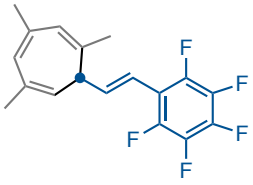
The title compound (amorphous white foam, 0.35 g, 86% yield) was obtained following General Procedure A from reagent **48** (0.43 g, 1.21 mmol) and phenanthrene-9-carbaldehyde (0.50 g, 2.41 mmol, 2 equiv) using LiHMDS (0.21 g, 1.27 mmol, 1.05 equiv) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane to cyclohexane/EtOAc 98:2 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.75 (d, *J* = 8.1 Hz, 1H), 8.68 (d, *J* = 7.5 Hz, 1H), 8.18 (d, *J* = 9.4 Hz, 1H), 7.92 (d, *J* = 9.3 Hz, 1H), 7.82 (s, 1H), 7.71 – 7.60 (m, 4H), 7.16 (d, *J* = 15.4 Hz, 1H), 6.51 (dd, *J* = 15.4, 8.3 Hz, 1H), 6.31 (s, 1H), 5.91 (s, 1H), 5.23 (d, *J* = 6.7 Hz, 1H), 3.04 (t, *J* = 7.5 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.04, 135.28, 134.56, 133.13, 131.94, 130.83, 130.35, 130.05, 129.42, 128.50, 128.14, 126.70, 126.51, 126.40, 126.27, 124.91, 124.53, 124.34, 123.01, 122.51, 118.56, 46.21, 24.71, 22.09, 22.00. **HRMS** (APCI Positive): calculated for $C_{26}H_{25}$ $[M+H]^+$: 337.1951; found: 337.1950.

**(*E*)-5-Bromo-6-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)benzo-[*d*][1,3]dioxole (44n)**



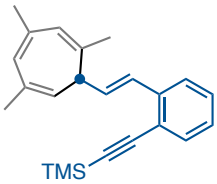

The title compound (pale yellow oil, 0.23 g, 90% yield, >20 *E*/*Z*) was obtained following General Procedure A from reagent **48** (0.25 g, 0.70 mmol) and 6-bromobenzo[*d*][1,3]dioxole-5-carbaldehyde (0.32 g, 1.40 mmol, 2 equiv) using LiHMDS (0.123 g, 0.74 mmol, 1.05 equiv) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane to cyclohexane/EtOAc 98:2 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 6.97 (d, *J* = 4.6 Hz, 2H), 6.63 (d, *J* = 15.7 Hz, 1H), 6.19 (s, 1H), 6.18 – 6.12 (m, 1H), 5.96 – 5.93 (m, 2H), 5.80 (s, 1H), 5.06 (d, *J* = 6.9 Hz, 1H), 2.87 (t, *J* = 7.6 Hz, 1H), 2.00 (s, 3H), 1.95 (d, *J* = 1.2 Hz, 3H), 1.87 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 147.95, 147.86, 138.27, 133.50, 131.30, 130.99, 129.63, 129.23, 124.70, 118.44, 114.61, 112.94, 106.64, 102.03, 46.16, 25.03, 22.51, 22.39. **HRMS** (APCI Pos): calculated for $C_{19}H_{20}BrO_2$ $[M+H]^+$: 359.0641; found: 359.0629.

**(*E*)-1,3,5-Trimethyl-7-(2,3,4,5,6-pentafluorostyryl)cyclohepta-1,3,5-triene (44o)**



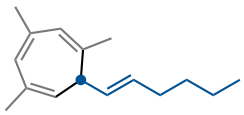

The title compound (pale yellow oil, 137 mg, 60% yield, 10:1 *E*/*Z*) was obtained following General Procedure A from reagent **48** (250 mg, 0.70 mmol) and 2,3,4,5,6-pentafluorobenzaldehyde (275 mg, 1.40 mmol, 2 equiv) using LiHMDS (123 mg, 0.74 mmol, 1.05 equiv) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 99:1 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 6.69 (dd, *J* = 16.3, 8.2 Hz, 1H), 6.29 (dd, *J* = 16.3, 1.1 Hz, 1H), 6.21 (s, 1H), 5.85 (s, 1H), 5.07 (d, *J* = 7.0 Hz, 1H), 2.93 (t, *J* = 7.6 Hz, 1H), 2.02 (s, 3H), 1.98 (d, *J* = 1.1 Hz, 3H), 1.91 (s, 3H). **$^{19}$F NMR** (376 MHz, Chloroform-*d*) δ -143.32 (m), -157.28 (t, *J* = 20.8 Hz), -163.10 (td, *J* = 21.7, 8.0 Hz). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 145.80, 143.37, 140.71, 139.58, 138.95, 136.40, 133.71, 133.13, 129.20, 124.69, 116.59, 114.11, 112.56, 46.79, 24.50, 22.22, 22.00. **HRMS** (APCI Positive): calculated for $C_{18}H_{16}F_5$ $[M+H]^+$: 327.1167; found: 327.1176.

**(*E*)-Trimethyl((2-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)phenyl)ethynyl)silane (44p)**




The title compound (pale yellow oil, 0.29 g, 78% yield) was obtained following General Procedure A from reagent **48** (0.40 g, 1.12 mmol) and 2-((trimethylsilyl)ethynyl)benzaldehyde (0.34 g, 1.68 mmol, 1.5 equiv) using LiHMDS (0.20 g, 1.18 mmol, 1.05 equiv) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane to cyclohexane/EtOAc 99:1 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.54 – 7.50 (m, 1H), 7.41 (ddd, *J* = 7.7, 1.4, 0.6 Hz, 1H), 7.27 (tdd, *J* = 8.0, 1.5, 0.6 Hz, 1H), 7.15 (td, *J* = 7.5, 1.3 Hz, 1H), 6.90 (dd, *J* = 15.9, 1.4 Hz, 1H), 6.47 (dd, *J* = 15.9, 7.7 Hz, 1H), 6.20 (s, 1H), 5.82 (t, *J* = 1.4 Hz, 1H), 5.14 (d, *J* = 7.0 Hz, 1H), 2.92 (t, *J* = 7.4 Hz, 1H), 2.00 (d, *J* = 1.3 Hz, 3H), 1.97 (d, *J* = 1.4 Hz, 3H), 1.87 (t, *J* = 1.0 Hz, 3H), 0.27 (s, 9H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.74, 140.17, 136.89, 135.43, 134.90, 133.64, 131.26, 130.87, 129.92, 128.88, 126.95, 126.56, 123.57, 120.02, 105.78, 101.25, 48.01, 26.60, 24.25, 24.01, 1.92. **HRMS** (APCI Pos): calculated for $C_{23}H_{27}Si$ $[M-H]^+$: 331.1877; found: 331.1873.

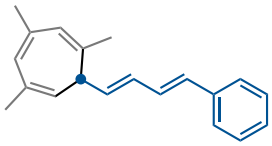
**(*E*)-1,3,5-Trimethyl-7-(hex-1-en-1-yl)cyclohepta-1,3,5-triene (44q)**



The title compound (pale yellow oil, 0.29 g, 97% yield) was obtained following General Procedure A from reagent **48** (0.60 g, 1.68 mmol) and pentanal (0.29 g, 3.37 mmol, 2 equiv) using LiHMDS (0.30 g, 1.77 mmol, 1.05 equiv) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (500 MHz, $CD_2Cl_2$, 1.0:0.6 CHT/NCD equilibrium) δ 6.18

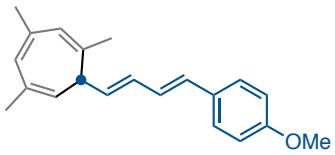
(d, *J* = 1.6 Hz, 1H), 5.72 (t, *J* = 1.5 Hz, 1H), 5.68 – 5.63 (m, 1H), 5.44 (ddd, *J* = 15.1, 6.8, 1.1 Hz, 1H), 4.97 – 4.93 (m, 1H), 2.52 (t, *J* = 7.6 Hz, 1H), 2.04 (qd, *J* = 6.8, 1.5 Hz, 2H), 1.97 (d, *J* = 1.3 Hz, 3H), 1.88 (d, *J* = 1.4 Hz, 3H), 1.82 (d, *J* = 1.2 Hz, 3H), 1.34 – 1.29 (m, 4H), 0.92 – 0.88 (m, 3H). **$^{13}$C NMR** (126 MHz, $CD_2Cl_2$) δ 138.22, 136.37, 132.48, 131.74, 129.92, 129.38, 123.89, 119.92, 46.01, 32.05, 27.39, 24.60, 22.50, 21.76, 21.33, 14.00. **GCMS** (EI): calculated for $C_{16}H_{24}$ $[M]^+$: 216.2; found: 216.2.

**1,3,5-Trimethyl-7-((1*E*,3*E*)-4-phenylbuta-1,3-dien-1-yl)cyclohepta-1,3,5-triene (44r)**



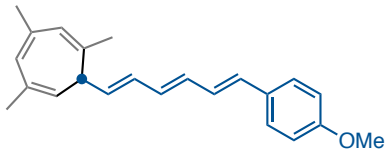
The title compound (pale yellow oil, 275 mg, 90% yield, 8:1 *E*/*Z* for the newly formed double bond) was obtained following General Procedure A from reagent **48** (400 mg, 1.12 mmol) and (*E*)-cinnamaldehyde (297 mg, 2.24 mmol, 2 equiv) using LiHMDS (197 mg, 1.18 mmol, 1.05 equiv) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 99:1 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.43 – 7.40 (m, 2H), 7.35 – 7.32 (m, 2H), 7.26 – 7.21 (m, 1H), 6.83 (ddd, *J* = 15.7, 10.4, 0.8 Hz, 1H), 6.50 (d, *J* = 15.7 Hz, 1H), 6.29 – 6.21 (m, 2H), 6.05 (dd, *J* = 15.1, 8.5 Hz, 1H), 5.83 (t, *J* = 1.5 Hz, 1H), 5.05 (d, *J* = 6.8 Hz, 1H), 2.79 (t, *J* = 7.7 Hz, 1H), 2.04 (d, *J* = 1.3 Hz, 3H), 1.97 (d, *J* = 1.4 Hz, 3H), 1.91 (t, *J* = 1.0 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 137.90, 137.56, 133.88, 132.95, 130.99, 130.93, 129.21, 128.58, 128.56, 127.24, 126.22, 124.15, 118.02, 45.71, 24.65, 21.98. **HRMS** (APCI Positive): calculated for $C_{20}H_{23}$ $[M+H]^+$: 263.1794; found: 263.1794.

**7-((1*E*,3*E*)-4-(4-Methoxyphenyl)buta-1,3-dien-1-yl)-1,3,5-trimethylcyclohepta-1,3,5-triene (44s)**



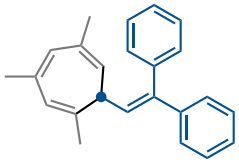

The title compound (yellow viscous oil, 1.75 g, 93% yield, 6:1 *E*/*Z*) was obtained following General Procedure A from reagent **48** (2.3 g, 6.45 mmol, 1.0 equiv) and (*E*)-3-(4-methoxyphenyl)acrylaldehyde (2.09 g, 12.9 mmol, 2.0 equiv) using LiHMDS (1.13 g, 6.78 mmol, 1.05 equiv) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 98:2 as eluent. **$^1$H NMR** (300 MHz, Chloroform-*d*) δ 7.34 (d, *J* = 8.8 Hz, 2H), 6.88 (s, 2H), 6.70 (dd, *J* = 15.6, 10.2 Hz, 1H), 6.44 (d, *J* = 15.6 Hz, 1H), 6.29 – 6.39 (m, 2H), 5.99 (dd, *J* = 15.1, 8.5 Hz, 1H), 5.83 – 5.79 (m, 1H), 5.04 (d, *J* = 6.7 Hz, 1H), 3.83 (s, 3H), 2.75 (t, *J* = 7.6 Hz, 1H), 2.03 (s, 3H), 1.98 – 1.94 (m, 3H), 1.89 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.38, 138.24, 133.18, 133.03, 133.01, 131.49, 130.91, 130.75, 129.56, 128.01, 127.75, 127.58, 124.41, 114.41, 55.66, 46.08, 25.00, 22.31, 22.28. **HRMS** (APCI Positive): calculated for $C_{21}H_{25}O$ $[M+H]^+$: 293.1900; found: 293.1910.

**7-((1*E*,3*E*,5*E*)-6-(4-Methoxyphenyl)hexa-1,3,5-trien-1-yl)-1,3,5-trimethylcyclohepta-1,3,5-triene (44t)**



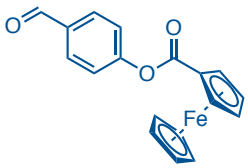

The title compound (pale yellow oil, 0.30 g, 81% yield, 4:1 *E*/*Z*) was obtained following General Procedure A from reagent **48** (0.205 g, 1.23 mmol, 1.0 equiv) and (2*E*,4*E*)-5-(4-methoxyphenyl)penta-2,4-dienal (0.22 g, 1.17 mmol, 1.0 equiv) using LiHMDS (0.205 g, 1.23 mmol, 1.05 equiv) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 98:2 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.35 (d, *J* = 8.7 Hz, 2H), 6.87 (dd, *J* = 9.0, 2.6 Hz, 3H), 6.74 – 6.68 (m, 1H), 6.54 – 6.48 (m, 1H), 6.34 – 6.31 (m, 1H), 6.22 – 6.14 (m, 2H), 5.95 (dd, *J* = 15.0, 8.5 Hz, 1H), 5.83 – 5.79 (m, 1H), 5.02 (d, *J* = 6.7 Hz, 1H), 3.83 (s, 3H), 2.73 (t, *J* = 7.6 Hz, 1H), 2.02 (s, 3H), 1.94 (s, 3H), 1.89 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 159.13, 137.87, 133.25, 132.85, 132.40, 132.01, 131.49, 131.04, 129.19, 127.58, 127.48, 127.23, 124.05, 118.05, 114.11, 55.32, 45.71, 24.62, 21.93, 21.88. **HRMS** (APCI Positive): calculated for $C_{23}H_{27}O$ $[M+H]^+$: 319.2056; found: 319.2067.

**7-(2,2-Diphenylvinyl)-1,3,5-trimethylcyclohepta-1,3,5-triene (44u)**



The title compound (100 mg, 38% yield) was obtained following General Procedure A from reagent **48** (300 mg, 0.84 mmol, 1.0 equiv) and benzophenone (307 mg, 1.17 mmol, 1.0 equiv) using LiHMDS (148 mg, 0.88 mmol, 1.05 equiv) after purification by flash column chromatography on $SiO_2$ using cyclohexane to cyclohexane/EtOAc 99:1 as eluent. **$^1$H NMR** (500 MHz, $CD_2Cl_2$) δ 7.33 – 7.25 (m, 5H), 7.25 – 7.21 (m, 3H), 7.13 – 7.09 (m, 2H), 6.32 (d, *J* = 10.4 Hz, 1H), 6.12 (d, *J* = 3.3 Hz, 1H), 5.76 (t, *J* = 1.5 Hz, 1H), 4.92 (d, *J* = 6.4 Hz, 1H), 2.66 (dd, *J* = 10.4, 6.4 Hz, 1H), 1.93 (dd, *J* = 3.2, 1.3 Hz, 6H), 1.83 (t, *J* = 1.1 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CD_2Cl_2$) δ 143.42, 142.61, 140.21, 138.01, 132.73, 130.18, 129.67, 129.31, 129.01, 128.39, 128.24, 127.94, 127.39, 127.34, 124.07, 117.93, 42.69, 24.55, 21.83, 21.68. **GCMS** (EI Positive): calculated for $C_{24}H_{24}$ $[M]^+$: 312.2; found: 312.3.

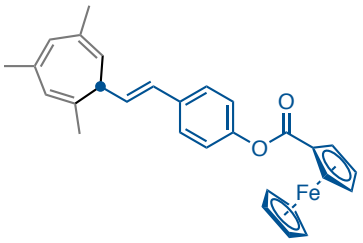
**4-Formylphenyl ferrocenecarboxylate**




To a solution of ferrocene carboxylic acid (1.13 g. 4.91 mmol, 1.2 equiv) in $CH_2Cl_2$ (30 mL, 0.15 M) under Ar, was added oxalyl chloride (0.39 mL, 0.57 g, 4.50 mmol, 1.1 equiv), followed by 5 drops of DMF. After stirring for 2 h, the solvent and excess oxalyl chloride was removed in high vacuum. The crude ferrocenoyl chloride was redissolved in 20 mL of $CH_2Cl_2$/triethylamine (1:1, 0.2 M), and to this mixture was added a solution of 4-

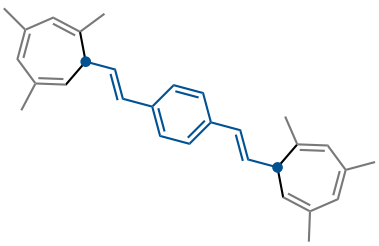
hydroxybenzaldehyde (0.50 g, 4.09 mmol, 1 equiv) and DMAP (0.25 g, 2.05 mmol, 0.5 equiv) in 10 mL of $CH_2Cl_2$. The resulting mixture was stirred at 25 ºC for 12 h, before it was quenched with water. The mixture was extracted with $CH_2Cl_2$ three times. Combined organic fractions were washed with water once, with brine once, and dried over anhydrous $Na_2SO_4$. After concentrating in vacuum, 4-formylphenyl ferrocenecarboxylate (0.97 g, 4.09 mmol, 71%) was obtained as an orange solid after CombiFlash column chromatography in $SiO_2$ using cyclohexane/EtOAc 7:3 as solvent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 10.00 (s, 1H), 7.95 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 4.96 (t, *J* = 2.0 Hz, 2H), 4.52 (t, *J* = 2.0 Hz, 2H), 4.30 (s, 5H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 191.34, 170.14, 156.13, 134.17, 131.63, 122.82, 72.67, 71.09, 70.42, 69.69. **HRMS** (ESI Pos): calculated for $C_{18}H_{14}FeNaO_3$ $[M+Na]^+$: 357.0185; found: 357.0180. **MP** 95–98 ºC.

**(*E*)-4-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)phenyl ferrocenecarboxylate (44v)**




The title compound (amorphous orange foam, 0.19 g, 97% yield) was obtained following General Procedure A from reagent **48** (0.15 g, 0.42 mmol, 1.0 equiv) and 4-formylphenyl ferrocenecarboxylate (0.16 g, 0.46 mmol, 1.1 equiv) using LiHMDS (75 mg, 0.44 mmol, 1.05 equiv) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane to cyclohexane/EtOAc 8:2 as eluent. **$^1$H NMR** (300 MHz, Chloroform-*d*) δ 7.45 – 7.40 (m, 2H), 7.16 – 7.11 (m, 2H), 6.42 (d, *J* = 6.1 Hz, 2H), 6.24 (s, 1H), 5.84 (t, *J* = 1.4 Hz, 1H), 5.11 (d, *J* = 6.7 Hz, 1H), 4.99 (t, *J* = 2.0 Hz, 2H), 4.52 (q, *J* = 1.8 Hz, 2H), 4.32 (s, 5H), 2.85 (t, *J* = 6.4 Hz, 1H), 2.04 (d, *J* = 1.2 Hz, 3H), 1.99 (d, *J* = 1.4 Hz, 3H), 1.91 (t, *J* = 1.1 Hz, 3H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 170.34, 149.94, 137.99, 135.29, 135.03, 132.98, 129.55, 129.46, 129.32, 127.11, 124.19, 121.73, 118.34, 71.94, 70.66, 70.11, 69.97, 53.45, 45.90, 24.67, 21.95, 21.89. **HRMS** (ESI Pos): calculated for $C_{29}H_{29}FeO_2$ $[M+H]^+$: 465.1512; found: 465.1507.

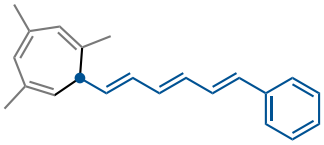
**1,4-Bis((*E*)-2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)benzene (44w)**



The title compound (viscous yellow oil, 139 mg, 94% yield) was obtained following General Procedure A from reagent **48** (306 mg, 0.86 mmol, 1.15 equiv) and terephthalaldehyde (50 mg, 0.37 mmol, 0.45 equiv) using LiHMDS (149 mg, 0.90 mmol, 1.20 equiv) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.30 (s, 4H), 6.42 – 6.34 (m, 4H), 6.22 – 6.20 (m, 2H), 5.80 (dt, *J* = 4.3, 1.5 Hz, 2H), 5.11 – 5.05 (m, 2H), 2.81 (t, *J* = 6.8 Hz, 2H), 2.00 (dd, *J* = 3.4, 1.2

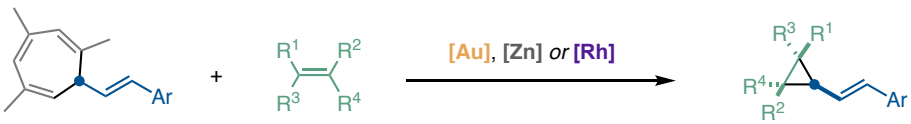
Hz, 6H), 1.95 (dd, *J* = 5.3, 1.5 Hz, 6H), 1.86 (dt, *J* = 4.0, 1.1 Hz, 6H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 139.83, 138.48, 136.79, 134.76, 131.66, 130.99, 130.67, 128.15, 125.95, 120.12, 47.83, 26.26, 23.53, 21.53. **HRMS** (APCI Pos): calculated for $C_{30}H_{35}$ $[M+H]^+$: 395.2733; found: 395.2736.

**1,3,5-Trimethyl-7-((1*E*,3*E*,5*E*)-6-phenylhexa-1,3,5-trien-1-yl)cyclohepta-1,3,5-triene (44x)**



The title compound (pale yellow oil, 190 mg, 73% yield) was obtained following General Procedure A from reagent **48** (320 mg, 0.898 mmol, 1.0 equiv) and (2*E*,4*E*)-5-phenylpenta-2,4-dienal (156 mg, 0.988 mmol, 1.1 equiv) using LiHMDS (158 mg, 0.943 mmol, 1.05 equiv) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 99:1 as eluent. **$^1$H NMR** (400 MHz, $CD_2Cl_2$) δ 7.44 (d, *J* = 7.8 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.25 (t, *J* = 6.6 Hz, 1H), 6.93 – 6.85 (m, 1H), 6.58 (d, *J* = 15.6 Hz, 1H), 6.40 (dd, *J* = 11.8, 9.3 Hz, 2H), 6.25 – 6.16 (m, 2H), 6.00 (dd, *J* = 15.1, 8.4 Hz, 1H), 5.81 (s, 1H), 5.03 (d, *J* = 6.8 Hz, 1H), 2.77 (t, *J* = 7.6 Hz, 1H), 2.05 – 2.01 (m, 3H), 1.95 (d, *J* = 1.2 Hz, 3H), 1.89 (s, 3H). **HRMS** (APCI Positive): calculated for $C_{22}H_{25}$ $[M+H]^+$: 289.1951; found: 289.1956.

**General Procedures B for the Au(I)- Zn(II)- or Rh(II)-Catalyzed Styrylcyclopropanation**




**General Procedure B1:** [Au] = [(JohnPhos)Au(MeCN)]$SbF_6$ (5 mol %), EtOAc, 25 ºC, 20 h
**General Procedure B2:** [Zn] = $ZnBr_2$ (10 mol %), DCE, 65 ºC, 30 h
**General Procedure B3:** [Rh] = $[Rh(TFA)_2]_2$ (3 mol%), DCE, 60 ºC, 18 h
**General Procedure B4:** [Zn] = $ZnEt_2$ (1.1 equiv), BINOL der. (1.0 equiv), 25 ºC, 16 h.

**General Procedure B1 (Gold(I) Catalysis)**: under air, a round-bottomed flask or a screw-cap culture tube equipped with a Teflon-coated magnetic stirring bar was charged with the corresponding 1,3,5-trimethyl-7-styryl-1,3,5-cycloheptatriene **44** (1.0 equiv) and the corresponding alkene (1.5 equiv). Both were dissolved in HPLC grade ethyl acetate (0.10–0.15 M) before [(JohnPhos)Au(MeCN)]$SbF_6$, (5 mol %) was added. The flask/vial was closed with a rubber septum/screw-cap and the homogeneous mixture was stirred at room-temperature (*ca.* 25 ºC) for 20 hours. After confirming that the reaction was finished by TLC, the resulting yellow-orange homogeneous solution was concentrated in vacuum, and the obtained residue analyzed by $^1$H NMR to determine the dr of the product. The crude product was purified by flash column chromatography or preparative TLC on silica gel, using pentane or gradients of pentane/diethyl ether.

**General Procedure B2 (Zinc(II) Catalysis)**: a screw-cap culture tube equipped with a magnetic stirring bar was charged with the corresponding 1,3,5-trimethyl-7-styryl-1,3,5-cycloheptatriene **44** (1.0 equiv) and the corresponding alkene (4 equiv). The tube was introduced in a nitrogen-filled glovebox, and both reagents were dissolved in anhydrous 1,2-dichloroethane (0.1 M) before anhydrous $ZnBr_2$ (99.999% purity, 10 mol %) was added. The tube was closed with the corresponding cap, taken outside the glovebox and further sealed with parafilm. The mixture was stirred at 65 ºC for 30 h using a heating block or an oil bath, making sure the entire volume of the reaction mixture is inside the block/bath. After confirming that the reaction was finished by TLC, the resulting yellow-orange mixture was concentrated in vacuum, and the obtained residue was analyzed by $^1$H NMR to determine the dr of the product. The product was purified by flash column chromatography or preparative TLC on silica gel, using pentane or gradients of pentane and diethyl ether.

**General Procedure B3 (Rhodium(II) Catalysis)**: a screw-cap culture tube or a microwave vial equipped with a Teflon-coated magnetic stirring bar was charged with the corresponding 1,3,5-trimethyl-7-styryl-1,3,5-cycloheptatriene **44** (1.0 equiv) and the corresponding alkene (4 equiv). The vial was introduced in an argon-filled glovebox, and both reagents were dissolved in anhydrous 1,2-dichloroethane (0.1 M), before $[Rh_2(TFA)_4]$ (3 mol %) was added. The vial was closed with the corresponding screw-cap and taken outside the glovebox, and then stirred at 60 ºC for 18 hours. After confirming that the reaction was finished by TLC, the resulting mixture was concentrated in vacuum, and the obtained residue analyzed by $^1$H NMR to determine the dr of the product. The crude product was purified by flash column chromatography or preparative TLC on silica gel, using pentane or gradients of pentane/diethyl ether.

**General Procedure B4 (BINOL–$ZnEt_2$ Catalysis)**: An HPLC vial or a round-bottom flask equipped with a magnetic stirring bar was charged with the corresponding 1,3,5-trimethyl-7-styryl-1,3,5-cycloheptatriene **44** (1.0 equiv), the corresponding alkene (4 equiv), diphenylmethane (internal standard for NMR yield, 1 equiv) and the corresponding BINOL derivative (1.0 equiv). The vial was closed with the corresponding cap or fitted with a rubber septum, and then the atmosphere was exchanged with Ar through three fast vacuum/Ar cycles. All the reagents were dissolved in anhydrous PhMe (0.2 M), before diethylzinc (1.1 equiv) was added as a commercially available 1.0 M solution in hexanes. The resulted mixture was stirred at room temperature (*ca.* 25 ºC) for 16 h, before water was added. The mixture is extracted with $Et_2O$, and after removal of the solvent in vacuum, the resulting residue was analyzed by $^1$H NMR. The products may be purified by flash column or preparative TLC in silica gel if required.

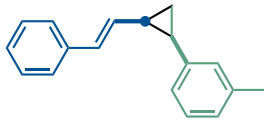
Each cyclopropane reported herein was prepared according to one or more of the four General Procedures B1–B4 (see discussions throughout Sections II.3 and II.4 for the outcomes of each method). Characterization data of all obtained cyclopropanes is shown below.

**Characterization Data of Styrylcyclopropanes (46) and (58)**

***cis*-((*E*)-2-(2-Phenylcyclopropyl)vinyl)benzene (46a)**

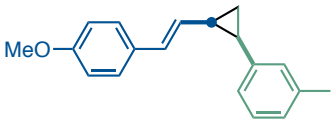

The title compound was obtained following General Procedure B1, B2, B3 or B4 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene and styrene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.36 – 7.11 (m, 10H), 6.53 (d, J = 15.7 Hz, 1H), 5.55 (dd, J = 15.7, 9.5 Hz, 1H), 2.48 (m, 1H), 2.05 (m, 1H), 1.39 (m, 1H), 1.16 (m, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.9, 137.9, 130.7, 129.7, 129.3, 128.5, 128.2, 126.7, 126.2, 125.8, 24.0, 22.8, 12.7 ppm. **HRMS** (APCI Pos): calculated for $C_{17}H_{17}$ $[M+H]^+$: 221.1325; found: 221.1322.

***cis*-(*E*)-1-Methyl-3-(2-styrylcyclopropyl)benzene (46b)**



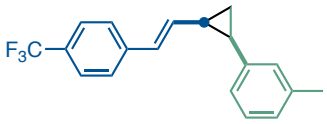
The title compound was obtained following General Procedure B1, B2 or B3 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene and 1-methyl-3-vinylbenzene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.25-7.12 (m, 7H), 7.08-7.03 (m, 2H), 6.54 (d, *J* = 15.7 Hz, 1H), 5.57 (dd, *J* = 15.7, 9.5 Hz, 1H), 2.49-2.42 (m, 1H), 2.36 (s, 3H), 2.04 (qd, *J* = 8.9, 5.5 Hz, 1H), 1.38 (td, *J* = 8.4, 5.2 Hz, 1H), 1.15 (dt, *J* = 6.3, 5.4 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.6, 137.8, 137.6, 130.8, 130.1, 129.4, 128.4, 128.0, 126.8, 126.5, 126.0, 125.7, 23.8, 22.7, 21.5, 12.6 ppm. **HRMS** (APCI Positive): calculated for $C_{18}H_{19}$ $[M+H]^+$: 235.1481; found: 235.1475.

***cis*-1-Methoxy-4-((E)-2-(2-phenylcyclopropyl)vinyl)benzene (46c)**



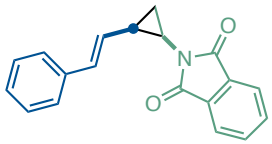

The title compound was obtained following General Procedure B1, B3 or B4 from (*E*)-7-(4-methoxystyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene and 1-methyl-3-vinylbenzene after purification by flash column chromatography on $SiO_2$ using pentane/$Et_2O$ 99:1 as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.20 (t, *J* = 7.5 Hz, 1H), 7.12-7.09 (m, 3H), 7.05 (dd, *J* = 16.4, 7.4 Hz, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 6.49 (d, *J* = 16.2 Hz, 1H), 5.44 (dd, *J* = 15.6, 9.4 Hz, 1H), 3.79 (s, 3H), 2.41 (q, *J* = 7.8 Hz, 1H), 2.36 (s, 3H), 2.01 (dq, *J* = 8.9, 5.4 Hz, 1H), 1.35 (td, *J* = 8.5, 5.3 Hz, 1H), 1.12 (q, *J* = 5.6 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.4, 138.7, 137.6, 130.8, 130.1, 128.9, 128.4, 127.9, 126.7, 126.0, 122.7, 113.8, 55.3, 23.7, 22.7, 12.4 ppm. **HRMS** (APCI Positive): calculated for $C_{19}H_{20}O$ $[M]^+$: 264.1509; found: 264.1513.

**_cis_-(_E_)-1-Methyl-3-(2-(4-(trifluoromethyl)styryl)cyclo-propyl)benzene (46d)**



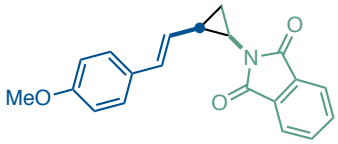
The title compound was obtained following General Procedure B1, B3 or B4 from (*E*)-1,3,5-trimethyl-7-(4-(trifluoromethyl)styryl)cyclo-hepta-1,3,5-triene and 1-methyl-3-vinylbenzene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.48-7.45 (m, 2H), 7.25-7.18 (m, 3H), 7.13-7.03 (m, 3H), 6.55 (d, *J* = 15.8 Hz, 1H), 5.65 (dd, *J* = 15.8, 9.6 Hz, 1H), 2.49 (td, *J* = 8.5, 6.5 Hz, 1H), 2.36 (d, *J* = 0.8 Hz, 3H), 2.10-2.00 (m, 1H), 1.41 (td, *J* = 8.4, 5.2 Hz, 1H), 1.19 (dt, *J* = 6.5, 5.4 Hz, 1H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.2, 138.3, 137.7, 133.9, 130.1, 128.1, 128.0, 127.0, 126.0, 125.7, 125.3 (q, $J_{C-F}$ = 3.8 Hz), 24.2, 22.7, 21.4, 12.8 ppm. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -62.48 ppm. **HRMS** (APCI Positive): calculated for $C_{19}H_{17}F_3$ $[M]^+$: 302.1277; found: 302.1286.

**_cis_-(_E_)-2-(2-(Styrylcyclopropyl)isoindoline-1,3-dione (46e)**



The title compound was obtained following General Procedure B1 or B3 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene and 1-methyl-3-vinylbenzene after purification by flash column chromatography on $SiO_2$ using pentane/$Et_2O$ 8:2 to 7:3 as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.83 (dd, J = 5.5, 3.0 Hz, 2H), 7.71 (dd, J = 5.5, 3.0 Hz, 2H), 7.26-7.17 (m, 4H), 7.17-7.12 (m, 1H), 6.48 (d, J = 15.8 Hz, 1H), 5.89 (dd, J = 15.8, 7.7 Hz, 1H), 3.03 (ddd, J = 7.8, 7.1, 4.9 Hz, 1H), 2.18-2.10 (m, 1H), 1.78 (td, J = 6.8, 4.9 Hz, 1H), 1.55 (ddd, J = 8.9, 7.9, 6.7 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 169.1, 137.3, 134.0, 131.7, 131.2, 128.4, 127.0, 126.2, 126.0, 123.2, 28.1, 20.1, 10.7 ppm. **HRMS** (APCI Pos): calculated for $C_{19}H_{15}NNaO_2$ $[M+Na]^+$: 312.0995; found: 312.1000.

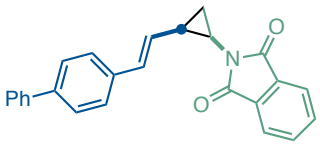
**_cis_-2-(2-((_E_)-4-Methoxystyryl)cyclopropyl)isoindoline-1,3-dione (46f)**



The title compound was obtained following General Procedure B1 or B3 from (*E*)-7-(4-methoxystyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene and *N*-vinylphtalimide after purification by flash column chromatography on $SiO_2$ using pentane/$Et_2O$ 8:2 to 6:4 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 8.5 Hz, 2H), 7.70 (d, *J* = 8.5 Hz, 2H), 7.13 (d, *J* = 8.5 Hz, 2H), 6.75 (d, *J* = 8.8 Hz, 2H), 6.42 (d, *J* = 15.8 Hz, 1H), 5.76 (dd, *J* = 15.8, 7.5 Hz, 1H), 3.76 (s, 3H), 3.00 (dd, *J* = 14.9, 4.8 Hz, 1H), 2.12 (p, *J* = 7.9, 7.4 Hz, 1H), 1.75 (td, *J* = 6.8, 4.9 Hz, 1H), 1.55 – 1.49 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 169.10, 158.79, 134.01, 131.69, 130.72, 130.14, 127.09, 123.88, 123.22, 113.80, 55.24, 28.00, 20.08, 10.49.

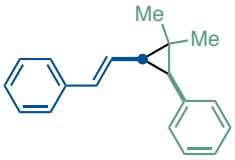
**HRMS** (APCI Pos): calculated for $C_{19}H_{21}NaO$ $[M+Na]^+$: 342.1101; found: 342.1097. **MP** 98–101 ºC.

***cis*-2-(2-((*E*)-4-Phenylstyryl)cyclopropyl)isoindoline-1,3-dione (46g)**



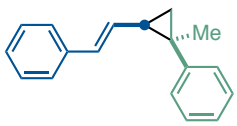

The title compound was obtained following General Procedure B1 from (*E*)-7-(4-phenylstyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene and *N*-vinylphtalimide after purification by flash column chromatography on $SiO_2$ using pentane/$Et_2O$ 8:2 to 6:4 as eluent. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.88 – 7.81 (m, 2H), 7.76 – 7.67 (m, 2H), 7.59 – 7.52 (m, 2H), 7.50 – 7.40 (m, 4H), 7.37 – 7.25 (m, 3H), 6.53 (d, *J* = 15.8 Hz, 1H), 5.95 (dd, *J* = 15.8, 7.7 Hz, 1H), 3.05 (ddd, *J* = 7.9, 7.1, 4.9 Hz, 1H), 2.25 – 2.10 (m, 1H), 1.81 (td, *J* = 6.9, 4.8 Hz, 1H), 1.57 (ddd, *J* = 8.9, 7.9, 6.7 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 169.07, 140.71, 139.78, 136.31, 134.08, 131.68, 130.79, 128.73, 127.19, 127.09, 126.85, 126.43, 126.39, 123.28, 77.30, 77.05, 76.80, 30.35, 29.72, 28.22, 20.26, 10.80 ppm.

***cis*-(*E*)-(2-(2,2-Dimethyl-3-phenylcyclopropyl)vinyl)benzene (46h)**



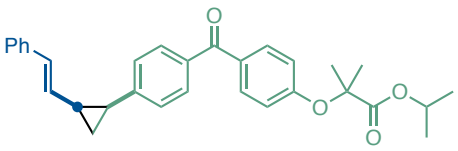

The title compound was obtained following General Procedure B1 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene and (2-methylprop-1-en-1-yl)benzene after purification by flash column chromatography on $SiO_2$ using pentane/$Et_2O$ 99:1 as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.34 – 7.14 (m, 10H), 6.59 (d, *J* = 15.7 Hz, 1H), 5.79 (dd, *J* = 15.7, 10.3 Hz, 1H), 2.24 (d, *J* = 8.8 Hz, 1H), 1.87 (dd, *J* = 10.2, 9.0 Hz, 1H), 1.35 (s, 3H), 1.07 (s, 3H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.09, 137.64, 131.13, 129.58, 129.33, 128.47, 128.04, 126.50, 126.04, 125.66, 34.95, 32.81, 28.93, 23.61, 17.83 ppm. **HRMS** (APCI Pos): calculated for $C_{19}H_{21}$ $[M-H]^+$: 249.1638; found: 249.1643.

***cis*-(1-Methyl-2-((*E*)-styryl)cyclopropyl)benzene (46i)**



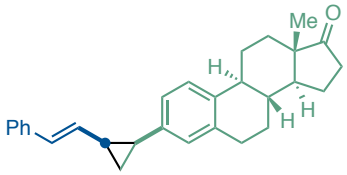

The title compound was obtained following General Procedure B1 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5- and prop-1-en-2-ylbenzene after purification by flash column chromatography on $SiO_2$ using pentane/$Et_2O$ 99:1 as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.36 – 7.31 (m, 5H), 7.24 – 7.21 (m, 3H), 7.15 – 7.12 (m, 2H), 6.49 (d, J = 15.8 Hz, 1H), 5.33 (dd, J = 15.8, 9.8 Hz, 1H), 1.85 (ddd, J = 5.9, 7.6, 9.8 Hz, 1H), 1.48 (s, 3H), 1.21 – 1.18 (m, 2H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 143.5, 137.9, 132.7, 129.6, 128.4, 128.3, 128.1, 126.4, 126.2, 125.6, 29.7, 28.8, 22.3, 21.1 ppm. **HRMS** (APCI Pos): calculated for $C_{18}H_{19}$ $[M+H]^+$: 235.1481; found: 235.1483.

**Isopropyl-2-methyl-2-(4-(4-(*cis*-2-((*E*)-styryl)cyclopropyl)benzoyl)phe-noxy)propanoate (46j)**



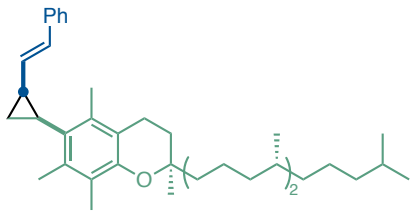
The title compound was obtained following General Procedure B1 from (*E*)-7-styryl-1,3,5-trimethylcyclohepta-1,3,5-triene and vinyl-fenofibrate after purification by flash column chromatography on $SiO_2$ using pentane/acetone 99:1 to 9:1 gradients as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.79 – 7.75 (m, 2H), 7.74 – 7.71 (m, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.26 – 7.22 (m, 2H), 7.18 – 7.15 (m, 3H), 6.90 – 6.87 (m, 2H), 6.56 (d, *J* = 15.7 Hz, 1H), 5.58 (dd, *J* = 15.7, 9.3 Hz, 1H), 5.10 (h, *J* = 6.3 Hz, 1H), 2.52 (td, *J* = 8.5, 6.4 Hz, 1H), 2.14 (qd, *J* = 8.8, 5.6 Hz, 1H), 1.68 (s, 6H), 1.47 (td, *J* = 8.4, 5.4 Hz, 1H), 1.29 – 1.24 (m, 2H), 1.23 (d, *J* = 6.3 Hz, 6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 195.25, 173.19, 159.38, 143.70, 137.46, 135.82, 131.93, 130.92, 130.41, 129.81, 129.50, 128.79, 128.44, 126.81, 125.70, 117.18, 79.36, 77.28, 77.03, 76.77, 69.29, 25.40, 25.38, 24.03, 23.46, 21.53, 12.93. **HRMS** (APCI Positive): calculated for $C_{31}H_{32}NaO_4$ $[M+H]^+$: 491.2193; found: 491.2191.

**(8*R*,9*S*,13*S*,14*S*)-13-Methyl-3-(*cis*-2-((*E*)-styryl)cyclopropyl)-6,7,8,9,11,12,13,14,15, 16-deca-hydro-17*H*-cyclopenta[a]phenanthren-17-one (46k)**



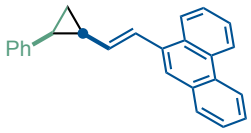
The title compound was obtained following General Procedure B1 (as a 1:1 mixture of the two possible *cis*-diastereomers) from (*E*)-7-styryl-1,3,5-trimethylcyclohepta-1,3,5-triene and vinyl-estrone after purification by flash column chromatography on $SiO_2$ using pentane/acetone 99:1 to 95:5 gradients as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.27 – 7.19 (m, 5H), 7.18 – 7.14 (m, 1H), 7.08 – 7.01 (m, 2H), 6.55 (d, *J* = 15.7 Hz, 1H), 5.64 (ddd, *J* = 15.8, 9.5, 6.3 Hz, 1H), 2.93 (dd, *J* = 9.8, 4.5 Hz, 2H), 2.54 (dd, *J* = 19.1, 8.7 Hz, 1H), 2.43 (dtd, *J* = 15.3, 8.4, 7.3, 4.0 Hz, 2H), 2.33 (td, *J* = 11.0, 3.9 Hz, 1H), 2.22 – 1.99 (m, 5H), 1.70 – 1.48 (m, 6H), 1.38 (td, *J* = 8.4, 5.1 Hz, 1H), 1.17 – 1.10 (m, 1H), 0.95 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 220.96, 137.86, 137.46, 136.10, 130.88, 129.87, 129.43, 128.37, 126.53, 126.38, 126.16, 125.72, 125.06, 50.57, 48.04, 44.32, 38.18, 35.89, 31.65, 29.43, 26.61, 25.71, 23.51, 22.81, 21.62, 13.90, 12.73. **HRMS** (APCI Positive): calculated for $C_{29}H_{32}NaO_4$ $[M+Na]^+$: 419.2345; found: 419.2339. **MP** 119–122 ºC.

**(*R*)-2,5,7,8-Tetramethyl-6-(*cis*-2-((*E*)-styryl)cyclopropyl)-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chromane (46l)**



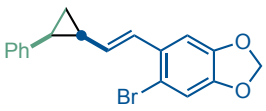

The title compound was obtained following General Procedure B1 (as a 1:1 mixture of the two possible *cis*-diastereomers) from (*E*)-7-styryl-1,3,5-trimethyl-cyclohepta-1,3,5-triene and vinyl-α-tocopherol after purification by preparative TLC (2000 micron) on $SiO_2$ using pentane to pentane/$Et_2O$ 99:1 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.43 – 7.39 (m, 2H), 7.34 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.25 – 7.21 (m, 1H), 6.59 (d, *J* = 15.7 Hz, 1H), 6.04 (dd, *J* = 15.7, 9.1 Hz, 1H), 2.64 (t, *J* = 6.8 Hz, 2H), 2.35 (s, 3H), 2.31 (s, 3H), 2.15 (s, 3H), 1.92 (dt, *J* = 9.1, 6.0 Hz, 1H), 1.86 (q, *J* = 6.8 Hz, 1H), 1.79 (dt, *J* = 13.2, 6.4 Hz, 1H), 1.66 – 1.30 (m, 15H), 1.28 (s, 3H), 1.26 – 1.06 (m, 9H), 0.92 – 0.88 (m, 12H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 194.96, 173.15, 159.48, 141.11, 137.23, 136.05, 131.92, 130.76, 130.22, 125.96, 117.20, 116.31, 79.38, 77.36, 77.04, 76.73, 69.30, 25.38, 21.52. **HRMS** (ESI Positive): calculated for $C_{40}H_{61}O$ $[M+H]^+$: 557.4717; found: 557.4725.

***cis*-9-((*E*)-2-(2-Phenylcyclopropyl)vinyl)phenanthrene (46m)**




The title compound was obtained following General Procedure B3 from (*E*)-9-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)phenanthrene and styrene after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.71 (d, *J* = 9.4 Hz, 1H), 8.63 (d, *J* = 8.1 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.76 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.70 – 7.54 (m, 5H), 7.46 (s, 1H), 7.37 (d, *J* = 4.2 Hz, 3H), 7.28 (s, 1H), 7.21 (d, *J* = 15.4 Hz, 1H), 5.68 (dd, *J* = 15.4, 9.2 Hz, 1H), 2.62 – 2.54 (m, 1H), 2.28 – 2.18 (m, 1H), 1.51 – 1.45 (m, 1H), 1.33 – 1.27 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.78, 134.46, 134.18, 131.89, 130.63, 130.31, 129.84, 129.43, 128.39, 128.18, 127.23, 126.58, 126.42, 126.28, 126.15, 126.08, 124.91, 124.24, 122.94, 122.43, 24.10, 22.76, 12.55. **HRMS**-APCI (Positive): calculated for $C_{25}H_{21}$ $[M+H]^+$: 321.1638; found: 321.1643. **MP** 91–93 ºC.

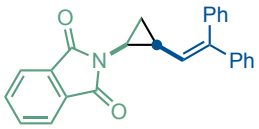
***cis*-5-Bromo-6-((*E*)-2-(2-phenylcyclopropyl)vinyl)benzo[*d*][1,3]dioxole (46n):**




The title compound was obtained following General Procedure B3 from (*E*)-5-bromo-6-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)-benzo[*d*][1,3]dioxole and styrene after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 99:1 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.31 – 7.22 (m, 4H), 7.18 (t, *J* = 7.1 Hz, 1H), 6.91 (s, 1H), 6.73 (d, *J* = 15.6 Hz, 1H), 6.55 (s, 1H), 5.89 – 5.84 (m, 2H), 5.29 (dd, *J* = 15.6, 9.4 Hz, 1H), 2.49 – 2.40

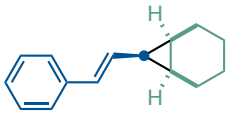
(m, 1H), 2.04 (qd, *J* = 8.8, 5.7 Hz, 1H), 1.36 (td, *J* = 8.4, 5.3 Hz, 1H), 1.16 – 1.10 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 147.79, 147.48, 138.93, 132.41, 131.35, 129.56, 129.32, 128.50, 128.44, 126.50, 112.81, 106.23, 101.88, 24.38, 23.01, 13.00. **HRMS**-APCI: calculated for $C_{18}H_{16}BrO_2$ $[M+H]^+$: 343.0328; found: 343.0325.

***cis*-2-(2-(2,2-Diphenylvinyl)cyclopropyl)isoindoline-1,3-dione (46o)**



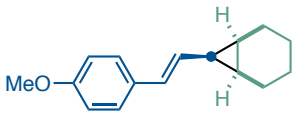

Racemic material of the title compound (as a 16:1 *cis*/*trans* mixture, white solid) was obtained following General Procedure B2 from (*E*)-7-(4-phenylstyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene and *N*-vinylphtalimide after purification by flash column chromatography on $SiO_2$ using pentane/$Et_2O$ 8:2 to 6:4 as eluent. Traces of the two enantiomers were separated by SFC using an UPC2 System with an IC chiral column, 10% of ethanol in $CO_2$ (1.2 mL/min). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.89 – 7.82 (m, 2H), 7.76 – 7.71 (m, 2H), 7.51 – 7.41 (m, 4H), 7.38 – 7.32 (m, 1H), 7.22 – 7.15 (m, 3H), 7.14 – 7.07 (m, 2H), 5.37 (d, *J* = 9.9 Hz, 1H), 3.02 (ddd, *J* = 7.8, 7.0, 5.0 Hz, 1H), 2.07 (ddt, *J* = 9.9, 9.0, 6.8 Hz, 1H), 1.73 (td, *J* = 6.6, 5.0 Hz, 1H), 1.51 (ddd, *J* = 9.0, 7.8, 6.4 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 169.02, 143.47, 142.70, 140.14, 134.10, 131.80, 130.47, 128.20, 127.97, 127.58, 127.18, 126.90, 126.23, 123.30, 29.71, 28.85, 18.88, 13.22.

***endo*-7-((*E*)-Styryl)bicyclo[4.1.0]heptane (58a)**




The title compound was obtained following General Procedure B1, B2, B3 or B4 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-cycloheptatriene and cyclohexene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.40 – 7.27 (m, 4H), 7.24 – 7.18 (m, 1H), 6.61 (d, *J* = 15.7 Hz, 1H), 6.20 (dd, *J* = 15.7, 9.3 Hz, 1H), 2.01 – 1.89 (m, 2H), 1.69 – 1.57 (m, 3H), 1.43 – 1.25 (m, 6H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.25, 131.22, 128.49, 128.42, 126.53, 125.58, 23.06, 22.61, 19.47, 15.20 ppm. **HRMS** (APCI Positive): calculated for $C_{15}H_{19}$ $[M+H]^+$: 199.1481; found: 199.1479.

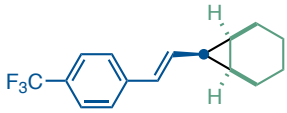
***endo*-7-((*E*)-4-Methoxystyryl)bicyclo[4.1.0]heptane (58b)**




The title compound was obtained following General Procedure B2 from (*E*)-7-(4-methoxystyryl)-1,3,5-trimethyl-cyclohepta-1,3,5-triene and cyclohexene after purification by preparative TLC on $SiO_2$ (2000 micron) using pentane/$Et_2O$ 98:2 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.33 – 7.29 (m, 2H), 6.88 – 6.84 (m, 2H), 6.54 (d, *J* = 15.7 Hz, 1H), 6.04 (dd, *J* = 15.7, 9.2 Hz, 1H), 3.83 (s, 3H), 1.98 – 1.90 (m, 2H), 1.63 – 1.56 (m, 3H), 1.40 – 1.23 (m, 6H). **$^{13}$C NMR**

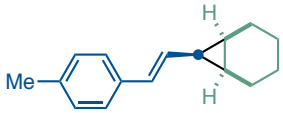
(101 MHz, $CDCl_3$) δ 158.51, 131.27, 130.68, 126.66, 126.04, 113.95, 55.31, 22.85, 22.61, 19.46, 14.84. **HRMS** (APCI Positive): calculated for $C_{16}H_{21}O$ $[M+H]^+$: 229.1587; found: 229.1587.

***endo*-7-((*E*)-4-(Trifluoromethyl)styryl)bicyclo[4.1.0]heptane (58c)**



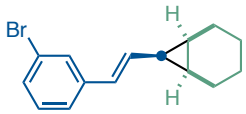
The title compound was obtained following General Procedure B2 (but stirring for 60 h at 80 ºC) from (*E*)-1,3,5-trimethyl-7-(4-(trifluoromethyl)-styryl)cyclohepta-1,3,5-triene and cyclohexene after purification by preparative TLC on $SiO_2$ (2000 micron) using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 6.62 (d, *J* = 15.7 Hz, 1H), 6.32 (dd, *J* = 15.7, 9.5 Hz, 1H), 2.02 – 1.92 (m, 2H), 1.78 – 1.55 (m, 2H), 1.46 – 1.38 (m, 1H), 1.35 – 1.25 (m, 6H), 1.18 – 1.12 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.41, 131.65, 129.90, 125.61, 125.45, 124.81, 23.37, 22.58, 19.47, 15.81. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -62.41 (minor *trans* isomer), -62.44 (major *cis* isomer). **HRMS** (APCI Positive): calculated for $C_{16}H_{18}F_3$ $[M+H]^+$: 267.1355; found: 267.1346.

***endo*-7-((*E*)-4-Methylstyryl)bicyclo[4.1.0]heptane (58d)**



The title compound was obtained following General Procedure B2 from (*E*)-1,3,5-trimethyl-7-(4-methylstyryl)cyclohepta-1,3,5-triene and cyclohexene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.29 – 7.26 (m, 2H), 7.15 – 7.10 (m, 2H), 6.58 (d, *J* = 15.7 Hz, 1H), 6.14 (dd, *J* = 15.7, 9.3 Hz, 1H), 2.36 (s, 3H), 1.99 – 1.90 (m, 2H), 1.67 – 1.58 (m, 3H), 1.44 – 1.36 (m, 2H), 1.34 – 1.28 (m, 2H), 1.28 – 1.23 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 136.25, 135.53, 131.12, 129.19, 127.29, 125.50, 22.97, 22.62, 21.14, 19.47, 15.03. **HRMS** (APCI Positive): calculated for $C_{16}H_{21}$ $[M+H]^+$: 213.1638; found: 213.1641.

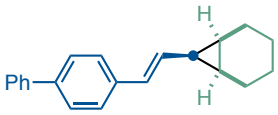
***endo*-7-((*E*)-3-Bromostyryl)bicyclo[4.1.0]heptane (58e)**



The title compound was obtained following General Procedure B2 (but stirring for 60 h at 80 ºC) from (*E*)-7-(3-bromostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene and cyclohexene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.50 (t, *J* = 1.8 Hz, 1H), 7.32 (ddd, *J* = 7.9, 2.0, 1.1 Hz, 1H), 7.27 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.20 – 7.13 (m, 1H), 6.51 (d, *J* = 15.7 Hz, 1H), 6.21 (dd, *J* = 15.7, 9.4 Hz, 1H), 2.00 – 1.92 (m, 2H), 1.67 – 1.55 (m, 3H), 1.40 (m, 2H), 1.30 (m, 4H). **$^{13}$C NMR** (126 MHz,

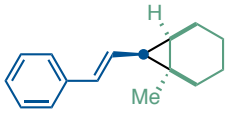
$CDCl_3$) δ 140.39, 137.22, 130.29, 130.01, 129.80, 129.35, 128.35, 124.27, 23.22, 22.59, 19.47, 15.59. **HRMS** (APCI Pos): calculated for $C_{15}H_{18}{}^{79}Br$ $[M+H]^+$: 277.0586; found: 277.0588.

***endo*-7-((*E*)-2-([1,1'-Biphenyl]-4-yl)vinyl)bicyclo[4.1.0]heptane (58f)**



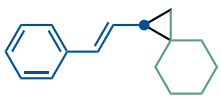

The title compound was obtained following General Procedure B2 from (*E*)-4-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)-1,1'-biphenyl and cyclohexene after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 99:1 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.66 – 7.61 (m, 2H), 7.59 – 7.55 (m, 2H), 7.49 – 7.44 (m, 4H), 7.39 – 7.35 (m, 1H), 6.65 (d, *J* = 15.7 Hz, 1H), 6.26 (dd, *J* = 15.7, 9.3 Hz, 1H), 1.97 (m, 2H), 1.71 – 1.61 (m, 3H), 1.47 – 1.39 (m, 2H), 1.38 – 1.29 (m, 5H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 140.95, 139.33, 137.34, 130.77, 128.76, 128.71, 127.23, 127.11, 126.89, 126.00, 23.22, 22.64, 19.51, 15.37. **HRMS** (APCI Positive): calculated for $C_{21}H_{23}$ $[M+H]^+$: 275.1794; found: 275.1795. **MP** 76–79 ºC.

**1-Methyl-7-((*E*)-styryl)bicyclo[4.1.0]heptane (58g)**




The title compound was obtained following General Procedure B2 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene and 1-methylcyclohex-1-ene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d,* mixture of diastereoisomers, unassigned) δ 7.38 – 7.28 (m, 8H), 7.22 – 7.15 (m, 2H), 6.55 (d, *J* = 15.7 Hz, 1H), 6.45 (d, *J* = 15.7 Hz, 1H), 6.21 (dd, *J* = 15.7, 9.3 Hz, 1H), 5.99 (dd, *J* = 15.7, 9.2 Hz, 1H), 2.04 – 1.90 (m, 2H), 1.87 – 1.57 (m, 7H), 1.45 – 1.23 (m, 11H), 1.17 (m, 5H), 1.07 (td, *J* = 8.8, 2.4 Hz, 1H), 1.00 – 0.89 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$, mixture of diastereoisomers, unassigned) δ 138.27, 138.16, 132.34, 130.80, 128.69, 128.47, 128.44, 127.21, 126.46, 126.29, 125.54, 125.49, 77.33, 77.01, 76.69, 32.51, 32.25, 31.52, 29.59, 27.90, 27.03, 24.29, 23.78, 23.56, 23.08, 22.56, 22.41, 21.62, 21.21, 20.83, 19.78, 0.00. **HRMS** (APCI Positive): calculated for $C_{16}H_{21}$ $[M+H]^+$: 213.1638; found: 213.1639.

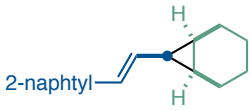
**(*E*)-1-Styrylspiro[2.5]octane (58h)**



The title compound was obtained following General Procedure B2 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene and methylenecyclohexane after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.36 – 7.29 (m, 4H), 7.19 (ddt, *J* = 7.6, 6.6, 1.5 Hz, 1H), 6.50 (d, *J* = 15.7 Hz, 1H), 6.06 (dd, *J* = 15.7, 9.0 Hz, 1H), 1.55 – 1.32 (m, 12H), 0.78 (dd, *J* = 8.2, 4.4 Hz, 1H), 0.54 (t, *J* = 4.8 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$)

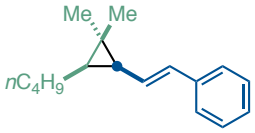
δ 138.10, 131.40, 129.01, 128.47, 126.43, 125.60, 37.69, 31.39, 27.90, 26.33, 25.57, 20.84. **HRMS** (APCI Positive): calculated for $C_{16}H_{21}$ $[M+H]^+$: 213.1638; found: 213.1633.

***endo*-2-((*E*)-2-(Bicyclo[4.1.0]heptan-7-yl)vinyl)naphthalene (58i)**



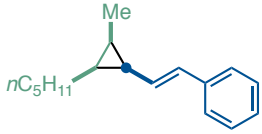

The title compound was obtained following General Procedure B2 from (*E*)-2-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)naphthalene and cyclohexene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.85 – 7.78 (m, 3H), 7.70 (d, *J* = 1.7 Hz, 1H), 7.63 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.46 (dddd, *J* = 20.8, 8.2, 6.8, 1.3 Hz, 2H), 6.78 (d, *J* = 15.7 Hz, 1H), 6.35 (dd, *J* = 15.7, 9.3 Hz, 1H), 1.98 (m, 2H), 1.74 – 1.64 (m, 3H), 1.47 – 1.41 (m, 2H), 1.40 – 1.35 (m, 2H), 1.34 – 1.30 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 135.70, 133.84, 132.58, 131.37, 128.97, 128.06, 127.83, 127.65, 126.14, 125.32, 124.75, 123.45, 23.35, 22.68, 19.54, 15.42. **HRMS** (APCI Positive): calculated for $C_{19}H_{21}$ $[M+H]^+$: 249.1638; found: 249.1635. **MP** 77–81ºC.

***cis*-((*E*)-2-(3-Butyl-2,2-dimethylcyclopropyl)vinyl)benzene (58j)**




The title compound was obtained following General Procedure B2 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene and 2-methylhept-2-ene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.34 – 7.30 (m, 4H), 7.21 – 7.16 (m, 1H), 6.53 (d, *J* = 15.7 Hz, 1H), 6.05 – 6.01 (m, 1H), 1.48 – 1.33 (m, 6H), 1.17 – 1.13 (m, 3H), 1.11 (s, 3H), 1.09 (dd, *J* = 9.1, 5.2 Hz, 1H), 0.94 (m, 3H), 0.87 (dt, *J* = 8.9, 7.1 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$, mixture of diastereoisomers, unassigned) δ 138.31, 138.15, 132.23, 130.13, 128.74, 128.55, 128.47, 126.37, 126.32, 125.55, 125.51, 77.27, 35.14, 33.99, 32.21, 32.18, 31.61, 31.08, 29.16, 28.89, 24.85, 23.86, 22.99, 22.62, 22.56, 22.22, 21.41, 15.71, 14.16. **HRMS** (APCI Positive): calculated for $C_{17}H_{25}$ $[M+H]^+$: 229.1951; found: 229.1951.

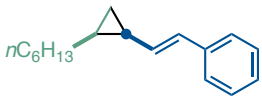
**(*E*)-(2-(2-Methyl-2-pentylcyclopropyl)vinyl)benzene, 1:1 *cis*/*trans* (58k)**




The title compound was obtained following General Procedure B2 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene and 2-methylhept-1-ene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*, mixture of diastereoisomers, unassigned) δ 7.36 – 7.28 (m, 4H), 7.19 (t, *J* = 7.2 Hz, 1H), 6.49 (dd, *J* = 15.7, 3.2 Hz, 1H), 6.03 (ddd, *J* = 15.7, 8.9, 2.9 Hz, 1H), 1.42 (m, 4H), 1.31 (m, 5H), 1.13 (s, 3H), 0.92 (m, 4H), 0.79 (dt, *J* = 7.7, 3.9 Hz, 1H), 0.53 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$,

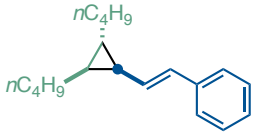
mixture of diastereoisomers, unassigned) δ 138.11, 138.03, 131.80, 131.68, 129.14, 129.01, 128.47, 126.48, 126.44, 125.60, 41.13, 34.84, 32.21, 32.05, 28.73, 27.90, 26.60, 26.32, 24.23, 23.87, 23.67, 22.76, 22.68, 22.02, 21.69, 18.20, 14.12, 14.08. **HRMS** (APCI Positive): calculated for $C_{17}H_{25}$ $[M+H]^+$: 229.1951; found: 229.1955.

***cis*-((*E*)-2-(2-Hexylcyclopropyl)vinyl)benzene (58l)**



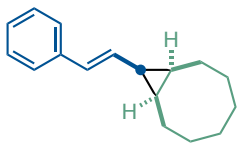

The title compound was obtained following General Procedure B2 or B3 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene and 1-octene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.36 – 7.29 (m, 4H), 7.22 – 7.15 (m, 1H), 6.52 (d, *J* = 15.7 Hz, 1H), 6.00 (dd, *J* = 15.7, 9.1 Hz, 1H), 1.71 – 1.61 (m, 1H), 1.42 (m, 3H), 1.36 – 1.26 (m, 6H), 1.12 – 1.03 (m, 1H), 1.00 (td, *J* = 8.2, 4.4 Hz, 1H), 0.91 – 0.87 (m, 4H), 0.36 (td, *J* = 5.6, 4.4 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.06, 131.23, 129.29, 128.46, 126.47, 125.60, 31.85, 29.74, 29.43, 29.17, 22.66, 19.65, 19.58, 14.09, 13.65. **HRMS** (APCI Positive): calculated for $C_{17}H_{25}$ $[M+H]^+$: 229.1951; found: 229.1951.

**((*E*)-2-(2,3-Dibutylcyclopropyl)vinyl)benzene (58m)**



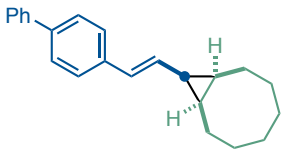

The title compound was obtained following General Procedure B2 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene and (*E*)-dec-5-ene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.36-7.29 (m, 4H), 7.18 (t, *J* = 7.1 Hz, 1H), 6.48 (d, *J* = 15.7 Hz, 1H), 6.01 (dd, *J* = 15.7, 9.3 Hz, 1H), 1.45-1.30 (m, 13H), 0.95-0.90 (m, 6H), 0.83 (m, 1H), 0.69 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.17, 131.43, 128.60, 128.46, 126.34, 125.53, 33.69, 32.04, 31.59, 28.98, 28.23, 27.44, 27.36, 22.55, 22.51, 14.13, 14.12. **HRMS** (APCI Positive): calculated for $C_{19}H_{29}$ $[M+H]^+$: 257.2264; found: 257.2267.

***endo*-9-((*E*)-Styryl)bicyclo[6.1.0]nonane (58n)**



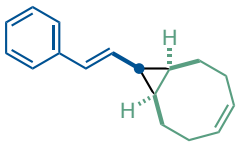

The title compound was obtained following General Procedure B1, B2 or B3 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene and (*Z*)-cyclooctene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.38 – 7.26 (m, 4H), 7.24 – 7.12 (m, 1H), 6.57 (d, *J* = 15.7 Hz, 1H), 6.15 (dd, *J* = 15.7, 9.8 Hz, 1H), 1.87 (m, 2H), 1.71 (m, 5H), 1.47 – 1.32 (m, 6H), 1.05 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.24, 134.86, 130.73, 128.45, 126.42, 125.57, 29.66, 26.60, 22.70, 22.62, 22.49. **HRMS** (APCI Positive): calculated for $C_{19}H_{29}$ $[M+H]^+$: 257.2264; found: 257.2267.

***endo*-9-((*E*)-2-([1,1'-Biphenyl]-4-yl)vinyl)bicyclo[6.1.0]nonane (58o)**



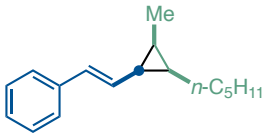

The title compound was obtained following General Procedure B2 from (*E*)-4-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)-1,1'-biphenyl and (*Z*)-cyclooctene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.65 – 7.62 (m, 2H), 7.58 – 7.54 (m, 2H), 7.49 – 7.43 (m, 4H), 7.40 – 7.35 (m, 1H), 6.62 (d, *J* = 15.7 Hz, 1H), 6.22 (dd, *J* = 15.7, 9.8 Hz, 1H), 1.94 – 1.87 (m, 2H), 1.79 – 1.66 (m, 4H), 1.50 – 1.35 (m, 6H), 1.13 – 1.05 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 140.97, 139.21, 137.32, 135.17, 130.27, 128.82, 127.20, 127.09, 126.89, 125.98, 29.68, 26.62, 22.88, 22.67. **HRMS** (APCI Positive): calculated for $C_{23}H_{27}$ $[M+H]^+$: 303.2107; found: 303.2103. **MP** 87–90 ºC.

***endo*-(*Z*)-9-((*E*)-Styryl)bicyclo[6.1.0]non-4-ene (58p)**



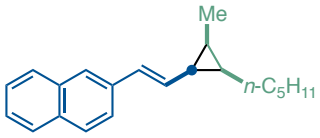

The title compound was obtained following General Procedure B2 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene and (1*Z*,5*Z*)-cycloocta-1,5-diene and purification by preparative TLC on $SiO_2$ (2000 micron) using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.37 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.34 – 7.29 (m, 2H), 7.22 – 7.19 (m, 1H), 6.59 (d, *J* = 15.7 Hz, 1H), 6.08 (dd, *J* = 15.7, 9.9 Hz, 1H), 5.74 – 5.64 (m, 2H), 2.50 – 2.41 (m, 2H), 2.22 – 2.13 (m, 2H), 2.05 – 1.98 (m, 2H), 1.81 – 1.76 (m, 2H), 1.30 – 1.22 (m, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.15, 130.78, 129.72, 128.49, 128.25, 126.55, 125.63, 27.69, 24.53, 23.00, 22.66. **HRMS** (APCI Positive): calculated for $C_{17}H_{21}$ $[M+H]^+$: 225.1638; found: 225.1634.

***cis*-((*E*)-2-(2-Methyl-3-pentylcyclopropyl)vinyl)benzene (58q)**



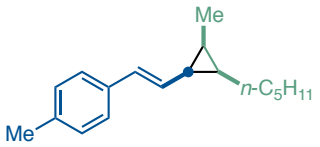

The title compound was obtained following General Procedure B2 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene and (*Z*)-oct-2-ene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.38 – 7.26 (m, 4H), 7.22 – 7.17 (m, 1H), 6.58 (d, *J* = 15.7 Hz, 1H), 6.06 (dd, *J* = 15.7, 10.0 Hz, 1H), 1.67 (dt, *J* = 9.9, 8.4 Hz, 1H), 1.46 – 1.33 (m, 8H), 1.26 – 1.18 (m, 1H), 1.12 (m, 3H), 1.11 – 1.05 (m, 1H), 0.94 – 0.90 (m, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.30, 135.22, 128.47, 128.00, 126.42, 125.57, 31.85, 29.53, 23.81, 22.84, 22.67, 22.47, 16.43, 14.09, 8.54. **HRMS** (APCI Positive): calculated for $C_{17}H_{25}$ $[M+H]^+$: 229.1951; found: 229.1949.

**_cis_-2-((_E_)-2-(2-Methyl-3-pentylcyclopropyl)vinyl)naphthalene (58r)**



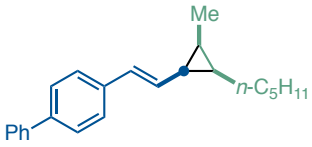

The title compound was obtained following General Procedure B2 from (*E*)-2-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)naphthalene and (*Z*)-oct-2-ene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.84 – 7.77 (m, 3H), 7.68 (d, *J* = 1.7 Hz, 1H), 7.59 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.45 (dqd, *J* = 9.5, 6.9, 1.3 Hz, 2H), 6.74 (d, *J* = 15.6 Hz, 1H), 6.19 (dd, *J* = 15.6, 9.9 Hz, 1H), 1.74 (dt, *J* = 10.0, 8.6 Hz, 1H), 1.52 – 1.35 (m, 8H), 1.26 (tt, *J* = 8.4, 5.4 Hz, 1H), 1.17 (m, 3H), 1.15 – 1.09 (m, 1H), 0.95 – 0.90 (m, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 135.75, 133.84, 132.50, 130.75, 128.56, 128.00, 127.78, 127.62, 126.11, 125.26, 124.64, 123.51, 31.86, 29.55, 23.86, 23.05, 22.72, 22.68, 16.62, 14.10, 8.60. **HRMS** (APCI Positive): calculated for $C_{21}H_{27}$ $[M+H]^+$: 279.2107; found: 279.2097.

**_cis_-1-Methyl-4-((_E_)-2-(2-methyl-3-pentylcyclopropyl)vinyl)benzene (58s)**




The title compound was obtained following General Procedure B2 from (*E*)-1,3,5-trimethyl-7-(4-methylstyryl)cyclohepta-1,3,5-triene and (*Z*)-oct-2-ene after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.27 – 7.24 (m, 2H), 7.13 (d, *J* = 7.9 Hz, 2H), 6.55 (d, *J* = 15.6 Hz, 1H), 6.00 (dd, *J* = 15.7, 9.9 Hz, 1H), 2.36 (s, 3H), 1.66 (dt, *J* = 10.1, 8.7 Hz, 1H), 1.45 – 1.34 (m, 8H), 1.23 – 1.17 (m, 1H), 1.12 (d, *J* = 6.5 Hz, 3H), 1.08 (ddd, *J* = 8.7, 6.9, 1.9 Hz, 1H), 0.92 (m, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 136.10, 135.57, 130.49, 129.16, 126.84, 125.48, 31.87, 29.54, 23.81, 22.69, 22.41, 21.13, 16.26, 14.10, 8.53. **HRMS** (APCI Positive): calculated for $C_{18}H_{27}$ $[M+H]^+$: 243.2107; found: 243.2095.

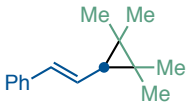
**_cis_-4-((_E_)-2-(2-Methyl-3-pentylcyclopropyl)vinyl)-1,1'-biphenyl (58t)**




The title compound was obtained following General Procedure B2 from (*E*)-4-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)-1,1'-biphenyl and (*Z*)-oct-2-ene after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 99:1 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.65 – 7.62 (m, 2H), 7.59 – 7.55 (m, 2H), 7.49 – 7.43 (m, 4H), 7.36 (td, *J* = 7.3, 1.5 Hz, 1H), 6.62 (d, *J* = 15.7 Hz, 1H), 6.12 (dd, *J* = 15.6, 10.0 Hz, 1H), 1.71 (q, *J* = 8.9 Hz, 1H), 1.48 – 1.35 (m, 8H), 1.25 (tt, *J* = 8.5, 6.4 Hz, 1H), 1.15 (m, 3H), 1.12 (td, *J* = 8.7, 7.7, 6.0 Hz, 1H), 0.95 – 0.92 (m, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 140.97, 139.21, 137.38, 130.16, 128.76, 128.30, 127.20, 127.09, 126.88, 125.98, 31.87, 29.56, 23.85, 23.01,

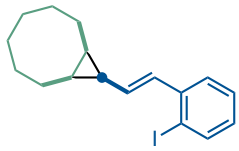
22.69, 22.63, 16.59, 14.11, 8.58. **HRMS** (APCI Positive): calculated for $C_{23}H_{29}$ $[M+H]^+$: 305.2264; found: 305.2253.

**(*E*)-(2-(2,2,3,3-Tetramethylcyclopropyl)vinyl)benzene (58u)**



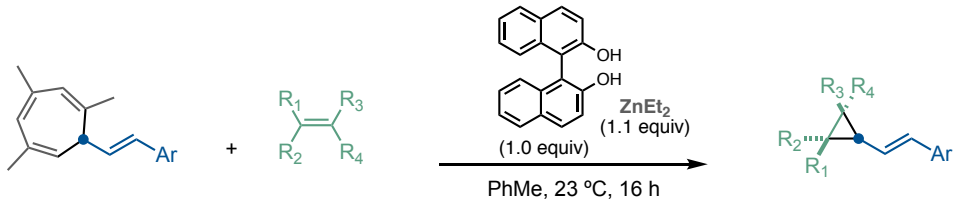

The title compound was obtained following General Procedure B2 from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene and 2,3-dimethylbut-2-ene after purification by preparative TLC on $SiO_2$ (2000 micron) using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.37 – 7.29 (m, 4H), 7.21 – 7.16 (m, 1H), 6.51 (d, *J* = 15.6 Hz, 1H), 6.06 (dd, *J* = 15.6, 9.7 Hz, 1H), 2.32 – 2.28 (m, 1H), 1.19 (s, 6H), 1.13 (s, 6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.29, 130.13, 129.35, 128.47, 126.36, 125.53, 38.28, 26.41, 23.58, 17.85. **HRMS** (APCI Positive): calculated for $C_{15}H_{21}$ $[M+H]^+$: 201.1638; found: 201.1637.

***endo*-9-((*E*)-2-Iodostyryl)bicyclo[6.1.0]nonane (58v)**

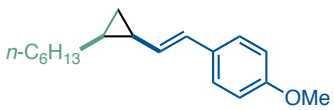



The title compound was obtained following General Procedure B3 from (*E*)-7-(2-iodostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene and (*Z*)-cyclooctene after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.84 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.45 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.29 (td, *J* = 6.4, 0.82 Hz, 1H), 6.89 (td, *J* = 7.7, 1.7 Hz, 1H), 6.73 (d, *J* = 15.4 Hz, 1H), 6.04 (dd, *J* = 15.4, 9.8 Hz, 1H), 1.89 (dd, *J* = 13.7, 2.8 Hz, 2H), 1.79 (q, *J* = 8.9 Hz, 1H), 1.75 – 1.63 (m, 4H), 1.50 – 1.39 (m, 4H), 1.38 – 1.28 (m, 2H), 1.10 (t, *J* = 9.6 Hz, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.50, 139.82, 134.67, 132.39, 128.56, 128.36, 127.27, 126.36, 99.42, 29.98, 26.94, 23.44, 23.01, 22.96. **HRMS**-APCI (Positive): calculated for $C_{17}H_{22}I$ $[M+H]^+$: 353.0761; found: 353.0759.

**mmol-Scale BINOL–$ZnEt_2$-Promoted Cyclopropanation**



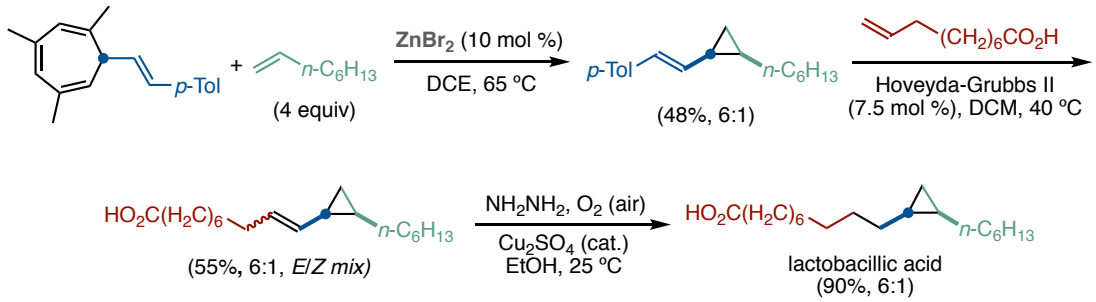

***cis*-1-((*E*)-2-(2-Hexylcyclopropyl)vinyl)-4-methoxybenzene (58w)**:




An oven dried 25 mL two-necked round-bottomed flask equipped with a magnetic stirring bar was charged with BINOL (0.43 g, 1.5 mmol, 1 equiv). After exchanging the atmosphere with Ar through three vacuum/Ar cycles, (*E*)-7-(4-methoxystyryl)-1,3,5-trimethylcyclohepta-

1,3,5-triene (0.40 g, 1.5 mmol, 1 equiv) was added as a solution in anhydrous PhMe, and then 1-octene (0.95 mL, 6.0 mmol, 4 equiv) was added via syringe. To the resulting stirring solution was added dropwise diethylzinc (1.58 mmol, 1.58 mL of a 1.0 M commercial solution in hexanes, 1.1 equiv), and the obtained mixture was stirred at room temperature (*ca.* 25 ºC) for 16 h, before the reaction was quenched by the addition of water. The mixture was extracted three times with $Et_2O$, and combined organic extracts were washed once with water, once with brine and then dried over anhydrous $Na_2SO_4$. After removal of the solvent, the product was purified by flash column in silica gel using pentane to pentane/$Et_2O$ 98:2 to give *cis*-1-((*E*)-2-(2-hexylcyclopropyl)vinyl)-4-methoxybenzene (0.202 g, 0.78 mmol, 52% yield) as a colorless oil, with 17:1 dr. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.24 (d, *J* = 8.8 Hz, 2H), 6.84 – 6.81 (m, 2H), 6.43 (d, *J* = 15.7 Hz, 1H), 5.83 (dd, *J* = 15.7, 9.0 Hz, 1H), 3.79 (s, 3H), 1.59 (qd, *J* = 8.5, 5.2 Hz, 1H), 1.39 – 1.25 (m, 10H), 1.05 – 0.97 (m, 1H), 0.94 (td, *J* = 8.3, 4.4 Hz, 1H), 0.86 (t, *J* = 6.9 Hz, 3H), 0.29 (q, *J* = 5.4 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.81, 131.37, 129.24, 129.11, 127.04, 114.28, 55.65, 32.23, 30.13, 29.78, 29.56, 23.04, 19.84, 19.78, 14.47, 13.78. **HRMS** (ESI Positive): calculated for $C_{18}H_{27}O$ $[M+H]^+$: 259.2056; found: 259.2049.

**Total Synthesis of Lactobacillic Acid**




**1. Gram Scale Zinc(II)-Catalyzed Cyclopropanation**

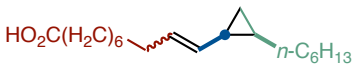
***cis*-1-((*E*)-2-(2-Hexylcyclopropyl)vinyl)-4-methylbenzene (58v)**


A dry two-necked 100 mL round-bottomed flask with a magnetic stirring bar was fitted, under Ar, with a reflux condenser. Anhydrous zinc(II) bromide (0.090 g, 0.399 mmol, 10 mol %) (99.999% pure, stored in the glovebox) was added to the flask and the system was purged three times with vacuum/Ar cycles. To the flask was added oct-1-ene (2.5 ml, 16 mmol, 4 equiv) and subsequently a solution of (*E*)-1,3,5-trimethyl-7-(4-methylstyryl)cyclohepta-1,3,5-triene (1 g, 3.99 mmol, 1 equiv) in anhydrous DCE (35 mL, 0.11 M) before the mixture is stirred at 65 ºC for 35 h. After confirming the disappearance of the starting cycloheptatriene by TLC and $^1$H NMR, crude product was taken up in SiO2 and purified by flash column in $SiO_2$ using pentane as eluent to give 1-((*E*)-2-(*cis*-

2-hexylcyclopropyl)vinyl)-4-methylbenzene (0.47 g, 1.94 mmol, 49% yield) as a 6:1 *cis*/*trans* mixture. The isolated product contained 15% w/w of mesitylene from the retro-Buchner reaction (the yield was corrected accordingly), but this does not interfere in the next reaction and it is very easily removed in the next purification step. Due to the relative volatility of **58v**, any attempts to selectively remove or distil mesitylene heating in high vacuum were not successful. **$^{1}$H NMR** (500 MHz, Chloroform-*d*) δ 7.26 – 7.23 (m, 2H), 7.15 – 7.11 (m, 2H), 6.50 (d, *J* = 15.6 Hz, 1H), 5.96 (dd, *J* = 15.7, 9.0 Hz, 1H), 2.32 (s, 3H), 1.65 (qd, *J* = 8.6, 5.2 Hz, 1H), 1.37 – 1.30 (m, 10H), 1.00 (td, *J* = 8.2, 4.4 Hz, 1H), 0.93 (d, *J* = 2.6 Hz, 3H), 0.37 – 0.33 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 136.16, 135.32, 133.70, 130.09, 129.17, 125.53, 31.88, 29.77, 29.44, 29.20, 22.68, 22.37, 21.12, 19.54, 14.11, 13.54. **HRMS** (APCI Positive): calculated for $C_{18}H_{27}$ $[M+H]^+$: 243.2107; found: 243.2102.

**2. Cross-Metathesis of Styryl Cyclopropanes with Unsaturated Fatty Acids**

**10-(*cis*-2-Hexylcyclopropyl)dec-9-enoic acid (*E*/*Z* mixture) (60)**

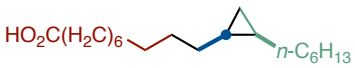



A screw-cap culture tube equipped with a Teflon-coated magnetic stirring bar was charged with 1-((*E*)-2-(*cis*-2-hexylcyclopropyl)vinyl)-4-methylbenzene (6:1 *cis*/*trans,* 68 mg, 0.278 mmol, 1 equiv) and dec-9-enoic acid (52 mg, 0.306 mmol, 1.1 equiv) and it was introduced in an Ar filled glovebox. Both materials were dissolved in anhydrous dichloromethane (0.7 mL, 0.4 M) and then Hoveyda–Grubbs 2$^{nd}$ Generation Catalyst (9 mg, 5 mol %) was added. The tube was closed with the corresponding cap, taken outside the glovebox and stirred at 40 ºC for 16 h. After that time, another solution containing another portion of dec-9-enoic acid (52 mg, 0.306 mmol, 1.1 equiv) and 4 mg of Hoveyda-Grubbs 2$^{nd}$ Generation Catalyst (2.5 mol %) in 0.4 mL of anhydrous dichloromethane was added in a single portion to the reaction mixture, which was stirred again for 20 h at 40 ºC. After that time, the crude product was taken up in $SiO_2$ and purified by flash column in $SiO_2$ using a slow gradient of pentane/$Et_2O$/acetic acid 95:5:1 to pentane/$Et_2O$/acetic acid 90:10:1 to give 10-(*cis*-2-hexylcyclopropyl)dec-9-enoic acid **60** (6:1 *cis*/*trans*, 44 mg, 54% yield, *ca.* 2:1 *E*/*Z* mixture, unassigned) as a pale yellow oil. **$^{1}$H NMR** (500 MHz, Chloroform-*d*, major isomer) δ 11.34 (br, 1H), 5.45 – 5.51 (m, 1H), 5.15 (dd, *J* = 14.9, 8. Hz, 1H), 2.33 (t, *J* = 7.9 Hz, 2H), 1.95 – 1.99 (m, 2H), 1.60 – 1.62 (m, 3H), 1.25 – 1.35 (m, 21H), 0.87 (t, *J* = 6.9 Hz 3H), 0.75 – 0.80 (m, 1H), 0.10 (q, *J* = 5.0 Hz 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$, major isomer) δ 180.20, 130.66, 130.02, 34.35, 33.05, 32.25, 30.08, 30.04, 29.58, 29.52, 29.47, 29.39, 29.27, 25.04, 23.03, 18.81, 18.65, 14.47, 12.71. **FTIR** (ATR) ν 2922, 2853, 1707, 1457, 1284, 958 $cm^{-1}$. **HRMS** (ESI Negative): calculated for $C_{19}H_{33}O_2$ $[M-H]^+$: 293.2486; found: 293.2487. Alternatively, the same procedure can carried out using 1-((*E*)-2-(*cis*-2-hexylcyclopropyl)vinyl)-4-methylbenzene (17:1 *cis*/*trans,* 55 mg, 0.213 mmol,

1 equiv), dec-9-enoic acid (80 mg, 0.468 mmol, 2.2 equiv) and Hoveyda-Grubbs 2nd Generation Catalyst (11 mg, 7.5 mol %), giving 10-(*cis*-2-hexylcyclopropyl)dec-9-enoic acid (17:1 *cis*/*trans*, 33 mg, 60% yield, *ca.* 2:1 *E*/*Z* mixture, unassigned).

**3. Diimide Reduction of the Double Bond**

**Lactobacillic acid (61)**



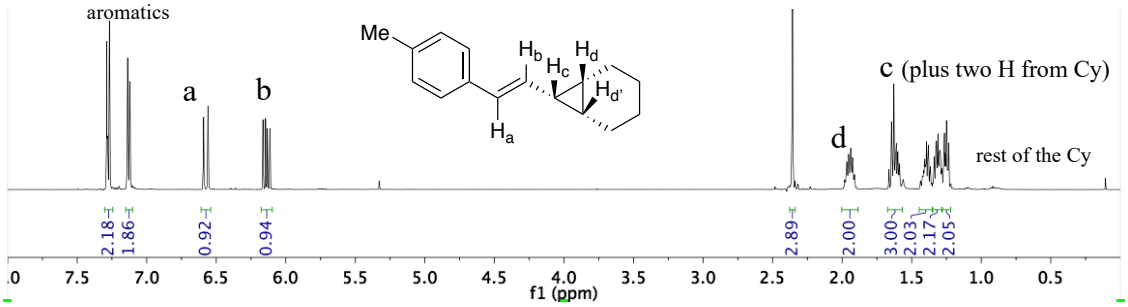

Following a similar reported procedure,[142] 10-(c*is*-2-hexylcyclopropyl)dec-9-enoic acid (35 mg, 0.119 mmol, 1.0 equiv, *E*/*Z* mixture) is dissolved in ethanol (3 mL, 0.04 M) in a round-bottomed flask open to air. To the stirring solution was added in one portion hydrazine monohydrate (0.6 mL, 11.9 mmol, 100 equiv). After that, a total amount of approximately 0.2 mL of a saturated aqueous solution of $CuSO_4$ was added in five portions, one every 24 h, while vigorous stirring was continued at room temperature and with the flask open to air (A brownish suspension is formed after the addition of copper sulfate, if the mixture becomes blue over the course of the reaction, it may indicate that hydrazine was consumed, and more equivalents can be added if the reaction is not complete.). More ethanol can be added over the course of the reaction to compensate for evaporation loses. After 5 days, the reaction was quenched by the addition of aqueous HCl (10%) and the aqueous phase was extracted three times with $Et_2O$. Combined organic fractions were washed once with aqueous HCl (10%) and once with brine, dried over anhydrous $Na_2SO_4$ and concentrated in vacuum. Crude product was purified by flash column in silica gel, using pentane/$Et_2O$/acetic acid 90:10:1 as eluent, giving lactobacillic acid (31 mg, 90% yield, 6:1 *cis*/*trans*) as a pale-yellow viscous oil that solidifies in the freezer and melts around room temperature. Spectroscopic data matched the previously reported ones.[143] **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 10.20 (br, 1H), 2.34 (t, *J* = 7.5 Hz, 2H), 1.62 (quint, *J* = 7.2 Hz, 2H), 1.32 – 1.25 (m, 22H), 1.14 – 1.09 (m, 2H), 0.88 – 0.86 (m, 3H), 0.66 – 0.60 (m, 2H), 0.58 – 0.51 (m, 1H), -0.35 (q, *J* = 5.3 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 180.02, 34.20, 32.11, 30.35, 30.34, 29.85, 29.78, 29.60, 29.51, 29.40, 29.23, 28.89, 28.86, 24.85, 22.85, 15.94, 15.92, 14.26, 11.07. **FTIR** (ATR) ν 2922, 2853, 1709, 1459, 1287, 722 $cm^{-1}$. **HRMS** (ESI Negative): calculated for $C_{19}H_{35}O_2$ $[M-H]^+$: 295.2643; found: 295.2649.

142 Lou, Y.; Horikawa, M.; Kloster, R. A.; Hawryluk, N. A.; Corey, E. J. A New Chiral Rh(II) Catalyst for Enantioselective [2 + 1]-Cycloaddition. Mechanistic Implications and Applications. *J. Am. Chem. Soc.* **2004**, *126*, 8916–8918.

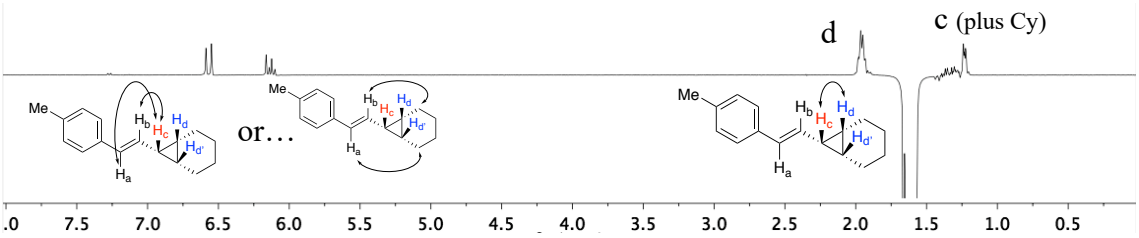
143 Shah, S.; White, J. M.; Williams, S. J. Total syntheses of cis-cyclopropane fatty acids: dihydromalvalic acid, dihydrosterculic acid, lactobacillic acid, and 9,10-methylenehexadecanoic acid. *Org. Biomol. Chem.*, **2014**, 9427–9438.

**Confirmation of the relative *cis*-configuration of the major products (nOe NMR and X-ray diffraction analysis)**

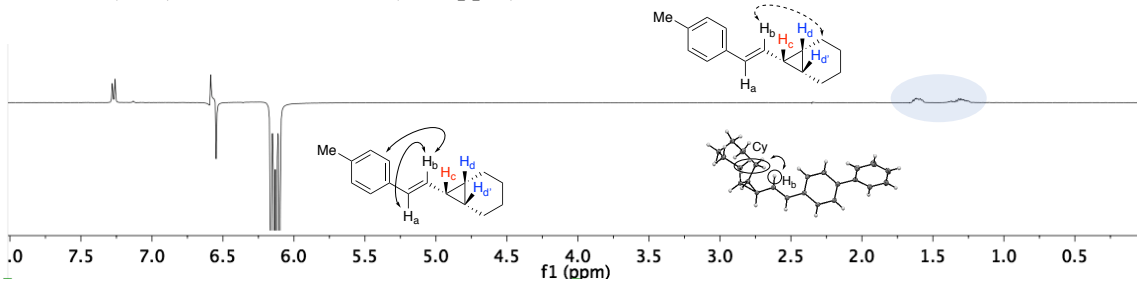
For space reasons, only some representative examples are shown here, for the rest of nOe experiments, see the original publication.[144]




GOESY (nOe) Irradiation on $H_c$ (plus two H from the cyclohexane) (1.67 ppm)

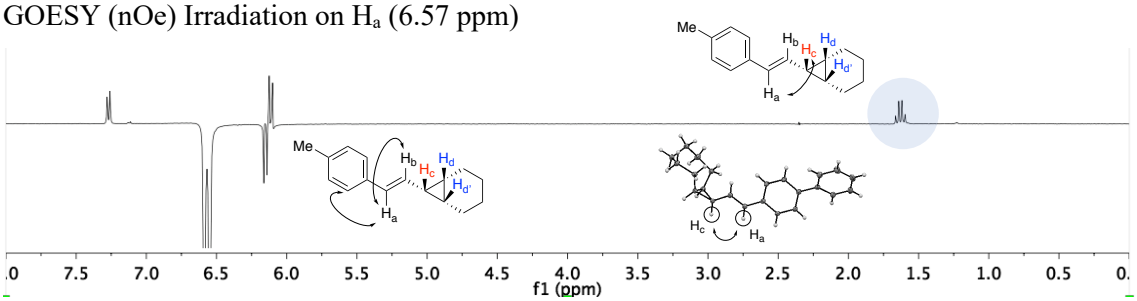



GOESY (nOe) Irradiation on $H_b$ (6.13 ppm)

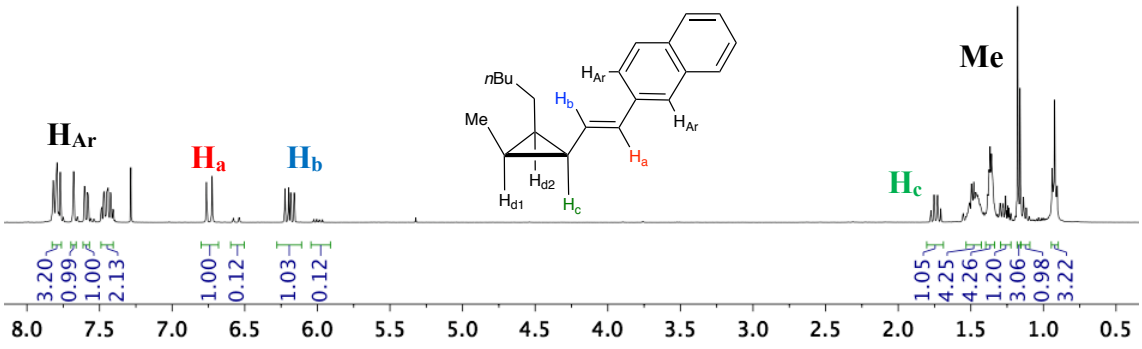



**No nOe between $H_b$ and $H_d$/$H_{d'}$, confirming the *cis* configuration**

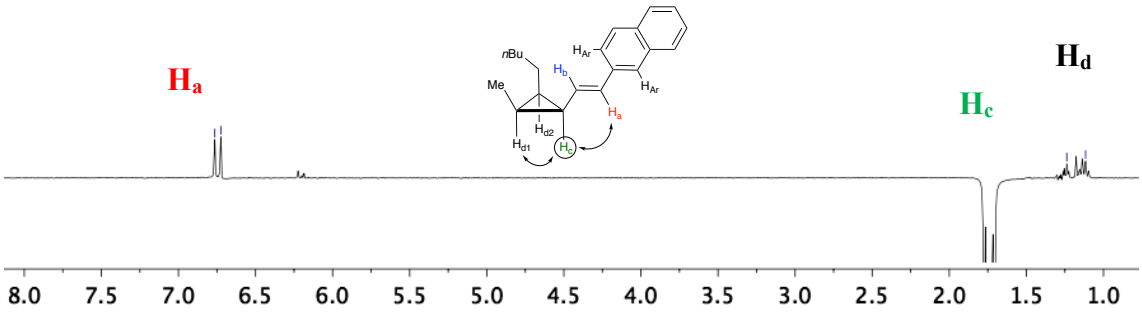
GOESY (nOe) Irradiation on $H_a$ (6.57 ppm)



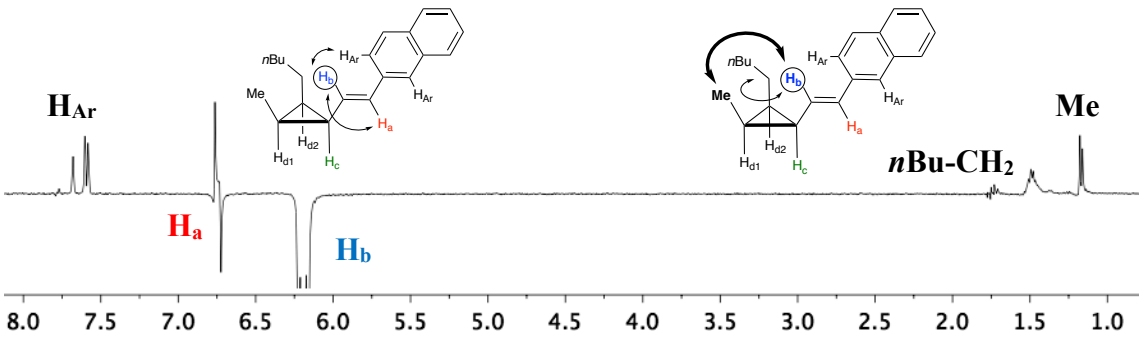

144 Mato, M.; Herlé, B.; Echavarren, A. M. Cyclopropanation by Gold- or Zinc-Catalyzed Retro-Buchner Reaction at Room Temperature. *Org. Lett.* **2018**, *20*, 4341–4345.




GOESY (nOe) Irradiation on $H_c$ (1.74 ppm)

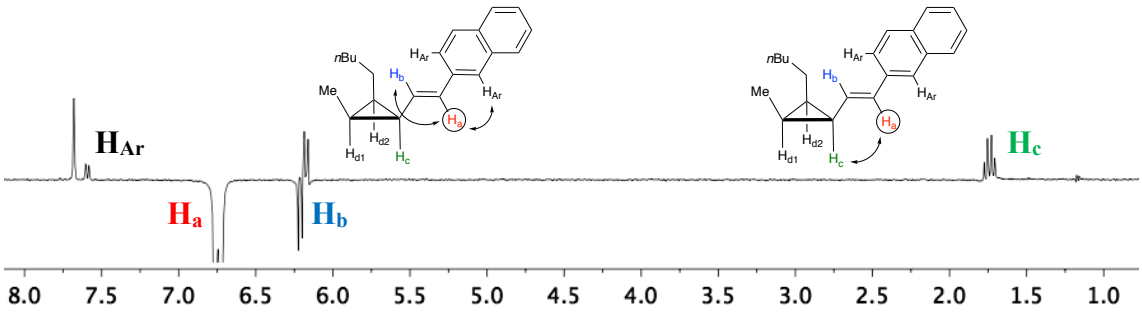


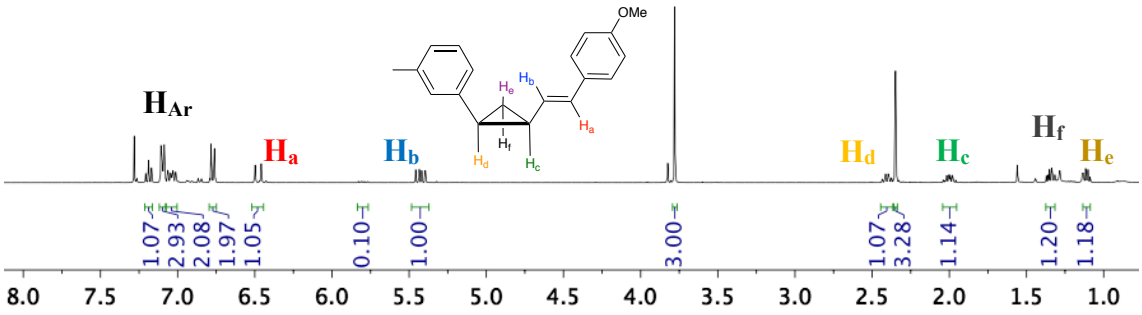

GOESY (nOe) Irradiation on $H_b$ (6.19 ppm)



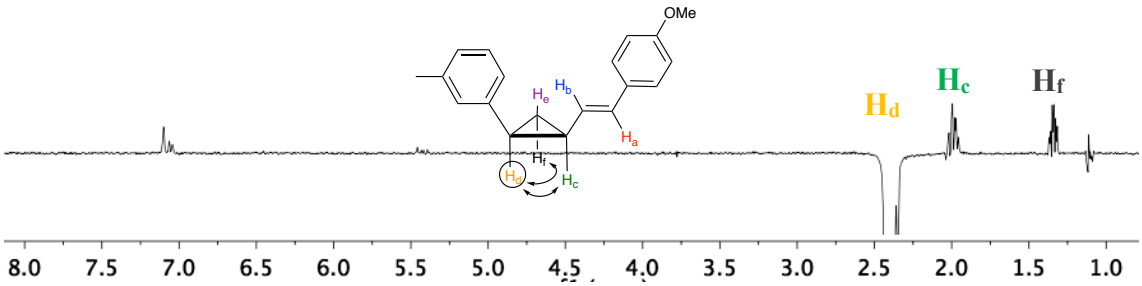

**nOe between $H_b$ and methyl group (d, 1.17 ppm, 3H) confirming the *cis* configuration**

GOESY (nOe) Irradiation on $H_a$ (6.74 ppm)

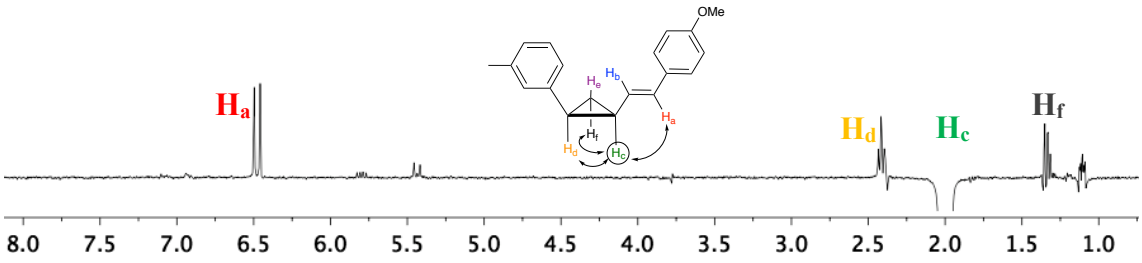




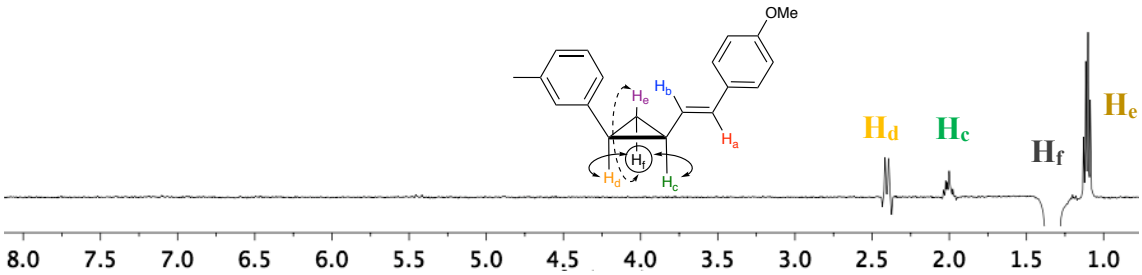

GOESY (nOe) Irradiation on $H_d$ (2.41 ppm)




GOESY (nOe) Irradiation on $H_d$ (2.00 ppm)

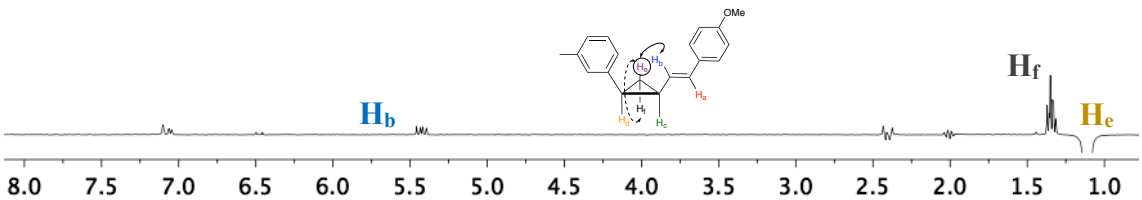



GOESY (nOe) Irradiation on $H_f$ (1.35 ppm)




**No nOe between $H_f$ and $H_b$ (confirming *cis* configuration)**

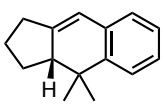
GOESY (nOe) Irradiation on $H_e$ (1.12 ppm)



**Cycloisomerization of Enynes with BINOL–Zn**

The cycloisomerization of enynes (and related processes) catalyzed by the BINOL–Zn system were carried out using a slight modifications of procedure B4. All the obtained products were previously reported,[145] and all the yields/ratios were determined by $^1$H NMR using diphenylmethane as internal standard.

An HPLC vial equipped with a magnetic stirring bar was charged with the corresponding enyne (1.0 equiv) and diphenylmethane (internal standard for NMR yield, 1 equiv) and the corresponding BINOL derivative (0.1–1.0 equiv, depending on the experiment). The vial was closed with the corresponding cap or fitted with a rubber septum, and then the atmosphere was exchanged with Ar through three vacuum-Ar cycles. All the reagents were dissolved in the corresponding solvent before diethylzinc (0.1–1.1 equiv, depending on the experiment) is added as a commercially available 1.0 M solution in hexanes (or as a freshly prepared dilution of that solution in anhydrous hexane, if necessary). The resulting mixture was stirred at the corresponding temperature for 16 h, before water was added. The mixture is extracted with $Et_2O$, and after removal of the solvent in vacuum, the resulting residue was analyzed by $^1$H NMR. The products may be purified by flash column or preparative TLC on silica gel if required.



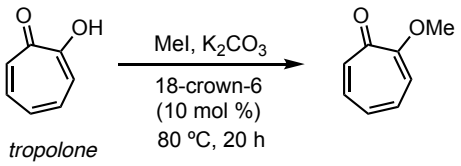

The (4+2) adduct **70** (colorless oil)[146] was isolated and purified (by flash column chromatography in cyclohexane), and the enantiomeric ratio of the different reactions was determined by SFC using an OJ chiral column and MeOH/$CO_2$ (85:15) as mobile phase (2 mL/min). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.30 – 7.26 (m, 1H), 7.14 – 7.08 (m, 2H), 7.01 – 6.96 (m, 1H), 6.28 (d, *J* = 2.6 Hz, 1H), 2.57 (dd, *J* = 18.0, 6.5 Hz, 1H), 2.47 (d, *J* = 9.6 Hz, 1H), 2.39 – 2.30 (m, 1H), 1.93 – 1.85 (m, 2H), 1.55 (dd, *J* = 10.4, 4.9 Hz, 2H), 1.41 (s, 3H), 0.89 (s, 3H).

145 For the characterization of the products and the original results obtained with gold catalysis, see: Nieto-Oberhuber, C.; Muñoz, M. P.; López, S.; Jiménez-Núñez, E.; Nevado, C.; Herrero-Gómez, E.; Raducan, M.; Echavarren, A. M. Gold(I)-Catalyzed Cyclizations of 1,6-Enynes: Alkoxycyclizations and *exo*/*endo* Skeletal Rearrangements. *Chem. Eur. J.* **2006**, *12*, 1677–1693 (and references therein).

146 Zuccarello, G.; Mayans, J. G.; Escofet, I.; Scharnagel, D.; Kirillova, M. S.; Pérez-Jimeno, A. H.; Calleja, P.; Boothe, J. R.; Echavarren, A. M. Enantioselective Folding of Enynes by Gold(I) Catalysts with a Remote C2-Chiral Element. *J. Am. Chem. Soc.* **2019**, *141*, 11858–11863.

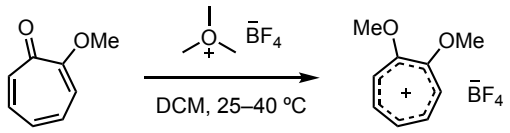
**Synthesis and Reactivity of New Tropylium Salts**

**2-Methoxycyclohepta-2,4,6-trien-1-one (49)**




To a 250 mL two necked round-bottom flask with a Teflon-coated magnetic stirring bar, fitted with a reflux condenser, was added 2-hydroxycyclohepta-2,4,6-trien-1-one (2.2 g, 18.0 mmol), potassium carbonate (7.47 g, 54 mmol) and 18-crown-6 (0.48 g, 1.80 mmol, 10 mol %) before submitting it to three vacuum-Ar cycles. Then, dry Acetonitrile (90 mL) was added, and the resulting yellow suspension was stirred at 80 ºC for 18 h. The mixture was cooled down to room temperature, filtered, and then the filtrate concentrated in vacuum (*careful, MeI*). The resulting residue was redissolved in dichloromethane, washed with water once, with $K_2CO_3$ aqueous saturated solution once, dried over $Na_2SO_4$, concentrated in vacuum and purified by CombiFlash chromatography, giving 2-methoxycyclohepta-2,4,6-trien-1-one (1.9 g, 13.96 mmol, 77% yield) as a pale-orange oil. Characterization data matched previously reported ones.

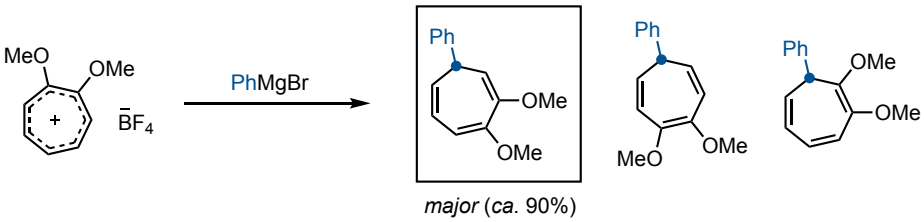
**1,2-Dimethoxytropylium tetrafluoroborate (50)**




A 50 mL round-bottom flask with a magnetic stirring bar was charged with 2-methoxycyclohepta-2,4,6-trien-1-one (1.00 g, 7.34 mmol) and introduced in the glovebox, where the starting material was dissolved in 10 mL of anhydrous dichloromethane, before tetrafluoro(trimethyl-l4-oxidanyl)-l5-borane (Meerwein's salt, 1.20 g, 8.08 mmol) was added as a suspension in 10 mL of dichloromethane (although the opposite procedure would be more advisable, since the Meerwein's salt is not soluble in dichloromethane). The flask was closed with a septum, taken out of the glovebox, and the resulting suspension was stirred for 1.5 h at 25 ºC under argon. Then, the mixture was warmed up to 40 ºC and further stirred for another 2 h. The warm mixture is filtered through a filtering plate and the filtrate was collected. Dry $Et_2O$ (30 mL) was added slowly to the filtrate, resulting in the precipitation of an off-white solid. HPLC-grade MeOH (*ca.* 2 mL) was added, and the mixture was swirled in order to quench any remaining Meerwein's salt. The solid was collected by filtration, washed twice with 5 mL of $Et_2O$ and then dried in high vacuum, giving the title compound (1.4 g, 5.88 mmol,

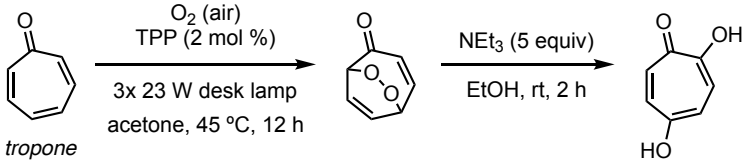
80% yield) as a white solid, apparently stable under air over several weeks. **$^{1}$H NMR** (500 MHz, $CD_3CN$) δ 8.61 – 8.52 (m, 2H), 8.33 (d, *J* = 11.2 Hz, 2H), 8.22 (d, *J* = 9.6 Hz, 1H), 4.31 (s, 6H). **$^{13}$C NMR** (126 MHz, $CD_3CN$) δ 169.37, 147.66, 139.11, 128.45, 59.65. **$^{19}$F NMR** (471 MHz, $CD_3CN$) δ -151.76. **MS** (ESI Positive): calculated for $C_9H_{11}O_2$ $[M\text{-}BF_4]^+$: 151.1; found: 151.1. **MP** 126–129 ºC.

**2,3-Dimethoxy-7-phenylcyclohepta-1,3,5-triene (major regioisomer) (51)**




In a 50 mL round-bottom flask, a solution of 1,2-dimethoxytropylium tetrafluoroborate (0.50 g, 2.10 mmol) in anhydrous THF (14 mL) was cooled down to -78 ºC, under argon. To the solution was added dropwise a commercial solution of phenylmagnesium bromide in THF (1.0 M, 2.52 mL, 2.52 mmol, 1.2 equiv). The resulting mixture was stirred while slowly coming to room temperature overnight. Water was added, and the mixture was extracted twice with $Et_2O$, dried over anhydrous $Na_2SO_4$. After removal of the solvent, CombiFlash chromatography gave 2,3-dimethoxy-7-phenylcyclohepta-1,3,5-triene (0.47 g, 2.06 mmol, 98% yield) as a yellow solid. **$^{1}$H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 4H), 7.33 – 7.28 (m, 1H), 6.11 (ddd, *J* = 9.3, 6.3, 1.6 Hz, 1H), 5.97 (d, *J* = 6.3 Hz, 1H), 5.67 (dd, *J* = 9.3, 5.4 Hz, 1H), 4.86 (d, *J* = 6.5 Hz, 1H), 3.81 (s, 3H), 3.64 (s, 3H), 3.13 (t, *J* = 5.9 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 155.45, 149.47, 144.36, 129.16, 128.71, 127.62, 126.59, 122.56, 105.40, 104.32, 55.97, 55.26, 41.49.

**2,5-Dihydroxycyclohepta-2,4,6-trien-1-one (53)**

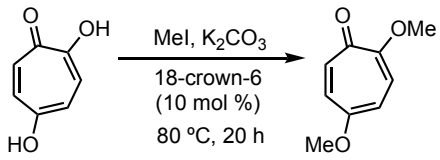



**Photocycloaddition:** A 25 mL glass culture tube was charged, open to air, with cyclohepta-2,4,6-trien-1-one (tropone, 0.25 g, 2.36 mmol) and 5,10,15,20-tetraphenylporphyrin (29 mg, 0.047 mmol, 2 mol %), and both were dissolved in HPLC-grade acetone (8 mL). The mixture was vigorously stirred (1200 rpm) while pointing three 23 W halogen desk lamps at the reaction vessel over 12 h (covering the sides with aluminum foil to increase efficiency). The solvent was removed and the product was purified by CombiFlash chromatography (7:3 to 1:1

cyclohexane/EtOAc) giving 6,7-dioxabicyclo[3.2.2]nona-3,8-dien-2-one (0.275 g, 1.89 mmol, 80% yield; *note: yield decreased down to 40% when the reaction time was increased to 60 h*) as a purple oil, due to contamination with roughly 2 mol % of porphyrin, which was used directly in the next step. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.13 – 7.01 (m, 2H), 6.54 (ddd, *J* = 8.8, 7.7, 1.0 Hz, 1H), 6.05 (ddd, *J* = 11.0, 2.3, 0.8 Hz, 1H), 5.11 (dddd, *J* = 9.2, 7.4, 1.7, 0.9 Hz, 1H), 5.03 (dddd, *J* = 7.7, 2.3, 1.5, 0.9 Hz, 1H).

**Peroxide cleavage:** A 25 mL round-bottom flask was charged with a solution of 6,7-dioxabicyclo[3.2.2]nona-3,8-dien-2-one (0.20 g, 1.45 mmol) (contaminated with *ca.* 2 mol % of porphyrin) in HPLC-grade ethanol (7 mL) under air, and to the resulting mixture, triethylamine (1.00 mL, 7.24 mmol) was added over *ca.* 30 sec. The mixture evolved rapidly from purple to dark orange-brown, and heated up significantly, so it was cooled down with an ice bath, and it was allowed to stir while comming to room temperature over 2 h. When TLC showed full conversion of the starting peroxide, which gave rise to a new very polar spot (Rf = 0.05 in EtOAc), the solvent and triethylamine were remove in vacuum. 2,5-Dihydroxycyclohepta-2,4,6-trien-1-one (yield not determined, but *ca.* quantitative) was purified by flash column chromatography in $SiO_2$ using a gradient between EtOAc and EtOAc/MeOH 8:2. **$^1$H NMR** (300 MHz, $CD_3CN$) δ 7.24 (dt, *J* = 11.8, 1.3 Hz, 2H), 7.04 (dt, *J* = 11.8, 1.3 Hz, 2H).

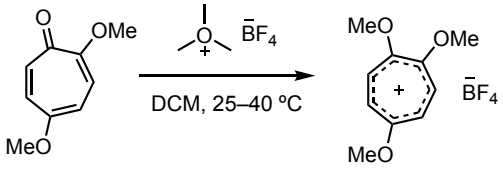
**2,5-Dimethoxycyclohepta-2,4,6-trien-1-one (54)**




A 50 mL round-bottom flask with a Teflon-coated magnetic stirring bar was charged with 2,5-dihydroxycyclohepta-2,4,6-trien-1-one (0.22 g, 1.59 mmol), potassium carbonate (1.10 g, 7.96 mmol) and 18-crown-6 (42 mg, 0.159 mmol, 10 mol %), and introduced in the glovebox. Then, dry acetonitrile (8 mL) was added, and the flask was fitted with a septum and taken out of the glovebox. Then iodomethane (0.51 mL, 7.96 mmol) was added and the flask was fitted with a reflux condenser. The resulting yellow suspension was stirred at 80 ºC for 14 h. The mixture was cooled down to room temperature and concentrated in vacuum (*careful, MeI*). The resulting residue was redissolved in dichloromethane, washed with water once, with brine once, dried over anhydrous $Na_2SO_4$, concentrated and dried in high vacuum, giving a brown-purple solid (due to traces of porphyrin). The solid was triturated in 9:1 pentane/$Et_2O$ and sonicated for half an hour to give, after filtration, 2,5-dimethoxycyclohepta-2,4,6-trien-1-one (0.188 g, 1.13 mmol, 71% yield) as a pale brown solid. **$^1$H NMR** (500 MHz, $CD_3CN$) δ 7.06

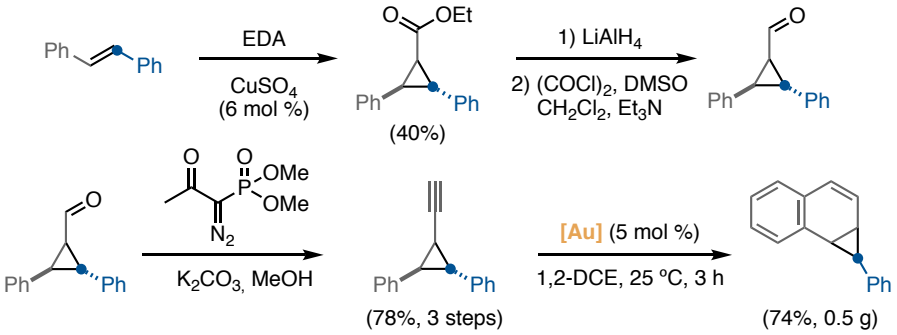
(dd, *J* = 13.2, 2.9 Hz, 1H), 7.00 (d, *J* = 13.2 Hz, 1H), 6.84 (d, *J* = 10.8 Hz, 1H), 6.44 (dd, *J* = 10.8, 2.9 Hz, 1H), 3.79 (s, 3H), 3.74 (s, 3H). **$^{13}$C NMR** (126 MHz, $CD_3CN$) δ 179.13, 160.15, 159.15, 137.13, 132.74, 114.03, 107.94, 70.46, 55.92, 55.74.

**1,2,5-Trimethoxytropylium tetrafluoroborate (55)**

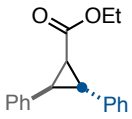



A 25 mL round-bottom flask with a magnetic stirring bar was introduced in the glovebox and charged with tetrafluoro(trimethyl-l4-oxidanyl)-l5-borane (Meerwein's salt, 0.166 g, 1.12 mmol), which was suspended in anhydrous dichloromethane (3.5 mL), before 2,5-dimethoxycyclohepta-2,4,6-trien-1-one (0.17 g, 1.02 mmol) was added directly as a solid, in a single portion. The flask was fitted with a septum, taken out of the glovebox and the resulting green suspension was stirred for 30 min at 25 ºC under argon. Then, the mixture was warmed up to 40 ºC and further stirred for another 2 h. The warm mixture is filtered through a filtering plate and the filtrate was collected. To the filtrate, dry Et2O (5 mL) was added slowly, resulting in the precipitation of an off-white solid. MeOH (0.2 mL) was added, and the mixture was swirled in order to quench any remaining Meerwein's salt. The solid was collected by filtration, washed twice with 3 mL of $Et_2O$ and then dried in high vacuum, giving (0.240 g, 0.91 mmol, 89% yield) as a greenish solid. **$^{1}$H NMR** (500 MHz, $CD_3CN$) δ 8.30 – 8.26 (m, 2H), 8.07 (dt, *J* = 12.6, 1.8 Hz, 2H), 4.23 (d, *J* = 0.6 Hz, 6H), 4.11 (s, 3H). **$^{13}$C NMR** (126 MHz, $CD_3CN$) δ 168.73, 163.88, 132.02, 129.82, 58.89, 58.15. **$^{19}$F NMR** (471 MHz, $CD_3CN$) δ -151.84.

**Synthesis of Carbene Precursors based on the Release of Naphthalene**

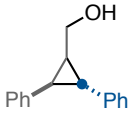



**Ethyl 2,3-diphenylcyclopropane-1-carboxylate (80)**



A dry two-necked 100 mL round-bottomed flask with a magnetic stirring bar was charged with (*E*)-1,2-diphenylethene (6.56 g, 36.4 mmol, 1.5 equiv) and $CuSO_4$ (232 mg, 1.46 mmol, 6 mol %), under Ar atmosphere. Both solids were dissolved in anhydrous toluene (30 mL, 0.8 M), and the resulting solution was heated to 75 ºC. After that, ethyl 2-diazoacetate (3 mL, 24.2 mmol, 1 equiv, 85% w/w commercial solution with $CH_2Cl_2$) was added by automatic syringe pump over 8 h (*ca.* 0.4 mL/h), while stirring at 75 ºC. After stirring for s total time of 18 hours, the reaction was allowed to cool down to room temperature and the solvent was removed in vacuum. CombiFlash chromatography in $SiO_2$, using a gradient from cyclohexane to cyclohexane/EtOAc 8:2 as eluent, giving ethyl (*exo*)-2,3-diphenylcyclopropane-1-carboxylate **80** (2.6 g, 24.2 mmol, 40% yield) as a yellow oil. Characterization data matched the reported ones for this product.[147] **$^1$H NMR** (500 MHz, $CDCl_3$) 7.30 – 7.20 (m, 6H), 7.19 – 7.13 (m, 4H), 3.88 (qd, $J$ = 7.1, 1.8 Hz, 2H), 3.14 (dd, $J$ = 7.0, 5.2 Hz, 1H), 2.85 (dd, $J$ = 9.5, 7.1 Hz, 1H), 2.34 (dd, $J$ = 9.6, 5.2 Hz, 1H), 0.96 (t, $J$ = 7.2 Hz, 3H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 170.1, 139.8, 136.3, 129.3, 128.7, 128.2, 127.0, 126.8, 126.8, 60.6, 34.6, 31.4, 29.4, 14.2 ppm.

**(2,3-Diphenylcyclopropyl)methanol**

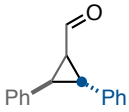


A two-necked 250 mL round-bottomed flask with a magnetic stirring bar was charged, under Ar, with $LiAlH_4$ (534 mg, 14.1 mmol, 1.5 equiv), and it was suspended in anhydrous THF (40 mL, 0.2 M). After cooling down the suspension to 0 ºC in an ice-water bath, a solution of ethyl 2,3-diphenylcyclopropane-1-carboxylate **80** (2.5 g, 9.4 mmol, 1 equiv) in 7 mL of anhydrous THF was added dropwise over 5 min, and

147 Scholz, S. O.; Farney, E. P.; Kim, S.; Bates, D. M.; Yoon, T. P. Spin-Selective Generation of Triplet Nitrenes: Olefin Aziridination through Visible-Light Photosensitization of Azidoformates. *Angew. Chem. Int. Ed.*, **2016**, **55**, 2239–2242.

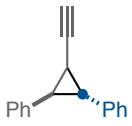
then the cooling bath was removed. The resulting suspension was stirred for 16 h while coming to room temperature, when no starting material was observed by TLC. The reaction was cooled down again to 0 ºC in an ice-water bath, and was quenched by careful addition of water, and then aqueous (10%) HCl. The aqueous phase was extracted twice with $Et_2O$, and the combined organic fractions were washed with water once, with brine once, dried over anhydrous $Na_2SO_4$ and concentrated in vacuum giving (2,3-diphenylcyclopropyl)methanol (*ca.* quantitative yield, 2.1 g) as a yellow oil, used on the next step without further purification. Characterization data matched the reported ones for this product.[147] **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.25 (dtd, *J* = 11.0, 6.8, 1.8 Hz, 6H), 7.18 – 7.09 (m, 4H), 3.58 (dd, *J* = 11.7, 6.2 Hz, 1H), 3.41 (dd, *J* = 11.7, 8.2 Hz, 1H), 2.55 (dd, *J* = 9.2, 5.6 Hz, 1H), 2.34 (t, *J* = 5.4 Hz, 1H), 1.83 (dddd, *J* = 9.3, 8.2, 6.2, 5.2 Hz, 1H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.6, 137.7, 128.9, 128.6, 126.7, 126.4, 126.2, 62.3, 31.8, 31.4, 26.5 ppm.

**2,3-Diphenylcyclopropane-1-carbaldehyde (81)**



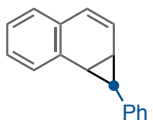

A dry 500 mL round-bottomed flask was charged under argon with a solution of dimethylsulfoxide (2.0 mL, 27.6 mL, 3.1 equiv) in dichloromethane (130 mL). After cooling this solution to -78 ºC, oxalyl chloride (1.6 mL, 18.72 mmol, 2.1 equiv) was added dropwise. After 30 min, a solution of (2,3-diphenylcyclopropyl)methanol (2.0 g, 8.92 mmol, 1 equiv) in dichloromethane (20 mL) was added. The mixture was stirred at -78 ºC for 1 h. After that, triethylamine (5 mL, 35.7 mmol, 4 equiv) was added to the mixture and it was maintained for 15 min at -78 ºC then it was allowed to warm to room temperature. The mixture was diluted with dichloromethane and water was added, and the mixture was extracted three times with dichloromethane. Combined organic fractions were washed with water and with brine, dried over $Na_2SO_4$ and concentrated under vacuum giving 2,3-diphenylcyclopropane-1-carbaldehyde (**81**) (*ca.* quantitative yield, 1.9 g) as an orange oil, used on the next step without further purification. Characterization data matched the reported ones for this product.[147] **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.88 (d, *J* = 6.3 Hz, 1H), 7.39 – 7.24 (m, 6H), 7.24 – 7.12 (m, 4H), 3.29 (dd, *J* = 6.9, 4.8 Hz, 1H), 3.12 (dd, *J* = 9.4, 6.7 Hz, 1H), 2.41 (ddd, *J* = 9.2, 6.3, 4.8 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 199.2, 138.5, 135.5, 129.3, 128.9, 128.8, 127.6, 127.2, 126.8, 39.9, 35.1, 29.9 ppm.

**(3-Ethynylcyclopropane-1,2-diyl)dibenzene (82)**




A modified reported procedure was followed.[148] A 250 mL round-bottomed flask was charged under air with a suspension of crude 2,3-diphenylcyclopropane-1-carbaldehyde **81** (1.9 g, 8.55 mmol, 1 equiv) and potassium carbonate (3.5 g, 25.6 mmol, 3 equiv) in HPLC-grade MeOH (71 mL, 0.12 M). Dimethyl (1-diazo-2-oxopropyl)phosphonate (neat, 3.0 g, 15.6 mmol, 1.8 equiv) was added, and the resulting mixture was stirred for 1 h. After confirming complete conversion of **81**, water was added, and the mixture was extracted three times with diethyl ether. Combined organic fractions were washed with brine, dried over $Na_2SO_4$ and concentrated under vacuum. CombiFlash chromatography in $SiO_2$, using a gradient from cyclohexane to cyclohexane/EtOAc 97:3 as eluent gave (*exo*)-(3-ethynylcyclopropane-1,2-diyl)dibenzene (**82**) (1.4 g, 8.55 mmol, 78% overall yield over 3 steps) as a pale yellow solid. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.21 (m, 6H), 7.21 – 7.11 (m, 4H), 2.63 – 2.52 (m, 2H), 2.05 (ddd, *J* = 8.8, 5.5, 2.2 Hz, 1H), 1.87 (d, *J* = 2.2 Hz, 1H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 140.0, 137.1, 128.7, 128.5, 128.2, 126.8, 126.8, 126.4, 82.4, 69.7, 32.9, 32.7, 19.2 ppm. **HRMS** (ESI Pos): calc. for $C_{17}H_{15}$ $[M+H]^+$: 219.1168; found: 219.1179. **MP** 88–90 ºC.

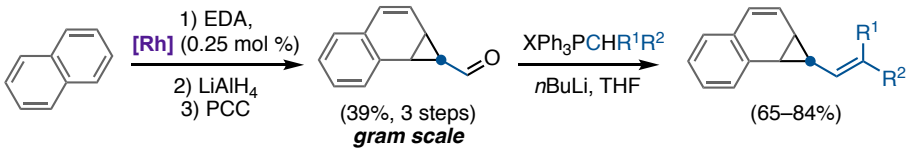
**1-Phenyl-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (83)**



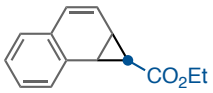

Under air, a 100 mL round-bottomed flask equipped with a magnetic stirring bar was charged (3-ethynylcyclopropane-1,2-diyl)dibenzene (**82**) (510 mg, 2.3 mmol, 1 equiv) and it was dissolved in HPLC-grade 1,2-DCE (23.4 mL, 0.1 M), before [(JohnPhos)Au(MeCN)]$SbF_6$ (5 mol %) was added. The resulting mixture was further stirred at room temperature for 3 h. After confirming complete conversion of (**82**), the resulting mixture was concentrated in vacuum and the crude product was purified by CombiFlash chromatography in $SiO_2$, using cyclohexane as eluent gave 1-phenyl-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (**83**) as a white solid. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.29 (m, 3H), 7.24 – 7.15 (m, 4H), 7.10 – 7.01 (m, 2H), 6.44 – 6.31 (m, 2H), 2.80 (dd, *J* = 7.9, 4.5 Hz, 1H), 2.39 (dtd, *J* = 7.9, 4.3, 1.0 Hz, 1H), 1.28 (t, *J* = 4.3 Hz, 1H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 142.8, 134.6, 130.8, 128.6, 128.4, 127.9, 127.9, 127.5, 126.3, 125.7, 125.4, 124.4, 32.5, 29.4, 26.9 ppm. **HRMS** (APCI Pos): calc. for $C_{17}H_{15}$ $[M+H]^+$: 219.1168; found: 219.1172. **MP** 74–77 ºC.

148 Hanessian, S.; Focken, T.; Mi, X.; Oza, R.; Chen, B.; Ritson, D.; Beaudegnies R. Total Synthesis of (+)-Ambruticin S: Probing the Pharmacophoric Subunit. *J. Org. Chem.*, **2010**, *75*, 5601–5618.

**Preparation of Alkenylcyclopropane Derivatives of Naphthalene**

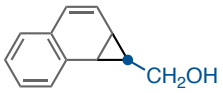



**Ethyl 1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene-1-carboxylate**




A two-necked 250 mL round-bottomed flask with a magnetic stirring bar was charged with naphthalene (25.9 g, 202 mmol, 5 equiv) and $Rh_2(TFA)_4$ (60 mg, 0.101 mmol, 0.25 mol %), under Ar atmosphere. Both solids were dissolved in anhydrous $CH_2Cl_2$ (67 mL, 0.6 M), and the resulting dark green solution was degassed by bubbling Ar through over 15 min. After that, ethyl 2-diazoacetate (5 mL, 40.4 mmol, 1 equiv, 85% w/w commercial solution with $CH_2Cl_2$) was added by automatic syringe pump over 18 h (0.3 mL/h), while stirring at 25 ºC. After stirring for one additional hour, the solvent was removed in vacuum, and the crude mixture was adsorbed into $SiO_2$, and then submitted to purification by CombiFlash column chromatography in $SiO_2$, eluting first with cyclohexane to remove excess naphthalene, and then with a slow gradient of cyclohexane/EtOAc from 95:5 to 85:15, giving ethyl 1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene-1-carboxylate (4.5 g, 20.8 mmol, 52%) as a colorless oil. Alternatively, the purification can be carried out more rapidly, giving a 7:1 mixture (77% of combined yield, based on ethyl diazoacetate) of the desired product and the formal insertion products (naphthalenes), which can be used in the next steps as is, and purified in later step of the synthetic route. Characterization data matched the reported ones for this product.[149] **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.42 – 7.39 (m, 1H), 7.24 – 7.18 (m, 2H), 7.13 – 7.11 (m, 1H), 6.39 (d, $J$ = 9.6 Hz, 1H), 6.29 (ddd, $J$ = 9.6, 5.0, 0.7 Hz, 1H), 4.18 (q, $J$ = 7.1 Hz, 2H), 3.07 (dd, $J$ = 8.3, 4.0 Hz, 1H), 2.66 – 2.59 (m, 1H), 1.27 (t, $J$ = 7.1 Hz, 3H), 0.84 (t, $J$ = 3.9 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 175.9, 133.0, 131.1, 129.1, 128.3, 128.0, 127.1, 126.3, 126.3, 61.3, 30.8, 27.9, 23.2, 14.7 ppm. **HRMS** (ESI Positive): calculated for $C_{14}H_{15}O_2$ $[M+H]^+$: 215.1067; found: 215.1069.

**1a,7b-Dihydro-1*H*-cyclopropa[*a*]naphthalen-1-yl)methanol**




A two-necked 250 mL round-bottomed flask with a magnetic stirring bar was charged under Ar, with $LiAlH_4$ (1.08 g, 28.4 mmol, 1.5 equiv), and it was suspended in anhydrous THF (50 mL, 0.12 M). After cooling down the suspension to 0 ºC in an ice-water bath, a solution of ethyl 1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene-1-

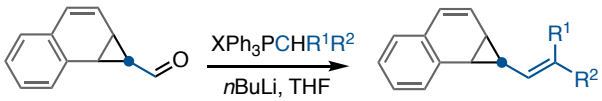
149 Pérez, P. J.; Díaz-Requejo, M. M.; Rivilla, I. Gold-catalyzed naphthalene functionalization. *Beilstein J. Org. Chem.*, **2011**, *7*, 653–657.

carboxylate (4.05 g, 18.9 mmol, 1 equiv) in 6 mL of anhydrous THF was added dropwise over 5 min, and then the cooling bath was removed. The resulting suspension was stirred for 14 h while coming to room temperature, when no starting material was observed by TLC. The reaction was cooled down again to 0 ºC in an ice-water bath, and was quenched by careful addition of water, and then aqueous (10%) HCl. The aqueous phase was extracted twice with $Et_2O$, and the combined organic fractions were washed with water once, with brine once, dried over anhydrous $Na_2SO_4$ and concentrated in vacuum. Fast filtration through $SiO_2$ washing with EtOAc gave (1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalen-1-yl)methanol (*ca.* quantitative yield, 3.3 g) as a colorless oil, used on the next step without further purification. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.16 (dtd, *J* = 18.2, 7.3, 1.5 Hz, 2H), 7.08 (dd, *J* = 7.4, 1.7 Hz, 1H), 6.29 – 6.23 (m, 2H), 3.82 (dt, *J* = 11.7, 6.0 Hz, 1H), 3.70 (ddd, *J* = 11.6, 7.0, 5.1 Hz, 1H), 2.35 (dd, *J* = 7.9, 4.4 Hz, 1H), 1.93 (dtd, *J* = 8.0, 4.0, 1.6 Hz, 1H), 0.42 (tt, *J* = 6.8, 4.2 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 134.3, 131.1, 128.3, 128.0, 127.6, 127.6, 126.3, 124.5, 66.5, 25.9, 24.4, 23.1 ppm. **HRMS** (APCI Positive): calculated for $C_{12}H_{11}$ $[M\text{-}OH]^+$: 155.0855; found: 155.0852.

**1a,7b-Dihydro-1*H*-cyclopropa[*a*]naphthalene-1-carbaldehyde (84)**

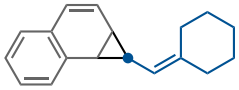
A 500 mL round-bottomed flask was charged under air with a solution of crude (1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalen-1-yl)methanol (3.3 g, 17 mmol, 1 equiv) in HPLC-grade $CH_2Cl_2$ (140 mL, 0.12 M). After cooling this solution to 0 ºC in an ice-water bath, was added pyridinium chlorochromate (7.34 g, 34 mmol, 2 equiv) in a single portion, and the resulting brown mixture was stirred while coming to room temperature for 14 h, when no starting material was observed by TLC. The mixture was filtered through Celite, concentrated in vacuum and then purified by CombiFlash chromatography in $SiO_2$ (95:5 to 9:1 cyclohexane/EtOAc gradient) to give 1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene-1-carbaldehyde (**84**) (1.6 g, 9.4 mmol, 38% overall yield over 3 steps) as a yellow oil. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 9.92 (d, *J* = 3.3 Hz, 1H), 7.45 – 7.41 (m, 1H), 7.29 – 7.26 (m, 2H), 7.22 – 7.18 (m, 1H), 6.50 (d, *J* = 9.6 Hz, 1H), 6.35 (ddd, *J* = 9.5, 5.1, 0.8 Hz, 1H), 3.29 (ddd, *J* = 8.4, 3.8, 0.7 Hz, 1H), 2.87 (dddd, *J* = 8.5, 5.1, 3.6, 0.6 Hz, 1H), 1.20 (q, *J* = 3.6 Hz, 1H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 202.7, 132.3, 130.9, 128.6, 128.2, 127.9, 127.1, 126.6, 125.8, 32.7, 31.2, 29.8 ppm. **HRMS** (APCI Positive): calculated for $C_{12}H_{11}O$ $[M+H]^+$: 171.0804; found: 171.0806.

**Wittig Reaction of Aldehyde (84) to Give Vinyl Cyclopropanes (85a–d)**



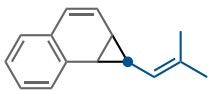

An alkyl phosphonium halide (1.3 equiv) was dried in high vacuum at 60 ºC for 4 h and, after cooling, it was suspended in anhydrous THF (0.2 M) under Ar. The suspension was cooled down to 0 ºC in an ice-water bath, and to this mixture was added dropwise a commercial solution of *n*-BuLi (2.5 M in hexanes, 1.4 equiv). After the addition, the mixture was stirred in the ice-water bath for 30 min, before 1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene-1-carbaldehyde (**84**) (1 equiv) was added as a solution in anhydrous THF (*ca.* 1 M). The mixture was stirred while coming to room temperature for 16–20 h. The reaction was quenched by the addition of aqueous $NH_4Cl$, and the aqueous phase was extracted twice with $Et_2O$. Combined organic fractions were washed with water once, with brine once, dried over anhydrous $Na_2SO_4$ and concentrated in vacuum. The products were purified by flash chromatography in $SiO_2$ or preparative TLC using pentane or cyclohexane as eluent.

**1-(Cyclohexylidenemethyl)-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (85a)**



The title compound (colorless oil, 136 mg, 65%) was prepared by Wittig reaction of aldehyde **84** (150 mg, 0.88 mmol, 1.0 equiv) using cyclohexyltriphenylphosphonium bromide (487 mg, 1.15 mmol, 1.3 equiv) after purification by CombiFlash chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.14 (dtd, *J* = 17.9, 7.3, 1.5 Hz, 2H), 7.06 (dd, *J* = 7.3, 1.6 Hz, 1H), 6.27 (dd, *J* = 9.6, 4.9 Hz, 1H), 6.21 (d, *J* = 9.6 Hz, 1H), 4.73 (dd, *J* = 9.1, 1.3 Hz, 1H), 2.34 (dd, *J* = 7.7, 4.3 Hz, 1H), 2.15 – 2.08 (m, 4H), 1.91 (dt, *J* = 8.1, 4.4 Hz, 1H), 1.53 (dd, *J* = 6.7, 3.5 Hz, 4H), 1.50 – 1.46 (m, 2H), 0.88 (ddd, *J* = 9.3, 4.9, 3.3 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.3, 134.9, 131.2, 128.4, 128.3, 127.8, 127.5, 126.1, 124.1, 122.9, 37.4, 30.0, 29.6, 28.9, 27.9, 27.2, 26.9, 21.9 ppm. **HRMS** (APCI Positive): calculated for $C_{18}H_{21}$ $[M+H]^+$: 237.1638; found: 237.1635.

**1-(2-Methylprop-1-en-1-yl)-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (85b)**



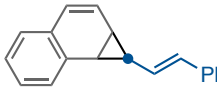
The title compound (colorless oil, 97 mg, 84%) was prepared by Wittig reaction of aldehyde **84** (100 mg, 0.59 mmol, 1.0 equiv) using isopropyltriphenylphosphonium iodide (330 mg, 0.76 mmol, 1.3 equiv) after purification by CombiFlash chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 7.1, 1.6 Hz, 1H), 7.14 (dtd, *J* = 16.5, 7.3, 1.6 Hz, 2H), 7.06 (dd, *J* = 7.3, 1.7 Hz, 1H), 6.29 – 6.20 (m, 2H), 4.80 (dp, *J* = 9.1, 1.4 Hz, 1H), 2.36 (dd, *J* = 7.7, 4.4 Hz, 1H),

1.92 (dddd, *J* = 7.6, 4.7, 3.8, 0.7 Hz, 1H), 1.74 (d, *J* = 1.4 Hz, 3H), 1.64 (d, *J* = 1.3 Hz, 3H), 0.85 (dt, *J* = 9.0, 4.1 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 134.9, 133.1, 131.2, 128.4, 128.2, 127.8, 127.5, 126.1, 126.1, 124.1, 29.8, 26.7, 26.2, 22.7, 18.7 ppm. **HRMS** (APCI Positive): calculated for $C_{15}H_{17}$ $[M+H]^+$: 197.1325; found: 197.1320.

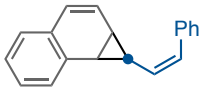
**1-(Styryl)-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene, *E* (85c) and *Z* (85d)**

The title compounds (white viscous oils, 196 mg, 68%, 2:1 *E*:*Z*) were prepared by Wittig reaction of aldehyde **84** (200 mg, 1.17 mmol, 1.0 equiv) using benzyltriphenylphosphonium chloride (548 mg, 1.41 mmol, 1.2 equiv) after purification by CombiFlash chromatography in $SiO_2$ using cyclohexane as eluent. Preparative TLC in $SiO_2$ using pentane as eluent allowed isolating each diastereoisomer separately (**85c** = *E*, bottom fraction, **85d** = *Z*, top fraction).

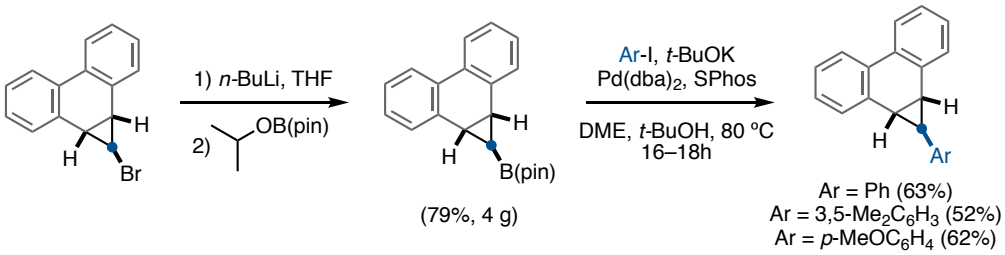
**1-((*E*)-Styryl)-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (85c) $^1$H NMR** (500 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 7.1, 1.7 Hz, 1H), 7.34 – 7.27 (m, 4H), 7.21 – 7.15 (m, 3H), 7.10 (dd, *J* = 7.3, 1.7 Hz, 1H), 6.41 (d, *J* = 15.8 Hz, 1H), 6.32 – 6.28 (m, 2H), 5.99 (dd, *J* = 15.7, 9.1 Hz, 1H), 2.61 (dd, *J* = 7.9, 4.3 Hz, 1H), 2.20 (dtd, *J* = 7.0, 3.7, 2.4 Hz, 1H), 0.98 (dt, *J* = 9.3, 4.0 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 137.8, 134.2, 132.5, 131.1, 129.1, 128.9, 128.4, 128.0, 127.7, 127.5, 127.1, 126.4, 126.0, 124.7, 31.2, 27.4, 26.8 ppm. **HRMS** (APCI Positive): calculated for $C_{19}H_{17}$ $[M+H]^+$: 245.1325; found: 245.1321.




**1-((*Z*)-Styryl)-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (85d) $^1$H NMR** (500 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 7.3, 1.5 Hz, 1H), 7.29 – 7.26 (m, 2H), 7.25 – 7.21 (m, 2H), 7.18 (td, *J* = 7.4, 1.6 Hz, 1H), 7.14 (td, *J* = 7.3, 1.6 Hz, 2H), 7.07 (dd, *J* = 7.5, 1.6 Hz, 1H), 6.47 (d, *J* = 11.4 Hz, 1H), 6.37 – 6.23 (m, 2H), 5.37 (dd, *J* = 11.5, 9.6 Hz, 1H), 2.56 (dd, *J* = 7.8, 4.3 Hz, 1H), 2.15 – 2.11 (m, 1H), 1.21 (dtd, *J* = 9.5, 4.1, 1.1 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 137.7, 134.1, 134.1, 131.1, 129.5, 128.9, 128.5, 128.5, 128.0, 127.6, 127.2, 126.9, 126.4, 124.9, 31.1, 27.9, 23.7 ppm. **HRMS** (APCI Positive): calculated for $C_{19}H_{17}$ $[M+H]^+$: 245.1325; found: 245.1321.



**Preparation of Aryl Cyclopropyl Dihydrophenanthrenes (90a–c)**

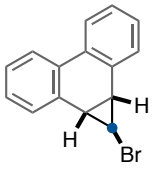



(79%, 4 g)

Ar = Ph (63%)
Ar = 3,5-$Me_2C_6H_3$ (52%)
Ar = *p*-$MeOC_6H_4$ (62%)

**1-Bromo-1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene (88)**

1,1-Dibromo-1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene was prepared in multigram scale by the treatment of phenanthrene with $CHBr_3$ and aqueous NaOH in $CH_2Cl_2$/EtOH (40:1), in the presence of 1 mol % of benzyltriethylammonium chloride, according to a reported procedure.[150]

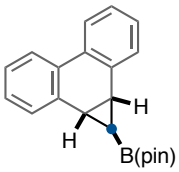



A two-necked 50 mL round-bottomed flask with a magnetic stirring bar was charged under Ar, with 1,1-dibromo-1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene (3.5 g, 10.0 mmol, 1 equiv), and it was suspended in anhydrous THF (40 mL, 0.25 M). After cooling down the suspension to -78 ºC, *n*-BuLi (4.4 mL, 2.5 M in hexane, 11.0 mmol, 1.1 equiv) was slowly added and the reaction was stirred for 1 h. Then, methanol (0.8 mL, 20.0 mmol, 2.0 equiv) was added and the reaction was allowed to warm to room temperature. The reaction was further quenched by the addition of water. The aqueous phase was extracted twice with $CH_2Cl_2$, and the combined organic fractions were washed with brine once, dried over anhydrous $Na_2SO_4$ and concentrated in vacuum. The crude product was purified by CombiFlash chromatography in $SiO_2$ using cyclohexane to give 1-bromo-1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene (**88**) (1.7 g, 10.0 mmol, 63% yield) as a white solid. Characterization data matched the reported ones for this product.[151] **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.97 – 7.92 (m, 2H), 7.52 – 7.46 (m, 2H), 7.35 – 7.26 (m, 4H), 3.01 (d, *J* = 3.1 Hz, 2H), 2.42 (t, *J* = 3.1 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 131.9, 129.8, 129.3, 128.1, 127.2, 123.3, 29.9, 27.7 ppm.

150 Nguyen, J. M.; Thamattoor, D. M. A Simple Synthesis of 1,1-Dibromo-1a,9b-dihydrocyclopropa-[*l*]phenanthrene. *Synthesis*, **2007**, *14*, 2093–2094.

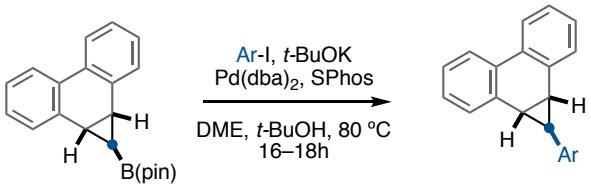
151 Graves, K. S.; Thamattoor, D. M.; Rablen, P. R. Experimental and Theoretical Study of the 2-Alkoxyethylidene Rearrangement. *J. Org. Chem.*, 2011, **76**, 1584–1591.

**2-(1a,9b-Dihydro-1*H*-cyclopropa[*l*]phenanthren-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (89)**




A two-necked 500 mL round-bottomed flask with a magnetic stirring bar was charged under Ar, with 1-bromo-1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene (4.0 g, 14.8 mmol, 1 equiv), and it was suspended in anhydrous THF (180 mL, 0.08 M). After cooling down the suspension to -78 ºC, *n*-BuLi (8.85 mL, 2.5 M in hexanes, 22.1 mmol, 1.5 equiv) was slowly added and the reaction was stirred for 1 h. Then, 2-isopropoxy-4,4,5,5- tetramethyl-1,3,2-dioxaborolane (4.5 mL, 22.1 mmol, 1.5 equiv) was added at -78 ºC. The reaction was stirred for 2 h while warming to room temperature. The reaction was quenched by the addition of a saturated solution of ammonium chloride. The aqueous phase was extracted twice with diethyl ether, and the combined organic fractions were washed with brine once, dried over anhydrous $Na_2SO_4$ and concentrated in vacuum, giving a pale yellow solid. The product was purified by trituration and washing with MeOH (3x10 mL), which was then removed by filtration to give pure 2-(1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthren-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**89**) (3.7 g, 14.75 mmol, 79% yield) as a white solid. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.99 – 7.93 (m, 2H), 7.46 – 7.42 (m, 2H), 7.28 – 7.18 (m, 4H), 2.77 (d, *J* = 5.3 Hz, 2H), 1.27 (s, 12H), -0.59 (t, *J* = 5.3 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 136.6, 129.5, 129.3, 127.6, 126.2, 123.3, 83.5, 26.2, 24.9 ppm. **HRMS** (APCI Positive): calculated for $C_{21}H_{24}BO_2$ $[M+H]^+$: 318.1900; found: 318.1903. **MP** 163–168 ºC.

**Suzuki Coupling for the Synthesis of Aryl Cyclopropyl Dihydrophenanthrenes**

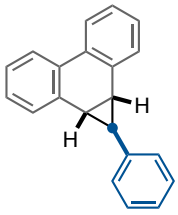



This procedure was adapted from a previously reported one.[152] A microwave vial was charged with $Pd(dba)_2$ (5 mol %), 2-di-cyclohexylphosphino-2',6'-dimethoxybiphenyl (10 mol %), boronic ester (**89**) (1 equiv), and an aryl iodide (3 equiv). The vial was introduced in an Ar-filled glovebox and *t*-BuOK (4 equiv) was added. The vial was sealed with its cap, and taken out of the glovebox before DME and *t*-BuOH (0.06 M, DME/*t*-BuOH 3:1) were added through the septum of the cap. The mixture was stirred at 80 ºC for 16–18 h. After cooling, the reaction

152 Murai, M.; Mizuta, C.; Taniguchi, R.; Takai, K. Synthesis of Borylcyclopropanes by Chromium-Promoted Cyclopropanation of Unactivated Alkenes. *Org. Lett.*, **2017**, *19*, 6104–6107.

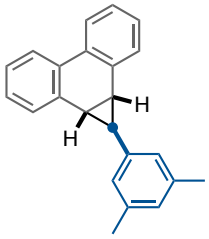
mixture was diluted with water, and extracted three times with EtOAc. The combined organic fractions were washed with brine, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography in $SiO_2$.

**1-Phenyl-1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene (90a)**



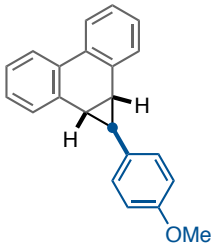
The title compound (white solid, 161 mg, 62%) was prepared by palladium-catalyzed Suzuki-Miyaura cross-coupling of boronic ester (**89**) (300 mg, 0.94 mmol, 1.0 equiv) with iodobenzene (577 mg, 2.83 mmol, 3 equiv), after purification by CombiFlash chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 7.8, 1.4 Hz, 2H), 7.42 (dd, *J* = 7.3, 1.7 Hz, 2H), 7.34 – 7.23 (m, 6H), 7.22 – 7.18 (m, 1H), 7.10 – 7.06 (m, 2H), 2.92 (d, *J* = 4.3 Hz, 2H), 1.40 (t, *J* = 4.3 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 142.5, 135.3, 129.7, 129.6, 128.9, 128.2, 126.8, 126.0, 125.7, 123.6, 31.7, 30.8 ppm. **HRMS** (APCI Positive): calculated for $C_{21}H_{17}$ $[M+H]^+$: 269.1325; found: 269.1318. **MP** 132–134 ºC.

**1-(3,5-Dimethylphenyl)-1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene (90b)**



The title compound (white solid, 144 mg, 52%) was prepared by palladium-catalyzed Suzuki-Miyaura cross-coupling of boronic ester (**89**) (300 mg, 0.94 mmol, 1.0 equiv) using 1-iodo-3,5-dimethylbenzene (656 mg, 2.83 mmol, 3 equiv) after purification by CombiFlash chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.43 (dd, *J* = 7.4, 1.7 Hz, 2H), 7.34 – 7.23 (m, 4H), 6.87 (s, 1H), 6.72 (s, 1H), 2.92 (d, *J* = 4.3 Hz, 2H), 2.33 (s, 6H), 1.36 (t, *J* = 4.3 Hz, 1H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 142.2, 138.2, 135.3, 129.5, 129.4, 127.9, 127.6, 126.6, 123.4, 123.3, 31.4, 30.6, 21.5 ppm. **HRMS (**APCI Positive): calculated for $C_{23}H_{21}$ $[M+H]^+$: 297.1638; found: 297.1634. **MP** 126–127 ºC.

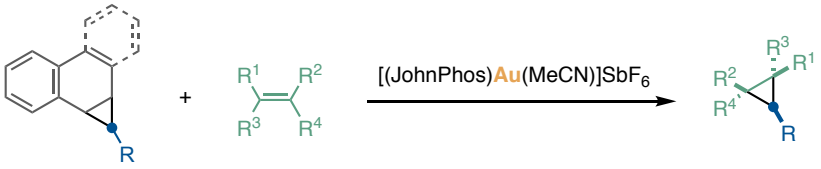
**1-(4-Methoxyphenyl)-1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene (90c)**




The title compound (white solid, 174 mg, 62%) was prepared by palladium-catalyzed Suzuki-Miyaura cross-coupling of boronic ester (**89**) (300 mg, 0.94 mmol, 1.0 equiv) using 4-iodoanisole (662 mg, 2.83 mmol, 3 equiv) after purification by CombiFlash chromatography in $SiO_2$ using cyclohexane/EtOAc 97:3 as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 7.7, 1.5 Hz, 2H), 7.43 (dd, *J* = 7.4, 1.6 Hz, 2H), 7.32 – 7.24 (m, 4H), 7.06 – 7.01 (m, 2H), 6.90 – 6.86 (m, 2H), 3.82 (s, 3H), 2.85 (d, *J* = 4.3 Hz, 2H), 1.38 (t, *J* = 4.3 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.1, 135.3, 134.0, 129.5, 129.4, 127.9, 126.5, 126.5, 123.4,

114.2, 55.5, 30.9, 29.9 ppm. **HRMS** (APCI Positive): calculated for $C_{22}H_{19}O$ $[M+H]^+$: 299.1430; found: 299.1424. **MP** 145–147 ºC.

**General Procedures C for the Au(I)-Catalyzed Cyclopropanation through Release of Polyaromatics**




**General Procedure C1:** [Au] (5 mol %), DCE, 80 ºC, 16–20 h
**General Procedure C2:** [Au] (10 mol %), DCE, 140–160 ºC (MW), 60 min

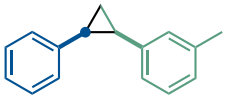
**General Procedure C1 (80 ºC)**: A microwave vial equipped with a Teflon-coated magnetic stirring bar was charged, under air, with the corresponding cyclopropyl dihydronaphthalene (**83** or **85**) (1.0 equiv) (or with alkyne **82** for the one-pot hydroarylation/decarbenation/ cyclopropanation sequence) and the corresponding alkene (3–6 equiv). Both reagents were dissolved in HPLC-grade 1,2-DCE (0.15 M), before [(JohnPhos)Au(MeCN)]$SbF_6$ (5 mol %) was added. The vial was closed with the cap and then stirred at 80 ºC for 16–20 hours, until complete consumption of the starting material, which was confirmed by TLC and GC-MS. The resulting mixture was concentrated in vacuum and the crude product was purified by flash column chromatography or preparative TLC on $SiO_2$. The configuration of the products was assigned by direct comparison or analogy with reported substrates, based on X-ray or nOe analysis.[153]

**General Procedure C2 (Microwave Heating, 140–160 ºC)**: A microwave vial equipped with a Teflon-coated magnetic stirring bar was charged, under air, with the corresponding aryl cyclopropyl dihydrophenanthrene (**90**) (1.0 equiv) and the corresponding alkene (2 equiv). Both reagents were dissolved in HPLC-grade 1,2-DCE (0.15 M), before [(JohnPhos)Au(MeCN)]$SbF_6$ (10 mol %) was added. The vial was closed with the cap and then stirred at 140–160 ºC for 60 min in a microwave reactor. The resulting mixture was concentrated in vacuum and the crude product was purified by flash column chromatography or preparative TLC on $SiO_2$. The configuration of the products was assigned by direct comparison or analogy with reported substrates, based on X-ray, $^1$H NMR, or nOe analysis.[153]

153 Solorio-Alvarado, C. R.; Wang, Y.; Echavarren, A. M. Cyclopropanation with Gold(I) Carbenes by Retro-Buchner Reaction from Cycloheptatrienes. *J. Am. Chem. Soc.* **2010**, *132*, 11881–11883. Correction of the relative configuration of some of the products: *J. Am. Chem. Soc.* **2017**, *139*, 2529.

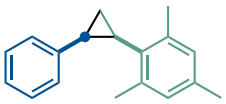
**Characterization Data for the Different Aryl (86) and Alkenyl (87) Cyclopropanes**

**(*cis*)-1-Methyl-3-(2-phenylcyclopropyl)benzene (86a)**



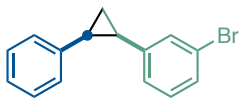
The title compound (colorless oil, 15 mg, 68% yield, 5:1 dr) was obtained following General Procedure C1 from 1-phenyl-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (**83**) (23 mg, 0.105 mmol) and 1-methyl-3-vinylbenzene (75 mg, 0.64 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (4.1 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.15 – 7.04 (m, 3H), 7.00 – 6.94 (m, 3H), 6.86 (d, *J* = 7.6 Hz, 1H), 6.81 (s, 1H), 6.75 – 6.67 (m, 1H), 2.47 (m, 2H), 2.20 (s, 3H), 1.46 (td, *J* = 8.6, 5.3 Hz, 1H), 1.36 (td, *J* = 6.3, 5.3 Hz, 1H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.6, 138.4, 137.2, 130.0, 129.1, 127.7, 127.6, 126.5, 125.9, 125.7, 24.4, 24.4, 21.5, 11.6 ppm. **HRMS** (APCI Positive): calculated for $C_{16}H_{17}$ $[M+H]^+$: 209.1325; found: 209.1319.

**(*cis*)-1,3,5-Trimethyl-2-(2-phenylcyclopropyl)benzene (86b)**



The title compound (colorless oil, 14 mg, 55% yield, 6:1 dr) was obtained following General Procedure C1 from 1-phenyl-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (**83**) (23 mg, 0.105 mmol) and 1,3,5-trimethyl-2-vinylbenzene (92 mg, 0.64 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (4.1 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.06 – 6.99 (m, 3H), 6.72 (s, 2H), 6.67 – 6.62 (m, 2H), 2.41 – 2.34 (m, 2H), 2.34 – 2.25 (m, 2H), 2.25 – 2.11 (m, 9H), 1.74 (td, *J* = 8.9, 5.4 Hz, 1H), 1.14 (dt, *J* = 7.6, 5.6 Hz, 1H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.2, 135.7, 130.9, 128.9, 127.5, 126.5, 125.1, 23.6, 23.1, 20.9, 20.8, 17.9 ppm. **HRMS** (APCI Positive): calculated for $C_{18}H_{21}$ $[M+H]^+$: 237.1638; found: 237.1633.

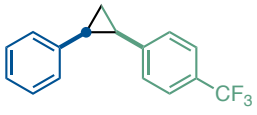
**(*cis*)-1-Bromo-3-(2-phenylcyclopropyl)benzene (86c)**




The title compound (colorless oil, 18 mg, 63% yield, 11:1 dr) was obtained following General Procedure C1 from 1-phenyl-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (**83**) (23 mg, 0.105 mmol) and 1-bromo-3-vinylbenzene (116 mg, 0.64 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (4.1 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. Alternatively, the same compound (60%, 6:1 dr) could be obtained following General Procedure C2 starting from phenanthrene derivative **90a**. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.20 – 7.09 (m, 4H), 7.10 – 7.06 (m, 1H), 6.98 – 6.94 (m, 2H), 6.91 (d, *J* = 7.8 Hz, 1H), 6.81 – 6.76 (m, 1H), 2.52 (td, *J* = 8.9, 6.4 Hz, 1H), 2.43 (td, *J* = 8.9, 6.2 Hz, 1H), 1.48 (td, *J* = 8.7, 5.6 Hz,

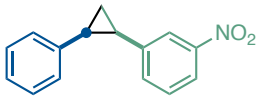
1H), 1.37 (q, $J$ = 6.1 Hz, 1H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.2, 137.8, 132.2, 129.2, 129.2, 128.8, 127.9, 127.5, 126.0, 121.9, 24.76, 23.9, 11.5 ppm. **HRMS** (APCI Positive): calculated for $C_{15}H_{14}Br$ $[M+H]^+$: 273.0273; found: 273.0263.

**(*cis*)-1-(2-Phenylcyclopropyl)-4-(trifluoromethyl)benzene (86d)**



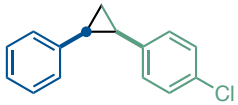

The title compound (colorless oil, 14 mg, 51% yield, 10:1 dr) was obtained following General Procedure C1 from 1-phenyl-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (**83**) (23 mg, 0.105 mmol) and 1-(trifluoromethyl)-4-vinylbenzene (109 mg, 0.64 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (4.1 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.32 (d, $J$ = 8.1 Hz, 2H), 7.16 – 7.04 (m, 3H), 7.02 – 6.93 (m, 4H), 2.59 (td, $J$ = 8.9, 6.4 Hz, 1H), 2.50 (td, $J$ = 8.9, 6.2 Hz, 1H), 1.58 – 1.52 (m, 1H), 1.42 (td, $J$ = 6.4, 5.5 Hz, 1H) ppm. **$^{19}$F NMR** (471 MHz, $CDCl_3$) δ -62.39 ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 143.1 (q, $J$ = 1.2 Hz), 137.5, 129.3, 128.9, 128.0, 127.7, 126.1, 125.5, 124.6 (q, $J$ = 3.8 Hz), 123.4, 121.2, 77.4, 25.1, 24.0, 11.9 ppm. **HRMS** (APCI Positive): calculated for $C_{16}H_{14}F_3$ $[M+H]^+$: 263.1042; found: 263.1033.

**(*cis*)-1-Nitro-3-(2-phenylcyclopropyl)benzene (86e)**




The title compound (viscous white oil, 11 mg, 41% yield, 8:1 dr) was obtained following General Procedure C1 from 1-phenyl-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (**83**) (23 mg, 0.105 mmol) and 1-nitro-3-vinylbenzene (94 mg, 0.64 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (4.1 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane/$Et_2O$ 97:3 as eluent. Alternatively, the same compound (52%, 7:1 dr) could be obtained following General Procedure C2 starting from phenanthrene derivative **90a**. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.88 (dt, $J$ = 7.6, 2.0 Hz, 1H), 7.84 – 7.78 (m, 1H), 7.25 – 7.15 (m, 2H), 7.14 – 7.09 (m, 2H), 7.08 – 7.03 (m, 1H), 6.99 – 6.93 (m, 2H), 2.63 (td, $J$ = 8.9, 6.4 Hz, 1H), 2.55 (td, $J$ = 8.9, 6.2 Hz, 1H), 1.61 – 1.55 (m, 1H), 1.50 (q, $J$ = 6.2 Hz, 1H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.1, 137.0, 134.9, 129.3, 128.5, 128.2, 126.4, 123.7, 120.9, 25.2, 23.8, 11.5 ppm. **HRMS** (APCI Pos): calculated for $C_{15}H_{12}NO_2$ $[M–H]^+$: 238.0863; found: 238.0857.

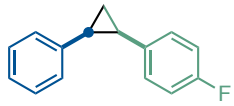
**(*cis*)-1-Chloro-4-(2-phenylcyclopropyl)benzene (86f)**




The title compound (colorless oil, 16 mg, 66% yield, 11:1 dr) was obtained following General Procedure C1 from 1-phenyl-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (**83**) (23 mg, 0.105 mmol) and 1-chloro-4-vinylbenzene (88 mg, 0.64 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (4.1

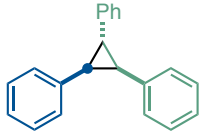
mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. Alternatively, the title compound (colorless oil, 12 mg, 57% yield, 12:1 dr) can be obtained in a one-pot procedure from (3-ethynylcyclopropane-1,2-diyl)dibenzene (**82**) (20 mg, 0.092 mmol) and 1-chloro-4-vinylbenzene (76 mg, 0.64 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (3.5 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.15 – 7.10 (m, 2H), 7.09 – 7.03 (m, 3H), 6.98 – 6.90 (m, 2H), 6.90 – 6.82 (m, 2H), 2.50 (td, *J* = 8.9, 6.3 Hz, 1H), 2.43 (td, *J* = 8.9, 6.3 Hz, 1H), 1.48 (td, *J* = 8.6, 5.5 Hz, 1H), 1.34 (td, *J* = 6.3, 5.5 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.0, 137.1, 130.3, 129.1, 127.9, 127.9, 125.9, 24.6, 23.8, 11.5 ppm. **HRMS** (APCI Positive): calculated for $C_{15}H_{14}Cl$ $[M+H]^+$: 229.0760; found: 229.0768.

**(*cis*)-1-Fluoro-4-(2-phenylcyclopropyl)benzene (86g)**




The title compound (colorless oil, 17 mg, 76% yield, 12:1 dr) was obtained following General Procedure C1 from 1-phenyl-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (**83**) (23 mg, 0.105 mmol) and 1-fluoro-4-vinylbenzene (77 mg, 0.64 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (4.1 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. Alternatively, the title compound (colorless oil, 12 mg, 62% yield, 12:1 dr) can be obtained in a one-pot procedure from (3-ethynylcyclopropane-1,2-diyl)dibenzene (**82**) (20 mg, 0.092 mmol) and 1-fluoro-4-vinylbenzene (67 mg, 0.55 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (3.5 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.18 – 7.02 (m, 3H), 6.95 – 6.86 (m, 4H), 6.83 – 6.74 (m, 2H), 2.46 (m, 2H), 1.47 (td, *J* = 8.6, 5.5 Hz, 1H), 1.33 (td, *J* = 6.2, 5.4 Hz, 1H) ppm. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -117.70 ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 161.1 (d, *J* = 243.5 Hz), 138.1, 133.9 (d, *J* = 3.0 Hz), 130.4 (d, *J* = 7.9 Hz), 128.8, 127.7, 125.6, 114.4 (d, *J* = 21.3 Hz), 24.0, 23.6, 11.4 ppm. **HRMS** (APCI Positive): calculated for $C_{15}H_{14}F$ $[M+H]^+$: 213.1074; found: 213.1069.

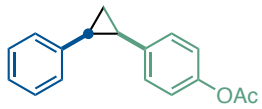
**(*exo*)-1,2,3-Triphenylcyclopropane (86h)**




The title compound (colorless oil, 20 mg, together with a 20% of product of phenyl cyclopropanation of **83**, 80% corrected yield) was obtained following General Procedure C1 from 1-phenyl-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (**83**) (23 mg, 0.105 mmol) and (*E*)-1,2-diphenylethene (114 mg, 0.64 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (4.1 mg, 5 mol %) after purification by CombiFlash chromatography in $SiO_2$ using cyclohexane as eluent. Alternatively, the title compound (colorless oil, 17 mg, together with a 20% of product of phenyl cyclopropanation of **83**, 71% corrected yield) can be obtained in a one-pot procedure from (3-

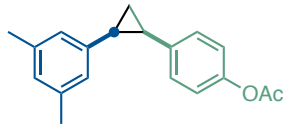
ethynylcyclopropane-1,2-diyl)dibenzene (**82**) (20 mg, 0.092 mmol) and (*E*)-1,2-diphenylethene (99 mg, 0.55 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (3.5 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.43 – 7.36 (m, 4H), 7.31 – 7.27 (m, 1H), 7.22 – 7.12 (m, 6H), 7.10 – 7.04 (m, 4H), 2.94 – 2.86 (m, 3H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 142.0, 137.7, 129.0, 128.6, 127.9, 126.5, 126.1, 126.0, 34.5, 30.7 ppm.

**(*cis*)-4-(2-Phenylcyclopropyl)phenyl acetate (86i)**



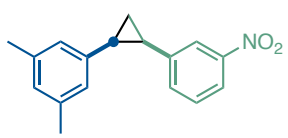

The title compound (viscous colorless oil, 21 mg, 54% yield, 10:1 dr) was obtained following General Procedure C1 from 1-phenyl-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (**83**) (32.7 mg, 0.150 mmol) and 4-vinylphenyl acetate (73 mg, 0.45 mmol, 3 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (4.1 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane/$Et_2O$ 9:1 as eluent. Alternatively, the same compound (36%, 1:1 dr) could be obtained following General Procedure C2 starting from phenanthrene derivative **90a**. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.17 – 7.07 (m, 3H), 6.99 – 6.94 (m, 4H), 6.88 – 6.82 (m, 2H), 2.50 (m, 2H), 2.25 (s, 3H), 1.51 (td, *J* = 8.6, 5.4 Hz, 1H), 1.40 – 1.33 (m, 1H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 169.4, 148.6, 138.1, 136.0, 129.9, 128.9, 127.7, 125.7, 120.7, 24.2, 23.8, 21.1, 11.7 ppm. **HRMS** (ESI Pos): calculated for $C_{17}H_{16}NaO_2$ $[M+Na]^+$: 275.1043; found: 275.1056.

**(*cis*)-4-(2-(3,5-Dimethylphenyl)cyclopropyl)phenyl acetate (86j)**




The title compound (viscous colorless oil, 14 mg, 59% yield, 3:1 dr) was obtained following General Procedure C2 from 1-(3,5-dimethylphenyl)-1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene (**90b**) (25 mg, 0.084 mmol) and 4-vinylphenyl acetate (27 mg, 0.17 mmol, 2 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (6.5 mg, 10 mol %) after purification by preparative TLC on $SiO_2$ using pentane/$Et_2O$ 97:3 as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$, *cis* isomer) δ 6.95 – 6.92 (m, 2H), 6.83 – 6.80 (m, 2H), 6.67 (s, 1H), 6.51 (d, *J* = 0.9 Hz, 2H), 2.43 – 2.35 (m, 2H), 2.22 (s, 3H), 2.13 (d, *J* = 0.7 Hz, 6H), 1.44 – 1.41 (m, 1H), 1.28 – 1.25 (m, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$, 3:1 *cis*/*trans*, unassigned) δ 169.8, 148.9, 138.4, 137.4, 136.7, 130.3, 127.7, 127.1, 123.9, 121.7, 120.9, 24.4, 24.0, 21.6, 21.5, 21.5, 12.2 ppm. **HRMS** (APCI Positive): calculated for $C_{19}H_{21}O_2$ $[M+H]^+$: 281.1536; found: 281.1536.

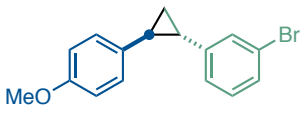
**(*cis*)-1,3-Dimethyl-5-(2-(3-nitrophenyl)cyclopropyl)benzene (86k)**




The title compound (colorless oil, 15 mg, 55% yield, 12:1 dr) was obtained following General Procedure C2 from 1-(3,5-

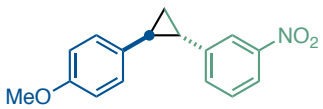
dimethylphenyl)-1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene (**90b**) (30 mg, 0.101 mmol) and 1-nitro-3-vinylbenzene (30 mg, 0.20 mmol, 2 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (7.8 mg, 10 mol %) after purification by preparative TLC on $SiO_2$ using pentane/$Et_2O$ 97:3 as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.88 (dt, *J* = 7.3, 2.1 Hz, 1H), 7.85 – 7.81 (m, 1H), 7.26 – 7.17 (m, 2H), 6.69 (s, 1H), 6.59 (s, 2H), 2.53 (m, 2H), 2.14 (s, 6H), 1.53 (td, *J* = 8.6, 5.7 Hz, 1H), 1.46 (q, *J* = 6.2 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.4, 137.5, 136.7, 134.9, 128.4, 128.0, 127.1, 123.6, 120.7, 25.2, 23.8, 21.3, 11.6 ppm. **HRMS** (APCI Positive): calculated for $C_{17}H_{16}NO_2$ $[M+H]^+$: 266.1176; found: 266.1173.

**(*trans*)-1-Bromo-3-(2-(4-methoxyphenyl)cyclopropyl)benzene (86l)**



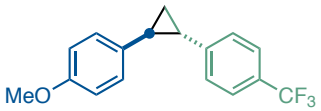

The title compound (colorless oil, 29 mg, 94% yield, 15:1 dr) was obtained following General Procedure C2 from 1-(4-methoxyphenyl)-1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene (**90c**) (30 mg, 0.101 mmol) and 1-bromo-3-vinylbenzene (37 mg, 0.20 mmol, 2 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (7.8 mg, 10 mol %) after purification by preparative TLC on $SiO_2$ using pentane/$Et_2O$ 98:2 as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.31 (ddd, *J* = 7.9, 2.0, 1.1 Hz, 1H), 7.27 (t, *J* = 1.9 Hz, 1H), 7.15 (t, *J* = 7.8 Hz, 1H), 7.10 – 7.04 (m, 3H), 6.89 – 6.82 (m, 2H), 3.80 (s, 3H), 2.13 (ddd, *J* = 8.8, 6.1, 4.5 Hz, 1H), 2.05 (ddd, *J* = 8.6, 5.9, 4.5 Hz, 1H), 1.40 (m, 2H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.2, 145.4, 134.1, 130.0, 128.9, 128.8, 127.1, 124.7, 122.7, 114.1, 55.5, 27.7, 27.2, 17.9 ppm. **HRMS** (APCI Pos): calculated for $C_{16}H_{16}{}^{79}BrO$ $[M+H]^+$: 303.0379; found: 303.0366.

**(*trans*)-1-(2-(4-Methoxyphenyl)cyclopropyl)-3-nitrobenzene (86m)**



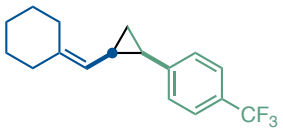

The title compound (pale yellow solid, 21 mg, 87% yield, 10:1 dr) was obtained following General Procedure C2 from 1-(4-methoxyphenyl)-1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene (**90c**) (30 mg, 0.089 mmol) and 1-nitro-3-vinylbenzene (27 mg, 0.18 mmol, 2 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (6.9 mg, 10 mol %) after purification by CombiFlash chromatography on $SiO_2$ using a cyclohexane/EtOAc gradient from 99:1 to 9:1. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.03 (ddd, *J* = 7.6, 2.3, 1.5 Hz, 1H), 7.96 (t, *J* = 2.0 Hz, 1H), 7.51 – 7.38 (m, 2H), 7.13 – 7.05 (m, 2H), 6.89 – 6.82 (m, 2H), 3.80 (s, 3H), 2.20 (m, 2H), 1.49 (m, 2H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.3, 148.7, 145.2, 133.5, 132.3, 129.3, 127.1, 120.8, 120.4, 114.1, 55.5, 28.2, 27.1, 18.4 ppm. **MP** 92–94 ºC. **HRMS** (APCI Pos): calculated for $C_{16}H_{15}NO_3$ $[M]^+$: 269.1046; found: 269.1052.

**(*trans*)-1-Methoxy-4-(2-(4-(trifluoromethyl)phenyl)cyclopropyl)benzene (86n)**



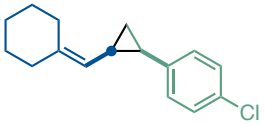

The title compound (colorless oil, 21 mg, 88% yield, 14:1 dr) was obtained following General Procedure C2 from 1-(4-methoxyphenyl)-1a,9b-dihydro-1*H*-cyclopropa[*l*]phenanthrene (**90c**) (24 mg, 0.080 mmol) and 1-(trifluoromethyl)-4-vinylbenzene (28 mg, 0.16 mmol, 2 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (6.2 mg, 10 mol %) after purification by preparative TLC on $SiO_2$ using pentane/diethyl ether 97:3 as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.57 – 7.50 (m, 2H), 7.27 – 7.16 (m, 2H), 7.12 – 7.06 (m, 2H), 6.89 – 6.83 (m, 2H), 3.80 (s, 3H), 2.16 (m, 2H), 1.46 (m, 2H) ppm. **$^{19}$F NMR** (471 MHz, $CDCl_3$) δ -62.33 ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.4, 147.4, 134.10, 128.2 (q, $J$ = 32.9 Hz), 127.3, 126.2, 125.7 (q, $J$ = 3.8 Hz), 124.9 (q, $J$ = 271.3 Hz), 114.3, 55.7, 28.4, 27.7, 18.6 ppm.

**(*cis*)-1-(2-(Cyclohexylidenemethyl)cyclopropyl)-4-(trifluoromethyl)benzene (87a)**




The title compound (colorless oil, 16 mg, 54% yield, 5:1 dr) was obtained following General Procedure C1 from 1-(cyclohexylidenemethyl)-1a,7b-dihydro-1*H*-cyclopropa[*a*]-naphthalene (**85a**) (25 mg, 0.106 mmol) and 1-(trifluoromethyl)-4-vinylbenzene (109 mg, 0.64 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (4.1 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.54 – 7.50 (m, 2H), 7.28 – 7.24 (m, 2H), 4.45 (dt, $J$ = 8.1, 1.2 Hz, 1H), 2.33 – 2.26 (m, 1H), 2.22 (m, 2H), 2.03 – 1.97 (m, 1H), 1.94 (m, 2H), 1.53 – 1.29 (m, 7H), 0.94 – 0.91 (m, 1H) ppm. **$^{19}$F NMR** (471 MHz, $CDCl_3$) δ -62.30 ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 142.6, 129.1, 125.7, 124.7, 124.7, 124.6, 124.6, 123.2, 118.9, 36.8, 29.3, 28.5, 27.6, 26.7, 22.9, 17.9, 13.3 ppm. **HRMS** (APCI Pos): calculated for $C_{17}H_{20}F_3$ $[M+H]^+$: 281.1512; found: 281.1504.

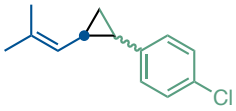
**(*cis*)-1-(2-(Cyclohexylidenemethyl)cyclopropyl)-4-chlorobenzene (87b)**




The title compound (colorless oil, 19 mg, 73% yield, 2:1 dr) was obtained following General Procedure C1 from 1-(cyclohexylidenemethyl)-1a,7b-dihydro-1*H*-cyclopropa[*a*]-naphthalene (**85a**) (25 mg, 0.106 mmol) and 1-chloro-4-vinylbenzene (88 mg, 0.64 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (4.1 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.27 – 7.20 (m, 2H), 7.13 – 7.07 (m, 2H), 4.41 (dt, $J$ = 8.4, 1.2 Hz, 1H), 2.26 – 2.19 (m, 3H), 1.96 – 1.90 (m, 3H), 1.58 – 1.51 (m, 4H), 1.43 – 1.36 (m, 1H), 1.31 – 1.25 (m, 2H), 0.83 (td, $J$ = 6.0, 5.0 Hz, 1H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.9, 138.1, 130.3, 127.9, 123.5, 119.4, 36.9, 29.3, 28.6, 27.7,

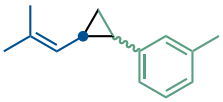
26.8, 22.3, 17.4, 12.9 ppm. **HRMS** (APCI Positive): calculated for $C_{16}H_{20}Cl$ $[M+H]^+$: 247.1248; found: 247.1243.

**1-Chloro-4-(2-(2-methylprop-1-en-1-yl)cyclopropyl)benzene (87c)**



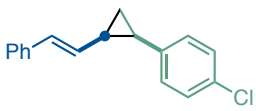

The title compound (colorless oil, 15 mg, 65% yield, 1:1 dr) was obtained following General Procedure C1 from 1-(2-methylprop-1-en-1-yl)-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (**85b**) (22 mg, 0.112 mmol) and 1-chloro-4-vinylbenzene (93 mg, 0.67 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (4.3 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$, *cis*/*trans* 1:1 mixture, unassigned) δ 7.23 – 7.18 (m, 4H), 7.09 – 7.05 (m, 2H), 7.01 – 6.95 (m, 2H), 4.71 (dp, *J* = 8.8, 1.4 Hz, 1H), 4.42 (dp, *J* = 8.7, 1.4 Hz, 1H), 2.20 (td, *J* = 8.6, 6.2 Hz, 1H), 1.87 (td, *J* = 8.7, 5.7 Hz, 1H), 1.80 – 1.75 (m, 1H), 1.69 (d, *J* = 1.4 Hz, 6H), 1.68 (d, *J* = 1.3 Hz, 3H), 1.67 – 1.62 (m, 1H), 1.55 (d, *J* = 1.4 Hz, 3H), 1.23 – 1.21 (m, 1H), 1.12 (dt, *J* = 8.6, 5.2 Hz, 1H), 0.96 (ddd, *J* = 8.5, 5.7, 4.9 Hz, 1H), 0.79 (td, *J* = 6.0, 5.0 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$, *cis*/*trans* 1:1 mixture, unassigned) δ 141.9, 138.4, 130.6, 128.7, 128.3, 127.3, 127.2, 123.0, 25.9, 25.8, 24.7, 23.7, 22.6, 18.8, 18.7, 18.6, 17.5, 12.9 ppm. **HRMS** (APCI Positive): calculated for $C_{13}H_{16}Cl$ $[M+H]^+$: 207.0935; found: 207.0937.

**(*cis*)-1-Methyl-3-(2-(2-methylprop-1-en-1-yl)cyclopropyl)benzene (87d)**



The title compound (colorless oil, 12 mg, 58% yield, 1:1 dr) was obtained following General Procedure C1 from 1-(2-methylprop-1-en-1-yl)-1a,7b-dihydro-1*H*-cyclopropa[*a*]-naphthalene (**85b**) (22 mg, 0.112 mmol) and 1-methyl-3-vinylbenzene (79 mg, 0.67 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (4.3 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, $CDCl_3$, *cis* isomer) δ 7.18 (t, *J* = 7.5 Hz, 1H), 7.04 – 6.96 (m, 4H), 4.55 (dt, *J* = 8.9, 1.3 Hz, 1H), 2.36 (s, 3H), 2.26 (td, *J* = 8.6, 6.5 Hz, 1H), 1.89 (qd, *J* = 8.8, 5.8 Hz, 1H), 1.74 (m, 4H), 1.61 – 1.60 (m, 4H), 1.25 (td, *J* = 8.5, 4.9 Hz, 1H), 0.90 – 0.85 (m, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$, *cis* isomer) δ 139.3, 137.3, 132.6, 129.9, 127.7, 126.4, 125.9, 123.1, 25.6, 22.7, 21.5, 18.3, 18.3, 12.3 ppm. **GC-MS** (EI): calculated for $C_{14}H_{18}$ $[M]^+$: 186.1; found: 186.1.

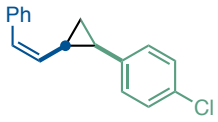
**(*cis*)-1-Chloro-4-(2-((*E*)-styryl)cyclopropyl)benzene (87e)**




The title compound (colorless oil, 10 mg, 50% yield, 20:1 dr) was obtained following General Procedure C1 from (*E*)-1-styryl-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (**85c**) (18 mg, 0.106 mmol)

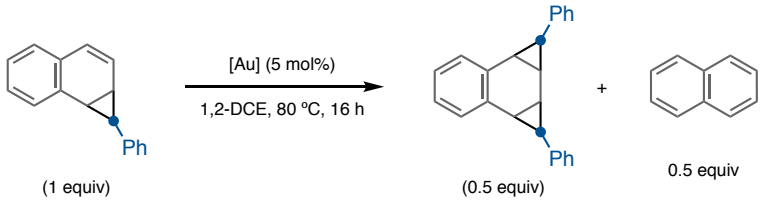
and 1-chloro-4-vinylbenzene (62 mg, 0.45 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (2.9 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.15 - 7.32 (m, 9H), 6.56 (d, J=15.8 Hz, 1H), 5.52 (dd, J=15.8, 9.4 Hz, 1H), 2.38 - 2.49 (m, 1H), 2.01 - 2.13 (m, 1H), 1.37 - 1.46 (m, 1H), 1.08 - 1.19 (m, 1H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 137.6, 137.4, 131.9, 130.7, 130.1, 130.0, 128.6, 128.3, 126.9, 125.8, 23.3, 22.8, 12.8 ppm. **GC-MS** (EI): calculated for $C_{17}H_{16}Cl$ $[M+H]^+$: 255.1; found: 255.1.

**(*cis*)-1-Chloro-4-(2-((*Z*)-styryl)cyclopropyl)benzene (87f)**

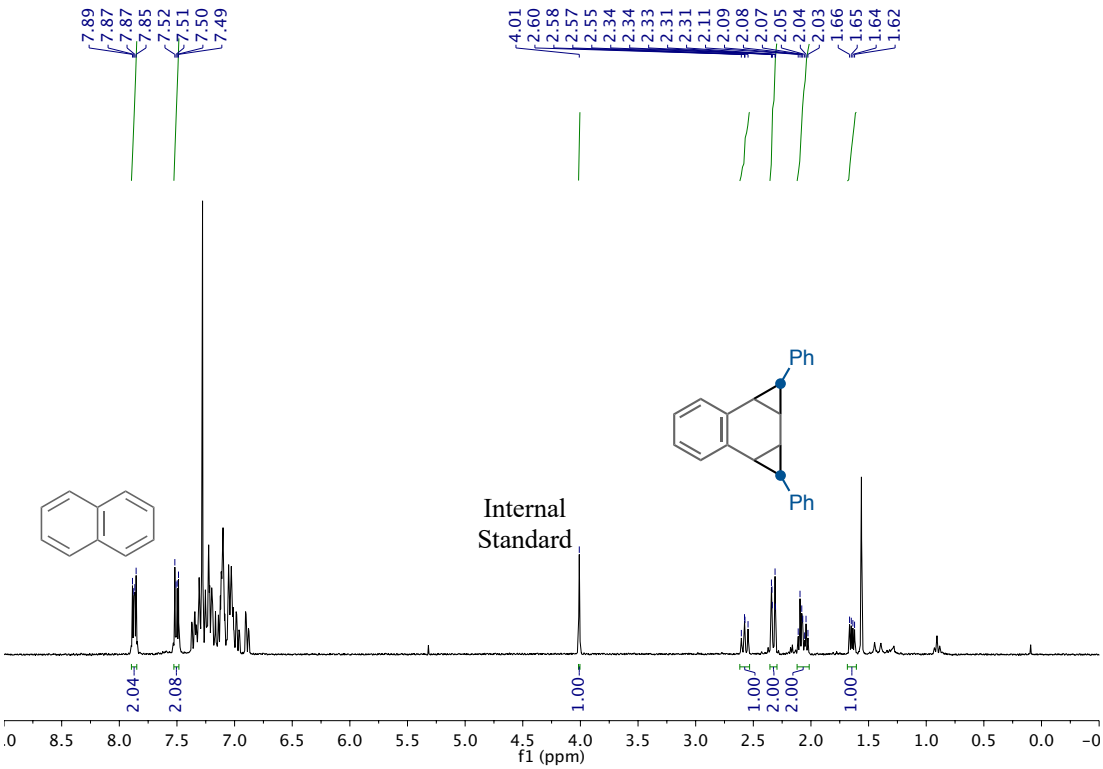



The title compound (colorless oil, 13 mg, 68% yield, 8:1 dr) was obtained following General Procedure C2 from (*Z*)-1-styryl-1a,7b-dihydro-1*H*-cyclopropa[*a*]naphthalene (**85d**) (18 mg, 0.075 mmol) and 1-chloro-4-vinylbenzene (63 mg, 0.45 mmol, 6 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (2.9 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.42 – 7.39 (m, 2H), 7.34 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.28 – 7.19 (m, 4H), 7.18 – 7.14 (m, 2H), 6.33 (d, *J* = 11.5 Hz, 1H), 4.91 (dd, *J* = 11.5, 9.7 Hz, 1H), 2.38 (td, *J* = 8.6, 6.3 Hz, 1H), 2.28 (dtdd, *J* = 9.8, 8.6, 5.7, 1.1 Hz, 1H), 1.39 (td, *J* = 8.4, 5.1 Hz, 1H), 1.05 (dt, *J* = 6.4, 5.4 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.0, 137.5, 132.2, 131.6, 130.8, 130.0, 129.1, 128.6, 128.6, 126.9, 24.1, 19.4, 14.2 ppm. **HRMS** (APCI Positive): calculated for $C_{17}H_{16}Cl$ $[M+H]^+$: 255.0935; found: 255.0923.

**Formation of biscyclopropane side-product by heating with gold(I)**




Dissolving (**83**) in 1,2-DCE, adding 5 mol % of [(JohnPhos)Au(MeCN)]$SbF_6$ and heating at 80 ºC for 16 h gives quantitative release of 0.5 equiv of naphthalene and 0.5 equiv of bisphenylcyclopropane, which is unreactive towards retro-cyclopropanation under the reaction conditions (determined by $^1$H NMR in $CDCl_3$ using 1 equiv of diphenylmethane as internal standard). Characterization data for the biscyclopropane matches the reported ones.[154]

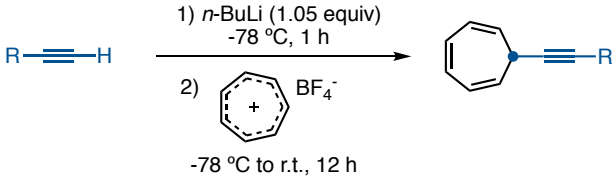



154 Wang, Y.; McGonigal, P. R.; Herlé, B.; Besora, M.; Echavarren, A. M. Gold(I) Carbenes by Retro-Buchner Reaction: Generation and Fate. *J. Am. Chem. Soc.* **2014**, *136*, 801–809.

**Synthesis of 7-Alkynylcycloheptatrienes (91)**

Some of the 7-alkynyl-1,3,5-cycloheptatrienes used in this work were already known and characterized by our group.[155] Both the new and known compounds **91** were prepared according to General Procedure D, and characterization data is listed below for new compounds only. Also, new substrates **91q–u** and **91e**/**91m–o** were prepared by collaborators Dr. M. Montesinos-Magraner and A. R. Sugranyes, respectively, and their characterization data is not included in this section.

**General Procedure D for the Synthesis of 7-Alkynylcycloheptatrienes from Alkynes**




A two-necked round-bottomed flask equipped with a Teflon-coated stirring bar was charged with the corresponding terminal alkyne before dissolving it, under argon, in anhydrous THF (*ca.* 0.15–0.25 M). The solution was cooled down to -78 ºC before a *n*-BuLi solution (2.50 M in hexane, 1.05 equiv) was added dropwise. The resulting mixture was stirred at -78 ºC for 1 h. After this time, solid tropylium tetrafluoroborate (1.05 equiv) was added in a single portion. After stirring for 5–10 min at -78 ºC, the flask was taken out of the cooling bath and stirred while coming to room temperature overnight (*ca.* 12 h). Water was added, and the mixture was extracted 3 times with diethyl ether. The combined organic fractions were washed once with water and once with brine, dried over anhydrous $MgSO_4$ and concentrated under vacuum. The crude material was purified by flash column chromatography or CombiFlash chromatography in $SiO_2$ using cyclohexane or gradients of cyclohexane/EtOAc as eluent to give the corresponding 7-alkynyl-cycloheptatriene **91**. Most 7-alkynyl-1,3,5-cycloheptatrienes can be safely stored under argon in the fridge (5 ºC) for more than a year, or under air at room temperature for several months without significant decomposition.

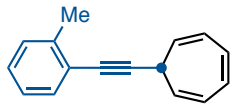
155 (a) McGonigal, P. R.; de León, C.; Wang, Y.; Homs, A.; Solorio-Alvarado, C. R.; Echavarren, A. M. Gold for the Generation and Control of Fluxional Barbaralyl Cations. *Angew. Chem. Int. Ed.* **2012**, *51*, 13093–13096. (b) Ferrer, S.; Echavarren, A. M. Synthesis of Barbaralones and Bullvalenes Made Easy by Gold Catalysis. *Angew. Chem. Int. Ed.* **2016**, *55*, 11178–11182.

**Characterization Data for New 7-Alkynylcycloheptatrienes (91)**

**(Cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane (91b)**

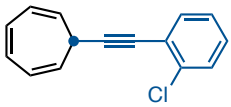

The title compound (pale yellow oil, 1.90 g, 67% yield) was obtained following General Procedure D from ethynyltrimethylsilane (1.47 g, 15.0 mmol, 1 equiv) and tropylium tetrafluoroborate (2.67 g, 15.0 mmol, 1 equiv) using *n*-BuLi (2.50 M in hexane, 6.30 mL, 15.8 mmol, 1.05 equiv) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (300 MHz, Chloroform-*d*) δ 6.66 (ddt, *J* = 3.5, 2.6, 0.8 Hz, 2H), 6.18 (dddd, *J* = 8.7, 3.8, 2.5, 1.4 Hz, 2H), 5.34 (ddq, *J* = 9.3, 5.5, 0.7 Hz, 2H), 2.52 (tt, *J* = 5.5, 1.5 Hz, 1H), 0.22 (s, 9H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 130.94, 124.67, 123.05, 108.04, 84.58, 32.59, 0.11. **HRMS** (APCI Pos): calculated for $C_{12}H_{17}Si$ $[M+H]^+$: 189.1094; found: 189.1092.

**7-(*o*-Tolylethynyl)cyclohepta-1,3,5-triene (91i)**



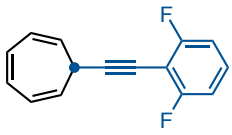

The title compound (colorless oil, 281 mg, 93% yield) was obtained following General Procedure D from 1-ethynyl-2-methylbenzene (171 mg, 1.47 mmol, 1 equiv) and tropylium tetrafluoroborate (275 mg, 1.55 mmol, 1.05 equiv) using *n*-BuLi (2.42 M in hexane, 0.65 mL, 1.56 mmol, 1.06 equiv) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.47 (dt, *J* = 7.5, 1.1 Hz, 1H), 7.27 – 7.22 (m, 2H), 7.21 – 7.14 (m, 1H), 6.79 – 6.69 (m, 2H), 6.27 (dddd, *J* = 8.9, 3.9, 2.6, 1.4 Hz, 2H), 5.49 (ddt, *J* = 9.3, 5.5, 0.7 Hz, 2H), 2.82 (tt, *J* = 5.5, 1.5 Hz, 1H), 2.50 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 140.20, 131.96, 131.07, 129.39, 127.94, 125.51, 124.81, 123.49, 123.22, 95.08, 79.50, 32.44, 20.78. **HRMS** (APCI Pos): calculated for $C_{16}H_{15}$ $[M+H]^+$: 207.1168; found: 207.1177.

**7-((2-Chlorophenyl)ethynyl)cyclohepta-1,3,5-triene (91j)**



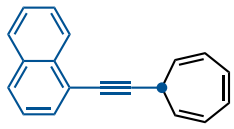

The title compound (colorless oil, 250 mg, 79% yield) was obtained following General Procedure D from 1-chloro-2-ethynylbenzene (191 mg, 1.40 mmol, 1 equiv) and tropylium tetrafluoroborate (262 mg, 1.47 mmol, 1.05 equiv) using *n*-BuLi (2.42 M in hexane, 0.61 mL, 1.48 mmol, 1.06 equiv) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.57 – 7.48 (m, 1H), 7.47 – 7.40 (m, 1H), 7.30 – 7.19 (m, 2H), 6.78 – 6.68 (m, 2H), 6.26 (dddd, *J* = 8.8, 3.8, 2.6, 1.4 Hz, 2H), 5.50 (ddt, *J* = 8.6, 5.5, 0.8 Hz, 2H), 2.82 (tt, *J* = 5.5, 1.5 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 136.04, 133.40, 131.07, 129.22, 128.95, 126.38, 124.92, 123.32, 122.87, 96.63, 77.54, 32.43. **HRMS** (APCI Pos): calculated for $C_{15}H_{12}Cl$ $[M+H]^+$: 227.0622; found: 227.0621.

**7-((2,6-Difluorophenyl)ethynyl)cyclohepta-1,3,5-triene (91k)**



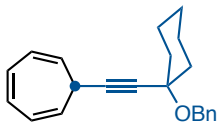

The title compound (colorless oil, 310 mg, 97% yield) was obtained following General Procedure D from 2-ethynyl-1,3-difluorobenzene (193 mg, 1.40 mmol, 1 equiv) and tropylium tetrafluoroborate (262 mg, 1.48 mmol, 1.05 equiv) using *n*-BuLi (2.42 M in hexane, 0.61 mL, 1.48 mmol, 1.05 equiv) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.32 – 7.20 (m, 1H), 6.98 – 6.88 (m, 2H), 6.72 (ddd, J = 3.5, 2.1, 0.8 Hz, 2H), 6.26 (dddd, J = 8.8, 3.8, 2.6, 1.4 Hz, 2H), 5.48 (ddt, J = 8.7, 5.5, 0.8 Hz, 2H), 2.84 (td, J = 5.6, 2.9 Hz, 1H). **$^{13}$C NMR** (101 MHz, CDCl3) δ 164.62 (d, J = 5.4 Hz), 162.10 (d, J = 5.5 Hz), 131.06, 129.22 (t, J = 9.9 Hz), 125.00, 122.47, 111.05 (m), 102.39 (t, J = 19.8 Hz), 101.50 (t, J = 3.2 Hz), 67.57, 32.54. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -107.78. **HRMS** (APCI Pos): calculated for $C_{15}H_{11}F_2$ $[M+H]^+$: 229.0823; found: 229.0832.

**1-(Cyclohepta-2,4,6-trien-1-ylethynyl)naphthalene (91p)**



The title compound (viscous pale-yellow oil, 230 mg, 68% yield) was obtained following General Procedure D from 1-ethynylnaphthalene (224 mg, 1.47 mmol) and tropylium tetrafluoroborate (249 mg, 1.48 mmol, 1.05 equiv) using *n*-BuLi (2.42 M in hexane, 0.61 mL, 1.48 mmol, 1 equiv) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.42 (dq, *J* = 8.4, 0.9 Hz, 1H), 7.91 – 7.82 (m, 2H), 7.73 (dd, *J* = 7.1, 1.2 Hz, 1H), 7.58 (dddd, *J* = 23.2, 8.1, 6.8, 1.4 Hz, 2H), 7.46 (dd, *J* = 8.3, 7.1 Hz, 1H), 6.81 – 6.72 (m, 2H), 6.31 (dddd, *J* = 8.8, 3.9, 2.6, 1.4 Hz, 2H), 5.59 (ddt, *J* = 8.7, 5.6, 0.8 Hz, 2H), 2.94 (tt, *J* = 5.6, 1.5 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 133.51, 133.22, 131.13, 130.36, 128.39, 128.27, 126.67, 126.34, 126.25, 125.24, 124.95, 123.24, 121.12, 96.06, 78.69, 32.56. **HRMS** (APCI Pos): calculated for $C_{19}H_{15}$ $[M+H]^+$: 243.1168; found: 243.1167.

**7-((1-(Benzyloxy)cyclohexyl)ethynyl)cyclohepta-1,3,5-triene (91v)**




The title compound (orange oil, 1.35 g, 95% yield) was obtained following General Procedure D from (((1-ethynylcyclohexyl)oxy)methyl)benzene (1.00 g, 4.67 mmol, 1 equiv, prepared according to a reported procedure[156]) and tropylium tetrafluoroborate (0.87 g, 4.9 mmol, 1.05 equiv) using *n*-BuLi (2.42 M in hexane, 2.00 mL, 4.9 mmol, 1.05 equiv) after

156 Bolte, B.; Odabachian, Y.; Gagosz, F. Gold(I)-Catalyzed Rearrangement of Propargyl Benzyl Ethers: A Practical Method for the Generation and in Situ Transformation of Substituted Allenes. *J. Am. Chem. Soc.* **2010**, *132*, 7294–7296.

purification by flash column chromatography in $SiO_2$ using a gradient between cyclohexane and cyclohexane/EtOAc 9:1 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.44 – 7.27 (m, 5H), 6.74 – 6.65 (m, 2H), 6.21 (dddd, *J* = 8.3, 3.8, 2.5, 1.4 Hz, 2H), 5.42 – 5.34 (m, 2H), 4.72 (s, 2H), 2.62 (tt, *J* = 5.6, 1.5 Hz, 1H), 2.03 (m, 2H), 1.79 – 1.70 (m, 4H), 1.64 (m, 3H), 1.41 – 1.30 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 139.54, 131.02, 128.28, 127.73, 127.22, 124.73, 123.72, 87.80, 81.73, 74.23, 65.44, 37.61, 31.71, 26.94, 25.59, 23.03. **HRMS** (ESI Pos): calculated for $C_{22}H_{24}NaO$ $[M+Na]^+$: 327.1719; found: 327.1729.

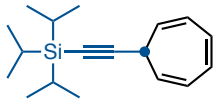
***tert*-Butyl(cyclohepta-2,4,6-trien-1-ylethynyl)dimethylsilane (91w)**


The title compound (pale yellow oil, 0.54 g, 79% yield) was obtained following General Procedure D from *tert*-butyl(ethynyl)dimethylsilane (0.42 g, 3.00 mmol, 1 equiv) and tropylium tetrafluoroborate (0.56 g, 3.15 mmol, 1.05 equiv) using *n*-BuLi (2.50 M in hexane, 1.25 mL, 3.15 mmol, 1.05 equiv) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (300 MHz, Chloroform-*d*) δ 6.72 – 6.61 (m, 2H), 6.19 (dddd, *J* = 8.7, 3.8, 2.5, 1.4 Hz, 2H), 5.41 – 5.29 (m, 2H), 2.55 (tt, *J* = 5.5, 1.5 Hz, 1H), 0.98 (s, 9H), 0.15 (s, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 130.94, 124.69, 123.25, 108.61, 82.68, 32.60, 26.11, 16.56, -4.49. **HRMS** (APCI Pos): calculated for $C_{15}H_{23}Si$ $[M+H]^+$: 231.1564; found: 231.1565.

**(Cyclohepta-2,4,6-trien-1-ylethynyl)dimethyl(phenyl)silane (91x)**

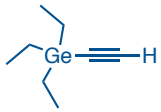

The title compound (pale yellow oil, 0.54 g, 72% yield) was obtained following General Procedure D from *tert*-butyl(ethynyl)dimethylsilane (0.56 g, 3.00 mmol, 1 equiv) and tropylium tetrafluoroborate (0.56 g, 3.15 mmol, 1.05 equiv) using *n*-BuLi (2.50 M in hexane, 1.25 mL, 3.15 mmol, 1.05 equiv) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (300 MHz, Chloroform-*d*) δ 7.77 – 7.65 (m, 2H), 7.47 – 7.40 (m, 3H), 6.76 – 6.63 (m, 2H), 6.22 (dddd, *J* = 8.7, 3.9, 2.6, 1.4 Hz, 2H), 5.47 – 5.34 (m, 2H), 2.62 (tt, *J* = 5.6, 1.5 Hz, 1H), 0.48 (d, *J* = 0.5 Hz, 6H). **$^{13}$C NMR** (75 MHz, CDCl3) δ 137.34, 133.73, 130.99, 129.39, 127.89, 124.83, 122.84, 109.89, 82.61, 32.69, -0.64. **HRMS** (APCI Pos): calculated for $C_{17}H_{19}Si$ $[M+H]^+$: 251.1251; found: 251.1249.

**(Cyclohepta-2,4,6-trien-1-ylethynyl)triisopropylsilane (91y)**



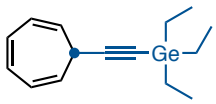
The title compound (pale yellow oil, 1.45 g, 88% yield) was obtained following General Procedure D from ethynyltriisopropylsilane (1.00 g, 5.48 mmol, 1 equiv) and tropylium tetrafluoroborate (1.02 g, 5.76 mmol, 1.05 equiv) using *n*-BuLi (2.50 M in hexane, 2.30 mL, 5.76 mmol, 1.05 equiv) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (300 MHz, Chloroform-*d*) δ 6.72 – 6.62 (m, 2H), 6.19 (dddd, *J* = 8.8, 3.8, 2.5, 1.4 Hz, 2H), 5.37 (ddd, *J* = 9.4, 5.5, 0.8 Hz, 2H), 2.58 (tt, *J* = 5.5, 1.5 Hz, 1H), 1.12 (d, *J* = 2.8 Hz, 21H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 130.95, 124.65, 123.69, 109.92, 80.38, 32.71, 18.65, 11.24. **HRMS** (APCI Pos): calculated for $C_{18}H_{29}Si$ $[M+H]^+$: 273.2033; found: 273.2027.

**Triethyl(ethynyl)germane**



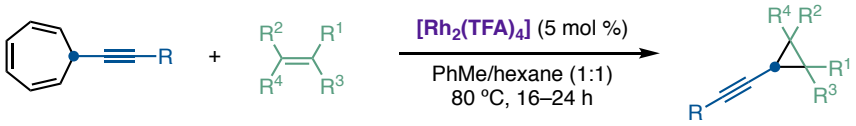
To a stirred solution of chlorotriethylgermane (0.580 g, 0.50 mL, 2.97 mmol, 1 equiv) in dry diethyl ether (12 mL, 0.5 M) under argon at 0 ºC was added dropwise over 2–3 min a commercial 0.5 M solution in THF of ethynylmagnesium bromide (8.91 mL, 4.5 mmol, 1.5 equiv). The mixture is then allowed to come slowly to room temperature and stirred for 20 h. After this time, water and more diethyl ether were added, and the mixture extracted with diethyl ether twice. The combined organic fractions were washed with water once, with brine once, and then washed with anhydrous $MgSO_4$. After filtration and concentration in vacuum, the product was purified by flash column chromatography in pentane. This gave triethyl(ethynyl)germane (0.49 g, 89% yield) as a colorless oil. **$^1$H NMR** (300 MHz, Chloroform-*d*) δ 2.29 (s, 1H), 1.15 – 1.09 (m, 9H), 0.94 – 0.86 (m, 6H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 93.16, 87.71, 8.84, 5.55.

**(Cyclohepta-2,4,6-trien-1-ylethynyl)triethylgermane (91z)**



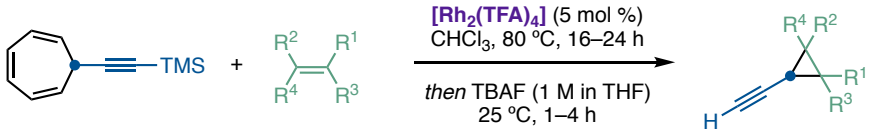
The title compound (very pale-yellow oil, 0.48 g, 81% yield) was obtained following General Procedure D from triethyl(ethynyl)germane (0.40 g, 2.16 mmol) and tropylium tetrafluoroborate (0.41 g, 2.27 mmol, 1.05 equiv) using *n*-BuLi (2.42 M in hexane, 0.95 mL, 2.29 mmol, 1.05 equiv) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 6.66 (ddd, *J* = 3.7, 2.6, 0.8 Hz, 2H), 6.18 (dddd, *J* = 8.7, 3.9, 2.5, 1.5 Hz, 2H), 5.37 (ddq, *J* = 9.3, 5.5, 0.7 Hz, 2H), 2.55 (tt, *J* = 5.5, 1.5 Hz, 1H), 1.14 (td, *J* = 7.9, 0.7 Hz, 9H), 0.89 (qd, *J* = 7.7, 0.9 Hz, 6H). **$^{13}$C NMR** (101 MHz, CDCl3) $^{13}$C NMR (101 MHz, $CDCl_3$) δ 130.90, 124.48, 124.02, 108.46, 81.37, 32.75, 8.98, 5.77. **HRMS** (APCI Pos): calculated for $C_{15}H_{23}{}^{70}Ge$ $[M+H]^+$: 273.1037; found: 229.0832.

**General Procedure E1 for the Rhodium(II)-Catalyzed Synthesis of Disubstituted Alkynylcyclopropanes**




A microwave vial or screw-cap culture tube equipped with a Teflon-coated magnetic stirring bar was charged with the corresponding 7-alkynyl-1,3,5-cycloheptatriene **91** (1 equiv) and the corresponding alkene (4 equiv). The vial was introduced in an argon-filled glovebox, and both reagents were dissolved in anhydrous solvent (0.15 M, either in $CHCl_3$ or a 1:1 PhMe/hexane mixture; specified for each reaction in the corresponding individual procedure below). Then, $[Rh_2(TFA)_4]$ (5 mol %) was added before the reaction vial was closed/sealed, and taken out of the glovebox. The mixture was stirred at 80 ºC until TLC and/or GCMS show full consumption of the starting cycloheptatriene **91** (*ca*. 16–24 h). The reaction was concentrated in vacuum and the obtained crude mixture was analyzed by $^1$H NMR to determine the dr of the product. Then, the crude product was purified by flash column chromatography, CombiFlash chromatography, or preparative TLC in $SiO_2$ using the corresponding solvent for each substrate to give alkynylcyclopropanes **98**, **99** or **101**.

**General Procedure E2 for the Rhodium(II)-Catalyzed One-Pot Synthesis of Terminal Alkynylcyclopropanes**

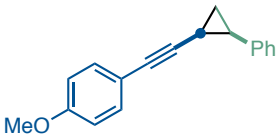



A microwave vial or screw-cap culture tube equipped with a Teflon-coated magnetic stirring bar was charged with (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane **91b** (1 equiv) and the corresponding alkene (4 equiv). The vial was introduced in an argon-filled glovebox, and both reagents were dissolved in anhydrous $CHCl_3$ (0.15 M). Then, $[Rh_2(TFA)_4]$ (5 mol %) was added before the reaction vial was closed/sealed, and taken out of the glovebox. The mixture was stirred at 80 ºC until TLC and/or GCMS show full consumption of the starting cycloheptatriene (*ca*. 16–24 h). Then, after cooling the mixture down to room temperature, a commercial solution of TBAF in THF (1.0 M, 1.5 equiv) was added in a single portion. The reaction was further stirred at room temperature until TLC and/or GCMS show full deprotection of the TMS-alkyne group. After this time, water was added, and the mixture was extracted with $Et_2O$ two times. The combined organic fractions were washed with brine once, dried over anhydrous $MgSO_4$, filtered, concentrated in vacuum and the obtained crude mixture

was analyzed by $^1$H NMR to determine the dr of the product. Then, the crude product was purified by flash column chromatography, CombiFlash chromatography, or preparative TLC in $SiO_2$ using the corresponding solvent for each substrate to give terminal alkynylcyclopropanes **100**.

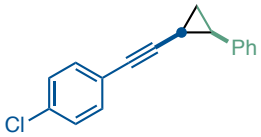
**Characterization Data for Alkynylcyclopropanes (98–101)**

***cis*-1-Methoxy-4-((2-phenylcyclopropyl)ethynyl)benzene (98b)**




The title compound (viscous colorless oil, 50 mg, 67% yield, 12:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-((4-methoxyphenyl)ethynyl)-cyclohepta-1,3,5-triene (67 mg, 0.30 mmol, 1 equiv) and styrene (125 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9.9 mg, 5 mol %) after purification by preparative TLC in $SiO_2$ using pentane/$Et_2O$ 97:3 as eluent. The minor (*trans*) isomer was already reported.[157] **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.36 – 7.23 (m, 5H), 7.14 – 7.06 (m, 2H), 6.77 – 6.72 (m, 2H), 3.78 (s, 3H), 2.40 (td, J = 8.5, 6.7 Hz, 1H), 2.00 (td, J = 8.5, 5.8 Hz, 1H), 1.46 (td, J = 8.6, 5.0 Hz, 1H), 1.32 – 1.29 (m, 1H). **$^{13}$C NMR** (101 MHz, CDCl3) δ 158.95, 138.15, 132.76, 128.35, 127.73, 126.20, 115.96, 113.70, 88.01, 79.99, 55.21, 23.89, 15.06, 10.26. **GCMS** (EI): calculated for $C_{18}H_{16}O$ $[M]^+$: 248.1; found: 248.1.

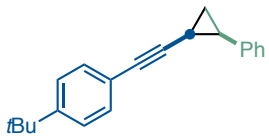
***cis*-1-Chloro-4-((2-phenylcyclopropyl)ethynyl)benzene (98c)**




The title compound (pale yellow solid, 53 mg, 70% yield, 14:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-((4-chlorophenyl)ethynyl)-cyclohepta-1,3,5-triene (68 mg, 0.30 mmol, 1 equiv) and styrene (125 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9.9 mg, 5 mol %) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.38 – 7.31 (m, 4H), 7.30 – 7.25 (m, 1H), 7.18 (td, J = 7.1, 6.7, 3.5 Hz, 2H), 7.07 (dd, J = 8.6, 1.9 Hz, 2H), 2.45 (qd, J = 8.4, 7.4, 1.6 Hz, 1H), 2.05 – 1.93 (m, 1H), 1.52 – 1.45 (m, 1H), 1.33 (ddd, J = 9.8, 5.6, 4.2 Hz, 1H). **$^{13}$C NMR** (101 MHz, CDCl3) δ 137.89, 133.31, 132.61, 128.38, 127.80, 126.37, 122.32, 90.95, 79.12, 24.07, 14.95, 10.15. **HRMS** (APCI Positive): calculated for $C_{17}H_{14}Cl$ $[M]^+$: 253.0779; found: 253.0784. **MP** 63–64 ºC.

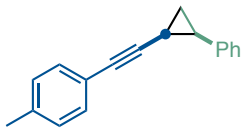
157 Li, C.-W.; Pati, K.; Lin, G.-Y.; Sohel, S. M. A.; Hung, H.-H.; Liu, R.-S. Gold-Catalyzed Oxidative Ring Expansions and Ring Cleavages of Alkynylcyclopropanes by Intermolecular Reactions Oxidized by Diphenylsulfoxide. *Angew. Chem. Int. Ed.* **2010**, *49*, 9891–9894.

**_cis_-1-_tert_-Butyl-4-((2-phenylcyclopropyl)ethynyl)benzene (98e)**



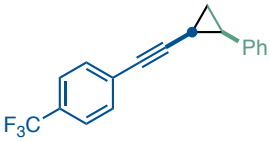

The title compound (yellow oil, 55 mg, 67% yield, 10:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-((4-*tert*-butyl-phenyl)ethynyl)-cyclohepta-1,3,5-triene (75 mg, 0.30 mmol, 1 equiv) and styrene (125 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9.9 mg, 5 mol %) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.38 – 7.33 (m, 4H), 7.30 – 7.23 (m, 3H), 7.15 – 7.09 (m, 2H), 2.42 (td, J = 8.5, 6.7 Hz, 1H), 2.02 (td, J = 8.5, 5.8 Hz, 1H), 1.48 (td, J = 8.6, 5.0 Hz, 1H), 1.34 – 1.31 (m, 1H), 1.30 (s, 9H). **$^{13}$C NMR** (101 MHz, CDCl3) δ 150.55, 138.11, 131.14, 128.37, 127.77, 126.24, 125.06, 120.81, 88.91, 80.27, 34.65, 31.19, 23.98, 15.12, 10.30. **HRMS** (APCI Positive): calculated for $C_{21}H_{23}$ $[M]^+$: 275.1794; found: 275.1798.

**_cis_-1-Methyl-4-((2-phenylcyclopropyl)ethynyl)benzene (98f)**




The title compound (pale yellow solid, 29 mg, 51% yield, 15:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-((4-methylphenyl)ethynyl)-cyclohepta-1,3,5-triene (50 mg, 0.24 mmol, 1 equiv) and styrene (101 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (8.0 mg, 5 mol %) in $CHCl_3$ at 80 ºC, after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.39 – 7.31 (m, 4H), 7.28 – 7.23 (m, 1H), 7.10 – 7.05 (m, 2H), 7.05 – 6.99 (m, 2H), 2.42 (td, J = 8.4, 6.7 Hz, 1H), 2.31 (s, 3H), 2.01 (td, J = 8.5, 5.8 Hz, 1H), 1.47 (td, J = 8.6, 5.0 Hz, 1H), 1.32 – 1.28 (m, 1H). **$^{13}$C NMR** (101 MHz, CDCl3) δ 138.09, 137.37, 131.29, 128.81, 128.35, 127.74, 126.23, 120.72, 88.86, 80.30, 23.95, 21.37, 15.09, 10.27. **HRMS** (APCI Positive): calculated for $C_{18}H_{17}$ $[M]^+$: 233.1325; found: 233.1323. **MP** 51–53 ºC.

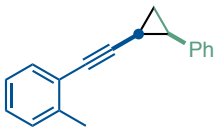
**_cis_-1-Trifluoromethyl-4-((2-phenylcyclopropyl)ethynyl)benzene (98g)**




The title compound (colorless oil, 47 mg, 55% yield, 15:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-((4-trifluoromethylphenyl)ethynyl)-cyclohepta-1,3,5-triene (78 mg, 0.30 mmol, 1 equiv) and styrene (125 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9.9 mg, 5 mol %) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.47 (d, J = 8.2 Hz, 2H), 7.39 – 7.32 (m, 4H), 7.31 – 7.25 (m, 1H), 7.25 – 7.18 (m, 2H), 2.49 (td, J = 8.4, 6.7 Hz, 1H), 2.02 (td, J = 8.6, 5.8 Hz, 1H), 1.51 (tdd, J = 8.6, 5.0, 1.0 Hz, 1H), 1.37 (dt, J = 6.8, 5.4 Hz, 1H). **$^{19}$F NMR** (376 MHz, Chloroform-d) δ -62.86. **$^{13}$C NMR** (101 MHz, CDCl3) δ 137.73, 131.54, 129.09 (q, J = 32 Hz, 2C) 128.40, 127.84, 126.46, 124.96 (q, J = 3.9 Hz, 1C), 124.01 (q, J = 273 Hz, 1C), 92.85,

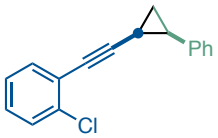
79.00, 24.22, 14.92, 10.08. **HRMS** (APCI Positive): calculated for $C_{18}H_{17}$ $[M]^+$: 287.1042; found: 287.1055.

***cis*-1-Methyl-2-((2-phenylcyclopropyl)ethynyl)benzene (98h)**



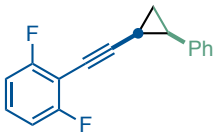

The title compound (colorless oil, 63 mg, 90% yield, 13:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-((2-methylphenyl)ethynyl)-cyclohepta-1,3,5-triene (62 mg, 0.30 mmol, 1 equiv) and styrene (125 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9.9 mg, 5 mol %) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.41 – 7.32 (m, 4H), 7.30 – 7.24 (m, 1H), 7.23 – 7.19 (m, 1H), 7.17 – 7.03 (m, 3H), 2.47 (td, J = 8.5, 6.7 Hz, 1H), 2.14 – 2.05 (m, 4H), 1.50 (td, J = 8.6, 5.0 Hz, 1H), 1.37 (ddd, J = 6.8, 5.8, 5.0 Hz, 1H). **$^{13}$C NMR** (101 MHz, CDCl3) δ 139.99, 138.05, 131.92, 129.14, 128.62, 127.92, 127.37, 126.35, 125.27, 123.58, 93.55, 79.04, 24.08, 20.38, 14.80, 10.39. **HRMS** (APCI Positive): calculated for $C_{18}H_{17}$ $[M]^+$: 233.1325; found: 233.1325.

***cis*-1-Chloro-2-((2-phenylcyclopropyl)ethynyl)benzene (98i)**




The title compound (viscous residue, 41 mg, 54% yield, 10:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-((2-chlorophenyl)ethynyl)-cyclohepta-1,3,5-triene (68 mg, 0.30 mmol, 1 equiv) and styrene (125 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9.9 mg, 5 mol %) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.40 – 7.23 (m, 6H), 7.18 – 7.06 (m, 3H), 2.47 (td, J = 8.4, 6.8 Hz, 1H), 2.09 (td, J = 8.5, 5.8 Hz, 1H), 1.52 (td, J = 8.6, 5.1 Hz, 1H), 1.39 (ddd, J = 6.8, 5.8, 5.1 Hz, 1H). **$^{13}$C NMR** (101 MHz, CDCl3) δ 137.76, 135.49, 133.35, 128.98, 128.47, 128.34, 127.90, 126.36, 126.16, 123.66, 95.33, 77.13, 24.32, 15.19, 10.42. **HRMS** (APCI Positive): calculated for $C_{17}H_{14}Cl$ $[M]^+$: 253.0779; found: 253.0774.

***cis*-1,3-Difluoro-2-((2-phenylcyclopropyl)ethynyl)benzene (98j)**




The title compound (colorless oil, 33 mg, 43% yield, 13:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-((2,6-difluorophenyl)ethynyl)cyclohepta-1,3,5-triene (68 mg, 0.30 mmol, 1 equiv) and styrene (125 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9.9 mg, 5 mol %) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.39 – 7.30 (m, 4H), 7.27 – 7.21 (m, 1H), 7.18 – 7.10 (m, 1H), 6.86 – 6.76 (m, 2H), 2.46 (td, J = 8.5, 6.8 Hz, 1H), 2.11 (td, J = 8.6, 5.9 Hz, 1H), 1.55 (td, J = 8.6, 5.0 Hz, 1H), 1.39 (ddd, J = 6.9, 5.9, 5.0 Hz, 1H). **$^{19}$F NMR** (376 MHz, CDCl3) δ -107.93.

**$^{13}$C NMR** (101 MHz, Chloroform-d) δ 164.57 (d, J = 5.5 Hz), 162.06 (d, J = 5.6 Hz), 128.47 (t, J = 9.9 Hz), 128.22, 127.87, 126.33, 111.00 (d, J = 5.9 Hz), 110.81 (d, J = 5.8 Hz), 102.68 (t, J = 19.8 Hz), 100.11 (t, J = 3.2 Hz), 67.23, 24.41, 15.59, 10.65. **HRMS** (APCI Positive): calculated for $C_{17}H_{13}F_2$ $[M]^+$: 255.0980; found: 255.0991.

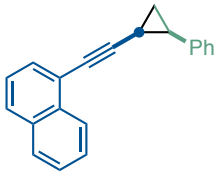
***endo*-7-(Phenylethynyl)bicyclo[4.1.0]heptane (98k)**

The title compound (viscous residue, 41 mg, 54% yield, 10:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-((2-chlorophenyl)ethynyl)-cyclohepta-1,3,5-triene (68 mg, 0.30 mmol, 1 equiv) and styrene (125 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9.9 mg, 5 mol %) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.40 – 7.23 (m, 6H), 7.18 – 7.06 (m, 3H), 2.47 (td, J = 8.4, 6.8 Hz, 1H), 2.09 (td, J = 8.5, 5.8 Hz, 1H), 1.52 (td, J = 8.6, 5.1 Hz, 1H), 1.39 (ddd, J = 6.8, 5.8, 5.1 Hz, 1H). **$^{13}$C NMR** (101 MHz, CDCl3) δ 137.76, 135.49, 133.35, 128.98, 128.47, 128.34, 127.90, 126.36, 126.16, 123.66, 95.33, 77.13, 24.32, 15.19, 10.42. **HRMS** (APCI Positive): calculated for $C_{17}H_{14}Cl$ $[M]^+$: 253.0779; found: 253.0774.

***endo*-7-(*p*-Tolylethynyl)bicyclo[4.1.0]heptane (98l)**

The title compound (pale yellow oil, 22 mg, 43% yield, >15:1 *endo*/*exo* ratio) was obtained following General Procedure E1 from 7-(p-tolylethynyl)cyclohepta-1,3,5-triene (50 mg, 0.24 mmol, 1 equiv) and cyclohexene (80 mg, 0.97 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (8.0 mg, 5 mol %) in $CHCl_3$, after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (500 MHz, Chloroform-d) δ 7.32 – 7.26 (m, 2H), 7.10 – 7.05 (m, 2H), 2.32 (s, 3H), 1.97 – 1.88 (m, 2H), 1.78 – 1.70 (m, 2H), 1.57 (t, J = 8.5 Hz, 1H), 1.44 (m, 2H), 1.29 – 1.22 (m, 5H). **$^{13}$C NMR** (126 MHz, CDCl3) δ 137.65, 131.73, 129.29, 121.68, 89.33, 83.07, 22.19, 21.72, 20.46, 15.71, 11.47. **HRMS** (APCI Positive): calculated for $C_{16}H_{19}$ $[M]^+$: 211.1481; found: 211.1477.

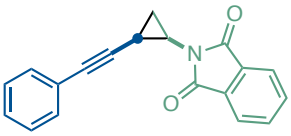
***cis*-1-((2-Phenylcyclopropyl)ethynyl)naphthalene (98m)**




The title compound (white solid, 65 mg, 81% yield, >15:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 1-(cyclohepta-2,4,6-trien-1-ylethynyl)naphthalene (73 mg, 0.30 mmol, 1 equiv) and styrene (125 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9.9 mg, 5 mol %) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.82 – 7.72 (m, 2H), 7.65 – 7.60 (m, 1H), 7.51 – 7.34 (m, 9H), 2.56 (td, J = 8.4, 6.7 Hz, 1H), 2.23 – 2.15 (m, 1H), 1.58 – 1.48 (m, 2H). **$^{13}$C NMR** (101 MHz,

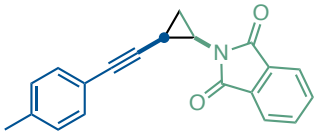
CDCl3) δ 138.08, 133.35, 133.06, 130.08, 128.87, 128.15, 127.94, 127.80, 126.56, 126.45, 126.34, 126.12, 125.14, 121.58, 94.79, 78.09, 24.23, 14.59, 10.51. **HRMS** (APCI Positive): calculated for $C_{21}H_{17}$ $[M]^+$: 269.1325; found: 269.1320. **MP** 69–72 ºC.

***cis*-2-(2-(Phenylethynyl)cyclopropyl)isoindoline-1,3-dione (98n)**



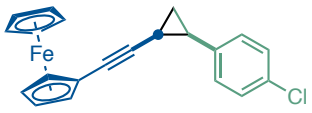
The title compound (white solid, 65 mg, 81% yield, >15:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 1-(cyclohepta-2,4,6-trien-1-ylethynyl)naphthalene (73 mg, 0.30 mmol, 1 equiv) and styrene (125 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9.9 mg, 5 mol %) after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.82 – 7.72 (m, 2H), 7.65 – 7.60 (m, 1H), 7.51 – 7.34 (m, 9H), 2.56 (td, J = 8.4, 6.7 Hz, 1H), 2.23 – 2.15 (m, 1H), 1.58 – 1.48 (m, 2H). **$^{13}$C NMR** (101 MHz, CDCl3) δ 138.08, 133.35, 133.06, 130.08, 128.87, 128.15, 127.94, 127.80, 126.56, 126.45, 126.34, 126.12, 125.14, 121.58, 94.79, 78.09, 24.23, 14.59, 10.51. **HRMS** (APCI Positive): calculated for $C_{21}H_{17}$ $[M]^+$: 269.1325; found: 269.1320.

***cis*-2-(2-(*p*-Tolylethynyl)cyclopropyl)isoindoline-1,3-dione (98o)**



The title compound (white solid, 53 mg, 52% yield, 12:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-(*p*-tolylethynyl)cyclohepta-1,3,5-triene (70 mg, 0.34 mmol, 1 equiv) and *N*-vinylphthalimide (118 mg, 0.68 mmol, 2 equiv) using $[Rh_2(TFA)_4]$ (11.2 mg, 5 mol %) using $CHCl_3$, after purification by flash column chromatography in $SiO_2$ using a gradient between from cyclohexane to 7:3 cyclohexane/EtOAc as eluent. **$^1$H NMR** (500 MHz, Chloroform-d) δ 7.83 (dd, J = 5.4, 3.0 Hz, 2H), 7.69 (dd, J = 5.5, 3.0 Hz, 2H), 6.88 (s, 4H), 3.07 (ddd, J = 7.8, 6.5, 5.1 Hz, 1H), 2.21 (s, 3H), 2.06 (dt, J = 9.1, 6.5 Hz, 1H), 1.94 (td, J = 6.5, 5.2 Hz, 1H), 1.59 – 1.55 (m, 1H). **$^{13}$C NMR** (126 MHz, CDCl3) δ 169.00, 138.00, 134.37, 132.14, 131.68, 129.07, 123.54, 120.46, 86.88, 79.86, 28.31, 21.64, 13.88, 8.88. **HRMS** (ESI Pos): calculated for $C_{20}H_{15}NNaO_2$ $[M+Na]^+$: 324.0995; found: 324.0992. **MP** 105–106 ºC.

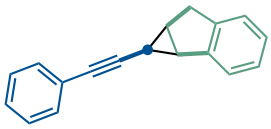
***cis*-1-Chloro-4-(2-(ferrocenylethynyl)cyclopropyl)benzene (98p)**



The title compound (orange solid, 55 mg, 45% yield, 9:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-((ferrocenyl)ethynyl)-cyclohepta-1,3,5-triene (100 mg, 0.33 mmol, 1 equiv) and 4-chlorostyrene (185 mg, 1.33 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (6.6 mg, 3 mol %) in $CHCl_3$ after purification by flash column chromatography in $SiO_2$ using

cyclohexane as eluent. Slow evaporation of a 9:1 MeCN/$CH_2Cl_2$ solution afforded X-ray diffraction-quality crystals. **$^1$H NMR** (500 MHz, Chloroform-d) δ 7.35 – 7.29 (m, 2H), 7.27 – 7.23 (m, 2H), 4.17 (h, J = 1.3 Hz, 2H), 4.06 (t, J = 1.9 Hz, 2H), 3.97 (s, 5H), 2.30 (td, J = 8.4, 6.6 Hz, 1H), 1.88 (td, J = 8.5, 5.8 Hz, 1H), 1.40 (td, J = 8.6, 5.1 Hz, 1H), 1.19 (ddd, J = 6.6, 5.8, 5.1 Hz, 1H). **$^{13}$C NMR** (126 MHz, CDCl3) δ 137.34, 132.35, 130.26, 128.23, 85.39, 78.78, 71.48, 71.41, 70.08, 68.51, 66.18, 23.51, 15.40, 10.86. **HRMS** (ESI Pos): calculated for $C_{21}H_{17}Cl^{55}Fe$ $[M]^+$: 360.0363; found: 360.0354. **MP** 82–84 ºC.

***endo*-1-(Phenylethynyl)-1,1a,6,6a-tetrahydrocyclopropa[*a*]indene (98q)**

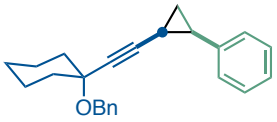


The title compound (pale yellow residue, 53 mg, 52% yield, 12:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-(*p*-tolylethynyl)cyclohepta-1,3,5-triene (70 mg, 0.34 mmol, 1 equiv) and *N*-vinylphthalimide (118 mg, 0.68 mmol, 2 equiv) using $[Rh_2(TFA)_4]$ (11.2 mg, 5 mol %) using $CHCl_3$, after purification by flash column chromatography in $SiO_2$ using a gradient between from cyclohexane to 7:3 cyclohexane/EtOAc as eluent. **$^1$H NMR** (500 MHz, Chloroform-d) δ 7.83 (dd, J = 5.4, 3.0 Hz, 2H), 7.69 (dd, J = 5.5, 3.0 Hz, 2H), 6.88 (s, 4H), 3.07 (ddd, J = 7.8, 6.5, 5.1 Hz, 1H), 2.21 (s, 3H), 2.06 (dt, J = 9.1, 6.5 Hz, 1H), 1.94 (td, J = 6.5, 5.2 Hz, 1H), 1.59 – 1.55 (m, 1H). **$^{13}$C NMR** (126 MHz, CDCl3) δ 169.00, 138.00, 134.37, 132.14, 131.68, 129.07, 123.54, 120.46, 86.88, 79.86, 28.31, 21.64, 13.88, 8.88. **HRMS** (ESI Pos): calculated for $C_{20}H_{15}NNaO_2$ $[M+Na]^+$: 324.0995; found: 324.0992.

***cis*-(2-(Oct-1-yn-1-yl)cyclopropyl)benzene (98ap)**

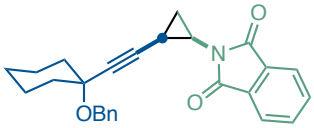
The title compound (pale yellow oil, 13 mg, 13% yield, 5:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-(oct-1-yn-1-yl)cyclohepta-1,3,5-triene (100 mg, 0.50 mmol, 1 equiv) and styrene (208 mg, 2.00 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9.9 mg, 3 mol %) using $CHCl_3$, after purification by flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.33 – 7.26 (m, 4H), 7.24 – 7.20 (m, 1H), 2.24 (td, *J* = 8.5, 6.6 Hz, 1H), 2.02 (td, *J* = 7.0, 2.0 Hz, 2H), 1.82 – 1.74 (m, 1H), 1.35 – 1.24 (m, 6H), 1.20 – 1.16 (m, 3H), 1.11 (ddd, *J* = 6.6, 5.9, 4.9 Hz, 1H), 0.90 (d, *J* = 7.0 Hz, 3H). **$^{13}$C NMR** (101 MHz, CDCl3) δ 138.40, 128.29, 127.61, 125.98, 80.52, 79.05, 31.36, 28.81, 28.32, 23.16, 22.52, 18.71, 14.61, 14.06, 9.81. **HRMS** (APCI Pos): calculated for $C_{17}H_{23}$ $[M+H]^+$: 227.1794; found: 227.1793.

***cis*-2-((1-(Benzyloxy)cyclohexyl)ethynyl)cyclopropyl)benzene (98at)**



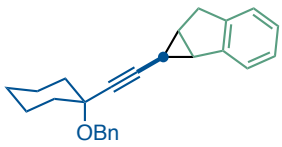

The title compound (pale yellow oil, 65 mg, 60% yield, 6:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-((1-(benzyloxy)cyclohexyl)ethynyl)cyclohepta-1,3,5-triene (100 mg, 0.33 mmol, 1 equiv) and styrene (137 mg, 1.31 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (11 mg, 5 mol %), after purification by flash column chromatography in $SiO_2$ using a gradient from cyclohexane to cyclohexane/EtOAc 95:5 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.39 – 7.21 (m, 10H), 4.32 (s, 2H), 2.37 (td, *J* = 8.4, 6.6 Hz, 1H), 1.87 (td, *J* = 8.5, 5.7 Hz, 1H), 1.78 – 1.73 (m, 2H), 1.59 – 1.47 (m, 4H), 1.41 – 1.36 (m, 1H), 1.35 – 1.19 (m, 4H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 139.72, 138.02, 128.60, 128.12, 127.82, 127.63, 127.01, 126.30, 85.94, 80.90, 74.19, 64.99, 37.58, 37.31, 25.51, 23.54, 22.77, 14.13, 9.50. **HRMS** (ESI Pos): calculated for $C_{24}H_{26}NaO$ $[M+Na]^+$: 353.1876; found: 353.1874.

***cis*-2-(2-((1-(Benzyloxy)cyclohexyl)ethynyl)cyclopropyl)isoindoline-1,3-dione (98au)**




The title compound (pale brown amorphous solid, 58 mg, 44% yield, 11:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-((1-(benzyloxy)cyclohexyl)ethynyl)cyclohepta-1,3,5-triene (100 mg, 0.33 mmol, 1 equiv) and *N*-vinylphthalimide (228 mg, 1.31 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (11 mg, 3 mol %), after purification by flash column chromatography in $SiO_2$ using a gradient from cyclohexane/EtOAc 95:5 to 70:30 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.83 – 7.76 (m, 2H), 7.72 – 7.63 (m, 2H), 7.36 – 7.18 (m, 5H), 4.40 – 4.27 (m, 2H), 3.05 (ddd, *J* = 7.9, 6.5, 5.2 Hz, 1H), 2.00 – 1.89 (m, 2H), 1.65 – 1.57 (m, 2H), 1.56 – 1.51 (m, 1H), 1.42 – 1.33 (m, 3H), 1.31 – 1.22 (m, 3H), 1.10 (dt, *J* = 11.0, 6.3 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 168.60, 139.30, 134.07, 131.69, 128.13, 127.59, 127.10, 123.10, 83.97, 80.58, 74.06, 65.13, 37.30, 27.63, 25.36, 22.76, 13.39, 7.85. **HRMS** (ESI Pos): calculated for $C_{26}H_{25}NNaO_3$ $[M+Na]^+$: 422.1727; found: 422.1730.

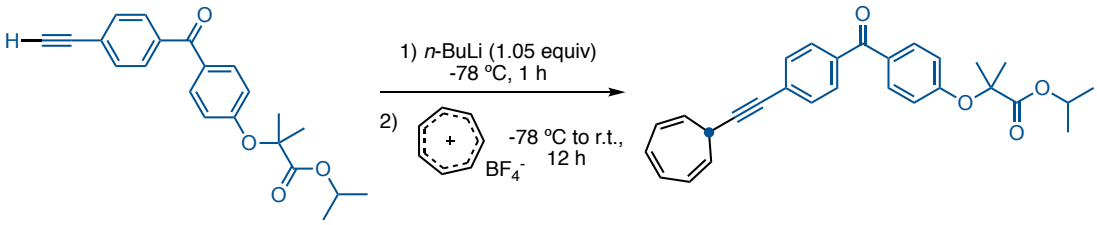
***cis*-1-((1-(benzyloxy)cyclohexyl)ethynyl)-1,1a,6,6a-tetrahydrocyclopropa[*a*]indene (98av)**




The title compound (pale yellow oil, 120 mg, 70% yield, 5:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-((1-(benzyloxy)cyclohexyl)ethynyl)cyclohepta-1,3,5-triene (152 mg, 0.50 mmol, 1 equiv) and 1*H*-indene (232 mg, 2.00 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (16 mg, 5 mol %), after purification by preparative TLC in $SiO_2$ using pentane/$Et_2O$ 97:3 as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.38 – 7.24 (m, 6H), 7.11 (tdd, J = 5.0, 3.3, 2.2 Hz, 3H),

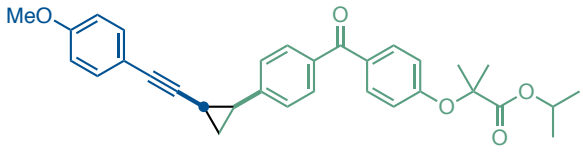
4.23 – 4.12 (m, 2H), 3.30 – 3.21 (m, 1H), 3.11 – 3.02 (m, 1H), 2.82 (ddd, J = 7.6, 6.0, 1.5 Hz, 1H), 2.20 – 2.12 (m, 1H), 1.93 (t, J = 7.7 Hz, 1H), 1.67 – 1.59 (m, 2H), 1.53 – 1.46 (m, 2H), 1.38 (m, 3H), 1.26 – 1.11 (m, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.75, 141.73, 139.73, 128.10, 127.67, 126.99, 126.21, 126.03, 124.61, 124.12, 82.84, 81.27, 74.24, 64.83, 37.67, 37.25, 32.75, 31.27, 25.47, 22.95, 22.83, 14.12. **HRMS** (ESI Pos): calculated for $C_{25}H_{26}NaO$ $[M+Na]^+$: 365.1876; found: 365.1877.

**Fenofibrate Alkynylcycloheptatriene: Isopropyl 2-(4-(4-(cyclohepta-2,4,6-trien-1-ylethynyl)benzoyl)phenoxy)-2-methyl-propanoate**




Fenofibrate Alkynylcycloheptatriene (viscous residue, 75 mg, 18% yield) was obtained following General Procedure D from isopropyl 2-(4-(4-ethynylbenzoyl)phenoxy)-2-methylpropanoate (337 mg, 0.20 mmol, 1 equiv, prepared according to a reported procedure)[158] and tropylium tetrafluoroborate (180 mg, 1.01 mmol, 1.05 equiv) using *n*-BuLi (2.42 M in hexane, 0.42 mL, 1.02 mmol, 1.06 equiv) after purification by flash column chromatography in $SiO_2$ using a gradient from 95:5 to 90:10 cyclohexane/EtOAc as eluent. **$^1$H NMR** (2:1 equilibrium of cycloheptatriene/norcaradiene) 400 MHz, Chloroform-*d*) δ 7.79 – 7.70 (m, 2H), 7.60 – 7.53 (m, 1H), 7.17 – 7.10 (m, 1H), 6.99 (ddt, *J* = 5.8, 3.6, 1.2 Hz, 1H), 6.92 – 6.85 (m, 1H), 6.74 – 6.67 (m, 1H), 6.61 (ddd, *J* = 3.3, 2.6, 0.7 Hz, 1H), 6.28 – 6.17 (m, 1H), 5.48 – 5.35 (m, 1H), 2.27 (t, *J* = 6.8 Hz, 1H), 1.68 (s, 3H), 1.22 (dd, *J* = 6.2, 0.8 Hz, 3H), 1.07 (m, 10H). **LCMS** (APCI Pos): calculated for $C_{29}H_{28}O_4$ $[M+H]^+$: 440.2; found: 440.3.

***cis*-Isopropyl 2-(4-(4-(2-((4-methoxyphenyl)ethynyl)cyclopropyl)benzoyl)phenoxy)-2-methylpropanoate (98ay)**

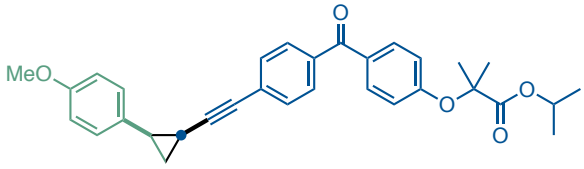



The title compound (viscous orange oil, 55 mg, 52% yield, 90% brsm, 10:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-((4-methoxyphenyl)ethynyl)-cyclohepta-1,3,5-triene (71 mg, 0.32 mmol, 1.5 equiv) and styrene (125 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (7 mg, 5

158 Zhao, B.; Wu, Y.; Yuan, Y.; Shi, Z. Copper-catalysed Csp3–Csp cross-couplings between cyclobutanone oxime esters and terminal alkynes induced by visible light. *Chem. Commun.* **2020**, *56*, 4676–4679.

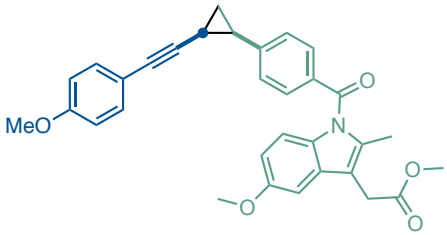
mol %) after purification by flash column chromatography in $SiO_2$ using a gradient from 95:5 to 75:25 cyclohexane/EtOAc as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.79 – 7.72 (m, 4H), 7.45 – 7.39 (m, 2H), 7.15 – 7.08 (m, 2H), 6.89 – 6.84 (m, 2H), 6.78 – 6.72 (m, 2H), 5.10 (p, J = 6.3 Hz, 1H), 3.78 (s, 3H), 2.46 (td, J = 8.4, 6.6 Hz, 1H), 2.09 (td, J = 8.5, 5.9 Hz, 1H), 1.68 (s, 6H), 1.54 (td, J = 8.6, 5.1 Hz, 1H), 1.36 (ddd, J = 6.6, 5.9, 5.1 Hz, 1H), 1.22 (d, J = 6.3 Hz, 6H). **$^{13}$C NMR** (101 MHz, CDCl3) δ 195.30, 173.19, 159.37, 159.14, 143.12, 135.93, 132.78, 131.95, 131.01, 129.42, 128.01, 117.17, 115.60, 113.81, 87.34, 80.52, 79.36, 69.30, 55.24, 25.40, 25.38, 24.01, 21.53, 15.70, 11.09. **HRMS** (ESI Positive): calculated for $C_{32}H_{33}O_5$ $[M]^+$: 497.2323; found: 497.2329.

***cis*-Isopropyl 2-(4-(4-((2-(4-methoxyphenyl)cyclopropyl)ethynyl)benzoyl)phenoxy)-2-methylpropanoate (98az)**




The title compound (viscous orange residue, 11 mg, 24% yield, >15:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from isopropyl 2-(4-(4-(cyclohepta-2,4,6-trien-1-ylethynyl)benzoyl)phenoxy)-2-methylpropanoate (40 mg, 1.5 equiv 0.091 mmol) and styrene (49 mg, 0.36 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (3 mg, 5 mol %) after purification by flash column chromatography in $SiO_2$ using a gradient from 95:5 to 80:20 cyclohexane/EtOAc as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.75 – 7.70 (m, 2H), 7.64 – 7.59 (m, 2H), 7.28 – 7.21 (m, 4H), 6.91 – 6.85 (m, 4H), 5.11 (p, *J* = 6.3 Hz, 1H), 3.83 (s, 3H), 2.43 (q, *J* = 8.2 Hz, 1H), 1.98 (td, *J* = 8.5, 5.7 Hz, 1H), 1.68 (s, 6H), 1.52 – 1.46 (m, 1H), 1.32 – 1.28 (m, 1H), 1.22 (d, *J* = 6.3 Hz, 6H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 194.98, 173.18, 159.58, 158.32, 136.55, 131.96, 131.10, 130.53, 129.85, 129.62, 129.45, 127.90, 117.21, 113.34, 93.65, 79.64, 79.39, 69.33, 55.35, 25.38, 23.60, 21.52, 15.09, 9.93. **HRMS** (ESI Positive): calculated for $C_{32}H_{32}NaO_5$ $[M]^+$: 519.2142; found: 519.2143.

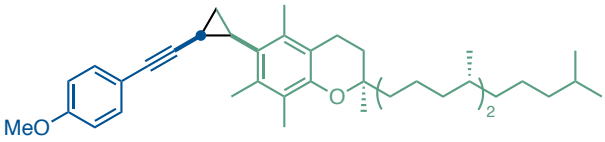
***cis*-Methyl 2-(5-methoxy-1-(4-(2-((4-methoxyphenyl)ethynyl)cyclopropyl)-benzoyl)-2-methyl-1*H*-indol-3-yl)acetate (98ba)**




The title compound (50 mg, pale brown solid, 30% yield, 73% brsm 15:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from 7-((4-methoxyphenyl)ethynyl)-cyclohepta-1,3,5-triene (110 mg, 0.50 mmol, 1.5 equiv) and vinyl-indomethacin methyl ester (120 mg, 0.33 mmol, 1 equiv) using $[Rh_2(TFA)_4]$ (11 mg, 5 mol %) in PhMe/$CHCl_3$ (2:1) after purification by flash column chromatography in $SiO_2$ using 8:2 cyclohexane/EtOAc as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.68 – 7.63 (m, 2H), 7.42

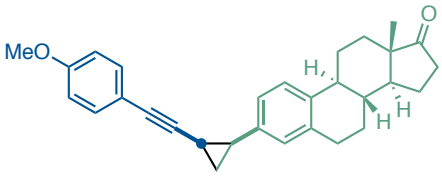
– 7.37 (m, 2H), 7.14 – 7.08 (m, 2H), 6.93 (d, *J* = 2.5 Hz, 1H), 6.83 (d, *J* = 9.0 Hz, 1H), 6.74 – 6.69 (m, 2H), 6.46 (dd, *J* = 9.0, 2.6 Hz, 1H), 3.78 (s, 3H), 3.75 (s, 3H), 3.68 (s, 3H), 3.64 (s, 2H), 2.44 (td, *J* = 8.4, 6.6 Hz, 1H), 2.34 (s, 3H), 2.09 (td, *J* = 8.6, 6.0 Hz, 1H), 1.53 (td, *J* = 8.5, 5.2 Hz, 1H), 1.36 – 1.32 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 171.82, 169.77, 159.57, 156.17, 144.51, 136.53, 133.18, 131.43, 130.80, 129.73, 128.84, 115.81, 115.31, 114.23, 112.26, 111.80, 101.50, 87.34, 81.02, 66.21, 56.03, 55.56, 52.45, 30.54, 24.44, 16.10, 13.51, 11.65. **HRMS** (ESI Pos): calculated for $C_{32}H_{29}NNaO_5$ $[M+Na]^+$: 530.1938; found: 530.1938. **MP** 59–63 ºC.

***cis*-6-(2-((4-Methoxyphenyl)ethynyl)cyclopropyl)-2,5,7,8-tetramethyl-2-((4*R*,8*R*)-4,8,12-trimethyltridecyl)chromane (98bb)**




The title compound (pale orange oil, 31 mg, 51% yield, 90% brsm, 3:1 *cis*/*trans* ratio, as a mixture of the two possible *cis* cyclopropanes) was obtained following General Procedure E1 from 7-((4-methoxyphenyl)ethynyl)-cyclohepta-1,3,5-triene (34 mg, 0.15 mmol, 1.5 equiv) and vinyl-alpha-Tocopherol (45 mg, 0.10 mmol, 1 equiv) using $[Rh_2(TFA)_4]$ (3.4 mg, 5 mol %) after purification by preparative TLC in $SiO_2$ using 98:2 pentane/$Et_2O$ as eluent. **$^1$H NMR** (unassigned mixture of the two possible *cis* diastereoisomers, 400 MHz, Chloroform-d) δ 7.43 – 7.38 (m, 1H), 7.03 – 6.97 (m, 2H), 6.88 – 6.83 (m, 1H), 6.74 – 6.69 (m, 1H), 3.83 (s, 1H), 3.77 (s, 2H), 2.68 – 2.59 (m, 2H), 2.20 (q, *J* = 8.1 Hz, 1H), 2.02 (td, *J* = 8.3, 5.7 Hz, 1H), 1.90 – 1.78 (m, 2H), 1.66 – 1.49 (m, 6H), 1.46 – 1.39 (m, 3H), 1.30 (m, 11H), 1.17 (ddd, *J* = 8.8, 6.9, 4.4 Hz, 3H), 1.13 – 1.05 (m, 4H), 1.01 – 0.95 (m, 1H), 0.91 – 0.87 (m, 13H). **$^{13}$C NMR** (unassigned mixture of the two possible *cis* diastereoisomers, 101 MHz, CDCl3) δ 159.04, 158.74, 150.35, 150.17, 135.84, 134.42, 133.08, 132.70, 128.88, 127.25, 126.90, 126.59, 126.57, 122.23, 121.93, 116.93, 116.71, 116.39, 116.15, 113.83, 113.62, 113.61, 91.31, 89.88, 78.18, 74.91, 74.70, 55.27, 55.19, 39.40, 37.54, 37.48, 33.45, 32.73, 31.53, 31.30, 29.72, 28.00, 24.82, 24.48, 24.47, 23.98, 22.74, 22.65, 21.38, 21.13, 21.07, 20.84, 20.78, 19.77, 19.66, 18.74, 17.52, 17.33, 16.56, 16.40, 12.45, 11.83, 11.78, 9.85. **HRMS** (APCI Positive): calculated for $C_{41}H_{61}O_2$ $[M+H]^+$: 585.4666; found: 585.4666.

**3*cis*-(8*R*,9*S*,13*S*,14*S*)-3-(2-((4-Methoxyphenyl)ethynyl)cyclopropyl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (98bc)**




The title compound (off-white solid, 29 mg, 64% yield, >15:1 *cis*/*trans* ratio, as a mixture of the two possible *cis* cyclopropanes) was obtained following General Procedure E1 from 7-((4-methoxyphenyl)ethynyl)-cyclohepta-1,3,5-triene (36 mg, 0.16 mmol, 1.5 equiv) and vinyl-Estrone (30 mg, 0.11 mmol, 1 equiv) using $[Rh_2(TFA)_4]$ (3.5 mg, 5 mol %) after purification by flash column chromatography in $SiO_2$ using a gradient from 95:5 to 75:25 cyclohexane/EtOAc as eluent. **$^1$H NMR** (unassigned mixture of the two possible *cis* diastereoisomers, 400 MHz, Chloroform-d) δ 7.22 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.11 (ddd, *J* = 6.5, 4.0, 1.9 Hz, 2H), 7.05 (dd, *J* = 7.5, 1.9 Hz, 1H), 6.76 – 6.69 (m, 2H), 3.75 (s, 3H), 2.89 (td, *J* = 7.0, 2.7 Hz, 2H), 2.49 (ddd, *J* = 18.9, 8.8, 0.9 Hz, 1H), 2.45 – 2.39 (m, 1H), 2.33 – 2.25 (m, 2H), 2.13 (dt, *J* = 18.9, 8.9 Hz, 1H), 2.07 – 1.90 (m, 4H), 1.67 – 1.38 (m, 8H), 1.21 – 1.16 (m, 1H), 0.91 (s, 3H). **$^{13}$C NMR** (unassigned mixture of the two possible *cis* diastereoisomers, 101 MHz, CDCl3) (126 MHz, $CDCl_3$) δ 221.35, 159.31, 137.99, 136.08, 133.14, 129.26, 129.12, 126.16, 125.87, 125.11, 116.48, 114.05, 88.68, 80.49, 55.59, 50.92, 48.40, 44.74, 38.68, 36.25, 32.01, 29.87, 26.99, 26.14, 21.98, 15.87, 14.25, 10.51. **HRMS** (ESI Pos): calculated for $C_{30}H_{32}NaO_2$ $[M+Na]^+$: 447.2295; found: 447.2292. **MP** 130–134 ºC.

***cis*-Trimethyl((2-phenylcyclopropyl)ethynyl)silane (99a)**

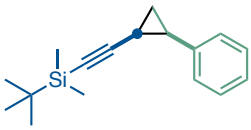

The title compound (colorless oil, 91 mg, 90% yield, 6:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane (94 mg, 0.47 mmol, 1 equiv) and styrene (198 mg, 1.90 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (15 mg, 5 mol %) after purification by flash column chromatography $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.30 – 7.24 (m, 4H), 7.22 – 7.18 (m, 1H), 2.29 (td, *J* = 8.5, 6.7 Hz, 1H), 1.80 (td, *J* = 8.6, 5.9 Hz, 1H), 1.35 (td, *J* = 8.6, 5.0 Hz, 1H), 1.20 (ddd, *J* = 6.8, 5.9, 5.0 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.16, 128.70, 127.97, 126.55, 106.75, 84.86, 24.30, 15.58, 10.84, 0.25. **HRMS** (APCI Positive): calculated for $C_{17}H_{15}$ $[M]^+$: 215.1251; found: 215.1246.

***cis*-Dimethyl(phenyl)((2-phenylcyclopropyl)ethynyl)silane (99b)**


The title compound (colorless oil, 120 mg, 87% yield, 4.5:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from (cyclohepta-2,4,6-trien-1-ylethynyl)dimethyl(phenyl)silane (125 mg, 0.50 mmol, 1 equiv) and styrene (208 mg, 2.00 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (16

mg, 5 mol %) after purification by flash column chromatography $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.48 – 7.45 (m, 2H), 7.43 – 7.28 (m, 8H), 2.42 (td, *J* = 8.4, 6.8 Hz, 1H), 1.94 (td, *J* = 8.6, 5.8 Hz, 1H), 1.45 (td, *J* = 8.6, 5.0 Hz, 1H), 1.39 – 1.33 (m, 1H), 0.34 (d, *J* = 2.0 Hz, 6H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 137.75, 137.45, 133.68, 129.16, 128.54, 127.84, 127.75, 126.40, 108.35, 82.32, 24.15, 15.03, 10.64, -0.67, -0.77. **HRMS** (APCI Positive): calculated for $C_{17}H_{15}$ $[M]^+$: 277.1407; found: 277.1403.

***cis-tert*-Butyldimethyl((2-phenylcyclopropyl)ethynyl)silane (99c)**




The title compound (pale yellow oil, 121 mg, 94% yield, 3:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from *tert*-butyl(cyclohepta-2,4,6-trien-1-ylethynyl)dimethylsilane (115 mg, 0.50 mmol, 1 equiv) and styrene (208 mg, 2.00 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (16 mg, 5 mol %) after purification by flash column chromatography $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.34 – 7.29 (m, 4H), 7.24 (ddd, *J* = 7.4, 4.1, 1.7 Hz, 1H), 2.34 (td, *J* = 8.4, 6.7 Hz, 1H), 1.86 (td, *J* = 8.6, 5.8 Hz, 1H), 1.41 – 1.36 (m, 1H), 1.28 – 1.23 (m, 1H), 0.79 (s, 9H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 137.75, 128.46, 127.78, 126.22, 106.84, 82.47, 26.16, 25.94, 23.96, 14.87, 10.50, -4.59. **HRMS** (APCI Positive): calculated for $C_{17}H_{25}Si$ $[M]^+$: 257.1720; found: 257.1720.

***cis*-Triisopropyl((2-phenylcyclopropyl)ethynyl)silane (99d)**


The title compound (colorless oil, 313 mg, 84% yield, 2:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from (cyclohepta-2,4,6-trien-1-ylethynyl)triisopropylsilane (340 mg, 1.25 mmol, 1 equiv) and styrene (520 mg, 5.00 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (25 mg, 3 mol %) after purification by flash column chromatography $SiO_2$ using cyclohexane as eluent gave the two diastereoisomer separately (>15:1 for each). ***cis*-Isomer: $^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.25 – 7.22 (m, 4H), 7.19 – 7.14 (m, 1H), 2.29 (td, *J* = 8.4, 6.7 Hz, 1H), 1.83 (td, *J* = 8.6, 5.8 Hz, 1H), 1.33 (td, *J* = 8.6, 4.9 Hz, 1H), 1.19 (ddd, *J* = 6.8, 5.8, 4.9 Hz, 1H), 0.92 – 0.84 (m, 21H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.14, 128.85, 128.15, 126.51, 108.01, 80.45, 24.27, 18.82, 15.09, 11.57, 10.90. **HRMS** (APCI Positive): calculated for $C_{17}H_{15}$ $[M]^+$: 299.2190; found: 299.2188. ***trans*-Isomer: $^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.26 (dd, *J* = 8.3, 7.0 Hz, 2H), 7.19 – 7.15 (m, 1H), 7.09 – 7.05 (m, 2H), 2.24 (ddd, *J* = 8.8, 6.1, 4.5 Hz, 1H), 1.57 (ddd, *J* = 8.7, 5.7, 4.5 Hz, 1H), 1.32 (ddd, *J* = 8.8, 5.6, 4.6 Hz, 1H), 1.23 (ddd, *J* = 8.7, 6.2, 4.7 Hz, 1H), 1.08 – 1.04 (m, 21H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.23, 128.76, 126.55, 126.25, 110.94, 27.30, 19.01, 18.93, 12.76, 11.70.

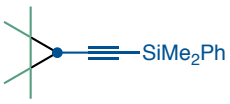
***endo*-((Bicyclo[4.1.0]heptan-7-yl)ethynyl)dimethyl(phenyl)silane (99e)**


The title compound (colorless oil, 60 mg, 79% yield, >15:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from (cyclohepta-2,4,6-trien-1-ylethynyl)dimethyl(phenyl)silane (75 mg, 0.30 mmol, 1 equiv) and cyclohexene (99 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9.9 mg, 5 mol %) after purification by flash column chromatography $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.68 – 7.64 (m, 2H), 7.37 (dd, *J* = 4.4, 2.3 Hz, 3H), 1.95 – 1.87 (m, 2H), 1.74 – 1.67 (m, 2H), 1.43 – 1.36 (m, 2H), 1.26 – 1.17 (m, 4H), 0.41 (s, 6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.15, 134.06, 129.55, 128.14, 109.13, 85.12, 22.02, 20.34, 15.95, 11.96, 1.23, -0.08. **HRMS** (APCI Positive): calculated for $C_{17}H_{23}Si$ $[M]^+$: 255.1564; found: 255.1558.

***endo*-((Bicyclo[4.1.0]heptan-7-yl)ethynyl)dimethyl(*tert*-butyl)silane (99f)**

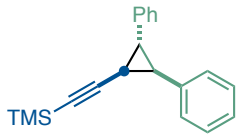

The title compound (colorless oil, 65 mg, 92% yield, >10:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from (cyclohepta-2,4,6-trien-1-ylethynyl)dimethyl(*tert*-butyl)silane (75 mg, 0.30 mmol, 1 equiv) and cyclohexene (99 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9.9 mg, 5 mol %) after purification by flash column chromatography $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 1.91 – 1.83 (m, 2H), 1.70 – 1.62 (m, 2H), 1.44 – 1.35 (m, 3H), 1.26 – 1.18 (m, 2H), 1.17 – 1.10 (m, 2H), 0.92 (s, 9H), 0.08 (s, 6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 107.50, 85.33, 26.50, 21.99, 20.28, 16.79, 15.67, 11.90, -3.87. **HRMS** (APCI Positive): calculated for $C_{15}H_{27}Si$ $[M]^+$: 235.1877; found: 235.1874.

**Dimethyl(phenyl)((2,2,3,3-tetramethylcyclopropyl)ethynyl)silane (99g)**



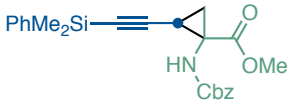

The title compound (colorless oil, 42 mg, 67% yield) was obtained following General Procedure E1 from (cyclohepta-2,4,6-trien-1-ylethynyl)dimethyl(phenyl)silane (60 mg, 0.24 mmol, 1 equiv) and 2,3-dimethylbut-2-ene (81 mg, 0.96 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (7.9 mg, 5 mol %) after purification by flash column chromatography $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.70 – 7.65 (m, 2H), 7.40 – 7.38 (m, 3H), 1.16 (s, 12H), 0.99 (s, 1H), 0.42 (s, 6H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 133.66, 133.02, 129.15, 127.76, 108.91, 82.28, 26.39, 25.96, 22.39, 18.35, 0.87, -0.33. **HRMS** (APCI Positive): calculated for $C_{17}H_{23}Si$ $[M]^+$: 255.1564; found: 255.1558.

**((2,3-Diphenylcyclopropyl)ethynyl)trimethylsilane (99h)**



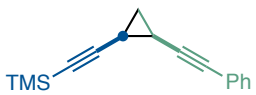

The title compound (pale brown viscous residue, 120 mg, 83% yield) was obtained following General Procedure E1 from (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane (94 mg, 0.50 mmol, 1 equiv) and (*E*)-stilbene (180 mg, 1.00 mmol, 2 equiv) using $[Rh_2(TFA)_4]$ (16 mg, 5 mol %) after purification by flash column chromatography $SiO_2$ using cyclohexane to cyclohexane/EtOAc 98:2 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 6.89 (d, *J* = 10.0 Hz, 2H), 2.44 (s, 6H), 2.33 – 2.30 (m, 3H), 2.06 (q, *J* = 8.1 Hz, 1H), 1.86 (tdd, *J* = 8.4, 5.5, 2.2 Hz, 1H), 1.68 (d, *J* = 2.2 Hz, 1H), 1.57 (td, *J* = 8.6, 4.8 Hz, 1H), 1.12 (ddd, *J* = 7.6, 5.6, 4.8 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 135.96, 131.28, 128.93, 128.82, 84.80, 66.40, 20.94, 20.74, 20.32, 17.16, 7.86. **HRMS** (APCI Positive): calculated for $C_{20}H_{23}Si$ $[M]^+$: 291.1564; found: 291.1565.

**Methyl 1-(((benzyloxy)carbonyl)amino)-2-((dimethyl(phenyl)silyl)ethynyl)cyclopropane-1-carboxylate (99i)**




The title compound (brownish residue, 65 mg, 67% yield, 1:1 *cis*/*trans*) was obtained following General Procedure E1 from (cyclohepta-2,4,6-trien-1-ylethynyl)dimethyl(phenyl)silane (60 mg, 0.24 mmol, 1 equiv) and *N*-Cbz-Dehydro-Ala-OMe (225 mg, 0.96 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (7.9 mg, 5 mol %) after purification by flash column chromatography $SiO_2$ using a gradient between 95:5 to 80:20 cyclohexane/EtOAc as eluent. **$^1$H NMR** (1:1 *cis*/*trans* mixture, unassigned; 400 MHz, Chloroform-*d*) δ 7.66 – 7.59 (m, 2H), 7.44 – 7.32 (m, 8H), 5.57 (two singlets, 1H for each diast), 5.17 (s, 2H), 3.77 – 3.61 (m, 3H), 2.39 (dd, *J* = 9.6, 7.4 Hz, 1H of 1 diast), 2.15 (m, 1H+1H of one diast), 1.53 (dd, *J* = 7.3, 5.2 Hz, 1H of one diast), 1.37 – 1.24 (m, 1H of one diast), 0.42 (d, *J* = 4.1 Hz, 6H). **$^{13}$C NMR** (1:1 *cis*/*trans* mixture, unassigned; 101 MHz, $CDCl_3$) δ 171.09, 156.24, 136.90, 136.62, 136.24, 136.02, 133.69, 133.58, 129.53, 129.44, 128.56, 128.52, 128.25, 128.17, 128.04, 127.97, 127.86, 103.32, 85.12, 84.14, 77.28, 67.51, 67.10, 52.95, 52.34, 41.74, 38.46, 26.94, 25.35, 23.67, 19.85, 19.29, 14.09, -0.85, -0.91. **HRMS** (ESI Pos): calculated for $C_{23}H_{25}NNaO_4Si$ $[M]^+$: 430.1445; found: 430.1442.

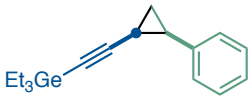
***cis*-Trimethyl((2-(phenylethynyl)cyclopropyl)ethynyl)silane (99j)**




The title compound (pale orange oil, 49 mg, 60% yield, 4:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane (65 mg, 0.34 mmol, 1 equiv) and but-3-en-1-yn-1-ylbenzene (177 mg, 1.38 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (11 mg, 5 mol %), at 80 ºC for 40 h, after purification by flash column chromatography $SiO_2$ using cyclohexane as eluent. **$^1$H**

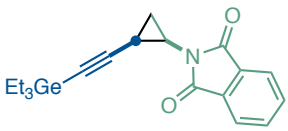
**NMR** (400 MHz, Chloroform-*d*) δ 7.48 – 7.43 (m, 2H), 7.32 – 7.28 (m, 3H), 1.90 – 1.82 (m, 1H), 1.78 (ddd, *J* = 8.6, 7.8, 6.2 Hz, 1H), 1.31 (dt, *J* = 8.5, 4.3 Hz, 1H), 1.11 (td, *J* = 6.1, 4.4 Hz, 1H), 0.17 (s, 9H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 131.81, 128.10, 127.69, 123.69, 105.35, 88.76, 83.86, 79.52, 17.63, 10.13, 9.76, 0.13. **HRMS** (APCI Positive): calculated for $C_{16}H_{19}Si$ $[M+H]^+$: 239.1251; found: 239.1252.

***cis*-Triethyl((2-phenylcyclopropyl)ethynyl)germane (101a)**




The title compound (colorless oil, 42 mg, 51% yield, 9:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from (cyclohepta-2,4,6-trien-1-ylethynyl)triethylgermane (75 mg, 0.27 mmol, 1 equiv) and styrene (114 mg, 1.10 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9 mg, 5 mol %) after purification by flash column chromatography $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.29 (s, 4H), 7.24 – 7.18 (m, 1H), 2.30 (td, *J* = 8.4, 6.7 Hz, 1H), 1.86 (td, *J* = 8.6, 5.9 Hz, 1H), 1.37 (td, *J* = 8.6, 4.9 Hz, 1H), 1.20 (ddd, *J* = 6.7, 5.9, 4.9 Hz, 1H), 0.98 – 0.88 (m, 9H), 0.70 (qd, *J* = 7.8, 1.0 Hz, 6H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.02, 128.38, 127.61, 126.05, 106.16, 81.45, 23.78, 15.09, 10.67, 8.80, 5.64. **HRMS** (APCI Pos): calculated for $C_{17}H_{25}{}^{70}Ge$ $[M+H]^+$: 299.1193; found: 299.1183.

***cis*-2-(2-((Triethylgermyl)ethynyl)cyclopropyl)isoindoline-1,3-dione (101b)**



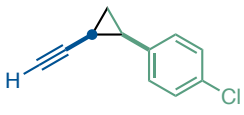

The title compound (white solid, 65 mg, 64% yield, >15:1 *cis*/*trans* ratio) was obtained following General Procedure E1 from (cyclohepta-2,4,6-trien-1-ylethynyl)triethylgermane (75 mg, 0.27 mmol, 1 equiv) and *N*-vinylphthalimide (189 mg, 1.10 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9 mg, 5 mol %) after purification by flash column chromatography $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.83 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.72 (dd, *J* = 5.5, 3.0 Hz, 2H), 3.07 – 2.95 (m, 1H), 1.98 – 1.86 (m, 2H), 1.54 – 1.44 (m, 1H), 0.83 – 0.71 (m, 9H), 0.55 – 0.46 (m, 6H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 168.55, 133.89, 131.86, 123.03, 103.99, 81.04, 27.88, 13.63, 8.85, 8.63, 5.44. **HRMS** (ESI Pos): calc. for $C_{19}H_{23}NNaO_2{}^{70}Ge$ $[M+ Na]^+$: 390.0863; found: 390.0864. **MP** 93–94 ºC.

***cis*-(2-Ethynylcyclopropyl)benzene (100a)**


The title compound (pale yellow oil, volatile, do not put under high vacuum, 1.10 g, 6:1 *cis*/*trans* ratio, 91% combine yield of both diastereoisomers) was obtained following General Procedure E2 from (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane **91b** (1.60 g, 8.5 mmol, 1 equiv) and styrene (3.54 g, 34 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (279 mg, 5 mol %), at 65 ºC for 40 h (lower temperature than in

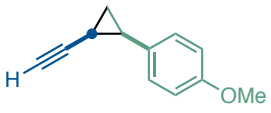
sealed microwave vials for the gram-scale procedure; alternatively, the reaction can be performed in toluene at 80 ºC in less than 24 h with similar result). Flash column chromatography in $SiO_2$ using pentane as eluent gave both diastereoisomers in pure form (0.88 g of *cis*/*trans* >20:1 dr, 73%; 0.16 g of *trans*/*cis* >20:1 dr, 13%). ***cis*-Isomer: $^1$H NMR** (500 MHz, Chloroform-d) δ 7.34 – 7.29 (m, 2H), 7.29 – 7.25 (m, 2H), 7.25 – 7.21 (m, 1H), 2.30 (td, J = 8.4, 6.7 Hz, 1H), 1.82 – 1.77 (m, 1H), 1.76 (d, J = 2.2 Hz, 1H), 1.35 (td, J = 8.6, 5.1 Hz, 1H), 1.21 (ddd, J = 6.8, 5.8, 5.0 Hz, 1H). **$^{13}$C NMR** (126 MHz, CDCl3) δ 137.99, 128.76, 128.21, 126.76, 83.92, 68.39, 23.70, 14.64, 9.51. ***trans*-Isomer: $^1$H NMR** (400 MHz, Chloroform-d) δ 7.33 – 7.27 (m, 2H), 7.25 – 7.19 (m, 1H), 7.14 – 7.09 (m, 2H), 2.31 (ddd, J = 8.8, 6.2, 4.5 Hz, 1H), 1.94 (d, J = 2.1 Hz, 1H), 1.54 (dddd, J = 8.8, 5.6, 4.6, 2.1 Hz, 1H), 1.36 (ddd, J = 8.9, 5.6, 4.8 Hz, 1H), 1.28 (ddd, J = 8.7, 6.2, 4.8 Hz, 1H). **$^{13}$C NMR** (101 MHz, CDCl3) δ 140.50, 128.45, 126.35, 126.00, 86.22, 64.79, 26.10, 17.46, 10.87. **HRMS** (APCI Positive): calculated for $C_{11}H_{11}$ $[M+H]^+$: 143.0855; found: 143.0856.

***cis*-1-Chloro-4-(2-ethynylcyclopropyl)benzene (100b)**




The title compound (pale yellow oil, 48 mg, 54% yield, 10:1 *cis*/*trans* ratio) was obtained following General Procedure E2 from (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane **91b** (94 mg, 0.50 mmol, 1 equiv) and 1-chloro-4-vinylbenzene (104 mg, 0.75 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (16.4 mg, 5 mol %) after flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.30 – 7.21 (m, 2H), 7.20 – 7.14 (m, 2H), 2.24 (td, *J* = 8.6, 6.8 Hz, 1H), 1.82 – 1.77 (m, 1H), 1.76 (d, *J* = 2.0 Hz, 1H), 1.38 – 1.33 (m, 1H), 1.17 – 1.11 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 136.57, 132.51, 130.09, 128.35, 83.56, 68.68, 23.09, 14.81, 9.60. **HRMS** (APCI Positive): calculated for $C_{11}H_{10}Cl$ $[M+H]^+$: 177.0466; found: 177.0461.

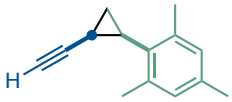
***cis*-1-(2-Ethynylcyclopropyl)-4-methoxybenzene (100c)**




The title compound (pale yellow solid, 63 mg, 73% yield, 4:1 *cis*/*trans* ratio) was obtained following General Procedure E2 from (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane **91b** (94 mg, 0.50 mmol, 1 equiv) and 1-methoxy-4-vinylbenzene (268 mg, 2.00 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (16.4 mg, 5 mol %) after flash column chromatography in $SiO_2$ using a gradient from cyclohexane to cyclohexane/EtOAc 95:5 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.27 – 7.20 (m, 2H), 6.93 – 6.87 (m, 2H), 3.83 (s, 3H), 3.81 (s, 1H), 2.28 (dtd, *J* = 8.4, 6.6, 1.9 Hz, 1H), 1.80 (d, *J* = 2.0 Hz, 1H), 1.79 – 1.73 (m, 1H), 1.35 (td, *J* = 8.7, 5.1 Hz, 1H), 1.19 – 1.14 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.24, 129.48, 127.25, 113.38, 83.93, 64.70,

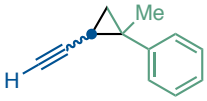
55.22, 22.63, 14.23, 8.82. **HRMS** (APCI Positive): calculated for $C_{12}H_{13}O$ $[M+H]^+$: 173.0961; found: 173.0963. **MP** 37–40 ºC.

***cis*-1-(2-Ethynylcyclopropyl)-1,3,5-trimethlybenzene (100d)**



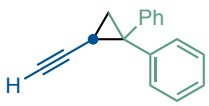
The title compound (pale orange oil, 66 mg, 65% yield, 6:1 *cis*/*trans* ratio) was obtained following General Procedure E2 from (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane **91b** (94 mg, 0.50 mmol, 1 equiv) and 1,3,5-trimethyl-4-vinylbenzene (292 mg, 2.00 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (16.4 mg, 5 mol %) after flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 6.91 (s, 2H), 2.33 – 2.30 (m, 3H), 2.06 (q, *J* = 8.1 Hz, 1H), 1.86 (tdd, *J* = 8.4, 5.5, 2.2 Hz, 1H), 1.68 (d, *J* = 2.2 Hz, 1H), 1.57 (td, *J* = 8.6, 4.8 Hz, 1H), 1.12 (ddd, *J* = 7.6, 5.6, 4.8 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.92, 135.96, 131.28, 128.93, 84.80, 66.40, 20.94, 20.74, 20.32, 17.16, 7.86. **HRMS** (APCI Positive): calculated for $C_{14}H_{17}$ $[M+H]^+$: 185.1325; found: 185.1330.

**(2-Ethynyl-1-methylcyclopropyl)benzene (100e)**



The title compound (pale pink oil, 30 mg, 64% yield, 1.2:1 ratio, unassigned) was obtained following General Procedure E2 from (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane **91b** (56 mg, 0.30 mmol, 1 equiv) and prop-1-en-2-ylbenzene (142 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (10 mg, 5 mol %) after flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (*cis*/*trans* mixture, unassigned; 500 MHz, Chloroform-*d*) δ 7.36 – 7.19 (m, 10H), 1.99 (d, *J* = 2.2 Hz, 1H), 1.73 (d, *J* = 2.2 Hz, 1H), 1.63 (ddd, *J* = 9.0, 5.7, 2.2 Hz, 1H), 1.56 – 1.52 (m, 1H), 1.41 (s, 3H), 1.38 (dd, *J* = 9.0, 4.5 Hz, 1H), 1.29 (t, *J* = 5.0 Hz, 1H), 1.13 (dd, *J* = 8.6, 4.6 Hz, 1H), 0.94 (dd, *J* = 5.7, 4.5 Hz, 1H). **$^{13}$C NMR** (*cis*/*trans* mixture, unassigned; 126 MHz, $CDCl_3$) δ 145.83, 142.49, 129.44, 128.78, 128.44, 127.64, 126.87, 126.71, 85.11, 84.91, 68.47, 67.35, 29.40, 27.83, 23.00, 22.81, 22.20, 15.22, 15.15. **HRMS** (APCI Positive): calculated for $C_{12}H_{13}$ $[M+H]^+$: 157.1012; found: 157.1013.

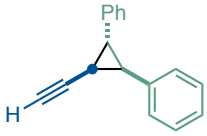
**(2-Ethynylcyclopropane-1,1-diyl)dibenzene (100f)**



The title compound (pale brown solid, 53 mg, 81% yield) was obtained following General Procedure E2 from (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane **91b** (56 mg, 0.30 mmol, 1 equiv) and ethene-1,1-diyldibenzene (216 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9.9 mg, 5 mol %) after flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.52 – 7.44 (m, 2H), 7.41 – 7.33 (m, 2H), 7.33 – 7.25 (m, 5H), 7.27 – 7.19

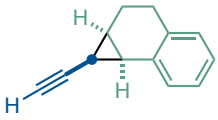
(m, 1H), 2.24 (ddd, *J* = 9.1, 5.9, 2.2 Hz, 1H), 1.92 (d, *J* = 2.2 Hz, 1H), 1.76 (dd, *J* = 5.9, 4.7 Hz, 1H), 1.69 (dd, *J* = 9.0, 4.7 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 144.77, 140.70, 130.16, 128.49, 128.15, 128.02, 126.84, 126.56, 83.94, 69.61, 37.65, 22.89, 15.59. **HRMS** (APCI Positive): calculated for $C_{17}H_{15}$ $[M+H]^+$: 219.1168; found: 219.1171. **MP** 56–58 ºC.

**(2-Ethynylcyclopropane-1,1-diyl)dibenzene (100g)**



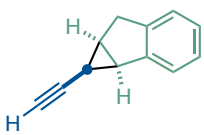

The title compound (pale yellow solid, 94 mg, 78% yield) was obtained following General Procedure E2 from (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane **91b** (94 mg, 0.50 mmol, 1 equiv) and (*E*)-stilbene (180 mg, 1.00 mmol, 2 equiv) using $[Rh_2(TFA)_4]$ (16 mg, 5 mol %) after flash column chromatography in $SiO_2$ using a gradient from cyclohexane to cyclohexane/EtOAc 95:5 as eluent. **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.21 (m, 6H), 7.21 – 7.11 (m, 4H), 2.63 – 2.52 (m, 2H), 2.05 (ddd, *J* = 8.8, 5.5, 2.2 Hz, 1H), 1.87 (d, *J* = 2.2 Hz, 1H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 140.0, 137.1, 128.7, 128.5, 128.2, 126.8, 126.8, 126.4, 82.4, 69.7, 32.9, 32.7, 19.2 ppm. **HRMS** (ESI Pos): calc. for $C_{17}H_{15}$ $[M+H]^+$: 219.1168; found: 219.1179. **MP** 88–90 ºC.

***endo*-1-Ethynyl-1a,2,3,7b-tetrahydro-1*H*-cyclopropa[*a*]naphthalene (100h)**




The title compound (yellow solid, 35 mg, 69% yield, >15:1 *endo*/*exo* ratio) was obtained following General Procedure E2 from (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane **91b** (56 mg, 0.30 mmol, 1 equiv) and 1,2-dihydronaphthalene (156 mg, 1.20 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (9.9 mg, 5 mol %) after flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.29 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.17 (td, *J* = 7.4, 1.6 Hz, 1H), 7.13 (td, *J* = 7.4, 1.6 Hz, 1H), 7.10 – 7.04 (m, 1H), 2.97 (ddd, *J* = 15.9, 9.0, 6.9 Hz, 1H), 2.68 (dt, *J* = 16.1, 6.1 Hz, 1H), 2.27 (t, *J* = 8.4 Hz, 1H), 2.16 – 2.03 (m, 2H), 1.85 (td, *J* = 8.4, 2.4 Hz, 1H), 1.79 (d, *J* = 2.4 Hz, 1H), 1.74 (tdd, *J* = 8.5, 5.7, 3.5 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 137.10, 133.66, 130.39, 128.58, 126.45, 126.31, 82.93, 70.61, 27.62, 21.44, 19.48, 19.10, 14.88. **HRMS** (APCI Positive): calculated for $C_{13}H_{13}$ $[M+H]^+$: 169.1012; found: 169.1011. **MP** 50–52 ºC

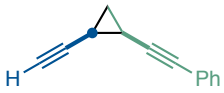
***endo*-1-Ethynyl-1,1a,6,6a-tetrahydrocyclopropa[*a*]indene (100i)**




The title compound (yellow oil, 65 mg, 84% yield, 15:1 *endo*/*exo* ratio) was obtained following General Procedure E2 from (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane **91b** (94 mg, 0.50 mmol, 1 equiv) and 1H-indene (232 mg, 2.00 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (16 mg, 5 mol %) after flash

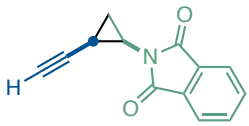
column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.41 – 7.35 (m, 1H), 7.23 – 7.16 (m, 3H), 3.32 – 3.23 (m, 1H), 3.14 – 3.07 (m, 1H), 2.81 (ddd, *J* = 7.6, 6.0, 1.5 Hz, 1H), 2.17 (dddd, *J* = 7.7, 6.8, 6.1, 1.0 Hz, 1H), 1.90 (td, *J* = 7.8, 2.2 Hz, 1H), 1.58 (d, *J* = 2.2 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 143.78, 141.28, 126.32, 126.06, 124.55, 124.10, 80.57, 68.04, 32.53, 31.06, 22.73, 13.80. **HRMS** (APCI Positive): calculated for $C_{12}H_{11}$ $[M+H]^+$: 155.0855; found: 155.0854.

***cis*-((2-Ethynylcyclopropyl)ethynyl)benzene (100j)**




The title compound (pale orange oil, 31 mg, 54% yield, 4:1 *cis*/*trans* ratio) was obtained following General Procedure E2 from (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane **91b** (65 mg, 0.34 mmol, 1 equiv) and but-3-en-1-yn-1-ylbenzene (177 mg, 1.38 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (11 mg, 5 mol %) after flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.46 (dddd, *J* = 6.4, 3.8, 2.8, 1.2 Hz, 2H), 7.34 – 7.29 (m, 3H), 2.04 (d, *J* = 2.1 Hz, 1H), 1.90 – 1.83 (m, 1H), 1.75 (dddd, *J* = 8.4, 7.8, 6.2, 2.1 Hz, 1H), 1.32 (dt, *J* = 8.5, 4.3 Hz, 1H), 1.10 (td, *J* = 6.2, 4.5 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 131.87, 128.16, 127.79, 123.57, 88.51, 83.00, 79.57, 67.31, 17.13, 9.22, 8.94. **HRMS** (APCI Positive): calculated for $C_{13}H_{11}$ $[M+H]^+$: 167.0855; found: 167.0854.

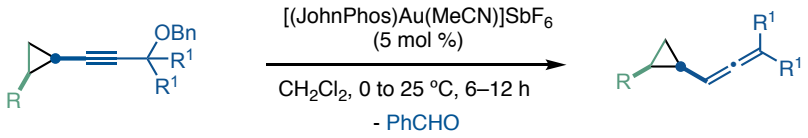
***cis*-2-(2-Ethynylcyclopropyl)isoindoline-1,3-dione (100k)**




The title compound (pale brown solid, 65 mg, 62% yield, 15:1 *cis*/*trans* ratio) was obtained following General Procedure E2 from (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane **91b** (94 mg, 0.50 mmol, 1 equiv) and *N*-vinylphthalimide (173 mg, 1.00 mmol, 2 equiv) using $[Rh_2(TFA)_4]$ (10 mg, 3 mol %) after flash column chromatography in $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.86 – 7.81 (m, 2H), 7.73 – 7.69 (m, 2H), 2.99 – 2.93 (m, 1H), 1.89 – 1.82 (m, 2H), 1.68 (d, *J* = 1.9 Hz, 1H), 1.53 – 1.45 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 168.91, 134.45, 132.06, 123.64, 81.92, 67.84, 27.69, 13.39, 8.10. **HRMS** (ESI Pos): calculated for $C_{13}H_9NNaO_2$ $[M+Na]^+$: 234.0525; found: 234.0522. **MP** 152–155 ºC.

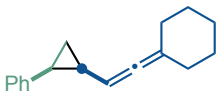
**Derivatization of Alkynylcyclopropanes**

**General Procedure F Synthesis of Allenylcyclopropanes**



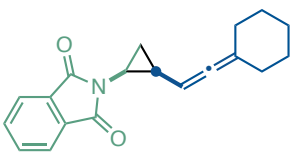

To a stirred solution of propargyl benzyloxy cyclopropane (1 equiv) in anhydrous dichloromethane (0.1 M) under argon at 0 ºC was added [(JohnPhos)Au(MeCN)]$SbF_6$ (5 mol %) in a single portion. The mixture was allowed to stir while coming to room temperature, until full consumption of the starting material was observed by TLC and/or GCMS (*ca*. 6–12 h). After this time, the solvent was removed, and the crude product was purified by flash column in silica gel or preparative TLC. The products were found to be slightly unstable under the reaction conditions. Therefore, it is highly recommended to purify, or filter them through silica gel (in order to remove the gold catalyst) as soon as most of the starting material is consumed. Characterization data for allenes **103d–f** is included below. Allenes **103a–c** were prepared by collaborator Dr. M. Montesinos-Magraner and characterization data is not included.

***cis*-((2-(2-Cyclohexylidenevinyl)cyclopropyl)benzene (103d)**




The title compound (colorless oil, 22 mg, 83% yield, 6:1 *cis*/*trans* ratio) was obtained following General Procedure F from *cis*-(2-((1-(benzyloxy)cyclohexyl)ethynyl)-cyclopropyl)benzene (39 mg, 1 equiv, 0.12 mmol) using [(JohnPhos)Au(MeCN)]$SbF_6$ (4.5 mg, 5 mol %) after flash column chromatography in $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.38 – 7.24 (m, 6H), 7.11 (tdd, J = 5.0, 3.3, 2.2 Hz, 3H), 4.23 – 4.12 (m, 2H), 3.30 – 3.21 (m, 1H), 3.11 – 3.02 (m, 1H), 2.82 (ddd, J = 7.6, 6.0, 1.5 Hz, 1H), 2.20 – 2.12 (m, 1H), 1.93 (t, J = 7.7 Hz, 1H), 1.67 – 1.59 (m, 2H), 1.53 – 1.46 (m, 2H), 1.38 (m 3H), 1.26 – 1.11 (m, 3H). **$^{13}$C NMR** (101 MHz, CDCl3) δ 143.75, 141.73, 139.73, 128.10, 127.67, 126.99, 126.21, 126.03, 124.61, 124.12, 82.84, 81.27, 74.24, 64.83, 37.67, 37.25, 32.75, 31.27, 25.47, 22.95, 22.83, 14.12. **HRMS** (APCI Positive): calculated for $C_{17}H_{21}$ $[M+H]^+$: 225.1638; found: 225.1638.

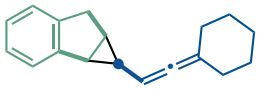
***cis*-2-(2-(2-Cyclohexylidenevinyl)cyclopropyl)isoindoline-1,3-dione (103e)**




The title compound (white solid, 15 mg, 51% yield, 11:1 *cis*/*trans* ratio) was obtained following General Procedure F from *cis*-2-(2-((1-(benzyloxy)cyclohexyl)ethynyl)-cyclopropyl)isoindoline-1,3-dione (40 mg, 0.10 mmol, 1 equiv) using

[(JohnPhos)Au(MeCN)]$SbF_6$ (3.9 mg, 5 mol %) after preparative TLC in $SiO_2$ using pentane/$Et_2O$ 9:1 as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.90 – 7.78 (m, 2H), 7.77 – 7.64 (m, 2H), 5.14 – 5.07 (m, 1H), 2.85 (ddd, J = 7.8, 6.9, 4.8 Hz, 1H), 2.11 – 2.03 (m, 1H), 1.95 (dddd, J = 13.1, 8.7, 4.1, 2.5 Hz, 1H), 1.76 (dtd, J = 8.8, 6.9, 5.8 Hz, 1H), 1.57 (ddd, J = 9.6, 6.4, 2.8 Hz, 1H), 1.51 – 1.44 (m, 4H), 1.40 – 1.36 (m, 1H), 1.35 – 1.29 (m, 3H). **$^{13}$C NMR** (101 MHz, CDCl3) δ 198.75, 169.13, 133.93, 131.87, 123.01, 105.41, 85.56, 31.58, 31.56, 28.10, 27.43, 27.41, 25.92, 15.81, 9.51. **HRMS** (ESI Pos): calculated for $C_{19}H_{19}NNaO_2$ $[M+Na]^+$: 316.1308; found: 316.1307. **MP** 85–88 ºC.

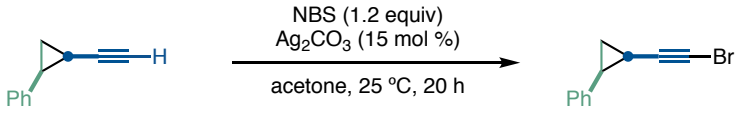
***cis*-1-(2-Cyclohexylidenevinyl)-1,1a,6,6a-tetrahydrocyclopropa[*a*]indene (103f)**



The title compound (colorless oil, 31 mg, 64% yield, 5:1 *cis*/*trans* ratio) was obtained following General Procedure F from *cis*-1-((1-(benzyloxy)cyclohexyl)ethynyl)-1,1a,6,6a-tetrahydrocyclopropa[*a*]indene (70 mg, 0.20 mmol, 1 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (7.9 mg, 5 mol %) after preparative TLC in $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.29 (dd, J = 6.8, 1.4 Hz, 1H), 7.15 – 7.10 (m, 3H), 4.20 (dp, J = 7.8, 2.2 Hz, 1H), 3.18 (ddd, J = 17.3, 7.2, 1.2 Hz, 1H), 3.00 – 2.92 (m, 1H), 2.72 (ddd, J = 8.0, 6.2, 1.7 Hz, 1H), 2.15 (dtd, J = 10.0, 5.6, 4.9, 2.1 Hz, 1H), 2.11 – 2.04 (m, 3H), 1.99 (m, 2H), 1.80 (q, J = 8.0 Hz, 1H), 1.62 – 1.52 (m, 4H). **$^{13}$C NMR** (101 MHz, CDCl3) δ 200.91, 144.02, 142.48, 126.10, 125.67, 124.59, 124.04, 102.38, 83.10, 35.65, 34.02, 31.82, 31.72, 31.56, 30.21, 27.32, 26.13, 22.51. **HRMS** (APCI Positive): calculated for $C_{18}H_{21}$ $[M+H]^+$: 237.1638; found: 237.1639.

**Alkyne Bromination**

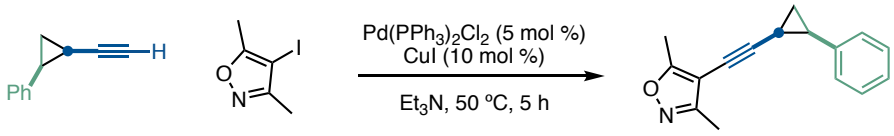
***cis*-(2-(Bromoethynyl)cyclopropyl)benzene (102a)**




Under air, *cis*-(2-(ethynyl)cyclopropyl)benzene (30 mg, 0.21 mmol, 1 equiv) was dissolved in 1 mL of HPLC-grade acetone (0.2 M), and to this solution was added first NBS (45 mg, 0.25 mmol, 1.2 equiv), and then silver carbonate (8.7 mg, 15 mol %). The mixture was stirred at room temperature for 20 h, showing full conversion of the starting material by TLC and GCMS. Volatiles were removed in vacuum and flash column chromatography in $SiO_2$ using cyclohexane as solvent gave *cis*-(2-(bromoethynyl)cyclopropyl)benzene (40 mg, 0.18 mmol, 86 %, >20:1 *cis*/*trans*) as a white solid. **$^1$H NMR** (400 MHz, Chloroform-d) δ 7.38 – 7.31 (m, 2H), 7.30 – 7.23 (m, 3H), 2.31 (td, J = 8.4, 6.7 Hz, 1H), 1.83 (td, J = 8.5, 5.8 Hz, 1H), 1.38 (td, J = 8.6, 5.1 Hz, 1H), 1.23 (ddd, J = 6.8, 5.8, 5.1 Hz, 1H). **$^{13}$C NMR** (101 MHz, CDCl3) δ

137.56, 128.17, 127.89, 126.42, 79.54, 37.69, 23.45, 14.42, 10.50. **HRMS** (APCI Pos): calculated for $C_{11}H_{10}{}^{79}Br$ $[M+H]^+$: 220.9960; found: 220.9955. **MP** 31–33 ºC.

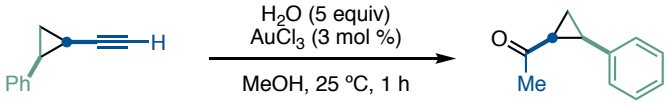
**Sonogashira Coupling**




***cis*-3,5-Dimethyl-4-((2-phenylcyclopropyl)ethynyl)isoxazole (102b)**

A vial was charged with *cis*-(2-ethynylcyclopropyl)benzene (brown solid, 25 mg, 0.18 mmol, 1 equiv), 4-iodo-3,5-dimethylisoxazole (47 mg, 1.2 equiv, 0.21 mmol), copper(I) iodide (3.4 mg, 10 mol %) and $Pd(PPh_3)_2Cl_2$ (6.2 mg, 5 mol %). Under argon, everything was suspended in 1.8 mL of anhydrous triethylamine before the vial was closed with the corresponding cap, and stirred at 50 ºC until full conversion of the starting material was observed by TLC and GCMS (5 h). Volatiles were removed in vacuum, and the crude product was purified by flash column chromatography in silica gel, using a gradient between 99:1 to 90:10 cyclohexane/EtOAc, giving cis-3,5-dimethyl-4-((2-phenylcyclopropyl)ethynyl)isoxazole (40 mg, 96%, >20:1 *cis*/*trans*) as an orange oil. **$^1$H NMR** (500 MHz, Chloroform-d) δ 7.30 – 7.25 (m, 4H), 7.22 – 7.18 (m, 1H), 2.44 – 2.40 (m, 1H), 2.13 (s, 3H), 1.98 – 1.93 (m, 4H), 1.42 (dt, J = 5.0, 3.5 Hz, 1H), 1.30 – 1.26 (m, 1H). **$^{13}$C NMR** (126 MHz, CDCl3) δ 171.07, 161.16, 138.09, 128.94, 128.28, 126.80, 101.57, 94.97, 67.98, 24.33, 14.76, 11.86, 10.52, 10.37. **HRMS** (ESI Pos): calculated for $C_{16}H_{15}NNaO$ $[M+Na]^+$: 260.1046; found: 260.1039. **MP** 63–66 ºC.

**Gold-Catalyzed Hydration**

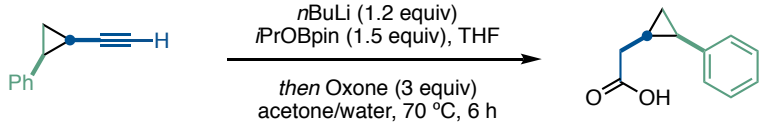



***cis*-1-(2-Phenylcyclopropyl)ethan-1-one (102c)**

In a vial under air, *cis*-(2-(ethynyl)cyclopropyl)benzene (30 mg, 0.21 mmol, 1 equiv) and water (15 mg, 0.85 mmol, 4 equiv) were dissolved in 1.5 mL of HPLC-grade methanol, before gold(III) chloride (2 mg, 3 mol %) was added. The vial was closed with the corresponding cap and the resulting suspension was stirred for 1 h at room temperature. After this time, the suspension had evolved into a solution, and TLC showed full conversion of the starting material. Volatiles were removed in vacuum, and the crude product was purified by flash column chromatography in silica gel, using a gradient between cyclohexane to 80:20

cyclohexane/EtOAc, giving *cis*-1-(2-Phenylcyclopropyl)ethan-1-one (27 mg, 80%, >20:1 *cis*/*trans*) as an pale yellow oil. **$^{1}$H NMR** (500 MHz, Chloroform-d) δ 7.27 – 7.23 (m, 2H), 7.23 – 7.14 (m, 3H), 2.72 – 2.63 (m, 1H), 2.41 (ddd, J = 9.4, 7.4, 5.8 Hz, 1H), 2.00 (s, 3H), 1.83 (ddd, J = 7.5, 5.8, 5.0 Hz, 1H), 1.29 (ddd, J = 8.6, 7.4, 4.9 Hz, 1H). **$^{13}$C NMR** (126 MHz, CDCl3) δ 204.56, 136.38, 129.44, 128.37, 127.08, 31.56, 30.70, 28.60, 12.02. **HRMS** (ESI Pos): calculated for $C_{11}H_{12}NaO$ $[M+Na]^+$: 183.0780; found: 183.0772.

**Lithiation/Borylation/Oxidation**



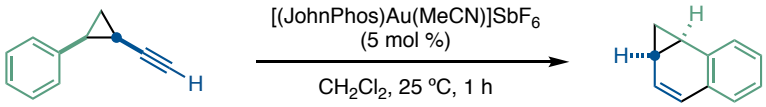

***cis*-2-(2-Phenylcyclopropyl)acetic acid (102d)**

To a solution of *cis*-(2-(ethynyl)cyclopropyl)benzene (45 mg, 0.32 mmol, 1 equiv) in dry THF (1.5 mL, 0.2 M) under argon at -78 ºC was added a solution of *n*BuLi in hexane (0.16 mL, 2.43 M, 0.38 mmol, 1.2 equiv). The mixture was stirred at -78 ºC for 1 h, before 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (88 mg, 1.5 equiv, 0.48 mmol) was added in 1 mL of dry THF. The mixture was stirred at -78 ºC for 1 h and at 25 ºC for 1 h, before the reaction was quenched by adding aqueous 1 M solution of HCl. The mixture was further diluted with $Et_2O$ and water, and three extractions with $Et_2O$ were performed. The combined organic fractions were washed once with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuum to afford crude boronic ester, which was dried in high vacuum and used directly in the next reaction step.

Under air, the crude boronic ester was dissolved in 1.5 mL (0.1 M) of HPLC-grade acetone, before a solution of Oxone (146 mg, 0.48 mmol, 1.5 equiv) in 1.5 mL of deionized water was added. The resulting suspension was stirred at 70 ºC for 6 h. After this time, saturated aqueous $NH_4Cl$ solution and EtOAc were added, and the aqueous phase was extracted a total of three times with EtOAc. The combined organic fractions were dried over anhydrous $MgSO_4$, filtered and concentrated in vacuum. The resulting crude product was purified by flash column chromatography in silica gel using a gradient from 8:2 to 6:4 cyclohexane/EtOAc as eluent, giving *cis*-2-(2-phenylcyclopropyl)acetic acid (31 mg, 56% over 2 steps, >20:1 *cis*/*trans*) as a viscous pale yellow oil. **$^{1}$H NMR** (500 MHz, Chloroform-d) δ 11.3 (br, 1 H), 7.30 – 7.24 (m, 2H), 7.23 – 7.14 (m, 3H), 2.26 (td, J = 8.7, 6.1 Hz, 1H), 2.12 (dd, J = 17.0, 6.8 Hz, 1H), 1.97 (dd, J = 17.0, 7.7 Hz, 1H), 1.50 – 1.43 (m, 1H), 1.10 (td, J = 8.5, 5.5 Hz, 1H), 0.80 (q, J = 5.7 Hz, 1H). **$^{13}$C NMR** (126 MHz, CDCl3) δ 179.80, 138.43, 129.53, 128.53, 126.60, 34.05, 20.90,

14.24, 9.46. **HRMS** (ESI Negative): calculated for $C_{11}H_{11}O_2$ $[M-H]^+$: 175.0765; found: 175.0758.

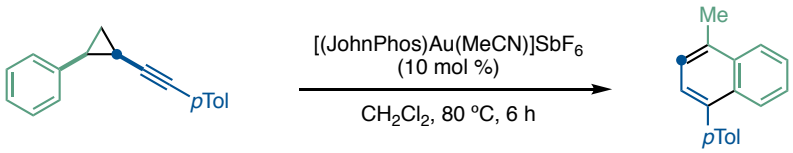
**Gold-Catalyzed Hydroarylation**




***endo*-1a,7b-Dihydro-1H-cyclopropa[*a*]naphthalene (102e)**

Under air, *cis*-(2-(ethynyl)cyclopropyl)benzene (34 mg, 0.24 mmol, 1 equiv) was dissolved in 1.6 mL of HPLC-grade dichloromethane (0.15 M). To this solution was added [(JohnPhos)Au(MeCN)]$SbF_6$ (9.2 mg, 5 mol %), and the mixture was stirred at room temperature for 1 h. After this time, TLC shows full conversion of the starting material. Removal of the volatiles in vacuum and flash column chromatography in silica gel using pentane as solvent afforded *endo*-1a,7b-dihydro-1H-cyclopropa[a]naphthalene (23 mg, 67%, >20:1 *endo*/*exo*) as a pale yellow oil. **$^1$H NMR** (500 MHz, Chloroform-d) δ 7.36 – 7.33 (m, 1H), 7.15 (dtd, J = 21.0, 7.3, 1.5 Hz, 2H), 7.08 (dd, J = 7.4, 1.6 Hz, 1H), 6.32 – 6.18 (m, 2H), 2.41 (ddd, J = 9.1, 7.5, 5.1 Hz, 1H), 1.97 (ddtd, J = 8.3, 7.5, 4.7, 0.8 Hz, 1H), 1.56 – 1.52 (m, 1H), -0.25 (td, J = 4.9, 3.6 Hz, 1H). **$^{13}$C NMR** (126 MHz, CDCl3) δ 135.73, 130.90, 129.28, 128.40, 127.93, 127.39, 125.95, 123.82, 20.80, 17.89, 9.62. **HRMS** (APCI Pos): calculated for $C_{11}H_{11}$ $[M+H]^+$: 143.0855; found: 143.0852.

**Sequential Formal (3+3) Cycloaddition**

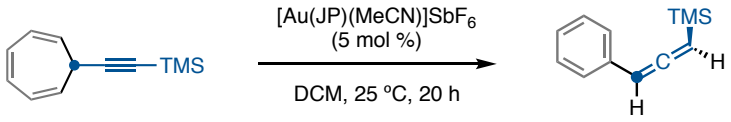



**1-Methyl-4-(*p*-tolyl)naphthalene (102f)**

In a vial under air, *cis*-1-methyl-4-((2-phenylcyclopropyl)ethynyl)benzene (25 mg, 0.11 mmol, 1 equiv) was dissolved in 0.7 mL of HPLC-grade 1,2-DCE (0.15 M), before [(JohnPhos)Au(MeCN)]$SbF_6$ (5 mg, 10 mol %) was added. The vial was closed, and the mixture was stirred at 80 ºC for 6 h. After this time, full conversion of the starting material was observed, volatiles were removed in vacuum, and the crude product was purified by flash column chromatography in silica gel using cyclohexane as eluent, giving 1-methyl-4-(*p*-tolyl)naphthalene (16 mg, 64%) as a colorless oil. Characterization data match the previously

reported ones for this product.[159] **$^{1}$H NMR** (500 MHz, Chloroform-d) δ 8.05 (ddd, J = 8.5, 1.3, 0.7 Hz, 1H), 7.92 (ddd, J = 8.5, 1.4, 0.7 Hz, 1H), 7.52 (ddd, J = 8.3, 6.7, 1.3 Hz, 1H), 7.42 (ddd, J = 8.2, 6.7, 1.3 Hz, 1H), 7.38 – 7.34 (m, 3H), 7.31 – 7.27 (m, 3H), 2.73 (d, J = 0.9 Hz, 3H), 2.44 (s, 3H). **$^{13}$C NMR** (126 MHz, CDCl3) δ 139.02, 138.44, 137.08, 133.94, 133.17, 132.15, 130.42, 129.27, 127.10, 126.91, 126.56, 125.91, 125.89, 124.71, 21.11, 19.91. **HRMS** (APCI Pos): calculated for $C_{18}H_{17}$ $[M+H]^+$: 233.1325; found: 233.1320.

**Trimethyl(3-phenylpropa-1,2-dien-1-yl)silane (95)**



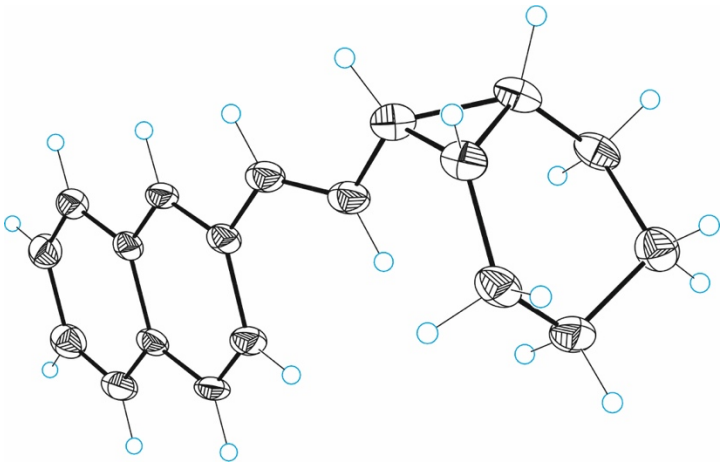

Under air, a vial was charged with (cyclohepta-2,4,6-trien-1-ylethynyl)trimethylsilane (60 mg, 0.32 mmol, 1 equiv) and dissolved in 2.1 mL of HPLC-grade dichloromethane. To this solution was added [(JohnPhos)Au(MeCN)]$SbF_6$ (12 mg, 5 mol %), and the resulting mixture was stirred at 25 ºC for 20 h. After this time, the crude product was adsorbed directly into silica gel, and purified by flash column chromatography in silica gel, using pentane as eluent, to give the title compound (45 mg, 75%) as a colorless oil. **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.33 – 7.24 (m, 4H), 7.19 – 7.14 (m, 1H), 5.89 (d, *J* = 6.9 Hz, 1H), 5.45 (dq, *J* = 6.9, 0.7 Hz, 1H), 0.20 (s, 9H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 210.24, 135.11, 128.58, 125.95, 87.91, 87.06, -0.76. **GCMS** (EI): calculated for $C_{12}H_{16}Si$ $[M]^+$: 188.1; found: 188.1.

159 Watanabe, T.; Abe, H.; Mutoh, Y.; Saito, S. Ruthenium-Catalyzed Cycloisomerization of 2-Alkynylstyrenes via 1,2-Carbon Migration That Leads to Substituted Naphthalenes. *Chem. Eur. J.* **2018**, *24*, 11545–11549.

### *Crystallographic Data*

### *endo*-2-((*E*)-2-(Bicyclo[4.1.0]heptan-7-yl)vinyl)naphthalene (58i)

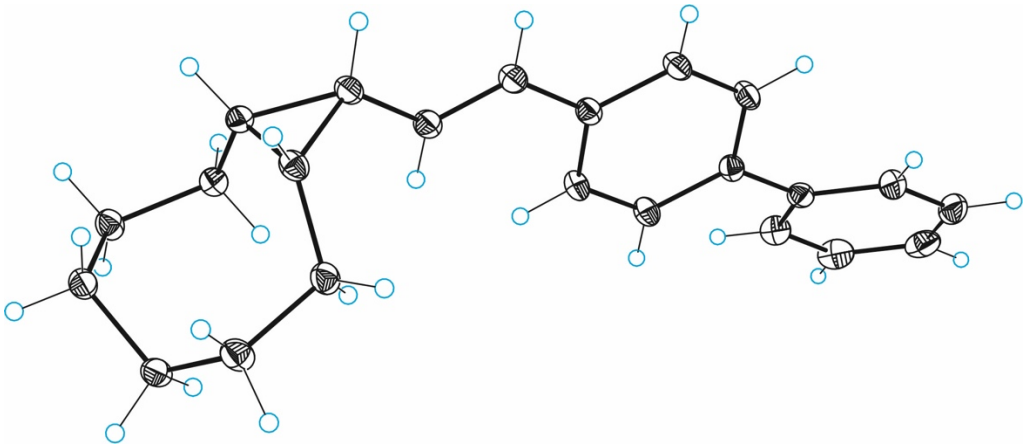
The single crystals of compound **58i** suitable for X-ray diffraction analysis were obtained by slow diffusion of methanol into a solution of **58i** in dichloromethane in an NMR tube, in the freezer (-20 ºC) over three days. The crystal structure information for this compound has been deposited at the Cambridge Crystallographic Data Centre. CCDC 1848067 contains the crystal structure information of this compound and can be obtained free of charge via http://www.ccdc.cam.ac.uk.



| | |
|---|---|
| Identification code | mmy4177f |
| Empirical formula | C19 H20 |
| Formula weight | 248.35 |
| Temperature | 100(2) K |
| Wavelength | 0.71073 Å |
| Crystal system | Triclinic |
| Space group | P-1 |
| Unit cell dimensions | a = 5.9984(2)Å a= 111.117(4)°.<br>b = 18.7613(7)Å b = 92.903(3)°.<br>c = 19.9913(9)Å g = 97.381(3)°. |
| Volume | 2069.87(15) Å3 |
| Z | 6 |
| Density (calculated) | 1.195 Mg/m3 |
| Absorption coefficient | 0.067 mm-1 |
| F(000) | 804 |
| Crystal size | ? x ? x ? mm3 |
| Theta range for data collection | 1.885 to 28.675°. |
| Index ranges | -7<=h<=7,-24<=k<=25,-26<=l<=26 |
| Reflections collected | 26399 |
| Independent reflections | 9456[R(int) = 0.0604] |
| Completeness to theta =28.675° | 88.6% |
| Absorption correction | Multi-scan |
| Max. and min. transmission | 0.999 and 0.768 |
| Refinement method | Full-matrix least-squares on F2 |
| Data / restraints / parameters | 9456/ 0/ 514 |
| Goodness-of-fit on F2 | 1.018 |
| Final R indices [I>2sigma(I)] | R1 = 0.0624, wR2 = 0.1304 |
| R indices (all data) | R1 = 0.1209, wR2 = 0.1524 |
| Largest diff. peak and hole | 0.312 and -0.274 e.Å-3 |

### *endo*-9-((*E*)-2-([1,1'-Biphenyl]-4-yl)vinyl)bicyclo[6.1.0]nonane (58o)

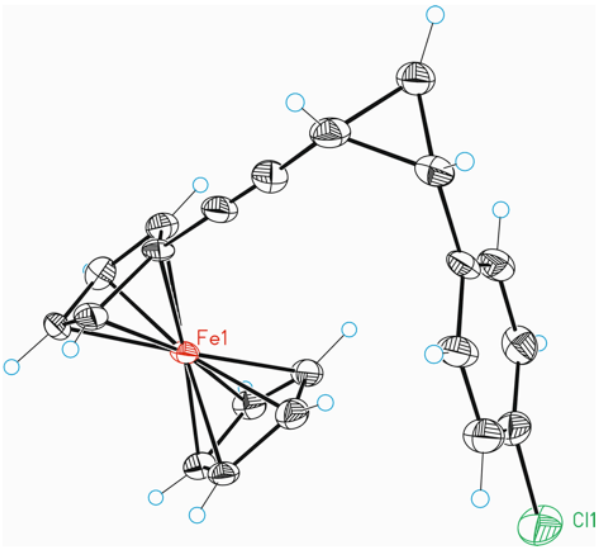
The single crystals of compound **6o** suitable for X-ray diffraction analysis were obtained by slow diffusion of methanol into a solution of **6o** in dichloromethane in an NMR tube, in the freezer (-20 ºC) over three days. The crystal structure information for this compound has been deposited at the Cambridge Crystallographic Data Centre. CCDC 1848066 contains the crystal structure information of this compound and can be obtained free of charge via http://www.ccdc.cam.ac.uk.



| | |
|---|---|
| Identification code | mmy182 |
| Empirical formula | C23H26 |
| Formula weight | 302.44 |
| Temperature | 100(2) K |
| Wavelength | 0.71073 Å |
| Crystal system | Monoclinic |
| Space group | P2(1)/c |
| Unit cell dimensions | a = 7.2732(2)Å a= 90°.<br>b = 7.8909(3)Å b = 96.882(3)°.<br>c = 30.0960(10)Å g = 90°. |
| Volume | 1714.83(10) Å3 |
| Z | 4 |
| Density (calculated) | 1.171 Mg/m3 |
| Absorption coefficient | 0.065 mm-1 |
| F(000) | 656 |
| Crystal size | ? x ? x ? mm3 |
| Theta range for data collection | 2.670 to 31.931°. |
| Index ranges | -9<=h<=10,-11<=k<=11,-43<=l<=44 |
| Reflections collected | 12790 |
| Independent reflections | 5429[R(int) = 0.0141] |
| Completeness to theta =31.931° | 91.9% |
| Absorption correction | Multi-scan |
| Max. and min. transmission | 0.990 and 0.762 |
| Refinement method | Full-matrix least-squares on F2 |
| Data / restraints / parameters | 5429/ 0/ 208 |
| Goodness-of-fit on F2 | 1.047 |
| Final R indices [I>2sigma(I)] | R1 = 0.0406, wR2 = 0.1164 |
| R indices (all data) | R1 = 0.0453, wR2 = 0.1197 |
| Largest diff. peak and hole | 0.448 and -0.200 e.Å-3 |

### *cis*-1-Chloro-4-(2-(ferrocenylethynyl)cyclopropyl)benzene (98p)

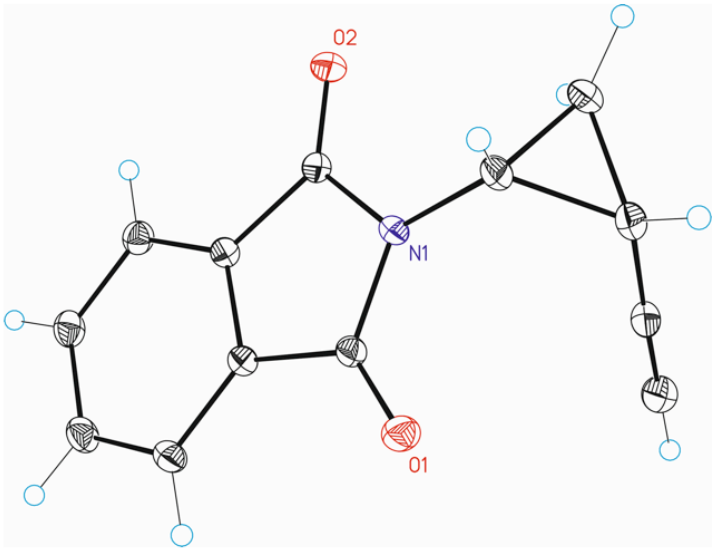
Single crystals of compound **98p** suitable for X-ray diffraction analysis were obtained by slow evaporation (*ca.* 24 h) of an acetonitrile/dichloromethane (*ca.* 9:1) solution of **98p**. The crystal structure information for this compound has been deposited at the Cambridge Crystallographic Data Centre. CCDC 2085763 contains the crystal structure information of this compound and can be obtained free of charge via http://www.ccdc.cam.ac.uk.




| | |
|---|---|
| Identification code | MM-4-22F_twin1_hklf5 |
| Empirical formula | C21 H17 Cl Fe |
| Formula weight | 360.65 |
| Temperature | 100(2)K |
| Wavelength | 0.71073 Å |
| Crystal system | monoclinic |
| Space group | P 21/n |
| Unit cell dimensions | a = 5.8803(8)Å a= 90°.<br>b = 36.366(6)Å b = 95.168(15)°.<br>c = 7.5321(16)Å g = 90°. |
| Volume | 1604.1(5) $Å^3$ |
| Z | 4 |
| Density (calculated) | 1.493 $Mg/m^3$ |
| Absorption coefficient | 1.102 $mm^{-1}$ |
| F(000) | 744 |
| Crystal size | 0.120 x 0.100 x 0.050 $mm^3$ |
| Theta range for data collection | 2.772 to 27.533°. |
| Index ranges | -7<=h<=7,-46<=k<=46,-9<=l<=9 |
| Reflections collected | 11314 |
| Independent reflections | 11314[R(int) = ?] |
| Completeness to theta =27.533° | 83.9% |
| Absorption correction | Multi-scan |
| Max. and min. transmission | 1.00 and 0.73 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 11314/ 602/ 407 |
| Goodness-of-fit on $F^2$ | 1.157 |
| Final R indices [I>2sigma(I)] | R1 = 0.0955, wR2 = 0.3129 |
| R indices (all data) | R1 = 0.1242, wR2 = 0.3288 |
| Largest diff. peak and hole | 1.532 and -1.496 $e.Å^{-3}$ |

### *cis*-2-(2-Ethynylcyclopropyl)isoindoline-1,3-dione (100k)

Single crystals of compound **100k** suitable for X-ray diffraction analysis were obtained by slow evaporation (*ca.* 24 h) of an acetonitrile/dichloromethane (*ca.* 9:1) solution of **100k**. The crystal structure information for this compound has been deposited at the Cambridge Crystallographic Data Centre. CCDC 2085762 contains the crystal structure information of this compound and can be obtained free of charge via http://www.ccdc.cam.ac.uk.




| | |
|---|---|
| Identification code | mo_MM442_0m |
| Empirical formula | C13 H9 N O2 |
| Formula weight | 211.21 |
| Temperature | 100(2)K |
| Wavelength | 0.71073 Å |
| Crystal system | triclinic |
| Space group | P -1 |
| Unit cell dimensions | a = 7.8827(8)Å a= 89.714(2)°.<br>b = 8.1648(7)Å b = 73.885(2)°.<br>c = 9.1516(8)Å g = 64.698(2)°. |
| Volume | 507.18(8) $Å^3$ |
| Z | 2 |
| Density (calculated) | 1.383 $Mg/m^3$ |
| Absorption coefficient | 0.095 $mm^{-1}$ |
| F(000) | 220 |
| Crystal size | 0.250 x 0.200 x 0.100 $mm^3$ |
| Theta range for data collection | 2.337 to 31.614°. |
| Index ranges | -11<=h<=11,-12<=k<=8,-13<=l<=13 |
| Reflections collected | 6678 |
| Independent reflections | 3289[R(int) = 0.0256] |
| Completeness to theta =31.614° | 96.7% |
| Absorption correction | Multi-scan |
| Max. and min. transmission | 0.74 and 0.70 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 3289/ 0/ 145 |
| Goodness-of-fit on $F^2$ | 1.043 |
| Final R indices [I>2sigma(I)] | R1 = 0.0396, wR2 = 0.1081 |
| R indices (all data) | R1 = 0.0441, wR2 = 0.1121 |
| Largest diff. peak and hole | 0.447 and -0.348 $e.Å^{-3}$ |

***Computational Data***

**General Computational Methods**

All density functional calculations were performed using the Gaussian09 suit.[160] The functional B3LYP[161] was used for all calculations, in conjunction with Grimme's D3 dispersion correction. The basis set used for Rh was LANL2DZ[162] (and the associated pseudopotential) and 6-31G(d,p)[163] for all other atoms. All structures were fully optimized, and frequency calculations were undertaken. No imaginary frequencies for minima, and a single imaginary frequency corresponding to the reaction coordinate in the case of the transition states were found. Frequency calculations were analyzed to characterize the nature of the stationary points as minima (no imaginary frequency) or transition state (one imaginary frequency). Additionally, relaxation of transition states towards previous and next intermediates was used to verify the connectivity of the transition states.

Finally, potential energies were refined using the LANL2TZ[164] basis set for metals, and the 6-311G(2d,2p)[165] (Section II.7) or 6-311++G(d,p) (Section III.5)[166] basis sets for all the other

160 Gaussian 09, Revision D.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, **2013**.

161 (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648-5652. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B.* **1988**, *37*, 785–789. (c) Stephens, P. J.; Devlin, F. J.; Chabalowsky, C. F.; Frisch, M. J. *J. Phys. Chem*. **1994**, *98*, 11623–11627.

162 (a) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.*, **1985**, *82*, 299–310. (b) Wadt, W. R.; Hay, P. J. *J. Chem. Phys.*, **1985**, *82*, 284–298.

163 Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257–2261.

164 Roy, Lindsay E.; Hay, P. J.; Martin, R. L *J. Chem. Theory Comput*., S186 **2008**, *4*, 1029–1031.

165 (a) Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. V. R. *J. Comp. Chem.*, **1983**, *4*, 294–301. (b) Frisch, M. J.; Pople, J. A. *J. Chem. Phys.*, **1984**, *80*, 3265–3269.

166 (a) Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. V. R. *J. Comput. Chem*., **1983**, *4*, 294–301. (b) Ditchfield, R.; Hehre, W. J.; Pople, J. A. *J. Chem. Phys*., **1971**, *54*, 724–728. (c) Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; G., Mark S.; DeFrees, D. J.; Pople, J. A. *J. Chem. Phys*., **1982**, *77*, 3654–3665. (d) Gordon, M. S.; Binkley, J. S.; Pople, J. A.; Pietro, W. J.; Hehre, W. J. *J. Am. Chem. Soc*., **1982**, *104*, 2797–2803. (e) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta*, **1973**, *28*, 213–222. (f) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys*., **1972**, *56*, 2257–2261 (g) Spitznagel, G. W.; Clark, T.; Schleyer, P. V. R.; Hehre, W. J. *J. Comput. Chem*., **1987**, *8*, 1109–1116

atoms. Solvation Model Based (SMD)[167] was used to simulate the solvent (1,2-dichloroethane) throughout all calculations. Unless otherwise stated, all the energies presented are potential (E) and free energies (G) in solution at 298.15 K and 1 atm in kcal/mol.

Optimized geometries were visualized using CYLview.[168] NCIPLOT was used to obtain the grid data for NCI (non-covalent interactions) analysis,[169] and the corresponding results were visualized with the VMD software.[170]

All these considerations are common for the calculations performed by the author of this thesis, which are presented both in Chapters II and III (particularly, in Sections II.7 and III.5).

*The details on the DFT calculations presented in the following pages correspond to the theory presented throughout Section II.7. This study was performed jointly by the author of this thesis (who developed the initial model for the retro-Buchner/cyclopropanation sequence) and Dr. Marc Montesinos-Magraner (who studied the competing 6-*endo*-dig cycloisomerization pathway and completed the full mechanistic picture).*

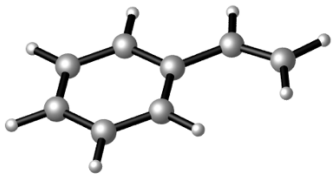
167 Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B*, **2009**, *113*, 6378–6396.

168 Legault, C. Y. CYLview; Universite de Sherbrooke: Sherbrooke, Canada, **2009**; http://www.cylview.org.

169 Contreras-García, J.; Johnson, E. R.; Keinan, S.; Chaudret, R.; Piquemal, J.-P.; Beratan, D. N.; Yang, W. NCIPLOT: A Program for Plotting Noncovalent Interaction Regions. *J. Chem. Theory Comput.* **2011**, *7*, 625–632.

170 Humphrey, W.; Dalke, A.; Schulten, K. VMD: Visual molecular dynamics. *J. Mol. Graph.* **1996**, *14*, 33–38.

**Styrene**

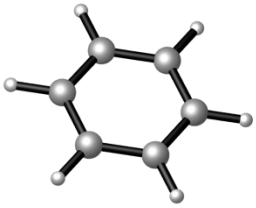


E (opt) = -309.673002005 Hartrees

G (opt) = -309.570760 Hartrees

E (SP) = -309.7583771 Hartrees

**Benzene**

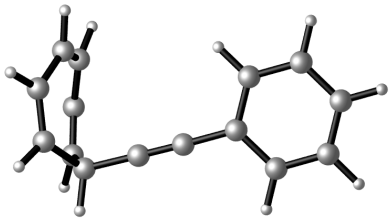


E (opt) = -232.266686119 Hartrees

G (opt) = -232.193560 Hartrees

E (SP) = -232.3309627 Hartrees

**Cycloheptatriene 91a**

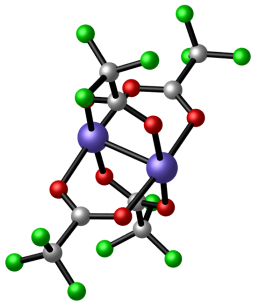


E (opt) = -578.7538372 Hartrees

G (opt) = -578.574960 Hartrees

E (SP) = -578.912744 Hartrees

**$[Rh_2(TFA)_4]$**

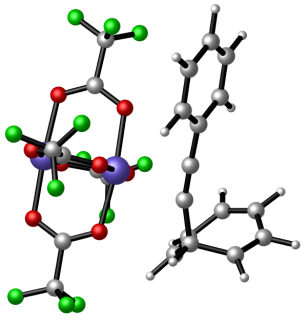


E (opt) = -2323.968200 Hartrees

G (opt) = -2323.914009 Hartrees

E (SP) = -2324.703656 Hartrees

**(I)-Rh**

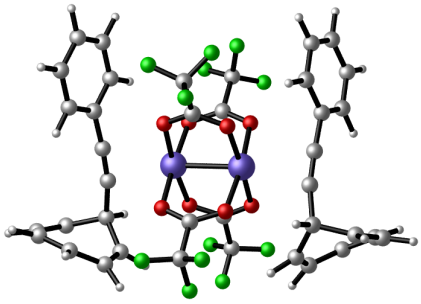


E (opt) = -2902.761142 Hartrees

G (opt) = -2902.503465 Hartrees

E (SP) = -2903.651256 Hartrees

**(0)-Rh**

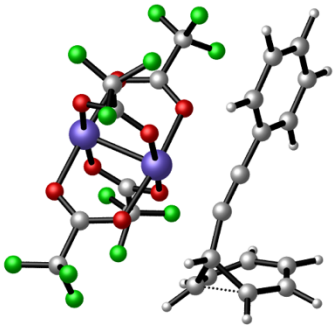


E (opt) = -3481.54663 Hartrees

G (opt) = -3481.088948 Hartrees

E (SP) = -3482.591732 Hartrees

**($TS_{I–II}$)-Rh**

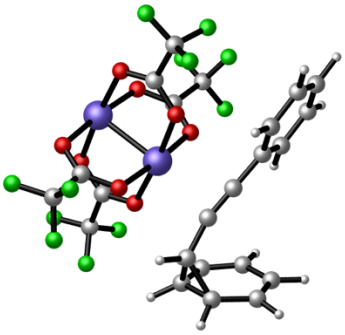


E (opt) = -2902.747973 Hartrees

G (opt) = -2902.491019 Hartrees

E (SP) = -2903.636331 Hartrees

**(II)-Rh**

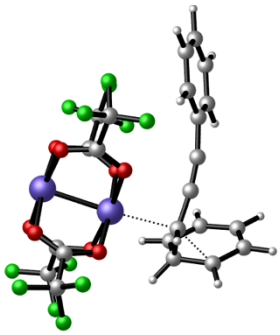


E (opt) = -2902.759835 Hartrees

G (opt) = -2902.502881 Hartrees

E (SP) = -2903.647612 Hartrees

**($TS_{II–III}$)-Rh**

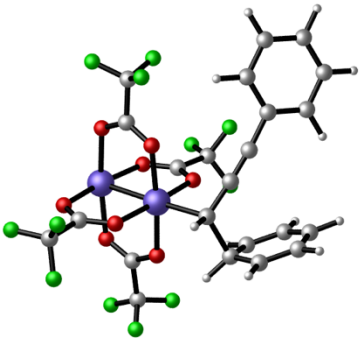


E (opt) = -2902.735161 Hartrees

G (opt) = -2902.478057 Hartrees

E (SP) = -2903.622428 Hartrees

**(III)-Rh**

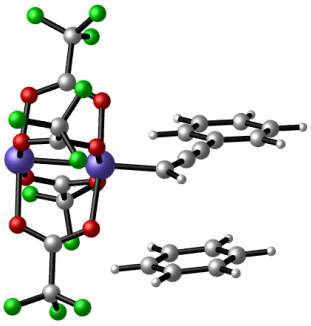


E (opt) = -2902.740893 Hartrees

G (opt) = -2902.486751Hartrees

E (SP) = -2903.628862 Hartrees

**(IV)-Rh**

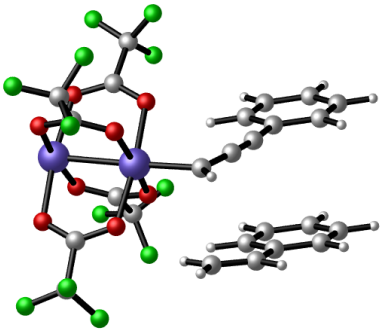


E (opt) = -2902.755687 Hartrees

G (opt) = -2902.506623 Hartrees

E (SP) = -2903.645744 Hartrees

**($V_{cis}$)-Rh**

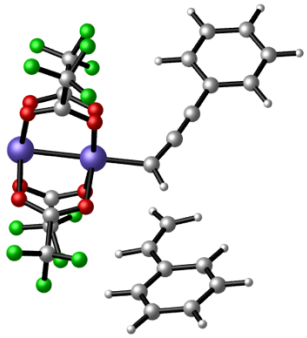


E (opt) = -2980.168265 Hartrees

G (opt) = -2979.884385 Hartrees

E (SP) = -2981.079095 Hartrees

**($V_{trans}$)-Rh**

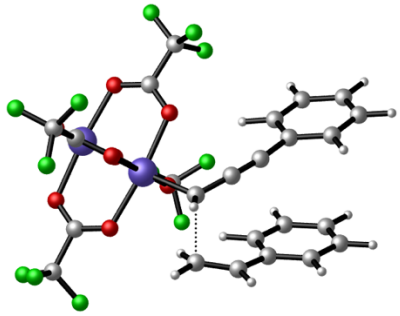


E (opt) = -2980.162121 Hartrees

G (opt) = -2979.879606 Hartrees

E (SP) = -2981.072838 Hartrees

**($TS_{V-VI\_cis}$)-Rh**

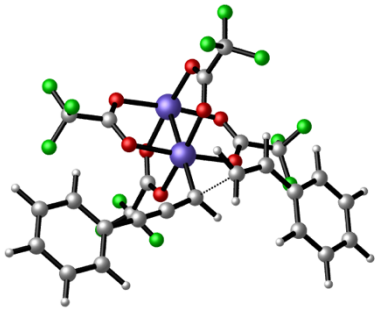


E (opt) = -2980.166632 Hartrees

G (opt) = -2979.881040 Hartrees

E (SP) = -2981.075983 Hartrees

**($TS_{V-VI\_trans}$)-Rh**

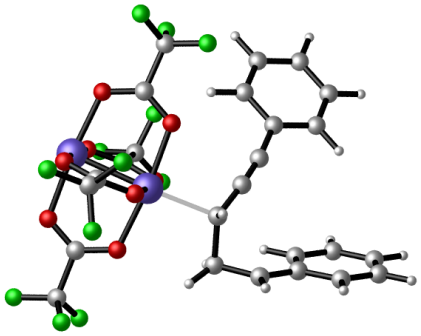


E (opt) = -2980.161826 Hartrees

G (opt) = -2979.876544 Hartrees

E (SP) = -2981.071548 Hartrees

**($VI_{cis}$)-Rh**

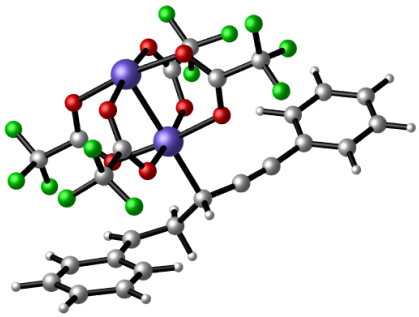


E (opt) = -2980.185087 Hartrees

G (opt) = -2979.896608 Hartrees

E (SP) = -2981.092798 Hartrees

**($VI_{trans}$)-Rh**

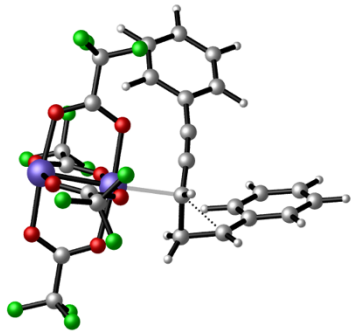


E (opt) = -2980.179503 Hartrees

G (opt) = -2979.890982 Hartrees

E (SP) = -2981.085827 Hartrees

**($TS_{VI-VII}$)-Rh**

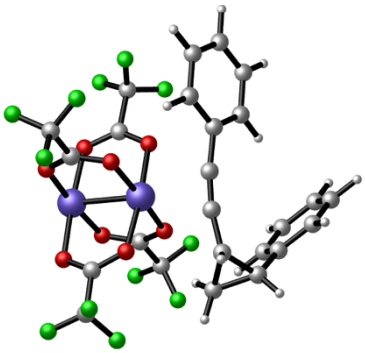


E (opt) = -2980,184425 Hartrees

G (opt) = -2.979,899182 Hartrees

E (SP) = -2.981.092016 Hartrees

**(VII)-Rh**

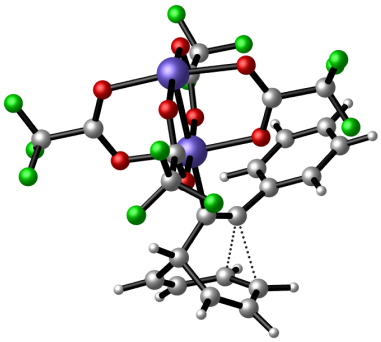


E (opt) = -2980.217933 Hartrees

G (opt) = -2979.927483 Hartrees

E (SP) = -2981.124620 Hartrees

**($TS_{I-VIII}$)-Rh**

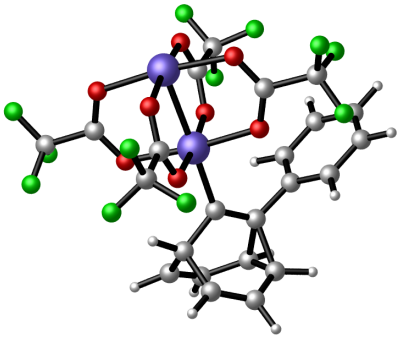


E (opt) = -2902.741037 Hartrees

G (opt) = -2902.484046 Hartrees

E (SP) = -2903.627219 Hartrees

**(VIII)-Rh**

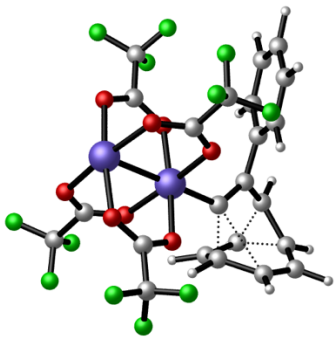


E (opt) = -2902.75850 Hartrees

G (opt) = -2902.497309 Hartrees

E (SP) = -2903.641935 Hartrees

**($TS_{VIII-IX}$)-Rh**

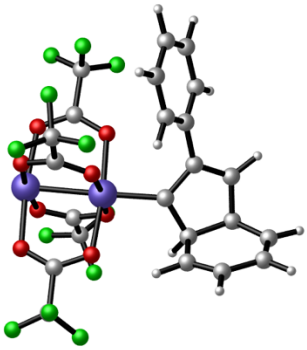


E (opt) = -2902.73870 Hartrees

G (opt) = -2902.478873 Hartrees

E (SP) = -2903.621106 Hartrees

**(IX)-Rh**

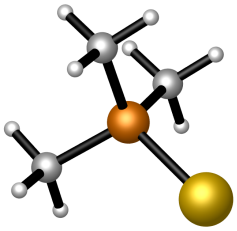


E (opt) = -2902.77778 Hartrees

G (opt) = -2902.518274 Hartrees

E (SP) = -2903.663031 Hartrees

**[($PMe_3$)Au]$^+$**

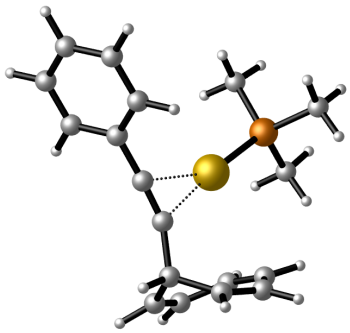


E (opt) = -596.477863 Hartrees

G (opt) = -596.396611 Hartrees

E (SP) = -596.552706 Hartrees

**(I)-Au**

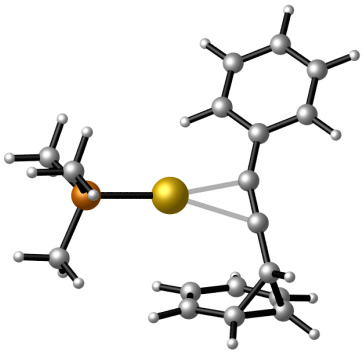


E (opt) = -1175.276777 Hartrees

G (opt) = -1174.996116 Hartrees

E (SP) = -1175.508081 Hartrees

**(II)-Au**

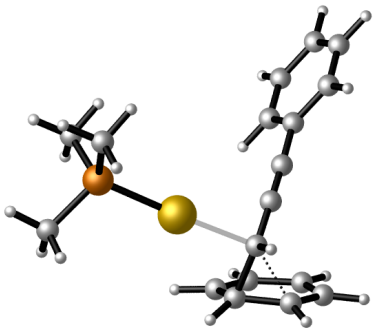


E (opt) = -1175.274408 Hartrees

G (opt) = -1174.993558 Hartrees

E (SP) = -1175.502215 Hartrees

**($TS_{II-III}$)-Au**

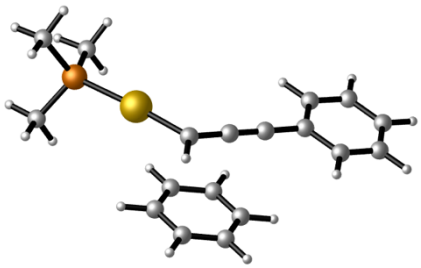


E (opt) = -1175.242406 Hartrees

G (opt) = -1174.963376 Hartrees

E (SP) = -1175.471652 Hartrees

**(IV)-Au**

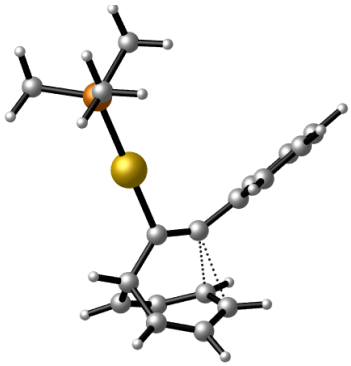


E (opt) = -1175.267591 Hartrees

G (opt) = -1174.993596 Hartrees

E (SP) = -1175.499982 Hartrees

**($TS_{I-VIII}$)-Au**

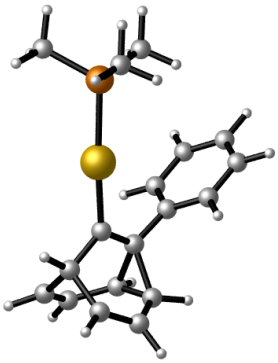


E (opt) = -1175.256084 Hartrees

G (opt) = -1174.974983 Hartrees

E (SP) = -1175.483935 Hartrees

**(VIII)-Au**

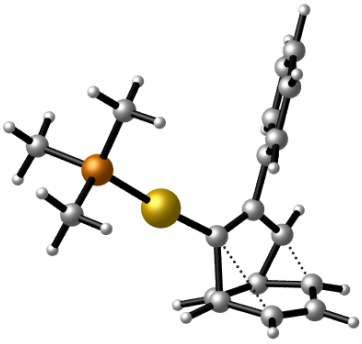


E (opt) = -1175.273115 Hartrees

G (opt) = -1174.988160 Hartrees

E (SP) = -1175.497917 Hartrees

**(TS$_{VIII–IX}$)-Au**

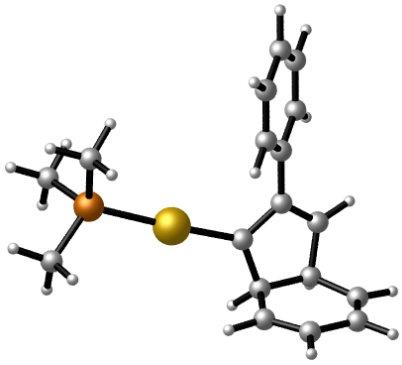


E (opt) = -1175.256768 Hartrees

G (opt) = -1174.970664 Hartrees

E (SP) = -1175.480471 Hartrees

**(IX)-Au**



E (opt) = -1175.296475 Hartrees

G (opt) = -1175.013254 Hartrees

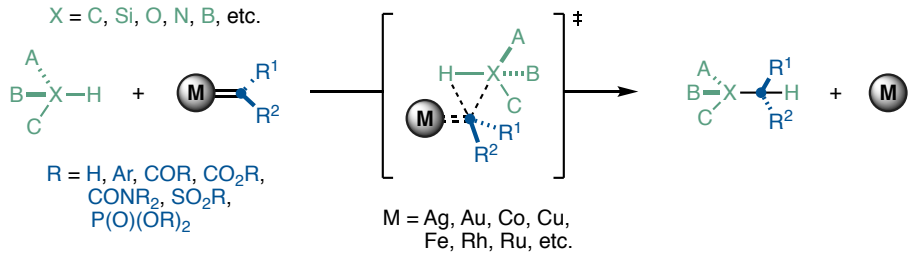
E (SP) = -1175.522572 Hartrees

# *Chapter III: "New Cycloheptatriene Derivatives as Tools for Reaction Discovery"*

*Part of the work described in this chapter was carried out in collaboration with* ***Dr. Cristina García-Morales, Dr. Xiang Yin*** *and* ***Helena Armengol-Relats****.*

## III.1. Background: Carbenes Beyond Cyclopropanations

The cyclopropanation of alkenes is the benchmark reaction of metal carbenes. As illustrated in the previous chapter, this reaction is often explored in the early stages of development of new carbene precursors. However, the remarkable reactivity of highly energetic carbene intermediates goes far beyond that.[171] For instance, they can engage in a variety of very selective X–H (X = C, Si, O, N, B, etc.) concerted insertion processes, a powerful, clean and efficient strategy to forge both C–C and C–heteroatom bonds (Scheme 72).[172]




**Scheme 72**. General mechanistic overview of concerted metal-carbene X–H insertions.

It is worth mentioning that the nature of the metal, its ligands, and the stereoelectronic properties of the carbene substituents play an important role in the chemo- regio- and stereoselectivity of the process. In this regard, non-acceptor carbene fragments are rather underexplored due to their challenging generation.[173]

These statements are also true for another general group of transformations in which metal carbenes can engage: higher formal cycloadditions (*i*+*j*) (in which at least either *i* or *j* > 2).[174] Among the different types of reactivities in which metal carbenes can take part, formal cycloadditions stand out for their potential to rapidly build up molecular complexity (Scheme 73).

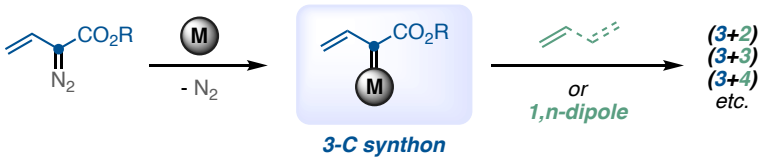
171 *Metal Carbenes is Organic Synthesis* (in Topics in Organometallic Chemistry, 2004). Ed.: Dötz, K. H. Springer-Verlag Berlin Heidelberg.

172 Doyle, M. P.; Duffy, R.; Ratnikov, M.; Zhou, L. Catalytic Carbene Insertion into C-H Bonds. *Chem. Rev.* **2010**, *110*, 704–724.

173 Davies, H. M. L.; Denton, J. R. Application of donor/acceptor-carbenoids to the synthesis of natural products. *Chem. Soc. Rev.* **2009**, *38*, 3061–3071.

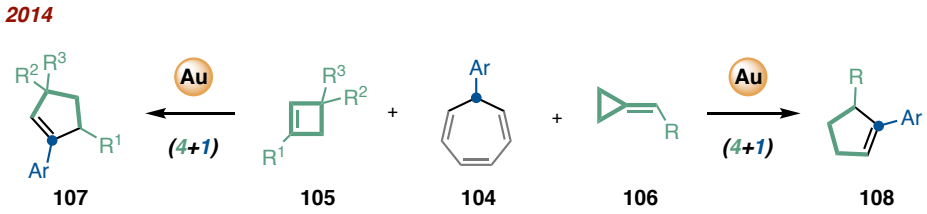
174 Xu, X.; Doyle, M. P. The [3 + 3]-Cycloaddition Alternative for Heterocycle Syntheses: Catalytically Generated Metalloenolcarbenes as Dipolar Adducts. *Acc. Chem. Res.* **2014**, *47*, 1396–1405.

More specifically, vinyl donor–acceptor carbenes have been identified as privileged substrates to develop this type of cycloaddition processes, as demonstrated by different research groups (Scheme 73).[175]




**Scheme 73**. Vinyl carbenes as 3-C synthons in formal cycloadditions.

Previous studies by our group showed that aryl donor carbenes generated by retro-Buchner reaction of cycloheptatrienes react with 4-carbon synthons such as cyclobutenes and methylenecyclopropanes to give cyclopentenes, in an overall (4+1) formal cycloaddition process (Scheme 74).[176]




**Scheme 74**. (4+1) cycloaddition of aryl gold(I) carbenes with methylenecyclopropanes or cyclobutenes.

Based upon these precedents (and other more specific ones which will be introduced in the appropriate sections of this chapter), we applied the knowledge gathered on new methods for the generation of metal carbenes for the discovery of new chemical transformations.

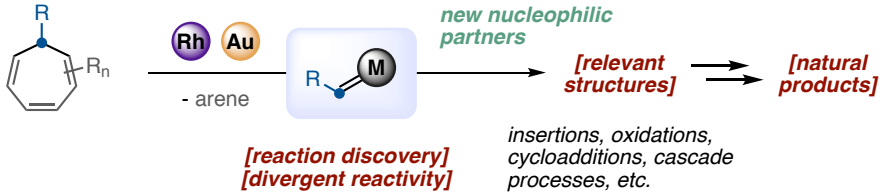
175 (a) Parr, B. T.; Davies, H. M. L. Highly stereoselective synthesis of cyclopentanes bearing four stereocentres by a rhodium carbene-initiated domino sequence. *Nat. Commun*. **2014**, *5*, 4455. (b) Lee, D. J.; Han, H. S.; Shin, J.; Yoo, E. J. Multicomponent [5 + 2] cycloaddition reaction for the synthesis of 1,4-diazepines: Isolation and reactivity of azomethine ylides. *J. Am. Chem. Soc.* **2014**, *136*, 11606–11609. (c) Zhang, C.; Hong, K.; Pei, C.; Zhou, S.; Hu, W.; Hashmi, A. S. K.; Xu, X. Gold(I)-catalyzed intramolecular cyclization/ intermolecular cycloaddition cascade as a fast track to polycarbocycles and mechanistic insights. *Nat. Commun.* **2021**, *12*, 1182.

176 Wang, Y.; Muratore, M. E.; Rong, Z.; Echavarren, A. M. Formal (4+1) Cycloaddition of Methylenecyclopropanes with 7-Aryl-1,3,5-cycloheptatrienes by Triple Gold(I) Catalysis. *Angew. Chem. Int. Ed.* **2014**, *53*, 14022–14026.

## III.2. Objectives

The global objective of the projects discussed in the third chapter was the application of the newly developed metal-carbene precursors in the discovery of new chemical transformations beyond cyclopropanations. In particular, we wanted to:

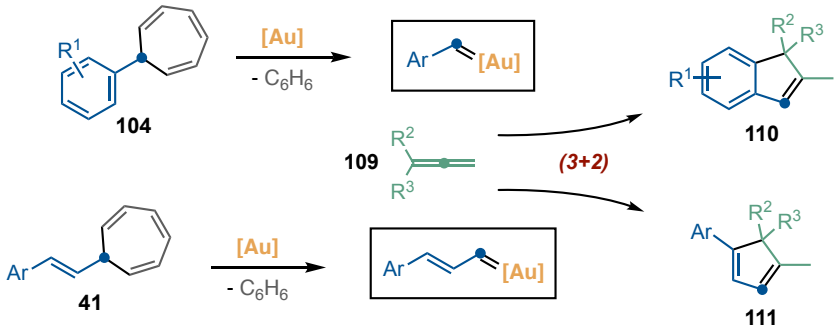
- Exploit the versatility of alkenyl carbene intermediates for the development of new synthetic methodologies based on higher cycloaddition processes.
- Evaluate a wide range of potential nucleophilic partners that can react satisfactorily with non-acceptor metal carbenes, which have not been explored thus far, due to the difficulties associated with the generation of this type of intermediates. This could result, for instance, in the development of insertion reactions or complex cascade processes.
- Study if the possibility of generating carbenes of different metals would potentially allow for unlocking new, divergent reactivity which was not possible by means of gold(I) catalysis.
- Study the mechanism of the new reactions using both theory and experiments.
- Illustrate the potential of the new methodologies through the short total synthesis of natural products.




**Scheme 75**. Aromative decarbenations as tools for the discovery of new reactions and the rapid assembly of molecular complexity.

## III.3. (3+2) Cycloaddition of Alkenyl Carbenes with Allenes

At the outset of our search for new reactions based on the intermediacy of non-acceptor gold(I) carbenes generated by retro-Buchner reaction of cycloheptatrienes, we identified allenes as effective nucleophilic trapping partners. Very recently at the time, our group had found that simple 7-aryl-1,3,5-cycloheptatrienes **104** react with allenes in the presence of cationic gold(I) complexes to give indenes, through a decarbenation/formal (3+2) cycloaddition sequence.[177] In parallel, we also found that the same type of 1,1-disubstituted allenes could be trapped with styryl gold(I) carbenes, generated from 7-styryl-1,3,5-cycloheptatrienes **41**, to afford densely substituted cyclopentadienes **111**, through a vinylogous version of the same process (Scheme 76). A similar type of transformation was also recently reported using instead vinyl donor–acceptor diazo compounds as carbene source.[178]



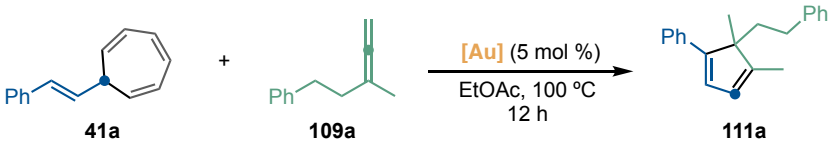

**Scheme 76**. Au(I)-catalyzed (3+2) cycloadditions of non-acceptor carbenes and allenes.

We started off by optimizing the gold(I) catalyst for the reaction between cycloheptatriene **41a** and 1.5 equiv of allene **109a** (Scheme 77, entries 1–4). We found that in this case, JohnPhos-type ligands with *t*Bu substituents in the phosphine were the ones promoting more cleanly the transformation. Out of these, [(*t*BuXPhos)Au(MeCN)]$SbF_6$ proved to be the best performing complex, giving tetrasubstituted cyclopentadiene **111a** in 52% yield. It is worth highlighting the unusually better result provided by EtOAc when using precursors such as **41a**, a solvent which is often outperformed by chlorinated solvents in aromative-decarbenation chemistry (Scheme 77, entry 5).

177 The (3+2) cycloaddition of aryl gold(I) carbenes with allenes to give indenes was developed by Dr. Xiang Yin in parallel to the reaction presented in this section, and both works were published together in 2017, see: Yin, X.; Mato, M.; Echavarren, A. M. Gold(I)-Catalyzed Synthesis of Indenes and Cyclopentadienes: Access to (±)-Laurokamurene B and the Skeletons of the Cycloaurenones and Dysiherbols. *Angew. Chem. Int. Ed.* **2017**, *56*, 14591–14595.

178 López, E.; Lonzi, G.; González, J.; López, L. A. Gold-catalyzed intermolecular formal (3+2) cycloaddition of stabilized vinyldiazo derivatives and electronically unbiased allenes. *Chem. Commun.* **2016**, *52*, 9398–9401.

Regarding temperature, 100 ºC allowed to reach full conversion in 12 h with the best yield. Lower temperatures slowed down the reaction significantly and working above 100 ºC led to a decrease in yield (Scheme 77, entries 6 and 7).[179]

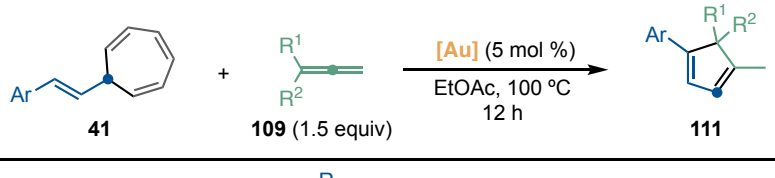



**41a** **109a** **111a**

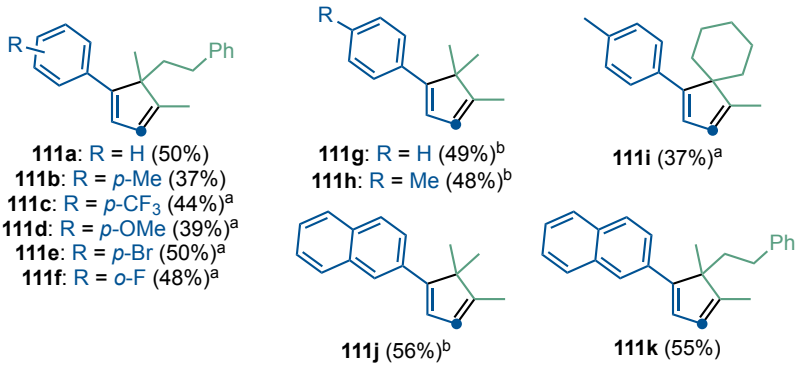
| *entry* | *deviation from standard conditions* | *yield of 111a* |
|---|---|---|
| 1 | **none**, [(*t*BuXPhos)Au(MeCN)]$SbF_6$ | **52% (50% isolated)** |
| 2 | [(JohnPhos)Au(MeCN)]$SbF_6$ | 45% |
| 3 | [(XPhos)Au(MeCN)]$SbF_6$ | n/d |
| 4 | [(IPr)Au(PhCN)]$SbF_6$ | 17% |
| 5 | DCE instead of EtOAc | 25% |
| 6 | 80 ºC | 33% |
| 7 | 120 ºC | 40% |

**Scheme 77**. Optimization of the synthesis of cyclopentadienes.

Then, we explored the scope of the transformation (Scheme 78). We found that, even though the effect was minimum in the synthesis of **111a**, in some cases the yield could be slightly increased using an excess of allene **109** (2–3 equiv). In combination with model allene **109a**, we transferred successfully styryl-carbene fragments with different substituents in the aromatic ring, obtaining a range of arylcyclopentadienes in moderate yields. Starting from a naphthyl-substituted alkenylcycloheptatriene, we assembled **111j** and **111k** in slightly better yields.




**41** **109** (1.5 equiv) **111**




**111a**: R = H (50%)
**111b**: R = *p*-Me (37%)
**111c**: R = *p*-$CF_3$ (44%)[a]
**111d**: R = *p*-OMe (39%)[a]
**111e**: R = *p*-Br (50%)[a]
**111f**: R = *o*-F (48%)[a]

**111g**: R = H (49%)[b]
**111h**: R = Me (48%)[b]

**111i** (37%)[a]

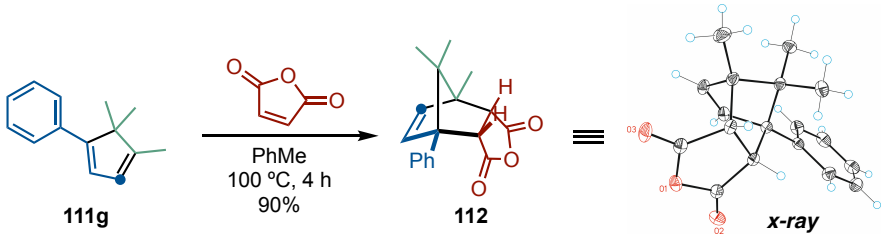
**111j** (56%)[b]

**111k** (55%)

**Scheme 78**. Scope of the synthesis of cyclopentadienes. [Au] = [(*t*BuXPhos)Au(MeCN)]$SbF_6$
[a] 2 equiv of **109**. [b] 3 equiv of **109**.

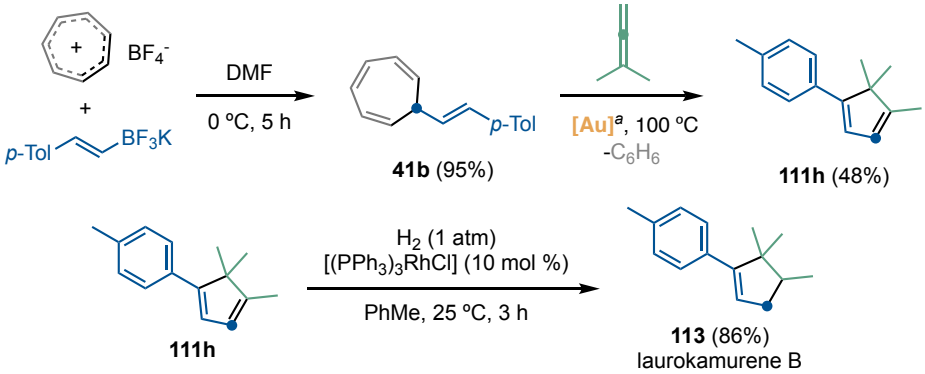
179 Since this project was carried out before the development of more reactive 7-styryl-1,3,5-trimethyl cycloheptatrienes **91**, these were not evaluated in the optimization of this reaction.

Finally, other allenes with the same substitution pattern were evaluated, leading to the formation of trimethylcyclopentadienes such as **111g** and **111h** or to spirocyclic product **111i** (Scheme 78). Diels–Alder reaction of cyclopentadiene **111g** and maleic anhydride led exclusively to crystalline *endo* adduct **112**. This allowed an indirect confirmation of the structure of cyclopentadienes **111** and illustrates the power of the combination of the two cycloaddition processes to rapidly build up complex polycyclic structures (Scheme 79).




**Scheme 79**. Diels–Alder cycloaddition of cyclopentadiene **111g**.

At this point, we envisioned that our gold(I)-catalyzed cycloaddition could be applied to develop a short synthesis of laurokamurene B, a natural sesquiterpenoid from a family of cytotoxic five-membered carbocyclic compounds.[180] Thus, cycloheptatriene **41b** was prepared in one step from commercially available tropylium tetrafluoroborate and Molander-type potassium *p*-methylstyryl tetrafluoroborate in quantitative yield. Then, **41b** was submitted to our reaction conditions with 3-methyl-1,2-butadiene, directly affording the typical skeleton of this family of natural compounds. Finally, selective hydrogenation of **111h** with a $H_2$ balloon and Wilkinson's catalyst gave directly laurokamurene B in good yield. This three-step strategy compares favorably to previously reported synthesis.[181]

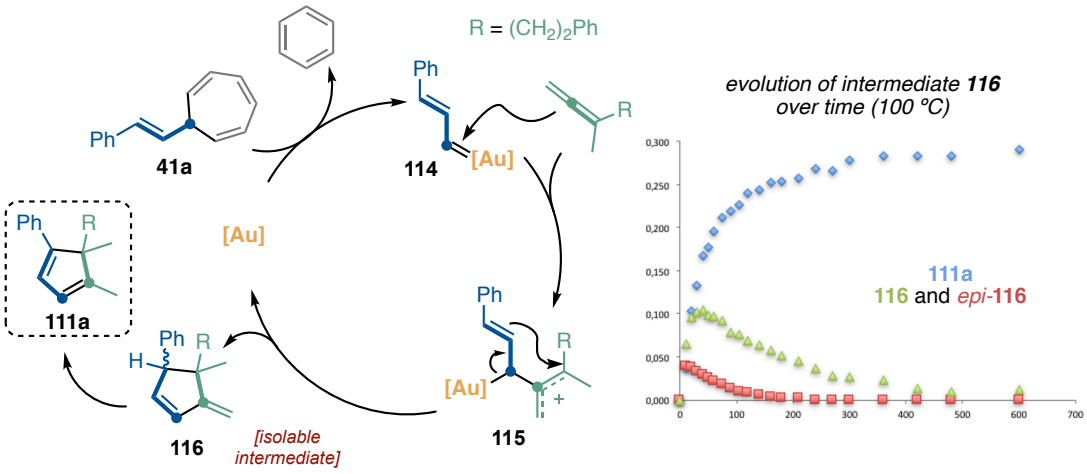



**Scheme 80**. Total synthesis of (±)-laurokamurene B.
[a] [Au] = [(*t*BuXPhos)Au(MeCN)]$SbF_6$

180 Yu, X.-Q.; He, W.-F.; Liu, D.-Q.; Feng, M.-T.; Fang, Y.; Wang, B.; Feng, L.-H.; Guo, Y.-W.; Mao, S.-C. A seco-laurane sesquiterpene and related laurane derivatives from the red alga *Laurencia okamurai* Yamada. *Phytochemistry* **2014**, *103*, 162–170.

181 Srikrishna, A.; Khan, I. A.; Ramesh Babu, R.; Sajjanshetty, A. The first total synthesis of (±)-laurokamurene B. *Tetrahedron* **2007**, *63*, 12616–12620.

Our mechanistic proposal for this process starts by the gold(I)-catalyzed retro-Buchner reaction of **41a** to give styryl carbene **114** upon release of a molecule of benzene. Nucleophilic attack by the central carbon of an allene leads to allylic cation **115**, which can evolve through a vinylogous Friedel–Crafts-type cyclization, to give a mixture of the two possible diastereoisomers of methylenecyclopentene **116**. Finally, isomerization of **116** affords fully conjugated cyclopentadiene **111a** (Scheme 81).




**Scheme 81**. Mechanistic proposal for the formal (3+2) cycloaddition (left) and evolution of intermediates **116** into product **111a** (right).

The proposed mechanism is consistent with our observation of the formation and accumulation of significant amounts of intermediate **116**. If the reaction is stopped after 25 min at 100 ºC and submitted to chromatographic purification, the three compounds shown in Figure 19 can be identified. Kinetic analysis shows the slow convergence of both *syn*- and *anti*-**116** (unassigned) into **111a**. Whether this isomerization is either thermal or promoted by gold(I) was not studied.

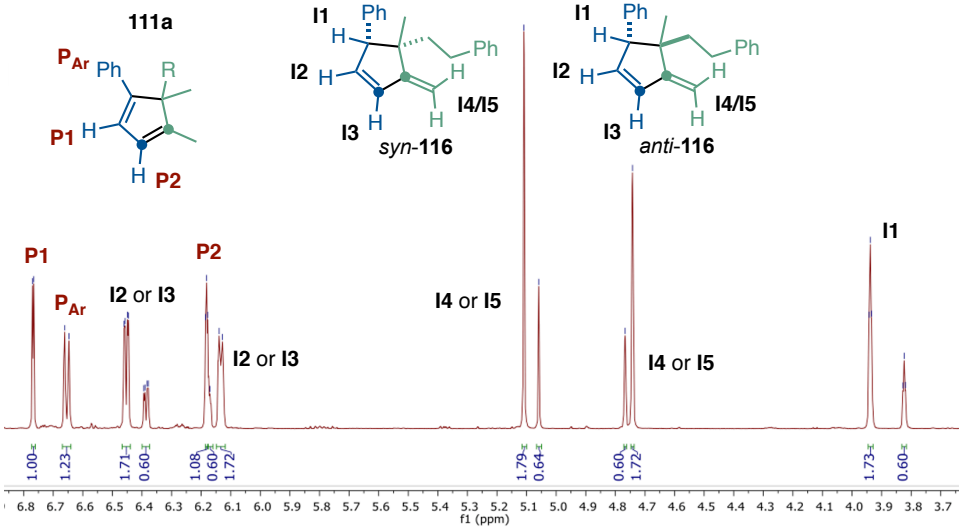
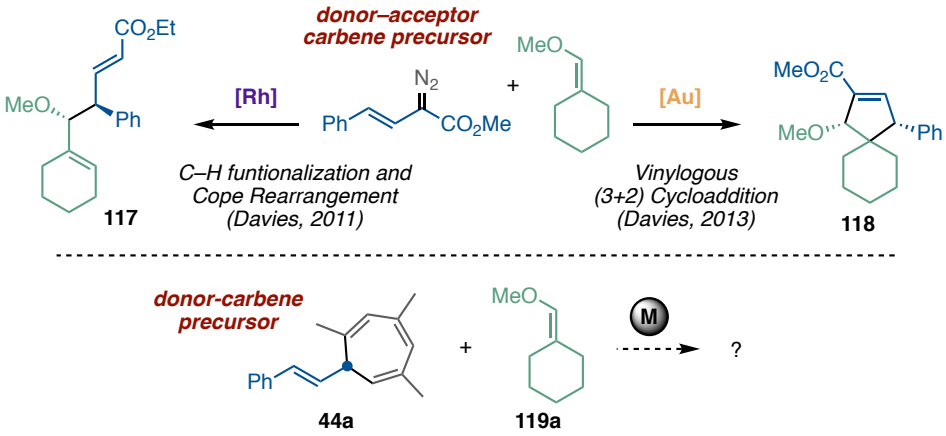



**Figure 19**. $^{1}$H NMR of the mixture of products isolated after 25 min at 100 ºC.

## III.4. Assembly and Disassembly of Cyclopropylethers to Give Trienes

After the discovery of 7-styryl-1,3,5-trimethylcycloheptatrienes **44** as powerful rhodium(II) donor-carbene precursors (Section II.4),[182] we wondered whether it would be possible to develop reactivity divergent to that observed when using classical acceptor or donor–acceptor analogs. The group of Davies reported in 2011 that styryl donor–acceptor carbenes react with enol ethers such as **119** under rhodium(II) catalysis to give products of sequential C–H insertion and Cope rearrangement (**117**).[183] Contrastingly, the same group found that, under gold(I) catalysis, the same two substrates give rise to **118**, the product of vinylogous (3+2) cycloaddition of the corresponding styryl donor–acceptor carbene and the enol ether.[184] Considering these precedents, we decided to explore the potentially divergent reactivity between enol ethers and donor carbenes.[185]




**Scheme 82**. Divergent reactivity of donor–acceptor or donor alkenyl carbenes.

Distinctly, when performing the reaction between cycloheptatriene **44a** and enol ether **119a** in the presence of catalytic amounts of $[Rh_2(TFA)_4]$, we found that, after 18 h at 40 ºC in DCE, spirocyclic cyclopropylether **120a** was obtained as the only product in 78% yield and in a 6:1 *cis*/*trans* (as suggested by nOe NMR experiments) ratio of diastereoisomers (Scheme 83, Conditions A). On the other hand, when exactly the same combination of substates, catalyst and solvent was heated at 120 ºC for 12 h, *E,E,E*-triene **121a** was obtained as major product (53%

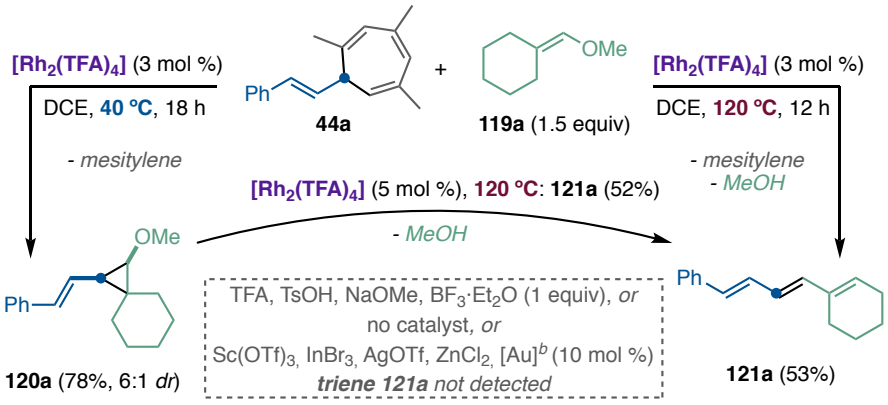
182 Mato, M.; Echavarren, A. M. Donor Rhodium Carbenes by Retro-Buchner Reaction. *Angew. Chem. Int. Ed.* **2018**, *58*, 2088–2092.

183 Lian, Y.; Davies, H. M. L. Combined C–H Functionalization/Cope Rearrangement with Vinyl Ethers as a Surrogate for the Vinylogous Mukaiyama Aldol Reaction. *J. Am. Chem. Soc.* **2011**, *133*, 11940−11943.

184 Briones, J. F.; Davies, H. M. L. Enantioselective Gold(I)-Catalyzed Vinylogous [3 + 2] Cycloaddition between Vinyldiazoacetates and Enol Ethers. *J. Am. Chem. Soc.* **2013**, *135*, 13314−13317.

185 In this Section, all DFT calculations were performed by Dr. Cristina García-Morales and all experiments were performed by Mauro Mato.

yield), and cyclopropane **120a** was not observed (Scheme 83, Conditions B). Control and optimization experiments for the cyclopropanation showed that gold(I) could also be used to promote the reaction but delivered **120a** as a 1:1 mixture of diastereoisomers at 65 ºC (Scheme 83, entry 2). However, when the reaction at 120 ºC was attempted under gold(I) catalysis, a complex mixture was obtained in which triene **121a** was not detected (Scheme 83, entry 8). The cyclopropanation can be carried out at room temperature (Scheme 83, entry 5), but slower rates were observed for other substrates. This led us to choosing 40 ºC as standard reaction temperature. Less electrophilic rhodium(II) sources also gave good results in the cyclopropanation (Scheme 83, entry 3) but led only to very poor yields of triene at high temperature (Scheme 83, entries 9 and 10). Non-methylated cycloheptatriene **41a** led to only 17% yield of cyclopropane at 60 ºC. Finally, the nature of the leaving group in the enol ether was studied, but neither OTBS or OAc led to the formation of significant amount of triene **121a**.




| Conditions A | |
|---|---|
| ***variations*** | ***120a yield (dr)*** |
| **(1)** None | **78% (6:1)**[a] |
| **(2)** [Au][b] (65 °C) | 65% (1:1) |
| **(3)** $Rh_2(esp)_2$ (90 °C) | 66% (9:1) |
| **(4)** $C_7H_7$Styrene[c] (60 °C) | 17% (n/d) |
| **(5)** 25 °C | 80% (6:1) |
| **(6)** 60 °C | 75% (3:1) |

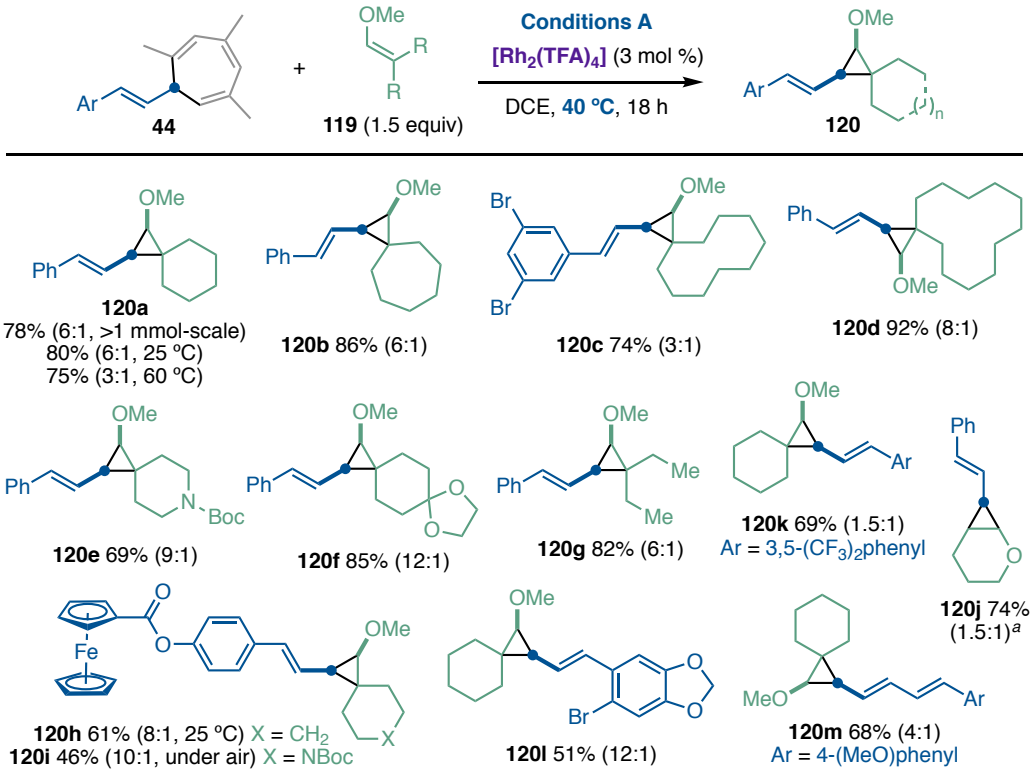
| Conditions B | |
|---|---|
| ***variations*** | ***121a yield*** |
| **(7)** None | **53%**[a] |
| **(8)** [Au][b] (100–120 °C) | n/d |
| **(9)** $Rh_2(esp)_2$ (110 °C) | 8% |
| **(10)** $Rh_2(OAc)_2$ (110 °C) | 11% |
| **(11)** OTBS, OAc instead of OMe | n/d |
| **(12)** TCE-*d2* (100 °C) | 44% |

**Scheme 83**. Optimization and control experiments of the assembly and disassembly of cyclopropylethers. [a] Isolated yield. [b] [Au] = [(JohnPhos)Au(MeCN)]$SbF_6$. [c] Non-methylated 7-styryl-1,3,5-cycloheptatriene **41a** instead of **44a**.

In order to prove the intermediacy of cyclopropane **120a** in the formation of **121a**, we treated the former with 5 mol % of $[Rh_2(TFA)_4]$ in DCE at 120 ºC. This gave triene **121a** in the same yield as when performing the assembly and disassembly of the **120a** in a single pot. We also tested a

range of Brønsted acids, Brønsted bases, and Lewis acids (including gold(I) complexes and zinc(II) halides), but only rhodium(II) dimers were active in this transformation.

In this manner, we found two new divergent reaction pathways for the reaction of styryl donor carbenes with enol ethers, which have not been found using classical donor–acceptor carbenes. The first is a diastereoselective rhodium(II)-catalyzed cyclopropanation leading to complex spirocyclic cyclopropylether structures. The second is the disassembly of the same cyclopropyl ethers upon elimination of methanol. Conveniently, the later process was only found to take place under catalysis of the same type of rhodium(II) dimers that promote the former. The second process, which complements the extensive studies based on the metal-catalyzed activation and opening of donor–acceptor cyclopropanes,[186] leads to the formation of trienes, in an overall formal insertion of the carbene in a C–O bond, followed by elimination. At this point, we decided to evaluate the scope of both methodologies, using the same conditions but only switching the temperature between 40 and 120 ºC (Schemes 84 and 85).

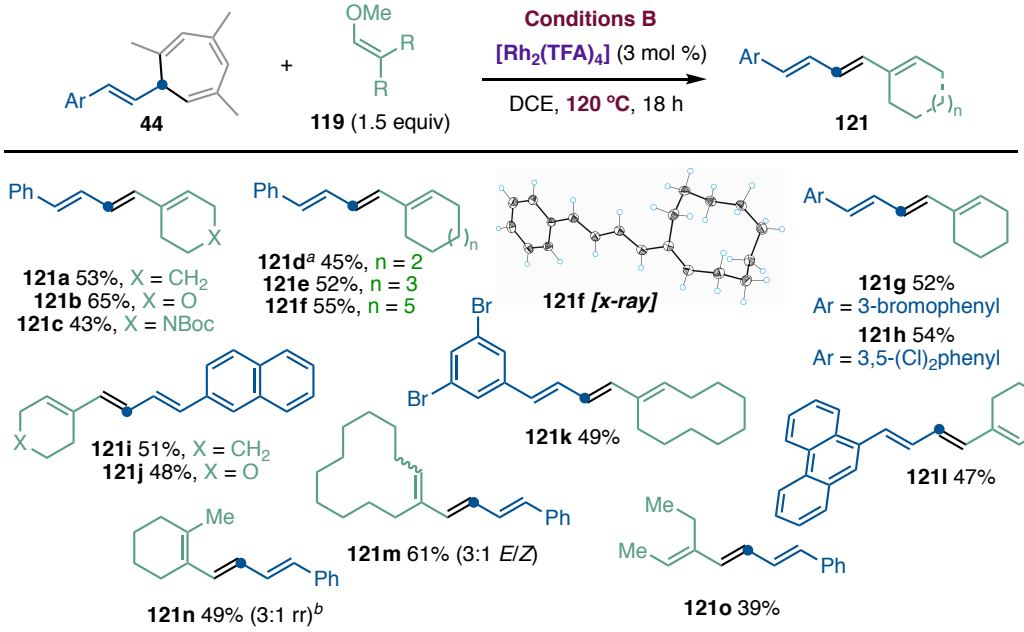



**Scheme 84**. Scope of the assembly of cyclopropylethers. [a] Obtained as a 1.5:1 mixture of unassigned diastereoisomers, using 4 equiv of 3,4-dihydropyran.

186 (a) Reissig, H.-U.; Zimmer, R. Donor−Acceptor-Substituted Cyclopropane Derivatives and Their Application in Organic Synthesis. *Chem. Rev.* **2003**, *103*, 1151–1196. (b) Schneider, T. F.; Kaschel, J.; Werz, D. B. A New Golden Age for Donor–Acceptor Cyclopropanes. *Angew. Chem. Int. Ed.* **2014**, *53*, 5504–5523.

We explored the styrylcyclopropanation of several trisubstituted enol ethers, obtaining spirocyclic structures of different ring sizes (**120a–d**) in good yields and moderate to good diastereoselectivities. Whereas *N*-benzyl protected amines did not work, it was possible to cyclopropanate, in good yield, an enol ether containing an *N*-Boc piperidine (**120e**, **120i**). Similarly, enol ethers containing a protected ketone (**120f**) or an acyclic structure (**120g**) also performed well in the reaction. 3,4-Dihydropyran could also be used to trap the corresponding styryl carbene but giving, in this case, bicyclic **120j** as an unassigned 1.5:1 mixture of diastereoisomers. Finally, styrylcarbene units with different electronic properties were tested, giving products containing electron-rich (**120l**) or electron-poor groups (**120k**), halogens (**120c**), or more complex features such as a ferrocenoyl group (**120h** and **120i**).

Then, we moved on to evaluate the range of all-*E* conjugated trienes that we could access through the one-pot assembly and disassembly of cyclopropanes at 120 ºC (Scheme 85). Different ring sizes can also be used on this transformation (**121a**, **121d–f**). Interestingly, when using large rings such as in the case of **121m**, both *cis* (*E*,*E*,*E*) and *trans* (*E*,*E*,*Z*) macrocycles could be isolated separately. This reaction is also tolerant to the use of *N*-Boc piperidines (**121c**), aryl halides (**121g–h**, **121k**), tetrahydropyrans (**121b**, **121j**), polyaromatic hydrocarbons (**121i–j**, **121l**), or non-cyclic enol ethers (**121o**). However, cyclopropanes with electron-rich aromatics did not open cleanly and led to complex mixtures of products. When using an asymmetrical enol ether (**121n**), a 3:1 mixture of regioisomers was obtained, favoring the product with the more substituted alkene. Finally, the structure of triene **121f** was confirmed by X-ray diffraction.




**Scheme 85**. Scope of the synthesis of trienes. [a] 100 ºC and 0.4 M instead of 120 ºC and 0.15 M. [b] 3:1 Ratio of regioisomers, favoring the tetrasubstituted endocyclic alkene over the trisubstituted one.

To paint a clear mechanistic picture of the entire process, we used a combination of experiments and theory. First, Dr. Cristina García-Morales modeled the rhodium(II)-catalyzed decarbenation/cyclopropanation sequence using DFT (Figure 20). In summary, we found that the rate-limiting step of these two processes is the cleavage of the first C–C bond in norcaradiene **III**, to give Wheland-type carbenoid intermediate **IV**. This is similar to what was previously determined for the gold(I)-catalyzed retro-Buchner reaction of simple, first-generation 7-aryl or 7-styryl cycloheptatrienes (Figure 12, page 54). In this case, there are two possibilities for that process to occur: one leading to trisubstituted carbocation **IV**, and the second one to disubstituted carbocation **IV***. As expected, both **IV** and the TS leading to it were lower in energy than **IV*** and $\mathbf{TS_{III–IV*}}$. The overall barrier of the process is 20.3 kcal/mol, consistent with the cyclopropanation taking place at ≥25 ºC.

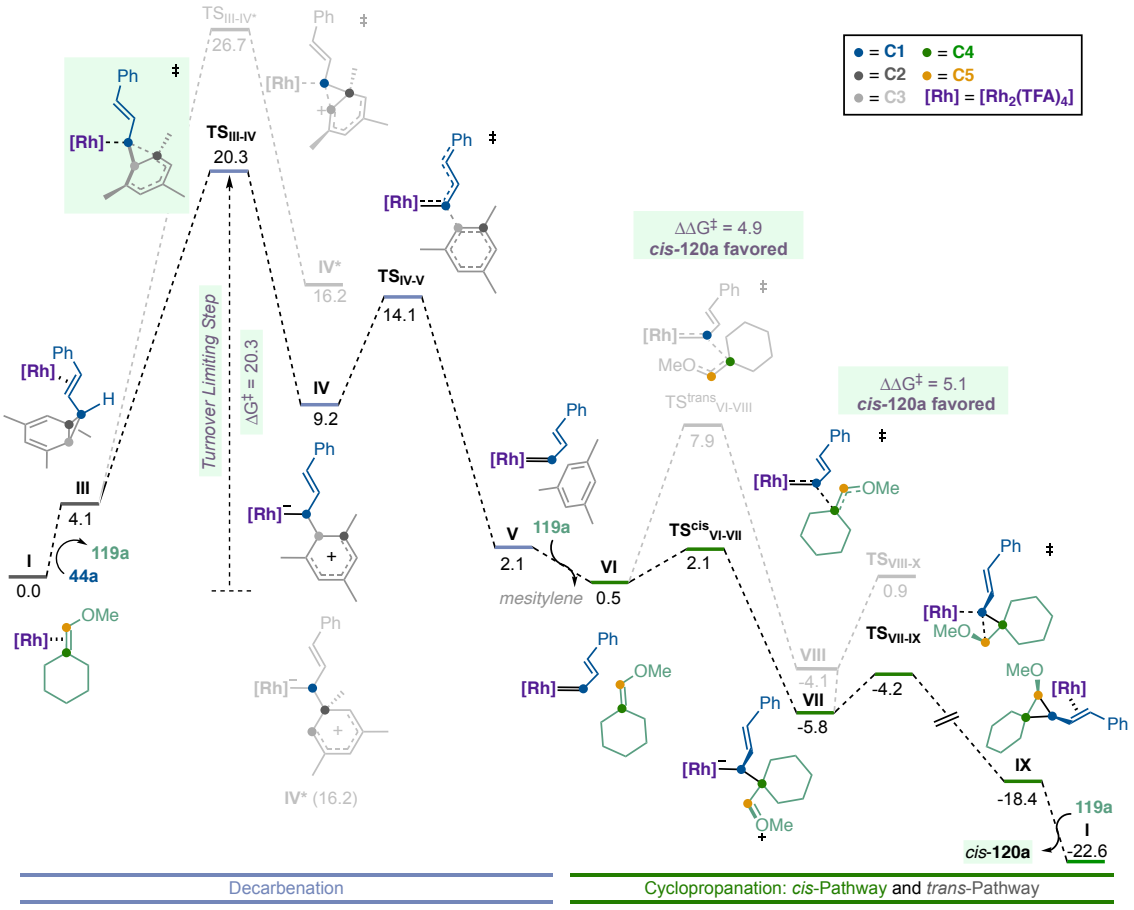
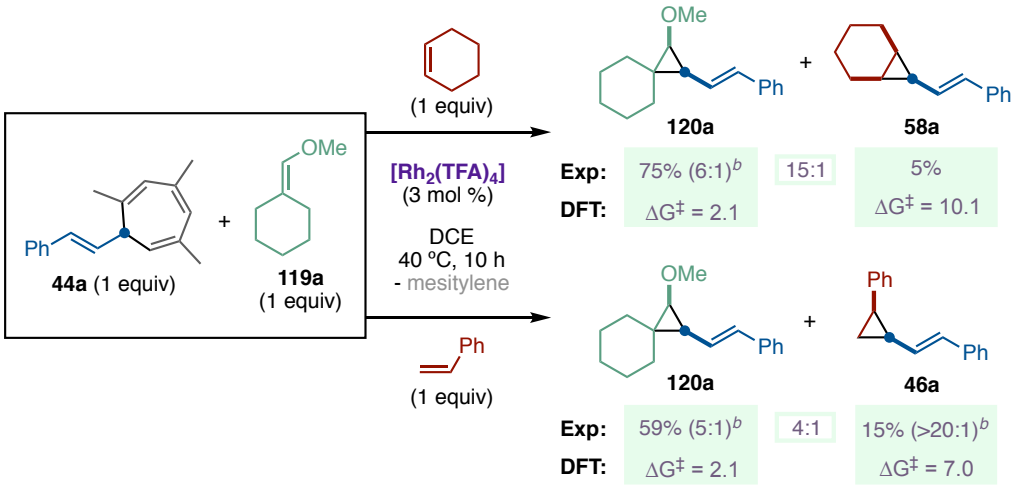



**Figure 20**. Free-energy profile (kcal/mol) for the Rh(II)-catalyzed retro-Buchner/cyclopropanation sequence, calculated by DFT.[187]

187 Cycloheptatriene–norcaradiene (**II**/**III**) equilibrium omitted for clarity. For details on this process, or about the DFT calculations presented in this Section in general, see the original publication: Mato, M.; García-Morales, C.; Echavarren, A. M. Synthesis of Trienes by Rhodium-Catalyzed Assembly and Disassembly of Non-Acceptor Cyclopropanes. *ACS Catal.* **2020**, *10*, 3564–3570.

Release of mesitylene through $\mathbf{TS_{IV-V}}$ leads to rhodium(II) carbene **V**, which upon ligand exchange with enol ether **119a**, evolves to give O-stabilized carbocationic intermediate **VII**.[188] Finally, **VII** closes up to give the corresponding Rh(II)-coordinated cyclopropyl ether **IX** through an almost barrierless and highly exothermic process.

With a wider range of alkenes that can get cyclopropanated by donor carbenes in our hands, we did some competition experiments, in order to evaluate the relative nucleophilicity of the different substates. Thus, a 1:1 mixture of enol ether **119a** and cyclohexene led to a 15:1 mixture of cyclopropyl ether **120a** and **58a**. Competition between **119a** and styrene also favored the formation of **120a**, but only in a 4:1 ratio. Both of these results are qualitatively consistent with the barriers obtained by DFT for the three cyclopropanation reactions and are in agreement with what one might expect by simple chemical intuition (Scheme 86).




**Scheme 86**. Experimental and theoretical competition studies between different alkenes.
[b] In parenthesis, *cis*/*trans* ratio for each of the two cyclopropanes.

A closer look at the opening/MeOH elimination of non-acceptor cyclopropane **120a** led us to the discovery of a rhodium(II)-catalyzed *cis*/*trans* isomerization of this compound (Figure 21, top). This type of process had already been observed for other types of cyclopropanes under gold(I) and gold(III) catalysis.[189]

188 A pathway for the concerted cyclopropanation of enol ether **119a** could not be located. Similar calculations for reveal than the pathway followed in cyclopropanation reactions can go through either type of mechanism depending on the type of alkene (i.e., the stabilization of the resulting carbocation). Styrene gives also a stepwise pathway, whereas for cyclohexene it is concerted.

189 (a) Herlé, B.; Holstein, P. M.; Echavarren, A. M. Stereoselective *cis*-Vinylcyclopropanation via a Gold(I)-Catalyzed Retro-Buchner Reaction under Mild Conditions. *ACS Catal.* **2017**, *7*, 3668–3675. (b) Reiersølmoen, A. C.; Østrem, E.: Fiksdahl, A. Gold(III)-Catalysed *cis*-to-*trans* Cyclopropyl Isomerization. *Eur. J. Org. Chem.* **2018**, 3317–3325.

Diastereopure *cis*-**120a** (>20:1) could be isolated by means of preparative TLC. Treatment of *cis*-**120a** with 5 mol % of $[Rh_2(TFA)_4]$ at 60 ºC for 24 h led to a 3:1 *cis*/*trans* mixture of diastereoisomers, and the ratio continued to decrease towards the *trans* isomer overtime (Figure 21, top). It was also possible to observe the same process at 23 ºC, but at a much lower rate (13:1 ratio after 6 days). If the same experiment is performed with diastereopure *trans*-**120a**, the formation of some *cis*-**120a** is also observed, confirming an equilibrium between two species which are significantly close in energy.

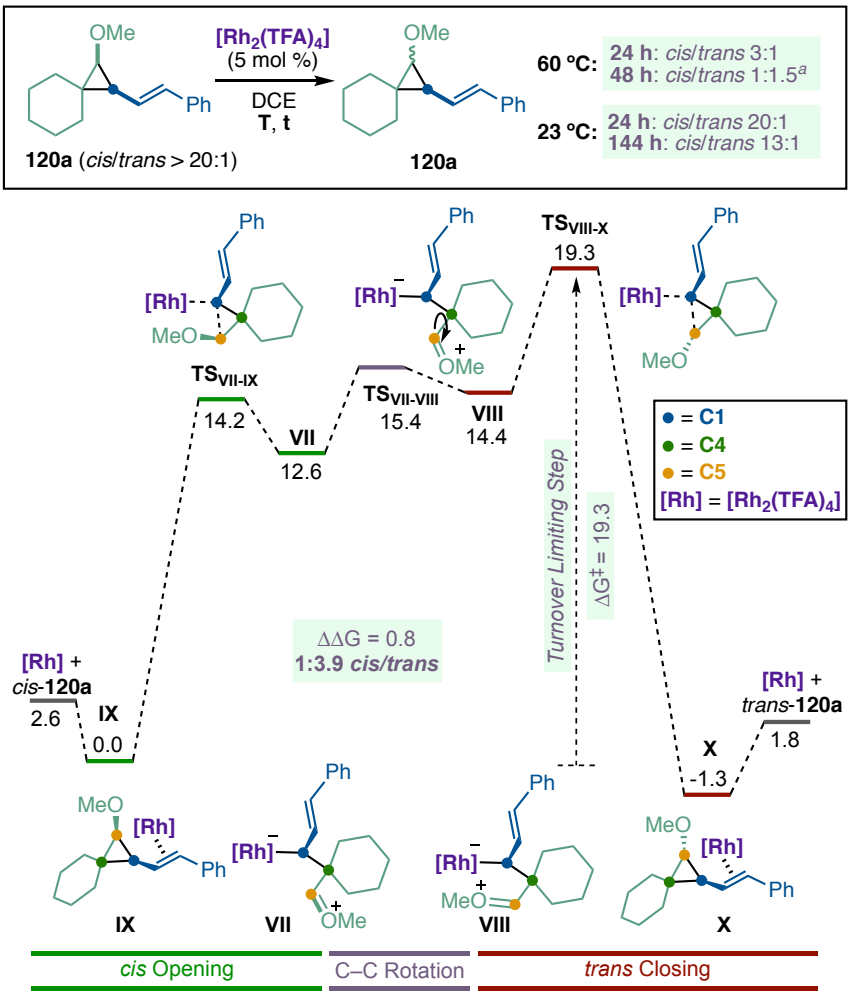



**Figure 21**. Experimental and theoretical study of the *cis*-to-*trans* isomerization.
[a] **120a** slowly decays into a mixture of unknown products.

Theoretical analysis of this process showed that *trans*-**120a** is thermodynamically more stable than *cis*-**120a**, and that an energetically feasible pathway ($\Delta G^{\ddagger}$ = 19.3 kcal/mol) does indeed exist through the means of rhodium(II) catalysis. This model, together with that for the kinetically favored *cis*-cyclopropanation, explains the interconversion that is observed over time. Interestingly, we found this *cis*-to-*trans* isomerization to be of key importance for the final process resulting in the formation of triene **121a** (Figure 22).

We investigated the cyclopropane opening process starting from either pure *cis*-**120a** and *trans*-**120a** (Figure 22, top). Following both processes by $^1$H NMR at 100 ºC, we observed full conversion after 2.5 h in TCE-$d_2$ with 5 mol % of [$Rh_2$(TFA)$_4$]. However, whereas the kinetically favored *cis* isomer led only to 40% of triene, starting from diastereopure *trans* isomer, 57% yield was obtained. If the kinetic 6:1 mixture is used, an intermediate 52% yield is obtained. These observations hinted at the *trans* isomer being the actual productive intermediate in the ring-opening/MeOH-elimination sequence, through a Curtin–Hammett-like scenario.

The opening process was also modeled by DFT (Figure 22, bottom) and we found that, indeed, the ring opening of *cis*-**120a** (**XIII**) has a very high barrier (28.6 kcal/mol) and is most likely an unproductive pathway. However, *trans*-**120a** (**XII**) can open up through **TS$_{XII–XV}$** with a reasonable barrier of 23.0 kcal/mol to give **XV**, in which OMe is directly bonded to rhodium. As expected from experimental observations, this is the rate-limiting step of the entire cyclopropanation/opening/elimination sequence. Finally, a smooth Rh–OMe-assisted elimination leads to triene **121a** upon release of methanol and regeneration of the rhodium(II) dimer.[190]

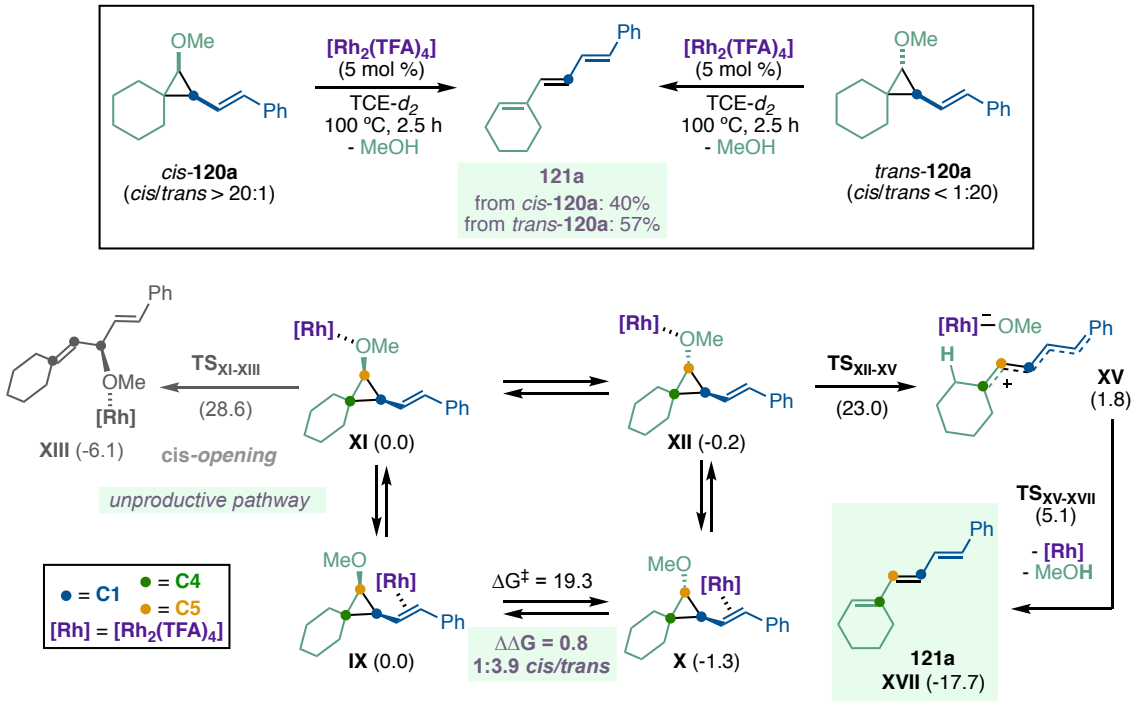
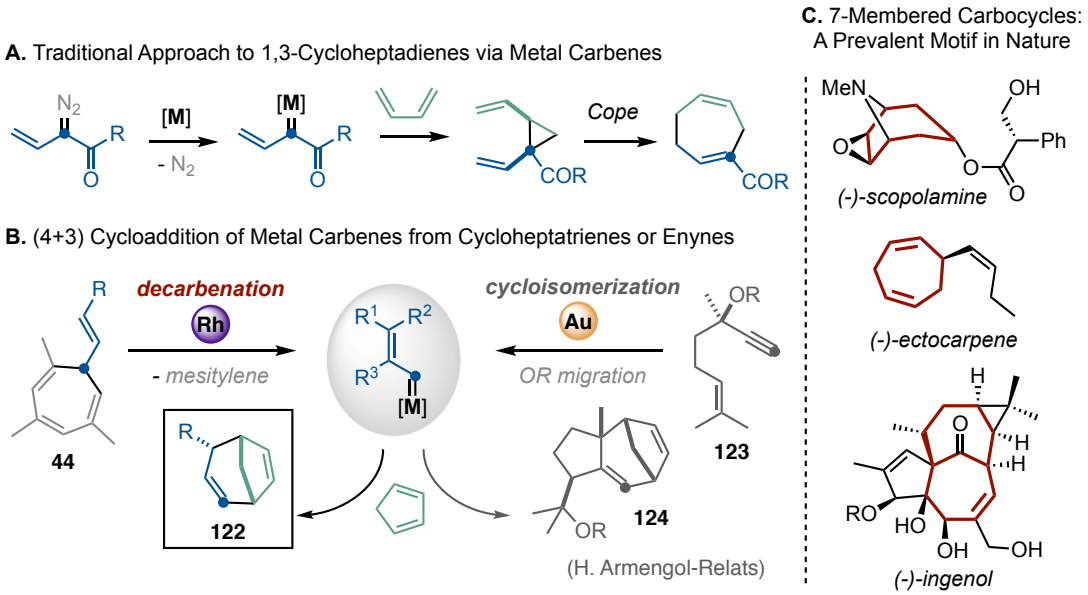



**Figure 22**. Experimental and computational study of the ring opening to form trienes.

190 Several possible pathways were located for the ring opening of **XII**, but only the more energetically feasible one, through **TSXII–XV** and **XV**, is depicted. For more details, see the original publication.

## III.5. (4+3) Cycloaddition of Alkenyl Carbenes with 1,3-Dienes

After realizing the potential of alkenyl donor carbenes for the fast assembly of synthetically complex molecules (see Sections III.3 and III.4), we continued our exploration of new nucleophilic partners that could unlock the access to new and interesting structures. One of the most successful partners were found to be simple, unbiased 1,3-dienes. These dienes have been reported to react with donor–acceptor vinyl carbenes generated from diazo compounds, giving 1,2-divinylcyclopropanes, which readily undergo a Cope rearrangement to form 1,4-cycloheptadienes (Scheme 87A).[191] This strategy was exploited by several groups, but presents the inherent drawbacks of the use of diazo compounds.[192]




**Scheme 87**. Synthesis and relevance of 7-membered rings.

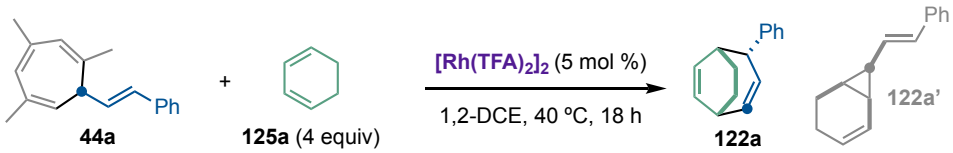
When we evaluated our carbene precursors, we found that the reaction of cycloheptatrienes **44** with cyclopentadiene, under rhodium(II) catalysis, afforded bicyclic 1,4-cycloheptadienes **122**, through a decarbenation/(4+3) cycloaddition sequence (Scheme 87B). This work was developed in parallel to the formal (4+3) cycloaddition between 1,3-dienes and alkenyl gold(I) carbenes generated by a cycloisomerization/migration cascade of enynes **123** to give 1,4-cycloheptadienes

191 (a) Krüger, S.; Gaich, T. Recent applications of the divinylcyclopropane–cycloheptadiene rearrangement in organic synthesis. *Beilstein J. Org. Chem.* **2014**, *10*, 163–193. (b) Davies, H. M. L.; Stafford, D. G.; Doan, B. D.; Houser, J. H. Tandem Asymmetric Cyclopropanation/Cope Rearrangement. A Highly Diastereoselective and Enantioselective Method for the Construction of 1,4-Cycloheptadienes. *J. Am. Chem. Soc.* **1998**, *120*, 3326–3331.

192 Fulton, J. R.; Aggarwal, V. K.; de Vicente, J. The Use of Tosylhydrazone Salts as a Safe Alternative for Handling Diazo Compounds and Their Applications in Organic Synthesis. *Eur. J. Org. Chem.* **2005**, 1489.

**124**.[193] The relevance of these methodologies is illustrated by the often encountered 7-membered carbocyclic motif in natural products which generally, due to thermodynamic considerations, cannot be assembled by classical cyclization pathways (Scheme 87C).[194]

The reaction of **44a** with 1,3-cyclohexadiene (4 equiv) in the presence of [$Rh_2(TFA_4)$] at 40 ºC for 18 h gives cleanly (4+3) cycloadduct **122a** in excellent yield, as a single diastereoisomer (Scheme 88, entry 1). Notably, after this time, no traces of dinvinylcyclopropane **122a'** (a plausible intermediate in the formation of **122a** through a Cope rearrangement) were observed. In this case, we found that the same reaction could be carried out using a cationic gold(I) catalyst with a bulky JohnPhos ligand, although with lower yield (Scheme 88, entry 5). In contrast, other Lewis acids such as $ZnBr_2$, or even less electrophilic Rh(II) complexes, failed to give significant amounts of product **122a** (Scheme 88, entries 6–8). Furthermore, the reaction could be carried out in a significantly wide range of temperatures, or without protective inert atmosphere, showing only moderate variations in yield (Scheme 88, entries 2–4).



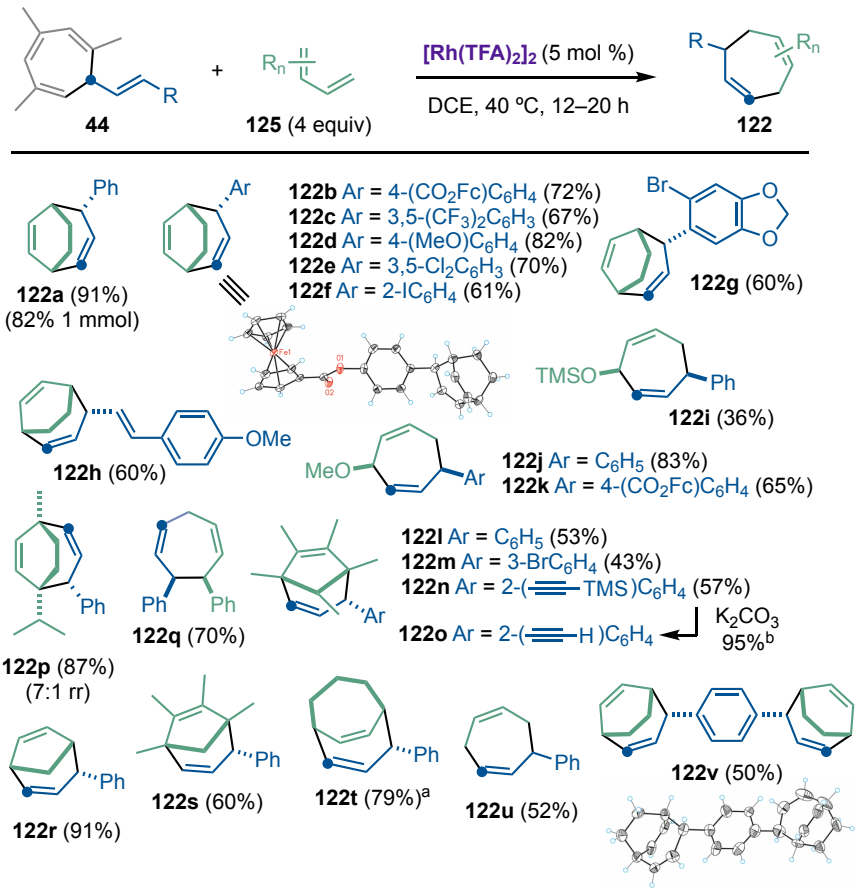

| entry | deviations from standard conditions | yield 122a |
|---|---|---|
| 1 | none | 91% |
| 2 | under air and non-dry solvent | 75% |
| 3 | 25 ºC instead of 40 ºC | 82% |
| 4 | 80 ºC instead of 40 ºC | 65% |
| 5 | [(JohnPhos)Au(MeCN)]$SbF_6$ instead of $[Rh(TFA)_2]_2$ | 70% |
| 6 | $ZnBr_2$ (20 mol %) instead of $[Rh(TFA)_2]_2$ | 8% |
| 7 | $InCl_3$ (20 mol %) instead of $[Rh(TFA)_2]_2$ | n/d |
| 8 | $Rh_2(esp)_2$ instead of $[Rh(TFA)_2]_2$ | 7% |

**Scheme 88**. Optimization and control experiments for the synthesis of **122a**.

193 The (4+3) cycloaddition of alkenyl gold(I) carbenes with 1,3-dienes was developed by Helena Armengol-Relats in parallel to the reaction presented in this section, and both works were published together in 2021, see: Armengol-Relats, H.; Mato, M.; Echavarren, A. M. Assembly of Complex 1,4-Cycloheptadienes by (4+3) Cycloaddition of Rhodium(II) and Gold(I) Non-Acceptor Carbenes. *Angew. Chem. Int. Ed.* **2021**, *60*, 1916–1922.

194 (a) de Oliveira, K. T.; Servilha, B. M.; Alves, L. de C.; Desiderá, A. L.; Brocksom, T. J. "The Synthesis of Seven-Membered Rings in Natural Products" in *Studies in Natural Products Chemistry* **2014**, *42*, 421–463. (b) Baldwin, J. E. Rules for ring closure. *J. Chem. Soc., Chem. Commun.* **1976**, 734–736

A range of styryl cycloheptatrienes **44** were successfully employed, showing the tolerance to both electron-rich and electron-poor aromatic rings on the carbene fragment (**122a–g**) (Scheme 89). Different aryl halides (**122e–g**, **122m**) and a dienyl carbene (**122h**) could be transferred, and even a TMS–alkyne was tolerated (**122n**), which could be easily deprotected afterwards under basic conditions (**122o**). A double decarbenation/(4+3) cycloaddition was also carried out giving directly **122v** in 50% yield as a single diastereoisomer, forging six new stereocenters in a single synthetic step. The relative configuration of the bicyclic products was unequivocally confirmed by X-ray analysis of both **122v** and ferrocene-derivative **122b**. Then, we explored the scope of 1,3-dienes. We found non-cyclic dienes to also be successful reaction partners (**122q**), including different 1-oxo-1,3-dienes which led to products **122i–k**.[195]



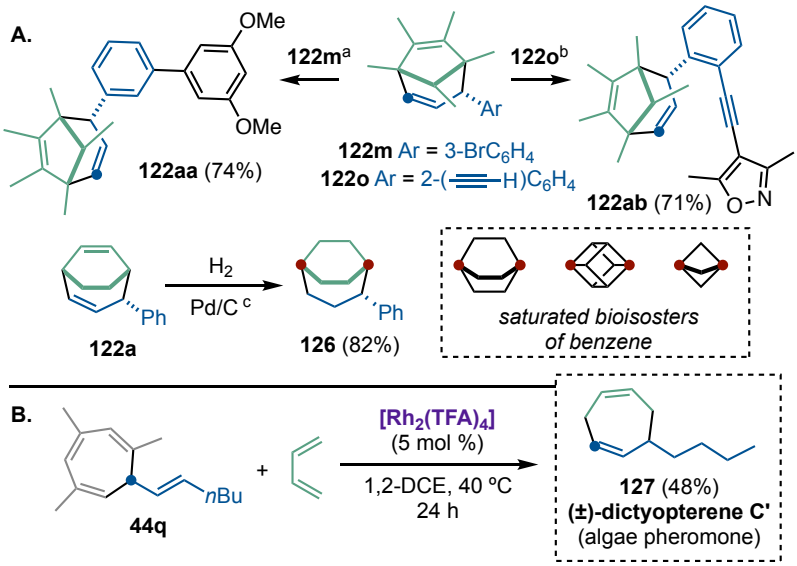

**Scheme 89**. Scope of the (4+3) cycloaddition.
[a] At 60 ºC for 20 h. [b] $K_2CO_3$ (2 equiv) in $MeOH/CH_2Cl_2$ at 25 ºC for 3 h.

The reaction of **44a** with α-terpinene afforded **122p** in high yield and 7:1 ratio of regioisomers, corresponding to a more favorable cyclopropanation of the less hindered double bond, followed

195 The *cis* configuration for **122i–k** was assigned based on a simple diastereospecific Cope rearrangement model.

by a diastereospecific Cope rearrangement. Cyclic dienes of several sizes (5–7) took part successfully in the (4+3) cycloaddition process (**122l-t**).

Diversification of some of these products allowed us to reach further into the chemical space of 7-membered carbocycles. Cycloheptadienes **122aa** and **122ab** were easily obtained from **122m** and **122o**, respectively, by palladium-catalyzed cross-coupling reactions (Scheme 90A). It was possible to fully hydrogenate **122a** under mild conditions, obtaining 2-phenylbicyclo-[3.2.2]nonane (**126**), which resembles an alternative type of saturated benzene bioisostere.[196]




**Scheme 90**. Diversification of products (A) and total synthesis of dictyopterene C' (B).
[a] 3,5-Dimethoxyphenyl boronic acid, $Cs_2CO_3$, $PdCl_2$/RuPhos (cat), dioxane/water, 80 ºC, 2 h.
[b] 4-Iodo-3,5-dimethylisoxazole, $Pd(PPh_3)_2Cl_2$ (cat), CuI (cat), triethylamine, 50 ºC, 20 h.
[c] $H_2$ (1 atm, balloon), Pd/C (cat), ethanol, 25 ºC, 18 h.

Furthermore, to illustrate the potential of the methodology, starting from **44q** and 1,3-butadiene, we prepared in a single reaction flask dictyopterene C' (Scheme 90B), a pheromone isolated from brown algae. Biosynthetically, this natural product also arises from the Cope rearrangement of the corresponding *cis*-divinylcyclopropane **127'**, which occurs smoothly at sea-level temperature.[197]

196 Mykhailiuk, P. K. Saturated bioisosteres of benzene: where to go next? *Org. Biomol. Chem.* **2019**, *17*, 2839–2849.

197 (a) Müller, D. G.; Jaenicke, L.; Donike, M.; Akintobi, T. Sex Attractant in a Brown Alga: Chemical Structure. *Science* **1971**, *171*, 815–817. (b) Moore, R. E.; Pettus, J. A.; Mistysyn, J. Odoriferous C11 hydrocarbons from Hawaiian Dictyopteris. *J. Org. Chem.* **1973**, *39*, 2201–2207. (c) Grandjean, D.; Pale, P.; Chuche, J. Enzymatic hydrolysis of cyclopropanes. Total synthesis of optically pure dictyopterenes a and c'. *Tetrahedron* **1991**, *47*, 1215–1230.

As it was already hinted at during the introduction of this section (Scheme 87A, page 227), the general mechanistic proposal for this type of formal (4+3) cycloaddition goes through the vinyl cyclopropanation of the 1,3-dienes, followed by Cope rearrangement of the corresponding *cis*-divinylcyclopropane **122'**. Theoretical exploration of the system by DFT calculations revealed an alternative pathway in which a cationic intermediate can potentially close up directly to the corresponding 1,4-cycloheptadiene **122** (Figure 23).

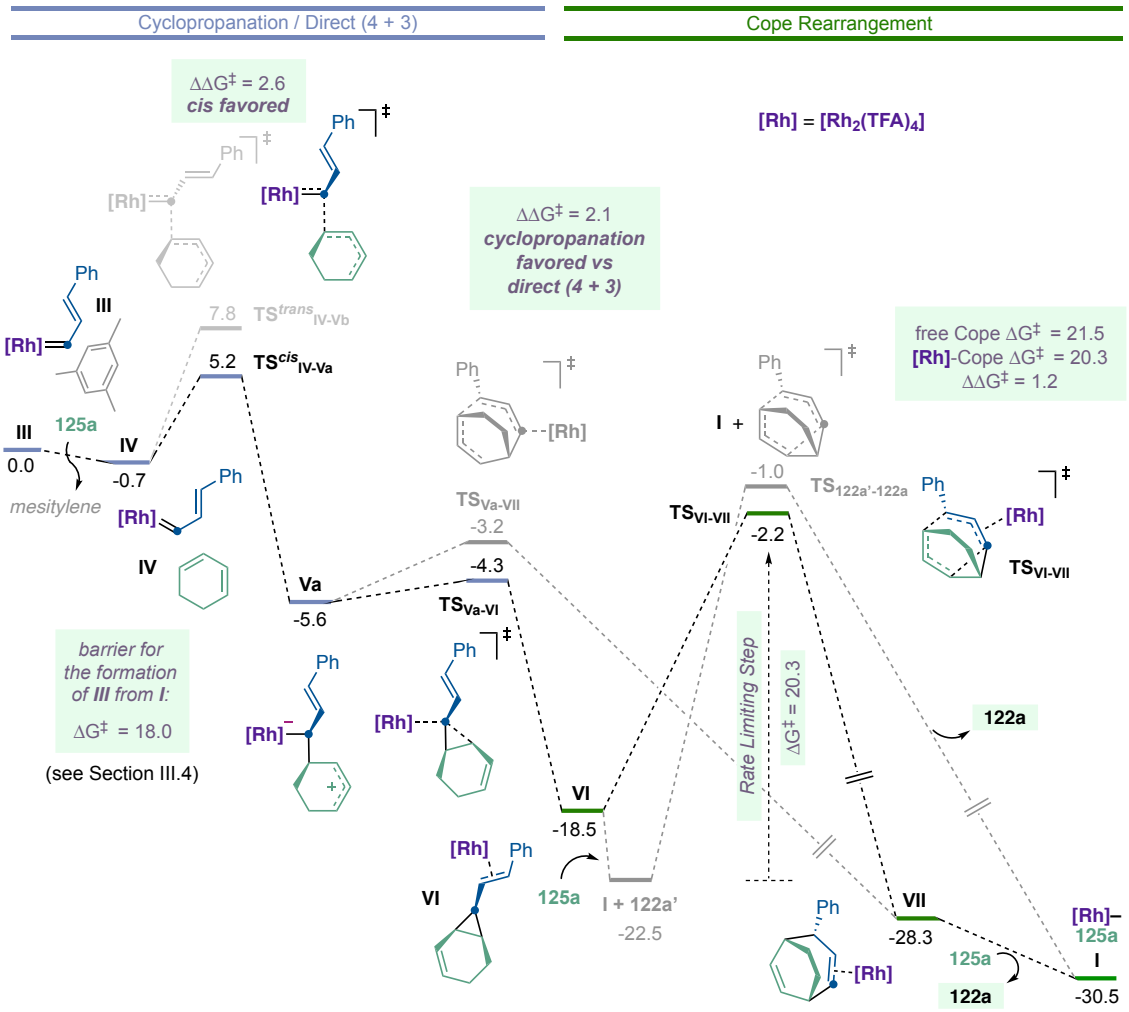



**Figure 23**. Free-energy profile (kcal/mol) for the formal (4+3) cycloaddition of styryl carbene **III** with 1,3-cyclohexadiene, calculated by DFT.

The entire mechanism begins by the rhodium(II)-catalyzed decarbenation by retro-Buchner reaction of **44a**, which has already been presented in the DFT calculations performed by Dr. Cristina García-Morales (Section III.4), in the context of the styryl cyclopropanation of enol ethers. In this case, starting from resting-state **I** (rhodium(II) trifluoroacetate dimer $\eta^2$-coordinated to 1,3-cyclohexadiene **125a**), the activation barrier for the decarbenation process to give **III** was calculated to be 18.0 kcal/mol.

After ligand exchange, **IV** undergoes C–C bond formation through a *cis*-selective ($\Delta\Delta G^{\ddagger}$ = 2.6 kcal/mol) process that gives cationic intermediates **V**. This would account for a perfect (>20:1) kinetic *cis* selectivity. Noteworthily, **Va** (*cis* intermediate) and **Vb** (*trans*) can interconvert through an energetically reasonable process (for details, see Figure 25 in page 235 and the corresponding explanation).

Then, intermediate **V** can follow two different pathways. First, we found that it can close up directly to give rhodium-coordinated 1,4-cycloheptadiene **VII**, the final product of the reaction. Alternatively, it can give Rh(II)-coordinated divinylcyclopropane **VI**. Both processes have reasonable barriers, with a $\Delta\Delta G^{\ddagger}$ of 2.1 kcal/mol, favoring the divinylcyclopropane formation. Rh(II)-coordinated cyclopropane **VI** can then undergo Cope rearrangement through $\mathbf{TS_{VI-VII}}$ to give Rh(II)-coordinated 1,4-cycloheptadiene **VII**. Alternatively, after decoordination of the divinylcyclopropane (through an exchange with another molecule of 1,3-cyclohexadiene, to give more stable **I** and free **122a'**), free **122a'** can also undergo a thermal Cope rearrangement to give free **122a**, with an almost identical activation energy ($\Delta\Delta G^{\ddagger}$ = 1.2 kcal/mol). This would account for the Cope rearrangement of **122a'** being the overall rate-limiting step of the entire process, either through direct forward reaction of **VI**, or going back to cationic intermediate **Va**, which then undergoes irreversible (4+3) closing. Considering the similarities in energy, both pathways can be considered feasible (Figure 23).

This hypothesis was verified by following the kinetic profile of the overall process by $^{1}$H NMR (Figure 24A). A significant accumulation of divinylcyclopropane intermediate **122a'** was observed, suggesting that the rearrangement of this intermediate to 1,4-cycloheptadiene **122a** is the rate-limiting step of the transformation, rather than the retro-Buchner reaction.

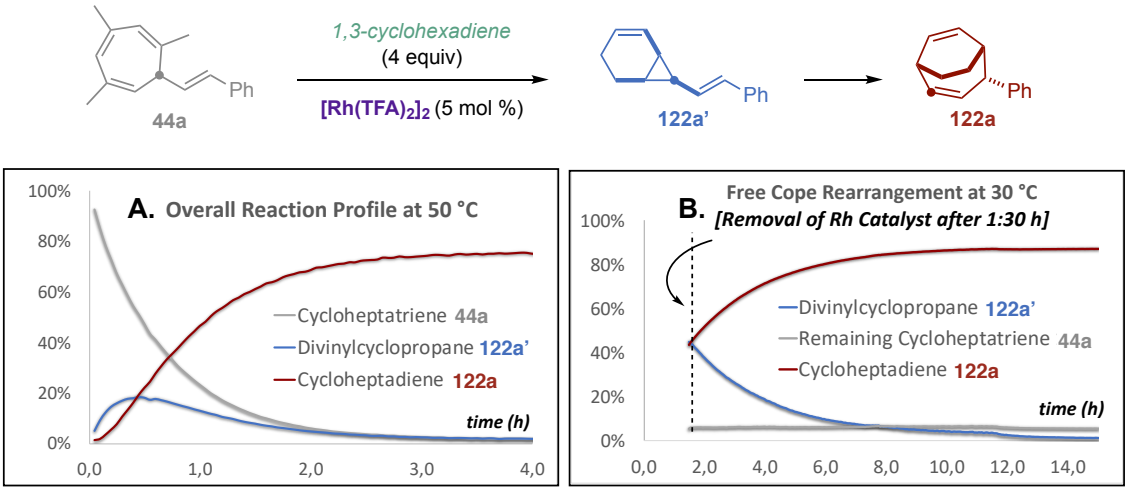
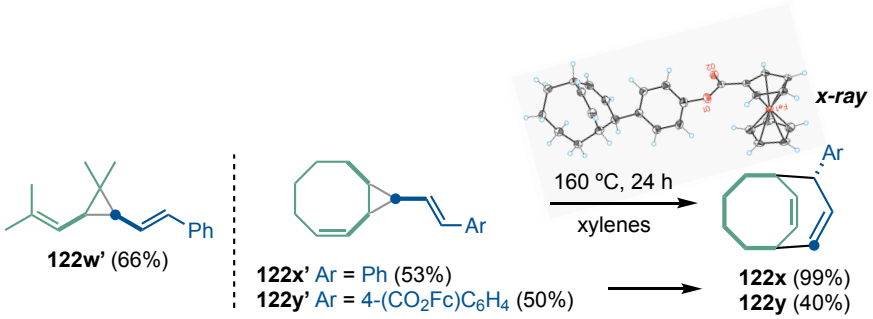



**Figure 24**. Kinetic profile of the entire process (A) and of the free Cope rearrangement (B).

Furthermore, in order to confirm experimentally the existence of the Rh(II)-free Cope rearrangement pathway, we stopped a reaction after 1.5 h and removed the rhodium catalyst by quick flash column purification, and then followed the evolution of the resulting mixture by $^1$H NMR. This showed a clean thermal conversion of intermediate divinylcyclopropane **122a'** into 1,4-cycloheptadiene **122a** during 12 h at 30 ºC. The successful removal of the Rh(II) catalyst was confirmed by the recovery of the remaining cycloheptatriene **44a** (Figure 24B).

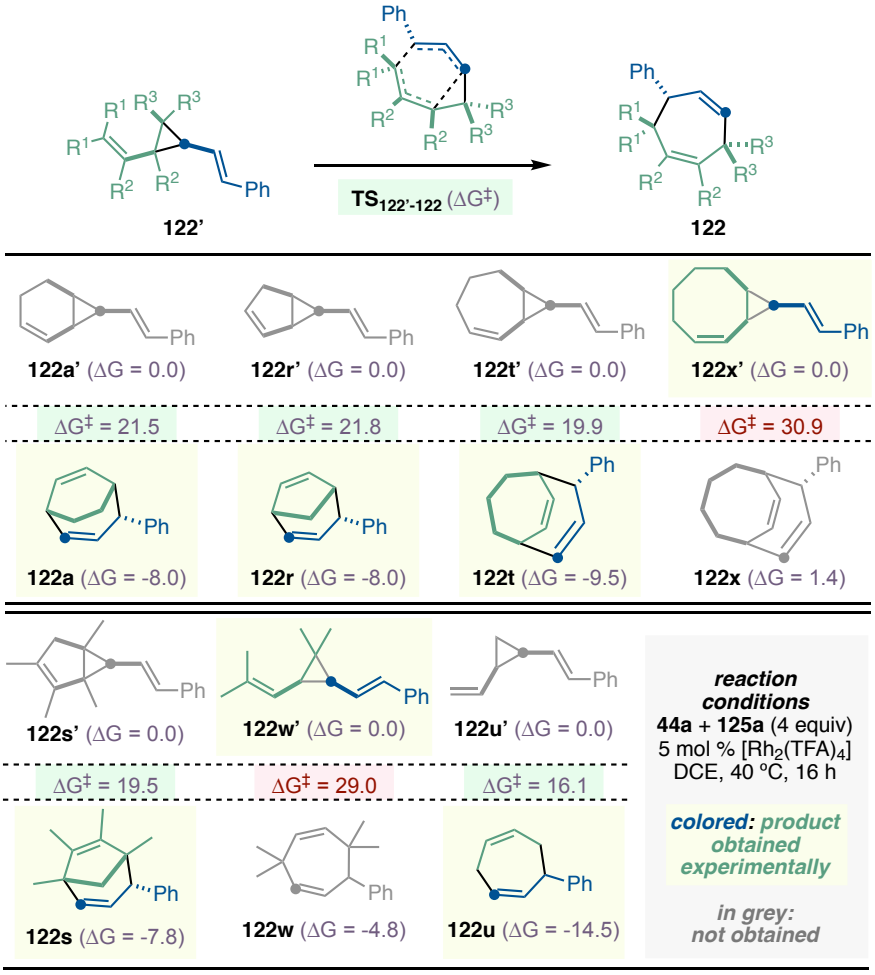
The barriers for the formation of these Cope (4+3) adducts are highly dependent on the substitution pattern of the substates. For instance, when the (4+3) cascade is attempted using 1,1,4,4-tetramethylbutadiene as nucleophile, only divinylcyclopropane **122w'** is obtained. Similarly, 1,3-cyclooctadiene gave exclusively **122x'** and **122y'** at temperatures lower than 100 ºC. However, thermal treatment of **122x'** at 160 ºC in xylenes for 24 h gave (4+3) adduct **122x** quantitatively. This reaction can be performed either with pure **122x'** or in the same pot when the cyclopropanation has finished, after a solvent swap. These results were further confirmed by X-ray analysis of ferrocenoyl derivative **122y**, which was obtained in lower yield due to partial decomposition at 160 ºC (Scheme 91).




**Scheme 91**. Substrates with high Cope-rearrangement barriers which provided divinylcyclopropanes at <100 ºC, and thermal Cope of **122x'** and **122y'** at 160 ºC.

Combining these observations with our theoretical studies, we proposed a simplified model based on the thermal Cope rearrangement of divinylcyclopropanes **122'**. This model correlates the substitution pattern of the 1,3-diene with which product (**122** or **122'**) is obtained experimentally at 40 ºC (Scheme 92). Thus, substrates with an activation barrier for the Cope rearrangement above *ca.* 25 kcal/mol give divinylcyclopropanes experimentally. If the barrier is lower, the (4+3) adducts are obtained. For instance, divinylcyclopropanes **122w'** and **122x'** from Scheme 91 present a Cope-rearrangement barrier of 29.0 and 30.9 kcal/mol, respectively. On the other hand, when 1,3-cyclohexadiene (**122a**) or cyclopentadiene (**122b**) are used as dienes, (4+3) adducts are obtained, as suggested by the calculated 21.5 and 21.8 kcal/mol barriers, respectively.

The model could also be applied in a predictive manner. With 1,3-cyclohexadiene, the (4+3) adduct is obtained at 40 ºC. However, 1,3-cyclooctadiene leads to divinylcyclopropane **122x'** exclusively at the same temperature. We calculated the barrier for 1,3-cycloheptadiene to be 19.9 kcal/mol. Subsequently, we performed the corresponding experiment, obtaining the expected (4+3) adduct **122t** exclusively. We also predicted beforehand the outcome of the reaction with simple 1,3-butadiene (**122u**), which allowed us to develop the one-pot assembly of natural-product dictyopterene C' (Scheme 90B, page 230).




**Scheme 92**. Free-energy barriers (kcal/mol) for the metal-free Cope rearrangement of each divinylcyclopropane **122'** towards the corresponding cycloheptadiene **122**. The product observed experimentally for each case is highlighted in yellow.

Finally, in order to explain the perfect selectivity observed in this decarbenation/(4+3) sequence (which gives 1,4-cycloheptadienes **122** as single diastereoisomers, without trace of the corresponding *trans* divinylcyclopropane) we used DFT calculations (Figure 25).

Kinetically, the formation of *cis*-**122'** is predicted to be more favorable ($\Delta\Delta G^{\ddagger}$ = 2.6 kcal/mol, Figure 23, page 231). On the other hand, *trans*-**122'** (**VIb**) is 3.2 kcal/mol more stable than *cis*-**122'**. Our calculations show that both a *cis*-to-*trans* and a *trans*-to-*cis* isomerization pathways are energetically feasible ($\Delta G^{\ddagger}$ = 21.7 and 24.9 kcal/mol, respectively), through $\mathbf{TS_{Va–Vb}}$. However, only the *cis* isomer can evolve through the irreversible stereospecific Cope rearrangement to give 1,4-cycloheptadienes **122**. Therefore, any *trans*-**122'** (or **Vb**/**VIb**) that could be formed, would reversibly swift back to the *cis* isomer (either **Va** or **VIa**), and eventually close up to also give 1,4-cycloheptadiene **122**. This convergent model explains the cleanness of the overall transformation observed experimentally.

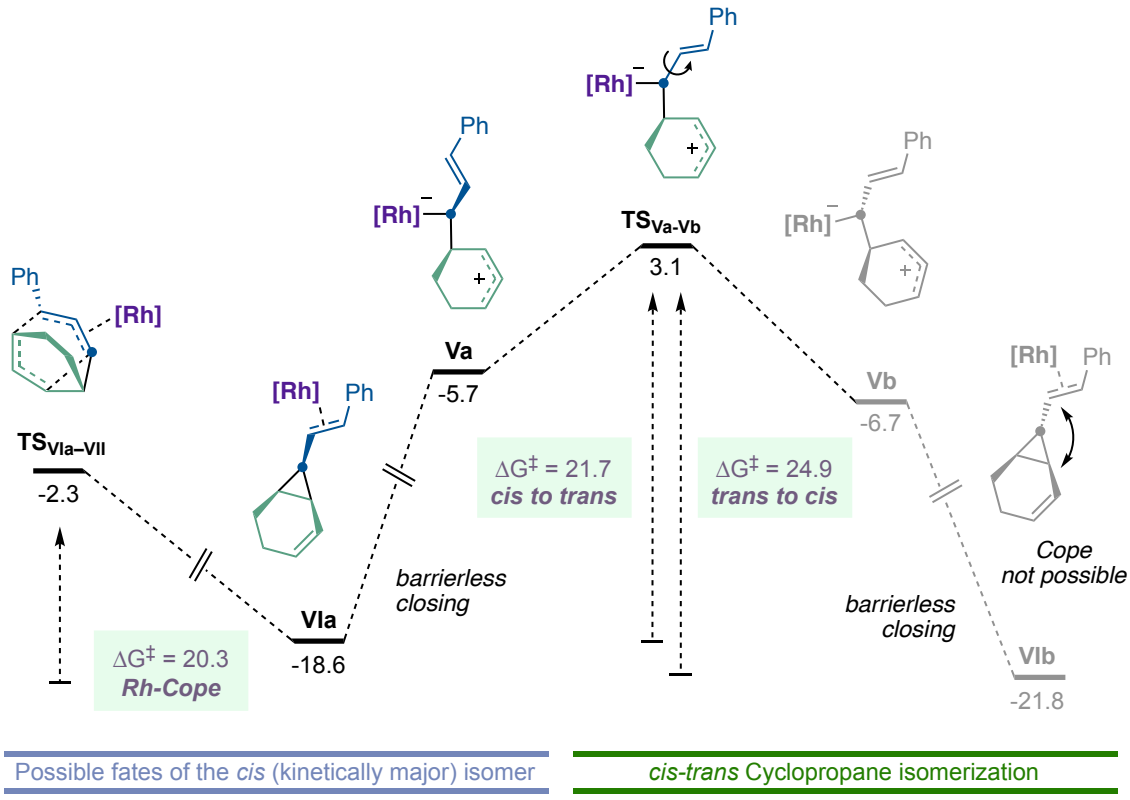
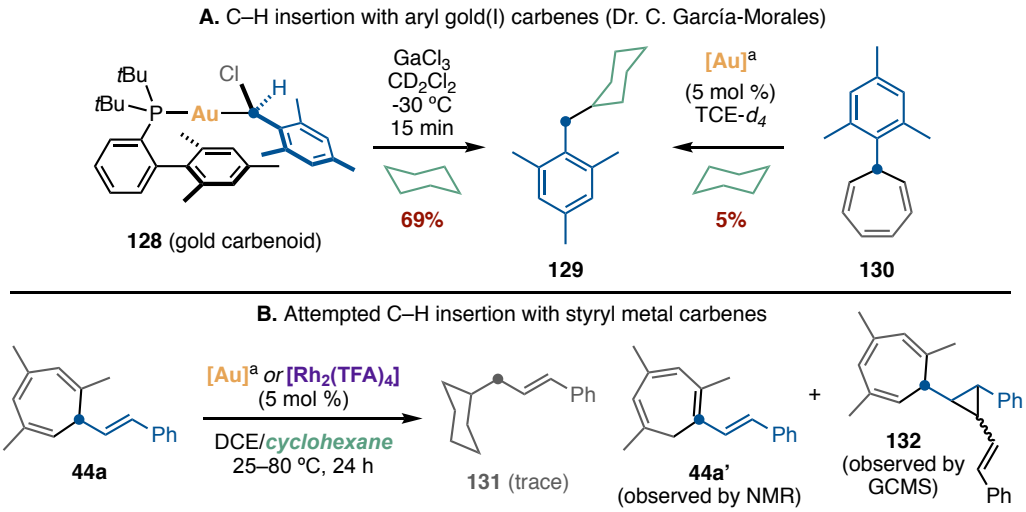



**Figure 25.** *cis-trans* Isomerization and Cope rearrangement.

## III.6. Insertions, Oxidations and Miscellaneous Reactivity

Donor metal carbenes were not only found to be successful partners in cyclopropanations and higher formal cycloadditions but can also participate in other types of chemical processes. First off, we wanted to evaluate the reactivity of these now readily accessible intermediates towards C–H and X–H bond functionalization. Insertion reactions, a well-established benchmark process of acceptor and non-acceptor metal carbenes,[198] have been considerably less studied with donor carbenes, due to the problems associated with their generation. Our group has recently shown how aryl gold(I) carbenes generated from carbenoids **128** undergo C–H insertion in the presence of cyclohexane, to give benzylated product **129** (Scheme 93A).[199] Nevertheless, when using cycloheptatrienes as carbene precursors, intermolecular C–H insertions are inherently challenging because of the presence of double bonds in the starting substrate, which can often get cyclopropanated through a much lower energy barrier than that for the C–H functionalization process itself (e.g., upon activation with $GaCl_3$, carbenoids **128** readily react with alkenes to form cyclopropanes even at -90 ºC, whereas temperatures of -30 ºC are required for the C–H insertion to proceed).




**Scheme 93**. C–H activation of cyclohexane with aryl gold(I) carbenes (A) and unsuccessful attempts with styryl metal carbenes (B).
[a] [Au] = [(JohnPhos)Au(MeCN)]$SbF_6$.

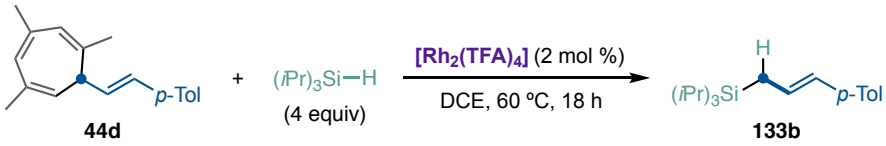
198 (a) Davies, H. M. L.; Manning, J. R. Catalytic C–H functionalization by metal carbenoid and nitrenoid insertion. *Nature.* **2008**, *451*, 417–424. (b) Besora, M.; Olmos, A.; Gava, R.; Noverges, B.; Asensio, G.; Caballero, A.; Maseras, F.; Pérez, P. J. A Quantitative Model for Alkane Nucleophilicity Based on C‑H Bond Structural/Topological Descriptors. *Angew. Chem. Int. Ed.* **2020**, *59*, 3112–3116.

199 García-Morales, C. Doctoral Thesis, "Reactivity and Characterization of Gold(I) Carbenes: Key Intermediates in Gold(I) Catalysis" (2019).

This problem is accentuated when 7-styryl cycloheptatrienes **44** are employed, since activation barriers for the cyclopropanation of styrenes with this type of donor carbenes were calculated to be in the order of 3–7 kcal/mol (e.g., see Figure 18, page 102 and Scheme 86, page 224). Thus, the reaction of **44a** with a large excess of cyclohexane, under either Rh(II) or Au(I) catalysis, barely afforded trace amounts of insertion product **131**. Rather, different products of cyclopropanation of **44a** itself (and further oligomerization) could be observed as major components of the reaction by GCMS, together with variable amounts of **44a'** (Scheme 93B).

### *Si–H Insertion Reactions*

Subsequently, we embarked upon the identification of X–H bonds nucleophilic enough to compete with the low barriers for the undesired cyclopropanation side-pathways. This search met with success with the discovery of silanes bearing Si–H bonds as competent nucleophilic partners for alkenyl donor rhodium carbenes. After optimization, we found that 2 mol % of $[Rh_2(TFA)_4]$ was enough to promote the reaction of cycloheptatriene **44d** and triisopropylsilane (4 equiv) in DCE at 60 ºC for 18 h. This afforded the product of decarbenation followed by Si–H insertion of the corresponding metal carbene, **133b**, in 65% yield (Scheme 94, entry 1). Very interestingly, while rhodium(II) is very active in this transformation, cationic gold(I) complexes did not afford any product of Si–H insertion. Experimentally, deposition of metallic gold on the surface of the reaction vial was observed. Presumably, this may come as a result of the mildly reductive reaction conditions, which decompose the gold(I) catalyst (Scheme 94, entry 2).




**44d** **133b**

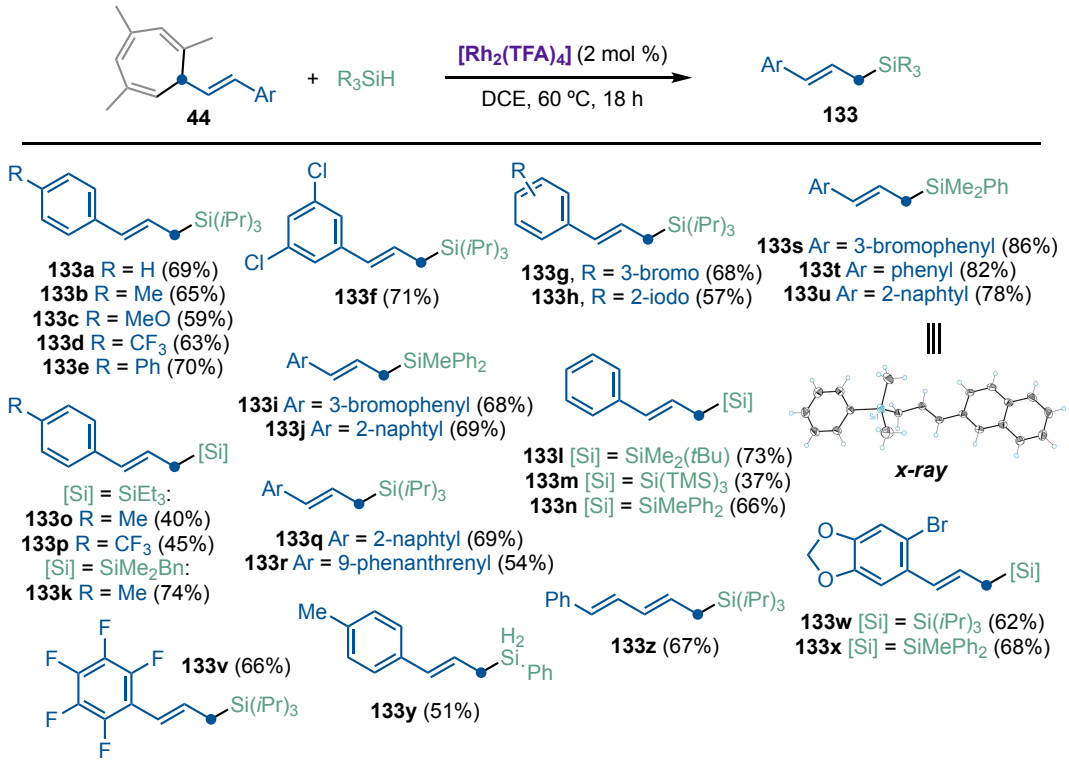
| *entry* | *deviation from standard conditions* | *yield* |
|---|---|---|
| **1** | **none** | **65%** |
| 2 | [(JohnPos)Au(MeCN)]$SbF_6$ (5 mol %) | **n/d** |
| 3 | $ZnBr_2$ (10 mol %) | 25% |
| 4 | $[Cu(MeCN)_4]PF_6$ (10 mol %), 65 ºC | n/d |
| 5 | 5 mol % of **$[Rh_2(TFA)_4]$** | 64% |
| 6 | 1 mol % of **$[Rh_2(TFA)_4]$** | 55% |
| 7 | 0.1 mol % of **$[Rh_2(TFA)_4]$** | 15% |
| 8 | 0.01 mol % of **$[Rh_2(TFA)_4]$** | trace |
| 9 | non-methylated styrylcycloheptatriene **41a** | n/d |
| 10 | no catalyst | n/d |

**Scheme 94**. Optimization and control experiments of the Si–H insertion.

On the other hand, zinc(II) salts were also active. However, the best attempt (with 10 mol % of $ZnBr_2$), afforded only 25% yield of allylsilane **133b** (Scheme 94, entry 3). We evaluated other transition metals, such as copper, but no reaction was observed. Catalyst loading was also studied, and we found that going below 1 mol % leads to a significant decrease in reaction rate (Scheme

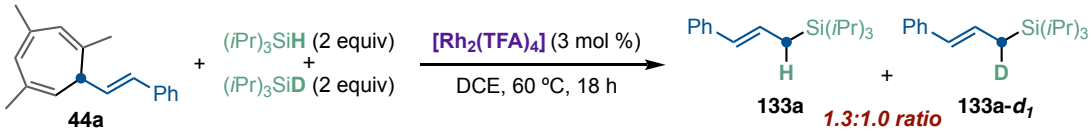
94, entries 5–8). Finally, we observed that, under the same reaction conditions, non-methylated 7-styryl-1,3,5-cycloheptatriene **41a** did not afford any conversion (Scheme 94, entry 9).

Henceforth, we analyzed the generality of this method (Scheme 95), and we found that most of the substrates employed reacted successfully under these conditions, giving allylsilanes in an average 70% yield. First, using triisopropylsilane as model nucleophile, we prepared the corresponding allylsilanes in good yields across a wide range of cycloheptatrienes **44**, bearing both electron-poor and electron-rich substituents in different positions of the aromatic ring (**133a–e**). Halides, from fluoride to iodide, were tolerated (**133f–h**, **133v**), and it was possible to transfer polyarene units such as naphthalene and phenanthrene (**133q–r**). Similarly, dienyl silane **133z** was also obtained in 67% yield. The scope of the reaction was also evaluated in terms of the silane group, allowing to perform the Si–H insertion in substrates as bulky as $(TMS)_3SiH$ (**133m**). Other commercially available silanes were tested and performed well in the reaction (**133k–p**). On the other hand, silyl ethers led only to poor yield of insertion product. Selective mono-insertion could also be carried out in a primary silane, $PhSiH_3$ (**133y**).



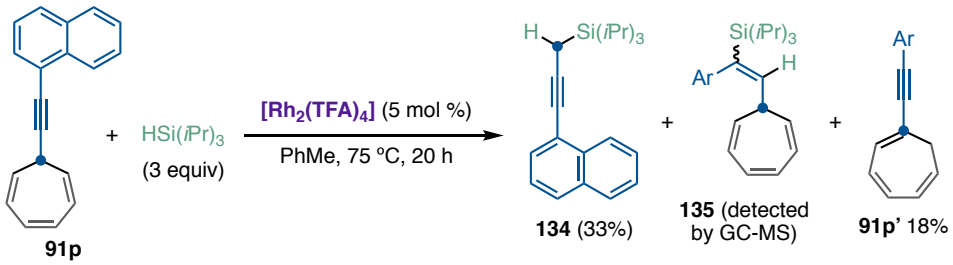

**Scheme 95**. Scope of the synthesis of allylsilanes.

Then, we performed a competition experiment between triisopropylsilane and deuterated triisopropylsilane. Under the standard reaction conditions, this led to the formation of the non-deuterated (**133a**) and deuterated (**133a-*d*$_1$**) allyl silane in a 1.3:1 ratio (Scheme 96). This significant kinetic isotope effect is consistent with previously reported values for concerted metal-carbene insertions in Si–H bonds.[200]




**Scheme 96**. Kinetic isotope effect experiment.

Later on, we studied a similar process in order to prove the possibility of also trapping alkynyl rhodium carbenes (see Section II.7) by Si–H insertion (Scheme 97).[201] This led to propargyl silane **134** only in moderate yield, due to the existence of two main competing side pathways. In the presence of silanes, we observed partial isomerization of alkynyl cycloheptatriene **91p** to **91p'**.[202] Also, different products of rhodium(II)-catalyzed hydrosilylation of alkynes were observed, mainly **135** (Scheme 97).[203]




**Scheme 97**. Trapping of an alkynyl rhodium(II) carbene by Si–H insertion.

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200 (a) Landais, Y.; Parra-Rapado, L.; Planchenault, D.; Weber, V. Mechanism of metal-carbenoid insertion into the Si–H bond. *Tetrahedron Lett.* **1997**, *38*, 229–232. (b) Chen, D.; Zhu, D.-X.; Xu, M.-H. Rhodium(I)-Catalyzed Highly Enantioselective Insertion of Carbenoid into Si–H: Efficient Access to Functional Chiral Silanes. *J. Am. Chem. Soc.* **2016**, *138*, 1498–1501

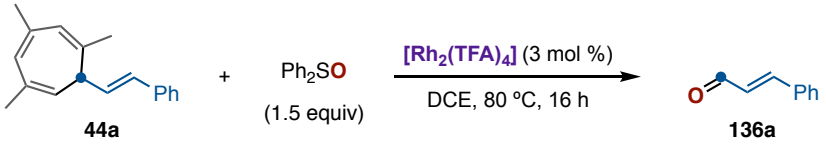
201 The Si–H insertion of alkynylcarbenes was studied by the Master student Arnau R. Sugranyes under co-supervision by the author of this Doctoral Thesis.

202 Conjugated isomers such as **91p'** are typical side-products in retro-Buchner chemistry. However, for 7-alkynylcycloheptatrienes, we only observed them in the presence of silanes, since both the decarbenation and the 6-*endo*-dig pathways are faster (see Section II.7).

203 Doyle, M. P.; High, K. G.; Nesloney, C. L.; Clayton Jr., T. W.; Lin, J. Rhodium(II) perfluorobutyrate catalyzed hydrosilylation of 1-alkynes. Trans addition and rearrangement to allylsilanes. *Organometallics* **1991**, *10*, 1225–1226.

### *Oxidative Trapping of Carbenes*

Mild oxidants such as sulfoxides or pyridine *N*-oxides have been extensively used in the metal-catalyzed activation of alkynes, as an alternative approach to generate α-oxo gold carbenes.[204] In 2016, our group showed that certain types of non-acceptor cyclopropylgold carbenes (e.g., gold(I)-stabilized barbaralyl cations) can be formally trapped by such oxidants to give ketones (i.e., barbaralones).[205] Accordingly, we hypothesized that our donor carbene intermediates could potentially be trapped oxidatively, to give aldehydes. This proved to be the case, as the treatment of **44a** with 1.5 equiv of diphenylsulfoxide in the presence of 3 mol % of $[Rh_2(TFA)_4]$ in DCE at 80 ºC for 16 h gave rise to cinnamaldehyde (**136a**), in 80% yield, as a single diastereoisomer (Scheme 98, entry 1).




**44a** **136a**

| *entry* | *deviation from standard conditions* | *yield* |
|---|---|---|
| **1** | **none** | **80%** |
| 2 | no catalyst | n/d |
| 3 | [(JohnPos)Au(MeCN)]$SbF_6$ (5 mol %) | 55% |
| 4 | [(JohnPos)Au(MeCN)]$SbF_6$ (5 mol %) and 3,5-$Br_2$-pyridine *N*-oxide | 60% |
| 5 | 3,5-$Br_2$-pyridine *N*-oxide (2 equiv), 70 °C | 19% |
| 6 | 5 equiv of $Ph_2SO$ | 52% |
| 7 | 1.2 equiv of $Ph_2SO$ | 72% |
| 8 | 40 °C | 24% |
| 9 | 100 °C | 72% |
| 10 | 0.05 M in DCE | 70% |
| 11 | 0.25 M in DCE | 78% |
| 12 | PhMe (0.1 M) | 65% |
| 13 | $CHCl_3$ (0.1 M) | 74% |

**Scheme 98**. Optimization of the oxidative retro-Buchner reaction.

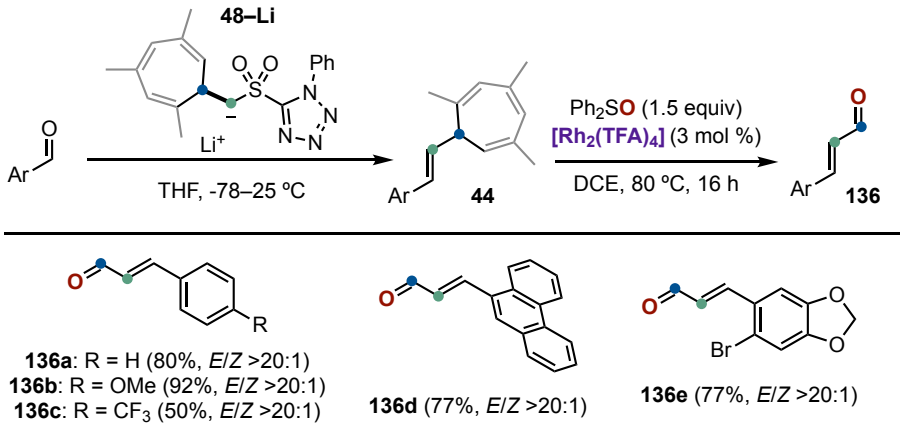
Whereas the Rh(II)-catalyzed oxidative decarbenation proceeded in a much worse 19% yield using a pyridine *N*-oxide as trapping agent (Scheme 98, entry 5), a cationic gold(I) complex also gave the same product in 55–60% yield using either diphenylsulfoxide or an *N*-oxide (Scheme 98, entries 3–4). Nevertheless, the best performing system was found to be the combination of $[Rh_2(TFA)_4]$ and $Ph_2SO$. Both a larger excess of oxidant or an amount lower than 1.5 equiv proved to be detrimental to the reaction yield (Scheme 98, entries 6–7). Similarly, temperatures lower than 80 ºC reduced the reaction rate significantly, whereas higher temperatures led to a slight

204 (a) Zhang, L. A Non-Diazo Approach to α-Oxo Gold Carbenes via Gold-Catalyzed Alkyne Oxidation. *Acc. Chem. Res.* **2014**, *47*, 877–888. (b) Ye, L.-W.; Zhu, X.-Q.; Sahani, R. L.; Xu, Y.; Qian, P.-C.; Liu, R.-S. Nitrene Transfer and Carbene Transfer in Gold Catalysis. *Chem. Rev.* **2020**, doi: 10.1021/acs.chemrev.0c00348.

205 Ferrer, S.; Echavarren, A. M. Synthesis of Barbaralones and Bullvalenes Made Easy by Gold Catalysis. *Angew. Chem. Int. Ed.* **2016**, *55*, 11178–11182.

decrease in yield (Scheme 98, entries 8–9). A brief evaluation of concentration and common solvents led to the identification of DCE and 0.1 M as the best set of conditions (Scheme 98, entries 10–13 vs entry 1).

If we consider that 7-styryl cycloheptatrienes **44** can be prepared by Julia–Kocienski olefination of aldehydes using the lithium salt of sulfone **48** (Scheme 22, page 56), we can see the combination of this reaction with the subsequent oxidative decarbenation as a two-step alternative for the diastereoselective *E*-vinylogation of aldehydes. Thus, lithiation of sulfone **48** with LiHMDS leads to **48–Li**, which can be treated with aldehydes to give cycloheptatrienes **44**. After purification, **44** is submitted to our newly optimized conditions, and the product of vinylogation of the starting aldehyde is obtained in good yield and excellent *E*/*Z* ratio. Accordingly, several cinnamaldehyde derivatives with different electronic and steric properties were prepared in good yield and as single *E*-diastereoisomers (Scheme 99, **136a–e**).

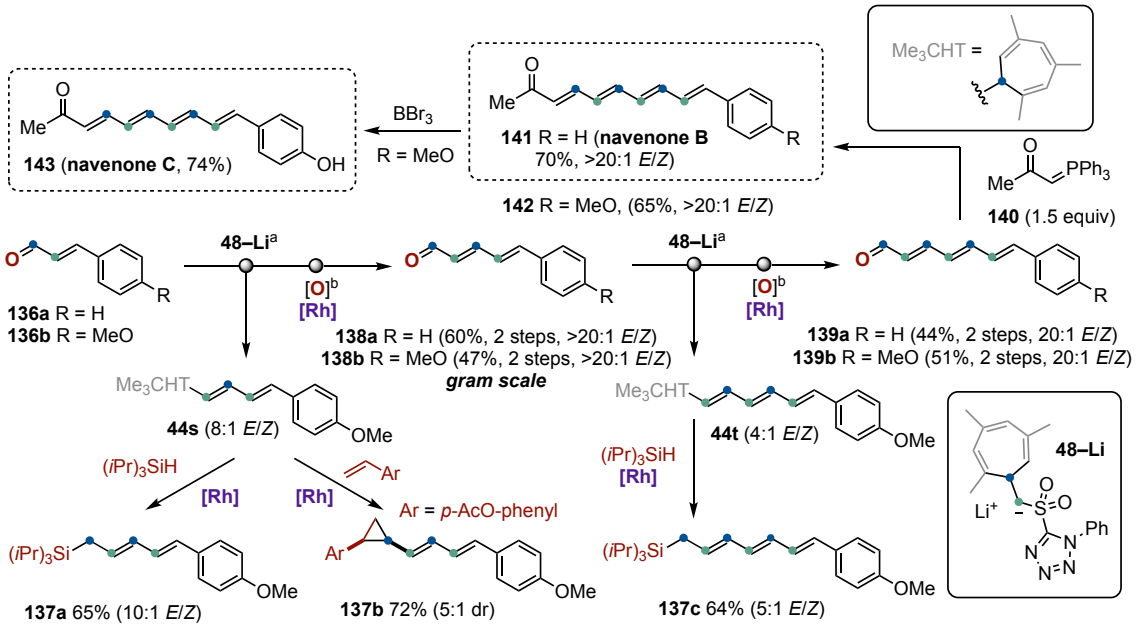



**Scheme 99**. Two-step vinylogation of aldehydes via oxidative retro-Buchner reaction.

Then, we considered the possibility of implementing this procedure in an iterative manner. The product of this two-step process has the same terminal functionality as the starting substrate: an aldehyde. Therefore, one could envision repeating the same Julia–Kocienski olefination with products **136**. Then, another oxidative retro-Buchner reaction would lead to dienyl aldehydes. Thus, *E*-polyene chains could be grown in a controlled fashion.

Following this hypothesis, we found that the Julia–Kocienski olefination of cinnamaldehyde with **48–Li**, followed by rhodium(II)-catalyzed oxidative retro-Buchner reaction afforded *E,E*-2,4-dienal **138a** in 60% yield over two steps (Scheme 100). Another iteration of the same two steps led to the preparation of *E,E,E*-2,4,6-trienal **139a** in 44% yield. We observed that the *E*-diastereoselectivity of the Julia–Kocienski olefination decreased as the length of the chain increased (e.g., **44s** vs **44t**) but, conveniently, the *E*-product could always be easily obtained as a single diastereoisomer after column chromatography.

Conjugated *E*-polyenes are a prevalent motif in Nature.[206] In order to illustrate the potential of this strategy, we applied our iterative chain growth to the diastereoselective total synthesis of the navenones, a family of trail-breaking pheromones from the marine opisthobranch *Navanax inermis* (Scheme 100).[207]




**Scheme 100**. Iterative total synthesis of natural and unnatural all-*E* polyenes.
[a] Julia–Kocienski olefination: 1.2 equiv of **2-Li** in THF (0.1 M), from -78 ºC to 25 ºC for 12 h.
[b] Decarbenation/oxidation sequence: 1.5 equiv of $Ph_2SO$ and 3 mol % of $[Rh(TFA)_2]_2$ in 1,2-DCE (0.1 M), at 80 ºC for 16 h.

Therefore, simply submitting *E,E,E*-2,4,6-trienal **139a** to a Wittig reaction with commercially available stabilized ylide **140** gave navenone B in 70% yield as a very bright yellow solid. Similarly, we submitted 4-methoxycinnamaldehyde to two iterations of the same chain-growth process, obtaining functionalized *E,E,E*-2,4,6-trienal **139b** in 24% overall yield (4 steps). Treatment of **139b** with ylide **140** and subsequent deprotection of the methoxy group with $BBr_3$ gave navenone C in 52% yield over two steps.

Finally, we decided to merge this iterative process with other methodologies based on donor rhodium(II) carbenes: cyclopropanation (described in Section II.4) and Si–H insertion (described earlier in this Section). Following this idea, we wanted to demonstrate how this strategy can be

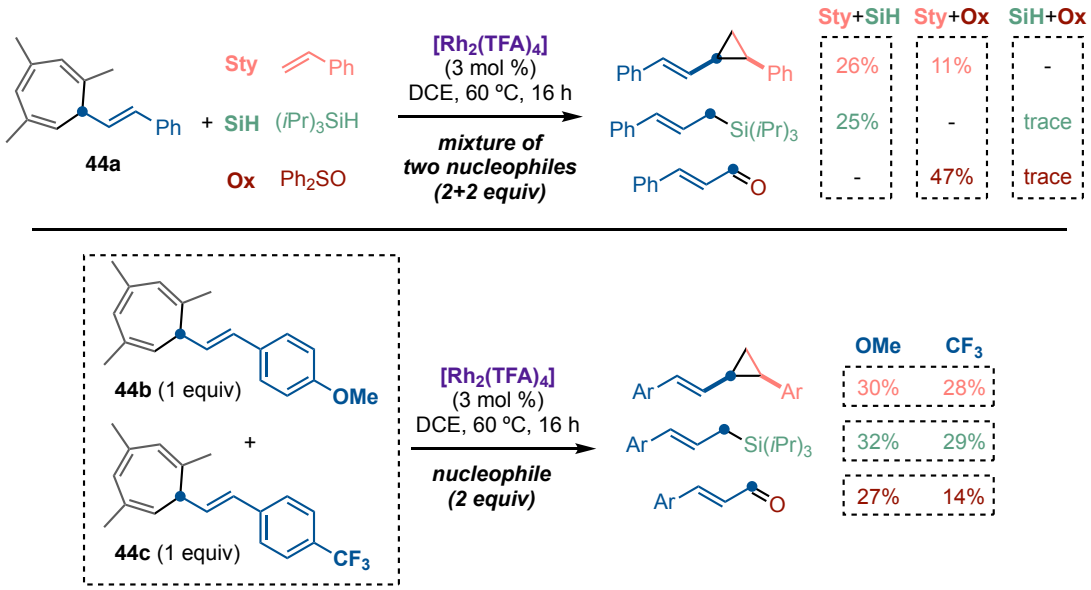
206 (a) Rychnovsky, S. D. Oxo Polyene Macrolide Antibiotics. *Chem. Rev.* **1995**, *95*, 2021–2024. (b) Woerly, E. M.; Roy, J.; Burke, M. D. Synthesis of most polyene natural product motifs using just 12 building blocks and one coupling reaction. *Nature Chemistry* **2014**, *6*, 484–491.

207 (a) Sleeper, H. L.; Fenical, W. Navenones A-C: trail-breaking alarm pheromones from the marine opisthobranch Navanax inermis. *J. Am. Chem. Soc.* **1977**, *99*, 2367–2368. (b) Soullez, D.; Ramondenc, Y.; Ple, G. Duhamel, L. Handy Access to Navenones A, B and C. *Natural Product Letters*, **1994**, *4*, 203–208.

used for the synthesis of *E*-polyenes bearing not only aldehyde groups, but also silanes, and cyclopropanes. Thus, we showed how 7-polyenyl-1,3,5-trimethyl-1,3,5-cycloheptatrienes **44s** and **44t** can be submitted to the corresponding Rh(II)-based reaction conditions to provide polyenyl *cis*-cyclopropanes (**137b**) or polyenyl silanes (**137a** and **137c**) in good yield and moderate to good diastereoselectivity (Scheme 100).

We started the investigations described in this Section with the aim of identifying new nucleophilic partners that could react with non-acceptor donor carbenes in a comparable or even faster rate than styrenes (see introduction of Section III.6, page 236), to avoid or minimize the competing cyclopropanation of starting substrates **44**. Once we discovered silanes and oxidants such as diphenylsulfoxide to be competent reaction partners, we wanted to evaluate their relative reactivities with our carbene precursors **44** under rhodium(II) catalysis (Scheme 101).

We performed the reaction of 1 equiv of **44a** with 2:2 equiv mixtures of two different nucleophiles, under standard rhodium(II)-catalyzed conditions (Scheme 101, top). A mixture of styrene and triisopropylsilane afforded a 1:1 mixture of cyclopropane and allylsilane, suggesting a similar rate for the cyclopropanation and the Si–H insertion of the corresponding rhodium(II) carbene. On the other hand, a mixture of styrene and diphenylsulfoxide leads to a *ca* 1:5 mixture of cyclopropane and aldehyde, showing that the oxidative decarbenation is even faster than the retro-Buchner/cyclopropanation sequence. A mixture of silane and oxidant led to almost no reactivity, presumably due to redox interactions between the two reagents.



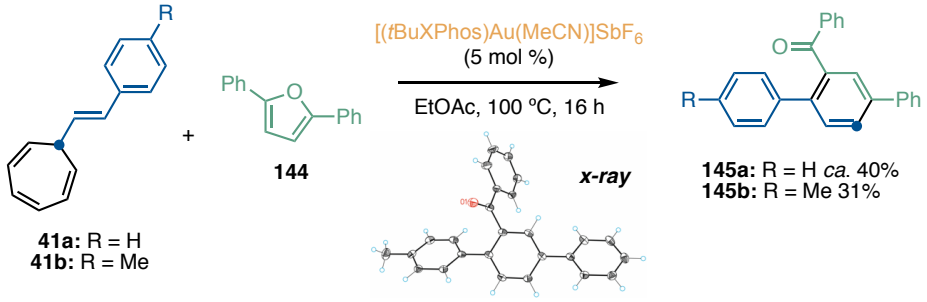

**Scheme 101**. Competition between different nucleophiles and electrophiles.

We also compared the relative performance of electronically different carbene precursors in the three processes (Scheme 101, bottom). For both the cyclopropanation and the Si–H insertion, a 1:1 statistical mixture of products was obtained, whereas only for the oxidation process a preference for the more electron-rich substrate is observed. These results highlight the similar reactivity of carbenes with different electronic properties, accounting for the wide scope of these transformations.

***Reactivity with Heterocycles***

During our investigations with donor carbenes generated by decarbenation of cycloheptatrienes, we never observed that these intermediates could engage in a Buchner ring expansion to give rise to a different cycloheptatriene (a reaction typical of acceptor carbenes). This is highlighted by the fact that most of our carbene-transfer reactions can be carried out in aromatic solvents such as toluene, without formation of any cycloheptatriene–arene metathesis product.

However, we found that this type of non-acceptor carbene can indeed be trapped by heteroaromatic compounds. We tested the reaction of 2,5-diphenylfuran with 7-styryl cycloheptatrienes **41** under gold(I) catalysis, expecting to obtain the corresponding (2+1) adducts. Instead, we isolated as major product polyaromatic compounds **145**, as confirmed by the single-crystal X-ray analysis of **145b** (Scheme 102).

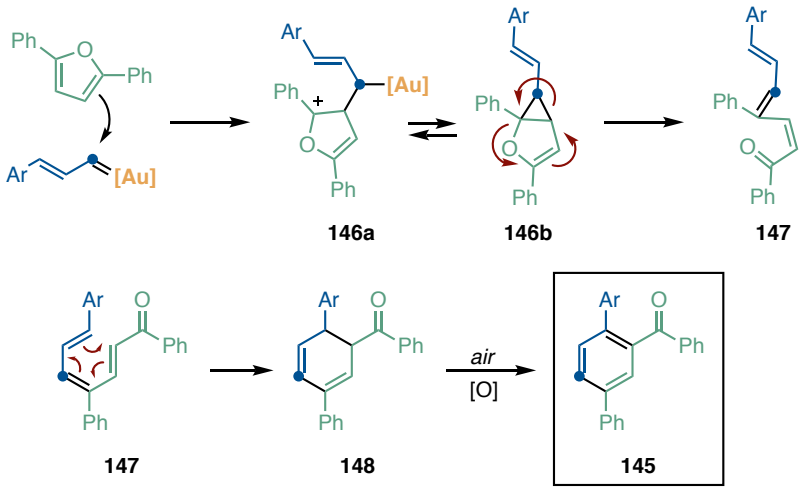



**Scheme 102**. Gold(I)-catalyzed synthesis of *p*-terphenyl ketones.

A mechanistic rationale for the formation of these *p*-terphenyl ketones is presented in Scheme 103. Gold(I)-catalyzed decarbenation by retro-Buchner reaction of **41** leads to the formation of a styryl gold(I) carbene, which is intercepted by the furan to give rise to either cationic intermediate **146a** or cyclopropane **146b**.[208] Either of the two intermediates can evolve through opening of the 5-membered ring to give linear trienyl ketone **147**. This triene would undergo an electrocyclization. Subsequent oxidation of cyclohexadiene **148** (which might take place

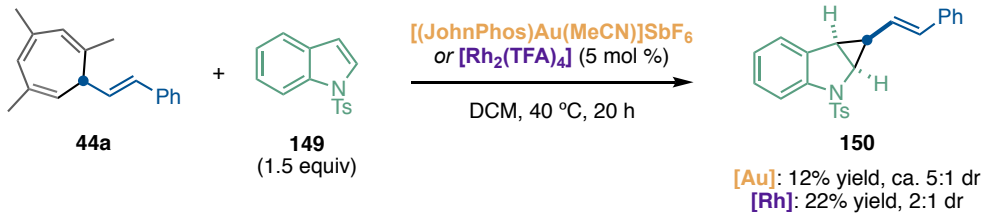
208 Our theoretical study on the cyclopropanation of enol ethers would suggest the intermediacy of the O-stabilized cationic intermediate **146a**, see Figure 20 in page 223.

aerobically or through a different mechanism) results in the formation of *p*-terphenyl ketone **145**. The formation of this highly conjugated molecule is most likely the driving force of the whole transformation (Scheme 103). A similar ring-opening process had been previously observed in the reaction of aryl gold(I) carbenes with furans, giving rise to dienes which, depending on the substitution pattern, either could be isolated or evolve through Friedel–Crafts-type cyclizations.[209]




**Scheme 103**. Mechanistic rationale for the assembly of *p*-terphenyl ketones from carbenes and furans.

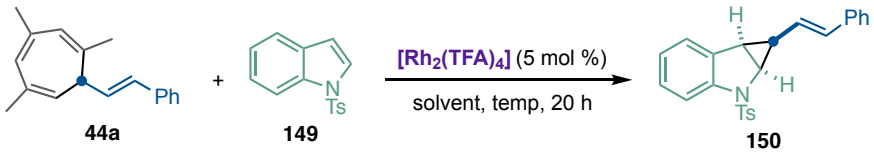
Similarly, these substrates reacted with indoles to afford the corresponding styrylcyclopropanes, although in low yields (Scheme 104).




**Scheme 104**. Styrylcyclopropanation of *N*-tosyl indole.

The reaction of **44a** with 1.5 equiv of *N*-tosyl indole gave rise to (2+1) cycloadduct **150**. Gold(I) catalysis afforded the product in 12% yield and in a 5:1 ratio of diastereoisomers. On the other hand, $[Rh_2(TFA)_4]$ gave **150** in a higher 22% yield, but in a lower 2:1 ratio of isomers. Both diastereoisomers could be isolated separately, and nOe -NMR experiments allowed assigning the structure of the major product to *cis*-**150**.

209 Leboeuf, D.; Gaydou, M.; Wang, Y.; Echavarren, A. M. Intermolecular reactions of gold(I)-carbenes with furans by related mechanisms. *Org. Chem. Front.* **2014**, *1*, 759–764.



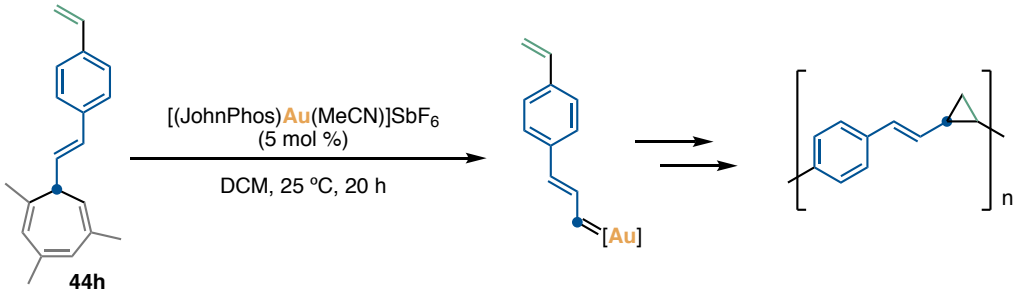

| *entry* | *44a/149 ratio* | *solvent* | *temperature* | *yield (dr)* |
|---|---|---|---|---|
| **1** | **1:2** | **DCE** | **40 ºC** | **23% (2.5:1)** |
| 2 | 3:1 | DCM | 40 ºC | 15% (2.4:1) |
| 3 | 1:3 | DCM | 40 ºC | 21% (2.3:1) |
| 4 | 1:2 | DCE | 25 ºC | 21% (2.5:1) |
| 5 | 1:2 | DCE | 80 ºC | 12% (1.4:1) |

**Scheme 105**. Preliminary screening of conditions of the cyclopropanation of indoles.

Preliminary screening of conditions under Rh(II) catalysis showed that an excess of indole was beneficial to the reaction efficiency (Scheme 105, entries 1–3). The reaction can be performed also at 25 ºC. On the other hand, higher temperatures lead to erosion of the diastereomeric ratio (entries 4–5).

***Decarbenation/Polymerization Sequence***

As a further application of these substrates, a decarbenation/polymerization sequence was envisioned. Cycloheptatriene **44h** could be prepared by Julia-Kocienski olefination of 4-vinyl-benzaldehyde and submitted to the usual room-temperature gold(I)-catalyzed retro-Buchner reaction conditions. NMR analysis of the resulting material, which can be isolated by addition of methanol and centrifugation, shows the typical broad $^{1}$H signals characteristic of polymers (Scheme 106).[210] Further characterization of the product by MS was not performed due to time constrains.



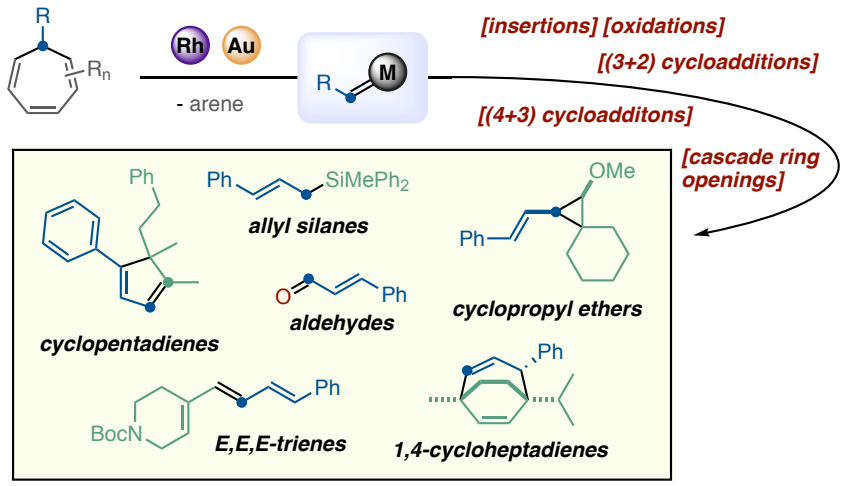

**Scheme 106**. Polymerization of a 4-vinyl-styryl carbene.

210 Nzulu, F.; Bontemps, A.; Robert, J.; Barbazanges, M.; Fensterbank, L.; Goddard, J.-P.; Malacria, M.; Ollivier, C.; Petit, M.; Rieger, J.; Stoffelbach, F. Gold-Catalyzed Polymerization Based on Carbene Polycyclopropanation. *Macromolecules* **2014**, *47*, 6652–6656.

## III.7. Conclusions

In summary, we developed a range of new chemical transformations based on the knowledge about metal-catalyzed aromative decarbenations gathered over the course of the studies described in Chapter II, and on the previous work carried out in our research group.

The metal-catalyzed decarbenation by retro-Buchner reaction of 7-substituted cycloheptatrienes grants access to gold(I)- and rhodium(II)-carbene intermediates which can take part in many different transformations besides simple cyclopropanations (Scheme 107).




**Scheme 107**. Selected examples of the reactions and structures that can be accessed through non-acceptor carbenes generated by retro-Buchner reaction.

For instance, we found that alkenyl carbenes can engage in (3+2) cycloadditions with allenes, and in (4+3) cycloadditions with 1,3-dienes, giving rise to synthetically complex cyclopentadienes and 1,4-cycloheptadienes, respectively. In contrast to gold(I) analogs, rhodium(II) styryl carbenes can engage in Si–H insertion processes to give allyl silanes. The same intermediates can be trapped oxidatively, to give aldehydes. This led to the development of a two-step vinylogation of aldehydes, which can be used iteratively to grow polyenes. We also found that, under rhodium(II) catalysis, cyclopropyl ethers could be assembled and disassembled to give conjugated *E,E,E*-trienes. A combination of experiments and DFT calculations shed light into the mechanistic scenarios that govern these newly discovered transformations. Preliminary studies on the reaction of the same intermediates with other nucleophiles, such as furans or indoles, further illustrate the potential of non-acceptor metal carbenes as powerful tools for the discovery of new chemistry.

Finally, we applied our new methodologies to the total synthesis of several natural products: laurokamurene B, navenones B and C, and dictyopterene C'.

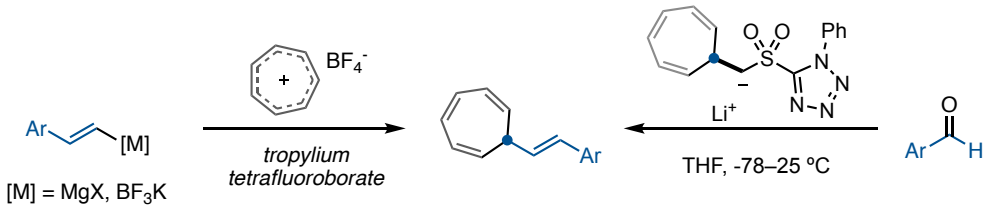
## III.8. Methods Section

*The General Considerations for the experimental section in this Chapter are exactly the same as those specified for Chapter II, which can be found in Section II.9 (page 105).*

### *Synthetic Procedures and Analytical Data*

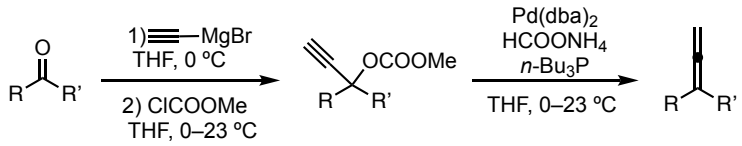
#### Preparation of First-Generation 7-Styryl-1,3,5-cycloheptatrienes (41)

All first-generation (non-methylated) styrylcyclohepatrienes employed in the chemistry described in Section II.2, and for reactivity-comparison purposes in other reactions described throughout this thesis were prepared according to already reported procedures, based on the nucleophilic addition or styryl-organometallic compounds to tropylium tetrafluoroborate (if said organometallic species are easily accessible) or by Julia–Kocienski olefination of aldehydes (for more challenging substrates).[211]




#### Preparation of Allenes (109)

Most allenes employed were commercially available. Non-commercial allenes such as **109a** were prepared according to a 3-step reported procedure.[212]

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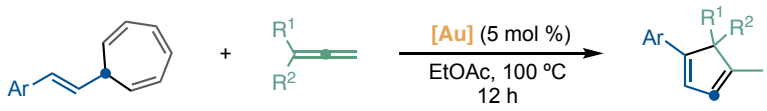
211 Herlé, B.; Holstein, P. M.; Echavarren, A. M. Stereoselective *cis*-Vinylcyclopropanation via a Gold(I)-Catalyzed Retro-Buchner Reaction under Mild Conditions. *ACS Catal.* **2017**, *7*, 3668–3675.

212 Takaya, J.; Iwasawa, N. Hydrocarboxylation of Allenes with CO2 Catalyzed by Silyl Pincer-Type Palladium Complex. *J. Am. Chem. Soc.* **2008**, *130*, 15254-15255

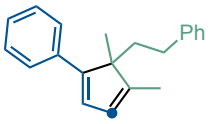
**General Procedure G for the Gold(I)-Catalyzed Synthesis of Cyclopentadienes**




Under air, a 2–5 mL microwave vial with a Teflon-coated magnetic stirring bar was charged with an allene **109** (1.5–3.0 equiv) and it was dissolved in EtOAc (HPLC grade, 0.1 M). Then, the 7-styryl-1,3,5-cycloheptatriene **41** (1.0 equiv) was added as a solid or as a liquid by glass pipette or Hamilton syringe (although order of addition was found to have no effect in the reaction outcome), and finally [(JohnPhos)Au(MeCN)]$SbF_6$ (5 mol %) was added. The vial was sealed with its corresponding cap and the resulting solution was stirred at 100 ºC in a heating block (covering the vial completely) for 12 h. The resulting yellow-orange solution was concentrated under vacuum and the obtained residue was purified by flash column chromatography ($SiO_2$, pentane or gradients of pentane/$Et_2O$).

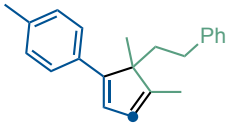
**Characterization Data of the Different Cyclopentadienes**

**(4,5-Dimethyl-5-phenethylcyclopenta-1,3-dien-1-yl)benzene (111a)**




This compound was obtained, following General Procedure G, form (*E*)-7-styrylcyclohepta-1,3,5-triene (50 mg, 0.257 mmol, 1.0 equiv) and (3-Methylpenta-3,4-dien-1-yl)benzene (61 mg, 0.386 mmol, 1.5 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (11.6 mg, 0.013 mmol, 5 mol %) after purification by flash column ($SiO_2$, eluent: pentane) as a colorless oil (35 mg, 0.128 mmol, 50%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.26 – 7.19 (m, 3H), 7.16 – 7.11 (m, 1H), 7.03 – 7.00 (m, 2H), 6.75 (d, *J* = 2.2 Hz, 1H), 6.17 (p, *J* = 1.6 Hz, 1H), 2.24 (td, *J* = 12.7, 4.7 Hz, 1H), 2.12 (td, *J* = 13.3, 4.7 Hz, 1H), 2.00 (dd, *J* = 12.9, 4.2 Hz, 1H), 1.96 (d, *J* = 1.5 Hz, 3H), 1.92 (td, *J* = 12.7, 4.4 Hz, 1H), 1.27 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 153.6, 151.2, 142.8, 136.6, 128.5, 128.3, 128.2, 128.0, 126.3, 125.8, 125.6, 125.4, 57.2, 37.9, 30.3, 22.9, 12.7 ppm. **HRMS** (APCI Positive): calculated for $C_{21}H_{23}$ $[M+H]^+$: 275.1794; found: 275.1788.

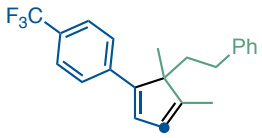
**1-(4,5-Dimethyl-5-phenethylcyclopenta-1,3-dien-1-yl)-4-methyl-benzene (111b)**




This compound was obtained, following General Procedure G, form (*E*)-7-(4-methylstyryl)cyclohepta-1,3,5-triene (70 mg, 0.340 mmol, 1.0 equiv) and (3-methylpenta-3,4-dien-1-yl)benzene (80 mg, 0.504 mmol, 1.5 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (15 mg, 0.017 mmol, 5 mol %) after purification by flash column ($SiO_2$, eluent: pentane) as a colorless oil (36 mg, 0.125 mmol, 37%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.3 Hz, 2H), 7.24 (t, *J* = 7.3 Hz, 2H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.16 (t *J* =

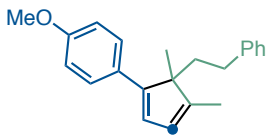
7.3 Hz, 1H), 7.05 (d, *J* = 8.1 Hz, 2H), 6.73 (d, *J* = 2.3 Hz, 1H), 6.18 (quint, *J* = 1.7 Hz, 1H), 2.40 (s, 3H), 2.26 (td, *J* = 12.6, 4.6 Hz, 1H) 2.15 (td, *J* = 12.6, 4.6 Hz, 1H), 1.98 (d, *J* = 1.6 Hz, 3H), 2.04-1.90 (m, 2H), 1.28 (s, 3H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 153.1, 151.2, 142.9, 136.0, 133.8, 129.2, 128.3, 128.2, 127.2, 125.7, 125.5, 125.4, 57.1, 37.9, 30.3, 22.9, 21.1, 12.7 ppm. **HRMS** (APCI Positive): calculated for $C_{22}H_{25}$ $[M+H]^+$: 289.1951; found: 289.1949.

**1-(4,5-Dimethyl-5-phenethylcyclopenta-1,3-dien-1-yl)-4-(tri-fluoromethyl)benzene (111c)**



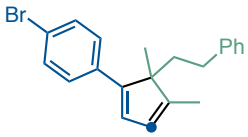

This compound was obtained, following General Procedure G, form (*E*)-7-(4-(trifluoromethyl)styryl)cyclohepta-1,3,5-triene (40 mg, 0.153 mmol, 1.0 equiv) and (3-methylpenta-3,4-dien-1-yl)benzene (48 mg, 0.305 mmol, 2.0 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (6.9 mg, 7.6 µmol, 5 mol %) after purification by flash column ($SiO_2$, eluent: pentane) as a colorless oil (23 mg, 0.153 mmol, 44%). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.6 Hz, 2H), 7.61 (d, *J* = 8.6 Hz, 2H), 7.23 (tt, *J* = 7.0, 1.4 Hz, 2H), 7.15 (tt, *J* = 7.2, 1.4 Hz, 1H), 7.03-6.99 (m, 2H), 6.90 (d, *J* = 2.4 Hz, 1H), 6.21 (quint, *J* = 1.7 Hz, 1H), 2.28-2.20 (m, 1H), 2.08-1.94 (m, 3H), 1.99 (d, *J* = 1.5 Hz, 3H), 1.28 (s, 3H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 155.4, 149.5, 142.4, 130.2, 129.0, 128.4, 128.4, 128.3, 128.2, 125.7, 125.5, 125.4 (q, $J_{C-F}$ = 3.8 Hz), 57.3, 37.9, 30.2, 22.9, 12.7 ppm. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -62.50 ppm. **HRMS** (APCI Positive): calculated for $C_{22}H_{22}F_3$ $[M+H]^+$: 343.1668; found: 343.1662.

**1-(4,5-Dimethyl-5-phenethylcyclopenta-1,3-dien-1-yl)-4-methoxybenzene (111d)**



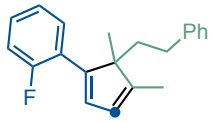

This compound was obtained, following General Procedure G, form (*E*)-7-(4-methoxystyryl)cyclohepta-1,3,5-triene (50 mg, 0.223 mmol, 1.0 equiv) and (3-methylpenta-3,4-dien-1-yl)benzene (71 mg, 0.446 mmol, 2.0 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (10 mg, 11 µmol, 5 mol %) after purification by flash column ($SiO_2$, eluent: pentane/$Et_2O$ 99:1) as a pale yellow syrup (27 mg, 0.089 mmol, 39%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.9 Hz, 2H), 7.24 (t, *J* = 7.7 Hz, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 7.9 Hz, 2H), 6.93 (d, *J* = 7.9 Hz, 2H), 6.64 (d, *J* = 2.2 Hz, 1H), 6.16 (quint, *J* = 1.8 Hz, 1H), 3.87 (s, 3H), 2.21 (td, *J* = 12.9, 4.7 Hz, 1H), 2.12 (td, *J* = 12.9, 4.5 Hz, 1H), 2.00 (td, *J* = 13.0, 4.5 Hz, 1H), 1.96 (d, *J* = 1.5 Hz, 3H), 1.91 (td, *J* = 12.9, 4.5 Hz, 1H), 1.26 (s, 3H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 158.2, 152.5, 150.9, 142.9, 129.6, 128.3, 128.2, 126.9, 126.4, 125.5, 125.4, 113.9, 77.3, 57.1, 55.3, 37.9, 30.3, 23.0, 12.6 ppm. **HRMS** (APCI Positive): calculated for $C_{22}H_{25}O$ $[M+H]^+$: 305.1900; found: 305.1904.

**1-Bromo-4-(4,5-dimethyl-5-phenethylcyclopenta-1,3-dien-1-yl)-benzene (111e)**



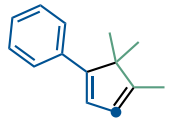

This compound was obtained, following General Procedure G, form (*E*)-7-(4-bromostyryl)cyclohepta-1,3,5-triene (60 mg, 0.220 mmol, 1.0 equiv) and (3-methylpenta-3,4-dien-1-yl)benzene (70 mg, 0.439 mmol, 2.0 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (9.9 mg, 11 µmol, 5 mol %) after purification by flash column ($SiO_2$, eluent: pentane) as a white syrup (39 mg, 0.110 mmol, 50%). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.50 (dt, *J* = 8.7, 2.2 Hz, 2H), 7.44 (dt, *J* = 8.6, 2.2 Hz, 2H), 7.24 (t, *J* = 7.2 Hz, 2H), 7.16 (tt, *J* = 7.2, 2.1 Hz, 1H), 7.02 (d, *J* = 7.2 Hz, 2H), 6.78 (d, *J* = 2.3, 1H), 6.18 (quint, *J* = 1.8 Hz, 1H), 2.19 (td, *J* = 12.4, 4.8 Hz, 1H), 2.08-1.90 (m, 3H), 1.97 (d, *J* = 1.5 Hz, 3H), 1.26 (s, 3H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 154.3, 149.9, 142.6, 135.4, 131.6, 128.6, 128.3, 128.2, 127.2, 125.7, 125.5, 120.0, 57.2, 37.9, 30.2, 22.9, 12.7 ppm. **HRMS** (APCI Positive): calculated for $C_{21}H_{22}Br$ $[M+H]^+$: 353.0899; found: 353.0895.

**1-(4,5-Dimethyl-5-phenethylcyclopenta-1,3-dien-1-yl)-2-fluoro-benzene (111f)**




This compound was obtained, following General Procedure G, form (*E*)-7-(2-fluorostyryl)cyclohepta-1,3,5-triene (40 mg, 0.188 mmol, 1.0 equiv) and (3-methylpenta-3,4-dien-1-yl)benzene (60 mg, 0.377 mmol, 2.0 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (8.5 mg, 9.4 µmol, 5 mol %) after filtering through silica gel and further purification by preparative TLC (1000 micron $SiO_2$, eluent: pentane) as a colorless viscous oil (28 mg, 0.096 mmol, 48%). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.47 (td, *J* = 7.9, 1.9 Hz, 1H), 7.26-7.21 (m, 3H), 7.18-7.12 (m, 3H), 7.08-7.04 (m, 2H), 6.79 (t, *J* = 2.2 Hz 1H), 6.20 (quint, *J* = 1.7 Hz, 1H), 2.25-2.17 (m, 1H), 2.12-2.03 (m, 2H), 1.97 (d, *J* = 1.6 Hz, 3H), 1.90-1.84 (m, 1H), 1.23 (s, 3H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 160.4 (d, $J_{C\text{-}F}$ = 248.1 Hz), 153.4, 144.6, 142.8, 132.7 (d, $J_{C\text{-}F}$ = 9.7 Hz), 128.6 (d, $J_{C\text{-}F}$ = 3.8 Hz), 128.2, 128.2, 127.6 (d, $J_{C\text{-}F}$ = 8.7 Hz), 125.7, 125.6, 123.7 (d, $J_{C\text{-}F}$ = 4.8 Hz), 116.2, 116.0, 58.3, 37.5, 30.1, 22.6, 12.8 ppm. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -111.30 ppm. **HRMS** (APCI Positive): calculated for $C_{21}H_{22}F$ $[M+H]^+$: 293.1700; found: 293.1701.

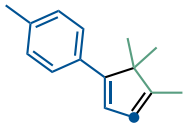
**(4,5,5-Trimethylcyclopenta-1,3-dien-1-yl)benzene (111g)**



This compound was obtained, following General Procedure G, form (*E*)-7-styrylcyclohepta-1,3,5-triene (0.26 g, 1.34 mmol, 1.0 equiv) and 3-methylbuta-1,2-diene (0.27 g, 4.01 mmol, 3.0 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (60 mg, 0.05 mmol, 5 mol %) after purification by flash column ($SiO_2$, eluent: pentane) as a colorless oil (121 mg, 0.66 mmol, 49%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.0 Hz, 2H), 7.32 (t, *J* = 7.9 Hz, 2H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.63 (d, *J* = 2.3 Hz, 1H), 6.02 (quint, *J* = 1.4 Hz, 1 H), 1.92 (d, *J* = 1.4 Hz, 3H), 1.22 (s, 6H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 156.3, 153.6, 136.5,

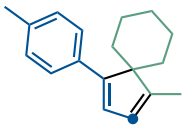
128.3, 126.1, 126.1, 126.0, 123.3, 53.1, 22.5, 12.5 ppm. **HRMS** (APCI Positive): calculated for $C_{14}H_{17}$ $[M+H]^+$: 185.1325; found: 185.1321.

**1-Methyl-4-(4,5,5-trimethylcyclopenta-1,3-dien-1-yl)benzene (111h)**



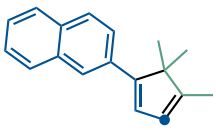
This compound was obtained, following General Procedure G, form (*E*)-7-(4-methylstyryl)cyclohepta-1,3,5-triene (0.21 g, 1.01 mmol, 1.0 equiv) and 3-methylbuta-1,2-diene (0.21 g, 3.02 mmol, 3.0 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (45 mg, 0.05 mmol, 5 mol %) after purification by flash column ($SiO_2$, eluent: pentane) as a colorless low boiling point oil (95 mg, 0.48 mmol, 43-48%). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.1 Hz, 2H), 7.18 (d, *J* = 8.1 Hz, 2H), 6.62 (d, *J* = 2.1 Hz, 1H), 6.04 (quint, *J* = 1.5 Hz, 1H), 2.38 (s, 3H), 1.95 (d, *J* = 1.4 Hz, 3H), 1.25 (d, *J* = 0.6 Hz, 6H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 155.8, 153.6, 135.8, 133.6, 129.0, 125.9, 125.3, 123.3, 53.0, 22.5, 21.1, 12.5 ppm. **HRMS** (APCI Positive): calculated for $C_{15}H_{19}$ $[M+H]^+$: 199.1481; found: 199.1482.

**1-Methyl-4-(*p*-tolyl)spiro[4.5]deca-1,3-diene (111i)**



This compound was obtained, following General Procedure G, form (*E*)-7-(4-methylstyryl)-cyclohepta-1,3,5-triene (67 mg, 0.32 mmol, 1.0 equiv) and vinylidenecyclohexane (77 mg, 0.643 mmol, 2.0 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (14 mg, 0.016 mmol, 5 mol %) after purification by flash column ($SiO_2$, eluent: pentane) as a colorless oil (28 mg, 0.117 mmol, 37%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.29 (t, *J* = 4.1 Hz, 2H), 7.16 (d, *J* = 7.6 Hz, 2H), 6.28 (d, *J* = 2.2 Hz, 1H), 6.00 (quint, *J* = 1.7 Hz, 1H), 2.38 (s, 3H), 2.16 (d, *J* = 1.6 Hz, 3H), 1.91-1.85 (m, 2H), 1.80-1.72 (m, 2H), 1.67-1.59 (m, 3H), 1.50-1.42 (m, 3H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 155.9, 155.4, 135.8, 135.7, 128.5, 128.1, 126.6, 124.7, 56.9, 30.5, 25.4, 22.4, 21.1, 17.3 ppm. **HRMS** (APCI Positive): calculated for $C_{18}H_{23}$ $[M+H]^+$: 239.1794; found: 239.1788.

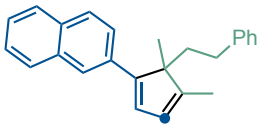
**2-(4,5,5-Trimethylcyclopenta-1,3-dien-1-yl)naphthalene (111j)**



This compound was obtained, following General Procedure G, form (*E*)-2-(2-(cyclohepta-2,4,6-trien-1-yl)vinyl)naphthalene (65 mg, 0.266 mmol, 1.0 equiv) and 3-methylbuta-1,2-diene (54 mg, 0.798 mmol, 3.0 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (12 mg, 13 µmol, 5 mol %) after purification by flash column ($SiO_2$, eluent: pentane) as a pale yellow solid (35 mg, 0.149 mmol, 56%). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.95 – 7.89 (m, 1H), 7.89 – 7.70 (m, 4H), 7.46 (m, 2H), 6.84 (d, *J* = 2.3 Hz, 1H), 6.17 – 6.08 (m, 1H), 2.01 (d, *J* = 1.6 Hz, 3H), 1.36 (s, 6H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 157.0, 153.3, 133.6, 133.5, 132.0, 128.1, 127.7, 127.5, 126.9, 126.0, 125.3, 125.2, 123.5, 123.4, 53.2, 22.8,

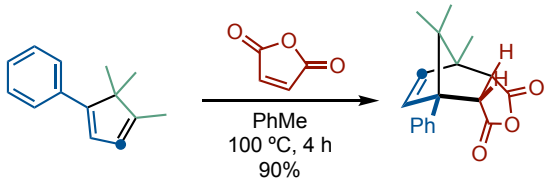
12.5. **HRMS** (APCI Positive): calculated for $C_{18}H_{19}$ $[M+H]^+$: 235.1481; found: 235.1485. **MP** 58–62 ºC.

**2-(4,5-Dimethyl-5-phenethylcyclopenta-1,3-dien-1-yl)naphthalene (111k)**




This compound was obtained, following General Procedure G, form (*E*)-2-(2-(cyclohepta-2,4,6-trien-1-yl)vinyl)naphthalene (30 mg, 0.123 mmol, 1.0 equiv) and (3-methylpenta-3,4-dien-1-yl)benzene (29 mg, 0.184 mmol, 1.5 equiv) using [(JohnPhos)Au(MeCN)]$SbF_6$ (5.5 mg, 6.1 µmol, 5 mol %) after filtering through silica gel and further purification by preparative TLC (1000 micron $SiO_2$, eluent: pentane) as a pale yellow syrup (22 mg, 0.068 mmol, 55%). **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.96 (br, 1H), 7.86-7.76 (m, 4H), 7.47 (p, *J* = 7.3 Hz, 2H), 7.20 (t, *J* = 7.3 Hz, 2H), 7.13 (t, *J* = 7.2 Hz, 1H), 7.04-7.00 (m, 2H), 6.93 (d, *J* = 2.3 Hz, 1H), 6.24 (p, *J* = 1.7 Hz, 1H), 2.43-2-36 (m, 1H), 2.19-2.10 (m, 1H), 2.06-1.95 (m, 2H), 2.01 (d, *J* = 1.5 Hz, 3H), 1.37 (s, 3H) ppm. **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 154.3, 150.8, 142.8, 133.8, 133.7, 132.2, 128.8, 128.3, 128.3, 128.2, 128.0, 127.5, 126.1, 125.6, 125.6, 125.5, 125.1, 123.1, 57.3, 38.4, 30.4, 23.3, 12.8 ppm. **HRMS** (APCI Positive): calculated for $C_{25}H_{25}$ $[M+H]^+$: 325.1951; found: 325.1949.

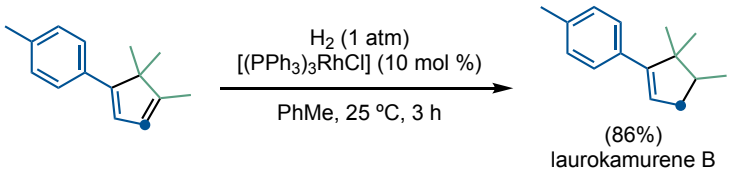
**Diels–Alder Reaction of (111g) with Maleic Anhydride to Give (112)**




To a solution of (4,5,5-trimethylcyclopenta-1,3-dien-1-yl)benzene **111g** (58 mg, 0.315 mmol, 1.0 equiv) in 1.5 mL of anhydrous toluene (0.2 M) open to air was added maleic anhydride (40 mg, 0.409 mmol, 1.3 equiv) and the resulting yellow mixture was stirred at 100 ºC for 4 h. The obtained colorless suspension was cooled to room temperature and the solvent was removed under reduced pressure. Purification by flash column chromatography on $SiO_2$ (eluent pentane/$Et_2O$ from 8:2 to 7:3) afforded *endo*-4,8,8-trimethyl-7-phenyl-3a,4,7,7a-tetrahydro-4,7-methano-isobenzofuran-1,3-dione **112** (80 mg, 90%, >20:1 dr) as a white solid. Slow evaporation overnight of a solution of **112** in heptane/$CH_2Cl_2$ afforded crystals suitable for X-ray analysis. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.47-7.42 (m, 2H), 7.38 (dd, *J* = 8.2, 2.2 Hz, 3H), 6.39 (d, *J* = 5.8 Hz, 1H), 6.20 (d, *J* = 5.8 Hz, 1H), 4.30 (d, *J* = 7.8 Hz, 1H), 3.49 (d, *J* = 7.8 Hz, 1H), 1.45 (s, 3H), 0.78 (s, 3H), 0.72 (s, 3H). ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 171.5, 170.6, 139.3, 136.8, 135.0, 128.5, 127.7, 127.7, 68.9, 67.9, 60.8, 52.5, 49.1, 17.42, 17.36, 12.8. ppm. **HRMS** (ESI Positive): calculated for $C_{18}H_{18}NaO_3$ $[M+Na+CH_3OH]^+$: 337.1410; found: 337.1413. **MP** 185–187 ºC.

**Total Synthesis of Laurokamurene B (113)**

The synthesis of (±)-laurokamurene B was achieved in one step directly from cyclopentadiene **111h**, (1-methyl-4-(4,5,5-trimethylcyclopenta-1,3-dien-1-yl)benzene, see above for preparation).



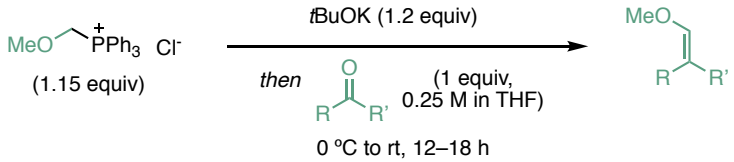

To a stirred solution of 1-methyl-4-(4,5,5-trimethylcyclopenta-1,3-dien-1-yl)benzene (50 mg, 0.252 mmol, 1.0 equiv) in 1.5 mL of anhydrous toluene (0.17 M) under Ar atmosphere, was added Wilkinson's Catalyst, $[Rh(PPh_3)_3Cl]$ (23 mg, 0.025 mmol, 10 mol %). The Ar atmosphere was exchanged for a $H_2$ atmosphere though 3 vacuum/$H_2$ cycles using a $H_2$ balloon which was finally left attached to the flask. The reaction mixture was allowed to stir at room temperature for 3 h. The reaction was followed using both TLC and GC/MS (the later allowed the separation of the starting cyclopentadiene, the desired product and the double hydrogenation byproduct) and it was found that longer reaction times were detrimental to the desired product yield, as the second olefin gets also hydrogenated. After that time, the reaction was filtered through silica gel, and then purified by slow flash column in $SiO_2$ using pentane as eluent to afford (±)-laurokamurene B (43 mg, 0.220 mmol, 86%). Characterization data matched those reported for the natural sample.[213] **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 5.71 (br, 1H), 2.45-2.40 (m, 1H), 2.35 (s, 3H), 2.07-1.99 (m, 2H), 1.11 (s, 3H), 1.02 (d, *J* = 6.7 Hz, 3H), 1.00 (s, 3H) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 152.8, 136.2, 135.5, 128.6, 127.5, 126.2, 47.7, 45.8, 37.9, 26.3, 21.1, 20.7, 14.1 ppm. **HRMS** (APCI Positive): calculated for $C_{15}H_{21}$ $[M+H]^+$: 201.1638; found: 201.1636.

213 Mao, S.-C.; Guo, Y.-W. A Laurane Sesquiterpene and Rearranged Derivatives from the Chinese Red Alga Laurencia okamurai Yamada. *J. Nat. Prod.* **2006**, *69*, 1209–1211.

**Synthesis of Substrates for the Assembly and Disassembly of Cyclopropyl Ethers**

Trimethylstyryl cycloheptatrienes **44** were prepared according to the procedure described in the Methods Section II.9 of Chapter II. Most enol ethers **119** are well known and were prepared by Wittig reaction of ketones using commercially available $MeOCH_2PPh_3Cl$. Spectroscopic data (shown below for most enol ethers) matched those for the reported products.

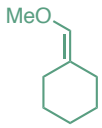
**General Procedure H for the Synthesis of Enol Ethers**




To a suspension of (methoxymethyl)triphenylphosphonium chloride (1.15 equiv) in anhydrous THF (0.25 M) under Ar, at 0 ºC (water-ice bath), was added potassium *tert*-butoxide (1.2 equiv), either as a solid in portions, or dropwise as a freshly prepared 0.5–1.0 M solution in anhydrous THF. The mixture immediately turned orange, and it was further stirred for 60 min at 0 ºC. After this time, the corresponding ketone was added in a single portion (1 equiv, neat *via* syringe for liquid ketones or as a 0.5–1.0 M solution in anhydrous THF for solid ketones). The resulting mixture was then stirred for 14–18 h while coming to room temperature (full conversion was observed by TLC). The reaction was quenched by the addition of $Et_2O$ and saturated aqueous ammonium chloride. The product was extracted twice with $Et_2O$, and the combined organic fractions were washed once with water, once with brine and dried over anhydrous $Na_2SO_4$. The solvent was removed under vacuum, and the product was purified by flash column chromatography. Most of the enol ethers are well known and spectroscopic data matched the reported ones.

**Characterization Data for the Different Enol Ethers**

**(Methoxymethylene)cyclohexane (119a)**

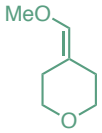



The title compound (colorless oil, 2.06 g, 80% yield) was obtained following General Procedure H from (methoxymethyl)triphenylphosphonium chloride (8.03 g, 23.4 mmol, 1.15 equiv) and cyclohexanone (2.0 g, 20.4 mmol, 1 equiv) using *t*BuOK (2.74 g, 24.5 mmol, 1.20 equiv) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 97:3 as eluent. Spectroscopic data matched the reported values.[214] **$^1$H**

214 Chepiga, K. M.; Feng, Y.; Brunelli, N. A.; Jones, C. W.; Davies, H. M. L. Silica-Immobilized Chiral Dirhodium(II) Catalyst for Enantioselective Carbenoid Reactions. *Org. Lett.* **2013**, *15* 6136–6139.

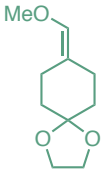
**NMR** (300 MHz, Chloroform-*d*) δ 5.76 (t, *J* = 1.3 Hz, 1H), 3.54 (d, *J* = 0.5 Hz, 3H), 2.23 – 2.15 (m, 2H), 2.00 – 1.90 (m, 2H), 1.57 – 1.46 (m, 6H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.77, 118.41, 59.25, 30.54, 28.39, 27.04, 26.89, 25.43. **GC-MS** (EI): calc. for $C_8H_{14}O$ $[M]^+$: 126.1; found: 126.1.

**4-(Methoxymethylene)tetrahydro-2*H*-pyran (119b)**



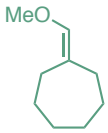
The title compound (colorless oil, 0.18 g, 88% yield) was obtained following General Procedure H from (methoxymethyl)triphenylphosphonium chloride (0.57 g, 1.84 mmol, 1.15 equiv) and tetrahydro-4*H*-pyran-4-one (0.16 g, 0.15 mL, 1.6 mmol, 1 equiv) using *t*BuOK (0.215 g, 1.92 mmol, 1.20 equiv) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 95:5 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 5.85 (q, *J* = 1.3 Hz, 1H), 3.65 (m, 4H), 3.57 (t, *J* = 0.8 Hz, 3H), 2.36 – 2.28 (m, 2H), 2.11 – 2.04 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 140.22, 112.93, 69.56, 68.38, 59.39, 30.46, 26.43. **GC-MS** (EI): calc. for $C_7H_{12}O_2$ $[M]^+$: 128.1; found: 128.1.

**8-(Methoxymethylene)-1,4-dioxaspiro[4.5]decane (119c)**



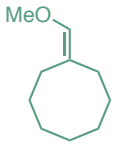
The title compound (colorless oil, 0.22 g, 78% yield) was obtained following General Procedure H from (methoxymethyl)triphenylphosphonium chloride (0.61 g, 1.77 mmol, 1.15 equiv) and 1,4-dioxaspiro[4.5]decan-8-one (0.24 g, 1.54 mmol, 1 equiv) using *t*BuOK (0.21 g, 1.84 mmol, 1.20 equiv) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane to cyclohexane/EtOAc 95:5 to 85:15 as eluent. **$^1$H NMR** (300 MHz, Chloroform-*d*) δ 5.80 (q, *J* = 1.2 Hz, 1H), 3.97 (d, *J* = 1.2 Hz, 4H), 3.56 (d, *J* = 1.1 Hz, 3H), 2.33 (ddt, *J* = 6.4, 5.1, 1.2 Hz, 2H), 2.11 (ddt, *J* = 7.8, 4.7, 1.2 Hz, 2H), 1.70 – 1.60 (m, 4H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 139.63, 115.22, 109.21, 64.29, 59.36, 36.12, 34.82, 27.31, 22.10. **GC-MS** (EI): calc. for $C_{10}H_{16}O_3$ $[M]^+$: 184.1; found: 184.1.

**(Methoxymethylene)cycloheptane (119d)**



The title compound (colorless oil, 1.11 g, 74% yield) was obtained following General Procedure H from (methoxymethyl)triphenylphosphonium chloride (3.95 g, 12.8 mmol, 1.2 equiv) and cycloheptanone (1.2 g, 1.26 mL, 10.7 mmol, 1 equiv) using *t*BuOK (1.44 g, 12.8 mmol, 1.20 equiv) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 97:3 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 5.79 (p, *J* = 1.4 Hz, 1H), 3.56 (s, 3H), 2.34 – 2.26 (m, 2H), 2.11 – 2.03 (m, 2H), 1.62 – 1.50 (m, 8H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.54, 120.15, 59.19, 31.57, 30.19, 30.15, 29.63, 27.50, 26.98. **GC-MS** (EI): calc. for $C_9H_{16}O$ $[M]^+$: 140.1; found: 140.1.

**(Methoxymethylene)cyclooctane (119e)**

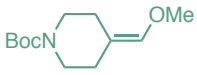



The title compound (colorless oil, 0.19 g, 77% yield) was obtained following General Procedure H from (methoxymethyl)triphenylphosphonium chloride (0.57 g, 1.84 mmol, 1.15 equiv) and cyclooctanone (0.20 g, 1.6 mmol, 1 equiv) using *t*BuOK (0.22 g, 1.92 mmol, 1.20 equiv) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 97:3 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 5.78 (p, *J* = 1.0 Hz, 1H), 3.56 (s, 3H), 2.23 – 2.18 (m, 2H), 2.05 – 2.01 (m, 2H), 1.65 – 1.57 (m, 4H), 1.56 – 1.48 (m, 6H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.99, 119.48, 59.13, 31.73, 27.04, 26.75, 26.64, 26.63, 26.45, 26.34. **GC-MS** (EI): calc. for $C_{10}H_{18}O$ $[M]^+$: 154.1; found: 154.1.

**(Methoxymethylene)cyclodecane (119f)**

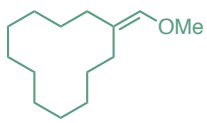

The title compound (colorless oil, 0.27 g, 93% yield) was obtained following General Procedure H from (methoxymethyl)triphenylphosphonium chloride (0.63 g, 1.84 mmol, 1.15 equiv) and cyclodecanone (0.25 g, 1.6 mmol, 1 equiv) using *t*BuOK (0.22 g, 1.92 mmol, 1.20 equiv) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 97:3 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 5.81 (p, *J* = 1.0 Hz, 1H), 3.56 (s, 3H), 2.21 (m, 2H), 2.07 – 2.02 (m, 2H), 1.69 – 1.56 (m, 4H), 1.54 – 1.44 (m, 10H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 144.04, 116.84, 59.17, 32.19, 27.29, 25.13, 25.11, 24.95, 24.41, 24.21, 23.90, 23.70. **GC-MS** (EI): calc. for $C_{12}H_{22}O$ $[M]^+$: 182.1; found: 182.2.

***tert*-Butyl 4-(methoxymethylene)piperidine-1-carboxylate (119g)**




The title compound (white solid, 0.29 g, 85% yield) was obtained following General Procedure H from (methoxymethyl)triphenylphosphonium chloride (0.53 g, 1.73 mmol, 1.15 equiv) and *tert*-butyl 4-oxopiperidine-1-carboxylate (0.30 g, 1.50 mmol, 1 equiv) using *t*BuOK (0.20 g, 1.80 mmol, 1.20 equiv) after purification by flash column chromatography on $SiO_2$ using cyclohexane to cyclohexane/EtOAc 9:1 to 7:3 as eluent. **$^1$H NMR** (300 MHz, Chloroform-*d*) δ 5.86 (p, *J* = 1.2 Hz, 1H), 3.56 (s, 3H), 3.37 (td, *J* = 5.9, 3.0 Hz, 4H), 2.24 (t, *J* = 5.6 Hz, 2H), 2.06 – 1.96 (m, 2H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 154.83, 140.60, 113.68, 79.36, 59.41, 29.57, 28.46, 25.27. **GC-MS** (EI): calc. for $C_8H_{14}O$ $[M]^+$: 227.2; found: 227.1 **MP** 43–45 ºC.

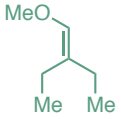
**(Methoxymethylene)cyclododecane (119h)**




The title compound (colorless oil, 0.27 g, 86% yield) was obtained following General Procedure H from (methoxymethyl)triphenylphosphonium chloride (0.53 g, 1.73 mmol, 1.15 equiv) and cyclododecanone (0.27 g, 1.5 mmol, 1 equiv) using *t*BuOK (0.20 g, 1.80 mmol, 1.20 equiv) after purification by flash column

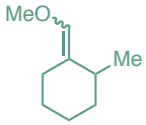
chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 97:3 as eluent. **$^1$H NMR** (300 MHz, Chloroform-*d*) δ 5.81 (t, *J* = 1.1 Hz, 1H), 3.54 (s, 3H), 2.11 (t, *J* = 6.7 Hz, 2H), 1.94 (td, *J* = 6.7, 1.3 Hz, 2H), 1.51 – 1.40 (m, 4H), 1.35 (m, 14H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 143.04, 116.68, 59.22, 28.85, 25.42, 24.57, 24.54, 24.18, 24.00, 23.98, 23.81, 23.50, 23.02. **GC-MS** (EI): calc. for $C_{14}H_{26}O$ $[M]^+$: 210.2; found: 210.2.

**3-(Methoxymethylene)pentane (119i)**



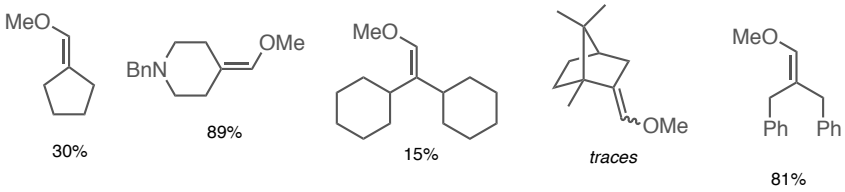

The title compound (colorless oil, 0.40 g, 60% yield) was obtained following General Procedure H from (methoxymethyl)triphenylphosphonium chloride (2.23 g, 6.7 mmol, 1.15 equiv) and pentan-3-one (0.50 g, 5.8 mmol, 1 equiv) using *t*BuOK (0.78 g, 7.0 mmol, 1.20 equiv) after fast filtration through $SiO_2$ using pentane/$Et_2O$ 9:1 as eluent, and then vacuum distillation at 50 mbar/100 ºC. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 5.71 (p, *J* = 1.0 Hz, 1H), 3.52 (d, *J* = 0.6 Hz, 3H), 2.06 (q, *J* = 7.6 Hz, 2H), 1.90 (qd, *J* = 7.5, 1.3 Hz, 2H), 0.95 (td, *J* = 7.5, 5.9 Hz, 6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.22, 122.36, 59.59, 24.57, 20.35, 13.52, 13.02. **GC-MS** (EI): calc. for $C_7H_{14}O$ $[M]^+$: 114.1; found: 114.1.

**1-(Methoxymethylene)-2-methylcyclohexane (119j)**

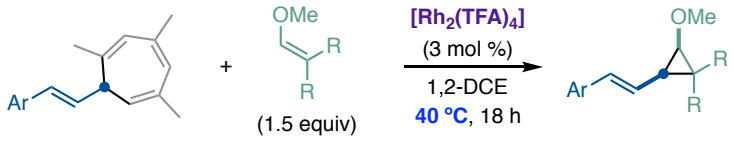



The title compound (colorless oil, 0.21 g, 50% yield, 4:1 *E*/*Z* ratio) was obtained following General Procedure H from (methoxymethyl)triphenylphosphonium chloride (1.18 g, 3.45 mmol, 1.15 equiv) and 2-methylcyclohexan-1-one (0.34 g, 3.00 mmol, 1 equiv) using *t*BuOK (0.40 g, 3.60 mmol, 1.20 equiv) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 99:1 to 98:2 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 5.71 (t, *J* = 1.4 Hz, 1H), 3.56 (s, 3H), 2.61 (ddd, *J* = 13.5, 5.4, 4.1 Hz, 1H), 2.12 – 2.02 (m, 1H), 1.86 – 1.76 (m, 1H), 1.75 – 1.67 (m, 2H), 1.65 – 1.59 (m, 1H), 1.46 – 1.27 (m, 3H), 1.03 (d, *J* = 6.8 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.30, 122.93, 59.31, 36.53, 34.21, 27.25, 25.32, 24.67, 18.49. **GC-MS** (EI): calc. for $C_9H_{16}O$ $[M]^+$: 140.1; found: 140.1.

The following enol ethers were prepared (or its preparation was attempted; the yield below the structures corresponds to the outcome of the Wittig reaction) but did not perform well in the rhodium(II) catalyzed reactions.



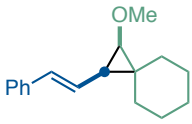
**General Procedure I for the Rhodium(II)-Catalyzed Synthesis of Cyclopropyl Ethers at Low Temperature**




A screw-cap culture tube, or glass vial, equipped with a Teflon-coated magnetic stirring bar was charged with the corresponding 1,3,5-trimethyl-7-styryl-1,3,5-cycloheptatriene **44** (1.0 equiv) and the corresponding enol ether **119** (1.5 equiv). The vial was introduced in an argon-filled glovebox, and both reagents were dissolved in anhydrous 1,2-DCE (0.15 M), before $[Rh_2(TFA)_4]$ (3 mol %) was added. The vial was closed with the corresponding screw-cap and taken outside the glovebox, and then stirred at 40 ºC for 18 hours. After confirming that the reaction was completed by TLC, the resulting mixture was concentrated in vacuum, and the obtained residue analyzed by $^1$H NMR to determine the dr of the product. The crude product was purified by flash column chromatography or preparative TLC on silica gel, using pentane or gradients of pentane/diethyl ether.

**Characterization Data for the Different Cyclopropyl Ethers**

***cis*-1-Methoxy-2-((*E*)-styryl)spiro[2.5]octane (120a)**



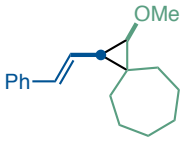

The title compound (colorless oil, 296 mg, 78% yield, 6:1 *cis*/*trans* ratio) was obtained following General Procedure I from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (370 mg, 1.57 mmol) and (methoxymethylene)cyclohexane (296 mg, 2.35 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (28 mg, 3 mol %) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane/EtOAc 98:2 as eluent.

A fraction of this 6:1 *cis*/*trans* mixture was further purified by preparative TLC in $SiO_2$ (2000 microns) to give each of the two diastereoisomers separately (>20:1 dr). The *cis* isomer is slightly less polar (top spot) than the *trans* isomer. Both diastereoisomers were fully characterized by NMR/nOe (see the corresponding section) and were used for the kinetic/mechanistic studies.

**$^1$H NMR (*cis*)** (400 MHz, Chloroform-*d*) δ 7.38 – 7.34 (m, 2H), 7.34 – 7.28 (m, 2H), 7.22 – 7.15 (m, 1H), 6.58 (d, *J* = 15.9 Hz, 1H), 6.17 (dd, *J* = 15.9, 9.9 Hz, 1H), 3.41 (s, 3H), 3.14 (d, *J* = 6.0 Hz, 1H), 1.69 (d, *J* = 5.0 Hz, 2H), 1.53 (m, 6H), 1.42 (dd, *J* = 9.9, 6.1 Hz, 1H), 1.34 (q, *J* = 6.4 Hz, 1H), 1.26 – 1.19 (m, 1H). **$^{13}$C NMR (*cis*)** (101 MHz, $CDCl_3$) δ 138.28, 130.05, 128.46, 126.41, 126.18, 125.61, 69.02, 58.61, 36.68, 31.63, 30.77, 26.57, 25.19, 24.68. **HRMS (*cis*)** (APCI+): calculated for $C_{17}H_{23}O$ $[M+H]^+$: 243.1743; found: 243.1746.

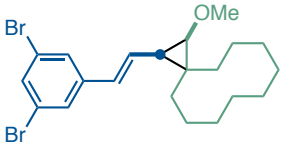
**$^{1}$H NMR (*trans*)** $^{1}$H NMR (500 MHz, Chloroform-*d*) δ 7.31 – 7.25 (m, 4H), 7.16 (ddt, *J* = 8.6, 6.5, 1.7 Hz, 1H), 6.47 (d, *J* = 15.7 Hz, 1H), 5.93 (dd, *J* = 15.7, 9.1 Hz, 1H), 3.38 (s, 3H), 3.09 (d, *J* = 3.0 Hz, 1H), 1.60 – 1.42 (m, 10H), 1.35 – 1.29 (m, 1H). **$^{13}$C NMR (*trans*)** (126 MHz, $CDCl_3$) δ 138.20, 130.15, 128.90, 128.87, 126.98, 125.95, 72.28, 58.74, 34.30, 33.97, 31.26, 31.10, 26.88, 26.10, 25.37. **HRMS (*trans*)** (APCI+): calculated for $C_{17}H_{23}O$ $[M+H]^+$: 243.1743; found: 243.1746.

***cis*-1-Methoxy-2-((*E*)-styryl)spiro[2.6]nonane (120b)**



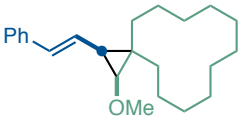

The title compound (pale yellow oil, 56 mg, 86% yield, 6:1 *cis*/*trans* ratio) was obtained following General Procedure I from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (60 mg, 0.254 mmol) and (methoxymethylene)cycloheptane (53 mg, 0.381 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (4.5 mg, 3 mol %) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane to cyclohexane/EtOAc 9:1 as eluent. **$^{1}$H NMR** (500 MHz, Chloroform-*d*) δ 7.35 – 7.31 (m, 2H), 7.29 – 7.24 (m, 2H), 7.15 (ddt, *J* = 7.8, 6.8, 1.4 Hz, 1H), 6.53 (d, *J* = 15.9 Hz, 1H), 6.09 (dd, *J* = 15.9, 10.0 Hz, 1H), 3.37 (s, 3H), 3.05 (d, *J* = 6.3 Hz, 1H), 1.85 – 1.78 (m, 1H), 1.75 – 1.69 (m, 1H), 1.68 – 1.49 (m, 10H), 1.47 (dd, *J* = 10.0, 6.2 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.63, 130.33, 128.82, 127.04, 126.78, 125.99, 70.06, 58.87, 39.35, 32.62, 32.23, 28.88, 28.69, 26.78, 26.28, 26.12. **HRMS** (APCI Pos): calculated for $C_{18}H_{25}O$ $[M+H]^+$: 243.1743; found: 243.1746.

***cis*-1-((*E*)-3,5-Dibromostyryl)-2-methoxyspiro[2.9]dodecane (120c)**



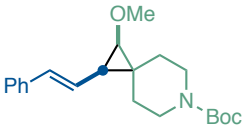

The title compound (pale yellow residue, 59 mg, 72% yield, 3:1 *cis*/*trans* ratio) was obtained following General Procedure I from (*E*)-7-(3,5-dibromostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (60 mg, 0.152 mmol) and (methoxymethylene)-cyclodecane (42 mg, 0.23 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (2.8 mg, 3 mol %) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane to cyclohexane/EtOAc 95:5 as a solvent. Prep TLC on $SiO_2$ using pentane/$Et_2O$ as eluent (98:2) allowed isolating pure ***cis*-3c**. **$^{1}$H NMR** (400 MHz, Chloroform-*d*) δ 7.46 (t, *J* = 1.7 Hz, 1H), 7.39 (d, *J* = 1.8 Hz, 2H), 6.39 (d, *J* = 15.8 Hz, 1H), 6.18 (dd, *J* = 15.8, 9.9 Hz, 1H), 3.39 (s, 3H), 3.13 (d, *J* = 6.2 Hz, 1H), 1.86 (dt, *J* = 15.0, 6.5 Hz, 1H), 1.78 – 1.69 (m, 1H), 1.59 (m, 14H), 1.44 (dd, *J* = 9.9, 6.2 Hz, 1H), 1.29 (dt, *J* = 14.6, 4.7 Hz, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.83, 131.46, 130.39, 127.35, 127.20, 123.02, 70.22, 58.68, 33.76, 33.34, 32.15, 26.33, 25.59, 25.37, 23.91, 23.55, 23.04, 23.02, 21.76. **HRMS** (APCI Pos): calculated for $C_{21}H_{29}{}^{79}Br_2O$ $[M+H]^+$: 455.0580; found: 455.0571.

**_cis_-1-Methoxy-2-((_E_)-styryl)spiro[2.11]tetradecane (120d)**



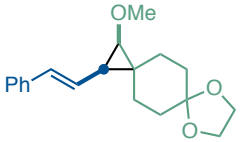

The title compound (pale yellow oil, 38 mg, 92% yield, 8:1 *cis*/*trans* ratio) was obtained following General Procedure I from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (30 mg, 0.127 mmol) and (methoxymethylene)cyclododecane (41 mg, 0.190 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (2.5 mg, 3 mol %) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane to cyclohexane/EtOAc 95:5 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.38 – 7.29 (m, 4H), 7.22 – 7.17 (m, 1H), 6.55 (d, *J* = 15.9 Hz, 1H), 6.20 (dd, *J* = 15.9, 10.0 Hz, 1H), 3.40 (s, 3H), 3.15 (d, *J* = 6.2 Hz, 1H), 1.74 – 1.65 (m, 1H), 1.62 – 1.51 (m, 5H), 1.45 (s, 1H), 1.43 – 1.34 (m, 16H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.30, 129.91, 128.46, 126.79, 126.40, 125.64, 68.89, 58.62, 32.99, 31.91, 31.82, 26.62, 26.27, 26.24, 22.34, 22.27, 22.17, 21.10, 20.67, 20.26. **HRMS** (APCI Pos): calculated for $C_{23}H_{35}O$ $[M+H]^+$: 327.2682; found: 327.2679.

***tert*-Butyl *cis*-1-methoxy-2-((*E*)-styryl)-6-azaspiro[2.5]octane-6-carboxylate (120e)**




The title compound (colorless viscous oil, 30 mg, 69% yield, 9:1 *cis*/*trans* ratio) was obtained following General Procedure I from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (30 mg, 0.127 mmol) and *tert*-butyl 4-(methoxymethylene)piperidine-1-carboxylate (44 mg, 0.190 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (2.4 mg, 3 mol %) after filtration through silica gel and purification by preparative TLC on $SiO_2$ using pentane/$Et_2O$ 9:1 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.32 – 7.25 (m, 4H), 7.18 – 7.14 (m, 1H), 6.57 (d, *J* = 15.9 Hz, 1H), 6.07 (dd, *J* = 15.9, 9.9 Hz, 1H), 3.51 – 3.38 (m, 4H), 3.37 (s, 3H), 3.18 (d, *J* = 6.1 Hz, 1H), 1.71 (dd, *J* = 20.9, 14.2 Hz, 2H), 1.49 (dd, *J* = 9.8, 6.1 Hz, 1H), 1.44 (s, 9H), 1.39 – 1.27 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 155.36, 138.24, 131.44, 128.88, 127.10, 126.03, 125.10, 79.72, 68.21, 58.99, 43.74, 31.28, 29.09, 28.83. **HRMS** (ESI Pos): calculated for $C_{21}H_{29}NNaO_3$ $[M+Na]^+$: 366.2040; found: 366.2036.

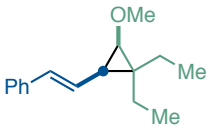
***cis*-1-Methoxy-2-((*E*)-styryl)-7,10-dioxadispiro[2.2.4$^6$.2$^3$]dodecane (120f)**




The title compound (amorphous residue, 38 mg, 85% yield, 12:1 *cis*/*trans* ratio) was obtained following General Procedure I from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (35 mg, 0.148 mmol) and 8-(methoxymethylene)-1,4-dioxaspiro[4.5]decane (41 mg, 0.222 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (2.8 mg, 3 mol %) after purification by flash column chromatography on $SiO_2$ using a gradient of pentane/$Et_2O$ 99:1 to 9:1 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.32 – 7.29 (m, 2H), 7.28 – 7.24 (m, 2H), 7.15 (ddt, *J* = 7.7, 6.7, 1.4 Hz, 1H), 6.55 (d, *J* = 15.9 Hz, 1H), 6.11 (dd, *J* = 15.9, 9.8 Hz, 1H), 3.95 – 3.92 (m, 4H), 3.38 (s, 3H), 3.17 (d, *J* = 6.1 Hz, 1H), 1.86 – 1.76 (m, 2H), 1.70 – 1.63 (m, 4H), 1.55 (ddd, *J* = 13.2, 8.1, 5.1 Hz, 1H), 1.45 (dd, *J* = 9.8, 6.1

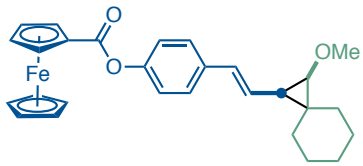
Hz, 1H), 1.31 (dt, *J* = 12.7, 5.6 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.47, 131.09, 128.82, 126.91, 126.03, 125.81, 109.60, 68.64, 64.65, 59.02, 33.96, 33.69, 33.54, 31.31, 29.63, 22.38. **HRMS** (APCI Pos): calculated for $C_{19}H_{25}O_3$ $[M+H]^+$: 301.1798; found: 301.1796.

***cis*-((*E*)-2-(2,2-Diethyl-3-methoxycyclopropyl)vinyl)benzene (120g)**



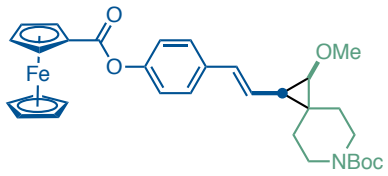

The title compound (yellow oil, 24 mg, 82% yield, 6:1 *cis*/*trans* ratio) was obtained following General Procedure I from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (30 mg, 0.127 mmol) and 3-(methoxymethylene)pentane (29 mg, 0.254 mmol, 2 equiv) using $[Rh_2(TFA)_4]$ (2.5 mg, 3 mol %) after purification by CombiFlash column chromatography on $SiO_2$ using a gradient of cyclohexane to cyclohexane/EtOAc 97:3 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.34 – 7.32 (m, 2H), 7.29 – 7.25 (m, 2H), 7.18 – 7.14 (m, 1H), 6.53 (d, *J* = 15.9 Hz, 1H), 6.15 (dd, *J* = 15.9, 10.0 Hz, 1H), 3.36 (d, *J* = 0.9 Hz, 3H), 3.09 (d, *J* = 6.2 Hz, 1H), 1.64 (m, 2H), 1.46 – 1.41 (m, 2H), 1.12 – 1.04 (m, 1H), 0.92 (dt, *J* = 12.2, 7.4 Hz, 6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.65, 130.47, 128.87, 128.82, 126.77, 125.99, 69.37, 59.31, 33.66, 32.03, 28.80, 17.32, 10.60, 10.02. **HRMS** (APCI Pos): calculated for $C_{16}H_{23}O$ $[M+H]^+$: 231.1743; found: 231.1742.

***cis*-4-((*E*)-2-(2-methoxyspiro[2.5]octan-1-yl)vinyl)phenyl ferrocenecarboxylate (120h)**




The title compound (amorphous orange residue, 49 mg, 61% yield, 8:1 *cis*/*trans* ratio) was obtained following General Procedure I from (*E*)-4-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)phenyl ferrocenecarboxylate (80 mg, 0.172 mmol) and (methoxymethylene)cyclohexane (44 mg, 0.345 mmol, 2 equiv) using $[Rh_2(TFA)_4]$ (3.1 mg, 3 mol %) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane/EtOAc 95:5 to 85:15 as eluent. This reaction was performed at 25 ºC instead of 40 ºC. Pure *cis* diastereoisomer was isolated by preparative TLC using 9:1 pentane/$Et_2O$ as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.38 – 7.33 (m, 2H), 7.11 – 7.04 (m, 2H), 6.54 (d, *J* = 15.9 Hz, 1H), 6.10 (dd, *J* = 15.9, 10.0 Hz, 1H), 4.94 (t, *J* = 2.0 Hz, 2H), 4.48 (t, *J* = 2.0 Hz, 2H), 4.28 (s, 5H), 3.37 (s, 3H), 3.10 (d, *J* = 6.1 Hz, 1H), 1.65 (s, 2H), 1.49 (s, 6H), 1.39 (dd, *J* = 9.9, 6.1 Hz, 1H), 1.31 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 170.72, 149.78, 136.26, 129.55, 126.82, 126.68, 122.02, 72.24, 71.01, 70.55, 70.31, 69.37, 58.98, 37.02, 31.96, 31.18, 30.06, 26.92, 25.55, 25.04. **HRMS** (ESI+): calculated for $C_{28}H_{30}{}^{56}FeNaO_3$ $[M+Na]^+$: 493.1437; found: 493.1428.

**_tert_-Butyl _cis_-1-((_E_)-4-((ferrocenecarbonyl)oxy)styryl)-2-methoxy-6-azaspiro[2.5]-octane-6-carboxylate (120i)**

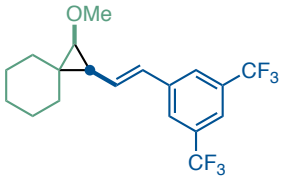



The title compound (amorphous orange foam, 17 mg, 46% yield, 10:1 *cis*/*trans* ratio) was obtained following General Procedure I from (*E*)-4-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)phenyl ferrocenecarboxylate (30 mg, 0.065 mmol) and *tert*-butyl 4-(methoxymethylene)piperidine-1-carboxylate (22 mg, 0.097 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (1.5 mg, 3 mol %) after purification by CombiFlash column chromatography with a 8:2 to 6:4 gradient of cyclohexane/EtOAc, and then preparative TLC on $SiO_2$ using pentane/$Et_2O$ 7:3 as eluent. This reaction was carried out under air, with HPLC grade solvent an a Rh(II) catalyst stored in a desiccator. Despite all our attempts, it was not possible to obtain this product in crystalline form. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.38 – 7.33 (m, 2H), 7.12 – 7.06 (m, 2H), 6.57 (d, *J* = 15.9 Hz, 1H), 6.04 (dd, *J* = 15.9, 9.8 Hz, 1H), 4.94 (t, *J* = 2.0 Hz, 2H), 4.48 (q, *J* = 1.7 Hz, 2H), 4.28 (s, 5H), 3.52 – 3.38 (m, 4H), 3.38 (s, 3H), 3.19 (d, *J* = 6.1 Hz, 1H), 1.75 (s, 2H), 1.50 (dd, *J* = 9.8, 6.1 Hz, 1H), 1.44 (s, 9H), 1.35 – 1.28 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 170.70, 150.03, 135.86, 130.57, 126.92, 125.24, 122.10, 79.75, 72.28, 71.01, 70.48, 70.32, 68.21, 59.01, 35.77, 31.27, 30.06, 29.14, 28.83. **HRMS** (ESI+): calculated for $C_{32}H_{37}NaO_3{}^{56}Fe$ $[M+Na]^+$: 594.1913; found: 594.1913.

**7-((_E_)-Styryl)-2-oxabicyclo[4.1.0]heptane (_endo_/_exo_ miture) (120j)**

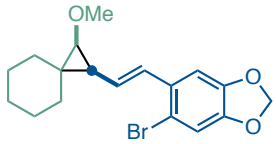

The title compound (pale yellow oil, 25 mg, 74% yield, 1.4:1 *endo*/*exo* mixture, unassigned) was obtained following General Procedure I from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (40 mg, 0.169 mmol) and 3,4-dihydro-2H-pyran (56 mg, 0.67 mmol, 4 equiv, commercially available) using $[Rh_2(TFA)_4]$ (3.0 mg, 3 mol %) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane to cyclohexane/EtOAc 97:3 as eluent. **$^1$H NMR** (*endo*/*exo* mixture, unassigned, 400 MHz, Chloroform-*d*) δ 7.42 – 7.38 (m, 2H), 7.34 – 7.29 (m, 5H), 7.23 – 7.18 (m, 2H), 6.64 (d, *J* = 16.0 Hz, 1H), 6.37 (dd, *J* = 15.9, 0.7 Hz, 1H), 6.28 (dd, *J* = 16.0, 8.8 Hz, 1H), 5.85 (dd, *J* = 15.8, 8.6 Hz, 1H), 3.84 – 3.75 (m, 2H), 3.65 (dtd, *J* = 10.8, 3.3, 1.4 Hz, 1H), 3.60 (dd, *J* = 7.3, 2.1 Hz, 1H), 3.47 – 3.34 (m, 2H), 2.13 – 1.94 (m, 3H), 1.91 – 1.83 (m, 1H), 1.70 – 1.61 (m, 2H), 1.60 – 1.52 (m, 3H), 1.31 – 1.19 (m, 2H). **$^{13}$C NMR** (*endo*/*exo* mixture, unassigned, 101 MHz, $CDCl_3$) δ 138.09, 137.68, 131.81, 130.78, 128.50, 128.46, 127.65, 126.65, 125.73, 125.62, 64.63, 64.52, 59.51, 55.34, 27.84, 24.16, 23.28, 22.40, 20.44, 19.32, 15.84, 15.24. **HRMS** (APCI Pos): calculated for $C_{14}H_{17}O$ $[M+H]^+$: 201.1274; found: 201.1278.

***cis*-1-((*E*)-3,5-Bis(trifluoromethyl)styryl)-2-methoxyspiro[2.5]octane (120k)**



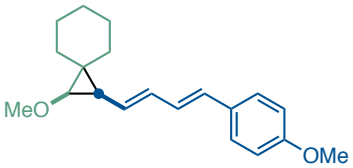

The title compound (pale yellow oil, 28 mg, 69% yield, 1.5:1 *cis*/*trans* ratio) was obtained following General Procedure I from (*E*)-7-(3,5-bis(trifluoromethyl)styryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (40 mg, 0.107 mmol) and (methoxymethylene)cyclohexane (21 mg, 0.161 mmol, 1.5 equiv) using [$Rh_2(TFA)_4$] (2.0 mg, 3 mol %) after purification by flash column chromatography on $SiO_2$ using pentane/$Et_2O$ 99:1 to 98:2 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.73 – 7.71 (m, 2H), 7.68 – 7.66 (m, 1H), 6.62 (d, *J* = 15.9 Hz, 1H), 6.33 (dd, *J* = 15.9, 10.0 Hz, 1H), 3.43 (s, 3H), 3.20 (t, *J* = 1.5 Hz, 1H), 1.74 – 1.69 (m, 1H), 1.64 – 1.61 (m, 1H), 1.53 (d, *J* = 10.8 Hz, 7H), 1.48 – 1.44 (m, 1H), 1.39 (d, *J* = 6.7 Hz, 1H). **$^{13}$C NMR** (101 MHz, Chloroform-*d*) δ 140.11, 131.66 – 131.52 (m), 131.03, 127.44, 125.67 – 124.84 (m), 123.44 (q, *J* = 273 Hz) 119.75 – 119.58 (m), 69.50, 58.75, 36.58, 34.27, 31.81, 30.66, 26.45, 25.22, 24.65. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -63.10. **HRMS** (APCI Pos): calculated for $C_{19}H_{21}F_6O$ $[M+H]^+$: 379.1491; found: 379.1499.

***cis*-5-Bromo-6-((*E*)-2-(2-methoxyspiro[2.5]octan-1-yl)vinyl)benzo[*d*][1,3]dioxole (120l)**




The title compound (pale yellow oil, 21 mg, 52% yield, 14:1 *cis*/*trans* ratio) was obtained following General Procedure I from (*E*)-5-bromo-6-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)benzo[*d*][1,3]dioxole (40 mg, 0.111 mmol) and (methoxymethylene)cyclohexane (22 mg, 0.167 mmol, 1.5 equiv) using [$Rh_2(TFA)_4$] (2.0 mg, 3 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 6.96 (s, 1H), 6.94 (s, 1H), 6.77 (d, *J* = 15.7 Hz, 1H), 5.93 (m, 3H), 5.92 (s, 2H), 3.36 (s, 3H), 3.10 (d, *J* = 6.0 Hz, 1H), 1.63 (t, *J* = 4.9 Hz, 2H), 1.54 – 1.47 (m, 6H), 1.42 (dd, *J* = 6.6, 3.3 Hz, 1H), 1.29 (dd, *J* = 6.8, 4.5 Hz, 1H), 1.22 – 1.17 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 147.96, 147.38, 131.83, 128.85, 128.00, 113.72, 112.89, 106.13, 101.95, 69.46, 59.00, 36.96, 31.97, 31.39, 26.91, 25.55, 25.53, 25.03. **HRMS** (APCI Pos): calculated for $C_{18}H_{22}{}^{79}BrO_3$ $[M+H]^+$: 365.0747; found: 365.0760.

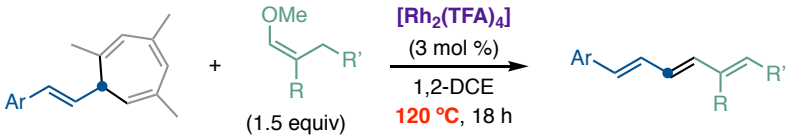
***cis*-1-Methoxy-2-((1*E*,3*E*)-4-(4-methoxyphenyl)buta-1,3-dien-1-yl)spiro[2.5]octane (120m)**




The title compound (pale yellow oil, 24 mg, 68% yield, 4:1 *cis*/*trans* ratio) was obtained following General Procedure I from 7-((1*E*,3*E*)-4-(4-methoxyphenyl)buta-1,3-dien-1-yl)-1,3,5-trimethylcyclohepta-1,3,5-triene (35 mg, 0.120 mmol) and (methoxy-methylene)cyclohexane (23 mg, 0.180 mmol, 1.5 equiv) using [$Rh_2(TFA)_4$] (2.3 mg, 3 mol %) after purification by preparative TLC on $SiO_2$ using pentane/$Et_2O$ 97:3 as eluent. **$^1$H NMR**

(500 MHz, Chloroform-*d*) δ 7.31 – 7.26 (m, 2H), 6.84 – 6.81 (m, 2H), 6.61 (ddd, *J* = 15.6, 10.5, 0.8 Hz, 1H), 6.37 (d, *J* = 15.6 Hz, 1H), 6.29 (ddt, *J* = 15.0, 10.5, 0.8 Hz, 1H), 5.48 (dd, *J* = 15.0, 9.3 Hz, 1H), 3.79 (s, 3H), 3.35 (s, 3H), 3.02 (d, *J* = 3.0 Hz, 1H), 1.61 – 1.42 (m, 10H), 1.40 (d, *J* = 5.7 Hz, 1H), 1.33 (dd, *J* = 9.3, 3.0 Hz, 1H), 1.30 – 1.27 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.21, 132.39, 131.13, 130.96, 129.21, 127.72, 127.58, 114.40, 72.54, 58.70, 55.65, 34.28, 34.20, 31.20, 31.09, 26.87, 26.08, 25.35. **HRMS** (APCI Pos): calculated for $C_{20}H_{27}O_2$ $[M+H]^+$: 299.2006; found: 299.2012.

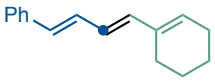
**General Procedure J for the One-Pot Assembly and Disassembly of Cyclopropyl Ethers to Give Trienes at 120 ºC**




A microwave vial equipped with a Teflon-coated magnetic stirring bar was charged with the corresponding 1,3,5-trimethyl-7-styryl-1,3,5-cycloheptatriene **44** (1.0 equiv) and the corresponding enol ether **119** (1.5 equiv). The vial was introduced in an argon-filled glovebox, and both reagents were dissolved in anhydrous 1,2-DCE (0.15 M), before $[Rh_2(TFA)_4]$ (3 mol %) was added. The vial was sealed with the corresponding microwave cap and taken outside the glovebox, and then stirred at 120 ºC for 18 hours. After confirming that the reaction was completed by TLC, the resulting mixture was concentrated in vacuum. The crude product was purified by flash column chromatography or preparative TLC on silica gel, using pentane or gradients of pentane/diethyl ether.

**Characterization Data for the Different *E,E,E*-Trienes**

**((1*E*,3*E*)-4-(Cyclohex-1-en-1-yl)buta-1,3-dien-1-yl)benzene (121a)**

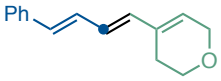



The title compound (white solid, 15 mg, 53% yield) was obtained following General Procedure J from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (30 mg, 0.127 mmol) and (methoxymethylene)cyclohexane (24 mg, 0.190 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (3 mg, 3 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. Characterization matched previously reported data.[215] **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.39 – 7.37 (m, 2H), 7.31 – 7.27 (m, 2H), 7.20 – 7.16 (m, 1H), 6.82 (dd, *J* = 15.6, 9.4 Hz, 1H), 6.52 (d, *J* = 15.6 Hz, 1H), 6.38 – 6.26 (m, 2H), 5.84 – 5.80 (m, 1H), 2.22 –

215 Tamura, R.; Kato, M.; Saegusa, K.; Kakihana, M.; Oda, D. Stereoselective E-olefin formation by Wittig-type olefination of aldehydes with allylic tributylphosphorus ylides derived from allylic nitro compounds. *J. Org. Chem.* **1987**, *52*, 4121–4124.

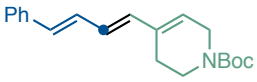
2.14 (m, 4H), 1.69 (tdd, *J* = 8.2, 5.1, 2.6 Hz, 2H), 1.62 (dtt, *J* = 9.2, 6.0, 2.6 Hz, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.12, 137.40, 136.42, 131.37, 131.15, 130.26, 128.94, 127.47, 126.50, 125.94, 26.54, 24.90, 22.87, 22.85. **HRMS** (APCI Positive): calculated for $C_{16}H_{19}$ $[M+H]^+$: 211.1487; found: 211.1487. **MP** 59–63 ºC.

**4-((1*E*,3*E*)-4-Phenylbuta-1,3-dien-1-yl)-3,6-dihydro-2*H*-pyran (121b)**



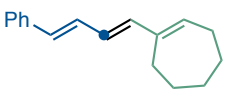

The title compound (yellow solid, 23 mg, 65% yield) was obtained following General Procedure J from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (40 mg, 0.169 mmol) and 4-(methoxymethylene)tetrahydro-2*H*-pyran (33 mg, 0.254 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (4 mg, 3 mol %) after purification by preparative TLC on $SiO_2$ using pentane/$Et_2O$ 98:2 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.40 – 7.37 (m, 2H), 7.32 – 7.28 (m, 2H), 7.22 – 7.18 (m, 1H), 6.86 – 6.80 (m, 1H), 6.56 (d, *J* = 15.5 Hz, 1H), 6.38 – 6.30 (m, 2H), 5.77 (tt, *J* = 3.1, 1.5 Hz, 1H), 4.26 (q, *J* = 2.7 Hz, 2H), 3.85 (t, *J* = 5.5 Hz, 2H), 2.32 (ttd, *J* = 5.5, 2.5, 1.4 Hz, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 137.79, 134.93, 133.98, 132.62, 129.57, 129.00, 127.79, 127.44, 127.39, 126.64, 66.22, 64.54, 25.35. **HRMS** (APCI Positive): calculated for $C_{15}H_{17}O$ $[M+H]^+$: 213.1274; found: 213.1272. **MP** 78–82 ºC.

***tert*-Butyl 4-((1*E*,3*E*)-4-phenylbuta-1,3-dien-1-yl)-3,6-dihydropyridine-1(2*H*)-carboxylate (121c)**




The title compound (amorphous yellow solid, 17 mg, 43% yield) was obtained following General Procedure J from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (30 mg, 0.127 mmol) and tert-butyl 4-(methoxymethylene)piperidine-1-carboxylate (44 mg, 0.190 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (2.3 mg, 3 mol %) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane/EtOAc 95:5 to 9:1 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.45 – 7.40 (m, 2H), 7.36 – 7.31 (m, 2H), 7.26 – 7.21 (m, 1H), 6.86 (ddd, *J* = 15.6, 7.6, 2.1 Hz, 1H), 6.60 (d, *J* = 15.6 Hz, 1H), 6.43 – 6.32 (m, 2H), 5.74 (s, 1H), 4.06 (d, *J* = 4.0 Hz, 2H), 3.62 – 3.57 (m, 2H), 2.35 (s, 2H), 1.50 (s, 9H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 154.85, 140.61, 137.42, 134.61, 132.26, 129.20, 128.63, 127.43, 127.27, 126.27, 79.67, 43.83, 31.63, 28.48, 24.71. **HRMS** (ESI Positive): calculated for $C_{20}H_{26}NO_2$ $[M+H]^+$: 312.1964; found: 312.1960.

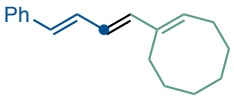
**1-((1*E*,3*E*)-4-Phenylbuta-1,3-dien-1-yl)cyclohept-1-ene (121d)**




The title compound (colorless amorphous residue, 25 mg, 44% yield) was obtained following General Procedure J from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (60 mg, 0.254 mmol) and (methoxymethylene)cycloheptane (53 mg, 0.381 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (5 mg, 3 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. This reaction was performed at 100 ºC and 0.4 M in 1,2-

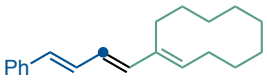
DCE. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.39 – 7.37 (m, 2H), 7.30 – 7.27 (m, 2H), 7.20 – 7.16 (m, 1H), 6.85 (ddd, *J* = 15.6, 6.9, 2.9 Hz, 1H), 6.52 (d, *J* = 15.6 Hz, 1H), 6.33 (d, *J* = 6.8 Hz, 2H), 5.97 (t, *J* = 6.9 Hz, 1H), 2.39 – 2.35 (m, 2H), 2.27 – 2.22 (m, 2H), 1.80 – 1.75 (m, 2H), 1.56 – 1.49 (m, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 143.73, 138.25, 135.90, 131.26, 130.33, 129.83, 128.94, 127.44, 126.50, 126.06, 32.64, 29.20, 27.70, 27.18, 26.68. **HRMS** (APCI Positive): calculated for $C_{17}H_{21}$ $[M+H]^+$: 225.1638; found: 225.1643.

**(*E*)-1-((1*E*,3*E*)-4-phenylbuta-1,3-dien-1-yl)cyclooct-1-ene (121e)**



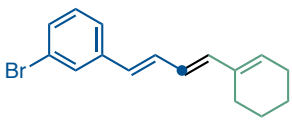

The title compound (pale yellow amorphous solid, 22 mg, 54% yield) was obtained following General Procedure J from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (40 mg, 0.169 mmol) and (methoxymethylene)cyclooctane (40 mg, 0.255 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (3.1 mg, 3 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.44 – 7.40 (m, 2H), 7.35 – 7.30 (m, 2H), 7.24 – 7.20 (m, 1H), 6.87 (ddd, *J* = 15.5, 8.5, 1.2 Hz, 1H), 6.56 (d, *J* = 15.6 Hz, 1H), 6.44 – 6.31 (m, 2H), 5.83 (t, *J* = 8.3 Hz, 1H), 2.52 – 2.45 (m, 2H), 2.31 – 2.24 (m, 2H), 1.65 – 1.48 (m, 9H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 139.58, 137.79, 136.91, 133.80, 130.95, 130.03, 128.59, 127.08, 126.20, 126.14, 30.42, 28.66, 27.44, 26.95, 26.01, 24.42. **HRMS** (APCI Positive): calculated for $C_{18}H_{23}$ $[M+H]^+$: 239.1794; found: 239.1793.

**(*E*)-1-((1*E*,3*E*)-4-Phenylbuta-1,3-dien-1-yl)cyclodec-1-ene (121f)**




The title compound (white solid, 25 mg, 55% yield) was obtained following General Procedure J from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (25 mg, 0.106 mmol) and (methoxymethylene)cyclodecane (47 mg, 0.254 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (3.1 mg, 3 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.44 – 7.39 (m, 2H), 7.33 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.24 – 7.19 (m, 1H), 6.86 (dd, *J* = 15.5, 9.3 Hz, 1H), 6.56 (d, *J* = 15.6 Hz, 1H), 6.45 – 6.31 (m, 2H), 5.62 (t, *J* = 8.6 Hz, 1H), 2.52 (t, *J* = 6.6 Hz, 2H), 2.41 (q, *J* = 7.4 Hz, 2H), 1.72 – 1.61 (m, 4H), 1.50 – 1.43 (m, *J* = 4.7, 4.0 Hz, 6H), 1.29 (d, *J* = 5.8 Hz, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 137.78, 137.55, 137.48, 135.41, 130.90, 130.15, 128.59, 127.08, 126.66, 126.13, 28.20, 27.85, 27.68, 25.15, 24.88, 23.47, 21.38, 20.70. **HRMS** (APCI Positive): calculated for $C_{20}H_{27}$ $[M+H]^+$: 267.2107; found: 267.2107. **MP** 84–86 ºC.

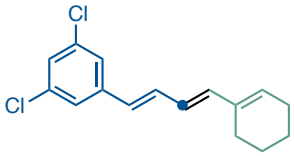
**1-Bromo-3-((1*E*,3*E*)-4-(cyclohex-1-en-1-yl)buta-1,3-dien-1-yl)benzene (121g)**




The title compound (pale yellow amorphous solid, 19 mg, 52% yield) was obtained following General Procedure J from (*E*)-7-(3-bromostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (40 mg, 0.127 mmol) and (methoxymethylene)cyclohexane (24 mg, 0.190 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$

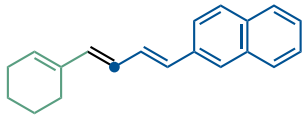
(2.3 mg, 3 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.55 (t, *J* = 1.8 Hz, 1H), 7.34 – 7.27 (m, 2H), 7.18 (t, *J* = 7.8 Hz, 1H), 6.84 (dd, *J* = 15.5, 10.1 Hz, 1H), 6.46 (d, *J* = 15.6 Hz, 1H), 6.40 (d, *J* = 15.4 Hz, 1H), 6.30 (dd, *J* = 15.4, 10.1 Hz, 1H), 5.92 – 5.84 (m, 1H), 2.22 (ddt, *J* = 8.6, 6.1, 3.1 Hz, 4H), 1.73 (qq, *J* = 4.8, 2.7, 2.2 Hz, 2H), 1.65 (qd, *J* = 5.9, 2.1 Hz, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 139.99, 138.13, 135.98, 131.56, 131.34, 130.04, 129.81, 129.23, 128.83, 125.06, 124.74, 122.82, 26.19, 24.50, 22.44. **HRMS** (APCI Pos): calculated for $C_{16}H_{18}{}^{79}Br$ $[M+H]^+$: 289.0592; found: 289.0592.

**1,3-Dichloro-5-((1*E*,3*E*)-4-(cyclohex-1-en-1-yl)buta-1,3-dien-1-yl)benzene (121h)**



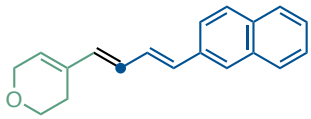

The title compound (pale yellow solid, 15 mg, 54% yield) was obtained following General Procedure J from (*E*)-7-(3,5-dichlorostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (30 mg, 0.098 mmol) and (methoxymethylene)cyclohexane (19 mg, 0.147 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (3.0 mg, 3 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.22 (d, *J* = 1.8 Hz, 2H), 7.14 (t, *J* = 1.8 Hz, 1H), 6.81 (dd, *J* = 15.5, 10.5 Hz, 1H), 6.36 (dd, *J* = 15.4, 12.2 Hz, 2H), 6.24 (dd, *J* = 15.4, 10.5 Hz, 1H), 5.90 – 5.84 (m, 1H), 2.18 (tt, *J* = 6.6, 4.6 Hz, 4H), 1.69 (tdd, *J* = 7.9, 4.8, 2.4 Hz, 2H), 1.63 – 1.58 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.23, 139.48, 136.28, 135.44, 133.01, 132.64, 128.25, 126.95, 125.00, 124.64, 30.07, 26.58, 24.83, 22.76. **HRMS** (APCI Positive): calculated for $C_{16}H_{17}Cl_2$ $[M+H]^+$: 279.0702; found: 279.0708. **MP** 80–85 ºC

**2-((1*E*,3*E*)-4-(Cyclohex-1-en-1-yl)buta-1,3-dien-1-yl)naphthalene (121i)**



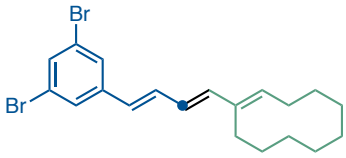
The title compound (amorphous yellow solid, 14 mg, 51% yield) was obtained following General Procedure J from (E)-2-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)naphthalene (30 mg, 0.105 mmol) and (methoxymethylene)cyclohexane (26 mg, 0.209 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (3.2 mg, 3 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.79 – 7.73 (m, 3H), 7.72 – 7.69 (m, 1H), 7.61 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.44 – 7.37 (m, 2H), 6.99 – 6.91 (m, 1H), 6.68 (d, *J* = 15.5 Hz, 1H), 6.42 – 6.30 (m, 2H), 5.87 – 5.82 (m, 1H), 2.22 (tt, *J* = 6.4, 2.0 Hz, 2H), 2.18 (ddt, *J* = 8.5, 6.3, 2.8 Hz, 2H), 1.73 – 1.68 (m, 2H), 1.65 – 1.60 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 137.60, 136.47, 135.66, 134.12, 133.17, 131.47, 131.31, 130.69, 128.51, 128.24, 128.02, 126.60, 126.22, 125.99, 123.84, 30.07, 26.56, 24.91, 22.86. **HRMS** (APCI Positive): calculated for $C_{20}H_{21}$ $[M+H]^+$: 261.1638; found: 261.1633.

**4-((1*E*,3*E*)-4-(Naphthalen-2-yl)buta-1,3-dien-1-yl)-3,6-dihydro-2*H*-pyran (121j)**



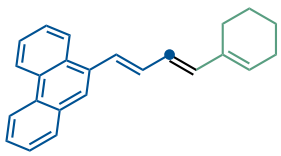
The title compound (pale yellow solid, 13 mg, 47% yield) was obtained following General Procedure J from (*E*)-2-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)naphthalene (25 mg, 0.106 mmol) and 4-(methoxymethylene)tetrahydro-2*H*-pyran (21 mg, 0.158 mmol, 1.5 equiv) using [$Rh_2(TFA)_4$] (3.1 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane/$Et_2O$ 97:3 as eluent. The product contained an inseparable impurity, and the yield was corrected by $^1$H NMR with an internal standard. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.77 (td, *J* = 6.0, 2.6 Hz, 3H), 7.72 (d, *J* = 1.7 Hz, 1H), 7.61 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.45 – 7.39 (m, 2H), 6.96 (ddd, *J* = 15.6, 6.8, 3.0 Hz, 1H), 6.73 (d, *J* = 15.5 Hz, 1H), 6.40 (d, *J* = 6.6 Hz, 2H), 5.79 (td, *J* = 3.1, 1.5 Hz, 1H), 4.27 (q, *J* = 2.7 Hz, 2H), 3.87 (t, *J* = 5.5 Hz, 2H), 2.36 – 2.32 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 135.33, 135.10, 134.08, 134.03, 133.31, 132.72, 129.97, 128.60, 128.30, 128.04, 127.56, 127.46, 126.68, 126.57, 126.19, 123.78, 66.23, 64.54, 25.37. **HRMS** (APCI Positive): calculated for $C_{19}H_{19}O$ $[M+H]^+$: 263.1430; found: 263.1426. **MP** 149–152 ºC.

**(*E*)-1-((1*E*,3*E*)-4-(3,5-Dibromophenyl)buta-1,3-dien-1-yl)cyclodec-1-ene (121k)**



The title compound (white solid, 31.5 mg, 49% yield) was obtained following General Procedure J from (*E*)-7-(3,5-dibromostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (60 mg, 0.152 mmol) and (methoxymethylene)cyclodecane (42 mg, 0.228 mmol, 1.5 equiv) using [$Rh_2(TFA)_4$] (2.9 mg, 3 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.44 (t, *J* = 1.7 Hz, 1H), 7.41 (d, *J* = 1.8 Hz, 2H), 6.79 (dd, *J* = 15.5, 9.4 Hz, 1H), 6.38 – 6.27 (m, 3H), 5.63 (t, *J* = 8.6 Hz, 1H), 2.47 (t, *J* = 6.6 Hz, 2H), 2.38 (q, *J* = 7.3 Hz, 2H), 1.67 – 1.58 (m, 4H), 1.42 (q, *J* = 6.1, 5.3 Hz, 5H), 1.28 – 1.22 (m, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.90, 140.12, 137.72, 137.30, 133.35, 132.32, 127.95, 127.89, 126.07, 123.47, 106.96, 28.47, 28.28, 27.99, 25.47, 25.19, 23.79, 21.77, 21.03. **HRMS** (APCI Pos): calculated for $C_{20}H_{25}{}^{79}Br_2$ $[M+H]^+$: 423.0318; found: 423.0317. **MP** 93–95 ºC.

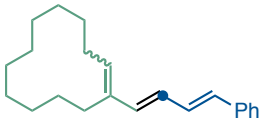
**9-((1*E*,3*E*)-4-(Cyclohex-1-en-1-yl)buta-1,3-dien-1-yl)phenanthrene (121l)**



The title compound (yellow solid, 13 mg, 47% yield) was obtained following General Procedure J from (*E*)-9-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)phenanthrene (30 mg, 0.089 mmol) and (methoxymethylene)cyclohexane (17 mg, 0.134 mmol, 1.5 equiv) using [$Rh_2(TFA)_4$] (2.7 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.77 – 8.73 (m, 1H), 8.67

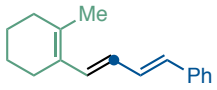
(dd, *J* = 7.6, 1.8 Hz, 1H), 8.27 – 8.23 (m, 1H), 7.72 – 7.58 (m, 6H), 7.33 (d, *J* = 15.2 Hz, 1H), 7.05 – 6.97 (m, 1H), 6.56 – 6.44 (m, 2H), 5.94 – 5.88 (m, 1H), 2.31 (td, *J* = 6.0, 2.1 Hz, 2H), 2.26 – 2.20 (m, 2H), 1.77 (qd, *J* = 6.3, 2.6 Hz, 2H), 1.71 – 1.65 (m, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 137.49, 136.07, 133.89, 133.09, 131.91, 131.16, 130.61, 130.47, 130.04, 128.60, 128.02, 126.76, 126.58, 126.43, 126.33, 125.78, 124.50, 123.82, 123.09, 122.51, 29.72, 26.22, 24.59, 22.52. **HRMS** (APCI Positive): calculated for $C_{24}H_{23}$ $[M+H]^+$: 311.1794; found: 311.1792. **MP** 101–105 ºC.

**1-((1*E*,3*E*)-4-Phenylbuta-1,3-dien-1-yl)cyclododec-1-ene (121m)**




The title compound (white solid, 23 mg, 61% combined yield *trans*/*cis*, confirmed by $^1$H NMR with an internal standard) was obtained following General Procedure J from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (30 mg, 0.127 mmol) and (methoxymethylene)cyclododecane (41 mg, 0.190 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (2.3 mg, 3 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. Further purification by preparative TLC on $SiO_2$ with pentane allowed separating both *trans* and *cis* macrocycles (the latter slightly impure). **$^1$H NMR** (major, *cis*-macrocycle, 400 MHz, Chloroform-*d*) δ 7.44 – 7.39 (m, 2H), 7.32 (dd, *J* = 8.5, 6.9 Hz, 2H), 7.24 – 7.19 (m, 1H), 6.85 (dd, *J* = 15.6, 9.8 Hz, 1H), 6.56 (d, *J* = 15.6 Hz, 1H), 6.43 – 6.27 (m, 2H), 5.60 (t, *J* = 8.1 Hz, 1H), 2.39 (t, *J* = 6.9 Hz, 2H), 2.21 (q, *J* = 7.5 Hz, 2H), 1.67 – 1.60 (m, 2H), 1.58 – 1.48 (m, 5H), 1.42 – 1.30 (m, 9H). **$^{13}$C NMR** (major, *cis*-macrocycle 101 MHz, $CDCl_3$) δ 138.38, 137.86, 137.80, 135.22, 130.82, 130.11, 128.58, 127.06, 126.83, 126.12, 26.92, 26.55, 25.74, 25.30, 25.25, 25.01, 23.68, 23.52, 23.08, 22.25. **$^1$H NMR** (minor, *trans*-macrocycle, 400 MHz, Chloroform-*d*) δ 7.45 – 7.41 (m, 2H), 7.36 – 7.32 (m, 2H), 7.23 (td, *J* = 5.6, 1.3 Hz, 1H), 6.94 (dd, *J* = 15.5, 10.5 Hz, 1H), 6.72 (d, *J* = 15.5 Hz, 1H), 6.60 (d, *J* = 15.6 Hz, 1H), 6.53 – 6.46 (m, 1H), 5.60 (t, *J* = 8.1 Hz, 1H), 2.37 – 2.28 (m, 4H), 1.61 – 1.57 (m, 4H), 1.41 – 1.31 (m, 12H). **MP** (major, *Z*-macrocycle) 73–76 ºC. **HRMS** (APCI Positive): calculated for $C_{22}H_{31}$ $[M+H]^+$: 295.2420; found: 295.2427.

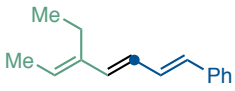
**((1*E*,3*E*)-4-(2-Methylcyclohex-1-en-1-yl)buta-1,3-dien-1-yl)benzene (121n)**




The title compound (pale yellow amorphous residue, 17 mg, 49% yield, 3:1 rr) was obtained following General Procedure J from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (25 mg, 0.106 mmol) and 1-(methoxymethylene)-2-methylcyclohexane (32 mg, 0.222 mmol, 1.5 equiv, 4:1 *E*/*Z* mixture) using $[Rh_2(TFA)_4]$ (2.7 mg, 3 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.41 – 7.36 (m, 2H), 7.30 – 7.27 (m, 2H), 7.20 – 7.18 (m, 1H), 6.89 (ddd, *J* = 15.6, 10.6, 0.9 Hz, 1H), 6.81 (d, *J* = 15.4 Hz, 1H), 6.52 (d, *J* = 15.5 Hz, 1H), 6.37 – 6.30 (m, 1H), 2.19 (d, *J* = 8.0 Hz, 2H), 2.11 (d, *J* = 6.5 Hz, 3H), 1.71 – 1.57 (m, 6H). **$^{13}$C NMR** (126 MHz,

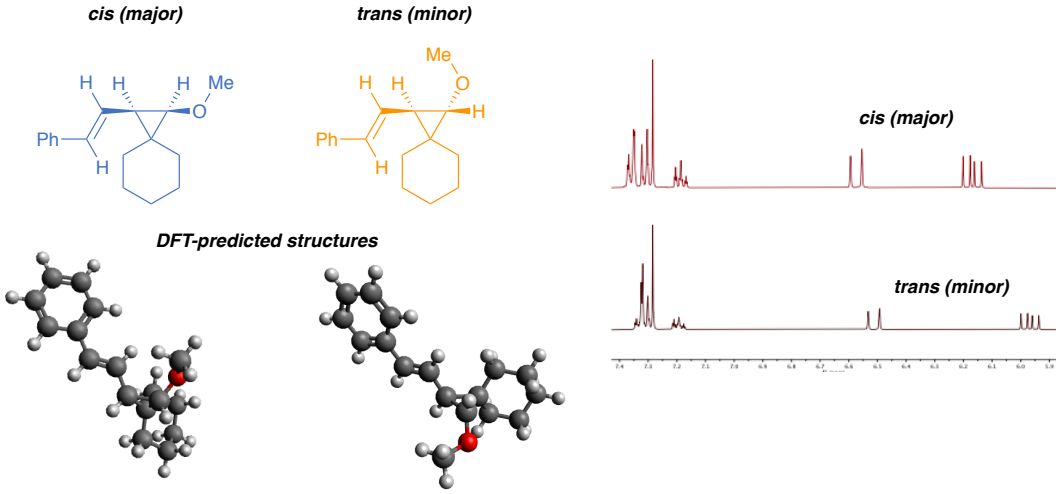
$CDCl_3$) δ 138.23, 135.33, 132.59, 130.94, 128.93, 128.80, 128.57, 127.35, 126.47, 126.28, 33.62, 30.69, 25.82, 23.23, 19.85. **HRMS** (APCI Positive): calculated for $C_{17}H_{19}$ $[M-H]^+$: 223.1481; found: 223.1482.

**((1*E*,3*E*,5*E*)-5-Ethylhepta-1,3,5-trien-1-yl)benzene (121o)**

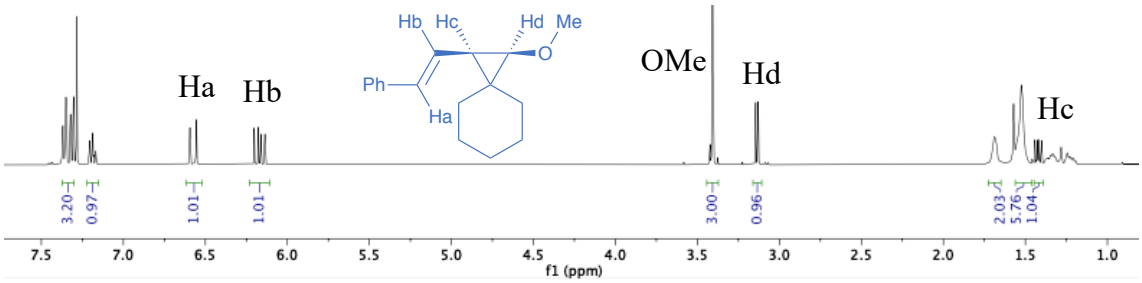



The title compound (pale yellow residue, 10 mg, 39% yield) was obtained following General Procedure J from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (30 mg, 0.127 mmol) and 3-(methoxymethylene)pentane (29 mg, 0.254 mmol, 2 equiv) using $[Rh_2(TFA)_4]$ (2.3 mg, 3 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.39 – 7.36 (m, 2H), 7.31 – 7.27 (m, 2H), 7.20 – 7.16 (m, 1H), 6.82 (dd, *J* = 15.6, 9.9 Hz, 1H), 6.52 (d, *J* = 15.6 Hz, 1H), 6.37 – 6.22 (m, 2H), 5.58 (q, *J* = 7.1 Hz, 1H), 2.29 (q, *J* = 7.6 Hz, 2H), 1.75 (d, *J* = 7.1 Hz, 3H), 1.03 (t, *J* = 7.6 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.64, 138.14, 137.40, 131.21, 130.41, 128.94, 127.85, 127.43, 126.48, 126.24, 30.06, 19.88, 14.12, 13.67. **HRMS** (APCI Positive): calculated for $C_{15}H_{17}$ $[M+H]^+$: 197.1325; found: 197.1321.

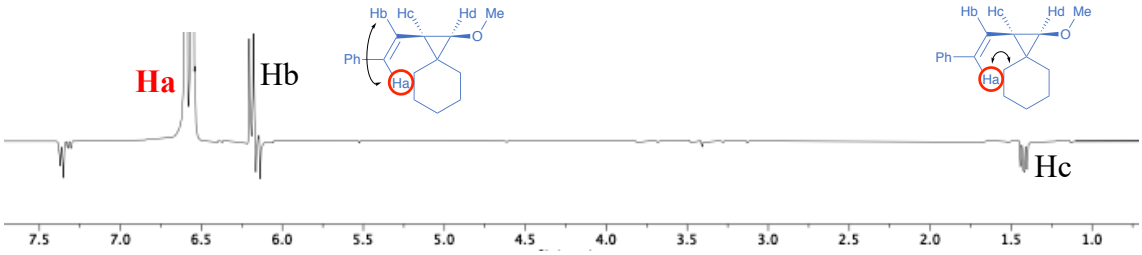
## Determination of the Relative Configuration of the Cyclopropyl Ethers by nOe NMR



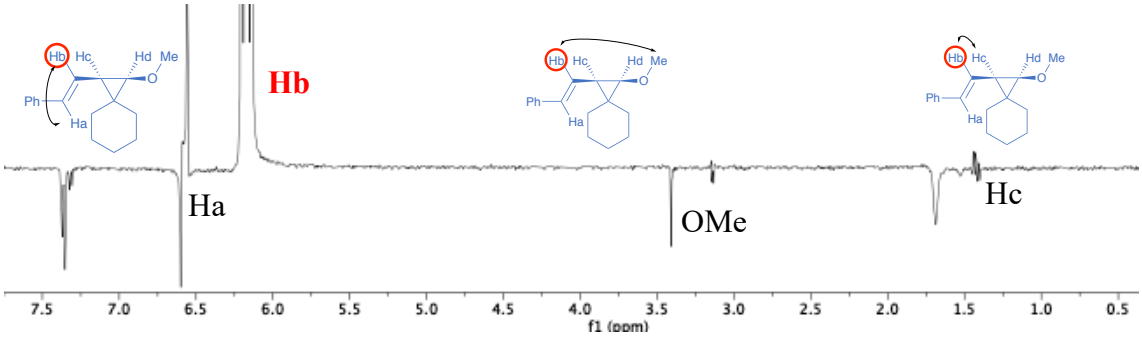

## Full characterization of *cis* isomer:



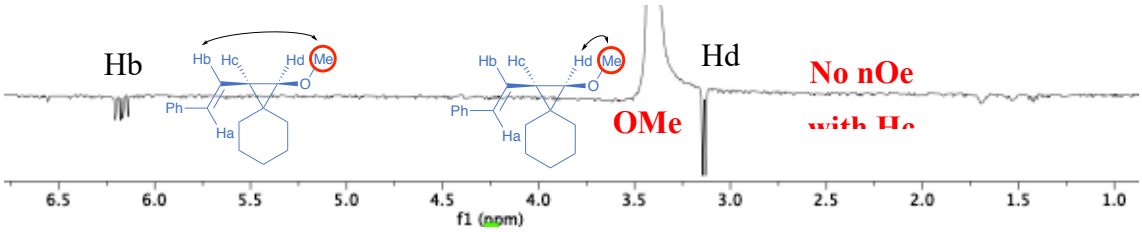

## GOESY (nOe) at 6.57 ppm (Ha)




## GOESY (nOe) at 6.17 ppm (Hb)

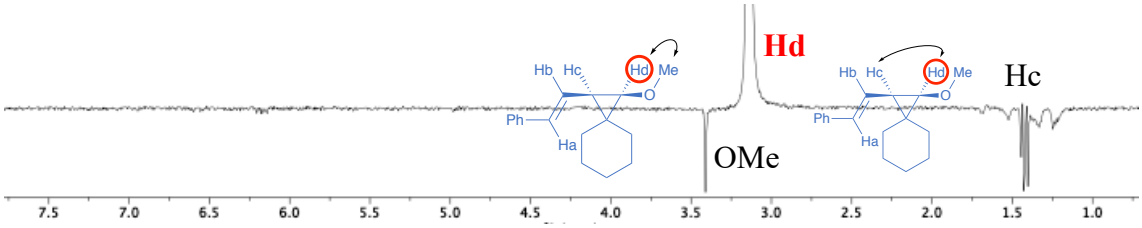


**GOESY (nOe) at 3.40 ppm (MeO)**



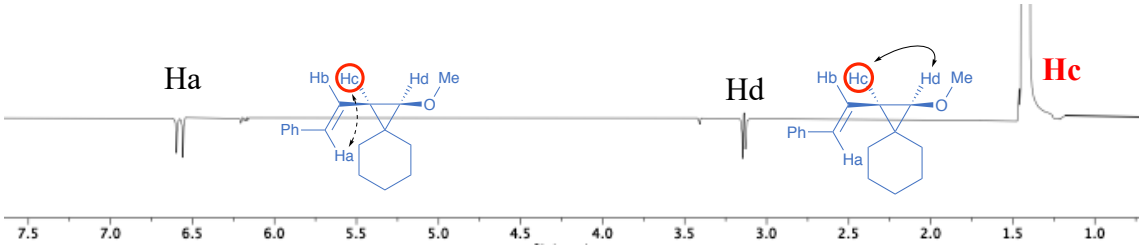

No nOe correlation between MeO and Hc: evidence of *cis* configuration.

**GOESY (nOe) at 3.17 (Hd)**



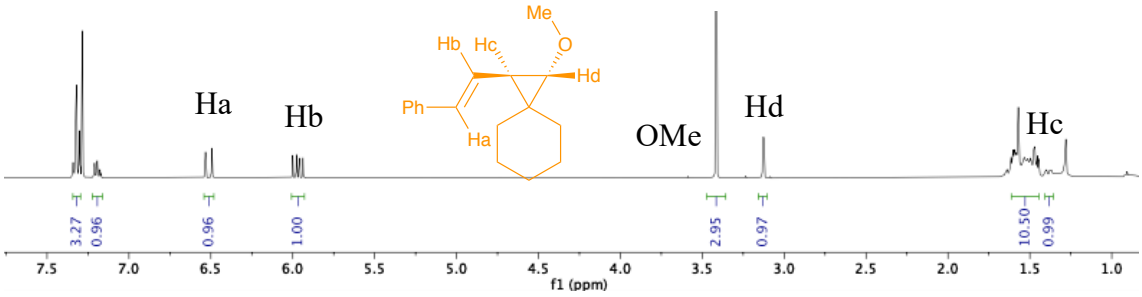

nOe correlation between Hd and Hc: evidence of *cis* configuration.

**GOESY (nOe) at 1.42 (Hc)**

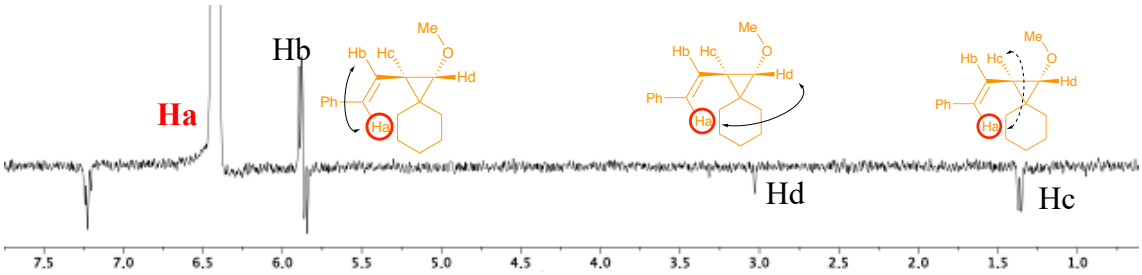



nOe correlation between Hc and Hd: evidence of *cis* configuration

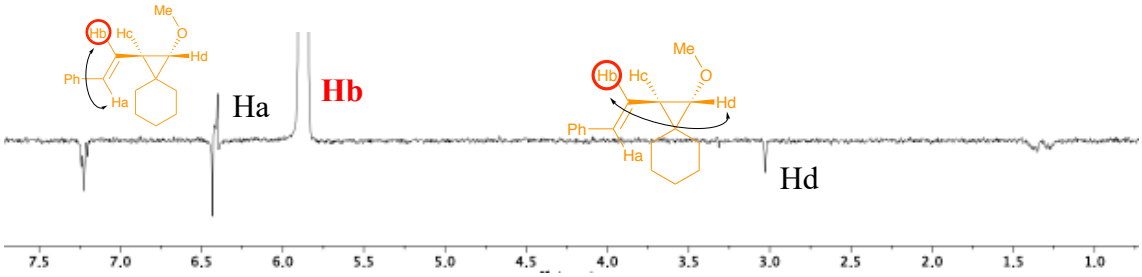
**Full characterization of *trans* isomer:**



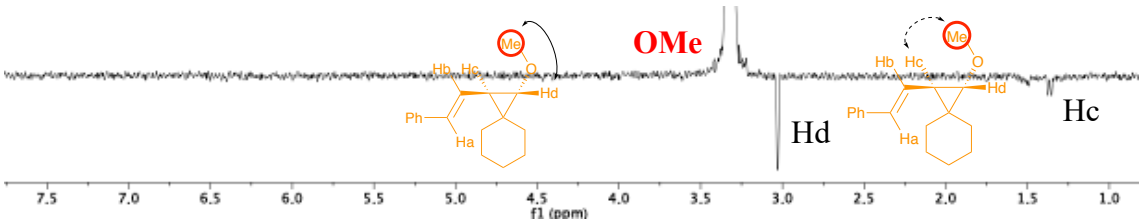

**GOESY (nOe) at 6.51 (Ha)**




**GOESY (nOe) at 5.96 (Hb)**

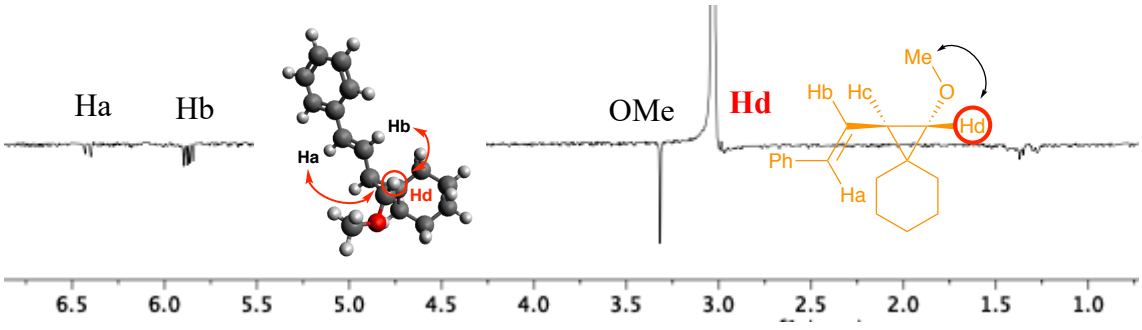



**GOESY (nOe) at 3.41 (MeO)**




nOe correlation between MeO and Hc: evidence of *trans* configuration

**GOESY (nOe) at 3.12 (Hd)**

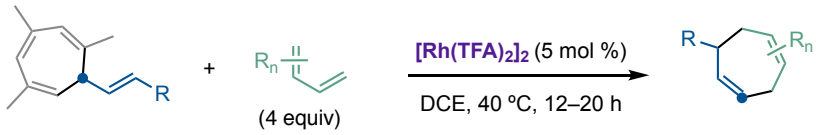



nOe correlation between Hd and Ha/Hb: evidence of *trans* configuration

### Synthesis of Substrates for the (4+3) Cycloaddition

Trimethylstyryl cycloheptatrienes **44** were prepared according to the procedure described in the Methods Section II.9 of Chapter II. Most 1,3-dienes were commercially available. 1,3-Cyclopentadiene was obtained by cracking and distillation of its commercial dimer and used immediately afterwards. 1,3-Butadiene was purchased from Sigma-Aldrich as a 20% solution in toluene.

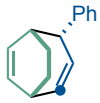
### General Procedure K for the Synthesis of 1,4-Cycloheptadienes




A screw-cap culture tube or microwave vial equipped with a Teflon-coated magnetic stirring bar was charged with the corresponding 1,3,5-trimethyl-7-styryl-1,3,5-cycloheptatriene **44** (1.0 equiv) and the corresponding 1,3-diene (4 equiv). The vial was introduced in an argon-filled glovebox, and both reagents were dissolved in anhydrous 1,2-DCE (0.1 M), before $[Rh_2(TFA)_4]$ (5 mol %) was added. The vial was closed and taken outside the glovebox, and then stirred at 40 ºC for 12–20 hours. After confirming that the reaction was completed by TLC, the resulting mixture was concentrated in vacuum, adsorbed into silica gel, and purified by flash column chromatography or preparative TLC on silica gel, using pentane or gradients of pentane/diethyl ether. For the cases in which the divinylcyclopropane **(122')** is obtained at 40 ºC, characterization data is also included for that product.

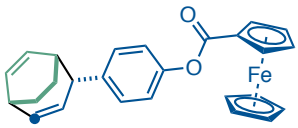
### Characterization Data for the Different 1,4-Cycloheptadienes (122)

#### (±)-(1*S*,4*R*,5*R*)-4-Phenylbicyclo[3.2.2]nona-2,6-diene (122a)



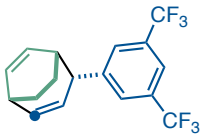

The title compound (pale yellow oil, 163 mg, 82% yield) was obtained following General Procedure K from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (240 mg, 1.02 mmol) and 1,3-cyclohexadiene (324 mg, 4.02 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (13.6 mg, 3 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.28 – 7.24 (m, 2H), 7.22 – 7.16 (m, 3H), 6.43 (dd, *J* = 8.8, 7.4 Hz, 1H), 6.16 (ddd, *J* = 10.7, 8.3, 2.3 Hz, 1H), 5.58 – 5.49 (m, 1H), 5.35 (ddd, *J* = 10.9, 3.8, 1.8 Hz, 1H), 3.51 (td, *J* = 3.8, 2.4 Hz, 1H), 2.75 – 2.65 (m, 2H), 2.11 (ddt, *J* = 12.0, 9.7, 2.5 Hz, 1H), 2.06 – 1.99 (m, 1H), 1.93 (dddd, *J* = 13.5, 11.3, 6.8, 2.9 Hz, 1H), 1.75 – 1.67 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 143.70, 138.70, 134.01, 130.77, 129.28, 128.65, 128.30, 126.49, 51.89, 39.94, 33.11, 30.84, 26.58. **HRMS** (APCI Pos): calculated for $C_{15}H_{15}$ $[M-H]^+$: 195.1168; found: 195.1168.

**(±)-(4-((1*R*,2*R*,5*S*)-Bicyclo[3.2.2]nona-3,6-dien-2-yl)phenyl ferrocenoylate (122b)**



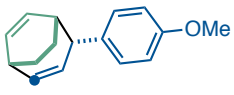

The title compound (orange solid, 36 mg, 72% yield) was obtained following General Procedure K from (*E*)-4-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)phenyl ferrocenoylate (55 mg, 0.118 mmol) and 1,3-cyclohexadiene (38 mg, 0.47 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (3.5 mg, 5 mol %) after purification by preparative TLC in 95:5 pentane/$Et_2O$ (3 elutions). **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.24 – 7.20 (m, 2H), 7.09 – 7.03 (m, 2H), 6.43 (dd, *J* = 8.7, 7.4 Hz, 1H), 6.16 (ddd, *J* = 10.7, 8.3, 2.3 Hz, 1H), 5.59 – 5.53 (m, 1H), 5.34 (ddd, *J* = 10.9, 3.8, 1.7 Hz, 1H), 4.95 (t, *J* = 1.7 Hz, 2H), 4.48 (t, *J* = 1.8 Hz, 2H), 4.30 (m, 5H), 3.53 (td, *J* = 3.8, 2.3 Hz, 1H), 2.74 – 2.65 (m, 2H), 2.11 (ddt, *J* = 12.1, 9.6, 2.6 Hz, 1H), 2.06 – 1.99 (m, 1H), 1.93 (dddd, *J* = 13.5, 11.2, 6.8, 2.9 Hz, 1H), 1.75 – 1.67 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 170.73, 149.60, 140.98, 138.80, 134.10, 130.62, 129.59, 129.22, 121.39, 72.34, 71.09, 70.72, 70.40, 51.27, 39.90, 33.11, 30.80, 26.48. **HRMS** (ESI+): calculated for $C_{26}H_{24}NaO_2{}^{56}Fe$ $[M+Na]^+$: 447.1018; found: 447.1013. **MP** 120–124 ºC.

**(±)-(1*S*,4*R*,5*R*)-4-(3,5-Bis(trifluoromethyl)phenyl)bicyclo[3.2.2]nona-2,6-diene (122c)**




The title compound (colorless oil, 60 mg, 67% yield) was obtained following General Procedure K from (*E*)-7-(3,5-bis(trifluoromethyl)styryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (100 mg, 0.27 mmol) and 1,3-cyclohexadiene (86 mg, 1.07 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (7.9 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.70 (d, *J* = 2.2 Hz, 1H), 7.63 (d, *J* = 1.7 Hz, 2H), 6.51 – 6.46 (m, 1H), 6.25 (ddd, *J* = 10.7, 8.4, 2.2 Hz, 1H), 5.47 – 5.41 (m, 1H), 5.28 (ddd, *J* = 10.9, 3.9, 1.8 Hz, 1H), 3.63 (td, *J* = 3.9, 2.3 Hz, 1H), 2.79 – 2.73 (m, 1H), 2.70 – 2.65 (m, 1H), 2.13 (ddt, *J* = 12.0, 9.5, 2.6 Hz, 1H), 2.06 – 1.94 (m, 2H), 1.76 – 1.69 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 146.03, 139.78, 135.64, 131.60 (q, *J* = 31 Hz), 128.87 (br), 128.59, 127.97, 123.87 (q, *J* = 273 Hz), 120.63 (quint, *J* = 3.9 Hz), 51.12, 39.63, 33.10, 30.52, 26.24. **$^{19}$F NMR** (471 MHz, $CDCl_3$) δ -63.11. **HRMS** (APCI Pos): calculated for $C_{17}H_{15}F_6$ $[M+H]^+$: 333.1072; found: 333.1073.

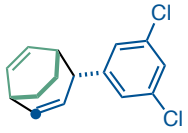
**(±)-(1*S*,4*R*,5*R*)-4-(4-Methoxyphenyl)bicyclo[3.2.2]nona-2,6-diene (122d)**




The title compound (pale yellow oil, 63 mg, 82% yield) was obtained following General Procedure K from (*E*)-7-(4-methoxystyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (90 mg, 0.338 mmol) and 1,3-cyclohexadiene (108 mg, 1.35 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (10.0 mg, 5 mol %) after purification by preparative TLC on $SiO_2$ using pentane/$Et_2O$ 99:1 as eluent (3 elutions). **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.18 – 7.13 (m, 2H), 6.87 – 6.82 (m, 2H), 6.50 – 6.43 (m, 1H), 6.17 (ddd, *J* = 10.7, 8.3, 2.3 Hz, 1H),

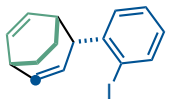
5.61 – 5.55 (m, 1H), 5.36 (dddd, *J* = 10.9, 3.8, 1.8, 0.6 Hz, 1H), 3.82 (s, 3H), 3.50 (td, *J* = 3.8, 2.3 Hz, 1H), 2.75 – 2.67 (m, 2H), 2.14 (ddt, *J* = 11.8, 9.4, 2.5 Hz, 1H), 2.08 – 1.91 (m, 2H), 1.77 – 1.70 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.04, 138.31, 135.58, 133.34, 130.78, 129.18, 129.05, 113.32, 55.23, 50.75, 39.69, 32.75, 30.48, 26.08. **HRMS** (APCI Pos): calculated for $C_{16}H_{19}O$ $[M+H]^+$: 227.1430; found: 227.1426.

**(±)-(1*S*,4*R*,5*R*)-4-(3,5-Dichlorophenyl)bicyclo[3.2.2]nona-2,6-diene (122e)**



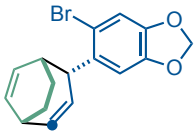

The title compound (colorless oil, 55 mg, 70% yield) was obtained following General Procedure K from (*E*)-7-(3,5-dichlorostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (90 mg, 0.295 mmol) and 1,3-cyclohexadiene (95 mg, 1.18 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (8.7 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.17 (t, *J* = 1.9 Hz, 1H), 7.06 (dd, *J* = 1.9, 0.5 Hz, 2H), 6.44 (dd, *J* = 8.8, 7.4 Hz, 1H), 6.18 (ddd, *J* = 10.7, 8.3, 2.2 Hz, 1H), 5.53 – 5.47 (m, 1H), 5.24 (dddd, *J* = 10.9, 3.8, 1.8, 0.6 Hz, 1H), 3.44 (td, *J* = 3.8, 2.3 Hz, 1H), 2.74 – 2.68 (m, 1H), 2.65 (tdd, *J* = 6.9, 3.7, 1.3 Hz, 1H), 2.12 – 2.06 (m, 1H), 2.02 – 1.89 (m, 2H), 1.69 (dddd, *J* = 12.3, 10.8, 6.3, 4.4 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 147.12, 139.35, 135.14, 134.73, 129.09, 128.46, 127.21, 126.72, 51.02, 39.59, 33.06, 30.57, 26.31. **HRMS** (APCI Pos): calculated for $C_{15}H_{15}Cl_2$ $[M+H]^+$: 265.0545; found: 265.0540.

**(±)-(1*S*,4*R*,5*R*)-4-(1-Iodophenyl)bicyclo[3.2.2]nona-2,6-diene (122f)**



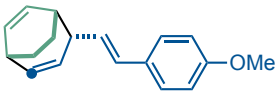

The title compound (viscous colorless oil, 70 mg, 61% yield) was obtained following General Procedure K from (*E*)-7-(2-iodostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (130 mg, 0.359 mmol) and 1,3-cyclohexadiene (115 mg, 1.44 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (10.7 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.80 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.22 (td, *J* = 7.5, 1.3 Hz, 1H), 7.13 (dd, *J* = 7.7, 1.8 Hz, 1H), 6.87 (ddd, *J* = 7.8, 7.2, 1.8 Hz, 1H), 6.42 (ddd, *J* = 8.6, 7.2, 1.0 Hz, 1H), 6.20 (ddd, *J* = 10.8, 8.3, 2.3 Hz, 1H), 5.50 – 5.44 (m, 1H), 5.31 – 5.23 (m, 1H), 3.76 (td, *J* = 3.6, 2.4 Hz, 1H), 2.79 (tq, *J* = 6.8, 3.8, 3.2 Hz, 1H), 2.74 – 2.68 (m, 1H), 2.12 (ddt, *J* = 11.9, 9.7, 2.5 Hz, 1H), 2.08 – 2.02 (m, 1H), 1.94 (dddd, *J* = 13.3, 11.6, 6.8, 2.9 Hz, 1H), 1.76 – 1.69 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 144.78, 139.52, 138.53, 134.37, 130.56, 128.93, 128.47, 128.21, 101.43, 54.87, 36.81, 33.08, 30.65, 26.27. **HRMS** (APCI Pos): calculated for $C_{15}H_{16}I$ $[M+H]^+$: 323.0291; found: 323.0291.

**(±)-5-((1*R*,2*R*,5*S*)-Bicyclo[3.2.2]nona-3,6-dien-2-yl)-6-bromobenzo[*d*][1,3]dioxole (122g)**



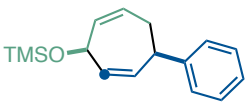

The title compound (pale yellow solid, 80 mg, 60% yield) was obtained following General Procedure K from (*E*)-5-bromo-6-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)benzo[*d*][1,3]dioxole (150 mg, 0.418 mmol) and 1,3-cyclohexadiene (134 mg, 1.67 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (12.4 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane/$Et_2O$ 99:1 to 9:1 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 6.97 (s, 1H), 6.70 (s, 1H), 6.40 (ddd, *J* = 8.7, 7.2, 1.0 Hz, 1H), 6.16 (ddd, *J* = 10.7, 8.3, 2.3 Hz, 1H), 5.91 (s, 2H), 5.54 – 5.48 (m, 1H), 5.20 (dddd, *J* = 10.9, 3.9, 1.8, 0.6 Hz, 1H), 3.83 (td, *J* = 3.7, 2.3 Hz, 1H), 2.78 – 2.72 (m, 1H), 2.69 (q, *J* = 7.9, 6.5 Hz, 1H), 2.09 (ddt, *J* = 12.2, 9.6, 2.6 Hz, 1H), 2.02 – 1.95 (m, 1H), 1.90 (dddd, *J* = 13.7, 11.3, 6.8, 3.0 Hz, 1H), 1.69 (dddd, *J* = 12.2, 10.8, 5.9, 4.5 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 147.40, 147.02, 138.50, 135.39, 134.45, 130.45, 129.20, 114.23, 112.62, 110.93, 101.81, 49.81, 36.78, 33.04, 30.66, 26.09. **HRMS** (APCI Pos): calculated for $C_{16}H_{16}{}^{79}BrO_2$ $[M+H]^+$: 319.0328; found: 319.0326. **MP** 102–105 ºC.

**(±)-(1*S*,4*S*,5*R*)-4-((*E*)-4-Methoxystyryl)bicyclo[3.2.2]nona-2,6-diene (122h)**




The title compound (pale yellow oil, 25 mg, 48% yield) was obtained following General Procedure K from 7-((1*E*,3*E*)-4-(4-methoxyphenyl)buta-1,3-dien-1-yl)-1,3,5-trimethylcyclohepta-1,3,5-triene (60 mg, 0.205 mmol) and 1,3-cyclohexadiene (66 mg, 0.82 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (6.0 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane/$Et_2O$ (99:1 to 97:3) as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.28 – 7.25 (m, 2H), 6.83 – 6.80 (m, 2H), 6.48 – 6.41 (m, 1H), 6.30 (d, *J* = 16.0 Hz, 1H), 6.06 (dd, *J* = 15.8, 8.0 Hz, 1H), 6.00 (ddd, *J* = 10.7, 8.3, 2.1 Hz, 1H), 5.89 (ddd, *J* = 8.4, 7.1, 1.0 Hz, 1H), 5.24 (ddd, *J* = 10.8, 4.1, 1.6 Hz, 1H), 3.78 (s, 3H), 2.98 (d, *J* = 7.6 Hz, 1H), 2.68 – 2.57 (m, 2H), 2.10 – 2.04 (m, 1H), 1.93 – 1.86 (m, 2H), 1.67 (ddd, *J* = 10.2, 7.9, 4.5 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.15, 139.30, 133.29, 130.91, 130.67, 130.16, 129.71, 128.90, 127.59, 114.26, 55.66, 49.75, 37.64, 33.15, 30.91, 25.88. **HRMS** (APCI Pos): calculated for $C_{18}H_{21}O$ $[M+H]^+$: 253.1587; found: 253.1592.

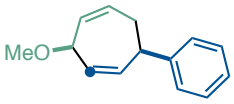
***cis*-Trimethyl((4-phenylcyclohepta-2,6-dien-1-yl)oxy)silane (122i)**




The title compound (pale yellow oil, 12 mg, 37% yield, >20:1 *cis*/*trans*) was obtained following General Procedure K from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (30 mg, 0.127 mmol) and (*E*)-(buta-1,3-dien-1-yloxy)trimethylsilane (72 mg, 0.51 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (3.7 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.30 – 7.25 (m, 4H), 7.21 – 7.18 (m, 1H), 5.84 – 5.79 (m, 1H), 5.77

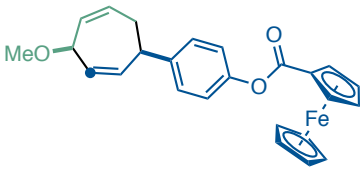
– 5.72 (m, 1H), 5.71 – 5.64 (m, 1H), 5.39 (dddd, *J* = 11.2, 4.1, 2.9, 0.9 Hz, 1H), 4.80 (s, 1H), 3.72 (dd, *J* = 6.5, 3.3 Hz, 1H), 3.12 – 3.03 (m, 1H), 2.75 (dt, *J* = 20.1, 7.0 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 140.82, 136.04, 130.81, 130.55, 128.54, 127.75, 126.74, 126.48, 72.07, 51.33, 28.98, 0.38. **GCMS** (EI): calculated for $C_{16}H_{22}OSi$ $[M]^+$: 258.1; found: 258.2.

***cis*-3-Methoxy-6-phenylcyclohepta-1,4-diene (122j)**



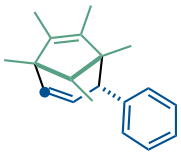

The title compound (pale yellow oil, 21 mg, 83% yield, >20:1 *cis*/*trans*) was obtained following General Procedure K from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (30 mg, 0.127 mmol) and (*E*)-1-methoxybuta-1,3-diene (43 mg, 0.51 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (3.7 mg, 5 mol %) after purification by CombiFlash column chromatography on $SiO_2$ using a gradient between cyclohexane and 95:5 cyclohexane/EtOAc as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.30 – 7.25 (m, 4H), 7.23 – 7.18 (m, 1H), 5.84 – 5.76 (m, 2H), 5.72 (dddd, *J* = 11.7, 6.1, 2.5, 0.7 Hz, 1H), 5.49 (ddd, *J* = 10.3, 5.9, 2.2 Hz, 1H), 4.43 (d, *J* = 5.4 Hz, 1H), 3.91 (tdd, *J* = 4.7, 3.9, 3.4, 2.0 Hz, 1H), 3.39 (s, 3H), 3.14 – 3.04 (m, 1H), 2.84 – 2.74 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 133.83, 130.56, 130.32, 127.93, 127.91, 126.86, 80.89, 57.25, 47.82, 29.10. **GCMS** (EI): calculated for $C_{14}H_{16}O$ $[M]^+$: 200.1; found: 200.1.

***cis*-4-(4-Methoxycyclohepta-2,5-dien-1-yl)phenyl ferrocenoylate (122k)**



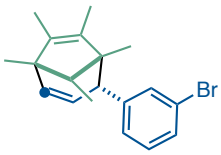

The title compound (amorphous orange residue, 48 mg, 65% yield, >20:1 *cis*/*trans*) was obtained following General Procedure K from (*E*)-4-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)phenyl ferrocenoylate (80 mg, 0.172 mmol) and (*E*)-1-methoxybuta-1,3-diene (58 mg, 0.69 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (5.1 mg, 5 mol %) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane/EtOAc 95:5 to 9:1 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.36 – 7.29 (m, 2H), 7.10 – 7.04 (m, 2H), 5.84 – 5.75 (m, 2H), 5.72 (ddd, *J* = 11.9, 6.1, 2.5 Hz, 1H), 5.49 (dt, *J* = 11.2, 3.7 Hz, 1H), 4.96 (s, 2H), 4.49 (s, 2H), 4.43 (s, 1H), 4.30 (s, 5H), 3.92 (dt, *J* = 6.4, 3.7 Hz, 1H), 3.39 (s, 3H), 3.09 (d, *J* = 20.3 Hz, 1H), 2.78 (dt, *J* = 20.3, 6.9 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 170.62, 149.96, 137.94, 133.83, 131.25, 130.43, 128.06, 127.93, 120.96, 80.79, 72.44, 71.18, 70.85, 70.49, 57.22, 47.29, 29.08. **HRMS** (ESI+): calculated for $C_{25}H_{24}NaO_3{}^{54}Fe$ $[M+Na]^+$: 449.1014; found: 439.1009.

**(±)-(1*S*,4*S*,5*S*)-1,5,6,7,8-Pentamethyl-4-phenylbicyclo[3.2.1]octa-2,6-diene (122l)**



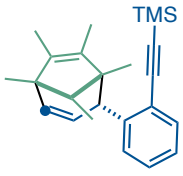
The title compound (pale yellow oil, 17 mg, 53% yield) was obtained following General Procedure K from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (30 mg, 0.127 mmol) and 1,2,3,4,5-pentamethylcyclopenta-1,3-diene (52 mg, 0.38 mmol, 3 equiv) using [$Rh_2(TFA)_4$] (3.8 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.28 – 7.18 (m, 3H), 7.07 – 6.99 (m, 2H), 6.12 (dd, *J* = 9.4, 2.4 Hz, 1H), 5.40 (dd, *J* = 9.4, 2.6 Hz, 1H), 3.17 (t, *J* = 2.6 Hz, 1H), 2.02 (q, *J* = 6.8 Hz, 1H), 1.62 (q, *J* = 1.2 Hz, 3H), 1.04 (s, 3H), 1.00 (s, 3H), 0.86 (q, *J* = 1.2 Hz, 3H), 0.78 (d, *J* = 6.8 Hz, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 142.04, 141.29, 140.37, 129.93, 129.14, 128.07, 127.41, 126.21, 57.10, 53.27, 52.54, 47.67, 18.39, 18.23, 12.26, 11.48, 10.46. **HRMS** (APCI Pos): calculated for $C_{19}H_{24}$ $[M]^+$: 252.1873; found 252.1876.

**(±)-(1*S*,4*S*,5*S*)-1,5,6,7,8-Pentamethyl-4-(3-bromophenyl)bicyclo[3.2.1]octa-2,6-diene (122m)**




The title compound (colorless viscous oil, 18 mg, 43% yield) was obtained following General Procedure K from (*E*)-7-(3-bromostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (40 mg, 0.127 mmol) and 1,2,3,4,5-pentamethylcyclopenta-1,3-diene (52 mg, 0.38 mmol, 3 equiv) using [$Rh_2(TFA)_4$] (3.8 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.31 (ddd, *J* = 7.9, 2.1, 1.1 Hz, 1H), 7.11 (t, *J* = 1.8 Hz, 1H), 7.08 (t, *J* = 7.8 Hz, 1H), 6.91 (dt, *J* = 7.7, 1.4 Hz, 1H), 6.09 (dd, *J* = 9.4, 2.4 Hz, 1H), 5.30 (dd, *J* = 9.4, 2.6 Hz, 1H), 3.08 (t, *J* = 2.5 Hz, 1H), 1.96 (q, *J* = 6.8 Hz, 1H), 1.58 (q, *J* = 1.2 Hz, 3H), 0.99 (s, 3H), 0.94 (s, 3H), 0.85 (q, *J* = 1.2 Hz, 3H), 0.73 (d, *J* = 6.8 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 144.94, 142.20, 141.31, 133.18, 129.65, 129.30, 129.20, 128.87, 127.66, 122.07, 57.44, 53.72, 52.57, 48.07, 18.67, 18.57, 12.57, 11.79, 10.83. **HRMS** (APCI Pos): calculated for $C_{19}H_{22}{}^{79}Br$ [M-H]: 329.0899; found: 329.0854.

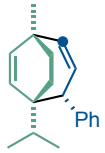
**(±)-Trimethyl((2-((1*S*,2*S*,5*S*)-1,5,6,7,8-pentamethylbicyclo[3.2.1]octa-3,6-dien-2-yl)phenyl)ethynyl)silane (122n)**




The title compound (viscous colorless oil, 34 mg, 57% yield) was obtained following General Procedure K from (*E*)-trimethyl((2-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)phenyl)ethynyl)silane (55 mg, 0.165 mmol) and 1,2,3,4,5-pentamethylcyclopenta-1,3-diene (90 mg, 0.66 mmol, 4 equiv) using [$Rh_2(TFA)_4$] (4.9 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.41

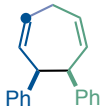
(ddd, *J* = 7.5, 1.6, 0.6 Hz, 1H), 7.12 (dtd, *J* = 23.6, 7.4, 1.5 Hz, 2H), 6.81 – 6.75 (m, 1H), 6.04 (dd, *J* = 9.4, 2.5 Hz, 1H), 5.27 (dd, *J* = 9.4, 2.6 Hz, 1H), 3.90 (t, *J* = 2.6 Hz, 1H), 2.06 (q, *J* = 6.8 Hz, 1H), 1.60 (q, *J* = 1.2 Hz, 3H), 0.99 (d, *J* = 5.8 Hz, 6H), 0.93 (q, *J* = 1.2 Hz, 3H), 0.74 (d, *J* = 6.8 Hz, 3H), 0.25 (s, 9H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 145.05, 140.95, 140.86, 132.26, 130.54, 129.43, 128.89, 128.49, 126.27, 124.04, 105.69, 98.35, 57.97, 55.35, 49.33, 48.04, 19.23, 18.71, 12.86, 11.67, 10.78, 0.34. **HRMS** (APCI Pos): calculated for $C_{24}H_{33}Si$ $[M+H]^+$: 349.2346; found: 349.2346.

**(±)-(1*S*,4*R*,5*R*)-5-Isopropyl-1-methyl-4-phenylbicyclo[3.2.2]nona-2,6-diene (122p)**



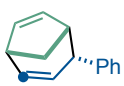

The title compound (viscous colorless oil, 37 mg, 87% yield, 7:1 rr) was obtained following General Procedure K from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (40 mg, 0.169 mmol) and α-terpinene (1-isopropyl-4-methylcyclohexa-1,3-diene) (69 mg, 0.51 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (5.0 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.27 – 7.20 (m, 4H), 7.19 – 7.15 (m, 1H), 6.11 (dt, *J* = 9.2, 0.7 Hz, 1H), 5.66 (dd, *J* = 11.1, 2.2 Hz, 1H), 5.27 (d, *J* = 9.2 Hz, 1H), 5.24 (dd, *J* = 11.1, 4.5 Hz, 1H), 3.46 (dd, *J* = 4.6, 2.2 Hz, 1H), 2.00 – 1.95 (m, 1H), 1.77 – 1.65 (m, 2H), 1.52 (p, *J* = 6.8 Hz, 1H), 1.41 (ddd, *J* = 12.0, 10.5, 8.2 Hz, 1H), 1.17 (s, 3H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.74 (d, *J* = 6.7 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.74, 140.88, 135.89, 133.45, 131.71, 130.26, 127.85, 126.73, 53.11, 43.68, 39.74, 35.33, 32.73, 28.40, 25.54, 17.78, 16.60. **HRMS** (APCI Pos): calculated for $C_{19}H_{25}$ $[M+H]^+$: 253.1951; found: 253.1949.

***cis*-6,7-Diphenylcyclohepta-1,4-diene (122q)**




The title compound (viscous colorless oil, 22 mg, 70% yield, >20:1 *cis*/*trans*) was obtained following General Procedure K from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (30 mg, 0.127 mmol) and (*E*)-buta-1,3-dien-1-ylbenzene (50 mg, 0.381 mmol, 3 equiv) using $[Rh_2(TFA)_4]$ (3.8 mg, 5 mol %) after purification by CombiFlash column chromatography on $SiO_2$ using cyclohexane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.20 – 7.10 (m, 6H), 6.91 – 6.79 (m, 4H), 5.91 (dddd, *J* = 10.8, 7.6, 3.1, 1.6 Hz, 2H), 5.76 (ddd, *J* = 11.1, 6.0, 2.9 Hz, 2H), 4.08 (s, 2H), 3.36 (dp, *J* = 19.8, 3.0 Hz, 1H), 2.80 (dt, *J* = 19.8, 7.6 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.91, 133.55, 130.03, 128.44, 127.79, 126.70, 50.64, 28.35. **HRMS** (APCI Pos): calculated for $C_{19}H_{19}$ $[M+H]^+$: 247.1481; found: 247.1480.

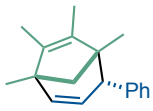
**(±)-(1*S*,4*R*,5*R*)-4-Phenylbicyclo[3.2.1]octa-2,6-diene (122r)**




The title compound (colorless oil, 29 mg, 94% yield) was obtained following General Procedure K from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (40 mg, 0.169 mmol) and freshly cracked/distilled 1,3-cyclopentadiene (45 mg, 0.68 mmol, 4 equiv) using

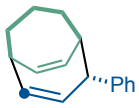
$[Rh_2(TFA)_4]$ (5.0 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.28 – 7.24 (m, 2H), 7.21 – 7.15 (m, 1H), 7.15 – 7.10 (m, 2H), 6.35 (ddd, *J* = 5.6, 2.8, 0.7 Hz, 1H), 6.30 (dddd, *J* = 9.7, 6.3, 2.5, 1.1 Hz, 1H), 5.37 (dddd, *J* = 9.6, 2.6, 1.8, 0.7 Hz, 1H), 5.22 (ddd, *J* = 5.7, 2.8, 0.6 Hz, 1H), 3.69 (dt, *J* = 5.0, 2.6 Hz, 1H), 3.00 (tdd, *J* = 4.8, 2.7, 1.9 Hz, 1H), 2.68 – 2.63 (m, 1H), 2.19 – 2.14 (m, 1H), 2.10 (dt, *J* = 9.5, 0.8 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 142.28, 141.70, 135.02, 129.95, 128.43, 128.13, 128.08, 126.51, 47.11, 44.69, 44.22, 38.73. **HRMS** (APCI Pos): calculated for $C_{14}H_{13}$ $[M-H]^+$: 181.1012; found: 181.1010.

**(±)-(1*R*,4*S*,5*S*)-1,5,6,7-Tetramethyl-4-phenylbicyclo[3.2.1]octa-2,6-diene (122s)**



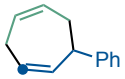

The title compound (colorless oil, 21 mg, 60% yield) was obtained following General Procedure K from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (35 mg, 0.148 mmol) and 1,2,3,4-tetramethylcyclopenta-1,3-diene (54 mg, 0.44 mmol, 3 equiv) using $[Rh_2(TFA)_4]$ (4.4 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.23 – 7.16 (m, 3H), 7.00 – 6.95 (m, 2H), 6.08 (ddd, *J* = 9.4, 2.5, 1.3 Hz, 1H), 5.39 (dd, *J* = 9.4, 2.6 Hz, 1H), 3.19 (t, *J* = 2.5 Hz, 1H), 1.82 (d, *J* = 9.1 Hz, 1H), 1.61 (q, *J* = 1.2 Hz, 3H), 1.59 (d, *J* = 1.4 Hz, 1H), 1.11 (d, *J* = 4.3 Hz, 6H), 0.82 (q, *J* = 1.2 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 144.14, 142.05, 139.58, 132.93, 129.95, 128.79, 127.84, 126.59, 58.71, 51.18, 50.35, 45.36, 23.07, 21.74, 12.24, 10.60. **HRMS** (APCI Pos): calculated for $C_{18}H_{21}$ $[M-H]^+$: 237.1638; found: 237.1636.

**(±)-(1*S*,4*R*,5*R*)-4-Phenylbicyclo[3.3.2]deca-2,9-diene (122t)**



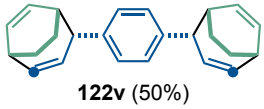

The title compound (colorless oil, 35 mg, 79% yield) was obtained following General Procedure K from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (50 mg, 0.212 mmol) and 1,3-cycloheptadiene (80 mg, 0.85 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (6.3 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.28 – 7.23 (m, 4H), 7.18 (ddt, *J* = 6.3, 4.8, 3.0 Hz, 1H), 6.25 – 6.18 (m, 1H), 5.88 – 5.78 (m, 2H), 5.65 – 5.59 (m, 1H), 3.47 (dt, *J* = 4.0, 2.0 Hz, 1H), 2.86 – 2.80 (m, 1H), 2.42 (dddd, *J* = 7.7, 6.5, 2.7, 1.5 Hz, 1H), 2.34 (tdt, *J* = 14.0, 12.8, 4.3 Hz, 1H), 1.92 (ddt, *J* = 13.5, 5.8, 3.9 Hz, 1H), 1.82 (dp, *J* = 14.5, 3.7 Hz, 1H), 1.70 (tdd, *J* = 13.6, 4.2, 2.5 Hz, 1H), 1.61 (tdd, *J* = 12.9, 3.6, 2.0 Hz, 1H), 1.56 – 1.51 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 145.61, 139.59, 135.37, 132.81, 128.95, 128.52, 128.38, 126.39, 48.42, 43.07, 36.81, 33.43, 28.23, 24.14. **HRMS** (APCI Pos): calculated for $C_{16}H_{19}$ $[M+H]^+$: 211.1481; found: 211.1479.

**6-Phenylcyclohepta-1,4-diene (122u)**




The title compound (colorless oil, 19 mg, 53% yield) was obtained following General Procedure K from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (50 mg, 0.212 mmol) and 1,3-butadiene (20% w/w solution in PhMe, 0.35 mL, 1.05 mmol, 5 equiv) using $[Rh_2(TFA)_4]$ (6.3 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.36 – 7.27 (m, 4H), 7.26 – 7.20 (m, 1H), 5.92 – 5.68 (m, 4H), 3.76 (ddt, *J* = 10.3, 3.4, 1.9 Hz, 1H), 3.07 – 2.89 (m, 2H), 2.62 (dddt, *J* = 13.5, 10.2, 4.9, 1.5 Hz, 1H), 2.51 – 2.43 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 146.27, 134.92, 129.78, 129.69, 128.37, 127.56, 126.13, 43.96, 35.30, 28.17. **HRMS** (APCI Pos): calculated for $C_{13}H_{15}$ $[M+H]^+$: 171.1168; found: 171.1168.

**(±)-1-((1*R*,2*R*,5*S*)-Bicyclo[3.2.2]nona-3,6-dien-2-yl)-4-((1*S*,2*S*,5*R*)-bicyclo[3.2.2]nona-3,6-dien-2-yl)benzene (122v)**


**122v** (50%)

The title compound (white solid, 30 mg, 50% yield, >20:1 dr for the carbon atoms linking to the phenyl ring) was obtained following General Procedure K from 1,4-bis((*E*)-2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)benzene (75 mg, 0.190 mmol) and 1,3-cyclohexadiene (122 mg, 1.52 mmol, 8 equiv) using $[Rh_2(TFA)_4]$ (11.3 mg, 10 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.08 (d, *J* = 1.8 Hz, 4H), 6.42 (ddt, *J* = 8.8, 7.3, 1.3 Hz, 2H), 6.13 (dddd, *J* = 10.8, 8.4, 2.4, 1.2 Hz, 2H), 5.54 (dd, *J* = 8.7, 7.1 Hz, 2H), 5.33 (dddd, *J* = 11.0, 3.6, 1.7, 0.8 Hz, 2H), 3.47 (q, *J* = 3.6 Hz, 2H), 2.72 – 2.64 (m, 4H), 2.10 (ddt, *J* = 12.1, 9.6, 2.5 Hz, 2H), 2.04 – 1.97 (m, 2H), 1.92 (dddd, *J* = 13.5, 11.2, 6.8, 2.9 Hz, 2H), 1.74 – 1.66 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.50, 141.48, 138.60, 138.59, 133.80, 131.03, 129.45, 128.18, 51.58, 39.90, 39.87, 33.11, 30.87, 26.58. **HRMS** (APCI Pos): calculated for $C_{24}H_{27}$ $[M+H]^+$: 315.2107; found: 315.2109. **MP** 147–149 ºC.

***cis*-((*E*)-2-(2,2-dimethyl-3-(2-methylprop-1-en-1-yl)cyclopropyl)vinyl)benzene (122w')**

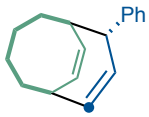

The title compound (colorless oil, 19 mg, 66% yield, >20:1 *cis*/*trans* ratio) was obtained following General Procedure K from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (30 mg, 0.127 mmol) and 2,5-dimethylhexa-2,4-diene (42 mg, 0.38 mmol, 3 equiv) using $[Rh_2(TFA)_4]$ (3.8 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.36 – 7.28 (m, 4H), 7.22 – 7.16 (m, 1H), 6.54 (d, *J* = 15.7 Hz, 1H), 6.10 – 5.99 (m, 1H), 5.11 (dtd, *J* = 6.6, 2.8, 1.4 Hz, 1H), 1.79 – 1.77 (m, 3H), 1.72 (d, *J* = 1.3 Hz, 3H), 1.67 – 1.63 (m, 2H), 1.21 (s, 3H), 1.13 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.17, 135.24, 130.40, 128.61, 128.45, 126.47,

125.66, 119.58, 33.48, 30.43, 28.73, 25.74, 24.03, 18.57, 16.41. **HRMS** (APCI Pos): calculated for $C_{17}H_{23}$ $[M+H]^+$: 227.1794; found: 227.1795.

**(*endo*,*Z*)-9-((*E*)-Styryl)bicyclo[6.1.0]non-2-ene (122x')**

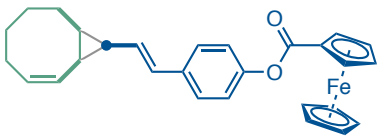

The title compound (colorless oil, 15 mg, 53% yield, >20:1 *cis*/*trans* ratio) was obtained following General Procedure K from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (30 mg, 0.127 mmol) and (1*Z*,3*Z*)-1,3-cyclooctadiene (55 mg, 0.51 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (3.8 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.36 – 7.27 (m, 4H), 7.22 – 7.16 (m, 1H), 6.57 (d, *J* = 15.7 Hz, 1H), 5.95 (dd, *J* = 15.8, 9.8 Hz, 1H), 5.85 (dddd, *J* = 11.4, 6.9, 4.8, 2.4 Hz, 1H), 5.46 – 5.39 (m, 1H), 2.49 (dddt, *J* = 16.2, 8.9, 7.0, 1.8 Hz, 1H), 2.13 – 1.97 (m, 2H), 1.89 – 1.77 (m, 3H), 1.70 – 1.60 (m, 1H), 1.55 – 1.46 (m, 1H), 1.42 – 1.32 (m, 1H), 1.29 – 1.19 (m, 1H). **GCMS** (EI): calculated for $C_{17}H_{20}$ $[M]^+$: 223.1; found: 223.2.

**(±)-(1*R*,6*S*,9*R*,*Z*)-9-Phenylbicyclo[4.3.2]undeca-7,10-diene (122x)**




The title compound (pale yellow oil, 13 mg, 90% yield) was obtained by dissolving **122x'** (15 mg, 0.127 mmol) in xylenes and heating at 160 ºC for 24 h, after purification by flash column chromatography on $SiO_2$ using pentane as eluent. This can also be performed as a one pot procedure, swapping the solvent of the cyclopropanation from 1,2-DCE to xylenes, and heating the crude mixture at 160 ºC for 24 h. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.31 – 7.28 (m, 2H), 7.26 – 7.22 (m, 2H), 7.18 – 7.13 (m, 1H), 5.77 (ddd, *J* = 11.3, 7.9, 1.3 Hz, 1H), 5.71 (ddt, *J* = 12.1, 6.5, 1.2 Hz, 1H), 5.66 – 5.58 (m, 2H), 3.50 (d, *J* = 6.2 Hz, 1H), 3.10 (dtdt, *J* = 7.9, 6.1, 2.7, 1.4 Hz, 1H), 2.64 (dt, *J* = 8.4, 4.0 Hz, 1H), 2.14 – 2.05 (m, 1H), 1.93 – 1.89 (m, 2H), 1.81 – 1.65 (m, 4H), 1.59 – 1.53 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 145.91, 134.36, 132.84, 131.85, 130.09, 129.05, 128.17, 126.27, 51.45, 44.96, 40.43, 39.27, 33.48, 27.57, 24.52. **HRMS** (APCI Pos): calculated for $C_{17}H_{19}$ $[M-H]^+$: 223.1481; found: 223.1482.

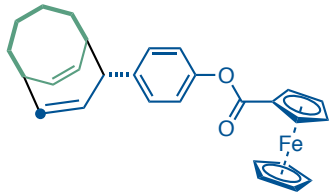
**4-((*E*)-2-((*endo*,*Z*)-Bicyclo[6.1.0]non-2-en-9-yl)vinyl)phenyl 1-ferrocenoylate (122y')**




The title compound (pale yellow oil, 22 mg, 50% yield, >20:1 *cis*/*trans* ratio) was obtained following General Procedure K from (*E*)-4-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)phenyl ferrocenoylate (45 mg, 0.097 mmol) and (1*Z*,3*Z*)-1,3-cyclooctadiene (42 mg, 0.39 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (2.9 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.41 – 7.33 (m, 2H), 7.14 – 7.08 (m, 2H), 6.57 (d, *J* = 15.8 Hz, 1H), 5.96 – 5.82 (m, 2H), 5.47 – 5.42 (m, 1H), 4.98 (t, *J* = 2.0 Hz, 2H), 4.53 – 4.50 (m, 2H), 4.32 (m, 5H), 2.49 (ddd, *J* = 16.2, 8.6, 6.6 Hz,

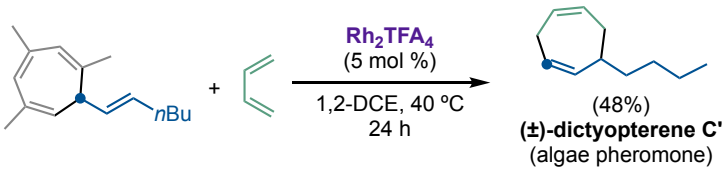
1H), 2.12 – 1.99 (m, 2H), 1.92 – 1.75 (m, 4H), 1.68 (m, 2H), 1.55 – 1.46 (m, 1H), 1.41 – 1.34 (m, 1H), 1.26 – 1.19 (m, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.36, 149.47, 136.29, 135.76, 129.48, 128.79, 126.48, 123.32, 121.65, 71.89, 70.65, 70.19, 69.95, 30.95, 30.03, 25.17, 25.13, 23.05, 22.97, 21.71.

**(±)-4-((1*S*,6*R*,7*R*,*Z*)-Bicyclo[4.3.2]undeca-8,10-dien-7-yl)phenyl ferrocenoylate (122y)**




The title compound (pale yellow oil, 9 mg, 45% yield) was obtained by dissolving **122y'** (22 mg, 0.049 mmol) in xylenes and heating at 160 ºC for 24 h, after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.35 – 7.30 (m, 2H), 7.08 – 7.03 (m, 2H), 5.81 – 5.75 (m, 1H), 5.74 – 5.69 (m, 1H), 5.67 – 5.58 (m, 2H), 4.94 (dt, *J* = 3.9, 1.9 Hz, 2H), 4.47 (m, 2H), 4.28 (d, *J* = 4.1 Hz, 5H), 3.52 (d, *J* = 6.0 Hz, 1H), 3.11 (d, *J* = 5.6 Hz, 1H), 2.65 (s, 1H), 2.09 (ddt, *J* = 14.2, 8.9, 4.8 Hz, 1H), 1.93 (m, 2H), 1.79 – 1.66 (m, 4H), 1.58 (dd, *J* = 9.9, 4.9 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 170.68, 149.47, 143.16, 134.44, 132.92, 131.82, 130.05, 129.97, 121.19, 72.16, 70.99, 70.74, 70.28, 50.89, 44.98, 40.46, 39.19, 33.46, 27.57, 24.53. **HRMS** (ESI Pos): calculated for $C_{28}H_{28}NaO_2{}^{56}Fe$ $[M+Na]^+$: 475.1331; found 475.1329. **MP** 130–135 ºC.

**Total Synthesis of Dictyopterene C' and Diversification of Products**

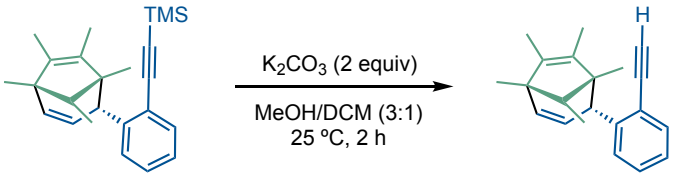



Under Ar, a microwave vial equipped with a Teflon-coated magnetic stirring bar was charged with 1,3,5-trimethyl-7-(hex-1-en-1-yl)-1,3,5-cycloheptatriene (120 mg, 0.56 mmol, 1.0 equiv) and 1,4-butadiene (0.75 mL of a 20% w/w solution in toluene, 2.22 mmol, 4 equiv). Both reagents were dissolved in anhydrous 1,2-DCE (0.15 M, 3.8 mL), before $[Rh_2(TFA)_4]$ (16 mg, 5 mol %) was added. The vial was sealed and then stirred at 40 ºC for 24 h. After confirming that the reaction was completed by TLC, the resulting mixture was concentrated in vacuum, adsorbed into silica gel, and purified by slow flash column chromatography on silica gel, using pentane as eluent, giving (±)-dictyopterene C' as an odorous colorless oil (48% yield). Characterization data matched with the reported ones for the natural product.[216] **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 5.73 – 5.58 (m, 4H), 2.93 (ddq, *J* = 19.7, 4.3, 2.2 Hz, 1H), 2.69 (dt, *J* = 19.7, 5.7 Hz, 1H), 2.44 (s,

216 (a) Moore, R. E.; Pettus, J. A.; Mistysyn, J. Odoriferous C11 hydrocarbons from Hawaiian Dictyopteris. *J. Org. Chem.* **1973**, *39*, 2201–2207. (b) Grandjean, D.; Pale, P.; Chuche, J. Enzymatic hydrolysis of cyclopropanes. Total synthesis of optically pure dictyopterenes a and c'. *Tetrahedron* **1991**, *47*, 1215–1230.

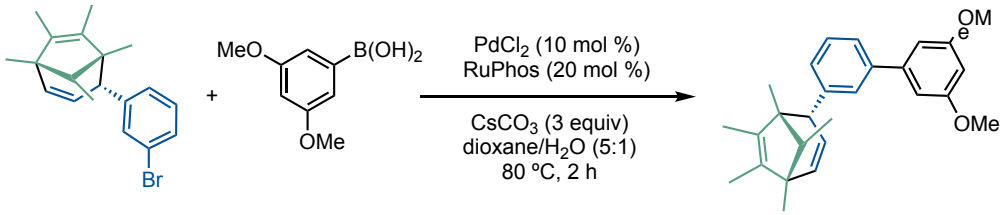
1H), 2.20 (ddt, *J* = 15.8, 6.3, 3.0 Hz, 1H), 2.13 – 2.05 (m, 1H), 1.34 – 1.28 (m, 7H), 0.89 – 0.87 (m, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 136.82, 129.87, 128.09, 127.19, 37.16, 35.98, 32.85, 29.40, 28.32, 22.81, 14.03. **GCMS** (EI): calculated for $C_{11}H_{18}$ $[M]^+$: 150.1; found: 150.1.

**(±)-(1*S*,4*S*,5*S*)-4-(2-Ethynylphenyl)-1,5,6,7,8-pentamethylbicyclo[3.2.1]octa-2,6-diene (122o)**




Under air, (**122n**) (32 mg, 0.092 mmol) was dissolved in 0.6 mL of 3:1 MeOH/ $CH_2Cl_2$ (HPLC grade) and to the mixture was added $K_2CO_3$ (25 mg, 0.18 mmol, 2 equiv). The reaction was stirred for 2 h (after this time the reaction was finished by NMR, even though in TLC, both SM and product have almost identical $R_f$). Water was added, and the mixture was extracted 3 times with $CH_2Cl_2$. Organic fractions were dried over $MgSO_4$, filtrated, concentrated, resuspended in pentane, and filtered through an HPLC filter. Then, the solvent was removed in vacuum, obtaining pure (**122o**) without further purification. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.48 – 7.42 (m, 1H), 7.18 (td, *J* = 7.6, 1.6 Hz, 1H), 7.12 (td, *J* = 7.5, 1.4 Hz, 1H), 6.81 (dd, *J* = 7.8, 1.5 Hz, 1H), 6.05 (dd, *J* = 9.4, 2.5 Hz, 1H), 5.26 (dd, *J* = 9.4, 2.6 Hz, 1H), 3.89 (t, *J* = 2.5 Hz, 1H), 3.22 (s, 1H), 2.08 (q, *J* = 6.8 Hz, 1H), 1.60 (q, *J* = 1.2 Hz, 3H), 0.99 (d, *J* = 3.7 Hz, 6H), 0.94 (q, *J* = 1.2 Hz, 3H), 0.74 (d, *J* = 6.8 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 145.22, 141.10, 141.03, 132.66, 130.63, 129.38, 128.76, 128.65, 126.38, 123.04, 84.01, 81.26, 57.86, 55.29, 49.34, 48.06, 19.11, 18.70, 12.90, 11.64, 10.82. **HRMS** (APCI Pos): calculated for $C_{21}H_{25}$ $[M+H]^+$: 277.1951; found: 277.1952.

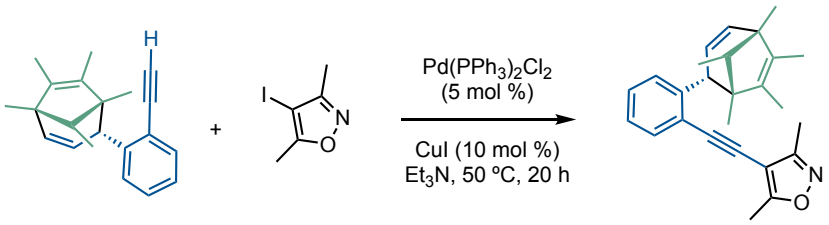
**(±)-(1*S*,4*S*,5*S*)-4-(3',5'-Dimethoxy-[1,1'-biphenyl]-3-yl)-1,5,6,7,8-pentamethylbicyclo [3.2.1]octa-2,6-diene (122aa)**




An HPLC vial was charged with (3,5-dimethoxyphenyl)boronic acid (17 mg, 0.091 mmol, 2 equiv), cesium carbonate (44 mg, 0.14 mmol, 3 equiv), $PdCl_2$ (0.8 mg, 10 mol %) and RuPhos (4.2 mg, 20 mol %). The vial was introduced in the glovebox, and then a solution of (**122m**) (15 mg, 0.045 mmol, 1 equiv) in 0.25 mL of dry dioxane (0.15 M) was added. The vial was closed,

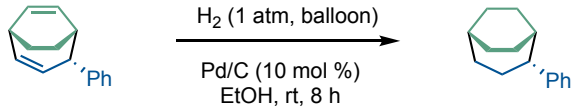
taken out of the glovebox, and then 0.05 mL of $H_2O$ were added via syringe. The mixture was stirred at 80 ºC for 2 h. After this time, full conversion of (**122m**) is observed by TLC. The mixture was diluted with water and extracted 3 times with diethyl ether. Combined organic fractions were washed once with brine, dried over anhydrous $Na_2SO_4$. filtered, concentrated under vacuum, and purified by CombiFlash chromatography in silica gel, using a gradient between cyclohexane and 99:1 cyclohexane/EtOAc, to give the title compound (**122z**, 13 mg, 74% yield) as an amorphous colorless residue. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.39 (ddd, *J* = 7.7, 1.9, 1.1 Hz, 1H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.19 (s, 1H), 6.99 (d, *J* = 7.5 Hz, 1H), 6.69 (d, *J* = 2.3 Hz, 2H), 6.44 (t, *J* = 2.3 Hz, 1H), 6.09 (dd, *J* = 9.4, 2.4 Hz, 1H), 5.38 (dd, *J* = 9.4, 2.6 Hz, 1H), 3.83 (s, 6H), 3.18 (t, *J* = 2.6 Hz, 1H), 2.02 – 1.98 (m, 1H), 1.61 (q, *J* = 1.2 Hz, 3H), 1.00 (s, 3H), 0.99 (s, 3H), 0.88 (q, *J* = 1.2 Hz, 3H), 0.75 (d, *J* = 6.8 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 161.36, 144.14, 142.77, 141.72, 140.80, 140.54, 129.61, 129.60, 129.08, 128.36, 128.06, 125.46, 105.71, 99.55, 57.47, 55.75, 53.68, 52.91, 48.09, 18.75, 18.64, 12.74, 11.82, 10.83 **HRMS** (APCI Pos): calculated for $C_{27}H_{33}O_2$ $[M+H]^+$: 389.2475; found: 389.2478.

**(±)-3,5-Dimethyl-4-((2-((1S,2S,5S)-1,5,6,7,8-pentamethylbicyclo[3.2.1]octa-3,6-dien-2-yl)phenyl)ethynyl)isoxazole (122ab)**




In the glovebox, a mixture of (**122o**) (20 mg, 0.072 mmol), 4-iodo-3,5-dimethylisoxazole (19 mg, 0.087, 1.2 equiv), $Pd(PPh_3)_3Cl_2$ (2.5 mg, 5 mol %), and copper iodide (1.4 mg, 10 mol %), was dissolved in 0.7 mL of anhydrous $NEt_3$ (0.1 M) in an HPLC vial. The vial was closed, taken out of the glovebox, and the mixture was stirred at 50 ºC for 20 h. After this time, the solvent was removed while adsorbing the crude product in silica gel, and it was purified by CombiFlash chromatography in $SiO_2$ using a gradient of cyclohexane/EtOAc 95:5 to 9:1, to give the title compound (**122aa**) as a yellow solid. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.44 (dd, *J* = 7.4, 1.6 Hz, 1H), 7.21 – 7.14 (m, 2H), 6.84 (dd, *J* = 7.6, 1.4 Hz, 1H), 6.07 (dd, *J* = 9.4, 2.5 Hz, 1H), 5.29 (dd, *J* = 9.4, 2.5 Hz, 1H), 3.89 (t, *J* = 2.5 Hz, 1H), 2.50 (s, 3H), 2.35 (s, 3H), 2.05 (q, *J* = 6.8 Hz, 1H), 1.63 – 1.59 (m, 3H), 1.00 (s, 6H), 0.98 – 0.95 (m, 3H), 0.74 (d, *J* = 6.8 Hz, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 171.21, 160.92, 144.38, 141.32, 141.22, 131.99, 130.72, 129.21, 128.63, 128.54, 126.54, 123.70, 101.88, 94.78, 81.31, 58.07, 55.21, 49.75, 48.12, 19.37, 18.67, 12.91, 12.43, 11.66, 11.09, 10.83. **HRMS** (ESI Pos): calculated for $C_{26}H_{30}NO$ $[M+H]^+$: 372.2322; found: 372.2334. **MP** 100–102 ºC.

**(±)-(1*R*,2*R*,5*S*)-2-Phenylbicyclo[3.2.2]nonane (126)**

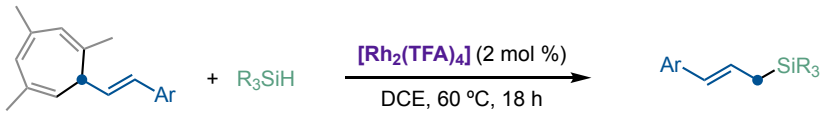



A vial was charged with a solution of (**122a**) (30 g, 0.153 mmol, 1 equiv) in 1.5 mL of HPLC grade EtOH. The vial was submitted to two vacuum-Ar cycles, before Pd/C (16 mg, 10% w/w on Pd, 10 mol %) was added. Then, the vial was submitted to three consecutive vacuum-$H_2$ cycles (using a hydrogen balloon). The mixture was then stirred under $H_2$ atmosphere at 25 ºC for 18 h. After this time, GCMS showed conversion to the tetrahydrogenated product. After filtration though Celite and evaporation of the solvent, flash column chromatography in silica gel using pentane as eluent gave the title compound (**126**) (25 mg, 82%) as a colorless oil. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.29 – 7.22 (m, 4H), 7.18 – 7.13 (m, 1H), 2.79 (dd, *J* = 12.1, 4.2 Hz, 1H), 1.99 – 1.85 (m, 5H), 1.79 – 1.61 (m, 7H), 1.57 – 1.45 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 149.78, 128.59, 127.20, 125.88, 51.72, 37.29, 35.62, 29.43, 28.83, 28.22, 24.12, 21.95. **HRMS** (APCI Pos): calculated for $C_{15}H_{19}$ $[M-H]^+$: 199.1481; found: 199.1476.

**Synthesis of Substrates for the Si–H Insertion or the Oxidation of Rhodium Carbenes**

Trimethylstyryl cycloheptatrienes **44** were prepared according to the procedure described in the Methods Section II.9 of Chapter II. All silanes and oxidants employed were commercially available.

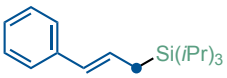
**General Procedure L for the Synthesis of Allylsilanes (133)**




A screw-cap culture tube equipped with a Teflon-coated magnetic stirring bar was charged with the corresponding 1,3,5-trimethyl-7-styryl-1,3,5-cycloheptatriene **44** (1.0 equiv) and the corresponding silane (4 equiv). The vial was introduced in an argon-filled glovebox, and both reagents were dissolved in anhydrous 1,2-DCE (0.1 M), before $[Rh_2(TFA)_4]$ (2 mol %) was added. The vial was closed with the corresponding screw-cap and taken outside the glovebox, and then stirred at 60 ºC for 18 hours. After confirming that the reaction was completed by TLC, the resulting mixture was concentrated in vacuum. The crude product was purified by flash column chromatography or preparative TLC on silica gel, using pentane or gradients of pentane/diethyl ether.

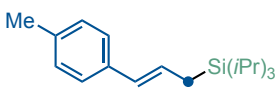
**Characterization Data for the Different Allylsilanes**

**Cinnamyltriisopropylsilane (133a)**




The title compound (colorless oil, 20 mg, 69% yield) was obtained following General Procedure L from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (25 mg, 0.106 mmol) and triisopropylsilane (67 mg, 0.423 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (2.1 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.27 – 7.24 (m, 4H), 7.14 (dq, *J* = 6.0, 2.8 Hz, 1H), 6.30 – 6.27 (m, 2H), 1.79 (d, *J* = 6.8 Hz, 2H), 1.07 (m, 21H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.92, 129.14, 128.82, 128.51, 126.51, 125.81, 19.08, 17.03, 11.43. **HRMS** (APCI Positive): calculated for $C_{18}H_{31}Si$ $[M+H]^+$: 275.2190; found: 275.2187.

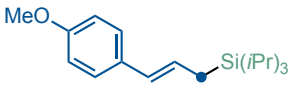
**(*E*)-Triisopropyl(3-(p-tolyl)allyl)silane (133b)**




The title compound (colorless oil, 23 mg, 63% yield) was obtained following General Procedure L from (*E*)-1,3,5-trimethyl-7-(4-methylstyryl)cyclohepta-1,3,5-triene (23 mg, 0.09 mmol) and triisopropylsilane (57 mg, 0.360 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (1.8 mg, 2 mol %) after purification by preparative TLC on

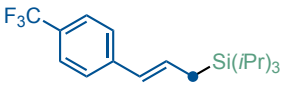
$SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.18 (d, *J* = 8.1 Hz, 2H), 7.07 (d, *J* = 7.9 Hz, 2H), 6.29 – 6.18 (m, 2H), 2.31 (s, 3H), 1.77 (d, *J* = 6.9 Hz, 2H), 1.11 – 1.03 (m, 21H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 136.15, 129.52, 128.36, 127.99, 125.71, 21.45, 19.08, 16.90, 11.43. **HRMS** (APCI Positive): calculated for $C_{19}H_{33}Si$ $[M+H]^+$: 289.2346; found: 289.2345.

**(*E*)-Triisopropyl(3-(4-methoxyphenyl)allyl)silane (133c)**



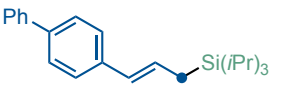

The title compound (colorless oil, 41 mg, 60% yield) was obtained following General Procedure L from (*E*)-7-(4-methoxystyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (60 mg, 0.23 mmol) and triisopropylsilane (143 mg, 0.90 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (4.5 mg, 2 mol %) after purification by preparative TLC on $SiO_2$ using pentane/$Et_2O$ (99:1). **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.27 – 7.21 (m, 2H), 6.88 – 6.82 (m, 2H), 6.27 (d, *J* = 15.7 Hz, 1H), 6.16 (dt, *J* = 15.7, 7.9 Hz, 1H), 3.82 (s, 3H), 1.83 – 1.75 (m, 2H), 1.14 – 1.07 (m, 21H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 158.21, 131.51, 127.52, 126.49, 126.46, 113.94, 55.30, 18.73, 16.41, 11.07. **HRMS** (APCI Positive): calculated for $C_{19}H_{33}OSi$ $[M+H]^+$: 305.2295; found: 305.2299.

**(*E*)-Triisopropyl(3-(4-(trifluoromethyl)phenyl)allyl)silane (133d)**




The title compound (colorless oil, 25 mg, 64% yield) was obtained following General Procedure L from (*E*)-1,3,5-trimethyl-7-(4-(trifluoromethyl)styryl)cyclohepta-1,3,5-triene (35 mg, 0.115 mmol) and triisopropylsilane (73 mg, 0.460 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (2.3 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.56 – 7.51 (m, 2H), 7.38 (d, *J* = 8.2 Hz, 2H), 6.45 (dt, *J* = 16.1, 8.1 Hz, 1H), 6.34 (d, *J* = 15.7 Hz, 1H), 1.86 (dd, *J* = 8.1, 1.2 Hz, 2H), 1.16 – 1.06 (m, 21H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.92, 132.02, 128.29 (q, *J* = 32 Hz), 126.90, 125.44 (q, *J* = 1.9 Hz), 121.60 (q, *J* = 273 Hz), 17.12, 11.08. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -62.42. **HRMS** (APCI Positive): calculated for $C_{19}H_{29}F_2Si$ $[M–F]^+$: 323.2001; found: 323.2002.

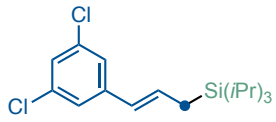
**(*E*)-(3-([1,1'-Biphenyl]-4-yl)allyl)triisopropylsilane (133e)**




The title compound (colorless oil, 51 mg, 70% yield) was obtained following General Procedure L from (*E*)-4-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)-1,1'-biphenyl (65 mg, 0.208 mmol) and triisopropylsilane (132 mg, 0.832 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (4.1 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.64 – 7.59 (m, 2H), 7.55 (d, *J* = 8.4 Hz, 2H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.39 (d, *J* = 8.3 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 1H), 6.46 – 6.32 (m, 2H), 1.86 (d, *J* = 6.8 Hz, 2H),

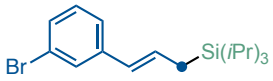
1.19 – 1.06 (m, 21H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.00, 138.96, 137.63, 129.07, 128.74, 127.70, 127.22, 127.04, 126.87, 125.84, 18.75, 16.85, 11.11. **HRMS** (APCI Positive): calculated for $C_{24}H_{35}Si$ $[M+H]^+$: 351.2503; found: 351.2501.

**(*E*)-(3-(3,5-Dichlorophenyl)allyl)triisopropylsilane (133f)**



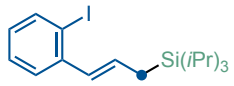

The title compound (colorless oil, 32 mg, 71% yield) was obtained following General Procedure L from (*E*)-7-(3,5-dichlorostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (40 mg, 0.131 mmol) and triisopropylsilane (83 mg, 0.524 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (2.6 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.18 – 7.08 (m, 3H), 6.33 (dt, *J* = 15.6, 8.4 Hz, 1H), 6.14 (dt, *J* = 15.7, 1.6 Hz, 1H), 1.79 (dd, *J* = 8.5, 1.4 Hz, 2H), 1.10 – 1.02 (m, 21H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.86, 135.32, 132.78, 126.23, 126.11, 124.06, 19.04, 17.45, 11.43. **GC-MS** (EI): calculated for $C_{18}H_{28}Cl_2Si$ $[M]^+$: 342.1; found: 342.1.

**(*E*)-(3-(3-Bromophenyl)allyl)triisopropylsilane (133g)**




The title compound (colorless oil, 36 mg, 64% yield) was obtained following General Procedure L from (*E*)-7-(3-bromostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (50 mg, 0.159 mmol) and triisopropylsilane (100 mg, 0.634 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (2.1 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.39 (t, *J* = 1.8 Hz, 1H), 7.27 – 7.24 (m, 1H), 7.17 (dt, *J* = 7.7, 1.2 Hz, 1H), 7.11 (t, *J* = 7.8 Hz, 1H), 6.34 – 6.26 (m, 1H), 6.19 (d, *J* = 15.6 Hz, 1H), 1.79 (dd, *J* = 8.2, 1.2 Hz, 2H), 1.10 – 1.02 (m, 21H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.06, 131.04, 130.32, 129.34, 128.67, 127.13, 124.36, 123.10, 19.06, 17.25, 11.43. **HRMS** (APCI Pos): calculated for $C_{18}H_{30}{}^{79}BrSi$ $[M+H]^+$: 353.1295; found: 353.1281.

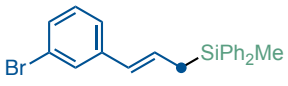
**(*E*)-(3-(2-Iodophenyl)allyl)triisopropylsilane (133h)**




The title compound (colorless oil, 16 mg, 57% yield) was obtained following General Procedure L from (*E*)-7-(2-iodostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (26 mg, 0.071 mmol) and triisopropylsilane (45 mg, 0.283 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (1.0 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.78 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.35 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.26 – 7.23 (m, 1H), 6.84 (td, *J* = 7.7, 1.7 Hz, 1H), 6.46 (d, *J* = 15.4 Hz, 1H), 6.16 (dt, *J* = 15.4, 8.4 Hz, 1H), 1.85 (dd, *J* = 8.4, 1.4 Hz, 2H), 1.08 (m, 21H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 141.91, 139.69, 132.63, 132.31, 128.62, 128.13,

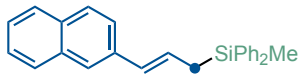
126.34, 99.41, 19.12, 17.36, 11.44. **HRMS** (APCI Positive): calculated for $C_{18}H_{30}ISi$ $[M+H]^+$: 401.1156; found: 401.1147.

**(*E*)-(3-(3-Bromophenyl)allyl)(methyl)diphenylsilane (133i)**



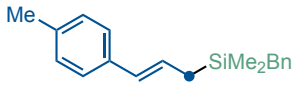

The title compound (amorphous solid, 38 mg, 68% yield) was obtained following General Procedure L from (*E*)-7-(3-bromostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (45 mg, 0.143 mmol) and methyldiphenylsilane (113 mg, 0.571 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (1.9 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.55 (dd, *J* = 7.8, 1.6 Hz, 4H), 7.44 – 7.35 (m, 7H), 7.28 (dt, *J* = 6.9, 1.9 Hz, 1H), 7.16 – 7.09 (m, 2H), 6.28 – 6.16 (m, 2H), 2.24 (d, *J* = 7.1 Hz, 2H), 0.61 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 140.78, 136.56, 134.91, 130.29, 129.85, 129.59, 128.86, 128.82, 128.61, 128.31, 124.58, 123.05, 22.04, -4.21. **HRMS** (APCI Pos): calculated for $C_{22}H_{22}{}^{79}BrSi$ $[M+H]^+$: 393.0669; found: 393.0670.

**(*E*)-Methyl(3-(naphthalen-2-yl)allyl)diphenylsilane (133j)**




The title compound (colorless viscous oil, 44 mg, 69% yield) was obtained following General Procedure L from (*E*)-2-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)-naphthalene (50 mg, 0.175 mmol) and methyldiphenylsilane (138 mg, 0.698 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (2.3 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.79 (dd, *J* = 7.8, 4.4 Hz, 2H), 7.75 (d, *J* = 8.6 Hz, 1H), 7.61 (dd, *J* = 7.5, 1.9 Hz, 5H), 7.50 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.48 – 7.38 (m, 8H), 6.51 – 6.33 (m, 2H), 2.33 (d, *J* = 7.4 Hz, 2H), 0.66 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 136.45, 135.71, 134.62, 133.77, 132.47, 129.81, 129.44, 127.99, 127.94, 127.75, 127.62, 127.10, 126.12, 125.30, 124.75, 123.51, 21.72, -4.52. **HRMS** (APCI Positive): calculated for $C_{26}H_{25}Si$ $[M+H]^+$: 365.1720; found: 365.1720.

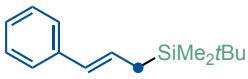
**(*E*)-Benzyldimethyl(3-(p-tolyl)allyl)silane (133k)**




The title compound (viscous amorphous oil, 31 mg, 79% yield) was obtained following General Procedure L from (*E*)-1,3,5-trimethyl-7-(4-methylstyryl)cyclohepta-1,3,5-triene (35 mg, 0.140 mmol) and dimethylbenzylsilane (84 mg, 0.559 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (1.8 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.26 – 7.21 (m, 4H), 7.13 (s, 1H), 7.13 – 7.10 (m, 2H), 7.04 (dd, *J* = 12.8, 7.2 Hz, 3H), 6.24 (d, *J* = 15.8 Hz, 1H), 6.15 (dt, *J* = 15.6, 7.8 Hz, 1H), 2.36 (s, 3H), 2.18 (s, 2H), 1.69 (d, *J* = 7.3 Hz, 2H), 0.06 (s, 3H), 0.02 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 139.95, 139.42, 135.99, 135.60, 129.16,

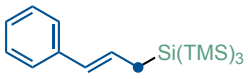
128.65, 128.35, 128.25, 128.18, 128.14, 126.07, 125.45, 124.07, 28.54, 25.33, 21.95, 21.10, -0.07, -3.71. **GC-MS** (EI): calculated for $C_{19}H_{24}Si$ $[M]^+$: 280.1; found: 280.1.

***tert*-Butyl(cinnamyl)dimethylsilane (133l)**



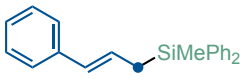

The title compound (colorless oil, 29 mg, 74% yield) was obtained following General Procedure L from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (40 mg, 0.169 mmol) and *tert*-butylmethylsilane (79 mg, 0.677 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (2.3 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.30 – 7.24 (m, 4H), 7.14 (tt, *J* = 7.3, 1.8 Hz, 1H), 6.28 – 6.18 (m, 2H), 1.70 – 1.66 (m, 2H), 0.90 (s, 9H), -0.02 (s, 6H) **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.89, 128.81, 128.65, 128.63, 126.54, 125.84, 26.93, 20.41, 17.21, -5.98. **GC-MS** (EI): calculated for $C_{15}H_{24}Si$ $[M+H]^+$: 232.1; found: 232.1.

**2-Cinnamyl-1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane (133m)**



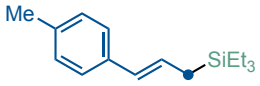

The title compound (colorless oil, 17 mg, 37% yield) was obtained following General Procedure L from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (30 mg, 0.127 mmol) and 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane (126 mg, 0.508 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (1.7 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.30 – 7.27 (m, 4H), 7.21 – 7.14 (m, 1H), 6.35 – 6.21 (m, 2H), 2.01 – 1.90 (m, 2H), 0.21 (s, 27H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 138.26, 130.80, 128.49, 127.26, 126.20, 125.42, 14.29, 1.08. **HRMS** (APCI Positive): calculated for $C_{18}H_{37}Si_4$ $[M+H]^+$: 365.1967; found: 365.1973.

**Cinnamyl(methyl)diphenylsilane (133n)**



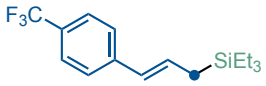

The title compound (colorless oil, 35 mg, 66% yield) was obtained following General Procedure L from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (40 mg, 0.169 mmol) and methyldiphenylsilane (134 mg, 0.677 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (2.2 mg, 3 mol %) after purification by flash column chromatography on $SiO_2$ using pentane to pentane/$Et_2O$ 99:1 as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.55 (dd, *J* = 7.7, 1.6 Hz, 4H), 7.42 – 7.34 (m, 6H), 7.27 – 7.22 (m, 4H), 7.15 (tt, *J* = 6.2, 1.9 Hz, 1H), 6.28 (d, *J* = 15.8 Hz, 1H), 6.22 (dt, *J* = 15.6, 7.5 Hz, 1H), 2.23 (d, *J* = 7.4 Hz, 2H), 0.59 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.64, 136.82, 134.95, 130.04, 129.75, 128.80, 128.27, 126.91, 126.77, 126.00, 21.85, -4.22. **HRMS** (APCI Positive): calculated for $C_{22}H_{23}Si$ $[M+H]^+$: 315.1564; found: 315.1549.

**(*E*)-Triethyl(3-(*p*-tolyl)allyl)silane (133o)**



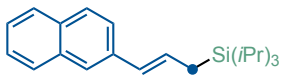

The title compound (colorless oil, 8.7 mg, 39% yield) was obtained following General Procedure L from (*E*)-1,3,5-trimethyl-7-(4-methylstyryl)cyclohepta-1,3,5-triene (23 mg, 0.090 mmol) and triethylsilane (43 mg, 0.360 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (1.8 mg, 3 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.18 (d, *J* = 8.1 Hz, 2H), 7.07 (d, *J* = 7.9 Hz, 2H), 6.24 – 6.13 (m, 2H), 2.30 (s, 3H), 1.67 (d, *J* = 7.0 Hz, 2H), 0.95 (t, *J* = 7.9 Hz, 9H), 0.55 (q, *J* = 7.9 Hz, 6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 136.16, 136.14, 129.49, 128.24, 127.33, 125.72, 21.44, 19.07, 7.73, 3.62. **HRMS** (APCI Positive): calculated for $C_{16}H_{27}Si$ $[M+H]^+$: 247.1877; found: 247.1876.

**(*E*)-Triethyl(3-(4-(trifluoromethyl)phenyl)allyl)silane (133p)**



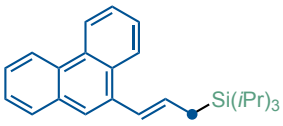

The title compound (colorless oil, 20 mg, 45% yield) was obtained following General Procedure L from (*E*)-1,3,5-trimethyl-7-(4-(trifluoromethyl)styryl)cyclohepta-1,3,5-triene (45 mg, 0.148 mmol) and triethylsilane (69 mg, 0.591 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (2.3 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 8.3 Hz, 2H), 6.46 – 6.34 (m, 1H), 6.29 (d, *J* = 15.7 Hz, 1H), 1.77 (dd, *J* = 8.1, 0.8 Hz, 2H), 1.00 (t, *J* = 7.9 Hz, 9H), 0.61 (q, *J* = 7.9 Hz, 6H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.95, 131.35, 127.93 (q, *J* = 34 Hz, 1C, *C*–$CF_3$), 126.78, 125.47, 125.39 (q, *J* = 3.8 Hz, 2C, *C*–C–$CF_3$), 124.39 (q, *J* = 272 Hz, *C*$F_3$), 19.33, 7.35, 3.27. **$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -62.42. **HRMS** (APCI Positive): calculated for $C_{16}H_{23}F_2Si$ $[M–F]^+$: 281.1532; found: 281.1528.

**(*E*)-Triisopropyl(3-(naphthalen-2-yl)allyl)silane (133q)**



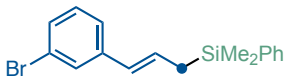

The title compound (colorless oil, 35 mg, 69% yield) was obtained following General Procedure L from (*E*)-2-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)-naphthalene (45 mg, 0.157 mmol) and triisopropylsilane (100 mg, 0.628 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (2.1 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 9.1 Hz, 2H), 7.73 (d, *J* = 8.6 Hz, 1H), 7.61 – 7.59 (m, 1H), 7.53 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.42 (ddd, *J* = 8.1, 6.9, 1.4 Hz, 1H), 7.37 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 6.49 – 6.38 (m, 2H), 1.89 – 1.80 (m, 2H), 1.17 – 1.05 (m, 21H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 136.35, 134.21, 132.73, 129.70, 128.68, 128.38, 128.06, 127.97, 126.44, 125.51, 124.76, 123.79, 19.11, 17.27, 11.48. **HRMS** (APCI Pos): calculated for $C_{22}H_{33}Si$ $[M+H]^+$: 325.2346; found: 325.2341.

**(*E*)-Triisopropyl(3-(phenanthren-9-yl)allyl)silane (133r)**



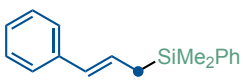

The title compound (viscous colorless oil, 20 mg, 53% yield) was obtained following General Procedure L from (*E*)-9-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)-phenanthrene (34 mg, 0.100 mmol) and triisopropylsilane (63 mg, 0.400 mmol, 4 equiv) using [$Rh_2$(TFA)$_4$] (1.4 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 8.71 (dd, *J* = 8.0, 1.5 Hz, 1H), 8.67 – 8.61 (m, 1H), 8.16 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.86 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.70 (s, 1H), 7.67 – 7.60 (m, 2H), 7.60 – 7.54 (m, 2H), 7.01 (d, *J* = 16.0 Hz, 1H), 6.39 (dt, *J* = 15.2, 8.3 Hz, 1H), 1.96 (dd, *J* = 8.3, 1.5 Hz, 2H), 1.20 – 1.10 (m, 21H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 135.51, 132.56, 132.48, 131.25, 130.74, 130.12, 128.74, 126.97, 126.81, 126.63, 126.31, 126.12, 125.14, 124.00, 123.36, 122.82, 19.17, 17.61, 11.53. **HRMS** (APCI Positive): calculated for $C_{26}H_{35}Si$ $[M+H]^+$: 375.2503; found: 375.2497.

**(*E*)-(3-(3-Bromophenyl)allyl)dimethyl(phenyl)silane (133s)**



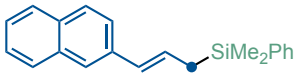

The title compound (colorless oil, 41 mg, 87% yield) was obtained following General Procedure L from (*E*)-7-(3-bromostyryl)-1,3,5-trimethylcyclohepta-1,3,5-triene (45 mg, 0.143 mmol) and dimethyl(phenyl)silane (78 mg, 0.571 mmol, 4 equiv) using [$Rh_2$(TFA)$_4$] (1.9 mg, 2 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.81 – 7.78 (m, 2H), 7.77 (d, *J* = 8.6 Hz, 1H), 7.63 (s, 1H), 7.60 – 7.58 (m, 1H), 7.55 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.48 – 7.45 (m, 1H), 7.43 – 7.41 (m, 2H), 6.47 – 6.35 (m, 2H), 2.00 (d, *J* = 7.3 Hz, 2H), 0.39 (s, 6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.90, 136.20, 134.17, 134.03, 132.80, 129.50, 129.45, 128.21, 126.47, 125.60, 124.99, 123.86, 23.63, -2.89. **GC-MS** (EI): calculated for $C_{17}H_{19}{}^{81}BrSi$ $[M+H]^+$: 330.9; found: 330.9.

**Cinnamyldimethyl(phenyl)silane (133t)**



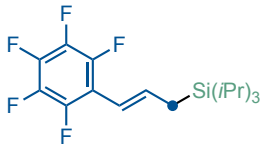

The title compound (colorless oil, 35 mg, 82% yield) was obtained following General Procedure L from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (40 mg, 0.169 mmol) and dimethyl(phenyl)silane (92 mg, 0.677 mmol, 4 equiv) using [$Rh_2$(TFA)$_4$] (2.3 mg, 3 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.56 – 7.50 (m, 2H), 7.40 – 7.34 (m, 3H), 7.30 – 7.25 (m, 4H), 7.18 – 7.13 (m, 1H), 6.28 – 6.17 (m, 2H), 1.96 – 1.84 (m, 2H), 0.33 (s, 6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.92, 138.76, 134.00, 129.47, 129.31, 128.82, 128.18, 127.51, 126.68, 125.94, 23.40, -2.94. **HRMS** (APCI Positive): calculated for $C_{17}H_{21}Si$ $[M+H]^+$: 253.1407; found: 253.1409.

**(*E*)-Dimethyl(3-(naphthalen-2-yl)allyl)(phenyl)silane (133u)**



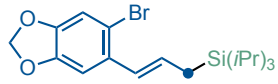

The title compound (pale yellow solid, 41 mg, 78% yield) was obtained following General Procedure L from (*E*)-2-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)-naphthalene (50 mg, 0.175 mmol) and dimethyl(phenyl)silane (95 mg, 0.698 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (2.3 mg, 2 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.64–7.50 (m, 3H), 7.44–7.37 (m, 6H), 7.30 (d, *J* = 6.4 Hz, 1H), 7.21–7.13 (m, 2H), 6.30–6.16 (m, 2H), 1.94 (d, *J* = 7.9 Hz, 2H), 0.36 (s, 6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 140.92, 140.20, 138.63, 133.97, 133.38, 130.31, 129.63, 129.57, 129.50, 129.43, 128.78, 128.23, 128.08, 127.89, 124.56, 123.08, 23.61, 1.24, -2.93. **GC-MS** (EI): calculated for $C_{21}H_{22}Si$ $[M+H]^+$: 302.1; found: 302.1. **MP** 60–63 ºC.

**(*E*)-Triisopropyl(3-(perfluorophenyl)allyl)silane (133v)**



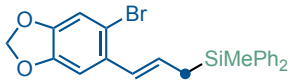

The title compound (colorless oil, 27 mg, 60% yield) was obtained following General Procedure L from (*E*)-1,3,5-trimethyl-7-(2-(perfluorophenyl)vinyl)cyclohepta-1,3,5-triene (40 mg, 0.123 mmol) and triisopropylsilane (78 mg, 0.490 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (1.8 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 6.70 (dt, *J* = 16.6, 8.5 Hz, 1H), 6.18 (dt, *J* = 16.0, 1.3 Hz, 1H), 1.93 – 1.86 (m, 2H), 1.14 – 1.06 (m, 21H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 145.45, 142.98, 140.03, 139.71, 138.88, 137.52, 136.41, 113.02, 112.06, 18.82, 18.61, 11.08. **$^{19}$F NMR** (376 MHz, Chloroform-*d*) δ -144.23 – -144.83 (m), -159.07 (t, *J* = 20.8 Hz), -163.51 (td, *J* = 21.1, 7.0 Hz). **GC-MS** (EI): calculated for $C_{18}H_{25}F_5Si$ $[M]^+$: 364.2; found: 364.2.

**(*E*)-(3-(6-Bromobenzo[*d*][1,3]dioxol-5-yl)allyl)triisopropylsilane (133w)**



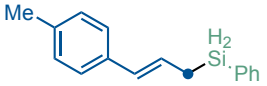

The title compound (viscous colorless oil, 34 mg, 62% yield) was obtained following General Procedure L from (*E*)-5-bromo-6-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)benzo[*d*][1,3]dioxole (50 mg, 0.139 mmol) and triisopropylsilane (88 mg, 0.557 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (1.8 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 6.95 (s, 1H), 6.88 (s, 1H), 6.52 (dt, *J* = 15.4, 1.3 Hz, 1H), 6.06 (dt, *J* = 15.3, 8.3 Hz, 1H), 5.92 (s, 2H), 1.81 (dd, *J* = 8.4, 1.4 Hz, 2H), 1.09 – 1.05 (m, 21H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 147.93, 147.19, 132.20, 130.78, 127.25, 113.62, 112.89, 106.22, 101.90, 19.08, 17.21, 11.43. **HRMS** (APCI Pos): calculated for $C_{19}H_{30}BrO_2Si$ $[M+H]^+$: 397.1193; found: 397.1177.

**(*E*)-(3-(6-Bromobenzo[*d*][1,3]dioxol-5-yl)allyl)(methyl)diphenylsilane (133x)**




The title compound (amorphous viscous solid, 33 mg, 68% yield) was obtained following General Procedure L from (*E*)-5-bromo-6-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)benzo[*d*][1,3]dioxole (40 mg, 0.111 mmol) and methyldiphenylsilane (88 mg, 0.445 mmol, 4 equiv) using [$Rh_2(TFA)_4$] (1.5 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.60 – 7.55 (m, 4H), 7.44 – 7.37 (m, 6H), 6.98 (s, 1H), 6.83 (s, 1H), 6.57 (dt, *J* = 15.5, 1.2 Hz, 1H), 6.05 – 5.97 (m, 1H), 5.95 (s, 2H), 2.28 (dd, *J* = 8.2, 1.3 Hz, 2H), 0.64 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 147.52, 147.03, 136.31, 134.56, 131.61, 129.43, 128.42, 128.26, 127.95, 113.46, 112.48, 106.08, 101.55, 21.61, -4.55. **HRMS** (APCI Positive): calculated for $C_{23}H_{22}BrO_2Si$ $[M+H]^+$: 437.0567; found: 437.0570.

**(*E*)-Phenyl(3-(p-tolyl)allyl)silane (133y)**



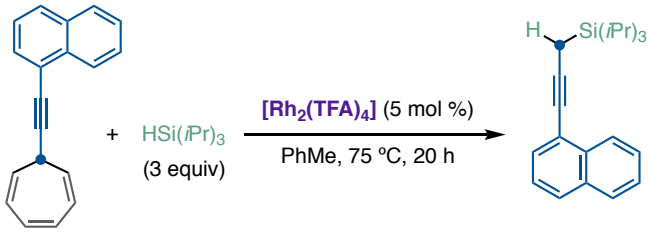

The title compound (colorless oil, 15 mg, 53% yield) was obtained following General Procedure L from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (30 mg, 0.120 mmol) and phenylsilane (78 mg, 0.719 mmol, 6 equiv) using [$Rh_2(TFA)_4$] (2.0 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.57 (dt, *J* = 6.6, 1.5 Hz, 2H), 7.42 – 7.38 (m, 1H), 7.37 – 7.32 (m, 2H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.07 (d, *J* = 7.9 Hz, 2H), 6.30 (d, *J* = 15.8 Hz, 1H), 6.20 (dt, *J* = 15.6, 7.8 Hz, 1H), 4.35 (t, *J* = 3.7 Hz, 2H), 2.30 (s, 3H), 2.04 (ddt, *J* = 6.6, 3.6, 1.9 Hz, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 136.68, 135.66, 135.53, 132.10, 130.25, 130.16, 129.52, 128.39, 125.94, 125.42, 21.47, 17.16. **HRMS** (APCI Positive): calculated for $C_{16}H_{19}Si$ $[M+H]^+$: 239.1251; found: 239.1250.

**Triisopropyl((2*E*,4*E*)-5-phenylpenta-2,4-dien-1-yl)silane (133z)**


The title compound (colorless oil, 20 mg, 67% yield10:1, *E*/*Z* ratio) was obtained following General Procedure L from 1,3,5-trimethyl-7-((1*E*,3*E*)-4-phenylbuta-1,3-dien-1-yl)cyclohepta-1,3,5-triene (26 mg, 0.100 mmol, 10:1 *E*/*Z* ratio) and triisopropylsilane (63 mg, 0.396 mmol, 4 equiv) using [$Rh_2(TFA)_4$] (1.8 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.37 – 7.33 (m, 2H), 7.27 (t, *J* = 7.7 Hz, 2H), 7.18 – 7.13 (m, 1H), 6.73 (dd, *J* = 15.6, 10.4 Hz, 1H), 6.34 (d, *J* = 15.6 Hz, 1H), 6.12 (dd, *J* = 14.9, 10.4 Hz, 1H), 5.90 (dt, *J* = 14.9, 8.5 Hz, 1H), 1.73 (dd, *J* = 8.4, 1.0 Hz, 2H), 1.08 – 1.05 (m, 21H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.34, 134.15, 130.28, 129.76, 128.87, 128.29, 127.08, 126.30, 19.07, 17.11, 11.46. **HRMS** (APCI Positive): calculated for $C_{20}H_{33}Si$ $[M–H]^+$: 301.2346; found: 301.2334.

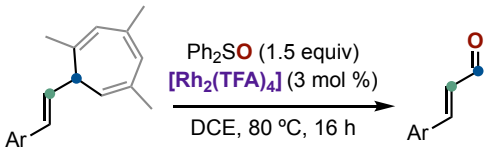
**Trapping of an Alkynylcyclopropane by Intermolecular Si–H Insertion**

**Triisopropyl(3-(naphthalen-1-yl)prop-2-yn-1-yl)silane**




A microwave vial equipped with a Teflon-coated magnetic stirring bar was charged with 7-(1-naphthyl)-1,3,5-cycloheptatriene (120 mg, 0.50 mmol, 1 equiv) and triisopropylsilane (235 mg, 1.49 mmol, 3 equiv). The vial was introduced in an argon-filled glovebox, and both reagents were dissolved in anhydrous PhMe (0.15 M). Then, $[Rh_2(TFA)_4]$ 16 mg, (5 mol %) was added before the reaction vial was sealed and taken out of the glovebox. The mixture was stirred at 75 ºC (until TLC and/or GCMS show full consumption of the starting cycloheptatriene, *ca*. 20 h). The reaction was concentrated in vacuum and the obtained crude mixture was analyzed by NMR and GCMS (in order to check the ratios of products and side-products), before it was purified by flash column chromatography in $SiO_2$ using pentane as eluent to give the title compound (colorless oil, 40 mg, 33% yield). **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 8.39 (ddt, *J* = 8.3, 1.5, 0.8 Hz, 1H), 7.89 – 7.83 (m, 1H), 7.77 (dt, *J* = 8.3, 1.1 Hz, 1H), 7.63 – 7.50 (m, 3H), 7.42 (dd, *J* = 8.3, 7.1 Hz, 1H), 1.98 (s, 2H), 1.35 – 1.27 (m, 3H), 1.21 (d, *J* = 6.7 Hz, 18H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 133.56, 133.28, 129.60, 128.16, 127.23, 126.48, 126.25, 126.12, 125.34, 122.83, 94.29, 77.65, 18.68, 11.19, 0.42. **HRMS** (APCI Pos): calculated for $C_{22}H_{31}Si$ $[M+H]^+$: 323.2190; found: 323.2191.

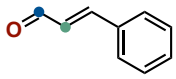
**General Procedure M for the Oxidative Retro-Buchner Reaction**




A microwave vial equipped with a Teflon-coated magnetic stirring bar was charged with the corresponding 1,3,5-trimethyl-7-styryl-1,3,5-cycloheptatriene **44** (1.0 equiv) and diphenylsulfoxide (1.5 equiv). The vial was introduced in an argon-filled glovebox, and both reagents were dissolved in anhydrous 1,2-DCE (0.1 M), before $[Rh_2(TFA)_4]$ (3 mol %) was added. The vial was sealed with the corresponding cap, taken outside the glovebox, and then stirred at 80 ºC for 16 hours. After confirming that the reaction was complete by TLC, the resulting mixture was concentrated in vacuum. The crude product was purified by flash column chromatography or preparative TLC on silica gel, using gradients of pentane/diethyl ether.

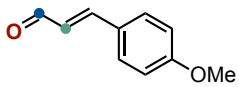
**Characterization Data for Different Aldehydes**

**Cinnamaldehyde (136a)**



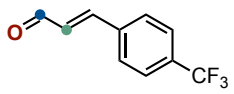
The title compound (pale yellow oil, 28 mg, 80% yield, >20:1 *E*/*Z* ratio) was obtained following General Procedure M from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (60 mg, 0.254 mmol) and diphenylsulfoxide (79 mg, 0.380 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (4.3 mg, 3 mol %) after purification by flash column chromatography on $SiO_2$ using pentane/$Et_2O$ 9:1 to 8:2 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) $^1$H NMR (400 MHz, Chloroform-*d*) δ 9.73 (d, *J* = 7.7 Hz, 1H), 7.61 – 7.57 (m, 2H), 7.50 (d, *J* = 16.0 Hz, 1H), 7.48 – 7.41 (m, 3H), 6.75 (dd, *J* = 16.0, 7.7 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 193.76, 152.84, 134.02, 131.30, 129.13, 128.61, 128.52. **GC-MS** (EI): calculated for $C_9H_8O$ $[M]^+$: 132.1; found: 132.1.

**(*E*)-3-(4-Methoxyphenyl)acrylaldehyde (136b)**



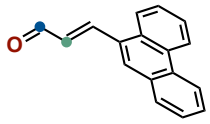
The title compound (yellow solid, 15 mg, 92% yield, >20:1 *E*/*Z* ratio) was obtained following General Procedure M from (*E*)-7-(4-methoxystyryl)-1,3,5-trimethyl-cyclohepta-1,3,5-triene (27 mg, 0.100 mmol) and diphenylsulfoxide (30 mg, 0.150 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (2.1 mg, 3 mol %) after purification by preparative TLC on $SiO_2$ using pentane/$Et_2O$ 8:2 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 9.68 (d, *J* = 7.7 Hz, 1H), 7.55 (d, *J* = 8.7 Hz, 2H), 7.45 (d, *J* = 15.8 Hz, 1H), 6.97 (d, *J* = 8.8 Hz, 2H), 6.63 (dd, *J* = 15.8, 7.8 Hz, 1H), 3.88 (s, 3H) **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 193.69, 162.22, 152.69, 130.36, 126.82, 126.57, 114.59, 55.47. **GC-MS** (EI): calculated for $C_{10}H_{10}O_2$ $[M]^+$: 162.1; found: 162.1.

**(*E*)-3-(4-(Trifluoromethyl)phenyl)acrylaldehyde (136c)**



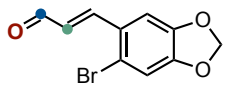
The title compound (pale orange residue, 10 mg, 50% yield, >20:1 *E*/*Z* ratio) was obtained following General Procedure M from (*E*)-1,3,5-trimethyl-7-(4-(trifluoromethyl)styryl)cyclohepta-1,3,5-triene (30 mg, 0.100 mmol) and diphenylsulfoxide (30 mg, 0.150 mmol, 1.5 equiv) using [$Rh_2(TFA)_4$] (2.1 mg, 3 mol %) after purification by preparative TLC on $SiO_2$ using pentane/$Et_2O$ 8:2 as eluent. Spectroscopic data matched the reported ones. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 9.78 (d, *J* = 7.5 Hz, 1H), 7.71 (d, *J* = 1.4 Hz, 4H), 7.53 (d, *J* = 16.1 Hz, 1H), 6.80 (dd, *J* = 16.0, 7.5 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 193.18, 150.26, 137.31, 132.80 (q, *J* = 32.1 Hz, 1C *C*-$CF_3$), 130.54, 128.57, 126.07 (q, *J* = 3.8 Hz, 2C, H*C*-C-$CF_3$), 121.20 (q, *J* = 231 Hz, 1C, *C*$F_3$) **GC-MS** (EI): calculated for $C_{10}H_7F_3O$ $[M+H]^+$: 200.0; found: 200.1.

**(*E*)-3-(Phenanthren-9-yl)acrylaldehyde (136d)**



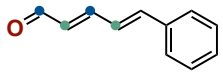
The title compound (pale yellow oil, 18 mg, 80% yield, >20:1 *E*/*Z* ratio) was obtained following General Procedure M from (*E*)-9-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)phenanthrene (30 mg, 0.127 mmol) and diphenylsulfoxide (39 mg, 0.190 mmol, 1.5 equiv) using [$Rh_2(TFA)_4$] (3.1 mg, 3 mol %) after purification by preparative TLC on $SiO_2$ using pentane/$Et_2O$ 8:2 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 9.92 (d, *J* = 7.7 Hz, 1H), 8.81 – 8.76 (m, 1H), 8.71 (d, *J* = 8.3 Hz, 1H), 8.35 (d, *J* = 15.7 Hz, 1H), 8.22 (dd, *J* = 8.0, 1.4 Hz, 1H), 8.07 (s, 1H), 7.96 (d, *J* = 9.1 Hz, 1H), 7.75 (pd, *J* = 7.1, 1.5 Hz, 3H), 7.67 (ddd, *J* = 8.0, 7.1, 1.1 Hz, 1H), 6.95 (dd, *J* = 15.7, 7.7 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 193.64, 150.04, 131.50, 130.91, 130.59, 130.09, 129.63, 129.57, 128.27, 127.53, 127.29, 127.27, 127.17, 123.80, 123.44, 122.69. **HRMS** (ESI Positive): calculated for $C_{17}H_{12}NaO$ $[M+Na]^+$: 255.0780; found: 255.0781. **MP** 160–162 ºC.

**(*E*)-3-(6-Bromobenzo[*d*][1,3]dioxol-5-yl)acrylaldehyde (136e)**



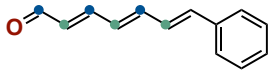
The title compound (pale yellow solid, 18 mg, 77% yield, >20:1 *E*/*Z* ratio) was obtained following General Procedure M from (*E*)-5-bromo-6-(2-(2,4,6-trimethylcyclohepta-2,4,6-trien-1-yl)vinyl)benzo[*d*][1,3]dioxole (34 mg, 0.100 mmol) and diphenylsulfoxide (30 mg, 0.150 mmol, 1.5 equiv) using [$Rh_2(TFA)_4$] (2.1 mg, 3 mol %) after purification by preparative TLC on $SiO_2$ using pentane/$Et_2O$ 75:25 as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 9.74 (d, *J* = 7.7 Hz, 1H), 7.85 (d, *J* = 15.8 Hz, 1H), 7.12 (s, 2H), 6.55 (dd, *J* = 15.8, 7.7 Hz, 1H), 6.08 (s, 2H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 193.45, 150.89, 150.51, 148.14, 128.93, 127.14, 118.71, 113.37, 106.60, 102.50. **HRMS** (APCI Positive): calculated for $C_{10}H_8{}^{79}BrO_3$ $[M+H]^+$: 254.9651; found: 254.9647. **MP** 155–157 ºC.

**(2*E*,4*E*)-5-Phenylpenta-2,4-dienal (138a)**



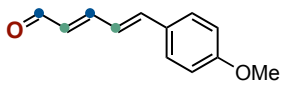
The title compound (orange oil, 252 mg, 70% yield, >20:1 *E*/*Z* ratio) was obtained following General Procedure M from 1,3,5-trimethyl-7-((1*E*,3*E*)-4-phenylbuta-1,3-dien-1-yl)cyclohepta-1,3,5-triene (600 mg, 2.29 mmol) and diphenylsulfoxide (694 mg, 3.43 mmol, 4 equiv) using [$Rh_2(TFA)_4$] (38 mg, 2.5 mol %) after purification by CombiFlash column chromatography on $SiO_2$ cyclohexane/EtOAc 9:1 to 8:2 as eluent. Spectroscopic data matched the reported ones.[217] **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 9.61 (d, *J* = 7.9 Hz, 1H), 7.53 – 7.45 (m, 2H), 7.40 – 7.31 (m, 3H), 7.26 (ddd, *J* = 15.2, 7.6, 2.6 Hz, 1H), 7.04 – 6.95 (m, 2H), 6.27 (dd, *J* = 15.2, 7.9 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 193.99, 152.41, 142.82, 135.97, 132.00, 130.06, 129.32, 127.91, 126.57. **GC-MS** (EI): calculated for $C_{11}H_{10}O$ $[M]^+$: 158.1; found: 158.1.

**(2*E*,4*E*,6*E*)-7-Phenylhepta-2,4,6-trienal (139a)**



The title compound (dark yellow solid, 50 mg, 60% yield, >20:1 *E*/*Z* ratio) was obtained following General Procedure M from 1,3,5-trimethyl-7-((1*E*,3*E*,5*E*)-6-phenylhexa-1,3,5-trien-1-yl)cyclohepta-1,3,5-triene (130 mg, 0.451 mmol) and diphenylsulfoxide (137 mg, 0.676 mmol, 1.5 equiv) using [$Rh_2(TFA)_4$] (15 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. Spectroscopic data matched the reported ones.[218] **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 9.60 (d, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 7.3 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.29 (t, *J* = 7.3 Hz, 1H), 7.20 (dd, *J* = 15.1, 11.2 Hz, 1H), 6.95 – 6.78 (m, 3H), 6.56 (dd, *J* = 14.1, 11.2 Hz, 1H), 6.23 (dd, *J* = 15.2, 8.0 Hz, 1H). **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 193.99, 152.12, 142.98, 138.51, 136.32, 131.14, 130.16, 128.89, 128.87, 127.71, 127.05. **GC-MS** (EI): calculated for $C_{13}H_{12}O$ $[M]^+$: 184.1; found: 184.1.

**(2*E*,4*E*)-5-(4-Methoxyphenyl)penta-2,4-dienal (138b)**



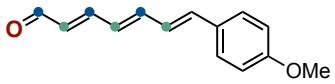
The title compound (colorless oil, 0.380 g, 51% yield, >20:1 *E*/*Z* ratio) was obtained following General Procedure M from 7-((1*E*,3*E*)-4-(4-methoxyphenyl)buta-1,3-dien-1-yl)-1,3,5-trimethylcyclohepta-1,3,5-triene (1.35 g, 3.92 mmol) and diphenylsulfoxide (1.19 g, 5.89 mmol, 1.5 equiv) using [$Rh_2(TFA)_4$] (52 mg, 2 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400

217 Duhamel, L.; Tombret, F. Efficient synthesis of a new nucleophilic acetaldehyde equivalent: (*Z*) 2-trimethylsiloxyvinyllithium. *J. Org. Chem.* **1981**, *46*, 3741–3742.

218 Kryshtal, G. V.; Zhdankina, G. M.; Ignat'ev, N. V.; Schulte, M.; Zlotin, S. G. Acidic ionic liquid-catalyzed homologation of the polyene chain in α,β-enals (polyenals). *Tetrahedron*, **2011**, *67*, 173–178

MHz, Chloroform-*d*) δ 9.62 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.7 Hz, 2H), 7.31 – 7.24 (m, 1H), 6.99 (d, *J* = 15.5 Hz, 1H), 6.95 – 6.86 (m, 3H), 6.25 (dd, *J* = 15.1, 8.0 Hz, 1H), 3.86 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 193.64, 160.98, 152.71, 142.30, 130.61, 129.15, 128.44, 124.11, 114.44, 55.40. **HRMS** (ESI Pos): calculated for $C_{12}H_{12}NaO_2$ $[M+Na]^+$: 211.0730; found: 211.0728.

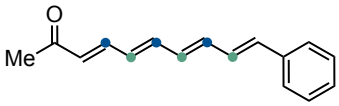
**(2*E*,4*E*,6*E*)-7-(4-methoxyphenyl)hepta-2,4,6-trienal (139b)**




The title compound (colorless oil, 63 mg, 62% yield, 20:1 *E*/*Z* ratio) was obtained following General Procedure M from 7-((1*E*,3*E*,5*E*)-6-(4-methoxyphenyl)hexa-1,3,5-trien-1-yl)-1,3,5-trimethylcyclohepta-1,3,5-triene (200 mg, 0.471 mmol, 4:1 *E*/*Z*) and diphenylsulfoxide (143 mg, 0.707 mmol, 1.5 equiv) using $[Rh_2(TFA)_4]$ (15 mg, 5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 9.63 (d, *J* = 8.0 Hz, 1H), 7.45 – 7.40 (m, 2H), 7.27 – 7.20 (m, 1H), 6.94 – 6.89 (m, 2H), 6.89 – 6.79 (m, 3H), 6.60 – 6.52 (m, 1H), 6.26 (dd, *J* = 15.1, 8.0 Hz, 1H), 3.85 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 193.34, 160.13, 151.94, 143.11, 137.98, 130.45, 128.99, 128.87, 128.30, 125.51, 114.16, 55.19. **HRMS** (ESI Pos): calculated for $C_{14}H_{14}NaO_2$ $[M+Na]^+$: 237.0886; found: 237.0883.

**Synthesis of Navenones B and C**

**Navenone B (141)**

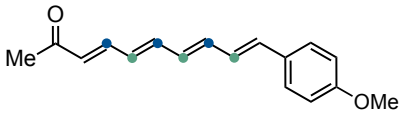



A microwave vial with a magnetic stirring bar was charged with (2*E*,4*E*,6*E*)-7-Phenylhepta-2,4,6-trienal **139a** (25 mg, 0.136 mmol) and 1-(triphenyl-l5-phosphanylidene)propan-2-one **140** (65 mg, 0.204 mmol, 1.5 equiv), introduced in an Ar-filled glovebox and dissolved in anhydrous toluene (1.35 mL, 0.1 M). The vial was sealed, taken out of the glovebox and stirred at 100 ºC for 20 h. After cooling down to room temperature and observing the formation of a slightly more polar spot by TLC, the solvent was removed in vacuum, and the resulting residue was purified by preparative TLC in $SiO_2$ using pentane/$Et_2O$ 8:2 as eluent (eluted twice), giving navenone B **141** (21 mg, 69%, >20:1 *E*/*Z*) as a bright yellow solid. Spectroscopic and physical data matched the reported ones for both natural and synthetic sample.[219] **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.41 (d, *J* = 7.8 Hz, 2H), 7.32 (t, *J* = 7.6 Hz, 2H), 7.25 (d, *J* = 7.3 Hz, 1H), 7.18 (dd, *J* = 15.6, 11.0 Hz, 1H), 6.86 (dd, *J* = 15.5, 10.8 Hz, 1H), 6.72 – 6.64 (m, 2H), 6.58 (dd, *J* = 14.8, 10.8 Hz, 1H), 6.40

219 (a) Sleeper, H. L.; Fenical, W. Navenones A-C: trail-breaking alarm pheromones from the marine opisthobranch Navanax inermis. *J. Am. Chem. Soc.* **1977**, *99*, 2367–2368. (b) Soullez, D.; Ramondenc, Y.; Ple, G.; Duhamel, L. *Nat. Prod. Lett.* Handy Access to Navenones A, B and C. **1994**, *4*, 203–208.

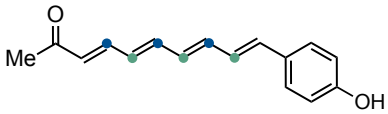
(ddd, *J* = 30.9, 14.7, 11.2 Hz, 2H), 6.15 (d, *J* = 15.4 Hz, 1H), 2.27 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 198.30, 143.21, 141.55, 137.69, 136.88, 135.33, 132.17, 130.52, 129.88, 128.73, 128.50, 128.15, 126.66, 27.39. **HRMS** (ESI Pos): calculated for $C_{16}H_{16}NaO$ $[M+H]^+$: 247.1093; found: 247.1083. **MP** 135–138 ºC.

**Methyl-Navenone C (141)**




A microwave vial with a magnetic stirring bar was charged with (2*E*,4*E*,6*E*)-7-(4-methoxyphenyl)hepta-2,4,6-trienal **139b** (30 mg, 0.140 mmol) and 1-(triphenyl-l5-phosphanylidene)propan-2-one **140** (67 mg, 0.210 mmol, 1.5 equiv), introduced in an Ar-filled glovebox and dissolved in anhydrous toluene (1.4 mL, 0.1 M). The vial was sealed, taken out of the glovebox and stirred at 100 ºC for 20 h. After cooling down to room temperature and observing the formation of a slightly more polar spot, the solvent was removed in vacuum and the resulting residue was purified by CombiFlash chromatography in $SiO_2$ using cyclohexane/EtOAc 9:1 to 8:2 as eluent, giving methyl-navenone C **141** (23 mg, 65%, >20:1 *E*/*Z*) as an orange solid. **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.36 (d, *J* = 8.7 Hz, 2H), 7.19 (dd, *J* = 15.3, 11.2 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.78 – 6.53 (m, 4H), 6.37 (td, *J* = 15.5, 14.8, 11.2 Hz, 2H), 6.14 (d, *J* = 15.4 Hz, 1H), 3.82 (s, 3H), 2.28 (s, 3H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 198.32, 159.79, 143.43, 141.87, 138.17, 135.09, 131.12, 129.91, 129.76, 129.55, 128.03, 126.52, 114.25, 55.33, 27.37. **HRMS** (ESI, Pos): calculated for $C_{17}H_{18}NaO_2$ $[M]^+$: 277.1199; found: 277.1201. **MP** 168–170 ºC.

**Navenone C (143)**

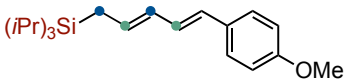



In a 25 mL round bottomed flask with a magnetic stirring bar, methyl-navenone C (20 mg, 0.079 mmol) was dissolved, under Ar, in anhydrous dichloromethane (1.0 mL, 0.08 M), and the yellow solution was cooled down to -78 ºC. Then, a 1.0 M solution of $BBr_3$ in dichloromethane (0.18 mL, 0.173 mmol, 2.2 equiv) was added dropwise. The mixture evolved immediately from yellow-orange to dark blue, and after stirring for 5 min at -78 ºC, it was allowed to slowly come to room temperature over 1 h, and then stirred for 3 h at 25 ºC. After this time, full conversion of the starting material was observed by TLC, and the reaction was quenched by the addition of 10 mL of $Et_2O$ and 10 mL of water (the organic phase evolved immediately back from dark blue to orange), and the aqueous phase was extracted twice more with $Et_2O$. Combined organic fractions were washed once with water, once with brine, dried over anhydrous $Na_2SO_4$ and then concentrated in vacuum. The resulting crude material was purified by CombiFlash chromatography in $SiO_2$ using cyclohexane/EtOAc 8:2 to 6:4 as eluent, giving navenone C **143** (14 mg, 74%) as an orange solid. Spectroscopic and physical data matched the reported ones for

both natural and synthetic sample.[219] **$^1$H NMR** (400 MHz, Acetone-$d_6$) δ 8.55 (br, 1H), 7.37 (d, *J* = 8.6 Hz, 2H), 7.27 (dd, *J* = 15.5, 11.2 Hz, 1H), 6.89 – 6.78 (m, 4H), 6.71 – 6.61 (m, 2H), 6.46 (dt, *J* = 14.8, 11.0 Hz, 2H), 6.13 (d, *J* = 15.5 Hz, 1H), 2.21 (s, 3H). **$^{13}$C NMR** (126 MHz, Acetone) δ 197.52, 158.60, 143.78, 142.42, 138.93, 135.94, 131.81, 130.78, 130.33, 129.66, 128.95, 126.78, 116.45, 27.09. **HRMS** (ESI Positive): calculated for $C_{16}H_{17}O_2$ $[M+H]^+$: 241.1223; found: 241.1227. **MP** 210–213 ºC.

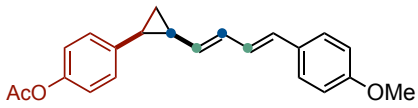
**Diversification of Polyene Intermediates**

**Triisopropyl((2*E*,4*E*)-5-(4-methoxyphenyl)penta-2,4-dien-1-yl)silane (137a)**



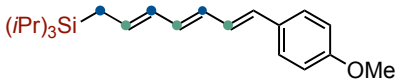

The title compound (pale yellow oil, 25 mg, 65% yield, 10:1 *E*/*Z* ratio) was obtained following General Procedure L from 7-((1*E*,3*E*)-4-(4-methoxyphenyl)buta-1,3-dien-1-yl)-1,3,5-trimethylcyclohepta-1,3,5-triene (40 mg, 0.116 mmol, 8:1 *E*/*Z* ratio) and triisopropylsilane (74 mg, 0.465 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (2.0 mg, 2.5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.28 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.8 Hz, 2H), 6.60 (dd, *J* = 15.5, 10.4 Hz, 1H), 6.29 (d, *J* = 15.6 Hz, 1H), 6.09 (dd, *J* = 14.6, 10.0 Hz, 1H), 5.84 (dt, *J* = 14.9, 8.4 Hz, 1H), 1.71 (d, *J* = 9.4 Hz, 2H), 1.07 – 1.05 (m, 21H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.01, 132.80, 131.19, 129.91, 128.36, 127.83, 127.42, 114.37, 55.65, 19.08, 16.96, 11.44. **HRMS** (APCI Positive): calculated for $C_{21}H_{35}OSi$ $[M+H]^+$: 331.2452; found: 331.2455.

***cis*-4-(2-((1*E*,3*E*)-4-(4-Methoxyphenyl)buta-1,3-dien-1-yl)cyclopropyl)phenyl acetate (137b)**




The title compound (pale yellow solid, 26 mg, 72% yield, >5:1 dr, favoring the all-*E*-*cis*-cyclopropane product) was obtained following General Procedure B3 from 7-((1*E*,3*E*)-4-(4-methoxyphenyl)buta-1,3-dien-1-yl)-1,3,5-trimethylcyclohepta-1,3,5-triene (35 mg, 0.108 mmol, 8:1 *E*/*Z* ratio) and styrene (70 mg, 0.431 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (1.8 mg, 2.5 mol %) after purification by flash column chromatography on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.24 – 7.19 (m, 4H), 7.00 (d, *J* = 8.5 Hz, 2H), 6.79 (d, *J* = 8.8 Hz, 2H), 6.48 – 6.42 (m, 1H), 6.34 – 6.26 (m, 2H), 5.05 (dd, *J* = 14.8, 9.5 Hz, 1H), 3.77 (s, 3H), 2.37 (q, *J* = 8.5 Hz, 1H), 2.28 (s, 3H), 1.92 (dt, *J* = 9.2, 4.4 Hz, 1H), 1.35 – 1.31 (m, 1H), 1.03 – 0.99 (m, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 169.92, 159.21, 149.31, 136.73, 133.90, 131.12, 130.86, 130.52, 129.33, 127.62, 127.03, 121.47, 114.35, 55.64, 23.84, 23.00, 21.53, 13.37. **HRMS** (APCI Pos): calculated for $C_{22}H_{22}NaO_3$ $[M+H]^+$: 357.1461; found: 357.1463. **MP** 90–93 ºC.

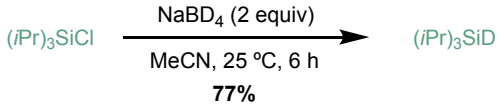
**Triisopropyl((2*E*,4*E*,6*E*)-7-(4-methoxyphenyl)hepta-2,4,6-trien-1-yl)silane (137c)**




The title compound (yellow oil, 17 mg, 68% yield, 5:1 *E*/*Z* ratio) was obtained following General Procedure L from 7-((1*E*,3*E*,5*E*)-6-(4-methoxyphenyl)hexa-1,3,5-trien-1-yl)-1,3,5-trimethylcyclohepta-1,3,5-triene (25 mg, 0.071 mmol, 4:1 *E*/*Z* ratio) and triisopropylsilane (45 mg, 0.283 mmol, 4 equiv) using $[Rh_2(TFA)_4]$ (1.3 mg, 2.5 mol %) after purification by preparative TLC on $SiO_2$ using pentane as eluent.[1] **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 7.33 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.69 (dd, *J* = 15.5, 10.0 Hz, 1H), 6.46 (d, *J* = 15.6 Hz, 1H), 6.35 – 6.18 (m, 2H), 6.08 (dd, *J* = 14.8, 10.0 Hz, 1H), 5.89 – 5.79 (m, 1H), 3.83 (s, 3H), 1.74 (d, *J* = 8.5 Hz, 2H), 1.08 (d, *J* = 2.0 Hz, 21H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 133.69, 133.57, 131.03, 130.57, 129.83, 129.44, 128.03, 127.64, 114.43, 55.66, 19.05, 11.44. **GC-MS** (EI): calculated for $C_{23}H_{36}OSi$ $[M]^+$: 356.3; found: 356.3.

**Deuteration Experiments**

A deuterated analog of triisopropylsilane, triisopropylsilane-*d1* was prepared by reduction of chlorotriisopropylsilane with $NaBD_4$.

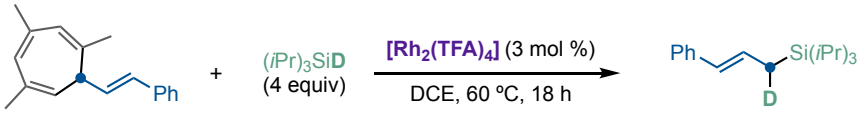



**Triisopropylsilane-*d*$_1$**

To a solution of chlorotriisopropylsilane (0.5 g, 2.59 mmol) under Ar atmosphere in anhydrous acetonitrile (5.2 mL, 0.5 M) at 25 ºC, was added in one portion sodium tetrahydroborate-*d4* (0.217 g, 5.19 mmol, 2 equiv). The resulting suspension was stirred at room temperature for 6 h (gas evolution stops after, <1 h, but the reactions is left stirring to ensure complete conversion), before water was added, and two extractions with $Et_2O$ are performed. Combined organic fractions were washed once with water and once with brine, before drying them over anhydrous $MgSO_4$. Crude product was filtered through $SiO_2$ using pentane as eluent. The solvent was removed carefully at 100 mbar/40 ºC, to avoid evaporation of the product, giving triisopropylsilane-*d*$_1$ (0.31 g, 2.00 mmol, 77%) as a colorless liquid. Spectroscopic data were in agreement with previously reported ones.[220] **$^1$H NMR** (400 MHz, Chloroform-*d*) δ 1.09 (s, 21H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 19.37, 10.16. **GC-MS (EI)**: calculated for $C_9H_{21}DSi$ $[M]^+$: 159.2; found: 159.2.

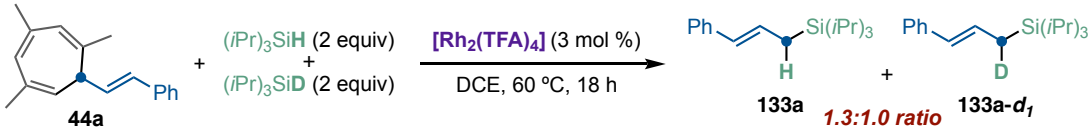
220 Ogata, K.; Atsuumi, Y.; Fukuzawa, S.-I. Nickel-Catalyzed Ring-Opening Three-Component Coupling of Methylenecyclopropane with Aldehydes and Silanes. *Org. Lett.* **2010**, *12*, 4536–4539.

**(*E*)-Triisopropyl(3-phenylallyl-1-*d*)silane (133a-$d_1$)**



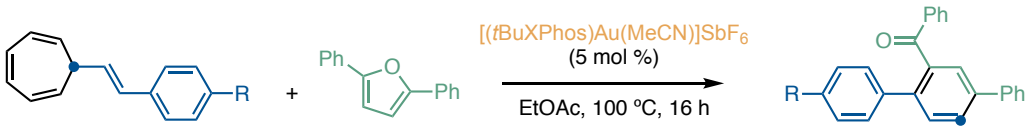

The title compound (colorless oil, 17 mg, 58% yield) was obtained following General Procedure L from (*E*)-1,3,5-trimethyl-7-styrylcyclohepta-1,3,5-triene (25 mg, 0.106 mmol) and triisopropylsilane-$d_1$ (68 mg, 0.423 mmol, 4 equiv) using [$Rh_2(TFA)_4$] (3.5 mg, 5 mol %), heating at 80 ºC instead of 60 ºC, after purification by preparative TLC on $SiO_2$ using pentane as eluent. **$^1$H NMR** (500 MHz, Chloroform-*d*) δ 7.27 – 7.24 (m, 4H), 7.14 (ddt, *J* = 8.5, 5.7, 2.8 Hz, 1H), 6.30 – 6.25 (m, 2H), 1.77 (ddq, *J* = 5.3, 3.8, 1.6 Hz, 1H), 1.09 – 1.05 (m, 21H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 138.93, 129.11, 128.82, 128.51, 126.51, 125.80, 100.36, 19.08, 16.68 (t, *J* = 18 Hz, *C*–D), 11.43. **HRMS** (APCI Positive): calculated for $C_{18}H_{30}DSi$ $[M+H]^+$: 276.2252; found: 276.2254.

Kinetic isotope effect competition experiments were performed according to the same procedure but using a mixture of 2 equiv of triisopropylsilane and 2 equiv of triisopropylsilane-$d_1$. The ratio of products was determined by $^1$H NMR.



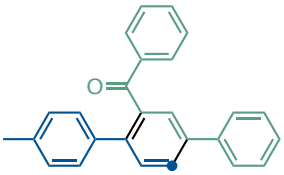
**Reactivity with Heterocycles**

**Synthesis of Terphenylketones from Furans**




Under air, a 2–5 mL microwave vial with a Teflon-coated magnetic stirring bar was charged with a styryl-1,3,5-cycloheptatriene **41** (1.0 equiv) and 2,5-diphenylfuran (2 equiv) and both were dissolved in EtOAc (HPLC grade, 0.1 M). Then, [(JohnPhos)Au(MeCN)]$SbF_6$ (5 mol %) was added. The vial was sealed with its corresponding cap and the resulting solution was stirred at 100 ºC in a heating block (covering the vial completely) for 16 h. The resulting solution was concentrated under vacuum and the obtained residue was purified by flash column chromatography ($SiO_2$, pentane or gradients of pentane/$Et_2O$).

**(4-Methyl-[1,1':4',1''-terphenyl]-2'-yl)(phenyl)methanone (145b)**

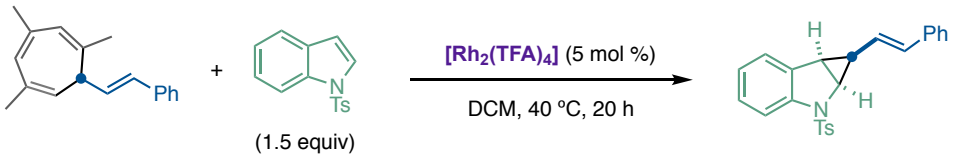



The title compound (yellowish solid, 45 mg, 31% yield) was prepared according to the procedure above using (*E*)-7-(4-methylstyryl)cyclohepta-1,3,5-triene (80 mg, 0.384 mmol, 1 equiv), 2,5-diphenylfuran (169 mg, 0.768 mmol, 2 equiv) and [(*t*BuXPhos)Au(MeCN)]$SbF_6$ (17 mg, 5 mol %), after filtration through $SiO_2$ and subsequent purification by preparative TLC using pentane/$Et_2O$ as eluent. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.78 – 7.74 (m, 3H), 7.70 – 7.66 (m, 2H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.51 – 7.48 (m, 2H), 7.43 – 7.39 (m, 1H), 7.35 – 7.33 (m, 2H), 7.25 – 7.23 (m, 2H), 7.11 (s, 1H), 7.07 (d, *J* = 7.9 Hz, 2H), 2.29 (s, 3H). **GCMS** (EI): calculated for $C_{26}H_{20}O$ $[M+]^+$: 348.1; found: 348.2.

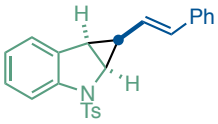
The same reaction was tested with (*E*)-7-styrylcyclohepta-1,3,5-triene to give simpler **145a**. This product was not isolated or characterized but the yield was estimated to be 40% by $^1$H NMR using diphenylmethane as internal standard.

The structure of both products was confirmed by single-crystal X-ray diffraction of **145b**.

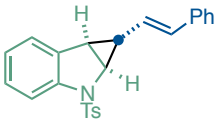
**Cyclopropanation of *N*-Tosylindole**




A screw-cap culture tube or a microwave vial equipped with a Teflon-coated magnetic stirring bar was charged with 1,3,5-trimethyl-7-styryl-1,3,5-cycloheptatriene **44a** (50 mg, 0.212 mmol, 1.0 equiv) and *N*-tosylindole (86 mg, 0.317 mmol, 1.5 equiv). The vial was introduced in an argon-filled glovebox, and both reagents were dissolved in anhydrous dichloromethane (0.15 M), before $[Rh_2(TFA)_4]$ (7.0 mg, 5 mol %) was added. The vial was closed with the corresponding screw-cap and taken outside the glovebox, and then stirred at 40 ºC for 20 h. After this time, the resulting mixture was concentrated in vacuum, and the obtained residue analyzed by $^1$H NMR to determine the dr of the product. GCMS analysis (m/z = 387.1) shows two main products corresponding to the *cis* and *trans* cyclopropane products (22% yield, 2:1 *cis*/*trans*) The crude product was purified preparative TLC on silica gel, performing two elutions with 95:5 pentane/$Et_2O$. This allowed the isolation of the pure major (*cis*) and minor (*trans*) products separately. NMR nOe experiments allowed to assign the relative configuration of each diastereoisomer.




***cis* Isomer**: **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.77 – 7.72 (m, 2H), 7.61 (d, *J* = 8.1 Hz, 1H), 7.25 – 7.20 (m, 2H), 7.12 – 7.04 (m, 3H), 7.01 – 6.95 (m, 3H), 6.77 – 6.70 (m, 2H), 6.30 (d, *J* = 15.8 Hz, 1H), 4.66 (dd, *J* = 15.8, 9.4 Hz, 1H), 4.50 (t, *J* = 6.4 Hz, 1H), 3.02 (dd, *J* = 8.7, 6.6 Hz, 1H), 1.95 (s, 3H), 1.79 (td, *J* = 9.1, 6.1 Hz, 1H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 144.88, 142.35, 137.13, 135.77, 132.39, 129.98, 129.48, 128.53, 128.04, 127.40, 127.23, 126.08, 126.02, 123.56, 122.12, 113.35, 46.34, 27.06, 21.54, 19.97.

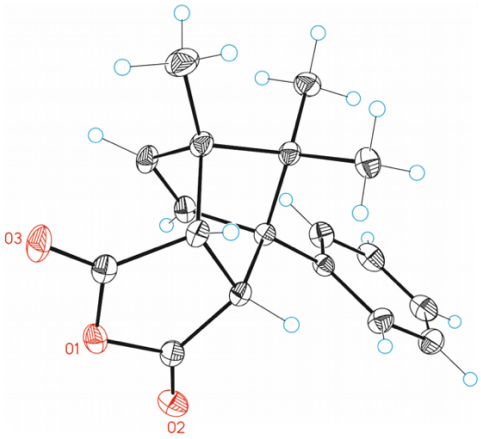



***trans* Isomer**: **$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.81 – 7.73 (m, 2H), 7.69 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.33 – 7.19 (m, 9H), 6.99 (td, *J* = 7.5, 1.0 Hz, 1H), 6.19 (d, *J* = 15.8 Hz, 1H), 5.78 (dd, *J* = 15.8, 8.9 Hz, 1H), 4.21 (dd, *J* = 6.6, 2.2 Hz, 1H), 2.78 (dd, *J* = 6.7, 3.3 Hz, 1H), 2.44 (s, 3H), 0.67 (dddd, *J* = 8.9, 3.1, 2.2, 0.7 Hz, 1H). **$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 144.35, 141.01, 136.82, 134.52, 133.17, 130.04, 129.67, 128.67, 127.77, 127.49, 127.34, 126.99, 125.79, 124.43, 123.45, 115.09, 46.00, 29.71, 25.48, 21.62.

### *Crystallographic Data*

### *endo*-4,8,8-Trimethyl-7-phenyl-3a,4,7,7a-tetrahydro-4,7-methano-isobenzofuran-1,3-dione (112)

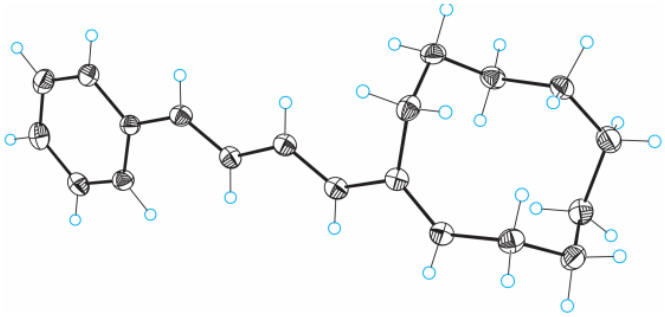
The single crystals of compound **112** suitable for X-ray diffraction analysis were obtained by slow evaporation of a solution of heptane/dichloromethane. The crystal structure information for this compound has been deposited at the Cambridge Crystallographic Data Centre. CCDC 1571037 contains the crystal structure information of this compound and can be obtained free of charge via http://www.ccdc.cam.ac.uk.




| | |
|---|---|
| Identification code | mo_MM143F_0m |
| Empirical formula | C18 H18 O3 |
| Formula weight | 282.32 |
| Temperature | 100(2) K |
| Wavelength | 0.71073 Å |
| Crystal system | Orthorhombic |
| Space group | P2(1)2(1)2(1) |
| Unit cell dimensions | a = 6.4200(5)Å a= 90°.<br>b = 12.0907(9)Å b = 90°.<br>c = 18.3454(14)Å g = 90°. |
| Volume | 1424.01(19) $Å^3$ |
| Z | 4 |
| Density (calculated) | 1.317 $Mg/m^3$ |
| Absorption coefficient | 0.089 $mm^{-1}$ |
| F(000) | 600 |
| Crystal size | 0.20 x 0.10 x 0.02 $mm^3$ |
| Theta range for data collection | 2.017 to 29.904°. |
| Index ranges | -8<=h<=9,-10<=k<=16,-24<=l<=25 |
| Reflections collected | 22310 |
| Independent reflections | 093[R(int) = 0.0436] |
| Completeness to theta =29.904° | 99.8% |
| Absorption correction | Multi-scan |
| Max. and min. transmission | 0.998 and 0.768 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 4093/ 0/ 193 |
| Goodness-of-fit on $F^2$ | 1.044 |
| Final R indices [I>2sigma(I)] | R1 = 0.0408, wR2 = 0.0931 |
| R indices (all data) | R1 = 0.0529, wR2 = 0.0995 |
| Flack parameter | x =0.3(5) |
| Largest diff. peak and hole | 0.300 and -0.233 e.Å |

### (*E*)-1-((1*E*,3*E*)-4-Phenylbuta-1,3-dien-1-yl)cyclodec-1-ene (121f)

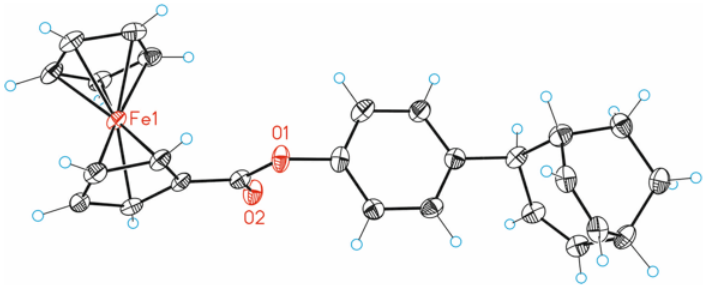
The single crystals of compound **121f** suitable for X-ray diffraction analysis were obtained by slow diffusion, layering methanol in top of a solution of **121f** in dichloromethane in an NMR tube (*ca.* 5:1 methanol/dichloromethane ratio), in the freezer (-20 ºC), over three days. The crystal structure information for this compound has been deposited at the Cambridge Crystallographic Data Centre. CCDC 1973559 contains the crystal structure information of this compound and can be obtained free of charge via http://www.ccdc.cam.ac.uk.



| | |
|---|---|
| Identification code | MM-y-429 |
| Empirical formula | C21 H22 Si |
| Formula weight | 302.47 |
| Temperature | 100(2) K |
| Wavelength | 0.71073 Å |
| Crystal system | Monoclinic |
| Space group | P2(1)/c |
| Unit cell dimensions | a = 11.1024(3)Å α= 90°.<br>b = 6.20124(15)Å β = 92.754(2)°.<br>c = 25.0157(6)Å γ = 90°. |
| Volume | 1720.32(7) Å3 |
| Z | 4 |
| Density (calculated) | 1.168 Mg/m3 |
| Absorption coefficient | 0.131 mm-1 |
| F(000) | 648 |
| Crystal size | 0.08 x 0.07 x 0.02 $mm^3$ |
| Theta range for data collection | 2.396 to 29.631°. |
| Index ranges | -15<=h<=15,-8<=k<=7,-34<=l<=34 |
| Reflections collected | 19500 |
| Independent reflections | 4438[R(int) = 0.0214] |
| Completeness to theta =29.631° | 91.299995% |
| Absorption correction | Multi-scan |
| Max. and min. transmission | 0.997 and 0.767 |
| Refinement method | Full-matrix least-squares on F2 |
| Data / restraints / parameters | 4438/ 419/ 418 |
| Goodness-of-fit on F2 | 1.023 |
| Final R indices [I>2sigma(I)] | R1 = 0.0365, wR2 = 0.0945 |
| R indices (all data) | R1 = 0.0443, wR2 = 0.0988 |
| Largest diff. peak and hole | 0.432 and -0.369 e.Å-3 |

### (±)-(4-((1*R*,2*R*,5*S*)-Bicyclo[3.2.2]nona-3,6-dien-2-yl)phenyl ferrocenoylate (122b)

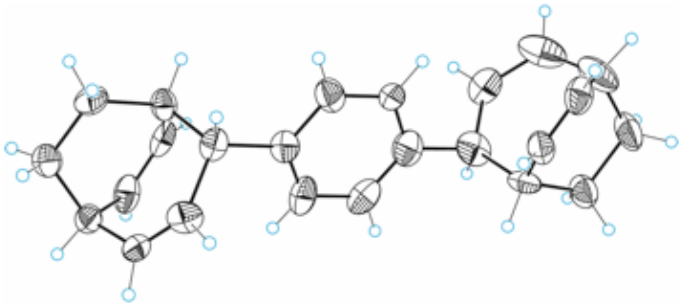
The single crystals of compound **122b** suitable for X-ray diffraction analysis were obtained by slow evaporation of a solution of **122b** in 9:1 MeCN/$CH_2Cl_2$ over 24 h. The crystal structure information for this compound has been deposited at the Cambridge Crystallographic Data Centre. CCDC 2027382 contains the crystal structure information of this compound and can be obtained free of charge via http://www.ccdc.cam.ac.uk.




| | |
|---|---|
| Identification code | MM-2-164 |
| Empirical formula | C26 H24 Fe O2 |
| Formula weight | 424.30 |
| Temperature | 100(2)K |
| Wavelength | 0.71073 Å |
| Crystal system | triclinic |
| Space group | P -1 |
| Unit cell dimensions | a = 6.7191(5)Å a= 68.128(11)°.<br>b = 12.4557(10)Å b = 79.019(9)°.<br>c = 12.803(2)Å g = 77.481(7)°. |
| Volume | 963.6(2) $Å^3$ |
| Z | 2 |
| Density (calculated) | 1.462 $Mg/m^3$ |
| Absorption coefficient | 0.803 $mm^{-1}$ |
| F(000) | 444 |
| Crystal size | 0.250 x 0.050 x 0.010 $mm^3$ |
| Theta range for data collection | 2.881 to 28.809°. |
| Index ranges | -8<=h<=9,-16<=k<=16,-16<=l<=17 |
| Reflections collected | 10838 |
| Independent reflections | 4201[R(int) = 0.0556] |
| Completeness to theta =28.809° | 83.7% |
| Absorption correction | Multi-scan |
| Max. and min. transmission | 1.00 and 0.65 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 4201/ 606/ 517 |
| Goodness-of-fit on $F^2$ | 1.024 |
| Final R indices [I>2sigma(I)] | R1 = 0.0543, wR2 = 0.1340 |
| R indices (all data) | R1 = 0.0833, wR2 = 0.1473 |
| Largest diff. peak and hole | 1.215 and -0.463 $e.Å^{-3}$ |

### (±)-1-((1*R*,2*R*,5*S*)-Bicyclo[3.2.2]nona-3,6-dien-2-yl)-4-((1S,2S,5R)-bicyclo[3.2.2]nona-3,6-dien-2-yl)benzene (122v)

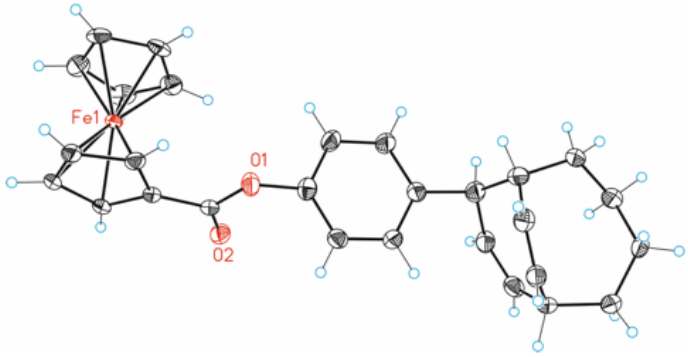
The single crystals of compound **122v** suitable for X-ray diffraction analysis were obtained by evaporation of a solution of **122v** in pentane. The crystal structure information for this compound has been deposited at the Cambridge Crystallographic Data Centre. CCDC 2027380 contains the crystal structure information of this compound and can be obtained free of charge via http://www.ccdc.cam.ac.uk.



| | |
|---|---|
| Identification code | mm-2-216 |
| Empirical formula | C24 H26 |
| Formula weight | 314.45 |
| Temperature | 100(2)K |
| Wavelength | 0.71073 Å |
| Crystal system | monoclinic |
| Space group | P 21 |
| Unit cell dimensions | a = 6.3048(5)Å a= 90°.<br>b = 11.2915(5)Å b = 98.845(6)°.<br>c = 12.2779(7)Å g = 90°. |
| Volume | 863.68(9) $Å^3$ |
| Z | 2 |
| Density (calculated) | 1.209 $Mg/m^3$ |
| Absorption coefficient | 0.068 $mm^{-1}$ |
| F(000) | 340 |
| Crystal size | 0.150 x 0.150 x 0.030 $mm^3$ |
| Theta range for data collection | 2.464 to 28.701°. |
| Index ranges | -7<=h<=8,-13<=k<=14,-14<=l<=16 |
| Reflections collected | 9489 |
| Independent reflections | 3418[R(int) = 0.0242] |
| Completeness to theta =28.701° | 87.1% |
| Absorption correction | Multi-scan |
| Max. and min. transmission | 1.00 and 0.85 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 3418/ 454/ 397 |
| Goodness-of-fit on $F^2$ | 1.839 |
| Final R indices [I>2sigma(I)] | R1 = 0.0798, wR2 = 0.2286 |
| R indices (all data) | R1 = 0.0926, wR2 = 0.2382 |
| Flack parameter | x =2.4(10) |
| Largest diff. peak and hole | 0.437 and -0.224 $e.Å^{-3}$ |

**(±)-1-((1*R*,2*R*,5*S*)-Bicyclo[3.2.2]nona-3,6-dien-2-yl)-4-((1S,2S,5R)-bicyclo[3.2.2]nona-3,6-dien-2-yl)benzene (122y)**

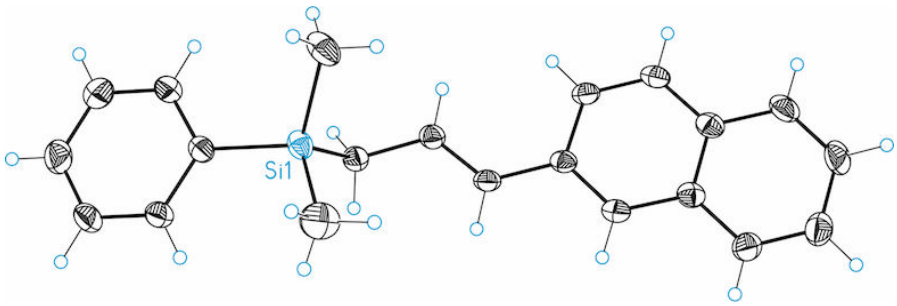
The single crystals of compound **122y** suitable for X-ray diffraction analysis were obtained by slow evaporation of a solution of **122y** in 9:1 MeCN/$CH_2Cl_2$ over 2 days. The crystal structure information for this compound has been deposited at the Cambridge Crystallographic Data Centre. CCDC 2027383 contains the crystal structure information of this compound and can be obtained free of charge via http://www.ccdc.cam.ac.uk.




| | |
|---|---|
| Identification code | MM-2-245_hklf5 |
| Empirical formula | C28 H28 Fe O2 |
| Formula weight | 452.35 |
| Temperature | 100(2)K |
| Wavelength | 0.71073 Å |
| Crystal system | triclinic |
| Space group | P -1 |
| Unit cell dimensions | a = 7.1763(2)Å a= 79.583(3)°.<br>b = 12.3501(4)Å b = 83.597(3)°.<br>c = 12.5306(6)Å g = 86.888(3)°. |
| Volume | 1084.78(7) $Å^3$ |
| Z | 2 |
| Density (calculated) | 1.385 $Mg/m^3$ |
| Absorption coefficient | 0.718 $mm^{-1}$ |
| F(000) | 476 |
| Crystal size | 0.150 x 0.120 x 0.030 $mm^3$ |
| Theta range for data collection | 2.561 to 31.963°. |
| Index ranges | -10<=h<=10,-17<=k<=17,-18<=l<=18 |
| Reflections collected | 15519 |
| Independent reflections | 15519[R(int) = ?] |
| Completeness to theta =31.963° | 89.6% |
| Absorption correction | Multi-scan |
| Max. and min. transmission | 1.00 and 0.66 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 15519/ 0/ 282 |
| Goodness-of-fit on $F^2$ | 2.005 |
| Final R indices [I>2sigma(I)] | R1 = 0.0801, wR2 = 0.2685 |
| R indices (all data) | R1 = 0.0906, wR2 = 0.2729 |
| Largest diff. peak and hole | 1.781 and -1.130 $e.Å^{-3}$ |

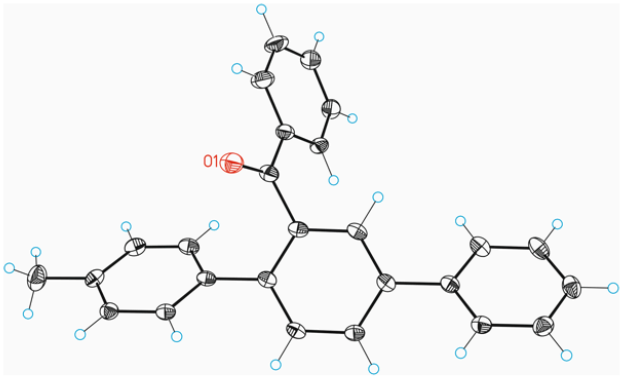
### (*E*)-Dimethyl(3-(naphthalen-2-yl)allyl)(phenyl)silane (133u)

The single crystals of compound **133u** suitable for X-ray diffraction analysis were obtained by slow diffusion, layering a 9:1 methanol/water mixture in top of a solution of **133u** in chloroform in an NMR tube, in the freezer (-20 ºC), over three days. The crystal structure information for this compound has been deposited at the Cambridge Crystallographic Data Centre. CCDC 1881564 contains the crystal structure information of this compound and can be obtained free of charge via http://www.ccdc.cam.ac.uk.




| | |
|---|---|
| Identification code | MM-y-429 |
| Empirical formula | C21 H22 Si |
| Formula weight | 302.47 |
| Temperature | 100(2) K |
| Wavelength | 0.71073 Å |
| Crystal system | Monoclinic |
| Space group | P2(1)/c |
| Unit cell dimensions | a = 11.1024(3)Å α= 90°.<br>b = 6.20124(15)Å β = 92.754(2)°.<br>c = 25.0157(6)Å γ = 90°. |
| Volume | 1720.32(7) Å3 |
| Z | 4 |
| Density (calculated) | 1.168 Mg/m3 |
| Absorption coefficient | 0.131 mm-1 |
| F(000) | 648 |
| Crystal size | 0.08 x 0.07 x 0.02 $mm^3$ |
| Theta range for data collection | 2.396 to 29.631°. |
| Index ranges | -15<=h<=15,-8<=k<=7,-34<=l<=34 |
| Reflections collected | 19500 |
| Independent reflections | 4438[R(int) = 0.0214] |
| Completeness to theta =29.631° | 91.299995% |
| Absorption correction | Multi-scan |
| Max. and min. transmission | 0.997 and 0.767 |
| Refinement method | Full-matrix least-squares on F2 |
| Data / restraints / parameters | 4438/ 419/ 418 |
| Goodness-of-fit on F2 | 1.023 |
| Final R indices [I>2sigma(I)] | R1 = 0.0365, wR2 = 0.0945 |
| R indices (all data) | R1 = 0.0443, wR2 = 0.0988 |
| Largest diff. peak and hole | 0.432 and -0.369 e.Å-3 |

**(4-Methyl-[1,1':4',1''-terphenyl]-2'-yl)(phenyl)methanone (145b)**



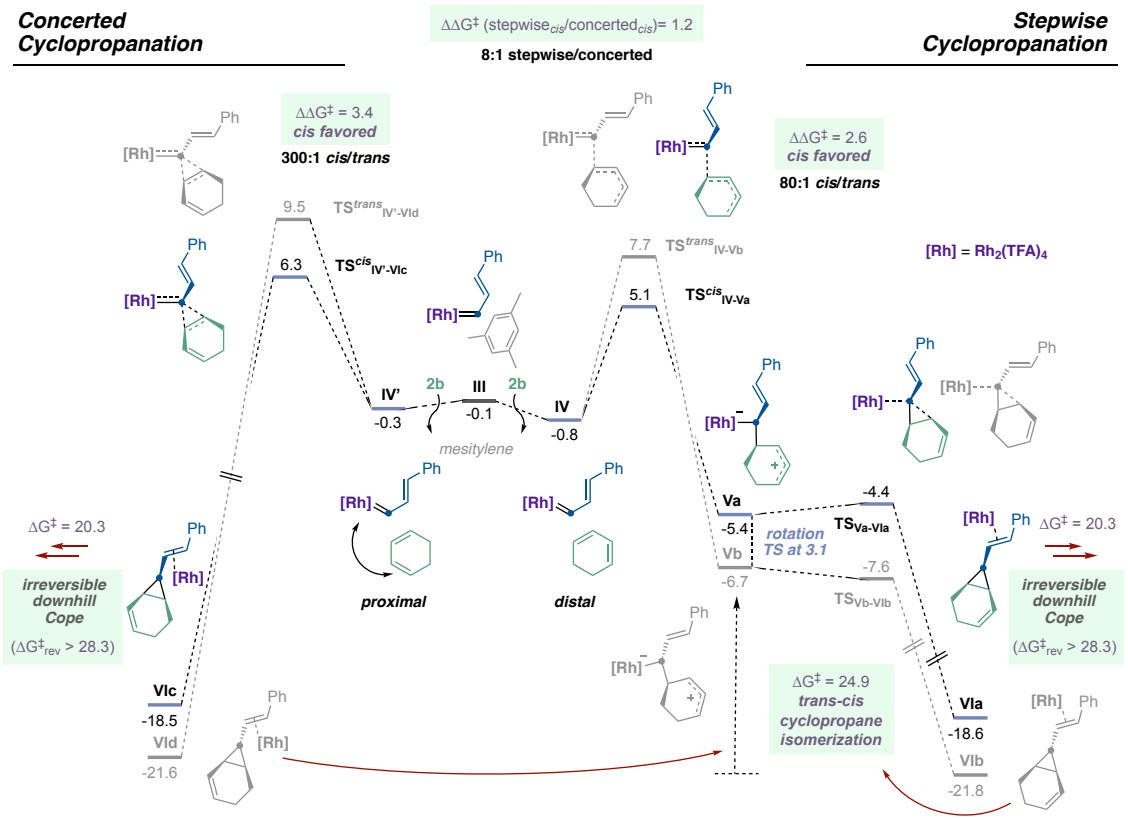

| | |
|---|---|
| Identification code | mo_MM119F_0m |
| Empirical formula | C26.50 H20.57 Cl1.43 O |
| Formula weight | 405.69 |
| Temperature | 100(2) K |
| Wavelength | 0.71073 Å |
| Crystal system | Monoclinic |
| Space group | P2(1)/n |
| Unit cell dimensions | a = 6.7475(6) a= 90°.<br>b = 16.6822(16)Å b = 99.941(3)°.<br>c = 18.5254(17)Å g = 90°. |
| Volume | 2054.0(3) $Å^3$ |
| Z | 4 |
| Density (calculated) | 1.312 $Mg/m^3$ |
| Absorption coefficient | 0.257 $mm^{-1}$ |
| F(000) | 848 |
| Crystal size | 1.00 x 0.30 x 0.10 $mm^3$ |
| Theta range for data collection | 1.654 to 30.700°. |
| Index ranges | -8<=h<=9,-21<=k<=23,-21<=l<=26 |
| Reflections collected | 22819 |
| Independent reflections | 6137[R(int) = 0.0539] |
| Completeness to theta =30.700° | 96.3% |
| Absorption correction | Multi-scan |
| Max. and min. transmission | 0.975 and 0.817 |
| Refinement method | Full-matrix least-squares on $F^2$ |
| Data / restraints / parameters | 6137/ 134/ 344 |
| Goodness-of-fit on $F^2$ | 1.039 |
| Final R indices [I>2sigma(I)] | R1 = 0.0520, wR2 = 0.1286 |
| R indices (all data) | R1 = 0.0817, wR2 = 0.1444 |
| Largest diff. peak and hole | 0.350 and -0.303 $e.Å^{-3}$ |

### *DFT Calculations*

*The General Considerations for the computational section of this Chapter are exactly the same as those specified for Chapter II, which can be found in Section II.9 (page 201). The DFT calculations corresponding to Section III.4 were performed by Dr. Cristina García-Morales and its details are not included in this thesis. The calculations corresponding to Section III.5 were performed by the author of this thesis, and its details are summarized in the following pages.*

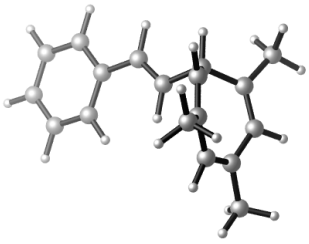
In the following pages, illustrations of all modeled structures discussed in the calculations of Section II.5 are presented, together with their optimization energies and single-point energies. For the coordinates of each structure and more details, see the original publication.[221]

For a more detailed mechanistic analysis of the cyclopropanation, in which both a stepwise and a concerted process are located (arising from the two possible dispositions, proximal or distal, of the second double bond of the 1,3-diene), see the figure below:




221 Armengol-Relats, H.; Mato, M.; Echavarren, A. M. Assembly of Complex 1,4-Cycloheptadienes by (4+3) Cycloaddition of Rhodium(II) and Gold(I) Non-Acceptor Carbenes. *Angew. Chem. Int. Ed.* **2021**, *60*, 1916–1922.

**(44a)**

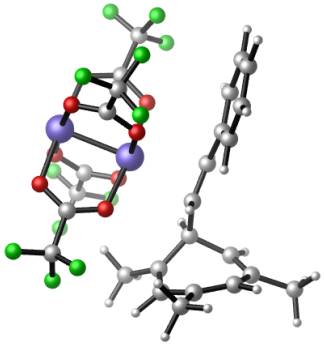


E (opt) = -697.981886190 Hartrees

G (opt) = -697.701940 Hartrees

E (SP) = -698.147888691 Hartrees

**(44a–Rh)**

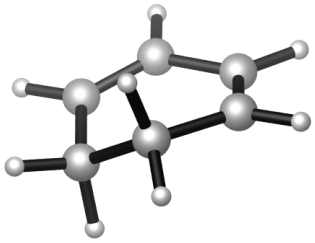


E (opt) = -3021.99506948 Hartrees

G (opt) = -3021.633602 Hartrees

E (SP) = -3022.88167338 Hartrees

**1,3-Cyclohexadiene (125a)**

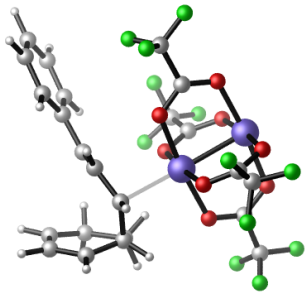


E (opt) = -233.441394064 Hartrees

G (opt) = -233.346671 Hartrees

E (SP) = -233.499816974 Hartrees

**(Va)**

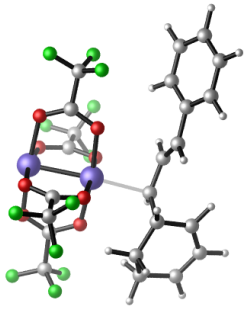


E (opt) = -2905.20533312 Hartrees

G (opt) = -2904.903381 Hartrees

E (SP) = -2906.06971495 Hartrees

**(Vb)**

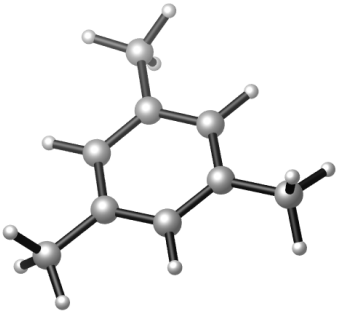


E (opt) = -2905.21192426 Hartrees

G (opt) = -2904.906928 Hartrees

E (SP) = -2906.07427445 Hartrees

**Mesitylene**

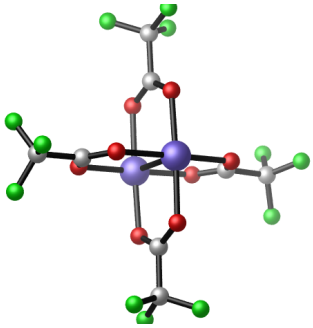


E (opt) = -350.235781599 Hartrees

G (opt) = -350.087583 Hartrees

E (SP) = -350.317575535 Hartrees

**[$Rh_2(TFA)_4$]**

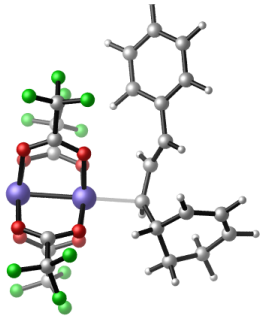


E (opt) = -2323.96839904 Hartrees

G (opt) = -2323.915912 Hartrees

E (SP) = -2324.70026139 Hartrees

**($TS_{Va-Vb}$) (*cis* to *trans*)**

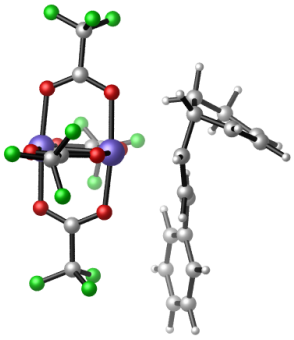


E (opt) = -2905.18831489 Hartrees

G (opt) = -2904.888390 Hartrees

E (SP) = -2906.05359905 Hartrees

**($TS_{Va-VIa}$) (*cis* closing)**

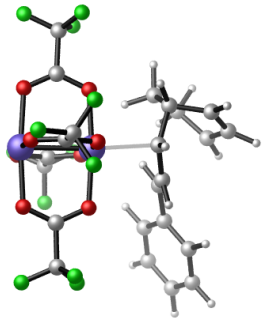


E (opt) = -2905.20487770 Hartrees

G (opt) = -2904.902311 Hartrees

E (SP) = -2906.06824292 Hartrees

**($TS_{Va–VII}$)**

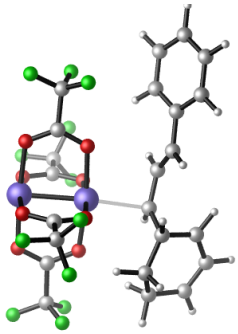


E (opt) = -2905.20402067 Hartrees

G (opt) = -2904.900089 Hartrees

E (SP) = -2906.06787304 Hartrees

**($TS_{Vb-VIb}$) (*trans* closing)**

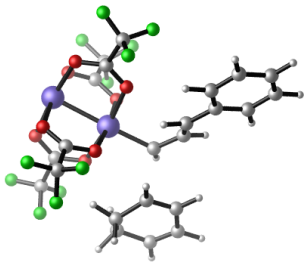


E (opt) = -2905.21188828 Hartrees

G (opt) = -2904.908654 Hartrees

E (SP) = -2906.07405476 Hartrees

**($TS_{IV-Vb}$) (*trans* cationic int. formation)**

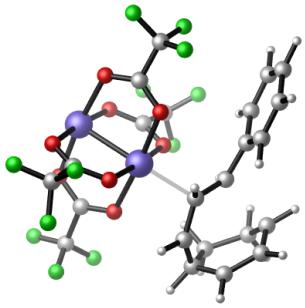


E (opt) = -2905.18381971 Hartrees

G (opt) = -2904.881464 Hartrees

E (SP) = -2906.04879948 Hartrees

**($TS_{VI\text{-}VII}$) (Rh–Cope)**

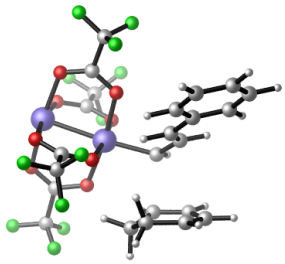


E (opt) = -2905.20674028 Hartrees

G (opt) = -2904.901189 Hartrees

E (SP) = -2906.06779063 Hartrees

**($TS^{cis}_{IV\text{-}Va}$)**

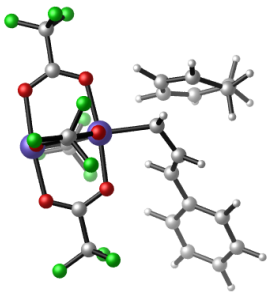


E (opt) = -2905.18666984 Hartrees

G (opt) = -2904.884581 Hartrees

E (SP) = -2906.05263362 Hartrees

**($TS^{cis}_{IV'\text{-}VIc}$)**

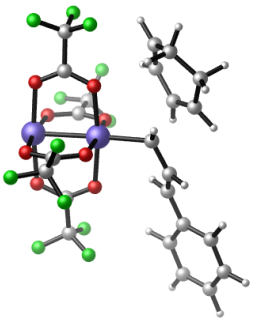


E (opt) = -2905.18019178 Hartrees

G (opt) = -2904.882789 Hartrees

E (SP) = -2906.04600316 Hartrees

**($TS^{trans}_{IV'\text{-}VId}$)**

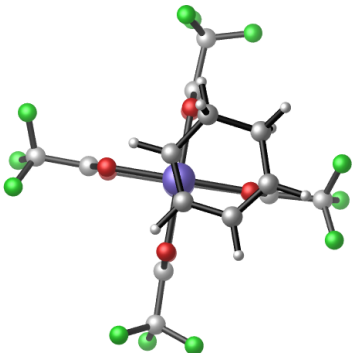


E (opt) = -2905.18069784 Hartrees

G (opt) = -2904.879530 Hartrees

E (SP) = -2906.04474935 Hartrees

**(I)**

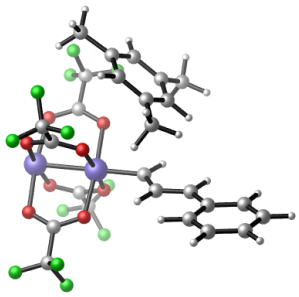


E (opt) = -2557.44508749 Hartrees

G (opt) = -2557.275250 Hartrees

E (SP) = -2558.22991796 Hartrees

**(III)**

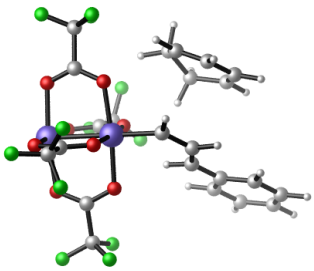


E (opt) = -3021.98855971 Hartrees

G (opt) = -3021.634693 Hartrees

E (SP) = -3022.87701519 Hartrees

**(IV-*cis*)**

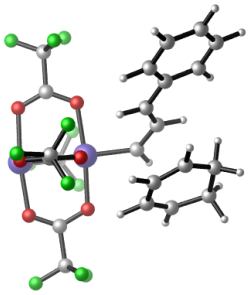


E (opt) = -2905.19181901 Hartrees

G (opt) = -2904.894354 Hartrees

E (SP) = -2906.05735450 Hartrees

**(IV'-*cis*)**

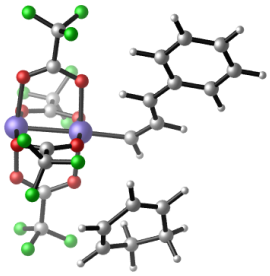


E (opt) = -2905.19227305 Hartrees

G (opt) = -2904.892736 Hartrees

E (SP) = -2906.05858903 Hartrees

**(IV'-*trans*)**

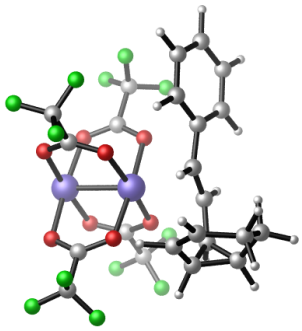


E (opt) = -2905.18888310 Hartrees

G (opt) = -2904.890781 Hartrees

E (SP) = -2906.05361988 Hartrees

**(VI) (*cis*)**

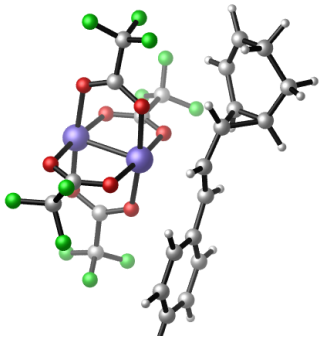


E (opt) = -2905.23316170 Hartrees

G (opt) = -2904.927567 Hartrees

E (SP) = -2906.09389530 Hartrees

**(VId) (*trans*)**

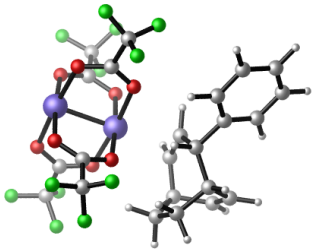


E (opt) = -2905.23852204 Hartrees

G (opt) = -2904.933444 Hartrees

E (SP) = -2906.10050890 Hartrees

**(VII)**

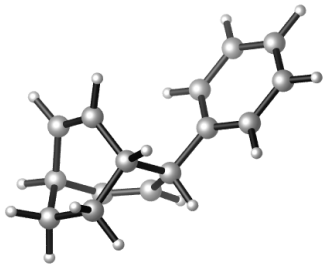


E (opt) = -2905.25115412 Hartrees

G (opt) = -2904.942942 Hartrees

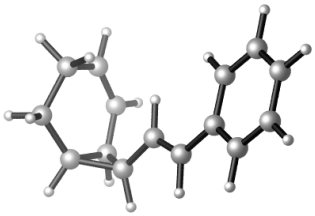
E (SP) = -2906.11196205 Hartrees

**(122a)**



E (opt) = -581.246405416 Hartrees
G (opt) = -581.015567 Hartrees
E (SP) = -581.383238242 Hartrees

**(122a')**



E (opt) = -581.229027278 Hartrees
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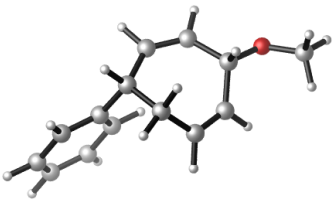
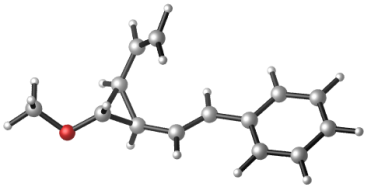
**(122i)**



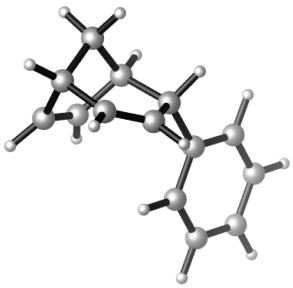
E (opt) = -618.340220152 Hartrees
G (opt) = -618.115712 Hartrees
E (SP) = -618.497265857 Hartrees

**(122i')**



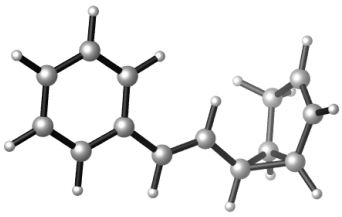
E (opt) = -618.310154072 Hartrees
G (opt) = -618.091008 Hartrees
E (SP) = -618.467580099 Hartrees

**(122r)**



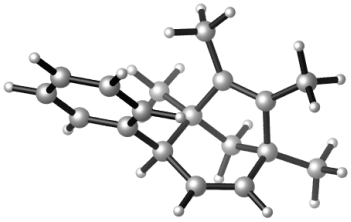
E (opt) = -541.921365626 Hartrees
G (opt) = -541.718166 Hartrees
E (SP) = -542.049682507 Hartrees

**(122r')**



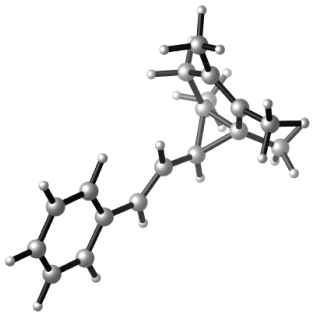
E (opt) = -541.902927014 Hartrees
G (opt) = -541.704719 Hartrees
E (SP) = -542.031908837 Hartrees

**(122s)**



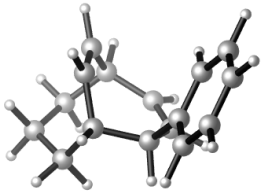
E (opt) = -699.218969493 Hartrees
G (opt) = -698.911395 Hartrees
E (SP) = -699.379158524 Hartrees

**(122s')**



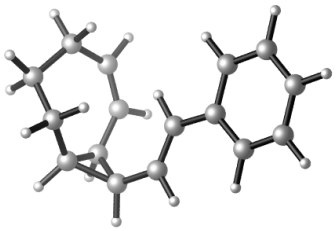
E (opt) = -699.199973162 Hartrees
G (opt) = -698.897969 Hartrees
E (SP) = -699.361243343 Hartrees

**(122t)**



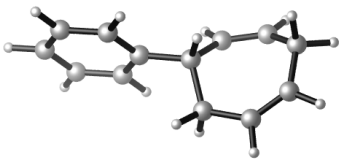
E (opt) = -620.560959775 Hartrees
G (opt) = -620.301639 Hartrees
E (SP) = -620.705644369 Hartrees

**(122t')**



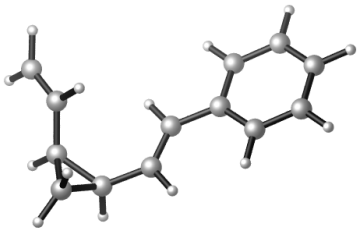
E (opt) = -620.540882545 Hartrees
G (opt) = -620.286072 Hartrees
E (SP) = -620.686057832 Hartrees

**(122u)**



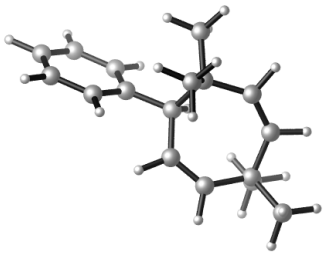
E (opt) = -503.818522385 Hartrees
G (opt) = -503.624163 Hartrees
E (SP) = -503.940830585 Hartrees

**(122u')**



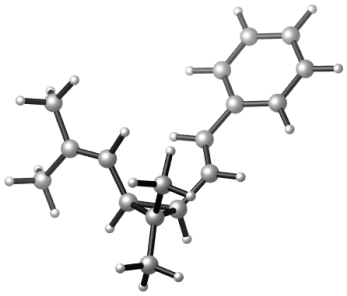
E (opt) = -503.790393893 Hartrees
G (opt) = -503.601092 Hartrees
E (SP) = -503.912655544 Hartrees

**(122w)**



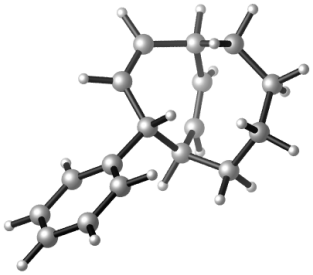
E (opt) = -661.095961715 Hartrees
G (opt) = -660.793266 Hartrees
E (SP) = -661.250805678 Hartrees

**(122w')**



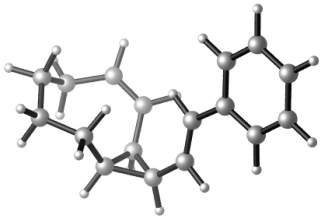
E (opt) = -661.080562034 Hartrees
G (opt) = -660.785991 Hartrees
E (SP) = -661.235025820 Hartrees

**(122x)**



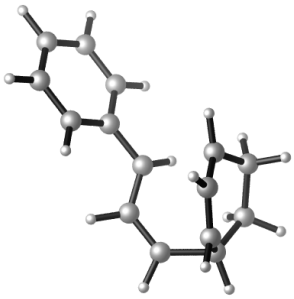
E (opt) = -659.864942957 Hartrees
G (opt) = -659.578502 Hartrees
E (SP) = -660.019044157 Hartrees

**(122x')**



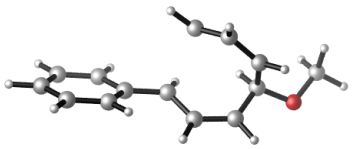
E (opt) = -659.858941570 Hartrees
G (opt) = -659.576856 Hartrees
E (SP) = -660.012507800 Hartrees

**($TS_{122a'-122a}$)**



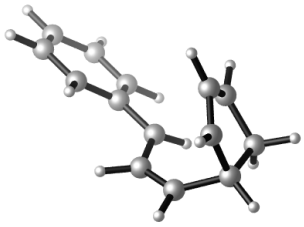
E (opt) = -581.194027887 Hartrees
G (opt) = -580.966638 Hartrees
E (SP) = -581.332809082 Hartrees

**($TS_{122i'-122i}$)**



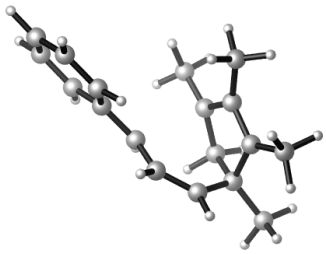
E (opt) = -618.289674726 Hartrees
G (opt) = -618.069034 Hartrees
E (SP) = -618.448499908 Hartrees

**($TS_{122r'-122r}$)**



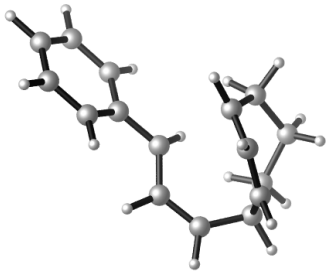
E (opt) = -541.867811533 Hartrees
G (opt) = -541.668666 Hartrees
E (SP) = -541.998098210 Hartrees

**($TS_{122s'-122s}$)**



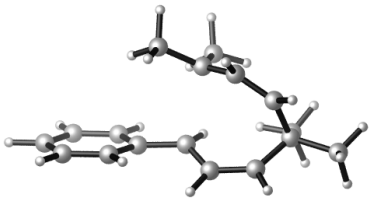
E (opt) = -699.168069245 Hartrees
G (opt) = -698.865737 Hartrees
E (SP) = -699.330441920 Hartrees

**($TS_{122t'-122t}$)**



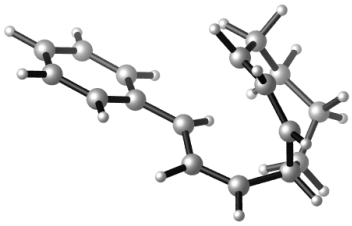
E (opt) = -620.508567559 Hartrees
G (opt) = -620.252744 Hartrees
E (SP) = -620.655300172 Hartrees

**($TS_{122w'-122w}$)**



E (opt) = -661.036834620 Hartrees
G (opt) = -660.737640 Hartrees
E (SP) = -661.193385128 Hartrees

**($TS_{122x'-122x}$)**

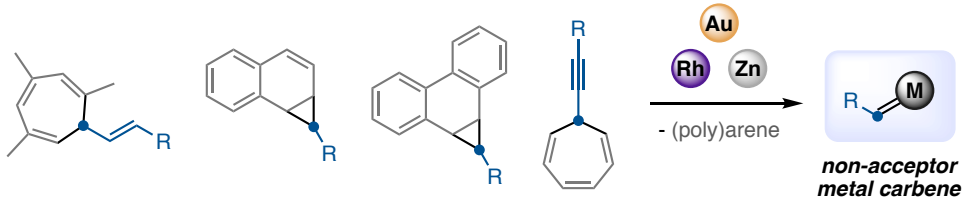


E (opt) = -659.810856802 Hartrees
G (opt) = -659.528222 Hartrees
E (SP) = -659.965996547 Hartrees

# *General Conclusions*

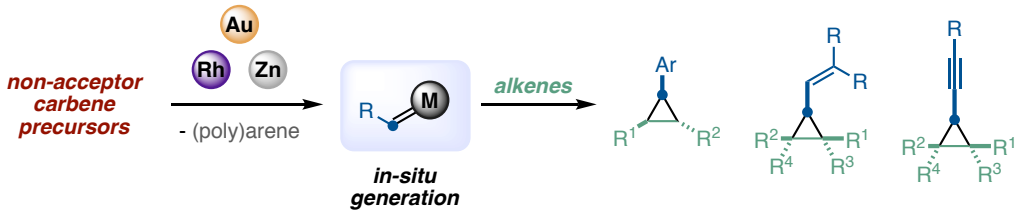
The research developed in this doctoral thesis has led to the following results:

Based upon the concept of aromative decarbenation via retro-Buchner reaction, we have designed a series of new metal carbene precursors. In the presence of different transition-metal complexes, these precursors release (poly)aromatic units (such as benzene, mesitylene, naphthalene or phenanthrene) while generating simple metal carbenes, with different types of non-acceptor substituents (aryl, alkenyl, alkynyl). The development of a more reactive generation of 7-substituted cyclohepatrienes unlocked the use of metals other than gold(I) (such as zinc(II) or rhodium(II)) to promote this type of process, under mild conditions (Scheme 108).




**Scheme 108**. New carbene precursors developed during this thesis.

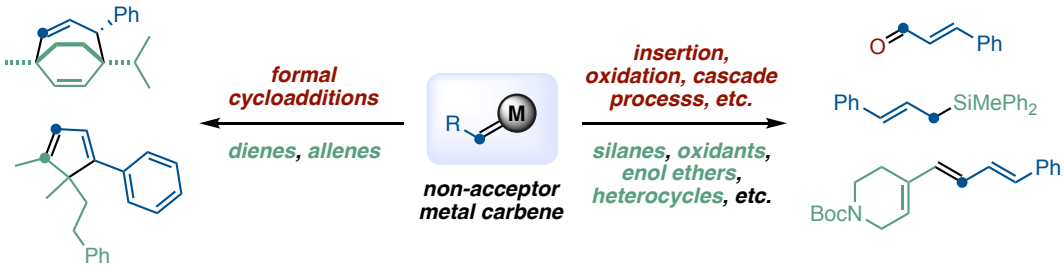
The development of these metal-carbene precursors led to the discovery of improved and new strategies for the cyclopropanation of alkenes. Thus, more than 150 di- to pentasubstituted cyclopropanes could be prepared (often in a highly *cis*-diastereoselective manner), bearing aryl, alkenyl, alkyl, allenyl, alkynyl, amino or alkoxy substituents, among others (Scheme 109).




**Scheme 109**. Illustrative examples of the synthesized cyclopropanes.

These findings pave the way for the further development of new precursors, or new carbene-transfer catalytic systems, based on a similar premise. Furthermore, we have proved the possibility of inducing enantioselectivity in these processes by the use of chiral gold(I)-, zinc(II)- or rhodium(II) catalysts. Our preliminary studies may set the scene for the development of the first, general enantioselective transfer of simple, monosubstituted non-acceptor carbenes.

Besides engaging in cyclopropanation reactions, we found these non-acceptor carbenes to be able to take part in higher cycloaddition processes. For instance, our alkenyl metal carbenes react with allenes and 1,3-dienes to form complex cyclopentadienes and 1,4-cycloheptadienes, through formal (3+2) and (4+3) cycloadditions, respectively. The same type of intermediate can be trapped by Si–H bonds to give allylsilanes through concerted insertions, by oxidants to give aldehydes, or by enol ethers to give cyclopropyl ethers. The latter, in the presence of the same rhodium(II)-based carbene-transfer catalyst, undergo ring opening to give trienes. Preliminary studies show that other nucleophiles, such as furans or indoles, also react with donor carbenes to give cyclopropanes or other products of further cascade rearrangements (Scheme 110).




**Scheme 110**. Selected examples of synthetically challenging structures prepared by cycloaddition, insertion, oxidation and other reactions of donor carbenes.

The synthetic methodologies that we developed as a consequence of these discoveries were applied to the assembly of natural products, versatile building blocks, and new derivatives of biologically active molecules. Natural compounds such as laurokamurene B, dictyopterene C', lactobacillic acid or navenones B–C were prepared in a straightforward manner (Figure 26).

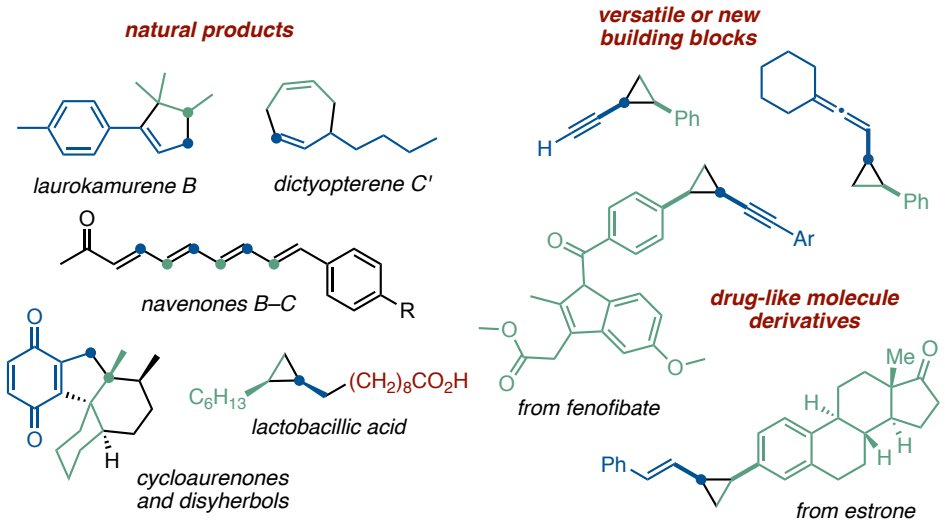



**Figure 26**. Relevant molecules accessed by means of aromative decarbenations.