Chapter 4

Catalytic asymmetric hydroboration of perfluoroalkenes and dihydroboration of internal alkynes. Recovery of the catalyst.

In this chapter we focus on the applicability of enantioselective B-H addition to interesting unsaturated substrates, such as perfluoroalkenes and internal alkynes.

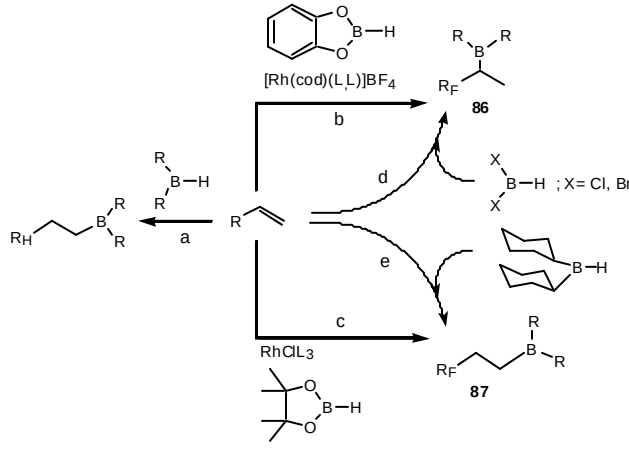
Because of the synthetic utility of chiral perfluoroalcohol and diol compounds, we decided to make for the fist time, a systematic study of the asymmetric rhodium-catalysed hydroboration/oxidation of perfluoroalkenes and dihydroboration/oxidation of internal alkynes, respectively.

We also felt that it would be interesting to find out how to convert these transformations into recyclable processes and even make possible a new concept of consecutive recyclability of substrate preparation and substrate transformation, as two consecutive recyclable catalytic cycles.

1. Introduction

The synthesis of fluoroorganic compounds involves synthesising molecules with fluorine instead of hydrogen. This often improves the biological activity properties of organic molecules. Also, fluorinated compounds are increasingly being used in analytical, materials, and polymer chemistry because of their unique properties [1]. The hydroboration of perfluoroalkenes is an interesting pathway to get perfluoro-organoboronates intermediates which can be furthermore functionalised.

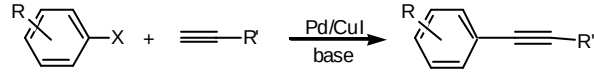
The directing effects of electronegative substituents on 2-substituted-1-alkenes can substantially modify the regioselectivity expected both in the transition-metal catalysed (Scheme 1, pathways b and c) [2] and uncatalysed (Scheme 2, pathways d and e) [3], hydroboration reaction. Thus, the reversed regioselectivity from the Markovnikov "B-H" addition in unfunctionalised terminal olefins to the *anti*-Markovnikov manner in perfluoroalkylethylenes, [4], makes it possible to obtain the branched product. However, other factors that must be taken into account to control the regioselectivity in the hydroboration of perfluoroalkenes are the hydroborating reagents, the reaction temperature and the electronic nature of the rhodium complex when it is used as a catalyst precursor, (Scheme 1).



Scheme 1

The regioselectivity for a series of fluorinated terminal olefins can be controlled by choosing the appropriate reaction conditions. This makes it possible to synthesise the suitable *anti*-Markovnikov perfluoroalkylborane isomer. Recently, P.V.Ramanchandran and H.C.Brown [2] studied the control of the regioselectivity of the hydroboration/oxidation of perfluoroalkenes where the neutral Rh(I) complexes with pinacolborane provided the terminal perfluoroalkylborane **87**, (Scheme 1, pathway c), whereas the cationic Rh(I) complexes with catecholborane provided the branched perfluoroalkylborane isomer **86** (Scheme 1, pathway b). However, the latter process has not been subjected to an asymmetric catalytic version in order to get the chiral product.

In another context, coupling reactions are important methods for carrying out carbon-carbon bond formation. These processes, developed from early work by Tsuji now have a central place in organic chemistry [5]. All coupling reactions are catalysed by a number of palladium complexes, or simply by a mixture of $Pd(OAc)_2$ and PR_3 ligands. Mild conditions are usually used for this reaction, often room temperature, which means that numerous functional groups can be tolerated. The reaction, known as the Sonogashira cross coupling (Scheme 2), converts terminal alkynes into internal alkynes and generally involves the use of a palladium catalyst in conjunction with copper iodide. The copper (I) seems to react with the alkyne to form an alkynylcuprate.

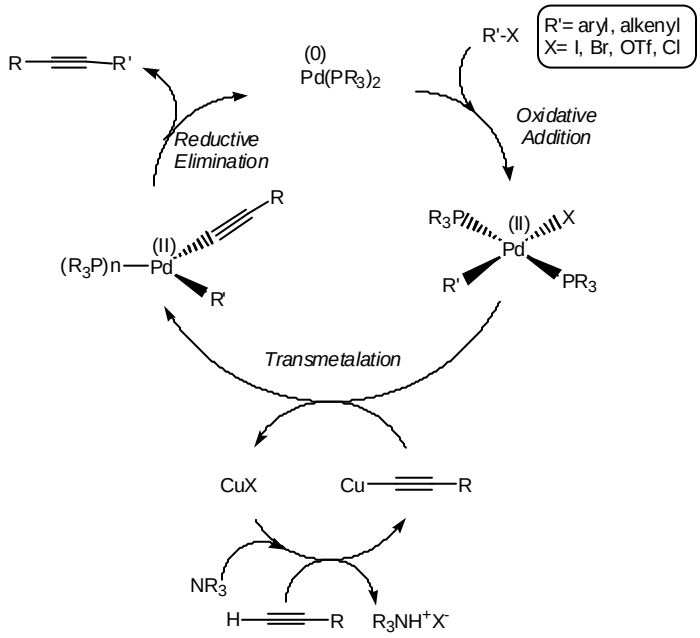


Scheme 2

Recently, Sonogashira proposed the catalytic cycle illustrated in Scheme 3, [6]. This cross-coupling reaction takes place through the oxidative addition of R-X to generate an R-Pd(II)-X intermediate, followed by a transmetalation step, and finally reductive elimination to give the C-C product and the regenerated Pd(0) catalytic system.

G.C.Fu et al. have recently reported examples of Suzuki, Sonogashira, and Stille couplings of the appropriate RX, where X=Cl, using a convenient catalytic

system [7]. The best ligands seem to be bulky and electron rich-phosphines, such as PCy_3 and P^tBu_3 [8]. The reactions are very sensitive to the bulk of the ligand. Also, Eberhard et al. [9] and Plenio et al. [10],obtained significant results in the coupling of aryl chlorides. They described high-yielding palladium catalytic system modified with phosphonito pincer ligands and bis-adamanthyl benzylphosphine ligands, respectively. In this context, the nucleophilic N-heterocyclic carbenes have attracted considerable attention as possible alternatives for the widely used phosphine ligands.



Scheme 3

The main advantages of these ligands are that they do not readily dissociate from the metal center, they have a strong σ-donor character and they are considered to be of low toxicity [11]. All these beneficial effects, together with the fact that they are synthesised more readily than many conventional phosphine ligands mean that they have become versatile ligands in catalysed organic transformations [12], such as cross

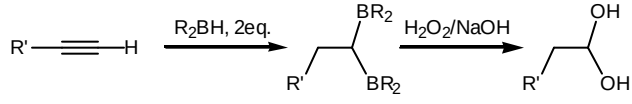
coupling reactions [13]. They have shown that they are efficient at coupling aryl halides with amines [14], amides [15], and alkenes (Heck reaction) [16]. The homogeneous coupling of aryl halides with terminal acetylenes to produce aryl alkynes in the Sonogashira reaction [17] has been extensively studied because it is frequently used as a key step in the synthesis of antimycotics [18], antibiotics [19], liquid crystals, polymers and optical or electronic materials [20]. However, the use of nucleophilic carbenes in the Sonogashira coupling has been studied much less [16b and 16d], [21], although recent results with palladium complexes modified with carbamoyl imidazolium salts under mild conditions [22] and imidazolium chloride assisted coupling of aryl bromides with alkynilsilanes, have been promising [23].

The Sonogashira reaction permits us to obtain internal alkynes such as diphenylacetylene and related compounds *via* a catalysed reaction. Functionalised alkynes are important building blocks for the synthesis of biologically active molecules and, surprisingly, have common structural features no natural products which have been isolated from plants and marine organisms, or synthetic drugs [6], [24-25]. Therefore, the Sonogashira reaction is frequently used as a key step in the synthesis of pharmaceuticals, such as the enediyne antibiotics or the contraceptive pill [26]. In addition, unsaturated internal alkynes are the unsaturated substrates of several hydrometalation reactions.

From the industrial point of view, the recyclability of palladium catalyst is interesting because it can compensate for the cost of the transition-metal catalyst in the process. The catalytic system in the Sonogashira cross-coupling reaction can be immobilised so that it can be recovered and reused in consecutive runs. However, there are few examples for this in the literature that in the case of Sonogashira reaction. As far as we know, in the last couple of years there have only been five attempts to immobilise the catalytic palladium system in: in an aqueous film supported on mesoporous silica [27], in a fluorous reversed-phase silica gel (FRPSG) [28], soluble polymers [29], in ionic liquids in microflow systems [30], in layered double hydroxide supported nanopalladium catalysts [31], and more recently, immobilisation in zeolite by ion exchange [32]. All these attempts succeeded in separating the palladium catalytic system from the products, but the recyclability was heavily dependent on the nature of the immobilisation.

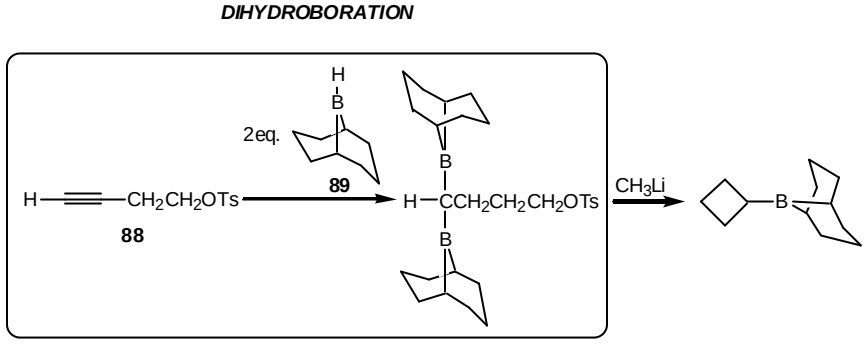
The enantiomerically pure hydrobenzoins have proved to be very useful chiral auxiliaries [33] and ligands [34-35], for stereoselective organic synthesis. These diols, which were previously accessible only through kinetic resolution [36], can now be obtained by dihydroxylation of olefins [37], reduction of benzyls [38] or *via* carbon-carbon bond formation [39], [40]. However, to the best of our knowledge, nobody has yet studied the enantioselective synthesis of hydrobenzoin through the catalytic asymmetric dihydroboration/oxidation of the diphenylacetylene with boranes such as hydroborating reagents.

Terminal alkynes can undergo the dihydroboration with an excess of hydroborating reagents (H-BR_2), giving rise to diborane adducts. In addition, the diorganoborane compounds can be transformed into several functionalised compounds such as diols through oxidation with alkaline hydrogen peroxide (Scheme 4).



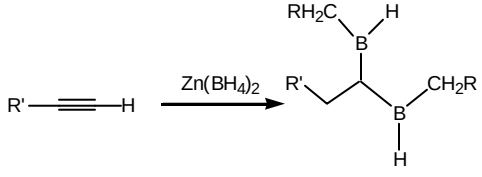
Scheme 4

The dihydroboration of terminal alkynes with dialkylboranes provides the synthesis of diborane, B-C-B, compounds. This reaction is used principally as an intermediate step in the synthesis of cycloalkylboranes. The first example was reported by Binger and Köster who reacted propargyl chloride with diethylborane *via* dihydroboration [41]. H.C.Brown and Rhodes [42], introduced 9-BBN (**89**) as reagent in the dihydroboration of the tosylate of 3-butyl-1-ol (**88**) followed by treatment with methyllithium (Scheme 5). Recently, there has been a slight increase in the number of reports about this reaction in the literature [43-45], although they all show the formation of gem-diboron compounds.



Scheme 5

From the point of view of catalytic synthesis, and to the best of our knowledge, only Narashimhan and Balakumar [46] have carried out the catalytic dihydroboration of terminal and internal alkynes with $Zn(BH_4)_2$, which also give the gem-diborone (Scheme 6).



Scheme 6

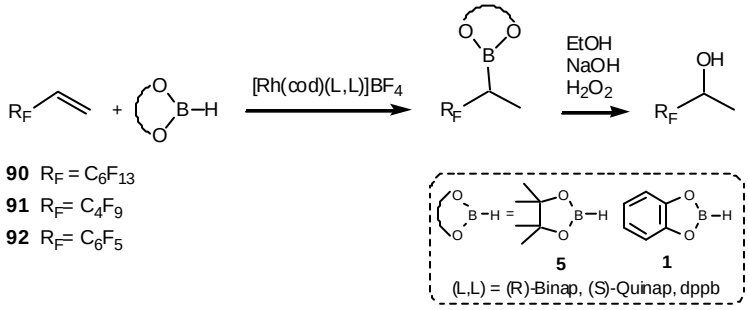
In this context, it seemed interesting to develop a catalytic asymmetric dihydroboration reaction of internal alkynes such as diphenylacetylene in order to get the vic-diborone chiral product. In addition, the immobilised catalytic dihydroboration would provide a clean economic methodology for synthesising chiral compounds, such as the hydrobenzoin, in few steps.

2. Results and discussion

2.1. Catalytic asymmetric hydroboration of perfluoroalkenes

2.1.a. Homogeneous version

As a consequence of the observations by P.V.Ramanchandran and H.C.Brown [2], that cationic Rh(I) complexes are effective for the Markovnikov hydroboration/oxidation of perfluoroalkenes with catecholborane, we decided to examine how a cationic catalytic system modified with chiral diphosphine ligands affected the process, (Scheme 7).



Scheme 7

For purposes of comparison with previous studies in which diphosphine dppb was used as the bidentate ligand, we chose (R)-Binap because both ligands make seven membered chelate with rhodium in the complex.

We started by examining the hydroboration/oxidation of a model substrate 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-1-octene (**90**) with 1 mol% of [Rh(cod)(R)-Binap]BF_4 (**69**) and catecholborane, (Scheme 7). The reaction was almost complete within 1h at room temperature, (Table 1, entry 1). Regioselection on the secondary alcohol was favoured and increased at low reaction temperatures, (Table 1, entries 2 and 3). Similar behaviour was attributed to the catalytic system [Rh(cod)(dppb)]BF_4, (Table 1, entries 4-6) [2], although in this case the regioselectivity was almost

quantitative. When (R)-Binap was used instead of dppb as the chiral ligand; enantiomeric excesses were between 60 and 65.5%, under these reaction conditions.

Table 1. Rh-diphosphine-catalysed enantioselective hydroboration/oxidation of perfluoroalkenes with catecholborane.[a]

Entry	Catalytic system [Rh(cod)(*L*,*L*)]BF_4	R_F	T(^{0}C)	Yield (%)	Branched (%)	e.e[b] (%)
1	(R)-Binap	C_6F_{13}	20	99	70	62(+)
2	"	"	0	99	84	65.5(+)
3	"	"	-78	23	81	60(+)
4[c]	dppb	"	20	82	72	-
5[c]	"	"	0	84	90	-
6[c]	"	"	-25	89	98	-
7[d]	(R)-Binap	"	20	99	46	60.5(+)
8[e]	"	"	20	99	35	50(+)
9[f]	"	"	20	99	-	-
10	"	C_4F_9	0	99	80	64(+)
11	"	C_6F_5	20	86	97	19.5[g]

[a] Standard conditions: alkene/catecholborane/Rh complex=1:1.1:0.01. Solvent: THF. T: 20^{0}C. Time: 1h; [b] Determined by GC with chiral column FS-Cyclodex β-IP, 50 m x 0.25mm; [c] Ref. [2] with 2 mol% of catalyst; [d] Precursor of catalyst: $[Rh(\mu\text{-}Cl)(cod)]_2$/(R)-Binap; [e] Addition of 0.03mmol of $BnMe_3NCl$; [f] Pinacolborane; [g] (R) Enantiomer.

Unlike the cationic catalysts, a preferentially primary insertion of the perfluoroalkenes into neutral-Rh complex formed from $[Rh(\mu\text{-}Cl)(cod)]_2$/2eq (R)-Binap has been detected. However, this had very little effect on enantioselectivity, as the e.e values remained at about 60.5%, (Table 1, entry 7). The neutralising influence of chlorine as a coordinated counterion was confirmed in a new experiment where the salt $BnMe_3NCl$ was added to the catalytic system [Rh(cod)(R)-Binap]BF_4. The results confirmed that the products were distributed similarly to those observed with the neutral system, (Table 1, entry 8). A complete undesired regioselection towards the primary alcohol was obtained when a sterically hindered borane pinacolborane, was

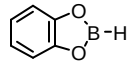
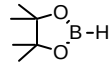
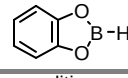
used instead of catecholborane as the hydroborating reagent in presence of [Rh(cod)(R)-Binap]BF_4 (Table 1, entry 9).

The generality of this reaction was demonstrated by carrying out the hydroboration/oxidation of 3,3,4,4,5,5,6,6,6-nonafluoro-1-hexene (**91**). The results were similar to those when catecholborane was used as the hydroborating reagent (Table 1, entry 10). Alkene isomerisation was not observed during the reaction, in contrast to the observed trend with hydroboration of unfunctionalised alkenes [47].

Because the steric factors of the catalyst alter as much as the electronics in the substrate to the access towards the sterically hindered 2-perfluoroalkyl-rhodium intermediate, we studied the influence of the [Rh(cod)(S)-Quinap]BF_4 [48]. The Quinap is less bulky than its parent ligand Binap and, in addition, the P,N ligand forms a six-member chelate ring with rhodium in the complex.

Using catecholborane as the hydroborating reagent, **90** and **91** were transformed into their corresponding alcohols with complete regioselectivity (Table 2, entries 1 and 3). However, the induced chirality was lower than the chirality provided

Table 2. Rh-Quinap-catalysed enantioselective hydroboration/oxidation of perfluoro-alkenes.[a]

Entry	Borane	R_F	T(^{0}C)	Yield (%)	Branched[b] (%)	e.e[b] (%)
1		C_6F_{13}	20	99	99	20(+)
2	"	"	0	99	99	19(+)
3	"	C_4F_9	20	99	99	25(+)
4		C_6F_{13}	20	99	99	55(+)
5	"	C_4F_9	20	99	99	53.5(+)
6		C_6F_5	20	97	97	18[c]

[a] Standard conditions: alkene/catecholborane or pinacolborane/Rh complex=1:1.1:0.01. Solvent: THF. T: 20^{0}C. Time: 1h.; [b] Determined by GC with chiral column FS-Cyclodex β-IP, 50 m x 0.25mm; [c] (S) Enantiomer.

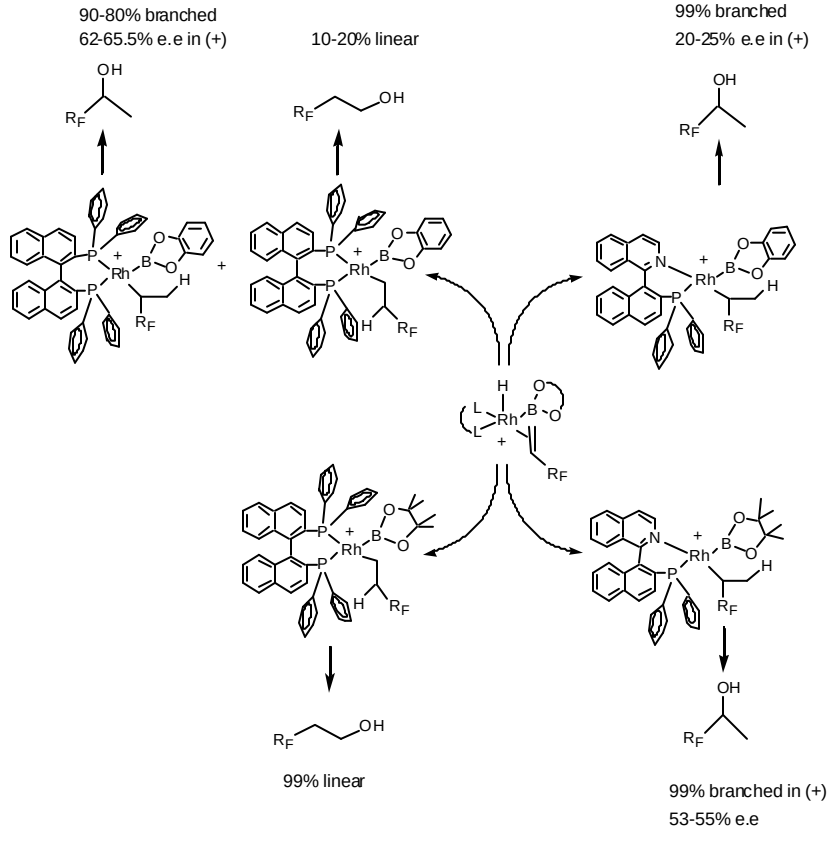
by the analogue (R)-Binap derived Rh-catalyst, even at low temperatures (Table 2, entry 2). We then conducted the hydroboration of **90** and **91** with the more sterically demanding hydroborating reagent pinacolborane, and surprisingly, we also obtained the secondary perfluoroalkylborane quantitatively, with e.e values as high as 55% (Table 2, entries 4 and 5). In the literature, there are examples of symmetrically internal alkyl pinacolboronate products formed in the presence of [$RhCl(CO)(PPh_3)_2$] and [$NiCpCl(cod)(PPh_3)Cl$] but not with $RhCl(PPh_3)_3$, [49].

It should be pointed out that both cationic Rh-catalytic systems behave differently towards the formation of the secondary-alkyl rhodium complexes, principally because of the steric properties of the hydroborating reagent involved in the intermediates. As can be seen in scheme 8, pinacolborane almost exclusively provides the secondary insertion of the perfluoroalkenes on the (S)-Quinap-Rh catalyst, but the primary insertion of the same substrates on the (R)-Binap-Rh catalyst. Presumably the more congested (R)-Binap-Rh-pinacolboryl intermediate could be the reason for the terminal olefin insertion. However, it cannot be excluded that this product may also be the result of the isomerisation of a plausible secondary alkyl-rhodium intermediate into the primary alkyl-rhodium, because of a β-H elimination process, which could also be favoured by the steric demand around the metal.

A high and complete degree of the secondary alkyl-rhodium complex is obtained by using both (R)-Binap-Rh and (S)-Quinap-Rh complexes, respectively, when catecholborane is involved in the reaction. In these cases, the lower steric demand around the reaction site means that the metal is affixation in the most hindered carbon, as is expected because of the electronic effect exerted by the fluorinated alkene.

To obtain a total picture of the process, it should be mentioned that the oxidation of the secondary alkyl-rhodium intermediate, obtained from both chiral complexes, (S)-Quinap-Rh and (R)-Binap-Rh, provided principally the same (+)-enantiomer. This contrasts substantially with the trend observed in the hydroboration/oxidation of styrene, where the (S)-Quinap-Rh catalyst provided the (S)-1-Phenylethanol and the (R)-Binap-Rh catalyst provided the (R)-enantiomer [50]. The enantiodifferentiation in the case of the vinylarenes has previously been explained by some intermolecular π-π stacking interactions between the ligand and the substrate

[51]. The lack of phenyl groups in the perfluoroalkenes **90** and **91** suggests that the coincidence in the main enantiomer formed could be due to the configuration of the Rh-H fragment when it is transferred to the coordinated alkenes. This extreme is confirmed by an additional experiment, where 2',3',4',5',6'-pentafluorostyrene was subjected to the hydroboration/oxidation reaction with catecholborane and both chiral catalytic systems. In accordance with the regioselective trend observed with the hydroboration/oxidation reaction with catecholborane and both chiral catalytic systems. In accordance with the regioselective trend observed with the hydroboration of vinylarenes, the aromatic perfluoroalkenes gave the (S) enantiomer product in the presence of the (S)-Quinap-Rh and the (R) enantiomer with (R)-Binap (Table 1, entry 11 and Table 2, entry 6, respectively).

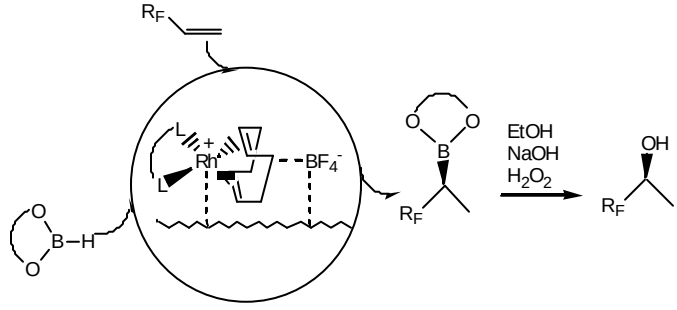


Scheme 8

The consistently moderate e.e values, (55-65%), that we obtained in the hydroboration/oxidation of aliphatic perfluoroalkenes were even higher than those observed in the asymmetric B-H addition on aromatic perfluoroalkenes, such as 2',3',4',5',6'-pentafluorostyrene (**92**), (18-19.5%), and in electron-deficient vinylarenes such as 3,5-bis-trifluoromethylstyrene (5%), and 2,6-difluorostyrene (<15%).

2.1.b. Heterogenised version

In a subsequent investigation, we focused on perfluoroalkenes as the substrates for the recyclable catalytic asymmetric hydroboration reaction with $[Rh(cod)(L_2)]BF_4$/ /MK-10_T (where MK-10_T= preheated montmorillonite K10, L_2= (R)-Binap and (S)-Quinap). We used a similar heterogenised procedure to that described for the hydroboration of vinylarenes in chapter 2, (Scheme 9).



Scheme 9

We started by examining the catalytic properties of the model rhodium complex $[Rh(cod)(R)\text{-Binap}]BF_4$ adsorbed onto preheated commercial montmorillonite K10, MK-10_T, using catecholborane as hydroborating reagent. In the homogeneous hydroboration/oxidation of 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-1-octene (**90**), the catalyst precursor provided high yields (99%), moderate regioselectivities for the branched alcohol and moderate enantioselectivities. As far as catalytic activity is concerned, the results were similar to those of the homogeneous counterpart.

However, in subsequent runs the regio- and enantioselectivity decreased slightly. After the third run, the selectivity remained constant (Figure 1).

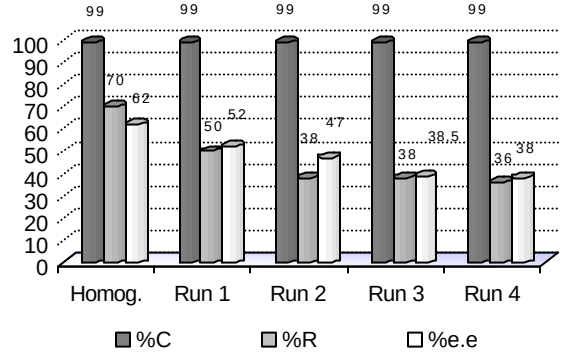


Figure 1

Catalytic activity provided by [Rh(cod)(R)-Binap]BF_4 in the homogeneous and heterogenised hydroboration of **90**.

Similar results were observed when the reaction was performed with the hydroboration/oxidation of 3,3,4,4,5,5,6,6,6-nonafluoro-1-hexene (**91**), under similar reaction conditions, (Figure 2).

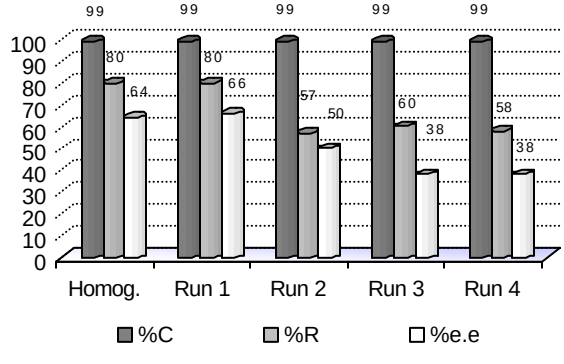


Figure 2

Catalytic activity provided by [Rh(cod)(R)-Binap]BF_4 in the homogeneous (0^0C) and heterogenised hydroboration of **91**.

When the rhodium catalytic system was based on [Rh(cod)(R)-Quinap]BF_4 anchored onto preheated commercial montmorillonite MK-10, (MK-10_T), the catalytic hydroboration/oxidation reaction of **90** with pinacolborane provided a slight decrease in regio- and enantioselectivity. In addition, unlike the homogeneous version, the selectivity continued decreasing in further consecutive runs until it remained constant after the third, (Figure 3).

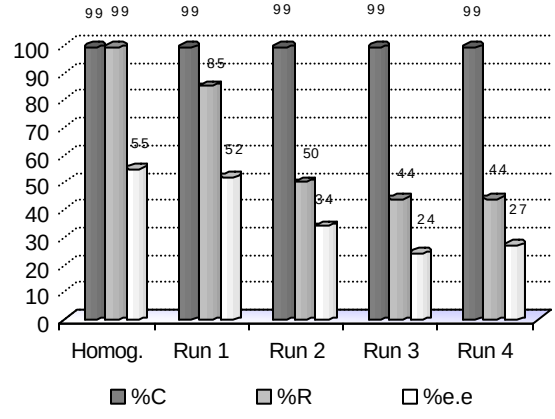


Figure 3

Catalytic activity provided by [Rh(cod)(S)-Quinap]BF_4 in the homogeneous and heterogenised hydroboration of **90**.

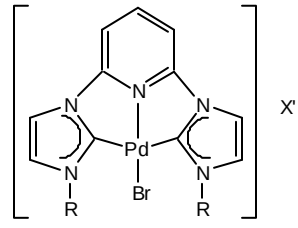
These results showed that, independently of the immobilised catalytic system and/or the perfluoroalkene, the heterogenised catalytic asymmetric hydroboration/oxidation reaction behaves in a similar way to the homogeneous version. However, we observed a slight loss of catalytic system during the filtration. This observation together with the decrease in the selectivity from the hydroboration/oxidation of perfluoroalkenes could be related to fluorides competing to interact with the external surface of montmorillonite K-10, probably through hydrogen bond interactions.

2.2. Catalytic dihydroboration of internal alkynes

2.2.a. Synthesis of internal alkynes *via* heterogenised Sonogashira C-C coupling

Generally the homogeneous Sonogashira reaction is carried out in an organic solvent such as toluene, THF or DMF, with at least a stoichiometric amount of base, and a Pd(0)/Cu(I) catalytic system [52]. Homogeneous Pd-catalysts make the separation and recovery of the catalysts tedious if not impossible and might result in unacceptable palladium contamination of the product. The intensive application of the Sonogashira reaction in the chemical industry depends on the development of new, stable heterogenised palladium catalysts. With this aim, we made a systematic study of immobilising organopalladium complexes onto clays through adsorptive and electrostatic interactions, following the same methodology described in previous sections.

Our work involved selecting an optimised palladium catalyst modified with the C,N,C-pincer bis-carbene ligand (**93**) [53], (Figure 4), in both homogeneous and heterogenised versions. Once we had established the methodology with model substrates, we extended it to include more attractive starting materials.



X'= Br^-, BF_4^-; R= Bu, Me, Bn

93

Figure 4

The pincer-heterocyclic-carbene ligands are very efficient at C-X activation and extremely stable at high temperatures, [16a,16b] which made it possible for them

to be used in the C-C coupling of the test substrates phenylacetylene and phenyliodide at the refluxing temperature (87^0C) of pyrrolidine, (which acts both as a solvent and as a base to intercept the HI formed). Of all the solutions described to date for suppressing the side reaction of the oxidative homocoupling (Glaser coupling) of the alkyne to the corresponding symmetrical diyne, [23], [54] we decided to perform the reaction under nitrogen by slow addition of the alkyne, keeping its concentration in the reaction mixture low. Under these homogeneous reaction conditions, the catalyst [PdBr(CNC-Bu_2)]Br proved to be highly efficient, and it afforded the desired product in a 99% yield in 45 min (Figure 5).

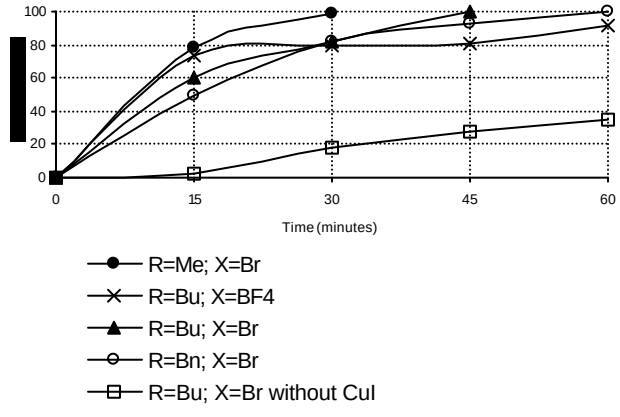


Figure 5

Reaction profiles for Sonogashira coupling of (C_6H_5)CCH and (C_6H_5)I with [PdBr(CNC-R_2)]X.

As has been shown above in scheme 3 for the Sonogashira reaction, the co-catalyst CuI, (probably involved in the transmetalation step), seems to be necessary because, otherwise, conversions are only moderate (38% yield in 1h, Figure 5). However, the addition of CuI to other palladium catalytic systems modified with carbene ligand [16d], surprisingly resulted in almost complete deactivation of the catalyst, probably because carbene ligands may be transferred to Cu [55].

A search for the best tridentate pincer bis-carbene ligand showed the influence of the wingtip groups (R= methyl, butyl and benzyl) on the catalytic activity. Whereas the solubility in non-polar solvents increases from C,N,C pincer bis-carbene with R=Me to R=Bu or Bn, the C-C coupling reaction was substantially affected by the difference in the nature of the substituents. The activity was highest activity (99% yield in 30 min) when the catalytic system was [PdBr(CNC-Me_2)]Br, (Figure 5). Similar increases in activity have been observed in the literature when non-hindered substituents on imidazolium chlorides modify the palladium catalytic system $Pd(OAc)_2$ [23]. The reaction rates were also significantly influenced by the identity of the counterion in the catalytic system [PdBr(CNC-Bu_2)]X. The C-C coupling proceeded more rapidly when the counterion was X=Br than when it was X=BF_4, (Figure 5). We did not observe the formation of Pd-black during the reaction, but the black deposit started to form some time after all the substrate had been consumed if the solution was maintained at the refluxing temperature of the solvent.

To test the long-term stability of the catalyst and its recovery and reuse in consecutive runs, we initiated the immobilisation of [PdBr(CNC-Me_2)]Br in smectite clays. We used the solvent-impregnation method [56] to immobilise the ionic palladium complex in three types of solids: montmorillonite K-10 (MK-10), bentonite A: (bA), bentonite B: (bB). Chapter 2 showed the structural differences between the montmorillonite K-10 and both bentonites and how these differences affect the immobilisation process. The higher crystallinity of bentonites A and B favours the immobilisation process to take place *via* cation exchange while the higher surface area of the MK-10 as a result of their partially destroyed lamellar structure means that the immobilisation will mainly take place *via* adsorption [57]. The different ways for grafting complex [PdBr(CNC-Me_2)]Br onto the clays affect the quantity of the palladium complex immobilised, attending to the chemical analyses of the solids (Table 3). This can also lead to differences in their catalytic behaviour when used as catalysts in the Sonogashira reaction.

The scanning electron microscopy analyses of MK-10_T/[Pd]Br, bA_T/[Pd]Br, and bB_T/[Pd]Br, (Table 3), provide the percentages of palladium complex which agree with the expected amount of metal in the solid catalytic system, (0.6-0.7%).

Table 3. Chemical analyses of solids and immobilised catalytic systems [PdBr(CNC-Me_2)]Br/clay.[a]

M^{n+}	MK-10_T[b]	MK-10_T/[Pd]Br	bA_T[b]	bA_T/[Pd]Br	bB_T[b]	bB_T/[Pd]Br
Si	32.3	31.9	28.7	26.3	25.2	23.9
Al	7.3	7.7	9.4	9.9	3.2	3.6
O	53.6	48.6	51.8	44.9	48.2	41.1
Mg	0.6	0.9	1.7	1.8	14.3	13.4
Na	0.2	0.2	2.0	1.9	---	---
K	1.3	0.8	0.8	0.9	0.7	0.4
Ca	0.2	0.3	1.3	0.7	0.3	0.1
Fe	1.5	2.1	1.9	2.5	1.5	1.1
Pd	---	0.6	---	0.7	---	0.7

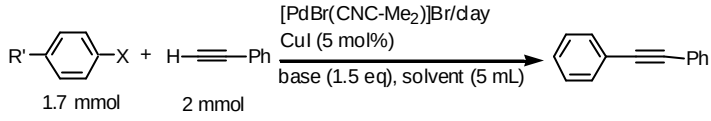
[a] Percentages calculated as (% by weight) from the scanning electro microanalyser analysis; [b] MK-10: montmorillonite K-10, bA: bentonite A, bB: bentonite B. All the clays were predried at 100^0C for 24h.

Initial experiments with the heterogenised catalytic system [PdBr(CNC-Me_2)]Br/clay, (catalyst loading of 1,7 mol% in MK-10_T/[Pd]Br and 1.8 mol% in bA_T/[Pd]Br and bB_T/[Pd]Br) were carried out using the previously optimised conditions for the homogeneous Sonogashira coupling between phenylacetylene and phenyliodide. The three supported catalysts proved to be highly efficient and afforded 92-94% yield of the product between 0.5 and 1h (Table 4, entries 1-3). Therefore, the different structural nature of the clay and the different grafting of the palladium complex did not make a significant difference to the catalytic activity of the solid system.

The coupling reaction of more challenging substrates, such as activated arylbromides with MK-10_T/[Pd]Br, bA_T/[Pd]Br, and bB_T/[Pd]Br, was almost complete within 0.5 h for *p*-nitrobromobenzene, and quantitative within 2.5 h for *p*-bromobenzaldehyde and *p*-bromoacetophenone (Table 4, entries 4-6).

These results indicate that the activity of the catalytic system is higher than of previously reported Pd-carbene catalysts [16d], [22] or Pd-immobilised catalytic systems [28-29], for the coupling of the same substrates. We also studied the role of pyrrolidine, piperidine and Cs_2CO_3 as the base, and we concluded that activity was highest with piperidine [23] (Table 4, entries 1, 7 and 9).

Table 4. Chemical analyses of solids and immobilised catalytic systems [PdBr(CNC-Me$_2$)]Br/MK-10$_T$.[a]



Entry	X	R'	Clay[b]	Base[c]	Solv.	T(^{0}C)	t(h)	Yield (%)[d]
1	I	H	MK-10$_T$	Pyrr	Pyrr	87	0.5	92
2	I	H	bA$_T$	Pyrr	Pyrr	87	1	94
3	I	H	bB$_T$	Pyrr	Pyrr	87	1	92
4	Br	NO_2	MK-10$_T$	Pyrr	Pyrr	87	0.5	99
5	Br	CHO	MK-10$_T$	Pyrr	Pyrr	87	2.5	77
6	Br	MeCO	MK-10$_T$	Pyrr	Pyrr	87	2.5	73
7	I	H	MK-10$_T$	Pip	Pip	106	0.5	99
8	I	H	MK-10$_T$	Pip	DMA	100	1	86
9	I	H	MK-10$_T$	Cs_2CO_3	DMA	100	1	64
10	I	H	bA$_T$	Pip	DMA	100	1	97
11	I	H	bB$_T$	Pip	DMA	100	1	93.5
12	Br	NO_2	MK-10$_T$	Pip	DMA	100	0.5	99
13	Br	CHO	MK-10$_T$	Pip	DMA	100	2	98
14	Br	MeCO	MK-10$_T$	Pip	DMA	100	2	72

[a] 0.029mmol [Pd]Br in 0.5 of MK-10$_T$; 0.032mmol [Pd]Br in 0.5 of bA and bB; [b] MK-10$_T$: montmorillonite K-10 predried, bA$_T$: bentonite A predried, bB$_T$: bentonite B predried; [c] Pyrr: pyrrolidine, Pip:piperidine; [d] Conversion of the arylalkynes determined by GC.

Before validating the concept of effective catalyst recycling, we selected an appropriate solvent to simplify the protocol of washing the solid catalyst system after it has been separated from the products via filtration. Therefore, we demonstrated that the use of DMA, (N,N-dimethylacetamide), as solvent, could be a suitable solvent for efficient catalysis and for removing all the products and ammonium salts involved in the reaction, from [PdBr(CNC-Me$_2$)]Br/clay (Table 4, entries 8-14). Catalyst recycling studies were carried out after [PdBr(CNC-

Me_2)]Br/clay had been recovered, and washed with DMA and CH_2Cl_2. Pd-black deposit was not observed in the washed solid, which confirmed the great stability of the catalyst when it is immobilised. The resulting recovered solids were successfully reused and the activity was the same as for the first run in the coupling of phenylacetylene and phenyliodide (Figure 6 i, ii and iii).

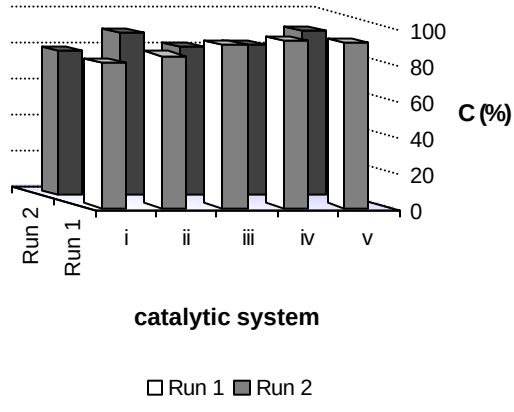


Figure 6

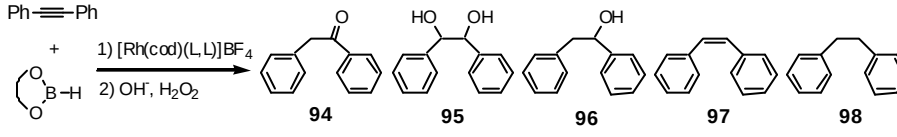
Reusability of [PdBr(CNC-Me_2)]Br/clay in the coupling of phenylacetylene and R'-C_6H_4-X. i) R'= H, X = I, clay = MK-10_T; ii) R'= H, X = I, clay = bA_T; iii) R'= H, X = I, clay = bB_T; iv) R'= NO_2, X = Br, clay = MK-10_T; v) R'= CHO, X = Br, clay = MK-10_T.

Encouraged by the satisfactory recycling capacity of these systems, we extended our study of the reusability of [PdBr(CNC-Me_2)]Br/MK-10_T to the consecutive coupling of phenylacetylene with *p*-nitrobromobenzene and *p*-bromobenzaldehyde, (Figure 6 iv and v, respectively). Reaction rates were similar for the first and second consecutive runs in both cases.

2.2.b. Study of the homogeneous and heterogenised catalytic dihydroboration of internal alkynes.

The internal alkyne diphenylacetylene, obtained from the Sonogashira cross-coupling, was used as a model substrate in the tandem dihydroboration/oxidation reaction. First we selected the optimised standard reaction conditions: solvent, catalytic system and hydroborating reagent in the homogeneous version. Once we had established the most suitable methodology, we extended it to the heterogenised version.

We started by examining the catalytic properties of the rhodium complex $[Rh(cod)(dppp)]BF_4$ in THF, with an equimolecular amount of catecholborane.



Scheme 10

Table 5. Hydroboration/oxidation and dihydroboration/oxidation of diphenylacetylene with $[Rh(cod)(dppp)]BF_4$.[a]

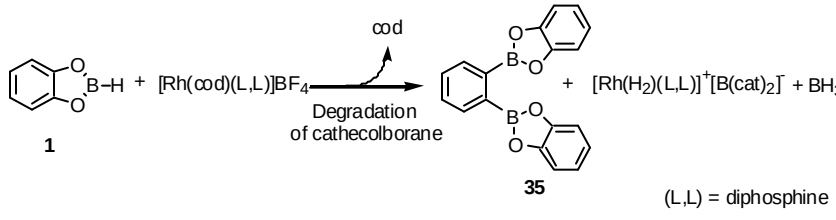
Entry	Eq. Borane	C (%)	Selectivity (%)				
			94	**95**	**96**	**97**	**98**
1	1.1eq	37	17	50	25	8	-
2	2.2eq	98	3	60	33	3	-

[a] Standard conditions: phenylacetylene/catecholborane/Rh complex=1:1.1 or 2.2:0.01. Solvent: THF. T: 25 ^{0}C. Time: 2h.

Although the ketone **94** was expected to be the major product obtained, in fact it was the diol diphenyl-1,2-ethanediol (**95,** hydroxybenzoin) that was the most favoured, (Scheme 10, Table 5, entry 1). The low conversion is consistent with the total consumption of catecholborane. Therefore, the double amount of borane reagent (2.2 equivalents) could guaranteed a higher conversion. However, not only was

conversion significantly improved, but selectivity towards the diol **95** also increased to 60%, (Table 5, entry 2).

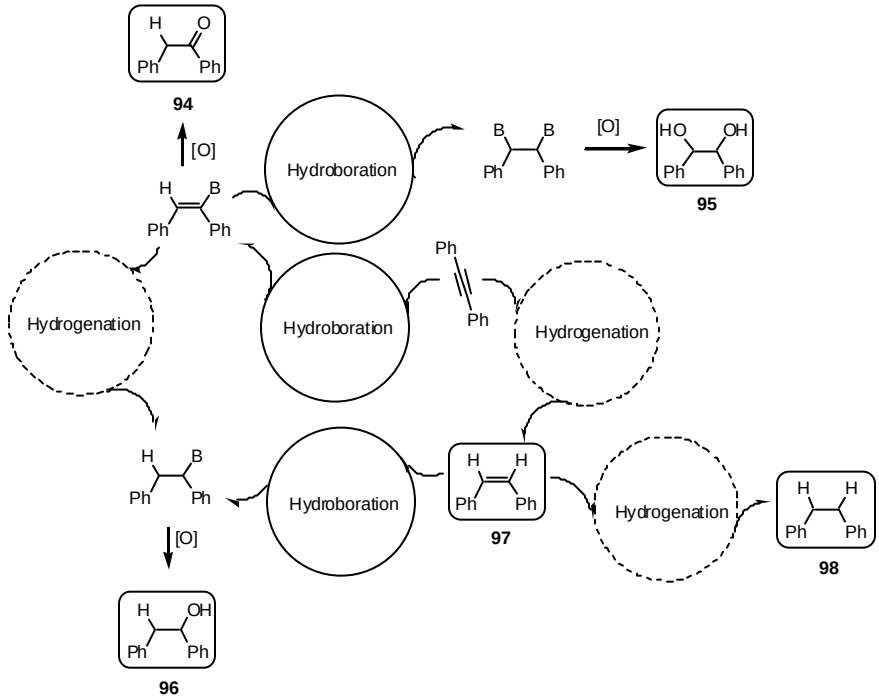
Some other by products, (scheme 10), were observed as a consequence of competitive catalytic reactions, such as hydrogenation. The reason for these secondary reactions could be related to the degradation of catecholborane in the reaction media which depends on the nature of the phosphine ligands, the rhodium complex and the solvent. It seems that, catecholborane breaks down to give a variety of boron products such as **35** plus metaldihydro species such as $[Rh(H_2)(dppb)]^+[B(cat)_2]^-$ (Scheme 11), [58]. The production of rhodium dihydrido species might be responsible for the formation of hydrogenation products.



Scheme 11

The ^{11}B NMR spectra determined during the dihydroboration reaction, showed two broad signals at $\delta(^{11}B)$= 33.00ppm and $\delta(^{11}B)$= 21.50ppm in agreement with the alkylboronate products and compound **35**, respectively.

On the basis of these observations, we suggest that diphenylacetylene was involved in competitive hydroboration and/or hydrogenation reactions as is illustrated in scheme 12. While the dihydroboration of diphenylacetylene provided the desired hydroxybenzoin **95**, hydroboration followed by the hydrogenation of the substrate gave the 1,2-diphenylethanol **96**. Alkene **97** and alkane **98**, were also formed from the catalytic hydrogenation of the alkyne and alkene, respectively.



Scheme 12

As far as the catalytic asymmetric dihydroboration of diphenylacetylene was concerned, the chiral complex [Rh(cod)(S,S)-bdpp]BF_4 with catecholborane provided conversion and selectivity, (Table 6, entry 1) similar to those of [Rh(cod)(dppb)]BF_4. However, the diphenyl-1,2-ethanediol (**95**) was characterised mainly as the ery*thro* compound, not the expected *threo*. Unfortunately, even modifying the rhodium complex with other chiral ligands, such as Quinap and Binap, did not change this trend towards the formation of the ery*thro* compound, (Table 6, entries 2 and 3). In addition, the formation of the diol **95** is not favoured in the latter bidentate ligands.

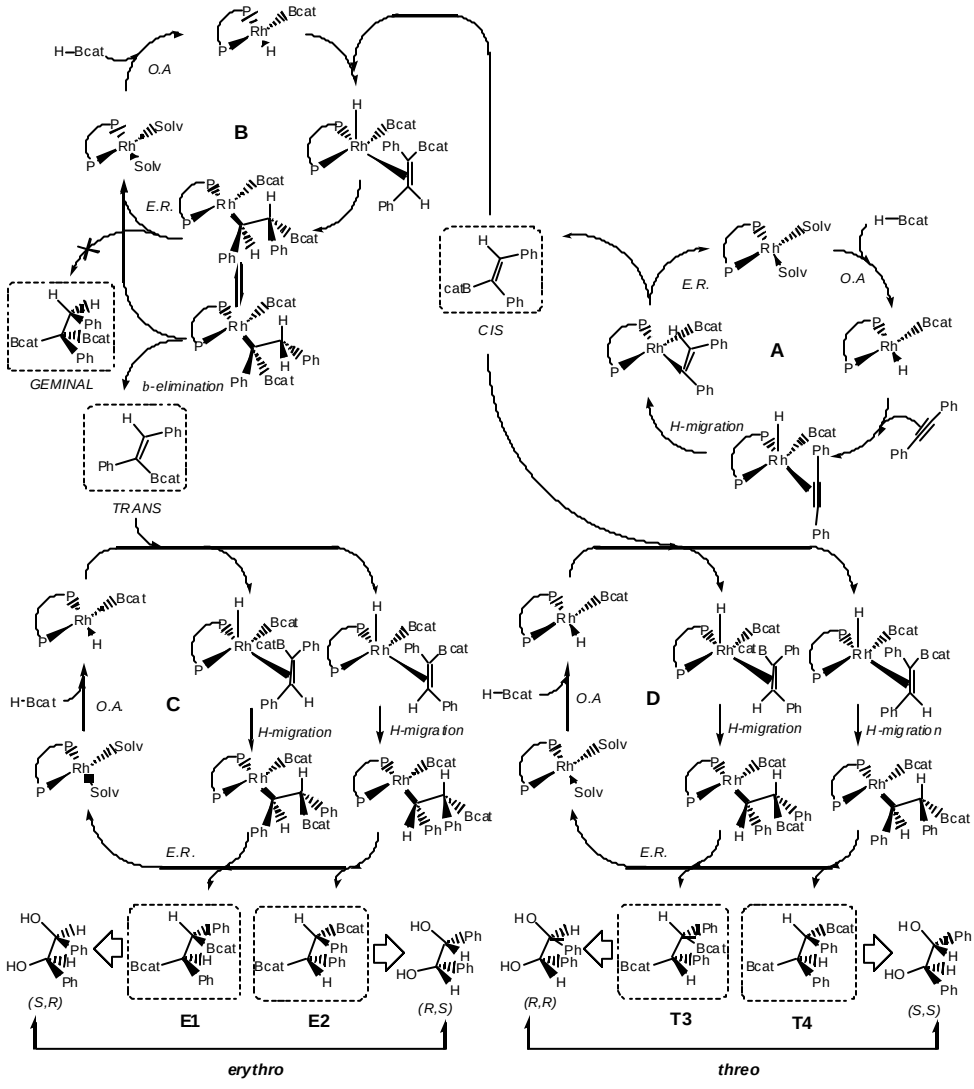
Table 6. Catalytic asymmetric dihydroboration of diphenylacetylene with $[Rh(cod)(L,L)]BF_4$ and catecholborane (**1**).[a]

Entry	L_2	run	C (%)[b]	Selectivity (%)[b]				
				94	**95** (erythro:threo)[c]	**96**	**97**	**98**
1	(S,S)-bdpp	-	98	4	68 (96:4)	26	2	-
2	(S)-Quinap	-	78	68	17	15	-	-
3	(R)-Binap	-	63	15	31 (88:12)	31	23	-
4[d]	(S,S)-bdpp	1	99	9	17 (58:42)	74	-	-
		2	56	23.5	47 (66:34)	29.5	-	-

[a] Standard conditions: phenylacetylene/catecholborane/Rh complex=1:2.2:0.01. Solvent: THF. T: 25^0C. Time: 2h.;[b] Determined by ^{1}H RMN; [c] Determined by HPLC; [d] 0.02mmol Rh system into 250mg MK-10_T

One explanation of the formation of the syn-diol, could be that the alkenylboronate ester isomerises from the *cis* to the *trans* isomer, because of the favoured β-elimination, (Scheme 13). The *trans* isomer could then be transformed into the *syn* diboronate, during the second catalytic hydroboration.

The heterogenisation of $[Rh(cod)(S,S)\text{-bdpp}]BF_4$ in montmorillonite K-10 (MK-10), yielded almost complete conversion in the first run, although the percentage of the diol **95** diminished substantially in comparison with the homogeneous version. Also, the erythro:threo ratio was 58:42 in this case, (Table 6, entry 4). In a second consecutive run, the conversion was only 56% but the percentage of diol **95** increased to 47% with a mixture of erythro:threo= 66:34. The more restricted environment in the heterogenised system could be the reason for these changes in selectivity. However, the decomposition of the catecholborane provided the compound B_2cat_3 (**35**), which is insoluble in THF and could justify the low conversion on recycling.


H–Bcat
O.A
B
E.R.
GEMINAL
b-elimination
TRANS
CIS
A
H-migration
C
D
H-migration
H-migration
(S,R)
E1
E2
(R,S)
erythro
(R,R)
T3
T4
(S,S)
threo

Scheme 13

3. Conclusions

It has been developed the catalytic asymmetric hydroboration of perfluoroalkenes in which the regioselectivity towards the branched perfluoroalkylboronate compound is controlled with the rhodium complex, the ligand and the borane reagent. The moderate e.e values (55-65%) obtained in the hydroboration of aliphatic perfluoroalkenes, are even higher than those observed in the aromatic perfluoroalkenes (18-19.5%), and in electron deficient vinylarenes such as 3,5-bis-trifluoromethylstyrene (5%), and 2,6-difluorostyrene (<15%).

It was possible to reuse the catalytic system in the heterogenised hydroboration/oxidation reaction of perfluoroalkenes but the selectivities diminished slightly.

Diphenylacetylene was synthesised through a suitable palladium phosphine-free catalytic system which has significant advantages in the Sonogashira coupling of alkynes with aryliodides and bromides. Not only does it catalyse the reaction successfully, it is also easily recovered and reused when it is immobilised on clays, because it is very stable.

Dihydroboration/oxidation of diphenylacetylene can provide 1,2-diphenyl-1,2-ethanediol (hydrobenzoin (**95**)) with a selectivity of 68% but the resulting diol is the ery*thro* isomer.

4. Experimental section

General comments. All reactions and manipulations were carried out with standard vacuum line techniques under an atmosphere of dry nitrogen. All rhodium organometallic complexes were synthesised using standard Schlenk techniques. All organic solvents were distilled, stored on a molecular sieve (0.4nm Aldrich), and degassed with a nitrogen flow prior to use. The complexes $[Rh(\mu\text{-}Cl)(cod)]_2$ [59], $[Rh(cod)_2BF_4$ [60], [61], $[Rh(cod)(R)\text{-}Binap]BF_4$ [62], $[Rh(cod)(S)\text{-}Quinap]BF_4$ [50b] were prepared as previously reported. They were characterised by elemental analysis, ^1H and ^{31}P NMR, and FTIR spectroscopies. MK-10 was purchased from Fluka and bentonite A and B was purchased as Majorbenton B from AEB Iberica S.A. Predried clays were obtained as follows: clay (5g) was kept in a melting pot in the oven at 100^0C for 24h. NMR spectra were recorded on a Varian Gemini 300 and Mercury 400 spectrometer. Chemical shifts were reported relative to tetramethylsilane for ^1H as internal reference, 85% H_3PO_4 for ^{31}P and BF_3OEt_2 for ^{11}B as the external reference. Gas chromatographic analyses were performed on a Hewlett-Packard 5890 II with a flame ionisation detector equipped with a chiral column FSCycoldex β-IP, 50m x 0.25mm. The HPLC analyses were performed in a chiral column Chiralcel OJH. BET surface areas were calculated from nitrogen adsorption isotherms at 77K by using a Micromeritics ASAP 2000 surface analyser and a value of $0.164nm^2$ for the cross section of the nitrogen molecule. The scanning electron microscopy analyses were made in a JEOL, JSM-640 with an accelerating voltage=15KV and a prove current = $(3\text{-}6)x10^{-9}$ A for a representative area (575 x 466 μm) for each sample.

Preparation of the supported complexes. The ionic rhodium complex and the palladium complex were immobilised in the following manner. The solid support (montmorillonite K-10 or bentonite A and B was added to an organometallic solution prepared with 10ml of deoxygenated dichloromethane and 0.2mmol of the complex under nitrogen. Then it was stirred for 24h under nitrogen at room temperature. The suspension was filtered off and the solid was washed with dichloromethane and dried

under vacuum. The amount of metal complex immobilised on the clay was determined by gravimetric analysis and SEM analysis.

Homogeneous catalytic hydroboration/oxidation of perfluoroalkenes 90, 91, 92 with catecholborane or pinacolborane. Perfluoroalkenes (2mmol) were added to a solution of catalyst (1 mol%) in THF (2mL) under nitrogen. The solution was stirred for 5 min and freshly distilled catecholborane or pinacolborane (2mmol) was then added. The mixture was stirred at ambient temperature for 1h because there is a risk of explosion when using peroxides with ether and THF. Afterwards, NaOH (2M, 2mL) and H_2O_2 (2mL) were added and the mixture was stirred for several hours. The reaction mixture was extracted with Et_2O (3x20) and washed (NaOH 2M, H_2O, saturated brine). The organic extracts were dried over $MgSO_4$, and evaporated under reduced pressure. The products were characterised by chromatography.

Heterogenised catalytic hydroboration/oxidation of perfluoroalkenes 90, 91 and 92 with catecholborane or pinacolborane. Perfluoroalkenes (2mmol) were added to a suspension of supported catalyst (1 mol% immobilised in 0.5g of solid) in THF (2mL) under nitrogen. The solution was stirred for 5 min and freshly distilled catecholborane (2mmol) was then added. The mixture was stirred at ambient temperature for 2h. The solution was filtered off under vacuum and the filtrates were then quenched with EtOH (2mL). Work up must be carried out carefully because there is a risk of explosion when using peroxides with ether and THF. The quenched filtrates were treated with NaOH (2M, 2mL) and H_2O_2 (2mL) and the mixture was stirred for several hours. The mixture was finally extracted into Et_2O, washed (NaOH 2M, H_2O, saturated brine) and dried over $MgSO_4$. The products were then characterised by chromatography. The solid that contained the complex was dried under vacuum for 10 minutes and put into the *schlenk* for another run.

Homogeneous catalytic Sonogashira reaction. To a solution of arylhalide (1,7mmol), Pd catalyst complex (17μmol, 1 mol%), and CuI (85μmol, 5 mol%) in dry base (pyridine, pyrrolidine or Cs_2CO_3) PhC≡CH (2mmol, 1.2eq) was added under

nitrogen, and the mixture were reacted at reflux temperature for 0.5-2.5h. The products were characterised by chromatography.

Heterogenised catalytic Sonogashira. CuI (85μmol, 5 mol%) in dry base (pyridine, pyrrolidine or Cs_2CO_3) was added to a suspension of supported Pd catalyst (1 mol% metal complex in 250mg of clay) under nitrogen and arylhalide (1.7mmol). The solution was stirred for several minutes and PhC≡CH (2mmol, 1.2 eq) was then added under nitrogen. The mixture was reacted at reflux temperature for 0.5-2.5h. The products were characterised by chromatography.

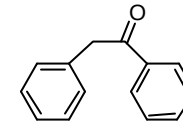
Homogeneous catalytic dihydroboration/oxidation of diphenylacetylene. Diphenylacetylene (1mmol) was added to a solution of catalyst (1 mol%) in solvent (THF or toluene) (2mL) under nitrogen. The solution was stirred for 5 min and freshly distilled catecholborane or pinacolborane (2.2mmol) was then added drop by drop for 15 min. The mixture was stirred at ambient temperature for 2h and then quenched with EtOH (2mL). Work up must be carried out carefully because there is a risk of explosion when using peroxides with ether and THF. Afterwards, NaOH (2M, 2mL) and H_2O_2 (2mL) were added and the mixture was stirred for several hours. The reaction mixture was extracted with ethyl acetate (3x20) and washed (NaOH 2M, H_2O, saturated brine). The organic extracts were dried over $MgSO_4$, and evaporated under reduced pressure. The products were characterised by ^{1}H NMR and chiral HPLC.

Heterogenised catalytic dihydroboration/oxidation of diphenylacetylene with catecholborane (1). Diphenylacetylene (1mmol) was added to a suspension of supported catalyst (2 mol% immobilised in 0.250g of solid) in THF (2mL) under nitrogen. The solution was stirred for 5 min and freshly distilled catecholborane (2.2mmol) was then added drop by drop for 15 min. The mixture was stirred at ambient temperature for 2h, using the chemical assembly exemplified in Figure 7. The solution was filtered off under vacuum and the filtrates were then quenched with EtOH (2mL). Work up must be carried out carefully because there is a risk of explosion when using peroxides with ether and THF. The quenched filtrates were treated with NaOH (2M, 2mL) and H_2O_2 (2mL) and the mixture was stirred for several hours. The mixture was

finally extracted into Et_2O, washed (NaOH 2M, H_2O, saturated brine) and dried over $MgSO_4$. The products were then characterised by ^1H NMR and HPLC. The solid that contained the complex was dried under vacuum for 10 minutes and put into the *schlenk* for another run.

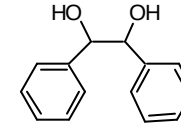
Deoxybenzoin (94) [63a]

^1H RMN($CDCl_3$): δ(ppm)= 7.99(d, 2H), 7.50(m, 2H); 7.46(m, 2H), 7.27(s, 4H), 4.25(s, 2H)



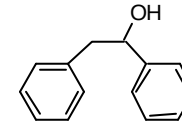
Hydroxybenzoin (95) [63b]

^1H RMN($CDCl_3$): δ(ppm)=7.09-7.22(m, 10H), 4.80(s, 2H), 2.17(br s, 2H); HPLC (diol): Chiralcel OJ-H, 10% ^{i}PrOH in Hexane, flow rate 1.0mL/min, t_R= 15.29 (R,R); t_R= 17.70 (S,S); t_R= 21.50 (R,S) and (S,R)



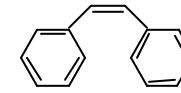
1,2-diphenylethanol (96) [50b]

^1H RMN($CDCl_3$): δ(ppm)= 7.40-7.10 (m, 10H), 4.90 (dd ,$^3J_{H-H}$=8.0 and 5.4Hz, 1H),3.20-2.90 (m, 2H), 1.80(br s, 1H)



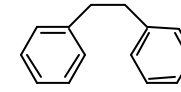
***cis*-stilbene (97)** [63a]

^1H RMN($CDCl_3$): δ(ppm)= 7.38-6.98 (m, 10H); 6.57 (s, 2H)



Bibenzyl (98) [63a]

^1H RMN($CDCl_3$): δ(ppm)= 7.42-6.99 (m, 10H); 2.91 (s, 4H)



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