2

N-donor Ligands: Oxazoline and Imidazoline Ligands

In recent years, the potential of N-donor ligands has been demonstrated in such metal-catalysed reactions as enantioselective cyclopropanation, hydrosilylation, Diels-Alder, hydrogenation and palladium catalysed allylic substitution, in which only P-donor ligands seemed to be effective. Oxazolines and imidazolines are two examples of N-donor ligands that are widely used in asymmetric catalysis and which are an attractive alternative to diphosphines for the hydrogenation of imines.

Chapter 2

2.1. Introduction

The development of new *N*-donor ligands with two different coordinative heteroatoms may be an attractive alternative to diphosphines. The bifunctional character of hybrid ligands has proven to be very useful in homogeneous catalysis and some important organic reactions catalysed by transition metal complexes with N⌒X ligands (X=coordinative atom, c.a. P, S, N…) are quite impressive in terms of selectivity and reactivity [1]. Thus, a transition metal complex with a bidentate ligand in which the two coordinating atoms are electronically different can impart stereoelectronic control in the formation of a specific product, resulting in enhanced selectivity [2]. Metal complexes with hybrid ligands containing N, S or P donor atoms are of increasing interest because of their ability to act as "hemilabile" ligands. For instance, nitrogen as a hard donor atom is capable of stabilizing metal ions in higher oxidation states whereas phosphorus or sulphur as soft donor atoms are best suited to stabilizing metals in lower to medium oxidation states.

Ligands containing the oxazoline moiety (**1a-f**) (Figure 1) have been widely explored in the last two decades and successfully used in such asymmetric reactions as enantioselective cooper and ruthenium cyclopropanation [3], iron, magnesium and copper catalysed Diels Alder [4], rhodium catalysed hydrosilylation [5], iridium catalysed hydrogenation [6] and palladium catalysed allylic substitution [7]. More recently, ligands carrying an imidazoline moiety (**1g-i**) (Figure 1) have been used in palladium catalysed copolymerisation [8], the ruthenium Diels Alder reaction [9], iridium catalysed enantioselective hydrogenation of prochiral olefins [10] and enantioselective diethyl zinc additions [11] affording promising results.

All these examples demonstrate the backbone variety and the ability of the hemilabile ligands to be coordinated to several metals. The coordination chemistry of these ligands and the structural characteristics of the resulting transition metal complexes have recently been reviewed [12].

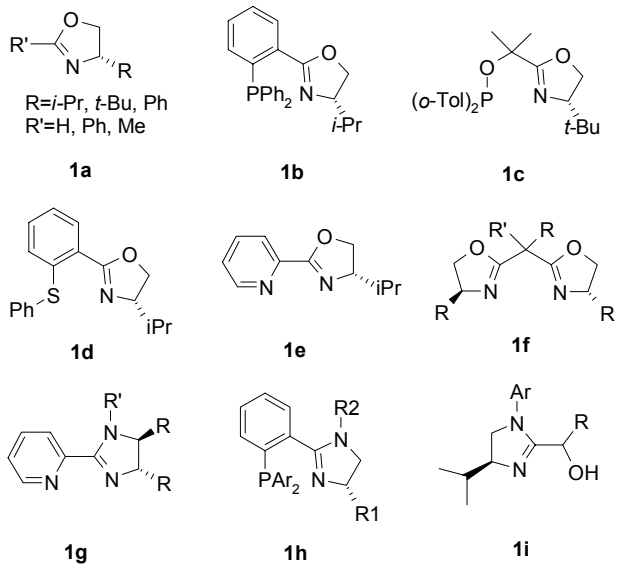


Figure 1

Oxazoline and imidazoline ligands are structurally similar and show attractive characteristics: versatility of the ligand design, the straightforward synthesis of ligands from readily available precursors, and the modulation of the chiral centers. The asymmetry induced by such heterobidentate systems is determined by a combination of steric and electronic interactions, so these ligands make it possible to control the enantioselectivity in catalytic reactions by creating an asymmetric environment provided by the oxazoline/imidazoline moiety and by combining soft and hard donor atoms (P, S, N) to modify the electronic properties on the metal center. Moreover, modifying the chelate ring size is another way of optimising the effectiveness of the catalytic system (Figure 2).

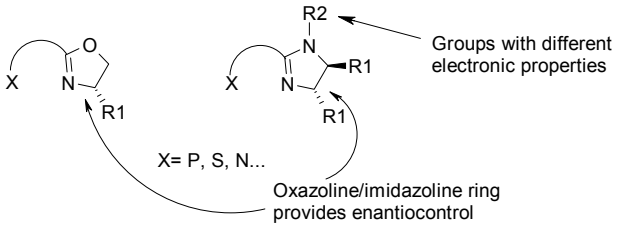
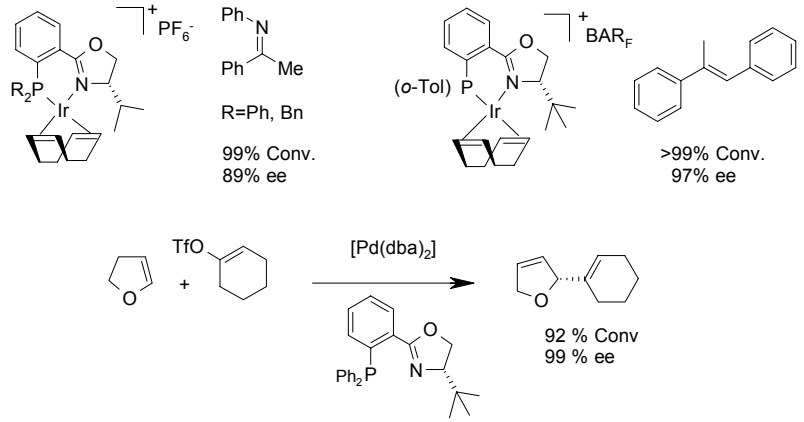


Figure 2

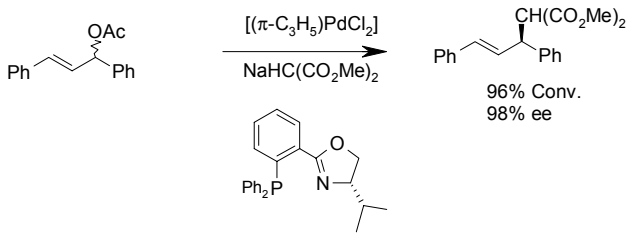
Nevertheless, oxazoline and imidazoline ligands have some important differences. For instance, the imidazoline ring is much more basic than the oxazoline ring [13]. Furthermore, the imidazoline unit makes it possible to introduce a variety of substituents into the aminic nitrogen, modifying its electronic properties. So these ligands are more tunable than the oxazoline analogues.

The phosphine-oxazoline ligands (P⌒N) were developed largely by Pfaltz [14] and proved to be versatile chiral ligands in a wide range of homogeneous catalytic reactions such as imine [15] and olefin [16] reductions with Ir(I) complexes as well as in Heck [17] reactions with Pd(0) (Scheme 1).



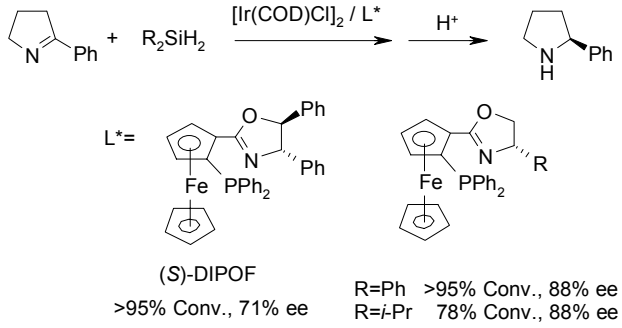
Scheme 1

At the same time, other groups worked independently on the synthesis of phosphinooxazoline ligands. Williams [18] and Helmchen [19], in particular, focused their attention on the palladium-catalysed allylic substitution (Scheme 2).



Scheme 2

Uemura and co-workers [20] proved that chiral ferrocenyl-phosphinooxazolines are effective ligands for the Ir(I)-catalysed asymmetric hydrosilylation of imines giving, after hydrolysis, the corresponding amines with high enantioselectivities (up to 88%) in almost quantitative yields (Scheme 3).



Scheme 3

In the field of N⌒S ligands, Pfaltz [21], Williams [18a] and Helmchen [19a] have reported the use of thioether-oxazoline ligands in palladium-catalysed allylic alkylation providing high enantiocontrol (Figure 3) [22,23].

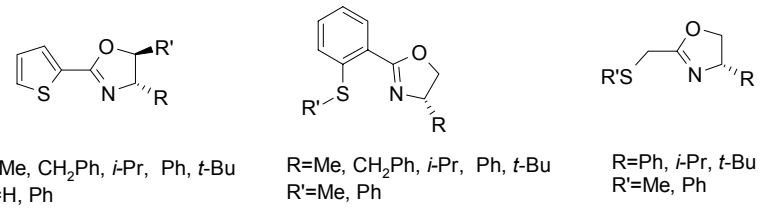


Figure 3

However, as far as we know, the use of N⌒S ligands in the hydrogenation of imines has not been reported.

Few examples of N⌒N ligands containing the oxazoline moiety are applied to the reduction of C=N [20], however, the results are disappointing. Oxazolinylpyridines are mainly used in palladium-catalysed allylic alkylation of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate (Figure 4) [7].

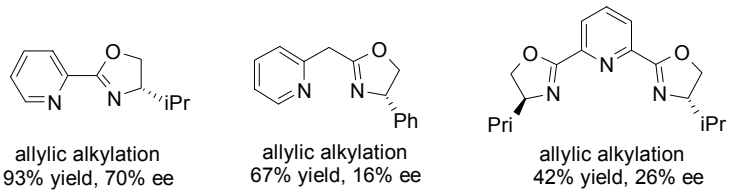


Figure 4

Ligands carrying an imidazoline unit have not received as much attention as

oxazoline ligands, although they are more electronically tunable by a proper choice of the group attached to the aminic atom. Pfaltz and co-workers [10] evaluated the use of phosphino-imidazoline ligands in the reduction of unfunctionalized olefins and, in several cases, ee's were higher than when phosphino-oxazoline ligands were used (Figure 5).

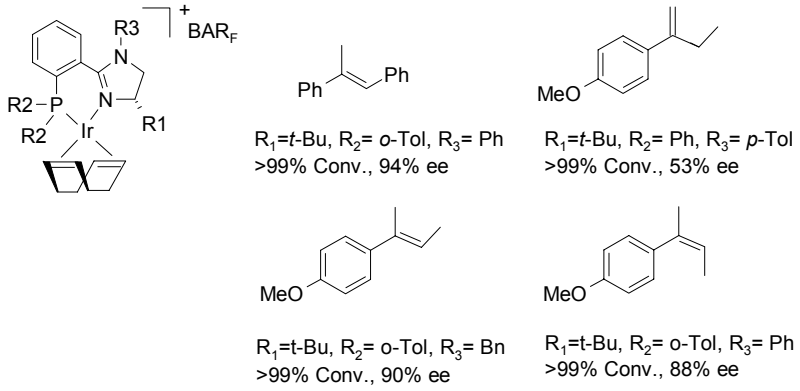


Figure 5

These results seem to indicate that *N*-donor ligands are gaining interest to replace the more widely used diphosphines in homogeneous catalysis. Moreover, the successful results of Pfaltz's cationic iridium catalysts based on diphenylphosphinooxazolines in imine reduction prompted us to check the aptitude of thioether-oxazoline (NS) and phosphino-imidazoline (NP) ligands towards the iridium-catalysed enantioselective reduction of prochiral imines, since they had not previously been used in this reaction.

2.2. Results and Discussion

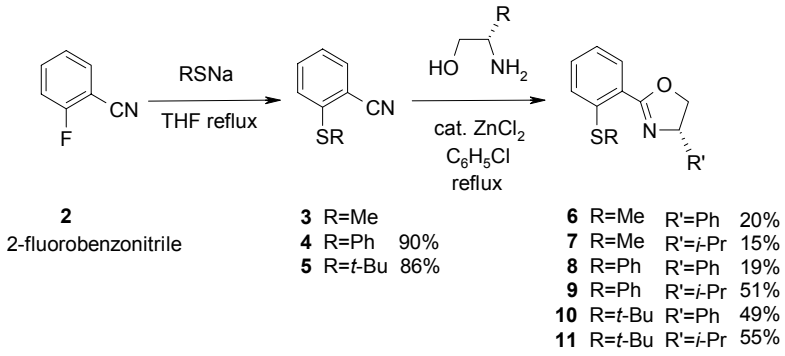
2.2.1. Thioether-oxazoline ligands

As mentioned above, although phosphino-oxazoline ligands have been successfully applied in the iridium-catalysed hydrogenation of imines, oxazoline-thioether ligands have never been used. These ligands can control the reactivities of metal sites owing to the different steric and electronic properties of the donor groups. It is worth noting that replacing the phosphorous moiety by sulphur creates a new stereogenic center, which can have a remarkable effect.

2.2.1.1. Synthesis of thioether-oxazoline ligands 6-11

We decided to prepare ligands **6-11,** which have methyl, phenyl or t-butyl groups attached to the sulphur atom, and phenyl or isopropyl on the stereogenic center of the ozaxoline ring. Compounds **6-9** have already been reported [22] and ligands **10** and **11** have been synthesized and characterized for the first time in this work. Oxazoline-thioether ligands **6-11** are readily accessible in a procedure of two steps; the reaction of 2-fluorobenzonitrile (**2**) with sodium thiolate salts affords compounds **3-5**. The reaction of **3-5** with homochiral amino alcohols (L-valinol and L- phenylglycinol) in the presence of a catalytic amount of zinc chloride using dry chlorobenzene as solvent allows to obtain the desired ligands **6-11** in poor to moderate yields (Scheme 4) [22].

Compound **3** was commercially available. The $ZnCl_2$ increases the electrophilicity of the ciano group, and favours condensation with the amino alcohol.



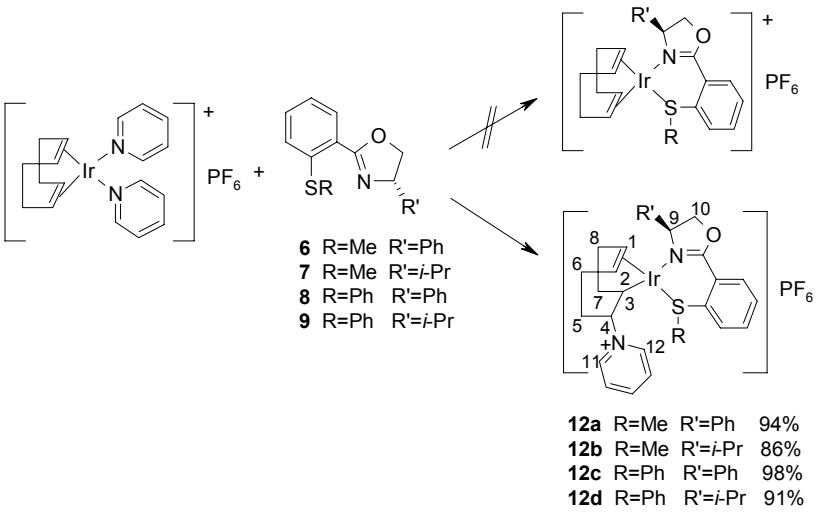
Scheme 4. Synthesis of thioether-oxazoline ligands **6-11**

Although this procedure is well established in the literature [22], the yields are only low or moderate. In an attempt to improve the yields, we used other catalysts like ytterbium triflate and solvents like *o*-dichlorobenzene (bp=178-180ºC), which makes it possible to increase the temperature of the reaction. The results, however, were not better. The use of an argon flow, which removes the ammonia formed, allows in some cases to obtain higher yields.

2.2.1.2. Synthesis and characterization of $[Ir(\sigma\text{-}\eta^2\text{-}PyC_8H_{12})L]PF_6$ (12a-d), $[Ir(\eta^4\text{-}COD)L]PF_6$ (13a) and $[Ir(\eta^4\text{-}COD)L]BF_4$ (13b)

With the aim of exploring the coordination chemistry of these ligands, we studied their reactivity towards different iridium (I) precursors. We initially selected $[Ir(\eta^4\text{-}COD)(Py)_2]PF_6$ (COD=C_8H_{12}=1,5-cyclooctadiene, Py=pyridine) which had been used as a precursor to prepare several Ir(I) complexes [24]. The reaction of the chiral oxazoline-thioether ligands **6-9** with $[Ir(\eta^4\text{-}COD)(Py)_2]PF_6$ in anhydrous CH_2Cl_2 at room temperature, was expected to occur with the displacement of the

two pyridine molecules affording the corresponding cationic Ir(I) complexes [Ir(η^4-COD)L]PF_6 (L=oxazoline-thioether ligands). However, this did not occur and the isolated complexes **12a-d** showed the structure depicted in Scheme 5.



Scheme 5. Synthesis of complexes**12a-d**

Isolated complexes **12a-d** were stable in air even in solution. Mass spectroscopy analysis and NMR experiments allowed us to elucidate the structure of compound **12a**.

The presence of pyridine was confirmed by ^1H and $^{13}C\{^1H\}$ NMR, and also by MS spectroscopy. The highest m/z 649.1 in the FAB spectrum corresponded to the M^+ $[C_{29}H_{32}SON_2Ir]^+$ and m/z 569 corresponded to M^+-Py.

The characteristic signals of the PF_6^- anion, which in this case is the counterion of the pyridinium salt, were also observed in the $^{31}P\{^1H\}$ spectrum at -144.1 ppm (septuplet, $J_{P\text{-}F}$= 712.8 Hz) and in $^{19}F\{^1H\}$ spectrum at -73.6 ppm (doublet, $J_{F\text{-}P=}$711.7 Hz).

^{1}H and $^{13}C\{^{1}H\}$ NMR spectra showed signals corresponding to the COD ligand and to the coordinated thioether-oxazoline ligand. The eight signals corresponding to the aliphatic CH_2 protons of COD were unambiguously assigned by COSY and TOCSY experiments and by correlation with their respective carbons (Figure 6). The assignment of the olefinic COD revealed that whereas three of these signals appeared at the expected chemical shift (3-5 ppm), a signal corresponding to H3 appeared at 2.59 ppm. The HETCOR experiment demonstrated the correlation of H3 with a carbon appearing at 3.57 ppm (!!!) (Figure 6). This carbon must be directly bonded to the metal and since there are no additional protons in the COD structure, pyridine must be bonded in the neighbouring carbon. In fact, the chemical shift of H4 and C4 are in agreement with the values expected for a carbon bonded to a pyriridium salt.

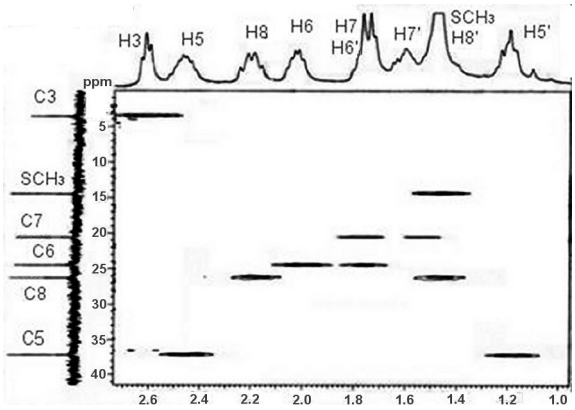


Figure 6 . A section of the HETCOR spectrum for **12a**

The stereochemistry of complex **12a** was proposed after a NOE experiment, which showed a signal enhancement of H11 and H12 of pyridine and H4 when the methyl group was irradiated (see Scheme 5).

Thus, the resulting structure, $[Ir(\sigma\text{-}\eta^2\text{-}PyC_8H_{12})L]PF_6$ (**12a**), consists of monomeric units with an Ir atom coordinated to a pyridinium-cyclooctaenyl via σ-C and π-C=C bonds and to the thioether-oxazoline ligand. The NMR data for **12a** are collected in Table 1.

Table 1. NMR Data of complex **12a**

	^{1}H NMR (ppm)		^{13}C{^{1}H} NMR (ppm)
H1	4.07	C1	87.1
H2	3.22	C2	67.3
H3	2.59	C3	3.6
H4	4.66	C4	70.9
H5, H5’	2.43, 1.21	C5	37.2
H6, H6’	2.03, 1.74	C6	24.5
H7, H7’	1.74, 1.54	C7	20.6
H8, H8’	2.20, 1.46	C8	26.3
H9	5.81	C9	66.6
H10, H10’	5.13 , 4.94	C10	77.9
H11	8.95	C11	154.8
H12	8.54	C12	152.6
Me	1.48	Me	14.5

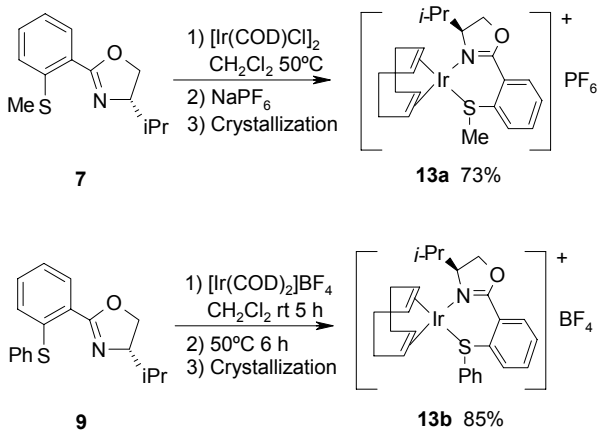
A reasonable explanation for these observations is that a nucleophilic attack of the removed pyridine to the C=C of the coordinated cyclooctadiene takes place, resulting in the formation of a piridinium salt and a C-Ir bond.

Olefins, which are usually unreactive to nucleophiles, do react with various nucleophiles such as malonates, acetates, hydroxides, etc, leading to new carbon-carbon bond formation when they are coordinated to metals [25]. Transition metals in high oxidation states such as palladium (II) or platinum (II) [26,27] are most suitable for this reaction, since they tend to withdraw electron density from the olefins. Likewise, several examples were reported with rhodium (I) [28] or iridium (I) [29] complexes, even with NR_nH_{3-n} as nucleophilic agents.

The ^{1}H NMR spectrum of complex **12b** showed only one species and the presence of pyridine, COD and oxazoline-thioether ligands, as in **12a**, although in this case the signals were broad even at -50ºC and could not be assigned unambiguously. ^{1}H NMR of complexes **12c-d** showed the presence of several species in equilibrium, where pyridine signals were also present. Lowering the temperature did not result in the resolution of one species. The presence of several species may be due to the formation of several regioisomers as a consequence of the nucleophilic attack of the pyridine on either C3 or C4. The formation of these regioisomeric complexes may be favored when a phenyl substituent is attached to the sulphur atom. Moreover, there is also the additional complexity that a new stereogenic center is created when the sulphur is coordinated to the metal center, which gives diastereoisomeric complexes. This behavior has previously been described for Rh [30] and Pd [31] complexes with thioether ligands.

Further investigation of the reaction of $[Ir(\eta^4\text{-COD})Cl]_2$ with ligand **7** in anhydrous CH_2Cl_2 at 50ºC for 1-2 hours under an inert atmosphere afforded the complex $[Ir(\eta^4\text{-COD})\mathbf{7}]PF_6$ (**13a**) after anion exchange by washing with an aqueous solution of $NaPF_6$ and crystallization from CH_2Cl_2/Et_2O (Scheme 4). Complex **13b** was synthesized by reacting $[Ir(\eta^4\text{-COD})_2]BF_4$ with ligand **9** in anhydrous CH_2Cl_2. These compounds were characterized by elemental analysis and NMR spectroscopy. The elemental analysis results showed that the compositions of the air-stable complexes **13a-b** correspond to a 1:1 metal complex of the M(COD) fragment and NS ligand. Although the ^{1}H NMR spectra of **13a-b** showed the signals corresponding to the coordinated oxazoline-thioether ligand and the η^4-cyclooctadiene appearing at the expected chemical shift, the signals were broad and a complete and unambiguous structural assignment on the basis of these data was not possible.

The catalytic behaviour of the systems formed by Ir/oxazoline-thioether ligands will be discussed later in section **2.2.3**.



7 **13a** 73%

9 **13b** 85%

Scheme 4. Synthesis of [Ir(η^4-COD)**7**]PF_6 (**13a**) and [Ir(η^4-COD)**9**]BF_4 (**13b**)

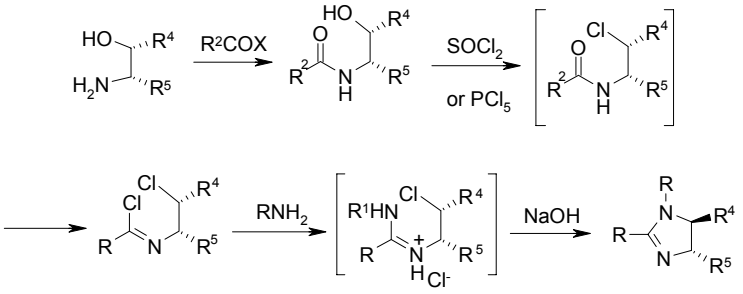
2.2.2. Phosphine-imidazoline ligands

Phosphine-imidazoline ligands are closely related to the phosphino-oxazoline reported by Pfaltz for the high effective asymmetric reduction of imines [15]. The imidazoline ring also makes it possible to modify the electronic properties by introducing electron-donor or withdrawing groups at the aminic nitrogen.

2.2.2.1. Synthesis and characterization of ligands 18a-c

The synthesis of imidazole derivatives has been reported using a variety of methods [32] but more specifically, the synthesis of imidazole derivatives bearing a 2-substituted aromatic group has been described in some recent papers by condensation of a diamine with aryl imidoesters [33]. This strategy involves the formation of the corresponding imidoesters, which were studied many years ago by Pinner [34]. However, following the imidoester procedure, the imidazoline ring is

normally constructed in only moderate yields [8,9,35]. An improved method for preparing imidazoline rings has recently been published by Casey and co-workers [36], while the present study was being made (Scheme 6).



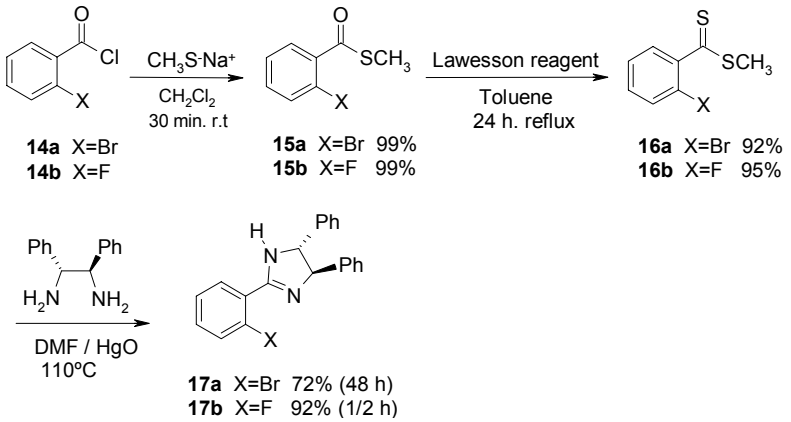
Scheme 6. Synthesis of 2-aryl-imidazolines

Enantiopure amino alcohols are converted into *N*-hydroxyethylamides, which are reacted with an excess of thionyl chloride to yield *N*-chloroethylimidoyl chlorides. These intermediates are treated with amines and anilines to produce *N*-chloroethylamidines, which are converted into imidazolines upon workup with aqueous hydroxide. This is a versatile method which allow to obtain the imidazolines from the corresponding amides in a 40-80% overall yield. Recently, Pfaltz published the synthesis of phosphine-imidazoline ligands on the basis of Casey's work and its application to the reduction of olefins [10].

Here, we report that dithioesters are useful precursors for the synthesis of *2*-arylimidazolines. After constructing the heterocycle moiety, we must then introduce the phosphino moiety to obtain the phosphine-imidazoline ligands.

As starting material, we selected the benzoyl chlorides **14a** and **14b**, which have a fluorine or bromine atom in the ortho position. These compounds should make it possible to introduce the phosphine moiety by different synthetic procedures.

Thus, 2-bromo-benzoylchloride and 2-fluoro-benzoylchloride (**14a-b**) reacted with methanethiolate sodium salt to afford 2-halo-thiobenzoic acid *S*-methyl esters (**15a-b**) in almost quantitative yield (Scheme 7). These compounds were subsequently treated with Lawesson's reagent to give dithioesters **16a-b** in excellent yield [37].



Scheme 7. Synthesis of 2-aryl-imidazolines **17a-b**

The imidazoline ring formation is due to the condensation of the dithioesters **16a-b** with a chiral diamine giving compounds **17a-b**. The driving force of the reaction is the precipitation of HgS by using a desulfurizing agent such as mercury (II) oxide [38]. Therefore, the reaction of **16a** with (1*R*,2*R*)-diphenylethylene diamine gave compound **17a** in a 66% overall yield. The condensation of compound **16b** with the chiral diamine worked considerably better, and the ring closure took place in only half an hour, isolating the compound **17b** in 92% yield. The overall yield was 86% in this case.

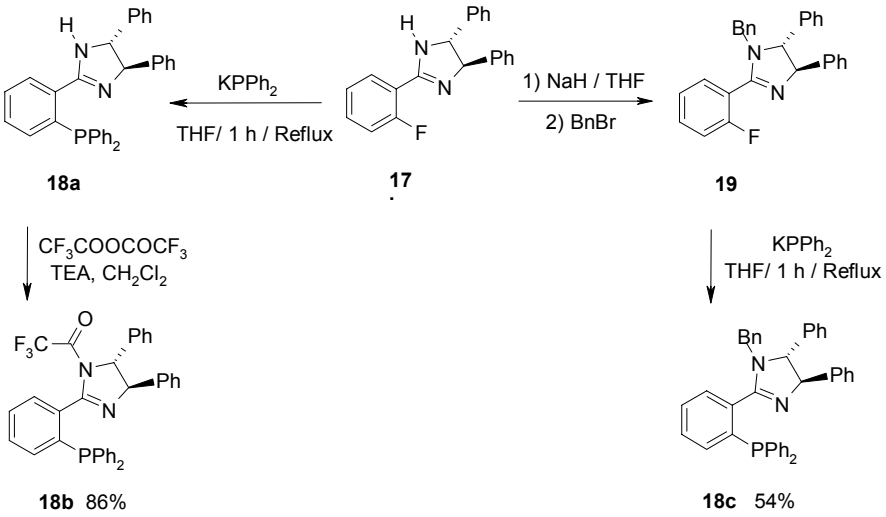
Having achieved our first goal, the next step was to introduce the phosphino moiety by lithium-halogen exchange prior to reaction with the electrophile, chlorodiphenylphosphine. However, despite numerous attempts, the

reaction of **17a** did not proceed with either n-BuLi or t-BuLi, even when the excess of lithium reagent was large. In almost all the cases the starting material was recovered. This suggests that the aryl-lithium intermediate was not formed. The only product that was isolated and charaterised was n-BuPPh_2, obtained by reaction of n-BuLi with Ph_2PCl.

Hence a different approach was required to introduce the phosphino group. Compound **17b** reacted with Ph_2PK in refluxing THF for an hour affording the phosphino-imidazoline ligand **18a** in 99% yield. The key step was now the reaction with Ph_2PK through an aromatic nucleophilic substitution reaction (Scheme 8) [35d,18a].

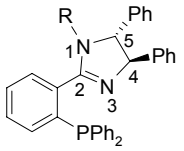
Tuning the electronic properties of ligands can have dramatic effects on the enantioselectivity in metal-catalysed reactions [39]. Accordingly, we decided to prepare the (*4R*,*5R*)-1-substituted-2-[(2-diphenylphosphine)phenyl]-4,5-diphenyl-4,5-dihydro-imidazoles (**18b, 18c**). Further reaction of **18a** with trifluoroacetate anhydride provided **18b** (Scheme 8). On the other hand, **17b** reacted with benzyl bromide to give compound **19** before the phosphine moiety was introduced to give **18c** (Scheme 8).

Ligands **18a-c** were characterized by ^{1}H, $^{13}C\{^{1}H\}$, $^{31}P\{^{1}H\}$, HSQC NMR spectroscopy, mass spectrometry (MS) and elemental analysis. Table 2 collects some NMR selected data for ligands **18a-c**.



Scheme 8. Synthesis of phosphine-imidazoline ligands **18a-c**

Table 2. Selected ^{1}H, $^{13}C\{^{1}H\}$ and $^{31}P\{^{1}H\}$ NMR data for ligands **18a-c** recorded in $CDCl_3$

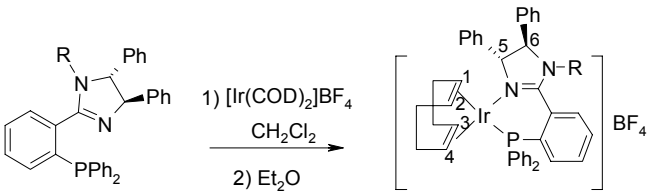


18a R=H
18b R=$COCF_3$
18c R=Bn

^{1}H (ppm)	**18a**	**18b**	**18c**
H4	4.48	5.16	4.36
H5	4.73	5.28	5.00
$^{13}C\{^{1}H\}$ (ppm)			
C=N	164.2	165.8	164.9
C4	71.3	70.0	72.2
C5	80.3	81.4	78.4
$^{31}P\{^{1}H\}$ (ppm)			
P	-10.3	-11.8	-12.3

2.2.2.2. Synthesis and characterization of $[Ir(\eta^4\text{-COD})L]BF_4$ (19a-c)

Cationic iridium(I) complexes **19a-c** (Scheme 9) were prepared by reaction between the cationic complex $[Ir(\eta^4\text{-COD})_2]BF_4$ (COD=cyclooctadiene) and a slight excess of the corresponding ligands in dichloromethane. The organometallic complexes $[Ir(\eta^4\text{-COD})L]BF_4$ (COD=1,5-cyclooctadiene, L=ligands **18a-c**) were precipitate by adding Et_2O.



18a R=H
18b R=$COCF_3$
18c R=Bn

19a R=H 97%
19b R=$COCF_3$ 61%
19c R=Bn 86%

Scheme 9. Synthesis of $[Ir(\eta^4\text{-COD})L]BF_4$ (**19a-c**)

The elemental analysis results showed that the compositions of the air-stable complexes **19a-b** correspond to a 1:1 metal complex of the M(COD) fragment and NP ligand. The FAB MS analysis of **19a** and **19b** showed the highest peaks at m/z 783.1 and 879.1, respectively, corresponding to M^+. The loss of cyclooctadiene is also observable at m/z 675.0 (**19a**, M^+-COD) and 771.0 (**19b**, M^+-COD).

The ^1H NMR spectra of **19a-c** showed signals for the cyclooctadiene ligand at the expected chemical shift (1.25-2.38 ppm, methylene protons) [15,40]. The olefinic protons of COD displayed two set of signals. Whereas H1 and H2 appeared as broad peaks at 4.14-5.12 ppm, H3 and H4 appeared at higher fields (2.77-3.41 ppm). In the $^{13}C\{^1H\}$ NMR spectra of **19a-b**, the C5 and C=N were shifted to lower

fields than the corresponding resonance in the free ligand (Tables 2 and 3). This observation is strong evidence of M-N coordination [41].

The $^{31}P\{^{1}H\}$ NMR spectra of **19a-c** displayed a singlet shifted to lower fields than the free ligand, which confirmed that the phosphorus atom was coordinated to the metal center [15].

Table 3. Selected ^{1}H and $^{31}P\{^{1}H\}$ NMR data for complexes **19a-c** recorded in $CDCl_3$

^{1}H (ppm)	**19a**	**19b**	**19c**
H1	4.85	4.91	5.12
H2	4.85	4.64	4.14
H3	2.90	3.41	2.80
H4	2.77	3.41	3.13
H5	4.93	5.20	5.59
H6	4.66	5.03	4.97
^{31}P (ppm)	15.5	15.3	15.5

Suitable single crystals were obtained for complex **19a**, which contains the phosphine-imidazoline ligand **18a**. The organometallic complex **19a** crystallized from 2-butanone and under inert conditions, in a monoclinic cell with the chiral space group $P2_1$. The molecular structure refined from the X-ray agrees with the proposed structure. The elementary cell of **19a** contains two independent molecules (*molecule A and molecule B*), which have the same chirality and are related by pseudosymmetry. Indeed, they are conformational isomers (Figure 7).

The two molecules of the unit cell adopt a three-dimensional configuration to minimize the electrostatic repulsions, and they also show an intermolecular π-stacking interaction between the two chelate phenyl rings that favours this arrangement, correlated by a local center of inversion (pseudosymmetry). The distance between the center of the benzene rings is about 3.84 Å.

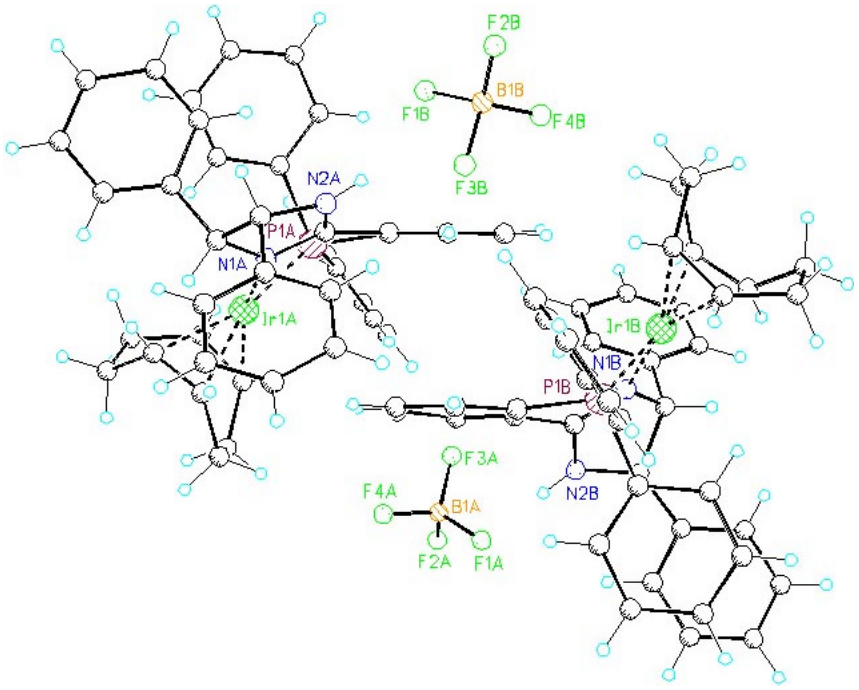


Figure 7. Crystal structure of **19a**

Moreover, an intramolecular π-stacking interaction is also observable in both *molecule A* and *molecule B*, between one of the phenyl groups of the phosphino moiety (C(30)-C(35)) and the phenyl group of the imidazoline moiety (C(12A)-C(17A), 4.336 Å in *molecule A* and C(18B)-C(23B), 3.90 Å in *molecule B*) (Figures 8 and 9).

Curiously the benzene ring (C(12A)-C(17A)) *at molecule A* is disordered in two positions with a ratio of 80:20, but there is no change in the chirality of *molecule A*.

The coordination geometry of the iridium atom in both molecules is square planar, since the midpoints of the double bonds of the COD ligands, the metal, P and N atoms all lie on a plane (main deviation from plane *molecule A*: 0.0264 Å

and *molecule B*: 0.0035 Å) [42]. The phenyl substituents on the phosphorous adopt a pseudoequatorial and a pseudoaxial position as was expected by comparison with the Ir-phosphine-oxazoline [6,15] and Ir-phosphine-imidazoline complexes [10].

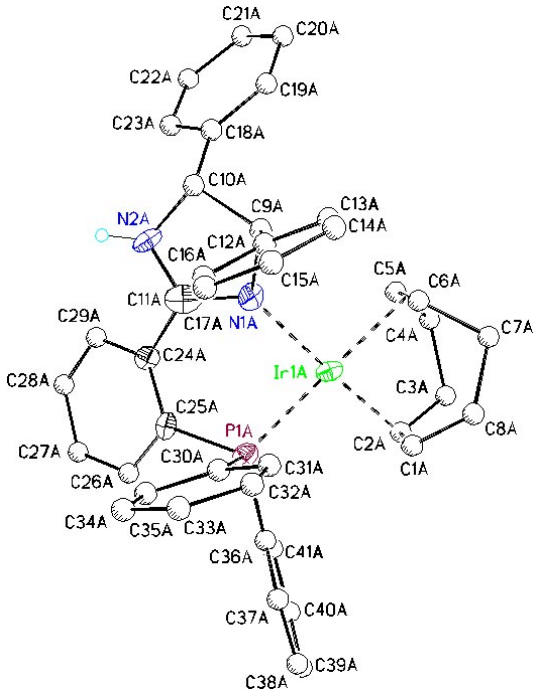


Figure 8. Crystal structure and atom numbering scheme of *molecule A* (**19a**)

The Ir-N distance (*molecule A:* 2.084(11) Å*; molecule B:* 2.095(11) Å) is shorter than the Ir-P distance (*molecule A*: 2.267(4) Å; *molecule B*: 2.279(4) Å) [42,43]. The distance from the metal to the midpoint of the C(5)=C(6) double bond *trans* to P (*molecule A*: 2.083(15) Å; *molecule B*: 2.102(12) Å) is significantly longer than the distance from the metal to the midpoint of the C(1)=C(2) double bond *trans* to N (*molecule A*: 2.010(13) Å; *molecule B*: 1.992(13) Å) indicating a clear *trans*-influence. This *trans*-influence is also observable for similar Ir/NP [42]

and Pd/NP[43] complexes. There are also differences between the C=C distances of COD.

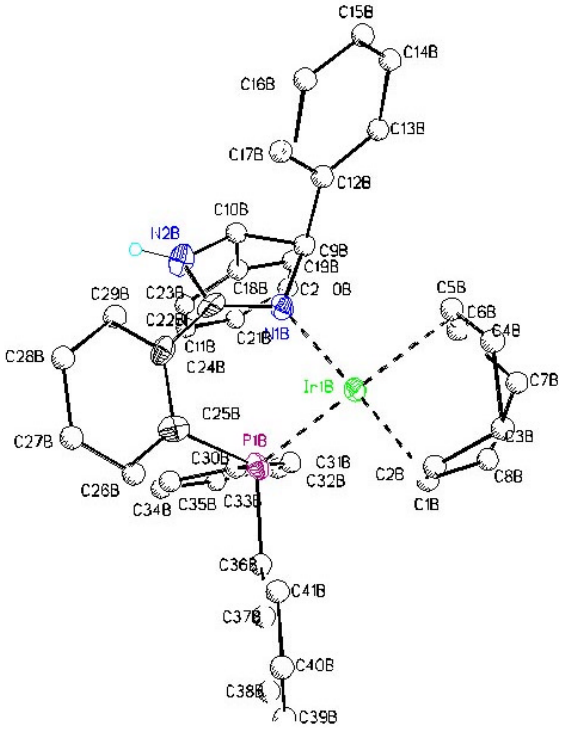
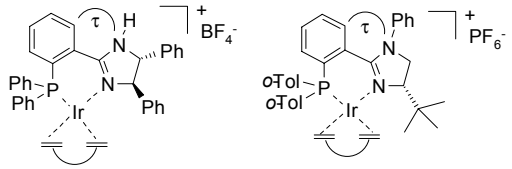


Figure 9. Crystal structure and atom numbering scheme of *molecule B* (**19a**)

In *molecule A*, the longer double bond is closer to the metal, *trans* to N (C(1)=C(2):1.368(17) Å vs C(5)=C(6): 1.34(2) Å), so backbonding from the metal appears to be greater *trans* to N [42]. In molecule B, these differences are smaller (C(1)=C(2):1.378(17) Å vs C(5)=C(6): 1.373(19) Å). Moreover, in *molecule A* the N(1)-C(11) and N(2)-C(11) bond distances, 1.337(17) and 1.323(15) Å, are consistent with a delocalization inside the N(1)-C(11)-N(2) fragment, as already

observed in the molecular structures of Ir/phosphine-imidazoline [10], Ru/pyridine-imidazoline [9] and Pd/pyridine-imidazoline complexes [8].

In both molecules, the rings of the chelating ligand (phenyl and imidazoline rings) are not coplanar, but slightly titled, as indicated by the C(29)-C(24)-C(11)-N torsion angle of -27.0º (in *molecule A*) and 45.2º (in *molecule B*). Although these values are similar to those reported by Pfaltz for a similar iridium complex (**20**) [10], the difference of 4º may be attributed to the different substitution of aminic nitrogen (Figure 10).



19a Molecule A τ=-27.0º **20** τ=-31º

Figure 10. Torsion angles in complexes **19a** and **20**

The absolute configuration for both molecules was determined with *R*(C(9)); *R*(C(10)) having a Flack Parameter of –0.003 with a standard deviation of 0.010 [44]. Expected values are 0 for correct and +1 for inverted absolute structure.

Table 4 shows a selection of bond lengths and angles of the molecular structures for *molecules A* and *B* of complex **19a**.

Table 4. Selected bond distances (Å) and angles (°) and geometrical parameters for complex **19a**

Empirical formula	$(C_{41}\ H_{39}\ B\ F_4\ Ir\ N_2\ P) \times 2$	
Formula weight	869.72	
Temperature	153(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 13.8464(7) Å	α= 90°.
	b = 13.5639(6) Å	β=98.779(2)°.
	c = 19.0698(8) Å	γ = 90°.
Ir(1A)···[C(1A)-C(2A)]	2.010(13)	
Ir(1A)···[C(5A)-C(6A)]	2.083(15)	
Ir(1A)-N(1A)	2.084(11)	
Ir(1A)-P(1A)	2.267(4)	
C(1A)-C(2A)	1.368(17)	
C(5A)-C(6A)	1.34(2)	
N(1A)-C(11A)	1.337(17)	
N(2A)-C(11A)	1.323(15)	
Ir(1B)···[C(1B)-C(2B)]	1.992(13)	
Ir(1B)···[C(5B)-C(6B)]	2.102(12)	
C(1B)-C(2B)	1.378(17)	
C(5B)-C(6B)	1.373(19)	
Ir(1B)-N(1B)	2.095(11)	
Ir(1A)-P(1B)	2.279(4)	
N(1B)-C(11B)	1.291(16)	
N(2B)-C(11B)	1.340(14)	
N(1A)-Ir(1A)-P(1A)	87.0(3)	
N(1B)-Ir(1B)-P(1B)	84.8(3)	
C(29A)-C(24A)-C(11A)-N(1A)	-27.0(15)	
C(29B)-C(24B)-C(11B)-N(1B)	45.2(15)	

2.2.3. Asymmetric Hydrogenation of Imines

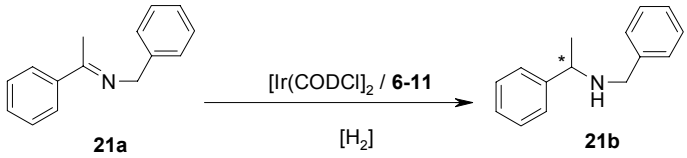
The Ir/thioether-oxazoline ligands **6-11**, the Ir/phosphine-imidazoline ligands **18a-c** and complex **12a** were tested as catalysts for the asymmetric hydrogenation of imines. Firstly, we focused on reducing the imine *N*-(phenylethylidene)benzylamine (**21a**) by systems generated *in situ* from $[Ir(COD)Cl]_2$/**6-11** and under 50 bar of H_2 pressure. The results are collected in Table 5.

When the catalytic precursor was formed by $[Ir(COD)Cl]_2$ in the presence of ligands **6**, **7**, **8** (Table 5, entries 2, 3, 4), conversions were lower than 50%. These results were similar to or lower than the conversion obtained with the iridium precursor when no ligand was added (entry 1). However, the iridium systems with ligands **9**, **10**, **11** (Table 5, entries 5, 6, 7) provided conversions between 80-100% in the same conditions. These results indicate that new catalytic systems are formed when the oxazoline-thioether ligands **9-11** are added to the iridium precursor. Conversions were higher when the electronic density on the sulphur atom of the thioether-oxazoline ligands was enhanced with the donor *t*-butyl group (Table 5, entries 6, 7).

It has been shown that in several Rh(I) [45] and Ir(I) [46] systems the presence of an additive improves the catalytic activity and the enantioselectivity. Among the most widely used additives are iodides and amines [47]. The experiments with ligands **6** and **7** (Table 5, entries 8, 9) provided higher conversion when Bu_4NI was used as additive. The results obtained in the experiments carried out with ligands **9** and **10** in the presence of Bu_4NI were maintained or were slightly lower than in the absence of additive.

No enantioselectivity was observed with these catalytic systems in the asymmetric hydrogenation of imine **21a**. Only the catalyst $[Ir(COD)Cl]_2$/**6** provided 15 % of enantiomeric excess.

Table 5. Hydrogenation of *N*-(phenylethylidene)benzylamine (**21a**)[a]



Entry	Precursor/Ligand	Solvent	Additive	Conv [%]
1	$[Ir(COD)Cl]_2$ / -	MeOH / DCE (1:1)	-	48
2	$[Ir(COD)Cl]_2$ / **6**	MeOH / DCE (1:1)	-	50
3	$[Ir(COD)Cl]_2$ / **7**	MeOH / DCE (1:1)	-	32
4	$[Ir(COD)Cl]_2$ / **8**	MeOH / DCE (1:1)	-	34
5	$[Ir(COD)Cl]_2$ / **9**	MeOH / DCE (1:1)	-	80
6	$[Ir(COD)Cl]_2$ / **10**	MeOH / DCE (1:1)	-	99
7	$[Ir(COD)Cl]_2$ / **11**	MeOH / DCE (1:1)	-	100
8	$[Ir(COD)Cl]_2$ / **6**	MeOH / DCE (1:1)	Bu_4NI	73
9	$[Ir(COD)Cl]_2$ / **7**	MeOH / DCE (1:1)	Bu_4NI	44
10	$[Ir(COD)Cl]_2$ / **8**	MeOH / DCE (1:1)	Bu_4NI	28
11	$[Ir(COD)Cl]_2$ / **9**	MeOH / DCE (1:1)	Bu_4NI	64
12	$[Ir(COD)Cl]_2$ / **10**	MeOH / DCE (1:1)	Bu_4NI	99
13	$[Ir(COD)Cl]_2$ / **10**	MeOH	-	95
14	$[Ir(COD)Cl]_2$ / **10**	C_6H_6	-	100
15	$[Ir(COD)Cl]_2$ / **10**	MeOH / C_6H_6 (1:1)	-	100
16[b]	**12a**	MeOH / DCE (1:1)	-	13
17	**12a**	MeOH / DCE (1:1)	-	39
18	**12a**	CH_2Cl_2	-	23

[a] 1% mol [Ir], 1.25% mol **6-11**, 1% mol Bu_4NI, 50 bar H_2, 25ºC, 24 h, DCE=dichloroethane [b] 30 bar

Such solvents as MeOH/$C_2H_4Cl_2$, MeOH, C_6H_6 and MeOH/C_6H_6 (Table 5, entries 12-15) have been tested, and they all gave total conversion.

The complex $[Ir(\sigma\text{-}\eta^2\text{-}PyC_8H_{12})L]PF_6$ **12a** was active in reducing imine **21a** into the corresponding amine (Table 5, entries 16, 17). Conversions were similar to those obtained with systems prepared *in situ* from $[Ir(COD)Cl]_2$/**7** and **8** (entries 3, 4 and 17).

After the results achieved with the Ir(I)/thioether-oxazoline catalysts, it can be concluded that replacing the phosphorus atom in the phosphine-oxazoline ligands by a sulphur atom has a dramatic effect. The Ir(I)/thioether-oxazoline catalysts do not provide stereocontrol in the hydrogenation of imine **21a**.

We then went on to explore the catalytic behavior of Ir(I)/phosphine-imidazoline catalysts with systems generated *in situ* from $[Ir(COD)Cl]_2$ or $[Ir(COD)_2]BF_4$ and **18a-c**, in order to evaluate the influence of the catalytic precursor. Precursors based on neutral complexes of Rh(I) and Ir(I) with diphosphines normally show higher enantioselectivities in the hydrogenation of some prochiral ketimines than the cationic ones, usually in a presence of an additive [46b-c,48]. We planned to investigate if this rule is also valid for cationic Ir(I)/phosphine-imidazoline systems.

Three different imines were chosen as models: the acyclic imines *N*-(phenylethylidene)benzylamine (**21a**) and *N*-(phenylethylidene)aniline (**22a**), and the cyclic imine 6,7-dimethoxy-1-methyl-3,4-dihydroisoquinoline (**23a**), in which the geometry of the C=N double bond is fixed to *E*-configuration.

The catalytic systems based on $[Ir(COD)_2]BF_4$/**18a-c** were more active than the catalyst precursors $[Ir(COD)Cl]_2$/**18a-b** in the reduction of acyclic imines **21a** and **22a**, and in some cases conversion was complete within 16 hours (Table 6, entries 1-8). However, only for the most constrained imine **22a**, moderate enantiomeric excess (up to 51%) was achieved (Table 6, entry 8) when the catalytic system $[Ir(COD)_2]BF_4$/**18b** was used.

Hydrogenolysis products were also detected together with the desired secondary amine **21b**, because of the cleavage of the nitrogen-benzylic bond, which decreased selectivity [49] (Table 6, entries 1-4).

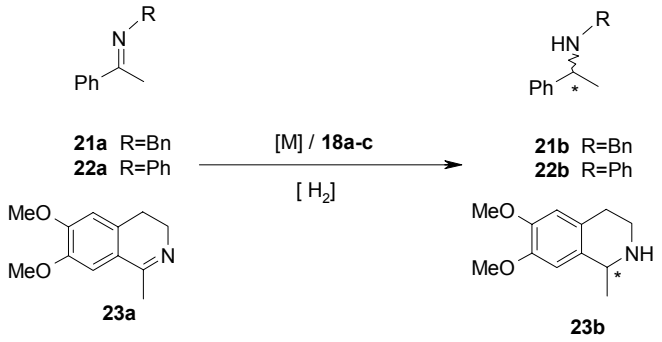
It should be noted that in the reduction of **22a**, the cationic system $[Ir(COD)_2]BF_4$/**18b** was more enantioselective than the neutral system $[Ir(COD)Cl]_2$/**18b** (Table 6, entries 6 and 8).

In general, the Ir(I) catalyst based on the withdrawing ligand **18b** was more effective than the catalysts Ir/**18a** under the conditions described (Table 6, entries 3, 4, 7, 8), which confirmed that the electronic properties of the ligands do not only influence the reaction rate but also the enantiocontrol of the process.

Four different metal precursors were tested, $[M(COD)Cl]_2$ and $[M(COD)_2]BF_4$ (M=Ir and Rh) in the reduction of cyclic imine **23a** and all conversions were very low (values of conversion <10%). Only with the cationic iridium precursor $[Ir(COD)_2]BF_4$ and ligands **18a-c** values of conversion between 20-40% were achieved in 18 h (Table 6, entries 9-11). It is reported that for the total hydrogenation of this imine, reaction times need to be longer (24-90h) [46b,c]. $[Ir(COD)_2]BF_4$/**18a** gave an enantiomeric excess up to 34%; the system $[Ir(COD)_2]BF_4$/**18b** based on the electro-withdrawing ligand **18b** afforded 26% ee, whereas the more electron-rich catalyst $[Ir(COD)_2]BF_4$/**18c** gave the worst value, nearly racemic.

In summary, Ir(I)/phosphine-imidazoline catalysts gave moderate to low enantioselectivities in the hydrogenation of the imines **21a**, **22a** and **23a.**

Table 6. Hydrogenation of *N*-(phenylethylidene)benzylamine (**21a**), *N*-(phenylethylidene)aniline (**22a**) and 6,7-dimethoxy-1-methyl-3,4-dihydroisoquinoline imine (**23a**)[a]



Entry	Imine	Ligand	Precursor	Conv [%]	Selec [%]	Ee [%][b]
1	**21a**	**18a**	$[IrCODCl]_2$	27	28	9 (+)
2	**21a**	**18b**	$[IrCODCl]_2$	44	38	11 (+)
3	**21a**	**18a**	$[Ir(COD)_2]BF_4$	48	64	3 (+)
4	**21a**	**18b**	$[Ir(COD)_2]BF_4$	75	83	5 (+)
5	**22a**	**18a**	$[IrCODCl]_2$	2	100	22 (-)
6	**22a**	**18b**	$[IrCODCl]_2$	14	100	14 (-)
7	**22a**	**18a**	$[Ir(COD)_2]BF_4$	100	100	15 (-)
8	**22a**	**18b**	$[Ir(COD)_2]BF_4$	100	100	51 (-)
9[c]	**23a**	**18a**	$[Ir(COD)_2]BF_4$	32	100	34 (-)
10[c]	**23a**	**18b**	$[Ir(COD)_2]BF_4$	42	100	26 (-)
11[c]	**23a**	**18c**	$[Ir(COD)_2]BF_4$	23	100	9 (-)

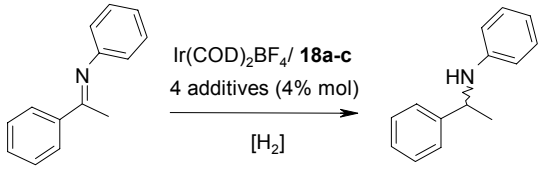
[a] 1% mol [Ir], 1.25% mol **18a-c**, 70 bar H_2, CH_2Cl_2, 25ºC, 16 h [b] no absolute configuration was determined [c] 60 bar H_2, 18 h

Since the best result was achieved by the more electron-poor catalyst formed by $[Ir(COD)_2]BF_4$/**18b** in the hydrogenation of **22a** with total conversion and 51% ee, we decided to investigate the role of additives in the hydrogenation of this imine. The selection of suitable halides or other additives, which can coordinate to the vacant site of the iridium complex, is important to improve the

enantioselectivity in the hydrogenation of imines [45a,46b,50] So two iodine derivatives and two amine derivatives were used as additives in the hydrogenation of **22a**.

The results obtained are summarized in the Table 7.

Table 7. Study of the effect of the additive on the hydrogenation of **22a**[a]



22a **22b**

Entry	Ligand	Additive	Conv [%]	Selec [%]	ee [%][b]
1	**18a**	--	100	100	15 (-)
2	**18a**	Bu_4NI	6	100	24 (+)
3	**18a**	I_2	100	100	0
4	**18a**	Phthalimide	99	100	12 (-)
5	**18a**	$BnNH_2$	92	99	13 (-)
6	**18b**	--	100	100	51 (-)
7	**18b**	Bu_4NI	81	100	27 (+)
8	**18b**	I_2	100	100	4 (+)
9	**18b**	Phthalimide	100	100	48 (-)
10	**18b**	$BnNH_2$	>99	99	24 (-)

[a] 1% mol [Ir], 1.25% mol **18a-c**, 4% mol additive, 70 bar H_2, CH_2Cl_2, 25ºC, 16 h [b] no absolute configuration was determined

Whereas the addition of Bu_4NI promoted the formation of the opposite enantiomer (Table 7, entries 1, 2, 6, 7), adding I_2 to the catalytic system gave racemic products (Table 7, entries 1, 3, 6, 8). Hence the cationic Ir(I)/phosphine-imidazoline/I^- systems did not lead to any improvement in the enantiocontrol of the process. This behavior has already been reported by Pfaltz [15] in the reduction of C=N with cationic Ir(I)/diphenylphosphinooxazolines catalysts, in which the

addition of Bu_4NI also decreased the ee and reversed the configuration of the final product. Besides, the catalytic system $[Ir(COD)_2BF_4]$/**18a**/Bu_4NI (Table 7, entry 2) induced a sharp decrease in the conversion.

The amine derivative additives generally did not have a strong influence on either conversion or enantioselectivity (Table 7, entries 1, 4, 5, 6, 9 and 10). The catalytic systems Ir(I)/**18a-b**/amine afforded complete conversions, demonstrating that in this particular case the strong coordinative amines do not poison the catalyst. A considerable decrease in the ee was only observed when benzylamine was added to $[Ir(COD)_2BF_4]$/**18b** (Table 7, entries 6 and 10).

2.3. Conclusions

In the preparation of iridium complexes containing oxazoline-thioether ligands starting from the iridium precursor $[Ir(\eta^4\text{-COD})Py_2]PF_6$, an unexpected nucleophilic attack of the pyridine on the coordinated cyclooctadiene with concomitant σ-Ir-C bond formation takes place, leading to the $[Ir(\sigma\text{-}\eta^2\text{-}PyC_8H_{12})L]PF_6$ (**12a-d**). When $[Ir(\eta^4\text{-COD})_2]BF_4$ was used as precursor the expected $[Ir(\eta^4\text{-COD})L]\ BF_4$ complexes were obtained.

Hydrogenation of imine **21a** with the catalytic systems formed *in situ* from $[Ir(\eta^4\text{-COD})Cl]_2$/**6-11** provided conversions of 30-100% in 24 hours, although no enantioselectivity was achieved. The new stereogenic center formed by the coordination of sulphur to the metal center may be responsible for the existence of different diastereomers during the catalytic cycle, which does not favour the stereoselectivity.

Complex **12a** was also active in the hydrogenation of imine **21a** although showed low conversions and no enantioselectivity.

A new improved synthetic procedure has been established to prepare 2-arylimidazolines starting from dithioesters.

The cationic Ir(I)-phosphine-imidazoline system is an efficient catalyst for the reduction of acyclic and cyclic imines, although the ee are only moderate.

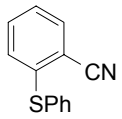
In general, the additives have a negative effect on the cationic iridium catalyst based on hemilabile ligands NX (X=S or P) and favour a change in the configuration of the final product, although the catalyst does not lose its activity when strong coordinative compounds such as amines are added.

2.4. Experimental Section

General Comments. All reactions were carried out in an argon atmosphere using standard Schlenk techniques. Solvents were distilled and degassed prior to use.
^{1}H, $^{13}C\{^{1}H\}$, $^{31}P\{^{1}H\}$ and $^{19}F\{^{1}H\}$ NMR spectra were recorded on a Varian Gemini spectrometer at 300 and 400 MHz. Chemical shifts were reported relative to tetramethylsilane for ^{1}H and $^{13}C\{^{1}H\}$ as internal reference, H_3PO_4 85% for $^{31}P\{^{1}H\}$ and trichlorofluoromethane for $^{19}F\{^{1}H\}$ as external references. Elemental analyses were carried out on a Carlo Erba Microanalyser EA 1108. VG-Autospect equipment was used for FAB mass spectral analyses with 3-nitrobenzylalcohol as matrix. EI mass spectra were obtained on an HP 5989 A spectrometer at an ionizing voltage of 70 eV. Optical rotations were measured on a Perkin-Elmer 241 MC polarimeter. Melting points were determinated in an open capillary tube with a Tottoli-Büchi 510 melting point apparatus and are uncorrected. IR spectra were recorded with the KBr disc for solid samples or the NaCl window for liquid samples on a MIDAC PROSPECT-IR spectrometer.

Single hydrogenation reactions were carried out in a Berghof or Parr 100 ml stainless steel autoclave and multi-screening hydrogenations were performed in a home-made 96-micro-titer plate in Bayer AG (Leverkusen-Germany). The catalytic reactions were monitored by GC on a Hewlett-Packard 5890A. Conversion was measured in an Ultra-2 (5 % diphenylsilicone/95% dimethylsilicone) column (25 m x 0.2 mm Ø). The enantiomeric excess of *N*-(phenylethylidene)benzylamine (**21a**) was determined by ^{1}H NMR (with mandelic acid as the resolution agent) or by chiral chromatography after derivation into the trifluoroacetamide compound.. The enantiomeric excess of *N*-(phenylethylidene)aniline (**22a**) was determined by chiral chromatography after derivation into the acetamide compound. The enantiomeric excess of the 6,7-dimethoxy-1-methyl-3,4-dihydroisoquinoline imine (**23a**) was determined by chiral chromatography.

2-phenylthio-benzonitrile (4) [22c]

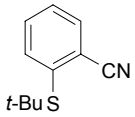


A solution of benzenethiol (18 mmols) in THF (4 ml) was added to a stirred mixture of sodium hydride (18 mmols) in THF (10 ml). To the resulting white precipitate, a solution of 2-fluorobenzonitrile (16 mmols) in THF (4 ml) was added.

The mixture was stirred under reflux for 48 h. The reaction mixture was poured into dichloromethane (40 ml) and washed with 15% aqueous NaOH (40 ml) and then with water (40 ml). The aqueous layers were extracted with dichloromethane (2x50 ml) and the combined extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. The crude product was purified by flash chromatography (Hexane/AcOEt 3:1) to afford a solid. The solid was recrystallized in THF/Hexane to afford 3g (90%) of compound **4** as a colourless crystalline solid. **NMR ^{1}H** (300 MHz, $CDCl_3$, ppm) 7.60-7.11 (m, 9H, arom.). **NMR ^{13}C** (74.5 MHz, $CDCl_3$, ppm) 141.3 (arom. C), 133.4, 133.2, 133.1, 132.9 (CH, arom.), 131.3 (C, arom.), 129.6,

128.7, 126.4 (CH, arom.), 116.5 (C≡N), 112.3 (C, arom.). **IR** (KBr, cm^{-1}): 3049 (=CH), 2217 (C≡N)

Synthesis of 2-terc-butylthio-benzonitrile (5)

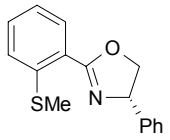


A solution of 2-methyl-2-propanethiol (9 mmols) in THF (2 ml) was added to a stirred mixture of sodium hydride (9 mmols) in THF (5 ml). To the resulting white precipitate a solution of 2-fluorobenzonitrile (8 mmols) in THF (2 ml) was added. The mixture was stirred under reflux for 48 h. The reaction mixture was poured into dichloromethane (20 ml) and washed with 15% aqueous NaOH (20 ml) and then with water (20 ml). The aqueous layers were extracted with dichloromethane (2x30 ml) and the combined extracts were dried (MgSO4), concentrated under reduced pressure and purified by column chromatography to give 1.3g (86%) of compound **5**. **NMR ^{1}H** (300 MHz, $CDCl_3$, ppm) 7.70-7.51 (m, 4H, arom.), 1.35 (s, 9H, $C(CH_3)_3$). **NMR ^{13}C** (74.5 MHz, $CDCl_3$, ppm) 138.8 (CH, arom.), 136.3 (C, arom.), 133.6- 132.3 (CH, arom.), 129.3 (CH, arom.), 121.0 (CH, arom.), 118.1 (C≡N), 48.8 ($\underline{C}(CH_3)_3$), 30.9 ($C(\underline{C}H_3)_3$).

General procedure for the synthesis of thioether-oxazoline ligands 6-11

In a 50-ml Schlenk flask, zinc chloride (44 mg, 0.32 mmols) was melted under high vacuum and cooled under nitrogen to room temperature. Chlorobenzene (20 ml) was then added followed by the corresponding thiobenzonitrile (6.4 mmol) and the aminoalcohol (9.6 mmol L-valinol or L-phenylglycinol). The mixture was heated under reflux for 48 h. The solvent was removed under reduced pressure to give an oily residue, which was dissolved in dichloromethane (30 ml). The solution was extracted with aqueous solution of NaCl (3x20 ml) and the aqueous phase with dichloromethane (30 ml). The combined organic extracts were dried ($MgSO_4$), and evaporated under reduced pressure.

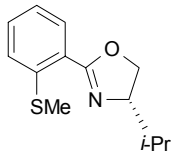
(*4S*)-4-phenyl-4,5-dihydro-2-[2-(methylthio)phenyl]-1,3-oxazoline (6) [22a]



Ligand **6** was obtained by following the general procedure described above. The reaction crude was purified by MPLC (CH_2Cl_2) to afford 344 mg (20% yield) of compound **6** as a solid product.

$[\alpha]_D^{25}$= + 78.3° (c=0.22, $CHCl_3$). **NMR ^{1}H** (300 MHz, $CDCl_3$, ppm) 7.8-7.1 (m, 9H, arom.), 5.45 (t, *J*=9Hz, 1H, CH), 4.66, (t, 1H, CH_2), 4.10 (t, *J*=7.7 Hz, 1H, CH_2), 2.4 (s, 3H, CH_3-S). **NMR ^{13}C** (74.5 MHz, $CDCl_3$, ppm) 163.9 (C=N), 142.6, 141.5 (arom. C), 131.2, 130.5, 128.8, 127.6, 126.8 (arom. CH), 124.8 (arom. C), 124.4, 123.7 (arom. CH), 74.2 (CH_2-O), 71.0 (CH-N), 16.0 (CH_3-S). **IR** (KBr, cm^{-1}): 3028 (=CH), 2980 (CH_3-S), 1636 (C=N).

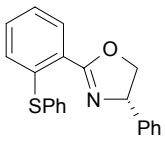
(*4S*)-4-isopropyl-4,5-dihydro-2-[2-(methylthio)phenyl]-1,3-oxazoline (7) [22a]



Ligand **7** was obtained by following the general procedure described above. The reaction crude was purified by MPLC (CH_2Cl_2) to afford 225 mg (15% yield) of compound **7** as a solid product.

$[\alpha]_D^{25}$= -81.4° (c= 0.24, $CHCl_3$). **NMR ^{1}H** (300 MHz, $CDCl_3$, ppm) 7.70-7.00 (m, 4H, arom.), 4.28 (dd, ^2J=9.3Hz, ^3J=7.8Hz 1H, CH), 4.12, (m, 1H, CH_2), 4.02 (t, *J*=7.8 Hz, 1H, CH_2), 2.36 (s, 3H, CH_3-S), 1.80 (m, ^3J=6.6 Hz, 1H, CH), 0.99 (d, ^3J=6.6 Hz, 3H, CH_3), 0.89 (d, ^3J=6.6 Hz, 3H, CH_3). **NMR ^{13}C** (74.5 MHz, $CDCl_3$, ppm) 162.3 (C=N), 141.1 (C, arom.), 130.9, 130.2 (CH, arom.), 125.2 (C, arom.), 124.3 (CH, arom.), 123.6 (CH, arom.), 73.6 (CH_2-O), 69.5 (CH-N), 33.1 (CH), 19.1 (CH_3), 18.4 (CH_3), 16.0 (CH_3-S). **IR** (KBr, cm^{-1}): 2958 (CH_3-S), 1649 (C=N).

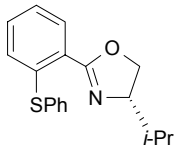
(*4S*)-4-phenyl-4,5-dihydro-2-[2-(phenylhylthio)phenyl]-1,3-oxazoline (8)



A total of 0.20 mmols (27.5 mg) of $ZnCl_2$ reacted with 4 mmols (845 mg) of 2-phenylthio-benzonitrile (**4**) and 6 mmols (825 mg) of L-phenylglycinol following the general procedure described above. The reaction crude was purified by MPLC (CH_2Cl_2) to afford 260 mg (19% yield) of compound **8** as a solid product.

$[\alpha]_D^{25}$= +58.5° (c= 0.22, $CHCl_3$). **NMR ^{1}H** (300 MHz, $CDCl_3$, ppm) 7.90-6.80 (m, 14H, arom.), 5.53 (dd, ^2J=10.4 Hz, ^3J=8.6 Hz, 1H, CH), 4.77, (dd, ^2J=10.4 Hz, ^3J=8.6 Hz, 1H, CH_2), 4.20 (t, ^3J=8.6 Hz, 1H, CH_2). **NMR ^{13}C** (74.5 MHz, $CDCl_3$, ppm) 163.9 (C=N), 142.5, 141.1 (C, arom.), 135.1 (CH, arom.), 133.4 (C, arom.), 131.1-126.8 (arom.), 125.1 (C, arom.), 124.7 (CH, arom.), 74.4 (CH_2-O), 70.9 (CH-N). **IR** (KBr, cm^{-1}) 3054 (=CH), 1629 (C=N).

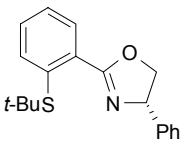
(*4S*)-4-isopropyl-4,5-dihydro-2-[2-(phenylthio) phenyl]-1,3-oxazoline (9) [22c]



A total of 0.25 mmols (34 mg) of $ZnCl_2$ reacted with 5 mmols (1 g) of 2-phenylthio-benzonitrile (**4**) and 7.5 mmols (775 mg) of L-valinol by following the general procedure described above. The reaction crude was purified by MPLC (CH_2Cl_2) to afford 756 mg (51% yield) of compound **9** as a solid product.

$[\alpha]_D^{20}$= – 49.3° (c=1.32, CH_3COCH_3). **NMR ^{1}H** (400 MHz, $CDCl_3$, ppm) 7.81-6.80 (m, 9H, arom.), 4.33 (t, ^3J=8 Hz, 1H, CH), 4.19 (m, 1H, CH_2), 4.07 (t, ^3J=8 Hz, 1H, CH_2), 1.85 (m, ^3J=6.6 Hz, 1H, CH), 1.07 (d, ^3J=6.6 Hz, 3H, CH_3), 0.96 (d, ^3J=6.6 Hz, 3H, CH_3). **NMR ^{13}C** (100.6 MHz, $CDCl_3$, ppm) 161.8 (C=N), 140.7 (C, arom.), 134.9 (CH, arom.), 133.2 (CH, arom.), 130.4 (C, arom.), 129.7- 127.2 (arom.), 124.9 (C, arom.), 124.1 (CH, arom.), 73.3 (CH_2-O), 69.5 (CH-N), 32.8 (CH), 18.7 (CH_3), 18.3 (CH_3). **IR** (NaCl, cm^{-1}) 3062, 2960 (=CH), 1650 (C=N).

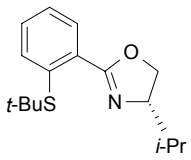
(*4S*)-4-phenyl-4,5-dihydro-2-[2-(terc-butylthio)phenyl]-1,3-oxazoline (10)



A total of 0.5 mmols (68 mg) of $ZnCl_2$ reacted with 10 mmols (1.91 g) of 2-terc-butylthio-benzonitrile (**5**) and 15 mmols (1.37 g) of L-phenylglycinol by following the general procedure described above. The residue was purified by column chromatography using CH_2Cl_2/Et_3N as solvent to give 1.5g (49% yield) of compound **10** as a yellow oil was obtained. Compound **10** decomposed slightly during the purification.

NMR ^{1}H (300 MHz, $CDCl_3$, ppm) 7.71-7.10 (m, 9H, arom.), 5.40 (dd, ^3J=8.4Hz, J=1.8Hz 1H, CH), 4.81, (dd, ^3J=8.4Hz, J=1.8Hz, 1H, CH_2), 4.30 (t, J=8.4 Hz, 1H, CH_2), 1.25 (s, 9H, $C(CH_3)_3$). **NMR ^{13}C** (74.5 MHz, $CDCl_3$, ppm) 166.1 (C=N), 142.5 (C, arom.), 138.6 (CH, arom.), 135.6 (C, arom.), 130.4 (C, arom.), 130.2-126.8 (arom.), 75.2 (CH_2-O), 70.5 (CH-N), 47.6 ($\underline{C}(CH_3)_3$), 31.4 ($C(\underline{C}H_3)_3$).

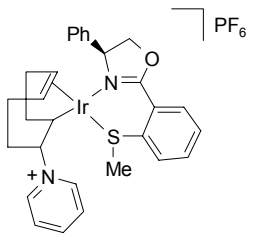
(*4S*)-4-isopropyl-4,5-dihydro-2-[2-(terc-butylthio)phenyl]-1,3-oxazoline (11)



A total of 0.25 mmols (68 mg) of $ZnCl_2$ reacted with 5 mmols (950 g) of 2-terc-butylthio-benzonitrile (**5**) and 7.5 mmols (685 mg) of L-valinol following the general procedure described above. The residue was purified by column chromatography using CH_2Cl_2/Et_3N as eluent to obtain 85.5 mg (55% yield) of compound **11** as a yellow oil.

$[\alpha]_D^{20}$= – 28.0° (c=0.33, CH_3COCH_3). **NMR ^{1}H** (300 MHz, $CDCl_3$, ppm) 7.71-6.80 (m, 4H, arom.), 4.37 (dd, ^3J=6.8 Hz, J=1.5Hz 1H, CH), 4.18 (t, ^3J=6.8 Hz, CH_2), 4.13 (m, 1H, CH_2), 1.84 (d, ^3J=6.6 Hz, 1H, CH), 1.35 (s, 9H, $C(CH_3)_3$), 1.04 (d, ^3J=6.6 Hz, 3H, CH_3), 0.96 (d, ^3J=6.6 Hz, 3H, CH_3). **NMR ^{13}C** (74.5 MHz, $CDCl_3$, ppm) 161.6 (C=N), 137.6-125.0 (arom.), 73.3 (CH_2-O), 69.7 (CH-N), 48.85 ($\underline{C}(CH_3)_3$), 32.7 (CH), 30.68 ($C(\underline{C}H_3)_3$), 18.6 (CH_3), 18.2 (CH_3). **IR** (NaCl, cm^{-1}) 3059, 2957 (=CH), 1648 (C=N).

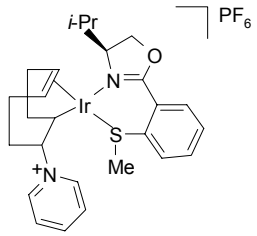
[Ir(σ-η^2-PyC$_8$H$_{12}$)6]PF$_6$ (12a)



A solution of ligand **6** (0.40 mmol) and [Ir(η^4-COD)(Py)$_2$]PF$_6$ (0.30 mmols) in 1 ml of anhydrous dichloromethane was stirred for two hours. Then cold degassed diethylether was added and a precipitate appeared. The solid was filtered and washed with cold and degassed diethylether to afford 223 mg (94%) of complex **12a**.

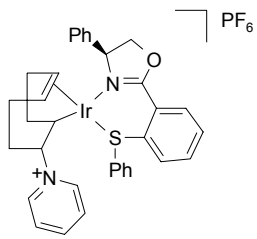
Elemental analysis calculated for C$_{29}$H$_{32}$F$_6$IrN$_2$OPS (%): C 43.88; H 4.06; N 3.53, S 4.04. **Found** (%): C 43.97; H 4.19; N 3.40, S 3.49. **MS FAB**: m/z (%): 649.1 (8.5, M$^+$), 572.1 (19.8, M$^+$-C$_6$H$_5$), 570.1 (63.5, M$^+$-Py), 462 (2.20, M$^+$-C$_{13}$H$_{17}$N), 136 (100, C$_8$H$_{10}$NO). **HRMS L-SIMS**: m/z [C$_{24}$H$_{27}$NOSIr]$^+$ **Calculated:** 570.14425 **Found**: 570.14537. **NMR ^{1}H** (400 MHz, CDCl$_3$, ppm) 8.95 (m, 1H, arom), 8.54 (m, 1H, arom), 7.79 (m, 4H, arom), 7.52 (m, 2H, arom), 7.41 (m, 2H, arom), 7.30 (m, 3H, arom), 7.05 (m 1H, arom), 5.81 (m, 1H, CH), 5.13 (m, 1H, CH$_2$), 4.96 (m, 1H, CH$_2$), 4.66 (m, 1H, CH), 4.07 (m, 1H, CH), 3.22 (m, 1H, CH), 2.59 (m, 1H, CH), 2.43 (m, 1H, CH$_2$), 2.22 (m, 1H, CH$_2$), 2.03 (m, 1H, CH$_2$), 1.74 (m, 1H, CH$_2$), 1.51 (s, 3H, CH$_3$-S), 1.21 (m, 1H, CH$_2$). **NMR ^{13}C** (100.6 MHz, CDCl$_3$, ppm) 176.5 (C=N), 154.7 (CH, arom.), 152.6 (CH, arom.), 147.8-123.4 (arom.), 87.1 (CH), 77.9 (CH$_2$-O), 70.9 (CH), 67.3 (CH), 66.6 (CH-N), 37.2 (CH$_2$), 26.3 (CH$_2$), 24.5 (CH$_2$), 20.6 (CH$_2$), 14.5 (CH$_3$-S), 3.6 (CH). **NMR ^{31}P** (161.9 MHz, CDCl$_3$, ppm) –144.1 (sept, $J_{P\text{-}F}$= 712.8 Hz). **NMR ^{19}F** (376 MHz, CDCl$_3$, ppm) –73.6 (d, $J_{F\text{-}P=}$711.7 Hz).

[Ir(σ-η^2-PyC$_8$H$_{12}$)7]PF$_6$ (12b)



Prepared following the same procedure described for **12a** in 86% yield. **NMR ^{1}H** (300 MHz, $CDCl_3$, ppm) 8.68 (m, 1H, arom), 8.48 (m, 1H, arom), 7.70 (m, 3H, arom), 7.19 (m, 3H, arom), 6,94 (m, 1H, arom), 4.68 (m, 2H, CH), 4.54 (m, 3H, CH), 4.33 (m, 1H, CH), 2.65 (m, 1H, CH), 2.51-0.82 (m, 8H, CH_2), 1.43 (s, 3H, CH_3-S), 1.07 (d, ^3J=6.9 Hz, 3H, CH_3), 0.64 (d, ^3J=6.9 Hz, 3H, CH_3)**. NMR ^{13}C** (74.5 MHz, $CDCl_3$, ppm) 197.5 (C=N), 154.7 (arom., CH), 152.7 (arom., CH), 138.9-123.7 (arom.), 87.5 (CH), 71.6 (CH_2-O), 70.8 (CH), 68.5 (CH), 65.9 (CH-N), 37.5 (CH_2), 30.3 (CH), 29.9 (CH_2), 26.8 (CH_2), 24.9 (CH_2), 20.9 (CH_3), 19.4 (CH_3), 14.9 (CH_3-S), 3.7 (CH).

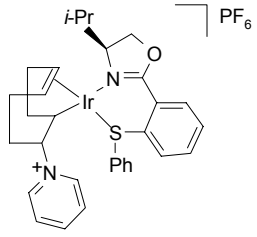
[Ir(σ-η^2-PyC$_8$H$_{12}$)8]PF$_6$ (12c)



Prepared following the same procedure described by **12a** in 98% yield. **Elemental analysis calculated for C$_{34}$H$_{34}$F$_6$IrN$_2$OPS** (%): C 47.71; H 4.00; N 3.27, S 3.75**. Found** (%): C 47.44 H 4.08; N 2.92, S 3.75.

NMR ^{1}H (400 MHz, $CDCl_3$, ppm) 8.33-6.81 (m, arom.), 5.89-4.22 (m, CH_2-O, CH-N, COD), 2.97-1.37 (m, COD).

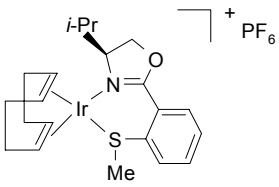
[Ir(σ-η^2-PyC$_8$H$_{12}$)9]PF$_6$ (12d)



Prepared following the same procedure described by **12a** in 91% yield. **Elemental analysis calculated for C$_{31}$H$_{36}$F$_6$IrN$_2$OPS** (%): C 45.30; H 4.41; N 3.41, S 3.9. **Found** (%): C 45.12; H 4.42; N 3.59, S 3.61. **MS FAB**: m/z (%) 598.1 (7.01, M^+-Py), 147 (100, C_9H_9NO).

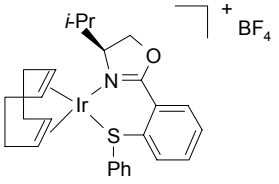
HRMS L-SIMS m/z $[C_{26}H_{31}NOSIr]^+$ **Calculated:** 598.1755 **Found:** 598.1752 **NMR ^{1}H** (400 MHz, $CDCl_3$, ppm) 10.59-6.84 (m, arom.), 5.51-3.81 (m, CH_2-O, CH-N, COD), 2.50-0.45 (m, COD, CH, CH_3). **NMR ^{31}P** (161.9 MHz, CDCl3, ppm) –143.9 (sept, $J_{P\text{-}F}$= 712.7 Hz). **NMR ^{19}F** (376 MHz, CDCl3, ppm) –73.26 (d, $J_{F\text{-}P=}$713.3 Hz).

[Ir(η^4-COD)(7)]PF_6 (13a)



A solution of ligand **7** (0.150 mmol) and [Ir(η^4-COD)Cl]$_2$ (0.132 mmol) in dichloromethane (5 ml) was heated for 2 h at 50ºC in a sealed tube under argon. After cooling to room temperature, the solution was washed twice with an aqueous solution of NH_4PF_6 (0.4 M, two 10 ml portions). The red dichloromethane solution was washed with water and dried over Na_2SO_4. Crystallization from CH_2Cl_2/Et_2O and drying afforded 65.6 mg (73%) of compound **13a**. **Elemental analysis calculated for $C_{21}H_{29}F_6IrNOPS$** (%): C 37.05; H 4.26; N 2.06, S 4.70. **Found** (%): C 38.30; H 4.13; N 1.96, S 4.46.

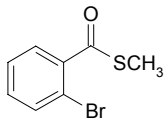
[Ir(η^4-COD)(9)]BF_4 (13b)



A solution of **9** (0.204 mmol) with dry and degassed dichloromethane (5 ml) was added dropwise to a chilled (-80ºC) solution of [Ir(η^4-COD)$_2$]BF_4 (0.204 mmol) with dry and degassed dichloromethane (4 ml). The solution was allowed to warm to 0ºC and stirred for 15 min. Then ethyl ether (30 ml) was added to precipitate 118.5 mg (85%) of complex **13b** as a yellow solid.

Elemental analysis calculated for $C_{26}H_{31}F_4IrNOBS$ (%): C 45.61; H 4.56; N 2.05, S 4.68. **Found** (%): C 45.92; H 4.31; N 1.92, S 4.81.

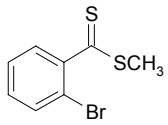
2-Bromo-thiobenzoic acid *S*-methyl ester (15a)



2-bromobenzoylchloride (1.96 ml, 15 mmol) was added dropwise at 0ºC to a suspension of 1.20 g (17 mmol) of methanethiolate sodium salt with 17 ml of dichloromethane. After 1 hour at room temperature, the reaction mixture was quenched with water (20 ml). After several extractions with dichloromethane, the combined organic layers were dried and concentrated to afford 3.5g (99 % yield) of compound **15a** as a yellow liquid, which was used without purification in the next reaction.

NMR ^{1}H (400 MHz, $CDCl_3$, ppm) 7.64-7.59 (m, 2H, arom.), 7.38-7.29 (m, 2H, arom.), 2.5 (s, 3H, CH_3). **NMR ^{13}C** (100.6 MHz, $CDCl_3$, ppm) 193.5 (C=O), 139.6 (C, arom.), 134.1 (CH, arom.), 132.4 (CH, arom.), 129.3 (CH, arom.), 127.4 (CH, arom.), 118.9 (C, arom.), 12.8 (CH_3).

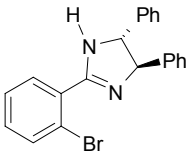
2-Bromo-dithiobenzoic acid *S*-methyl ester (16a)



Lawesson's reagent (2 g, 5.4 mmol) was added under argon to a solution of **15a** (325 mg, 1.4 mmol) in dry toluene (17 ml) and the mixture was heated to reflux. The reaction was monitored by TLC. When no starting material could be detected (ca. 24 hours), the reaction mixture was allowed to cool, and filtered. The solid was washed with toluene and the combined toluene solutions were evaporated and purified by flash column chromatography to afford 318 mg (92 % yield) of compound **16a** as a red liquid.

NMR ^{1}H (400 MHz, $CDCl_3$, ppm) 7.57 (m, 1H, arom.), 7.35-7.20 (m, 3H, arom.), 2.78 (s, 3H, CH_3). **NMR ^{13}C** (100.6 MHz, $CDCl_3$, ppm) 230.4 (C=S), 147.7 (C, arom.), 133.6 (CH, arom.), 130.4 (CH, arom.), 128.2 (CH, arom.), 127.4 (CH, arom.), 118.6 (C, arom.), 20.9 (CH_3).

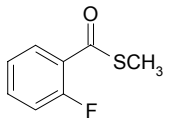
(*4R,5R*)-2-(2-bromophenyl)-4,5-diphenyl-4,5-dihydroimidazole (17a)



A solution of 2-bromo-dithiobenzoic acid *S*-methyl ester (**16a**) (914 mg, 3.7 mmol) in dimethylformamide (4ml) was added to a suspension of (*1R,2R*)-diphenylethylene diamine (786 mg, 3.7 mmol) and red mercury (II) oxide (814 mg, 3.7 mmol) in dimethylformamide (9 ml) at room temperature and vigorously stirred. The solution was heated at 110ºC for 48 hours. Then, the reaction mixture was filtered, concentrated under reduced pressure and purified by flash column chromatography (hexane/ethyl acetate 1:7) to afford 1 g (72% yield) of compound **17a** as a white powder.

m.p.= 148-150 ºC. $\mathbf{[\alpha]_D^{20}}$**=** + 0.601º (c=1.07, CH_2Cl_2). **Elemental analysis calculated for $C_{21}H_{17}BrN_2$.** (%): C, 67.34; H, 4.58; N, 7.44. **Found** (%): C, 67.22; H, 4.60; N, 7.46. **NMR ^{1}H** (300 MHz, $CDCl_3$, ppm) 7.72 (m, 1H, arom.), 7.59-7.57 (m, 1H, arom.), 7.35-7.24 (m, 12H, arom.), 4.83 (s, 2H, CH). **NMR ^{13}C** (75.4 MHz, $CDCl_3$, ppm) 163.1 (C=N), 143.2 (CH, arom.), 133.4 (CH, arom.), 132.6 (C, arom.), 131.5 (CH, arom.), 131.4 (CH, arom.), 129.2 (C, arom.), 128.7 (CH, arom.), 128.4 (CH, arom.), 127.6 (CH, arom.), 127.1 (CH, arom.), 126.8 (CH, arom.), 121.1 (C, arom.), 75.3 (CH).

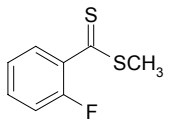
2-Fluoro-thiobenzoic acid *S*-methyl ester (15b)



Prepared following the procedure described for **15a** in 99% yield, and was used without purification in the next reaction.

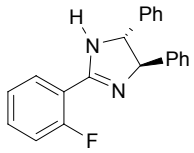
NMR ^{1}H (400 MHz, $CDCl_3$, ppm) 7.82 (m, 1H, arom.), 7.45 (m, 1H, arom.), 7.18-7.08 (m, 2H, arom), 2.45 (s, 3H, CH_3). **NMR ^{13}C** (100.6 MHz, $CDCl_3$, ppm) 188.6 (C=O), 159.9 (d, $^1J_{C\text{-}F}$=257.1 Hz, C, arom.,), 134.2 (d, $^3J_{C\text{-}F}$=8.8 Hz, CH, arom.), 129.5 (CH, arom.), 125.2 (d, $^2J_{C\text{-}F}$=11.3 Hz, C, arom.), 124.1 (d, $^3J_{C\text{-}F}$=3.4 Hz, CH, arom.), 116.6 (d, $^2J_{C\text{-}F}$=22.2 Hz, CH, arom.), 12.0 (CH_3).

2-Fluoro-dithiobenzoic acid *S*-methyl ester (16b)



Prepared following the procedure described for **16a** in 95% yield. .**NMR ^{1}H** (400 MHz, $CDCl_3$, ppm) 7.56 (m, 1H, arom.), 7.34 (m, 1H, arom.), 7.13-7.03 (m, 2H, arom), 2.71 (s, 3H, CH_3). **NMR ^{13}C** (100.6 MHz, $CDCl_3$, ppm) 224.2 (C=S), 157.3 (d, $^{1}J_{C\text{-}F}$=253.1 Hz, C, arom.), 134.5 (d, $^{2}J_{C\text{-}F}$=12.4Hz, C, arom.), 132 (d, $^{3}J_{C\text{-}F}$=8.5 Hz, CH, arom.), 129.5 (CH, arom), 123.9 (d, $^{3}J_{C\text{-}F}$=3.7 Hz, C, arom.), 116.3 (d, $^{2}J_{C\text{-}F}$=22.2 Hz, CH, arom.), 20.9 (CH_3).

(4*R*,5*R*)-2-(2-fluorophenyl)-4,5-diphenyl-4,5-dihydroimidazole (17b)

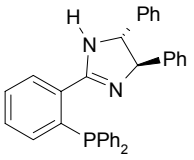


A solution of 2-fluoro-dithiobenzoic acid *S*-methyl ester (**16b**) (326 mg, 1.75 mmol) in dimethylformamide (3ml) was added to a suspension of (1*R*,2*R*)-diphenylethylene diamine (407 mg, 1.92 mmol) and red mercury (II) oxide (414 mg, 1.9 mmol) in dimethylformamide (2 ml) at room temperature and vigorously stirred. The solution was heated at 110ºC for 30 minutes. Then, the reaction mixture was filtered, concentrated under reduced pressure and purified by flash column chromatography to afford 509 mg (92% yield) of compound **17b** as a white powder.

$[\alpha]_D^{20}$= + 0.485º (c=0.811, CH_2Cl_2). **Elemental analysis calculated for $C_{21}H_{17}FN_2$** (%): C, 79.72, H, 5.42; N, 8.85. **Found** (%): C, 80.10, H, 5.32; N, 8.95. **HRMS:** m/z, $C_{21}H_{17}N_2F$ **Calculated**: 316.1376, **Found:** 316.1365. **MS (EI) m/z (%)**: 316 (11.3, M^+), 239 (1.28, M^+-Ph), 211 (100, $C_{14}H_{10}NF$) **NMR ^{1}H** (400 MHz, $CDCl_3$, ppm) 8.28 (dt, 1H, *J*=7.6 Hz, *J*=1.6 Hz, arom.), 7.49-7.12 (m, 13H, arom.), 5.99 (s, 1H, NH), 4.89 (s, 2H, CH). **NMR ^{13}C** (100.6 MHz, $CDCl_3$, ppm) 162.1 (C=N), 159.4 (d, ^{1}J=32.9 Hz, C, arom.), 143.3 (C, arom.), 132.6 (d, ^{3}J=9.15 Hz, CH, arom.), 131.3 (d, ^{4}J=2.3 Hz, CH, arom.), 128 (CH, arom.), 127.5 (CH, arom.), 126.6 (CH, arom.), 124.6 (d, ^{3}J=3.1 Hz, CH, arom.), 117.6 (d, ^{2}J=10.6 Hz, C,

arom.), 116.1 (d, ^{2}J=23.6 Hz, CH, arom.). **NMR ^{19}F** (376.5 MHz, $CDCl_3$), -114.2 (m).

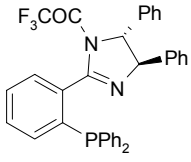
(4*R*,5*R*)-2-[(2-diphenylphosphine)phenyl]-4,5-diphenyl-4,5-dihydroimidazole (18a)



A mixture of 150 mg (0.475 mmols) of (4*R,*5*R*)-2-(2-fluorophenyl)-4,5-diphenyl-4,5-dihydroimidazole (**17b**) in 40 µl of anhydrous tetrahydrofuran and 1.04 ml (0.522 mmols) of potassium diphenylphosphide (0.5 M in tetrahydrofuran) was heated at 60ºC for 1 hour. The reaction crude was then poured into water and extracted twice with dichloromethane. The organic layer was dried with anhydrous $MgSO_4$ and purified by column chromatography under argon to give 226 mg (99% yield) of compound **18a** as a white solid.

$[\alpha]_D^{20}$= -0.192º (c=0.57, CH_2Cl_2). **Elemental analysis calculated for $C_{33}H_{27}N_2P$** (%): C, 82.14, H, 5.64; N, 5.81 **Found** (%): C, 82.17, H, 5.48; N, 5.29. **HRMS (EI):** m/z, $C_{33}H_{27}N_2P$ **Calculated** 482.1912, **Found** 482.1911. **MS (EI) m/z (%)**: 482 (3.78, M^+), 405 (9.61, M^+-Ph), 301 (100, $C_{19}H_{14}N_2P$), 222 (3.59, $C_{15}H_{14}N_2$) **NMR ^{1}H** (400 MHz, $CDCl_3$, ppm) 7.80 (m, 1H, arom.), 7.32-7.11 (m, 22H, arom.), 6.80 (m, 1H, arom), 5.86 (s broad, 1H, NH), 4.73 (m, 1H, CH), 4.48 (m, 1H, CH). **NMR ^{13}C** (100.6 MHz, $CDCl_3$, ppm) 164.2 (C=N), 143.3-126.7 (arom), 80.3 (CH), 71.3 (CH). **NMR ^{31}P** (161.9 MHz, $CDCl_3$), -10.3.

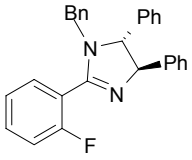
(4*R*,5*R*)-1-trifluoroacetate-2-[(2-diphenylphosphine)phenyl]-4,5-diphenyl-4,5-dihydroimidazole (18b)



A total of 45 µl (0.31 mmol) of trifluoroacetate anhydride was added to a solution of 100 mg (0.207 mmol) of (4*R*,5*R*)-2-(2-diphenylphosphine)-*trans*-diphenyl-4,5-dihydroimidazole **18a** and 60 µl of triethylamine in 1 ml of anhydrous dichloromethane. The solvent was

removed after 1 hour and the residue was purified by column chromatography with silica under argon to give 102.8 mg (86% yield) of compound **18b** as a white solid. **Elemental analysis calculated for $C_{35}H_{26}F_3N_2OP$** (%): C, 72.66, H, 4.53; N, 4.84, **Found** (%): C, 72.63, H, 4.34; N, 4.41. **NMR ^{1}H** (400 MHz, $CDCl_3$, ppm) 7.60 (ddd, *J*=8 Hz, *J*=4.4 Hz, *J*=3 Hz, 1H, arom.), 7.47 (dt, *J*=7.6 Hz, *J*=0.8 Hz, 1H, arom.), 7.41-7.20 (m, 19H, arom), 7.11 (ddd, *J*=7.6 Hz, *J*=4 Hz, *J*=0.8 Hz, 1H, arom), 7.15 (t, *J*=1.2 Hz, 1H, arom), 7.00 (d, *J*=2.4 Hz, 1H, arom), 5.28 (d, ^{3}J=4.6 Hz, 1H, CH), 5.16 (d, ^{3}J=4.6 Hz, 1H, CH). **NMR ^{13}C** (100.6 MHz, $CDCl_3$, ppm) 165.8 (C=N), 155.1 (d, $^{2}J_{C\text{-}F}$=39.8 Hz, C=O), 141-125 (arom), 115.4 (d, $^{1}J_{C\text{-}F}$=289.1 Hz, CF_3), 81.4 (CH), 70.0 (CH). **NMR ^{31}P** (161.9 MHz, $CDCl_3$), -11.8. **NMR ^{19}F** (376.5 MHz, $CDCl_3$) –71.7.

(4*R*,5*R*)-1-benzyl-2-[(2-fluorophenyl)phenyl]-4,5-diphenyl-4,5-dihydroimidazole (19)

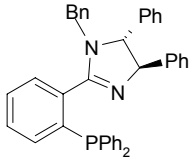


A total of 125 mg (0.395 mmol) of (4*R*,5*R*)-2-(2-fluorophenyl)-4,5-diphenyl-4,5-dihydroimidazole (**17b**) in 1 ml of anhydrous tetrahydrofuran was added to a cooled solution (0ºC) of 17.4 mg (0.43 mmol) of NaH (60% in oil suspension) and 0.5 ml of anhydrous tetrahydrofuran. The mixture was stirred for 30 min and then benzyl bromide (47 µl, 0.395 mmol) was added dropwise. After 3 hours, the reaction was stopped by adding a few drops of methanol and further purification gave 88.5 mg (55% yield) of compound **19** as a pale yellow solid. Several attempts of purification were unsuccessful, and final product contained a 5% of starting material.

MS (EI) m/z (%): 406 (4.04, M^+), 315 (6.08, M^+-Bn), 211 (81.78, $C_{14}H_{10}NF$), 91 (100, C_7H_7). **HRMS (EI):** m/z, $C_{28}H_{23}FN_2$ **Calculated** 406.1845, **Found** 406.1853. **NMR ^{1}H** (400 MHz, $CDCl_3$, ppm) 7.70 (m, 1H, arom.), 7.48 (m, 1H, arom), 7.47-7.19 (m, 15H, arom.), 6.90 (m, 2H, arom), 5.00 (d, ^{3}J=8.2 Hz, CH), 4.44 (d, ^{2}J=15.6 Hz, CH_2), 4.36 (d, ^{3}J=8.2 Hz, CH), 3.90 (d, ^{2}J=15.6 Hz, CH_2). **NMR ^{13}C**

(100.6 MHz, $CDCl_3$, ppm) 161.9 (C=N), 159.4 -116.1 (arom.), 78.4 (CH), 72.2 (CH), 49.0 (CH_2). **NMR ^{19}F** (376.5 MHz, $CDCl_3$), -112.9.

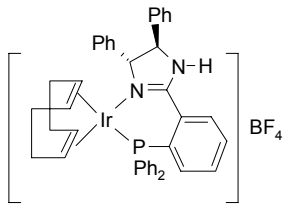
(4*R*,5*R*)-1-benzyl-2-[(2-diphenylphosphine)phenyl]-4,5-diphenyl-4,5-dihydroimidazole (18c)



A mixture of 88.5 mg (0.218 mmols) of (4*R*,5*R*)-1-benzyl-2-(2-fluorophenyl)-4,5-diphenyl-4,5-dihydroimidazole **19** and 0.5 ml (0.239 mmols) of potassium diphenylphosphide (0.5 M in tetrahydrofuran) was heated at 60ºC for 1 hour. The reaction crude was then poured into water and extracted twice with dichloromethane. The organic layer was dried with anhydrous $MgSO_4$ and purified by column chromatography under argon to give 68 mg (54% yield) of compound **18c** as a white solid. Several attempts of purification were unsuccessful, and final product contained a 5% of starting material.

MS (EI) m/z (%): 481 (100, M+-Bn), 91 (26.11, C_7H_7). **NMR ^{1}H** (400 MHz, $CDCl_3$, ppm) 7.70 (m, 1H, arom.), 7.44 (m, 1H, arom), 7.38-7.10 (m, 25H, arom.), 6.90 (m, 2H, arom), 4.93 (d, ^{3}J=9.8 Hz, CH), 4.44 (d, ^{3}J=9.8 Hz, CH), 4.28 (d, ^{2}J=17 Hz, CH_2), 3.70 (d, ^{2}J=17 Hz, CH_2). **NMR ^{13}C** (100.6 MHz, $CDCl_3$, ppm) 164.9 (C=N), 143.9-126.8 (arom), 78.8 (CH), 72.8 (CH), 49.3 (CH_2). **NMR ^{31}P** (161.9 MHz, $CDCl_3$), -12.3.

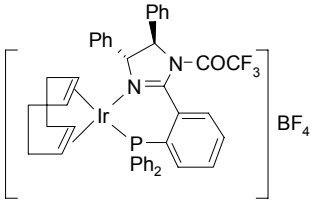
Synthesis of [Ir(η^4-COD)(18a)]BF_4 (19a)



A solution of **18a** (81.7 mg, 0.17 mmol) in dry and degassed dichloromethane (2.5 ml) was added dropwise to a chilled (-80ºC) solution of $[Ir(COD)_2]BF_4$ (70 mg, 0.141 mmol) in dry and degassed dichloromethane (3.5 ml) The solution was allowed to warm to 0ºC and stirred for 30 min. Then, ethyl ether (30 ml) was added to precipitate119 mg (97% yield) of compound **19a** as a pale red orange solid.

MS FAB m/z (%): 783.1 (100, M^+). **HRMS L-SIMS:** m/z, $[C_{41}H_{39}N_2PIr]^+$ **Calculated** 783.2480, **Found** 783.2467. **NMR ^{1}H** (400 MHz, $CDCl_3$, ppm) 8.50-6.70 (m, 24H, CH arom), 4.93 (m, 1H, CH), 4.85 (m, 2H, CH, COD), 4.66 (m, 1H, CH), 2.90 (m, 1H, CH, COD), 2.77 (m, 1H, CH, COD), 2.37 (m, 1H, CH_2, COD), 2.14 (m, 1H, CH_2, COD), 2.03 (m, 3H, CH_2, COD), 1.67 (m, 1H, CH_2, COD), 1.48 (m, 2H, CH_2, COD). **NMR ^{13}C** (100.6 MHz, $CDCl_3$, ppm) 162.2 (C=N), 141.9-125.4 (arom), 95.6 (CH, COD), 93.2 (CH, COD), 78.8 (CH), 67.5 (CH), 59.8 (CH, COD), 59.5 (CH, COD), 34.4 (CH_2, COD), 31.5 (CH_2, COD), 29,8 (CH_2, COD), 27.5 (CH_2, COD). **NMR ^{31}P** (161.9 MHz, $CDCl_3$), 15.5.

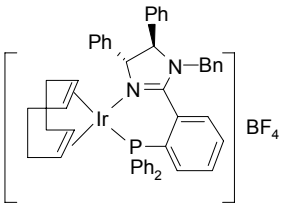
Synthesis of [Ir(η^4-COD)(18b)]BF_4 (19b)



A solution of **18b** (76.5 mg, 0.132 mmol) in dry and degassed dichloromethane (2 ml) was added dropwise to a chilled (-80ºC) solution of $[Ir(COD)_2]BF_4$ (55 mg, 0.11 mmol) in dry and degassed dichloromethane (2.8 ml). The solution was allowed to warm to 0ºC and stirred for 30 min. Then, ethyl ether (30 ml) was added to precipitate 64.9 mg (61% yield) of compound **19b** as a pale black-green solid.

MS FAB m/z (%): 879.1 (22.2, M^+). **HRMS L-SIMS:** m/z, $[C_{43}H_{38}F_3N_2OPIr]^+$ **Calculated** 879.2303, **Found** 879.3130. **NMR ^{1}H** (400 MHz, $CDCl_3$, ppm) 8.00-6.51 (m, 24H, arom), 5.20 (m, 1H, CH), 5.03 (m, 1H, CH), 4.91 (m, 1H, CH, COD), 4.64 (m, 1H, CH, COD), 3.41 (m, 2H, CH, COD), 2.48 (m, 1H, CH_2, COD), 2.35 (m, 2H, CH_2, COD), 2.16 (m, 2H, CH_2, COD), 1.79 (m, 1H, CH_2, COD), 1.53 (m, 1H, CH_2, COD), 1.39 (m, 1H, CH_2, COD). **NMR ^{13}C** (100.6 MHz, $CDCl_3$, ppm) 163.3 (C=N), 157.4 (d, $^2J_{C\text{-}F}$=41.3Hz, C=O), 137.0-121.5 (arom, CF_3), 96.3 (CH, COD), 95.1 (CH, COD), 80.4 (CH), 69.7 (CH), 68.1 (CH, COD), 66.3 (CH, COD), 35.8 (CH_2, COD), 32.4 (CH_2, COD), 28,8 (CH_2, COD), 26.7 (CH_2, COD). **NMR ^{31}P** (161.9 MHz, $CDCl_3$), 15.3. **NMR ^{19}F** (376.5 MHz, $CDCl_3$), -71.1 (CF_3), -154.3 (BF_4).

Synthesis of [Ir(η^4-COD)(18c)]BF_4 (19c)



A solution of **18c** (63.5 mg, 0.11 mmol) in dry and degassed dichloromethane (2.5 ml). was added dropwise to a chilled (-80ºC) solution of $[Ir(COD)_2]BF_4$ (50 mg, 0.10 mmol) in dry and degassed dichloromethane (2.5 ml). The solution was allowed to warm to 0ºC and stirred for 30 min. Then, ethyl ether (30 ml) was added to precipitate 82.4 mg (86% yield) of compound **19c** as a pale red solid.

NMR ^{1}H (400 MHz, $CDCl_3$, ppm) 8.14-6.59 (m, 29H, arom), 5.59 (m, 1H, CH), 5.12 (m, 1H, CH, COD), 4.97 (m, 1H, CH), 4.65 (br, 1H, CH_2), 4.14 (br, 1H, CH, COD), 4.02 (d, ^2J=15.2 Hz, 1H, CH_2), 3.13 (m, 1H, CH, COD), 2.80 (m, 1H, CH, COD), 2.10-1.42 (m, 8H, CH_2, COD). **NMR ^{31}P** (161.9 MHz, $CDCl_3$), 15.5

Crystal Structure Determinations

Crystal structure determination for 19a was carried out using a Siemens P4 diffractometer equipped with a SMART-CCD-1000 area detector, a MACScience

Co rotating anode with MoK radiation, a graphite monochromator and a Siemens low temperature device LT2 (T = -120 °C). The measurements were made in the range 1.70 to 31.55° for theta. Fullsphere data collection omega and phi scans. Programs used: Data collection Smart V. 5.060 (BrukerAXS 1999), data reduction Saint + Version 6.02 (Bruker AXS 1999) and absorption correction SADABS (Bruker AXS 1999). Crystal structure solution for 19a was achieved using direct methods as implemented in SHELXTL Version 5.10 (Sheldrick, Universtität Göttingen (Germany), 1998) and visualized using XP program. Missing atoms were subsequently located from difference Fourier synthesis and added to the atom list. Least-squares refinement on F2 using all measured intensities was carried out using the program SHELXTL Version 6.10 (Sheldrick, Universtität Göttingen (Germany),2000). All non hydrogen atoms were refined including anisotropic displacement parameters. Hydrogen atoms were invariably placed in geometrically optimized positions and forced to ride on the atom to which they are attached.

General procedure for the Ir-catalysed hydrogenation of imines

$[Ir(COD)Cl]_2$ (0.022 mmol) or $[Ir(COD)_2]BF_4$ (0.045 mmol) was dissolved in 10 ml of dry, degassed solvent (usually MeOH/CH_2Cl_2 1:1 or CH_2Cl_2) in a Schlenk tube. The thioether-oxazoline or phosphine-imidazoline ligand (0.055 mmol) was then added, followed by the corresponding imine (4.4 mmol for a 100:1 imine:Ir ratio). The solution was transferred under argon to the autoclave via a syringe.

The reaction mixture was stirred overnight at room temperature under 70 bar of H_2 pressure.

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