Iridium Complexes with P-Stereogenic Phosphino Imidazole Ligands: Synthesis, Structure and Catalysis.

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Dedicated to Steve Buchwald for his inspiring contributions to modern organic synthesis and catalysis

ABSTRACT: The synthesis of optically and diastereomerically pure P-stereogenic phosphine-imidazole ligands is reported. The new ligands contain either a benzoimidazole or a 4-phenylimidazole as a N-donor fragment. The ligands have been coordinated to iridium and the structure of the corresponding cationic COD complexes has been determined by X-ray analysis. The combination of the chiral phosphorus atom and the imidazole substituents generate a strong chiral environment around the metal

center. Preliminary hydrogenation reactions with a model cyclic β-enamide are also reported.

INTRODUCTION

The use of P-stereogenic ligands (P*) is as old as organometallic asymmetric catalysis.[1] Although at some point this family of ligands fell from favor, in the last decades a number of research groups have developed new type of P*-ligands which may be recognized among the most effective ligands in the chemist toolbox.[2-4] Since 2010, our group has developed different P-stereogenic synthons that can be conveniently used to assemble P-P, P-O and P-N ligands.[5-7] Among these synthons, we have recently reported the synthesis of optically pure *tert*-butylmethylphosphinous acid borane **1,** which we used in the synthesis of P-stereogenic phosphino-oxazoline MaxPHOX family of ligands. MaxPHOX ligands have provided excellent results in the Ir-catalyzed asymmetric isomerization and hydrogenation reactions.[8-12] P,N-Iridium complexes with imidazole as heterocyclic N-donor group have been reported in the literature, however, to our knowledge none of these contain a P-stereogenic phosphine.[13,14] In this work we report on the synthesis, coordination and X-ray structures of phosphine-imidazole ligands derived from phosphinous acid **1** and valine. Preliminary asymmetric hydrogenation reactions of a model cyclic β-enamide are also reported.

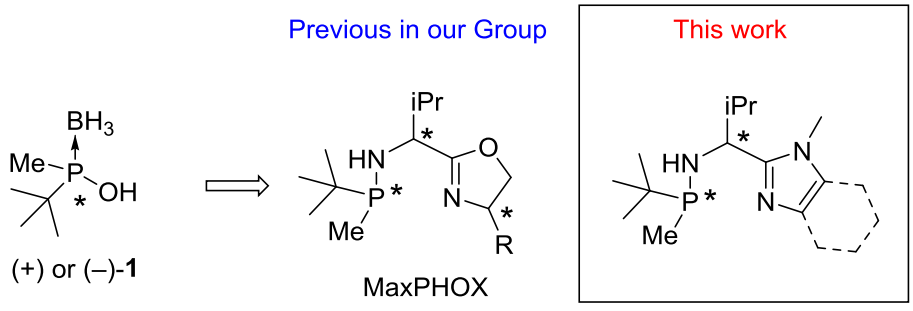
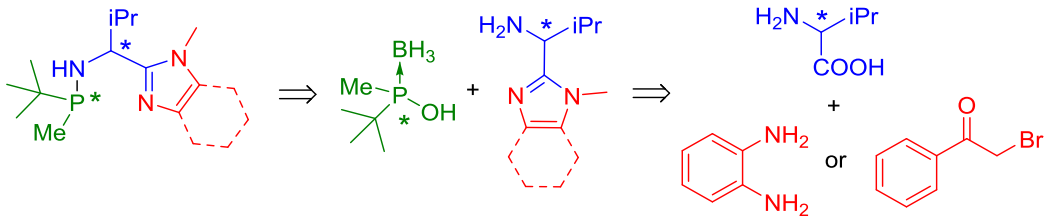


Figure 1: General structure of the ligands.

RESULTS AND DISCUSSION

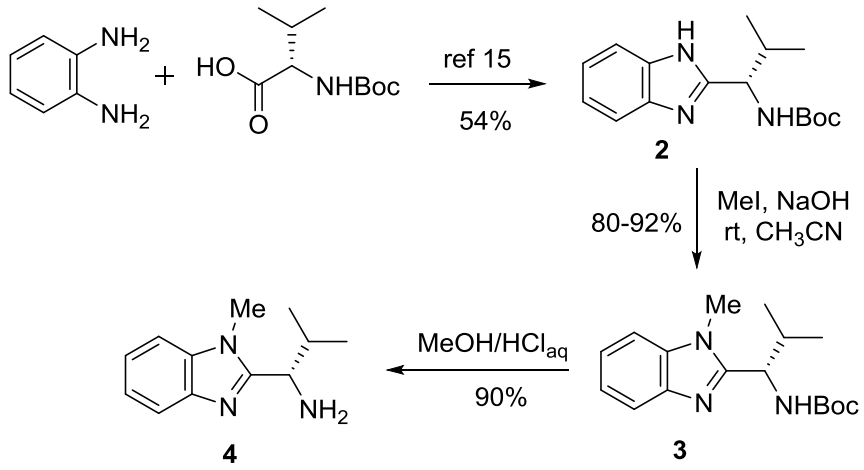
Ligand Synthesis. Phosphino imidazole ligands have been synthetized according to the retrosynthetic analysis shown in Scheme 1. Condensation of valine with *ortho*-phenylenendiamine and 2-bromoacetophenone should provide the corresponding chiral protected benzo- and 4-phenylimidazole amines. *N*-Alkylation and Boc deprotection would provide the corresponding primary amines. These will be coupled with either enantiomer of the optically pure *tert*-butylmethylphosphinous acid borane in a S_N2 reaction at the stereogenic P-center (S_N2@P) to afford the desired ligands.



Scheme 1: Retrosynthetic plan for the synthesis of phosphino imidazole ligands.

The synthesis of free (*R*)-2-methyl-1-(1-methylbenzoimidazol-2-yl)propan-1-amine **4** was conducted as shown in Scheme 2. Condensation of *N*-Boc valine with *ortho*-phenylenendiamine was carried out through a two-step procedure as described in the literature.[15] Isobutyl chlorocarbonate-mediated amide coupling and cyclization with AcOH at 65 ºC provided the desired *N*-Boc protected benzoimidazole **2** in 54% yield. Next, N-methylation of the benzoimidazole heterocycle was carried selectively with MeI and NaOH pellets in acetonitrile. This cleanly afforded **3** in 90% yield. Finally, Boc deprotection was performed in MeOH/HCl(aq) which afforded the desired benzoimidazole amine **4** in excellent yield and purity.

Scheme 2: Synthesis of benzoimidazole amine **4**.



Phenylimidazole amine was synthesized as indicated in Scheme 3. Compound **5** was synthesized as described in the literature in a two-step process.[16] Reaction of the phenacylbromide with *N*-Boc valine in Et_3N/EtOAc afforded the phenacyl ester which was cyclized with NH_4OAc in refluxing toluene to yield *N*-Boc protected phenylimidazole **5** in 63% overall yield. *N*-methylation of **5** with MeI/NaOH at 0 ºC provided a 1:10 mixture of regioisomers **6a/6b** as determined by ^1H NMR. After separation of the isomers by flash chromatography, NOESY experiments showed a cross-peak between the imidazole hydrogen and the *N*-CH_3 group in the major isomer **6a**, while for **6b** a cross peak was observed for Ph-H_{ortho} and the *N*-CH_3 group (Figure 2). This means that the alkylation takes place preferably at the less hindered nitrogen on the azole ring. Finally, from pure **6a**, MeOH/HCl_{aq} deprotection of the Boc group afforded the desired phenylimidazole amine **7** in 68 % yield.

Scheme 3: Synthesis of 1-methyl-4-phenylimidazole amine **7**.

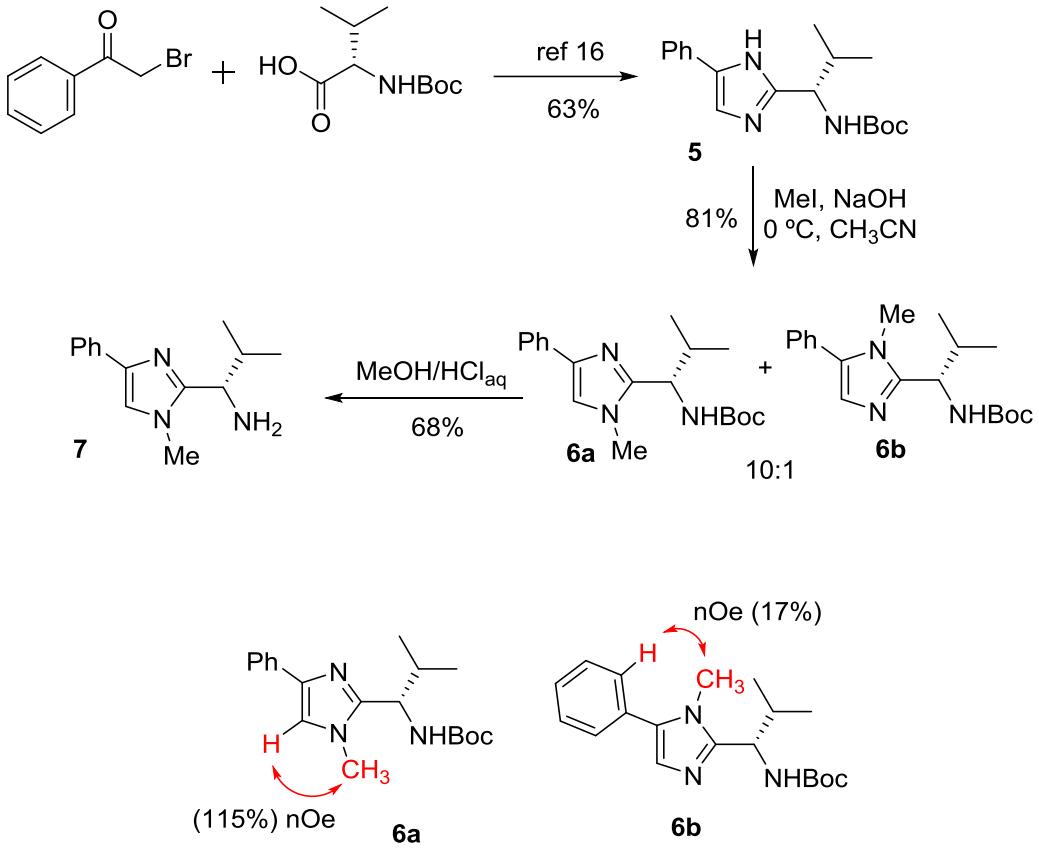
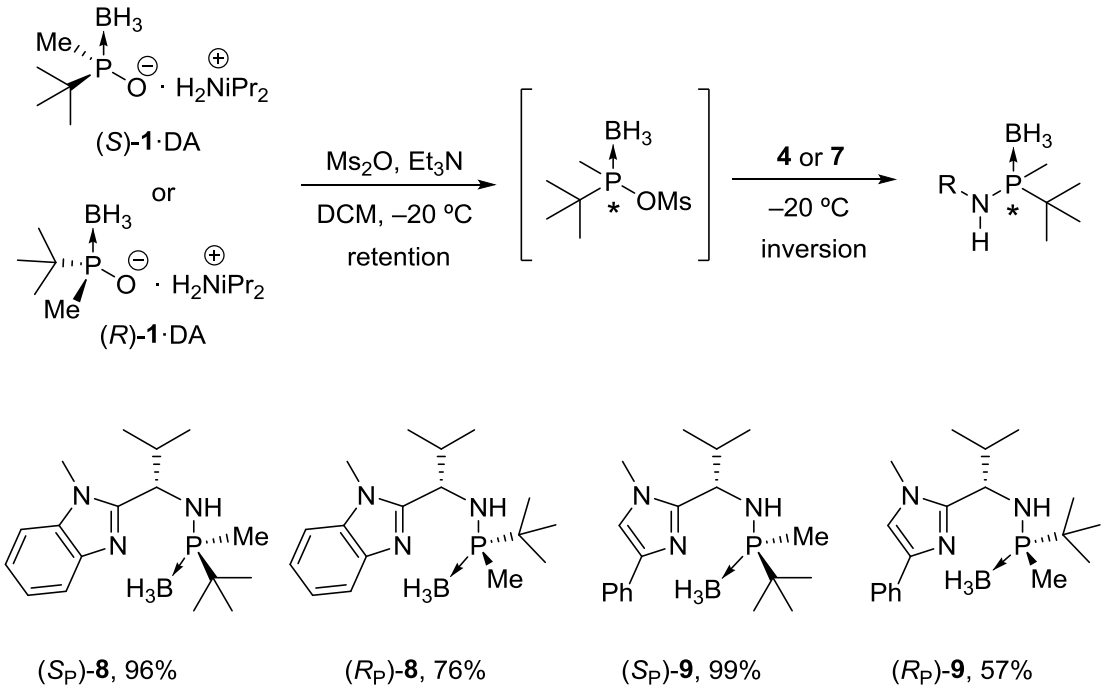


Figure 2: NOESY experiments on **6a** and **6b** isomers. nOe % was calculated with respect the C*H*(NHBoc)/C*H*$_3$(iPr) nOe signal.

With the pure imidazole amines **4** and **7** in hand we proceeded to couple them with the chiral phosphorus synthon. As we have recently reported,[17] pure *tert*-butylmethylphosphinous acid borane **1** has limited stability, while the corresponding dialkylammonium salts are shelf-stable crystalline solids that can be stored indefinitely. Moreover, they can be directly used in coupling reactions with primary amines. Thus, activation at -20 ºC of either enantiomer of **1**·DA (diisopropylammonium salt) with the methansulfonic anhydride provides the corresponding mixed anhydride which undergoes reaction with amines with inversion of configuration (Scheme 4). Reaction with benzoimidazole amine **4** provided diastereomers (S_P)-**8** and (R_P)-**8**, which only differ from the configuration at the phosphorus center, with 96 and 76% yield respectively. In the same manner, reaction with phenyl imidazole **7** provided diastereomer (S_P)-**9** (99%) and

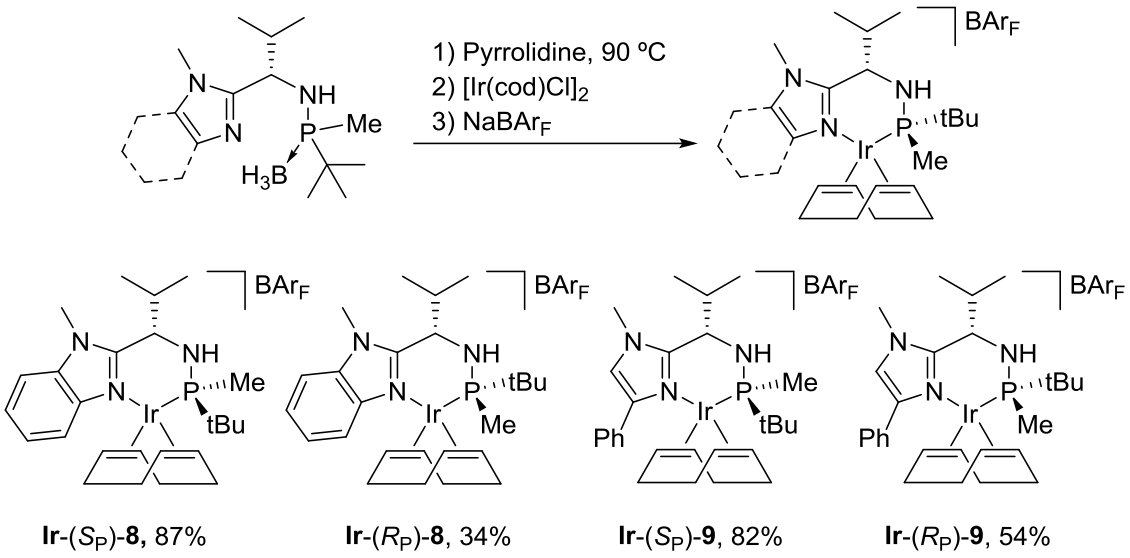
(R_P)-**9** (57%). In all four cases the compounds were isolated as diastereomerically pure substances as judged by ^{1}H NMR analysis.

Scheme 4: Amine coupling with the P-stereogenic phosphinous acid salt.



Iridium complexes: Synthesis, structure and catalysis. Ligands **8** and **9** were coordinated to iridium in a one pot 3-step procedure, as shown in Scheme 5. Borane deprotection was carried out in neat pyrrolidine (90 ºC) under nitrogen atmosphere, the pyrrolidine was removed under vacuum and $[Ir(COD)Cl]_2$ in CH_2Cl_2 was added. Finally, addition of $NaBAr_F$ produced the counteranion exchange. The cationic complexes were easily purified by flash chromatography in hexanes/DCM. Higher yields were observed for complexes **Ir-**(S_P)**-8** and **Ir-**(S_P)**-9** with *trans* configuration of *t*Bu/iPr groups, which may respond to a major chelate stability.

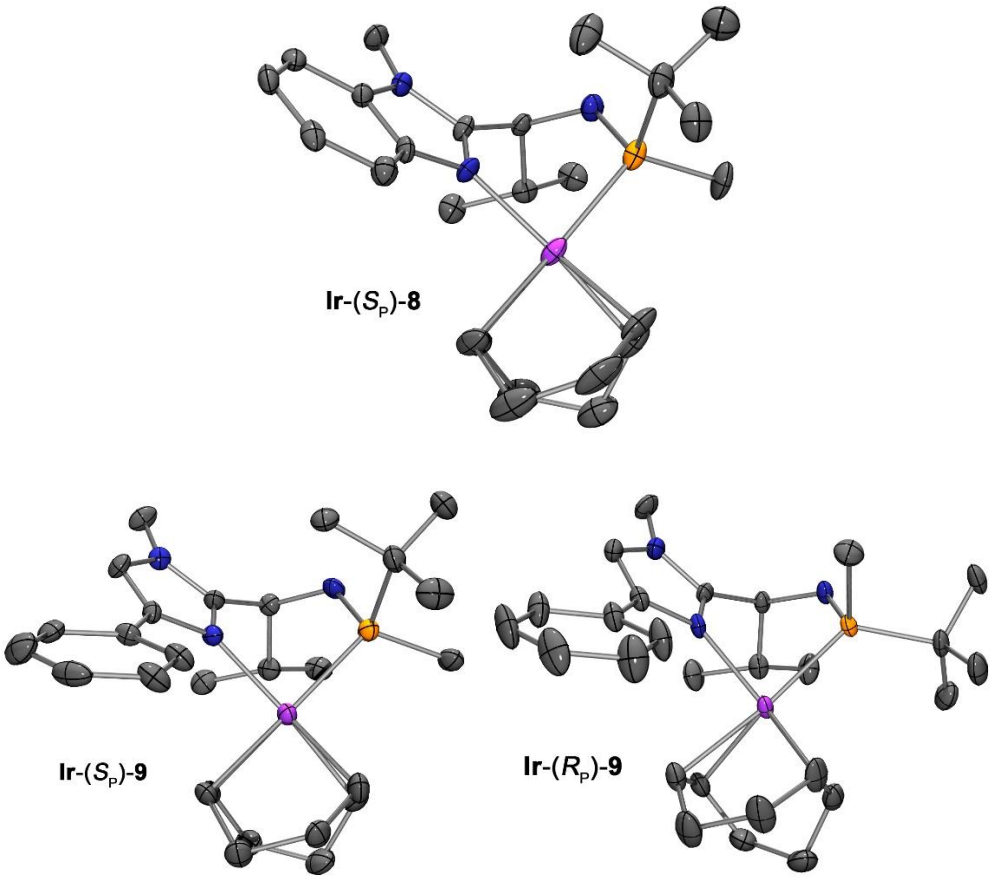
Scheme 5: Synthesis of P-stereogenic phosphino imidazole iridium catalysts.



To figure out how these ligands accommodate around the iridium metal center we sought to determine the solid-state structure of such complexes. Upon layering hexanes on top of a DCM solution of the pure samples, we could obtain single crystals suitable for X-ray analysis for complexes **Ir-**(S_P)-**8**, **Ir-**(S_P)-**9** and **Ir-**(R_P)-**9.**[18] Compound **Ir-**(R_P)-**8** precipitated as an oil. The corresponding Ortep drawings are depicted in Figure 3. All three structures share a boat conformation of the 6-membered ligand-metal chelate. The isopropyl group is in axial position for all 3 structures, thus avoiding steric strain with the *N*-methyl group on the imidazole heterocycle. Because of this, the -CH- proton of the iPr group is in close proximity to the Ir centre (2.64-2.80 Å). For **Ir-**(S_P)-**8** and **Ir-**(S_P)-**9** with S_P,*S* configuration,[19] the *t*Bu group is axial, in what it seems its preferred disposition, away from the cyclooctadiene ligand. In **Ir-**(R_P)-**9** the *t*Bu group is in equatorial position and to some extent clashes with the cyclooctadiene ligand producing a noticeable distortion. X-ray structure of **Ir-**(S_P)-**9** and **Ir-**(R_P)-**9** confirmed that *N*-methylation had taken place at the less hindered nitrogen atom of the imidazole. Finally, we should also highlight that both benzoimidazole and phenylimidazole P*,N ligands produce an effective chiral environment around the metal centre. For the phenylimidazole

derivatives, the phenyl group lies right above the metal producing slightly higher steric encumbrance.

Figure 3: X-ray structures for complexes **Ir-**(S_P)**-8**, **Ir-**(S_P)**-9** and **Ir-**(R_P)**-9**. Ortep drawing displays ellipsoids at 50% probability. BAr_F counter ions have been omitted for the sake of clarity.

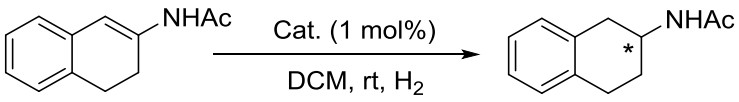


Finally, we tested the complexes **Ir-8** and **Ir-9** in the asymmetric hydrogenation of *N*-acetyl-3,4-dihydronaphthalen-2-amine. Cyclic β-enamides are challenging substrates to reduce and the resulting chiral amines have biological and therapeutical interest since they are precursors of drugs like rotigotine, a treatment for Parkinson's disease.[20]

Hydrogenation of such substrates has been reported recently by our group with excellent conversions and ee using Ir-MaxPHOX family of catalysts.[9]

In the present case the reaction conditions we employed were: 1 mol % catalyst loading, 3 bars of H_2 overnight at room temperature in DCM. With this set of conditions, the conversions were low for all four catalysts (Table 1, entries 1-4). To attain higher conversions, we increased the pressure to 50 bars of hydrogen (Table 1, entries 4-8). Indeed, higher conversions and selectivities were observed, the best result being with **Ir-**(R_P)**-8** which reported almost complete conversion and 89% enantiomeric excess (Table 1, entry 6). The activity of the present catalytic system is somewhat reduced with respect to the MaxPHOX family of catalysts which contain an oxazoline as a N-donor group. Such a decrease on activity could be caused by structural/steric differences between the two N-donor moieties. Also, electronic factors could be involved. *N*-Alkyl imidazoles are more electron rich that oxazolines. It is know that phoshino imidazole ligands are among the most electron-rich P,N systems.[14]

Table 1: Asymmetric hydrogenation of *N*-acetyl-3,4-dihydronaphthalen-2-amine.



Entry	Catalyst	H_2	Conv. (%)[a]	ee (%)[b]
1	**Ir-**(S_P)**-8**	3 bar	5	n.d.[c]
2	**Ir-**(R_P)**-8**	3 bar	12	n.d.[c]
3	**Ir-**(S_P)**-9**	3 bar	35	57
4	**Ir-**(R_P)**-9**	3 bar	10	n.d.[c]
5	**Ir-**(S_P)**-8**	50 bar	35	86
6	**Ir-**(R_P)**-8**	50 bar	98	89

7	**Ir-(S_P)-9**	50 bar	59	59
8	**Ir-(R_P)-9**	50 bar	72	72

a) Conversion was determined by ^{1}H NMR analysis of the reaction crude. b) Enantiomeric excess determined by chiral HPLC. c) n.d. = not determined.

CONCLUSIONS

A synthetic route to prepare optically and diastereomerically pure P-stereogenic phosphino imidazole ligands has been optimized. Up to 4 ligands have been prepared in good yields. The ligands contain either a benzoimidazole or a 4-phenylimidazole N-donor fragment. These ligands have been coordinated to iridium to afford the corresponding cationic COD complexes. The solid-state structures of **Ir-8S**, **Ir-9S** and **Ir-9R** have been determined by X-ray analysis. The combination of the chiral phosphorus atom and the imidazole substituents generate a strong chiral environment around the metal center; however, the catalytic activity of the imidazole ligands is low in comparison with the oxazoline analogs.

EXPERIMENTAL SECTION

General methods. All reactions were carried out in dried solvents under nitrogen atmosphere. Et_2O and CH_2Cl_2 were dried in a purification system. Other commercially available reagents and solvents were used with no further purification. Thin layer chromatography was carried out using TLC-aluminum sheets with silica gel. Flash chromatography was performed by using an automated chromatographic system with hexane/ethyl acetate or hexane/dichloromethane gradients as eluents, unless otherwise stated. NMR spectra were recorded at 23°C on a 400 MHz, 500 MHz or 600 MHz apparatus. ^{1}H NMR and ^{13}C NMR spectra were referenced either to relative internal TMS or to residual solvent peaks. ^{31}P NMR spectra were referenced to phosphoric acid. Optical

rotations were measured at room temperature (25°C) and concentration is expressed in g/100 mL. Melting points were determined using a Büchi apparatus and were not corrected. IR spectra were recorded in a FT-IR apparatus. HRMS were recorded in a LTQ-FT spectrometer using the Nanoelectrospray technique. Boc protected amines **2** and **5** were prepared according to described procedures.[15,16]

(*R*)-*N*-Boc-2-methyl-1-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)propan-1-amine, (3). [15]

N-Boc protected imidazole amine **2** (3.50 g, 12 mmol), NaOH (pellets) (1,10 g, 28 mmol) in acetonitrile (30 mL) was stirred at room temperature. Iodomethane (0.75 ml, 12 mmol) was added and the solution was stirred overnight at room temperature. Upon completion of the reaction as monitored by TLC, the solvent was removed under reduced pressure. The crude was partitioned with H_2O/CH_2Cl_2 and the aqueous phase was extracted three times with CH_2Cl_2. The organic phase was washed with water and dried over anhydrous $MgSO_4$ and the solvent was removed under vacuum to afford **3** as white solid (2.95 g, 80%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.71 (m, 1H), 7.38 – 7.26 (m, 4H), 7.25 (d, *J* = 2 Hz, 0H), 5.43 (d, *J* = 10 Hz, 1H), 4.80 (dd, *J* = 10, 8 Hz, 1H), 3.83 (s, 3H), 2.30 (dq, *J* = 14, 7 Hz, 1H), 1.41 (s, 9H), 1.06 (d, *J* = 7 Hz, 3H), 0.92 (d, *J* = 7 Hz, 3H) ppm.

(*R*)-2-methyl-1-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)propan-1-amine, (4).[15]

Methyl imidazole amine **3** (1.95 g, 6.4 mmol), MeOH (32 ml) and HCl 3M (32 ml) were stirred overnight at room temperature. Then, the MeOH was removed under reduced pressure and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent evaporated under vacuum. This afforded **4** as a white solid **(**1.15 g, 88%).

IR (KBr) υ_{max}: 3366, 3053, 2959, 2869, 1614, 1467 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.71 (m, 1H), 7.35 – 7.31 (m, 1H), 7.29 – 7.23 (m, 2H), 3.91 (d, *J* = 7 Hz, 1H), 3.79 (s, 3H), 2.17 (h, *J* = 7 Hz, 1H), 1.05 (d, *J* = 7 Hz, 3H), 0.95 (d, *J* = 7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.6 (C), 142.2 (C), 135.77 (C), 122.2 (CH), 121.9 (CH),

119.4 (CH), 109.1 (CH), 54.8 (CH), 34.3 (CH), 30.0 (CH_3), 20.0 (CH_3), 18.1 (CH_3) ppm. HRMS (ESI): calc for $[M+H]^+$: 204.1495, found 204.1493.

(*R*)-*N*-Boc-2-methyl-1-(1-methyl-4-phenyl-1*H*-imidazol-2-yl)propan-1-amine, (6a).

N-Boc protected imidazole amine **5**[16] (2.50 g, 8 mmol), NaOH (pellets) (0.63 g, 16 mmol) in acetonitrile (50 mL) was stirred at 0 ºC. Iodomethane (0.49 ml, 12 mmol) was added and the solution was let to warm stirring overnight to room temperature. Upon completion of the reaction as monitored by TLC, the solvent was removed under reduced pressure. The crude was partitioned with H_2O/CH_2Cl_2 and the aqueous phase was extracted three times with CH_2Cl_2. The CH_2Cl_2 phase was washed with water and dried over anhydrous $MgSO_4$, and the solvent was removed under vacuum to afford a **6a/6b** as an oil. Flash column chromatography (SiO_2, hexane/EtOAc) allowed separation of both isomers to yield 1.93 g (74%) of **6a** and 0.19 g (7%) of **6b**.

6a: $[\alpha]_D$: –91.8 (*c* 1.00, $CHCl_3$). IR (KBr) υ_{max}: 3302, 2972, 1705, 1496, 1170 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.68 (m, 2H), 7.34 (dd, *J* = 8, 7 Hz, 2H), 7.27 – 7.16 (m, 1H), 7.01 (d, *J* = 2 Hz, 1H), 5.52 (d, *J* = 9 Hz, 1H), 4.56 (dd, *J* = 9 and 8 Hz, 1H), 3.64 (s, 3H), 2.25 (dp, *J* = 8, 7 Hz, 1H), 1.43 (s, 9H), 1.04 (d, *J* = 7 Hz, 3H), 0.90 (d, *J* = 7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.71 (C), 155.4 (C), 136.3 (C), 135.1 (C), 129.0 (CH), 128.0 (CH), 126.8 (CH), 123.0 (CH), 119.6 (CH), 110.4 (CH), 79.8 (C), 52.5 (CH), 47.3 (CH), 33.1 (CH_3), 28.4 (3xCH_3), 19.8 (CH_3), 18.5 (CH_3) ppm. HRMS (ESI): Calc for $[M+H]^+$: 330.2176, found 330.2180.

6b: $[\alpha]_D$: –66.0 (*c* 1.02, $CHCl_3$). IR (KBr) υ_{max}: 3295, 2973, 2931, 1682, 1508, 1169 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.40 (m, 2H), 7.40 – 7.34 (m, 3H), 7.26 (s, 1H), 7.03 (s, 1H), 5.38 (d, *J* = 10 Hz, 1H), 4.64 (dd, *J* = 10 and 8 Hz, 1H), 3.62 (s, 3H), 2.33 – 2.19 (m, 1H), 1.44 (d, *J* = 4 Hz, 9H), 1.05 (d, *J* = 7 Hz, 3H), 0.93 (d, *J* = 7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.9 (C), 133.6 (C), 130.2 (CH), 129.0 (CH), 128.8 (CH), 128.1 (CH), 126.3 (CH), 79.6 (C), 52.6 (CH), 33.6 (CH), 31.5 (CH_3), 28.5 (3xCH_3), 19.7 (CH_3), 18.6 (CH_3) ppm. HRMS (ESI): Calc for $[M+H]^+$: 330.2176, found 330.2180.

(*R*)-2-methyl-1-(1-methyl-4-phenyl-1*H*-imidazol-2-yl)propan-1-amine, (7).

Methyl imidazole amine **6a** (1.54 g, 4.7 mmol), MeOH (25 ml) and HCl 3M (25 ml) were stirred overnight at room temperature. Then, MeOH was removed under reduced pressure and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent evaporated under reduced pressure. The resulting crude was disaggregated with Et_2O and filtered to afford **7** as a white solid **(**0.73 g, 68%).

$[\alpha]_D$: –27.0 (*c* 1.04, $CHCl_3$). IR (KBr) υ_{max}: 3418, 3133, 2965, 2876, 1607 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.69 (m, 2H), 7.39 – 7.30 (m, 2H), 7.20 (ddt, *J* = 8, 7 and 1 Hz, 1H), 7.04 (s, 1H), 3.70 (d, *J* = 7 Hz, 1H), 3.66 (s, 3H), 2.16 – 2.01 (m, 1H), 1.05 (d, *J* = 7 Hz, 3H), 0.89 (d, *J* = 7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.3 (C), 140.1 (C), 134.6 (C), 128.6 (CH), 126.6 (CH), 125.0 (CH), 116.5 (CH), 54.7 (CH), 34.7 (CH), 33.0 (CH_3), 20.0 (CH_3), 18.7 (CH_3) ppm. HRMS (ESI): calc for $[M+H]^+$: 230.1652 found 230.1649.

General method for P-stereogenic phosphine coupling.

A solution of *tert*-butylmethylphosphinous acid borane diisopropyl ammonium salt (1 eq) and methansulfonic anhydride 97% (1.2 eq) in CH_2Cl_2 (0.2 M) was cooled down to –20 ºC. To this solution, anhydrous NEt_3 (2.5 eq) was slowly added, and the mixture was stirred 1.5 h at –20 ºC. A solution of the corresponding amine (2 eq) in CH_2Cl_2 (0.2 M) was then added dropwise and the solution was stirred overnight at –20 ºC. Water was added to quench the reaction and the mixture was allowed to warm to room temperature. The organic layer was separated and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic extracts were washed with NaOH (1M), HCl (1M) and water. Finally, the solution was dried over anhydrous $MgSO_4$ and the volatiles were removed under vacuum.

(*S*)-1-*tert*-butyl-1-methyl-N-((*S*)-2-methyl-1-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)propyl)phosphanamine borane complex, (Ir-(S_P)-8).

Following the general procedure, benzoimidazole amine **4** (360 mg, 1.8 mmol), Ms_2O (185 mg, 1.1 mmol), phosphinite salt (*R*)-**1**·DA (208 mg, 0.9 mmol) and NEt_3 (0.3 ml, 2.2 mmol) were employed. White solid; 273 mg (96%).

$[\alpha]_D$: –18.3 (*c* 1.00, $CHCl_3$). IR (KBr) υ_{max}: 3317, 3032, 2963, 2378, 1467 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.65 (m, 1H), 7.40 – 7.31 (m, 1H), 7.31 – 7.20 (m, 2H), 4.44 (dt, *J* = 11 and 8 Hz, 1H), 3.83 (s, 3H), 2.79 (dd, *J* = 12 and 6Hz, 1H), 2.06 (h, *J* = 7 Hz, 1H), 1.18 (d, J_P = 14 Hz, 9H), 1.08 (d, *J* = 7 Hz, 3H), 1.02 (d, J_P = 9 Hz, 3H), 0.91 (d, *J* = 7 Hz, 3H), 0.81 – -0.03 (m, 3H, BH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4 (C), 142.0 (C), 135.3 (C), 122.3 (CH), 122.1 (CH), 118.9 (CH), 109.6 (CH), 55.1 (CH), 35.7 (d, J_P = 8 Hz, CH), 30.6 (C), 30.1 (CH_3), 24.4 (d, J_P = 3 Hz, 3xCH_3), 19.4 (CH_3), 18.6 (CH_3), 10.4 (d, J_P = 32 Hz, CH_3) ppm. ^{31}P NMR (202 MHz, $CDCl_3$) δ 71.5 (q, *J* = 51 Hz) ppm. HRMS (ESI): calc for $[M+H]^+$: 318.2265, found 318.2265.

(*R*)-1-*tert*-butyl-1-methyl-*N*-((*S*)-2-methyl-1-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)propyl)phosphanamine borane complex, (Ir-(R_P)-8).

Following the general procedure, benzoimidazole amine **4** (403 mg, 2 mmol), Ms_2O (213 mg, 1.2 mmol), phosphinite salt (*S*)-**1**·DA (233 mg, 1 mmol) and NEt_3 (0.3 ml, 2.5 mmol). Oil; 240 mg (76%).

$[\alpha]_D$: –42.9 (*c* 1.06, $CHCl_3$). IR (KBr) υ_{max}: 3345, 2963, 2870, 2377, 1467 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.74 (m, 1H), 7.48 – 7.33 (m, 3H), 4.51 (q, *J* = 10 Hz, 1H), 3.91 (s, 3H), 3.63 (d, *J* = 11 Hz, 1H), 2.33 (dp, *J* = 8 and 7 Hz, 1H), 1.39 (d, *J* = 9 Hz, 3H), 1.30 (d, *J* = 7 Hz, 3H), 1.13 (d, *J* = 7 Hz, 3H), 0.89 (d, *J* = 14 Hz, 9H), 0.78 (d, *J* = 7 Hz, 3H) 0.65 – 0.00 (m, 3H, BH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2 (C), 137.5 (C), 133.4 (C), 124.1 (CH), 123.9 (CH), 117.7 (CH), 110.3 (CH), 55.6 (d, J_P = 4 Hz, CH), 35.8 (d, J_P = 8 Hz, CH), 31.1 (C), 30.7 (CH_3), 24.3 (d, J_P = 3 Hz, 3xCH_3), 19.3 (CH_3), 19.2 (CH_3), 11.4 (d, J_P = 43 Hz, CH_3) ppm. ^{31}P NMR (202 MHz, $CDCl_3$) δ 74.4 (q, *J* = 56 Hz) ppm. HRMS (ESI): calc for $[M+H]^+$: 320.2421, found 320.2422.

(*S*)-1-*tert*-butyl-1-methyl-*N*-((*S*)-2-methyl-1-(1-methyl-4-phenyl-1*H*-imidazol-2-yl)propyl)phosphanamine borane complex, (Ir-(S_P)-9).

Following the general procedure; phenylimidazole amine **7** (402 mg, 1.8 mmol), Ms_2O (186 mg, 1.1 mmol), phosphinite salt (*R*)-**1**·DA (205 mg, 0.9 mmol) and NEt_3 (0.3 ml, 2.2 mmol). White solid; 300 mg (99%).

Mp = 117 – 119 ºC. $[\alpha]_D$: –73.4 (*c* 1.09, $CHCl_3$). IR (KBr) υ_{max}: 2962, 2870, 2378, 1607 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.65 (m, 2H), 7.40 – 7.32 (m, 2H), 7.24 – 7.19 (m, 1H), 7.03 (s, 1H), 4.12 (dt, *J* = 11 and 8 Hz, 1H), 3.70 (s, 3H), 1.99 (h, *J* = 7 Hz, 1H), 1.18 (d, J_P = 14 Hz, 9H), 1.06 (d, *J* = 7 Hz, 3H), 1.03 (d, J_P = 9 Hz, 3H), 0.88 (d, *J* = 7 Hz, 3H), 0.80 – -0.05 (m, 3H, BH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.9 (C), 140.0 (C), 128.5 (2xCH), 126.5 (CH), 124.8 (2xCH), 115.9 (CH), 54.9 (CH), 35.9 (d, J_P = 9 Hz, CH), 33.0 (CH_3), 30.5 (C), 24.4 (d, J_P = 2 Hz, CH_3), 19.4 (CH_3), 18.9 (CH_3), 10.3 (d, J_P = 31 Hz, CH_3) ppm. ^{31}P NMR (202 MHz, $CDCl_3$) δ 71.4 – 69.9 (m) ppm. HRMS (ESI): calc for $[M+H]^+$: 346.2578, found 346.2584.

(*R*)-1-*tert*-butyl-1-methyl-*N*-((*S*)-2-methyl-1-(1-methyl-4-phenyl-1*H*-imidazol-2-yl)propyl)phosphanamine borane complex, (Ir-(R_P)-9).

Following the general procedure; phenylimidazole amine **7** (399 mg, 1.8 mmol), Ms_2O (186 mg, 1.1 mmol), phosphinite salt (*S*)-**1**·DA (206 mg, 0.9 mmol) and NEt_3 (0.3 ml, 2.2 mmol). White solid; 172 mg (57%).

Mp = 185 – 187 ºC. $[\alpha]_D$: –122.0 (*c* 1.02, $CHCl_3$). IR (KBr) υ_{max}: 3333, 2957, 2872, 2370, 2347, 1463 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.68 (m, 2H), 7.39 – 7.32 (m, 2H), 7.25 – 7.19 (m, 1H), 6.99 (s, 1H), 4.19 (td, *J* = 10 and 8 Hz, 1H), 3.68 (s, 3H), 2.79 (d, J_P = 11 Hz, 1H, NH), 2.02 (m, 1H), 1.35 (d, J_P = 9 Hz, 3H), 1.06 (d, *J* = 7 Hz, 3H), 0.90 (d, J_P = 14 Hz, 9H), 0.82 (d, *J* = 7 Hz, 3H), 0.53 (m, 3H, BH_3) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.4 (C), 140.2 (C), 134.4 (C), 128.5 (2xCH), 126.6 (CH), 124.8 (2xCH), 115.4 (CH), 55.0 (d, J_P = 3 Hz, CH), 36.1 (d, J_P = 6 Hz, CH), 33.0 (CH_3), 30.5 (C), 24.3 (d, J_P = 3 Hz, CH_3), 19.2 (CH_3), 19.0 (CH_3), 11.1 (d, J_P = 45 Hz, CH_3) ppm. ^{31}P NMR (202 MHz, $CDCl_3$) δ 73.0 (q, *J* = 57 Hz) ppm. HRMS (ESI): calc for $[M+H]^+$: 346.2580, found 346.2582.

General procedure for the synthesis of Ir-[P,N] catalysts.

The corresponding borane protected ligand (1 eq) was dissolved in dry distilled pyrrolidine under nitrogen (0.06 M) and stirred overnight at 90 ºC. Pyrrolidine was then removed in high vacuum. The crude was further dried under vacuum for 30 min at 50 ºC. A solution of $[Ir(COD)(Cl)]_2$ (0.5 eq) in CH_2Cl_2 (0.06 M) was added to the free ligand via cannula. The resulting mixture was stirred for 40 min at room temperature. $NaBAr_F$ (1 eq) was then added and the solution was stirred 1 h at room temperature. The resulting

crude was filtered through a small plug of silica gel under N_2 and washed with dry Et_2O, eluting with hexanes/CH_2Cl_2 (50-100%). The orange coloured fraction was collected and concentrated to yield the corresponding Ir complexes as orange solids.

[Ir(COD)(*S*$_P$-8)][BAr$_F$].

Following the general procedure; ligand (*S*$_P$)-**8** (45 mg, 0.14 mmol), pyrrolidine (2.5 ml), $[Ir(COD)(Cl)]_2$ (47 mg, 0.07mmol), $NaBAr_F$ (125 mg, 0.14 mmol) were employed. Orange solid; 180 mg (87 %).

Mp = 187 – 188 ºC. $[\alpha]_D$: +34.9 (*c* 1.02, $CHCl_3$). IR (KBr) υ_{max}: 3417, 2958, 2918, 2843, 1606, 1454, 1351, 1270, 1124 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.75 (m, 1H), 7.71 (m, 8H, BAr_F^-), 7.52 (s, 4H, BAr_F^-), 7.46 – 7.37 (m, 3H), 5.37 (p, *J* = 8 Hz, 1H, COD), 4.72 (d, *J* = 5 Hz, 1H, COD), 4.03 (d, *J* = 6 Hz, 1H, COD), 3.92 (ddd, *J* = 23, 11 and 7 Hz, 1H), 3.80 (s, 3H), 3.61 (m, 1H), 3.48 – 3.41 (m, 1H, COD), 2.64 (m, 2H, COD), 2.36 (d, J_P = 15 Hz, 1H, COD), 2.30 (d, J_P = 6 Hz, 1H, NH), 2.24 – 2.06 (m, 3H, COD), 1.41 (d, J_P = 8 Hz, 3H), 1.20 (d, *J* = 6 Hz, 3H), 0.83 (d, *J* = 7 Hz, 3H), 0.76 (d, J_P = 15 Hz, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.7 (q, J_B = 50 Hz, BAr_F, 4xC) 155.4 (C), 138.8 (C), 136.0 (BAr_F, 8xCH), 134.0 (C), 129.2 (m, BAr_F, C), 128.9 (m, BAr_F, CF_3), 126.1 (CH), 125.2 (CH), 117.9 (BAr_F, 4xCH), 117.7 (CH), 115.7 (CH), 96.0 (COD, CH), 91.4 (COD, CH), 61.5 (COD, CH), 61.1 (COD, CH), 59.2 (d, J_P = 4 Hz, CH), 39.8 (d, J_P = 4 Hz, CH), 37.2 (d, J_P = 4 Hz, COD, CH_2), 36.4 (d, J_P = 37 Hz, C), 32.8 (d, J_P = 2 Hz, COD, CH_2), 31.0 (CH_3), 28.7 (COD, CH_2), 25.8 (3xCH_3), 25.7 (COD, CH_2) 20.0 (CH_3), 18.6 (CH_3), 8.8 (d, J_P = 35 Hz, CH_3) ppm. ^{31}P NMR (202 MHz, $CDCl_3$) δ 56.2 (s) ppm. HRMS (ESI): calc for $[M+H]^+$: 606.2584, found 606.2588; calc for $[M–H]^–$: 863.0643, found 863.0636.

[Ir(COD)(*R*$_P$-8)][BAr$_F$]

Following the general procedure; ligand (*R*$_P$)-**8** (50 mg, 0.16 mmol), pyrrolidine (2.5 ml), $[Ir(COD)(Cl)]_2$ (53 mg, 0.07mmol), $NaBAr_F$ (139 mg, 0.14 mmol) were employed. Orange solid; 80 mg (35 %).

Mp =152 – 155 ºC. $[\alpha]_D$: +66.0 (*c* 1.01, $CHCl_3$). IR (KBr) υ_{max}: 3417, 2950, 2914, 2851, 1601, 1484, 1353, 1271, 1116 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.85 (m, 1H), 7.70 (p, *J* = 2 Hz, 8H, BAr_F^-), 7.51 (s, 4H, BAr_F^-), 7.48 – 7.42 (m, 2H), 7.42 – 7.36 (m,

1H), 4.98 (s, 1H, COD), 4.80 (s, 2H, COD), 4.01 (d, *J* = 7 Hz, 1H, COD), 3.90 – 3.77 (m, 1H, COD), 3.74 (s, 3H), 3.30 (br. s, 1H, COD), 2.59 (br. s, 1H, COD), 2.45 (br. s, 1H, COD), 2.19 (br. s, 4H), 2.08 (br. s, 1H, NH), 1.55 (br. s, 2H), 1.31 (d, J_P = 6 Hz, 3H), 1.13 (d, J_P = 16 Hz, 9H), 0.91 (d, *J* = 7 Hz, 3H), 0.78 (d, *J* = 7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.6 (q, J_B = 50 Hz, BAr_F, 4xC), 138.4 (C), 135.9 (BAr_F, 8xCH), (m, BAr_F, C), 128.9 (m, BAr_F, CF_3), 126.0 (CH), 125.2 (CH), 118.5 (BAr_F, 4xCH), 117.6 (CH), 111.8 (CH), 110.2 (C), 94.3 (COD, CH), 85.6 (COD, CH), 65.7 (COD, CH), 58.0 (CH), 56.6 (COD, CH), 38.0 (CH), 37.5 (COD, 2xCH_2), 34.8 (C), 33.5 (COD, CH_2), 31.0 (CH_3), 29.5 (COD, CH_2), 25.8 (3xCH_3), 25.3 (COD, CH_2) 20.8 (CH_3), 19.0 (CH_3), 14.2 (CH_3) ppm. ^{31}P NMR (202 MHz, $CDCl_3$) δ 60.6 (s), ppm. HRMS (ESI): calc for $[M+H]^+$: 606.2584, found 606.2580; calc for $[M–H]^–$: 863.0643, found 863.0672.

[Ir(COD)(*S*$_P$-9)][BAr$_F$].

Following the general procedure; ligand (*S*$_P$)-**9** (50 mg, 0.15 mmol), pyrrolidine (2.5 ml), $[Ir(COD)(Cl)]_2$ (45 mg, 0.07mmol), $NaBAr_F$ (128 mg, 0.14 mmol) were employed. Orange solid; 173 mg (82 %).

Mp = 201 – 203 ºC. $[\alpha]_D$: +46.6 (*c* 1.02, $CHCl_3$). IR (KBr) υ_{max}: 3417, 2954, 2923, 2851, 1614, 1459, 1353, 1271, 1127 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 2H), 7.73 – 7.69 (m, 8H), 7.53 (s, 4H), 7.48 – 7.43 (m, 3H), 7.00 (s, 1H), 4.62 (br. s, 1H, COD), 4.17 (m, 1H, COD), 3.75 (ddd, J_P = 23, *J* = 11 and 7 Hz, 1H), 3.64 (s, 3H), 3.59 (m, 1H+1H COD), 3.34 (m, 1H, COD), 2.45 (m, 2H, COD), 2.27 – 2.17 (m, 2H, COD), 2.13 – 1.99 (m, 2H, COD), 1.46 (m, 2H, COD), 1.42 (d, J_P = 8 Hz, 3H), 1.16 (d, *J* = 6 Hz, 3H), 0.92 (d, J_P = 15 Hz, 9H), 0.77 (d, *J* = 7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.8 (q, J_B = 50 Hz, BAr_F, 4xC), 149.8 (C), 140.9 (C), 134.9 (BAr_F, 8xCH), 129.7 (2xCH), 129.2 (m, BAr_F, C), 128.9 (CH), 128.9 (m, BAr_F, CF_3), 127.9 (2xCH), 120.6 (C), 120.1 (CH), 117.6 (d, *J* = 4 Hz, BAr_F, 4xCH) 110.2 (C), 96.3 (d, *J* = 11 Hz, COD, CH), 92.1 (d, *J* = 13 Hz, COD, CH), 61.7 (COD, CH), 61.3 (COD, CH), 58.8 (d, *J* = 4 Hz, CH), 39.5 (CH), 37.4 (d, *J* = 4 Hz, COD, CH_2), 34.4 (CH_3), 33.3 (COD, CH_2), 29.9 (C), 28.3 (COD, CH_2), 25.4 (d, *J* = 5 Hz, 3x CH_3), 20.0 (CH_3), 18.6 (CH_3), 9.7 (d, *J* = 35 Hz, CH_3) ppm. ^{31}P NMR (202 MHz, $CDCl_3$) δ 54.7 (s) ppm. HRMS (ESI): calc for $[M+H]^+$: 632.2740, found 632.2725; calc for $[M–H]^–$: 863.0643, found 863.0640.

[Ir(COD)(*R*$_P$-9)][BAr$_F$]

Following the general procedure; ligand (*R*$_P$)-**9** (50 mg, 0.15 mmol), pyrrolidine (2.5 ml), [Ir(COD)(Cl)]$_2$ (45 mg, 0.07mmol), NaBAr$_F$ (128 mg, 0.14 mmol) were employed. Orange solid; 118 mg (54 %).

Mp = 173 – 175 ºC. $[\alpha]_D$: +52.8 (*c* 1.03, $CHCl_3$). IR (KBr) υ_{max}: 3412, 2959, 2918, 2843, 1606, 1476, 1353, 1274, 1119 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.87 (m, 2H), 7.73 – 7.67 (m, 10H), 7.52 (s, 4H), 7.50 – 7.44 (m, 3H), 7.01 (s, 1H), 5.02 (d, *J* = 8 Hz, 1H, COD), 4.63 (d, *J* = 6 Hz, 1H, COD), 3.90 (d, *J* = 8 Hz, 1H, COD), 3.73 – 3.60 (m, 1H), 3.59 (s, 3H), 3.42 (p, *J* = 8 Hz, 1H), 3.32 (m, 1H, COD), 2.43 – 2.30 (m, 1H), 2.18 (dd, *J* = 15 and 8 Hz, 1H), 2.13 – 2.00 (m, 4H), 1.54 (s, 2H), 1.27 (d, J_P = 6 Hz, 3H), 1.25 (d, *J* = 8 Hz, 3H), 1.16 (d, J = 15 Hz, 9H), 0.76 (d, *J* = 7 Hz, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.7 (q, J_B = 50 Hz, BAr$_F$, 4xC), 150.0 (C), 141.3 (C), 134.9 (BAr$_F$, 8xCH), 129.2 (2xCH), 129.2 (m, BAr$_F$, C), 128.9 (m, BAr$_F$, CF_3), 126.0 (C), 127.3 (2xCH), 123.3 (C), 120.2 (CH), 117.6 (BAr$_F$, 4xCH), 94.1 (d, *J* = 10 Hz, COD, CH), 87.7 (d, *J* = 15 Hz, CH), 65.1 (COD, CH), 56.0 (COD, CH), 37.6 (CH), 37.3 (COD, CH_2), 37.3 (COD, CH_2), 34.5 (CH_3), 33.6 (COD, CH_2), 29.9 (COD, CH_2), 20.0 (COD, CH_2), 26.0 (d, *J* = 4 Hz, 3x CH_3), 20.9 (CH_3), 19.0 (CH_3), 15.7 (CH_3) ppm. ^{31}P NMR (202 MHz, $CDCl_3$) δ 58.2 (s) ppm. HRMS (ESI): Calc for $[M+H]^+$: 632.2740, found 632.2750; calc for $[M–H]^–$: 863.0643, found 863.0687.

Hydrogenation reactions.

N-acetyl-3,4-dihydronaphthalen-2-amine (1 eq) and the corresponding catalyst (0.01 eq) were weighted in a test tube and then placed in a stainless steel high pressure reactor. The corresponding solvent was added and the reactor was closed and connected to a hydrogen manifold. While stirring, the reactor was purged with vacuum-nitrogen cycles and then vacuum-hydrogen cycles. Finally it was charged at the corresponding hydrogen pressure. The hydrogen manifold was unplugged and the mixture was left to stir overnight at room temperature. The reactor was depressurized. The mixture crude was dried, and at this point the conversion was determined by ^{1}H NMR analysis. Determination of the optical purity was carried out by chiral HPLC upon solving the sample in heptane/isopropyl alcohol (1:1) and filtration.

^{1}H NMR (400 MHz, $CHCl_3$) δ 7.19 – 7.01 (m, 3H), 4.37 – 4.24 (m, 1H), 3.18 – 3.08 (m, 1H), 2.98 – 2.79 (m, 2H), 2.69 – 2.59 (m, 1H), 2.05 (m, 1H), 1.98 (s, 3H), 1.79 (m, 1H) ppm. HPLC: CHIRALCEL OJ. Heptane/*i*-PrOH 70:30-0.2% NEt_3, 0.5 mL/min, λ = 254 nm. $t_{(S)}$ (–)= 8.1 min, $t_{(R)}$ (+)= 9.4 min.

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Supplementary Data. Crystallographic data in CIF format file for **Ir-**(*S*$_P$)-**8**, **Ir-**(*S*$_P$)-**9** and **Ir-**(*R*$_P$)-**9**. NMR spectra for new compounds.

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