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Simple Proline-Derived Phosphine-Thiazole Iridium Complexes for Asymmetric Hydrogenatation of Trisubstituted Olefins

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Dedication ((optional))

Abstract: Proline based phosphine thiazole ligands have been synthesized and successfully applied in the homogeneous iridium-catalyzedasymmetric hydrogenation of trisubstituted olefins. Five different sets of ligands were prepared and evaluated for their catalytic activity and enantioselectivity in asymmetric hydrogenation.

Keywords: Phosphine-Thiazole/imidazole Ligands, Iridium-Complexes, Asymmetric hydrogenation

Introduction

Asymmetric hydrogenation that makes use of molecular hydrogen to reduce prochiral olefins, ketones, and imines has become one of the most efficient, practical and atom economical methods for the construction of chiral compounds.[1] During the latter decades of the 20th century, considerable attention has been devotedto the discovery of asymmetric olefin hydrogenation by rhodium[2] and ruthenium- diphosphine[3] complexes. Both rhodium and ruthenium complexes need the presence of a coordinating functional group which is often an amide derivatives or an allylic alcohol that are typical substrate classes adjacent to the C=C double bond. This group, together with the olefinic double bond, chelate to the metal center to form a cyclic intermediate that governs the stereo chemical outcome of the hydrogenation reaction.[4] The application of rhodium or ruthenium based catalysts has thus been restricted to the effective asymmetric hydrogenation of olefinic substrates without coordinating groups or with less-coordinating groups.[5,6]

The first crucial outcomein the hydrogenation of unfunctionalized olefins appeared in literature in 1998 when Pflatz and co-workers unveiled a new class of chiral iridium *N,P*-ligand complexes that overcame the limitations of the rhodium and ruthenium based systems.[7] Additionally, iridium *N,P*-complexes showedremarkably high activity in the hydrogenation of unfunctionalized tri- and tetra-substituted alkenes. These are the chiral analogue of the Crabtree catalyst,[8] [Ir(pyridine)(Cy_3P)(COD)]PF_6 (Cy = cyclohexyl, COD = cyclooctadiene) that provided the reason for ~~the~~ this preliminary investigation. In addition, these iridium *N,P*-ligand based catalysts presentedfavorable results of asymmetric hydrogenation of various functionalized alkenes and imines.

Our research is focused on the development of new ligands for Ir-catalyzed asymmetric hydrogenation of olefins and imines that display high activities and selectivities.[9] Iridium complexes of phosphine-oxazoline ligands derived from bicyclic proline (Scheme **1**)such as **1** are highly effective catalysts for asymmetric hydrogenation of both olefins and imines.[10] It was discovered that the removal of the additional chiral center in complex **1** by replacement of the oxazoline with thiazole rings to produce complex **2**, generated catalysts that continue to display high activities andenatioselectivities for asymmetric hydrogenation of various alkenes, especially trisubstituted ones.[11]

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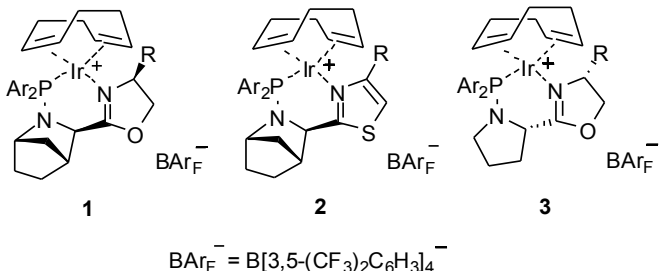


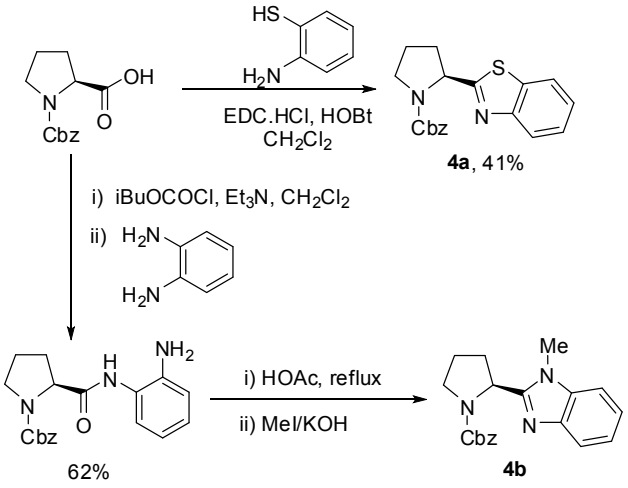
Scheme 1. Examples of Proline-based Ir-complexes

The Gilbertson group has synthesized a series of Ir-complexes **3** derived from proline-based phosphine-oxazoline ligand and has demonstrated their potential as catalysts for asymmetric hydrogenation of highly substituted olefins.[12]

The objective of this study was to synthesize Ir-complexes of *N*,*P*-ligands derived from L-proline and evaluate them as chiral catalysts for asymmetric hydrogenation of trisubstituted olefins.

Results and Discussion

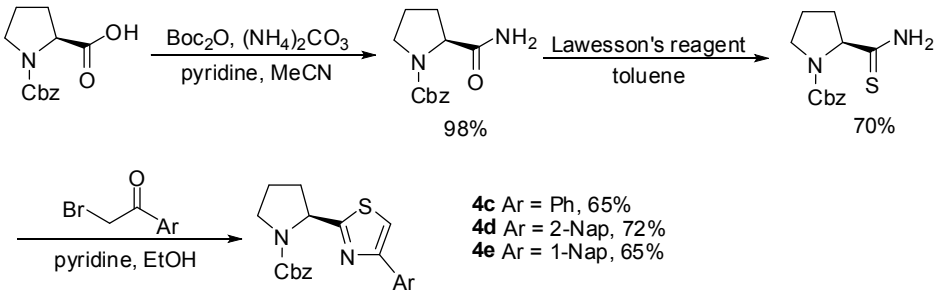
Five proline-based *N*,*P*-ligand precursors were prepared from Cbz-L-proline as shown in Schemes **2** and **3**. The benzothiazole ligand precursor (**4a**) was synthesized by amide coupling with 2-aminothiophenol and Cbz-L-proline. The benzothiazole ring formed spontaneously without formation of the intermediate aminothioester/amidethiol. However the corresponding reaction with *o*-phenylenediamine produced the mono-amide, that was first cyclized by refluxing in acetic acid[13] and secondly underwent N-methylation with MeI in the presence of KOH as a base to form the desired benzimidazole (**4b**). Chiral HPLC analysis revealed that no racemization occurred during both reaction sequences (>99%).The thiazole ligand precursors were also prepared from simple Cbz-protected L-proline. In this reaction the acid functionality of L-proline was first converted to the corresponding amide precursor in the presence of Boc_2O, $(NH_4)_2CO_3$ and pyridine in acetonitrile with a 98% yield.



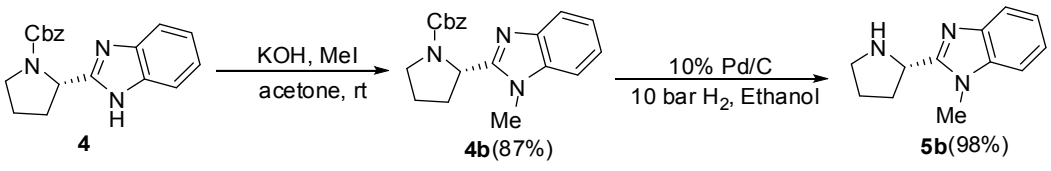
Scheme 2. Synthesis of Proline based bezothiazole/benzimidazole ligands

The amide group reacted with Lawesson's reagent and formed thiomide in 70% yield. The Cbz-protected L-proline thioamide[14]cyclized with α-bromoketones in the presence of pyridine in ethanol (Scheme **3**) to produce the different types of thiazole ligands. In the case of the ligand with the phenyl substitutent, the reaction was initially performed with phenacyl bromide (R = Ph) using the reflux conditions as described by Pichota.[15]Although the desired product **4c** was obtained in 63% yield, some racemization occurred which resulted in the cyclized product of only 90% ee according to chiral HPLC analysis. When the reaction was carried out at room temperature, the product was obtained in 65% yield and >99% ee. Using the same procedure, the ligand precursors **4d** and **4e** carrying bulky 2- and 1-naphthyl substitutents was prepared with 72% and 65% yield and enantiomeric purity >99% ee.

The ligand precursors **4a**–**4e**were then subjected to two different methods for Cbz-deprotection. One method was effective for ligand precursors **4b**, where the deprotection was carried out in the presence of 10% (Pd/C) in ethanol at10 bar hydrogen pressure in the reaction vessel to give **5b** in 98% yield (Scheme**4**).



Scheme 3. Synthesis of Proline based thiazole ligands

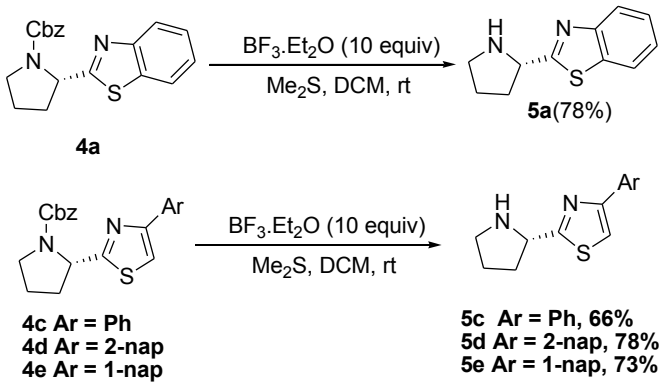


Scheme 4. Deprotection of Cbz-group from benzimidazole ligand

The second method for the deprotection of ligand precursors **4a**, **4c**, **4d** and **4e** was by treatment with 10 equiv of $BF_3.Et_2O$, dimethyl sulphide in dry dicholoromethane to produce various N-H prolinethiazole ligands **5a**, **5c**, **5d** and **5e** in good yields (Scheme **5**).

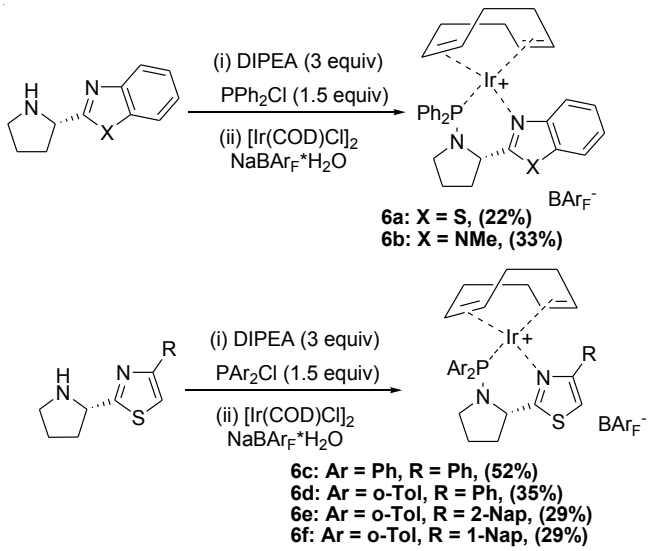
Phosphanylation of the pyrrolidine nitrogen atoms of all the ligands **5a-5e***via* Ar_2PCl (Ar = Ph or 2-Tolyl) and complex formation with $Ir(COD)_2Cl_2$was achieved. This was followed by counterion exchange with $NaBAr_F$ in a one pot reaction to furnish the iridium complexes **6a**–**6f** in moderate to good overall yield in the range of 22-33% (**6a** and **6b**) and 29-52% (**6c-6f**) (Scheme **6**). In the first step N-H prolinethiazole ligands react with di-arylphosphine chloride in the presence of N,N-diisopropylethylamineform the N,P ligands precursors. In the second step the precursors form a complex with $Ir(COD)_2Cl_2$ followed by counter anion exchange with NaBArF*H_2O .

The iridium complexes **6a**–**6f** were evaluated as catalysts for asymmetric hydrogenation of various trisubstituted alkenes (**7a**–**7e**, see Table **1**). The thiazole complex **6c** consistently gave superior results (84–99% ee) for most substrates tested compared to the benzothiazole and benzimidazole complexes **6a** and **6b**. Most notably, hydrogenation of the cyclic alkene substrate **7e** catalyzed by the thiazole complex **6c** gave the hydrogenated product in 84% ee compared to only 11% and 26% obtained from the complexes **6a** and **6b**, respectively.



Scheme 5. Deprotection of Cbz-group from benzothiazole/thiazole ligand

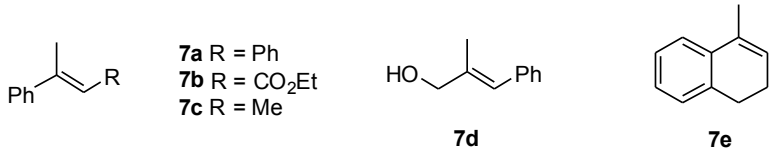
On the other hand, ethyl 3-methylcinnamate (**7b**) gave the *S*-enantiomer of the hydrogenated product in only 47% ee with **6c**. This particular substrate also yielded poor results with the complexes **6a** and **6b**, affording the almost same enantiomer of the product with *ee* values of 64% and 68% respectively. The enantioselectivity against this particular substrate was improved dramatically when the phosphine substituent was changed from phenyl in complex **5c** to the more sterically hindered *o*-tolyl group in **6d**, while the enantioselectivities against other substrates remained the same.



Scheme 6. Phophanylation and complex formation of imidazole/thiazole ligand

An additional advantage of the *o*-tolyl complexes is that the conversions improve considerably and in most cases, complete conversion (>99%) was observed. Further increasing the steric bulkiness of the thiazole substituent in **6d** by replacing the phenyl with 2-naphthyl (**6e**) and 1-naphthyl (**6f**) groups resulted in marginal improvement. The complex **6e** gave thehighest enantioselectivities with substrates **7a**, **7b** and **7c** while the complex **6f** appeared to be more general for this particular set of substrates. The enantioselectivities obtained with the best catalyst **6f** (84–97%) compares favorably with more structurally complexes with multiple chiral centers for the same set of substrates. For example, complex**2** derived from bicyclic proline gave ee in the range of 83–97% (Ar = Ph; R = Ph) and 76–99% (Ar = *o*-Tol; R = Ph)[11]. The proline-oxazoline complex **3** (Ar = 2-EtC_6H_4; R = ^{t}Bu) developed by Gilbertson[12] gave ee in the range of 68–94% for the same set of substrates.

Table 1. Results for the evaluation of complexes **6** as catalyst for asymmetric hydrogenation of various trisubstituted alkenes



Complex	6a		6b		6c		6d		6e		6f	
Substrate	conv.	ee	conv.	ee	conv.	ee	conv.	ee	conv.	ee	conv.	ee
7a	73	87(S)	51	82(S)	31	95(S)	87	95(S)	>99	96(S)	>99	97(S)
7b	84	64(S)	86	68(S)	61	47(S)	>99	91(S)	>99	94(S)	>99	84(S)
7c	>99	71(2)	>99	78(2)	>99	94(2)	>99	92(2)	>99	93(2)	>99	91(2)
7d	99	52(S)	71	38(S)	98	88(S)	>99	86(S)	>99	88(S)	>99	94(S)
7e	97	11(1)	73	26(1)	95	84(1)	>99	62(1)	>99	64(1)	>99	89(1)

Conclusion

In this study we have developed a series of simple proline based heterocyclic *N,P*- ligands for the asymmetric hydrogenation of olefins. Theseproline based thiazoles ligands efficiently catalyze both functionalized and unfunctionalizedtrisubstituted alkenes. The results, based on theenantioselectivity obtained in this hydrogenation, are among the best compared to what has been reported in literature.

Experimental Section

Experimental

Benzothiazole 4a

Cbz-L-proline (0.550 g, 2.2 mmol) was treated with 2-aminothiophenol (2 mmol) and EDC·HCl (2 mmol) in CH_2Cl_2 (5 mL) at room temperature overnight. The mixture was diluted with more CH_2Cl_2 (20 mL) and washed three times with water (3×20 mL). The combined organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by column chromatography (EtOAc:hexanes 1:4; R_f = 0.35) to give the desired product as yellow oil (0.278 g, 41%). The enantiomeric excess as determined by chiral HPLC was >99% (Chiralcel OD-H 0.46×25 cm; ^{i}PrOH:*n*-hexane 1:9, flow rate 0.5 mL/min; t_R(*S*) = 26.2 min, t_R (*R*) = 32.8 min).

^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 7.95 (d *J* = 5.7 Hz, 1H, ArH), 7.85 (d, *J* = 7.6 Hz, 1H, ArH), 7.50–6.90 (m, 7H, ArH), 5.44–5.05 [m, 3H, CH_2 Cbz and CH(2′)], 3.80–3.58 [m, 2H, CH_2 (5′)], 2.50–2.00 [m, 4H, CH_2(3′) and CH_2(4′)]; ^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 176.2 and 175.3 (C), 154.8 (CO Cbz), 153.1 (C), 136.6 (C), 136.2 (C), 134.6 (C), 128.5 (CH), 128.2 (CH), 128.1 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 126.1 (CH), 125.0 (CH), 122.8 (CH), 121.7 (CH), 67.3 (CH_2 Cbz), 60.0 and 59.8 [CH (2′) rotamers], 47.3 and 47.0 [CH_2 (5′) rotamers], 34.2 and 33.0 [CH_2 (3′) rotamers], 24.1 and 23.3 [CH_2 (4′) rotamers]; $[\alpha]_D^{25}$= -108.8 (*c*=1, $CHCl_3$); IR ν_{max}(cm^{-1}) 2169, 1636 ,1572, 1459, 952; HRMS (ESI+) $C_{19}H_{18}N_2O_2S{\cdot}Na^+$ *m/z* calcd: 361.0987, found: 361.0999.

Cbz-L-proline Benzimidazole 4

Cbz-L-proline (1.001 g, 4 mmol) was treated with *o*-phenylenediamine (0.429 g, 3.8 mmol) and dicyclohexylcarbodiimide (0.873 g, 4 mmol) in CH_2Cl_2 (10 mL) at room temperature overnight. The dicyclohexylurea precipitate was filtered off and the solvent was removed under reduced pressure. The residue was dissolved in glacial acetic acid (5 mL) and heated at 60 ^{o}C for 2 hours. After removal of the solvent, the residue was partitioned in water/CH_2Cl_2 and extracted with CH_2Cl_2 (3×20 mL). The combined organic extracts were washed with brine and dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The residue was purified by column chromatography (EtOAc:hexanes 1:4; R_f = 0.32) to the product give as yellow oil (0.74 g, 58% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 7.62–7.10 (m, 9H, ArH), 5.35–5.15 [m, 3H, CH_2Cbz and CH_2(2′)], 3.72–3.49 [m, 2H, CH_2 (5′)], 3.08–2.95 and 2.62–1.90 (m, 4H, CH_2(3′) and CH_2(4′)]; ^{13}C NMR (100 MHz, $CDCl_3$) δ(ppm): 156.8 (CO Cbz), 154.2 (C), 137.6 (C), 136.2 (C), 128.6 (CH), 128.2 (CH), 127.8 (CH), 123.0 (C), 122.8 (CH), 115.1 (CH), 67.6 (CH_2 Cbz), 55.5 and 55.2 [CH_2 (2′) rotamers], 47.6 and 47.2 [CH_2 (5′) rotamers], 32.3 and 28.6 [CH_2 (3′) rotamers], 24.9 and 23.9 [CH_2 (4′) rotamers]; $[\alpha]_D^{25}$= -109.5 (*c*=1, $CHCl_3$); IR ν_{max}(cm^{-1}): 2150, 1674 ,1585, 1468, 1296; HRMS (ESI+) $C_{19}H_{19}N_3O_2{\cdot}Na^+$*m/z*calcd: 344.1375, found: 344.1397.

Cbz-L-proline N-methyl Benzimidazole 4b

Compound **4** (100 mg, 0.31 mmol, 1 eq) was dissolved in acetone (3 mL). KOH pellets (207 mg) were added followed by MeI (0.12 mL, 1.93 mmol, 6 eq) and reaction solution was stirred for 6.5 hours. Water (10 mL) was added and acetone was evaporated under reduced pressure. The product was extracted with DCM (2 x 15 mL), the combined organic phase was washed with brine (20 mL), dried over Na_2SO_4 and evaporated. Chromatography on silica (pentane:EtOAc 75:25 to 0:100) afforded 91 mg (87 %) of compound **4b** as a solid**.** ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 7.62 (t, 1H, *J* = 8.3 Hz), 7.49 (dd, 1H, *J* = 7.8, *J* = 7.3 Hz), 7.40-7.10 (m, 5H), 6.98 (t, 1H, *J* = 6.8 Hz), 6.78 (d, 1H, *J* = 6.8 Hz), 5.24 (brs, 1H), 5.10-4.80 (m, 2H), 3.84 (s, 2H), 3.72-3.60 (m, 2H), 3.54 (t, 1H, *J* = 7.8 Hz), 2.40-1.86 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 155.2, 153.4, 141.8, 136.4, 135.4, 127.6, 127.0, 126.6, 121.2, 120.8, 118.3, 109.2, 65.5, 52.7, 46.2, 31.6, 29.1, 23.0; $[\alpha]_D^{25}$= -31.1 (*c*=1, $CHCl_3$); IR ν_{max}(cm^{-1}) 2879, 1695, 1615, 1453, 1149, 855, 740; HRMS (ESI+) $C_{20}H_{21}N_3O_2{\cdot}H^+$*m/z* calcd: 336.1707, found: 336.1718.

Cbz-L-proline thioamide

A mixture of Cbz-L-proline (2.5 g, 10 mmol), Boc_2O (2.02 g, 10 mmol,), $(NH_4)_2CO_3$ (1.06 g 10 mmol) and pyridine (0.16 mL 2 mmol) in acetonitrile (20 mL) was stirred at room temperature overnight. The acetonitrile was removed and the residue partitioned in water/EtOAc and extracted with EtOAc (3×20 mL). The combined organic layers were washed with water, brine and dried over Na_2SO_4 and the solvent removed under reduced pressure. The crude Cbz-L-prolinamide (assume quantitative yield) was treated with Lawesson's reagent (5 mmol, 2.02 g) in THF (10 mL). After stirring at room temperature overnight, the solvent was removed under vacuum and the residue extracted with EtOAc (3×20 mL). The combined organic layer was dried over Na_2SO_4 and the solvents removed under reduced pressure. The residue was purified by column chromatography (EtOAc:hexanes7:3; R_f = 0.45) to give a pale yellow oil (2.37 g, 90 % yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 8.34 and 8.10 (br m, 2H, NH_2), 7.40–7.31 (m, 5H, ArH), 5.20–5.12 (m, 2H, CH_2 Cbz), 4.78–4.72 [m, 1H, CH(2′)], 3.65–3.50 [m, 2H, CH_2(5′)], 2.45–1.80 [m, 4H, CH_2 (3′) and CH_2(4′)]; ^{13}C NMR (100 MHz, $CDCl_3$) δ(ppm): 208.6 (C=S), 155.5 (C Cbz), 136.2 (C), 128.6 (CH), 128.2 (CH), 127.9 (CH), 67.6 (CH_2 Cbz), 66.2 [CH_2(2′) rotamer], 47.7 [CH_2(5′)], 32.4 [CH_2(3′)], 24.0 [CH_2(4′)] ppm.

Phenylthiazole 4c

Cbz-L-proline thioamide (0.801 g, 3.25 mmol) was treated with phenacyl bromide (0.597 g, 3 mmol) and pyridine (1 mL) in CH_2Cl_2 (10 mL). The mixture was stirred at room temperature overnight. The mixture was extracted with CH_2Cl_2 (3×20 mL). The organic layer was dried with Na_2SO_4 and the solvent removed under reduced pressure. The residue was purified by column chromatography (EtOAc:hexanes; 1:4, R_f 0.32) to give yellow oil product (0.776 g, 71% yield). The enantiomeric excess as determined by chiral HPLC was >99% (Chiralcel OD-H 0.46×25 cm; ^{i}PrOH:*n*-hexane 1:9, flow rate 0.5 mL/min; t_R(*S*) = 24.9 min, t_R (*R*) = 32.7 min).

^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 7.75 (d, *J* = 7.5 Hz, 2H, ArH), 7.30–6.95 (m, 9H, ArH), 5.28–4.90 [m, 3H, CH_2 Cbz and CH(2′)], 3.65–3.35 [m, 2H, CH_2 (5′)], 2.30–1.75 [m, 4H, CH_2(3′) and CH_2(4′)]; ^{13}C NMR (100 MHz, $CDCl_3$) δ(ppm): 174.5 and 173.4 [(C) rotamers], 155.4 (C Cbz), 155.2 and 154.8 [(C) rotamers], 136.8 and 136.4 [(C) rotamers], 134.7 and 134.5 [(C) rotamers], 128.7 (CH), 128.5–127.7(CH), 126.4 (CH), 112.6 and 112.3 [(C) rotamers], 67.1 (CH_2 Cbz), 59.6 and 59.5 [CH_2(2′) rotamer], 47.2 and 46.8 [CH_2(5′) rotamers], 34.2 and 32.8 [CH_2(3′) rotamers], 24.0 and 23.1 [CH_2(4′) rotamers] ppm; $[\alpha]_D^{25}$= -61.4 (*c*=1, $CHCl_3$); IR ν_{max}(cm^{-1}): 2182, 1654 ,1571, 1465, 952; HRMS (ESI+) $C_{21}H_{20}N_2O_2S{\cdot}Na^+$*m/z* calcd: 387.1143, found : 387.1177.

2-Naphthylthiazole 4d

Cbz-L-proline thioamide (0.530 g, 2.2 mmol) was treated with 2-bromoacetylnaphthalene (0.510 g, 2 mmol) and pyridine (0.8 mL) in CH_2Cl_2 (5 mL). Following the same procedure described for compound **4c** above, the desired product was obtained as a yellow oil (0.588 g, 71% yield) after column chromatography (EtOAc:hexanes 1:4; R_f 0.33). The enantiomeric excess as determined by chiral HPLC was 99% (Chiralcel OD-H 0.46×25 cm; ^{i}PrOH:*n*-hexane 1:9, flow rate 0.5 mL/min; t_R(*S*) = 27.6 min, t_R (*R*) = 34.9 min).

^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 8.45 (s, 1H, ArH), 8.00–7.80 (m, 4H, ArH), 7.55–7.15 (m, 8H, ArH), 5.50–5.10 [m, 3H, CH_2 Cbz and CH(2′)], 3.85-3.55 [m, 2H, CH_2(5′)], 2.50–2.00 [m, 4H, CH_2(3′) and CH_2(4′)]; ^{13}C NMR (100 MHz, $CDCl_3$) δ(ppm) : 175.2 and 174.1 [(C) rotamers], 155.2 (C), 154.8 (C), 136.7 and 136.3 [(C) rotamers], 133.6 and 133.2 [(C) rotamers], 131.5 (C) , 128.5 (CH), 127.9–127.8 (CH), 127.7 (CH), 126.4 (CH), 126.2 (CH), 125.5 (CH), 124.3 (CH), 112.9 and 112.7 [(CH) rotamers], 67.2 (CH_2 Cbz), 59.5 [CH_2 (2′) rotamers], 47.2 and 46.9 [CH_2 (5′) rotamers], 34.3 and 33.0 [CH_2 (3′) rotamers], 24.0 and 23.1 [CH_2 (4′) rotamers]; $[\alpha]_D^{25}$= -33.6 (*c*=1, $CHCl_3$); IR ν_{max}(cm^{-1}): 2186, 1673 ,1576, 1463, 961; HRMS (ESI+) $C_{25}H_{22}N_2O_2S{\cdot}Na^+$*m/z* calcd: 437.1300, found: 437.1307.

1-Naphthylthiazole 4e

Cbz-L-proline thioamide (0.530 g, 2.2 mmol) was treated with 1-bromoacetylnaphthalene (0.512 g, 2 mmol) and pyridine (0.8 mL) in CH_2Cl_2 (5 mL). Following the same procedure described for compound **4c** above, the desired product was obtained as a yellow oil (0.538 g, 65% yield) after column chromatography (EtOAc:hexanes 1:4; R_f 0.35). The enantiomeric excess as determined by chiral HPLC was >99% (Chiralcel OD-H 0.46×25 cm; ^{i}PrOH:*n*-hexane 1:9, flow rate 0.5 mL/min; t_R(*S*) = 30.8 min, t_R (*R*) = 36.8 min).

^{1}H (400 MHz, $CDCl_3$) δ(ppm): 8.30–8.15 (m, 1H, ArH), 7.95–7.90 (m, 2H, ArH), 7.75–7.70 (m, 1H, ArH), 7.56–7.15 (m, 9H, ArH), 5.55–5.10 [m, 3H, CH_2 Cbz and CH(2′)], 3.82–3.60 [m, 2H, CH_2(5′)], 2.55-2.00 [m, 4H, CH_2(3′) and CH_2(4′)]; ^{13}C NMR (400 MHz, $CDCl_3$) δ(ppm): 175.0 and 174.9 [(C) rotamers], 155.4 and 154.9 (C), 154.5 (C), 136.5 (C), 134.0 (C), 132.0 (C), 131.4 (C),130.2 (C), 129.1 (CH), 128.4 (CH), 128.1 (CH), 127.9 (CH), 127.8 (CH), 126.6 (CH), 125.7–125.6 (CH), 125.3 (CH), 116.6 and 116.4 [(CH) rotamers], 67.2 (CH_2 Cbz), 59.6 and 59.4 [CH_2 (2′) rotamers], 47.3 and

47.0 [CH_2(5′) rotamers], 34.4 and 33.1 [CH_2 (3′) rotamers], 24.0 and 23.2 [CH_2 (4′) rotamers]; $[\alpha]_D^{25}$= -40.9 (*c*=1, $CHCl_3$); IR ν_{max}(cm^{-1}) 2184, 1674 ,1575, 1469, 956; HRMS (ESI+) $C_{25}H_{22}N_2O_2S{\cdot}Na^+$ *m/z* cald: 437.1300, found : 437.1311.

(S)-2-(pyrrolidin-2-yl)benzo[d]thiazole (5a)

Under nitrogen atmosphere Compound **4a** (0.15 g, 0.44 mmol, 1 eq) and DCM (4 mL) was added, followed by dimethyl sulfide (0.88 mL) and $BF_3{*}OEt_2$ (0.56 mL, 4.4 mmol, 10 eq). The reaction was stirred at room temperature for 3 hours, after that another portion of dimethyl sulfide (0.71 mL) was added and stirring was continued for 2.5 hours. On completion by TLC, reaction was quenched with aqueous 7% ammonia (10 mL), and then product was extracted with DCM (2 x 20 mL). The combined organic phase was washed with brine (20 ml) and dried over Na_2SO_4. Then the solvent was evaporated to reduce the volume. Residue was purified by chromatography on silica (DCM:MeOH 100:0 to 92:8) to give 71 mg (78%) of compound **5a** as crystalline product. ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 7.94 (d, 1H, *J* = 8.3 Hz), 7.84 (d, 1H, *J* = 7.8 Hz), 7.43 (t, 1H, *J* = 7.3 Hz), 7.33 (t, 1H, *J* = 7.8 Hz), 4.72-4.66 (m, 1H), 3.22-3.08 (m, 2H), 2.93 (brs, 1H), 2.42-2.33 (m, 1H), 2.12-2.04 (m, 1H), 1.96-1.82 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 179.8, 154.0, 135.2, 125.9, 124.6, 122.7, 121.8, 60.2, 47.2, 34.0, 25.8; $[\alpha]_D^{25}$= +81.9 (*c*=1, $CHCl_3$); IR ν_{max}(cm^{-1}) 3314, 2860, 1600, 1443, 1317, 1190, 956; HRMS (ESI+) $C_{11}H_{12}N_2S{\cdot}Na^+$ *m/z*calcd: 227.0721, found: 227.0729.

(S)-1-methyl-2-(pyrrolidin-2-yl)-1-H-benzo[d]imidazole (5b)

Compound **4b** (67 mg, 0.20 mmol) was dissolved in 99.5 % ethanol (5 mL). Pd/C(10%) (12 mg) was added to the reaction mixture and after applying a 10 bar hydrogen pressure, reaction was stirred for 2 hours. The reaction solution was filtered through a short plug of Celite and solvent was evaporated to afford 40 mg (quant.) of compound **5b** that was used in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 7.70 (d, 1H, *J* = 7.8 Hz), 7.26-7.18 (m, 3H), 4.44 (t, 1H, *J* = 7.3 Hz), 3.96 (brs, 1H), 3.70 (s, 3H), 3.29-3.22 (m, 1H), 3.02-2.95 (m, 1H), 2.28-2.20 (m, 1H), 2.08-1.85 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 155.8, 142.0, 136.3, 122.5, 122.0, 119.4, 109.2, 55.0, 47.2, 31.6, 29.8, 26.1; $[\alpha]_D^{25}$= -36.9 (*c*=1, $CHCl_3$); IR ν_{max}(cm^{-1}) 3298, 2943, 1616, 1281, 921, 739; HRMS (ESI+) $C_{12}H_{15}N_3{\cdot}Na^+$ *m/z*calcd: 224.1266, found: 224.1272.

(S)-4-phenyl-2-(pyrrolidin-2-yl)thiazole (5c)

According to synthesis of general procedure of **5a**, following amounts were used: Compound **4c** (207 mg, 0.57 mmol, 1 eq), DCM (6 mL), dimethyl sulfide (1.1 mL+ 0.89 mL) and $BF_3{*}OEt_2$ (0.72 mL, 5.7 mmol, 10 eq). Chromatography on silica (DCM:MeOH 100:0 to 90:10) afforded 86 mg (66 %) of compound **5c** as crystalline product. ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 7.87 (d, 2H, *J* = 7.3 Hz), 7.43-7.38 (m, 2H), 7.36 (s, 1H), 7.33-7.28 (m, 1H), 4.62 (t, 1H, *J* = 7.3 Hz), 3.96 (brs, 1H), 3.24-3.10 (m, 2H), 2.39-2.30 (m, 1H), 2.11-2.03 (m, 1H), 1.95-1.83 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 176.5, 155.4, 134.6, 128.6, 127.8, 126.2, 112.6, 59.7, 46.7, 33.8, 25.2; $[\alpha]_D^{25}$= -86.5 (*c*=1, $CHCl_3$); IR ν_{max}(cm^{-1}) 2964, 1760, 1600, 1496, 1298, 1189, 902, 834; HRMS (ESI+) $C_{13}H_{14}N_2S{\cdot}Na^+$ *m/z*calcd: 253.0878, found: 253.0871.

(S)-4-(napthalen-2-yl)-2-(pyrrolidin-2-yl)thiazole (5d)

According to synthesis of general procedure of **5a**, following amounts were used: Compound **4d** (146 mg, 0.35 mmol, 1 eq), DCM (5 mL), dimethyl sulfide (0.70 mL + 0.56 mL) and $BF_3{*}OEt_2$ (0.45 mL, 3.55 mmol, 10 eq). Chromatography on silica (DCM:MeOH 100:0 to 90:10) afforded 77 mg (78 %) of compound **5d** as crystalline product. ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 8.42 (s, 1H), 8.02-7.80 (m, 4H), 7.53-7.44 (m, 3H), 4.74-4.66 (m, 1H), 3.38 (brs, 1H), 3.27-3.07 (m, 2H), 2.45-2.32 (m, 1H), 2.20-1.82 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 177.8, 155.6, 133.8, 133.2, 132.2, 128.6, 128.4, 127.8, 126.4, 126.1, 125.3, 124.4, 113.2, 59.9, 47.0, 34.2, 25.6; $[\alpha]_D^{25}$= +95.5 (*c*=1, $CHCl_3$); IR ν_{max}(cm^{-1}) 3304, 2968, 2841, 1627, 1490, 1358, 1180, 948, 856; HRMS (ESI+) $C_{17}H_{16}N_2S{\cdot}Na^+$ *m/z*calcd: 303.0926, found: 303.0936.

(S)-4-(napthalen-1-yl)-2-(pyrrolidin-2-yl)thiazole (5e)

According to synthesis of general procedure of **5a**, following amounts were used: Compound **4e** (158 mg, 0.38 mmol, 1 eq), DCM (5 mL), dimethyl sulfide (0.75 mL + 0.61 mL) and $BF_3{*}OEt_2$ (0.48 mL, 3.79 mmol, 10 eq). Chromatography on silica (DCM:MeOH 100:0 to 92:8) afforded 78 mg (73 %) of compound **5e** as crystalline product. ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 8.30-8.20 (m, 1H), 7.94-7.80 (m, 2H), 7.68 (d, 1H, *J* = 6.8 Hz), 7.57-7.44 (m, 3H), 7.34 (s, 1H), 4.77-4.66 (m, 1H), 3.26-3.04 (m, 3H), 2.44-2.30 (m, 1H), 2.15-2.04 (m, 1H), 2.02-1.81 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 177.6, 155.2, 134.1, 133.2, 131.6, 128.8, 128.4, 127.6, 126.5, 126.0, 125.4, 116.7, 59.9, 47.1, 34.2, 25.7; $[\alpha]_D^{25}$= -69.0 (*c*=1, $CHCl_3$); IR ν_{max}(cm^{-1}) 3318, 2868, 1733, 1592, 1456, 1140, 902, 804, 751; HRMS (ESI+) $C_{17}H_{16}N_2S{\cdot}Na^+$ *m/z*calcd: 303.0926, found: 303.0948.

Complex 6a

In dry toluene (2 mL), compound **5a** (63 mg, 0.31 mmol, 1 eq) was added under argon followed by DIPEA (0.16 ml, 0.92 mmol, 3 eq) and reaction was cooled in ice bath. The diphenylphosphine chloride (86 ml, 0.46 mmol, 1.5 eq) was added drop wise and reaction was stirred for 1.5 hours. On completion of reaction by ^{1}H NMR, solution was filtered through a plug of cotton and solids were washed with dry toluene. The clear solution was evaporated and the residue was co-evaporated with dry toluene (3 x 6 mL) to remove DIPEA. Dry DCM (5 mL) was added to the crude phosphine product under argon followed by $[Ir(COD)Cl]_2$ (104 mg, 0.15 mmol, 0.5 eq) and solution was refluxed for 1.5 hour. After cooling to room temperature, water (5 mL) was added followed by $NaBAr_{F*}H_2O$ (348 mg, 0.37 mmol, 1.2 eq) and solution was stirred vigorously for 30 minutes. The product was extracted with DCM (2 x 15 mL). The combined organic phase was dried over Na_2SO_4, evaporated and the residue was purified by chromatography on silica (DCM:pentane 1:1) to give 104 mg (22 %) of complex **6a** as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 8.40 (d, 1H, *J* = 8.3 Hz), 7.86 (d, 1H, *J* = 7.8 Hz), 7.78-7.71 (m, 9H), 7.58-7.46 (m, 10H), 7.37-7.20 (m, 5H), 5.82-5.76 (m, 1H), 5.01-4.88 (m, 2H), 4.10 (brs, 1H), 3.38-3.30 (m, 1H), 2.83-2.62 (m, 4H), 2.52-2.05 (m, 7H), 1.92-1.82 (m, 1H), 1.75-1.66 (m, 1H), 1.52-1.40 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 176.3, 162.9, 162.2, 161.5, 160.9, 150.0, 135.0, 134.6 (d, *J* = 14.8 Hz), 132.6 (d, *J* = 14.8 Hz), 132.3-131.9 (m), 131.2 (d, *J* = 10.8 Hz), 130.2, 129.5-128.7 (m), 128.5, 127.9, 126.5, 125.8, 123.8, 122.9, 121.8, 119.3, 117.9-117.4 (m), 98.3 (d, *J* = 10.3 Hz), 90.2 (d, *J* = 14.3 Hz), 67.7, 66.0, 64.8 (d, *J* = 14.3 Hz), 46.7-46.5 (m), 37.2-36.8 (m), 33.8, 30.9 (d, *J* = 8.0 Hz), 28.4, 27.0-26.7 (m), 25.9; ^{31}P NMR (202 MHz, $CDCl_3$) δ(ppm): 53.6 (s); ^{19}F NMR (337 MHz, $CDCl_3$) δ(ppm): -62.8; $[\alpha]_D^{25}$= +33.9 (*c*=1, $CHCl_3$); IRν_{max}(cm^{-1}) 2960, 2029, 1610, 1459, 1353, 1115, 929, 885, 745. HRMS (ESI): Calcd. for $C_{31}H_{33}IrN_2PS^+$ (M^+): 689.1725, found: 689.1788.

Complex 6b

According to the synthesis of general procedure **6a**, following amounts were used: the compound **5b** (40 mg, 0.20 mmol, 1 eq), DIPEA (0.10 mL, 0.57 mmol, 3 eq), diphenylphosphine chloride (55 µL, 0.30 mmol, 1.5 eq), $[Ir(COD)Cl]_2$ (67 mg, 0.10 mmol, 0.5 eq) and $NaBAr_{F*}H_2O$ (224 mg, 0.24 mmol, 1.2 eq). The compound **6b** 101 mg (33 %) was isolated as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 7.96 (d, 1H, *J* = 8.3 Hz), 7.76-7.60 (m, 10 H), 7.54-7.20 (m, 15H), 5.78-5.72 (m, 1H), 5.22-5.15 (m, 1H), 4.82 (brs, 1H), 3.88-3.78 (m, 4H), 3.38-3.30 (m, 1H), 2.83-2.76 (m, 1H), 2.70-2.34 (m, 5H), 2.30-2.02 (m, 4H), 1.92-1.83 (m, 1H), 1.75-1.66 (m, 1H), 1.58-1.24 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 162.9, 162.2, 161.5, 160.9, 154.8, 138.8, 135.5-134.9 (m), 133.3, 132.6-132.3 (m), 131.9, 131.3 (d, *J* = 10.8 Hz), 130.1, 129.9-128.7 (m), 127.5, 126.7-126.4 (m), 125.8, 125.2, 122.9, 119.3, 117.8-117.4 (m), 111.7, 98.3 (d, *J* = 11.4Hz), 91.2 (d, *J* = 14.3 Hz), 65.4, 63.8, 63.3 (d, *J* = 13.1Hz), 46.1, 36.6, 33.0 (d, *J* = 27.4 Hz), 30.0-29.5 (m), 28.9, 27.5 (d, *J* = 4.5 Hz), 26.5; ^{31}P NMR (202 MHz, $CDCl_3$) δ(ppm): 54.6 (s); ^{19}F NMR (337 MHz, $CDCl_3$) δ(ppm): -62.8; $[\alpha]_D^{25}$= +35.3 (*c*=1, $CHCl_3$); IRν_{max}(cm^{-1}) 3290, 2948, 2036, 1610, 1454, 1115, 923, 742. HRMS (ESI): Calcd. for $C_{32}H_{36}IrN_3P^+$ (M^+): 686.2271, found: 686.2328.

Complex 6c

According to the synthesis of general procedure **6a**, following amounts were used: the compound **5c** (47 mg, 0.20 mmol, 1 eq), DIPEA (0.11 mL, 0.63 mmol, 3 eq), diphenylphosphine chloride (57 µL, 0.31 mmol, 1.5 eq), $[Ir(COD)Cl]_2$ (69 mg, 0.10 mmol, 0.5 eq) and $NaBAr_{F*}H_2O$ (230 mg, 0.24 mmol, 1.2 eq). The compound **6c** 166 mg (52 %) was isolated as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 7.78-7.70 (m, 9H), 7.56-7.28 (m, 19H), 5.86-5.66 (m, 1H), 4.68 (brs, 1H), 4.01 (brs, 1H), 3.30-3.13 (m, 1H), 3.10-2.90 (m, 3H), 2.85-2.65 (m, 1H), 2.45-2.06 (m, 7H), 1.98-1.80 (m, 1H), 1.37-1.16 (m, 3H);^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 175.0, 162.9, 162.2, 161.5, 160.9, 158.7, 135.0, 133.0, 132.4-130.8 (m), 130.1, 129.8-128.8 (m), 128.4, 126.5, 125.6, 124.8, 122.9, 119.3, 117.9-117.4 (m), 116.6, 96.7 (d, *J* = 10.8Hz), 90.8(d, *J* = 14.3 Hz), 66.4, 64.5 (d, *J* = 14.3 Hz), 63.9, 47.6-47.4 (m), 36.7 (d, *J* = 4.0Hz), 33.5 (m), 31.3 (d, *J* = 8.0 Hz), 28.4, 27.3 (d, *J* = 4.5 Hz), 25.5; ^{31}P NMR (202 MHz, $CDCl_3$) δ(ppm): 50.4 (s); ^{19}F NMR (337 MHz, $CDCl_3$) δ(ppm): -62.8; $[\alpha]_D^{25}$= +19.1 (*c*=1, $CHCl_3$); IRν_{max}(cm^{-1}) 2876,1610, 1352, 1160, 930, 887, 743. HRMS (ESI): Calcd. for $C_{33}H_{35}IrN_2PS^+$ (M^+): 715.1882, found: 715.1940.

Complex 6d

According to the synthesis of general procedure 6a, following amounts were used: the compound **5c** (76 mg, 0.33 mmol, 1 eq), DIPEA (0.17 mL, 0.98 mmol, 3 eq), chlorodi(o-tolyl)phosphine (164 mg, 0.66 mmol, 2 eq) dissolved in toluene (2 mL), $[Ir(COD)Cl]_2$ (111 mg, 0.17 mmol, 0.5 eq) and $NaBAr_{F*}H_2O$ (465 mg, 0.49 mmol, 1.5 eq). The compound **6d** 184 mg (35 %) was isolated as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 7.86-7.70 (m, 8H), 7.66-7.44 (m, 8H), 7.42-7.02 (m, 10H), 6.65 (t, 1H, *J* = 9.2 Hz), 5.48 (brs, 1H), 4.72-4.62 (m, 2H), 3.53 (brs, 1H), 3.16-2.94 (m, 5H), 2.82-2.44 (m, 6H), 2.42-1.80 (m, 8H), 1.60-1.48 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 173.2, 162.9, 162.2, 161.5, 160.9, 158.5, 141.4 (d, *J* = 10.8 Hz), 139.5 (d, *J* = 15.0 Hz), 135.3, 133.6, 133.5-132.2 (m), 131.6, 129.8, 128.5, 126.6, 125.4, 124.7, 123.1, 119.3, 117.5, 116.3, 95.7 (d, *J* = 10.6 Hz), 90.2 (d, *J* = 12.0 Hz), 72.8, 67.1, 62.8 (d, *J* = 14.0 Hz), 53.7, 48.2, 35.4, 33.9, 31.5 (d, *J* = 8.0 Hz), 29.6, 28.4, 25.5; ^{19}F NMR (337 MHz, $CDCl_3$) δ(ppm): -62.8; $[\alpha]_D^{25}$= +24.4 (*c*=1, $CHCl_3$); IRν_{max}(cm^{-1})2926, 1610, 1450, 1353, 1116, 886, 753. HRMS (ESI): Calcd. for $C_{35}H_{39}IrN_2PS^+$ (M^+): 743.2195, found: 743.2328.

Complex 6e

According to the synthesis of general procedure 6a, following amounts were used: the compound **5d** (73 mg, 0.26 mmol, 1 eq), DIPEA (0.14 mL, 0.80 mmol, 3 eq), chlorodi(o-tolyl)phosphine (129 mg, 0.52 mmol, 2 eq) dissolved in toluene (2 mL), $[Ir(COD)Cl]_2$ (87 mg, 0.13 mmol, 0.5 eq) and $NaBAr_{F*}H_2O$ (367 mg, 0.39 mmol, 1.5 eq). The compound **6e** 125 mg (29 %) was isolated as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 7.92-7.68 (m, 13H), 7.62-7.43 (m, 9H), 7.37-7.18 (m, 5H), 7.05 (t, 1H, , *J* = 7.3 Hz), 6.62 (t, 1H, , *J* = 9.2 Hz), 5.50-5.46 (m, 1H), 5.30 (brs, 1H), 4.74-4.65 (m, 2H), 3.60-3.50 (m, 1H), 3.12-2.98 (m, 4H), 2.92-2.85(m, 1H), 2.68 (s, 3H), 2.57-2.45 (m, 2H), 2.36-2.04 (m, 5H), 1.82-1.38 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 173.5, 162.9, 162.2, 161.5, 160.9, 158.3, 141.7 (d, *J* = 12.0 Hz), 139.7 (d, *J* = 15.4 Hz), 135.5-134.7 (m), 133.8, 133.4-132.3 (m), 131.8, 130.1, 130.0-127.5 (m), 127.0, 126.5, 124.6, 123.0, 121.4, 119.3, 117.7, 116.5, 92.9 (d, *J* = 8.5 Hz), 82.2 (d, *J* = 16.0 Hz), 72.6, 66.9, 62.5 (d, *J* = 12.5 Hz), 53.5, 48.0, 35.4, 33.7, 31.3 (d, *J* = 7.4 Hz),

29.4, 26.9, 25.0-24.4 (m), 21.3 (d, J = 6.8Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ(ppm): 50.8 (s); ^{19}F NMR (337 MHz, $CDCl_3$) δ(ppm): -62.8; $[\alpha]_D^{25}$ = +51.6 (c=1, $CHCl_3$); IR ν_{max}(cm^{-1})2883, 1610, 1452, 1115, 886, 756. HRMS (ESI): Calcd. for $C_{39}H_{41}IrN_2PS^+$ (M^+): 793.2352, found: 793.2478.

Complex 6f

According to the synthesis of general procedure 6a, following amounts were used: the amine **5e** (67 mg, 0.24 mmol, 1 eq), DIPEA (0.12 mL, 0.69 mmol, 3 eq), chlorodi(o-tolyl)phosphine (133 mg, 0.53 mmol, 2 eq) dissolved in toluene (2 mL), $[Ir(COD)Cl]_2$ (80 mg, 0.12 mmol, 0.5 eq) and $NaBAr_{F*}H_2O$ (337 mg, 0.36 mmol, 1.5 eq). The compound **6f** 115 mg (29 %) was isolated as an orange solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 8.01-7.90 (m, 2H), 7.78-7.69 (m, 10H), 7.62-7.34 (m, 12H), 7.31-7.08 (m, 4H), 6.72 (t, 1H, , J = 9.8Hz), 5.40 (t, 1H, , J = 5.8 Hz), 4.80-4.68 (m, 1H), 4.58-4.48 (m, 1H), 3.50-3.38 (m, 1H), 3.14-2.98 (m, 4H), 2.80-2.45 (m, 7H), 2.36-2.04 (m, 4H), 1.76-1.26 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$); δ(ppm): 173.0, 162.8, 162.3, 161.5, 160.9, 141.7 (d, J = 12.0 Hz), 140.3 (d, J = 15.4 Hz), 135.4-134.8 (m), 133.6, 133.0-132.4 (m), 132.2, 131.8, 131.2, 130.1-128.3 (m), 127.8-126.8 (m), 126.5, 124.5, 123.5, 122.9, 119.3, 118.8, 117.7, 92.0 (d, J = 6.8 Hz), 81.2 72.9, 66.9, 62.0 (d, J = 12.5 Hz), 48.2, 35.4, 33.8, 31.4 (d, J = 6.8 Hz), 29.3, 26.9, 25.0-24.4 (m), 21.4 (d, J = 7.4 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ(ppm): 50.6 (s); ^{19}F NMR (337 MHz, $CDCl_3$) δ(ppm): -62.8; $[\alpha]_D^{25}$= +17.8 (c=1, $CHCl_3$); IRν_{max}(cm^{-1}) 2954, 1610, 1451, 1353, 1273, 1118, 886, 756. HRMS (ESI): Calcd. for $C_{39}H_{41}IrN_2PS^+$ (M^+): 793.2352, found: 793.2385.

General Hydrogenation Procedure:

Alkene Substrate (0.25 mmol) and a magnet were charged into a glass vial. Stock solution of the catalyst (2.07 mg, 1.25 μmol, 0.005 eq, in 1 mL DCM) was added under argon and reaction was stirred at 50 bar hydrogen for 18 hours. The solvent was removed under reduced pressure and residue was analyzed by ^{1}H NMR spectroscopy. A small amount of the crude product was passed through a 1 cm pad of silica with pentane:Et_2O (1:1) and after removal of the solvent the product was analyzed with HPLC-UV or GC-MS.

Acknowledgements((optional))

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