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The synthesis of new chiral P,N-ligands on the basis of camphor

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ABSTRACT

The synthesis of new chiral P,N-ligands has been developed starting from 1,3-dicarbonyls, which are readily available from camphor. Iridium complexes derived from these ligands are also described. Furthermore, some preliminary results related to catalytic hydrogenation with these iridium complexes are presented.

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1. Introduction

The mixed-donor bidentate P,N-ligands have proven to be highly versatile and efficient ligands for a broad range of catalytic transformations.[1–6] Particularly in asymmetric catalysis P,N-ligands **B** (Scheme 1) bearing a chiral oxazoline moiety have attracted the most attention due to their easy preparation from an amino acid chiral pool.[7–10] In addition to its straightforward synthesis in both enantiomeric forms, *N*,*N*-dimethyl-1-ferrocenylethylamine has found huge popularity for the construction of modular P,N- and P,P-ligands.[11,12] Bidentate chiral ligands **A** containing phosphine as well as a pyrazole moiety were prepared from this unique chiral source.[13] These ligands were shown to promote different types of asymmetric transformations with high enantioselectivities.[14–16] Non-chiral *N*-(2-diphenylphosphino-phenyl)-pyrazoles have been found to be very useful in certain cross-coupling[17–19] and hydroamination[20] reactions. Their chiral versions will extend the scope of these types of ligands enabling asymmetric induction. The most prominent structure closely associated with this respect represents 'quinap' (ligand **C**) with a chiral environment induced via axial chirality.[21] Although significant progress has been made in the synthesis of this[22–24] and related ligands[3,25,26] in enantiomerically pure form, a chiral resolution still remains the method of choice.

One strategy for the construction of a chiral scaffold bearing N-heterocycles is the annulation of naturally occurring monoterpenes as a source of chirality.[27–32] Numerous examples of homochiral camphor annulated pyrroles and pyrazoles have been reported as potentially useful mono-, bi- and tridentate ligands.[33–35]

These encouraging findings prompted us to design a new pyrazole containing ligand **D** with chirality introduced from enantiomerically pure camphor. The methoxy group at the 6′-position of the phenyl ring is expected to be sufficiently bulky to prevent rotation around the C(aryl)–N(pyrazole) bond and fixes one preferred atropisomer upon coordination to the metalic center. This will reduce the number of possible diastereomeric intermediates in the catalytic reactions and thus increase the asymmetric induction. Herein we report a straightforward synthesis of such chiral P,N-ligands. Furthermore, the coordinative behavior of these ligands to iridium, as well as the preliminary results of application in the asymmetric hydrogenation of *trans*-α-methylstilbene are also described.

2. Results and discussion

β-Diketones **1** easily available from camphor[36] were employed as the starting material in the synthesis of ligands. In our preliminary attempts to build the desired scaffold, we prepared 7,8,8-trimethyl-1-phenyl-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole by the condensation of commercially available phenylhydrazine with 3-hydroxymethylenecamphor according to the literature.[37] However, direct deprotonation at the *ortho*-position of phenyl ring using *n*-BuLi and subsequent addition of chlorodiphenylphosphine gave a complex reaction mixture. ^{31}P NMR analysis of the reaction mixture showed an absence of resonance in the range of 0 to −10 ppm, which is typical for diphenylarylphosphines. Therefore, the *ortho*-bromo substituted arylhydrazine was employed as a building block since metallation via metal-halogen exchange proceeds under much milder conditions. Condensation of (2-bromo-6-methoxyphenyl)hydrazine with 3-formyl- **1a** or 3-acyl-camphor **1b** resulted in the clean formation of hydrazones which furnish pyrazoles **2a**,**b** after the treatment with catalytic amounts of hydrobromic acid at 80 °C. Next, lithiation with *n*-BuLi at low

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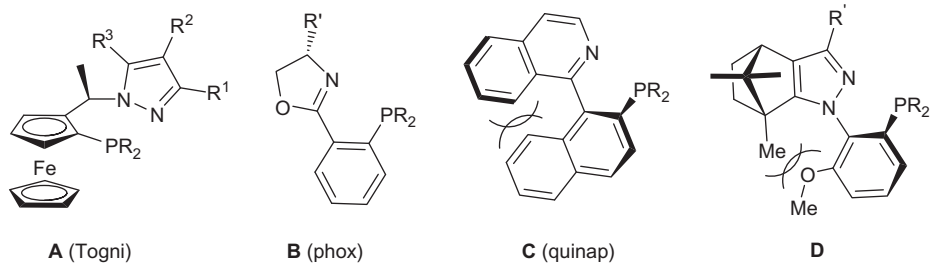
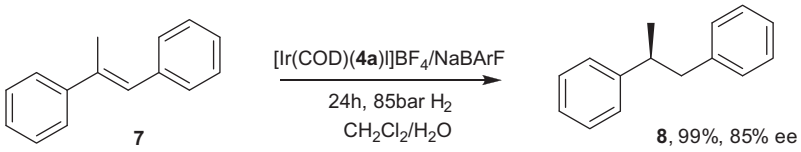


Scheme 1. Design of new ligand **D**.

temperature, followed by the slow addition of chlorophosphines $ClPR_2$ gave the desired ligands **3a**,**b**–**6a**,**b** in satisfactory yields (Scheme 2).

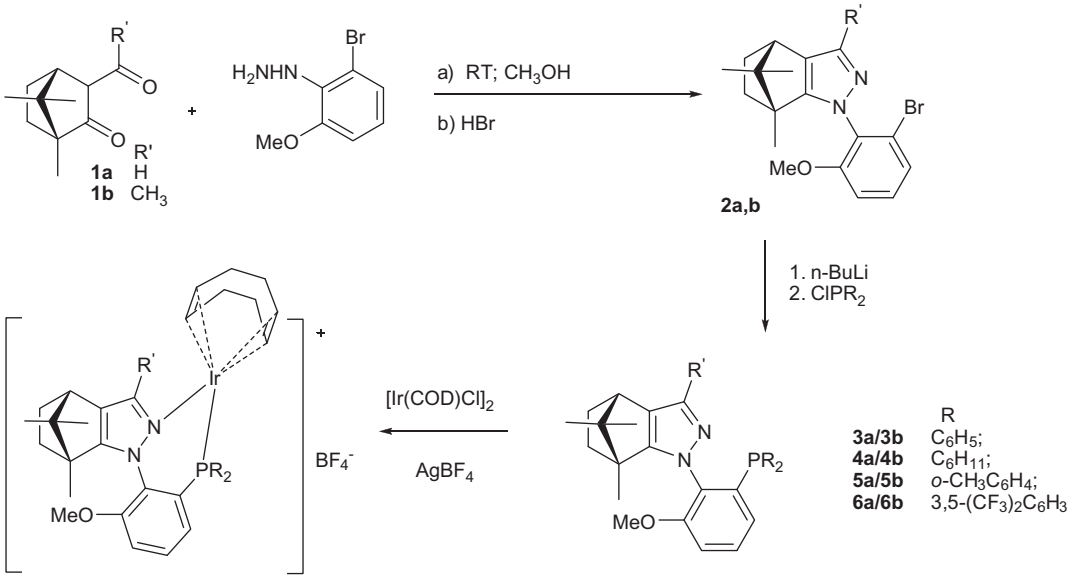
The cationic iridium complexes $[Ir(L)(COD)]BF_4$ can be easily prepared by the reaction of 2 equiv of ligand (L) with 1 equiv of $[Ir(COD)Cl]_2$ in CH_2Cl_2 at 50 °C followed by the exchange of the chloride in the presence of $AgBF_4$. After filtration from the precipitated AgCl, the expected complexes were isolated in appropriate yields. However, the NMR spectra of all of the prepared Ir-complexes showed very broad NMR signals. The structural characterization of the [Ir(**4a**)(COD)]BF_4 complex was performed by X-ray diffraction. The complex shows a square-planar coordination geometry around the iridium atom (Fig. 1). The chelating 6-ring adopts a distorted boat conformation with a typical axial–equatorial disposition of the two substituents at the P atom. The torsion angle between the phenyl ring and the five-membered pyrazole-ring (C(3)–N(2)–C(12)–C(17) = 55.1°) is significantly larger than in the analogous Ir–phox complexes (24° and 31°).[38,39] A key feature in this structure is the orientation of the phenyl ring with a methoxy-group disposed under the bornene moiety, as shown in Scheme 1 (**D**). Therefore, we can assume that this is the preferred conformation of these ligands upon coordination to the metal center. The conformation with an alternative orientation of the phenyl group (with the methoxy group disposed above the bornene moiety) should be significantly disfavored due to the steric interaction of the methoxy group with both methyl groups of bornene fragment. This gives rise to the hope that high asymmetric induction in catalytic transformations with metal complexes bearing these new ligands should be observed.

The iridium complexes were evaluated in the enantioselective hydrogenation of *trans*-α-methylstilbene **7**. The highest enantiomeric excess of 85% was obtained using [Ir(**4a**)(COD)]BF_4 as a catalyst.



3. Conclusion

In conclusion, novel chiral bidentate P,N-ligands have been prepared from camphor. The coordination behavior of the ligands has been illustrated through the synthesis of cationic Ir complexes. Preliminary catalytic results performed with these Ir complexes showed good results in the hydrogenation of C=C bonds.



Scheme 2. Synthesis of ligands and Ir-complexes $[Ir(L)(COD)]BF_4$.

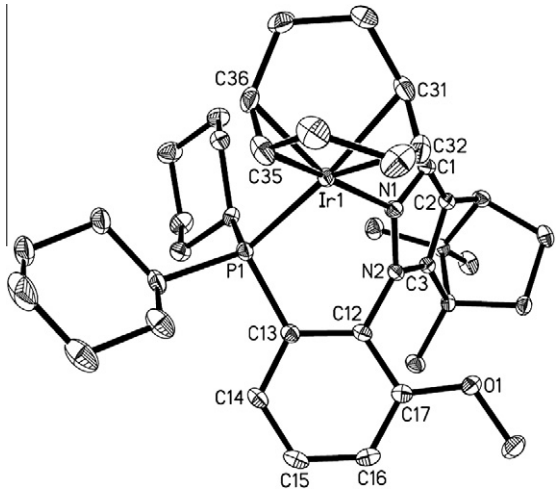


Figure 1. ORTEP view of the complex [Ir(**4a**)(COD)]BF_4, Hydrogen atoms and the BF_4 anion are omitted for the sake of clarity. Selected bonds lengths (Å) and angles (°): Ir(1)–P(1) 2.319(1), Ir(1)–N(1) 2.078(3), Ir(1)–C(31) 2.204(4), Ir(1)–C(32) 2.177(3), Ir(1)–C(35) 2.148(4), Ir(1)–C(36) 2.109(4), P(1)–C(13) 1.838(4), C(12)–C(13) 1.410(5), C(12)–N(2) 1.430(4), N(1)–N(2) 1.377(2), C(1)–N(1) 1.350(4), C(1)–C(2) 1.383(4), C(2)–C(3) 1.374(4), C(3)–N(2) 1.352(4), C(31)–C(32) 1.364(8), C(35)–C(36) 1.391(7), N(1)–Ir(1)–P(1) 85.58(9), Ir(1)–N(1)–N(2) 126.8(2), Ir(1)–P(1)–C(13) 106.62(12), P(1)–C(13)–C(12) 119.4(3), C(13)–C(12)–N(2) 121.4(3), C(12)–N(2)–N(1) 123.9(3), C(1)–N(1)–N(2) 106.1(2), C(3)–N(2)–N(1) 109.4(3), C(2)–C(3)–N(2) 108.3(3), C(1)–C(2)–C(3) 106.0(3), N(1)–C(1)–C(2) 110.2(3).

4. Experimental

4.1. General

NMR spectra were recorded on Brucker ARX 300 MHz and Brucker ARX 400 MHz spectrometer at rt. ^{1}H NMR and ^{13}C NMR spectra are reported in parts per million with TMS (δ = 0.00 ppm) as the internal standard. ^{31}P NMR spectra are reported in parts per million with 85% H_3PO_4 as an external reference. Proton chemical shifts (δ) and coupling constants (J) are given in ppm and in Hertz, respectively. Spin multiplicities are given as s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), and m (multiplet) as well as br (broad). High resolution mass spectra (HRMS) were performed on ESI-TOF/MS mass instrument. Optical rotations were measured on a Fluke GYROMAT-HP polarimeter at 21–3 °C. Reactions were monitored by thin layer chromatography (TLC, silica gel G254 plates). Column chromatography purifications were carried out using silica gel (200–300 mesh). Toluene, ether, and THF were distilled from sodium and benzophenone. CH_2Cl_2 was distilled over CaH_2 under argon. 6-Bromo-2-anisidine,[40] (1*R*)-3-hydroxymethylenecamphor,[33] and (1*R*)-3-acethylcamphor[41] were synthesised according to literature procedures. All other chemicals were obtained commercially and used as received without further purification.

4.2. 6-Bromo-2-methoxyphenylhydrazine

To a cooled (in an ice bath) suspension of 6-bromo-2-anisidine (63.52 g, 0.314 mol) in concentrated hydrochloric acid (130 ml) was added dropwise a solution of sodium nitrite (22 g, 0.32 mol) in water (100 ml) while the temperature was kept below 5 °C. After stirring for a further 30 min at 4 °C the red solution of the diazo compound was filtered and to the filtrate the chilled solution of tin(II) chloride dihydrate (175 g, 0.78 mol) in concentrated hydrochloric acid (200 ml) was added dropwise while occasionally adding water (all together ca. 500 ml water were added), while hydrazine hexachlorostannane precipitated. The reaction mixture was allowed to warm to room temperature and stirred for 3 h, after which the product was filtered off, and washed with saturated brine once. The solid was dissolved by the careful addition to a chilled aqueous solution of 25% sodium hydroxide (200 ml) containing ca. 40 g of potassium tartrate. The product was extracted with dichloromethane (4 × 50 ml). The combined organic layers were washed with 2 M NaOH and water, dried over $MgSO_4$ and evaporated to give 59.4 g (87%) of desired product as a tan solid. Mass spectrum, m/z (I rel., %): 219 (9), 218 (95), 217(10), 216 (100), 203 (64), 201(74), 200 (83), 198 (80), 186 (39).

4.3. (4*S*,7*R*)-7,8,8-Trimethyl-1-(2-bromo-6-methoxyphenyl)-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole 2a

(a) A solution of (2-bromo-6-methoxyphenyl)hydrazine in 100 ml of methanol was added to a solution of (1*R*)-2-hydroxymethylenecamphor in MeOH (50 ml), the product precipitated immediately with an exothermic reaction. The reaction mixture was allowed to cool to room temperature within 2 h and additionally cooled in an ice bath to complete the precipitation, filtered off, washed with 95% ethanol and air dried to give 32.7 g of hydrazone as a colorless solid. (3-[2-(2-bromo-6-methoxyphenyl)-hydrazo] methylenecamphor decomposes slowly at room temperature).

(b) To the suspension of 3-[2-(2-bromo-6-methoxyphenyl)hydrazo]methylenecamphor (21.69 g, 57.2 mmol) in acetic acid(150 ml), 0.5 ml of 47% HBr was added and the mixture was heated at 80 °C for 2 h. The resulting clear red solution was allowed to cool to ambient temperature, after which the reaction mixture was evaporated in vacuum and treated with chilled aq 2 M NaOH (50 ml). The product was extracted with ether (3 × 50 ml), and the combined organic layers were washed with aqueous sodium bicarbonate then with brine, dried over $MgSO_4$, filtered, diluted with heptane and the ether slowly removed on a rotary evaporator to give 16.21 g (78%) of pure product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 1H), 7.26 (d, J = 8.2, 1H), 7.16 (dd, J = 2.0, J = 8.4, 1H), 7.11 (d, J = 1.9, 1H), 3.77 (s, 3H), 2.80 (d, J = 3.8, 1H), 2.07 (tdd, J = 3.8, J = 9.4, J = 11.8, 1H), 1.75 (ddd, J = 3.8, J = 9.5, J = 12.0, 1H), 1.38 (m, 1H), 1.19 (ddd, J = 3.6, J = 9.0, J = 12.0, 1H), 0.91 (s, 3H), 0.88 (s, 3H), 0.75 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 155.69, 154.68, 132.87, 129.52, 128.70, 128.68, 123.70, 122.66, 115.11, 63.40, 55.73, 52.86, 47.48, 32.97, 27.61, 20.25, 19.67, 10.19. Mass spectrum, m/z (I rel., %): 362, 360 (95), 347 (60), 345 (60), 319 (100), 317 (100).

4.4. (4*S*,7*R*)-3,7,8,8-Tetramethyl-1-(2-bromo-6-methoxyphenyl)-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole 2b

(1*R*)-3-Acetylcamphor (7.93 g, 36.5 mmol) was added to a solution of (2-bromo-6-methoxyphenyl)hydrazine (7.1 g, 36.5 mmol) in methanol (50 ml). After 30 min of stirring, 10 drops of 47% HBr were added and refluxed for 5 h. Methanol was evaporated and the residue dissolved in a 100 ml mixture of ethyl acetate and hexane (1:1) and filtered through a short pad silica gel, and washed with 200 ml of ethyl acetate–hexane (1:1). The combined filtrates were evaporated, the residue dissolved in hot hexane (100 ml) cooled in an ice-bath, the precipitated product filtered off and washed twice with cold pentane to give 7.25 g (53%) of the desired product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, J = 8.2, 1H), 7.14 (dd, J = 2.0, J = 8.4, 1H), 7.08 (d, J = 2.0, 1H), 3,76 (s, 3H), 2.74 (d, J = 3.8, 1H), 2.24 (s, 3H), 2.05 (tdd, J = 3.8, J = 9.4, J = 11.7, 1H), 1.72 (ddd, J = 3.8, J = 9.3, J = 12.0, 1H), 1.38 (m, 1H), 1.17 (ddd, J = 3.4, J = 8.9, J = 12.0, 1H), 0.89 (s, 3H), 0.87 (s, 3H), 0.77 (s, 3H). ^{13}C NMR ($CDCl_3$) δ: 156.27, 154.62, 141.96, 129.60, 128.76, 127.48, 123.69, 122.29, 114.96, 63.29, 55.65, 53.29, 46.94, 32.92,

27.40, 20.30, 19.74, 12.63, 10.18. Mass spectrum, *m*/*z* (I rel., %): 376 (18), 374 (18), 361 (24), 359 (24), 333 (100) 331 (100).

4.5. General procedure for the synthesis of the ligands 3–6

A solution of 1.6 M *n*-BuLi in hexane (2.6 mmol) was added to a stirred solution of **2a** or **2b** (2 mmol) in dry THF (30 ml) at −70 °C. After 15 min of stirring, the appropriate chlorophosphine (2 mmol) in 3 ml of THF was added dropwise keeping the temperature below −70 °C and allowed to warm to room temperature with stirring over night, then quenched by the careful addition of aq NH_4Cl (50 ml) solution. The product was extracted with 10 ml ether, the organic layer was dried over $MgSO_4$, and concentrated in vacuum. The crude product was purified by column chromatography using 25% ethyl acetate in hexane as eluent.

4.6. (4*S*,7*R*)-7,8,8-Trimethyl-1-(2-diphenylphosphino-6-methoxyphenyl)-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole 3a

Prepared from **2a** (722 mg, 2 mmol) and chloro-diphenylphosphine (441 mg, 2 mmol). Yield 548 mg, (54%). $[\alpha]_D^{21} = -3.7$ (*c* 0.5, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29–7.25 (m, 12H), 6.85 (dd, *J* = 1.5, *J* = 8.3, 1H), 6.81 (ddd, *J* = 1.5, *J* = 6.4, *J* = 7.9, 1H), 3.55 (s, 3H), 2.72 (d, *J* = 3.8, 1H), 1.99 (tdd, *J* = 3.9, *J* = 9.4, *J* = 11.8, 1H), 1.66 (ddd, *J* = 3.7, *J* = 9.4, *J* = 12.0, 1H), 1.32 (br m, 1H), 1.12 (ddd, *J* = 3.5, *J* = 9.0, *J* = 12.1, 1H), 0.85 (s, 3H), 0.81 (s, 3H), 0.68 (s, 3H). ^{31}P NMR ($CDCl_3$) δ -3.00. HMRS (ESI) calcd for: $C_{30}H_{32}N_2OP$ $(M+H)^+$ 467.2247, found: 467.2251.

4.7. (4*S*,7*R*)-3,7,8,8-Tetramethyl-1-(2-diphenylphosphino-6-methoxyphenyl)-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole 3b

Prepared from **2b** (751 mg, 2 mmol) and chloro-diphenylphosphine (441 mg, 2 mmol). Yield 532 mg (53%). $[\alpha]_D^{22} = +7.5$ (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.25 (m 11H), 6.84 (dd, *J* = 1.5, *J* = 8.3, 1H), 6.79 (ddd, *J* = 1.5, *J* = 6.4, *J* = 7.9, 1H), 3.55 (s, 3H), 2.65 (d, *J* = 3.8, 1H), 2.18 (s, 3H), 1.98–1.92 (m, 1H), 1.63 (ddd, *J* = 3.7, *J* = 9.4, *J* = 12.0, 1H), 1.30–1.35 (m, 1H), 1.09 (ddd, *J* = 3.5, *J* = 9.0, *J* = 12.1, 1H), 0.83 (s, 3H), 0.80 (s, 3H), 0.69 (s, 3H). ^{13}C NMR (CD_2Cl_2) δ 153.21, 152.85 (d, *J* = 9.1), 140.59, 138.04 (d, *J* = 12.8), 136.21 (d, *J* = 11.9), 136.19 (d, *J* = 11.9), 132.98 (d, *J* = 20.1), 128.76, 128.16, 127.80 (d, *J* = 7.3), 127.48 (d, *J* = 6.4), 126.36, 124.75 (d, *J* = 15.5), 115.65 (d, *J* = 25.6), 62.39, 54.41, 52.54, 46.20, 32.07, 26.61, 19.30, 18.73, 11.49, 9.12. ^{31}P NMR ($CDCl_3$) δ −3.05. HMRS (ESI) calcd for: $C_{31}H_{34}N_2OP$ $(M+H)^+$ 481.2403, found: 481.2400.

4.8. (4*S*,7*R*)-7,8,8-Trimethyl-1-(2-dicyclohexylphosphino-6-methoxyphenyl)-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole 4a

Prepared from **2a** (722 mg, 2 mmol) and chloro-dicyclohexylphosphine (465 mg, 2 mmol). Yield 560 mg (56%). $[\alpha]_D^{23} = +4.2$ (*c* 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.23 (dd, *J* = 7.7, *J* = 0.8, 1H), 7.12 (s, 1H), 7.04 (ddd, *J* = 7.7, *J* = 5.3, *J* = 1.5, 1H), 7.01 (dd, *J* = 7.7, *J* = 1.3, 1H), 3.71 (s, 3H), 2.71 (d, *J* = 3.8, 1H), 2.00 (ddt, *J* = 11.7, *J* = 9.4, *J* = 3.9, 1H), 1.68, (ddd, *J* = 11.9, J = 9.4, *J* = 3.8, 1H), 1.26 (qt, *J* = 12.6, *J* = 3.2, 1H), 0.85–1.92 (m, 23H), 0.80 (s, 6H), 0.66 (s, 3H). ^{13}C NMR (CD_2Cl_2) δ: 155.98, 153.58 (d, *J* = 10.3), 137.56 (d, *J* = 20.6), 132.56, 130.15, 128.86, 127.91 (d, *J* = 5.8), 126.39 (d, *J* = 13.5), 118.43 (d, *J* = 27.7), 63.76, 55.79, 53.20, 47.95, 33.30, 33.08 (d, *J* = 12.2), 33.04, (d, *J* = 12.2), 30.41 (d, *J* = 16.7), 29.28 (d, *J* = 7.1), 29.27 (d, *J* = 7.1), 28.08, 27.64 (d, *J* = 12.9), 27.40 (d, *J* = 7.7), 26.85, 20.46, 19.85, 10.15. ^{31}P NMR (CD_2Cl_2) δ 5.08. HMRS (ESI) calcd for: $C_{30}H_{44}N_2OP$ $(M+H)^+$ 479.3186, found: 479.3190.

4.9. (4*S*,7*R*)-3,7,8,8-Tetramethyl-1-(2-dicyclohexylphosphino-6-methoxyphenyl)-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole 4b

Prepared from **2b** (751 mg, 2 mmol) and chloro-dicyclohexylphosphine (465 mg, 2 mmol). Yield 671 mg (67%). $[\alpha]_D^{22} = -12.9$ (*c* 1, ethyl acetate). ^{1}H NMR (400 MHz, CD_2Cl_2) δ: 7.21 (dd, *J* = 7.7, *J* = 0.8, 1H), 7.02 (ddd, *J* = 7.7, *J* = 5.2, *J* = 1.5, 1H), 6.98 (dd, *J* = 7.7, *J* = 1.6, 1H), 3.71 (s, 3H), 2.65 (d, *J* = 3.8, 1H), 2.11 (s, 3H), 1.98 (ddt, *J* = 11.6, *J* = 9.3, *J* = 3.9, 1H), 1.66 (ddd, *J* = 11.9, *J* = 9.4, *J* = 3.8, 1H), 0.79 (s, 6H), 0.86–1.87 (m, 24H), 0.67 (s, 3H). ^{13}C NMR (CD_2Cl_2) δ 156.45, 153.49 (d, *J* = 5.1), 141.58, 137.04 (d, *J* = 21.2), 130.22, 127.87 (d, *J* = 5.8), 127.58, 126.33 (d, *J* = 13.5), 118.35 (d, *J* = 27.7), 63.60, 55.70, 53.61, 47.37, 33.26, 33.07 (d, *J* = 12.2), 33.02 (d, *J* = 12.9), 30.41 (d, *J* = 16.7), 29.26 (d, *J* = 7.7), 29.23 (d, *J* = 7.7), 27.76 (d, v = 6.4), 27.49 (d, *J* = 8.4), 27.34, 26.84, 20.47, 19.89, 12.69, 10.1. ^{31}P NMR (CD_2Cl_2) δ: 4.78. HMRS (ESI) calcd for: $C_{31}H_{46}N_2OP$ $(M+H)^+$ 493.3342, found: 493.3349.

4.10. (4*S*,7*R*)-7,8,8-Trimethyl-1-[2-(di-*o*-tolylphosphino)-6-methoxyphenyl]-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole 5a

Prepared from **2a** (722 mg, 2 mmol) and chloro-di-o-tolylphosphine (497 mg, 2 mmol). Yield 524 mg (52%). $[\alpha]_D^{22} = -13.2$ 13.2 (*c* 0.5, CD_2Cl_2). ^{1}H NMR (400 MHz, CD_2Cl_2) δ: 7.23 (dd, *J* = 7.8, *J* = 1.4, 1H), 6.99–7.21 (m, 7H), 6.86 (dd, *J* = 8.3, *J* = 1.5, 1H), 6.74 (ddd, *J* = 7.9, *J* = 6.4, *J* = 1.6, 1H), 6.67–72 (m, 2H), 3.55 (s, 3H), 2.71 (d, *J* = 3.8), 2.33 (d, *J* = 0.9, 6H), 1.99 (ddt, *J* = 11.7, *J* = 9.4, *J* = 3.9, 1H), 1.67 (ddd, *J* = 12.0, *J* = 9.4, *J* = 3.7, 1H), 1.03–1.35 (m, 2H), 0.83 (s, 3H), 0.80 (s, 3H), 0.65 (s, 3H). ^{13}C NMR (CD_2Cl_2) δ: 156.02, 143.06, 142.72, 138.16 (d, *J* = 11.6), 135.29 (d, *J* = 11.6), 135.26 (d, *J* = 10.9), 133.19, 132.69, 130.51 (d, *J* = 5.2), 130.37, 129.30, 128.99, 128.83 (d, *J* = 7.1), 126.58 (d, *J* = 16.1), 126.58, 117.40 (d, *J* = 26.4), 63.81, 55.64, 53.23, 47.94, 32.28, 28.05, 21.42, 21.13, 20.42, 19.84, 10.16. ^{31}P NMR (CD_2Cl_2) δ −19.66. HMRS (ESI) calcd for: $C_{32}H_{36}N_2OP$ $(M+H)^+$ 495.2560, found: 495.2566.

4.11. (4*S*,7*R*)-3,7,8,8-Tetramethyl-1-[2-(di-*o*-tolylphosphino)-6-methoxyphenyl)-4,5,67-tetrahydro-4,7-methano-1*H*-indazole 5b

Prepared from **2b** (751 mg, 2 mmol) and chloro-di-*o*-tolylphosphine (497 mg, 2 mmol). Yield 560 mg (66%). $[\alpha]_D^{22} = -0.55$ (*c* 1, ethyl acetate). ^{1}H NMR (400 MHz, CD_2Cl_2) δ: 7.21 (dd, *J* = 7.8, *J* = 1.4, 1H), 7.13–7.19 (m, 4H), 6.99–7.05 (m, 2H), 6.84 (dd, *J* = 8.4, *J* = 1.6, 1H), 6.74 (ddd, *J* = 7.8, *J* = 6.4, *J* = 1.4, 1H), 6.67–6.72 (m, 2H), 3.55 (s, 3H), 2.65 (d, *J* = 3.8), 2.31 (m, 6H), 2.11 (s, 3H), 1.98 (ddt, *J* = 11.6, *J* = 9.4, *J* = 3.8, 1H), 1.65 (ddd, *J* = 12.0, *J* = 9.4, *J* = 3.6, 1H), 1.02–1.35 (m, 2H), 0.80 (s, 3H), 0.79 (s, 3H), 0.67 (s, 3H). ^{13}C NMR (CD_2Cl_2) δ: 156.47, 142.83 (d, *J* = 25.8), 141.70, 137.72 (d, *J* = 11.6) 135.31 (d, *J* = 11.6), 135.29 (d, *J* = 11.6), 133.14, 130.45 (d, *J* = 4.5), 130.42, 129.22, 128.82, 128.73, 127.70, 126.55 (d, *J* = 16.1), 126.52, 117.30 (d, *J* = 27.7), 62.36, 55.54, 53.62, 47.33, 32.24, 27.74, 21.37, 21.09, 20.42, 19.85, 12.65, 10.16. ^{31}P NMR (CD_2Cl_2) δ −19.70. HMRS (ESI) calcd for: $C_{33}H_{38}N_2OP$ $(M+H)^+$ 509.2716, found: 509.2721.

4.12. (4*S*,7*R*)-7,8,8-Trimethyl-1-[2-bis(3,5-ditrifluoromethylphenyl)phosphino-6-methoxyphenyl]-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole 6a

Prepared from **2a** and chloro-bis(3,5-ditrifluoromethylphenyl)phosphine (985 mg, 2 mmol). Yield 654 mg (65%).

$[\alpha]_D^{22} = -8.4$ (*c* 0.5, CD_2Cl_2). ^1H NMR (300 MHz, CD_2Cl_2) δ: 7.88 (s, 2H), 7.72 (dd, *J* = 6.6, *J* = 1.7, 4H), 7.38 (dd, *J* = 7.8, *J* = 1.7, 1H), 7.19 (s, 1H), 6.92 (dd, *J* = 9.3, *J* = 1.7, 1H), 6.85 (td, *J* = 7.6, *J* = 1.7, 1H), 3.62 (s, 3H), 2.72 (d, *J* = 3.7, 1H), 2.01 (ddt, *J* = 11.7, *J* = 9.5, *J* = 3.9, 1H), 1.70 (ddd, *J* = 12.0, *J* = 9.5, *J* = 3.7, 1H), 1.27–1.36 (m, 1H), 1.09 (ddd, *J* = 12.0, *J* = 8.8, *J* = 3.4, 1H), 0.83 (s, 3H), 0.81(s, 3H), 0.65 (s, 3H). ^{13}C NMR (CD_2Cl_2) δ 156.21, 154.82 (d, *J* = 11.0), 139.84 (d, *J* = 18.3), 139.79 (d, *J* = 18.3), 137.97 (d, *J* = 17.4), 134.68 (d, *J* = 11.9), 133.76 (d, *J* = 21.0), 133.73 (d, *J* = 19.2), 132.55 (q, *J* = 33.5), 132.49 (q, *J* = 33.5), 130.84, 129.75(d, *J* = 8.2), 129.51, 126.50 (d, *J* = 18.3), 124.01 (sept, *J* = 3.8), 123.50 (q, *J* = 272.9), 117.03 (d, *J* = 27.4), 64.03, 55.90, 53.39, 47.93, 33.20, 27.99, 20.37, 19.81, 10.04. ^{31}P NMR (CD_2Cl_2) δ −2.66. HMRS (ESI) calcd for: $C_{34}H_{28}F_{12}N_2OP$ $(M+H)^+$ 739.1742, found: 739.1755.

4.13. (4*S*,7*R*)-3,7,8,8-Tetramethyl-1-[2-bis(3,5-ditrifluoromethylphenyl)phosphino-6-methoxyphenyl]-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole 6b

Prepared from **2b** (751 mg, 2 mmol) and chloro-bis(3,5-ditrifluoromethylphenyl)phosphine (985 mg, 2 mmol). Yield 733 mg (73%). $[\alpha]_D^{23} = -13$ (*c* 0.5, CD_2Cl_2); ^1H NMR (400 MHz, CD_2Cl_2) δ: 7.86 (sept, *J* = 0.7, 2H), 7.71 (dd, *J* = 6.6, *J* = 1.7, 4H), 7.36 (dd, *J* = 7.9, *J* = 1.6, 1H), 6.90 (dd, *J* = 9.2, *J* = 1.6, 1H), 6.83 (td, *J* = 7.6, *J* = 1.7, 1H), 3.61 (s, 3H), 2.65 (d, *J* = 3.7, 1H), 2.10 (s, 3H), 1.98 (ddt, *J* = 11.7, *J* = 9.4, *J* = 3.9, 1H), 1.67 (ddd, *J* = 12.0, *J* = 9.4, *J* = 3.7, 1H), 1.27–1.35 (m, 1H), 1.03–1.11 (m, 1H), 1.06 (s, 3H), 0.81 (s, 3H), 0.79 (s, 3H), 0.66 (s, 3H). ^{13}C NMR (CD_2Cl_2) δ: 156.71, 154.70 (d, *J* = 11.0), 142.38, 139.96 (d, *J* = 19.2), 139.94(d, *J* = 18.3), 138.01 (d, *J* = 18.3), 133.76 (d, *J* = 21.0), 133.74 (d, *J* = 20.1), 132.56 (q, *J* = 33.5), 132.50(q, *J* = 33.5), 132.26, 129.72 (d, *J* = 7.3), 128.37, 126.55 (d, *J* = 18.3), 123.98 (p, *J* = 3.7), 123.53(q, *J* = 272.9), 116.98 (d, *J* = 27.4), 63.95, 55.84, 53.87, 47.39, 33.20, 27.74, 20.43, 19.89, 12.63, 10.09. ^{31}P NMR (CD_2Cl_2) δ −2.62. HMRS (ESI) calcd for: $C_{35}H_{28}F_{12}N_2OP$ $(M+H)^+$ 753.1899, found: 753.1911.

4.14. General procedure for the preparation of iridium complexes

In a sealed Schlenk tube, the $[Ir(COD)Cl]_2$ (168 mg, 0.25 mmol) and the ligand (0.5 mmol) in 10 ml of CH_2Cl_2 was heated at 50 °C for 3 h. The resulting deep red solution was allowed to cool to ambient temperature and a solution of $AgBF_4$ (97 mg, 0.5 mmol) in 2 ml of CH_2Cl_2 was then added at once. The precipitated AgCl was filtered off and the solvent evaporated. The product was crystallized from CH_2Cl_2/diethyl ether.

4.15. [(4*S*,7*R*)-7,8,8-Trimethyl-1-(2-diphenylphosphino-6-methoxyphenyl)-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole] (1,5-cyclooctadiene) iridium(I) tetrafluoroborate

Prepared from **3a** (233 mg, 0.5 mmol) following the general procedure as an orange solid. Yield 295 mg (68%). HMRS (ESI) calcd for: $C_{38}H_{43}IrN_2OP$ (M^*+) 765.2713, found: 765.2718.

4.16. [(4*S*,7*R*)-7,8,8-Trimethyl-1-(2-dicyclohexylphosphino-6-methoxyphenyl)-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole (1,5-cyclooctadiene) iridium(I) tetrafluoroborate

Prepared from **4a** (239 mg, 0.5 mmol) following the general procedure as an orange solid. Yield 315 mg (71%) characterized by X-ray analysis.

4.17. [(4*S*,7*R*)-3,7,8,8-Tetramethyl-1-(2-di-o-tolylphosphino-6-methoxyphenyl)-4,5,6,7-tetrahydro-4,7-methano-1*H*–indazole] (1,5-cyclooctadiene) iridium(I) tetrafluoroborate

Prepared from **5b** (254 mg, 0.5 mmol) following the general procedure as an orange solid. Yield 320 mg (71%). HMRS (ESI) calcd for: $C_{43}H_{49}IrN_2OP$ (M^*+) 831.3179, found: 831.3179.

4.18. {(4*S*,7*R*)-7,8,8-Trimethyl-1-[2-bis(3,5-ditrifluoromethylphenyl)phosphino-6-methoxyphenyl]-4,5,6,7-tetrahydro-4,7-methano-1*H*-indazole} (1,5-cyclooctadiene) iridium(I) tetrafluoroborate

Prepared from **6a** (369 mg, 0.5 mmol) following the general procedure as an orange solid. Yield (451 mg, 79%). HMRS (ESI) calcd for: $C_{42}H_{39}F_{12}IrN_2OP$ (M^*+) 1037.2209, found: 1037.2222.

4.19. General hydrogenation procedure

An aliquot (200 μl) of the Ir-complex solution in CH_2Cl_2 (0.05 M, 0.01 mmol) was added to a solution of 1 mmol substrate and 198 mg of tetradecane in 4 ml of CH_2Cl_2 under argon. The catalyst–substrate–tetradecane solution was transferred to the inertized autoclave charged with NaBArF (0.015 mmol), then 1 ml of water was added and the autoclave pressurized with hydrogen to 40 bar and stirred for 24 h. After releasing the hydrogen, the organic layer was dried over $MgSO_4$, passed through a short pad of silica gel and used directly for chiral HPLC analysis to measure the enantiomeric excess and for GC analysis to measure the conversion.

4.20. X-ray crystal structure analysis

Single crystals of complex [Ir(**4a**)(COD)]BF_4 were grown by slow diffusion of diethyl ether into a saturated solution in CH_2Cl_2.

Data were collected on a STOE IPDS II diffractometer using graphite-monochromated Mo Kα radiation. The structure was solved by direct methods (SIR2004)[42] and refined by full-matrix least-squares procedures on F^2 (SHELXL-97).[43] XP (Bruker AXS) was used for graphical representation.

Crystal data for [Ir(**4a**)(COD)]$BF_4 \cdot 0.5CH_2Cl_2$: $C_{38.5}H_{56}BClF_4IrN_2OP$, $M = 908.28$, crystal size: $0.50 \times 0.22 \times 0.15$ mm, orange crystal, monoclinic, space group *C*2, $a = 16.8787(4)$, $b = 11.8658(3)$, $c = 20.4194(5)$ Å, $\beta = 111.142(2)°$, $V = 3814.3(2)$ Å^3, $T = 150$ K, $Z = 4$, $\rho_{calcd} = 1.582$ g cm^{-3}, $\mu = 3.665$ mm^{-1}, absorption correction: numerical (max. and min. transmission: 0.6146 and 0.3355), 32071 reflections measured, 9110 independent reflections ($R_{int} = 0.0263$), final *R* values ($I > 2\sigma(I)$): $R_1 = 0.0219$, $wR_2 = 0.0499$, final *R* values (all data): $R_1 = 0.0252$, $wR_2 = 0.0504$, GOF on $F^2 = 0.961$, 438 parameters.

CCDC 840596 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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