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Iridium(I)-Catalyzed Asymmetric Intermolecular Hydroarylation of Norbornene with Benzamide

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Summary. Starting from the dinuclear chloro-bridged Ir(I) complexes $[IrCl(PP)]_2$ ($PP = (R)$-(6,6′-dimethylbiphenyl-2,2′-diyl)-1,1′-*bis*-(diphenylphosphine), (*R*)-(6,6′-dimethoxy-biphenyl-2,2′-diyl)-1,1′-*bis*-(diphenylphosphine), and (*R*)-1-((*S*)-2-(diphenylphosphino-ferrocenyl))-ethyldicyclohexyl-phosphine), a new class of cyclopentadienyl Ir(I) complexes containing a chiral bisphosphine ([Ir*Cp*(*PP*)]) was prepared and characterized. These new complexes are suited precatalysts for the direct hydroarylation of norbornene with benzamide. 2-(*exo*-Norbornyl)-benzamide is formed with an enantiomeric excess of up to 94% by the use of 1 mol% iridium, albeit in low yield.

Keywords. Iridium; Asymmetric Catalysis; Hydroarylation; Hydroamination; Norbornene.

Introduction

The catalytic addition of aromatic C–H bonds to unsaturated functionalities is still a rare process and, to the best of our knowledge, no such asymmetric process has been reported. *Murai* has shown that several Ru(II) complexes give active catalysts for the addition of functionalized aromatics to olefins and acetylenes [1] *via* C–H activation [2]. On the other hand, the asymmetric hydroarylation of norbornene has been achieved *via* Pd catalysis starting from aryl triflates or halides and in the presence of a hydride source in varying yields and stereoselectivities of up to 86% *ee* [3]. Furthermore, extremely active phosphapalladacyclic catalysts have been described most recently [4]. Turnover numbers as high as *ca.* 2×10^8 have been achieved for the reaction of norbornene with phenyl iodide and with formic acid as the hydride source. The use of Ir in catalytic C–C bond forming reactions is also a very underdeveloped field of homogeneous catalysis. In allylic alkylation, a system that affords regioselectivities opposed to those typically observed for Pd catalysts has recently been reported [5].

In the course of our investigations with the electron-rich Ir(I) complexes of the type $[IrCl(PP)]_2$ (**1**, PP = chiral chelating diphosphine), mainly aiming at the development of asymmetric olefin hydroamination [6], we have also shown that

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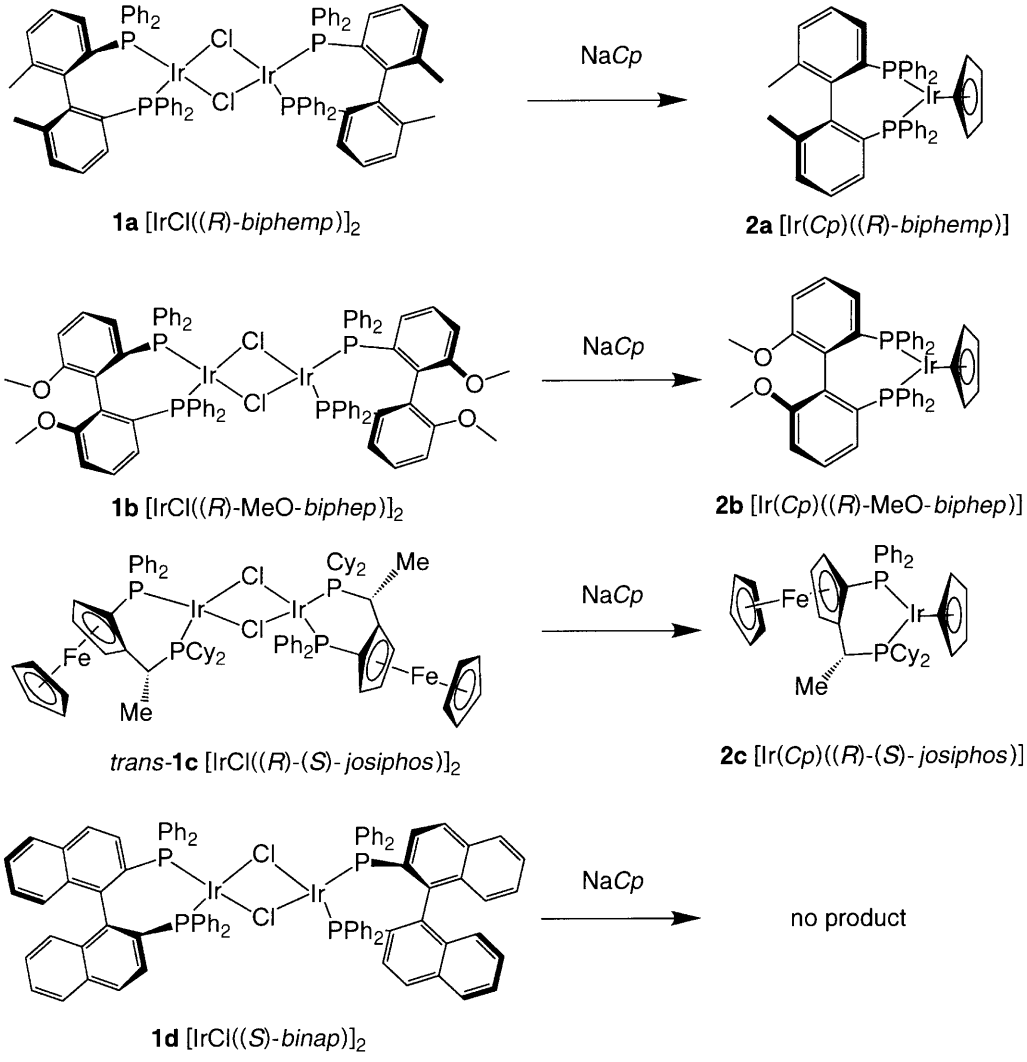
such complexes undergo smooth and reversible O–H and C–H bonds activation processes [7]. Looking for catalyst precursors alternative to **1a–d**, we prepared the new complexes [Ir*Cp*(*PP*)] (**2a–d**) and were surprised to find that they catalyze the direct asymmetric hydroarylation of norbornene. The use of *Cp*Ir complexes in asymmetric catalysis is new, although an η^5-indenyliridium(I) complex has very recently been reported to catalyze the hydroboration of olefins with catecholborane [8].

Results and Discussion

The cyclopentadienyliridium complexes **2** (Scheme 1) are easily obtained by reacting the respective precursor **1** with Na*Cp* in *THF*. Compounds **2** were isolated as dark red, air sensitive, microcrystalline materials in moderate to good yield, with

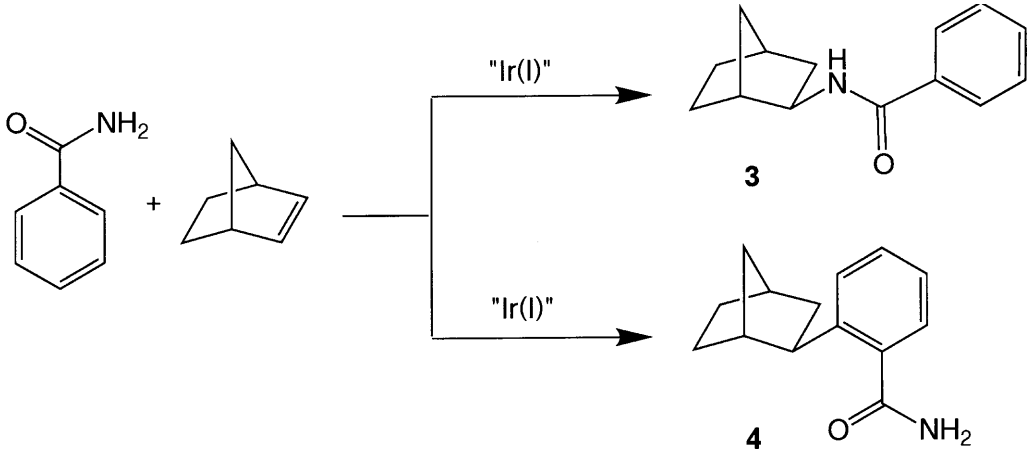


Scheme 1

the exception of the *BINAP* derivative **2d** in which case invariably the formation of Ir metal was observed upon reacting **1d** with Na*Cp*. Complexes **2a–c** containing (*R*)-*biphemp* ((*R*)-(6,6′-dimethylbiphenyl-2,2′-diyl)-1,1′-*bis*-(diphenylphosphine)), (*R*)-MeO-*biphep* ((*R*)-(6,6′-dimethoxy-biphenyl-2,2′-diyl)-1,1′-*bis*-(diphenylphosphine)), and (*R*)-(*S*)-*josiphos* ((*R*)-1((*S*)-2-(diphenylphosphinoferrocenyl))-ethyldicyclohexylphosphine), respectively, were characterized by NMR spectroscopy and elemental analysis. These complexes are Ir(I) 18-electron systems, as indirectly suggested by the equivalence of the P atoms in the ^{31}P NMR spectrum of **2a**,**b** and by the fact that the *Cp* ligand in all compounds gives a sharp singlet in the ^{1}H NMR spectrum, indicative of the η^5-coordination mode. It is therefore to be expected that the reactivity of these complexes could depend on either phosphine-chelate ring opening or *Cp* ring slippage phenomena [9].

When used in the prototype asymmetric hydroamination of norbornene with aniline [6a, 10], complexes **2** were found to be practically inactive as catalysts, *i.e.* unable to activate the N–H bond by oxidative addition [10]. Only in the case of **2a** we observed the formation of traces of N-phenyl-*exo*-aminonorbornane, however with an *ee* of 73%. We therefore decided to use a compound containing an activated N–H bond, such as benzamide, instead of aniline. With this nitrogen source typical catalytic experiments were carried out using 1 mol% of Ir in toluene. The reaction mixtures were stirred at 100°C for 72 h and thereafter subjected to chromatographic product isolation (see Experimental). The reaction is illustrated in Scheme 2, and the results are summarized in Table 1.

The expected hydroamination product N-benzoyl-*exo*-aminonorbornane (**3**) was formed only when complexes of type **1** were used as catalyst precursors. The enantioselectivity reached thereby 79% *ee* in the case of the MeO-*biphep* catalyst **1b**, and no other addition product was detected. On the other hand, catalyst **1a**, containing the less electron-rich ligand *biphemp*, reacted slower than **1b** and furnished both reaction products **3** and **4** in a 1:2 ratio. The C–H activation product **4** displayed an *ee* of 85%. The Ir*Cp* derivatives **2** afforded 2-(*exo*-norbornyl)-benzamide as only isolable product, *i.e.* the outcome of the uncommon direct hydroarylation reaction. The enantiomeric excesses amounted to 87% *ee* for **2a** and



Scheme 2

Table 1. Reaction of norbornene with benzamide in toluene

Precatalyst (mol% Ir)	*t*/°C	Product	Yield/%	*ee*/%
2a (1)	100	**4**	16	87
2a (10)	100	**4**	35	87
2b (1)	100	**4**	12	94
2c (1)	100	[b]		
1a (1)	100	**3**	5	65
		4	10	85
1b (1)	100	**3**	50	79
1c (1)	100	[b]		
1d (1)	100	**3**	30	70
		4	4	81

[a] Isolated yield after a reaction time of 72 h; [b] no product detected

94% *ee* in the case of **2b**. To the best of our knowledge these are the highest *ee* values ever reported for these kind of reaction. It is astonishing that with the catalysts **1c** and **2c**, containing the ferrocenyl diphosphine *josiphos*, no reaction took place under the conditions indicated, showing that the reaction of norbornene with benzamide is highly influenced by the electronic and steric nature of the ligand.

This highly selective hydroarylation reaction poses interesting mechanistic questions that have not yet been addressed experimentally. Complexes **2**, being 18-electron systems, require ligand dissociation processes in order to coordinate and activate benzamide and norbornene. This could happen *via* a change of the hapticity of the cyclopentadienyl ring from η^5 to η^3 (to η^1) (ring slippage [9]), or, less likely, *via* a phosphine dissociation step. The *ortho*-selectivity in the C–H activation process clearly indicates that the amide functional group must interact with the Ir center, probably *via* the oxygen atom.

In conclusion, we showed that the Ir(I) system, originally conceived for the first highly enantioselective hydroamination of norbornene occurring *via* N–H activation, is also capable of performing a catalytic C–H activation process instead when modified with a *Cp* ligand. The catalytic enantioselective formation of 2-(*exo*-norbornyl)-benzamide presented here constitutes the first example of a direct asymmetric hydroarylation process. We are currently pursuing this type of reaction in view of clarifying mechanistic aspects as well as in order to improve the catalytic activity and explore its synthetic utility with aryl substrates other than benzamide. Corresponding results will be reported in due course.

Experimental

All experiments were performed under purified N_2 in a glove box or under purified Ar using standard *Schlenk* techniques. All glasware and stirrer bars were oven-dried at 120°C. The solvents were freshly distilled before use (pentane and hexane over $CaCl_2$, *THF* from Na/K, benzene from Na/benzophenone, toluene and heptane from Na) or kept in dispenser flasks in the glove box. NMR spectra were recorded on a Bruker DPX 250 spectrometer operating at 250.133 MHz (^{1}H), 62.860 MHz (^{13}C), and 101.256 MHz (^{31}P) at room temperature. Chemical shifts (δ) are given in ppm

relative to internal *TMS* and to external H_3PO_4 (85%). Elemental analyses were carried out at the *Microelementaranalytisches Laboratorium*, ETH Zürich.

Cyclopentadienyl-((S)-2,2′-bis-(diphenylphosphino)-6,6′-dimethyl-1,1′biphenyl)-iridium (**2a**; $C_{43}H_{37}IrP_2$)

To a solution of 492 mg of **1a** (0.32 mmol) in 10 cm^3 of *THF*, 0.3 cm^3 of a 2 *M* solution of cyclopentadienyl-Na in *THF* were added. The reaction mixture was stirred at room temperature for 16 h. After evaporation of the volatile components, the reddish residue was extracted with pentane until the mother liquor was colorless. Evaporation of the solvent afforded a dark red powder.

Yield: 389 mg (80%); calcd.: C 63.93, H 4.62; found: C 64.07, H 4.81; ^{1}H NMR (250 MHz, δ, C_6D_6): 6.55–8.13 (m, 26H, aromat.), 4.84 (s, 5H, *Cp*), 1.37 (s, 6H, $-CH_3$) ppm; ^{31}P{^{1}H} NMR (101 MHz, δ, C_6D_6): 14.8 (s) ppm.

Cyclopentadienyl-((R)-(6,6′-dimethoxybiphenyl-2,2′-diyl)-1,1′-bis-(diphenylphosphine))-iridium (**2b**; $C_{43}H_{37}IrO_2P_2$)

2b was prepared analogously to **2a** from 98 mg of **1b** (0.06 mmol) in 1 cm^3 of *THF* and 0.1 cm^3 of a 2 *M* solution of cyclopentadienyl-Na in *THF*.

Yield: 55 mg (54%); ^{1}H NMR (259 MHz, δ, C_6D_6): 6.78–7.35 (m, 26H, aromat.), 4.97 (s, 5H, *Cp*), 3.07 (s, 6H, O–CH_3) ppm; ^{31}P{^{1}H} NMR (101 MHz, δ, C_6D_6): 14.7 (s) ppm.

Cyclopentadienyl-((R)-1-((S)-2-(diphenylphosphino)-ferrocenyl)-ethyldicyclohexylphosphine)-iridium (**2c**; $C_{41}H_{49}FeIrP_2$)

2c was prepared analogously to **2a** from 200 mg of **1c** (0.12 mmol) in 5 cm^3 of *THF* and 0.2 cm^3 of a 2 *M* solution of cyclopentdienyl-Na in *THF*. The reaction mixture was stirred at room temperature for 6 h. After filtration, heptane was added, inducing crystallization of the product. The resulting orange/red microcrystalline powder was filtered off and dried *in vacuo*.

Yield: 136 mg (66%); NMR spectroscopy indicated 0.8 equivalents of heptane; calcd.: C 60.01, H 6.63; found: C 60.14, H 6.52; ^{1}H NMR (250 MHz, δ, C_6D_6): 8.51–8.64 (m, 2H, aromat.), 7.42–7.53 (m, 2H, aromat.), 7.32–7.42 (m, 2H, aromat.), 7.10–7.21 (m, 3H, aromat.), 6.99–7.09 (m, 1H, aromat.), 5.13 (s, 5H, Ir*Cp*), 4.29 (m, 1H, C_5H_3), 4.23 (m, 1H, C_5H_3), 3.99 (*pseudo*-t, 1H, C_5H_3), 3.57 (m, 1H, CCH_3*H*P), 3.52 (s, 5H, Fe*Cp*), 2.32–2.46 (m, 2H, PCHR_2), 1.97 (*pseudo*-d, 3H, CCH_3*H*P), 0.31 (m, 1H, *cy*CH_2) ppm; ^{31}P{^{1}H} NMR (101 MHz, δ, C_6D_6): 44.5 (d, J(PP′) = 32 Hz), 1.7 (d, J(PP′) = 32 Hz) ppm.

Ir(I)-catalyzed addition of benzamide to norbornene (typical procedure)

The catalyst precursor (1 mol% of Iridium; for **2a**: 17 mg, 0.19 mmol) was dissolved in 1 cm^3 of toluene and added to 173 mg of norbornene (1.83 mmol). The resulting solution was transferred into a 20 cm^3 *Young-Schlenk* tube previously charged with 237 mg of benzamide (1.9 mmol). These manipulations were carried out in a glove box. The reaction mixture was then heated for 72 h at 100°C. Afterwards, the reaction was quenched by exposure to air, and product(s) purified by chromatography (silica gel 60 (Fluka), hexane:ethylacetate = 1:1). The enantiomeric excess was determined by HPLC (Daicel Chiralcel OD-H column, hexane:^{i}PrOH = 95:5).

N-Benzoyl-exo-aminonorbornane (**3**; $C_{14}H_{17}NO$)

Calcd.: C 78.10, H 7.96, N 6.51; found: C 78.14, H 7.94, N 6.60; ^{1}H NMR (250 MHz, δ, $CDCl_3$): 7.26–7.91 (5H, m, aromat.), 5.96 (1H, bs, NH), 3.92 (1H, m, CHR_2NHR), 1.09–2.51 (12H, m,

norbornyl) ppm; $^{13}C\{^1H\}$ NMR (63 MHz, δ, $CDCl_3$): 166.7 (1C, CO), 134.9 (1C, *C*CO*R*), 131.2 (1C, *para*-C, aromat.), 128.5 (2C, aromat.), 126.8 (2C, aromat.) 53.3, 42.4, 40.6, 35.7, 35.7, 28.1, 26.5 (7C, norbornyl) ppm; $[\alpha]_D^{25}$: +14 ($c = 1.849$, CH_2Cl_2; sample with 79% *ee*): HPLC retention times: 36.5 min (−)-N-benzoyl-*exo*-aminonorbornane, 39.9 min (+)-N-benzoyl-*exo*-aminonorbornane (major enantiomer).

2-Norbornyl-benzamide (**4**; $C_{14}H_{17}NO$)

Calcd.: C 78.10, H 7.96, N 6.51; found; C 77.81, H 8.06, N 6.49; ^1H NMR (250 MHz, δ, $CDCl_3$): 7.15–7.37 (m, 4H, aromat.), 6.32 (s, 1H, NH), 5.84 (s, 1H, NH′), 3.17 (m, 1H, CHR_2, $J_{gem} = 5.9$ Hz, $J_{endo,endo} = 9.1$ Hz), 2.35 (m, 2H), 1.86 (m, 1H), 1.21–1.57 (m, 7H) ppm; $^{13}C\{^1H\}$ NMR (63 MHz, δ, $CDCl_6$): 172.8 (1C, CO), 145.3 (1C, *C*CONH$_2$), 135.8 (1C, norbornyl-C*R*$_2$), 130.0 (1C, NH$_2$COC*C*H), 126.7, 126.1, 125.3 (3C, CH aromat.), 43.4, 42.8, 40.1, 36.9, 30.6, 28.6 (7C, norbornyl) ppm; $[\alpha]_D^{25}$: +65 ($c = 1.051$, CH_2Cl_2; sample with 94% *ee*); HPLC retention times: 30.5 min (−)-2-norbornyl-benzamide, 32.4 min (+)-2-norbornyl-benzamide (major enantiomer).

References

[1] Murai S, Chatani N, Kakiuchi F (1997) Pure Appl Chem **69**: 589
[2] a) Shilov AE, Shul'pin GB (1997) Chem Rev **97**: 2879; b) Chen H, Schlecht S, Semple TC, Hartwig JF (2000) Science **287**: 1995
[3] Namyslo JC, Kaufmann DE (1997) Chem Ber/Recueil **130**: 1327
[4] Brunel JM, Heumann A, Buono G (2000) Angew Chem **122**: 2022 (Angew Chem Int Ed **39**: 1946)
[5] Takeuchi R, Kashio M (1998) J Am Chem Soc **120**: 8647
[6] a) Dorta R, Egli P, Zürcher F, Togni A (1997) J Am Chem Soc **119**: 10857; b) Togni A, Dorta R, Köllner C, Pioda G (1998) Pure Appl Chem **70**: 1477; c) Togni A, Bieler N, Burckhardt U, Köllner C, Pioda G, Schneider R, Schnyder A (1999) Pure Appl Chem **71**: 1531; d) Senn HM, Blöchl PE, Togni A (2000) J Am Chem Soc **122**: 4098
[7] Dorta R, Togni A (1998) Organometallics **17**: 3423
[8] Brinkman JA, Nguyen TT, Sowa JR Jr (2000) Org Lett **2**: 981
[9] a) O'Connor JM, Casey CP (1987) Chem Rev **87**: 307; b) Calhorda MJ, Veiros LF (1999) Coord Chem Rev **186**: 37; c) Simanko W, Tesch W, Sapunov VN, Mereiter K, Schmid R, Kirchner K, Codington J, Wherland S (1998) Organometallics **17**: 5674

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