

The [IrCl(Diphosphine)]₂/Fluoride System. Developing Catalytic Asymmetric Olefin Hydroamination

Romano Dorta,[†] Patrick Egli,[‡] Fabio Zürcher,[§] and Antonio Togni^{*}

Laboratory of Inorganic Chemistry, ETH-Zentrum
Swiss Federal Institute of Technology
CH-8092 Zürich, Switzerland

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We report the first example of intermolecular enantioselective olefin hydroamination catalyzed by an Ir diphosphine system for which a remarkable fluoride ion effect on both activity and selectivity was found. Selectivities of up to 95% ee (enantiomeric excess) and average turnover frequencies (N_t) of up to 3.4 h⁻¹ at 75 °C with a substrate to Ir ratio of 100 were obtained for the model reaction of norbornene and aniline. We also report a general synthesis of chiral dinuclear chloride-bridged Ir(I) diphosphine complexes used as catalyst precursors for the title reaction and the X-ray crystallographic characterization of one of them.

Despite its synthetic potential and practical relevance, the asymmetric catalytic olefin hydroamination is still an undeveloped reaction. Indeed, in addition to the lanthanide-catalyzed enantioselective olefin hydroamination/cyclization reported by Marks and co-workers,¹ to the best of our knowledge no *intermolecular* version of this reaction is known. So far, transition metal catalysts for the intermolecular hydroamination of unactivated olefins hardly afford turnover numbers of more than ca. 0.08 h⁻¹ at 1 atm and medium temperature.² Organofluorine complexes are able to catalyze the same reaction of unactivated olefins, such as 1-pentene, at a rate of up to $N_t = 0.4$ h⁻¹ at 60 °C.^{1b}

Casalnuovo, Calabrese, and Milstein^{2a} have shown the feasibility of catalytic hydroamination via N–H activation.³ In particular, they demonstrated that the electron-rich Ir complex [Ir(PEt₃)₂(C₂H₄)Cl] (**1**)⁴ cleanly oxidatively adds, e.g., aniline. The Ir(III) hydrido amido species thus formed undergoes insertion of norbornene leading to a well-characterized complex containing a chelating alkylamino ligand, from which the amination product is released upon reductive elimination. However, this system did not afford more than up to 6 turnovers in the catalytic experiments, in the presence of apparently beneficial Lewis acids such as ZnCl₂.

In view of preparing complexes analogous to **1**, containing chiral chelating diphosphines, we found that [IrCl(C₂H₄)₄]⁵ or

* Author to whom correspondence should be addressed at the following; e-mail: togni@inorg.chem.ethz.ch.

[†] Part of the planned Ph.D. thesis of R.D. at ETH-Zürich.

[‡] Part of the Diploma thesis of P.E. at ETH-Zürich, 1997.

[§] X-ray structural study of complex **5**.

(1) See, e.g.: (a) Giardello, M. A.; Conticello, V. P.; Brard, L.; Gagné, M. R.; Marks, T. J. *J. Am. Chem. Soc.* **1994**, *116*, 10241. (b) Li, Y.; Marks, T. J. *Organometallics* **1996**, *15*, 3770. (c) Li, Y.; Marks, T. J. *J. Am. Chem. Soc.* **1996**, *118*, 9295 and further references cited therein.

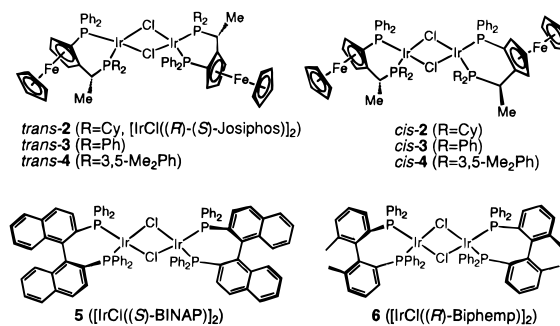
(2) (a) Casalnuovo, A. L.; Calabrese, J. C.; Milstein, D. *J. Am. Chem. Soc.* **1988**, *110*, 6738. (b) Brunet, J.-J.; Neibecker, D.; Philippot, K. *J. Chem. Soc., Chem. Commun.* **1992**, 1215. (c) Brunet, J.-J.; Commenges, G.; Neibecker, D.; Philippot, K. *J. Organomet. Chem.* **1994**, *469*, 221. For recent reviews, see, e.g.: (d) Brunet, J.-J. *Gazz. Chim. Ital.* **1997**, *127*, 111. (e) Roundhill, D. M. *Catal. Today* **1997**, *37*, 155.

(3) (a) Casalnuovo, A. L.; Calabrese, J. C.; Milstein, D. *Inorg. Chem.* **1987**, *26*, 971. (b) Schulz, M.; Milstein, D. *J. Chem. Soc., Chem. Commun.* **1993**, 318. See also: (c) Schaad, R. D.; Landis, C. R. *J. Am. Chem. Soc.* **1990**, *112*, 1628. (d) Hartwig, J. F.; Andersen, R. A.; Bergman, R. G. *Organometallics* **1991**, *10*, 1875.

(4) Aizenberg, M.; Milstein, D.; Tulip, T. H. *Organometallics* **1996**, *15*, 4093.

(5) Onderdelinden, A. L.; van der Ent, A. *Inorg. Chim. Acta* **1972**, *6*, 420.

Chart 1



[IrCl(COE)]₂ smoothly reacts with Josiphos-type ligands⁶ and with the axial chiral auxiliaries BINAP⁷ and Biphemp,⁸ respectively, in toluene solution, affording in good yields the new dinuclear derivatives **2–6** shown in Chart 1.⁹ Complexes **2–4** were isolated as an inseparable mixture of *cis/trans* isomers.⁹ Well-characterized examples of this type of Ir(I) complexes are extremely rare, although they are postulated intermediates in a number of catalytic and stoichiometric reactions.¹⁰ Derivative **5** has been characterized by X-ray crystallography (see the Supporting Information for full details) and an ORTEP view is shown in Figure 1.¹¹ As expected, the core of the dinuclear complex is butterfly-shaped, with an angle of 126° between the coordination planes of the two only slightly distorted square-planar Ir centers. The dihedral angles between the two pairs of naphthyl planes are 74.06° and 76.83°, respectively, values that lie in the upper range for BINAP complexes.⁷

Complexes **2–6** were used as catalyst precursors in the model hydroamination of norbornene with aniline (Scheme 1). The reactions were performed without solvent and with a catalyst concentration of 1 or 2 mol % Ir throughout (Table 1). In order to compare the catalytic activity of the different precatalysts, a common reaction time of 72 h was adopted. First experiments, performed with the (*R*)-(*S*)-Josiphos complexes (**2** at 50 °C, have shown the clean but slow formation of *exo*-(2-phenylamino)norbornane (**7**) in 12% yield and 51% ee (2*S*).¹² The corresponding *endo*-isomer was formed in traces, whereas the product derived from *o*-alkylation of aniline^{2c} was not detected. We reasoned that the good π -donating properties of fluoride as

(6) Togni, A.; Breutel, C.; Schnyder, A.; Spindler, F.; Landert, H.; Tijani, A. *J. Am. Chem. Soc.* **1994**, *116*, 4062.

(7) Noyori, R.; Takaya, H. *Acc. Chem. Res.* **1990**, *23*, 345 and references cited therein.

(8) Schmid, R.; Broger, E. A.; Cereghetti, M.; Cramer, Y.; Foricher, J.; Lalonde, M.; Müller, R. K.; Scalone, M.; Schoettel, G.; Zutter, U. *Pure Appl. Chem.* **1996**, *68*, 131 and references cited therein.

(9) See the Supporting Information for preparative details. For Josiphos, starting from [IrCl(COE)]₂, mainly a mixture of [IrCl(Josiphos)]₂ and [IrCl(Josiphos)COE] in variable ratios was formed, depending on the reaction conditions (COE = cyclooctene).

(10) (a) Rybtchinski, B.; Vigalok, A.; Ben-David, Y.; Milstein, D. *J. Am. Chem. Soc.* **1996**, *118*, 12406. (b) Hoel, E. L.; Talebinasab-Savari, M.; Hawthorne, M. F. *J. Am. Chem. Soc.* **1977**, *99*, 4356. (c) Del Paggio, A. A.; Andersen, R. A.; Muetterties, E. L. *Organometallics* **1987**, *6*, 1260. (d) Fryzuk, M. D.; McConville, D. H.; Rettig, S. J. *J. Organomet. Chem.* **1993**, *445*, 245. (e) Grotjahn, D. B.; Lo, H. C. *Organometallics* **1995**, *14*, 5463. (f) Tani, K.; Onouchi, J.; Yamagata, T.; Kataoka, Y. *Chem. Lett.* **1995**, 955.

(11) Dinuclear, halide-bridged complexes containing BINAP that have been structurally characterized are extremely rare. For an anionic Ru(II) derivative, see: Ohta, T.; Tonomura, Y.; Nozaki, K.; Takaya, H.; Mashima, K. *Organometallics* **1996**, *15*, 1521 and references cited therein. Complex **5** has recently been prepared and characterized independently by Tani and co-workers (Yamagata, T.; Iseki, A.; Tani, K. *Chem. Lett.* In press.

(12) The absolute configuration has been determined by internal comparison of the X-ray crystal structure of the salt **8** obtained from an enriched sample (92% ee) of (–)-**7** with (*R*)-(–)-1,1'-binaphthyl-2,2'-diyl hydrogen phosphate. For a recent example of resolution and determination of configuration of a chiral amine utilizing the latter reagent, see: Wilen, S. H.; Zhong Qi, J.; Williard, P. G. *J. Org. Chem.* **1991**, *56*, 485 and references cited therein.

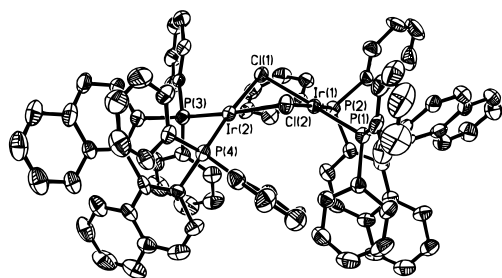


Figure 1. ORTEP view of **5** (50% probability ellipsoids). Selected interatomic distances (Å) and angles (deg) are as follows: Ir(1)–P(1) 2.196(2), Ir(1)–P(2) 2.200(2), Ir(1)–Cl(1) 2.398(2), Ir(1)–Cl(2) 2.425(2), Ir(2)–P(3) 2.202(2), Ir(2)–P(4) 2.205(2), Ir(2)–Cl(1) 2.425(2), Ir(2)–Cl(2) 2.417(2), Ir(1)–Ir(2) 3.322(2); P(1)–Ir(1)–P(2) 91.16(8), Cl(1)–Ir(1)–Cl(2) 79.27(7), Ir(1)–Cl(1)–Ir(2) 87.00(6), Ir(1)–Cl(2)–Ir(2) 86.58(7), Cl(1)–Ir(2)–Cl(2) 78.89(7), P(3)–Ir(2)–P(4) 90.93(8).

Scheme 1

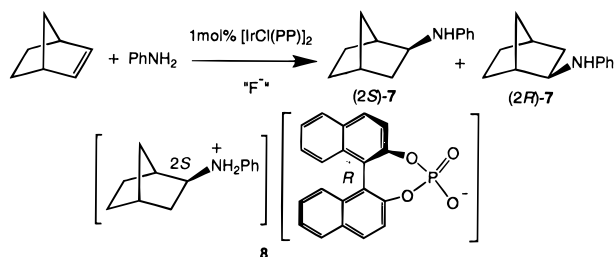


Table 1. Fluoride Effect on Activity and Stereoselectivity in the Ir-Catalyzed Addition of Aniline to Norbornene^a

catalyst precursor	<i>T</i> [°C]	[F ⁻]/[Ir]	yield [%] ^d (<i>N</i> _t , h ⁻¹)	ee[%] ^f (abs conf)
2 ^b	50	0	12 (0.17)	51 (2S)
2 ^b	50	0.25	76 (1.05)	31 (2R)
2 ^b	50	1	81 (1.11)	50 (2R)
2 ^b	50	4	51 (0.71)	16 (2R)
2 ^b	25	1	12 (0.17)	60 (2R)
2 ^b	75	1	81 (3.37) ^e	38 (2R)
3 ^b	50	1	27 (0.38)	9 (2R)
4 ^b	50	1	36 (0.50)	26 (2R)
5 ^c	50	0	12 (0.08)	57 (2R)
5 ^c	75	2	45 (0.31)	78 (2R)
5 ^c	75	4	22 (0.15)	95 (2S)
6 ^c	50	1	13 (0.09)	51 (2S)
6 ^c	75	1	37 (0.26)	43 (2S)
6 ^c	75	2	27 (0.19)	69 (2S)
6 ^c	75	4	24 (0.17)	92 (2S)

^a Reaction conditions: [IrCl(PP)]₂ + commercially available P2-fluoride (0.5 M in benzene), no solvent, workup after 72 h. ^b 1 mol% Ir. ^c 2 mol% Ir. ^d Determined after flash chromatography. Traces of the *endo*-isomer of the product were detected only if experiments were carried out in absence of fluoride. ^e Reaction time = 24 h. ^f Determined by HPLC using a Daicel Chiralcel OJH column and eluting with an hexane/*i*-PrOH mixture (90:10 v/v; 0.5 mL/min; *T* = 25 °C; retention times (2R)-7 15.5 min, (2S)-7 17.2 min).

a ligand, together with its tendency to form hydrogen bridges,¹³ could enhance the propensity toward N–H oxidative addition.

(13) For a review on fluoro complexes, see, e.g.: Doherty, N. M.; Hoffman, N. W. *Chem. Rev.* **1991**, *91*, 553.

However, we were not able, so far, to prepare the fluoro analogues of any of the complexes **2–6**. Nevertheless, both activity and enantioselectivity benefitted from the addition of co-catalytic amounts of “naked” fluoride,¹⁴ added as a benzene solution of phosphazanium fluoride-P₂.¹⁵ Inspection of Table 1 shows that for complexes **2** the presence of 1 equiv of fluoride leads to an increase of the catalytic activity by a factor of ca. 6.5 and, strikingly, to a reversal of enantioselectivity, as compared to the case without fluoride.¹⁶ Furthermore, **7** is the only product formed (81% isolated yield). Other Josiphos-type ligands (precatalysts **3** and **4**) afforded much lower activities and selectivities.

Similarly, the (*S*)-BINAP complex **5** was found to act as a rather modest catalyst precursor when used without fluoride (12% yield, 57% ee). The addition of 4 equiv of fluoride and a higher reaction temperature of 75 °C doubled the yield and raised the ee to 95%, the highest ee ever observed in hydroamination. Matching results were obtained with complex **6**, containing the ligand (*R*)-Biphemp (up to 92% ee).

Due to the high basicity of the “naked” fluoride anion,^{14b} anilide could be produced by deprotonation of aniline. It has been shown that addition of LiNHPPh is necessary to promote the condensation of aniline with norbornene when a rhodium catalyst is used.^{2b,c} However, when 1 equiv of LiNHPPh per Ir was added to **2**, instead of fluoride, the catalyst lost all its activity.

In conclusion, we have shown that Ir¹⁷ complexes of the type **2–6** in the presence of “naked” fluoride constitute suitable catalyst precursors for the enantioselective addition of the aniline N–H bond across the double bond of norbornene. We are currently broadening the scope of this reaction and attempting to elucidate the decisive role of the fluoride anion in this catalytic process.

Acknowledgment. We are grateful to Arianna Martelletti and Volker Gramlich for the X-ray structural study of **8**. R.D. thanks Novartis Ltd. for financial support.

Supporting Information Available: Procedure for catalytic experiments, synthetic and characterization details for complexes **2–6**, and full details of the crystal structure analyses of **5** and **8** including associated tables (29 pages). See any current masthead page for ordering and Internet access instruction.

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(14) We recently reported on the beneficial effect of added fluoride in the Pd-catalyzed allylic amination: (a) Burckhardt, U.; Baumann, M.; Togni, A. *Tetrahedron: Asymmetry* **1997**, *8*, 155. For comments about “naked” fluoride, see: (b) Seppelt, K. *Angew. Chem.* **1992**, *104*, 299; *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 292. For recent observations of the superior properties of fluoro complexes in catalysis, see: (c) Gauthier, D. R.; Carreira, E. M. *Angew. Chem.* **1996**, *108*, 2521; *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2363. (d) Duthaler, R. O.; Hafner, A. *Angew. Chem.* **1997**, *109*, 43; *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 43.

(15) 1,1,1,3,3,3-Hexakis(dimethylamino)diphosphazanium fluoride. See: (a) Schwesinger, R. *Angew. Chem.* **1991**, *103*, 1376; *Angew. Chem., Int. Ed. Engl.* **1991**, *29*, 1372. (b) Wollenweber, M.; Pinkos, R.; Leonhardt, J.; Prinzbach, H. *Angew. Chem.* **1994**, *106*, 84; *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 117.

(16) Addition of chloride, bromide, or iodide instead of fluoride has either no effect or only detrimental effects on activity and selectivity.

(17) The corresponding Rh complexes did not show any catalytic activity without fluoride, and with fluoride, under the same reaction conditions and at 75 °C, the product was formed in traces (ca. 2% yield) and with an ee of 62%, in the case of the ligand Josiphos.