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Asymmetric Hydrogenation of Imines Catalysed by Carboxylato(diphosphine)iridium(III) Complexes
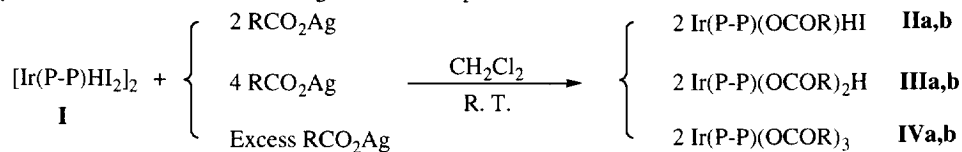
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Abstract: The synthesis of three new families of monomeric carboxylato(diphosphine)-iridium(III) complexes is described (e.g. diphosphine = diop, binap, bdpp). Some of these complexes catalyse the asymmetric hydrogenation of prochiral imines to amines in good activity and enantioselectivity. Copyright © 1996 Elsevier Science Ltd

Optically active compounds play an important role in agrochemistry and the pharmaceutical industry[1]. Catalytic asymmetric hydrogenation has emerged as being an efficient route to such molecules and the most intensive studies and impressive results have concentrated on the reduction of prochiral alkenes and ketones[2]. Recently, various homogeneous catalysts have been found to reduce ketimines to the corresponding amines[3-6], the most widely used catalyst systems for this process deriving from diphosphine/rhodium(I)[3] and iridium(I)[4,5] complexes although titanocene type catalysts[6] have also shown marked success. We showed that although dimeric iridium(III) catalysts, $[Ir(P-P)HI_2]_2$[5], **I**, were very efficient for this reduction, the active species in this case was a small quantity of the unsaturated pentacoordinate monomer, $Ir(P-P)HI_2$, which is in equilibrium with **I**. Analogous monomer complexes may thus be expected to increase the efficiency of the catalyst system in turnover rate and, hopefully, in enantioselectivity. We report here the synthesis and catalytic studies of closely related monomeric Ir(III) complexes with potentially bidentate anions such as carboxylates, where arm-off behaviour of the anion could produce a desired pentacoordinate active species.

The three new families (**II, III** and **IV**) of monomeric carboxylato(diphosphine)iridium(III) compounds (especially **IV**) display good activity and enantioselectivity for the reduction of imines (**A, B** and **C**) under mild conditions (40 bar, at 30°C).These complexes were obtained in 50 to 80% yield by the reaction of the dimeric complexes $[Ir(P-P)HI_2]_2$[5] (P-P = diop, binap, bdpp[7]) with 2, 4 equivalents or excess of silver carboxylate in methylene chloride in the absence of light at room temperature:

$$
[Ir(P-P)HI_2]_2 + \left\{ \begin{array}{l} 2\ RCO_2Ag \\[1.2em] 4\ RCO_2Ag \\[1.2em] \text{Excess } RCO_2Ag \end{array} \right. \xrightarrow[\text{R. T.}]{CH_2Cl_2} \left\{ \begin{array}{ll} 2\ Ir(P-P)(OCOR)HI & \textbf{IIa,b} \\[1.2em] 2\ Ir(P-P)(OCOR)_2H & \textbf{IIIa,b} \\[1.2em] 2\ Ir(P-P)(OCOR)_3 & \textbf{IVa,b} \end{array} \right.
$$

(a: R = CH₃; b: R = CF₃)

After AgI was filtered off, the yellow to light brown complexes were obtained by precipitation with ether or pentane. Microanalyses and mass spectra agree with the formulation proposed above, but the ^1H and ^{31}P NMR spectra showed that the complexes existed as mixtures of isomers which we were not able to separate by recrystallisation or chromatography. However, the NMR spectra for isomers of **II** and **III** indicated that the

hydride ligand was *cis* to both phosphorus atoms of the diphosphine ligand[8] and since both mono and bidentate carboxylate groups are found in **III** and **IV**, we propose the structures below for the three diastereomers formed.
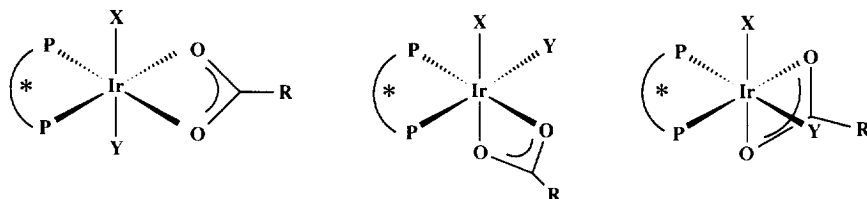
II: X = H; Y = I. **III**: X = H; Y = η^1-OCOR. **IV**: X = Y = η^1-OCOR.

Further **IIb** (where P-P = bdpp) consists of a diastereomeric pair of monomers (with the carboxylate bidentate) along with a dimeric form with bridging iodides and monodentate carboxylates. However, since under catalytic conditions these isomers are probably converted into one active species, we carried out the hydrogenation of imines **A**, **B** and **C** using **II**, **III**, and **IV**, some results of which are listed in Table 1.
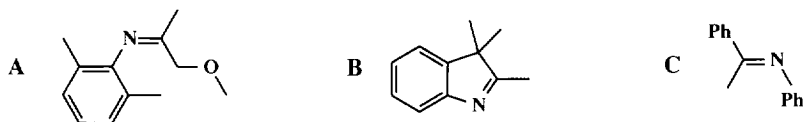
The data in Table 1 shows that for the model herbicide precursor **A**[10] the highest catalytic rates are achieved using the complexes **II** (entry 1) and **IV** (entries **7-11**), but in general the complexes containing the trifluoroacetate ligand show much higher enantioselectivity. The best catalyst precursor for this reduction is Ir[(-)-bdpp](OCOCF$_3$)$_3$ where ee's of 84 to 89 % are reached at 30°C (or 90% at 0°C; entries **8-11**), which are superior to that found in the iodide catalysts **I**[5] (*ca.* 65% ee). Further this catalyst appears to be somewhat more active and stable (i.e. longer lifetime, larger number of turnovers) than the iodide system. Unfortunately, these observations cannot be readily extended to imine **B** where almost no variation in enantioselectivity is found on exchanging either the chiral diphosphine or the carboxylate anion (entries **12-17**). In this case, {Ir[(-)-bdpp]HI$_2$}$_2$ remains the best catalyst (80% ee). For the hydrogenation of imine **C**, Ir[(-)-binap](OCORCF$_3$)$_3$ gave superior enantioselectivity (entry **19**), but was less rapid than the iodide catalysts. Two other observations must be made. Firstly, the results obtained with the mixed monocarboxylated catalysts **II** Ir(P-P)(OCOR)HI are similar (but not identical) to those described for the dimers **I** ([Ir(P-P)HI$_2$]$_2$)[5]. Also, inactive polyhydride dinuclear iridium complexes[4,11] are eventually formed, as with **I**[12]. This suggests that the catalysis may proceed in part via initial dissociation of the carboxylate ligand followed by the steps already proposed for **I**[5]. Secondly, and surprisingly, the compounds of type **III** exhibit both much lower activity and enantioselectivity in comparison with complexes **IV**. This is curious since one might anticipate that under H$_2$, **IV** would be initially converted into **III**. However, we find that although the complexes **IV** react with molecular hydrogen to form a monohydride Ir(P-P)(OCOR)$_2$H species, NMR data shows this to be an isomer with the hydride ligand *cis* to one phosphorus and *trans* to the other. Hence the variations in reactivity and enantioselectivity found between **III** and **IV** may result from stereochemical differences in such isomeric hydride intermediates. In view of these possible complications, an attempt to apply a simplified structural model to interpret the source of enantioselectivity appears premature.

Finally as observed in other systems[3(a,d,e,f,g),4], the optical yields increase at lower temperature (entries **8** and **9**), but with a lower hydrogenation rate. Increasing in pressure of H$_2$ increases the catalytic activity without

changing the enantiomeric excess. Although we have used CH_2Cl_2/THF generally as the solvent for these reactions, pure THF was found to give the faster hydrogenation rate in some cases (compare entries **8** and **10**), but with no change in enantioselectivity. An opposite behaviour was observed for reactions carried out in toluene (entries **8** and **11**).

Table 1: the asymmetric hydrogenation of imines **A**, **B** and **C**[a].

Entry	imine	catalyst	P-P	$t_{1/2}$ (h)[b]	t (h)	yield (%)	ee (%)[c]
1	A	IIa	(+)-diop	1	4	99	41 (S)
2	A	IIa	(+)-binap	35	197	98	29 (S)
3	A	IIb	(-)-bdpp	16	71	88	74 (R)
4	A	IIIa	(+)-diop	64	233	75	29 (S)
5[d]	A	IIIa	(+)-binap	110	188	54	2 (S)
6[d]	A	IVa	(+)-binap	-	19	29	56 (S)
7	A	IVb	(+)-binap	2.5	8.5	100	67 (S)
8	A	IVb	(-)-bdpp	3.5	10	100	84 (R)
9[e]	A	IVb	(-)-bdpp	50	145	96	90 (R)
10[f]	A	IVb	(-)-bdpp	1	2.5	94	85 (R)
11[g]	A	IVb	(-)-bdpp	4.5	11	95	89 (R)
12	B	IIa	(+)-diop	2.5	24	99	30 (-)
13	B	IIIa	(-)-diop	45	140	85	33 (+)
14[d]	B	IIIb	(-)-diop	20	69	96	23 (+)
15[d]	B	IVa	(+)-diop	20	70	90	35 (-)
16[d]	B	IVb	(+)-diop	22	51	100	31 (-)
17	B	IVb	(+)-binap	43	79	86	31 (-)
18	C	IVb	(-)-bdpp	32	170	97	33 (S)
19	C	IVb	(+)-binap	16	38	95	60 (R)

a) Standard conditions: catalyst = 0.016 mmol; imine = 7.84 mmol (500 eq.); solvent: THF/CH_2Cl_2 (3/1,v/v) = 10 mL; P_{H_2} = 40 bar; T = 30°C; b) $t_{1/2}$ (h) is time for the reduction of 50% of the substrate; c) ee of amines are measured by optical activity (reduced A^4 and C^9) or ^1H NMR (300 MHz, reduced B^5; d) imine/catalyst = 200/1; e) T = 0°C; f) solvent: 10 mL of THF.

Work is currently in progress in order to obtain more detailed mechanistic information concerning the catalysis described above, the results of which will be discussed separately.

References and Notes

1. Stinson, S.C. *Chem. Eng. News*, **1992**, *Sept.28*, 46-63.

2. For compilations, see: a) Noyori, R. *Asymmetric Catalysis in Organic Synhtesis*; Wiley: New York, **1994**. b) Kagan, H. B. In *Comprehensive Organometallic Chemistry*; Pergamon Press: Oxford, **1982**, *8*, pp 463-498. c) Bosnich, B. *Asymmetric Catalysis*, Martinus Nijhoff: Dordrecht, **1986**.
   d) Noyori, R. *Chem. Tech .*, **1992**, *June*, 360-372. e) Noyori, R.; *Chem. Soc. Rev.*, 1989, **18**, 187.
   e) Brown, J. M. *Chem. Soc. Rev.*, **1993**, *22*, 25-41.

3. a) Bakos, J.; Toth, I.; Heil B.; Szalontai, G.; Parkanyi L.; Fulop, V.*J. Organomet. Chem.*, **1989**, *370*, 263-276. b) Bakos, J.; Orosz, A.; Heil, B.; Laghmari, M.; Lhoste P.; Sinou, D. *J. Chem. Soc., Chem. Commun.*, **1991**, 1684-1685. c) Amrani, Y.; Lecomte, L.; Sinou, D.; Bakos, J.; Toth I.; Heil, B.

Organometallics, **1989**, *8*, 542-547. d) Kang, G.-J.; Cullen, W.R.; Fryzuk, M.D.; James, B.R.; Kutney, J.P. *J. Chem. Soc., Chem. Commun.*, **1988**, 1466-1467. e) Cullen, W.R.; Fryzuk, M.D.; James, B.R.; Kutney, J.P.; Kang, G.-J.; Herb, G.; Thorburn, I.S.; Spogliarich, R. *J. Mol. Catal.*, **1990**, *62*, 243-253. f) Bekalski, A.G.; Cullen, W.R.; Fryzuk, M.D.; James, B.R.; Kang, G.-J.; Rettig, S.J. *Inorg. Chem*, **1991**, *30*, 5002-5008. g) Burk, M.J.; Feaster, J.E. *J. Am. Chem. Soc.*, **1992**, *114*, 6266-6267. h) Lensink C.; de Vries, J.G. *Tetrahedron: Asymm.*, **1992**, *3*, 235-238.

4.   a) Spindler, F.; Pugin, B.; Blaser, H.-U. *Angew. Chem. Int. Ed. Engl.*, **1990**, *29*, 558-559. b) Morimoto, T.; Nakajima, N.; Achiwa, K. *Synlett*, **1995**, 748-750. c) Morimoto, T.; Achiwa, K. *Tetrahedron: Asymm.*, **1995**, *6*, 2661-2664. d) Sablong, R.; Osborn, J.A. *Tetrahedron: Lett.*, **1996**, *37*, 4937-4940.

5.   Chan Y.P.N.C.; Osborn, J.A. *J. Am. Chem. Soc.*, **1990**, *112*, 9400-9401.

6.   a) Kobayashi, K.; Okamoto, T.; Oida, T.; Tarimato, S. *Chem. Lett.*, **1986**, 2031-2034. b) Willoughby, C.A.; Buchwald, S.L. *J. Am. Chem. Soc.*, **1992**, *114*, 8652-8665. c) Willoughby, C.A.; Buchwald S.L. *J. Org. Chem.* 1993, **58**, 7627. d) Verdaguer X.; Lange U.E.W.; Reding M.T.; Buchwald S.L. *J. Am. Chem. Soc.*, 1996, **118**, 6784. e) Oppolzer W.; Wills M.; Starkemann C.; Bernadinelli G. *Tetrahedron Lett.*, 1990, **31**, 4117.

7.   The diphosphine structures are given below:
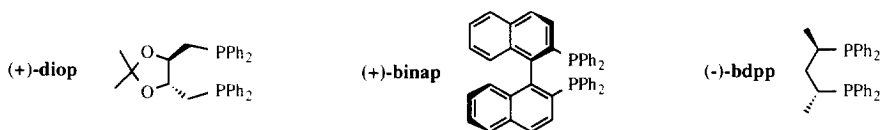
8.   The complexes have been characterised by ^{1}H and ^{31}P NMR, FAB mass spectroscopy, IR and elemental analyses; ^{1}H (200 MHz, CD_2Cl_2, hydride region, δ in ppm, $^2J_{PH}$ in Hz) and ^{31}P{^{1}H} (81 MHz, CD_2Cl_2/CH_2Cl_2, δ in ppm, $^2J_{PP}$ in Hz). NMR data for selected catalysts (isomer proportions in %) : **IIa**: **P-P** = **(+)-diop**, ^{1}H: -15.6 (t, J = 16, 25%), -26.9 (dd, ΣJ = 41, 10%), -27.3 (dd, ΣJ = 42, 65%), ^{31}P{^{1}H}: 0.3 and -19.7 (m, 1, 25%), -4.5 and -16.4 (m, 1, 10%), -6.4 and -8.6 (m, 1, 65%); **P-P** = **(+)-binap**, ^{1}H: -25.8 (dd, ΣJ = 39, 98%), -26.2 (dd, ΣJ = 39, 2%), ^{31}P{^{1}H}: -0.5 (s 1); **IIb**: **P-P** = **(-)-bdpp**, (these species exist as a mixture of monomeric Ir[(-)-(bdpp)](OCOCF$_3$)HI and dimeric {Ir[(-)-bdpp](OCOCF$_3$)H(μ-I)}$_2$ complexes), ^{1}H: -24.8 (t, J = 21, 30%), -24.9 (t, J = 18, 20%), -23.4 (t, 1, 20%). **IIIa**: **P-P** = **(+)-diop**, ^{1}H: -23.4 (t, 1, J = 19, 5%), -23.7 (dd, ΣJ = 39, 7%), -26.3 (t 1, J=23, 88%), ^{31}P{^{1}H}: -8.2 and -14.7 (AX, J = 16), **P-P** = **(+)-binap**, ^{1}H: -25.3 (dd, ΣJ = 44, 100%), ^{31}P{^{1}H}: 3.2 and -1.4 (AX, J = 18). **IVa**: **P-P** = **(+)-diop**, ^{31}P{^{1}H}: -37.9 (s, 100%); **IVb**: **P-P** = **(+)-binap**, ^{31}P{^{1}H}: -24.1 and -26.8 (AX, J = 21, 90%), -25.1 and -28.4 (AX, J = 21, 10%); **P-P** = **(-)-bdpp**, ^{31}P{^{1}H}: -4.2 and -17.1 (AX, J = 31, 35%), -14.5 and -19.9 (AX, J = 26, 65%).

9.   Ogata, Y.; Takeushi, K.J. *J. Org. Chem.*, **1970**, *35*, 1642-1645.

10. a) Moser, H.; Rihs, G.; Sauter, H. *Z. Naturforsch.*, **1982**, *37b*, 451-462. b) U.S. Pats. 3 937 730 and 4 022 611 (1972) to Ciba-Geigy Ltd.

11. Chadosh, D.; Crabtree,R.; Felkin, H.; Morehouse,S.; Morris,G. *Inorg. Chem.*, **1982**, *21*, 1307-1311.

12. Chan, Y.P.N.C.; Osborn, J.A. unpublished results.