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The Asymmetric Hydrogenation of Imines using Tridentate C_2 Diphosphine Complexes of Iridium(I) and Rhodium(I).

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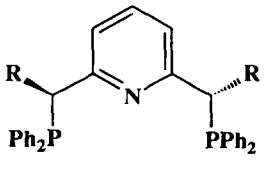
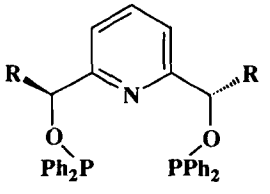
Abstract: We report the synthesis of $[M(PNP)(diene)]^+$ complexes (M = Ir or Rh; diene = COD or NBD), where PNP represents a tridentate diphosphine ligand of C_2 symmetry. These complexes are active catalysts for the hydrogenation of imines. Reduction of prochiral imines in the presence of chiral ligands leads to the corresponding amines with 7 to 55% ee. Copyright © 1996 Elsevier Science Ltd

The asymmetric hydrogenation of imines has attracted significant attention of late since it offers an attractive route for the synthesis of chiral amines. Reduction of imines however is seemingly not as easily carried out as other unsaturated functions (e.g. olefins, ketones) and the most successful catalysts have been based on rhodium(I)[1-6] and iridium(I)[7-9] or (III)[10] using chiral bidentate phosphines or titanocene type[11] complexes. We now report the synthesis of Ir(I) and Rh(I) complexes containing tridentate ligands of C_2 symmetry possessing a P-N-P donor set, and preliminary results concerning the highly active catalytic properties displayed by the iridium compounds.

The ligands **1** and **2** and their chiral analogues **3** and **4** were synthesised by recently published procedures (Scheme 1).[12-13]



1 R = H
3 R = CH_3

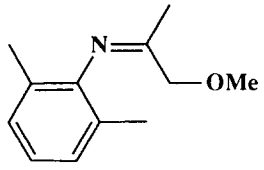


2 R = H
4 R = CH_3

Scheme 1

Ir(I) complexes of the type $[Ir(PNP)(COD)]^+$ (where COD = 1,5-cyclooctadiene), **1a-3a**, were prepared by treatment of a THF solution of $[Ir(COD)Cl]_2$ containing 2.1eq. of $NaClO_4$ with 2eq. of the PNP ligand in THF. After removal of the solvent, the residue was taken up into CH_2Cl_2, the insoluble NaCl removed by filtration over celite, and the crystalline orange complexes **1a-3a** obtained by recrystallisation from CH_2Cl_2/Et_2O. The $^{31}P\{^1H\}$ NMR spectra show clean singlets at δ 11.3 (**1a**), δ 94.5 (**2a**), δ 27.2 (**3a**) and unexceptional ^1H spectra. However **4a** proved difficult to obtain pure so in the catalytic reactions described below **4** was used *in situ* with $[Ir(COD)Cl]_2$. The analogous $[Rh(PNP)(NBD)]^+$ complexes (where NBD = norbornadiene), **3b-4b**, were prepared in an identical manner ($^{31}P\{^1H\}$: **3b**, δ 69.9 (d, $^1J_{Rh-P}$ = 126.8Hz); **4b**, δ 119.8 (d, $^1J_{Rh-P}$ = 146.3Hz)). All compounds have satisfactory analyses and show M^+ and $(M\text{-diene})^+$ as the principal ions in the FAB MS. X-ray structures of **1a** and **2a** show that they possess a distorted trigonal bipyramidal geometry with the PNP ligand in a quasi-facial coordination.[14]

The iridium complexes are very active for the hydrogenation of imines (Scheme 2).



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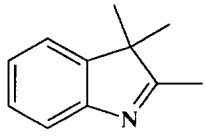

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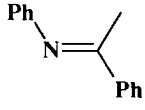

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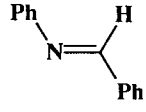

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Scheme 2

Hence the imine **5** is reduced (500 eq., 30°C, P_{H_2} = 40 bar, THF) at an initial rate (r_i) of 680 turnovers/Ir/hr using **1a** and is fully hydrogenated after 1.5hrs. The r_i for the imines **6** (80 t/Ir/hr), **7** (30 t/Ir/hr) and **8** (300 t/Ir/hr) are also some of the largest reported but we note that eventually the reductions are far from complete for **6** and **7** as a result of a rapid deactivation of the catalyst.

Table 1. Hydrogenation of Imines catalysed by $[Ir(PNP)(COD)]ClO_4$ Complexes

Catalyst	Imine	Yield(%)	Time(h)	r_i(t/Ir/h)
$[Ir(\mathbf{1})(COD)]ClO_4$	**5**	96	1.5	680
	6	4	0.25	80
	7	26	11	30
	8	99	1.5	300
$[Ir(\mathbf{2})(COD)]ClO_4$	**8**	100	1	715
	5	16	23	60

Standard Conditions: [Ir] = 1.57 10^{-2} mmol; [Imine]/[Ir] = 500; T = 30°C; P_{H_2} = 40 bar; solvent = THF (10 mL).

2a is in general less efficient catalyst except for the aldimine **8** where the hydrogenation is complete after 1hr with ri =715 t/Ir/hr.

The results of the asymmetric hydrogenation catalysed by **3a**, **4a**, **3b** and **4b** are shown in Table 2. **5** is rapidly (r_i= 280 t/Ir/hr) converted by **3a** into the chiral amine with modest enantioselectivity (ee= 40%); **4a** (prepared *in situ*) gave a higher ee (55%) but unfortunately deactivated more quickly. Using the rhodium complexes we found although **3b** shows no activity, **4b** is slightly active giving an ee of 41%. The reduction of **6** with **3a** and **4a** produced *in situ* as catalysts are surprisingly quite efficient but yield only low product enantioselectivities. The imine **7** gave both poor rates and ee values with all catalysts tested.

Table 2. Asymmetric Hydrogenation of Imines

Catalyst	Imine	Imine/M	P_{H_2}(bar)	Yield(%)	Time(h)	r_i(t/Ir/h)	ee(%)[a]
{Ir[(R,R)-**3**](COD)}ClO_4	**5**	500	40	87	3	280	40(S)
[Ir(COD)Cl]$_2$/2 ClO_4^-/2 (S,S)-**3**	**5**	500	40	65	1	520	34(R)
	6[b]	100	80	100	24	25	8(-)
	7	500	60	6	5	20	26(S)
{Rh[(R,R)-**3**](NBD)}ClO_4[c]	**5**	300	60	0	20	-	-
[Ir(COD)Cl]$_2$/(R,R)-**4**	**5**	500	60	5	18	5	-
[Ir(COD)Cl]$_2$/2 ClO_4^-/2 (R,R)-**4**	**5**	150	60	31	1	85	55(S)
Ir(COD)Cl]$_2$/2 ClO_4^-/2 (S,S)-**4**	**5**	500	80	37	20	120	53(R)
	6	100	50	6	10	10	-
	6[b]	100	80	88	23	40	7(-)
{Rh[(R,R)-**4**](NBD)}ClO_4[c]	**5**	500	60	9	22	30	41(S)

Standard Conditions: [M] = 1.57 10^{-2} mmol; T = 30°C; solvent = THF (10 mL). (**a**): For ee measurements, see references 7 and 11. (**b**): T = 50°C. (**c**): solvent = MeOH/CH_2Cl_2 9/1 (10 mL).

These preliminary results are promising. The hydrogenation rates of imines with these systems are very high but at present yields are limited in several cases by the deactivation of the catalyst. However, we have shown[14] that deactivation is a result of the irreversible formation of the dihydrido complex, $[Ir(PNP)H_2]^+$, which is susceptible to control by electronic and/or steric effects on the tridentate ligand. Similarly the enantioselectivities observed are only modest by today's standards but given that this family of ligands can be

modulated relatively easily, improvements in enantioselectivity for a target product can be anticipated. Finally complexes of these tridentate ligands[13] are also active hydrogenation catalysts for other unsaturated substrates (e. g. olefins, ketones) details of which will be reported separately[14].

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