Chemoselective Hydrogenation of Imines catalysed by Ir^{III} Complexes

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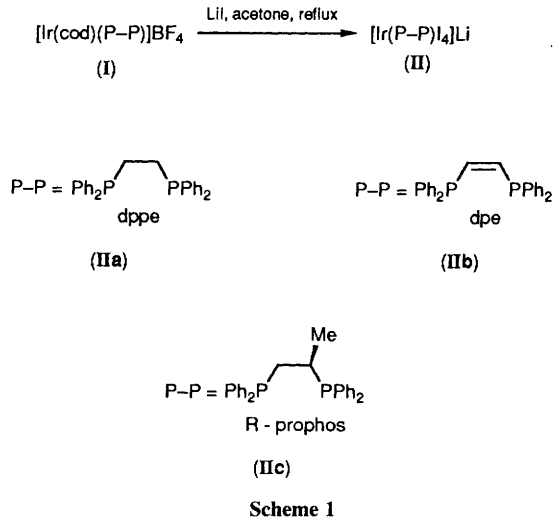
A new family of iridium(III) anionic complexes {Li[Ir(P–P)I_4]; P–P = 1,2-bis(diphenylphosphino)ethane, *cis*-1,2-bis(diphenylphosphino)ethylene, and *R*-(+)-1,2-bis(diphenylphosphino)propane} has been synthesised; they are efficient for catalytic and chemoselective hydrogenation of aldimines and ketimines at 20 °C and 25 bar H_2 (1 bar = 10^5 Pa).

The selective catalytic hydrogenation of the carbon to nitrogen double bond to the corresponding amine under mild conditions is important for organic synthesis. In homogeneous systems, only a few catalysts are effective for aldimine and ketimine[1—6] reduction but they are mostly, if not all, also effective for alkene and/or ketone hydrogenation. Rh^I/phosphine combinations have been generally used, particularly for enantioselective ketimine reduction, but recently the first Ir^I/chiral diphosphine[7] system has been successfully used to reduce prochiral ketimines.

We report herein the synthesis of a new family of anionic iridium(III)–tetraiododiphosphine complexes (**II**) that are efficient for catalytic hydrogenation of imines (**1**)—(**6**) under 25 bar H_2 (1 bar = 10^5 Pa) at 20 °C. Under similar conditions, alkenes, ketones, esters, nitriles, and nitro functionalities are not reduced and can be tolerated during imine reduction. This unprecedented high chemoselectivity and tolerance appears to be superior to that known for hydrogenation catalysts (both homogeneous and heterogeneous) as well as stoicheiometric reducing agents. The complexes Li[Ir(P–P)I_4] (**II**) [P–P = 1,2-bis(diphenylphosphino)ethane (dppe), *cis*-1,2-bis(diphenylphosphino)ethylene (dpe), and *R*-(+)-1,2-bis(diphenylphosphino)propane (*R*-prophos)] are conveniently prepared in 50—60% yield by refluxing the corresponding [Ir(cod)(P–P)]BF_4 (**I**) complex (cod = cyclo-octa-1,5-diene)

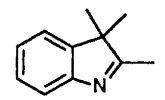


Scheme 1

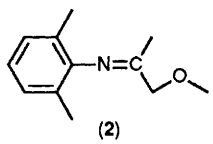
Table 1. Hydrogenation of imines (**1**)—(**6**) catalysed by Li[Ir(P–P)I_4] complexes.

Entry	Complex	S	S/Ir	$p(H_2)$/bar, T/°C	Time[a] /h
1	(**IIa**)	(**1**)	150	25, 20	2
2	(**IIa**)	(**2**)	150	25, 20	1
3	(**IIa**)	(**2**)	1500	25, 20	6
4	(**IIa**)	(**3**)	150	25, 20	0.5
5	(**IIa**)	(**4**)	300	25, 30	1
6	(**IIa**)	(**5**)	100	25, 30	2
7	(**IIa**)	(**6**)	150	25, 30	1
8	(**IIb**)	(**2**)	100	25, 30	2
9	(**IIc**)	(**1**)	250	25, 30	4
10	(**IIc**)	(**2**)	250	25, 30	6
11	(**IIc**)	(**3**)	250	25, 30	5

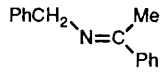
[a] Reaction time for quantitative conversion (99—100%, GC analysis).



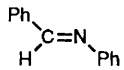
(**1**)



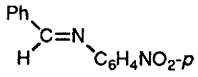
(**2**)



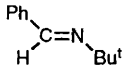
(**3**)



(**4**)



(**5**)



(**6**)

with excess lithium iodide in acetone for a few hours.† They are all air stable red crystalline solids. The oxidation from Ir^{I} to Ir^{III} probably occurs due to the presence of water, by an as yet unknown mechanism.

Metathesis of Li[Ir(dppe)I_4] with Ph_4AsBF_4 in acetone gave crystals of Ph_4As[Ir(dppe)I_4]·Me_2CO which has been analysed by *X*-ray diffraction.‡ The PLUTO plot of the anion is shown in Figure 1.

The catalytic hydrogenation of the imines (**1**)—(**6**) was carried out as follows. For example (entry 1), (**IIa**) (0.031 mmol) was dissolved in tetrahydrofuran (THF) (15 ml), then CH_2Cl_2 (5 ml) was added followed by the substrate (**1**) (4.65 mmol). The mixture was transferred to a 50 ml stainless steel autoclave, degassed three times with H_2 (25 bar) then pressurised to 25 bar. The reaction is followed by GC of a sample withdrawn at regular time intervals. After completion of the reaction, the amine is recovered in quantitative yield from the reaction mixture by pumping off the solvent followed by distillation under vacuum. The results are compiled in Table 1.

† For example, [Ir(dppe)(cod)]BF_4 (700 mg; 1.12 mmol) was refluxed with LiI (5.0 g; 37 mmol) in acetone (10 ml) for 3 h, whereby the colour changed from yellow to red. Acetone (10 ml) was then added to the solution which was allowed to cool to room temperature. After two days, red crystals of Li[Ir(dppe)I_4] could be isolated (332 mg). The mother liquor was left aside for a few days, giving more red crystals (total yield; 60%). All new complexes gave satisfactory elemental analyses. $^{31}P\{^1H\}$ NMR [81 MHz, ext. ref. 85% H_3PO_4, $(CD_3)_2CO$] for Li[Ir(dppe)I_4]: δ −2.7 ppm; Li[Ir(dpe)I_4]: δ 10.1 ppm; Li[Ir(*R*-prophos)I_4]; 11.1 (s) and −6.4 (s) ppm.

‡ *Crystal data* for Ph_4As[Ir(dppe)I_4]·Me_2CO: $C_{53}H_{50}OIrI_4P_2As$, deep red crystals, M = 1539,67, monoclinic, space group $P2_1/c$, a = 12.094(3), b = 13.206(4), c = 31.543(7) Å, β = 92.41(2)°, U = 5033.7 Å^3, Z = 4, D_c = 2.032, μ(Mo-K_α) = 58.207 cm^{-1}, crystal dimensions 0.2 × 0.1 × 0.1 mm, 4760 reflections [$I > 3\sigma(I)$], $2\theta_{max.}$ = 50°, R = 0.028, R_w = 0.031. Data were collected with the 2θ–ω scan method at 20° using a CAD-4 F diffractometer. The structure was solved by the direct method (MULTAN) and refined by full-matrix least-square techniques using the 'SDP, Structure Determination Package.'[8] Absorption corrections were applied. Hydrogen atoms were included in the structure factor calculation at idealized positions (d_{C-H} = 0.95 Å) and were assigned isotropic thermal parameters B(H) = 1.3 B_{eq}(C) Å^2. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

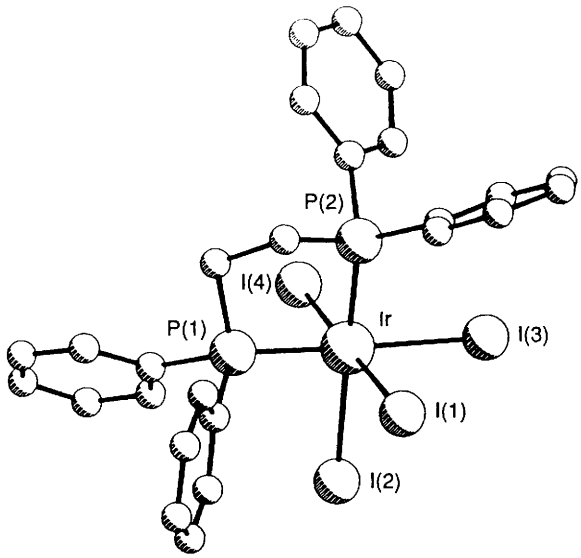


Figure 1. PLUTO plot of the [Ir(dppe)I_4] anion. Selected bond lengths (Å) and angles (°): Ir–P(1) 2.285(2), Ir–P(2) 2.291(2), Ir–I(1) 2.6954(6), Ir–I(2) 2.7578(6), Ir–I(3) 2.7619(6), Ir–I(4) 2.6926(6), P(1)–Ir–P(2) 86.49(7), I(2)–Ir–I(3) 88.21(2), I(1)–Ir–I(4) 176.85(2).

Examples of *N*-aryl, benzyl, and alkyl imines with a variety of carbon substituents have been smoothly reduced using a substrate to catalyst molar ratio (S/C) of 100—1500. For S/C = 1500 (entry 3) an initial turnover number of 1700 cycles h^{-1} was measured for reduction of the sterically hindered substrate (**2**). Short or negligible periods of induction were observed in every case. The solvent mixture THF/CH_2Cl_2 was found to give the fastest rates.

Chemoselectivity and tolerance tests were performed by carrying out the hydrogenation of an imine in presence of the other potential substrate or inhibitor **S** with imine/**S**/(**IIa**) = 100 : 100 : 1 at 25 bar H_2 and 30 °C. In presence of the substrate (**2**) and **S** = cyclohexane, acetophenone, benzylideneacetone,

nitrobenzene, or benzonitrile, (**2**) was quantitatively reduced with no reduction of **S** even over a long period of time ($t > 15$ h). Similar behaviour was observed with the combinations (**1**) and cyclopentanone and (**4**) and methyl benzoylformate. The rate of imine reduction was found to be unaffected by the presence of all **S** except in the case of benzonitrile where the initial rate for the hydrogenation of (**2**) was reduced by a factor of three. Although competition between the nitrile and the imine for co-ordination to the catalyst probably occurs, the former is not reduced. Further, for all **S** no reduction is observed in the absence of imine or amine. With diphenylacetylene and (**2**), reduction of (**2**) was completed without appreciable inhibition, but after 24 h, 10% of the acetylene was converted to a mixture of *cis*- and *trans*-stilbene in a 4 : 1 ratio.

In summary, these Ir^{III} complexes, which are easily prepared and conveniently handled, catalyse efficiently and chemoselectively the reduction of imines. There is evidence that a monohydrido-Ir^{III} complex is formed as the active species and detailed mechanistic studies will be reported separately. The use of chiral complexes such as (**IIc**) to achieve asymmetric reduction of prochiral imines is being investigated.

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