Iridium-catalysed Homogeneous Hydrogenation of Prochiral Enamides Containing Tetrasubstituted Alkene Moieties

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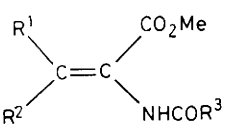
The tetrasubstituted prochiral amido-alkenes (**1a, b**), (**2a, b**), and (**3b**) have been homogeneously hydrogenated under very mild conditions by iridium complexes of the type $[Ir(cod)(bzn)(L)][ClO_4]$ (cod = cyclo-octa-1,5-diene, bzn = benzonitrile, L = tricyclohexylphosphine or neomenthyldiphenylphosphine).

Though much effort has been devoted to the synthesis of optically active amino-acid precursors *via* asymmetric hydrogenation of prochiral enamides with rhodium(I) complexes containing chiral phosphine ligands,[1] these catalytic systems are generally unable to reduce tetrasubstituted alkenes such as (**1a, b**). On the other hand, to the best of our knowledge, no related iridium catalysts have been studied for these purposes.

Crabtree *et al.*[2] have reported that the mixed-ligand complex $[Ir(cod)(py)(PCy_3)][PF_6]$ (py = pyridine, Cy = cyclohexyl) is a very active olefin hydrogenation catalyst in non-co-ordinating solvents, although it is generally deactivated in absence of substrate. Interestingly, this complex is able to hydrogenate the tetrasubstituted olefin 2,3-dimethylbut-2-ene, but it is deactivated progressively during the reaction giving rise to an inactive hydride cluster.[3]

We report herein the effectiveness of mixed-ligand cationic iridium(I) complexes for the hydrogenation of prochiral tetrasubstituted olefins. The results reported in Table 1 show that the complex $[Ir(cod)(py)(PCy_3)][ClO_4]$ is an effective catalyst precursor for the hydrogenation of the olefins (**1a, b**). However, the analogous complex $[Ir(cod)(py)(nmdpp)][ClO_4]$, containing the chiral neomenthyldiphenylphosphine is inactive under similar conditions. Interestingly, better results are found for the benzonitrile derivatives $[Ir(cod)(bzn)(L)][ClO_4]$ (L = PCy_3 or nmdpp). Thus, 200 mg of substrate [(**1a, b**) or (**2a, b**)] are completely hydrogenated after 15 s with 20 mg of $[Ir(cod)(bzn)(PCy_3)][ClO_4]$ as catalyst precursor, whilst 30 min [for (**1a, b**)] or 48 h [for (**2a, b**)] are required when the $[Ir(cod)(bzn)(nmdpp)][ClO_4]$ complex is used.

During this work we have only used the ClO_4^- anion,



(**1**) $R^1 = R^2 = Me$
(**2**) $R^1 = Me$; $R^2 = Ph$
(**3**) $R^1 = Ph$; $R^2 = Me$
(**4**) $R^1 = H$; $R^2 = Ph$
(**5**) $R^1 = Ph$; $R^2 = H$
a; $R^3 = Me$
b; $R^3 = Ph$

Table 1. Hydrogenation results.[a]

Catalyst precursor[b]	Substrate	Time	Yield/ %[c]	E.e./ %[d]
[Ir(cod)(py)(PCy_3)][ClO_4]	(**1a**)	6 h	100	—
	(**1b**)	6 h	100	—
[Ir(cod)(py)(nmdpp)][ClO_4]	(**1a**)	21 h	0	—
	(**1b**)	21 h	0	—
[Ir(cod)(bzn)(PCy_3)][ClO_4]	(**1a**)	15 s	100	—
	(**1b**)	15 s	100	—
	(**2a**)	15 s	100	—
	(**2b**)	15 s	100	—
[Ir(cod)(bzn)(nmdpp)][ClO_4]	(**1a**)	30 min	100	6.7
	(**1b**)	30 min	100	4.0
	(**2a**)	48 h	100	27.0
	(**2b**)	48 h	100	18.9
	(**3b**)	5 h	100	8.2
	(**4a**)	6 h	17	—
	(**4b**)	50 h	18	—
	(**5b**)	50 h	75[e]	—

[a] In a typical run 200 mg of substrate, 20 mg of catalyst precursor, 12 ml of dichloromethane, and 1 atm of H_2 at 293 K were used. After the required time the solvent was removed and the residue extracted with hot water or hot hexane and filtered to separate the catalyst. Evaporation to dryness left the product. [b] Abbreviations: cod = cyclo-octa-1,5-diene; py = pyridine; Cy = cyclohexyl; nmdpp = neomenthyldiphenylphosphine; bzn = benzonitrile. [c] Estimated by ^1H n.m.r. integration of the methyl ester singlet. [d] Enantiomeric excess estimated by tris-[3-(trifluoromethylhydroxymethylene)-(−)-camphorato]europium [$Eu(tfc)_3$] perturbed ^1H n.m.r. integration of the methyl ester singlet. All the predominant products correspond to the (+)-isomers. [e] 8% of (**4b**) is observed in the reaction mixture.

since previous work on the hydrogenation activity of [Ir(cod)(PR_3)$_2$]$^+$ complexes has shown that the use of various non-co-ordinating anions (ClO_4^-, PF_6^-, BF_4^-) does not appear to affect the results. Furthermore, related studies on cationic rhodium complexes containing chiral phosphines and two different anions (Knowles *et al.*[1e,4]) have shown that both gave the same optical yield of the reduction products. With these catalytic systems some unexpected and interesting features are observed: (a) the catalytic species are neither deactivated during the reaction nor when the substrate has been consumed; (b) the hindered tetrasubstituted olefins (**1a, b**), (**2a, b**), or (**3b**) are hydrogenated much faster than the less hindered trisubstituted (**4a, b**) or (**5b**); and (c) the (*E*) derivatives [(**3b**) and (**5b**)] are hydrogenated faster than the (*Z*) ones [(**2b**) and (**4b**)] in contrast with the reported observations with rhodium catalysts.[1]

Received, 25th July 1983; Com. 996

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