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FACILE HOMOGENEOUS HYDROGENATIONS OF HINDERED OLEFINS WITH $[Ir(cod)py(PCy_3)]PF_6$

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ABSTRACT: The title complex readily hydrogenates a number of hindered steroidal olefin groups from the α face, without reducing ketone carbonyl groups, carbon-halogen bonds or cyclopropane rings.

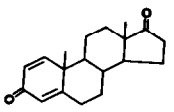
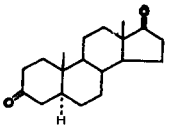
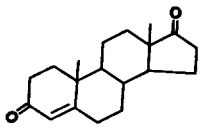
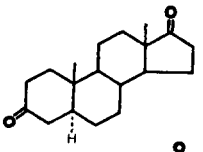
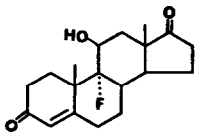
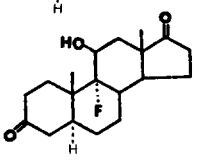
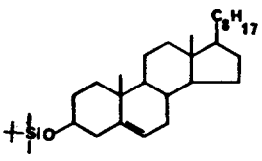
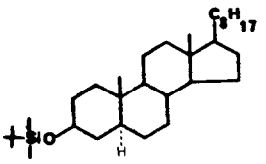
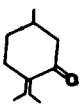
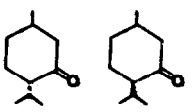
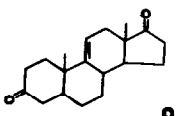
Many homogeneous hydrogenation catalysts share one shortcoming--hindered olefins are not reduced at useful rates. Normally, homogeneous hydrogenation solutions contain either coordinating solvents or dissociated ligands which compete with the olefin for catalytically active metal sites, preventing hydrogenation of most hindered olefins. An exception is the complex $[Ir(cod)L(py)]PF_6$ (cod = 1,5-cyclooctadiene, py = pyridine, L = tricyclohexylphosphine), which, when treated with hydrogen in a non-coordinating solvent, produces cyclooctane and an active iridium system that hydrogenates even 1-methylcyclohexane and 2,3-dimethyl-2-butene at synthetically useful rates.[1]

In connection with some synthetic studies, we wished to hydrogenate several Δ^4-3-keto-steroids to the corresponding 5α-3-ketosteroids. Heterogeneous catalysts normally give mixtures of 5α- and 5β-steroids, with the 5β isomer predominating. An enormous amount of work has been done to find conditions for selective reduction to one or the other isomer, and while fascinating directing effects have been discovered, a general solution based on heterogeneous catalysts has not been found.[2]

Only $RhCl(PPh_3)_3$ selectively and reproducibly hydrogenates Δ^4-steroids from the α face.[3] However, the reduction requires days and yields are low. The high activity of $[Ir(cod)L(py)]PF_6$ with simple olefins encouraged us to investigate its reactivity with unsaturated steroids.

TABLE I

Hydrogenations with $[Ir(cod)L(py)]PF_6$ [a]

	Olefin	Mol % [Ir] [b]	Time (hr)	Product [c]		Yield %
1.		15(3)	18		(4.9)	73 [d]
2.		20(4)	4		(3.5)	70 [d]
3.		39(2)	18		(1)	38 [d]
4.		25(1)	1		(4)	100 [e]
5.		12(1)	0.5	 61% 39%	(6)	73 [d]
6.		36(2)	3	no reaction		0
7.		4(1)	22		(24)	94 [d]

a) Hydrogen was bubbled through all solutions except the first and last, which were run under 1 atm of H_2.

b) The numbers in parenthesis refer to the number of equivalent portions of catalyst added which gave the final mole per cent of catalyst.

c) All products had the correct melting or boiling points and spectral properties and were homogeneous by tlc. Turnover numbers (mol product/ mol Ir) appear in brackets.

d) Yield after isolation by preparative tlc on silica gel.

e) Yield by nmr integration. Isolated yield was 10 percent lower.

f) We thank Prof. R. Danheiser and Mr. J. M. Morin, Jr., MIT, for allowing us to include their result of this experiment.

The results summarized in Table 1 show $[Ir(cod)L(py)]PF_6$ has high activity, much greater than the commonly used $RhCl(PPh_3)_3$ and retains the 5α selectivity of $RhCl(PPh_3)_3$. No 5β products could be seen by nmr or tlc. Experimentally, we obtained the best rates by bubbling hydrogen though the solution rather than by working under one atmosphere of hydrogen with magnetic stirring. Bubbling may help to maintain a higher hydrogen partial pressure in solution. Addition of the catalyst in portions was advantageous, since dimerization or trimerization of the coordinatively unsaturated catalytically active species to inactive complexes is a known side reaction. Polar groups, especially alcohols, deactivate the catalyst but this can be avoided by using the t-butyldimethylsilyl protecting group. Where the alcohol is very hindered, as is the 11β hydroxyl of example 3, hydrogenation takes place, but sluggishly. Finally, even under five atmospheres of hydrogen, the very hindered $\Delta^{9,11}$ olefin in example 6 was inert. Of parallel importance with the catalyst's high activity is the observation that the catalyst is unaffected by the presence of carbon-halogen bonds or the cyclopropane functionality in the substrate. The cyclopropane bond in 7, for example, is cleaved by heterogeneous hydrogenation catalysts, and organic halides frequently poison heterogeneous catalysts. The unreactivity of $[Ir(cod)L(py)]PF_6$ with oxidizing functionality distinguishes it from most other hydrogenation systems.

Enones of the type 1-3, and 5 seem to be excellent ligands, binding via oxygen. This binding may be an important factor in the success of the system, since protection of the catalyst from deactivation increases yields in the reductions of simple alkenes.[1] The enone must subsequently dissociate and bind via the C=C bond for reduction to take place. Novel O-bound intermediates[4] have been detected by ^1H NMR spectroscopy at -60°. For example, 1 reacts with $[IrH_2(H_2O)_2(PPh_3)_2]^+$ in CD_2Cl_2 to give cis,cis,trans-$[IrH_2(1)_2(PPh_3)_2]^+$ 8, PMR: IrH, -23.68, J_{PH} 16Hz and with $[IrH_2(Me_2CO)_2Lpy]^+$ to give largely cis$[IrH_2(1)_2$-$Lpy]^+$ 9, IrH, -28.58, J_{PH} 18Hz. 8 does not transfer H_2 to 1 on warming; 9 does so at -20°. Qualitative studies give the displacement order dienone > enone > ketone for these systems. Presumably, the extended π-delocalization for the dienone leads to a better metal-ligand π-bond. This may help account for the observation that while the two C=C bonds of 1 are reduced sequentially ($^1\Delta$ first), they are also hydrogenated at the same rate. 1 must bind the active site via oxygen better than does 2, counteracting the intrinsically greater reactivity of the $^1\Delta$ double bond.

A typical experimental procedure follows: 5α-Androstan-3,17-dione. To a solution of Δ^4-androstan-3,17-dione (.068g, .24mmols) in 10 ml of CH_2Cl_2 under argon was added one-fourth of a solution of $[Ir(cod)py(PCy_3)]PF_6$[5](.040g, .05mmoles) in 2 ml of CH_2Cl_2. Hydrogen was bubbled through the solution and the remaining catalyst solution added in 0.5 ml portions at one hour intervals. Normally the solution reddens with H_2 and becomes yellow when the catalyst is expended. After four hours no further reaction took place, and the 5α-androstan-3,17-dione was isolated by preparative thin layer chromatography on silica gel. The crude reaction mixture contained an 80% yield of the 5α-steroid by nmr, the isolated yield of chromatographically pure material was 70%. Recrystallization from hexane gave material with the nmr, ir, mp and mixed mp of authentic material. The catalyst and its solutions are stable to air. Chromatography can be avoided by precipitating the catalyst with hexane, when the product is hexane soluble.

REFERENCES AND NOTES

1. R. H. Crabtree, Accts. Chem. Res., 12, 331 (1979); R. H. Crabtree, H. Felkin and G. E. Morris, J. Organometal Chem., 141, 205 (1977).
2. R. L. Augustine, "Organic Reactions in Steroid Chemistry", Vol. 1, J. Fried and J. A. Edwards, Eds, Van Nostrand Reinhold Company, New York, 1972. Sodium in ethanol and analogous reagents do give 5α-steroids from Δ^4-3-ketosteroids; however, numerous functional groups are also reduced by this reagent.
3. W. Voelter and C. Djerassi, Chem. Ber., 101, 58 (1968).
4. The intermediates seem to be O-bound by comparison with the known O- and C=C-bound examples: R. H. Crabtree, H. Felkin, T. Fillebeen-Khan and G. E. Morris, J. Organometal Chem., 168, 183 (1979).
5. R. H. Crabtree and G. E. Morris, J. Organometal Chem., 135, 395 (1977). Briefly, the complex is prepared by heating H_2IrCl_6 in i-PrOH at reflux with excess cod for six hours and removing volatiles to give $[IrHCl_2(cod)]_2$. Dissolving 0.3g of this in 15 ml EtOH, 1 ml py, and 0.5g of NH_4PF_6 gives a precipitate of $[Ir(cod)py_2]PF_6$ which, upon treatment with a small excess of PCy_3 in acetone gives $[Ir(cod)py(PCy_3)]PF_6$. It can be isolated by addition of EtOH and concentration of the solution.

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