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TRANSFER OF HYDROGEN FROM ALCOHOLS TO KETONES CATALYZED BY IRIDIUM COMPLEXES WITH 2,2'-BIPYRIDINE, 1,10-PHENANTHROLINE, AND THEIR DERIVATIVES

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Summary

Complexes of the type Ir(I)chelCODCl (chel = bipy; 4,4'-Me_2bipy; phen; 4,7-Me_2phen; 3,4,7,8-Me_4phen; 4,7-Ph_2phen; COD = 1,5-cyclooctadiene) catalyze the hydrogen transfer from alcohols to ketones. The dependence of the rate and the stereoselectivity on the complex, the concentrations of the water and KOH is studied in detail, and a reaction mechanism is proposed. The most active of the above complexes is the 3,4,7,8-Me_4phen derivative, which gaves turnovers of up to 1150 cycles/min and is still efficient at 4×10^{-6} *M* concentration. Furthermore it favours the formation of the *trans* alcohol in the reduction of the t-butylcyclohexanone with high stereoselectivity.

Introduction

Reduction of unsaturated organic substrates catalyzed by complexes of transition metals can be accomplished by hydrogenation (eq. 1) or by hydrogen transfer from a donor (alcohol, amine, olefins, cyclic ethers . . .) to the acceptor (eq. 2) [1—4].

$$S + H_2 \overset{cat}{\rightleftharpoons} SH_2 \quad (1)$$

$$DH_2 + S \overset{cat}{\rightleftharpoons} D + SH_2 \quad (2)$$

Among the numerous homogeneous catalysts suitable for such reactions, the most active are complexes of rhodium, ruthenium and iridium, with phosphines, cyclopentadienyls and DMSO as supporting ligands. These usually show satisfactory catalytic activities in the reduction of olefins, ketones [1,2,5] Schiff bases [6—8] and nitro-derivatives [9—11]. Rhodium and iridium complexes with 2,2'-bipyridine (bipy), 1,10-phenanthroline (phen) and related derivatives, are good catalysts for the reduction of ketones and α,β-unsaturated ketones [12—16].

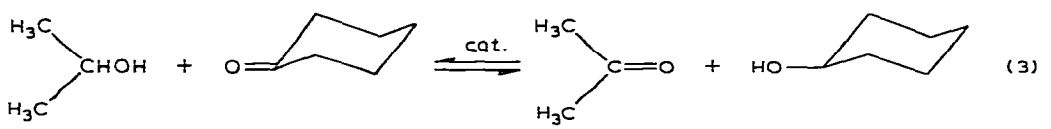
This paper presents the results of a detailed study of hydrogen transfer from alcohols to ketones catalyzed by iridium complexes of the type IrchelCODCl (chel = bipy; 4,4-Me_2bipy; phen; 4,7-Me_2phen; 3,4,7,8-Me_4phen; 4,7-Ph_2phen; COD = 1,5-cyclooctadiene). Isopropanol was used as hydrogen donor; the substrates were cyclohexanone (for the study of the catalytic activity of the complexes) and 4-t-butyl-cyclohexanone (for the study of the stereoselectivity).

Results

Activation of the catalysts

The formation of catalytically active species from the starting complexes IrchelCODCl requires the displacement of the coordinated COD. This step was accomplished by air oxidation of the isopropanol solutions at room temperature, followed by refluxing under argon in the presence of small amounts of potassium hydroxide. The addition of KOH without previous oxidation of the complex gives deep blue inactive solutions. The rate of the reduction of the oxidized species increases on increasing the concentration of the complex and the hydroxide. Incomplete prereduction is associated with a substantial loss of activity (Fig. 1).

Table 1 summarizes some conversion data at different [S]/[cat] ratios for the reduction (eq. 3) of cyclohexanone with the extremely active 3,4,7,8-Me_4phen derivative.



(3)

The catalytic activity depends on the concentrations of the complex, water, KOH, and substrate.

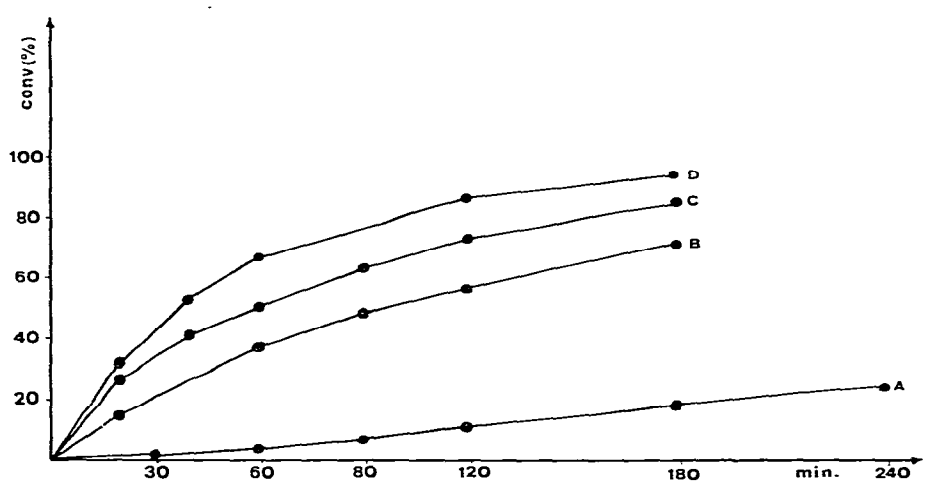


Fig. 1. Reduction of cyclohexanone with iso-PrOH in the presence of Ir(3,4,7,8-Me_4phen)CODCl: catalytic activity versus prereduction time. Prereduction (min): A, 0; B, 15; C, 30; D, 45.

TABLE 1

REDUCTION OF CYCLOHEXANONE WITH iso-PrOH IN THE PRESENCE OF Ir(3,4,7,8-Me_4phen)-CODCl.

[S]/[cat]	[KOH]/[cat]	H_2O (%)	Conversion (%)	Time (h)	Rate (cycles/min) [c]
7940	8	2	96.8	1.5	201
7940	8	1.3	99.75	1.5	378
39700	40	1.3	95	3	694
79400	80	0.6	98	8	820
99250	100	0.6	98.35	16	602
158800 [a]	80	0.6	98.55	19	1159
198500 [b]	200	0.6	94.1	18	1095

[S] = 0.766; [a] [S] = 1.532; [KOH] = 8×10^{-4}; [b] [cat] = 4×10^{-6}; [c] average, at about 30% conversion.

Fig. 2 shows the relationship between reaction rate and catalyst concentration (see also Figs. 3 and 4) at constant KOH concentration and varying percentages of water. Surprisingly, the catalytic activity increases on decreasing the concentration of the catalyst, this effect becoming more marked on decreasing the water concentrations.

As can be seen from Fig. 5 the rate depends on the water concentration, passing through a maximum, which is shifted to lower percentages of water by decreasing the concentrations of KOH. The rate also passes through a maximum on changing the KOH concentration at a constant water percentage (Fig. 6).

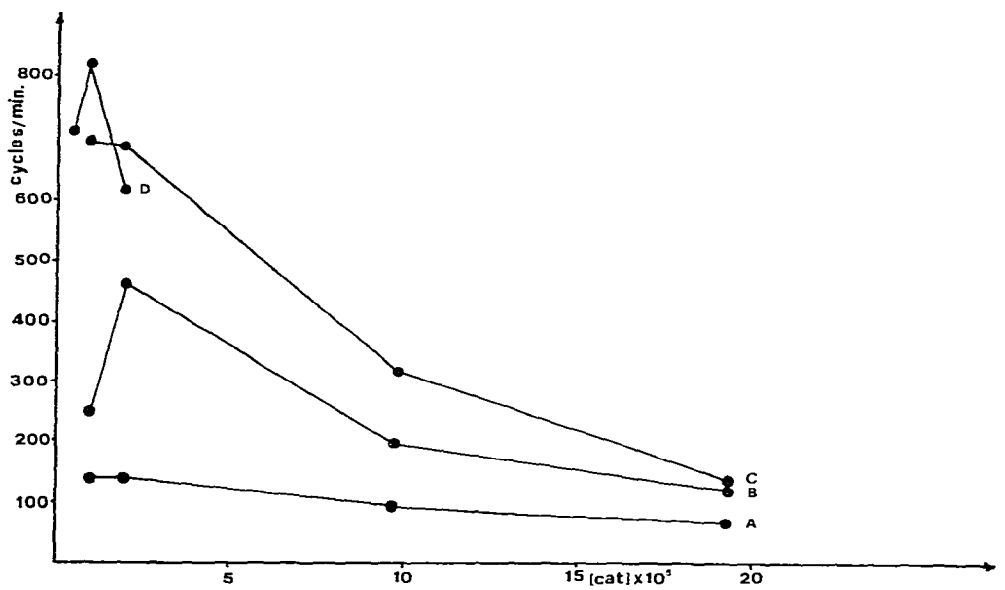


Fig. 2. Reduction of cyclohexanone with iso-PrOH in the presence of Ir(3,4,7,8-Me_4phen)CODCl: reaction rate versus catalyst concentration at different amounts of water. [S] = cost = 0.766; [KOH] = cost = 8×10^{-4}; H_2O (%): A, 4; B, 2; C, 1.3; D, 0.6.

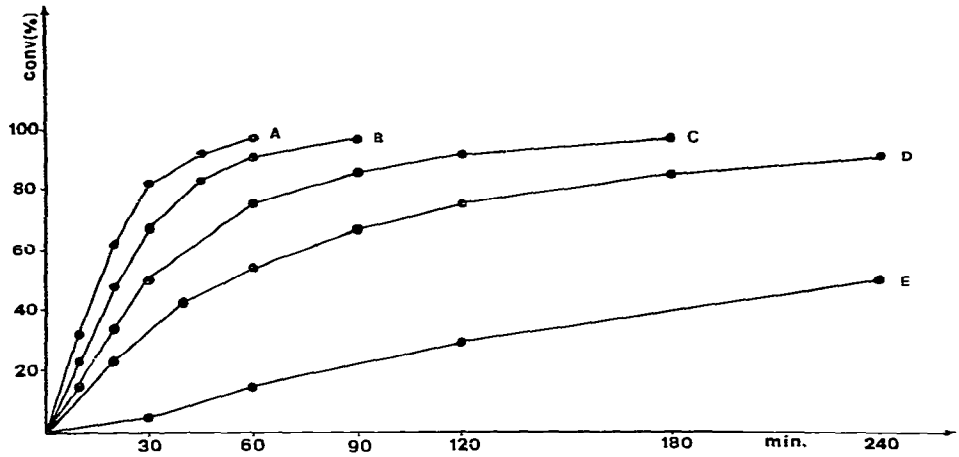


Fig. 3. Reduction of cyclohexanone with iso-PrOH in the presence of Ir(3,4,7,8-Me_4phen)CODCl: conversion (%) versus time at different [S]/[cat] ratios. [S] = cost = 0.766; [KOH] = cost = 8×10^{-4}; H_2O = 2%; [S]/[cat] = A, 3970; B, 7940; C, 19850; D, 39700; E, 79400.

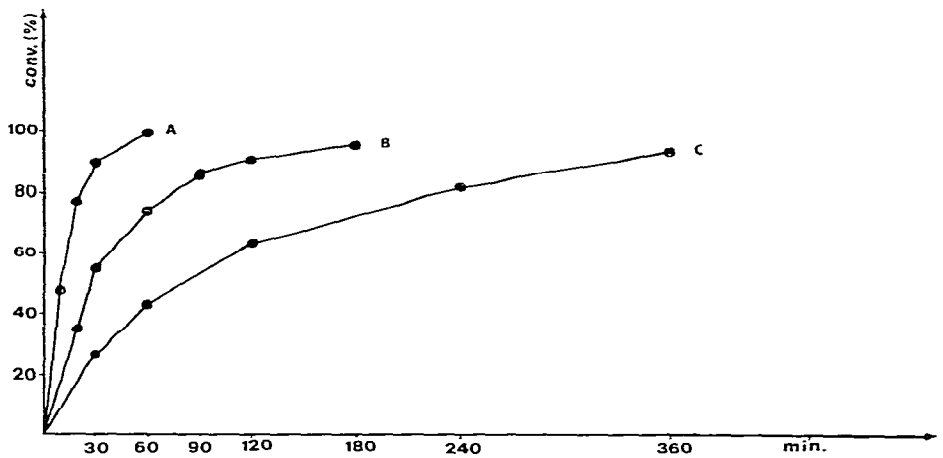


Fig. 4. Reduction of cyclohexanone with iso-PrOH in the presence of Ir(3,4,7,8-Me_4phen)CODCl: conversion (%) versus time. [S] = cost = 0.766; [KOH] = cost = 8×10^{-4}; H_2O = cost = 1.3%; [S]/[cat] = A, 7940; B, 39700; C, 79400.

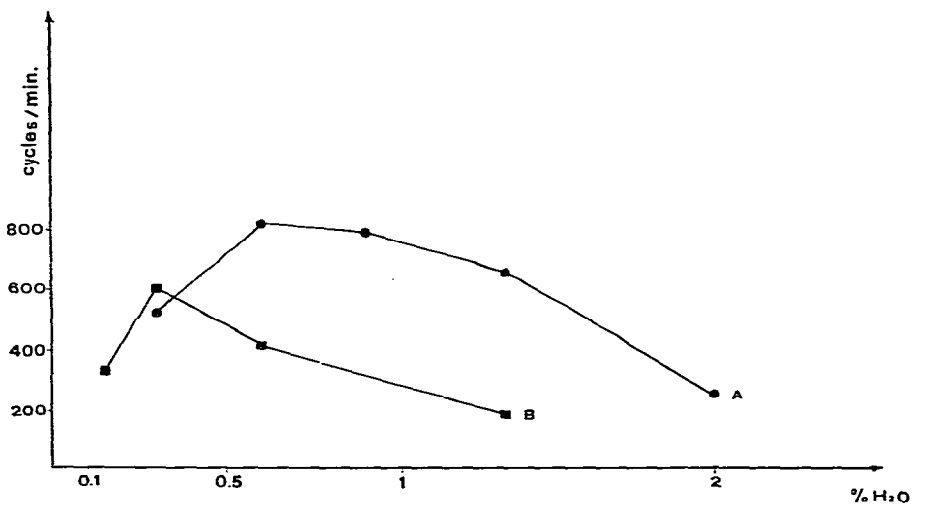


Fig. 5. Reduction of cyclohexanone with iso-PrOH in the presence of Ir(3,4,7,8-Me_4phen)CODCl: reaction rate versus water (%). [S] = cost = 0.766; [KOH] = A, 8×10^{-4}; B, 4×10^{-4}; [S]/[cat] = 79400.

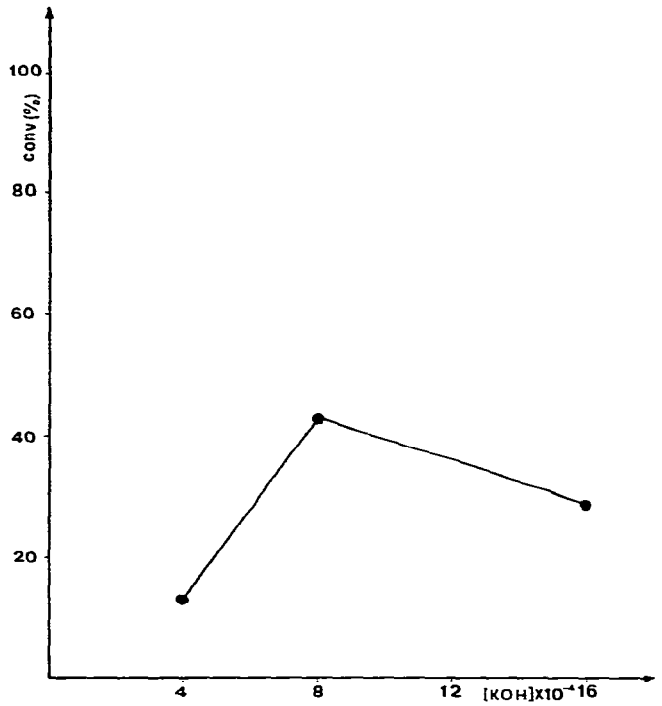


Fig. 6. Reduction of cyclohexanone with iso-PrOH in the presence of Ir(3,4,7,8-Me_4phen)CODCl: conversion (%) at different amounts of KOH. Time reaction: 1 h; H_2O = cost = 1.2%; [S]/[cat] = 79400.

Fig. 7 shows a plot of the reaction rate versus the substrate concentration. Again a maximum is reached, followed in this case by a rather sharp fall of catalytic activity.

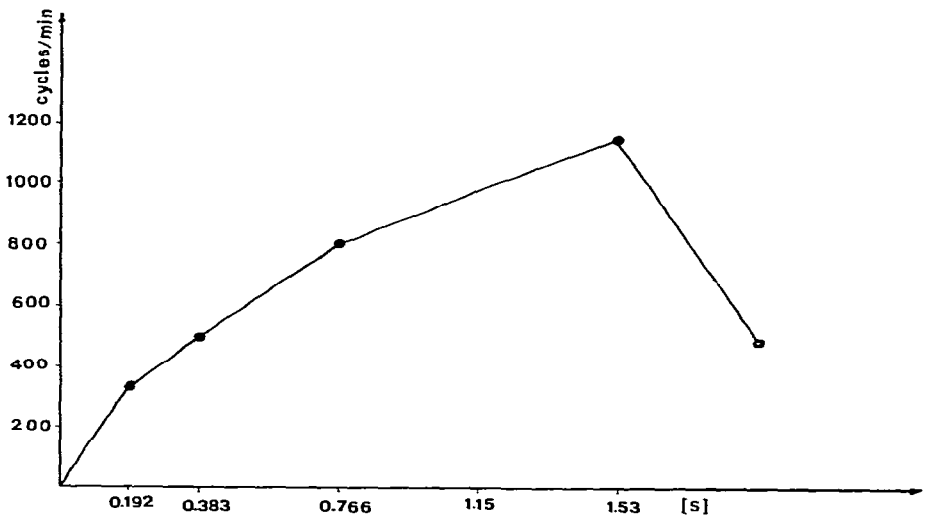


Fig. 7. Reduction of cyclohexanone with iso-PrOH in the presence of Ir(3,4,7,8-Me_4pgen)CODCl: reaction rate versus substrate concentration. [Cat] = 1×10^{-5}; [KOH] = 8×10^{-4}; H_2O = 0.6%.

TABLE 2

REDUCTION OF CYCLOHEXANONE WITH iso-PrOH, IN THE PRESENCE OF DIFFERENT Ir(chel)-CODCl COMPLEXES

chel	Conversion (%) [a]	p*Ka*
3,4,7,8-Me_4phen	95.0	6.31
4,7-Me_2phen	18.9	5.94
5,6-Me_2phen	10.5	5.60
phen	4.3	4.86
4,7-Ph_2phen	12.1	4.84
4,4-Me_2bipy	8.9	5.32
bipy	13.7	4.44

[S] = 0.766; [KOH] ~ 8×10^{-4}; H_2O = 0.6% [S]/[cat] = 38300.
[a] After 3 h.

TABLE 3

REDUCTION OF CYCLOHEXANONE WITH iso-PrOH, IN THE PRESENCE OF DIFFERENT Ir(chel)-CODCl COMPLEXES

chel	[S]/[cat]	Conversion (%)	Time (h)
4,7-Me_2phen	3.800	90	3
5,6-Me_2phen	3.800	66.4	4
phen [a]	3.120	94	1
4,7-Ph_2phen	3.800	88.3	3
bipy	7.600	56	4
4,4-Me_2bipy	3.800	80.4	4

[KOH] = 1.6×10^{-3}; [a] [KOH] = 3.5×10^{-2}; H_2O = 2%.

TABLE 4

REDUCTION OF 4-t-BUTYLCYCLOHEXANONE WITH iso-PrOH IN THE PRESENCE OF DIFFERENT Ir(chel)CODCl COMPLEXES: RELATIONSHIP BETWEEN STEREOSELECTIVITY AND NATURE OF THE CHELATING LIGAND

chel	Conversion (%)	Time (min)	*trans*-Isomer (%)
3,4,7,8-Me_4phen	100	30	82.0
4,7-Me_2phen	94.4	90	63.5
phen	33.6	120	57.6
4,7-Ph_2phen	97.1	120	39.7
4,4-Me_2bipy	97.2	90	52.4
bipy	80.5	120	68.6

[S]/[cat] = 1630; [KOH]/[cat] = 5.

TABLE 5

REDUCTION OF 4-t-BUTYL CYCLOHEXANONE WITH iso-PrOH IN THE PRESENCE OF Ir(3,4,7,8-Me_4phen)CODCl: STEREOSELECTIVITY AT DIFFERENT PERCENTAGES OF WATER

H_2O (%)	Conversion (%)	Time (min)	*trans*-Isomer (%)
0.03	99	40	95.8
2	98.3	30	95.8
4	99.5	30	94.8
4	100	40	93.7

[Cat] = 4×10^{-4}; [KOH]/[cat] = 1; [S]/[cat] = 1630.

TABLE 6

REDUCTION OF 4-t-BUTYLCYCLOHEXANONE WITH iso-PrOH IN THE PRESENCE OF Ir(3,4,7,8-Me_4phen)CODCl: RELATIONSHIP BETWEEN STEREOSELECTIVITY AND [KOH]/[cat] RATIO

[KOH]/[cat]	Conversion (%)	Time (min)	*trans*-Isomer (%)
1	98.3	30	95.8
2.5	96.7	45	86.5
5	100	30	82.0
10	99.35	30	78.7

[Cat] = 4×10^{-4}; [S]/[cat] = 1630.

TABLE 7

REDUCTION OF KETONES WITH iso-PrOH IN THE PRESENCE OF Ir(3,4,7,8-Me_4phen)CODCl

Substrate	[S]/[cat]	Conversion (%)	Time (min)
Acetophenone	5140	93.4	180
Propiophenone	4480	95.2	120
Benzophenone	3300	95.5	165
Benzil [a]	3300	100	120

[a] The benzil is reduced to 1,2-diphenylethandiol.

Catalytic activity and nature of the nitrogencontaining chelating ligand

Table 2 lists comparable conversion data for the cyclohexanone reduction catalyzed by the different complexes. The results show clearly that the derivative with the 3,4,7,8-Me_4phen is by far the most active. Among the phenanthroline complexes the catalytic activity increases appreciably with the pK_a of the chelating ligand, except for 4,7-Ph_2phen. An opposite effect is observed for the bipy and 4,4′-Me_2bipy derivatives. All the above complexes, however, give high percentages of conversion by operating at higher concentrations and/or increasing the amount of KOH (Table 3).

Reduction of 4-t-butylcyclohexanone

The thermodynamically more stable alcohol (equatorial OH) is preferentially formed in the reduction of 4-t-butylcyclohexanone with iridium complexes under the conditions used. The relationship between the stereoselectivity and the nature of the chelating ligand is shown in Table 4: the 3,4,7,8-Me_4phen derivative, which is again the most active complex, also gives the highest stereoselectivity. The stereoselectivity is scarcely affected by the water concentration (Table 5), but is improved markedly by lowering the concentration of KOH (Table 6).

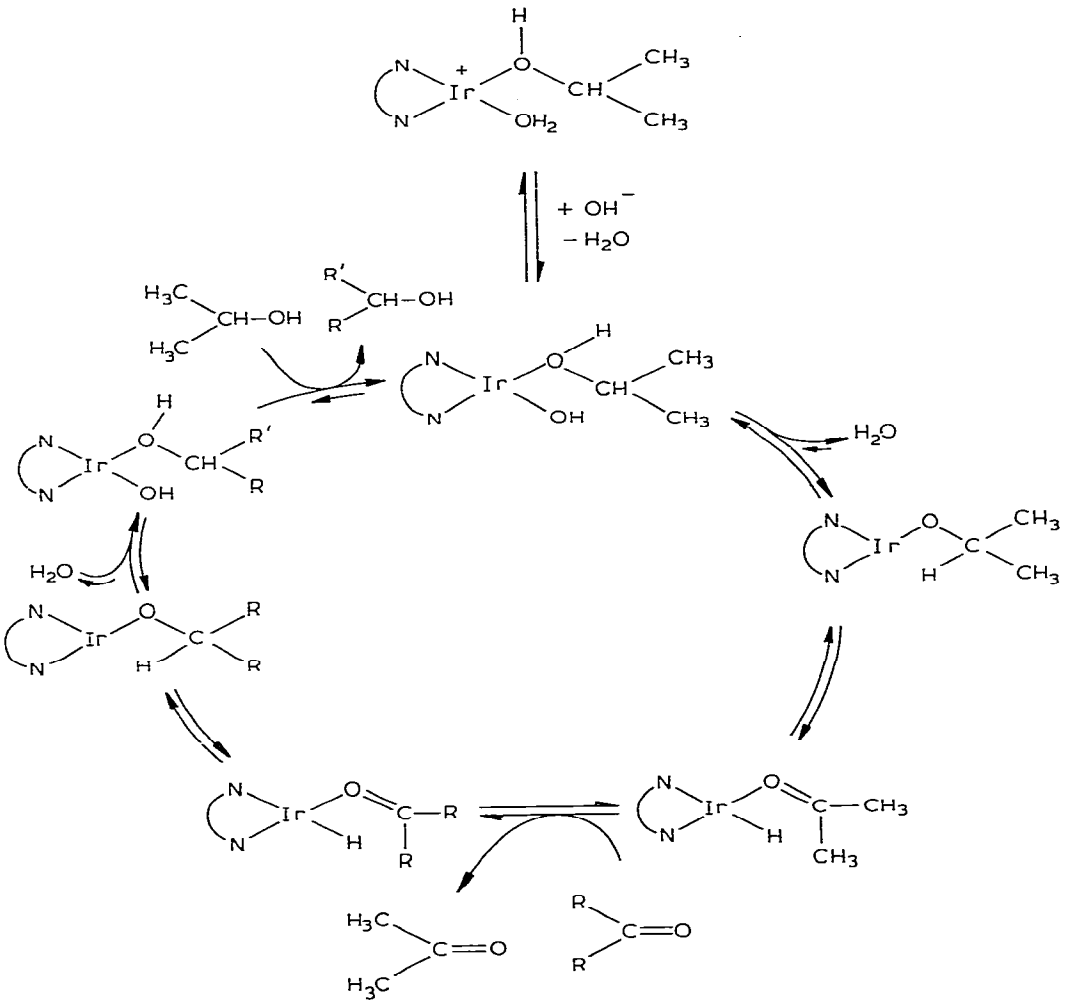
The complex with 3,4,7,8-Me_4phen shows also a high catalytic activity in the reduction of other substrates (Table 7).

Discussion

The mechanism proposed for the above reactions is represented in Scheme 1. The active species obtained after the reduction in isopropanol of the original oxidized complex, namely after the COD displacement, must be a cationic

SCHEME 1

Mechanism of reduction of ketones with iso-PrOH in the presence of Ir^I complexes with bipy, phen and derivatives. Only the essential molecules of solvent are taken into account.



solvated Ir^I species, in equilibrium with the neutral form with coordinated chloride (eq. 4).

$$Irchel(S)_2^+Cl^- \rightleftharpoons Irchel(S)_2Cl \quad (S = solvent) \tag{4}$$

In the presence of alkali the cationic form is in turn in equilibrium with a neutral isopropoxo derivative. The rate-determining step of the catalytic cycle, as already reported for other mechanisms [17], is a β-elimination reaction to form acetone and an Ir^I monohydride derivative, followed by coordination of the ketone (via oxygen) and transfer of the hydride tc the electrophilic carbon, through a mechanism which is a reverse of the β-elimination. The alkoxo-derivative so formed reacts with a molecule of water or solvent, giving the alcohol and a hydroxo or isopropoxo species, which enters the cycle again.

An increase in the concentration of either KOH or water causes an initial acceleration and then a retardation. For KOH the higher rates must be due mainly to a higher concentration of the isopropoxo species, which has to compete with the increasing stability of the alkoxo species. Analogously, a higher water concentration (at constant KOH) must favour hydrolysis of either the alkoxo-derivative or of the isopropoxo-derivative, with opposite effects. This explains how the water concentration at which the maximum rate is obtained is related to the KOH concentration, and decreases with the latter. Furthermore the presence of water can reduce the reaction rate owing to coordination to the metal which competes with that of the ketone.

The hypothesis of ketone coordination via oxygen is in agreement with the fact that the reaction is of zero order with respect to the solvent (contemporaneously hydrogen donor) but first order with respect to the ketone *. In effect benzophenone and benzil are reduced very rapidly.

The influence of the catalyst concentration on the rate is due, at least in part, to inhibition by the chloride ion **. Association phenomena cannot be excluded.

The rate increase associated with the increasing pK_a of the phenanthrolines must be related to a higher lability of the iridium in this series of complexes.

The better stereoselectivity obtained with a low KOH concentration may be due, at least in part, to the higher protonation rate of the alkoxo derivative. It is difficult, however, to explain why the equatorial alcohol is preferentially formed.

Conclusions

The above results show that the derivative containing 3,4,7,8-Me_4phen is an extraordinarly active species for the reduction of ketones (turnover of 1150 cycles/min) and effective at very low concentrations (4×10^{-6} *M*). The preferential formation of alcohols with the —OH group in equatorial position increases the interest of this complex, since in general the other catalysts favour the formation of the axial alcohols, and the equatorial alcohols usually have to be made with stoichiometric reagents ***.

It should also be noted that the reactions do not give side-products and that the catalyst can be recovered and recycled without loss of activity, evidently because of the high stabilities of the catalytic species. Furthermore it is probable that catalytic activity for this kind of reactions can be further improved by using similar complexes involving chelating ligands of higher pK_a.

Experimental

The iridium complexes were made by published methods [18]. The other reagents were commercial products, and were distilled or recrystallized before use.

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* Coordination via enol or enolate should give a zero order also for the ketone, as observed for the α,β-unsaturated ketones.

** The low solubility prevented examination of complexes containing less coordinated anions.

*** In some respects the behaviour of the above complexes is similar to that of the dehydrogenases: the activities, selectivities and mechanisms will be compared in a future paper.

Methods

Suitable amounts of the complexes were dissolved in 50 ml of iso-PrOH (1% H_2O) and oxidized overnight by atmospheric oxygen at room temperature *. The yellow solutions were transferred to a three-necked flask and heated under reflux in an argon stream. To the boiling solution were added appropriate amounts of deaerated aqueous KOH. When the reduction was complete (brown colour) the deaerated substrate was added, and the reaction carried out under reflux.

The reactions were followed by GLC on samples removed under argon from time to time. The withdrawn samples are immediately oxidized by air and the reaction stops.

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* The solution of the oxidized complex is stable and can be stored for weeks without loss of activity.