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# Aspects of Catalysis. Part I. Reduction of Unhindered Cyclohexanones to Axial Alcohols in the Presence of a Soluble Iridium–Phosphite Catalyst

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Some unhindered alkyl-substituted cyclohexanones are reduced by phosphorous acid in aqueous propan-2-ol solution containing a catalyst prepared in situ from iridium chloride and phosphorous acid (or an easily hydrolysed ester of this acid) to give exceptionally high proportions (often >96%) of axial alcohols.

Most reagents that reduce ketones to secondary alcohols give a preponderance of the more stable equatorial alcohol when applied to alkyl-substituted, relatively unhindered cyclohexanones. Reagents that contravene this general tendency include (each figure refers to the proportion of cis-axial alcohol from the reduction of 4-t-butylcyclohexanone): hydrogen-platinum-acetic and hydrochloric acids  $(78 \pm 3\%)$ ;<sup>1</sup> isobornyloxyaluminium dichloride in ether (80-92%);<sup>2</sup> propan-2-ol containing hydrochloric acid (65-70%);<sup>3</sup> propan-2-ol in the presence of platinum and hydrochloric acid (90%);<sup>4</sup> and propan-2-ol in the presence of the soluble hydridoiridium catalyst, HCl<sub>2</sub>Ir(Me<sub>2</sub>SO)<sub>3</sub> (77%).<sup>3,5</sup> A reagent, di-isoamylborane, that affords a 79:21 ratio of cis- to trans-alcohols from the reduction of 2-methylcyclohexanone<sup>6</sup> gives a low proportion (7%) of *cis*-alcohol when applied to 4-t-butylcyclohexanone.<sup>7</sup>

The present work represents an extension of the finding that unhindered ketones can be reduced by propan-2-ol in the presence of catalytic amounts of iridium sulphoxide complexes. As already noted, reduction of

<sup>4</sup> H. B. Henbest and A. Zurquiyah, unpublished work. <sup>5</sup> H. B. Henbest and J. Trocha-Grimshaw, *Chem. Comm.*, 1967, 544.

<sup>6</sup> H. C. Brown and V. Varma, J. Amer. Chem. Soc., 1966, 88, 2871.

7 H. C. Brown, personal communication.

<sup>&</sup>lt;sup>1</sup> E. L. Eliel and R. S. Ro, J. Amer. Chem. Soc., 1957, 79, 5992.

<sup>&</sup>lt;sup>2</sup> E. L. Eliel and D. Nasipuri, *J. Org. Chem.*, 1965, **30**, 3809. <sup>3</sup> Y. M. Y. Haddad, H. B. Henbest, J. Husbands, and T. R. B. Mitchell, Proc. Chem. Soc., 1964, 361.

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4-t-butylcyclohexanone by this system gives a preponderance of the *cis*-alcohol (77%). It was of interest to see if this proportion could be raised by use of other ligands, in particular those containing phosphorus. The survey was carried out by heating a mixture of 4-t-butylcyclohexanone, iridium tetrachloride, and a potential ligand in aqueous propan-2-ol solution for 16 hr. Under these conditions the ketone was essentially not reduced when a phosphine (n-Bu<sub>3</sub>P or Ph<sub>3</sub>P) was present as the stabilising ligand. [Subsequent experiment showed that the hydride, HCl<sub>2</sub>Ir(PPh<sub>3</sub>)<sub>3</sub>,<sup>8</sup> is not active as a hydrogen-transfer catalyst; the related trihydride, Reduction of  $5\alpha$ -cholestanone gave a 92:8 ratio of  $3\alpha$ -(axial) to  $3\beta$ -(equatorial) cholestanols.

A possible source of hydrogen for reduction of carbonyl compounds by the new procedure is propan-2-ol, which could thereby be converted into acetone. However, although acetone could be detected as a product from some of the experiments with the iridium-phosphite catalyst in aqueous propan-2-ol, it was formed in low yield (5% or less) and none was obtained from a reaction conducted in a sealed tube. A further indication that the reaction did not depend on equilibration between carbonyl and alcohol components was that the presence

Reduction of carbonyl compounds in a boiling mixture of propan-2-ol (10 ml.) and water (5 ml.)

Carbonyl compound	Phosphite (mmoles)	Iridium tetrachloride	Time (hr)	Reduction	Stereoselectivity: cis- to trans-alcohol
(minores)		(innoies)	()	(%)	ratio $(\pm 2\%)$
4-t-Butylcyclohexanone	H <sub>3</sub> PO <sub>3</sub> °	0.97	10	100	<b>0m 0</b>
(0.75)	(12)	0.27	10	100	97:3
3-t-Butylcyclohexanone	P(OMe) <sub>3</sub>	0.97	10	100	0.07
		0.27	10	100	3:97
4-Methylcyclonexanone	(11)	0.97	e	100	04 0
(0.75)		0.27	0	100	94:0
(0.75)		0.27	9	100	96:4
(0.75)		0.27	10	100	89:11
(0.75)	(11)	0.11	12	100	87:13
$(1.0)^{\circ}$	$\mathbf{D}(\mathbf{OM}_{2})$	0.11	10	100	95:5
2-Methylcyclonexanone	$P(OMe)_3$	0.97	16	00	05 - 0
(0.75)	(8.9)	0.27	10	80 05	97:3
(U·D)	H DO	0.94	10	90	97:3
2,2-Dimethylcyclonexatione	$\Pi_3 \Gamma U_3$	0.54	00	- 60	
(0) 9.9.6 Trimetheleveleborrenone	$P(OM_{o})$	0.94	30	<i>ca</i> . 00	
2,2,0-1 milletinyicycionexanone	$\Gamma(OMe)_3$	0.54	40	0	
(U·D) 2.2.5 Trimethylayolehovenone		0.04	40	0	
(0.5)	(9.5)	0.54	16	100	0.100
Nonadooan 2 ono	P(OMe) 6	0.04	10	100	0:100
(0.75)	$(0.110)_3$	0.27	16	97	
(0.13)	H.PO	0 21	10	21	
(0.5)	(12)	0.54	48	08 đ	
Bongoldebyde	HP(O)(OMe)	001	10	00	
(1.5) <b>d</b>	(10)	0.54	22	<b>\95</b>	
Pinacolone	P(OMe).	0.01		200	
(1.3)	(11)	0.36	16	0	
Renzonhenone	P(OMe).			0	
(1.5)	(8.5)	0.27	16	0	

• Determined by g.l.c.; conditions given in Experimental section. • Easily hydrolysed phosphite esters give essentially the same results; details in Experimental section. • Partly or extensively hydrolysed under the reaction conditions. • The amount of water was also changed (to 2 ml.).

 $H_{3}Ir(PPh_{3})_{3}$ ,<sup>9</sup> is active; see later]. However, the ketone was reduced (96–98% of the *cis*-axial alcohol was produced) when phosphorous acid or an easily hydrolysed phosphite ester was present. Table 1 summarises the results obtained with various carbonyl compounds.

Unhindered alkyl-substituted cyclohexanones afford high proportions of the corresponding axial alcohols on reduction by this iridium-phosphite procedure. The reactions are appreciably sensitive to steric hindrance. 2-Methylcyclohexanone is reduced more slowly than 4-methylcyclohexanone. The rate (extent) of reduction decreased further for 2,2-dimethylcyclohexanone, and 2,2,6-trimethylcyclohexanone was not reduced under the standard conditions. Pinacolone and benzophenone were also unreactive. of acetone (added initially) did not appreciably affect the rate of reduction of 4-t-butylcyclohexanone.

Further experiments indicated that phosphite is the reductant: the amount of phosphite in solution (estimated by its capacity to reduce mercury(II) chloride<sup>10</sup>) decreased during reduction of 4-t-butylcyclohexanone. Determination of the amount of ketone reduced when less than 1 mol. of phosphite was present initially indicated that reduction may correspond to equation (1).

ketone + phosphite + water  $\xrightarrow{\text{catalyst}}$ sec. alcohol + phosphate (1)

At least 450 moles of ketone can be reduced per g. atom of iridium in solution. Solutions containing the iridium-

<sup>10</sup> A. Vogel, 'Textbook of Quantitative Inorganic Analysis,' Longmans, London, 3rd edn., 1961, p. 577.

<sup>&</sup>lt;sup>8</sup> L. Vaska, J. Amer. Chem. Soc., 1961, 83, 756.

<sup>&</sup>lt;sup>9</sup> R. G. Hayter, J. Amer. Chem. Soc., 1961, 83, 1259.

phosphite catalyst remained homogeneous (*i.e.* no metal was precipitated) during the reactions provided that an excess of phosphite was present, and this catalyst seems to be relatively robust.

4-t-Butylcyclohexanone was not appreciably reduced when treated with phosphite in aqueous propan-2-ol in the presence of other Group VIII transition metal salts.

The 97:3 cis- to trans-alcohol product ratio from reduction of 4-t-butylcyclohexanone appears to be characteristic of reactions in which a phosphite containing the group HP(:O)  $\leq$   $\rightarrow$  HO·P $\leq$  is used, *i.e.* phosphorous acid and its mono- and di-esters. Trialkyl phosphites give this ratio only if they are hydrolysed sufficiently quickly under the reaction conditions. This is more easily achieved with trimethyl phosphite than with the less readily hydrolysed triethyl phosphite. (Several of the earlier experiments were performed with trimethyl phosphite in the presence of water, but later, phosphorous acid was generally employed.) When less easily hydrolysable trialkyl phosphites (triethyl, triallyl, and tri-isopropyl) are used the product ratio changes to 80-90: 20-10, the precise values probably depending on the extent to which hydrolysis takes place as a competing reaction before reduction occurs.

The values given refer to reactions in which the proportion of water was at least 10% by volume. No ethers were formed under these conditions. In the absence of water, reductive etherification of the ketone can occur in a reaction that involves the solvent alcohol.<sup>3</sup>

Although only a few experiments were carried out with hypophosphorous acid, they showed that this acid is a good reductant, the rate of reduction being faster than that with phosphorous acid. Provisional evidence was obtained that indicated that hypophosphorous acid could reduce more than 1 mol. of ketone.

The conclusion that propan-2-ol was not appreciably involved as a reductant was examined by using  $[2-^{2}H]$ propan-2-ol as co-solvent (with water) in the iridiumphosphite system. Reduction of 4-t-butylcyclohexanone occurred without incorporation of deuterium into the product; this might have occurred at C-1 by analogy with the Meerwein–Ponndorf–Verley reaction.<sup>11</sup> Also the use of t-butyl alcohol, a less likely source of hydrogen than propan-2-ol, did not prevent the reduction proceeding readily with the same degree of stereoselectivity as before.

Iridium tetrachloride (containing some chloroiridic acid; see Experimental section) was generally used as starting material. Its violet-red colour rapidly disappears on treatment with phosphites, derivatives of trivalent iridium probably being formed. Ammonium hexachloroiridate(IV) can be used as an alternative source of catalyst.

An attempt was made to isolate an iridium-phosphite complex. Reaction between iridium tetrachloride and phosphorous acid in hot aqueous propan-2-ol solution afforded a pale brown solution from which a noncrystalline acidic material was obtained on evaporation. Treatment of this acid with appropriate amines gave solids, analyses of which indicated the composition,  $(amine)_2(Cl_4IrPO_5H_8)$ . These derivatives were ineffective as catalysts for the reduction of ketone in aqueous propan-2-ol, but a catalytically active species was generated when the 4-bromoisoquinoline derivative was used in the presence of an excess of phosphorous acid, although reduction (of 4-t-butylcyclohexanone) proceeded more slowly than when the iridium-containing acid itself was used. An experiment referred to later indicates that the presence of chlorine may not be an essential feature of the active catalyst.

Reactions of iridium tetrachloride with phosphite esters were briefly studied. When several dialkyl phosphites were heated with the metal chloride, and excess of phosphite was evaporated off, hygroscopic vellow-brown solids were obtained. The carbon content of these materials was generally low (e.g. <2%) showing that dealkylation had occurred. A yellow amorphous substance (containing ca. 9% carbon) was obtained by treating iridium tetrachloride with trimethyl phosphite. When this material was used as the iridium component in the reduction of 4-t-butylcyclohexanone in aqueous propan-2-ol, the normal 97:3 ratio of alcohols was obtained. Thus for this catalyst (source), propan-2-ol can act as reductant (no additional phosphite had been added), and this was confirmed by the detection of acetone (88%) as a product.

With phosphorous acid present as reductant, a 97:3 ratio of alcohols was obtained from 4-t-butylcyclohexanone from reactions in various low molecular weight alcohols containing water, although propan-2-ol was generally used. Acidic conditions may be necessary for the functioning of this catalyst: addition of piperidine inhibits the reaction and, as already noted, amine derivatives of the iridium-phosphite acid are catalytically ineffective.

At least two roles for the acid may be envisaged. First, the reactivity of the ketone may be enhanced by protonation, cf. the increase in the proportion of axial alcohol produced by hydrogenation of ketones in acidic solution in the presence of metal catalysts. Alternatively, or in addition, protons may be required in one or more subsequent stages of the reaction, for example, for cleaving a carbon-iridium bond. If an intermediate is formed [>C(OH)Ir etc.] in which the bulky iridiumcontaining group preferentially occupies an equatorial position, protonolysis of it may be expected to give the axial alcohol as final product. Evidence bearing on this point was obtained by using an O-deuteriated solvent mixture (Me<sub>2</sub>CHOD and D<sub>2</sub>O). The C-1 (alcohol) position in the product was extensively deuteriated in accord with a protonolysis mechanism, although other mechanisms cannot be excluded at present.

The effect of using other phosphorus-containing compounds in place of phosphorous acid and its esters was examined. Many of these  $[H_3PO_4, (RO)_3PO,$ 

<sup>&</sup>lt;sup>11</sup> W. von E. Doering and J. Aschner, J. Amer. Chem. Soc., 1953, 75, 393; E. D. Williams, K. A. Krieger, and A. R. Day, *ibid.*, p. 2404.

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 $RP(OH)_2O$ ,  $RP(OR)_2O$ , and  $R_3PO$ ] were not effective in converting the iridium into a form that was stable to hot aqueous propan-2-ol; black precipitates separated. A phosphorothioate,  $(EtO)_3PS$ , gave a soluble, catalytically active species, but reduction was less selective than with phosphite, a 64:36 cis- to trans-ratio of alcohols being obtained from 4-t-butylcyclohexanone.

The triphenylphosphine complexes  $(PPh_3)_3IrH_3^9$  and  $(PPh_3)_2IrH_3^{12}$  catalyse the transfer of hydrogen from propan-2-ol to cyclohexanone, acetone also being produced. The stereochemistry of the reaction was determined by use of 4-t-butylcyclohexanone: 88-90% of the *trans*-alcohol was formed in contrast with the iridium-phosphite system. High proportions of *trans*-alcohol were also obtained when the hydrides HRu- $(CO)Br(PEt_2Ph)_3$ ,  $^{13}H_5Re(PPh_3)_3$ ,  $^{14,15}$  and  $H_7Re(PPh_3)_2$ ,  $^{15}$  were used as hydrogen-transfer catalysts.

The 97:3 phosphite ratio can also be obtained by first heating certain other complexes,  $(PPh_3)_3IrH_3$  and  $H[Cl_4Ir(Me_2SO)_2]$ , with phosphorous acid, and then using the product as the catalyst in the standard way; presumably phosphorous acid displaces one or more ligands in the first stage. Halogen cannot be present in the active product from the former complex. Addition of lithium chloride to the standard reaction mixture, containing the iridium-phosphite catalyst made from iridium tetrachloride, caused the reaction to proceed more slowly.

The effect of replacing phosphorus by other elements in the ligand was briefly studied. 4-t-Butylcyclohexanone was slowly reduced to an  $88:12\ cis$ - to transalcohol mixture when heated with arsenic(III) oxide and iridium tetrachloride in aqueous propan-2-ol; an orange precipitate separated during the reaction. Antimony-(III) oxide gave less selective reduction (65:35) and a dark precipitate separated. Sulphites (sulphur dioxide and dialkyl sulphites) stabilised the iridium and afforded 75-85% of the *cis*-alcohol.

Choice of solvent can affect the ratio of alcohols obtained. When the otherwise standard phosphite procedure was used the proportion of *cis*-product diminished when propan-2-ol was replaced as solvent by dioxan, pentan-3-one, or benzene.

### EXPERIMENTAL

The iridium tetrachloride used (from Johnson, Matthey Ltd.) contained some chloroiridic acid, iridium content 51.5% (Calc. for IrCl<sub>4</sub>: 57.5%), and calculations are based on the former figure. Unless stated otherwise reactions were carried out under reflux conditions with no provision for the exclusion of air.

Gas Chromatography.—Products from the reduction of the carbonyl compounds given in Table 1 were analysed with 4 ft. columns containing the following packings on a Pye Argon Chromatograph: 3- and 4-t-butylcyclohexanones (poly-

\* Other soluble iridium compounds, e.g. chloroiridic acid and iridium trichloride, can be used instead.

<sup>†</sup> Phosphorous acid can replace the ester; the latter is probably largely or wholly hydrolysed when it is used as a starting material. phenyl ether at 95°); 4-methylcyclohexanone (glycerol at 50°); 2-methylcyclohexanone (trixylyl phosphate at 70°; also glycerol at 50°); 3,3,5-trimethylcyclohexanone (polyphenyl ether at 70°); 2,2,6-trimethylcyclohexanone (trixylyl phosphate at 58°); benzaldehyde (Carbowax 20M at 83°); and pinacolone (trixylyl phosphate at 20°). Nonadecan-2-one and -2-ol were separated by chromatography on alumina; they are also separable by g.l.c.

Reduction of 4-t-Butylcyclohexanone (Large Scale).—A mixture of the ketone (4.62 g., 0.03 mole), iridium tetrachloride \* (1·23 g., 0·003 mole), trimethyl phosphite † (15 ml., 0·13 mole), propan-2-ol (200 ml.), and water (50 ml.) was heated under reflux for 21 hr. Much of the solvent was then distilled off (ca. 215 ml.) and the organic products were isolated with ether. If reduction is essentially complete the product at this stage may be sufficiently pure for most preparative purposes. Pure components can be obtained by chromatography over alumina; a representative experiment (on this scale) gave unchanged ketone (0·13 g.), cisalcohol (4.36 g.), and trans-alcohol (0·16 g.) (eluted in this order by pentane, and then by pentane-ether).

Reduction of  $5\alpha$ -Cholestanone (Y. M. Y. HADDAD).—A solution of cholestanone (390 mg., 1 mmole), iridium tetrachloride (134 mg., 0.35 mmole), trimethyl phosphite (2 ml., 17 mmoles) and water (4 ml.) in propan-2-ol (30 ml.) was boiled under reflux for 16 hr. and worked up in the usual way. Chromatography of the product on deactivated alumina (40 g.) gave cholestanone (161 mg.), cholestan-3 $\alpha$ -ol (209 mg.), and cholestan-3 $\beta$ -ol (19 mg.). Results for the reduction of other compounds are given in Table 1.

Stoicheiometry of the Catalysed Reaction.—(a) 4-t-Butylcyclohexanone (2.5 mmoles), iridium tetrachloride (0.054 mmole), phosphorous acid (5 mmoles), propan-2-ol (10 ml.) and water (2 ml.) were heated at  $82^{\circ}$  in a sealed tube for 17 hr. All the ketone was reduced. A sample of the solution was analysed by the mercury(II) chloride method:<sup>10</sup> 37% of the phosphorous acid remained whereas when the ketone was omitted 94% of this acid remained.

(b) The following experiments (Table 2) show that reduction is incomplete when less than 1 mol. of phosphite is added. The ketone (1 mmole), iridium tetrachloride, phosphite, propan-2-ol (10 ml.), and water (2 ml.) were heated under reflux. The amount of ketone reduced was estimated from g.l.c.

(c) Table 3 gives additional results that show how the extent of reduction depends on the ratio of reactants. Ketone (1.5 mmole), propan-2-ol (10 ml.), and water (2 ml.) were used.

 $\left( d\right)$  The following experiments were concerned with the possible formation of acetone.

4-t-Butylcyclohexanone (4.62 g.), iridium tetrachloride (0.492 g.), phosphorous acid (14.75 g.), propan-2-ol (100 ml.), and water (20 ml.) were refluxed for 21 hr. About 20 ml. of the solvent was distilled out, but this gave little acetone 2,4-dinitrophenylhydrazone (<5%).

A similar result was obtained when dimethyl phosphite was used instead of phosphorous acid, either with or without 4-t-butylcyclohexanone being present.

<sup>12</sup> L. Malatesta, C. Caglio, and M. Angoletta, *J. Chem. Soc.*, 1965, 6974; J. Chatt, R. S. Coffey, and B. L. Shaw, *ibid.*, p. 7391.

<sup>13</sup> J. Chatt, B. L. Shaw, and (in part) A. E. Field, *J. Chem.* Soc., 1964, 3466.

<sup>14</sup> L. Malatesta, M. Freni, and V. Valenti, *Gazzetta*, 1964, **94**, 1278.

<sup>15</sup> J. Chatt and R. S. Coffey, Chem. Comm., 1966, 545.

	TABLE $2$		
Phosphite (mmoles)	Iridium tetrachloride (mmoles)	Time (hr.)	Reduction (%)
$H_3PO_3$ (0.66) $HD('O)(OM_2)$	0.022	16	62
(0.66)	0.022	16	48
(0.33)	0.022	16	33
$\begin{array}{c} (0.33) \\ (0.33) \\ (0.33) \\ (0.33) \end{array}$	0·055 0·055 0·055	$\begin{array}{c} 12\\ 24\\ 120 \end{array}$	$5\\14\\25$
	TABLE 3		
Phosphite (mmoles)	Iridium tetrachloride (mmoles)	Time (hr.)	Reduction (%)
$H_{3}PO_{3}$ (10) (1)	0.033	16     16	100 62 ª
$HP(:O)(OMe)_{2}$ (10)	0.033	16	96
(2) (1.5)	0·033 0·033	$\frac{16}{16}$	92 62
(1)	0.033	33 16 16	71 48 ª 22 a
(0.5) (60) <sup>b</sup>	0.066	10 24 48	33 " 51 93
		<del>7</del> 4	99

<sup>a</sup> Small amount of white precipitate formed. <sup>b</sup> Larger quantities of ketone (30 mmoles), propan-2-ol (40 ml.), and water (8 ml.) were used in this experiment concerned with the efficiency of the catalyst. More than 450 mol. of ketone can be reduced.

No acetone was obtained when the following reaction was carried out in a sealed tube, although reduction was complete. A mixture of ketone (1.5 mmole), dimethyl phosphite (5.4 mmoles), iridium tetrachloride (0.15 mmole), propan-2-ol (5 ml.), and water (1 ml.) was heated at  $82^{\circ}$ for 23 hr.

Reactions with Other Phosphites. The ketone (0.75 mmole), iridium tetrachloride (0.27 mmole), phosphite (see later), propan-2-ol (10 ml.), and water (5 ml.) were refluxed for 16 hr. The extent of reduction, and the *cis-trans*-alcohol product ratio are given in brackets after each phosphite: phosphorous acid (1 g.) (100%; 97:3); ethylene phosphite (1 ml.) (100%; 97:3); triethyl phosphite (5 ml.) (98%; 80:20); di-isopropyl phosphite (1 ml.) (100%; 97:3); triisopropyl phosphite (1 ml.) (100%; 97:3); triisopropyl phosphite (1 ml.) (100%; 97:3); triisopropyl phosphite (1 ml.) (100%; 88:12); triallyl phosphite (1 ml.) (5%; 85:15); 1-methyl-4-phospha-3,5,8-trioxobicyclo[2,2,2]octane (1 g.) (100%; 97:3).

Other Phosphorus-containing Ligands.—Experiments were carried out as described in the preceding section, and the results are summarised in the same way: hypophosphorous acid (1 ml. of 50:50 w/w solution in water) (100%; 97:3); OOO-triethyl phosphorothioate (0.15 ml.) (96%; 64:36); tributylphosphine (1 ml.) (0%); triphenylphosphine (1 ml.) (1%; sealed tube experiment); chloro(diphenyl)phosphine (1 ml.) (10%; 35:65). A black precipitate formed when each of the following compounds was used, and the reactions were not studied further: tributyl- (0.5 g.) and triphenyl- (1 g.) phosphine oxides; phenylphosphonic acid (1 g.); dimethyl methylphosphonate (1 ml.); 90% phosphoric acid (0.6 ml.).

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Sulphur, Arsenic, and Antimony Compounds as Potential Ligands.—Reactions were performed as in the preceding section. Results: dimethyl sulphite  $(2 \cdot 5 \text{ ml.})$  (100%; 85:15); diethyl sulphite (5 ml.) (85%; 81:19); water saturated at 20° with sulphur dioxide (5 ml.) (75%; 74:26); thiacyclopentane  $(1 \cdot 5 \text{ ml.})$  (1%).

Iridium tetrachloride (102 mg., 0.27 mmole), arsenic(III) oxide (100 mg., 0.50 mmole), propan-2-ol (20 ml.), and water (4 ml.) were heated together for 2.5 hr. to yield a redorange solution and precipitate. 4-t-Butylcyclohexanone (231 mg., 1.5 mmole) was added and the mixture was heated for 16 hr. Analysis of the product showed that 80% of the ketone had been reduced to an 88: 12 *cis-trans*-alcohol mixture.

Hypophosphorous Acid.—4-t-Butylcyclohexanone (2 mmoles), iridium tetrachloride (10·2 mg., 0·027 mmole), hypophosphorous acid (0·66 mmole, as a 30-32% w/w solution in water), propan-2-ol (20 ml.), and water (4 ml.) were refluxed for 24 hr.; 73% of the ketone was then reduced to a 97:3 *cis-trans*-alcohol mixture. When the reaction time was increased to 48 hr., 95% of the ketone was reduced.

Relative Rates of Reduction of 4-t-Butylcyclohexanone with Use of Various Phosphites (Table 4).—The ketone (1.5 mmole), iridium tetrachloride (0.16 mmole), the phosphite (20 mmoles), propan-2-ol (20 ml.), and water (4 ml.) were refluxed, and samples were removed for analysis at intervals.

TABLE 4						
Phosphite	Reduction (%) (time in hr.)					
$P(OEt)_{3}$ $P(OMe)_{3}$ $HP(:O)(OEt)_{2}$ $HP(:O)(OMe)_{2}$ $H_{3}PO_{3}$ $H_{3}PO_{2}$	$\begin{matrix} 0(1) \\ 0(1) \\ 5(1) \\ 4(1) \\ 12(1) \\ 15(1) \end{matrix}$	$\begin{array}{c} 0(2) \\ 0(2) \\ 13(2) \\ 10(2) \\ 25(2) \\ 44(2) \end{array}$	$\begin{array}{c} 0.5(4) \\ 2(4) \\ 36(4) \\ 47(4) \\ 69(4) \\ 81(4) \end{array}$	4(7) 20(8) 81(7) 83(7) 93(7) 95(6.5)	$\begin{array}{c} 27(11\cdot5)\\ 61(12)\\ 96(11\cdot5)\\ 99(11)\\ 99(10) \end{array}$	96(24) 100(24)

The effect of using slightly higher temperatures was briefly studied; ketone (0.5 mmole), iridium tetrachloride (0.054 mmole), dimethyl phosphite (6.5 mmoles), propan-2-ol (6.7 ml.); and water (1.3 ml.) were heated in sealed tubes (Table 5).

		TABL	Е 5			
Temp.		Reduction (%) (time in hr.)				
82°	(4(2))	22(4)	49(6)	74(8)	99(11)	
97	11(2) 17(1)	52(2)	91(3)	98(4)		

Effect of acetone. 4-t-Butylcyclohexanone was 89% reduced when it (1.5 mmole), dimethyl phosphite (2 mmoles), iridium tetrachloride (0.033 mmole), propan-2-ol (10 ml.), and water (2 ml.) were heated at  $82^{\circ}$  in a sealed tube for 16 hr. When acetone (1.1 ml.) was also present the ketone was 92% reduced.

Other Transition Metals.—4-t-Butylcyclohexanone (115 mg., 0.75 mmole), ammonium hexachloroiridate(IV) (110 mg., 0.25 mmole), trimethyl phosphite (1 ml., 8.5 mmoles), propan-2-ol (10 ml.), and water (2 ml.) were heated under reflux for 16 hr. The product contained *cis*- and *trans*-4-t-butylcyclohexanols (97:3) and no starting ketone.

In similar experiments the salts used were ammonium hexachloroplatinate(IV), ammonium hexachlororhodate(III), ammonium hexachloro-osmate(IV), ammonium hexachlororuthenate(IV), palladium(II) chloride, nickel(II) chloride, cobalt(II) chloride, and ammonium iron(III) chloride. In no case was more than 1% of the ketone reduced. Precipitates formed in the reactions involving the platinum, rhodium, ruthenium, and palladium compounds.

Effects of Piperidine and Lithium Chloride.—Ketone (1.5 mmole), iridium tetrachloride (0.033 mmole), dimethyl phosphite (2 mmoles), propan-2-ol (10 ml.), and water (2 ml.) were refluxed for 16 hr.; 95% of the ketone was reduced. Repetition with (a) piperidine (6 mmoles) present led to only 3% reduction, and (b) lithium chloride (6 mmoles) to 38% reduction.

Iridium-Phosphite Compounds.—(a) Iridium tetrachloride (407 mg., 1.08 mmole), phosphorous acid (200 mg., 2.4 mmoles), and water (2 ml.) were heated at  $90^{\circ}$  for 1 hr. The pale red-brown solution was cooled and added to a solution of isoquinoline (260 mg., 2 mmoles) in propan-2-ol (2 ml.). The precipitate (391 mg.) had m.p. ca. 135° (Found: C, 30.25; H, 3.15; Cl, 20.05; N, 3.8; P, 4.6. C<sub>18</sub>H<sub>22</sub>Cl<sub>4</sub>IrN<sub>2</sub>O<sub>5</sub>P requires C, 30.4; H, 3.25; Cl, 19.95; N, 3.95; P, 4.35%).

This experiment was repeated with 4-bromoisoquinoline (414 mg., 2 mmoles) instead of isoquinoline. A granular solid (655 mg.), m.p. 140-150° (indefinite) separated which could be crystallised from water (Found: C, 25.4; H, 2.35; Cl, 15.6; N, 3.35; P, 4.6. C<sub>18</sub>H<sub>20</sub>Br<sub>2</sub>Cl<sub>4</sub>IrN<sub>2</sub>O<sub>5</sub>P requires C, 24.9; H, 2.3; Cl, 16.3; N, 3.2; P, 3.55%). A similar preparation with less phosphorous acid (100 mg.) gave 530 mg. of bromoisoquinoline derivative.

When each of the salts just mentioned (30 mg.) was heated with 4-t-butylcyclohexanone (115 mg., 0.75 mmole), in water (2 ml.) and propan-2-ol (10 ml.) for 17 hr., no reduction of the ketone occurred. The initial addition of phosphorous acid (100 mg.) to the bromoisoquinoline salt reaction caused the reduction (60%) of the ketone to the usual 97:3 cis-trans-4-t-butylcyclohexanol mixture in the same time.

(b) Dimethyl phosphite (0.7 ml., 8 mmoles), iridium tetrachloride (0.5 g., 1.35 mmole), and propan-2-ol (15 ml.) were heated under reflux for 17 hr. Evaporation under reduced pressure left a pink, non-crystalline solid (Found: C, 1.4; H,  $2\cdot3\%$ ). A mixture of this solid (100 mg.), 4-t-butylcyclohexanone (308 mg., 2 mmoles), propan-2-ol (20 ml.), and water (4 ml.) was heated under reflux for 22 hr. All of the ketone was reduced to give a 97: 3 cis-trans-alcohol ratio. A similar reaction in a sealed tube gave the same result and acetone was isolated as its 2,4-dinitrophenylhydrazone (80% based on starting ketone).

(c) Trimethyl phosphite (10 ml., 85 mmoles), iridium tetrachloride (1 g., 2.7 mmoles), and propan-2-ol (50 ml.) were heated under reflux for 24 hr. Ether and water were added. The ethereal layer was dried and evaporated to leave a yellow solid (Found: C, 9.3; H, 3.8%). When this material was used to reduce 4-t-butylcyclohexanone [cf. procedure under (b)] a 97: 3 cis-trans-alcohol ratio was obtained. A similar sealed tube experiment afforded an 88% yield of acetone, and a 97: 3 alcohol ratio.

(d) Iridium tetrachloride (1.08 mmole) was heated, in two separate experiments, with triethyl phosphite (2 and 3 mmoles) in dry ethanol (10 ml.) for 40 hr. Evaporation gave an orange-brown solid in each case (Found: C, 12.05; H, 2.55; Cl, 11.3; P, 12.1; and C, 13.5; H, 2.95; Cl, 11.5; P, 11.6%, respectively).

Other Solvents.-4-t-Butylcyclohexanone (231 mg., 1.5 mmole), chloroiridic acid (61 mg., 0.16 mmole), dimethyl phosphite (0.5 ml., 3.5 mmoles), water (1 ml.), and t-butyl alcohol (5 ml.) were heated in a sealed tube for 17 hr. at 82°. Complete reduction of the ketone to give a 97: 3 cis-trans-4-t-butylcyclohexanol mixture occurred.

Use of dioxan (5 ml.) instead of t-butyl alcohol and a reaction time of 19.5 hr. and temperature of  $ca. 90^{\circ}$  led to 57% reduction to a 75: 25 cis-trans-4-t-butylcyclohexanol mixture.

Diethyl ketone (5 ml.) as organic solvent led to 38% reduction to an 89: 11 cis-trans-alcohol mixture upon heating for 24 hr. at 82°.

Benzene (3 ml.) as organic solvent led to 54% reduction to an 86: 14 cis-trans-alcohol mixture on heating for 3 days at 82°.

Use of Deuteriated Propan-2-ol.-(a) 4-t-Butylcyclohexanone (115 mg., 0.75 mmole), iridium tetrachloride (20.4 mg., 0.054 mmole), propan-2-[2-2H]-ol (3 ml.), dimethyl phosphite (0.36 ml.), and water (0.6 ml.) were heated in a sealed tube for 19 hr. at 83°. The ketone was completely reduced to a 97:3 alcohol mixture. The mixture was separated from iridium-containing materials by chromatography over alumina; i.r. spectra of two fractions did not show any C-D absorption.

(b) The experiment was repeated with propan-2-[2H]-ol and deuterium oxide. Again complete reduction occurred. A sample of the alcohol product, purified over alumina, showed i.r. peaks at 2200 and 2100 cm.<sup>-1</sup>, attributed to C-D absorptions. The n.m.r. spectrum showed a peak at  $\tau$  6.08 (0.16H) attributed to C(1)H; presumably the signal was weak owing to extensive deuteriation at this position. The methylene spectrum was also weak (ca. 5H); deuteriation at C-2 and C-6 probably occurred via enolisation of the original ketone.

Other Complexes .- The action of these on 4-t-butylcyclohexanone (1 mmole) was studied under reflux conditions in aqueous propan-2-ol. The results are shown in Table 6.

	ABL	E 6		
Complex (mmoles)	Propan- 2-ol (ml.)	Time (hr.)	Reduc- tion (%)	Stereo- selectivity (cis- to trans- alcohol)
$HCl_2Ir(PPh_3)_3$ (0.1)	15ª	17	0 0	
H <sub>2</sub> Cllr(PPh <sub>3</sub> ) <sub>3</sub> (0.05)	20	16	<10	15:85
trans H <sub>3</sub> Ir(PPh <sub>3</sub> ) <sub>3</sub> * (0.025)	10	16.5	100 %	12:88 °
$H_{3}Ir(PPh_{3})_{2}^{\dagger}$ (0.026)	10	16.5	100 b	10:90
$\frac{\mathrm{HRu}(\mathrm{CO})\mathrm{Br}(\mathrm{PEt}_{2}\mathrm{Ph})_{3}}{(0.025)}$	10	16	100	9:91
$\begin{array}{c} H_5 \operatorname{Re}(\operatorname{PPh}_3)_3 \$^{\P} \\ (0.025) \\ H_2 \end{array}$	20	17 <sup>d</sup>	100 •	20:80
$\begin{array}{c} H_{7} \operatorname{Ke}(PPh_{3})_{3} \\ (0.05) \\ H_{7}(20) \operatorname{Cl}(DDL) \end{array} $	10	17 ª	100 •	24:76
(0.05)	20	16	<10	20:80

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" Ketone (0.23 mmole), benzene (10 ml.), and water (2 ml.) were used. • Some insoluble material present in reaction mixture. • A similar reaction in a sealed tube at 82° for 22 hr. led to the isolation of acetone 2,4-dinitrophenylhydrazone <sup>d</sup> Performed under nitrogen and in the dark because (70%). of the sensitivity of this hydride. A black precipitate

separated from the brown solution. \* Ref. 9. † Ref. 12. ‡ Ref. 13. § Ref. 14. ¶ Ref. 15. \*\* L. Vaska and J. W. Diluzio, J. Amer. Chem. Soc., 1961, 83, 2784.

The complex (PPh<sub>3</sub>)<sub>3</sub>IrH<sub>3</sub> (50 mg., 0.05 mmole), phosphorous acid (165 mg., 2 mmoles), propan-2-ol (20 ml.),

and water (4 ml.) were refluxed under nitrogen for 6 hr. (The solvents were first boiled to remove oxygen). Most of the solid dissolved quickly but a cloudiness then developed. The mixture was concentrated, and water \* and ether were added. The material in the ether layer was chromatographed on alumina to give impure triphenyl-phosphine (16.5 mg.), m.p. 75–78°, converted by treatment with methyl iodide into the salt [Ph<sub>3</sub>PMe]I.

In another experiment the complex (25 mg.) and phos-

\* The material in this layer was active, after the addition of propan-2-ol, for the reduction of 4-t-butylcyclohexanone to give a 90: 10 cis-trans-alcohol ratio.

phorous acid (82 mg.) were heated for 6 hr. in aqueous propan-2-ol. Ketone (154 mg.) was added and heating was continued for a further 21 hr. The ketone was 46% reduced to give a 97:3 *cis-trans*-alcohol mixture. Without water only 7% reduction occurred to give a >90: <10 alcohol ratio.

We thank Dr. R. S Coffey, I.C.I. Ltd., for samples. One of us (T. R. B. M.) thanks the Ministry of Education for Northern Ireland for a studentship, and Queen's University for a foundation studentship.

[9/1901 Received, November 10th, 1969]