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ASYMMETRIC CATALYSIS BY CHIRAL PHOSPHINE COBALT CARBONYL COMPLEXES. HYDROGENATION OF α,β-UNSATURATED KETONES

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Summary

Hydrogenation of α,β-unsaturated ketones catalysed by cobalt complexes was carried out in the presence of chiral phosphine ligands ($P(C_6H_5)_2$neomenthyl and $P(C_6H_5)_2$-6-deoxo-1,2 : 3,4-diisopropylidene-D-galactose) to give the corresponding optically active ketones. The nature of the ligand and the olefin were the primary factors controlling asymmetric induction. The highest induction efficiencies, up to 16% e.e., were obtained in the hydrogenation of isophorone. The presence of carbon monoxide (10 atm) resulted in racemic products.

Introduction

Cobalt carbonyl-catalysed hydroformylation using tertiary phosphines as cocatalysts has been used on an industrial scale [1]. This modified system is more selective for linear products than $Co_2(CO)_8$, and shows strong hydrogenation activity with concomitant formation of alcohols [2]. Its reducing power is often employed in conjunction with the oxo reaction but rarely for laboratory-scale organic preparations [3] and even more rarely in asymmetric synthesis [4]. We decided to examine the hydrogenation of olefinic substrates catalysed by chiral, phosphine substituted cobalt carbonyl complexes [5] with the aim of developing new asymmetric syntheses using cheap and easily prepared complexes, and of extending the knowledge of the mechanism of a widely used catalytic process.

Since our previous studies on the hydrogenation of terpenes did not show any optical induction [6], α,β-unsaturated ketones were chosen as substrates in order to increase the double bond reactivity and to avoid side reaction such as isomerization [6,7]. The absence of racemization was first confirmed for the hydrogenation of (+)-pulegone to menthone and isomenthone catalysed by $Co_2(CO)_6\{PBu_3\}_2$ [5]. We now report the first asymmetric hydrogenation of α,β-unsaturated ketones to ketones catalysed by $Co_2(CO)_8$/chiral phosphine. The dependance of the optical yield on carbon monoxide pressure has been also examined.

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Results

Hydrogenation of α,β-unsaturated ketones catalysed by $Co_2(CO)_6\{PBu_3\}_2$ (1)

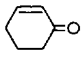
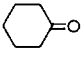
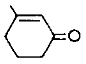
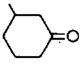
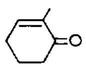
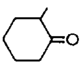
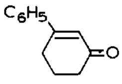
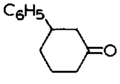
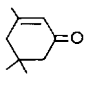
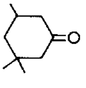
α,β-Unsaturated ketones undergo hydrogenation to saturated ketones rather than hydroformylation with dicobalt octacarbonyl as catalyst under oxo conditions, while the aliphatic α,β-unsaturated esters generally undergo hydroformylation [8]. The formation of π-oxapropenyl structure in the case of α,β-unsaturated ketones has been suggested by Goetz and Orchin to account for this difference in behaviour. The rate data obtained by these authors for the stoichiometric addition of $HCo(CO)_4$ to various substrates have been rationalized in terms of stabilization of the π-oxapropenyl complex by electron-donor groups [9].

In order to check whether the prochiral substrates used in the present study show the same behaviour under our catalytic conditions, reactivities of several substituted cyclohexenones were first compared [10], and results of hydrogenations catalysed by $Co_2(CO)_6\{PBu_3\}_2$ are summarized in Table 1.

The double bonds in unsaturated ketones were hydrogenated without concurrent carbonyl reduction. Higher temperatures are needed to hydrogenate ketones to alcohols with this catalyst [11]. Except for 2-methyl-2-cyclohexenone, the reduced carbonyl compounds were obtained in high yields. Relative α,β-unsaturated carbonyl substrate reactivities were also determined after 4 h reaction (Table 1) [12]; the results show that substitution β to the carbonyl moderately slows the reduction (entries 1,2,4,5), while substitution α to C=O caused rapid decomposition of the catalyst, resulting in a very low yield (compare entries 1 and 3). This contrasting behavior will be discussed later along with previous results [9] and the results in asymmetric syntheses.

TABLE 1

CATALYTIC HYDROGENATION USING $Co_2(CO)_6(PBu_3)_2$ IN BENZENE [a]

Entry	Substrate	Product	Yield (%)	Time (h)
1			86 (35) [b]	13
2			71 (27)	12
3			5 [c]	4
4			60 (15)	12
5			70 (33)	16

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[a] 30 atm H_2, 110°C, 50/1 substrate/catalyst. [b] Numbers in parentheses correspond to % of reduced substrate after 4 h. [c] Since the catalyst was entirely destroyed the reduction stopped after 4 h.

Catalytic hydrogenations using $Co_2(CO)_6\{P(C_6H_5)_2neomenthyl\}_2$ (2)

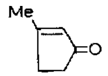
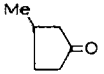
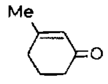
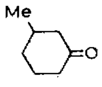
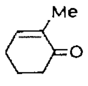
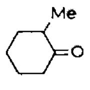
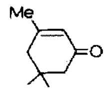
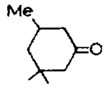
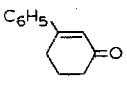
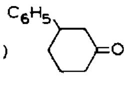
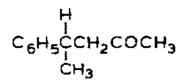
The binuclear complex, $Co_2(CO)_6\{P(C_6H_5)_2\text{neomenthyl}\}_2$ (**2**), was prepared in a one-step reaction from $Co_2(CO)_8$ and two equivalents of neomenthyl diphenylphosphine (eq. 1) $|\alpha|_D^{23}$ +90° [13]. After removal of traces of the monoadduct by chromatography, **2** was obtained as an orange oil $|\alpha|_D^{23}$ +41°. Solutions of **2** in benzene catalyse the reduction of the olefinic bond in high yield, but only modest optical rotations are obtained, and the best asymmetric synthesis is obtained with

$$Co_2(CO)_8 + 2\{P(C_6H_5)_2\text{neomenthyl}\} \rightarrow Co_2(CO)_6\{P(C_6H_5)_2\text{neomenthyl}\}_2 + 2CO \quad (1)$$

the hydrogenation of isophorone (o.p. 16%, entry 4). Asymmetric induction also seems to be very sensitive to steric effects: ring contraction from cyclohexenone to cyclopentenone (compare entries 2,4 and 1) greatly lowers the optical yield, and hydrogenation of a linear olefin gives very low optical yields (entry 6). It should be noted that 3-phenyl-2-cyclohexenone gave a positive result, but since, to our knowledge, the optical rotation of 3-phenyl-cyclohexanone is unknown, no optical purity was determined. 2-Methyl-2-cyclohexenone is also reduced, but with difficulty, and the saturated ketone does not show any optical rotation. Moreover, the extent of asymmetric induction varies widely, and depends primarily on the substrate structure, but the temperature also has a slight effect, lower temperatures giving higher

TABLE 2

ASYMMETRIC HYDROGENATION CATALYZED BY $Co_2(CO)_6\{P(C_6H_5)_2\text{neomenthyl}\}_2$ [a]

Entry	Substrate	Product (configuration)	Yield (%)	Optical [b] yield (%)	Time (h)	Temperature (°C)
1		(S)-(−) 	52	1.4	12	100
2		(S)-(−) 	40	10	11	100
3			16	–	20	100
4		(S)-(+) 	80	16	4	100
5		(−)  [c]	49	–	17	90
6	$C_6H_5C(CH_3)=$ $CHCOCH_3$	 $C_6H_5CH(CH_3)CH_2COCH_3$	95 60	1.05 2	2 5	100 60

[a] 30 atm H_2, 50/1 substrate/catalyst, solvent: benzene. [b] Optical yields are calculated relative to published values for the optically pure compounds: see Experimental section. [c] α_D^{25} −1.4° ($CHCl_3$).

e.e. values, as expected (entry 6). Finally no significant solvent effect was observed in the hydrogenation of 3-methyl-2-cyclohexenone (benzene or cyclohexane); this is consistent with a system in which such solvents do not compete with ligand coordination.

Dependence on chiral phosphine structure

In order to examine the dependence of the optical yield on the ligand structure, various phosphines were used (Table 3). The reduction of isophorone with [$P(C_6H_5)_2$neomenthyl] and [$P(C_6H_5)_2$-6-deoxo-1,2 : 3,4-diisopropylidene-D-galactose] [14] gave comparable optical yields, whereas use of (−)-Diop [15] as ligand did not result in any optical rotation; the latter negative result may be accounted for by the fact that (−)-Diop probably does not form a chelate ring around the cobalt.

Although use of various phosphines leads to asymmetric synthesis, the effectiveness of the present catalyst in asymmetric hydrogenation is far removed from the essentially complete optical selectivity observed for certain chiral rhodium catalysts [16,17]. This marked difference may reflect the presence on the cobalt atom of two carbonyl ligands which do not contribute to asymmetric synthesis (vide infra).

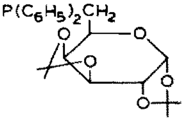
Reduction under carbon monoxide pressure

The use of high pressure IR spectroscopy has provided experimental evidence for the presence of specific intermediates during the oxoreaction catalysed by cobalt carbonyl phosphine systems. It has been found that the catalytically active species $HCo(CO)_4$ was only to a minor extent converted into $HCo(CO)_3PBu_3$ even although PBu_3 was present in excess (100°C, P(CO) 11 bar, $P(H_2)$ 49 bar) [19]. The decrease in the optical yield with increasing CO pressure agrees with this previous investigation. The hydrogenation of isophorone catalysed by **2** under carbon monoxide gives interesting results, which are summarized in Table 4.

The presence of 1 atm of carbon monoxide along with the solution greatly lowers the activity of the catalytic system and the optical yield falls from 16 to 1.8 e.e. Moreover samples taken periodically from the solution show increasing formation of $Co_2(CO)_7P(C_6H_5)_2$neomenthyl (ν(C=O) 1995 cm^{-1}). The effect is even more pronounced with 10 atm of CO, since the dihydroisophorone is found to be optically

TABLE 3

HYDROGENATION OF ISOPHORONE CATALYSED BY $Co_2(CO)_8/L_2$ [a]

L	Yield (%)	Optical yield (%)	Configuration	Time (h)	Temperature (°C)
$P(C_6H_5)_2$neomenthyl	80	16	*S*	4	100
 [b]	20	12.2	*R*	22	110
PMe_2menthyl [c]	25	1.2	*R*	21	100
(−)-Diop [d]	36	–	–	14	100

[a] 30 atm H_2, 50/1 substrate/catalyst, solvent: benzene. [b] Ref. 14. [c] Ref. 18. [d] Ref. 15.

TABLE 4

HYDROGENATION OF ISOPHORONE CATALYSED BY $Co_2(CO)_6[P(C_6H_5)_2\text{neomenthyl}]_2$ UNDER CARBON MONOXIDE PRESSURE[a]

P(CO) (atm.)	Optical yield	Yield (%)	Time (h)	Temperature (°C)
0	16	80	4	100
1	1.8	70	22	100
10	0	78	12	130

[a] 40 atm H_2, 50/1 substrate/catalyst, solvent: benzene.

inactive. The results confirm previous work [19] and are best explained by assuming that in the presence of carbon monoxide the following equilibria operate:

$$Co_2(CO)_6\{P(C_6H_5)_2\text{neomenthyl}\}_2 + CO \rightleftarrows Co_2(CO)_7P(C_6H_5)_2\text{neomenthyl} + P(C_6H_5)_2\text{neomenthyl} \quad (2)$$

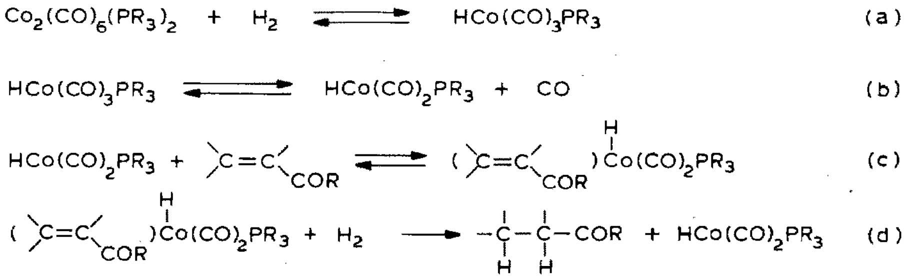
$$Co_2(CO)_7P(C_6H_5)_2\text{neomenthyl} + H_2 \rightleftarrows HCo(CO)_4 + HCo(CO)_3P(C_6H_5)_2\text{neomenthyl} \quad (3)$$

Under carbon monoxide pressure, $HCo(CO)_4$ is probably present. Since the latter is by far the more active catalyst, absence of any asymmetric synthesis under 10 atm of CO is easily understood.

Discussion

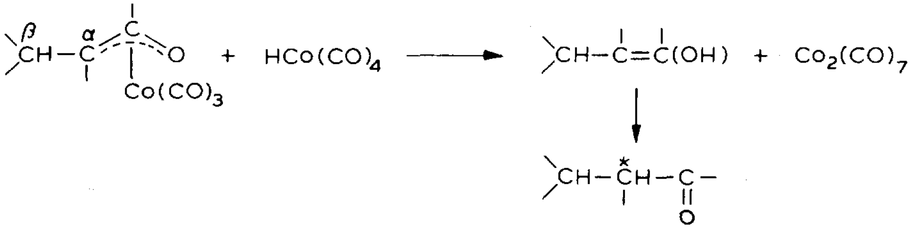
A generally agreed scheme for the hydrogenation of olefin with phosphine-modified cobalt carbonyl catalysts is given in eqs. a, b, c and d (Scheme 1) [20]. The importance of the second equilibrium (b) in the catalytic cycle is confirmed by the fact that basic phosphines such as PBu_3 lower the catalytic activity (Tables 1–3). The electron density at the metal center, and hence the electron back-donation to the coordinated carbon monoxide, would be expected to be more marked in complexes containing basic phosphines, and so the equilibrium probably lies far to the left with PBu_3. The fact that increase in the carbon monoxide pressure lowers the rate is also consistent with equilibrium b (Table 4).

SCHEME 1



There remains, however, an interesting point which cannot be settled simply from few asymmetric syntheses, namely, the interaction of the cobalt atom with the substrate (eq. c). Goetz and Orchin [9] has suggested that the hydrogenation of α,β-unsaturated ketones with $HCo(CO)_4$ proceeds via the formation of a π-oxapropenyl complex. The next step would be the addition of the proton from $HCo(CO)_4$ to the oxygen atom to give the enol form of the carbonyl adduct (Sch. 2).

SCHEME 2



Whether this mechanism operates under our catalytic conditions is a matter for speculation. One immediate implication of this mechanism is that hydrogenated ketones bearing a chiral carbon in the α-position relative to the carbonyl group should be racemic. The fact that racemic ketones are formed in the reduction of 2-methyl-2-cyclohexenone using $P(C_6H_5)_2$neomenthyl and $P(C_6H_5)_2$-6-deoxo-1,2 : 3,4-diisopropylidene-D-galactose [21], whereas in the same conditions hydrogenation of isophorone gives optically active product (Table 3), is consistent with this mechanism. However these reactions might alternatively involve labile Co–C intermediates [22]. It should also be noted that radical species have been detected recently in hydrogenation of aromatic olefins with $HCo(CO)_4$ [23]. This aspect is currently under investigations.

Experimental section

All preparations were performed in Schlenk tubes under dried, oxygen-free nitrogen. Solvents were distilled from appropriate drying agents and stored under nitrogen before used. IR spectra were recorded on a Unicam SP 1100 Infrared spectrophotometer, and gas-liquid chromatography was carried out with a Intersmat gas chromatograph [6]. Optical rotations were measured with a Perkin–Elmer polarimeter. Routine ^1H NMR spectra were recorded on a Varian T60 spectrometer.

The substrates: 3-methyl-2-cyclohexenone, isophorone, 3-methyl-2-cyclopentenone, 2-cyclohexenone were purchased from Aldrich Chemical Co., while 2-methyl-2-cyclohexenone [24], 3-phenyl-2-cyclohexenone [25], 4-phenyl-pent-3-en-2-one [26], were prepared by published procedures. Optical yields are calculated relative to the following values for the optically pure compounds (*R*)-3-methylcyclohexanone [27] α_D^{25} +14°; (*S*)-3,3,5-trimethylcyclohexanone [28] α_D^{25} +10.3°; (*R*)-3-methylcyclopentanone [29], α_D^{25} +154° and 4-phenyl-2-pentanone [30] α_D^{25} −74.5°.

Tributylphosphine and neomenthyl diphenylphosphine were purchased from Strem Chemicals Inc.; 6-diphenylphosphino-6-deoxo-1,2 : 3,4-diisopropylidene-D-galactose was prepared by a published procedure [14].

Dicobalt octacarbonyl was purchased from Strem Chemicals Inc.; Co_2-

$(CO)_6PBu_3$ [2] and $Co_2(CO)_6\{P(C_6H_5)_2\text{neomenthyl}\}_2$ [6] were prepared by published procedures. In the case of menthyldimethylphosphine and 6-diphenylphosphino-6-deoxo-1,2 : 3,4-diisopropylidene-D-galactose, the catalysts were prepared in situ by adding the relevant ligand to $Co_2(CO)_8$ in 2/1 ratio.

The reactions were carried out in a 300 ml Engineers autoclave with a magnetic stirrer. After introduction of a solution of the catalyst and substrate in benzene, hydrogenation was immediately started by injection of H_2 and heating. Samples were taken through a capillary line and analysed under ambient conditions by IR spectroscopy and GLC.

Acknowledgments

We thank Prof. Sinou for a generous gift of 6-diphenylphosphino-6-deoxo-1,2 : 3,4-diisopropylidene-D-galactose and the CNRS for financial support to V.M.

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