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Preliminary communication

ASYMMETRIC SYNTHESIS BY CHIRAL COBALT CATALYSTS: HOMOGENEOUS REDUCTION OF KETONES TO OPTICALLY ACTIVE ALCOHOLS

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Summary

The hydrogenation of ketones with $Co_2(CO)_6(PR_3)_2$ (PR_3 = PPh_2-neomenthyl, PPh_2-6-deoxo-1,2:3,4-diisopropylidene D-galactose and PMe_2-menthyl) as catalysts gives optically active alcohols in optical yields of 1.6 to 5%.

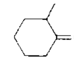
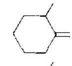
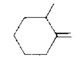
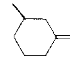
We previously reported that $Co_2(CO)_6(PPh_2\text{-neomenthyl})_2$ is an effective catalyst for the asymmetric reduction of carbon—carbon double bonds in α,β-unsaturated ketones [1]; saturated, optically active ketones were obtained under enhanced hydrogen pressures from prochiral substrates. We have now extended our investigation on the catalytic activity of the $Co_2(CO)_8$/chiral phosphine system to hydrogenation of ketones to give optically active alcohols.

Examples of hydrogenation of ketones in the presence of cobalt carbonyl complexes containing tertiary phosphine ligands are known [2], but no asymmetric reduction has previously been reported; the severe conditions used for the hydrogenation (200°C and 150—200 atm pH_2) prevented asymmetric synthesis. More suitable substrates were selected through a series of experiments in which various ketones were reduced with $Co_2(CO)_6(Pbu_3)_2$ as catalyst (Table 1). Cyclic aliphatic ketones were reduced at 110°C under 30 atm of hydrogen, whereas 130°C was required to hydrogenate acetophenone under the same conditions. Therefore, hydrogenation of 2- and 3-methylcyclohexanone was first undertaken with chiral cobalt catalysts; two complexes bearing different chiral phosphines were used: $Co_2(CO)_6(PPh_2\text{-neomenthyl})_2$ [3] and $Co_2(CO)_6[PPh_2\text{-6-deoxo-1,2:3,4-diisopropylidène-D-galactose}]_2$ (ν(CO): 1960, 1975 cm^{-1} (Nujol); m.p. 108°C; $[\alpha]_{545}$ + 25° (C_6H_6)). The results are summarized in Table 1.

It can be seen that reduction of 2-methylcyclohexanone gives both *cis*-

TABLE 1

HYDROGENATION UNDER PRESSURE OF KETONES WITH $Co_2(CO)_6(PR_3)_2$ SPECIES AS CATALYSTS [a]

PR_3	Substrate	Reaction time (h)	Yield (%)	Reaction product isomer %	RCH(OH)R′ O.Y. [b] (conf.) [c]
PBu_3		24	60	cis : 35 trans: 65	— —
NMDPP [d]		17	25	cis : 40 trans: 60	— 5 (1S, 2S)
GDPP [e]		25	26	cis : 27 trans: 73	2.6 (1S, 2R) —
NMDPP		28	15	cis : 33 trans: 67	— —
MDMP [f]	$C_6H_5COCH_3$	30	30	—	1.6 (S)

[a] 30 atm H_2, 110°C, 50/1 substrate/catalyst. [b] O.Y.: optical yield. [c] conf.: configuration of the prevailing enantiomer. [d] NMDPP: (+)-neomenthyldiphenylphosphine [4]. [e] GDPP: (—) 6-Deoxo-1,2:3,4-diisopropylidene-D-galactosediphenylphosphine [5]. [f] MDMP: (—)-menthyldimethylphosphine [6], 130°C.

and *trans*-2-methylcyclohexanol. The *cis/trans* ratio is slightly dependent on the nature of the phosphine (PBu_3: 40/60; NMDPP: 33/67 and GDPP: 27/73) and the thermodynamically more stable trans isomer is favoured [7]. The highest optical yield is obtained using $Co_2(CO)_6(NMDPP)_2$ as catalyst, but only the *trans*-2-methylcyclohexanol is optically active. In contrast a positive optical yield is obtained with *cis*-2-methylcyclohexanol when GDPP is employed as a chiral ligand in the cobalt complex. The nature of the chiral phosphine is obviously critical for the enantioselectivity. Reduction of 3-methylcyclohexanone also gives *cis*- and *trans*-isomers, but both alcohols are racemic.

We have also examined the influence of the phenyl group on the enantioselectivity. The presence of this group does, however, affect the reactivity. As shown in Table 1, reduction of acetophenone needs higher temperature (130°C) and a more basic phosphine ($Co_2CO_6(MDMP)_2$, ν(CO) 1950, 1970 cm^{-1}; m.p. 82°C; $[\alpha]_{545}$ $-21°$ (C_6H_6)). At this latter temperature considerable decomposition of the catalyst is observed, and the optical yield is low (1.6%).

Work is in progress to elucidate the mechanism by which the phosphine exerts its influence on the enantioselectivity of the catalyst.

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