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HOMOGENEOUS CATALYTIC ASYMMETRIC HYDROGENATION WITH A NEW LIPOPHILIZED BISPHOSPHINE-RHODIUM COMPLEX IN ALIPHATIC HYDROCARBONS[1)]

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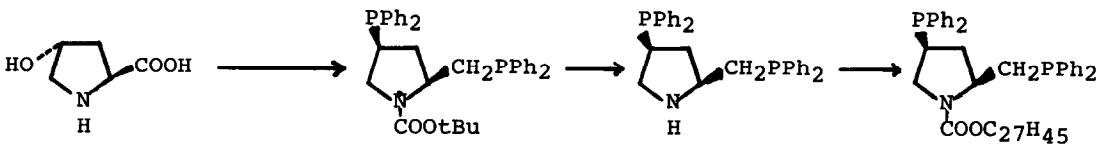
The catalytic asymmetric synthesis[2)] with phosphine-rhodium complexes has been proven comercially useful for the synthesis of optically active α-amino acids and the accumulated data[2-4)] have also indicated that, in most cases, the optical yields of this hydrogenation depended markedly on the nature of used solvents, and benzene was employed as the most non-polar aprotic homogeneous solvent mainly because of the insolubility of the chiral phosphine-rhodium complexes in aliphatic hydrocarbons.

We wish to describe here a new functionalized chiral bisphosphine, (2S,4S)-N-cholesteryloxycarbonyl-4-diphenylphosphino-2-diphenylphosphinomethylpyrrolidine(CPPM) (4) which consists of two bisphosphines as the metal ligands and a third functional group, N-cholesteryloxycarbonyl, expected to increase the solubility of CPPM in aliphatic hydrocarbons and also its lipophilic interaction with the substrates.

The new bisphosphine was synthesized from L-hydroxyproline(1) via the key intermediates, BPPM(2)[4)] and PPM(3)[4)], as shown in Scheme I.

Scheme I.



L-Hydroxyproline(1) BPPM(2) PPM(3) CPPM(4)

Thus, conventional treatment of BPPM(2) with a excess of trifluoroacetic acid at 0°c for 3h gave PPM(3)[5,6], mp 103-104°c, $[\alpha]_D^{20}$ -7° (c 1.84, benzene), in an almost quantitative yield, which on subsequent reaction with cholesteryloxycarbonyl chloride in pyridine at 0°c for 3h was converted to CPPM(4)[5], mp 82-84°c, $[\alpha]_D^{20}$ -31° (c 1.6, benzene), in a good yield.

Hydrogenations of pyruvates(5) were carried out with a neutral catalyst formed in situ from 2 or 4 and $[Rh(1,5\text{-hexadiene})Cl]_2$ in benzene or cyclohexane as solvents. CPPM-rhodium complex was found to be freely soluble in cyclohexane and slightly in n-hexane[7].

$$CH_3COCOOR \xrightarrow[\text{BPPM-Rh or CPPM-Rh}]{H_2} CH_3\underset{OH}{C}HCOOR$$

5 6

5a, 6a; R= C_2H_5
5b, 6b; R= $n\text{-}C_4H_7$

Table I. Catalytic asymmetric hydrogenation of pyruvates[a]

Substrate	Chiral reagent	Solvent	Time (h)	Conversion[b] (%)	Optical y.[c]	(config.)
5a	BPPM	benzene	(24)	100	65.3	(R)
5a	CPPM	benzene	(24)	100	63.8	(R)
5a	CPPM	cyclohexane	(45)	99	67.3	(R)
5b	CPPM	benzene	(45)	97	61.7	(R)
5b	CPPM	cyclohexane	(90)	98	62.8	(R)

a) All hydrogenations were run with 15 mmol of pyruvate, 3.8 $\times 10^{-2}$ mmol of $[Rh(1,5\text{-hexadiene})Cl]_2$, and 9.0 $\times 10^{-2}$ mmol of bisphosphine in 4 ml of solvent at 20°c under initial hydrogen pressure of 20 atm.

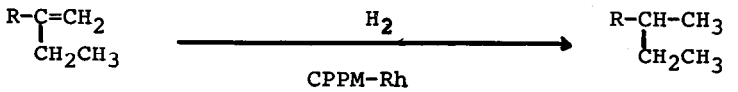
b) Yields were determined by vpc analysis.

c) Calculated on the basis of reported values for the optically pure compounds; R-6a, $[\alpha]_D^{18.9}$ +11.26° (neat), R-6b; $[\alpha]_D^{17}$ +14.7° (neat) (C. E. Wood, J. E. Such, and F. Scarf, J. Chem. Soc., 123, 600 (1923)).

Table I shows that the homogeneous hydrogenation of pyruvates with CPPM-rhodium complex proceeded smoothly in cyclohexane to give 63-67% optical yields of lactates in almost quantitative yields although the dramatic solvent effects on the optical yields were not observed.

For further demonstration of the usefullness of CPPM-rhodium catalyst[8], the hydrogenations of 2-ethyl-1-hexene(7a) and α-ethylstyrene(7b) were run in the absence of solvents to avoid the troublesome separation procedures of the volatill products from added solvents.

Thus, the homogeneous solution of CPPM(7.5×10^{-2}mmol)-rhodium(2.5×10^{-2}mmol) complex in 7a or 7b (10 mmol) was stirred at 20°c for 45h under initial hydrogen pressure of 50 atm to give in a 100% conversion yield the hydrocarbon, S-8a; bp 116°c, $[\alpha]_D^{20}$ +0.54° (neat)(5.8% optical yield)[9], or S-8b; bp 108° (113 mmHg), $[\alpha]_D^{20}$ +6.73 (neat)(24.7% optical yield)[10], on simple distillation of the reaction mixture.



7a, 8a; R= $CH_3(CH_2)_3$
7b, 8b; R=Ph

CPPM is therefore characterized as the most lipophilized and highly effective chiral bisphosphine ligand which can form its rhodium(I) complex soluble in aliphatic hydrocarbons.

Further investigations along these lines are in progress[11].

REFERENCES AND NOTES

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7) CPPM is freely soluble in aliphatic hydrocarbons (n-hexane, pentane, etc).

8) Asymmetric hydrogenation of dimethyl itaconate with CPPM-rhodium complex in benzene gave dimethyl methylsuccinate in a 29.5% optical yield, which is better than that with BPPM-rhodium complex (24.1%).

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