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NEW CHIRAL PHOSPHINE-RHODIUM CATALYSTS FOR ASYMMETRIC SYNTHESIS OF (R)- AND (S)-N-BENZYLOXYCARBONYLALANINE1)

Kazuo ACHIWA
Faculty of Pharmaceutical Sciences, University of Tokyo,
Bunkyo-ku, Tokyo 113

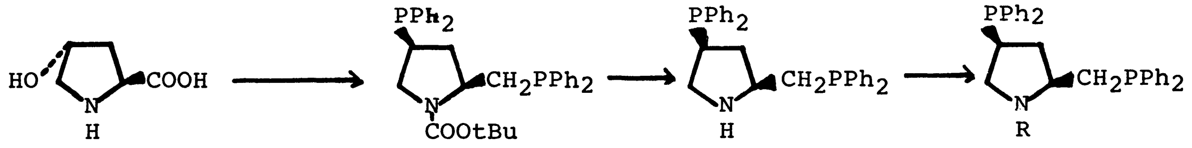
The synthesis of new chiral bisphosphine ligands (APPM (4) and PPPM (5)) and their application to the catalytic asymmetric synthesis of (R)- and (S)-N-benzyloxycarbonylalanine were described.

Although the catalytic asymmetric synthesis of optically active phenylalanine derivatives with chiral phosphine-rhodium complexes has been proven commercially useful, but the studies on aliphatic α-amino acids have remained without success2).

We wish to describe here new chiral bisphosphine reagents, (2S,4S)-N-acetyl-4-diphenylphosphino-2-diphenylphosphinomethylpyrrolidine(APPM) (4) and (2S,4S)-N-pivaloyl-4-diphenylphosphino-2-diphenylphosphinomethylpyrrolidine (PPPM) (5) and their application to the asymmetric synthesis of optically active N-benzyloxycarbonylalanine.

The new bisphosphines were synthesized from L-hydroxyproline(1) via the key intermediates, BPPM(2)3) and PPM(3)3), as shown in Scheme I.

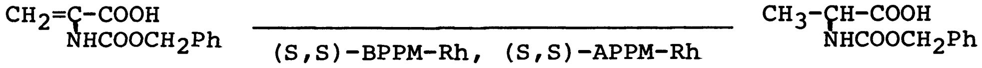
Scheme I.



L-Hydroxyproline(1) BPPM(2) PPM(3) APPM(4) ; R=CH_3CO-
PPPM(5) ; R=$(CH_3)_3CCO$-

Thus, conventional treatment of BPPM(2) with an excess of trifluoroacetic acid at 0°C for 3 hr gave PPM(3)4), mp 103-104°C, $[\alpha]_D^{20}$ -7°(c 1.84, benzene), in an almost quantitative yield, which on subsequent acylation with acetyl chloride or pivaloyl chloride was converted to APPM(4)4), mp 118-119°C, $[\alpha]_D^{20}$ -12°(c 1.08, benzene) or PPPM(5)4), mp 155-156°C $[\alpha]_D^{20}$ -2°(c 1.02, benzene), in good yields.

Hydrogenation of N-benzyloxycarbonyldehydroalanine(6)[5] was carried out with a catalyst formed in situ from 2,4 or 5 and $[Rh(1,5\text{-hexadiene})Cl]_2$. The product was isolated in 85-95% yields according to the same procedure previously reported[3].



$$CH_2{=}\underset{NHCOOCH_2Ph}{C}{-}COOH \xrightarrow[\text{(S,S)-BPPM-Rh, (S,S)-APPM-Rh or (S,S)-PPPM-Rh}]{} CH_3{-}\underset{NHCOOCH_2Ph}{CH}{-}COOH$$

6 7

Table I. Asymmetric synthesis of N-benzyloxycarbonylalanine[a]

Chiral reagent	Solvent	Optical Y.	(Conf.)[c]
BPPM	EtOH	50	(R)
BPPM	EtOH[b]	5	(R)
APPM	EtOH	57	(R)
APPM	EtOH[b]	8	(S)
PPPM	EtOH	59	(R)
PPPM	EtOH[b]	21	(S)

a) All hydrogenations were carried out with 2 mmol of substrate, 0.01 mmol of $[Rh(1,5\text{-hexadiene})Cl]_2$ and 0.022 mmol of bisphosphine in 15 ml of solvent at 20°C for 20 hr under initial hydrogen presure of 50 atm. b) Triethylamine(0.06 mmol) was used. c) Calculated on the basis of reported value for optically pure S-7; $[\alpha]_D^{17}$ -14.3°(c 9, AcOH)(M.Bergmann and L.Zervas; Chem. Ber., 65, 1192 (1932)).

Table I shows that APPM- and PPPM-Rh complexes gave (S)- and (R)-N-benzyloxycarbonylalanine depending respectively upon whether triethylamine was present or not, whereas BPPM-Rh complex gave only the R product even in the presence of the amine although the optical yield decreased. This fact may suggest that the N-substituents of PPM play an important role in affecting the optical yield of this asymmetric hydrogenation.

Although the optical yields of N-benzyloxycarbonylalanine in this hydrogenation are comparable to those reported using DIOP-Rh complex as a catalyst for the synthesis of N-acetylalanine[2b], N-benzyloxycarbonylalanine is more practically useful for the peptide synthesis than N-acetylalanine. It should be also noted that the effect of triethylamine on the optical yield of N-benzyloxycarbonylalanine is opposite to that observed in the synthesis of N-acetylphenylalanine[3].

Further studies along this line are under way[6].

REFERENCES AND NOTES

1) Asymmetric Reactions Catalyzed by Transition Metal Complexes. II.
Part I: K. Achiwa, J. Am. Chem. Sco., 98, 8265 (1976).
2)(a) J.D.Morrison, W.F.Masler, and M.K.Neuberg; Advan. Catal., 25, 81 (1976).
(b) T.Hayashi, M.Tanaka, and I.Ogata; Tetrahedron Lett., 1977, 295 and references cited therein.
3) K. Achiwa, J. Am. Chem. Soc., 98, 8265 (1976).
4) Satisfactory analytical and spectral data were obtained for this substance.
5) I. Photaki, J. Am. Chem. Soc., 85, 1123 (1963).
6) The author thanks emeritus professor S. Yamada, University of Tokyo, for his encouragement.

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