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ASYMMETRIC HYDROGENATION CATALYZED BY A CHIRAL FERROCENYLPHOSPHINE-RHODIUM COMPLEX

Tamio Hayashi, Takaya Mise, Seiko Mitachi, Keiji Yamamoto, and Makoto Kumada*
Department of Synthetic Chemistry, Kyoto University, Yoshida, Kyoto 606, Japan

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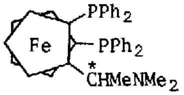
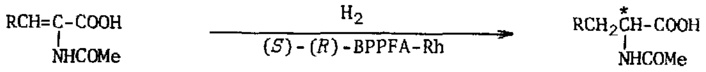
There has been a considerable interest recently in asymmetric synthesis catalyzed by transition metal complexes with a chiral ligand. We have previously reported the preparation of several chiral ferrocenylphosphine ligands and their application to catalytic asymmetric hydrosilylation of prochiral ketones.[1] We now wish to report that rhodium complex-catalyzed asymmetric hydrogenation[2-7] has been successfully achieved using (*S*)-α-[(*R*)-1',2-bis(diphenylphosphino)ferrocenyl]ethyldimethylamine, abbreviated as (*S*)-(*R*)-BPPFA, as a chiral ligand.



(*S*)-(*R*)-BPPFA

In the presence of $[Rh(1,5\text{-hexadiene})Cl]_2$ and (*S*)-(*R*)-BPPFA in a 1 : 2.4 ratio, hydrogenation of α-acetamidoacrylic acids (1a-1d) was completed in 20 hr at 50 atm initial hydrogen pressure and room temperature. The hydrogenated products (2a-2d) were isolated in 86-94% yield by means of the procedure reported by Kagan *et al.*[6]



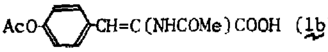
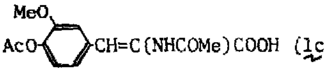
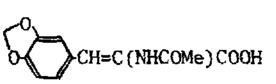
$$\underset{\displaystyle \text{NHCOMe}}{\text{RCH=C-COOH}} \xrightarrow[(S)\text{-}(R)\text{-BPPFA-Rh}]{H_2} \underset{\displaystyle \text{NHCOMe}}{\text{RCH}_2\overset{*}{\text{C}}\text{H-COOH}}$$

1a, R = phenyl
1b, R = 4-acetoxyphenyl
1c, R = 3-methoxy-4-acetoxyphenyl
1d, R = 3,4-methylenedioxyphenyl

2a-2d

Table 1 shows the results obtained for the asymmetric hydrogenation in a variety of solvents. The reaction of 1a always gives L-*N*-acetylphenylalanine (2a) with extremely high stereoselectivity regardless of the solvent employed. In cases of 1b and 1c, however, the optical yields were dependent markedly on the nature of solvents. It can be seen from Table 1 that the (*S*)-(*R*)-BPPFA-Rh complex shows the highest catalytic ability in aqueous solution rather than in methanol or ethanol. Such a high ability as an asymmetry-inducing ligand may be attributed to, in addition to the expected steric effects, attractive interactions forming an ammonium carboxylate between the amino group in (*S*)-(*R*)-BPPFA and the carboxy group in the olefinic substrate.

Table 1. Asymmetric Hydrogenation Catalyzed by (*S*)-(*R*)-BPPFA-Rh Complex[a]

Olefin	Solvent	$[\alpha]_D$	Optical yield (%)[b] (Configuration)
PhCH=C(NHCOMe)COOH (**1a**)	MeOH	+42.8°	93 (*S*)
	H_2O/EtOH(1/1)	+42.1°	92 (*S*)
	H_2O/MeOH(1/1)	+41.0°	89 (*S*)
 (**1b**)	MeOH	+3.1°	8 (*S*)
	EtOH	+15.3°	38 (*S*)
	H_2O/MeOH(1/3)	+35.1°	87 (*S*)
 (**1c**)	EtOH	+14.7°	36 (*S*)
	H_2O/MeOH(1/2)	+35.1°	86 (*S*)
 (**1d**)	H_2O/MeOH(3/4)	+27.7°	52 (*S*)

[a] $P(H_2)$ = 50 atm; (*S*)-(*R*)-BPPFA/Rh = 1.2/1; Rh/Substrate = 0.5 mol%. [b] Calculated on the basis of reported values for the optically pure compounds: (*S*)-**2a**; $[\alpha]_D^{26}$ +46.0° (*c* 1, EtOH), ref. 6b; (*S*)-**2b**; $[\alpha]_D^{27}$ +40.4° (*c* 0.5, H_2O), (R. R. Sealock, *J. Biol. Chem.*, **166**, 1 (1946)); (*S*)-**2c**; $[\alpha]_D^{20}$ +40.8° (*c* 1, MeOH), ref. 3c; (*R*)-**2d**; $[\alpha]_D^{19}$ -53.4° (*c* 1.8, EtOH) (S. Yamada, T. Fujii, and T. Schiori, *Chem. Pharm. Bull.*, **10**, 680 (1962)).

Relatively low optical yields were observed in the hydrogenation of methyl α-acetamidocinnamate (*S* 21% e.e.)[8] and of **1a** with one equivalent of triethylamine added (*S* 23% e.e.). This fact may support the attractive interactions mentioned above.

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