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ASYMMETRIC HYDROGENATION OF ENOL PHOSPHINATES CATALYZED BY A CHIRAL FERROCENYLPHOSPHINE-RHODIUM COMPLEX. ASYMMETRIC SYNTHESIS OF OPTICALLY ACTIVE SECONDARY ALKYL ALCOHOLS

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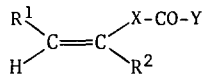
Summary: Catalytic asymmetric synthesis of secondary alkyl alcohols (up to 78% ee) was accomplished by asymmetric hydrogenation of enol diphenylphosphinates, derived from prochiral ketones such as acetophenone, 3-methyl-2-butanone, and 2-octanone, in the presence of a cationic rhodium complex of (*R*)-1-[(*S*)-1',2-bis(diphenylphosphino)ferrocenyl]ethanol (BPPFOH).

There has been intense interest and activity in asymmetric hydrogenation of prochiral olefins catalyzed by chiral phosphine-rhodium complexes,[1] and high optical yields (>85%) have been often attained in the reaction of α-(acylamino)-[1] and α-(acetyloxy)acrylic acids or esters,[2] itaconic acid derivatives,[3] and α-(acylamino)styrenes.[4] These olefins have the structural features shown below, containing the carbonyl oxygen three atoms away from the



X = NH, O, CH_2
Y = R, OR

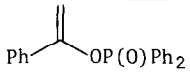
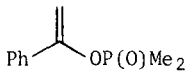
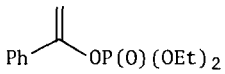
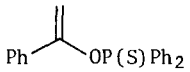
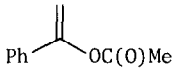
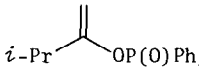
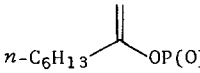
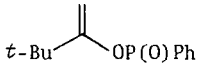
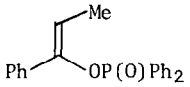
carbon-carbon double bond, and the chelation formed by coordination of the carbonyl as well as the olefin to rhodium has been recognized to enhance the stereoselectivity in diastereomeric transition states.[1e,5]

We report here that secondary alkyl alcohols of high optical purity could be obtained by asymmetric hydrogenation of enol phosphinates, which can be prepared regio- and stereoselectively from carbonyl compounds[6] and have analogous structure to the olefins mentioned above, capable of coordinating to rhodium with P=O instead of C=O. The present method provides a new efficient route to the preparation of optically active alcohols. Although there have been several attempts for the preparation by asymmetric hydrogenation of prochiral ketones,[7] the optical yields are generally low except for the reaction of those containing functional substituents, i.e., α-keto acids and esters[8] and α-amino ketones.[9]

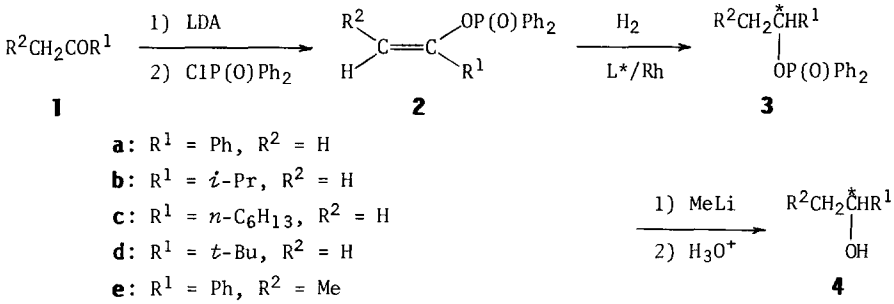
As shown in eq. 1, unsymmetrical ketones **1** were converted into enol phosphinates **2** with high regio- and stereoselectivity by phosphorylation of lithium enolates generated under kinetically controlled conditions (lithium diisopropylamide in THF at -78°). The phosphinates **2** were hydrogenated in the presence of a chiral phosphine-rhodium complex to give optically active secondary alkyl phosphinates **3**. Conversion of **3** into alcohol **4** was effected by treatment with an excess of methyllithium in ether followed by hydrolysis. Direct acid or base hydrolysis of **3** was unsuccessful. The results obtained for the asymmetric hydrogenation of **2** are summarized in Table 1.

For the reaction of 1-phenylvinyl diphenylphosphinate (**2a**), we have examined several rhodium catalysts with chiral bisphosphine ligands, which have been reported to be effective

Table 1. Asymmetric Hydrogenation of Enol Diphenylphosphinates **2** Catalyzed by Chiral Phosphine-Rhodium Complexes.[a]

Substrate	Ligand[b]	Solvent	Temp. (°C)	Conversion[c] (%)	% ee of **4**[d] (Configuration)
 (**2a**)	(*R*)-(*S*)-BPPFOH	Benzene	20	100	78 (*R*)
	(*R*)-(*S*)-BPPFOH	Benzene	30	100	63 (*R*)
	(*R*)-(*S*)-BPPFOH	Benzene	20[e]	100	64 (*R*)
	(*R*)-(*S*)-BPPFOH	THF	30	98	48 (*R*)
	(*R*)-(*S*)-BPPFOH	Methanol	20	0	——
	(*S*)-(*R*)-BPPFA	Benzene	20	94	43 (*R*)
	(-)-DIOP	Benzene	20	54 (15)[f]	80 (*S*)
	BPPM	Benzene	20	73 (26)[f]	57 (*S*)
	BPPM	Methanol	20	28	16 (*S*)
	(*S*)-prophos	Benzene	20	0	——
	(*R*)-(*S*)-BPPFOH	THF	20	96	39 (*R*)
	(*R*)-(*S*)-BPPFOH	Benzene	20	79 (18)[f]	33 (*R*)
	(*R*)-(*S*)-BPPFOH	Benzene	30[e]	18	24 (*S*)
	(*R*)-(*S*)-BPPFOH	Benzene	20	26	25 (*R*)
 (**2b**)	(*R*)-(*S*)-BPPFOH	Benzene	20	100	60 (*R*)
	(-)-DIOP	Benzene	20	17	55 (*S*)
	BPPM	Benzene	20	12	40 (*S*)
 (**2c**)	(*R*)-(*S*)-BPPFOH	Benzene	20[g]	100	48 (*R*)
 (**2d**)	(*R*)-(*S*)-BPPFOH	Benzene	30[e,h]	36	39 (*S*)
 (**2e**)	(*R*)-(*S*)-BPPFOH	Benzene	30[e,h]	40 (20)[i]	49 (*S*)

[a] The reaction was carried out at 5 atm initial hydrogen pressure for 40 h in the presence of cationic rhodium complex prepared in situ from a chiral ligand, $[Rh(NBD)_2]^+ClO_4^-$, and Et_3N (**2** : L* : $[Rh(NBD)_2]^+ClO_4^-$: Et_3N = 1 : 0.01 : 0.01 : 0.05). [b] See text. [c] Conversion was determined by ^1H NMR spectra of the reaction mixture. Isolated yields of alcohol **4** were over 70% when the conversion is >90%. [d] Obtained by a chiral shift reagent study with tris(3-trifluoroacetyl-*d*-camphorato)europium(III) [Eu(facam)$_3$] or tris(*d*,*d*-dicampholylmethanato)-europium(III) [Eu(dcm)$_3$]. [e] At 50 atm initial hydrogen pressure. [f] Yield of ethylbenzene. [g] For 170 h. [h] For 70 h. [i] Yield of propylbenzene.



a: R^1 = Ph, R^2 = H
b: R^1 = *i*-Pr, R^2 = H
c: R^1 = *n*-C_6H_{13}, R^2 = H
d: R^1 = *t*-Bu, R^2 = H
e: R^1 = Ph, R^2 = Me

(1)

for the hydrogenation of α-acylaminoacrylic acids. A rhodium cationic complex with (*R*)-1-[(*S*)-1',2-bis(diphenylphosphino)ferrocenyl]ethanol [(*R*)-(*S*)-BPPFOH][10] was the best catalyst exhibiting both high enantioselectivity (78% *R*) and high catalytic activity (100% conversion in 40 h). The (*S*)-*N*,*N*-dimethyl-1-[(*R*)-1',2-bis(diphenylphosphino)ferrocenyl]ethylamine [(*S*)-(*R*)-BPPFA][10] rhodium complex also catalyzed the hydrogenation in good yield, but the stereoselectivity was lower. The hydrogenation with (-)-2,3-*O*-isopropylidene-1,4-bis(diphenylphosphino)-2,3-butanediol [(-)-DIOP][11] or (2*S*,4*S*)-*N*-(*tert*-butoxycarbonyl)-4-(diphenylphosphino)-2-[(diphenylphosphino)methyl]pyrrolidine [BPPM][3c,12] as ligands resulted in low conversion and formation of ethylbenzene as a by-product, though the stereoselectivity was not low. Low catalytic activity of the (-)-DIOP- and BPPM-rhodium complex was also observed in the reaction of 1-isopropylvinyl diphenylphosphinate (**2b**). The rhodium complex with (*S*)-1,2-bis(diphenylphosphino)propane [(*S*)-prophos][2b] was entirely inactive for the present hydrogenation.

The BPPFOH-rhodium catalyzed-hydrogenation of **2a** gave rise to higher optical yields at lower reaction temperature and at lower hydrogen pressure, as is usually observed in the asymmetric hydrogenation of α-acylaminoacrylic acids.[1,3c,13] Solvent effects on the catalytic activity and stereoselectivity were remarkable; benzene leads to high conversion and high selectivity while methanol leads to complete inhibition of the hydrogenation.

Substitution of the diphenylphosphinyl group in **2a** for other phosphorus-containing functional groups lowered the stereoselectivity. Thus, the optical purities of the products obtained for hydrogenation of 1-phenylvinyl dimethylphosphinate, diethyl phosphate, and diphenylphosphinothioate in the presence of the (*R*)-(*S*)-BPPFOH-Rh catalyst were 39% (*R*), 33% (*R*), and 24% (*S*), respectively. The hydrogenation of 1-phenylvinyl acetate resulted in low conversion and low stereoselectivity (25% *R*) under the present reaction conditions.[14]

The rhodium catalyst with (*R*)-(*S*)-BPPFOH ligand was also effective for the asymmetric hydrogenation of diphenylphosphinates (**2b**,**2c**) derived from 3-methyl-2-butanone and 2-octanone, giving quantitatively 3-methyl-2-butanol (**4b**) (60% ee *R*) and 2-octanol (**4c**) (48% ee *R*). It should be noted that the optical yields attained here are much higher than those reported for direct hydrogenation of prochiral dialkyl ketones.[7] Phosphinates **2d** and **2e** gave the corresponding hydrogenated products with opposite configuration *S* in moderate optical yields.

We are presently continuing studies on mechanistic aspects of this asymmetric hydrogenation, focusing attention upon the coordinating ability of the diphenylphosphinyl group toward rhodium.

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REFERENCES AND NOTES

1. For reviews see (a) H. B. Kagan and J. C. Fiaud, "Topics in Stereochemistry," ed. by E. L. Eliel and N. L. Allinger, Wiley-Interscience, New York (1978), Vol. 10, p. 175; (b) D. Valentine, Jr. and J. W. Scott, *Synthesis*, 329 (1978); (c) R. Pearce, *Catalysis*, **2**, 176 (1978); (d) B. Bosnich and M. D. Fryzuk, "Topics in Inorganic and Organometallic Stereochemistry" ed. by G. Geoffroy, Wiley-Interscience, New York (1981), p. 119; (e) R. E. Merrill, "Asymmetric Synthesis Using Chiral Phosphine Ligands," Reaction Design Corp., New Jersey (1979).
2. (a) B. D. Vineyard, W. S. Knowles, M. J. Sabacky, G. L. Bachman, and D. J. Weinkauff, *J. Am. Chem. Soc.*, **99**, 5946 (1977); (b) M. D. Fryzuk and B. Bosnich, *J. Am. Chem. Soc.*, **100**, 5491 (1978).
3. (a) K. Achiwa, *Chem. Lett.*, 561 (1978); (b) I. Ojima, T. Kogure, and K. Achiwa, *Chem. Lett.*, 567 (1978); (c) I. Ojima, T. Kogure, and N. Yoda, *J. Org. Chem.*, **45**, 4728 (1980); (d) W. C. Christopfel and B. D. Vineyard, *J. Am. Chem. Soc.*, **101**, 4406 (1979).
4. D. Sinou and H. B. Kagan, *J. Organometal. Chem.* **114**, 325 (1976).
5. A. S. C. Chan, J. J. Pluth, and J. Halpern, *J. Am. Chem. Soc.*, **102**, 5952 (1980), and references cited therein.
6. (a) R. E. Ireland and G. Pfister, *Tetrahedron Lett.*, 2145 (1969); (b) I. J. Borowitz, S. Firstenberg, E. W. R. Casper, and R. K. Crouch, *J. Org. Chem.*, **36**, 3282 (1971); (c) I. J. Borowitz, E. W. R. Casper, R. K. Crouch, and K. C. Yee, *J. Org. Chem.*, **37**, 3873 (1972); (d) S. C. Welch and M. E. Walters, *J. Org. Chem.*, **43**, 2715 (1978).
7. (a) P. Bonvicini, A. Levi, G. Modena, and G. Scorrano, *J. C. S. Chem. Commun.*, 1188 (1972); (b) M. Tanaka, Y. Watanabe, T. Mitsudo, H. Iwane, and Y. Takegami, *Chem. Lett.*, 239 (1973); (c) C. J. Sih, J. B. Heather, R. Sood, P. Price, G. Peruzzotti, L. F. H. Lee, and S. S. Lee, *J. Am. Chem. Soc.*, **97**, 865 (1975); (d) A. Levi, G. Modena, and G. Scorrano, *J. C. S. Chem. Commun.*, 6 (1975); (e) S. Toros, B. Heil, and L. Marko, *J. Organometal. Chem.*, **159**, 401 (1978); (f) S. Toros, B. Heil, L. Kollar, and L. Marko, *J. Organometal. Chem.*, **197**, 85 (1980).
8. (a) T. Hayashi, T. Mise, and M. Kumada, *Tetrahedron Lett.*, 4351 (1976); (b) I. Ojima, T. Kogure, T. Terasaki, and K. Achiwa, *J. Org. Chem.*, **43**, 3444 (1978); (c) I. Ojima and T. Kogure, *J. Organometal. Chem.*, **195**, 239 (1980).
9. T. Hayashi, A. Katsumura, M. Konishi, and M. Kumada, *Tetrahedron Lett.*, 425 (1979).
10. T. Hayashi, T. Mise, M. Fukushima, M. Kagotani, N. Nagashima, Y. Hamada, A. Matsumoto, S. Kawakami, M. Konishi, K. Yamamoto, and M. Kumada, *Bull. Chem. Soc. Jpn.*, **53**, 1138 (1980).
11. H. B. Kagan and T. P. Dang, *J. Am. Chem. Soc.*, **94**, 6429 (1972).
12. K. Achiwa, *J. Am. Chem. Soc.*, **98**, 8265 (1976).
13. M. Fiorini and G. M. Giongo, *J. Mol. Catal.*, **5**, 303 (1979).
14. Asymmetric hydrogenation of 1-phenylvinyl acetate with the diPAMP-Rh catalyst has been reported to proceed in 55% optical yield; K. E. Koenig, G. L. Bachman, and B. D. Vineyard, *J. Org. Chem.*, **45**, 2362 (1980).

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