Pergamon

Tetrahedron Letters, Vol. 36, No. 45, pp. 8271-8274, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(95)01775-5

A New *P*-Chiral Bisphosphine, (*S,S*)-1,2-Bis[(*o*-ethylphenyl)phenylphosphino]ethane, as an Effective Ligand in Catalytic Asymmetric Hydrogenation of α-(Acylamino)acrylic Acids

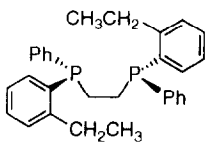
Tsuneo Imamoto,*[a] Hideyuki Tsuruta,[a] Yoshiyuki Wada,[b] Hideki Masuda[b] and Kentaro Yamaguchi[c]

[a]*Department of Chemistry, Faculty of Science, Chiba University, Inage, Chiba 263, Japan*
[b]*Ogawa and Co. Ltd., Okayama Laboratory, Shoocho, Katsuta, Okayama, 709-43, Japan*
[c]*Chemical Analysis Center, Chiba University, Inage, Chiba 263, Japan*

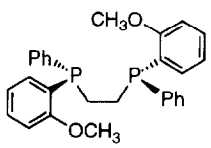
Abstract: (*S,S*)-1,2-Bis[(*o*-ethylphenyl)phenylphosphino]ethane has been prepared via optically active phosphine–boranes. Asymmetric hydrogenation of α-(acylamino)acrylic acids by a rhodium complex with this ligand affords *N*-acylamino acids in 86–93% ee.

Optically active phosphines possessing chiral centers at phosphorus have potential utility as ligands in catalytic asymmetric reactions, and many ligands of this class have been reported so far.[1] Among them, the *P*-chiral phosphines having *o*-methoxyphenyl groups are exceptionally effective in catalytic asymmetric hydrogenation of α-(acylamino)acrylic acids.[2] The role of the methoxy group in the asymmetric reaction has not yet been completely explained, but a weak interaction of the methoxy oxygen with the rhodium atom is suggested as one of the factors in effecting the enantioselectivity of the reduction on the basis of the X-ray analysis of a rhodium complex of (*R,R*)-1,2-bis[(*o*-methoxyphenyl)phenylphosphino]ethane (DIPAMP).[2c] We considered that a steric effect of *ortho*-methoxy group might be an important factor rather than the coordinative interaction.

In order to demonstrate this idea, we designed a new *P*-chiral phosphine ligand, (*S,S*)-1,2-bis[(*o*-ethylphenyl)phenylphosphino]ethane (**(*S,S*)-1**) which structurally resembled (*S,S*)-DIPAMP but possessed no oxygen functional groups. Synthesis of this ligand was accomplished via phosphine–boranes as the intermediates (Scheme 1).[3]



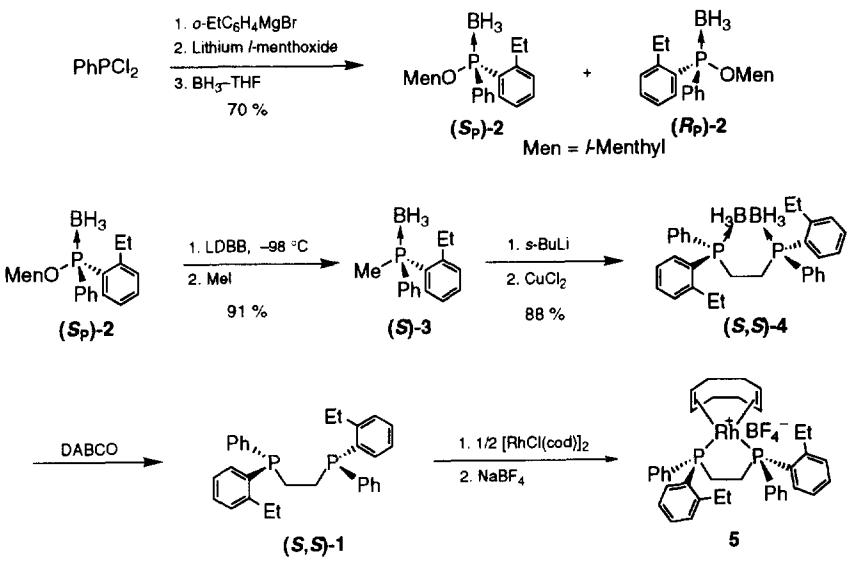
(*S,S*)-1



(*S,S*)-DIPAMP

Dichlorophenylphosphine was treated sequentially with *o*-ethylphenylmagnesium bromide, lithium *l*-menthoxide, and borane–THF to afford a mixture of two diastereomers, (**S**p)-**2** and (**R**p)-**2**, in 70 % combined yield. The two compounds were separated by preparative HPLC (ODS, MeOH),[4] and one compound was subjected to single crystal X-ray analysis to determine its absolute configuration at chiral phosphorus.[5,6] The molecular structure of compound (**S**p)-**2**, whose chirality at phosphorus is *S*, is shown in Figure 1.[7] Compound (**S**p)-**2** was reduced by lithium 4,4'-di-*t*-

Scheme 1



butylbiphenylide (LDBB) at –98 °C, followed by the treatment with iodomethane, to furnish (*S*)-**3** with 88% ee in 91% yield.[8,9] Without further purification, (*S*)-**3** was dimerized via successive reactions with *s*-BuLi and copper(II) chloride, and the resulting product was recrystallized from hexane-dichloromethane to yield optically pure bisphosphine–borane (*S,S*)-**4**.[10] The two boranato groups of this compound were removed by the reaction with DABCO in toluene at 50 °C for 30 min to furnish the desired phosphine ligand (*S,S*)-**1** in almost quantitative yield.[11] Complexation of this ligand with $[RhCl(cod)]_2$, followed by treatment with $NaBF_4$, afforded a rhodium cation complex **5**.

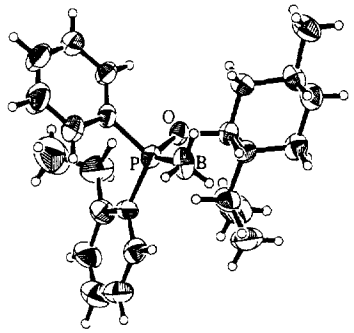


Figure 1

This complex was employed for catalytic asymmetric reduction of α-(acylamino)acrylic acids. The reductions were carried out under almost the same conditions as those conducted by Knowles *et al.* using a rhodium complex of (*R,R*)-DIPAMP in order to compare the enantioselectivities of the two ligands.[2b,c] The results are summarized in Table 1, together with the reported ones.

It is noted that markedly high asymmetric inductions (86–93%ee) were observed in these catalytic hydrogenations.[12] Another significant fact is that the catalysts prepared from (*S,S*)-**1** and (*R,R*)-DIPAMP provided the hydrogenation products with opposite chiralities, respectively. That is, both ligands, (*S,S*)-**1** and (*S,S*)-DIPAMP, with the same chirality at phosphorus afford products possessing the same configuration. These comparable results indicate that the *o*-ethyl group in (*S,S*)-**1** plays almost the same role as the *o*-methoxy group in DIPAMP and that a coordinative interaction of the methoxy group of DIPAMP is not a main factor in effecting the asymmetric induction.

Table 1. Asymmetric Hydrogenations of α-(Acylamino)acrylic Acids Using a Rhodium Complex **5**[a]

entry	R	R'	R"	substrate / rhodium	solvent	time (h)	% ee of product[b]	
1	Ph	H	CH_3	500	*i*-PrOH	3	90*R*	(96*S*)[c,d]
2	Ph	H	Ph	500	*i*-PrOH	4	86*R*	(93*S*)[c,d]
3	Ph	CH_3	CH_3	500	*i*-PrOH	6	93*R*	(97*S*)[c,d]
4	Ar[e]	H	CH_3	1000	88 % *i*-PrOH	8	89*R*	(94*S*)[c,f]
5[g]	H	H	CH_3	500	EtOH	6	93*R*	(90*S*)[c,d]
6[g]	H	CH_3	CH_3	500	MeOH	3	91*R*	(95*S*)[c,h]

[a] All reactions were carried out at 50 °C and under 3 atm of H_2 pressure, unless otherwise stated. [b] Enantiomeric excesses were determined by measuring the rotations of the products. [c] Reported data obtained by the use of (*R,R*)-DIPAMP. [d] See Ref. 2c and 2g. [e] Ar = 4-AcO-3-$MeOC_6H_3$. [f] See Ref. 2b and 2g. [g] The reaction was carried out at room temperature. [h] See Ref. 2e.

In summary, we have demonstrated that optically active 1,2-bis[(*o*-ethylphenyl)phenylphosphino]ethane exhibits high asymmetric inductions in rhodium-catalyzed asymmetric hydrogenations of α-(acylamino)acrylic acids. Synthesis and catalytic activities of related *P*-chiral ligands are currently under investigation in our laboratory, and the results will be published in due course.

Acknowledgement: This work was supported by Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture, Japan.

References and Notes

1. For recent representaive reviews, see the following: Valentine, Jr. D. in *Asymmetric Synthesis*, Morrison, J. D.; Scott, J. W. Eds., Academic Press, New York, Vol. 4, Chap. 3, 1984; Morrison, J. D. Ed. *Asymmetric Synthesis*, Vol. 5, Academic Press, New York, 1985; Brunner, H. in *Topics in Stereochemistry*, Vol. 18, Eliel, E. L.; Wilen, S. H. Eds.; John Wiley, New York, pp 129-247, 1988; Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581; Ojima, I. *Tetrahedron* **1989**, *45*, 6901; Kagan, H. B.; Sasaki, M. in *The Chemistry of Organophosphorus Compounds*, Hartley, F. R. Ed.; John Wiley, New York, 1990, Vol. 1. Chapter 3; Pietrusiewicz, K. M.; Zablocka, M. *Chem. Rev.* **1994**, *94*, 1375; Noyori, R. *Asymmetric Catalysis in Organic Synthesis*, John Wiley, New York, 1995.

2. (a) Knowles, W. S.; Sabacky, M. J.; Vineyard, B. D. *J. Chem. Soc. Chem. Commun.* **1972**, 10. (b) Knowles, W. S.; Sabacky, M. J.; Vineyard, B. D.; Weinkauff, D. J. *J. Am. Chem. Soc.*, **1975**, *97*, 2567. (c) Vineyard, B. D.; Knowles, W. S.; Sabacky, M. J.; Bachman, G. L.; Weinkauff, D. J. *J. Am. Chem. Soc.*, **1977**, *99*, 5946. (d) Horner, L.; Schlotthauer, B. *Phosphorus Sulfur* **1978**, *4*, 155. (e) Scott, J. W.; Keith, D. D.; Nix, Jr. G.; Parrish, D. R.; Remington, S.; Roth, G. P.; Townsend, J. M.; Valentine, Jr. D.; Yang, R. *J. Org. Chem.* **1981**, *46*, 5086. (f) Knowles, W. S.; Christopfel, W. C.; Koenig, K. E.; Hobbs, C. F. *Adv. Chem. Ser.* **1982**, *196*, 325. (g) Vineyard, B. D.; Knowles, W. S.; Sabacky, M. J. *J. Mol. Cat.* **1983**, *19*, 159. (h) Johnson, C. R.; Imamoto, T. *J. Org. Chem.* **1987**, *52*, 2170. (i) Nagel, U.; Krink, T. *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1052.

3. Imamoto, T.; Oshiki, T.; Onozawa, T.; Kusumoto, T.; Sato, K. *J. Am. Chem. Soc.* **1990**, *112*, 5244; Imamoto, T. *Pure Appl. Chem.* **1993**, *65*, 655; Imamoto, T.; Oshiki, T.; Onozawa, T.; Matsuo, M.; Hikosaka, T.; Yanagawa, M. *Heteroatom Chem.* **1993**, *3*, 563; Imamoto, T.; Matsuo, M.; Nonomura, T.; Kishikawa, K.; Yanagawa, M. *Heteroatom Chem.* **1994**, *4*, 475.

4. The product was recrystallized from methanol to separate each diastereomer. However, colorless needles (mp 74–75 °C) consisting of (***S*P**)-**2** and (***R*P**)-**2** in a 1 : 1 molar ratio were preferentially formed. The molecular structure of the crystal is shown in Figure 2. The X-ray crystallographic data are as follows: prismatic, $P2_1$ (#4), a = 14.733(2), b = 8.4430(6), c = 19.109(2)Å, β = 94.49(1)°, V = 2369.7(5)Å^3, Z = 4, D_{calc} = 1.072 g/cm^3, temperature of data collection 296K, 3180 observed reflections (I>3.00σ(I)), R = 0.065, R_W = 0.062. The supplementary materials have been deposited at the Cambridge Crystallographic Centre.

5. (***S*P**)-**2**: Colorless prisms; mp 80.0–80.5 °C (MeOH); $[\alpha]^{26}_D$ -103° (c 0.97, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.11 (dd, J = 14.7, 7.6Hz, 1H), 7.7–7.1 (m, 8H), 4.36 (m, 1H), 2.54 (m, 2H), 2.2–0.6 (m, 12H), 0.89 (d, J = 6.6 Hz, 3H), 0.78 (t, 3H), 0.75 (d, J = 6.9 Hz, 3H), 0.48 (d, J = 6.9 Hz, 3H); IR (KBr) 2370 cm^{-1}; MS (FAB) m/z 382 (M^+). Anal. Calcd for $C_{24}H_{36}BOP$: C, 75.40; H, 9.49. Found: C, 75.66; H, 9.69.

6. (***R*P**)-**2**: Colorless crystals; mp 57.5–58.5 °C; $[\alpha]^{24}_D$ -25.0° (c 1.05, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 8.07 (dd, J = 11.7, 7.8 Hz, 1H), 7.7–7.2 (m, 8H), 4.34 (m, 1H), 2.57 (m, 2H), 2.1–0.2 (m, 12H), 0.86 (t, J = 7.4 Hz, 3H), 0.86 (d, J = 7.3 Hz, 3H), 0.80 (d, J = 6.3 Hz, 3H), 0. 67 (d, J = 6.9 Hz, 3H); IR (KBr) 2350 cm^{-1}; MS (FAB) m/z 382 (M^+). Anal. Calcd for $C_{24}H_{36}BOP$: C, 75.40; H, 9.49. Found: C, 75.22; H, 9.47.

7. X-ray crystallographic data for (***S*P**)-**2**: FW = 382.33, prismatic, $P2_12_12_1$ (#19), a = 14.368(2), b = 17.042(1), c = 9,8810(8)Å, V = 2419.4(4)Å^3, Z = 4, D_{calc} = 1.050 g/cm^3, temperature of data collection 296K, 1428 observed reflections (I>3.00σ(I)), R = 0.067, R_W = 0.072. The supplementary materials have been deposited at the Cambridge Crystallographic Centre.

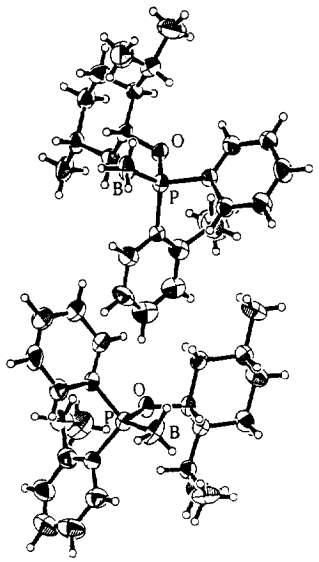


Figure 2

8. The enantiomeric excess of the product was determined by HPLC analysis using a chiral column (Daisel, CHIRALCEL OJ, *i*-PrOH/hexane = 1/9).

9. (***S*)-3**: Colorless oil; $[\alpha]^{26}_D$ +21.2° (c 1.04, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.7–7.2 (m, 9H), 2.8–2.4 (m, 2H), 1.0–0.8 (m, 3H), 2.0–0.1 (br m, 3H), 1.86 (d, J = 9.6 Hz, 3H); IR (Neat) 2350 cm^{-1}; HRMS (FAB) Calcd for $C_{12}H_{20}BKP$ ($M+K^+$) 281.1028 found 281.1037.

10. (***S*,*S*)-4**: Colorless needles; mp 151.5–152.5 °C (Hexane/CH_2Cl_2 = 5/1); $[\alpha]^{26}_D$ +51.8° (c 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.7–7.2 (m, 18H), 2.7–2.1 (m, 8H), 0.86 (t, J = 7.4 Hz, 3H); IR (KBr) 2350 cm^{-1}; MS (FAB) m/z 482 (M^+). Anal. Calcd for $C_{30}H_{38}B_2P_2$: C, 74.73; H, 7.94. Found: C, 74.47; H, 7.88.

11. (***S*,*S*)-1**: Colorless oil; $[\alpha]^{24}_D$ -10.8° (c 0.50, toluene); ^{1}H NMR ($CDCl_3$) δ 7.3–7.1 (m, 18H), 3.0–2.7 (m, 4H), 1.0–0.8 (m, 3H), 2.1–2.05 (m, 4H), 1.13 (t, J = 7.5 Hz, 6H); HRMS (FAB) Calcd for $C_{30}H_{33}P_2$ ($M+H^+$) 455.2050 found 455.2068.

12. Yoshikuni and Bailar, Jr. reported that asymmetric reduction of acetamidoacrylic acid catalyzed by a rhodium complex of optically active bis[(*o*-methylphenyl)phenylphosphino]ethane afforded *N*-acetylalanine in 49.3% ee. Yoshikuni, T.; Bailar, Jr. J. C. *Inorg. Chem.* **1982**, *21*, 2129.

(*Received in Japan* 10 *August* 1995; *revised* 8 *September* 1995; *accepted* 14 *September* 1995)