JOC*Note*

Synthesis of Monodentate Chiral Spiro Phosphonites and the Electronic Effect of Ligand in Asymmetric Hydrogenation

Yu Fu, Guo-Hua Hou, Jian-Hua Xie, Liang Xing,
Li-Xin Wang, and Qi-Lin Zhou*

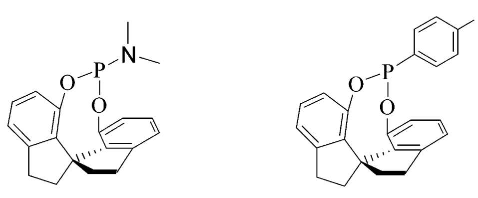
State Key Laboratory and Institute of Elemento-organic Chemistry, Nankai University, Tianjin 300071, China

glzhou@nankai.edu.cn

Received May 20, 2004

Abstract: New monodentate chiral phosphonites were synthesized from enantiomerically pure 1,1′-spirobiindane-7,7′-diol. The phosphonites **2** were efficient ligands for the Rh-catalyzed asymmetric hydrogenation of α- and *β*-dehydroamino acid derivatives, providing the amino acids in high enantioselectivities. The study of electronic effect showed that the electron-withdrawing substitutent on the *P*-phenyl ring of the phosphonite ligand dramatically decreased both the reactivity and enantioselectivity of the ligand.

The design and synthesis of new chiral ligands is the key to developing highly efficient enantioselective transition-metal-catalyzed reactions. In the past three decades, a tremendous amount of chelating diphosphane ligands have been prepared and applied in asymmetric hydrogenation with excellent enantioselectivities.[1] In contrast, the development of monodentate chiral phosphorus ligands for asymmetric hydrogenation has not attracted much attention, although the earliest chiral ligands used by Knowles and Horner were monophosphines.[2] Recently, the potential of chiral monodentate phosphorus ligands was rediscovered,[3] and several efficient chiral monophosphorus compounds, such as phospholane,[4] phosphonites,[5] phosphites,[6] and phosphoamidites,[7] were successfully applied in asymmetric hydrogenation of functionalized olefins with good to excellent enantioselectivities. We demonstrated that the chiral spiro phosphoramidite (SIPHOS, **1**) derived from 1,1′-spirobiindane-7,7′-diol was highly enantioselective for Rh-catalyzed asymmetric hydrogenation of α-dehydroamino acid derivatives and α-arylenamides (Figure 1).[8]



1 (SIPHOS) **2**

FIGURE 1. Chiral spiro monophosphorus ligands.

In the design of a chiral ligand applied in asymmetric catalyzed reaction, most considerations are based on the steric effect.[1c] By contrast, the electronic effect of ligands has been less explored.[9] In the optimization of SIPHOS ligands for Rh-catalyzed hydrogenation, we found that the ligand with smaller *N*-alkyl groups provided a higher enantioselectivity.[8b,10] However, when the substituents possessing different electronic properties were introduced into the rings of the spirobiindane backbone of SIPHOS ligands, only a weak electronic effect was observed in the Rh-catalyzed hydrogenations.[11] The weakness of the electronic effect might be attributed to the fact that the rings of spirobiindane in SIPHOS ligands are not directly connected to the *P*-atom and the electronic property of the substituents could not be efficiently transferred to the *P*-atom. To study the real electronic effect of monodentate phosphorus ligand in asymmetric hydrogenation, we herein describe the synthesis of chiral spiro phosphonite ligands **2** and the investigation on their behaviors in the enantioselective Rh-catalyzed hydrogenations of α- and *β*-dehydroamino acid derivatives.

The phosphonites **2** were easily prepared by the reaction of optically pure 1,1′-spirobiindane-7,7′-diol and the corresponding dichloroarylphosphine ($ArPCl_2$) in the presence of Et_3N (Scheme 1) at room temperature in 56–81% yields. To minimize the influence of steric hindrance, the substituents were introduced into the para position of the *P*-phenyl group.

The Rh-catalyzed hydrogenation of methyl (*Z*)-2-acetaminocinnamate, which is a standard reaction to test

---

[1] (a) *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley-VCH: New York, 2000. (b) *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999. (c) Tang, W.; Zhang, X. *Chem. Rev.* **2003**, *103*, 3029.

[2] (a) Knowles, W. S.; Sabacky, M. J. *J. Chem. Soc., Chem. Commun.* **1968**, 1445. (b) Horner, L.; Siegel, H.; Büthe, H. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 942.

[3] For reviews, see: (a) Lagasse, F.; Kagan, H. B. *Chem. Pharm. Bull.* **2000**, *48*, 315. (b) Komarov, I. V.; Börner, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 1197. (c) Ansell, J.; Wills, M. *Chem. Soc. Rev.* **2002**, *31*, 259.

[4] (a) Guillen, F.; Fiaud, J. C. *Tetrahedron Lett.* **1999**, *40*, 2939. (2) Junge, K.; Oehme, G.; Monsees, A.; Riermeier, T.; Dingerdissen, U.; Beller, M. *Tetrahedron Lett.* **2002**, *43*, 4977.

[5] (a) Claver, C.; Fernandez, E.; Gillon, A.; Heslop, K.; Hyett, D. J.; Martorell, A.; Orpen, A. J.; Pringle, P. G. *Chem. Commun.* **2000**, 961. (b) Reetz, M. T.; Sell, T. *Tetrahedron Lett.* **2000**, *41*, 6333.

[6] (a) Reetz, M. T.; Mehler, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 3889. (b) Reetz, M. T.; Sell, T. *Tetrahedron Lett.* **2000**, *41*, 6333. (c) Chen, W.; Xiao, J. *Tetrahedron Lett.* **2001**, *42*, 2897. (d) Reetz, M. T.; Sell, T.; Meiswinkel, A.; Mehler, G. *Angew. Chem., Int. Ed.* **2003**, *42*, 790.

[7] (a) van den Berg, M.; Minnaard, A. J.; Schudde, E. P.; van Esch, J.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. *J. Am. Chem. Soc.* **2000**, *122*, 11539. (b) van den Berg, M.; Minnaard, A. J.; Haak, R. M.; Leeman, M.; Schudde, E. P.; Meetsma, A.; Feringa, B. L.; de Vries, A. H. M.; Maljaars, C. E. P.; Willans, C. E.; Hyett, D.; Boogers, J. A. F.; Henderickx, H. J. W.; de Vries, J. G. *Adv. Synth. Catal.* **2003**, *345*, 308. (c) Zeng, Q.; Liu, H.; Mi, A.; Jiang, Y.; Li, X. S.; Choi, M. C. K.; Chan, A. S. C. *Tetrahedron* **2002**, *58*, 8799. (d) Jia, X.; Guo, R.; Li, X.; Yao, X.; Chan, A. S. C. *Tetrahedron Lett.* **2002**, *43*, 5541.

[8] (a) Fu, Y.; Xie, J.-H.; Hu, A.-G.; Zhou, H.; Wang, L.-X.; Zhou, Q.-L. *Chem. Commun.* **2002**, 480. (b) Hu, A.-G.; Fu, Y.; Xie, J.-H.; Zhou, H.; Wang, L.-X.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2002**, *41*, 2348.

[9] For recent papers, see: (a) Zhang, Z.; Qian, H.; Longmire, J.; Zhang, X. *J. Org. Chem.* **2000**, *65*, 6223. (b) Saito, T.; Yokozawa, T.; Ishizaki, T.; Moroi, T.; Sayo, N.; Miura, T.; Kumobayashi, H. *Adv. Synth. Catal.* **2001**, *343*, 264. (c) Pai, C. C.; Li, Y. M.; Zhou, Z. Y.; Chan, A. S. C. *Tetrahedron Lett.* **2002**, *43*, 2789. (d) Jeulin, S.; de Paule, S. D.; Ratovelomanana-Vidal, V.; Genêt, J.-P.; Champion, N.; Dellis, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 320.

[10] A favorable influence of small groups on the nitrogen in the MonoPhos ligands was also described by another group; see: Peña, D.; Minnaard, A. J.; de Vries, J. G.; Feringa, B. L. *J. Am. Chem. Soc.* **2002**, *124*, 14552.

[11] Zhu, S.-F.; Fu, Y.; Xie, J.-H.; Liu, B.; Xing, L.; Zhou, Q.-L. *Tetrahedron: Asymmetry* **2003**, *14*, 3219.

10.1021/jo049146x CCC: $27.50

SCHEME 1. Syntheses of Spiro Phosphonite Ligands 2

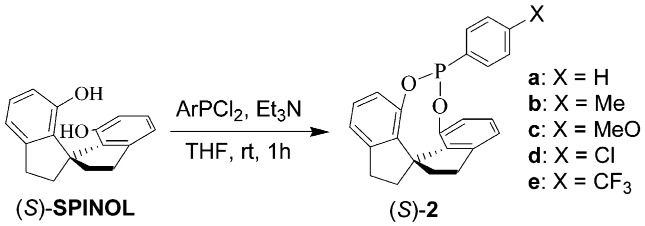
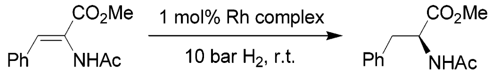


TABLE 1. Asymmetric Hydrogenation of Methyl (*Z*)-2-Acetamidocinnamate Using Rh/(*S*)-2 Catalysts[a]



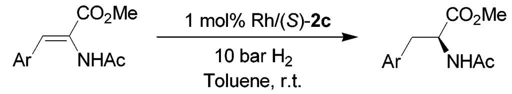
ligand	solvent	time[b] (h)	ee[c] (%)
(*S*)-**2a**	MeOH	4	74
(*S*)-**2a**	CH_2Cl_2	2	91
(*S*)-**2a**	acetone	4	81
(*S*)-**2a**	THF	3	95
(*S*)-**2a**	EtOAc	2	96
(*S*)-**2a**	toluene	3	98
(*S*)-**2b**	toluene	3	97
(*S*)-**2c**	toluene	2	99
(*S*)-**2d**	toluene	10	93
(*S*)-**2e**	toluene	24	82
(*S*)-**1**	toluene	4	97

[a] $Rh(COD)_2BF_4$/**2**/substrate = 1:2:100. [b] Time for 100% conversion. Quantitative yields were obtained in all reactions. [c] Determined by chiral GC using a Varian Chiralsil-L-Val column. The absolute configurations of product were *S*.

the efficiency of new phosphorus ligands, was chosen to study the electronic effect in ligands **2**. The reaction was carried out in different solvents, and the toluene was found to be the best choice. In toluene, the hydrogenation product was obtained in quantitative yield and 98% ee by using ligand **2a** under 10 bar H_2 at room temperature for 3 h (Table 1). This result is slightly better than that obtained by using phosphoramidite ligand SIPHOS (97% ee in 4 h). The spiro phosphonite ligands with different substituents were compared in toluene. The ligand **2c** bearing an electron-donating *p*-methoxy group was found to have slightly higher reactivity and enantioselectivity than its parent ligand **2a**, producing the hydrogenation product in 99% ee. However, the ligands **2d** and **2e**, which contained electron-withdrawing substituents on the *P*-phenyl group, had much lower reactivities and enantioselectivities.

Using ligand **2c**, a variety of α-dehydroamino acid derivatives were hydrogenated in quantitative yield with excellent enantioselectivities (97–99% ee). The electronic and steric nature of a substituent on the phenyl ring of substrate had little influence on the enantioselectivity of the reaction (Table 2).

TABLE 2. Hydrogenation of α-Dehydroamino Acid Derivatives with Ligand (*S*)-2c[a]



substrate (Ar)	ee[b] (%)	config
C_6H_5	99	*S*
4-MeC_6H_4	99	*S*
4-$MeOC_6H_4$	98	*S*
2-ClC_6H_4	99	*S*
3-ClC_6H_4	99	*S*
4-ClC_6H_4	98	*S*
2-$NO_2C_6H_4$	97	*S*
3-$NO_2C_6H_4$	99	*S*
4-$NO_2C_6H_4$	98	*S*

[a] $Rh(COD)_2BF_4$/(*S*)-**2c**/substrate = 1:2:100, 6 h, 100% conversions and quantitative yields were obtained in all reactions. [b] Determined by chiral GC using Varian Chiralsil-L-Val column or by chiral HPLC using a Chiralcel OJ or OD column.

Catalytic asymmetric hydrogenation of *β*-(acylamino)acrylate derivatives provides a convenient method for the synthesis of *β*-amino acid derivatives and has attracted much attention. Among the ligands used in the Rh-catalyzed hydrogenation of *β*-(acylamino)acrylate derivatives, the diphosphines have been most effective.[12] Recently, monophosphoramidites were also successfully employed in the Rh-catalyzed asymmetric hydrogenation of *β*-(acylamino)acrylates, giving excellent enantioselectivities.[10] However, for most of these catalytic systems, high enantioselectivity can only be obtained when pure *Z*- or *E*-isomers of *β*-(acylamino)acrylate substrates are used in the hydrogenation. Very few catalysts have been reported to be efficient for the hydrogenation of *Z*/*E* mixtures of *β*-(acylamino)acrylates.[12a,13] Since the *β*-(acylamino)acrylates are normally formed as a mixture of *Z*- and *E*-isomers, the development of a new efficient catalyst that can hydrogenate the mixture of two isomers is significantly important.

The hydrogenation of methyl (*Z*/*E*)-*β*-(acetamino)cinnamate (*Z*/*E* = 88:12) was used to optimize reaction conditions. Screening of solvents showed that the CH_2Cl_2 was the suitable solvent for obtaining high enantioselectivity. The comparison of ligand was performed in CH_2Cl_2 under 100 bar H_2 at room temperature. The results are summarized in Table 3. The reactivities of ligands **2a** and **2b** were similar to those of ligand SIPHOS, while their enantioselectivities (92% ee) were higher than that of ligand SIPHOS (90% ee). By introducing an electron-donating *p*-methoxy group, ligand **2c** slightly increased the enantioselectivity to 93% ee. But ligands **2d** and **2e**, with electron-withdrawing groups, gave incomplete reactions and much lower enantioselectivities.

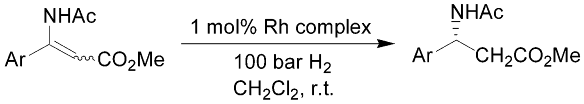
Different (*Z*/*E*)-*β*-aryl-*β*-(acetamino)acrylates (*Z*/*E* = 98:2–50:50) were hydrogenated by the rhodium complex of **2c** (Table 3). The electronic property of a substituent also has a significant influence on the reaction rate and enantioselectivity. The substrates with an electron-

---

(12) For a review, see ref 1c. For recent papers, see: (a) Zhou, Y.-G.; Tang, W.; Wang, W.-B.; Li, W.; Zhang, X. *J. Am. Chem. Soc.* **2002**, *124*, 4952. (b) Tang, W.; Wu, S.; Zhang. X. *J. Am. Chem. Soc.* **2003**, *125*, 9570. (c) Tang, W.; Wang, W.; Chi, Y.; Zhang, X. *Angew. Chem., Int. Ed.* **2003**, *42*, 3509. (d) Holz, J.; Monsees, A.; Jiao, H.; You, J.; Komarov, I. V.; Fischer, C.; Drauz, K.; Börner, A. *J. Org. Chem.* **2003**, *68*, 1701. (e) Wu, J.; Chen, X.; Guo, R.; Yeung, C.-H.; Chan, A. S. C. *J. Org. Chem.* **2003**, *68*, 2490. (f) Jerphagnon, T.; Renaud, J.-L.; Demonchaux, P.; Ferreira, A.; Bruneau, C. *Tetrahedron: Asymmetry* **2003**, *14*, 1973. (g) Dubrovina, N. V.; Tararov, V. I.; Monsees, A.; Kadyrov, R.; Fischer, C.; Börner, A. *Tetrahedron: Asymmetry* **2003**, *14*, 2739. (h) You, J.; Drexler, H.-J.; Zhang, S.; Fischer, C.; Heller, D. *Angew. Chem. Int. Ed.* **2003**, *42*, 913.

(13) 3. (a) Tang, W.; Zhang. X. *Org. Lett.* **2002**, *4*, 4159. (b) Lee, S.-G.; Zhang, Y. J. *Org. Lett.* **2002**, *4*, 2429. (c) Jerphagnon, T.; Renaud, J.-L.; Demonchaux, P.; Ferreira, A.; Bruneau, C. *Adv. Synth. Catal.* **2004**, *346*, 33.

TABLE 3. Hydrogenation of Methyl *β*-Aryl-*β*-(acetamino)acrylates[a]



ligand	substrate (Ar)	time (h)	conv[b] (%)	ee[c] (%)
(*S*)-**1**	Ph	40	100	90
(*S*)-**2a**	Ph	40	100	92
(*S*)-**2b**	Ph	40	100	92
(*S*)-**2c**	Ph	40	100	93
(*S*)-**2d**	Ph	48	70	87
(*S*)-**2e**	Ph	48	30	40
(*S*)-**2c**	4-CH_3Ph	36	100	94
(*S*)-**2c**	2-CH_3OPh	36	100	95
(*S*)-**2c**	4-CH_3OPh	36	100	98
(*S*)-**2c**	4-ClPh	48	100	90
(*S*)-**2c**	3-BrPh	48	100	85
(*S*)-**2c**	4-BrPh	48	100	91

[a] $Rh(COD)_2BF_4$/ligand/substrate = 1:2:100. [b] Determined by GC. Quantitative yields were obtained unless mentioned otherwise. [c] Determined by chiral GC using a Varian Chiralsil-L-Val column or chiral HPLC using a Chiralcel OD-H column. The absolute configurations were *R*.

donating substituent afforded faster reaction and higher enantioselectivity. The highest enantioselectivity (98% ee) was achieved in the hydrogenation of methyl *β*-(4-methoxyphenyl)-*β*-(acetamino)acrylate. However, the substrates with electron-withdrawing substituents had lower reaction rates and enantioselectivities. Methyl *β*-(2-boromophenyl)-*β*-(acetamino)acrylate cannot be hydrogenated at the same conditions.

In conclusion, we have developed novel chiral monodentate phosphonite ligands with spirobiindane as a backbone, which are highly effective for the Rh-catalyzed asymmetric hydrogenations of α- and *β*-dehydroamino acid derivatives. The enantioselectivities achieved in hydrogenation of (*Z*/*E*)-*β*-aryl-*β*-(acetamino)acrylates represent the highest level of enantiocontrol in the hydrogenation of *Z*/*E* mixtures of *β*-dehydroamino acid derivatives by using monophosphorus ligands. We also demonstrated that the electron-donating substituents on the *P*-phenyl ring of phosphonite ligands **2** have a limited influence on the enantioselectivity of ligand, while the electron-withdrawing substituents resulted in a significant decrease in both reactivity and enantioselectivity of ligand. To probe whether this detrimental effect was caused by the electronic effect of ligand on the catalyst or by the less efficiency of electron-poor ligand in the coordination, we compared the coordinative behavior of ligands **2a**, **2c** and **2e** to rhodium. The coordinations of all these three ligands to rhodium were complete in 5 min at the reaction conditions,[14] which indicated that the lower reaction rates and enantioselectivities of ligands with electron-withdrawing substituents were mainly attributed to the electronic effect of ligand on the catalyst.

Experimental Section

General Methods. All reactions and manipulations were performed in an argon atmosphere using standard Schlenk techniques. Anhydrous toluene and THF were distilled from sodium benzophenone ketyl. Anhydrous EtOAc, acetone, and CH_2Cl_2 were distilled from calcium hydride. Anhydrous MeOH was distilled from magnesium. SPINOL,[15] α-dehydroamino esters,[16] and *β*-dehydroamino esters[17] were prepared by reported methods.

General Procedure for Synthesis of Spiro Phosphonite Ligands. To a stirred solution of (*S*)-SPINOL (250 mg, 1.0 mmol) and Et_3N (0.5 mL) in 5 mL of THF was added $ArPCl_2$ (1.2 mmol) slowly at room temperature. The reaction mixture was stirred at rt for 1 h, and the product was purified by flash chromatography on a silica gel column using petroleum/EtOAc as eluent.

(*S*)-*O*,*O*′-[7,7′-(1,1′-Spirobiindan)]phenylphosphonite (2a): oil; 77% yield; $[\alpha]^{20}_D = -132$ (*c* 0.5, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$) δ 1.98−2.12 (m, 2H), 2.21−3.33 (m, 2H), 2.84−2.92 (m, 2H), 3.01−3.16 (m, 2H), 5.76 (d, $J = 8$ Hz, 1H), 6.68 (t, $J = 8$ Hz, 1H), 6.91 (d, $J = 8$ Hz, 1H), 7.00 (d, $J = 8$ Hz, 1H), 7.10 (d, $J = 8$ Hz, 1H), 7.23−7.32 (m, 5H), 7.38−7.42 (m, 1H); ^{31}P NMR (121 MHz, $CDCl_3$) δ 154.11; ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.8, 31.2, 37.6, 38.2, 38.8, 59.2, 114.5, 117.9, 120.8, 121.0, 121.7, 122.2, 127.4, 128.6, 128.7, 129.1, 130.9, 131.2, 135.0, 140.8, 142.1, 142.6, 145.1, 145.7; IR (KBr) 2950, 2848, 1609, 1584, 1464, 1435, 1323, 1233, 1221, 1162, 1131, 1102, 1063, 1014, 992, 953, 922 cm^{-1}; HRMS (EI) for $C_{23}H_{19}O_2P$ calcd 358.1122, found 358.1114.

(*S*)-*O*,*O*′-[7,7′-(1,1′-Spirobiindan)]-4-methylphenylphosphonite (2b): oil; 81% yield; $[\alpha]^{20}_D = -120$ (*c* 0.5, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$) δ 1.98−2.16 (m, 2H), 2.22−3.34 (m, 5H), 2.84−2.92 (m, 2H), 3.01−3.18 (m, 2H), 5.80 (d, $J = 8$ Hz, 1H), 6.68−6.74 (m, 2H), 6.88−7.26 (m, 7H); ^{31}P NMR (121 MHz, $CDCl_3$) δ 156.2; ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.8, 31.2, 38.2, 38.8, 59.3, 120.9, 121.8, 122.1, 127.4, 127.9, 128.0, 129.2, 130.8, 131.1, 131.7, 137.8, 138.2, 140.8, 142.6, 145.1, 145.7, 145.9, 149.; IR (KBr) 2950, 2849, 1584, 1464, 1233, 1221, 1162, 1102, 1014, 992, 922 cm^{-1}; HRMS (FAB) for $C_{24}H_{21}O_2P + H^+$ calcd 373.1352, found 373.1352.

(*S*)-*O*,*O*′-[7,7′-(1,1′-Spirobiindan)]-4-methoxyphenylphosphonite (2c): oil; 77% yield; $[\alpha]^{20}_D = -160$ (*c* 0.5, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$) δ 1.98−2.12 (m, 2H), 2.20−3.32 (m, 2H), 2.83−2.91 (m, 2H), 3.01−3.16 (m, 2H), 2.80 (s, 3H), 5.79 (d, $J =$ 8 Hz, 1H), 6.70−6.79 (m, 3H), 6.91−7.00 (m, 2H), 7.08−7.27 (m, 4H); ^{31}P NMR (121 MHz, $CDCl_3$) δ 155.48; ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.8, 31.3, 38.2, 38.9, 55.4, 59.3, 113.4, 120.8, 121.3, 121.7, 122.3, 127.5, 129.2, 129.4, 129.8, 132.7, 133.1, 140.9, 142.6, 145.1, 145.7, 145.9, 150.1, 162.5; IR (KBr) 2949, 2844, 1594, 1500, 1464, 1293, 1253, 1222, 1179, 1162, 1132, 1105, 1014, 991, 921 cm^{-1}; HRMS (FAB) for $C_{24}H_{21}O_3P + H^+$ calcd 389.1301, found 389.1301.

(*S*)-*O*,*O*′-[7,7′-(1,1′-spirobiindan)]-4-chlorophenylphosphonite (2d): oil; 76% yield; $[\alpha]^{20}_D = -120$ (*c* 0.5, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$) δ 1.98−2.14 (m, 2H), 2.21−3.33 (m, 2H), 2.84−2.92 (m, 2H), 3.02−3.18 (m, 2H), 5.78 (d, $J = 8$ Hz, 1H), 6.74 (t, $J = 8$ Hz, 1H), 6.93 (d, $J = 8$ Hz, 1H), 6.99 (d, $J = 8$ Hz, 1H), 7.11 (d, $J = 8$ Hz, 1H), 7.18−7.28 (m, 5H); ^{31}P NMR (121 MHz, $CDCl_3$) δ 151.2; ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.8, 31.2, 38.2, 38.9, 59.3, 114.5, 117.9, 120.9, 121.1, 122.0, 127.6, 128.3, 129.1, 132.2, 132.6, 136.3, 136.7, 138.0, 140.7, 142.5, 145.3, 145.8, 149.6; IR (KBr) 2948, 2846, 1918, 1609, 1581, 1464, 1386, 1319, 1300, 1233, 1221, 1161, 1132, 1086, 1012, 991, 952, 921 cm^{-1}; HRMS (EI) for $C_{23}H_{18}ClO_2P$, calcd 392.0733, found 392.0737.

(*S*)-*O*,*O*′-[7,7′-(1,1′-Spirobiindan)]-4-trifluoromethylphenylphosphonite (2e): oil; 56% yield; $[\alpha]^{20}_D = -108$ (*c* 0.5, CH_2Cl_2); ^1H NMR (300 MHz, $CDCl_3$) δ 1.98−2.12 (m, 2H), 2.21−3.34 (m, 2H), 2.84−2.93 (m, 2H), 3.04−3.18 (m, 2H), 5.74 (d, J = 8 Hz, 1H), 6.69 (t, $J = 8$ Hz, 1H), 6.92 (d, $J = 8$ Hz, 1H), 7.00 (d, $J = 8$ Hz, 1H), 7.13 (d, $J = 8$ Hz, 1H), 7.25−7.29 (m, 1H),

---

(14) ^{31}P NMR: $[Rh(\mathbf{2a})(COD)]BF_4$ δ 140.7 (d, $J_{Rh-P} = 208.8$ Hz); $[Rh(\mathbf{2c})(COD)BF_4]$ δ 141.0 (d, $J_{Rh-P} = 197.1$ Hz); $Rh(\mathbf{2e})(COD)BF_4]$ δ 137.7 (d, $J_{Rh-P} = 210.9$ Hz).

(15) (a) Birman, V. B.; Rheingold, A. L.; Lam, K.-C. *Tetrahedron: Asymmetry* **1999**, *10*, 125. (b) Zhang, J.-H.; Liao, J.; Cui, X.; Yu, K.-B.; Deng, J.-G.; Zhu, S.-F.; Wang, L.-X.; Zhou, Q.-L.; Chung, L.-W.; Ye, T. *Tetrahedron: Asymmtry* **2002**, *13*, 1363.

(16) Herbst, R. M.; Shemin, D. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, p 1.

(17) (a) Lubell, W. D.; Kitamura, M.; Noyori, R. *Tetrahedron: Asymmetry* **1991**, *2*, 543. (b) Krapacho, A. P.; Diamanti, J.; Zayen, C.; Binghan, R. *Org. Synth.* **1973**, *5*, 198.

7.40−7.45 (m, 2H), 7.53 (d, $J = 8$ Hz, 2H); ^{31}P NMR (121 MHz, CDCl$_3$) δ 149.2; ^{13}C NMR (75 MHz, CDCl$_3$) δ 30.6, 31.0, 38.0, 38.7, 59.1, 114.3, 117.7, 120.5, 121.0, 121.5, 121.9, 124.5, 127.4, 129.1, 130.9, 140.4, 141.9, 142.3, 131.3, 145.1, 145.4, 145.6, 149.1; IR (KBr) 2957, 2921, 2848, 1925, 1610, 1584, 1465, 1397, 1325, 1235, 1220, 1163, 1130, 1119, 1060, 1014, 991, 953, 921 cm^{-1}; HRMS (EI) for $C_{24}H_{18}F_3O_2P$ calcd 426.0996, found 426.0995.

General Procedure for Catalytic Asymmetric Hydrogenation of α-Dehydroamino Esters. A reaction tube equipped with a stirring bar, in which 5 μmol of Rh(COD)$_2$BF$_4$, 11 μmol of ligand, and 0.5 mmol of α-dehydroamino ester were added under an inert atmosphere, was put into an autoclave. After 5 mL of toluene was added, the inert atmosphere was replaced by 10 hydrogen/release cycles and the reaction mixture was left stirring under 10 bar H$_2$ pressure at room temperature for a proper time. The resulting mixture was filtered through a short silica column and submitted to analysis for conversion and ee values.

(*S*)-Methyl 2-acetamido-3-phenylpropionate: 99% ee, chiral GC Varian Chirasil-L-Val column, 25 m × 0.25 mm × 0.25 μm; N$_2$, 1.8 mL/min, 90 °C then 4 °C/min to 160 °C, $t_R = 17.54$ min, $t_S = 18.40$ min.

(*S*)-Methyl 2-acetamido-3-(4-methylphenyl)propionate: 99% ee, chiral HPLC Chiralcel OJ column, 25 cm, ^{i}PrOH/Hex = 10:90, 1.0 mL/min, $t_R = 9.33$ min, $t_S = 15.34$ min.

(*S*)-Methyl 2-acetamido-3-(4-methoxyphenyl)propionate: 98% ee, HPLC Chiralcel OJ column, 25 cm, ^{i}PrOH/Hex = 10:90, 1.0 mL/min, $t_R = 6.42$ min, $t_S = 11.43$ min.

(*S*)-Methyl 2-acetamido-3-(2-chlorophenyl)propionate: 99% ee, chiral HPLC Chiralcel OJ column, 25 cm, ^{i}PrOH/Hex = 10:90, 1.0 mL/min, $t_R = 11.17$ min, $t_S = 13.89$ min.

(*S*)-Methyl 2-acetamido-3-(3-chlorophenyl)propionate: 99% ee, chiral HPLC: Chiralcel OJ column, 25 cm, ^{i}PrOH/Hex = 10:90, 1.0 mL/min, $t_R = 19.83$ min, $t_S = 28.34$ min.

(*S*)-Methyl 2-acetamido-3-(4-chlorophenyl)propionate: 98% ee, chiral HPLC Chiralcel OJ column, 25 cm, ^{i}PrOH/Hex = 10:90, 1.0 mL/min, $t_R = 12.86$ min, $t_S = 17.21$ min.

(*S*)-Methyl 2-acetamido-3-(2-nitrophenyl)propionate: 97% ee, HPLC Chiralcel OD column, 25 cm, ^{i}PrOH/Hex = 15:85, 1.0 mL/min, $t_R = 19.92$ min, $t_S = 29.33$ min.

(*S*)-Methyl 2-acetamido-3-(3-nitrophenyl)propionate: 99% ee, HPLC Chiralcel OD column, 25 cm, ^{i}PrOH/Hex = 15:85, 1.0 mL/min, $t_R = 13.76$ min, $t_S = 17.20$ min.

(*S*)-Methyl 2-acetamido-3-(4-nitrophenyl)propionate: 98% ee, HPLC Chiralcel OD column, 25 cm, ^{i}PrOH/Hex = 15:85, 1.0 mL/min, $t_R = 17.13$ min, $t_S = 19.74$ min.

General Procedure for Asymmetric Hydrogenation of β-Dehydroamino Esters. A reaction tube equipped with a stirring bar, in which 5 μmol of Rh(COD)$_2$BF$_4$, 11 μmol of ligand. and 0.5 mmol of β-dehydroamino ester were added under an inert atmosphere, was put into an autoclave. After 5 mL of toluene added, the inert atmosphere was replaced by 10 hydrogen/release cycles and the reaction mixture was allowed to stir under 100 bar of H$_2$ pressure at room temperature for a proper time. The resulting mixture was filtered through a short silica column and submitted to analysis for conversion and ee values.

(*R*)-Methyl 3-acetylamido-3-phenylpropionate: 93% ee, chiral GC Varian Chirasil-L-Val column, 25 m × 0.25 mm × 0.25 μm; N$_2$ 1.8 mL/min, 120 °C then 1 °C/min to 150 °C, $t_R = 27.57$ min, $t_S = 28.24$ min.

(*R*)-Methyl 3-acetamido-3-(4-methylphenyl)propionate: 94% ee, chiral GC Varian Chirasil-L-Val column, 25 m × 0.25 mm × 0.25 μm; N$_2$ 2.0 mL/min, 120 °C then 1 °C/min to 160 °C, $t_R = 33.07$ min, $t_S = 33.97$ min.

(*R*)-Methyl 3-acetamido-3-(2-methoxylphenyl)propionate: 95% ee, chiral HPLC Chiralcel OD-H column, 25 cm, ^{i}PrOH/Hex = 10:90, 1.0 mL/min, $t_R = 21.91$ min, $t_S = 33.42$ min.

(*R*)-Methyl 3-acetamido-3-(4-methoxylphenyl)propionate: 98% ee, chiral GC Varian Chirasil-L-Val column, 25 m × 0.25 mm × 0.25 μm; N$_2$ 1.8 mL/min, 100 °C then 1 °C/min to 170 °C, $t_R = 67.03$ min, $t_S = 67.82$ min.

(*R*)-Methyl 3-acetamido-3-(4-chlorophenyl)propionate: 90% ee, chiral GC Varian Chirasil-L-Val column, 25 m × 0.25 mm × 0.25 μm; N$_2$ 1.8 mL/min, 120 °C then 1 °C/min to 170 °C, $t_R = 44.35$ min, $t_S = 45.28$ min.

(*R*)-Methyl 3-acetamido-3-(3-bromophenyl)propionate: 85% ee, chiral GC Varian Chirasil-L-Val column, 25 m × 0.25 mm × 0.25 μm; N$_2$ 2.0 mL/min, 120 °C then 1 °C/min to 160 °C, $t_R = 26.28$ min, $t_S = 26.93$ min.

(*R*)-Methyl 3-acetamido-3-(4-bromophenyl)propionate: 91% ee, chiral GC Varian Chirasil-L-Val column, 25 m × 0.25 mm × 0.25 μm; N$_2$ 2.0 mL/min, 120 °C then 1 °C/min to 160 °C, $t_R = 32.08$ min, $t_S = 32.67$ min.

Acknowledgment. We thank the National Natural Science Foundation of China, the Major Basic Research Development Program (Grant No. G2000077506), the Ministry of Education of China, and the Committee of Science and Technology of Tianjin for financial support.

JO049146X