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A Novel Class of P−O Monophosphite Ligands Derived from D-Mannitol: Broad Applications in Highly Enantioselective Rh-Catalyzed Hydrogenations

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Received November 5, 2003

We report on a new class of P−O monophosphite ligands (designated **3a**−**k**) with a double six-membered-ring backbone onto which are attached additional groups and on applications of their Rh complexes in the hydrogenation of enamides, α-dehydroamino acid esters, dimethyl itaconate, and *β*-(acylamino)acrylates. Our results demonstrate that the Rh complexes with ligands **3a**−**k** exhibit high enantioselectivity and reactivity in asymmetric hydrogenation reactions. An ee value of up to 98.0% was obtained for the hydrogenation of α-dehydroamino acid esters, and the ee values were all over 99% for the other three types of substrate, with a turnover number of up to 5000.

Introduction

Transition-metal-catalyzed asymmetric hydrogenation is one of the most powerful methods for the synthesis of optically active compounds, and the design of new phosphorus chiral ligands plays a central role in this area.[1] Although excellent enantioselectivities have been obtained by using chiral bisphosphane ligands, only a few ligands have found broad applications in various types of asymmetric hydrogenation reaction.[2]

Recently, some new classes of easily prepared monophosphorus ligands developed by Pringle,[3a] Reetz,[3b,c] and Feringa[3d] have proven to be highly effective for Rh-catalyzed asymmetric hydrogenation.[4] This pioneering work has opened a new frontier in the design and synthesis, through a simple route, of efficient monophosphorus ligands with high commercial value.[5] However, the enantioselectivities obtained with the monophosphite ligands developed thus far are not always sufficiently high, which is probably attributable to rotation of the Rh−P bond.

More recently, Reetz[4a] and ourselves[6] have independently reported carbohydrate-derived[7] monophosphite ligands **1** and **2**, which contain additional groups in the proper spatial configuration to effectively restrain the rotation of the Rh−P bond by secondary interactions.[8] Those ligands exhibited excellent enantioselectivities in Rh-catalyzed asymmetric hydrogenation of enamides and dimethyl itaconate. The excellent enantioselectivities and the pronounced effect of carbohydrate backbones in those ligands indicated that the additional groups orientated in a spatial configuration in monophosphites that improved the enantioselectivity. To establish the general utility of the design concept and to enhance the versatility

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10.1021/jo035627p CCC: $27.50 © 2004 American Chemical Society
Published on Web 02/27/2004

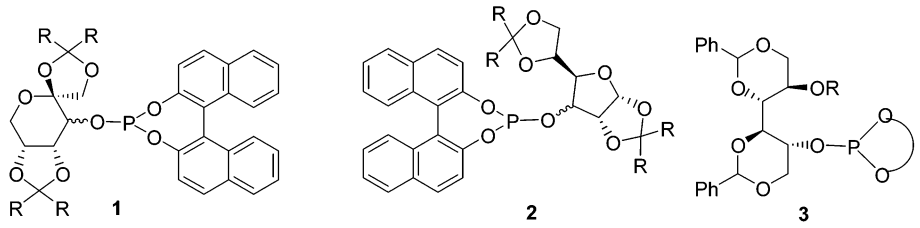
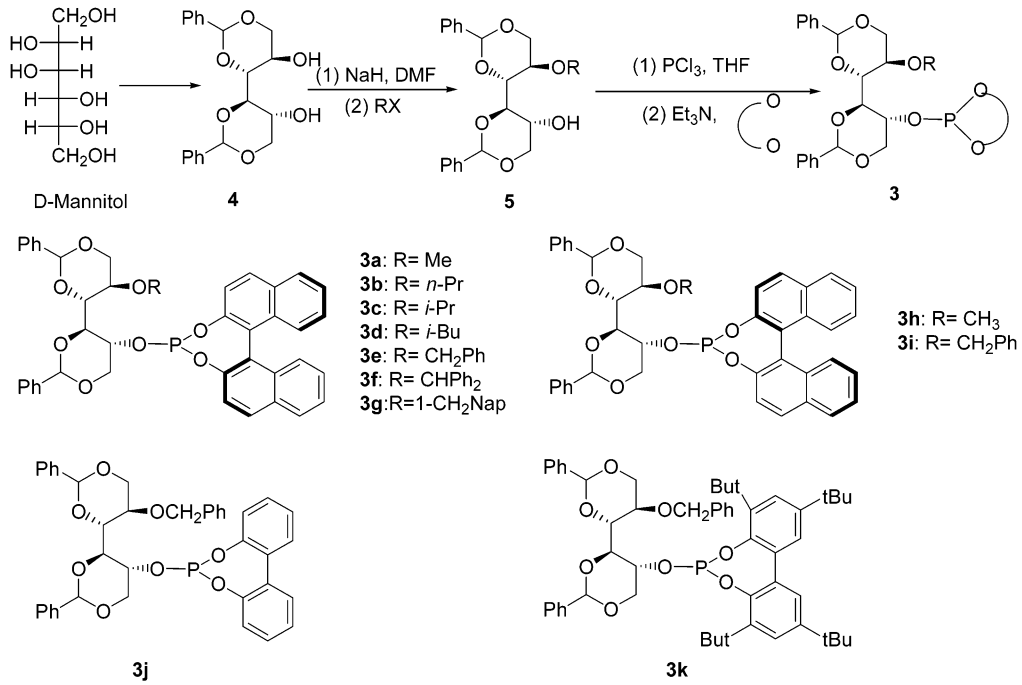


FIGURE 1. Monophosphites **1**−**3**.

SCHEME 1. Synthesis of Monophosphites 3



of this type of ligand and the selectivity in asymmetric reactions, the present paper reports on the development of a new class of chiral monophosphite ligands (designated **3**; abbreviated **ManniPhos**, Figure 1) based on D-mannitol, containing an extra chiral scaffold with an fair degree of rigidity and flexibility in attaching additional groups in a proper spatial configuration such that the ligands may not only offer the effect of additional groups but also act like hemilabile ligands[9] to enhance the enantioselectivity. Their applications to Rh-catalyzed asymmetric hydrogenations of functionalized olefins are also described. They were found to exhibit excellent catalytic properties and enantioselectivities in Rh-catalyzed enantioselective hydrogenations of four types of functionalized olefins: enamides, α-dehydroamino acid esters, dimethyl itaconate, and *β*-(acylamino)acrylates.

Results and Discussion

1. Synthesis of New Chiral Monophosphite Ligands. The chiral ligands **3a**−**k** were conveniently synthesized from commercially available D-mannitol[10] in three steps, as illustrated in Scheme 1. Commercially available D-mannitol was converted into 1,3:4,6-di-*O*-benzylidene-D-mannitol **4**[11] followed by selective monoalkylation of one of the remaining alcoholic groups affording compound **5**. Reaction of compound **5** with PCl_3 in the absence of Et_3N afforded $RO-PCl_2$, which was then directly reacted with BINOL or biphenol derivatives in the presence of Et_3N to afford the desired product. Ligands **3a**−**k** were easily purified through a short silica gel plug and were stable in the solid state.

2. Asymmetric Hydrogenation of Enamides. The catalytic performance of ligands **3a**−**k** was thoroughly explored in Rh-catalyzed asymmetric hydrogenation reactions. In a first set of experiments, we used these ligands in the Rh-catalyzed asymmetric hydrogenation

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(10) For some selected chiral phosphine ligands made from D-mannitol, see: (a) Holz, J.; Quirmbach, M.; Schmidt, U.; Heller, D.; Sturmer, R.; Börner, A. *J. Org. Chem.* **1998**, *63*, 8031. (b) Carmichael, D.; Doueet, H.; Brown, J. M. *Chem. Commun.* **1999**, 261. (c) Li, W.; Zhang, Z.; Xiao, D.; Zhang, X. *Tetrahedron Lett.* **1999**, *40*, 6701. (d) Reetz, M. T.; Neugebauer, T. *Angew. Chem., Int. Ed.* **1999**, *38*, 179. (e) Yan, Y.-Y.; RajanBabu, T. V. *Org. Lett.* **2000**, *2*, 199. (f) Yan, Y.-Y.; RajanBabu, T. V. *J. Org. Chem.* **2000**, *65*, 900. (g) Li, W.; Zhang, Z.; Xiao, D.; Zhang, X. *J. Org. Chem.* **2000**, *65*, 3489. (h) Li, W.; Zhang, X. *J. Org. Chem.* **2000**, *65*, 5871.

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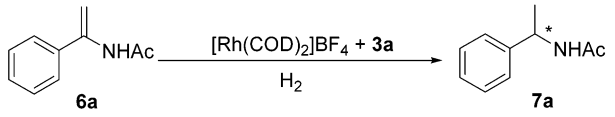
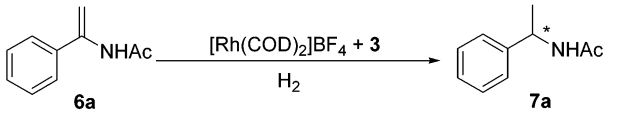
TABLE 1. The Effect of Solvent and H_2 Pressure on the Enantioselective Hydrogenation of *N*-Acetylphenylethenamine 6a[a]



entry	solvent	$P(H_2)$, atm	conv, %	ee, % (config)[b]
1	CH_2Cl_2	10	100	99.8 (*S*)
2	CH_2Cl_2	1.2	100	99.7 (*S*)
3	EtOAc	10	100	99.5 (*S*)
4	toluene	10	100	99.6 (*S*)
5	CH_3OH	10	78	95.5 (*S*)
6	THF	10	98	99.5 (*S*)

[a] T = 20 °C; reaction time: 12 h; substrate:$[Rh(COD)_2]BF_4$:**3a** = 1:0.01:0.022. [b] Determined by chiral capillary GC on a Varian Chirasil-L-Val column and a Supelco Chiral select 1000 column. The absolute configuration was assigned by comparison of the optical rotation with reported data.

TABLE 2. Asymmetric Hydrogenation of *N*-Acetylphenylethenamine Catalyzed by Rh-3[a]



entry	ligand	ee, % (config)[b]	entry	ligand	ee, % (config)[b]
1	**3a**	99.8 (S)	7	**3g**	99.5 (S)
2	**3b**	99.8 (S)	8	**3h**	91.3 (R)
3	**3c**	99.4 (S)	9	**3i**	92.1 (R)
4	**3d**	97.7 (S)	10	**3j**	49.7 (R)
5	**3e**	98.1 (S)	11	**3k**	9.7 (R)
6	**3f**	99.6 (S)			

[a] Solvent = CH_2Cl_2; $p(H_2)$ = 10 atm; T = 20 °C; reaction time = 12 h; substrate:$[Rh(COD)_2]BF_4$:**3** = 1:0.01:0.022; 100% conversion was obtained in all cases. [b] Determined by chiral capillary GC on a Varian Chirasil-L-Val column and a Supelco Chiral select 1000 column. The absolute configuration was assigned by comparison of the optical rotation with reported data.

of enamides (**6**).[12] The reactions proceeded smoothly at room temperature. In general, the catalysts were prepared in situ by mixing $[Rh(COD)_2]BF_4$ and the corresponding monophosphite ligands in CH_2Cl_2.

To study the effect of H_2 pressure and solvents on the reaction, the reaction with $[Rh(COD)_2]BF_4$/**3a** as a catalyst precursor and enamide **6a** as a model substrate was studied in more detail. The results, summarized in Table 1, show that the nature of the solvent had little effect on the enantioselectivity, but had a significant effect on the conversion. Reaction in a more polar solvent such as CH_3OH or THF resulted in a lower conversion rate (entries 5 and 6, Table 1). The catalyst performance was best when CH_2Cl_2 was used (entries 1 and 2, Table 1). Changes in H_2 pressure had little effect on the enantioselectivity and conversion (entries 1 and 2, Table 1); due to the high activity of the catalyst, the reaction can proceed smoothly under a lower H_2 pressure without deterioration (entry 2, Table 1).

To identify the most efficient ligands, the remaining ligands were tested under "standard" conditions (a ligand-to-Rh ratio of 2.2, an H_2 pressure of 10 atm, and CH_2Cl_2 as a solvent); the results are given in Table 2.

The screening of our ligands shows that the monophosphites we prepared are efficient ligands for an asymmetric hydrogenation reaction. However, the enantioselectivities proved to be influenced dramatically by the structure of the ligands. The results in Table 2 show that the enantiomeric excess depends strongly on the moiety of the P/O heterocycle in the chiral ligands. The ee values of over 90% were achieved with ligands **3a**−**i**, which contain (*S*)- or (*R*)-BINOL in the P/O heterocycle. Moreover, the ee values increased significantly when *R*-BINOL was introduced in these ligands (entries 1−7, Table 2). Values of ee up to 99.8% have been achieved with Rh-**3a** and Rh-**3b** as catalysts, which demonstrates that *R*-BINOL is matched cooperatively to the corresponding D-mannitol-derived backbone. In marked contrast, ligands **3j** and **3k** derived from conformationally flexible biphenols gave ee values of only 9.7−49.7%. In contrast, the enantioselectivities produced by these ligands are somewhat affected by the −OR groups contained in the ligands, which can be attributed to their effects on the degree of rigidity and flexibility of the D-mannitol-derived double-ring backbone. As can be seen from Table 2, less bulky substituents generally induce a higher ee value, and the simplest and more easily prepared ligand **3a** is the most efficient.

To broaden the scope of this reaction, we subsequently applied the most efficient monophosphite **3a** in the Rh-catalyzed hydrogenation of a variety of enamides under the above optimal reaction conditions. The results in Table 3 indicate that most of the reactions gave extremely high ee values with full conversions (96−99.9%, entries 1−5 and 7−10, Table 3), except in the case of hydrogenation of highly hindered substrates (entrie 6, Table 3).[13] The results also revealed that there is no major electronic effect on the substitution pattern of the α-phenylenamides. Hydrogenation of the 2-naphthyl derivative also gave an excellent ee value (entry 8, Table 3). A high ee value (99.2%) was also obtained for β-substituted enamide mixtures (*Z*/*E*) (entry 9, Table 3). Asymmetric hydrogenation of the cyclic enamide 1-(*N*-acetylamido)-indene also proceeded smoothly to give (*S*)-(+)-*N*-(indan-1-yl)acetamide in a quantitative yield and with an ee value of 96.0% (entry 10, Table 3), which provides a first example of using chiral monophosphorus ligands in the asymmetric hydrogenation of cyclic enamide with a high ee value. A high turnover number (ca. 5000) with a slight drop in ee was also observed in the hydrogenation of *N*-acetylphenylethenamine (entry 12, Table 3). The enantioselectivities of the hydrogenation of α-arylenamides with ligand **3a** are higher than or comparable to other reported families of efficient mono- and bidentate chiral phosphorus ligands.[12]

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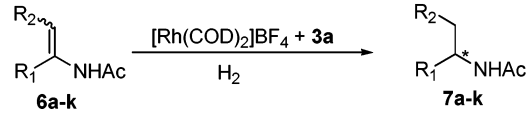
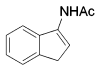
(13) The ee values given hy Reetz's monophosphites were typically 76−97%, see ref 4g.

TABLE 3. Asymmetric Hydrogenation of Enamides Catalyzed by Rh-3a[a]



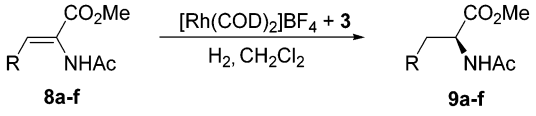
Entry	Substrate (R_1, R_2)	Ee% (config)[b]
1	**6a** (Ph, H)	99.8 (*S*)
2	**6b** (*p*-FC_6H_4, H)	99.9 (*S*)
3	**6c** (*p*-BrC_6H_4, H)	99.9 (*S*)
4	**6d** (*p*-ClC_6H_4, H)	99.7 (*S*)
5	**6e** (*p*-$CH_3OC_6H_4$, H)	99.5 (*S*)
6	**6f** (*o*-ClC_6H_4, H)	79.1 (*S*)
7	**6g**(*p*-$CF_3C_6H_4$, H)	99.9 (*S*)
8	**6h** (2-naphthyl, H)	99.5 (*S*)
9	**6i** (Ph, Me)	99.2 (*S*)
10	 **6j**	96.0 (*S*)
11[c]	**6a** (Ph, H)	99.5 (*S*)
12[d]	**6a** (Ph, H)	95.9 (*S*)

[a] Solvent = CH_2Cl_2; $p(H_2)$ = 10 atm; T = 20 °C; reaction time = 12 h; substrate:[$Rh(COD)_2$]BF_4:**3a** = 1:0.01:0.022; 100% conversion was obtained in all cases otherwise mentioned. [b] Determined by chiral capillary GC on a Varian Chirasil-L-Val column and a Supelco Chiral select 1000 column. The absolute configuration was assigned by comparison of the optical rotation with reported data. [c] Substrate-to-catalyst ratio (S/C) = 1000. [d] S/C = 5000, 88% conversion.

3. Asymmetric Hydrogenation of α-Dehydroamino Acid Derivatives. Encouraged by these findings, we investigated expanding the substrate scope of asymmetric hydrogenations by using ligands **3a**−**g**. The results, summarized in Table 4, follow the same trend as observed for substrate **6**, but with somewhat lower ee values. The catalyst precursor with ligand **3a** produced the highest ee value for **9a** (97.7%, entry 1, Table 4). With the best ligand **3a**, a variety of α-dehydroamino acid derivatives (**8a**−**f**) with different electronic properties were employed as substrates for the Rh-catalyzed hydrogenation reaction under atmospheric pressure. An ee value of over 96% was obtained for all substrates, indicating their minimal electronic effect. The highest ee value (up to 98.0%, entry 9, Table 4) was obtained for **9c**.

4. Asymmetric Hydrogenation of Dimethyl Itaconate. The Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate (**10**) was also investigated. Similarly, ligands **3a**−**g** turned out to be very active in this reaction. The high activity of these ligands means that the reaction can also be carried out at an H_2 pressure of 1.2 atm (entry 7, Table 5). An ee value of more than 98.0% can be produced by employing any of these ligands; the catalyst precursor containing ligand **3g** induced the highest ee value (99%, entry 9, Table 5). To evaluate further the catalytic efficiency of the Rh-**3** system in this asymmetric hydrogenation, we increased the ratio of substrate to catalyst. Hydrogenation of dimethyl itaconate **10** in the presence of Rh-**3g** (with a turnover number of 5000) within 3 h afforded the product **11** in 100% yield and with an ee value of 99.1% (entry 10, Table 5).

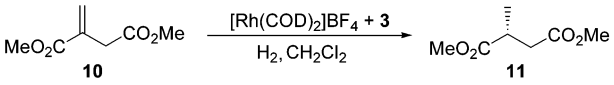
TABLE 4. Rh-Catalyzed Asymmetric Hydrogenation of α-Dehydroamino Acid Esters 8[a]



entry	ligand	substrate	R	ee, % (config)[b]
1	**3a**	**8a**	H	97.7 (*S*)
2	**3b**	**8a**	H	96.3 (*S*)
3	**3c**	**8a**	H	95.9 (*S*)
4	**3d**	**8a**	H	95.5 (*S*)
5	**3e**	**8a**	H	94.4 (*S*)
6	**3f**	**8a**	H	96.9 (*S*)
7	**3g**	**8a**	H	93.9 (*S*)
8	**3a**	**8b**	Ph	96.8 (*S*)
9	**3a**	**8c**	*p*-MeOPh	98.0 (*S*)
10	**3a**	**8d**	*o*-MeOPh	97.4 (*S*)
11	**3a**	**8e**	*p*-ClPh	97.1 (*S*)
12	**3a**	**8f**	*o*-ClPh	96.6 (*S*)

[a] Solvent = CH_2Cl_2; $p(H_2)$ = 1.2 atm; T = 20 °C; reaction time = 12 h; substrate:[$Rh(COD)_2$]BF_4:**3** = 1:0.01: 0.022; 100% conversion was obtained in all cases. [b] Determined by chiral capillary GC on a Varian Chirasil-L-Val column and a Supelco Chiral select 1000 column. The absolute configuration was assigned by comparison of the optical rotation with reported data.

TABLE 5. Rh-Catalyzed Asymmetric Hydrogenation of Dimethyl Itaconate 10[a]

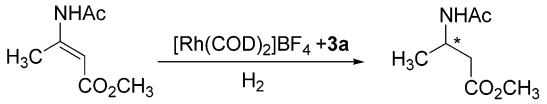


entry	ligand	$P(H_2)$, atm	ee, % (config)[b]
1	**3a**	10	98.8 (*R*)
2	**3b**	10	98.3 (*R*)
3	**3c**	10	98.5 (*R*)
4	**3d**	10	98.5 (*R*)
5	**3e**	10	98.5 (*R*)
6	**3e**	5	98.5 (*R*)
7	**3e**	1.2	98.6 (*R*)
8	**3f**	10	98.8 (*R*)
9	**3g**	10	99.0 (*R*)
10[c]	**3g**	10	99.1 (*R*)

[a] Solvent = CH_2Cl_2; T = 20 °C; reaction time = 12 h; substrate: [$Rh(COD)_2$]BF_4:**3** = 1:0.01:0.022; 100% conversion was obtained in all cases. [b] Determined by chiral capillary GC on a γ-DEX 225 column. The absolute configuration was assigned by comparison of the optical rotation with reported data. [c] S/C= 5000.

5. Asymmetric Hydrogenation of β-Alkyl-Substituted (*E*)-β-(Acylamino)acrylates. Unlike the above-mentioned three types of functionalized olefins, only a few Rh-catalyst and Ru-catalyst systems can fulfill the highly enantioselective hydrogenation of β-(acylamino)-acrylates.[14] The exciting results obtained in the Rh-**3** catalyzed hydrogenation of the above three types of substrates led us to attempt to use these ligands in this challenging asymmetric reaction. The catalysts were also prepared in situ by reacting the appropriate ligand with [$Rh(COD)_2$]BF_4 in the corresponding solvent at room temperature. The effects of solvent and H_2 pressure were investigated for the catalytic precursor containing ligand **3a**; the results are summarized in Table 6.

TABLE 6. The Effect of Solvent and H_2 Pressure on the Enantioselective Hydrogenation of (*E*)-Methyl 3-Acetamido-2-butenoate Catalyzed by Rh-3a[a]

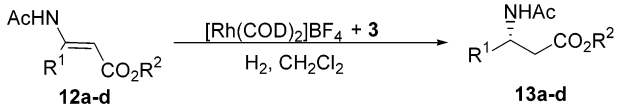


12a 13a

entry	solvent	$P(H_2)$, atm	conv, %	ee, % (config)[b]
1	CH_2Cl_2	10	72	99.6 (*S*)
2	EtOAc	10	2	89.0 (*S*)
3	toluene	10	0	N/A
4	THF	10	9	91.3 (*S*)
5	CH_3OH	10	93	1.1 (*S*)
6	CH_2Cl_2	35	82	99.4 (*S*)
7	CH_2Cl_2	40	98	96.7 (*S*)
8	CH_2Cl_2	50	94	92.5 (*S*)

[a] T = 20 °C; reaction time = 12 h; substrate:[$Rh(COD)_2$]BF_4:**3a** = 0.5:0.01:0.022. [b] Determined by chiral capillary GC on a Supelco Chiral select 1000 column. The absolute configuration was assigned by comparison of the optical rotation with reported data.

TABLE 7. Rh-Catalyzed Asymmetric Hydrogenation of (*E*)-β-(Acylamino)acrylates 12a−d[a]



12a-d 13a-d

entry	ligand	substrate	R^1	R^2	conv, %	ee, % (config)[b]
1	**3a**	**12a**	Me	Me	98	96.7 (*S*)
2	**3b**	**12a**	Me	Me	97	97.3 (*S*)
3	**3c**	**12a**	Me	Me	94	96.1 (*S*)
4	**3d**	**12a**	Me	Me	94	98.9 (*S*)
5	**3e**	**12a**	Me	Me	94	96.9 (*S*)
6	**3f**	**12a**	Me	Me	92	99.2 (*S*)
7	**3g**	**12a**	Me	Me	97	99.1 (*S*)
8	**3g**	**12b**	Me	Et	93	98.7 (*S*)
9	**3g**	**12c**	Et	Me	99	99.8 (*S*)
10	**3g**	**12d**	*i*-Pr	Me	100	99.9 (*S*)

[a] Solvent = CH_2Cl_2; $p(H_2)$ = 40 atm; T = 20 °C; reaction time = 12 h; substrate:[$Rh(COD)_2$]BF_4:**3** = 0.5:0.01:0.022. [b] Determined by chiral capillary GC on a Supelco Chiral select 1000 column and a γ-DEX 225 column. The absolute configuration was assigned by comparison of the optical rotation with reported data.

The results show that the efficiency of the process depended strongly on the nature of the solvent and the H_2 pressure: the catalyst performance was best when CH_2Cl_2 was used under higher H_2 pressure (entry 7, Table 6). The ligands were screened under these optimal conditions with **12a** as the model substrate. Table 7 shows that these are excellent ligands for hydrogenation, giving nearly full conversion and ee values of up to 99%. Ligand **3g** is superior to the other ligands in terms of the activity and enantioselectivity (entries 1−7, Table 7). The asymmetric hydrogenation of a variety of β-alkyl-substituted (*E*)-β-(acylamino)acrylates (**12a−d**) catalyzed by Rh-**3g** was studied, and consistently high enantioselectivities were obtained in all cases (entries 7−10, Table 7). Substrate **12d** with a bulky alkyl substituent gave the best ee value (up to 99.9%, entry 10, Table 7). We know of no reports of monophosphite ligands employed in the asymmetric hydrogenation of β-(acylamino)acrylates that exhibit such high enantioselectivities.[15]

In contrast to other chiral monophosphites, the ligands reported here can be used in a wide range of hydrogenation reactions under ambient temperature and atmospheric pressure. We assume that one of the critical factors underlying the efficient catalytic properties of these ligands is their double six-membered-ring backbone structure derived from D-mannitol and the additional groups attached to it. One of the ether moieties present in the backbone may behave as a hemilabile ligand, and thus reduce the conformational freedom. Although a rational explanation of the observed enantioselectivities is difficult at present, the short and convenient synthesis of the new ligands and the superb enantioselectivities obtained in asymmetric catalysis, combined with our previous observations,[6] provide new insights into the design of efficient monophosphorus ligands.

Conclusion

In summary, we have developed novel and easily prepared chiral ligands that provide the first examples of highly efficient monophosphite ligands for the asymmetric hydrogenation of all four types of functionalized olefins: enamides, α-dehydroamino acid esters, dimethyl itaconate, and β-(acylamino)acrylates. Furthermore, the air-stable ligands can be readily prepared in three steps from commercially available D-mannitol and BINOL, which offers the benefits of simple processes and low cost. Further studies to demonstrate the function of the additional groups attached in these ligands and extension of the scope of these ligands to other transition-metal-catalyzed reactions are in progress.

Experimental Section

General. All reactions and manipulations were performed in a nitrogen-filled glovebox or with standard Schlenk-type techniques. All solvents were dried and degassed by standard methods and stored under nitrogen. Commercially available methyl 2-acetamidoacrylate and dimethyl itaconate were used. All other α-dehydroamino acid esters, enamides, and β-(acylamino)acrylates are known compounds which were synthesized by using procedures described elsewhere.[16] All other chemicals were obtained commercially.

Synthesis of 1,3:4,6-Di-*O*-benzylidene-D-mannitol (4). This compound was prepared by using procedures described elsewhere.[11]

General Procedure for the Synthesis of the Chiral Alcohols 5a−f. Sodium hydride (80% oil suspension, 330 mg, 10 mmol) was washed with hexane, and then 1,3:4,6-di-*O*-benzylidene-D-mannitol **4** (3.58 g, 10 mmol) was added. To the mixture was added DMF (30 mL), the resulting mixture was

(14) For recent example see: (a) Heller, D.; Holz, J.; Drexler, H. J.; Lang, J.; Drauz, K.; Krimmer, H. P.; Börner, A. *J. Org. Chem.* **2001**, *66*, 6816. (b) Lee, S.; Zhang, Y. J. *Org. Lett.* **2002**, *4*, 2429. (c) Holz, J.; Monsees, A.; Jiao, H.; You, J.; Komarov, I. V.; Fischer, C.; Drauz, K.; Börner, A. *J. Org. Chem.* **2003**, *68*, 1701. (d) Tang, W.; Zhang, X. *Org. Lett.* **2002**, *4*, 4159. (e) Zhou, Y.-G.; Tang, W.; Wang, W.-B.; Li, W.; Zhang, X. *J. Am. Chem. Soc.* **2002**, *124*, 4952. (f) You, J.; Drexler, H. J.; Zhang, S.; Fischer, C.; Heller, D. *Angew. Chem., Int. Ed.* **2003**, *42*, 913. (g) Yasutake, M.; Gridnev, I. D.; Higashi, N.; Imamoto, T. *Org. Lett.* **2001**, *3*, 1701. (h) Ohashi, A.; Kikuchi, S.; Yasutake, M.; Imamoto, T. *Eur. J. Org. Chem.* **2002**, *8*, 5196. (i) Tang, W.; Wang, W.; Chi, Y.; Zhang, X. *Angew. Chem., Int. Ed.* **2003**, *42*, 3509.

(15) Reetz's monophosphites only gave 12% ee for β-(acylamino)-acrylates, see: Pena, D.; Minnaard, A. J.; Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. *Org. Lett.* **2003**, *5*, 475.

(16) (a) Herbst, R. M.; Shemin, D. *Organic Syntheses*; Wiley: New York, 1943; Collect. Vol. II, p 1. (b) Burk, M. J.; Casy, G.; Johnson, N. B. *J. Org. Chem.* **1998**, *63*, 6084. (c) Zhang, Z.; Zhu, G.; Jiang, Q.; Xiao, D.; Zhang, X. *J. Org. Chem.* **1999**, *64*, 1774. (d) Zhu, G.; Chen, Z.; Zhang, X. *J. Org. Chem.* **1999**, *64*, 6907.

stirred at room temperature for 0.5 h, and then RX (10 mmol) was added. The reaction mixture was stirred for 1−12 h at room temperature, diluted with water, and then extracted with ethyl acetate. The combined extracts were washed with water and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel with EtOAc/hexane (at ratios of 1/20−1/5) to give the corresponding product at yields of 30−95%.

1,3:4,6-Di-*O*-benzylidene-2-*O*-methyl-D-mannitol (5a). The above procedure was followed with use of **4** and iodomethane. After workup, **5a** was obtained as a white solid. Mp 154−155 °C, $[\alpha]^{22}_D$ −23.11 (*c* 0.77, THF); ^{1}H NMR (DMSO-d_6) δ 3.40 (m, 3H), 3.56−3.60 (m, 3H), 3.78−3.87 (m, 2H), 3.99 (d, J = 7.6 Hz, 1H), 4.16−4.19 (m, 1H), 4.39−4.46 (m, 1H), 5.58 (s, 1H), 5.61 (s, 1H), 7.35−7.44 (m, 10H); ^{13}C NMR (DMSO-d_6) δ 58.1, 58.7, 58.8, 68.5, 68.6, 70.9, 76.6, 78.4, 100.0, 100.2, 126.0, 126.1, 128.0, 128.1, 128.6, 138.0, 138.2; HRMS (APCI) calcd for $C_{21}H_{24}O_6$ (M^+ + 1) 373.1645, found 373.1641.

1,3:4,6-Di-*O*-benzylidene-2-*O*-propyl-D-mannitol (5b). The above procedure was followed with use of **4** and 1-bromopropane. After workup, **5b** was obtained as a white solid. Mp 94−95 °C, $[\alpha]^{22}_D$ −29.97 (*c* 0.69, THF); ^{1}H NMR (DMSO-d_6) δ 0.81−0.90 (m, 3H), 1.47−1.56 (m, 2H), 3.43−3.46 (m, 1H), 3.55−3.66 (m, 4H), 3.82−3.85 (m, 2H), 3.98 (d, J = 9.2 Hz, 1H), 4.16−4.20 (m, 1H), 4.37−4.40 (m, 1H), 5.52 (s, 1H), 5.54 (s, 1H), 7.35−7.42 (m, 10H); ^{13}C NMR (DMSO-d_6) δ 10.5, 22.7, 58.7, 58.8, 66.9, 68.8, 70.9, 71.6, 76.7, 78.4, 100.1, 100.2, 125.9, 126.1, 127.9, 128.1, 128.6, 138.1, 138.2; HRMS (APCI) calcd for $C_{23}H_{28}O_6$ (M^+ + 1) 401.1958, found 401.1971.

1,3:4,6-Di-*O*-benzylidene-2-*O*-isopropyl-D-mannitol (5c). The above procedure was followed with use of **4** and 2-bromopropane. After workup, **5c** was obtained as a white solid. Mp 106−107 °C, $[\alpha]^{22}_D$ −33.33 (*c* 0.62, THF); ^{1}H NMR (DMSO-d_6) δ 1.11 (s, 6H), 3.56−3.58 (m, 2H), 3.71 (m, 2H), 3.83 (m, 2H), 3.95−3.97 (d, J = 8.8 Hz, 1H), 4.16−4.18 (m, 1H), 4.31−4.33 (m, 1H), 5.52 (d, J = 9.6 Hz, 2H), 7.35−7.42 (m, 10H); ^{13}C NMR (DMSO-d_6) δ 22.1, 22.2, 58.7, 64.7, 69.4, 70.8, 76.7, 78.1, 100.2, 125.9, 126.1, 127.9, 128.1, 128.6, 138.1; HRMS (APCI) calcd for $C_{23}H_{28}O_6$ (M^+ + 1) 401.1958, found 401.1965.

1,3:4,6-Di-*O*-benzylidene-2-*O*-isobutyl-D-mannitol (5d). The above procedure was followed with use of **4** and 1-bromo-2-methylpropane. After workup, **5d** was obtained as a white solid. Mp 107−108 °C, $[\alpha]^{22}_D$ −24.49 (*c* 0.59, THF); ^{1}H NMR (DMSO-d_6) δ 0.85−0.88 (m, 6H), 1.17−1.80 (m, 1H), 3.21 (t, J = 8.0 Hz, 1H), 3.40−3.42 (m, 1H), 3.58−3.67 (m, 3H), 3.88−3.90 (m, 2H), 4.02 (d, J = 8.8 Hz, 1H), 4.18−4.21 (m, 1H), 4.40 (d, J = 5.6 Hz, 1H), 5.51 (s, 1H), 5.55 (s, 1H), 7.35−7.43 (m, 10H); ^{13}C NMR (DMSO-d_6) δ 19.1, 19.1, 28.2, 58.6, 67.3, 68.8, 70.9, 76.7, 78.5, 100.2, 125.9, 126.1, 127.9, 128.1, 128.6, 138.1, 138.1; HRMS (APCI) calcd for $C_{24}H_{30}O_6$ (M^+ + 1) 415.2115, found 415.2128.

1,3:4,6-Di-*O*-benzylidene-2-*O*-benzyl-D-mannitol (5e). The above procedure was followed with use of **4** and benzyl bromide. After workup, **5e** was obtained as a white solid. Mp 155−156 °C, $[\alpha]^{22}_D$ −38.17 (*c* 0.81, THF); ^{1}H NMR (DMSO-d_6) δ 3.56−3.68 (m, 2H), 3.79−3.84 (m, 2H), 3.90 (d, J = 9.6 Hz, 1H), 4.08 (d, J = 9.2 Hz, 1H), 4.18 (t, J = 5.2 Hz, 1H), 4.42−4.43 (d, J = 5.6 Hz, 1H), 4.57−4.66 (m, 2H), 5.49 (s, 1H), 5.57 (s, 1H), 7.22−7.44 (m, 15H); ^{13}C NMR (DMSO-d_6) δ 58.7, 66.1, 68.7, 70. 9, 71.3, 76.5, 78.2, 99.9, 100.2, 126.1, 126.1, 127.7, 127.9, 128.3, 128.5, 128.6, 138.0, 138.1, 138.2; HRMS (APCI) calcd for $C_{27}H_{28}O_6$ (M^+ + 1) 449.1958, found 449.1972.

1,3:4,6-Di-*O*-benzylidene-2-*O*-diphenylmethyl-D-mannitol (5f). The above procedure was followed with use of **4** and bromodiphenylmethane. After workup, **5f** was obtained as a white solid. Mp 107−108 °C, $[\alpha]^{22}_D$ −16.44 (*c* 0.69, THF); ^{1}H NMR (DMSO-d_6) δ 3.59−3.62 (m, 1H), 3.73−3.86 (m, 3H), 3.95 (d, J = 9.2 Hz, 1H), 4.16−4.21 (m, 2H), 4.31−4.45 (m, 1H), 5.46 (s, 1H), 5.70 (s, 1H), 5.75 (s, 1H), 7.12−7.43 (m, 20H); ^{13}C NMR (DMSO-d_6) δ 58.8, 58.9, 64.6, 68.8, 70.9, 76.5, 78.2, 80.9, 100.1, 100.3, 126.1, 126.5, 126.9, 127.4, 127.5, 127.8, 127.9, 128.3, 128.5, 128.6, 137.9, 141.8, 142.7; HRMS (APCI) calcd for $C_{33}H_{32}O_6$ (M^+ − 1) 523.2115, found 523.2144.

1,3:4,6-Di-*O*-benzylidene-2-*O*-1-naphthylmethyl-D-mannitol (5g). The above procedure was followed with **4** and 1-chloromethyl-naphthalene. After workup, **5g** was obtained as a white solid. Mp 148−149 °C, $[\alpha]^{22}_D$ −37.46 (*c* 0.58, THF); ^{1}H NMR (DMSO-d_6) δ 3.40 (m, 1H), 3.67−3.76 (m, 3H), 3.85 (m, 1H), 4.07−4.13 (m, 2H), 4.58−4.61 (m, 1H), 4.93−4.98 (m, 2H), 5.14 (d, J = 12.0 Hz, 1H), 5.58 (s, 1H), 7.12−7.13 (m, 2H), 7.30−7.42 (m, 9H), 7.48−7.56 (m, 3H), 7.79 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 8.14 (d, J = 8.0 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 58.7, 65.2, 68.7, 69.2, 70.9, 76.3, 78.1, 99.7, 100.3, 124.2, 125.2, 125.9, 126.1, 127.5, 127.8, 127.9, 128.4, 128.5, 128.6, 128.8, 131.5, 133.3, 133.4, 137.8, 138.0; HRMS (APCI) calcd for $C_{31}H_{30}O_6$ (M^+ + 1) 499.2115, found 499.2123.

General Procedure for the Synthesis of the Monophosphite Ligands (3a−k). PCl_3 (132 μL, 1.5 mmol) as a solution in THF (4 mL) was slowly added to a stirred solution of **5** (1.5 mmol) in THF (5 mL), and the resulting mixture was stirred for 1 h at room temperature. The reaction mixture was then cooled to −10 °C, and Et_3N (1.07 mL, 4.5 mmol) was slowly added. The reaction mixture was allowed to warm to room temperature, maintained under these conditions for 0.25 h, and then cooled to 0 °C, solid BINOL or biphenol was added, and the resulting mixture was allowed to warm to room temperature and stirred overnight prior to dilution with diethyl ether. The solids were removed by filtration through a pad of Celite, the solvent was removed in vacuo, and the residue was purified by flash chromatography (EtOAc/hexane 1/20−1/10), which furnished the title ligand as a white foam at a yield of 75−87%.

1,3:4,6-Di-*O*-benzylidene-2-*O*-methyl-3-*O*-((*R*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-mannitol (3a). The above procedure was followed with use of **5a** and *R*-BINOL. After workup, **3a** was obtained. Mp 152−153 °C, $[\alpha]^{22}_D$ −289.21 (*c* 0.65, THF); ^{1}H NMR (DMSO-d_6) δ 3.39 (s, 3H), 3.47−3.49 (m, 1H), 3.59 (m, 1H), 3.79 (d, J = 9.2 Hz, 1H), 3.91 (m, 1H), 4.10 (d, J = 9.6 Hz, 1H), 4.42−4.43 (m, 1H), 4.58 (m, 1H), 4.61 (m, 1H), 5.48 (s, 1H), 5.76 (s, 1H), 7.22−7.36 (m, 2H), 7.38−7.62 (m, 16H), 8.09−8.18 (m, 4H); ^{13}C NMR (DMSO-d_6) δ 58.1, 62.9, 63.1, 68.2, 68.8, 76.2, 76.5, 99.9, 100.1, 121.6, 121.9, 123.4, 125.3, 125.5, 125.9, 126.7, 126.8, 128.1, 128.2, 128.7, 130.3, 130.9, 131.3, 131.7, 132.0, 137.4, 137.7, 146.7, 147.0; ^{31}P NMR (DMSO-d_6) δ 154.81; HRMS (APCI) calcd for $C_{41}H_{35}O_8P$ (M^+ + 1) 687.2142, found 687.2110.

1,3:4,6-Di-*O*-benzylidene-2-*O*-propyl-3-*O*-((*R*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-mannitol (3b). The above procedure was followed with use of **5b** and *R*-BINOL. After workup, **3b** was obtained. Mp 127−128 °C, $[\alpha]^{22}_D$ −229.40 (*c* 0.57, THF); ^{1}H NMR (DMSO-d_6) δ 0.80−0.83 (m, 3H), 1.43−1.48 (m, 2H), 3.41 (m, 1H), 3.48−3.52 (m, 2H), 3.64−3.66 (m, 1H), 3.81−3.83 (m, 1H), 3.91 (m, 1H), 4.07−4.09 (m, 1H), 4.37−4.38 (m, 1H), 4.57−4.60 (m, 1H), 4.70 (m, 1H), 5.51 (s, 1H), 5.68 (s, 1H), 7.21−7.23 (m, 2H), 7.34−7.61 (m, 16H), 8.06−8.14 (m, 4H); ^{13}C NMR (DMSO-d_6) δ 10.5, 22.7, 62.8, 63.1, 66.5, 68.6, 68.8, 71.6, 76.2, 76.6, 100.1, 100.2, 121.6, 121.9, 123.4, 125.3, 125.4, 125.9, 125.9, 126.7, 126.8, 128.1, 128.2, 128.7, 128.8, 130.3, 130.9, 131.3, 131.7, 132.1, 137.4, 137.7, 146.7, 147.0; ^{31}P NMR (DMSO-d_6) δ 155.01; HRMS (APCI) calcd for $C_{43}H_{39}O_8P$ (M^+ + 1) 715.2455, found 715.2445.

1,3:4,6-Di-*O*-benzylidene-2-*O*-isopropyl-3-*O*-((*R*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-mannitol (3c). The above procedure was followed with use of **5c** and *R*-BINOL. After workup, **3c** was obtained. mp 135−136 °C, $[\alpha]^{22}_D$ −278.62 (*c* 0.62, THF); ^{1}H NMR (DMSO-d_6) δ 1.05−1.06 (s, 6H), 3.45−3.50 (m, 1H), 3.69−3.81 (m, 3H), 3.92 (t, J = 10.0 Hz, 1H), 4.06−4.09 (m, 1H), 4.32−4.33 (m, 1H), 4.58 (m, 1H), 4.68−4.70 (m, 1H), 5.54 (s, 1H), 5.68 (s, 1H), 7.20−7.63 (m, 18H), 8.07−8.17 (m, 4H); ^{13}C NMR (DMSO-d_6) δ 22.0, 22.5, 23.2, 62.9, 63.1, 64.2, 68.8, 69.2, 70.8, 76.1, 76.3, 100.0, 100.2, 121.6, 121.9, 123.4, 125.3, 125.4, 125.9, 126.7, 126.8, 128.1, 128.2, 128.7, 128.9, 130.3, 130.9, 131.3, 131.8, 132.0, 137.4,

137.7, 146.7, 146.9; ^{31}P NMR (DMSO-d_6) δ 155.22; HRMS (APCI) calcd for $C_{43}H_{39}O_8P$ ($M^+ + 1$) 715.2455, found 715.2433.

1,3:4,6-Di-*O*-benzylidene-2-*O*-isobutyl-3-*O*-((*R*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-mannitol (3d). The above procedure was followed with use of **5d** and *R*-BINOL. After workup, **3d** was obtained. Mp 142−143 °C, $[\alpha]^{22}_D$ −270.19 (*c* 0.62, THF); ^{1}H NMR (DMSO-d_6) δ 0.80−0.82 (m, 6H), 1.69−1.75 (m, 1H), 3.19−3.21 (m, 1H), 3.33−3.39 (m, 1H), 3.48−3.51 (m, 1H), 3.64−3.65 (m, 1H), 3.81−3.84 (m, 1H), 3.89 (t, J = 10.0 Hz, 1H), 4.07 (d, J = 9.2 Hz, 1H), 4.37−4.39 (m, 1H), 4.58−4.60 (m, 1H), 4.68−4.71 (m, 1H), 5.52 (s, 1H), 5.66 (s, 1H), 7.19−7.61 (m, 18H), 8.06−8.16 (m, 4H); ^{13}C NMR (DMSO-d_6) δ 19.0, 19.1, 28.1, 31.4, 62.8, 63.0, 66.9, 68.5, 68.8, 76.2, 76.6, 100.1, 100.2, 121.6, 121.9, 122.1, 123.4, 125.3, 125.4, 125.8, 125.9, 126.4, 126.7, 126.8, 128.1, 128.2, 128.7, 128.8, 130.3, 130.9, 131.2, 131.8, 132.0, 137.4, 137.7, 146.7, 147.0; ^{31}P NMR (DMSO-d_6) δ 154.98; HRMS (APCI) calcd for $C_{44}H_{41}O_8P$ ($M^+ + 1$) 729.2611, found 729.2640.

1,3:4,6-Di-*O*-benzylidene-2-*O*-benzyl-3-*O*-((*R*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-mannitol (3e). The above procedure was followed with use of **5e** and *R*-BINOL. After workup, **3e** was obtained. Mp 122−123 °C, $[\alpha]^{22}_D$ −251.81 (*c* 0.69, THF); ^{1}H NMR (DMSO-d_6) δ 3.51 (m, 1H), 3.75 (m, 1H), 3.85−3.90 (m, 2H), 4.12 (d, J = 9.2 Hz, 1H), 4.37−4.39 (m, 1H), 4.52−4.55 (m, 3H), 4.57−4.60 (m, 1H), 5.55 (s, 1H), 5.64 (s, 1H), 7.20−7.55 (m, 23H), 8.08−8.14 (m, 4H); ^{13}C NMR (DMSO-d_6) δ 62.9, 63.1, 65.6, 68.5, 68.7, 71.2, 76.1, 76.4, 99.9, 100.0, 121.6, 121.9, 125.3, 125.5, 125.9, 126.7, 126.8, 127.7, 127.8, 128.1, 128.3, 128.7, 130.3, 130.9, 131.2, 137.3, 137.6, 138.0, 146.7, 147.0; ^{31}P NMR (DMSO-d_6) δ 154.86; HRMS (APCI) calcd for $C_{47}H_{39}O_8P$ ($M^+ + 1$) 763.2455, found 763.2490.

1,3:4,6-Di-*O*-benzylidene-2-*O*-diphenylmethyl-3-*O*-((*R*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-mannitol (3f). The above procedure was followed with use of **5f** and *R*-BINOL. After workup, **3f** was obtained. Mp 125−126 °C, $[\alpha]^{22}_D$ −232.59 (*c* 0.58, THF); ^{1}H NMR (DMSO-d_6) δ 3.44 (t, J = 10.4 Hz, 1H), 3.73−3.79 (m, 1H), 3.87−3.95 (m, 2H), 4.17 (d, J = 9.6 Hz, 1H), 4.37 (d, J = 6.0 Hz, 1H), 4.54−4.57 (m, 1H), 4.65−4.68 (m, 1H), 5.45 (s, 1H), 5.55 (s, 1H), 5.64 (s, 1H), 7.06 (m, 1H), 7.14−7.27 (m, 7H), 7.28−7.39 (m, 17H), 7.48−7.56 (m, 4H), 8.05−8.20 (m, 4H); ^{13}C NMR (DMSO-d_6) δ 62.8, 62.9, 64.2, 68.4, 68.7, 75.9, 76.3, 99.7, 121.7, 122.0, 125.3, 125.4, 125.9, 126.1, 126.4, 126.7, 127.4, 127.5, 127.8, 128.1, 128.3, 128.7, 130.3, 130.8, 131.3, 131.8, 137.6, 141.6, 142.6, 146.7, 147.0; ^{31}P NMR (DMSO-d_6) δ 154.69; HRMS (APCI) calcd for $C_{53}H_{43}O_8P$ ($M^+ + 1$) 839.2768, found 839.2803.

1,3:4,6-Di-*O*-benzylidene-2-*O*-(1-naphthylmethyl)-3-*O*-((*R*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-mannitol (3g). The above procedure was followed with use of **5g** and *R*-BINOL. After workup, **3g** was obtained. Mp 141−142 °C, $[\alpha]^{22}_D$ −239.12 (*c* 0.76, THF); ^{1}H NMR (DMSO-d_6) δ 3.51 (m, 1H), 3.68 (m, 1H), 3.82 (m, 2H), 3.89 (d, J = 9.2 Hz, 1H), 4.47−4.51 (m, 3H), 4.91 (d, J = 12.4 Hz, 1H), 5.03 (s, 1H), 5.08 (d, J = 12.4 Hz, 1H), 5.47 (s, 1H), 7.06 (m, 2H), 7.19 (m, 2H), 7.21−7.41 (m, 11H), 7.48−7.53 (m, 6H), 7.60 (d, J = 8.8 Hz, 1H), 7.80 (d, J = 8.8 Hz, 1H), 7.82 (m, 1H), 8.06−8.14 (m, 5H); ^{13}C NMR (DMSO-d_6) δ 62.7, 62.9, 64.7, 68.4, 68.8, 69.1, 75.8, 76.3, 99.7, 100.1, 121.6, 121.9, 123.4, 124.1, 125.2, 125.3, 125.5, 125.8, 125.9, 126.3, 126.7, 126.9, 127.3, 127.9, 128.1, 128.5, 128.7, 130.3, 130.9, 131.3, 131.8, 132.0, 133.2, 133.4, 137.0, 137.6, 146.6, 147.0; ^{31}P NMR (DMSO-d_6) δ 154.36; HRMS (APCI) calcd for $C_{51}H_{41}O_8P$ ($M^+ + 1$) 813.2612, found 813.2641.

1,3:4,6-Di-*O*-benzylidene-2-*O*-methyl-3-*O*-((*S*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-mannitol (3h). The above procedure was followed with use of **5a** and *S*-BINOL. After workup, **3h** was obtained. Mp 117−118 °C, $[\alpha]^{22}_D$ 215.29 (*c* 0.74, THF); ^{1}H NMR (DMSO-d_6) δ 3.49 (s, 3H), 3.65−3.67 (m, 1H), 3.77−3.89 (m, 2H), 4.17−4.21 (m, 2H), 4.32−4.36 (m, 1H), 4.53−4.57 (m, 2H), 5.68 (s, 1H), 5.75 (s, 1H), 7.18−7.28 (m, 7H), 7.38−7.41 (m, 7H), 7.52−7.54 (m, 2H), 7.63 (d, J = 8.8 Hz, 1H), 7.76 (d, J = 8.8 Hz, 1H), 8.10−8.19 (m, 2H), 8.21−8.24 (m, 2H); ^{13}C NMR (DMSO-d_6) δ 58.2, 63.0, 63.1, 68.4, 68.8, 76.3, 99.9, 100.2, 121.2, 121.7, 123.3, 125.3, 125.5, 125.7, 125.9, 126.0, 126.1, 126.8, 127.9, 128.1, 128.5, 128.6, 128.7, 130.5, 130.7, 131.1, 131.3, 131.8, 131.9, 137.3, 137.6, 146.6, 147.2; ^{31}P NMR (DMSO-d_6) δ 144.50; HRMS (APCI) calcd for $C_{41}H_{35}O_8P$ ($M^+ + 1$) 687.2142, found 687.2112.

1,3:4,6-Di-*O*-benzylidene-2-*O*-benzyl-3-*O*-((*S*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-mannitol (3i). The above procedure was followed with use of **5e** and *S*-BINOL. After workup, **3i** was obtained. Mp 123−124 °C, $[\alpha]^{22}_D$ 184.97 (*c* 0.76, THF); ^{1}H NMR (DMSO-d_6) δ 3.81−3.86 (m, 3H), 4.17 (d, J = 9.6 Hz, 1H), 4.27−4.34 (m, 2H), 4.49−4.55 (m, 2H), 4.64 (d, J = 12.0 Hz, 1H), 4.72 (d, J = 11.6 Hz, 1H), 5.60 (s, 1H), 5.68 (s, 1H), 7.16−7.42 (m, 19H), 7.48−7.50 (m, 2H), 7.62 (d, J = 8.8 Hz, 1H), 7.72 (d, J = 8.8 Hz, 1H), 8.06−8.16 (m, 4H); ^{13}C NMR (DMSO-d_6) δ 63.0, 65.8, 68.7, 68.8, 71.3, 76.2, 99.9, 100.2, 121.2, 121.7, 125.3, 125.4, 125.7, 125.9, 126.8, 127.9, 127.9, 128.4, 128.6, 128.7, 130.4, 130.7, 131.1, 131.3, 131.9, 137.2, 137.5, 138.1, 146.6, 147.2; ^{31}P NMR (DMSO-d_6) δ 144.79; HRMS (APCI) calcd for $C_{47}H_{39}O_8P$ ($M^+ + 1$) 763.2455, found 763.2496.

1,3:4,6-Di-*O*-benzylidene-2-*O*-benzyl-3-*O*-(2,2′-*O*,*O*-(1,1′-biphenyl)dioxophosphite)-D-mannitol (3j). The above procedure was followed with use of **5e** and 2,2′-biphenol. After workup, **3j** was obtained. Mp:75−76 °C, $[\alpha]^{22}_D$ −35.81 (*c* 0.81, THF); ^{1}H NMR (DMSO-d_6) δ 3.68−3.79 (m, 2H), 3.89−3.92 (m, 1H), 4.07 (d, J = 8.8 Hz, 1H), 4.15 (d, J = 9.2 Hz, 1H), 4.41−4.47 (m, 2H), 4.56−4.67 (m, 3H), 5.52 (s, 1H), 5.62 (s, 1H), 7.22−7.53 (m, 19H), 7.53−7.56 (m, 2H); ^{13}C NMR (DMSO-d_6) δ 62.7, 62.8, 65.7, 68.6, 68.8, 71.3, 76.2, 76.3, 99.9, 100.1, 121.5, 122.1, 125.8, 125.9, 127.8, 127.9, 128.1, 128.3, 128.6, 128.8, 129.7, 130.0, 130.2, 130.4, 137.3, 137.5, 138.0, 148.2, 148.8; ^{31}P NMR (DMSO-d_6) δ 145.39; HRMS (APCI) calcd for $C_{39}H_{35}O_8P$ ($M^+ + 1$) 663.2142, found 663.2102.

1,3:4,6-Di-*O*-benzylidene-2-*O*-benzyl-3-*O*-(2,2′-*O*,*O*-(3,3′,5,5′-tetra-*tert*-butyl-1,1′-biphenyl)dioxophosphite)-D-mannitol (3k). The above procedure was followed with use of **5e** and 3,3′,5,5′-tetra-*tert*-butyl-1,1′-biphenyl-2,2′-diol. After workup, **3k** was obtained. Mp 120−121 °C, $[\alpha]^{22}_D$ 19.36 (*c* 0.83, THF); ^{1}H NMR (DMSO-d_6) δ 1.25 (s, 9H), 1.31 (s, 9H), 1.41 (s, 9H), 1.42 (s, 9H), 3.42 (m, 1H), 3.76−3.83 (m, 3H), 4.11−4.20 (m, 2H), 4.41−4.43 (m, 1H), 4.56−4.67 (m, 3H), 5.10 (s, 1H), 5.59 (s, 1H), 7.06 (m, 1H), 7.14−7.33 (m, 15H), 7.45 (m, 2H); ^{13}C NMR (DMSO-d_6) δ 31.0, 31.2, 34.2, 34.3, 35.0, 62.6, 65.6, 68.7, 68.9, 71.2, 76.1, 76.3, 99.9, 100.2, 124.1, 124.3, 125.8, 125.9, 126.3, 126.5, 127.6, 127.6, 127.9, 128.2, 128.5, 128.7, 132.1, 132.4, 137.2, 137.3, 138.2, 139.7, 139.9, 144.4, 144.7, 146.6; ^{31}P NMR (DMSO-d_6) δ 146.24; HRMS (APCI) calcd for $C_{55}H_{68}O_8P$ ($M^+ + 1$) 887.4646, found 887.4604.

General Procedure for Asymmetric Hydrogenation. Ligand **3** (0.011 mmol) was added to a solution of $[Rh(COD)_2]BF_4$ (2.0 mg, 0.005 mmol) in anhydrous and degassed CH_2Cl_2 (1 mL) in a nitrogen-filled glovebox. After the mixture was stirred for 30 min, a substrate (0.5 mmol) dissolved in CH_2Cl_2 (1 mL) was added. The reaction mixture was transferred to a stainless autoclave. The autoclave was purged three times with H_2 and the pressure was set to the desired value, and hydrogenation was performed at room temperature for 12 h. After carefully releasing the H_2, the reaction mixture was passed through a short silica gel plug to remove the catalyst. The resulting solution was used directly for chiral GC to measure enantiomeric excesses.

Acknowledgment. Financial support from the National Natural Science Foundation of China (29933050) is gratefully acknowledged. We also thank Prof. Y-G. Zhou for helpful discussions.

Supporting Information Available: NMR spectra of new ligands **3a**−**k** and ee value determination conditions of GC. This material is available free of charge via the Internet at http://pubs.acs.org.

JO035627P