Chiral Diphosphites Derived from D-Glucose: New Highly Modular Ligands for the Asymmetric Catalytic Hydrogenation

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A series of novel diphosphite ligands derived from readily available D-(+)-glucose have been synthesized. These ligands were screened in the Rh-catalyzed hydrogenation of a series of α,β-unsaturated carboxylic acid derivatives. Both excellent enantioselectivities (ee up to >99%) and activities were achieved. The advantage of these ligands is that their modular nature allows an easy systematic variation in the configuration of the stereocenters (C-3, C-5) at the ligand backbone and in the biaryl substituents, so the optimum configuration for maximum enantioselectivity in asymmetric hydrogenation can be determined. Results show that enantiomeric excesses depend strongly on the absolute configuration of C-3 and slightly on the stereocenter carbon C-5, while the sense of the enantiodiscrimination is predominantly controlled by the configuration of the biaryls at the phosphite moieties. Moreover, the presence of bulky substituents at the *ortho*-positions of the biaryl diphosphite moieties has a positive effect on enantioselectivity.

Introduction

The asymmetric hydrogenation of functionalized prochiral olefins is one of the most important applications of asymmetric catalysis. Over many years, the scope of this reaction has been gradually extended in both reactant structure and catalyst efficiency.[1] Many chiral diphosphines[1,2] and diphosphinites[3] have been synthesized as ligands for enantioselective metal-catalyzed hydrogenation. Recently, a group of less electron-rich phosphorus compounds—phosphite ligands—has received more attention.[4] Phosphite ligands are a very attractive group of compounds for catalysis and have been successfully applied in other transition-metal-catalyzed reactions such as hydroformylation, hydrocyanation, and allylic alkylation.[5] They have many advantages; for example, they are easy to prepare from readily available starting materials, and they are less sensitive to air than phosphines.[5j,6] However, only Reetz et al. have reported a successful enantioselective hydrogenation using phosphite ligands.[4a,b] Therefore, it is important to develop new phosphite ligands and to scope their applicability in the hydrogenation reaction.

For this purpose, chiral auxiliaries from the chiral pool are particularly advantageous. Of them, sugar-derived ligands have provided good conversions and excellent enantioselectivities in different types of catalytic reactions.[3c,4a,5f,i,7] Particularly, some 1,2-protected furanoses derived from D-(+)-xylose and D-(+)-glucose have been shown to be successful ligands for asymmetric catalysis.[5e,f,i,l,8] However, the success of these ligands highly depends on the studied reaction. For example, in diphosphite furanoside ligands **1** and **2** (Figure 1), the introduction of a stereogenic center at the C-5 position (ligands **3**−**6a,b**, Figure 2) improved the rate and enantioselectivity in the Rh-catalyzed asymmetric hydroformylation of styrene,[5e,f] while it hardly affected the enantioselectivity in the Pd-catalyzed asymmetric allylic alkylation of *rac*-1,3-diphenyl-2-propenyl acetate.[5i,l] As far

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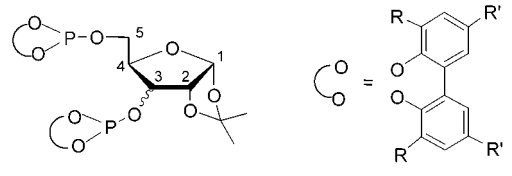

1 D-*xylo*
2 L-*ribo*

Figure 1.

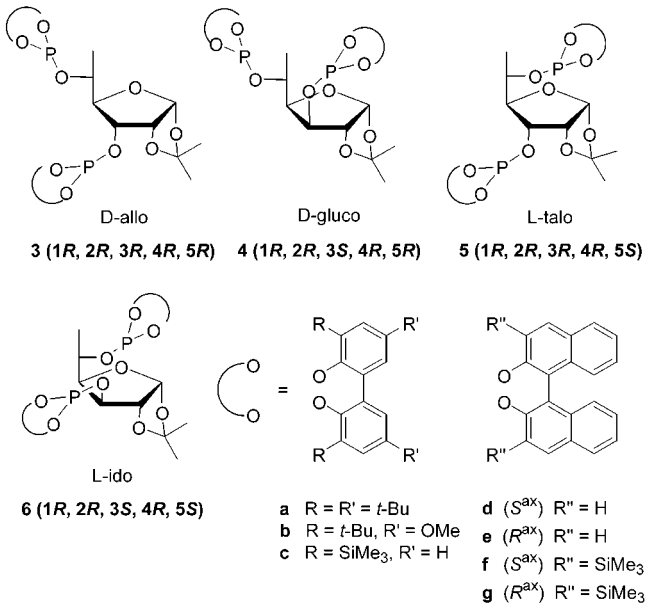

Figure 2.

as the asymmetric hydrogenation reaction is concerned, ligands **1** and **2** provided moderate results.[4e,f]

The objective of the study presented here is 2-fold: (a) to test whether introducing a stereocenter at the carbon C-5 position would improve enantioselectivity in the Rh-catalyzed asymmetric hydrogenation reaction and (b) to investigate the existence of a cooperative effect between the stereogenic centers of the ligand backbone and the stereogenic biaryl substituents. Such effects have recently been described for other ligands[5b,9] and were beneficial.

With these purposes, we synthesized the new chiral diphosphite ligands **3**−**6c**−**g** (Figure 2) so that the complete family of ligands **3**−**6a**−**g** combine the systematic variation of the configurations at C-3 and C-5 of the ligand backbone and different substituents and configurations in the biaryl phosphite moieties. This allows the optimum configuration for maximum enantioselectivity to be determined and may provide some insight into the origin of the stereochemistry of the reaction.

(7) See also, for instance: (a) RajanBabu, T. V.; Ayers, T. A. *Tetrahedron Lett.* **1994**, *35*, 4295. (b) RajanBabu, T. V.; Casalnuovo, A. L. *Pure Appl. Chem*. **1994**, *94*, 149. (c) Yonehara, K.; Hashizuma, T.; Mori, K.; Ohe, K.; Uemura, S. *Chem. Commun*. **1999**, 415. (d) Clyne, D. S.; Mermet-Bouvier, Y. C.; Nomura, N.; RajanBabu, T. V. *J. Org. Chem*. **1999**, *64*, 7601. (e) Yonehara, K.; Ohe, K.; Uemura, S. *J. Org. Chem*. **1999**, *64*, 937. (f) Park, H.; RajanBabu, T. V. *J. Am. Chem. Soc.* **2002**, *124*, 734.

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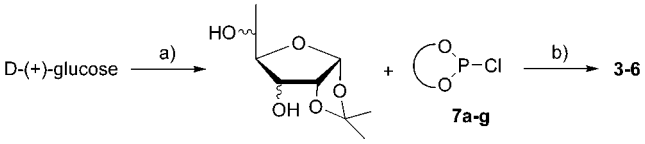
Scheme 1. Synthesis of Ligands 3−6[a]



[a] Reagents and conditions: (a) ref 5f; (b) Py, toluene, 100 °C.

Results and Discussion

Ligand Design. Ligands **3**−**6** consist of chiral 1,2-*O*-protected furanoside backbones, which determine their underlying structure, and two hydroxyl groups at the C-3 and C-5 positions. Several phosphoric acid biaryl esters **7** were attached to these basic frameworks (Scheme 1).

The influence of the different groups attached to the *ortho*- and *para*-positions of the biphenyl moieties on enantioselectivity was investigated using ligands **3a**−**c**, which have the same configuration on the carbon atoms C-3 and C-5.

We studied the effects of the stereogenic carbon atoms C-3 and C-5 on enantioselectivity and the possibility of a cooperative effect between them by comparing diastereomeric ligands **3**−**6**.

To determine whether there is a cooperative effect between the stereocenters of the ligand backbone and the configuration of the biaryl phosphite moieties, we prepared a series of enantiomerically pure binaphthol-based ligands **3d**−**g**.

Ligand Synthesis. The new ligands **3c**−**g** and **4c** were synthesized very efficiently in one step from the corresponding diols, which were prepared on a large scale from D-(+)-glucose, as previously described for ligands **3a,b** and **4a,b** (Scheme 1).[5f] Therefore, reaction of the corresponding diol with 2 equiv of the desired in situ formed phosphorochloridite **7c**−**g** in the presence of base afforded the desired ligands.

All the ligands were stable during purification on neutral silica gel under an atmosphere of argon and were isolated in moderate-to-good yields (45−80%) as white solids. The ^{31}P NMR spectra of ligands **3c**−**g** show two singlets—one for each phosphorus moiety, while for ligand **4c**, two doublets—one for each phosphorus—were observed. The large J_{PP} value for ligand **4c** is similar to those of the related diphosphite ligands **4a** and **4b**.[5f] Moroever, due to the axial chirality of the biphenyl groups, two pairs of signals should be expected for ligands **3c** and **4c**. However, the existence of a single set of signals for each phosphorus atom for ligands **3c** and **4c** in the variable-temperature ^{31}P NMR suggested rapid ring inversions (atropoisomerization) of the seven-membered dioxaphosphepin rings on the NMR time scale.[10]

Asymmetric Hydrogenation of α,β-Unsaturated Carboxylic Acid Derivatives. The catalytic performance of ligands **3**−**6** was thoroughly explored in the enantioselective rhodium-catalyzed hydrogenation reaction. In a first set of experiments, we used these ligands in the rhodium-catalyzed hydrogenation of dimethyl itaconate (**8**). The reaction proceeded smoothly at room temperature. In general, the catalysts were prepared in situ by adding the corresponding diphosphite ligands to the catalyst precursor $[Rh(cod)_2]BF_4$.

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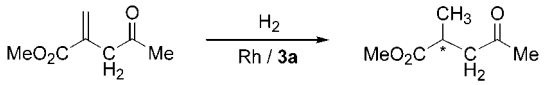
Table 1. Asymmetric Hydrogenation of Dimethyl Itaconate 8 Using Rh/Diphosphite 3a[a]



8 9

entry	solvent	P_{H_2}, bar	% convn[b] (t, h)	% ee[c]
1	toluene	5	16 (8)	2 (*S*)
2	CH_2Cl_2	5	90 (8)	90 (*R*)
3	AcOEt	5	8 (8)	2 (*R*)
4	THF	5	99 (8)	12 (*R*)
5	CH_2Cl_2	1	100 (20)	10 (*R*)
6	CH_2Cl_2	2	66 (8)	90 (*R*)
7	CH_2Cl_2	10	90 (3)	90 (*R*)
8	CH_2Cl_2	30	100 (0.8)	91 (*R*)
9[d]	CH_2Cl_2	5	89 (8)	90 (*R*)
10[d]	CH_2Cl_2	5	90 (8)	90 (*R*)

[a] Amount of $[Rh(cod)_2]BF_4$ 0.01 mmol, ligand/Rh = 1.1, substrate/Rh = 100, amount of solvent 6 mL, T = 25 °C. [b] Percent conversion measured by GC. [c] Percent enantiomeric excess measured by GC using a Chiraldex G-TA column. [d] Ligand/Rh = 2. [e] Using preformed complex $[Rh(cod)(3a)]BF_4$ (0.01 mmol).

The effects of different reaction parameters (i.e., solvent, hydrogen pressure, catalyst preparation, ligand-to-rhodium ratio, and temperature) were investigated for the catalytic precursor containing ligand **3a**. The results are summarized in Table 1.

The results show that the efficiency of the process depended strongly on the nature of the solvent (entries 1−4). Thus, the catalyst performance (activity and enantioselectivity) was best when dichloromethane was used (entry 2).

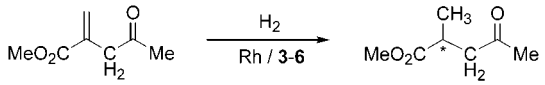
Interestingly, both enantioselectivity and activity were notably enhanced when the hydrogen pressure was raised from 1 to 2 bar (entry 5 vs entry 6). However, though increasing the hydrogen pressure further had a positive effect on activity, enantioselectivity remained the same (entries 7 and 8). This contrasts with the usual decrease in enantioselectivity with bidentate ligands when the hydrogen pressure is raised.[1a,11]

Using preformed catalyst precursor $[Rh(cod)(\mathbf{3a})]BF_4$ (cod = 1,3-cyclooctadiene) did not affect the efficiency of the process (entry 10). Also, adding a 1-fold excess of ligand did not affect the outcome of the reaction (entry 9).

For comparison purposes, the rest of the ligands were tested under "standard" conditions (a ligand-to-rhodium ratio of 1.1, a hydrogen pressure of 5 bar, and dichloromethane as a solvent). The results are shown in Table 2.

Using ligand **3b** with methoxy groups instead of *tert*-butyl groups in the *para*-positions of the biphenyl moieties led to lower enantioselectivity and activity than those of catalytic system Rh/**3a** (entry 1 vs entry 2).[12] The

Table 2. Rh-catalyzed Asymmetric Hydrogenation of 8 Using Diphosphites 3−6[a]



8 9

entry	ligand	% convn[b] (t, h)	% ee[c]
1	**3a**	90 (8)	90 (*R*)
2	**3b**	82 (8)	85 (*R*)
3	**3c**	100 (6)	97 (*R*)
4	**3d**	50 (8)	50 (*S*)
5	**3e**	46 (8)	52 (*R*)
6	**3f**	100 (8)	90 (*S*)
7	**3g**	100 (8)	92 (*R*)
8	**4a**	100 (8)	2 (*R*)
9	**4b**	98 (8)	2 (*R*)
10	**4c**	100 (8)	3 (*R*)
11	**5a**	87 (8)	67 (*R*)
12	**5b**	80 (8)	63 (*R*)
13	**6a**	73 (8)	29 (*R*)
14	**6b**	69 (8)	27 (*R*)
15	**1a**	12 (8)	22 (*R*)
16	**2a**	28 (8)	64 (*R*)

[a] Amount of $[Rh(cod)_2]BF_4$ 0.01 mmol, ligand/Rh = 1.1, substrate/Rh = 100, amount of CH_2Cl_2 6 mL, P_{H_2} = 5 bar, T = 25 °C. [b] Percent conversion measured by GC. [c] Percent enantiomeric excess measured by GC using a Chiraldex G-TA column.

presence of trimethylsilyl groups in the *ortho*-positions of the biphenyl moieties (ligand **3c**) had a positive effect on both activity and enantioselectivity (97% ee, entry 3). Ligands **3d** and **3e**, which contain stereogenic binaphthyl moieties, resulted in lower activity and enantioselectivity (entries 4 and 5). Ligand **3d**, which has (*S*)-binaphthyl moieties, resulted in an ee of 50% (*S*), whereas diastereomer **3e**, which has (*R*)-binaphthyl moieties, resulted in an ee of 52 (*R*). We can therefore conclude that the sense of the enantiodiscrimination is predominantly controlled by the configuration of the biaryl at the phosphite moieties.

As with ligand **3c**, ligands **3f** and **3g**, which contain bulky trimethylsilyl groups in the *ortho*-positions of the binaphthyl moieties, led to higher reaction rates and enantioselectivities (entries 6 and 7) than the less steric nonsubstituted binaphthyl ligands **3d** and **3e**. Thus, both enantiomers of **9** can be obtained in good enantioselectivities (entries 6 and 7). The enantioselectivity observed for the catalytic system Rh/**3c**, which was higher than for Rh/**3f** and Rh/**3g**, can be attributed to the different dihedral angles of the biphenyl and binaphthyl moieties, which affect the characteristics of the phosphorus and therefore the geometry of the species responsible for the catalytic activity.[5b]

Ligands **4a**−**c**, whose configuration of carbon atom C-3 is opposite that of ligands **3** (Figure 2), produced slightly better activities, but the enantioselectivity dropped considerably (entries 8−10).

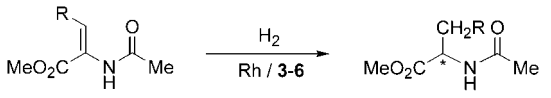
Ligands **5**, which resulted from changing the configuration of carbon C-5 from *R* to *S* in ligands **3**, led to a slightly lower activity and a lower enantioselectivity than the catalytic systems Rh/**3** (entries 1 and 2 vs entries 11 and 12).

Ligands **6**, whose configuration of carbon atom C-3 is opposite to that of ligands **5** (Figure 2), produced lower activities and enantioselectivities (entries 11 and 12 vs entries 13 and 14).

(11) (a) Pfaltz, A.; Brown, J. M. In *Houben-Weyl Methods of Organic Chemisty*; Helchem, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme: Stuttgart, Germany, 1995; Vol. E21, Section D.2.5.1.2. (b) Zhang, X. *Enantiomer* **1999**, *4*, 541. (c) Burk, M. J.; Bienewald, F. In *Transition Metals For Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, Germany, 1998; Vol. 2; Chapter 1.1.2. (d) 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.

(12) This behavior contrasts with the positive effect on enantioselectivity observed in the Rh-catalyzed hydroformylation and Pd-catalyzed allylic alkylation reactions for ligands containing methoxy substituents in the *para*-positions of the biphenyl moieties; see refs 5f and 5i.

Table 3. Asymmetric Hydrogenation of Methyl (*N*)-Acetylaminoacrylate (10) and Methyl (*Z*)-(*N*)-Acetylaminocinnamate (12) with $[Rh(cod)_2]BF_4$/3−6[a]



10 R = H
12 R = Ph

11 R = H
13 R = Ph

entry	substrate	ligand	% convn[b] (*t*, h)	% ee[c]
1	**10**	**3a**	98 (8)	92 (*S*)
2	**12**	**3a**	96 (8)	91 (*S*)
3	**10**	**3c**	100 (6)	97 (*S*)
4	**12**	**3c**	100 (6)	98 (*S*)
5	**10**	**4a**	100 (8)	3 (*S*)
6	**12**	**4a**	100 (8)	2 (*S*)
7	**10**	**5a**	97 (8)	71 (*S*)
8	**12**	**5a**	98 (8)	70 (*S*)
9	**10**	**6a**	92 (8)	29 (*S*)
10	**12**	**6a**	96 (8)	32 (*S*)

[a] Amount of $[Rh(cod)_2]BF_4$ 0.01 mmol, ligand/Rh = 1.1, substrate/Rh = 100, amount of CH_2Cl_2 6 mL, P_{H_2} = 5 bar, T = 25 °C. [b] Percent conversion measured by GC. [c] Percent enantiomeric excess measured by GC using a Permabond L-Chiralsil-Val column.

Comparison of entries 1, 8, 11, and 13 clearly shows that the enantiomeric excesses depend strongly on the absolute configuration of C-3 and depend slightly on the stereocenter carbon C-5 of the carbohydrate backbone. The best enantioselectivities were obtained therefore with allofuranoside ligands **3** with *R* configuration on both C-3 and C-5 stereocenters.[13] Further evidence is provided by using related diphosphite ligands **1a** and **2a** with xylo- and ribofuranoside backbones (Figure 1).[14] Ligand **2a**, with *R* configuration on C-3, produced a better enantioselecitivity than ligand **1a** with opposite configuration on C-3 (entry 15 vs entry 16). Moreover, the similar enantioselecitivities obtained with ligands **2a** and **5a** suggest that they both adopt a similar spatial arrangement around the metal center in the species responsible for the catalytic activity. This is also true for ligands **1a** and **6a**. Interestingly, in contrast with the hydroformylation results,[5f] the sense of enantioselectivity, in the biphenyl-based ligands, is not controlled by the absolute configuration of the stereogenic carbon atom C-3. Thus, in all cases the (*R*)-**9** enantiomer is predominantly formed (entries 1−3 and 9−16).

We can also conclude that the presence of a methyl substituent on the carbon C-5 significantly increased the activity (entries 1−14 vs entries 15 and 16).[15]

We subsequently applied these new highly efficient diphosphites **3**−**6** in the Rh-catalyzed hydrogenation of other benchmark dehydroamino acid derivatives **10** and **12**. The results are summarized in Table 3. The results followed the same trend as observed for substrate **8**, but the activities were somewhat higher. The absolute configuration of the hydrogenated products **11** and **13** is opposite that of the hydrogenated product **9**, but they have the same spatial arrangement.[16] The catalyst precursor with ligand **3c** produced the highest enantiomeric excess (98%, entry 4).

Table 4. Asymmetric Hydrogenation with Low Catalyst Loading at Elevated Pressure Using $[Rh(cod)_2]BF_4$/3c[a]

entry	substrate	*T*, °C	% convn[b] (*t*, min)	% ee[c]
1	**8**	25	99 (25)	97 (*R*)
2	**10**	25	100 (25)	98 (*S*)
3	**12**	25	95 (25)	97 (*S*)
4	**8**	5	100 (240)[d]	>99 (*R*)
5	**10**	5	100 (240)[d]	>99 (*S*)
6	**12**	5	100 (240)[d]	>99 (*S*)

[a] Amount of $[Rh(cod)_2]BF_4$ 0.01 mmol, ligand/Rh = 1.1, substrate/Rh = 1000, amount of CH_2Cl_2 6 mL, P_{H_2} = 30 bar. [b] Percent conversion measured by GC. [c] Percent enantiomeric excess measured by GC. [d] Reaction time not optimized.

Also, we performed the hydrogenation of substrates **8**, **10**, and **12** at high pressure and low catalyst concentration (0.1 mol %) using ligand **3c** in dichloromethane (see Table 4). Under these conditions, the reactions proceeded fast (TOF > 2500 h^{-1}) with enantioselectivities up to 98% (entries 1−3). An increase in enantioselectivity (ee > 99%) combined with good activity was found for all substrates by lowering the reaction temperature (Table 4, entries 4−6).

Conclusions

We have designed a series of diphosphite ligands **3**−**6** based on the simple but highly effective furanoside backbone. These ligands have been easily prepared in few steps from readily available D-(+)-glucose. The possibility and necessity of tuning the ligand was demonstrated by the synthesis of 14 diphosphite ligands and their application in the Rh-catalyzed asymmetric hydrogenation of several α,β-unsaturated carboxylic acid derivatives. Both excellent enantioselectivities (ee up to >99%) and activities were achieved. Systematic variation of stereocenters C-3 and C-5 at the ligand backbone revealed that enantiomeric excesses depend strongly on the absolute configuration of C-3 and slightly on that of the stereocenter carbon C-5. Therefore, enantioselectivities were best with ligands **3** with *R* configuration on both C-3 and C-5 stereocenters. Variation in chirality at the axial chiral binaphthyl substituents in ligands **3** indicates that the sense of the enantiodiscrimination is predominantly controlled by the configuration of the biaryls at the phosphite moieties. The presence of bulky substituents at the *ortho*-positions of the biaryl diphosphite moieties has a positive effect on enantioselectivity. The highest enantiomeric excess was found for allofuranoside ligand **3c**, which have *o*-trimethylsilyl substituents in the biphenyl moieties.

The systematic variation in the configuration of the stereocenters at the ligand backbone and in the biaryl substituents provides therefore a rational approach to the optimum ligand parameters for high activity and enantioselectivity (ee up to >99%). Exploiting the fact that these sugar ligands can be easily modified, further research into other types of hydrogenation reactions is now in progress.

(13) This behavior contrasts with the high copperative effect between stereocenters C-3 and C-5 observed in the Rh-catalyzed hydroformylation, which results in a matched combination for ligands with gluco- and talofuranoside backbones; see ref 5f.

(14) For comparative purposes diphosphite ligands **1a** and **2a** were tested in the Rh-catalyzed enantioselective hydrogenation of **8** under the same reaction conditions.

(15) Similar behavior has been observed in the Rh-catalyzed asymmetric hydrogenation using related diphosphine ligands. See: Diéguez, M.; Pàmies, O.; Ruiz, A.; Castillón, S.; Claver, C. *Tetrahedron: Asymmetry* **2000**, *11*, 4701.

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Experimental Section

General Comments. All syntheses were performed using standard Schlenk techniques under an argon atmosphere. Solvents were purified by standard procedures. Ligands **1a**[17] and **2a**[4f] were prepared according to the literature procedures. Compounds **3a,b**, **4a,b**, **5a,b**, and **6a,b** were prepared by previously described methods.[5f] 6-Desoxy-1,2-*O*-isopropylidene-α-D-allofuranose (**14**) and 6-desoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (**15**) were synthesized as previously described.[5f] Phosphorochloridites **7c**−**g** were prepared in analogy with literature procedures.[5b,18] All other reagents were used as commercially available. ^{1}H, ^{13}C{^{1}H}, and ^{31}P{^{1}H} NMR spectra were recorded using a 400 MHz spectrometer. Chemical shifts are relative to that of $SiMe_4$ (^{1}H and ^{13}C) as internal standard or H_3PO_4 (^{31}P) as external standard. All assignments in NMR spectra were determined by COSY and HETCOR spectra. Hydrogenation reactions were carried out in a homemade 100 mL stainless steel autoclave.

3,5-Bis[(3,3′-bis(trimethylsilyl)-1,1′-biphenyl-2,2′-diyl)-phosphite]-6-deoxy-1,2-*O*-*isopropylidene*-α-D-allofuranose (3c). In situ formed phosphorochloridite **7c** (2.2 mmol) was dissolved in toluene (5 mL) to which pyridine (0.36 mL, 4.6 mmol) was added. **14** (0.21 g, 1 mmol) was azeotropically dried with toluene (3 × 1 mL) and dissolved in toluene (10 mL) to which pyridine (0.18 mL, 2.3 mmol) was added. The diol solution was transferred slowly over 30 min to the solution of phosphorochloridite at room temperature. The reaction mixture was stirred overnight at reflux, and the pyridine salts were removed by filtration. Evaporation of the solvent gave a white foam which was purified by flash chromatography (eluent toluene, R_f 0.85) to produce 0.79 g (86%) of a white powder. Anal. Calcd for $C_{45}H_{62}O_9P_2Si_4$: C, 58.67; H, 6.78. Found: C, 58.76; H, 6.89. ^{31}P NMR: δ 145.0 (s), 145.5 (s). ^{1}H NMR: δ 0.24 (s, 9H, CH_3Si), 0.26 (s, 9H, CH_3Si), 0.27 (s, 9H, CH_3Si), 0.35 (s, 9H, CH_3Si), 0.63 (d, 3H, H-6, $^3J_{6-5}$ = 7.2 Hz), 1.25 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 3.88 (t, 1H, H-2, $^3J_{2-1}$ = 3.6 Hz, $^3J_{2-3}$ = 3.6 Hz), 4.05 (d, 1H, H-4, $^3J_{4-5}$ = 6.8 Hz), 4.36 (m, 1H, H-3), 4.48 (m, 1H, H-5), 5.56 (d, 1H, H-1, $^3J_{1-2}$ = 3.6 Hz), 7.1−7.5 (m, 12H, CH═). ^{13}C NMR: δ 0.1 (CH_3Si), 0.2 (CH_3Si), 0.2 (CH_3Si), 16.9 (C-6), 27.1 (CH_3), 27.3 (CH_3), 71.2 (C-5), 72.9 (d, C-3, J_{C-P} = 6.4 Hz), 78.9 (C-2), 83.1 (m, C-4), 104.8 (C-1), 113.8 (CMe_2), 124.7 (CH═), 124.8 (CH═), 124.9 (CH═), 130.8 (C), 130.9 (C), 131.1 (C), 132.3 (CH═), 132.5 (CH═), 132.6 (CH═), 134.8 (CH═), 135.1 (CH═), 135.3 (CH═), 150.9 (C), 151.1 (C), 151.2 (C).

3,5-Bis[((*S*)-1,1′-binaphthyl-2,2′-diyl)phosphite]-6-deoxy-1,2-O-isopropylidene-α-D-allofuranose (3d). Treatment of in situ formed phosphorochloridite **7d** (2.2 mmol) and **14** (0.21 g, 1 mmol) as described for compound **3c** afforded diphosphite **3d**, which was purified by flash chromatography (eluent toluene, R_f 0.45) to produce 0.42 g (51%) of a white powder. Anal. Calcd for $C_{49}H_{38}O_9P_2$: C, 70.67; H, 4.60. Found: C, 70.84; H, 4.78. ^{31}P NMR: δ 144.4 (s), 147.9 (s). ^{1}H NMR: δ 1.22 (d, 3H, H-6, $^3J_{6-5}$ = 7.2 Hz), 1.32 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 4.08 (d, 1H, H-4, $^3J_{4-5}$ = 7.2 Hz), 4.50 (m, 2H, H-2, H-3), 4.62 (m, 1H, H-5), 5.63 (d, 1H, H-1, $^3J_{1-2}$ = 3.2 Hz), 7.0−8.0 (m, 24H, CH═). ^{13}C NMR: δ 18.3 (C-6), 26.8 (CH_3), 26.9 (CH_3), 70.6 (d, C-5, J_{C-P} = 12.9 Hz), 73.2 (d, C-3, J_{C-P} = 9.1 Hz), 79.3 (C-2), 80.7 (m, C-4), 103.6 (C-1), 113.3 (CMe_2), 121.8 (CH═), 121.9 (CH═), 121.9 (CH═), 122.2 (CH═), 124.7 (CH═), 124.8 (CH═), 125.0 (CH═), 125.1 (CH═), 125.3 (CH═), 126.8 (CH═), 127.0 (CH═), 128.1 (CH═), 128.3 (CH═), 128.9 (CH═), 129.4 (CH═), 129.7 (CH═), 130.3 (CH═), 131.0 CH═), 131.5 (CH═), 132.2 (C), 132.6 (C), 132.7 (C), 132.8 (C), 146.9 (C), 147.4 (C), 147.9 (C), 148.4 (C).

3,5-Bis[((*R*)-1,1′-binaphthyl-2,2′-diyl)phosphite]-6-deoxy-1,2-O-isopropylidene-α-D-allofuranose (3e). Treatment of in situ formed phosphorochloridite **7e** (2.2 mmol) and **14** (0.21 g, 1 mmol) as described for compound **3c** afforded diphosphite **3e**, which was purified by flash chromatography (eluent toluene, R_f 0.45) to produce 0.39 g (48%) of a white powder. Anal. Calcd for $C_{49}H_{38}O_9P_2$: C, 70.67; H, 4.60. Found: C, 70.39, H, 4.68. ^{31}P NMR: δ 140.3 (s), 146.3 (s). ^{1}H NMR: δ 1.05 (d, 3H, H-6, $^3J_{6-5}$ = 6.4 Hz), 1.31 (s, 3H, CH_3), 1.55 (s, 3H, CH_3), 4.12 (m, 1H, H-4), 4.28 (m, 2H, H-2, H-3), 4.59 (m, 1H, H-5), 5.62 (d, 1H, H-1, $^3J_{1-2}$ = 3.2 Hz), 6.8−7.8 (m, 24H, CH═). ^{13}C NMR: δ 17.1 (d, C-6, J_{C-P} = 3 Hz), 26.7 (CH_3), 26.9 (CH_3), 71.0 (m, C-5), 72.0 (C-3), 79.0 (d, C-2, J_{C-P} = 1.9 Hz), 81.2 (m, C-4), 103.7 (C-1), 113.5 (CMe_2), 121.5 (CH═), 121.7 (CH═), 121.9 (CH═), 124.8 (CH═), 124.9 (CH═), 125.0 (CH═), 126.1 (CH═), 126.3 (CH═), 126.8 (CH═), 126.9 (CH═), 127.0 (CH═), 128.1 (CH═), 128.3 (CH═), 128.4 (CH═), 128.5 (CH═), 129.6 (CH═), 130.3 (CH═), 132.5 (C), 132.5 (C), 132.6 (C), 132.7 (C), 146.8 (C), 147.4 (C), 147.7 (C), 148.5 (C).

3,5-Bis[((S)-3,3′-bis(trimethylsilyl)-1,1′-binaphthyl-2,2′-diyl)phosphite]-6-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose (3f). Treatment of in situ formed phosphorochloridite **7f** (2.2 mmol) and **14** (0.21 g, 1 mmol) as described for compound **3c** afforded diphosphite **3f**, which was purified by flash chromatography (eluent toluene, R_f 0.50) to produce 0.39 g (35%) of a white powder. Anal. Calcd for $C_{61}H_{70}O_9P_2Si_4$: C, 65.33; H, 6.29. Found: C, 65.45; H, 6.37. ^{31}P NMR: δ 145.1 (s, 1P), 145.5 (s, 1P). ^{1}H NMR, δ: 0.31 (s, 9H, CH_3Si), 0.34 (s, 18H, CH_3Si), 0.36 (s, 9H, CH_3Si), 1.04 (d, 3H, H-6, $^3J_{6-5}$ = 7.2 Hz), 1.11 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 4.01 (m, 1H, H-4), 4.19 (d, 1H, H-2, $^3J_{2-1}$ = 3.6 Hz), 4.50 (m, 1H, H-3), 4.55 (m, 1H, H-5), 5.69 (d, 1H, H-1, $^3J_{1-2}$ = 3.6 Hz), 6.8−8.0 (m, 20H, CH═). ^{13}C NMR: δ −1.0 (CH_3Si), −0.2 (CH_3Si), 0.1 (CH_3Si), 0.5 (CH_3Si), 18.2 (C-6), 26.3 (CH_3), 26.5 (CH_3), 69.5 (m, C-5), 74.3 (m, C-3), 82.4 (C-4), 82.9 (C-2), 103.9 (C-1), 110.9 (CMe_2), 124.1 (CH═), 124.3 (CH═), 124.6 (CH═), 124.8 (CH═), 125.3 (CH═), 125.7 (CH═), 125.9 (CH═), 127.1 (CH═), 127.5 (CH═), 127.7 (CH═), 128.1 (CH═), 128.5 (CH═), 128.5 (CH═), 130.1 (C), 130.2 (C), 130.3 (C), 130.6 (C), 132.1 (C), 132.5 (C), 133.0 (C), 133.2 (C), 133.4 (C), 134.0 (C), 136.7 (CH═), 136.9 (CH═), 137.4 (CH═), 137.3 (CH═), 150.9 (C), 151.1 (C), 151.3 (C).

3,5-Bis[((*R*)-3,3′-bis(trimethylsilyl)-1,1′-binaphthyl-2,2′-diyl)phosphite]-6-deoxy-1,2-O-isopropylidene-α-D-allofuranose (3g). Treatment of in situ formed phosphorochloridite **7g** (2.2 mmol) and **14** (0.21 g, 1 mmol) as described for compound **3c** afforded diphosphite **3g**, which was purified by flash chromatography (eluent toluene, R_f 0.50) to produce 0.35 g (32%) of a white powder. Anal. Calcd for $C_{61}H_{70}O_9P_2Si_4$: C, 65.33; H, 6.29. Found: C, 65.27; H, 6.45. ^{31}P NMR: δ 146.2 (s, 1P), 148.0 (s, 1P). ^{1}H NMR: δ 0.34 (s, 9H, CH_3Si), 0.39 (s, 9H, CH_3Si), 0.41 (s, 9H, CH_3Si), 0.42 (s, 9H, CH_3Si), 0.92 (s, 3H, CH_3), 0.99 (d, 3H, H-6, $^3J_{6-5}$ = 7.2 Hz), 1.28 (s, 3H, CH_3), 4.12 (m, 1H, H-4), 4.38 (m, 2H, H-2, H-3), 4.51 (m, 1H, H-5), 5.41 (d, 1H, H-1, $^3J_{1-2}$ = 3.6 Hz), 7.0−8.0 (m, 20H, CH═). ^{13}C NMR: δ −0.8 (CH_3Si), −0.5 (CH_3Si), 0.1 (CH_3Si), 0.3 (CH_3Si), 18.7 (br, C-6), 27.4 (CH_3), 27.5 (CH_3), 71.4 (m, C-5), 77.5 (m, C-3), 82.1 (C-4), 82.9 (m, C-2), 104.3 (C-1), 112.1 (CMe_2), 125.1 (CH═), 125.2 (CH═), 125.3 (CH═), 125.5 (CH═), 127.0 (CH═), 127.1 (CH═), 127.6 (CH═), 127.8 (CH═), 127.9 (CH═), 128.1 (CH═), 128.4 (CH═), 128.5 (CH═), 128.7 (CH═), 130.4 (C), 130.5 (C), 130.6 (C), 130.8 (C), 131.9 (C), 132.1 (C), 132.5 (C), 132.7 (C), 132.8 (C), 133.9 (C), 134.1 (C), 136.5 (CH═), 136.6 (CH═), 137.1 (CH═), 137.2 (CH═), 137.4 (CH═), 151.2 (C), 151.3 (C), 151.5 (C), 151.6 (C).

3,5-Bis[(3,3′-bis(trimethylsilyl)-1,1′-biphenyl-2,2′-diyl)-phosphite]-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (4c). Treatment of in situ formed phosphorochloridite **7c** (2.2 mmol) and **15** (0.21 g, 1 mmol) as described for compound **3c** afforded diphosphite **4c**, which was purified by flash chromatography (eluent toluene, R_f 0.85) to produce 0.80 (86%) of a white powder. Anal. Calcd for $C_{45}H_{62}O_9P_2Si_4$: C, 58.67; H, 6.78. Found: C, 58.87; H, 6.86. ^{31}P NMR: δ 146.2 (d, 1P, $^6J_{P-P}$ = 23 Hz), 147.3 (d, 1P, $^6J_{P-P}$ = 23 Hz). ^{1}H NMR: δ 0.35 (s, 18H, CH_3Si), 0.36 (s, 9H, CH_3Si), 0.41 (s, 9H, CH_3Si), 1.02 (s, 3H, CH_3), 1.08 (d, 3H, H-6, $^3J_{6-5}$ = 6 Hz), 1.38 (s, 3H, CH_3), 3.38 (d, 1H, H-2, $^3J_{2-1}$ = 3.6 Hz), 4.03 (dd, 1H, H-4, $^3J_{4-5}$ = 7.6 Hz, $^3J_{4-3}$ = 2.4 Hz), 4.68 (m, 1H, H-5), 4.70 (dd, 1H, H-3, $^3J_{3-4}$ = 2.4 Hz, J_{3-P} = 5.2 Hz), 5.41 (d, 1H, H-1, $^3J_{1-2}$

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= 3.6 Hz), 7.0−7.6 (m, 12H, CH=). ^{13}C NMR: δ −0.2 (CH_3Si), 0.1 (CH_3Si), 0.2 (CH_3Si), 19.7 (C-6), 25.7 (CH_3), 26.4 (CH_3), 68.6 (C-5), 76.4 (d, C-3, J_{C-P} = 9.2 Hz), 82.7 (9 (t, C-4, J_{C-P} = 4.8 Hz), 83.8 (C-2), 104.6 (C-1), 111.4 (CMe_2), 124.4 (CH=), 124.6 (CH=), 124.9 (CH=), 130.9 (C), 131.1 (C), 131.2 (C), 132.0 (CH=), 132.2 (CH=), 132.5 (CH=), 134.9 (CH=), 135.1 (CH=), 153.4 (C), 153.5 (C), 153.6 (C).

Asymmetric Hydrogenation Reactions. In a typical experiment, the autoclave was filled with a dichloromethane solution (6 mL) of substrate (1 mmol), $[Rh(cod)_2]BF_4$ (4.95 mg, 0.01 mmol), and ligand (0.011 mmol). This was then purged three times with H_2 and a vacuum. The reaction mixture was then stirred under H_2 (5 atm) at room temperature. To remove the catalyst, the solution was placed on a short silica gel column and eluted with CH_2Cl_2. Conversion and enantiomeric excesses were determined by gas chromatography.

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