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Carbohydrate-derived monophosphite ligands for Rh-catalyzed enantioselective hydrogenation of α- and β-dehydroamino acid esters

Hanmin Huang, Xiongcai Liu, Song Chen, Huilin Chen and Zhuo Zheng*

Dalian Institute of Chemical Physics, The Chinese Academy of Sciences, Dalian 116023, PR China

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Abstract—A series of monophosphite ligands derived from D-fructose and D-glucose have been synthesized and employed in Rh-catalyzed asymmetric hydrogenation of α- and β-dehydroamino acid esters. A variety of chiral α- and β-amino acid esters have been obtained in excellent enantiomeric excess (up to 98.4% ee).

1. Introduction

The enantioselective hydrogenation of prochiral olefins constitutes a standard tool for the synthesis of optically active amino acids.[1] Although many efficient diphosphorus chiral ligands have been developed for this asymmetric reaction, only a few efficient monophosphorus ligands are reported to date, which may be ascribed to the free rotation of M–P bond in the complexes of monodentate ligands. With leading efforts by Pringle et al.,[2] Reetz and Mehler[3] and Feringa et al.,[4] some easily prepared and efficient chiral monophosphorus ligands have been developed, and these have exhibited high enantioselectivity in asymmetric hydrogenation.[5]

For many years, carbohydrates have been extensively explored as backbones for chiral ligands due to their easy modification and ready availability. Excellent results have been obtained with carbohydrate-based bidentate ligands in asymmetric hydrogenation.[6] However, few good monodentate chiral ligands have been reported based on carbohydrates.[5a,b,8] Recently, we have designed and synthesized a new class of chiral monophosphorus ligands **1**–**4** from carbohydrates, which contain additional groups in the appropriate spatial configuration to effectively restrain the rotation of M–P bond by secondary interactions between the metal and the ligand.[7] These ligands exhibited excellent enantioselectivity in the Rh-catalyzed asymmetric hydrogenation of dimethyl itaconate (up to 99.6%) and *E*/*Z* mixtures of enamides (up to 98.5%).[8] Further interest in establishing the general utility of the design concept and continuing our research interest to develop carbohydrate-derived chiral ligands[9] for asymmetric catalysis led us to examine the asymmetric hydrogenation of α- and β-dehydroamino acid esters by using these ligands.

2. Results and discussion

2.1. Synthesis of chiral monophosphite ligands

The ligands **1**–**4** were synthesized very efficiently from commercial BINOL and the corresponding monosaccharide alcohols, which were synthesized on a large scale from D-fructose and D-glucose.[10] The RO–PCl_2 intermediates were prepared by the reaction of alcohols with PCl_3 in the absence of Et_3N. These were then directly reacted with BINOL in the presence of Et_3N to afford the desired product. Ligands **1**–**4** were easily purified through a short silica gel plug and were stable in the solid state (Fig. 1).

2.2. Asymmetric hydrogenation of acetamidoacrylic acid esters

The active catalyst employed in our study was generated in situ from cationic $[Rh(COD)_2]BF_4$ and the

* Corresponding author. Tel.: +86-411-84379276; fax: +86-411-8468-4746; e-mail: zhengz@dicp.ac.cn

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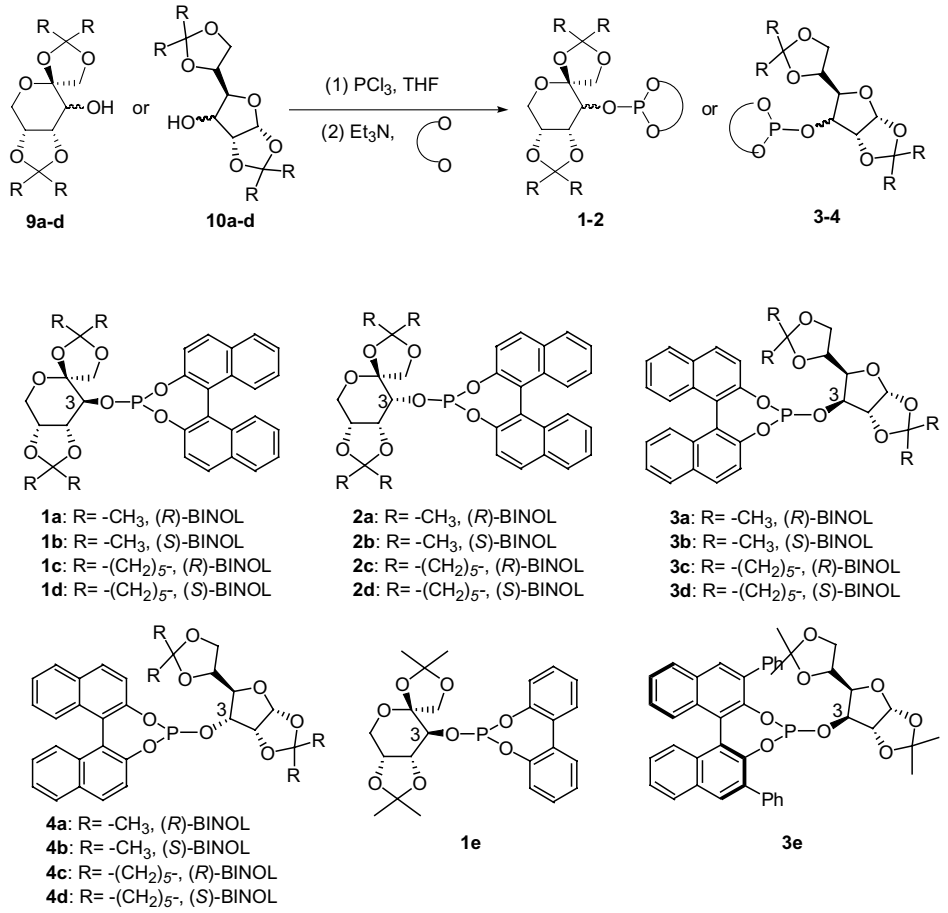
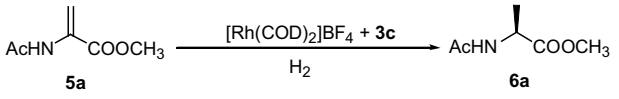


Figure 1. Synthesis of monophosphite ligands **1**–**4**.

monophosphite (1:2.2). Methyl acetamidoacrylate **5a** was chosen as a model substrate and **3c** was chosen as a ligand to screen various reaction conditions. As shown in Table 1, the enantioselectivity of the reaction was sensitive to the solvent used, and CH_2Cl_2 is the solvent of choice. In contrast, the hydrogen pressure has only a small influence on these asymmetric catalytic systems, lower hydrogen pressures gave higher ee values. As a result of the high activity of these catalysts, the reaction can be carried out at ambient hydrogen pressure in quantitative conversion with higher ee value.

Optimal reaction conditions with the Rh-monophosphite catalyst use CH_2Cl_2 as the solvent and an initial hydrogen pressure of 1.2 atm. Under these conditions, we next examined the catalytic properties of the other ligands for the hydrogenation of **5a**. The results are summarized in Table 2 and show that the carbohydrate-derived monophosphites are efficient ligands for this asymmetric hydrogenation reaction. However, the enantioselectivities proved to be dramatically influenced by the structure of the ligands. Comparison of the results in the Table 2 shows that the enantiomeric excess depends strongly on the absolute configuration of carbon atom at C-3 in carbohydrate backbone. In general, D-fructose-derived ligands **2a**–**d**, with *R* configuration at C-3, produced much higher enantioselectivities than

Table 1. The effect of solvent and H_2 pressure on the asymmetric hydrogenation of methyl 2-acetamidoacrylate[a]



5a 6a

Entry	Solvent	$P(H_2)$ (atm)	Ee% (config.)[b]
1	CH_2Cl_2	10	87.7 (*S*)
2	CH_2Cl_2	5	87.7 (*S*)
3	CH_2Cl_2	1.2	89.1 (*S*)
4	EtOAc	1.2	83.9 (*S*)
5	Toluene	1.2	86.7 (*S*)
6[c]	CH_3OH	1.2	21.1 (*S*)
7	THF	1.2	87.3 (*S*)

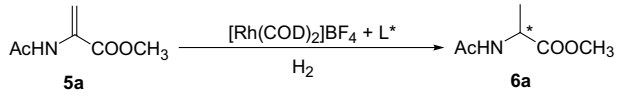
[a] The reactions were carried out at room temperature for 12 h, substrate/$[Rh(COD)_2]BF_4$/**3c** = 1.0/0.01/0.022. 100% conversion in all cases.

[b] Determined by GC with a Supelco Chiral Select 1000 capillary column and the absolute configuration was determined by comparing the sign of specific rotation.

[c] 22% conversion.

ligands **1a**–**d** with the opposite configuration on C-3. Similarly, for the D-glucose-derived ligands **3**–**4**, the absolute configuration at C-3 in the carbohydrate backbone also dramatically influenced the enantiomeric excesses. These observations are in agreement with those observed in the hydrogenation of dimethyl itaconate

Table 2. Enantioselective hydrogenation of methyl 2-acetamidoacrylate[a]



Entry	Ligand	Ee% (config.)[b]
1	**1a**	47.5 (*R*)
2	**1b**	0
3	**1c**	63.3 (*R*)
4	**1d**	33.6 (*S*)
5	**2a**	85.9 (*S*)
6	**2b**	45.0 (*R*)
7	**2c**	85.0 (*S*)
8	**2d**	5.5 (*R*)
9	**1e**	24.8 (*R*)
10	**3a**	87.9 (*S*)
11	**3b**	79.9 (*R*)
12	**3c**	89.1 (*S*)
13	**3d**	75.3 (*R*)
14	**4a**	26.5 (*R*)
15	**4b**	5.5 (*S*)
16	**4c**	38.1 (*R*)
17	**4d**	4.4 (*S*)
18	**3e**	39.0 (*R*)

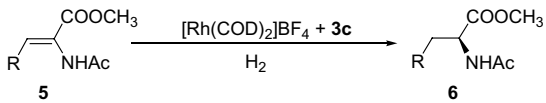
[a] The reactions were carried out in CH_2Cl_2 at room temperature for 12 h, $P(H_2) = 1.2$ atm, substrate/$[Rh(COD)_2]BF_4$/ligand = 1.0/0.01/0.022. 100% conversion in all cases.

[b] Determined by GC with a Supelco Chiral Select 1000 capillary column and the absolute configuration was determined by comparing the sign of specific rotation.

and α-arylenamides.[8] However, all carbohydrate backbones regardless of the *R* or *S* configuration at C-3 are matched co-operatively to (*R*)-BINOL, which is quite different to those observed in the hydrogenation of dimethyl itaconate and α-arylenamides, in which the carbohydrate backbones with (*R*)-configuration at C-3 are matched with (*R*)-BINOL while (*S*)-BINOL is matched to the corresponding carbohydrate backbones with (*S*)-configuration at C-3 in it.[8] On the other hand, comparison of the results obtained by ligand **3b** (entry 11, Table 2, 79.9% ee) and **3e** (entry 18, Table 2, 39.0% ee) indicated that introducing an additional substitutent in the 3,3′-positions of the BINOL-framework has a disadvantageous influence on the enantioselectivity. This is consistent with Börner's report.[11]

To expand the utility of these monophosphite ligands, we subsequently applied the efficient monophosphite **3c** in the Rh-catalyzed hydrogenation of other acetamidoacrylic acid esters **5b–f**, (Table 3). It was found that good enantioselectivities were observed for the desired products and the substitutents on the phenyl ring of the methyl (*Z*)-2-acetamidocinnamate had little effect on the enantioselectivity. Introducing an electron-withdrawing group into the acetamidoacrylic acid esters resulted in lower enantioselectivity (entries 5 and 6, Table 3) while substrates with an electron-donating group showed higher enantioselectivity (entry 2, Table 3, 88.5% ee). The substitution at the *ortho* position of the phenyl ring led to a lower ee value (entry 3 vs entry 4, entry 5 vs 6, Table 3).

Table 3. Enantioselective hydrogenation of acetamidoacrylic acid esters[a]



Entry	Substrate	R	Ee% (config.)[b]
1	**5a**	H	89.1 (*S*)
2	**5b**	Ph	86.1 (*S*)
3	**5c**	*p*-$CH_3OC_6H_4$	88.5 (*S*)
4	**5d**	*o*-$CH_3OC_6H_4$	85.7 (*S*)
5	**5e**	*p*-ClC_6H_4	86.1 (*S*)
6	**5f**	*o*-ClC_6H_4	80.3 (*S*)

[a] The reactions were carried out in CH_2Cl_2 at room temperature for 12 h, $P(H_2) = 1.2$ atm, substrate/$[Rh(COD)_2]BF_4$/**3c** = 1.0/0.01/0.022. 100% conversion in all cases.

[b] Determined by GC with a Supelco Chiral Select 1000 and a CP-Chrialsil-L-Val capillary column, the absolute configuration was determined by comparing the sign of specific rotation.

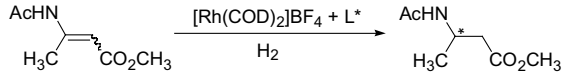
2.3. Asymmetric hydrogenation of β-(acylamino)acrylates

Chiral β-amino acids have attracted great interest for their utility as chiral building blocks in the synthesis of β-peptides and β-lactams.[12] One of the most promising methodologies for their synthesis is the asymmetric hydrogenation of the appropriate β-dehydroamino acid precursors catalyzed by homogeneous Rh or Ru complexes containing chiral phosphane ligands.[13] However, in striking contrast to the application of this methodology for the synthesis of α-amino acids, which was developed over the last three decades to a standard procedure in organic chemistry, there are few efficient monophosphorus ligands employed in this reaction.[5a,i,n] To broaden further the utility of our inexpensive monophosphite ligands, we applied the monophosphite **1–4** in the Rh-catalyzed hydrogenation of β-(acylamino)acrylates. 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.

To identify the most efficient ligands, the catalytic performance of ligands **1–4** was thoroughly examined under 'standard' conditions (a ligand-to-Rh ratio of 2.2, an hydrogen pressure of 10 atm, *i*-PrOH as a solvent for *Z*-isomer, CH_2Cl_2 as a solvent for *E*-isomer); the results are given in Tables 4 and 5.

The screening of our ligands showed that the observed enantioselectivities and activities were again strongly sensitive to the configuration at C-3 and the protecting groups of the carbohydrate skeletons. Fructose-derived ligands **1a–d**, with an *S* configuration at C-3, demonstrated much higher activities and enantioselectivities for both the *E*- and *Z*-β-(acylamino)acrylates than ligands **2a–d** with the opposite configuration at C-3. On the other hand, the protecting groups on the carbohydrate moieties dramatically influenced the activities and enantioselectivities of catalysts. In all cases, the sterically more bulky cyclohexanone-protected ligands gave much higher catalytic activity and enantioselectivity than the corresponding acetone-protected ligands (**1c–d** vs **1a–b**).

Table 4. Enantioselective hydrogenation of methyl 3-acetamido-2-butenoate[a]

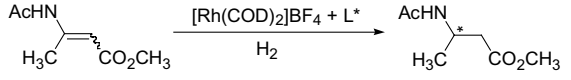


(*E*) or (*Z*)-7a — 8a

Entry	Ligand	Substrate	Conv.%	Ee% (config.)[b]
1	**1a**	*E*-**7a**	<5	N/A
2	**1b**	*E*-**7a**	<5	N/A
3	**1c**	*E*-**7a**	40	85.3 (*R*)
4	**1d**	*E*-**7a**	10	69.1 (*S*)
5	**2a**	*E*-**7a**	<5	N/A
6	**2b**	*E*-**7a**	<5	N/A
7	**2c**	*E*-**7a**	<5	N/A
8	**2d**	*E*-**7a**	<5	N/A
9	**1a**	*Z*-**7a**	25	29.7 (*S*)
10	**1b**	*Z*-**7a**	73	28.1 (*S*)
11	**1c**	*Z*-**7a**	100	20.1 (*R*)
12	**1d**	*Z*-**7a**	6	69.0 (*R*)
13	**2a**	*Z*-**7a**	<5	N/A
14	**2b**	*Z*-**7a**	53	7.1 (*S*)
15	**2c**	*Z*-**7a**	13	6.7 (*S*)
17	**2d**	*Z*-**7a**	12	29.3 (*R*)

[a] The reactions were carried out at room temperature for 12 h, the solvent for *E*-substrate is CH_2Cl_2, for *Z*-substrate is *i*-PrOH, $P(H_2) = 10$ atm, Substrate/$[Rh(COD)_2]BF_4$/ligand = 0.5/0.01/0.022.
[b] Determined by GC with Chiral Select 1000 capillary column and the absolute configuration was determined by comparing the sign of specific rotation.

Table 5. Enantioselective hydrogenation of methyl 3-acetamido-2-butenoate[a]



(*E*) or (*Z*)-7a — 8a

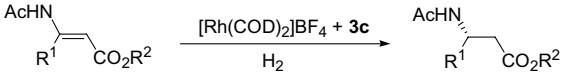
Entry	Ligand	Substrate	Conv.%	Ee% (config.)[b]
1	**3a**	*E*-**7a**	<5	N/A
2	**3b**	*E*-**7a**	<5	N/A
3	**3c**	*E*-**7a**	40	97.5 (*S*)
4	**3d**	*E*-**7a**	52	88.4 (*R*)
5	**4a**	*E*-**7a**	7	87.1 (*S*)
6	**4b**	*E*-**7a**	<5	N/A
7	**4c**	*E*-**7a**	<5	N/A
8	**4d**	*E*-**7a**	10	15.0 (*R*)
9	**3e**	*E*-**7a**	<5	N/A
10	**3a**	*Z*-**7a**	88	7.5 (*S*)
11	**3b**	*Z*-**7a**	37	51.5 (*R*)
12	**3c**	*Z*-**7a**	96	4.1 (*S*)
13	**3d**	*Z*-**7a**	64	60.5 (*R*)
14	**4a**	*Z*-**7a**	6	50.9 (*S*)
15	**4b**	*Z*-**7a**	37	17.1 (*S*)
16	**4c**	*Z*-**7a**	<5	N/A
17	**4d**	*Z*-**7a**	30	29.9 (*S*)
18	**3e**	*Z*-**7a**	19	55.7 (*R*)

[a] The reactions were carried out at room temperature for 12 h, the solvent for *E*-substrate is CH_2Cl_2, for *Z*-substrate is *i*-PrOH, $P(H_2) = 10$ atm, substrate/$[Rh(COD)_2]BF_4$/ligand = 0.5/0.01/0.022.
[b] Determined by GC with Chiral Select 1000 capillary column and the absolute configuration was determined by comparing the sign of specific rotation.

These observations are in contrast to those observed in hydrogenations of other types of functionalized olefins.[8] Similar observations were made with D-glucose-derived ligands **3** and **4**. In terms of reactivity and enantioselectivity, **1c**, **3c** and **3d** are better chiral ligands, with ligand **3c**, the higher ee value 97.5% was obtained with 40% conversion in the hydrogenation of *E*-methyl 3-acetamido-2-butenoate.

The screening of solvents demonstrated that CH_2Cl_2 is the best solvent for the *E*-isomer. The effect of hydrogen pressure was also investigated with **3c** as a ligand and *E*-methyl 3-acetamido-2-butenoate as a modular substrate, the results were collected in Table 6. The results show that activity was notably enhanced when the hydrogen pressure was raised from 10 to 30 atm (entries 1–3, Table 6), however, increasing the hydrogen pressure further had a negative effect on activity (entry 4, Table 6). In addition, on prolonging the reaction time from 12 to 48 h, the conversion reminded the same (entry 3 vs entry 4, Table 6). The enantioselectivity was also slightly decreased when the H_2 pressure increased (entries 1–3, Table 6).

Table 6. Enantioselective hydrogenation of β-(acylamino)acrylates[a]



7a: $R^1 = CH_3$, $R^2 = CH_3$
7b: $R^1 = CH_3$, $R^2 = C_2H_5$
7c: $R^1 = C_2H_5$, $R^2 = CH_3$
7d: $R^1 = Ph$, $R^2 = C_2H_5$

8a-d

Entry	Substrate	$P(H_2)$ (atm)	Conv.%	Ee% (config.)[b]
1	*E*-**7a**	10	40	97.5 (*S*)
2	*E*-**7a**	20	52	95.0 (*S*)
3	*E*-**7a**	30	73	95.3 (*S*)
4[c]	*E*-**7a**	30	78	95.5 (*S*)
5	*E*-**7a**	40	44	96.5 (*S*)
6	*E*-**7b**	30	65	95.7 (*S*)
7	*E*-**7c**	30	92	98.4 (*S*)
8	**7d**	30	80	93.0 (*S*)

[a] The reactions were carried out at room temperature for 12 h, the solvent is CH_2Cl_2, substrate/$[Rh(COD)_2]BF_4$/**3c** = 0.5/0.01/0.022.
[b] Determined by GC with Chiral Select 1000 capillary column and the absolute configuration was determined by comparing the sign of specific rotation.
[c] The reaction time is 48 h.

The hydrogenation of a series of *E*-β-alkyl-substituted β-(acylamino)acrylates and β-aryl-substituted β-(acylamino)acrylates was examined in CH_2Cl_2 under an H_2 pressure of 30 atm at room temperature with $[Rh(COD)_2]BF_4$/**3c** as a catalyst precursor (entries 6–8, Table 6). For β-alkyl-substituted β-(acylamino) acrylates, the ligand **3c** exhibited excellent enantioselectivities (95.0–98.4% ee) with moderate to good conversion. Moreover, for the β-phenyl-substituted β-(acylamino)acrylates, high ee value (93% ee, entry 8, Table 6) with good conversion also being obtained.

3. Conclusions

In conclusion, we have carried out the asymmetric hydrogenation of α- and β-dehydroamino acid esters using Rh-complexes of the carbohydrate-derived monophosphites **1**–**4** as catalysts. The pronounced effect of the carbohydrate backbones of these ligands observed in this asymmetric reaction further confirmed that the additional groups orientated in a proper spatial configuration contained in monophosphites are beneficial for improvement of enantioselectivity, which also provides new insights into the design of efficient chiral monophosphorus ligands. The design and synthesis of more effective chiral monophosphorus ligands containing additional groups and their applications in asymmetric catalytic hydrogenation are currently in progress.

4. Experimental

4.1. General methods

All reactions were carried out under an N_2 atmosphere. NMR spectra were measured on a Bruker DRX-400 NMR spectrometer. Optical rotations were measured with a JASCO P-1020 automatic polarimeter. High resolution mass spectra were recorded on Applied Biosystems Mariner System 5303. Enantiomeric excess (ee) determination was carried out using GC with a Supelco Chiral Select 1000 and a CP-chiralsil-L-Val capillary column on an Agilent HP-4890 GC instrument with FID as detector. All solvents were dried and degassed by standard methods. 1,2:4,5-Di-*O*-isopropylidene-D-fructose **9a**, 1,2:4,5-Di-*O*-cyclohexylidene-D-fructose **9b**, 1,2:4,5-Di-*O*-isopropylidene-β-D-fructopyranose **9c**, 1,2:4,5-Di-*O*-*cyclo*-hexylidene-β-D-fructopyranose **9d**, 1,2:5,6-Di-*O*-isopropylidene-D-glucose **10a**, 1,2:5,6-Di-*O*-cyclohexylidene-D-glucose **10b**, 1,2:5,6-Di-*O*-isopropylidene-β-D-glucofuranose **10c**, 1,2:5,6-Di-*O*-cyclohexylidene-β-D-glucofuranose **10d** and (*S*)-3,3′-diphenyl-2,2′-dihydroxy-1,1′-binaphthyl were prepared according to the literature procedures.[10,14] All other chemicals were obtained commercially.

4.2. General procedures for the synthesis of monophosphite ligands 1–4

To a stirred solution of **9** or **10** (1.5 mmol) in THF (5 mL) was slowly added PCl_3 (132 μL, 1.5 mmol) as a solution in THF (4 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 solid 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), furnished the title ligands as white foam in 75–90% yield.

4.2.1. 1,2:4,5-Di-*O*-isopropylidene-3-*O*-((*R*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-fructose 1a. The above procedure was followed using **9a** and *R*-BINOL. After workup, it gave **1a**. Mp 121–122 °C; $[\alpha]_D^{12} = -430.5$ (*c* 1.06, THF); ^{1}H NMR (DMSO-d_6): δ 1.27 (s, 3H), 1.34 (s, 3H), 1.43 (s, 3H), 1.53 (s, 3H), 3.99 (m, 3H), 4.09 (t, $J = 6.4$ Hz, 1H), 4.24 (d, $J = 9.2$ Hz, 1H), 4.30 (t, $J = 4.8$ Hz, 1H), 4.43 (t, $J = 8.4$ Hz, 1H), 7.21–7.24 (m, 2H), 7.34–7.36 (m, 2H), 7.47–7.57 (m, 4H), 8.05–8.10 (m, 3H), 8.17 (d, $J = 8.8$ Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 26.15, 27.87, 59.96, 71.44, 73.35, 73.94, 74.11, 75.16, 103.74, 108.88, 111.62, 121.67, 122.00, 122.26, 123.56, 125.13, 125.37, 125.89, 126.01, 126.60, 126.78, 128.57, 128.71, 129.95, 130.75, 130.87, 131.20, 131.71, 132.02, 146.79, 147.36; ^{31}P NMR (DMSO-d_6): δ 159.37; HRMS (APCI) calcd for $C_{32}H_{32}O_8P$ (M^++1): 575.1829, found: 575.1850.

4.2.2. 1,2:4,5-Di-*O*-isopropylidene-3-*O*-((*S*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-fructose 1b. The above procedure was followed using **9a** and *S*-BINOL. After workup, it gave **1b**. Mp 107–108 °C; $[\alpha]_D^{12} = +197.0$ (*c* 1.20, THF); ^{1}H NMR (DMSO-d_6): δ 0.90 (s, 3H), 1.33 (s, 3H), 1.39 (s, 3H), 1.51 (s, 3H), 3.84 (d, $J = 9.2$ Hz, 1H), 3.95–3.99 (m, 3H), 4.27–4.37 (m, 3H), 7.21–7.23 (m, 2H), 7.33–7.35 (m, 2H), 7.51–7.54 (m, 3H), 7.61 (d, $J = 8.8$ Hz, 1H), 8.04–8.17 (m, 4H); ^{13}C NMR (DMSO-d_6): δ 25.19, 26.37, 26.60, 27.92, 59.61, 70.54, 73.16, 73.31, 73.43, 75.51, 103.54, 108.92, 111.69, 121.70, 122.04, 123.50, 125.08, 125.31, 125.87, 126.02, 126.49, 126.72, 128.54, 128.69, 129.99, 130.76, 131.17, 131.64, 132.07, 146.96, 147.36; ^{31}P NMR (DMSO-d_6): δ 158.48; HRMS (APCI) calcd for $C_{32}H_{32}O_8P$ (M^++1): 575.1829, found: 575.1841.

4.2.3. 1,2:4,5-Di-*O*-cyclohexylidene-3-*O*-((*R*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-fructose 1c. The above procedure was followed using **9b** and *R*-BINOL. After workup, it gave **1c**. Mp 135–136 °C; $[\alpha]_D^{25} = -382.45$ (*c* 1.08, THF); ^{1}H NMR (DMSO-d_6): δ 1.24–1.75 (m, 20H), 3.97–4.04 (m, 3H), 4.10 (t, $J = 6.4$ Hz, 1H), 4.23 (d, $J = 9.2$ Hz, 1H), 4.30 (d, $J = 4.4$ Hz, 1H), 4.42 (t, $J = 8.4$ Hz, 1H), 7.21–7.24 (m, 2H), 7.33–7.38 (m, 2H), 7.46–7.53 (m, 4H), 8.05–8.09 (m, 3H), 8.18 (d, $J = 8.8$ Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 23.32, 23.56, 23.68, 24.40, 24.54, 35.05, 35.16, 35.47, 37.32, 60.25, 71.06, 73.03, 74.25, 74.43, 74.80, 403.34, 109.45, 112.20, 121.49, 122.01, 122.32, 123.62, 125.14, 125.38, 125.89, 126.02, 126.62, 126.81, 128.59, 128.73, 129.76, 130.77, 130.95, 131.19, 131.73, 132.06, 146.83, 147.41; ^{31}P NMR (DMSO-d_6): 159.55; HRMS (APCI) calcd for $C_{38}H_{40}O_8P$ (M^++1): 655.2455, found: 655.2508.

4.2.4. 1,2:4,5-Di-*O*-cyclohexylidene-3-*O*-((*S*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-fructose 1d. The above procedure was followed using **9b** and *S*-BINOL. After workup, it gave **1d**. Mp 153–154 °C; $[\alpha]_D^{25} = +147.9$ (*c* 0.98, THF); ^{1}H NMR (DMSO-d_6): δ 1.07–1.69 (m, 20H), 3.83–4.00 (m, 4H), 4.30–4.32 (m, 2H), 4.38 (m,

1H), 7.21–7.22 (m, 2H), 7.32–7.36 (m, 2H), 7.47–7.62 (m, 4H), 8.05–8.17 (m, 4H); ^{13}C NMR (DMSO-d_6): δ 22.10, 22.54, 22.97, 23.38, 23.50, 24.28, 24.45, 34.29, 35.28, 36.05, 37.42, 59.78, 70.16, 73.14, 73.32, 73.47, 75.19, 103.19, 109.48, 112.17, 121.71, 121.96, 122.11, 123.52, 125.07, 125.32, 125.87, 126.01, 126.50, 126.73, 128.55, 128.70, 130.04, 130.77, 131.17, 131.67, 132.08, 146.99, 147.41; ^{31}P NMR (DMSO-d_6): δ 158.47; HRMS (APCI) calcd for $C_{38}H_{40}O_8P$ (M^++1): 655.2455, found: 655.2481.

4.2.5. 1,2:4,5-Di-*O*-isopropylidene-3-*O*-(2,2′-*O*,*O*-(1,1′-biphenyl)dioxophosphite)-D-fructose 1e. The above procedure was followed using **9a** and biphenol. After workup, it gave **1e**. Mp 117–118 °C; $[\alpha]_D^{25} = -123.6$ (*c* 1.06, THF); ^{1}H NMR (DMSO-d_6): δ 1.15 (s, 3H), 1.36 (s, 3H), 1.39 (s, 3H), 1.51 (s, 3H), 3.92 (d, $J = 8.8$ Hz, 1H), 3.99 (s, 2H), 4.07 (d, $J = 9.2$ Hz, 1H), 4.19 (t, $J = 6.4$ Hz, 1H), 4.33–4.38 (m, 2H), 7.23–7.26 (m, 2H), 7.33–7.36 (m, 2H), 7.41–7.46 (m, 2H), 7.55 (m, 2H), ^{13}C NMR (DMSO-d_6): δ 25.66, 26.32, 26.50, 27.92, 59.75, 70.95, 73.24, 73.40, 75.45, 103.67, 108.87, 111.75, 122.11, 125.48, 129.44, 129.86, 130.60, 148.59; ^{31}P NMR (DMSO-d_6): δ 155.69; HRMS (APCI) calcd for $C_{24}H_{28}O_8P$ (M^++1): 475.1516, found: 475.1502.

4.2.6. 1,2:4,5-Di-*O*-isopropylidene-3-*O*-((*R*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-β-D-fructopyranose 2a. The above procedure was followed using **9c** and *R*-BINOL. After workup, it gave **2a**. Mp 120–121 °C; $[\alpha]_D^{25} = -360.7$ (*c* 1.20, THF); ^{1}H NMR (DMSO-d_6): δ 1.27 (s, 3H), 1.33 (s, 3H), 1.40 (s, 3H), 1.46 (s, 3H), 3.57 (d, $J = 13.2$ Hz, 1H), 3.67 (d, $J = 9.2$ Hz, 1H), 3.82 (d, $J = 13.2$ Hz, 1H), 4.04 (d, $J = 9.2$ Hz, 1H), 4.40 (d, $J = 7.6$ Hz, 1H), 4.72 (d, $J = 8.0$ Hz, 1H), 4.91 (d, $J = 10.4$ Hz, 1H), 7.20–7.22 (m, 2H), 7.34–7.38 (m, 2H), 7.49–7.58 (m, 4H), 8.08–8.19 (m, 4H); ^{13}C NMR (DMSO-d_6): δ 24.60, 25.86, 26.06, 26.27, 62.59, 70.55, 71.09, 71.26, 73.40, 73.78, 104.70, 108.69, 109.02, 121.45, 121.98, 125.22, 125.47, 125.85, 126.01, 126.68, 126.85, 128.64, 128.72, 130.09, 130.86, 131.01, 131.26, 131.80, 132.03, 146.59, 147.08; ^{31}P NMR (DMSO-d_6): δ 157.75; HRMS (APCI) calcd for $C_{32}H_{32}O_8P$ (M^++1): 575.1829, found: 575.1786.

4.2.7. 1,2:4,5-Di-*O*-isopropylidene-3-*O*-((*S*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-β-D-fructopyranose 2b. The above procedure was followed using **9c** and *S*-BINOL. After workup, it gave **2b**. Mp 147–148 °C; $[\alpha]_D^{25} = +201.1$ (*c* 0.89, THF); ^{1}H NMR (DMSO-d_6): δ 1.23 (s, 3H), 1.32 (s, 3H), 1.48 (s, 3H), 1.58 (s, 3H), 3.58 (d, $J = 13.2$ Hz, 1H), 3.82–3.85 (m, 2H), 4.32–4.36 (m, 2H), 4.42–4.44 (m, 1H), 4.92 (m, 1H), 7.23–7.25 (m, 2H), 7.34–7.36 (m, 2H), 7.50–7.52 (m, 2H), 7.59 (d, $J = 8.8$ Hz, 1H), 7.77 (d, $J = 8.8$ Hz, 1H), 8.07–8.20 (m, 4H); ^{13}C NMR (DMSO-d_6): δ 24.49, 25.44, 25.98, 26.06, 62.65, 70.90, 72.82, 73.03, 73.51, 73.87, 105.07, 108.86, 109.07, 121.46, 122.04, 123.43, 125.24, 125.40, 125.88, 126.00, 126.65, 126.80, 128.57, 128.69, 130.27, 130.81, 130.92, 131.20, 131.75, 132.04, 146.69, 147.75; ^{31}P NMR (DMSO-d_6): δ 160.52; HRMS (APCI) calcd for $C_{32}H_{32}O_8P$ (M^++1): 575.1829, found: 575.1797.

4.2.8. 1,2:4,5-Di-*O*-cyclohexylidene-3-*O*-((*R*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-β-D-fructopyranose 2c. The above procedure was followed using **9d** and *R*-BINOL. After workup, it gave **2c**. Mp 134–135 °C; $[\alpha]_D^{25} = -325.4$ (*c* 1.05, THF); ^{1}H NMR (DMSO-d_6): δ 1.35–1.72 (m, 20H), 3.57 (d, $J = 13.2$ Hz, 1H), 3.67 (d, $J = 9.2$ Hz, 1H), 3.84 (d, $J = 12.8$ Hz, 1H), 4.00 (t, $J = 9.2$ Hz, 1H), 4.41 (d, $J = 7.6$ Hz, 1H), 4.72 (d, $J = 8.0$ Hz, 1H), 4.94 (d, $J = 10.4$ Hz, 1H), 7.20–7.24 (m, 2H), 7.34–7.37 (m, 2H), 7.48–7.57 (m, 4H), 8.08 (m, 3H), 8.17–8.20 (d, $J = 8.8$ Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 23.24, 23.36, 23.50, 24.56, 33.77, 35.21, 35.33, 35.52, 62.69, 70.06, 71.10, 71.29, 73.13, 73.53, 104.18, 109.29, 109.67, 121.37, 121.99, 122.08, 123.52, 125.23, 125.48, 125.84, 126.01, 126.68, 126.86, 128.66, 128.72, 129.98, 130.87, 131.05, 131.26, 131.79, 132.04, 146.54, 147.10; ^{31}P NMR (DMSO-d_6): δ 153.43; HRMS (APCI) calcd for $C_{38}H_{40}O_8P$ (M^++1): 655.2455, found: 655.2434.

4.2.9. 1,2:4,5-Di-*O*-cyclohexylidene-3-*O*-((*S*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-β-D-fructopyranose 2d. The above procedure was followed using **9d** and *S*-BINOL. After workup, it gave **2d**. Mp 143–144 °C; $[\alpha]_D^{25} = +151.8$ (*c* 1.23, THF); ^{1}H NMR (DMSO-d_6): δ 1.33–1.85 (m, 20H), 3.58 (d, $J = 13.2$ Hz, 1H), 3.79–3.85 (m, 2H), 4.29–4.41 (m, 3H), 4.91 (d, $J = 8.4$ Hz, 1H), 7.21–7.23 (m, 2H), 7.34–7.38 (m, 2H), 7.51 (m, 2H), 7.58 (d, $J = 8.8$ Hz, 1H), 7.76 (d, $J = 8.8$ Hz, 1H), 8.06–8.10 (m, 2H), 8.14 (d, $J = 9.2$ Hz, 1H), 8.17 (d, $J = 8.8$ Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 23.19, 23.34, 23.50, 24.56, 33.78, 34.56, 35.01, 35.48, 62.77, 70.58, 72.96, 73.18, 73.69, 104.72, 109.62, 109.72, 121.32, 121.49, 125.23, 125.42, 125.90, 126.01, 126.65, 126.78, 128.60, 128.67, 130.33, 130.80, 130.92, 131.21, 131.74, 132.02, 146.63; ^{31}P NMR (DMSO-d_6): δ 154.91; HRMS (APCI) calcd for $C_{38}H_{40}O_8P$ (M^++1): 655.2455, found: 655.2470.

4.2.10. 1,2:5,6-Di-*O*-isopropylidene-3-*O*-((*R*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-glucose 3a. The above procedure was followed using **10a** and *R*-BINOL. After workup, it gave **3a**. Mp 113–114 °C; $[\alpha]_D^{25} = -303.1$ (*c* 1.14, THF); ^{1}H NMR (DMSO-d_6): δ 1.28 (s, 3H), 1.33 (s, 3H), 1.38 (s, 3H), 1.42 (s, 3H), 3.74–3.77 (m, 1H), 3.96–4.02 (m, 2H), 4.15–4.18 (m, 1H), 4.69 (d, $J = 9.6$ Hz, 1H), 4.81 (d, $J = 3.6$ Hz, 1H), 5.80 (d, $J = 3.2$ Hz, 1H), 7.21–7.23 (m, 2H), 7.34–7.37 (m, 2H), 7.49–7.53 (m, 2H), 7.59 (d, $J = 8.4$ Hz, 1H), 7.66 (d, $J = 8.8$ Hz, 1H), 8.08–8.21 (m, 4H); ^{13}C NMR (DMSO-d_6): δ 25.33, 26.09, 26.54, 26.66, 66.41, 71.72, 77.69, 77.82, 80.12, 83.68, 104.53, 108.62, 111.59, 121.55, 121.85, 125.25, 125.51, 125.98, 126.05, 126.69, 126.86, 128.68, 128.74, 130.40, 130.77, 131.06, 131.28, 131.64, 131.99, 146.52, 147.66; ^{31}P NMR (DMSO-d_6): δ 147.75; HRMS (APCI) calcd for $C_{32}H_{32}O_8P$ (M^++1): 575.1829, found: 575.1802.

4.2.11. 1,2:5,6-Di-*O*-isopropylidene-3-*O*-((*S*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-glucose 3b. The above procedure was followed using **10a** and *S*-BINOL. After workup, it gave **3b**. Mp 107–108 °C; $[\alpha]_D^{25} = +291.9$ (*c* 1.11, THF); ^{1}H NMR (DMSO-d_6): δ 1.20 (s, 3H), 1.38 (s, 3H), 1.39 (s, 3H), 1.42 (s, 3H), 3.80–3.83 (m, 1H), 3.96–4.00 (m, 1H), 4.08–4.10 (m, 1H), 4.22–4.25 (m, 1H), 4.59 (d, $J = 3.6$ Hz, 1H), 4.79–4.82 (m, 1H), 5.82 (d, $J = 3.6$ Hz, 1H), 7.20–7.22 (m, 2H), 7.35–7.36 (m, 2H), 7.49–7.52 (m, 2H), 7.57 (d, $J = 8.8$ Hz, 1H), 7.66 (d, $J = 8.8$ Hz, 1H), 8.08–8.21 (m, 4H); ^{13}C NMR (DMSO-d_6): δ 25.20, 25.86, 26.43, 26.55, 66.21, 71.88, 77.16, 77.31, 80.18, 83.74, 104.54, 108.57, 111.40, 121.56, 121.64, 121.95, 123.35, 125.30, 125.49, 125.95, 126.75, 126.87, 128.66, 128.74, 130.30, 130.82, 131.03, 131.28, 131.74, 132.00, 146.65, 147.25; ^{31}P NMR (DMSO-d_6): δ 152.58; HRMS (APCI) calcd for $C_{32}H_{32}O_8P$ (M^++1): 575.1829, found: 575.1795.

4.2.12. 1,2:5,6-Di-*O*-cyclohexylidene-3-*O*-((*R*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-glucose 3c. The above procedure was followed using **10b** and *R*-BINOL. After workup, it gave **3c**. Mp 121–122 °C; $[\alpha]_D^{25} = -267.7$ (*c* 1.13, THF); ^{1}H NMR (DMSO-d_6): δ 1.33–1.59 (m, 20H), 3.74 (m, 1H), 3.97–4.12 (m, 3H), 4.79 (m, 2H), 5.85 (d, $J = 3.6$ Hz, 1H), 7.22–7.24 (m, 2H), 7.35–7.37 (m, 2H), 7.50–7.54 (m, 3H), 7.65 (d, $J = 8.4$ Hz, 1H), 8.08–8.15 (m, 3H), 8.18 (d, $J = 8.8$ Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 22.39, 23.22, 23.58, 24.30, 24.65, 32.39, 33.47, 34.46, 35.17, 35.43, 35.91, 36.03, 66.34, 71.43, 77.77, 77.94, 80.40, 83.29, 104.31, 105.33, 109.10, 112.13, 121.38, 121.73, 121.86, 123.53, 125.22, 125.49, 125.91, 126.04, 126.67, 126.85, 128.67, 130.36, 130.79, 131.03, 131.25, 131.70, 132.02, 146.58, 147.47; ^{31}P NMR (DMSO-d_6): δ 149.34; HRMS (APCI) calcd for $C_{38}H_{40}O_8P$ (M^++1): 655.2455, found: 655.2463.

4.2.13. 1,2:5,6-Di-*O*-cyclohexylidene-3-*O*-((*S*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-D-glucose 3d. The above procedure was followed using **10b** and *S*-BINOL. After workup, it gave **3d**. Mp 118–119 °C; $[\alpha]_D^{25} = +262.7$ (*c* 1.08, THF); ^{1}H NMR (DMSO-d_6): δ 1.33–1.68 (m, 20H), 3.81–3.83 (m, 1H), 4.01–4.06 (m, 2H), 4.25–4.27 (m, 1H), 4.57 (m, 1H), 4.71 (d, $J = 9.6$ Hz, 1H), 5.87 (d, $J = 3.6$ Hz, 1H), 7.20–7.22 (m, 2H), 7.33–7.36 (m, 2H), 7.50–7.52 (m, 2H), 7.57 (d, $J = 8.8$ Hz, 1H), 7.65 (d, $J = 8.8$ Hz, 1H), 8.06–8.10 (m, 2H), 8.13 (d, $J = 8.8$ Hz, 1H), 8.18 (d, $J = 9.2$ Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 23.19, 23.43, 23.51, 23.62, 24.31, 24.63, 34.34, 34.91, 35.74, 35.99, 66.18, 71.63, 77.49, 77.64, 80.33, 83.36, 104.28, 109.04, 111.81, 121.53, 121.92, 125.25, 125.44, 125.97, 126.70, 126.81, 128.60, 128.72, 130.38, 130.79, 131.00, 131.26, 131.77, 132.01, 146.69; ^{31}P NMR (DMSO-d_6): δ 149.05; HRMS (APCI) calcd for $C_{38}H_{40}O_8P$ (M^++1): 655.2455, found: 655.2507.

4.2.14. 1,2:5,6-Di-*O*-isopropylidene-3-*O*-((*R*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-β-D-glucofuranose 4a. The above procedure was followed using **10c** and *R*-BINOL. After workup, it gave **4a**. Mp 76–77 °C; $[\alpha]_D^{25} = -248.7$ (*c* 0.98, THF); ^{1}H NMR (DMSO-d_6): δ 1.28 (s, 3H), 1.30 (s, 3H), 1.33 (s, 3H), 1.44 (s, 3H), 3.74–3.78 (m, 1H), 3.98–4.08 (m, 2H), 4.20–4.23 (m, 1H), 4.53–4.60 (m, 2H), 5.73 (d, $J = 3.6$ Hz, 1H), 7.19–7.21 (m, 2H), 7.34–7.38 (m, 2H), 7.49–7.51 (m, 3H), 7.60 (d, $J = 8.8$ Hz, 1H), 8.07–8.19 (m, 4H); ^{13}C NMR (DMSO-d_6): δ 25.00, 26.15, 26.54, 26.63, 64.67, 73.88, 73.98, 74.71, 78.11, 78.44, 103.54, 108.89, 112.49, 121.62, 121.73, 121.88, 123.41, 125.21, 125.42, 125.90, 125.99, 126.67, 126.81, 128.61, 128.70, 130.12, 130.77, 130.95, 131.22, 131.77, 132.01, 146.70, 147.37; ^{31}P NMR (DMSO-d_6): δ 148.81; HRMS (APCI) calcd for $C_{32}H_{32}O_8P$ (M^++1): 575.1829, found: 575.1786.

4.2.15. 1,2:5,6-Di-*O*-isopropylidene-3-*O*-((*S*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-β-D-glucofuranose 4b. The above procedure was followed using **10c** and *S*-BINOL. After workup, it gave **4b**. Mp 111–112 °C; $[\alpha]_D^{25} = +318.4$ (*c* 1.15, THF); ^{1}H NMR (DMSO-d_6): δ 1.33 (s, 3H), 1.37 (s, 3H), 1.38 (s, 3H), 1.46 (s, 3H), 3.73–3.76 (m, 1H), 3.96–4.01 (m, 2H), 4.17 (t, $J = 5.6$ Hz, 1H), 4.55–4.59 (m, 1H), 4.81 (t, $J = 4.2$ Hz, 1H), 5.75 (d, $J = 3.2$ Hz, 1H), 7.20–7.24 (m, 2H), 7.33–7.36 (m, 2H), 7.48–7.58 (m, 4H), 8.06–8.19 (m, 4H); ^{13}C NMR (DMSO-d_6): δ 25.17, 26.28, 26.54, 26.60, 65.11, 74.14, 74.30, 74.82, 77.41, 78.54, 103.44, 109.01, 112.29, 121.58, 121.84, 122.35, 123.56, 125.13, 125.43, 125.87, 126.05, 126.54, 126.80, 128.59, 128.71, 129.89, 130.93, 131.24, 131.67, 132.02, 146.71, 147.51; ^{31}P NMR (DMSO-d_6): δ 151.85; HRMS (APCI) calcd for $C_{32}H_{32}O_8P$ (M^++1): 575.1829, found: 575.1864.

4.2.16. 1,2:5,6-Di-*O*-cyclohexylidene-3-*O*-((*R*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-β-D-glucofuranose 4c. The above procedure was followed using **10d** and *R*-BINOL. After workup, it gave **4c**. Mp 110–111 °C; $[\alpha]_D^{25} = -192.45$ (*c* 1.00, THF); ^{1}H NMR (DMSO-d_6): δ 1.31–1.68 (m, 20H), 3.70–3.74 (m, 1H), 3.97–4.00 (m, 1H), 4.07–4.10 (m, 1H), 4.14–4.17 (m, 1H), 4.52–4.54 (m, 1H), 4.60 (t, $J = 4.0$ Hz, 1H), 5.75 (d, $J = 3.6$ Hz, 1H), 7.20–7.22 (m, 2H), 7.34–7.37 (m, 2H), 7.49–7.56 (m, 4H), 8.07–8.13 (m, 3H), 8.18 (d, $J = 8.8$ Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 23.38, 24.32, 24.61, 34.20, 35.54, 35.83, 64.83, 74.71, 78.03, 78.25, 103.32, 109.42, 113.12, 121.52, 121.80, 122.00, 123.40, 125.15, 125.37, 125.89, 126.00, 126.61, 126.78, 128.61, 128.69, 130.07, 130.77, 130.92, 131.16, 131.77, 132.03, 146.90, 147.44; ^{31}P NMR (DMSO-d_6): δ 148.71; HRMS (APCI) calcd for $C_{38}H_{40}O_8P$ (M^++1): 655.2455, found: 655.2395.

4.2.17. 1,2:5,6-Di-*O*-cyclohexylidene-3-*O*-((*S*)-2,2′-*O*,*O*-(1,1′-binaphthyl)dioxophosphite)-β-D-glucofuranose 4d. The above procedure was followed using **10d** and *S*-BINOL. After workup, it gave **4d**. Mp 131–132 °C; $[\alpha]_D^{25} = +358.5$ (*c* 1.00, THF); ^{1}H NMR (DMSO-d_6): δ 1.37–1.65 (m, 20H), 3.70–3.74 (m, 1H), 3.92–3.95 (m, 1H), 3.98–4.02 (m, 1H), 4.15–4.18 (m, 1H), 4.60–4.66 (m, 1H), 4.82 (t, $J = 4.0$ Hz, 1H), 5.77 (d, $J = 3.6$ Hz, 1H), 7.20–7.25 (m, 2H), 7.33–7.39 (m, 2H), 7.48–7.57

(m, 4H), 8.07–8.09 (m, 3H), 8.18 (d, $J = 8.8$ Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 23.46, 24.38, 24.71, 34.38, 35.63, 35.83, 65.25, 74.51, 74.70, 77.41, 78.18, 103.09, 109.55, 112.88, 121.33, 121.94, 122.46, 123.59, 125.15, 125.44, 125.83, 126.05, 126.57, 126.84, 128.60, 128.72, 129.75, 130.99, 131.21, 131.68, 132.05, 146.75, 147.48; ^{31}P NMR (DMSO-d_6): δ 153.48; HRMS (APCI) calcd for $C_{38}H_{40}O_8P$ (M^++1): 655.2455, found: 655.2416.

4.2.18. 1,2:5,6-Di-*O*-isopropylidene-3-*O*-((*S*)-2,2′-*O*,*O*-(3,3′-diphenyl-1,1′-binaphthyl)dioxophosphite)-D-glucose 4e. The above procedure was followed using **10a** and (*S*)-3,3′-diphenyl-2,2′-dihydroxy-1,1′-binaphthyl. After workup, it gave **4e**. Mp 118–119 °C; $[\alpha]_D^{25} = +350.0$ (*c* 0.86, THF); ^{1}H NMR (DMSO-d_6): 1.12 (s, 3H), 1.15 (s, 3H), 1.17 (s, 3H), 1.28 (s, 3H), 3.20–3.22 (m, 1H), 3.55–3.57 (m, 2H), 3.70–3.72 (m, 1H), 3.93 (d, $J = 3.2$ Hz, 1H), 4.24 (d, $J = 9.6$ Hz, 1H), 5.57 (d, $J = 3.2$ Hz, 1H), 7.21–7.24 (m, 2H), 7.38–7.57 (m, 10H), 7.70–7.75 (m, 4H), 8.14–8.30 (m, 4H); ^{13}C NMR (DMSO-d_6): δ 25.31, 25.87, 26.29, 26.59, 65.67, 71.19, 77.02, 79.42, 82.88, 104.19, 108.21, 111.14, 123.13, 125.67, 125.99, 126.80, 126.95, 127.70, 127.91, 128.33, 128.81, 129.93, 129.61, 130.78, 131.17, 131.41, 131.73, 133.61, 133.73, 136.48, 137.08, 143.66, 144.84; ^{31}P NMR (DMSO-d_6): δ 146.13; HRMS (APCI) calcd for $C_{44}H_{40}O_8P$ (M^++1): 727.2455, found: 727.2505.

4.3. General procedures for asymmetric hydrogenation

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

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