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Novel Disaccharide Chiral Ligands Derived from α,α-Trehalose and Their Applications to Asymmetric Hydrogenation of Enamides

Koji Yonehara, Tomohiro Hashizume, Kouichi Ohe,* and Sakae Uemura*

Department of Energy and Hydrocarbon Chemistry, Graduate School of Engineering, Kyoto University, Sakyo-ku, Kyoto 606-8501

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New chiral diphosphinite ligands such as 4,6 : 2′,3′ : 4′,6′-tri-*O*-cyclohexylidene-2,3-di-*O*-diphenylphosphino-α,α-trehalose (**1**), 3,3′-di-*O*-benzyl-4,6 : 4′,6′-di-*O*-benzylidene-2,2′-di-*O*-diphenylphosphino-α,α-trehalose (**2**), 4,6 : 4′,6′-di-*O*-benzylidene-2,2′-di-*O*-diphenylphosphino-3,3′-di-*O*-methyl-α,α-trehalose (**3**), and 2,2′-di-*O*-benzyl-4,6 : 4′,6′-di-*O*-benzylidene-3,3′-di-*O*-diphenylphosphino-α,α-trehalose (**4**) were prepared from α,α-trehalose which is an inexpensive natural reserve sugar. These ligands work as chiral ligands for Rh-catalyzed hydrogenation of α-acetamidoacrylic and cinnamic acid derivatives to afford both enantiomers of amino acids up to 84%ee (*S*) and 72%ee (*R*).

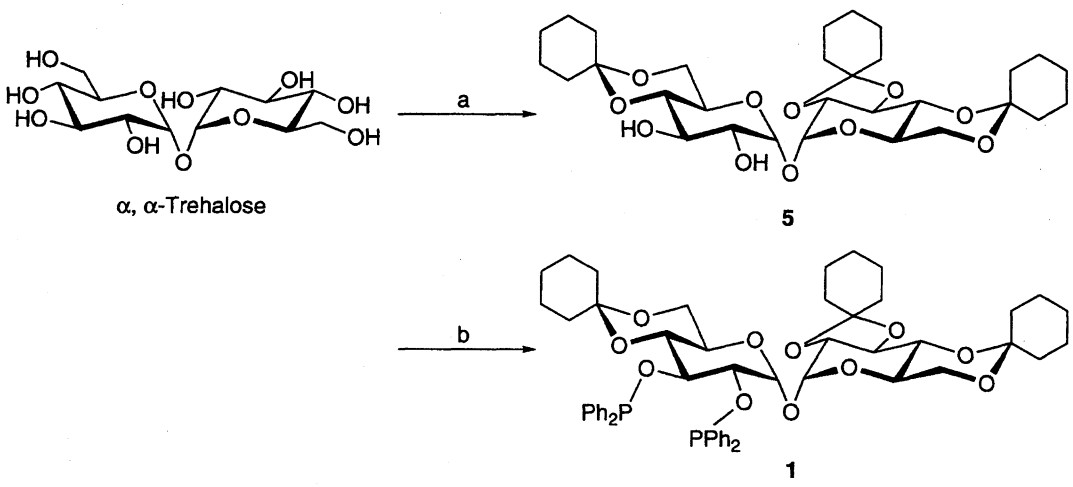
Transition metal-catalyzed enantioselective hydrogenation of dehydroamino acids has been well studied during the last three decades[1] because it is extremely important for the synthesis of biologically active substances. So far, a quite highly enantioselective hydrogenation has been done using several chiral bidentate phosphine ligands.[1,2] While they are excellent ligands, expensive chiral sources and multi-step synthesis are sometimes needed. For that reason, transformation of carbohydrates, especially monosaccharides, into chiral ligands has also been developed[3] because monosaccharides exist widely in nature and they have some advantages for asymmetric synthesis in such properties as ready availability and many chiral centers in their skeletones. In fact, high enantioselectivities using chiral ligands derived from monosaccharides were obtained not only in hydrogenation[3a—e] but also in hydrocyanation,[3f] hydroformylation,[3g] and allylation.[3h—i] However, there is a big drawback of these ligands based on natural products: their chiralities are limited by nature and the opposite enantiomer of the ligands cannot be easily synthesized because of the unavailability of the appropriate carbohydrate starting materials. RajanBabu et al. recently succeeded in the synthesis of (*S*)- or (*R*)-amino acids in hydrogenation by using 2,3-diphosphinites or 3,4-diphosphinites derived from D-glucopyranoside.[3e] Some limitations remained, however, and therefore the search for new chiral ligands derived from natural carbohydrates are yet awaited in the field of asymmetric synthesis.

Toward this end, we chose α,α-trehalose as a natural chiral source for new chiral ligands. It is found in many bacteria and fungi, in plants, and in the blood of most insects. Despite its ready availability, little work has been done on its use as a chiral ligand molecule. Recently, a few 6,6′-bis(diphenylphosphino)-6,6′-deoxytrehalose derivatives were reported, which were only one type of diphosphine ligands derived from α,α-trehalose to the best of our knowledge, but enantioselectivities obtained by using these ligands were not high in hydroformylation ("vanishingly small" as reported in the literature)[4] and hydrogenation (5—23% ee at r.t. and 53—82% ee at −10 °C).[5] These aspects stimulated us to make the best use of α,α-trehalose for new ligand synthesis. There is merit in it for the following reasons: (i) it is an inexpensive natural reserve sugar, and has a simple twofold axis of symmetry through the central glycosidic oxygen, which makes the D-glucopyranosyl residues chemically and physically indistinguishable, (ii) disaccharide chiral ligands have been little studied so far, and (iii) it is easily modified into several ligands to provide characteristic asymmetric environments. We report herein the synthesis of some new phosphinite chiral ligands from α,α-trehalose and the Rh-catalyzed hydrogenation of dehydroamino acids and their esters using these ligands aiming at the selective preparation of both enantiomers.

Results and Discussion

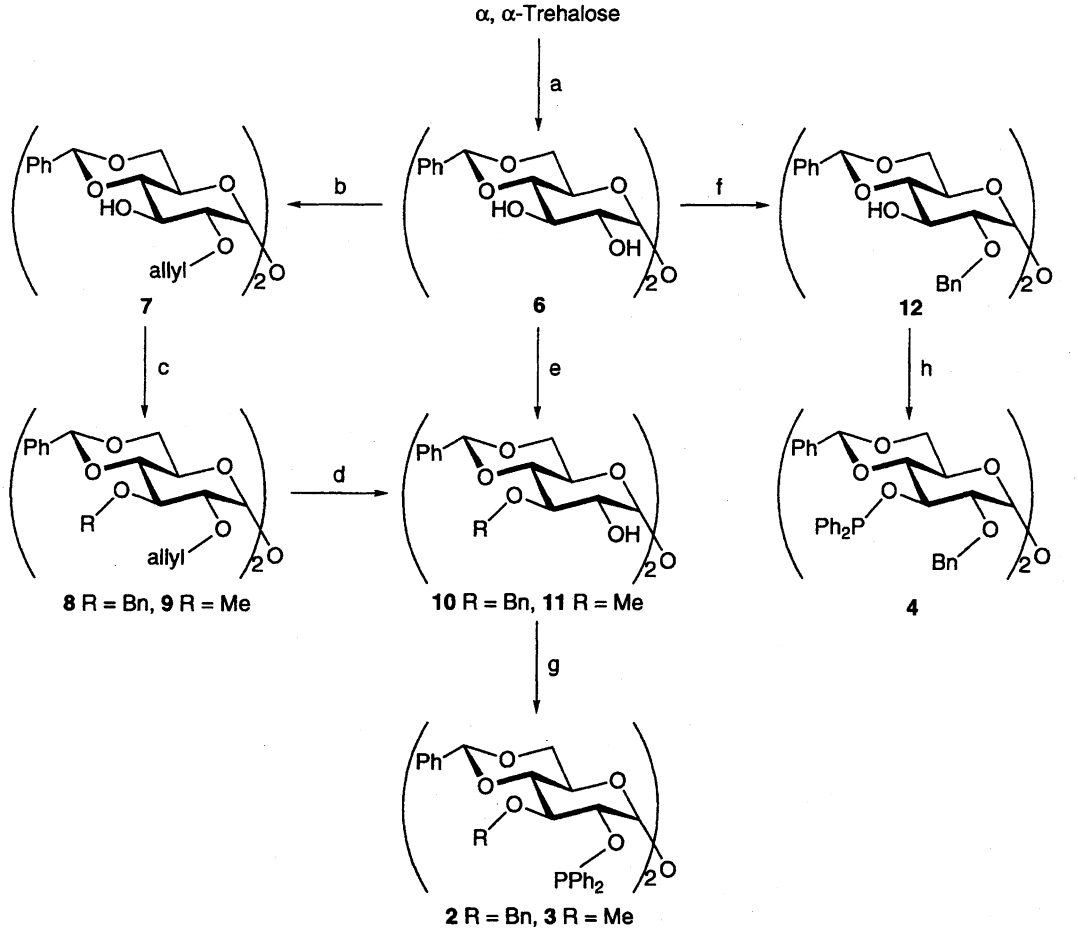
First, we prepared 4,6 : 2′,3′ : 4′,6′-tri-*O*-cyclohexylidene-α,α-trehalose (**5**)[6] which has 2,3-vicinal hydroxy groups, and transformed it into 4,6 : 2′,3′ : 4′,6′-tri-*O*-cyclohexylidene-2,3-di-*O*-diphenylphosphino-α,α-trehalose (**1**) using chlorodiphenylphosphine and triethylamine (Scheme 1). Because it can be counted among D-glucopyranosyl 2,3-diphosphinite bidentate ligand derivatives, we may expect that the (*S*)-amino acid is the major product in Rh-catalyzed hydrogenation using **1** as a chiral ligand similar to traditional ligands from monosaccharides.[3a,3c—e]

Next, aiming at preparing the unnatural (*R*)-enantiomer, we tried to synthesize chiral ligands with diphenylphosphinite groups at 2,2′ or 3,3′ positions (Scheme 2). After 4,6 : 4′,6′-positions of α,α-trehalose were protected by benzylidene groups to reduce the glucopyranosyl ring flexibility,[7] 2,2′-regioselective allylations of 4,6 : 4′,6′-di-



a) (i) 1, 1-dimethoxycyclohexane, *p*-TsOH·H_2O, MS4A, DMF, 80 ℃, 6 h. (ii) Ac_2O, C_5H_5N, rt, overnight, 2 steps 53 %. (iii) K_2CO_3, MeOH, rt, 5 h, 68 %. b) Ph_2PCl, cat. DMAP (4-dimethylaminopyridine), Et_3N-CH_2Cl_2, rt, overnight, 65 %.

Scheme 1. Synthesis of 2,3-diphenylphosphinite.

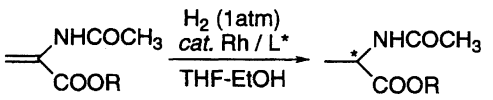


a) Benzaldehyde dimethylacetal, *p*-TsOH·H_2O, DMF, 100 ℃, 2 h, 91 %. b) Bu_2SnO, MS3A, CH_3CN, refrux, 48 h, then allyl bromide, *N*-methylimidazole, reflux, 48 h, 75 %. c) (i) NaH, DMF, rt, 1 h (ii) BnBr or MeI, cat. Bu_4N^+I, rt, 4 h, 92 % (R =Bn); 63 % (R = Me). d) cat. trans-[$PdCl_2(NH_3)_2$], *t*-BuOH, reflux, 72 h, 56 % (R = Bn); 24% (R = Me). e) BnBr or MeI, Ag_2O, acetone, reflux, 48 h, MS3A, 51 % (R = Bn); 41 % (R = Me). f) Bu_2SnO, MS3A, CH_3CN, reflux, 48 h, then BnBr, *N*-methylimidazole, reflux, 48 h, 40%. g) Ph_2PCl, cat. DMAP, Et_3N-CH_2Cl_2, rt, overnight, 62 % (R= Bn); 58 % (R = Me). h) Ph_2PCl, cat. DMAP, Et_3N-CH_2Cl_2, rt, overnight, 53 %.

Scheme 2. Synthesis of 2,2′- and 3,3′-diphenylphosphinites.

O-benzylidene-α,α-trehalose (**6**) with dibutyltin oxide[8] followed by benzylation or methylation of 3,3′ positions gave 2,2′-di-*O*-allyl-3,3′-di-*O*-benzyl-4,6 : 4′,6′-di-*O*-benzylidene-α,α-trehalose (**8**)[8] or 2,2′-di-*O*-allyl-4,6 : 4′,6′-di-*O*-benzylidene-3,3′-di-*O*-methyl-α,α-trehalose (**9**). Deallylation of **8** and **9** using a catalytic amount of *trans*-$[PdCl_2(NH_3)_2]$[9] gave 3,3′-di-*O*-benzyl-4,6 : 4′,6′-di-*O*-benzylidene-α,α-trehalose (**10**) and 4,6 : 4′,6′-di-*O*-benzylidene-3,3′-di-*O*-methyl-α,α-trehalose (**11**), respectively. One-step operation of **6** using silver oxide could also provide compounds **10** and **11**, respectively.[10] Treatment of **10** and **11** with chlorodiphenylphosphine and triethylamine gave the desired products, 3,3′-di-*O*-benzyl-4,6 : 4′,6′-di-*O*-benzylidene-2,2′-di-*O*-diphenylphosphino-α,α-trehalose (**2**) and 4,6 : 4′,6′-di-*O*-benzylidene-2,2′-di-*O*-diphenylphosphino-3,3′-di-*O*-methyl-α,α-trehalose (**3**). 2,2′-Di-*O*-benzyl-4,6 : 4′,6′-di-*O*-benzylidene-3,3′-di-*O*-diphenylphosphino-α,α-trehalose (**4**) could be prepared from **6** by the methods mentioned above. In addition to their C_2 symmetry having an axis through the anomeric oxygen, the compounds **2** and **3** having the diphenylphosphinite groups at 2,2′ positions and the compound **4** having them at 3,3′ positions were expected to have different asymmetric environments, and so it may be possible that (*R*)-enantiomer can be obtained using either **2**, **3**, or **4** as a chiral ligand.

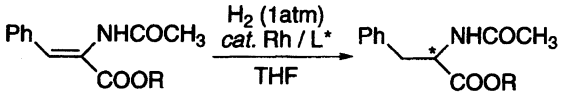
Hydrogenation of α-acetamidoacrylic acid and its methyl ester was done at room temperature with 1 atm of hydrogen in the presence of the catalyst (0.02 mol amt.) formed in situ from $[Rh(cod)_2]BF_4$ and diphosphinite **1**—**4** (Eq. 1). The results are listed in Table 1.



(1)

Although the enantioselectivity was not very high through the reactions (23—66% ee), it is worth noting that the 2, 3- and 3,3′-diphosphinite ligands **1** and **4** gave (*S*)-product (Entries 1 and 4), while 2,2′-diphosphinite ligands **2** and **3** gave (*R*)-product (Entries 2, 3, 5, and 6).

Next, we tested the ligands (**1**—**4**) for the hydrogenation of α-acetamidocinnamic acid and its methyl ester (Eq. 2). The results are summarized in Table 2.



(2)

The ee values were improved to 84%ee (*S*) using the ligand **1** (Entry 1) and 72%ee (*R*) using the ligand **2** (Entry 9), respectively. The amount of catalyst could be reduced to 0.01 mol amt., although the ee value was slightly decreased (Entry 4). The displacement of the counter anion from BF_4

Table 1. Asymmetric Hydrogenation of α-Acetamidoacrylic Acid and Its Methyl Ester[a]

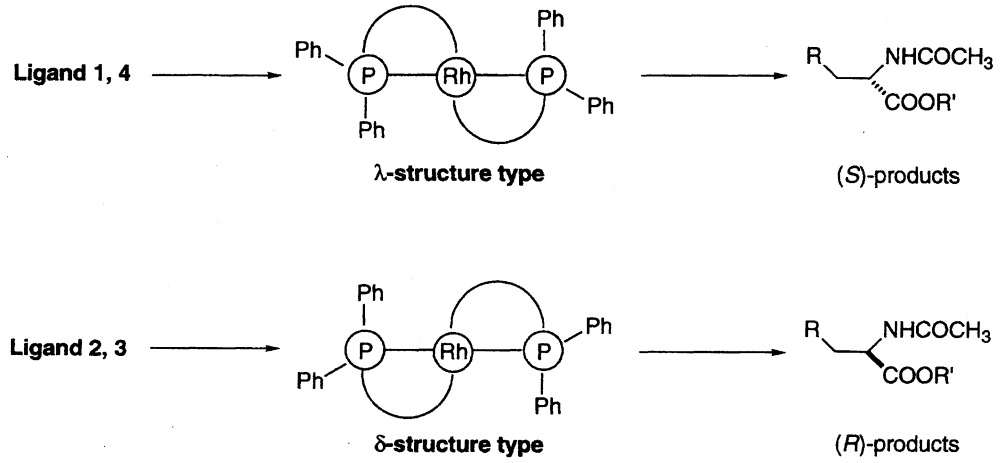
Entry	Ligand (L*)	R	Temp (°C)	Time (h)	Conv. (%)	%ee[b]	Config.[c]
1	**1**	CH_3	r.t.	1	100	66	*S*
2	**2**	CH_3	r.t.	5	100	24	*R*
3	**3**	CH_3	r.t.	5	100	38	*R*
4	**4**	CH_3	r.t.	5	100	23	*S*
5	**2**	H	r.t.	5	100	24[d]	*R*
6	**3**	H	r.t.	5	100	26[d]	*R*

a) The reaction was performed in THF–EtOH (3/1) under atmospheric hydrogen (substrate/$[Rh(cod)_2]$-BF_4/ligand = 50/1/1.1). b) The ee(%) values were determined by HPLC. c) The absolute configuration was determined by comparing optical rotations with reported values.[2a] d) The ee(%) values were determined on its methyl ester.

Table 2. Asymmetric Hydrogenation of α-Acetamidocinnamic Acid and Its Methyl Ester[a]

Entry	Ligand (L*)	R	Temp (°C)	Time (h)	Conv. (%)	%ee[b]	Config.[c]
1	**1**	CH_3	r.t.	6	100	84	*S*
2	**2**	CH_3	r.t.	12	100	70	*R*
3[d]	**2**	CH_3	r.t.	12	100	70	*R*
4[e]	**2**	CH_3	r.t.	17	100	68	*R*
5	**2**	CH_3	45	6	100	60	*R*
6[f]	**2**	CH_3	r.t.	4	100	38	*R*
7	**3**	CH_3	r.t.	24	100—90	58—25[g]	*R*
8	**4**	CH_3	r.t.	12	53—25	77—43[g]	*S*
9	**2**	H	r.t.	24	100	72[h]	*R*
10	**3**	H	r.t.	12	70	75[h]	*S*

a) The reaction was performed in THF under atmospheric hydrogen (substrate/$[Rh(cod)_2]BF_4$/ligand = 50/1/1.1). b) The ee(%) values were determined by HPLC. c) The absolute configuration was determined by comparing optical rotation with reported values.[2a] d) $[Rh(cod)_2]SbF_6$ was used instead of $[Rh(cod)_2]BF_4$. e) Substrate/$[Rh(cod)_2]BF_4$/ligand = 100/1/1.1. f) H_2 = 3 atm. g) These results showed poor reproducibility. h) The ee(%) values were determined on its methyl ester.



Scheme 3. Empirical rule in hydrogenation of dehydroamino acids.

to SbF_6 did not affect the ee values with the ligand **2** (Entries 2 and 3), but higher H_2 pressure and higher temperature decreased the obtained ee values (Entries 5 and 6).

The chelation of phosphinite ligands to rhodium was investigated by ^{31}P NMR study. In the ^{31}P NMR of rhodium complexes [Rh(cod)(L*)]BF_4 (L* = **2**, **3**, and **4**) prepared in situ from equimolar amounts of [Rh(cod)$_2$]BF_4 and chiral ligands (**2**, **3**, and **4**) in $CDCl_3$, only one resonance of a phosphorus nucleus was observed as a doublet for each complex: [Rh(cod)(**2**)]BF_4: δ = 119.1 (J_{Rh-P} = 183.2 Hz), [Rh(cod)(**3**)]BF_4: δ = 119.5 (J_{Rh-P} = 183.1 Hz), and [Rh(cod)(**4**)]BF_4: δ = 120.1 (J_{Rh-P} = 177.0 Hz).[11] These results show that the ligands **2**, **3**, and **4** all coordinate to rhodium in a bidentate fashion.

The mechanism of the hydrogenation of enamides has been identified by Halpern[12] and Brown,[13] and there exists a good empirical rule in the case of five and seven-membered chelates: The diphosphine ligands that form the λ configuration of the aromatic rings attached to phosphorus atoms generally yield naturally occurring (*S*)-amino acid derivatives, but the phosphines that form the δ configuration of them yield unnatural (*R*) enantiomers as major products (Scheme 3).[14] According to this rule, our results might suggest that the ligands **1** and **4** form a λ-like structure and that **2** and **3** form a δ-like structure. However, with **3** as a ligand, the product of opposite configuration to the expected product was exceptionally obtained in the reaction of the acid in contrast to the corresponding ester (Table 2, Entry 10). It is probably because the ligand **3** is so flexible compared to **2** that a change of absolute configuration from δ type to λ type occurred easily by hydrogen bonding or π–π interaction between substrate and catalyst.

In conclusion, we synthesized novel disaccharide phosphinite chiral ligands **1**—**4** from α,α-trehalose which is a natural reserve sugar, and succeeded in the synthesis of both enantiomers by rhodium-catalyzed hydrogenation of enamides using them as ligands. While their ee values were not yet satisfactory compared to those of some other excellent ligands, we could show a new way to overcome a big drawback of ligands based on natural products.

Applications of these ligands to other asymmetric reactions are now in progress.

Experimental

General. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under argon. Dichloromethane and triethylamine were distilled from calcium hydride. Analytical thin-layer chromatographies (TLC) were done with silica gel 60 Merck F-254 plates or aluminum oxide 60 Merck F-254. Column chromatographies were done with Wakogel C-300 silica gel or ICN Alumina Akt I (neutral). An LC-908 recycling preparative HPLC instrument with JAIGEL-1H and JAIGEL-2H columns (20×600 mm) was used for purification of **10** and **11**. NMR spectra were measured on JEOL EX-400 and JEOL JNM-GSX270 spectrometers for solutions in $CDCl_3$ with Me_4Si as an internal standard (^1H and ^{13}C) or with $P(OMe)_3$ as an external standard (^{31}P): the following abbreviations are used; s: singlet, d: doublet, t: triplet, m: multiplet. IR spectra were recorded with a Nicolet Impact 400 FT-IR spectrometer: the following abbreviations are used; s: strong, m: medium, w: weak. Optical rotations were measured on a JASCO DIP-1000. GLC analyses were done with a Shimadzu GC-14A with flame ionization detector with a 5% silicone OV-17A column. HPLC analyses were done on an HLC-803A instrument (Tosoh) with UV-8011 detector or L-7100 instrument (HITACHI) with L-7400 detector using either a Daicel Chiralcel OD or OJ column (4.6×250 mm) at 40 °C. Melting points are uncorrected. Elemental analyses were done at the Microanalytical Center of Kyoto University. α,α-Trehalose dihydrate was purchased from Nacalai Tesque. The compounds **5**,[6] **6**,[7] **7**,[8] **8**,[8] and **12**[8] were prepared by the reported methods, respectively.

2,2′-Di-*O*-allyl-4,6 : 4′,6′-di-*O*-benzylidene-3,3′-di-*O*-methyl-α,α-trehalose (9): To a stirred mixture of **7** (5.7 g, 9.6 mmol) and sodium hydride (0.51 g, 21 mmol) in *N*,*N*-dimethylformamide (50 mL) was added methyl iodide (2.7 g, 19 mmol). After 6 h, methanol was added to this solution, and the mixture was diluted with chloroform. The organic layer was washed with water and dried over $MgSO_4$. The solvent was removed under vaccum and the residue was chromatographed on a column of SiO_2 with $CHCl_3$–AcOEt (v/v = 6 : 1) as an eluent to give **9** (3.8 g, 6.1 mmol, 63%), as a white solid: Mp 123—125 °C. $[\alpha]_D^{23}$ = +86.8° (*c* 0.5, $CHCl_3$). ^1H NMR δ = 3.43 (2H, dd, *J* = 3.7, 9.3 Hz), 3.53 (2H, t, *J*=9.3 Hz), 3.67 (6H, s), 3.69 (2H, m), 3.77 (2H, t, *J* = 9.3 Hz), 4.13—4.25 (8H, m), 5.13 (2H, d, *J* = 3.7 Hz), 5.20 (2H, d, *J* = 10.3 Hz), 5.33 (2H, d, *J*=17.1 Hz), 5.53 (2H, s), 5.91 (2H, ddt, *J* = 5.4, 10.3, 17.1 Hz), 7.25—7.51 (10H, m); ^{13}C NMR δ = 61.1, 62.6, 69.0, 72.4, 78.7,

79.6, 82.2, 94.8, 101.4, 117.3, 126.1, 128.2, 128.9, 134.5, 137.5; IR (KBr) 654 (w), 699 (m), 749 (m), 967 (m), 991 (s), 1010 (m), 1089 (s), 1175 (m), 1375 (m), 1450 (w), 1640 (w), 2855 (m), 2928 (m) cm^{-1}. Found: C, 65.03; H, 6.78; O, 27.97%. Calcd for $C_{34}H_{42}O_{11}$: C, 65.16; H, 6.76; O, 28.08%.

3,3′-Di-*O*-benzyl-4,6 : 4′,6′-di-*O*-benzylidene-α,α-trehalose (10): (method A), This compound was prepared by the reported method.[10] A mixture of **6** (5.2 g, 10 mmol), acetone (30 mL), MS3A (5 g), benzyl bromide (7.6 g, 44 mmol), and silver oxide (11.4 g, 49 mmol) was boiled under reflux for 48 h. After filtration through Celite, the volatile components were removed under a high vaccum and the residue was chromatographed on a column of SiO_2 with hexane–AcOEt (v/v = 1 : 1) as an eluent to give **10** (3.6 g, 5.1 mmol, 51%).

(method B), To a solution of **8** (5.0 g, 6.5 mmol) in *t*-BuOH (70 mL) was added *trans*-$[PdCl_2(NH_3)_2]$[9] (0.45 g, 2.2 mmol) and the mixture was stirred under reflux for 3 d. After filtration through Celite, the solvent was evaporated and column chromatography of the residue on SiO_2 with hexane–AcOEt (v/v = 1 : 1) as an eluent and HPLC purification of the residue gave **10** (2.5 g, 3.6 mmol, 56%). NMR data were consistent with those of the reported one.[8]

4,6 : 4′,6′-di-*O*-benzylidene-3,3′-di-*O*-methyl-α,α-trehalose (11): (method A), The compound was prepared by the reported method.[10] A mixture of **6** (10.4 g, 20 mmol), acetone (50 mL), MS3A (10 g), methyl iodide (125 g, 88 mmol), and silver oxide (20 g, 86 mmol) was boiled under reflux for 48 h. After filtration through Celite, the solution was evaporated and column chromatography of the residue on SiO_2 with $CHCl_3$–AcOEt (v/v = 2 : 1) as an eluent gave **11** (4.4 g, 8.1 mmol, 41%).

(method B), To a solution of **9** (1.9 g, 3.0 mmol) in *t*-BuOH (30 mL) was added *trans*-$[PdCl_2(NH_3)_2]$[9] (0.22 g, 1.0 mmol) and the mixture was stirred under reflux for 3 d. After filtration through Celite, the solvent was evaporated and column chromatography of the residue on SiO_2 with $CHCl_3$–AcOEt (v/v = 2 : 1) as an eluent and HPLC purification of the residue gave **11** (0.39 g, 0.71 mmol, 24%). NMR data were consistent with those of the reported one.[10]

A Typical Procedure for the Synthesis of a Diphenylphosphinite Compound: To a solution of **5** (0.23 g, 0.40 mmol) and a catalytic amount of 4-dimethylaminopyridine in 4 mL of degassed CH_2Cl_2/Et_3N (v/v = 1 : 1) was added chlorodiphenylphosphine (0.15 mL, 0.84 mmol) at room temperature and the mixture was stirred overnight. The mixture was concentrated to dryness and column chromatography of the residue on Al_2O_3 with degassed benzene–$CHCl_3$ (v/v = 10 : 1) as an eluent gave 4,6 : 2′,3′ : 4′,6′-tri-*O*-cyclohexylidene-2,3-di-*O*-diphenylphosphino-α,α-trehalose (**1**) (0.25 g, 0.26 mmol, 65%), as a white solid: Mp 86—89 °C. $[\alpha]_D^{23}$ = +73.5° (*c* 0.5, $CHCl_3$). ^{1}H NMR δ = 0.90—2.13 (30H, m), 3.46—4.38 (12H, m), 5.12 (1H, d, *J*=2.8 Hz), 5.31 (1H, d, *J* = 2.8 Hz), 6.99—7.60 (20H, m); ^{13}C NMR δ = 22.0, 22.4, 22.5, 22.7, 23.6, 23.9, 25.0, 25.5, 25.6, 26.9, 28.0, 36.0, 36.2, 37.5, 37.7, 61.3, 61.4, 64.0, 66.4, 72.9, 73.0, 76.3, 77.6 (dd, *J*=3.7, 12.9 Hz), 79.8 (dd, *J* = 3.6, 18.7 Hz), 94.6, 96.0 (d, *J* = 6.8 Hz), 99.6, 112.4, 127.7—131.1 (12 carbons of 4 phenyls), 140.6 (d, *J* = 17.1 Hz), 141.9 (d, *J* = 22.3 Hz), 142.9 (d, *J* = 16.1 Hz), 143.4 (d, *J* = 18.7 Hz); ^{31}P NMR δ = 111.5, 114.6; IR (KBr) 696 (m), 741 (w), 792 (w), 827 (w), 955 (m), 976 (m), 1005 (s), 1058 (s), 1096 (s), 1380 (m), 1435 (m), 1462 (s), 1643 (w), 2854 (s), 2935 (s) cm^{-1}. Found: C, 68.60; H, 6.70; P, 6.33%. Calcd for $C_{54}H_{64}O_{11}P_2$: C, 68.20; H, 6.78; P, 6.51%.

3,3′-Di-*O*-benzyl-4,6 : 4′,6′-di-*O*-benzylidene-2,2′-di-*O*-diphenylphosphino-α,α-trehalose (2): 62% yield, a white solid: Mp 52—55 °C. $[\alpha]_D^{23}$ = +78.5° (*c* 0.5, $CHCl_3$). ^{1}H NMR δ = 3.54 (2H, t, *J*=10.2 Hz), 3.65 (2H, m), 3.82 (2H, dd, *J* = 4.8, 10.2 Hz), 4.08—4.11 (4H, m), 4.21 (2H, dt, *J* = 4.8, 9.6 Hz), 4.40 (2H, d, *J* = 11.1 Hz), 4.80 (2H, d, *J* = 11.1 Hz), 5.25 (2H, d, *J* = 2.4 Hz), 5.47 (2H, s), 7.10—7.60 (40H, m); ^{13}C NMR δ=63.4, 68.5, 74.8, 77.9, 78.5 (d, *J* = 16.5 Hz), 82.6, 94.9 (d, *J* = 7.4 Hz), 101.3, 126.2, 127.3, 128.0, 128.30 (d, *J* = 7.3 Hz), 128.5 (d, *J* = 7.3 Hz), 128.8, 129.2, 129.5, 130.4 (d, *J* = 22 Hz), 130.7 (d, *J* = 22.1 Hz), 137.6, 138.3, 141.4 (d, *J* = 16.6 Hz), 142.7 (d, *J* = 18.4 Hz); ^{31}P NMR δ = 114.6; IR (KBr) 696 (s), 749 (m), 788 (m), 806 (w), 999 (s), 1036 (s), 1074 (s), 1084 (s), 1373 (m), 1435 (m), 1455 (w), 1620 (w), 2861 (w), 2935 (w), 3057 (w) cm^{-1}. Found: C, 71.76; H, 5.74; P, 5.84%. Calcd for $C_{64}H_{62}O_{11}P_2$: C, 72.04; H, 5.67; P, 5.81%.

4,6 : 4′,6′-di-*O*-benzylidene-2,2′-di-*O*-diphenylphosphino-3,3′-di-*O*-methyl-α,α-trehalose (3): 58% yield, a white solid: Mp 70—72 °C. $[\alpha]_D^{22}$ = +99.6° (*c* 0.5, $CHCl_3$). ^{1}H NMR δ = 3.21 (6H, s), 3.53 (2H, t, *J*=10.0 Hz), 3.57 (2H, t, *J*=10.0 Hz), 3.78 (2H, t, *J*=10.0 Hz), 3.80 (2H, dd, *J* = 4.9, 10.0 Hz), 4.04 (2H, m), 4.23 (2H, dt, *J* = 4.9, 10.0 Hz), 5.25 (2H, d, *J* = 3.6 Hz), 5.46 (2H, s), 7.21—7.68 (30H, m); ^{13}C NMR δ=60.4, 63.2, 68.5, 79.0 (d, *J* = 16.1 Hz), 79.7, 82.7, 95.5 (d, *J* = 8.3 Hz), 101.3, 126.2, 127.9, 128.3 (d, *J* = 7.8 Hz), 128.4 (d, *J* = 6.8 Hz), 128.8, 129.2, 130.2 (d, *J* = 10.9 Hz), 130.5 (d, *J* = 11.9 Hz), 137.6, 142.1 (d, *J* = 17.1 Hz), 142.9 (d, *J* = 16.6 Hz); ^{31}P NMR δ = 116.4; IR (KBr) 697 (s), 750 (m), 789 (m), 807 (w), 999 (s), 1037 (s), 1072 (s), 1091 (s), 1374 (m), 1434 (m), 1455 (w), 1618 (w), 2855 (m), 2927 (s), 3052 (w), 3056 (w) cm^{-1}. Found: C, 68.18; H, 5.83; P, 6.51%. Calcd for $C_{52}H_{52}O_{11}P_2$: C, 68.26; H, 5.73; P, 6.77%.

2,2′-Di-*O*-benzyl-4,6 : 4′,6′-di-*O*-benzylidene-3,3′-di-*O*-diphenylphosphino-α,α-trehalose (4): 53% yield, a white solid: Mp 187—189 °C. $[\alpha]_D^{23}$ = +22.3° (*c* 0.5, $CHCl_3$). ^{1}H NMR δ = 3.53 (2H, t, *J* = 10.0 Hz), 3.61 (2H, t, *J* = 10.0 Hz), 3.65 (2H, dd, *J* = 3.9, 10.0 Hz), 3.90 (2H, dd, *J* = 4.8, 10.0 Hz), 4.19 (2H, dt, *J* = 4.8, 10.0 Hz), 4.38 (2H, d, *J* = 12.0 Hz), 4.43 (2H, d, *J* = 12.0 Hz), 4.65 (2H, m), 5.10 (2H, d, *J* = 3.9 Hz), 5.27 (2H, s), 7.06—7.53 (40H, m); ^{13}C NMR δ = 62.9, 68.7, 73.1, 79.1 (d, *J* = 4.6 Hz), 79.4 (d, *J* = 20.2 Hz), 81.6, 94.9, 101.4, 126.2, 127.38, 127.42, 127.8, 127.9 (d, *J* = 6.4 Hz), 128.0 (d, *J* = 7.4 Hz), 128.1, 128.3, 128.6, 129.9 (d, *J* = 21.1 Hz), 131.3 (d, *J* = 23.0 Hz), 137.0, 137.6, 142.7 (d, *J* = 15.6 Hz), 143.1 (d, *J* = 16.6 Hz); ^{31}P NMR δ = 115.0; IR (KBr) 697 (s), 751 (m), 829 (w), 978 (s), 998 (s), 1012 (s), 1052 (m), 1107 (s), 1371 (m), 1435 (m), 1453 (w), 1638 (w), 2859 (w), 2926 (w), 3055 (w) cm^{-1}. Found: C, 72.06; H, 5.70; P, 5.85%. Calcd for $C_{64}H_{62}O_{11}P_2$: C, 72.04; H, 5.67; P, 5.81%.

A General Procedure for the Hydrogenation Reaction: A rhodium complex, $[Rh(cod)_2]BF_4$ (0.5×10^{-2} mmol), and a ligand (0.55×10^{-2} mmol) were dissolved in a degassed solvent under Ar, and the solution was stirred at room temperature for 1 h. The catalyst solution was transferred quantitatively by a syringe using degassed solvent (0.5 mL) into the hydrogenation flask containing the substrate (0.25 mmol), and the mixture was stirred vigorously at room temperature under atmospheric hydrogen. After the complete conversion was confirmed by GC or TLC monitoring, the reaction mixture was concentrated and a portion was passed through a short column on SiO_2 with petroleum ether–AcOEt (v/v = 1 : 10) to remove the catalyst. The enantiomeric excess was measured by HPLC using either a Daicel Chiralcel OD or OJ column.

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