Novel Water-Soluble Bisphosphinite Chiral Ligands Derived from α,α- and *β,β*-Trehalose. Application to Asymmetric Hydrogenation of Dehydroamino Acids and Their Esters in Water or an Aqueous/Organic Biphasic Medium

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Received March 11, 1999

Novel 2,3:4,6-di-*O*-isopropylidene-α-D-glucopyranosyl-(1,1)-4,6-*O*-isopropylidene-2,3-di-*O*-diphenylphosphino-α-D-glucopyranoside (**2**), 2,3:4,6-di-*O*-cyclohexylidene-α-D-glucopyranosyl-(1,1)-4,6-*O*-cyclohexylidene-2,3-di-*O*-diphenylphosphino-α-D-glucopyranoside (**4**), and 2,3:4,6-di-*O*-cyclohexylidene-*β*-D-glucopyranosyl-(1,1)-4,6-*O*-cyclohexylidene-2,3-di-*O*-diphenylphosphino-*β*-D-glucopyranoside (**11**) were prepared from the corresponding α,α- or *β,β*-trehalose. The ligands were transformed into cationic Rh complexes, such as [Rh(α-D-glucopyranosyl-(1,1)-2,3-di-*O*-diphenylphosphino-α-D-glucopyranoside)(cod)]BF_4 (**3**) and [Rh(*β*-D-glucopyranosyl-(1,1)-2,3-di-*O*-diphenylphosphino-*β*-D-glucopyranoside)(cod)]BF_4 (**12**) bearing free hydroxy groups. These complexes were soluble in water and were efficient catalysts for the asymmetric hydrogenation of dehydroamino acids and their esters in water or an aqueous/organic biphasic medium with high enantioselectivity (up to 99.9% ee). Aqueous biphasic systems offer an easy separation of the aqueous catalyst phase from the product phase and allow recycling of the catalyst phase without the loss of enantioselectivity.

Introduction

Homogeneous catalysts have many attractive advantages over their heterogeneous counterparts, because the former have well-defined active sites with steric and electronic properties influenced by their ligands. Therefore, higher activities and selectivities are exhibited under milder operating reaction conditions.[1] Industrial large-scale applications of homogeneous catalysts, however, encounter serious drawbacks, such as the cumbersome separation of the expensive catalysts from reaction products and the quantitative recovery of the catalyst in an active form. In many cases, the separation of the product phase from the miscible molecular catalyst phase includes thermal operation, such as distillation, decomposition, transformation, and rectification, which normally causes thermal stress on the catalyst, sacrificing the catalytic activity. As a way of solving these problems, an aqueous biphasic system using a water-soluble complex has attracted a great deal of interest.[2] Ruhrchemie/Rhône-Poulenc's oxo process[3] is a benchmark in the field of homogeneous catalyst in aqueous media, and its success stimulated the application of this principle to a broad spectrum of catalytic reactions. The principle of this biphasic catalytic system is depicted in Figure 1. Generally, after the reaction the water-soluble organometallic complex loaded as a catalyst and the reaction product are maintained in an aqueous phase and an organic phase, respectively. This intrinsic nature of phase separation can facilitate the isolation of the product from the catalyst and the recycle of the catalyst phase. In addition, since water is used as solvent, this system is economically and environmentally attractive.

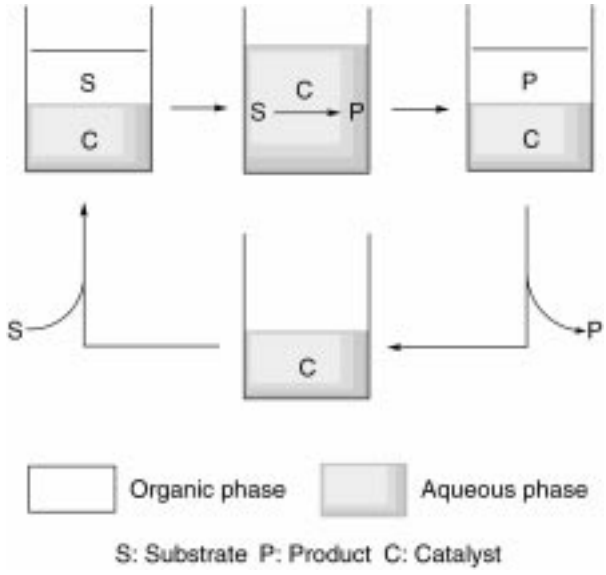

Figure 1. General principle of biphasic catalysis in an aqueous/organic medium.

Solubilization of transition-metal complexes in aqueous media has been usually accomplished by the attachment of charged or polar substituents, such as sulfonate, carboxylate, ammonium, phosphonium, and polyether, to their ligands. Complexes bearing such ligands have been

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10.1021/jo990448m CCC: $18.00
Published on Web 07/02/1999

applied to various reactions in water.[2] Furthermore, several water-soluble chiral ligands incorporating these substituents have been developed as well over the past decade, providing fair to good enantioselectivity in the hydrogenation[4] and hydroformylation[5] of alkenes and the hydrogenolysis of epoxides.[6]

In contrast, water-soluble ligands incorporating polyhydroxy groups have been used to a lesser extent.[7] For this reason, transformation of carbohydrates, especially monosaccharides, into water-soluble ligands now receives increased attention.[8] Carbohydrates have some advantages for ligand synthesis, since they are ubiquitously present in nature, and therefore readily available. Moreover, since they contain both many chiral centers and hydroxy groups in their skeletons, they are applicable to the synthesis of a variety of water-soluble chiral ligands. Recently, Selke, Oehme, and co-workers reported the application of the water-soluble or sparingly water-soluble rhodium complexes derived from α- or *β*-D-glucose to asymmetric reactions.[9] Although such complexes were active in asymmetric hydrogenation of dehydroamino acids and their derivatives in water, the addition of a surfactant was still necessary to achieve high reactivity as well as high enantioselectivity.[9a,b]

In this paper, we report the synthesis of novel water-soluble disaccharide chiral ligands in which one sugar moiety is attached to the 2,3-diphosphinite glucopyranoside moiety at the anomeric position by a glycosid linkage in order to increase the water-solubility (Figure 2). Their application to asymmetric hydrogenation of dehydroamino acids and their esters in water or an aqueous/organic biphasic medium will be described. Since the catalysts having such ligands are more soluble in water than those based on monosaccharides, their use as ligands of transition-metal catalysts may allow the asymmetric reaction in an immiscible biphasic system.

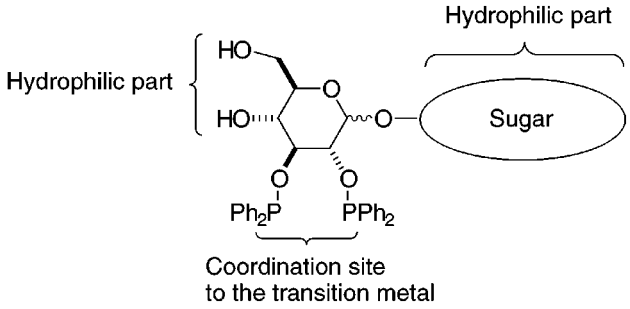

Figure 2. Concept for the water-soluble disaccharide chiral ligand.

Results and Discussion

We initially chose the α,α-trehalose (α-D-glucopyranosyl-(1,1)-α-D-glucopyranoside) as a starting material and planned to synthesize the Rh complex **3** in which α-D-glucopyranosyl-(1,1)-2,3-di-*O*-diphenylphosphino-α-D-glucopyranoside was introduced as a poly-hydroxy chiral ligand. α,α-Trehalose is found in many bacteria and fungi, in plants, and in the blood of most insects. In addition to its ready availability, we could take advantage of some features of it for the synthesis of a water-soluble poly-hydroxy chiral ligand: (i) 2,3-Di-*O*-diphenylphosphino-α,α-trehaloses which are protected in the 4,6:2′,3′:4′,6′ positions by cyclic acetals can be synthesized, and these protecting groups can be easily removed under acidic conditions. (ii) Because α,α-trehalose does not contain a reducing sugar in its structure, both D-glucopyranosyl structures may not be influenced by the isomerization under acidic conditions. The preparative sequence for such ligand and complex is depicted in Scheme 1.

First, 2,3:4,6-di-*O*-isopropylidene-α-D-glucopyranosyl-(1,1)-4,6-*O*-isopropylidene-α-D-glucopyranoside (**1**)[10] was prepared and then was transformed into 2,3:4,6-di-*O*-isopropylidene-α-D-glucopyranosyl-(1,1)-4,6-*O*-isopropylidene-2,3-di-*O*-diphenylphosphino-α-D-glucopyranoside (**2**) by treatment with Ph_2PCl and Et_3N. A complex [Rh(**2**)(acac)] was formed in situ by the reaction of [Rh(acac)(cod)] with chiral ligand **2** in degassed THF under Ar, and then 40% aqueous HBF_4 was added to this solution at 50 °C. After 4 h, degassed dry Et_2O was added and a separated orange syrup was rinsed with degassed Et_2O to give a water-soluble cationic Rh complex **3** in 76% yield (Scheme 1, Path A). On the other hand, we previously reported the synthesis of 2,3:4,6-di-*O*-cyclohexylidene-α-D-glucopyranosyl-(1,1)-4,6-*O*-cyclohexylidene-2,3-di-*O*-diphenylphosphino-α-D-glucopyranoside (**5**) from α,α-trehalose via the compound **4** and its application to the asymmetric hydrogenation of dehydroamino acids and their esters.[11] Then, we could prepare the complex **3** from **5** (Scheme 1, Path B). If two protection methods were compared, the efficiency of the tri-protection step by cyclohexylidene groups was higher (53%, 2 steps) than that by isopropylidene groups (20%, 2 steps), while the deprotection step of alkylidene groups from the Rh complex of **2** and **5** proceeded similarly in both cases. As

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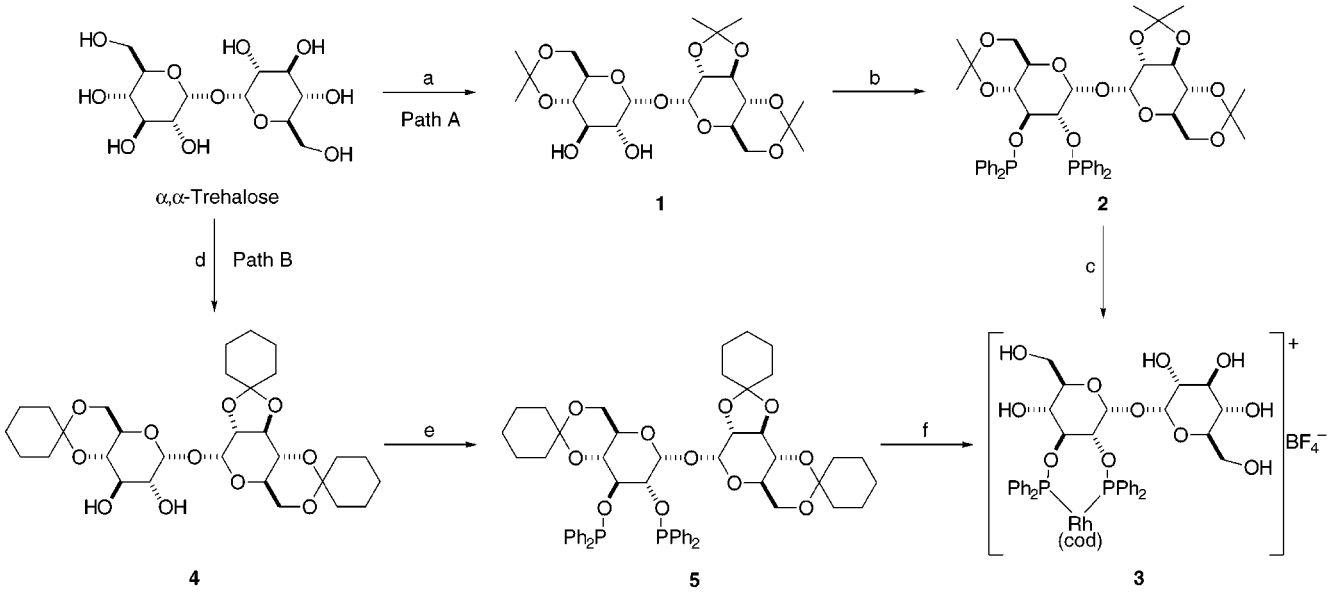
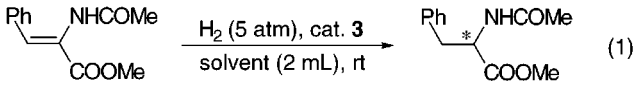
Scheme 1[a]



[a] (i) $Me_2C(OMe)_2$, cat. *p*-TsOH·H_2O, DMF, 80 °C, 6 h; (ii) Ac_2O, C_5H_5N, rt, overnight, 20% (2 steps); (iii) K_2CO_3, MeOH, rt, 1 h, 70%. (b) Ph_2PCl, cat. DMAP, Et_3N-THF, rt, 15 min, 63%. (c) (i) [Rh(acac)(cod)], THF, rt, 20 min; (ii) 40% aqueous HBF_4, 50 °C, 4 h, 76% (2 steps). (d) 1,1-dimethoxycyclohexane, cat. *p*-TsOH·H_2O, DMF, 80 °C, 6 h; (ii) Ac_2O, C_5H_5N, rt, overnight, 53% (2 steps); (iii) K_2CO_3, MeOH, rt, 1 h, 68%. (e) Ph_2PCl, cat. DMAP, Et_3N-THF, rt, 15 min, 65%. (f) (i) [Rh(acac)(cod)], THF, rt, 20 min; (ii) 40% aqueous HBF_4, 50 °C, 4 h, 72% (2 steps).

Table 1. Asymmetric Hydrogenation of Methyl α-Acetamidocinnamate Using 3 in Water or an Aqueous/Organic Medium[a]



(1)

13

entry	solvent	cat. (mol %)	time (h)	ee (%)[b] (*S*)[c]
1	H_2O	5	6	55
2[d]	H_2O	1	1	90
3	H_2O/AcOEt = 1/1	2	1.5	68 (66)[e]
4	H_2O/CH_3OH/AcOEt = 0.6/0.4/1	1	3	76
5	H_2O/CH_3OH = 3/2	1	1.5	75

[a] Complete conversion of **3** in all cases. [b] The ee (%) values were determined by HPLC. [c] The absolute configuration was determined by optical rotation. [d] Sodium dodecyl sulfate (10 mol %) was added. [e] The enantiomeric excess obtained from the second use of the catalyst aqueous solution is shown in parentheses.

can be expected, the complex **3** was soluble in water, at ca. 5 g/100 mL at 20 °C.

Asymmetric hydrogenation of methyl α-acetamidocinnamate (**13**) was carried out using the complex **3** in water or an aqueous/organic biphasic medium at room temperature under H_2 pressure (5 atm) (eq 1). The results are summarized in Table 1.

The reaction proceeded even in H_2O to give moderate selectivity (55% ee) (entry 1). The addition of sodium dodecyl sulfate (SDS) as an amphiphile improved its selectivity to 90% ee (entry 2). In a biphasic system (H_2O−AcOEt = 1:1), the reaction also occurred smoothly to give higher ee value (68% ee) than that in H_2O (entry 3). Furthermore, after the reaction was completed the organic phase including the product was easily separated by decantation. The aqueous phase containing the catalyst could be reused for the same hydrogenation to give almost the same enantiomeric excess (66% ee), albeit, with lower catalytic activity (70% conversion) under identical conditions. The best result (76% ee) in a biphasic system was obtained when the reaction was carried out in H_2O−MeOH−AcOEt = 0.6:0.4:1 (entry 4). Almost the same ee value (75% ee) was also observed in a homogeneous system (H_2O−MeOH = 3:2) (entry 5).

Next, we tried to synthesize the analogous water-soluble Rh complex (**12**) from *β*,*β*-trehalose (*β*-D-glucopyranosyl-(1,1)-*β*-D-glucopyranoside)[12] (Scheme 2). The *β*,*β*-trehalose is not nature's reserve sugar but it can be easily prepared from penta-*O*-acetyl-*β*-D-glucopyranoside by the following procedures. After the bromination of penta-*O*-acetyl-*β*-D-glucopyranoside (**6**) at the anomeric position with 25% HBr/AcOH,[13] the obtained compound **7**, 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide, was treated with H_2O and Ag_2CO_3 to give 2,3,4,6-tetra-*O*-acetyl-*β*-D-glucopyranoside (**8**).[14] Glycosidation of **8** with phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-*β*-D-glucose using *N*-iodosuccinimide/cat. trifluoromethanesulfonic acid (TfOH) as an activator[15] followed by deacetylation gave *β*,*β*-trehalose (**9**). The compound **9** was dissolved in dry DMF, and the solution was stirred at 80 °C in the presence of 1,1-dimethoxycyclohexane and a catalytic amount of *p*-toluenesulfonic acid. After 4 h, isolation of the mixture followed by acetylation produced crude 2,3:4,6-di-*O*-cyclohexylidene-*β*-D-glucopyranosyl-(1,1)-4,6-*O*-cyclohexylidene-2,3-di-*O*-acetyl-*β*-D-glucopyranoside. Deacetylation of this compound gave 2,3:4,6-di-*O*-cyclohexylidene-*β*-D-glucopyranosyl-(1,1)-4,6-*O*-cyclohexylidene-*β*-D-glucopyranoside (**10**). Treatment of **10** with Ph_2PCl and Et_3N afforded 2,3:4,6-di-*O*-cyclohexylidene-*β*-D-glucopyranosyl-(1,1)-4,6-*O*-cyclohexylidene-2,3-di-*O*-diphenylphosphino-*β*-D-glucopyranoside (**11**). The rhodium complex

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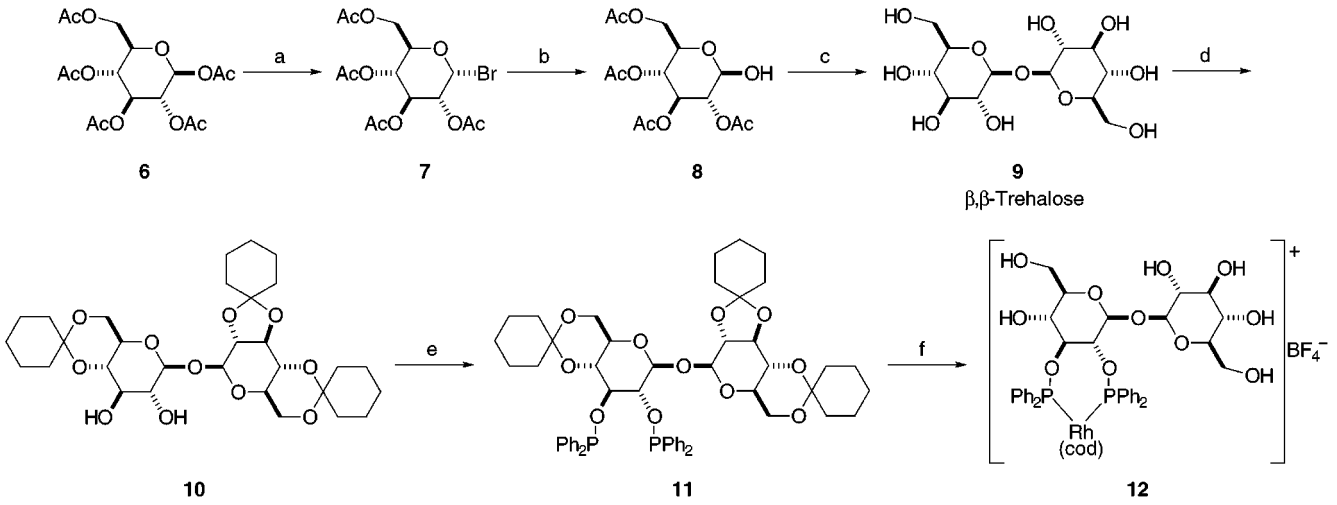
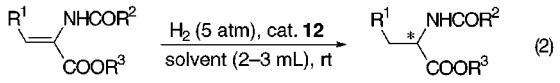
Scheme 2[a]



[a] (a) 25% HBr/AcOH, CH_2Cl_2, rt, 12 h, 90%. (b) Ag_2CO_3, H_2O, 0 °C, 1 h, 85%. (c) (i) phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-*β*-D-glucose, NIS(*N*-iodosuccinimide), cat. TfOH, MS 4A, CH_2Cl_2, rt, 30 min; (ii) NaOMe, MeOH, reflux, 15 min, 36% (2 steps). (d) (i) 1,1-dimethoxycyclohexane, cat. *p*-TsOH, DMF, 80 °C, 4 h; (ii) Ac_2O, C_5H_5N, rt, overnight; (iii) K_2CO_3, MeOH, rt, 1 h, 32% (3 steps). (e) Ph_2PCl, cat. DMAP, Et_3N-THF, rt, 15 min, 65%. (f) (i) [Rh(acac)(cod)], THF, rt, 20 min; (ii) 40% aqueous HBF_4, 50 °C, 4 h, 79% (2 steps).

Table 2. Asymmetric Hydrogenation of Dehydroamino Acids Using 12 in Water or an Aqueous/Organic Medium[a]



13: R^1 = Ph, R^2 = Me, R^3 = Me **16**: R^1 = 4-methoxyphenyl, R^2 = Me, R^3 = Me
14: R^1 = Ph, R^2 = Me, R^3 = H **17**: R^1 = 2-naphthyl, R^2 = Me, R^3 = Me
15: R^1 = Ph, R^2 = Ph, R^3 = Me **18**: R^1 = H, R^2 = Me, R^3 = Me

entry	substrate	solvent	cat. (mol %)	time (h)	ee (%)[b] (*S*)[c]
1	**13**	H_2O	5	6	88
2[d]	**13**	H_2O	1	1	99.9
3	**13**	H_2O/AcOEt = 1/1	2	1.5	87 (85)[e]
4	**13**	H_2O/CH_3OH/AcOEt = 0.6/0.4/1	1	3	98
5	**13**	H_2O/CH_3OH = 3/2	1	1.5	94
6	**14**	H_2O/CH_3OH/AcOEt = 0.6/0.4/2	1	3	96[f]
7	**14**	H_2O/CH_3OH = 3/2	1	1.5	95[f]
8	**15**	H_2O/CH_3OH/AcOEt = 0.6/0.4/1	1	3	92
9	**15**	H_2O/CH_3OH = 3/2	1	1.5	90
10	**16**	H_2O/CH_3OH/AcOEt = 0.6/0.4/1	1	3	98
11	**16**	H_2O/CH_3OH = 3/2	1	3	98
12	**17**	H_2O/CH_3OH/AcOEt = 0.6/0.4/1	1	3	96
13	**17**	H_2O/CH_3OH = 3/2	1	3	95
14	**18**	H_2O	2	1.5	80

[a] Complete conversion of alkenes in all cases. [b] The ee (%) values were determined by HPLC. [c] The absolute configuration was determined by optical rotation. [d] Sodium dodecyl sulfate (10 mol %) was added. [e] The enantiomeric excess obtained from the second use of the catalyst aqueous solution is shown in parentheses. [e] The ee (%) values were determined on its methyl ester.

[Rh(**11**)(acac)] formed in situ by the reaction of [Rh(acac)-(cod)] with the chiral ligand **11** in degassed THF under Ar was treated with 40% aqueous HBF_4 at 50 °C for 4 h to give a cationic Rh complex (**12**) in 79% yield. The water solubility of the complex **12** was almost the same as that of the complex **3**, being ca. 4.3 g/100 mL at 20 °C.

The results of asymmetric hydrogenation of dehydroamino acids and their esters (**13**−**18**) using the complex **12** in water or an aqueous/organic biphasic medium at room temperature under H_2 pressure (5 atm) (eq 2) are listed in Table 2. The hydrogenation of **13** proceeded smoothly in H_2O and the enantiomeric excess (88% ee) was higher than in the case of the complex **3** (entry 1). Moreover, complete enantioselectivity (99.9% ee) could be achieved in the presence of SDS as an amphiphile (entry 2). This ee value was much higher than that obtained by monosaccharide chiral ligands under the same conditions.[9a,b] When the hydrogenation was carried out in H_2O−AcOEt = 1:1 biphasic system, the ee value of product was 87%. The aqueous phase containing the complex **12** could be reused after the separation. The same level of enantiomeric excess of the product was maintained in 85% ee, although the conversion of the starting material was decreased to 82% (entry 3). The ee value was improved to 98% when the reaction was carried out in H_2O−MeOH−AcOEt = 0.6:0.4:1 biphasic system (entry 4). In H_2O−MeOH = 3:2 homogeneous system, the ee value was 94% (entry 5). In this case, the product could be extracted with AcOEt after the reaction and the catalyst phase was separated by a simple phase separation. The hydrogenation of **14** bearing a carboxylic acid group also proceeded both in H_2O−MeOH−AcOEt = 0.6:0.4:2 and in H_2O−MeOH = 3:2 with 96% ee and 95% ee, respectively (entries 6 and 7). Several

dehydroamino acid derivatives (**15**−**17**) were effectively hydrogenated with good enantioselectivities (90−98% ee) under homogeneous and heterogeneous conditions (entries 8−13). Since the compound **18** was quite soluble in water, the reaction proceeded completely in water within 1.5 h even in the absence of methanol as a cosolvent with 80% ee (entry 14). The reason for the high selectivity and the high reactivity observed in asymmetric hydrogenation using the catalyst **12** in water or aqueous solvent without surfactant might be ascribed to a high solubility as well as an ability of effective micelle formation of **12** in water.

Summary

We successfully prepared the novel disaccharide chiral ligands **2**, **5**, and **11** from natural reserve sugars. The water-soluble cationic Rh complexes **3** and **12** possessing free poly-hydroxy groups could be synthesized by the reaction of [Rh(cod)(acac)] with the ligands **2**, **5**, and **11** derived from α,α- or *β*,*β*-trehalose, followed by treatment with 40% aqueous HBF_4. These complexes were effective catalysts for the hydrogenation of dehydroamino acids and their esters in water or an aqueous/organic biphasic medium with high enantiomeric excesses (up to 99.9% ee). In the present biphasic system, the catalysts are immobilized in the aqueous phase. The catalyst could be recovered by simple phase separation. The aqueous catalyst phase could be reused for further operation in hydrogenation to give almost the same enantiomeric excesses. These results show that origosaccharides are applicable to the synthesis of water-soluble chiral ligands. Although the addition of MeOH as a cosolvent to the biphasic system was required, the highest enantiomeric excess (98% ee), which has never been accomplished in an aqueous medium using other water-soluble chiral ligands, could be obtained.

Experimental Section

General. Tetrahydrofuran (THF) and diethyl ether were distilled from sodium benzophenone ketyl under argon. Dichloromethane, *N*,*N*-dimethylformamide (DMF), and triethylamine were distilled from calcium hydride. NMR spectra were measured for solutions in $CDCl_3$, d_4-MeOH, or d_8-THF with Me_4Si as an internal standard (^1H and ^{13}C) or with $P(OMe)_3$ as an external standard (^{31}P). Melting points are uncorrected. Elemental analyses were performed at Microanalytical Center of Kyoto University. α,α-Trehalose dihydrate was purchased from Hayashibara Corporation. Pentaacetyl-*β*-D-glucopyranoside was purchased from Tokyo Chemical Industry Co, Ltd.

***β*-D-Glucopyranosyl-(1,1)-*β*-D-glucopyranoside (*β*,*β*-trehalose) (9).** This compound was prepared by the modified procedure of Brown et al.[12] The phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-*β*-D-glucose (6.6 g, 15 mmol) and alcohol **8** (5.2 g, 15 mmol) were dissolved in dry CH_2Cl_2 under argon, and *N*-iodosuccinimide (3.8 g, 17 mmol) and pulverized MS4A (5 g) were added to the solution. A solution of trifluoromethanesulfonic acid in CH_2Cl_2 (ca. 0.15 M) was added dropwise to this solution until TLC indicated that the substrate had been consumed. After filtration through a Celite pad, the solution was washed with aqueous $NaHCO_3$ followed by aqueous $Na_2S_2O_3$ and dried over $MgSO_4$. The solvent was evaporated under vacuum and the residue was subjected to column chromatography on SiO_2 with $CHCl_3$−AcOEt (v/v = 1:1) as an eluent to give a crude octaacetyl *β*,*β*-trehalose. To this crude product was added a small amount of Et_2O to precipitate a pure octaacetyl *β*,*β*-trehalose (3.9 g, 5.7 mmol). To methanolic NaOMe (2.6 mL, 0.1 M) was added a solution of octaacetyl *β*,*β*-trehalose in hot methanol, and this solution was refluxed for 15 min. The solvent was removed under vacuum. The solid was recrystallized from methanol/ethanol and dried under vacuum. Pure compound **9** (1.8 g, 5.4 mmol, 36%) was obtained as a white solid. NMR data were consistent with those of the reported ones.

2,3:4,6-Di-*O*-cyclohexylidene-*β*-D-glucopyranosyl-(1,1)-4,6-*O*-cyclohexylidene-*β*-D-glucopyranoside (10). To the compound **9** (0.51 g, 1.5 mmol) in dry DMF (10 mL) were added 1,1-dimethoxycyclohexane (1.0 g, 6.9 mmol) and a catalytic amount of *p*-toluenesulfonic acid, and the mixture was stirred at 80 °C for 4 h. If necessary, more 1,1-dimethoxycyclohexane was added. After the mixture was cooled, solid $NaHCO_3$ was added to quench the reaction. Solvent was removed under vacuum. The resulting crude syrup was dissolved in dry pyridine (15 mL), and then acetic anhydride (5 mL) was added. This solution was stirred overnight and then poured into ice−water. The product was extracted with $CHCl_3$, and the organic layer was washed successively with aqueous $CuSO_4$ and saturated aqueous NaCl, and dried over $MgSO_4$. The solvent was evaporated under vacuum, and the residue was subjected to column chromatography on SiO_2 with petroleum ether−AcOEt (v/v = 8:3) as an eluent to give crude 2,3:4,6-di-*O*-cyclohexylidene-*β*-D-glucopyranosyl-(1,1)-4,6-*O*-cyclohexylidene-2,3-di-*O*-acetyl-*β*-D-glucopyranoside. To a solution of this compound in methanol (10 mL) was added K_2CO_3 (0.1 g, 0.7 mmol), and the mixture was stirred for 1 h. The solvent was evaporated under vacuum and the residue was subjected to column chromatography on SiO_2 with petroleum ether−AcOEt (v/v = 1:1) as an eluent to give **10** (0.28 g, 0.48 mmol, 32%) as a white solid: mp 157.2−157.3 °C; $[\alpha]_D^{24} = -43.5°$ (c = 0.5, $CHCl_3$); ^1H NMR (400 Mz, $CDCl_3$) δ 1.30−2.40 (m, 30H), 3.31 (m, 2H), 3.42 (t, J = 8.5 Hz, 1H), 3.54 (t, J = 8.0 Hz, 1H), 3.59−3.72 (m, 3H), 3.82−3.97 (m, 5H), 4.72 (d, J = 6.9 Hz, 1H), 5.00 (d, J = 8.0 Hz, 1H) ppm; ^{13}C NMR (100 Mz, $CDCl_3$) δ 22.5, 22.7, 22.8, 23.5, 24.9, 25.5, 27.7, 27.8, 35.8, 36.1, 37.7, 37.8, 61.1, 61.3, 68.0, 70.4, 71.6, 71.8, 73.7, 73.9, 98.6, 99.8, 99.9, 100.0, 113.1 ppm; IR (KBr) 1100, 3484 cm^{-1}; HRMS (FAB) calcd for $C_{30}H_{47}O_{11}$ ($M+H^+$) 583.3118, found 583.3109.

A Typical Procedure for Synthesis of a Diphenylphosphinite Compound. To a solution of **1** (0.23 g, 0.5 mmol) and a catalytic amount of 4-(dimethylamino)pyridine in 2 mL of degassed THF/Et_3N (v/v = 1:1) was added chlorodiphenylphosphine (0.2 mL, 1.1 mmol) at room temperature, and the mixture was stirred for 15 min. The mixture was concentrated to dryness and the residue was subjected to column chromatography on Al_2O_3 with degassed hexane−CH_2Cl_2 (v/v = 1:2) as an eluent to give 2,3:4,6-di-*O*-isopropylidene-α-D-glucopyranosyl-(1,1)-4,6-*O*-isopropylidene-2,3-di-*O*-diphenylphosphino-α-D-glucopyranoside (**2**) (0.27 g, 0.32 mmol, 63%) as a white solid: mp 86.5−86.8 °C; $[\alpha]_D^{24} = +59.4°$ (c = 0.27, $CHCl_3$); ^1H NMR (400 Mz, $CDCl_3$) δ 0.92 (s, 3H), 1.11 (s, 3H), 1.39 (s, 3H), 1.46 (s, 3H), 1.49 (s, 3H), 1.53 (s, 3H), 3.5−3.8 (m, 7H), 3.92 (t, J = 9.3 Hz, 1H), 4.0−4.1 (m, 2H), 4.18 (t, J = 9.3 Hz, 1H), 4.45 (m, 1H), 5.14 (d, J = 2.3 Hz, 1H), 5.30 (d, J = 2.4 Hz, 1H), 7.0−7.6 (m, 20H) ppm; ^{13}C NMR (100 Mz, $CDCl_3$) δ 17.9, 19.2, 26.2, 26.8, 28.6, 28.9, 61.9, 62.2, 63.8, 66.1, 73.6, 73.7, 76.5, 77.6 (dd, J = 5.5, 12.9 Hz), 80.1 (dd, J = 3.7, 20.2 Hz), 94.7, 96.0 (d, J = 5.6 Hz), 99.3, 99.4, 111.8, 127.7−130.9 (12 carbons), 140.5 (d, J = 16.5 Hz), 142.0 (d, J = 22.0 Hz), 142.6 (d, J = 12.9 Hz), 143.6 (d, J = 20.2 Hz) ppm; ^{31}P NMR (161.9 Mz, $CDCl_3$) δ 111.9, 115.1 ppm; IR (KBr) 1434 cm^{-1}; HRMS (FAB) calcd for $C_{45}H_{52}O_{11}P_2$ M^+ 830.2985, found 830.2969. Anal. Calcd for $C_{45}H_{52}O_{11}P_2$: C, 65.05; H, 6.31; P, 7.46. Found: C, 65.33; H, 6.38; P, 7.12.

2,3:4,6-Di-*O*-cyclohexylidene-*β*-D-glucopyranosyl-(1,1)-4,6-*O*-cyclohexylidene-2,3-di-*O*-diphenylphosphino-*β*-D-glucopyranoside (11). 65% yield, a white solid; mp 116.1−116.2 °C; $[\alpha]_D^{24} = -38.5°$ (c = 0.24, $CHCl_3$); ^1H NMR (400 Mz, $CDCl_3$) δ 0.60−2.20 (m, 30H), 2.61 (t, J = 9.3 Hz, 1H), 3.03 (dt, J = 4.9, 9.3 Hz, 1H), 3.33 (dt, J = 5.8, 10.4 Hz, 1H), 3.42 (t, J = 9.3 Hz, 1H), 3.50 (t, J = 9.3 Hz, 1H), 3.57 (t, J = 9.3 Hz, 1H), 3.67 (t, J = 10.4 Hz, 1H), 3.77−3.82 (m, 2H), 3.86 (dd, J = 5.8, 10.4 Hz, 1H), 4.24−4.28 (m, 2H), 4.78 (d, J = 9.3 Hz, 1H), 4.93 (d, J = 7.3 Hz, 1H), 7.01−7.52 (m, 20H) ppm; ^{13}C NMR (100 Mz, $CDCl_3$) δ 22.1, 22.4, 22.7, 23.5, 25.0, 25.4,

25.5, 26.4, 28.0, 35.8, 36.2, 37.4, 37.7, 61.2, 67.0, 69.6, 71.4, 71.7, 76.5, 77.2, 82.9 (dd, J = 3.7, 23.9 Hz), 83.1 (dd, J = 5.5, 20.2 Hz), 96.4, 96.8, 99.7, 99.8, 112.5, 127.6−131.5 (12 carbons), 142.3 (d, J = 11.1 Hz), 142.5 (d, J = 11.0 Hz), 143.9 (d, J = 11.0 Hz), 144.6 (d, J = 9.2 Hz) ppm; ^{31}P NMR (161.9 Mz, $CDCl_3$) δ 109.9, 115.5 ppm; IR (KBr) 1435 cm^{-1}; HRMS (FAB) calcd for $C_{54}H_{64}O_{11}P_2$ M^+ 950.3924, found 950.3931. Anal. Calcd for $C_{54}H_{64}O_{11}P_2$: C, 68.20; H, 6.78; P, 6.51. Found: C, 68.29; H, 7.00; P, 6.52.

A Typical Procedure for Synthesis of a Water-Soluble Rh Complex. [Rh(acac)(cod)] (15.5 mg, 0.05 mmol) and **2** (41.5 mg, 0.05 mmol) [or **5** (47.6 mg, 0.05 mmol)] were dissolved in degassed dry THF (1.0 mL) and the mixture was stirred under Ar. After 20 min, 40% aqueous HBF_4 was added to the solution and the mixture was stirred at 50 °C for 4 h. Degassed dry Et_2O (5.0 mL) was added, and the complex was separated out as an orange syrup. The supernatant solution was decanted, and degassed dry Et_2O (5.0 mL) was again added to the obtained syrup. The product, [Rh(α-D-glucopyranosyl-(1,1)-2,3-di-*O*-diphenylphosphino-α-D-glucopyranoside)(cod)]BF_4 (**3**), was crystallized as an orange powder (36.0−38.0 mg, 0.036−0.038 mmol, 72−76%): ^{31}P NMR (161.9 MHz, d_4-MeOH) δ 131.0 (dd, ^1J (Rh, P) = 180 Hz, ^2J (P, P) = 28 Hz), 138.7 (dd, ^1J (Rh, P) = 180 Hz, ^2J (P, P) = 28 Hz) ppm; LRMS (FAB) m/z 921 (M^+−BF_4).

[Rh(*β*-D-glucopyranosyl-(1,1)-2,3-di-*O*-diphenylphosphino-*β*-D-glucopyranoside)(cod)]BF_4 (12). ^{31}P NMR (161.9 MHz, d_8-THF) δ 131.6 (dd, ^1J (Rh, P) = 177 Hz, ^2J (P, P) = 24 Hz), 132.5 (dd, ^1J (Rh, P) = 177 Hz, ^2J (P, P) = 24 Hz) ppm; LRMS (FAB) m/z 921 (M^+−BF_4).

A Typical Procedure for the Hydrogenation of Dehydroamino Acids in an Aqueous/Organic Medium. H_2O-MeOH−AcOEt System. The Rh complex **3** [or **12**] (1.5 mg, 0.15×10^{-2} mmol) was dissolved in H_2O−MeOH = 3:2 solution (1.0 mL), and the solution was injected to a stainless steel autoclave with glass container by a syringe under Ar. To this solution was added a solution of the substrate (0.15 mmol) in AcOEt (1.0−2.0 mL) by a syringe under Ar, and the mixture was stirred vigorously under H_2 pressure (5 atm). After the end of the reaction was confirmed by GLC, TLC, or ^{1}H NMR, the organic phase was separated by decantation and the solvent was evaporated under vacuum to give the product (85−93% yield). The enantiomeric excess was determined by HPLC using either a Daicel Chiralcel OD or OJ column (4.6 × 250 mm) at 40 °C.

H_2O-MeOH System. To the Rh complex **3** [or **12**] (1.5 mg, 0.15×10^{-2} mmol) and substrate (0.15 mmol) in a stainless steel autoclave with glass container was added a H_2O−MeOH = 3:2 solution (2.0 mL) by a syringe under Ar, and the mixture was stirred vigorously under H_2 pressure (5 atm). After the end of the reaction was confirmed by GLC, TLC, or ^{1}H NMR, AcOEt (1.5 mL) and H_2O (0.5 mL) were added and the mixture was stirred vigorously for 10 min. The organic phase was separated by decantation and the solvent was evaporated under vacuum to give the product (80−90% yield). The enantiomeric excess was determined by HPLC using either a Daicel Chiralcel OD or OJ column (4.6 × 250 mm) at 40 °C.

JO990448M