Asymmetric Hydrogenation Using Diphenylphosphinite Derivatives of Carbohydrates as the Chiral Ligand of Rhodium Catalysts

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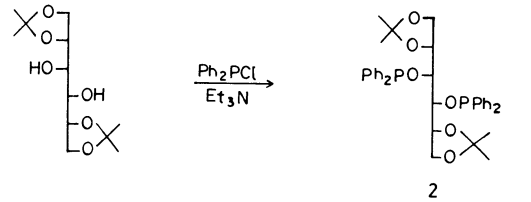
Synopsis. Diphenylphosphinite derivatives of carbohydrates (L-rhamnose, D-mannitol, and cellulose), which have asymmetric centers on the skeletons were synthesized. Asymmetric hydrogenations of prochiral substrates using rhodium catalysts with the prepared chiral phosphinite ligand were carried out to obtain chiral substances in 8—78% optical yield.

Monosaccharides have several chiral carbon atoms in their skeletons, however, their applications to homogeneous asymmetric hydrogenation are found only in several papers.[1-6] Cellulose, which widely exists in nature, is one of the most important naturally occurring resources and will work as a functional polymer, however, the investigation to apply the chirality to asymmetric induction are very much limited. As the result, the application of a bisphosphinite of cellulose to a chiral ligand for the rhodium catalyst was reported.[7]

In our preceding paper we reported the asymmetric hydrogenation of prochiral unsaturated acid derivatives to afford the corresponding saturated acid derivatives in an optical yields up to 100%, where methyl 2,3-*O*-isopropylidene-4-*O*-(diphenylphosphino)-α-L-rhamnopyranoside was revealed to be a good ligand for di-μ-chloro-bis(cyclooctadiene)dirhodium(I) catalyst.[6b] In this note we tried to clarify the efficiency of asymmetric hydrogenation catalysts in comparison with the preparative methods for the catalyst as well as the structure to spread the utility of carbohydrate ligands for asymmetric inductions.

Results and Discussion

Synthesis of Carbohydrate Ligands. Methyl 2,3-*O*-isopropylidene-4-*O*-(diphenylphosphino)-α-L-rhamnopyranoside (**1**) was prepared by the reaction of the anion of methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside with diphenylphosphinous chloride in ether, compound **1** thus prepared being agreed with that reported.[6b] 1,2:5,6-Di-*O*-isopropylidene-3,4-di-*O*-(diphenylphosphino)-D-mannitol (**2**) was prepared from 1,2:5,6-di-*O*-isopropylidene-D-mannitol by an action of diphenylphosphinous chloride in the presence of triethylamine (Eq. 1). 2,3,6-Tri-*O*-(diphenylphosphino)cellulose (**3**) was prepared from cellulose and diphenylphosphinous chloride in the presence of pyridine (Eq. 2).



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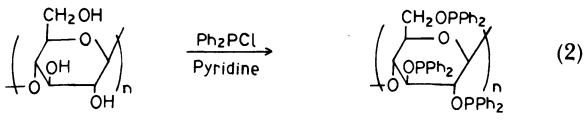

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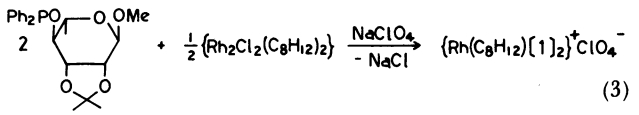
Preparation of Cationic Rhodium(I) Perchlorate Catalyst 4. Rhodium(I) perchlorate catalyst **4** was prepared by the reaction of di-μ-chloro-bis(cyclooctadiene)dirhodium(I) with ligand **1** and sodium perchlorate (Eq. 3).



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Asymmetric Hydrogenation of Prochiral Substrates. Asymmetric hydrogenation of prochiral substrates such as (*Z*)-α-acetylaminocinnamic acid, methyl (*Z*)-α-acetylaminocinnamate, (*Z*)-α-benzoylaminocinnamic acid, itaconic acid, dimethyl itaconate, tiglic acid, and acetophenone was carried out. The hydrogenation using rhodium(I) perchlorate catalyst **4** proceeded in 100% chemical yield for such a substrate as (*Z*)-α-acetylaminocinnamic acid to afford *N*-acetylphenylalanine ethyl ester. The optical yield was 54% with *R* configuration, being improved in optical yield over the previous work.[6b] The results are shown in Table 1. The complex was effective enough for the asymmetric hydrogenation, however, the chemical yields were not improved.

The asymmetric hydrogenation of prochiral olefins using di-μ-chloro-bis(cyclooctadiene)dirhodium(I) and mannitol **2** or cellulose **3** gave the results summarized in Table 2.

These results suggest that the cellulose ligand seems not to bring about a good asymmetric induction enough toward prochiral olefins owing mainly to its poor coordinating power to the rhodium catalyst because of its bulkiness, which cancels the merit of cellulose ligand in the hydrogenation procedure. Asymmetric hydrogenation of prochiral olefins with rhodium(I) catalysts having a cyclic carbohydrate ligand was expected to proceed excellently, because the tetrahydropyran ring has more rigid conformation

Table 1. Asymmetric Hydrogenation of Prochiral Substrates with $\{Rh(C_8H_{12})[\mathbf{1}]_2\}^+ClO_4^-$ (**4**)[a]

Substrate	Product	Chemical yield/%	$[\alpha]_D$/° (Solvent)	Optical yield/%[b]	(Configuration)
(*Z*)-α-Acetylaminocinnamic acid	*N*-Acetylphenylalanine ethyl ester[c]	100	−7.4 (*c* 0.85, EtOH)	54	(*R*)
Methyl (*Z*)-α-acetylaminocinnamate	*N*-Acetylphenylalanine methyl ester	50	−6.8 (*c* 1.02, MeOH)	32	(*R*)
(*Z*)-α-Benzoylaminocinnamic acid	*N*-Benzoylphenylalanine	53	+12.5 (*c* 0.28, MeOH)	31	(*R*)
Itaconic acid	Methylsuccinic acid	50	−13.3 (*c* 0.84, EtOH)	78	(*S*)
Dimethyl itaconate	Dimethyl methylsuccinate	96	−4.5 (*c* 0.96, EtOH)	73	(*S*)
Tiglic acid	2-Methylbutyric acid	60	+1.5 (*c* 0.77, EtOH)	8	(*R*)
Acetophenone	1-Phenylethanol	21	+19.4 (*c* 0.33, CH_2Cl_2)	37	(*R*)

a) The ratio of the substrate to the Rh complex was 25:1. All hydrogenations were carried out in 2 ml of benzene–ethanol (1:1) for 24 h at room temperature under atmospheric pressure of hydrogen in the presence of Et_3N (0.04 ml). b) Calculated on the basis of reported values of specific rotation for the optically pure compouds: (*S*)-*N*-acetylphenylalanine ethyl ester,[9] (*S*)-*N*-acetylphenylalanine methyl ester,[9] (*S*)-*N*-acetylphenylalanine,[10] (*S*)-*N*-benzoylphenylalanine,[11] (*R*)-methylsuccinic acid,[1] dimethyl (*R*)-methylsuccinate,[12] (*S*)-2-methylbutyric acid,[13] and (*S*)-1-phenylethanol.[14] c) Ethyl esterification proceeded at the deionization process of the catalyst with Dowex 50W (H^+).

Table 2. Asymmetric Hydrogenation of Prochiral Olefins with $[Rh(C_8H_{12})Cl]_2$ and Ligand **2** or **3**[a]

Substrate	Ligand	Product	Chemical yield/%	$[\alpha]_D$/° (Solvent)	Optical yield/%[b]	(Configuration)
(*Z*)-α-Acetylaminocinnamic acid[c]	**3**	*N*-Acetylphenylalanine	100	−3.8 (*c* 0.32, EtOH)	8.2	(*R*)
Methyl (*Z*)-α-acetylaminocinnamate[c]	**3**	*N*-Acetylphenylalanine methyl ester	100	+3.4 (*c* 1.39, MeOH)	16	(*S*)
(*Z*)-α-Benzoylaminocinnamic acid[c]	**3**	*N*-Benzoylphenylalanine	43	−3.6 (*c* 0.73, MeOH)	9.0	(*S*)
Itaconic acid	**2**	Methylsuccinic acid	50	−13.3 (*c* 0.84, EtOH)	78	(*S*)
Dimethyl itaconate[c,d]	**3**	Dimethyl methylsuccinate	100	+2.3 (*c* 1.00, EtOH)	38	(*R*)
Dimethyl itaconate	**2**	Dimethyl methylsuccinate	50	−1.2 (*c* 0.50, EtOH)	20	(*S*)

a) The ratio of the ligand to the Rh complex was 4:1. The reaction conditions were the same as that of Table 1 except otherwise noted. b) Calculated on the basis of the reported values of specific rotation for the optically pure compounds in Table 1. c) Conducted in 4 ml of the solvent. d) Conducted at 30°C under 50 atm of hydrogen.

than cyclohexane ring.[7] Ligands with less rigid and/or less soluble framework in solvents did not afford any good results in the asymmetric hydrogenation.

Experimental

Measurements. ^1H NMR spectra were measured on a Hitachi R-24B (60 MHz) spectrometer with tetramethylsilane as an internal standard, mass spectra were measured on a Hitachi RMU 7MG GC–MS spectometer, and IR spectra on a Japan Spectroscopic Co., Ltd. A-3 infrared spectrophotometer. Optical rotations were measured on Japan Spectroscopic Co., Ltd. DIP-4 digital polarimeter. Melting and boiling points were uncorrected.

Materials. The following materials were synthesized according to reported methods: di-μ-chloro-bis(cyclooctadiene)dirhodium(I),[6a] methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside,[6a] and 1,2:5,6-di-*O*-isopropylidene-D-mannitol.[8]

Synthesis of (Cyclooctadiene)bis[methyl 2,3-*O*-isopropylidene-4-*O*-(diphenylphosphino)-α-L-rhamnopyranoside]rhodium(I) Perchlorate (4). To a mixture of di-μ-chloro-bis(cyclooctadiene)dirhodium(I) (0.30 g) in dichloromethane (6 ml) and sodium perchlorate (0.15 g) in water (6 ml) was added methyl rhamnopyranoside **1** (1.0 g). The mixture was stirred for 5 h at room temperature. The reaction mixture was washed with water (6 ml×3) and the organic layer was dried over anhydrous sodium sulfate. Concentration of the solvent up to 2 ml followed by addition of cyclohexane (30 ml) gave precipitates (0.18 g), which was filtered off. Concentration of the mother liquid up to 2 ml followed by addition of hexane (20 ml) gave the cationic rhodium catast (**4**, 0.13 g) in 13% yield, mp 135 °C.

^1H NMR ($CDCl_3$) δ=1.0—1.7 (m, 18H, $2C(CH_3)_2$, $2CHCH_3$), 2.0—2.4 (m, 8H, C_4H_8), 3.4—4.3 (m, 8H, $2C_{2,3,4,5}$–H), 4.4—5.0 (m, 4H, C_4H_4), 5.35 (s, 2H, $2C_1$–H), 7.1—8.2 (m, 20H, 4Ph).

Synthesis of 1,2:5,6-Di-*O*-isopropylidene-3,4-di-*O*-(diphenylphosphino)-D-mannitol (2). Reaction of 1,2:5,6-di-*O*-isopropylidene-D-mannitol (0.50 g, 1.9 mmol) with diphenylphosphinous chloride (0.42 g) (0.92 mmol) in the presence of triethylamine (2 ml) for 48 h at room temperature followed

by filtration and evaporation gave **2** (0.50 g) in 44% yield.

^{1}H NMR ($CDCl_3$) δ=1.25, 1.35 (2s, 12H, $2C(CH_3)_2$), 3.5—4.3 (m, 8H, $2CH_2CHCH$), 7.0—8.2 (m, 20H, 4Ph); Found: C, 46.11; H, 6.23%. Calcd for $C_{36}H_{40}O_6P_2$: C, 46.46; H, 6.39%.

Synthesis of 2,3,6-Tri-*O*-(diphenylphosphino)cellulose (3). Reaction of cellulose (1.0 g) with diphenylphosphinous chloride (3.7 g) in pyridine (30 ml) for 8 d at room temperature followed by washing the reaction mixture with ethanol, separation of the product by successive centrifuging and decantation, and evaporation of the solvent in vacuo gave **3** (1.8 g) in 43% yield.

IR ν_{max} (neat, cm^{-1}) 1440 (P-Ph), 1020 (P-O-C), but no OH absorption.

Asymmetric Hydrogenation of *N*-Acetylaminocinnamic Acid with Cationic Rhodium(I) Perchlorate Catalyst 4. Asymmetric hydrogenation of *N*-acetylaminocinnamic acid (1.0 g) was carried out in dried benzene–ethanol (1:1 v/v, 2 ml) in the presence of rhodium catalyst **4** (21.8 mg, 0.82 mmol) and triethylamine (0.04 ml) for 24 h at room temperature under hydrogen atmosphere. Removal of the rhodium catalyst from the reaction mixture with ion-exchange resince Dowex 50 W (H^+ form, 10 g), where ethyl esterification proceeded quantitatively, followed by decolorization with active charcoal and evaporation of the solvent in vacuo afforded *N*-acetylphenylalanine ethyl ester (0.12 g) in 100% conversion. The structure of the product was confirmed by ^{1}H NMR,[6a] $[\alpha]_D^{13}$=−7.4° (*c* 0.85, EtOH), optical yield 54% with *R* configuration [lit,[9] for (*S*)-*N*-acetylphenylalanine ethyl ester $[\alpha]_D^{20}$=+13.8° (*c* 2.0, 95% EtOH)].

Asymmetric Hydrogenation of *N*-Acetylaminocinnamic Acid with Di-μ-chloro-bis(cyclooctadiene)dirhodium(I) and Cellulose 3. Asymmetric hydrogenation of *N*-acetylaminocinnamic acid (1.0 g) was carried out in dried benzene–ethanol (1:1 v/v, 4 ml) in the presence of di-μ-chloro-bis(cyclooctadiene)dirhodium(I) (1.0 mg, 0.020 mmol), cellulose **3** (29 mg), and triethylamine (0.04 ml) for 24 h at 30 °C under 50 atm of hydrogen in autoclave. Removal of the rhodium catalyst from the reaction mixture by filtration followed by decolorization with active charcoal and evaporation of the solvent in vacuo afforded *N*-acetylphenylalanine (0.077 g) in 100% conversion. The structure of the product was confirmed by ^{1}H NMR,[6b] $[\alpha]_D^{12}$=−3.8° (*c* 0.32, EtOH), optical yield 8.2% with *R* configuration [lit[10] for (*S*)-*N*-acetylphenylanine $[\alpha]_D^{26}$=+46.0° (*c* 2.0, EtOH)].

References

1) T. Iwami, T. Yoshida, and M. Sato, *Nippon Kagaku Kaishi*, **1976**, 1652.
2) W. R. Cullen and Y. Sugi, *Tetrahedron Lett.*, **1978**, 1635.
3) Y. Sugi and W. R. Cullen, *Chem. Lett.*, **1979**, 39.
4) T. H. Johnson and G. Rangerjan, *J. Org. Chem.*, **45**, 62 (1980).
5) D. Lafont, D. Sinou, and G. Descotes, *J. Organomet. Chem.*, **169**, 87 (1979).
6) a) M. Yamashita, K. Hiramatsu, M. Yamada, N. Suzuki, and S. Inokawa, *Bull. Chem. Soc. Jpn.*, **55**, 2917 (1982); b) M. Yamashita, M. Kobayashi, M. Sugiura, K. Tsunekawa, T. Oshikawa, S. Inokawa, and H. Yamamoto, *ibid.*, **59**, 175 (1986).
7) Y. Kawabata, M. Tanaka, and I. Ogata, *Chem. Lett.*, **1976**, 1213.
8) E. Baer and H. O. L. Fischer, *J. Biol. Chem.*, **128**, 463 (1939); *Chem. Abstr.*, **33**, 7276 (1939).
9) G. Schiavon, S. Zecchin, and G. Pilloni, *J. Organomet. Chem.*, **121**, 261 (1976).
10) T. P. Dang, J. C. Poulin, and H. B. Kagan, *J. Organomet. Chem.*, **91**, 105 (1975).
11) M. D. Fryzuk and B. Bosnich, *J. Am. Chem. Soc.*, **99**, 6262 (1977).
12) R. Rossi, P. Diversi, and G. Ingrosso, *Gazz. Chem. Ital.*, **98**, 1391 (1968).
13) Y. Asahina and T. Shimizu, *Nippon Yakugaku Kaishi*, **479**, 1 (1922).
14) A. Levi, G. Modena, and G. Scorrano, *J. Chem. Soc., Chem. Commun.*, **1975**, 6.