Preparation of Enantiopure 2,2,5,5-Tetramethyl-3,4-hexanediol and Its Use in Catalytic Enantioselective Oxidation of Sulfides to Sulfoxides

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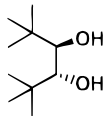
Introduction

Optically active 1,2-diols and related substrates play significant roles as chiral auxiliaries in the synthesis of natural products and biologically active compounds.[1] Recently, chiral catalysts derived from certain C_2-symmetric 1,2-diol ligands have been found to show high enantioselectivities in some asymmetric reactions.[2] These successful results led us to design a more effective chiral ligand. We considered that 2,2,5,5-tetramethyl-3,4-hexanediol (**1**) might be an efficient chiral ligand because it has a remarkable steric contrast between the bulky *tert*-butyl group and the hydrogen atom. This compound, however, has not been synthesized in optically pure form,[3] and, furthermore, its utility in organic synthesis has not yet been examined. In this paper we report a new preparation of enantiopure diol **1** and its utilization as a chiral ligand in titanium(IV)-catalyzed enantioselective oxidation of sulfides.



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Results and Discussion

Optical Resolution of 2,2,5,5-Tetramethyl-3,4-hexanediol. Our synthetic route to enantiopure 2,2,5,5-tetramethyl-3,4-hexanediol (**1**) is shown in Scheme 1. Initially, the racemic 1,2-diol **1** was prepared by reductive coupling of pivalaldehyde. After screening various coupling reagents, we found that a low-valent titanium reagent[4] gave the best result. Pivalaldehyde was treated with the titanium reagent (prepared in situ from $TiCl_4$ and Mg powder[4b,c]) to provide the 1,2-diol **1** as a 98/2 mixture of *dl*- and *meso*-isomers in 42% yield. Recrystallization of the mixture from hexane gave a pure *dl*-isomer as colorless needles.

We next examined the optical resolution of racemic compound **1**. Among many methods for optical resolution of diols,[5] the use of diastereomer phosphate esters[6,7] and related compounds[8,9] was found to be highly effective. Taking account of these previously established methods, we devised a new method for the resolution of the *dl*-**1** via the formation of the corresponding phosphine−borane bearing an *l*-menthyloxy group. Racemic diol **1** was converted by successive reactions with *n*-BuLi, dichloro(*l*-menthyloxy)phosphine, and BH_3−THF to a diastereomer mixture of 2-boranato-2-(1′*R*,2′*S*,5′*R*)-((2′-isopropyl-5′-methylcyclohexyl)oxy)-4,5-di-*tert*-butyl-1,3,2-dioxaphospholane. Separation of two diastereomers was achieved by fractional recrystallization from methanol. Reaction of one diastereomer **2** with excess MeLi (5 equiv) in toluene provided enantiopure (+)-diol **1** in 95%. In a similar manner, enantiopure (−)-diol **1** was also prepared in 90% from the other diastereomer **3**.

The absolute configuration of diol (+)-**1** was determined on the basis of X-ray structural analysis of diastereomer **2**. The ORTEP drawing of compound **2** is shown in Figure 1. The configuration of this diol was assigned to be (*S*,*S*) based on the relative stereochemistry to the known configuration of the *l*-menthyloxy group. Accordingly, (−)-diol **1** should possess (*R*,*R*) configuration.

Catalytic Asymmetric Oxidation of Sulfides. Asymmetric oxidation of sulfides has recently become a useful means of the preparation of optically active sulfoxides.[10,11] The most straightforward procedures involve the use of commercially available enantiopure reagents as chiral auxiliaries. For example, the employment of Ti(IV)−diethyl tartrate[12a−h] or Ti(IV)−binaphthol[12i−k] systems has resulted in high levels of enantioselectivity. However, the possibility of different diols has been scarcely explored.[12l,m] To test the catalytic efficiency of chiral diol **1**, we examined asymmetric oxidation of sulfides using a Ti(IV)−diol **1** complex as a catalyst.

The asymmetric oxidation of methyl *p*-tolyl sulfide was carried out as a model reaction. The results are summarized in Table 1. The chiral titanium complex was prepared in situ from $Ti(O^iPr)_4$ and (3*S*,4*S*)-2,2,5,5-tetramethyl-3,4-hexanediol. In the presence of this chiral titanium catalyst, methyl *p*-tolyl sulfide reacted with *tert*-

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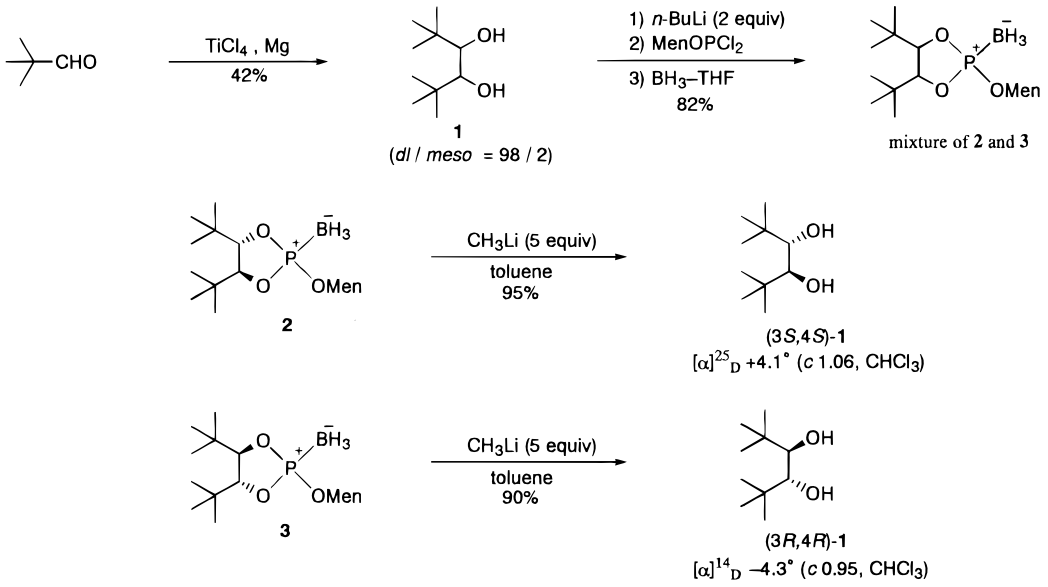
Scheme 1



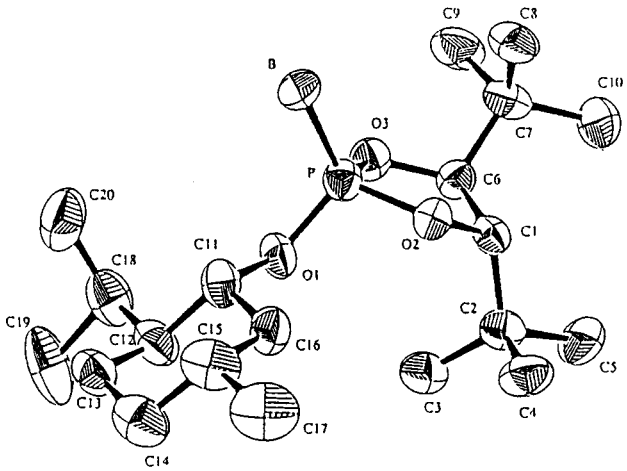


Figure 1. ORTEP drawing of compound **2**.

butyl hydroperoxide at −20 °C to afford the corresponding sulfoxide in 70% yield, but the enantiomeric excess was shown to be 10% (entry 1). After screening various reaction conditions, we found that beneficial effects were observed in the presence of molecular sieves 4A (MS4A) (entry 3). Although the role of MS4A is not clear at present, we consider that it plays an important role in the formation of the reactive Ti(IV)−diol **1** complex. In addition, the use of cumyl hydroperoxide instead of *tert*-butyl hydroperoxide improved greatly the enantiomeric excess (entry 4). The solvent showed a marked effect on both optical and chemical yields (entries 4 and 5). It was found that nonpolar aromatic solvents were appropriate for this asymmetric oxidation. In toluene, methyl *p*-tolyl sulfoxide was obtained in the highest optical yield (95% ee), although a considerable amount of sulfone was also observed. In contrast, the reaction in CH_2Cl_2 was sluggish, and the enantiomeric excess of the product was only moderate. Although the precise structure of the catalyst has not yet been clarified, it was found that 1:2 ratio of $Ti(O^iPr)_4$ and diol **1** gave the maximum enantiomeric excess. The reaction temperature also affected both chemical and optical yields. It was found that optimum temperature for this reaction was around −20 °C.

To clarify the generality and scope of this asymmetric reaction, enantioselective oxidations of several prochiral sulfides were examined. The results are shown in Table 2. Although this catalyst has proved to be ineffective in the case of dialkyl sulfides (entries 9 and 10), aryl alkyl sulfoxides with various substituents on the aromatic ring were obtained in good to high enantioselectivities (entries 1−8).

A kinetic study was carried out in order to examine the mechanism of this system using methyl *p*-tolyl sulfide as a model substrate. The results are shown in Figure 2. Enantiomeric excess of the sulfoxide largely depended on reaction time. For example, at the initial stage of the reaction the sulfoxide was obtained in 40% ee (5 h, 20% yield), and after 30 h enantiomeric excess of the product increased to 95% ee (42% yield). These facts indicate that kinetic resolution[14] of the sulfoxide may follow the asymmetric oxidation. Accordingly, we next examined the enantioselective oxidation of racemic methyl *p*-tolyl sulfoxide with this chiral titanium−(3*S*,4*S*)-**1** complex as a chiral catalyst at −20 °C. The relationship between optical yield and conversion of sulfoxide is shown in Figure 3. The optical purity of the sulfoxide increased

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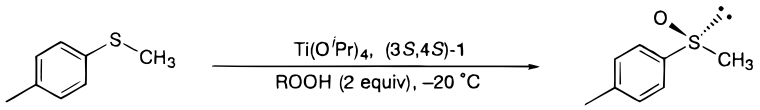
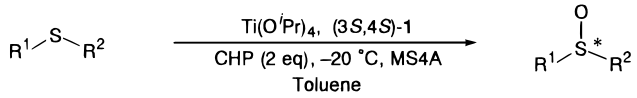
Table 1. Asymmetric Oxidation of Methyl *p*-Tolyl Sulfide[a]



					sulfoxide		sulfone
entry	ROOH	solvent	time (h)	additive	yield (%)[b]	ee (%)[c]	yield (%)
1	TBHP[d]	toluene	30	–	70	10	10
2	TBHP	toluene	30	H_2O[f]	66	14	8
3	TBHP	toluene	30	MS4A[g]	69	30	14
4	CHP[e]	toluene	30	MS4A	42	95	40
5	CHP	CH_2Cl_2	90	MS4A	75	41	14

[a] Sulfide (0.5 mmol), $Ti(O^iPr)_4$ (0.025 mmol), (3*S*,4*S*)-**1** (0.05 mmol). [b] Isolated yield. [c] Enantiomeric excess was determined by HPLC analysis. [d] *tert*-Butyl hydroperoxide. [e] Cumyl hydroperoxide. [f] H_2O (1 mmol) was added. [g] MS4A (70 mg) was added.

Table 2. Asymmetric Oxidation of Sulfides to Sulfoxides[a]



				sulfoxide			sulfone
entry	R^1	R^2	time (h)	yield (%)[b]	ee (%)[c]	config[d]	yield (%)[b]
1	*p*-tolyl	Me	30	42	95	(*S*)	40
2	Ph	Me	30	36	87	(*S*)	45
3	Ph	Et	35	40	82	(*S*)	51
4	*p*-BrC_6H_4	Me	55	58	65	(–)	40
5	*o*-BrC_6H_4	Me	40	92	33	(–)	–
6	*p*-$MeOC_6H_4$	Me	30	30	40	(–)	55
7	*o*-$MeOC_6H_4$	Me	60	45	87	(*S*)	40
8	2-naphthyl	Me	40	46	80	(*S*)	48
9	benzyl	Me	15	80	3	(*S*)	trace
10	^{n}octyl	Me	25	83	<1	(–)	trace

[a] Sulfide (0.5 mmol), $Ti(O^iPr)_4$ (0.025 mmol), (3*S*,4*S*)-**1** (0.05 mmol). [b] Isolated yield. [c] Enantiomeric excess was determined by HPLC analysis. [d] Absolute configurations were determined by comparison of the sign of $[\alpha]_D$ to literature values.[11–13]

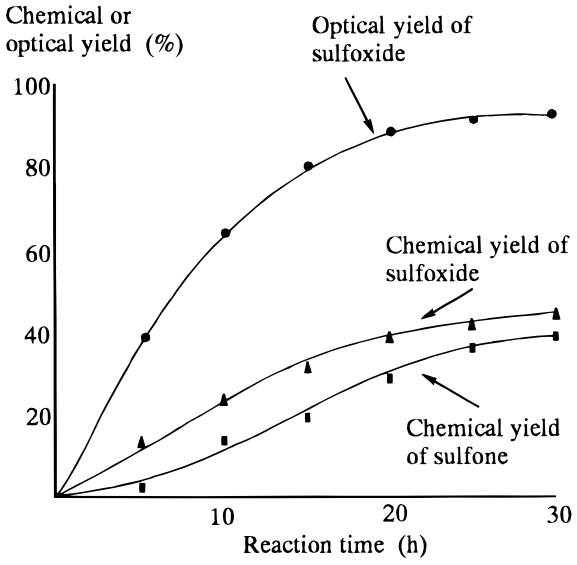


Figure 2. Dependence of yield of products [methyl *p*-tolyl sulfoxide (▲); methyl *p*-tolyl sulfone (■)] and optical yield of methyl *p*-tolyl sulfoxide (○) on the time (h) in the enantioselective oxidation of methyl *p*-tolyl sulfide.

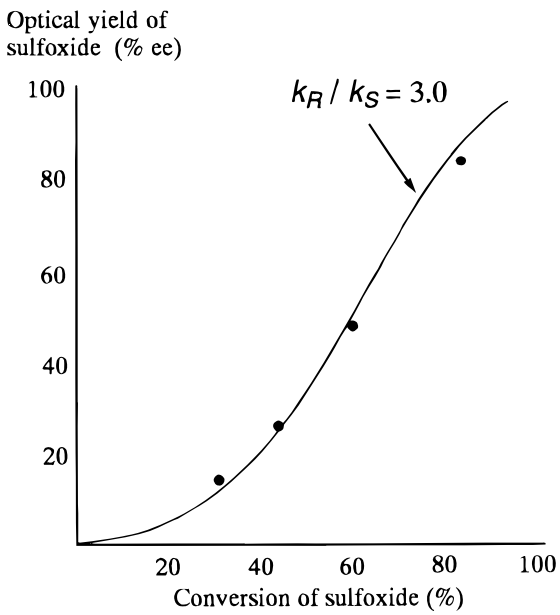
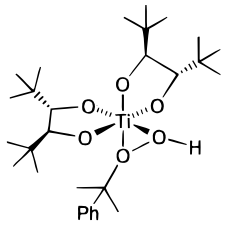


Figure 3. Kinetic resolution of methyl *p*-tolyl sulfoxide.

as the preferential oxidation of the *R*-isomer to sulfone took place. The relative rate of oxidation of enantiomers, k_R/k_S, was determined to be ca. 3.0 according to the reported equation.[14a]

Although the mechanistic details of this reaction are not yet clear, we presume the presence of a mononuclear titanium with two diol ligands as a catalyst. Reaction of this catalyst with cumyl hydroperoxide can form intermediate **4** which reacts with sulfides to afford optical active sulfoxides. However, this catalytic activity is also promoted by the accompanying oxidation of the resulting sulfoxides to sulfone by virtue of coordination of sulfoxide to Ti(IV). A combination of asymmetric oxidation and kinetic resolution gave the sulfoxide in high optical purity.



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In conclusion, we prepared enantiopure 2,2,5,5-tetramethyl-3,4-hexanediol (**1**) via the diastereomeric phosphine−boranes **2** and **3**. This chiral diol **1** has been proved useful as an effective chiral ligand in catalytic enantioselective oxidation of sulfides to sulfoxides.

Experimental Section

Melting points were determined in open capillaries using a Yamato micro melting point apparatus and were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded using a JEOL GSX-400 instrument (^{1}H at 400 MHz and ^{13}C at 100 MHz). IR spectra were recorded on a Hitachi IR 215 spectrophotometer. Optical rotations were measured with a JASCO DIP-370 digital polarimeter with 1-dm-long cell. Optical purities were determined by HPLC analysis performed on a Hitachi L-6000 pump and Hitachi L-4000 UV detector with an appropriate chiral column. Recycling preparative HPLC was performed on JAI LC-908 and RI Detector RI-5. Mass spectra were obtained on JEOL JMS-HX110. Microanalysis were performed on a Perkin-Elmer 240B at the Chemical Analysis Center of Chiba University. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under argon prior to use. Toluene and methylene chloride were distilled from CaH_2 and stored over molecular sieves 4A. Titanium(IV) tetraisopropoxide was distilled before use. Dichloro(*l*-menthyloxy)phosphine was prepared by reaction of lithium *l*-menthoxide with PCl_3 (bp 105 °C/2 mmHg; lit.[10c] 120−122 °C/3 mmHg). 2-Naphthyl methyl sulfide, *o*-bromophenyl methyl sulfide, *o*-anisyl methyl sulfide, and *p*-anisyl methyl sulfide were prepared from the corresponding thiophenol derivatives by methylation with iodomethane in the presence of DBU.[15] *tert*-Butyl hydroperoxide (5.0−6.0 M decane solution) was purchased from Aldrich, and cumyl hydroperoxide was obtained as a gift from NOF Corporation. All experiments were carried out under argon atmosphere. The products were isolated by preparative TLC on silica gel (Wakogel B-5F) or column chromatography on silica gel (Wakogel C-200).

Preparation of Diastereomerically Pure Phosphine−Boranes 2 and 3. To a solution of *dl*-2,2,5,5-tetramethyl-3,4-hexanediol (8.7 g, 50 mmol) in THF was added *n*-BuLi (61 mL of 1.63 M hexane solution, 100 mmol) at 0 °C. The mixture was added to a solution of dichloro(*l*-menthyloxy)phosphine (12.1 g, 50 mmol) in THF at −78 °C, and the reaction mixture was warmed to rt. The flask was immersed in an ice−water bath and then BH_3−THF (50 mL of 1.0 M THF solution, 50 mmol) was added. The reaction mixture was slowly added to vigorously stirred water. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate three times. The combined extracts were washed with brine and dried (Na_2SO_4). The solvent was evaporated under reduced pressure, and the residue was dissolved in hexane. The solution was passed through a short column packed with silica gel (hexane/ethyl acetate = 100/1). The eluent was evaporated to give a mixture of **2** and **3** as a white powder (15.3 g, 82%). It was recrystallized from MeOH to give a pure diastereomer **2** (5.0 g). Another diastereomer **3** was obtained from the mother solution (4.5 g).[16]

2-Boranato-(1′*R*,2′*S*,5′*R*)-((2′-Isopropyl-5′-methylcyclohexyl)oxy)-(4*S*,5*S*)-4,5-di-*tert*-butyl-1,3,2-dioxaphospholane (2): colorless cubes; mp 106.5−107.5 °C; $[\alpha]^{25}_D$ −102.8° (*c* 1.05, $CHCl_3$); IR (KBr) 2950, 2420, 2380, 2350, 1480, 1370 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81−1.16 (7H, m), 0.82 (3H, d, J = 7.1 Hz), 0.89 (3H, d, J = 6.8 Hz), 0.92 (3H, d, J = 6.6 Hz), 0.98 (3H, d, J = 8.3 Hz), 1.25−1.27 (1H, m), 1.46 (1H, m), 1.65 (2H, m), 2.02 (1H, m), 2.17 (1H, m), 4.03−4.12 (2H, m), 4.26−4.29 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.2, 20.8, 22.0, 23.2, 25.6, 25.9, 26.3, 31.5, 34.1, 34.4, 35.1 (d, J = 2.5 Hz), 43.2, 48.4 (d, J = 5.8 Hz), 80.3, 87.8 (d, J = 6.6 Hz), 88.2 (d, J = 7.4 Hz); EI MS *m*/*z* 370 (M − 2H). Anal. Calcd for $C_{20}H_{42}BO_3P$: C, 64.52; H, 11.37. Found: C, 64.82; H, 11.65.

2-Boranato-(1′*R*,2′*S*,5′*R*)-((2′-Isopropyl-5′-methylcyclohexyl)oxy)-(4*R*,5*R*)-4,5-di-*tert*-butyl-1,3,2-dioxaphospholane (3): colorless plates; mp 84.5−85.5 °C; $[\alpha]^{16}_D$ +13.3° (*c* 1.04, $CHCl_3$); IR (KBr) 2950, 2440, 2390, 2350, 1480, 1370 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84−2.08 (12H, m), 0.85 (3H, d, J = 7.1 Hz), 0.90 (3H, d, J = 3.4 Hz), 0.92 (3H, d, J = 2.7 Hz), 0.98 (18H, d, J = 5.6 Hz), 4.02−4.13 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.1, 21.0, 22.0, 22.9, 25.7, 25.9, 26.1, 31.5, 34.0, 34.4, 35.2 (d, J = 3.3 Hz), 43.2, 48.4 (d, J = 5.0 Hz), 80.6 (d, J = 2.9 Hz), 88.0 (d, J = 7.4 Hz), 88.1 (d, J = 6.6 Hz); FABMS *m*/*z* 369 (M − 3H). Anal. Calcd for $C_{20}H_{42}BO_3P$: C, 64.52; H, 11.37. Found: C, 64.75; H, 11.31.

X-ray Crystallographic Analysis of Compound 2.[17] A well-shaped orthorhombic crystal of **2** was obtained by recrystallization from methanol: $C_{20}H_{42}BO_3P$; space group $P2_12_12_1$ (#19); Z = 4; D = 1.035 g/cm^{-3}; cell constants a = 10.727(5) Å, b = 23.211(4) Å, c = 9.600(2) Å, V = 2390(1) Å^3; temperature of data collection 300 K; 1306 unique reflections ($I > 3.00\sigma(I)$); R = 0.070, Rw = 0.086. Selected bond distances (Å) and angles (deg): P(1)−B(1) 1.87(1), P(1)−O(1) 1.591(5), P(1)−O(2) 1.600-(5), P(1)−O(3) 1.566(6), O(1)−P(1)−B(1) 116.4(4), O(2)−P(1)−B(1) 117.7(4), O(3)−P(1)−B(1) 113.9(4), O(2)−P(1)−O(3) 102.4(3), O(1)−P(1)−O(3) 108.1(3), O(1)−P(1)−O(2) 96.2(3).

Preparation of Enantiomerically Pure 2,2,5,5-Tetramethyl-3,4-hexanediol from Phosphine−Boranes 2 and 3. Diastereomerically pure **2** (3.7 g, 10 mmol) in toluene (50 mL) was treated with MeLi (33 mL of 1.5 M Et_2O solution, 50 mmol) at rt for 5 h. The reaction mixture was poured into vigorously stirred water. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate three times. The combined extracts were washed with brine and dried over Na_2SO_4. The solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography ($CHCl_3$) to give crude (3*S*,4*S*)-**1** as a white powder (1.7 g, 95%). It was recrystallized from hexane to afford enantiomerically pure (3*S*,4*S*)-**1** as colorless needles. In a similar manner, enantiomerically pure antipode (3*R*,4*R*)-**1** was obtained from **3** (1.6 g, 90%).

(3*S*,4*S*)-2,2,5,5-Tetramethyl-3,4-hexanediol: colorless needles; mp 146.0−147.5 °C; $[\alpha]^{25}_D$ +4.1° (*c* 1.06, $CHCl_3$); IR (KBr) 3360, 2950, 2920, 2860, 1480, 1410, 1360, cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (18H, s), 2.35 (2H, d), 3.30 (2H, d); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.8, 35.2, 74.9; FABMS *m*/*z* 174 (M^+). Anal. Calcd for $C_{10}H_{22}O_2$: C, 68.92; H, 12.72. Found: C, 69.14; H, 13.02.

(3*R*,4*R*)-2,2,5,5-Tetramethyl-3,4-hexanediol: colorless needles; mp 146.0−148.0 °C; $[\alpha]^{14}_D$ −4.3° (*c* 0.95, $CHCl_3$); IR (KBr) 3360, 2950, 2920, 2860, 1480, 1410, 1360 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (18H, s), 2.38 (2H, d), 3.33 (2H, d); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.8, 35.2, 74.9; FABMS *m*/*z* 174 (M^+). HRMS calcd for $C_{10}H_{22}O_2$ *m*/*z* 174.1620, found *m*/*z* 174.1633.

Determination of Enantiomeric Purity of Optically Active 2,2,5,5-Tetramethyl-3,4-hexanediol. To a solution of (3*S*,4*S*)-2,2,5,5-tetramethyl-3,4-hexanediol (87 mg, 0.5 mmol) in THF, *n*-BuLi (0.6 mL of 1.63 M hexane solution, 1 mmol) was added. The contents were added to a solution of dichlorophenylphosphine (67 μL, 0.5 mmol) in THF at −78 °C. After the addition, the reaction mixture was warmed to rt. The flask was immersed in an ice−water bath, and then BH_3−THF (0.5 mL of 1.0 M THF solution, 0.5 mmol) was added. The reaction mixture was poured into vigorously stirred water. The organic layer was separated, and the aqueous layer was extracted with ethyl

(15) Ono, N.; Miyake, H.; Saito, T.; Kaji, A. *Synthesis* **1980**, 952.

(16) The mother solution was concentrated under reduced pressure, and the residue was dissolved in hot MeOH. The solution was seeded with optically pure diastereopure **3** (ca. 20 mg), which was obtained by preparative HPLC (ODS) using MeOH as the eluent. It was kept overnight at room temperature to give 4.5 g of diastereomer **3** as colorless plates.

(17) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

acetate three times. The combined extracts were washed with brine and dried (Na_2SO_4). The solvent was evaporated under reduced pressure, and the residue was purified by column chromatography (hexane/ethyl acetate = 10/1) to give 2-boranato-2-phenyl-(4*S*,5*S*)-di-*tert*-butyl-1,3,2-dioxaphospholane as colorless needles (135 mg, 93%). The enantiomeric excess was determined to be 100% ee by chiral HPLC analysis: Chiralcel OJ (Daicel, hexane/2-propanol = 9/1, flow rate = 1.00 mL/min): $t_r(S,S) = 4.8$ min, $t_r(R,R) = 6.4$ min.

(4*S*,5*S*)-2-Phenyl-2-boranato-4,5-di-*tert*-1,3,2-dioxaphospholane: colorless needles; mp 139.0−140.0 °C; $[\alpha]^{20}_D$ −38.8° (*c* 1.19, $CHCl_3$); IR (KBr) 3000, 2420, 2360, 2330, 1480 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.68 (9H, s), 1.09 (9H, s), 4.18−4.26 (2H, m), 7.26−7.72 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 26.5, 34.3, 35.2 (J = 5.2 Hz), 89.1 (J = 6.6 Hz), 89.2 (J = 5.8 Hz), 128.3, 129.7, 129.8, 132.0 (J = 1.7 Hz), 135.0, 135.5; FABMS *m*/*z* 291 (M −3H); HRMS calcd for $C_{16}H_{25}BO_2P$ *m*/*z* 291.1685, found *m*/*z* 291.1696.

(4*R*,5*R*)-2-Phenyl-2-boranato-4,5-di-*tert*-1,3,2-dioxaphospholane: colorless needles; mp 136.0−138.0 °C; $[\alpha]^{20}_D$ +39.0° (*c* 1.09, $CHCl_3$); IR (KBr) 3000, 2420, 2360, 2330, 1480 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.68 (9H, s), 1.09 (9H, s), 4.18−4.26 (2H, m), 7.26−7.72 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 26.5, 34.3, 35.2 (J = 5.2 Hz), 89.1 (J = 6.6 Hz), 89.2 (J = 5.8 Hz), 128.3, 129.7, 129.8, 132.0 (J = 1.7 Hz), 135.0, 135.5; FABMS *m*/*z* 291 (M − 3H); HRMS calcd for $C_{16}H_{25}BO_2P$ *m*/*z* 291.1685, found *m*/*z* 291.1690.

A Typical Experimental Procedure for the Asymmetric Oxidation. A solution of $Ti(^iOPr)_4$ (7.4 μL, 0.025 mmol) in toluene (1 mL) was added in a flask containing MS4A (70 mg) and (3*S*,4*S*)-2,2,5,5,-tetramethyl-3,4-hexanediol (0.05 mmol, 8.9 mg). This solution was stirred for 2 h at rt, and then methyl *p*-tolyl sulfide (68 μL, 0.5 mmol) was added. The solution was cooled to −20 °C, and 80% cumyl hydroperoxide (190 μL, 1 mmol) was added. After stirring for 30 h at the same temperature, the reaction was quenched with ca. 10% aqueous solution of sodium sulfite. The aqueous layer was extracted with ethyl acetate three times. The combined organic layer was washed with brine and dried over Na_2SO_4. The solvent was evaporated under reduced pressure, and column chromatography (ethyl acetate) on silica gel afforded 32 mg of (*S*)-methyl *p*-tolyl sulfoxide (42%, 95% ee) and 34 mg of methyl *p*-tolyl sulfone (40%). The enantiomeric excess was measured by chiral HPLC analysis using Chiralcel OD-H column. Absolute configuration was assigned by comparison of the sign of specific rotation with literature data.[11−13]

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