Pergamon

Tetrahedron, Vol. 53, No. 49, pp. 16663-16678, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)10094-1

General Method for Asymmetric Synthesis of Substituted 2,2'-Biaryldiols via Asymmetric Desymmetrization of 2,2',6,6'-Tetrahydroxybiphenyl with *l*-Menthone

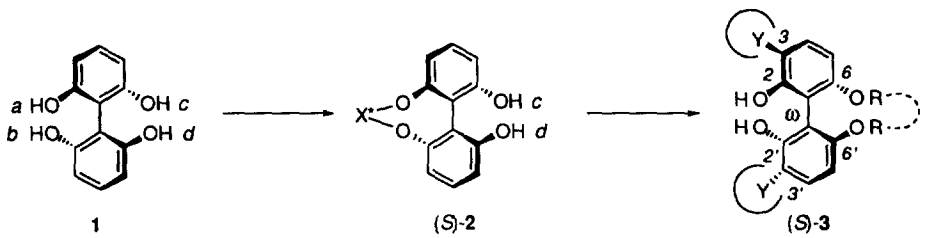
Toshiro Harada,* Shinji Ueda, Tran Mai Thi Tuyet, Atsushi Inoue, Katsuhiro Fujita, Masahiro Takeuchi, Nobuhiro Ogawa, Akira Oku, and Motoo Shiro†

Department of Chemistry, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606, Japan
† Rigaku Corporation, Matsubara-cho 3-9-12, Akishima, Tokyo 196, Japan

Abstract: Asymmetric desymmetrization of prochiral 2,2',6,6'-biphenyltetrol by acetalization with *l*-menthone affords isomenthonide **5b** of *S*-axial chirality. A variety of (*S*)-6,6'-dialkoxy-2,2'-biphenyldiols of high enantiomeric purities are synthesized by using **5b** as an intermediate. Thus, etherification of the hydroxy groups of **5b** followed by hydrolysis of the isomenthonide moiety give the corresponding 6,6'-dialkoxy-2,2'-biphenyldiols (**12**). Intermolecular cyclization of **5b** with 1,ω-dibromoalkanes followed by hydrolysis yields 2,2'-biphenyldiols **13** with alkylenedioxy bridges at the 6 and 6' positions. Regioselective functionalization of **13** leading to 3,3'-dimethyl, -diphenyl, and -bis(TBS) derivatives is achieved either via directed lithiation of a carbamate derivative or via regioselective bromination reaction of **13**. Origin of the stereoselectivity in acetalization reaction as well as thermal stability of the axial chirality of 2,2'-biphenyldiols is also discussed.

Axially chiral 2,2'-biaryldiols have been utilized as chiral ligands in catalytic asymmetric reactions as well as chiral elements in host-guest chemistry and molecular recognitions. Complexes of the biaryldiols with Lewis acids, in particular those of 1,1'-bi-2-naphthol (BINOL), have shown significant catalytic activity for asymmetric induction in Diels-Alder, carbonyl-ene, allylation, and other reactions.[1] Recently, attention has been focused on improvement of their performance by modification of a parent structure. The stereochemical features of 2,2'-biphenyldiols **3**, and their Lewis acid complexes, are governed both by the size and shape of the substituents (Y) attached at the 3 and 3' positions and by the torsional angle ω for the benzene rings (Scheme 1). The structural optimization of biaryldiol ligands with respect to the both factors is a promising approach to the development of an efficient Lewis acid catalysts. Successful results have been reported by increasing the asymmetry around the hydroxy groups via introducing proper substituents at the adjacent positions.[2] However, the effect of torsional angles has not been studied extensively.[3] This is probably due to the lack of a general method for the asymmetric synthesis of 2,2'-biphenyldiols with 6,6'-substituents by which the torsional angles could be controlled.[4]

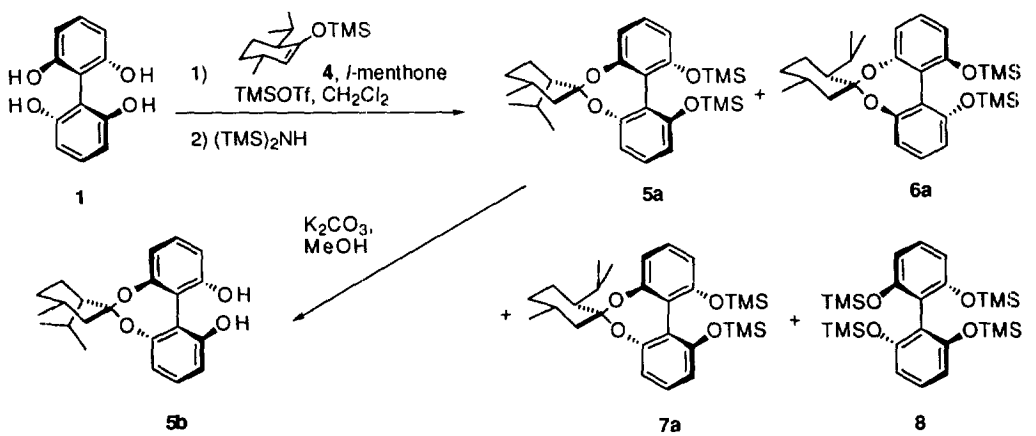
2,2',6,6'-Biphenyltetrol (**1**) is a prochiral precursor for a variety of polysubstituted 2,2'-biphenyldiols (Scheme 1). Asymmetric desymmetrization of **1** by enantiotopic group-selective transformation[5] of the hydroxy groups *a* and *b* would afford chiral derivative **2** of *S*-axial chirality. Manipulation of the free hydroxy groups *c*, *d* and removal of chiral auxiliary X* would lead to 2,2'-biphenyldiols (*S*)-**3** (Y = H) whose torsional angles are controlled by the alkoxy (or alkylenedioxy) groups attached at the 6 and 6' positions. Regioselective functionalization at the 3 and 3' positions would furnish the 3,3'-disubstituted derivatives (*S*)-**3**. We wish to report herein desymmetrization of **1** by group-selective acetalization with *l*-menthone. The reaction is successfully applied to a general method for asymmetric synthesis of polysubstituted 2,2'-biphenyldiols.[6]



Scheme 1

RESULTS AND DISCUSSION

Asymmetric Desymmetrization of Tetrol 1. We recently reported an asymmetric desymmetrization of prochiral diols by using acetalization with *l*-menthone.[5b,7] Use of *l*-menthone as a chiral template was applied to the asymmetric desymmetrization of tetrol **1** (Scheme 2). Attempted acetalization of the tetrakis(TMS) ether **8** with *l*-menthone catalyzed by TMSOTf[8] resulted in recovery of the starting materials. We recently reported an efficient method for the preparation of menthonides by acid catalyzed reaction of diols and *l*-menthone enol silyl ether **4**.[9] The method was successfully employed in the acetalization of **1**. Thus, tetrol **1** was treated with **4** (2.4 equiv) and *l*-menthone (0.7 equiv) in the presence of TMSOTf (0.4 equiv) in CH_2Cl_2 at -20 °C for 20 h. Silylation of the mixture with $(TMS)_2NH$ and subsequent purification of the crude products by flash chromatography (silica gel) gave a 15:1 mixture of **5a** and **7a** (45%), **6a** (16%), and the tetrakis(TMS) ether **8** (24%). Pure **5a** was obtained by a single recrystallization of the mixture from methanol. Desilylation of **5a** under basic conditions (K_2CO_3, MeOH) gave acetal **5b** quantitatively.



Scheme 2

In acetalization using enol silyl ether **4**, hydroxy groups of a substrate initially undergo partial silylation. Because 2.8 equiv total of silylating reagents (**4** and TMSOTf) were employed in the reaction of tetrol **1**, approximately 75% of the hydroxy groups was initially converted into the trimethylsilyloxy groups with the simultaneous formation of *l*-menthone and triflic acid. We previously proposed that free alcohols are kinetically more reactive in acetalization than the TMS ether derivatives.[9] Through the course of the acetalization in which

the more reactive hydroxy groups participated, the trimethylsilyl groups might act as a dehydrating agent by their conversion to $(TMS)_2O$ preventing the product acetals from hydrolysis. The products thus obtained is a mixture of the partially silylated derivatives, which was fully silylated with $(TMS)_2NH$ before isolation.

The structure of the major product **5a** was determined by X-ray analysis (Fig 1).[10] The analysis disclosed that **5a** is an isomenthonide of *S* axial chirality in which the isopropyl group takes an unusual axial position. The structure of the second major product **6a** was determined to be the menthonide of *R* chirality by X-ray diffraction analysis of the TBS ether derivative **6c** (Fig 2).[10] Minor product **7a** was assigned to a menthonide of *S*-chirality based on the observed rapid interconversion of the hydroxy derivatives **6b** and **7b** at rt (*vide infra*).

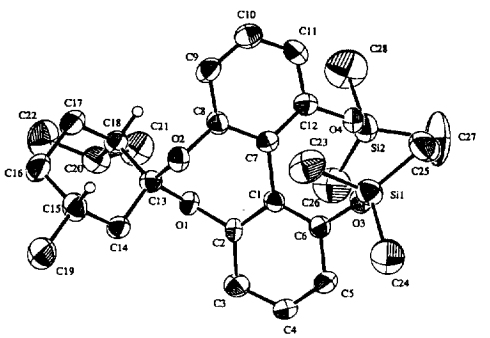


Fig 1. ORTEP drawing of TMS ether **5a**

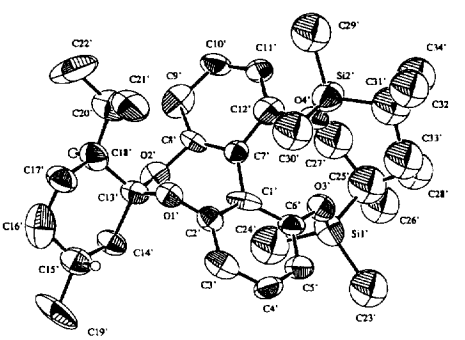
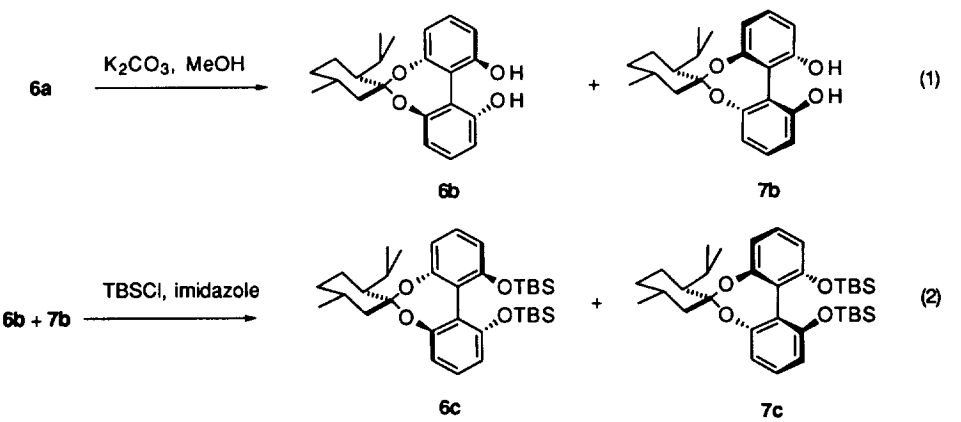


Fig 2. ORTEP drawing of TBS ether **6c**

Although (1*R*,4*R*)-isomenthone is formed reversibly in an acid catalyzed acetalization with *l*-menthone, the formation of thermodynamically less stable isomenthonides[11] has never been observed in the reactions of 1,n-alkanediols (n = 2, 3, and 4).[7] In the acetalization of **1**, formation of menthonides **6a** and **7a** is unfavorable probably due to a repulsive interaction between the isopropyl group and the benzene ring. On the other hand, such unfavorable interaction is absent in isomenthonide **5a**. This may explain the apparently unusual formation of isomenthonide **5a** as a major product.

Desilylation of **6a** with K_2CO_3 in MeOH at rt afforded hydroxy derivatives **6b** and **7b** as a 2.6:1 inseparable mixture (eq 1). Silylation of the mixture with $(TMS)_2NH$ gave a 2.7:1 mixture of **6a** and **7a**, which could be separated by silica gel flash chromatography. A 2.6:1 mixture of TBS derivatives **6c** and **7c** was obtained by treatment of the mixture of **6b** and **7b** with TBSCl and imidazole (eq 2). Separation of the mixture



by flash chromatography afforded **6c** and **7c** in 59 and 23% yield, respectively. Desilylation of **7a** (K_2CO_3, MeOH, rt), **6c**, and **7c** (Bu_4NF, THF, rt) all resulted in the formation of a *ca.* 2.5:1 mixture of **6b** and **7b**. These results suggests that hydroxy derivatives (*R*)-**6b** and (*S*)-**7b** are in rapid equilibrium at rt. On the other hand, the axial chirality of the TMS and TBS derivatives **6a,c** and **7a,c** are thermally stable at least at rt.

Support for the equilibrium between hydroxy derivatives **6b** and **7b** was obtained by the following VT-^{1}H NMR (300 MHz) experiments (Fig 3). In d_6-DMSO, at 30 °C, sets of signals derived from **6b** and **7b** were observed; H-4 and H-4' of **6b** appeared at 7.09 (t) and 7.16 (t) ppm while those of **7b** resonated at 7.08 (t) and 7.15 (t) ppm. These signals were broadened as the increase of the temperatures. The coalescence of the signals were observed at 120 °C. While the recooling of the mixture from 120° to 30° C, regenerate a similar NMR spectrum, at the higher temperatures (140 °C), partial decomposition of the mixture to unknown compounds was observed with line sharpening of the averaged signals; H-4 and H-4' appeared at 7.13 and 7.16 ppm.

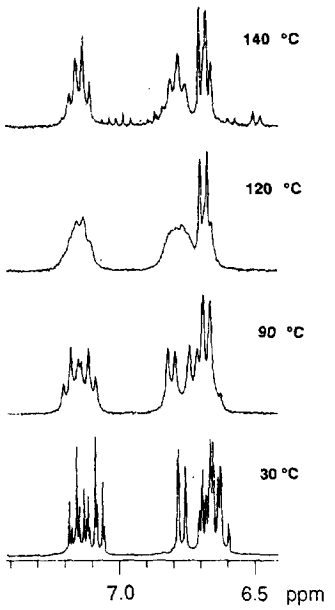
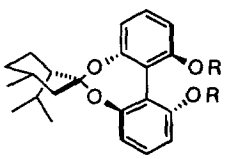


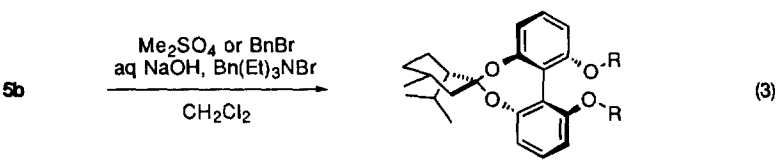
Fig 3. VT-^{1}H NMR Spectra of a mixture of **6b** and **7b**

In the acetalization of tetrol **1**, formation of diastereomeric isomenthonide **9a** with *R* axial chirality was not observed. Desylilation of acetal **5a** gave diol **5b** without concomitant formation of diasteromeric diol **9b**. A molecular model analysis suggested that **9a,b** would be highly unstable due to the unfavorable steric interaction between the axial isopropyl group and the benzene ring. Molecular mechanics calculation (MM3)[12] showed that **9b** is 3.6 kcal/mol less stable than **5b**.



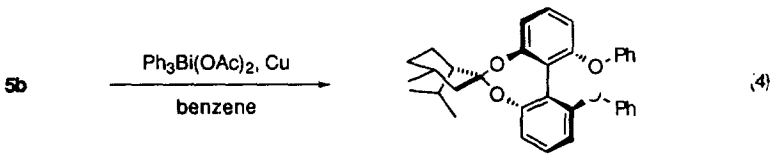
9a; R = TMS, **9b**; R = H

Synthesis of (*S*)-6,6'-Dialkoxy-2,2'-biphenyldiols 12 and (*S*)-6,6'-Alkylenedioxy-2,2'-biphenyldiols 13. Etherification of isomenthonide **5b** with dimethyl sulfate and benzyl bromide afforded the corresponding 6,6'-dialkoxy derivatives **10a** and **10b**, respectively, in high yields (eq 3). Di-



(3)

10a; R = Me (90%)
10b; R = Bn (91%)



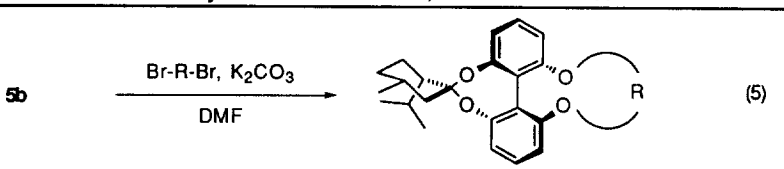
(4)

10c (48%)

phenylation of **5b** was achieved by using an organobismuth reagent developed by Barton *et al.* (eq 4).[13] Treatment of **5b** with triphenylbisumuth diacetate in the presence of copper powder (1.3 equiv) in benzene at 50 °C afforded diphenoxy derivative **10c** in 48% yield.

Axially chiral biphenyls **11a-e** with -O(CH$_2$)$_n$O- (n = 3-6) bridges were prepared by intermolecular cyclization of **5b** with the corresponding 1,ω-dibromoalkanes (eq 5 and Table 1).[14] The reactions were carried out under high dilution conditions in DMF by adding a solution of the dibromoalkanes slowly using a syringe pump. The efficiency of the cyclization was high in the nine- and ten-membered ring formation (entries 1,2 and 5). Although the product yields were decreased as the increase of the alkylene-chain length, the reaction can be applicable to penta- and hexamethylenedioxy derivatives **11c,d** (entries 3 and 4).

Table 1 Intramolecular Cyclization of **5b** with 1,ω-dibromoalkanes

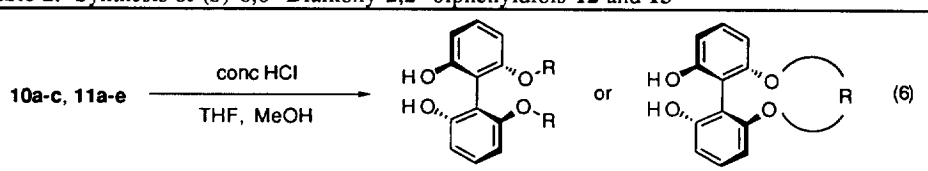


(5)

11a-e

entry	dibromo compound	product	isolated yield (%)
1	Br(CH$_2$)$_3$Br	**11a**	83
2	Br(CH$_2$)$_4$Br	**11b**	88
3	Br(CH$_2$)$_5$Br	**11c**	70
4	Br(CH$_2$)$_6$Br	**11d**	56
5	BrCH$_2$(*o*-C$_6$H$_4$)CH$_2$Br	**11e**	96

Table 2. Synthesis of (*S*)-6,6'-Dialkoxy-2,2'-biphenyldiols **12** and **13**



(6)

12a-c **13a-e**

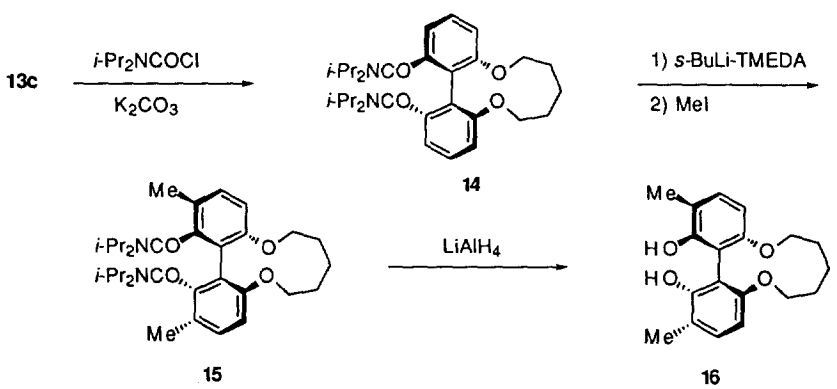
entry	substrate	product	isolated yield (%)	ee (%)	[α]$_D$ (*c*, solvent)
1	**10a**	**12a**; R = Me	96	91	+21.2 (0.60, EtOH)
2	**10b**	**12b**; R = Bn	97	96	+60.0 (0.70, EtOH)
3	**10c**	**12c**; R = Ph	96	96	+80.0 (0.52, EtOH)
4	**11a**	**13a**; -R- = -(CH$_2$)$_3$-	100	80	+169 (1.06, THF)
5	**11b**	**13b**; -R- = -(CH$_2$)$_4$-	97	98	+141 (0.60, THF)
6	**11c**	**13c**; -R- = -(CH$_2$)$_5$-	82	98	+189 (0.98, THF)
7	**11d**	**13d**; -R- = -(CH$_2$)$_6$-	100	99	+152 (0.77, EtOH)
8	**11e**	**13e**; -R- = -CH$_2$(*o*-C$_6$H$_4$)CH$_2$-	99	86	-51.0 (0.79, THF)

Hydrolysis of **10a-c** and **11a-e** under acidic conditions afforded chiral biphenyldiols **12a-c** and **13a-e** in high yields (Table 2). The enantiomeric purities, determined by HPLC analysis using a chiral column (Chiracel OD), were generally high (>95% ee). Although partial racemization was observed during hydrolysis

for **12a** and **13a**,**e**, enantiomerically pure (>95% ee) **12a** and **13a** were obtained after a single recrystallization.[15]

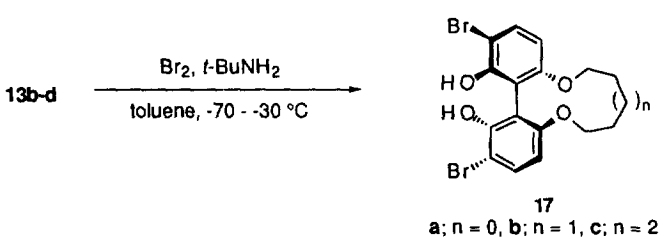
The axial chirality of biphenyldiols **12a-c** and **13a-e** are thermally stable during practical use. Thus, no detectable racemization was observed upon heating **12b**,**c** and **13b** in ethanol at 60 °C for 18 h. The rate of racemization was determined from kinetic runs for **12a** and **13b**. Dimethoxy derivatives **12a** exhibited the rate constant of 6.4×10^{-8} sec^{-1} at 78°C in ethanol and 3.4×10^{-5} sec^{-1} at 111°C in toluene, indicating that **12a** can be handled without loss of axial chirality with appropriate caution. The rate for **13b** ($k = 3.5 \times 10^{-6}$ sec^{-1}; 111°C in toluene) was found to be about ten times slower than that for **12a**. This suggests that the rotation of the bond between aryl rings are more restricted by the introduction of alkylenedioxy chain.

Synthesis of 3,3'-Disubstituted (*S*)-2,2'-Biphenyldiols. Recently, Snieckus et al. have reported an efficient route to 3,3'-disubstituted BINOL by directed *ortho*-metalation method.[17,18] For the regioselective functionalization of 2,2'-biphenyldiols at the 3,3'-positions, we first examined directed lithiation of carbamate derivative **14** (Scheme 3). Thus, carbamoylation of biphenyldiol **13c** with *i*-Pr_2NCOCl gave **14** in 80% yield. Lithiation of **14** with *s*-BuLi (4.4 equiv) in the presence of TMEDA in THF at -78 °C followed by treatment with MeI afforded dimethyl derivative **15** in 80% yield. It should be noted that no lithiation proceeded at the positions adjacent to the alkylenedioxy group under these conditions. Removal of the carbamoyl groups by $LiAlH_4$ reduction in refluxing dioxane furnished 3,3-dimethyl-2,2'-biphenyldiol **16** of 96% ee in 70% yield.



Scheme 3

3,3'-Dibromo derivatives of 1,2-biphenyldiols would serve as useful intermediates for the 3,3'-disubstituted 2,2'-biphenyldiols. Although directed dilithiation/bromination reaction of dicarbamates, such as **14**, would afford the 3,3'-dibromo derivatives, it was found that they could be obtained more straightforwardly by bromination of **13** (eq 7). It has been reported that phenols undergo regioselective *ortho*-bromination by treatment with bromine in the presence of *t*-butylamine at low temperatures.[19] The bromination reaction was



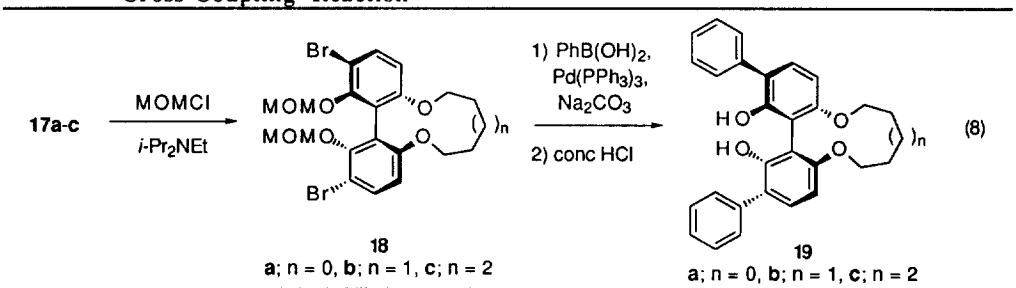
(7)

17
a; n = 0, **b**; n = 1, **c**; n = 2

successfully applied to the regioselective synthesis of 3,3'-dibromo derivatives **17a-c**. Treatment of biphenyldiol **13b** with bromine (2.2 equiv) in the presence of *t*-butylamine (4 equiv) at -70 - -40 °C afforded **17a** in 70% yield together with minor formation of the 3,3',5-tribromo derivative (18%). Under similar conditions, dibromo derivatives **17b** and **17c** were obtained in 72% and 71% yield, respectively, starting from the corresponding biphenyldiols. Dibromination of BINOL was also examined under similar conditions. However, the reaction resulted in the formation of a complex mixture of several bromination products.

The utility of 3,3'-diboromobiphenyldiols **17a-c** was demonstrated in the asymmetric synthesis of 3,3'-diphenyl derivatives **19a-c** (Table 3). Thus, protection of the hydroxy groups of **17a-c** with MOMCl afforded **18a-c** in high yields. The bis(MOM) derivatives were treated with phenylboronic acid under the Suzuki-Miyaura cross-coupling conditions to give diphenylation products in satisfactory yields.[20] Final deprotection under acidic conditions furnished (*S*)-**19a-c** in quantitative yields. Dibromides **17** can be also used for the synthesis of 3,3'-disilyl derivatives **20** (eq 9).[21] Silylation of **17b** with TBSCl and subsequent treatment of the bis(siloxy) derivative with *t*-BuLi gave 3,3'-bis(TBS) derivative **20a** in 43% overall yield. Similar reaction of **17a** using TMSCl afforded bis(TMS) derivative **20b** in 62% yield.

Table 3 Synthesis of (*S*)-3,3'-Diphenyl Derivatives 19a-c via Palladium-Catalyzed Cross-Coupling Reaction

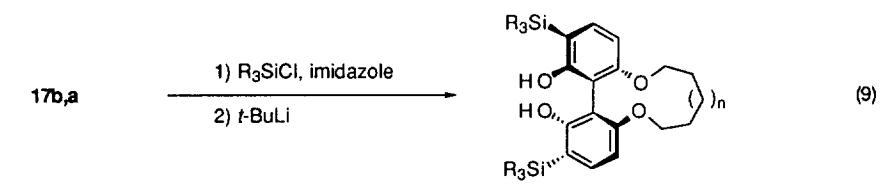


18
a; n = 0, **b**; n = 1, **c**; n = 2

19
a; n = 0, **b**; n = 1, **c**; n = 2

entry	substrate	18	yield (%)	19	yield (%)	$[\alpha]_D^{25}$ (*c*, THF)
1	**17a**	**18a**	78	**19a**	72	+272 (0.93)
2	**17b**	**18b**	80	**19b**	40	+241 (0.60)
3	**17c**	**18c**	71 [a]	**19c**	70	+287 (0.53)

[a] Overall yield starting from **13d**.



20a; R_3Si = *t*-BuMe$_2$Si, n = 1
20b; R_3Si =Me$_3$Si, n = 0

In summary, we have developed a general method for asymmetric synthesis of polysubstituted 2,2'-biaryldiols via desymmetrization of biphenyltetrol **1**. Each of the chiral biphenyldiols synthesized in the present study has a unique structure related to its torsional angle and 3,3'-substituent. Use of their Lewis acid complexes in catalytic asymmetric reactions are now underway.

EXPERIMENTAL

Unless otherwise noted ^{1}H- and ^{13}C-NMR spectra were recorded at 300 MHz and 75.6 MHz, respectively, in $CDCl_3$. Microanalyses were performed at the Microanalysis Center of Kyoto University. Unless otherwise noted, organic extracts were dried over Na_2SO_4. Flash chromatography was conducted on silica gel (Wakogel C-300). The ee values of 2,2'-biphenyldiols were established by HPLC analyses using a Chiracel OD column with 85:15:0.07 hexane:2-propanol:acetic acid as the mobile phase at a flow rate of 1 mL/min. All commercially available reagents were used without further purification unless otherwise noted. THF was distilled from sodium benzophenone ketyl. CH_2Cl_2 and DMF were distilled from CaH_2.

Bis(TMS) Ether 5a. To a stirred suspension of biphenyltetrol **1**[22] (1.00 g, 4.59 mmol) in CH_2Cl_2 (9.2 mL) under argon at -85 °C was added enol silyl ether **4**[9] (2.8 mL, 11 mmol), *l*-menthone (0.56 mL, 3.2 mmol), and TMSOTf (0.36 mL, 1.8 mmol) in this order. The mixture was allowed to warm to -20 °C and stirred for 20 h at this temperature. Hexamethyldisilazane (3.9 mL, 19 mmol) was added and the reaction mixture was stirred for 1 h at rt. The resulting mixture was diluted with hexane, poured into water, and extracted twice with hexane. The organic layers were washed with brine, dried, and concentrated. Unreacted menthone was recovered by vacuum distillation (bath temperature 60 °C). The residue was purified by silica gel flash chromatography (cold benzene/hexane, gradient elution from 10/90 to 25/75) to give, in the order of elution, the tetrakis(TMS) ether **8** (552 mg, 24%), a 15:1 mixture of isomenthonide **5a** and menthonide **7a** (1.04 g, 45%), and menthonide **6a** (364 mg, 16%) . Recrystallization of the mixture of **5a** and **7a** in methanol gave pure **5a**: mp 96-7 °C; ^{1}H NMR (C_6D_6) δ -0.05 (9H, s), -0.03 (9H, s), 0.68 (3H, d, *J* = 6.6 Hz), 0.85 (3H, d, *J* = 6.3 Hz), 0.92 (1H, m), 1.04 (3H, d, *J* = 6.2 Hz), 1.37 (1H, br d, *J* = *ca.* 12 Hz), 1.41 (1H, t, *J* = 12.6 Hz), 1.74 (1H, br d, *J* = *ca.* 12.5 Hz), 1.80-1.95 (2H, m), 2.02 (1H, tt, *J* = 3.9 and 13.9 Hz), 2.11 (1H, br d, *J* = *ca.* 13 Hz), 6.71 (1H, dd, *J* = 1.0 and 7.7 Hz), 6.72 (2H, br d, *J* = 8.0 Hz), 6.82 (1H, dd, *J* = 1.2 and 8.0), 7.00 (1H, t, *J* = 8.1 Hz), 7.02 (1H, t, *J* = 8.1 Hz); IR (KBr disk) 1250, 1230, 1040, 880, 840,745, 725 cm^{-1}; MS m/z (relative intensity) 498 (M^+, 48), 455 (10), 362 (56), 73 (100); HRMS: Calcd for $C_{28}H_{42}O_4Si_2$: 498.2623, found 498.2611. Anal. Calcd for $C_{28}H_{42}O_4Si_2$: C, 67.42; H, 8.49. Found: C, 67.20; H, 8.37. **6a**: mp 67-68 °C (recrystallized from methanol); ^{1}H NMR (C_6D_6) δ -0.05 (9H, s), -0.04 (9H, s), 0.75 (3H, d, *J* = 6.6 Hz), 0.79 (1H, m), 0.87 (6H, d, *J* = 6.9 Hz), 1.24 (1H, dd, *J* = 12.7 and 13.1 Hz), 1.45-1.65 (3H, m), 1.76 (1H, ddd, *J* = 0.9, 4.6, and 11.7 Hz), 1.80 (1H, m), 2.08 (1H, ddd, *J* = 1.9, 3.3, and 14.2 Hz), 2.56 (1H, br sept, *J* = 6.6 Hz), 6.63 (1H, dd, *J* = 1.4 and 7.8 Hz), 6.69 (1H, dd, *J* = 1.1 and 8.1 Hz), 6.76 (1H, dd, *J* = 1.1 and 8.0 Hz), 6.91 (1H, dd, *J* = 1.4 and 8.1 Hz), 6.96 (1H, t, *J* = 8.1 Hz), 6.98 (1H, t, *J* = 8.0 Hz); IR (KBr disk) 1250, 1040, 875, 750, 725 cm^{-1}; MS m/z (relative intensity) 498 (M^+, 24), 483 (20), 455 (6), 362 (56), 73 (100); HRMS: Calcd for $C_{28}H_{42}O_4Si_2$: 498.2623, found 498.2597. Anal. Calcd for $C_{28}H_{42}O_4Si_2$: C, 67.42; H, 8.49. Found: C, 67.23; H, 8.37. **7a**: ^{1}H NMR (C_6D_6) δ -0.03 (9H, s), -0.02 (9H, s), 0.66 (3H, d, *J* = 6.6 Hz), 0.80 (3H, d, *J* = 6.9 Hz), 0.85 (1H, m), 1.02 (3H, d, *J* = 6.6 Hz), 1.12 (1H, t, *J* = 12.6 Hz), 1.18-1.95 (5H, m), 2.00-2.15 (2H, m), 6.65 (1H, dd, *J* = 1.2 and 8.1 Hz), 6.70 (1H, dd, *J* = 1.1 and 8.1 Hz), 6.76 (1H, dd, *J* = 1.1 and 7.9 Hz), 6.83 (1H, dd, *J* = 1.3 and 8.1 Hz), 6.96 (1H, t, *J* = 8.0 Hz), 7.00 (1H, t, *J* = 8.1 Hz); IR (KBr disk) 1255, 1235, 1040, 1020, 780, 755, 720 cm^{-1}; MS m/z (relative intensity) 498 (M^+, 26), 483 (24), 455 (6), 362 (29), 73 (100); HRMS: Calcd for $C_{28}H_{42}O_4Si_2$: 498.2623, found 498.2624.

Isomenthonide 5b. To a stirred solution of **5a** (2.6 g, 5.21 mmol) in methanol (52 mL) at rt was added K_2CO_3 (2.2 g, 15.6 mmol) in one portion. After being stirred for 5 min, the reaction mixture was concentrated in vacuo. The residue was diluted with ether and washed successively with 1 N aq HCl and with brine. Concentrate of the dried organic layer was purified by silica gel flash chromatography (EtOAc/hexane = 10/90) to give **5b** (1.8 g, 98%): ^{1}H NMR δ 0.88 (3H, d, *J* = 6.6 Hz), 0.965 (3H, d, *J* = 6.5 Hz), 0.973 (3H, d, *J* = 6.7 Hz), 1.18 (1H, m), 1.49 (1H, t, *J* = 12.6 Hz), 1.54 (1H, m), 1.70-2.08 (6H, m), 6.76 (1H, dd, *J* = 1.0 and 7.8 Hz), 6.78-6.85 (3H, m), 7.19 (1H, t, *J* =7.8 Hz), 7.20 (1H, t, *J* = 8.1 Hz), 7.81 (2H, br); IR

(KBr disk) 3300 (br), 1155, 1110, 790, 750 cm^{-1}; MS m/z (relative intensity) 354 (M^+, 79), 339 (68), 311 (16), 81 (100); HRMS: Calcd for $C_{22}H_{26}O_4$: 354.1832, found 354.1836.

Menthonide 6b and 7b. Desilylation of bis(TMS) ethers **6a** by a procedure similar to that described above gave a 2.3:1 mixture of **6b** and **7b** in 100% yield. Under similar conditions, **7a** yield a 2.6:1 mixture of **6b** and **7b** in 97% yield. Desilylation of bis(TBS) ethers **6c** and **7c** was carried out in THF by using 5 equiv of Bu_4NF (1M solution in THF). The reaction of **6c** and **7c** gave *ca* 2.5:1 mixture of **6b** and **7b** in 80% and 95% yield, respectively. The ratios were determined by ^1H NMR analysis. **6b** and **7b**: ^1H NMR δ 0.67 (3H for **6b**, d, J = 6.6 Hz), 0.79 (6H for **7b**, d, J = 6.8 Hz), 0.88 (6H for **6b**, d, J = 6.8 Hz), 0.89 (3H, for **7b**, d, J = 6.6 Hz), 0.99 (1H, m), 1.23 (1H, m), 1.5-2.05 (6H, m), 2.34 (1H for **6b**, br sept, J = *ca.* 7 Hz), 6.25 (2H, br), 6.77-6.91 (4H, m), 7.18 (1H for **7b**, t, J = 8.1 Hz), 7.20 (1H for **6b**, t, J = 8.1 Hz), 7.25 (1H, t, J = 8.1 Hz); ^1H NMR (d^6-DMSO) δ 0.59 (3H for **6b**, d, J = 6.9 Hz), 0.70 (3H for **7b**, d, J = 6.5 Hz), 0.72 (3H for **7b**, d, J = 6.6 Hz), 0.75-1.0 (7H for **6b** and 4H for **7b**, m), 1.14 (1H, m), 1.4-2.0 (6H, m), 2.31 (1H for **6b**, br sept, J = *ca.* 7 Hz), 6.60-6.73 (3H, m), 6.77 (1H, dd, J = 1.0 and 8.1 Hz), 7.08 (1H for **7b**, t, J = 8.2 Hz), 7.09 (1H for **6b**, t, J = 8.2 Hz), 7.15 (1H for **7b**, t, J = 8.2 Hz), 7.16 (1H for **6b**, t, J = 8.2 Hz), 9.48 (2H, br).

Bis(TBS) Ethers 6c and 7c. To a solution of a 2.6:1 mixture of **6b** and **7b** (172 mg, 0.49 mmol) and imidazole (165 mg, 2.4 mmol) in DMF (2 mL) at rt was added TBSCl (293 mg, 1.9 mmol). After being stirred for 20 h, the mixture was poured into 1N aq HCl and extracted twice with ether. The organic layers were washed with brine, dried, and concentrated. The residue was purified by silica gel flash chromatography (benzene/hexane = 10/90) to give **6c** (168 mg, 59%) and **7c** (64 mg, 23%). **6c**: mp 90-91 °C (recrystallized from ethanol); ^1H NMR δ -0.38 (3H, s), -0.36 (3H, s), -0.03 (3H, s), 0.08 (3H, s), 0.66 (3H, d, J = 6.9 Hz), 0.78-0.93 (24H, m, including s (9H) at 0.79 and s (9H) at 0.80), 0.93-1.98 (8H, m), 2.31 (1H, br sept, J = 6.6 Hz), 6.62 (1H, br d, J = 7.2 Hz), 6.67 (1H, br d, J = 8.1 Hz), 6.77 (1H, br d, J = 8.1 Hz), 6.86 (1H, br d, J = 8.4 Hz), 7.08 (1H, t, J = 8.1 Hz), 7.12 (1H, t, J = 8.1 Hz); IR (KBr disk) 1250, 1230, 1075, 1035, 865, 840, 780 cm^{-1}; MS m/z (relative intensity) 582 (M^+, 5), 525 (15), 389 (34), 73 (100); HRMS: Calcd for $C_{34}H_{54}O_4Si_2$: 582.3562, found 582.3559. Anal. Calcd for $C_{34}H_{54}O_4Si_2$: C, 70.05; H, 9.34. Found: C, 70.08; H, 9.54. **7c**: mp 84-85 °C (recrystallized from ethanol); ^1H NMR δ -0.36 (3H, s), -0.34 (3H, s), -0.02 (3H, s), 0.03 (3H, s), 0.77 (3H, d, J = 6.8 Hz), 0.78 (3H, d, J = 6.7 Hz), 0.806 (9H, s), 0.814 (9H, s), 0.85 (3H, d, J = 6.3 Hz), 0.89 (1H, m), 1.15 (1H, br t, J = 12.0 Hz), 1.28 (3H, m), 1.4-1.95 (4H, m), 6.60 (1H, dd, J = 1.0 and 8.1 Hz), 6.67 (1H, dd, J = 1.0 and 8.0 Hz), 6.69 (1H, dd, J = 1.1 and 8.0 Hz), 6.75 (1H, dd, J = 1.0 and 8.1 Hz), 7.07 (1H, t, J = 8.1 Hz), 7.12 (1H, t, J = 8.1 Hz); IR (KBr disk) 1250, 1235, 1040, 1015, 870, 840, 795, 780 cm^{-1}; MS m/z (relative intensity) 582 (M^+, 4), 525 (14), 389 (32), 137 (73), 73 (100); HRMS: Calcd for $C_{34}H_{54}O_4Si_2$: 582.3562, found 582.3564. Anal. Calcd for $C_{34}H_{54}O_4Si_2$: C, 70.05; H, 9.34. Found: C, 69.91; H, 9.20.

Dimethoxy Derivative 10a. To a solution of **5b** (178 mg, 0.50 mmol) and Me_2SO_4 (0.19 mL, 2.0 mmol) in CH_2Cl_2 (2.5 mL) at rt were added aq 0.6 N NaOH (2.5 mL) and benzyltributylammonium bromide (89 mg, 0.25 mmol). After being stirred at rt for 3 h, the resulting mixture was poured into water and extracted twice with ether. The organic layers were washed with brine, dried, and concentrated in vacuo. The residue was purified by silica gel flash chromatography (EtOAc/hexane = 30/70) to give 175 mg (91%) of **10a**: ^1H NMR δ 0.86 (3H, d, J = 6.6 Hz), 0.96 (6H, d, J = 6.6 Hz), 1.0-2.1 (9H, m), 3.84 (3H, s), 3.90 (3H, s), 6.72 (1H, dd, J = 0.7 and 8.0 Hz), 6.76 (1H, br d, J = *ca.* 8 Hz), 6.83 (2H, br d, J = *ca.* 8 Hz), 7.25 (2H, t, J = *ca.* 8 Hz); IR (KBr disk) 1240, 1085, 950, 780, 720 cm^{-1}; MS m/z (relative intensity) 382 (M^+, 66), 367 (60), 246 (100), 136 (34); HRMS: Calcd for $C_{24}H_{30}O_4$: 382.2145, found 382.2137.

Dibenzyloxy Derivative 10b. To a solution of **5b** (169 mg, 0.48 mmol) and benzyl bromide (0.23 mL, 1.7 mmol) in CH_2Cl_2 (2.4 mL) at rt were added aq 0.6 N NaOH (2.4 mL) and benzyltributylammonium bromide (83 mg, 0.23 mmol). After being stirred at rt for 18 h, the resulting mixture was poured into water and extracted twice with ether. The organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel flash chromatography (EtOAc/hexane = 10/90) to give 231 mg

(90%) of **10a**: ^{1}H NMR δ 0.87 (3H, d, *J* = 6.4 Hz), 0.97 (3H, d, *J* = 6.7 Hz), 0.98 (3H, d, *J* = 6.5 Hz), 1.08 (1H, m), 1.46 (1H, t, *J* = 12.5 Hz), 1.52 (1H, m), 1.72-2.02 (6H, m), 4.77 (1H, d, *J* = 11.8 Hz), 4.80 (1H, d, *J* = 11.8 Hz), 4.98 (1H, d, *J* = 11.8 Hz), 4.99 (1H, d, *J* = 11.8 Hz), 6.76 (1H, dd, 1.1 and 8.0 Hz), 6.82 (3H, m), 7.08-7.30 (12H, m); IR (KBr disk) 1270, 1230, 1085, 1070, 735, cm^{-1}; MS m/z (relative intensity) 534 (M^+, 10), 443 (22), 148 (14), 91 (100); HRMS: Calcd for $C_{36}H_{38}O_4$: 534.2771, found 534.2761.

Diphenoxy Derivative 10c. To a solution of **5b** (36 mg, 0.10 mmol) and $Ph_3Bi(OAc)_2$ (229 mg, 0.41 mmol) in benzene (1 mL) under argon at 50 °C was added copper powder (8.6 mg). The resulting suspension was stirred at this temperature for 26 h. The mixture was diluted with ethyl acetate and filtered. The filtrate was washed with 1N HCl, dried, and concentrated in vacuo. The residue was purified by silica gel flash chromatography (benzene/hexane = 5/95) to give 24.2 mg (48%) of **10c**: ^{1}H NMR δ 0.92 (3H, d, *J* = 6.3 Hz), 1.00 (3H, d, *J* = 6.8 Hz), 1.03 (3H, d, *J* = 6.5 Hz), 1.10 (1H, m), 1.51 (1H, t, *J* = 13.8 Hz), 1.6-2.1 (m, 7H), 6.67 (1H, dd, *J* = 0.9 and 8.4 Hz), 6.72 (1H, dd, *J* = 0.9 and 8.4 Hz), 6.8-7.0 (8H, m), 7.11-7.22 (6H, m); IR (KBr disk) 1230, 1210, 1030, 780, 720, 695 cm^{-1}; MS m/z (relative intensity) 506 (M^+, 100), 491 (55), 81 (99); HRMS: Calcd for $C_{34}H_{34}O_4$: 506.2458, found 506.2447.

General Procedure for Intermolecular Cyclization Reaction of 5b. To a solution of **5b** (1.0 mmol) in DMF (25 mL) under argon at rt was added K_2CO_3 (2.3 mmol). A solution of a 1,ω–dibromoalkane (1.0 mmol) in DMF (9 mL) was added slowly to the resulting suspension during 2-4 h at 80 °C by using a syringe pump. After the addition, the reaction mixture was stirred further for 2-3 h, then poured into water, and extracted twice with benzene. The organic layers were washed with brine, dried, and concentrated in vacuo. The residue was purified by flash chromatography (EtOAc/hexane = 10/90 - 30/70) to give 6,6'-alkylenedioxy derivatives **11a-e**.

6,6'-Propylenedioxy Derivative 11a: ^{1}H NMR δ 0.86 (3H, d, *J* = 6.6 Hz), 0.94 (6H, d, *J* = 6.6 Hz), 1.04 (1H, m), 1.44 (1H, t, *J* = 12.5 Hz), 1.50 (1H, m), 1.71-2.12 (8H, m), 4.40 (4H, m), 6.77 (1H, dd, *J* = 0.9 and 8.1 Hz), 6.81 (1H, br d, *J* = ca 8 Hz), 6.94 (2H, br d, *J* = *ca.* 8 Hz), 7.21 (1H, t, *J* = 8.1 Hz), 7.22 (1H, t, *J* = 8.1 Hz); IR (KBr disk) 1240, 1215, 1080, 1065, 785, 720 cm^{-1}; MS m/z (relative intensity) 394 (M^+, 100), 379 (76), 258 (92); HRMS: Calcd for $C_{25}H_{30}O_4$: 394.2145, found 394.2152.

6,6'-Butylenedioxy Derivative 11b: ^{1}H NMR δ 0.86 (3H, d, *J* = 6.6 Hz), 0.94 (6H, d, *J* = 6.6 Hz), 1.05 (1H, m), 1.45 (1H, t, *J* = 12.5 Hz), 1.52 (1H, m), 1.75-2.00 (10H, m), 4.11 (2H, br t, *J* = ca 10 Hz), 4.45-4.56 (2H, m), 6.73 (1H, dd, *J* = 0.9 and 7.9 Hz), 6.77 (1H, dd, *J* = 0.9 and 8.0 Hz), 6.88 (2H, br d, *J* = *ca.* 8 Hz), 7.227 (1H, t, *J* = 8.1 Hz), 7.233 (1H, t, *J* = 8.1 Hz); IR (KBr disk) 1100, 780, 750, 720 cm^{-1}; MS m/z (relative intensity) 408 (M^+, 72), 393 (42), 55 (100); HRMS: Calcd for $C_{26}H_{32}O_4$: 408.2302, found 408.2296.

6,6'-Pentylenedioxy Derivative 11c: ^{1}H NMR δ 0.88 (3H, d, *J* = 6.6 Hz), 0.97 (6H, d, *J* = 6.6 Hz), 1.07 (1H, m), 1.46 (1H, t, *J* = 12.0 Hz), 1.53 (1H, m), 1.6-2.05 (12H, m), 4.1-4.3 (4H, m), 6.72 (1H, dd, *J* = 1.0 and 8.0 Hz), 6.76 (1H, dd, *J* = 1.0 and 8.0 Hz), 6.82 (2H, br d, *J* = *ca.* 8 Hz), 7.24 (1H, t, *J* = 8.0 Hz), 7.25 (1H, t, *J* = 8.0 Hz); IR (KBr disk) 1230, 1090, 775, 715 cm^{-1}; MS m/z (relative intensity) 422 (M^+, 100), 407 (50), 286 (78); HRMS: Calcd for $C_{27}H_{34}O_4$: 422.2448, found 422.2460.

6,6'-Hexylenedioxy Derivative 11d: ^{1}H NMR δ 0.86 (3H, d, *J* = 6.5 Hz), 0.95 (6H, d, *J* = 6.6 Hz), 1.01 (1H, m), 1.43 (1H, t, *J* = 12.5 Hz), 1.52 (5H, m), 1.55-2.10 (10H, m), 4.03 (2H, m), 4.21 (2H, m), 6.69 (1H, br d *J* = 7.9 Hz), 6.72 (1H, br d, *J* = 8.0 Hz), 6.90 (2H, br d, *J* = *ca.* 8 Hz), 7.22 (1H, t, *J* = 8.2 Hz), 7.23 (1H, t, *J* = 8.1 Hz); IR (KBr disk) 1230, 1110, 1070, 720 cm^{-1}; MS m/z (relative intensity) 436 (M^+, 84), 421 (42), 300 (72), 55 (100); HRMS: Calcd for $C_{28}H_{36}O_4$: 436.2615, found 436.2611.

6,6'-(2",3"-Benzo)-2"-butenylenedioxy Derivative 11e: ^{1}H NMR δ 0.86 (3H, d, *J* = 6.6 Hz), 0.93 (3H, d, *J* = 6.6 Hz), 0.94 (3H, d, *J* = 6.6 Hz), 1.04 (1H, m), 1.4-1.5 (2H, m), 1.7-2.0 (6H, m), 5.25 (1H, d, *J* = 11.4 Hz), 5.27 (1H, d, *J* = 11.4 Hz), 5.36 (2H, d, *J* = 11.4 Hz), 6.72 (1H, d, *J* = 7.8 Hz), 6.78 (1H, d, *J* = 8.1 Hz), 7.01 (2H, m), 7.17-7.24 (2H, m), 7.30 (2H, m), 7.43 (2H, m); IR (KBr disk) 1220,

1080, 740 (s), 720 (s) cm^{-1}; MS m/z (relative intensity) 456 (M^+, 100), 41 (34), 352 (16), 175 (54), 104 (88); HRMS: Calcd for $C_{30}H_{32}O_4$: 456.2302, found 456.2305.

General Procedure for the Synthesis of 2,2'-Biphenyldiols 12a-c and 13a-e. To a stirred solution of **10a-c** or **11a-e** (1.0 mmol) in MeOH (2 mL) and THF (4 mL) at rt was added conc. HCl (1.0 mL). The mixture was stirred overnight at rt and concentrated in vacuo. The mixture was diluted with ether and washed successively with water and brine. Concentration of the dried organic layer and silica gel flash chromatography (EtOAc/hexane = 5/95-20/80) of the reside afforded **12a-c** and **13a-e.**

(*S*)-6,6'-Dimethoxy-2,2'-biphenyldiol (12a): mp 135-140 °C (recrystallized from ethyl acetate and hexane); $[\alpha]^{25}_D$ + 23.4 (*c* 0.64, EtOH), $[\alpha]^{25}_D$ - 141 (*c* 1.0, $CHCl_3$) [lit.[25] $[\alpha]^{20}_D$ - 167.0 (*c* 1, $CHCl_3$), lit.[4g] $[\alpha]^{20}_D$ - 144 (*c* 0.77, $CHCl_3$)]; ^1H NMR δ 3.76 (6H, s), 5.10 (2H, br), 6.62 (2H, br d, *J* = 8.3 Hz), 6.72 (2H, br d, *J* = 8.2 Hz), 7.30 (2H, t, *J* = 8.2 Hz); IR (KBr disk) 3460 (br), 1160, 1075, 785, 730 cm^{-1}; MS m/z (relative intensity) 246 (M^+, 100), 215 (50), 200 (12), 171 (26), 73 (50); HRMS: Calcd for $C_{14}H_{14}O_4$: 246.0892, found 246.0900.

(*S*)-6,6'-Di(phenylmethoxy)-2,2'-biphenyldiol (12b): $[\alpha]^{25}_D$ + 60.0 (*c* 0.70, EtOH); ^1H NMR (200 MHz) δ 5.02 (4H, AB quartet, *J* = 12.3 Hz, Δδ = 12.2 Hz), 5.13 (2H, br s), 6.63 (2H, br d, *J* = ca 8 Hz), 6.74 (2H, br d, *J* = *ca.* 8 Hz), 7.2 (10H, m), 7.27 (2H, t, *J* = 8.0 Hz); IR (KBr disk) 3470 (br), 1255, 1185, 1060, 780, 735 cm^{-1}; MS m/z (relative intensity) 398 (M^+, 8), 307 (13), 191 (6), 91 (100); HRMS: Calcd for $C_{26}H_{22}O_4$: 398.1519, found 398.1518.

(*S*)-6,6'-Diphenoxy-2,2'-biphenyldiol (12c): mp 159-161 °C (recrystallized from benzene and hexane); $[\alpha]^{25}_D$ + 80.0 (*c* 0.52, EtOH); ^1H NMR δ 5.21 (2H, br s), 6.49 (2H, dd, *J* = 0.9 and 8.3 Hz), 6.81 (2H, dd, *J* = 0.9 and 8.2 Hz), 6.85 (4H, m), 7.02 (2H, br t , *J* = *ca.* 7.5 Hz), 7.21 (6H, m); IR (KBr disk) 3480 (br), 3380 (br), 1210, 1020, 800, 790, 730 cm^{-1}; MS m/z (relative intensity) 370 (M^+, 48), 276 (26), 73 (100); HRMS: Calcd for $C_{24}H_{18}O_4$: 370.1205, found 370.1197. Anal. Calcd for $C_{24}H_{18}O_4$: C, 77.82; H, 4.90. Found: C, 77.54; H, 5.00.

(*S*)-6,6'-Propylenedioxy-2,2'-biphenyldiol (13a): mp 275-277 °C (recrystallized from MeOH); $[\alpha]^{25}_D$ +220 (*c* 1.11, THF); ^1H NMR (acetone-d_6) δ 1.87 (2H, quintet, *J* = *ca.* 5 Hz), 2.85 (2H, br s), 4.21 (2H, td, *J* = 5.7 and 11.4 Hz), 4.29 (2H, td, *J* = 4.5 and 11.4 Hz), 6.62 (2H, dd, *J* = 0.9 and 8.1 Hz), 6.68 (2H, br d, *J* = *ca.* 8 Hz), 7.12 (2H, t, *J* = 8.1 Hz); IR (KBr disk) 3230 (br), 1250, 1220, 1070, 1055, 790 cm^{-1}; MS m/z (relative intensity) 258 (M^+, 18), 200 (4), 149 (100); HRMS: Calcd for $C_{15}H_{14}O_4$: 258.0892, found 258.0881. Anal. Calcd for $C_{15}H_{14}O_4$: C, 69.76; H, 5.46. Found: C, 69.71; H, 5.40.

(*S*)-6,6'-Butylenedioxy-2,2'-biphenyldiol (13b): mp 251-252 °C (recrystallized from EtOH); $[\alpha]^{30}_D$ + 142 (*c* 0.595, THF); ^1H NMR (acetone-d_6) δ 1.64-1.72 (2H, m), 1.79-1.85 (2H, m), 2.85 (2H, br s), 4.10-4.16 (2H, m), 4.24-4.31 (2H, m), 6.57 (2H, dd, *J* = 0.9 and 8.1 Hz), 6.65 (2H, dd, *J* = 0.9 and 8.1 Hz), 7.10 (2H, t, *J* = 8.1 Hz); IR (KBr disk) 3250 (br), 1240, 1045, 780 cm^{-1}; MS m/z (relative intensity) 272 (M^+, 12), 220 (20), 205 (60), 57 (100); HRMS: Calcd for $C_{16}H_{16}O_4$: 272.1049, found 272.1034. Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.28; H, 5.95.

(*S*)-6,6'-Pentylenedioxy-2,2'-biphenyldiol (13c): mp 177-179 °C (recrystallized from benzene); $[\alpha]^{25}_D$ + 184 (*c* 1.10, THF); ^1H NMR δ 1.18-1.23 (2H, m), 1.68-1.76 (4H, m), 3.98-4.10 (2H, m), 4.25-4.38 (2H, m), 5.00 (2H, br s), 6.63 (2H, br d, *J* = ca 8 Hz), 6.68 (2H, dd, *J* = 0.9 and 8.1 Hz), 7.26 (2H, t, *J* = 8.1 Hz); IR (KBr disk) 3270 (br), 1230, 1080, 780, 750, 720 cm^{-1}; MS m/z (relative intensity) 286 (M^+, 100), 218 (66), 200 (38), 149 (42); HRMS: Calcd for $C_{17}H_{18}O_4$: 286.1205, found 286.1208. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.15; H, 6.36.

(*S*)-6,6'-Hexylenedioxy-2,2'-biphenyldiol (13d): mp 180-181 °C (recrystallized form benzene and hexane); $[\alpha]^{25}_D$ +152 (*c* 0.765, EtOH); ^1H NMR δ 1.31-1.45 (4H, m), 1.55-1.67 (4H m), 3.98 (2H, m), 4.18 (2H, m), 4.91 (2H, br), 6.60 (2H, br d, *J* = *ca.* 8 Hz), 6.66 (2H, dd, *J* = 0.8 and 8.2 Hz), 7.26 (2H, t, *J* = 8.2 Hz); ^{13}C NMR δ 24.2, 25.9, 67.8, 104.7, 107.5, 108.3, 130.3, 154.9, 158.1; IR (KBr disk) 3500 (br), 3500, 3400 (br), 1185, 1065, 800, 730 cm^{-1}; MS m/z (relative intensity) 300 (M^+, 95), 218 (100), 200 (48);

HRMS: Calcd for $C_{18}H_{20}O_4$: 300.1362, found 300.1359. Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 71.94; H, 6.72.

(*S*)-6,6'-(2",3"-Benzo)-2"-butenylenedioxy-2,2'-biphenyldiol (13e): mp 252-254 °C (recrystallized from ethyl acetate and hexane); $[\alpha]^{25}_D$ - 51.0 (*c* 0.79, THF); ^{1}H NMR (THF-d^8) δ 5.12 (2H, d, *J* =11.4 Hz), 5.26 (2H, d, *J* = 11.4 Hz), 6.48 (2H, d, *J* = 8.1 Hz), 6.68 (2H, d, *J* = 8.1 Hz), 7.01 (2H, t, *J* = 8.1 Hz), 7.22-7.28 (2H, m), 7.36-7.40 (2H, m), 7.80 (2H, br); IR (KBr disk) 3300 (br), 2950, 1580, 1450, 1070, 780, 740, 720 cm^{-1}; MS m/z (relative intensity) 320 (M^+, 16), 302 (4), 205 (400, 149 (14), 80 (100); HRMS: Calcd for $C_{20}H_{16}O_4$: 320.1049, found 320.1043. Anal. Calcd for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03. Found: C, 75.07; H, 5.23.

Determination of the Rate Constant of Racemization. HPLC grade toluene and EtOH were used in the kinetic experiments. A biphenyldiol (15.0 mg) was dissolved in a refluxing toluene or EtOH (12 mL) and the solution was stirred for 8-9 h. At various intervals, a *ca.* 0.30 mL sample was removed from the solution and the ee was determined by HPLC analysis with a Chiracel OD column. The rate constants were calculated with a least-squares program that fits an exponential expression to the experimental data.

(*S*)-6,6'-Pentylenedioxybiphenyl-2,2'-diyl Bis(*N*,*N*-diisopropylcarbamate) 14. To a solution of **13c** (412 mg, 1.44 mmol) in THF (5.0 mL) was added K_2CO_3 (430 mg, 3.11 mmol) and *N*,*N*-diisopropylcarbamoyl chloride (761 mg, 4.65 mmol) at rt. After being stirred for 5.0 h at 65 °C, the mixture was poured into water and extracted twice with ether. The organic layers were washed with brine, dried, and concentrated in vacuo. The residue was purified by silica gel flash chromatography (10% EtOAc in hexane) to give 621 mg (80%) of **14**: ^{1}H NMR δ 0.6-1.4 (24H, br), 1.52 (2H, m), 1.6-1.8 (4H, m), 3.5-3.75 (2H, br), 3.75-4.0 (2H, br), 4.10 (2H, ddd, *J* = 3.0, 6.6, and 11.4 Hz), 4.29 (2H, ddd, *J* = 3.6, 7.2, and 11.1 Hz), 6.79 (2H, dd, *J* = 1.2 and 8.4 Hz), 6.92 (2H, dd, *J* = 1.2 and 8.4 Hz), 7.22 (2H, t, *J* = 8.4 Hz); IR (liquid film) 1720, 1705, 1230, 765, 750 cm^{-1}; MS (CI) m/z (relative intensity) 541 (MH^+, 16), 414 (6), 128 (100); HRMS (CI): Calcd for $C_{31}H_{45}O_6N_2$: 541.3277, found 541.3288.

(*S*)-3,3'-Dimethyl-6,6'-pentylenedioxybiphenyl-2,2'-diyl Bis(*N*,*N*-diisopropylcarbamate) 15. To a solution of **14** (574 mg, 1.06 mmol) and TMEDA (0.69 mL, 4.57 mmol) in THF (9.7 mL) at -78 °C was slowly added *s*-BuLi (4.35 mL, 1.05 M in hexane). The mixture was stirred at this temperature for 5 h. To this was added MeI (0.65 mL, 10.4 mmol) and the resulting mixture was allowed to warm to rt. After being stirred for 5.0 h, the mixture was poured into aq NH_4Cl and extracted twice with ether. The organic layers were washed with brine, dried, and concentrated in vacuo. The residue was purified by silica gel flash chromatography (10% EtOAc in benzene) to give 481 mg (80%) of **15**: ^{1}H NMR δ 0.98 (12H, d, *J* = 7.2 Hz), 1.06 (6H, d, *J* = 7.2 Hz), 1.14 (6H, d, *J* = 7.2 Hz), 1.4-1.75 (6H, m), 2.10 (6H, s), 3.3-3.6 (2H, m), 3.9-4.15 (4H, m), 4.25 (2H, m), 6.70 (2H, d, *J* = 8.8 Hz), 7.05 (2H, d, *J* = 8.8 Hz); IR (KBr disk) 1700, 1680, 1580, 780, 740 cm^{-1}; MS m/z (relative intensity) 568 (M^+, 7), 441 (30), 314 (46), 128 (80), 86 (100); HRMS: Calcd for $C_{33}H_{48}O_6N_2$: 568.3512, found 568.3503.

(*S*)-3,3'-Dimethyl-6,6'-pentylenedioxy-2,2'-biphenyldiol (16). To a solution of **15** (323 mg, 0.568 mmol) in dioxane (5.5 mL) was added $LiAlH_4$ (124 mg, 3.27 mmol). The mixture was heated at 90 °C for 24 h. The mixture was poured into aq 2N HCl and extracted twice with ether. The organic layers were dried and concentrated in vacuo. The residue was purified by silica gel flash chromatography (10% EtOAc in hexane) to give 125 mg (70%) of **16**: $[\alpha]^{25}_D$ +161 (*c* 0.52, EtOH); ^{1}H NMR δ 1.45-1.6 (2H, m), 1.6-1.8 (4H, m), 2.22 (6H, s), 4.03 (2H, ddd, *J* = 3.8, 6.3, and 12.5 Hz), 4.29 (2H, ddd, *J* = 3.8, 7.5, and 12.5 Hz), 4.98 (2H, br s), 6.55 (2H, d, *J* = 8.8 Hz), 7.12 (2H, d, *J* = 8.8 Hz); IR (KBr disk) 3500 (br), 1190, 1060, 785 cm^{-1}; MS m/z (relative intensity) 314 (M^+, 100), 246 (61), 229 (22), 109 (21); HRMS: Calcd for $C_{19}H_{22}O_4$: 314.1517, found 314.1514

(*S*)-3,3'-Dibromo-6,6'-butylenedioxy-2,2'-biphenyldiol (17a) (Representative Procedure for Bromination of 2,2'-Biphenyldiols 13). To a solution of *t*-butylamine (0.063 mL, 0.60 mmol) in THF (1.5 mL) was added Br_2 (0.017 mL, 0.33 mmol) at -30 °C and the mixture was cooled to -70 °C. To this was added a solution of **13b** (40.9 mg, 0.15 mmol) in THF (0.9 mL). The mixture was

allowed to warm to -30 °C and stirred for 7 h. The mixture was poured into aq 1N HCl and extracted twice with ether. The organic layers were dried and concentrated in vacuo. The residue was purified by silica gel flash chromatography (10% EtOAc in hexane) to give 45.2 mg (70%) of **17a** and 3,3',5-tribromo derivative 13.6 mg (18%). **17a**: mp 85-86 °C (recrystallized from benzene); ^{1}H NMR δ 1.7-1.9 (4H, m), 4.15-4.3 (4H, m), 5.7 (2H, br), 6.62 (2H, d, *J* = 8.5 Hz), 7.45 (2H, d, *J* = 8.5 Hz); ^{13}C NMR δ 25.9, 70.5, 103.0, 109.3, 112.9, 131.8, 150.7, 157.4; IR (KBr disk) 3430 (br), 1135, 790, 680 cm^{-1}; MS m/z (relative intensity) 431, 430, 429 (M^+, 50, 100, 50), 376 (45), 294 (21); HRMS: calcd for $C_{16}H_{14}O_4{}^{81}Br^{79}Br$ 429.9240, found 429.9238. Anal. Calcd for $C_{16}H_{14}O_4Br_2$: C, 44.68; H, 3.28. Found: C, 44.58; H, 3.42. (*S*)-3,3'-Tribromo-6,6'-butylenedioxy-2,2'-biphenyldiol: mp 231-232 °C (recrystallized from EtOH); ^{1}H NMR δ 2.0 (4H, m); 3.98 (1H, ddd, *J* = 2.1, 10.2, and 12.0 Hz), 4.12 (1H, br t, *J* = *ca.* 11 Hz), 4.57 (1H, br d, *J* = *ca.* 12 Hz), 5.02 (1H, td, *J* = 3.5 and 11.0 Hz); 5.48 (1H, s), 5.52 (1H, s), 6.65 (1H, d, *J* = 9.0 Hz), 7.47 (1H, d, *J* = 9.0 Hz), 7.69 (1H, s). Anal. Calcd for $C_{16}H_{13}O_4Br_3$: C, 37.76; H, 2.57; Br, 47.10. Found: C, 37.72; H, 2.42; Br, 46.99.

(*S*)-3,3'-Dibromo-6,6'-pentylenedioxy-2,2'-biphenyldiol (17b). The dibromide was prepared by a procedure similar to that described above. **17b**: $[\alpha]^{20}_D$ +198° (*c* 0.575, EtOH); ^{1}H NMR δ 1.40-1.62 (2H, m), 1.62-1.84 (4H, m), 4.05 (2H, ddd, *J* = 3.8, 6.3, and 12.5 Hz), 4.33 (2H, ddd, *J* = 3.8, 6.3, and 12.5 Hz), 5.57 (2H, br s), 6.55 (2H, d, *J* = 8.8 Hz), 7.45 (2H, d, *J* = 8.8 Hz); IR (KBr disk) 3500, 1590, 1480, 1440, 1310, 1240, 1180, 1080, 820, 795 cm^{-1}; MS m/z (relative intensity) 446, 444, 442 (M^+, 22, 44, 22), 378, 376, 374 (22, 44, 22), 295 (10), 69 (100); HRMS: Calcd for $C_{17}H_{16}O_4{}^{79}Br^{81}Br$: 443.9395, found 441.9395.

(*S*)-3,3'-Dibromo-6,6'-hexylenedioxy-2,2'-biphenyldiol (17c): The dibromide was obtained as a 4.9:1 mixture with 3,3',5-tribromo derivative by a procedure similar to that described above. The mixture was used for subsequent reaction. **17c**; ^{1}H NMR δ 1.40 (4H, m), 1.64 (4H, m), 3.95-4.05 (2H, m), 4.12-4.2 (2H, m), 6.53 (2H, d, *J* = 8.9 Hz), 7.44 (2H, d, *J* = 8.9 Hz); ^{13}C NMR δ 24.0, 25.6, 67.7, 101.3, 105.8, 110.4, 131.9, 150.7, 157.1; IR (KBr disk) 3440 (br), 1060, 820, 790 cm^{-1}.

(*S*)-3,3'-Dibromo-2,2'-di(methoxymethoxy)-6,6'-pentylenedioxybiphenyl (18b) (Representative Procedure for MOM Protection). To a solution of **17b** (132.3 mg, 0.298 mmol) and *i*-Pr_2NEt (0.21 mL, 1.2 mmol) in CH_2Cl_2 (3.0 mL) at 0 °C was added chloromethyl methyl ether (0.14 mL, 1.8 mmol). After being stirred for 15 h at rt, the mixture was poured into water and extracted twice with ether. The organic layers were dried and concentrated in vacuo. The residue was purified by silica gel flash chromatography (10 % EtOAc in benzene) to give 127 mg (80%) of **18b**: ^{1}H NMR δ 1.50-1.65 (2H, m), 1.65-1.85 (4H, m), 3.04 (6H, s), 4.0-4.15 (2H, m), 4.25-4.4 (2H, m), 4.71 (2H, d, *J* = 6.0 Hz), 4.82 (2H, d, *J* = 6.0 Hz), 6.71 (2H, d, *J* = 9.0 Hz), 7.50 (2H, d, *J* = 9.0 Hz); IR (KBr disk) 1570, 1460, 1380, 1200, 1160, 1050, 970, 915, 800 cm^{-1}; MS m/z (relative intensity) 534, 532, 530 (M^+, 5, 10, 5), 458, 456, 454 (36, 72, 36), 69 (100); HRMS: Calcd for $C_{21}H_{24}O_6{}^{79}Br^{81}Br$: 531.9919, found 531.9891.

(*S*)-3,3'-Dibromo-2,2'-di(methoxymethoxy)-6,6'-butylenedioxybiphenyl (18a). The compound was prepared from **17a** in 78% yield by a procedure similar to that described for **18b**: ^{1}H NMR δ 1.7-1.9 (4H, m), 2.98 (6H, s), 4.25 (4H, m), 4.74 (2H, d, *J* = 6.2 Hz), 4.83 (2H, d, *J* = 6.2 Hz), 6.79 (2H, d, *J* = 8.9 Hz), 7.51 (2H, d, *J* = 8.9 Hz); IR (KBr disk) 1200, 1150, 1030, 920, 800 cm^{-1}.

(*S*)-3,3'-Dibromo-2,2'-di(methoxymethoxy)-6,6'-hexylenedioxybiphenyl (18c). Bromination of **13d** and MOM protection of the resulting crude dibromide without isolation, by a procedure similar to that described above, gave **18c** in 71% overall yield. **18c**: ^{1}H NMR δ 1.42 (4H, m), 1.64 (4H, m), 3.08 (6H, s), 3.94-4.02 (2H, m), 4.11-4.20 (2H, m), 4.66 (2H, d, *J* = 5.3 Hz), 4.81 (2H, d, *J* = 5.3 Hz), 6.68 (2H, d, *J* = 9.0 Hz), 7.49 (2H, d, *J* = 9.0 Hz); ^{13}C NMR δ 24.1, 25.6, 56.9, 67.6, 99.0, 108.1, 108.9, 120.2, 132.5, 153.3, 157.0; IR (KBr disk) 1570, 1160, 1055, 950, 800 cm^{-1}.

(*S*)-4',4"-Butylenedioxy-1,1':3',3":1",1'"-quaterphenyl-2',2"-diol (19a). To a mixture of **18a** (101 mg, 0.195 mmol), $PhB(OH)_2$ (119 mg, 0.975 mmol), and $Pd(PPh_3)_4$ (67.6 mg, 0.059 mmol) in DME (2 mL) at rt under Ar was added aq 2M Na_2CO_3 (0.59 mL). The mixture was stirred at 75 °C for 48 h.

Then, H_2O_2 (5 mL) and aq 1M NaOH (5 mL) were added and the resulting mixture was stirred at 60°C for 30 min. The mixture was diluted with ether, poured into water, and extracted twice with ether. The organic layers were dried and concentrated in vacuo. The residue was purified by silica gel flash chromatography (15% ethyl acetate in hexane) to give 84.6 mg (85%) of (*S*)-4',4"-butylenedioxy-2',2"-bis(methoxymethyl)-1,1':3',3":1",1'"-quaterphenyl: ^{1}H NMR δ 1.8-2.0 (4H, m), 2.73 (6H, s), 4.2-4.3 (2H, m), 4.35-4.45 (4H, m, including d (2H, *J* = 5.9 Hz) at 4.39), 4.76 (2H, d, *J* = 5.9 Hz), 6.95 (2H, d, *J* = 8.5 Hz), 7.29 (2H, m), 7.32 (2H, d, *J* = 8.5 Hz), 7.41 (4H, m), 7.64 (4H, m); ^{13}C NMR δ 26.0, 56.2, 70.3, 98.9, 111.6, 121.1, 126.5, 128.1, 128.9, 129.5, 130.3, 139.0, 153.8, 157.2; IR (KBr disk) 1260, 1155, 1035, 750 cm^{-1}.

Conc. HCl (0.33 mL) was added to a solution of the diphenylation product (84.6 mg, 0.165 mmol) in MeOH (0.9 mL) and THF (3.5 mL) and the mixture was stirred at rt for 5.0 h. The mixture was poured into water and extracted twice with ether. The organic layers were dried and concentrated in vacuo. The residue was purified by silica gel flash chromatography (15-30% EtOAc in hexane) to give 59.8 mg (85%) of **19a**: mp 159-159.5 °C (recrystallized from hexane and benzene); $[\alpha]^{25}_D$ +272 (*c* 0.93, THF); ^{1}H NMR δ 1.8-2.05 (4H, m), 4.25-4.45 (4H, m), 5.58 (2H, br s), 6.80 (2H, d, *J* = 8.4 Hz), 7.30 (2H, d, *J* = 8.4 Hz), 7.32 (2H, m), 7.42 (4H, m), 7.53 (4H, m); ^{13}C NMR δ 26.0, 70.3, 108.5, 111.3, 122.8, 127.1, 128.3, 129.3, 130.7, 137.6, 150.7, 157.6; IR (KBr disk) 3520, 3400 (br), 1090, 1035, 765, 700 cm^{-1}; MS m/z (relative intensity) 424 (M$^+$, 100), 370 (8), 352 (8); HRMS: Calcd for $C_{28}H_{24}O_4$: 424.1675, found 424.1663. Anal. Calcd for $C_{28}H_{24}O_4$: C, 79.23; H, 5.70. Found: C, 78.79; H, 5.61.

(*S*)-4',4"-Pentylenedioxy-1,1':3',3":1",1'"-quaterphenyl-2',2"-diol (19b). Palladium(0) catalyzed coupling reaction of **18b** by a procedure similar to that described above gave (*S*)-4',4"-pentylenedioxy-2',2"-bis(methoxymethyl)-1,1':3',3":1",1'"-quaterphenyl (50%): ^{1}H NMR δ 1.60-1.70 (2H, m), 1.60-1.95 (4H, m), 2.73 (6H, s), 4.05-4.13 (2H, m), 4.39 (2H, d, *J* = 6.0 Hz), 4.48 (2H, d, *J* = 6.0 Hz), 4.38-4.47 (2H, m), 6.86 (2H, d, *J* = 8.4 Hz), 7.26-7.35 (4H, m), 7.40 (2H, t, *J* = 8.4 Hz), 7.41 (2H, d, *J* = 7.2 Hz), 7.64 (2H, d, *J* = 8.4 Hz), 7.63 (2H, d, *J* = 7.2 Hz); IR (KBr disk) 1600, 1580, 1385, 1380, 1310, 1295, 1205, 1160, 1100, 1080, 1060, 810, 750, 700 cm^{-1}; MS m/z (relative intensity) 526 (M$^+$, 18), 450 (80), 433(19), 314 (9), 128 (38), 69 (100); HRMS: Calcd for $C_{33}H_{34}O_6$: 526.2355, found 526.2351. The compound was hydrolyzed by a procedure similar to that described above to give **19b** (80%): mp 150-152 °C (recrystallized from benzene and hexane); $[\alpha]^{25}_D$ +241 (*c* 0.60, THF); ^{1}H NMR δ 1.60-1.70 (2H, m), 1.70-1.90 (4H, m), 4.11 (2H, ddd, *J* = 3.2, 6.2, and 10.8 Hz), 4.33 (2H, ddd, *J* = 3.6, 7.8, and 10.8 Hz), 5.45 (2H, s), 6.73 (2H, d, *J* = 8.4), 7.33 (2H, d, *J* = 8.4 Hz), 7.32 (2H, tt, *J* = 1.2 Hz and 7.2 Hz), 7.423 (2H, tt, *J* = 1.2 and 7.2 Hz), 7.56 (2H, dd, *J* = 1.2 and 7.2 Hz), 7.56 (2H, dd, *J* = .1.2 and 7.2 Hz); IR (KBr disk) 3510, 3400 (br), 1600, 1580, 1490, 1100, 805, 780, 760 cm^{-1}; MS m/z (relative intensity) 438 (M$^+$, 63), 341 (6), 325 (4), 167 (29), 149 (100), 73 (87); HRMS: Calcd for $C_{29}H_{26}O_4$: 438.1830, found 438.1836. Anal. Calcd for $C_{29}H_{26}O_4$: C, 79.43; H, 5.98. Found: C, 79.07; H, 6.12.

(*S*)-4',4"-Hexylenedioxy-1,1':3',3":1",1'"-quaterphenyl-2',2"-diol (19c). Palladium(0) catalyzed coupling reaction of **18c** by a procedure similar to that described above gave (*S*)-4',4"-hexylenedioxy-2',2"-bis(methoxymethyl)-1,1':3',3":1",1'"-quaterphenyl: ^{1}H NMR δ 1.45-1.6 (4H, m), 1.72 (4H, m), 2.74 (6H, s), 3.98-4.07 (2H, m), 4.2-4.3 (2H, m), 4.36 (2H, d, *J* = 5.6 Hz), 4.50 (2H, d, *J* = 5.6 Hz), 6.84 (2H, d, *J* = 8.5 Hz), 7.28 (2H, m), 7.31 (2H, d, *J* = 8.5 Hz), 7.40 (4H, m), 7.63 (4H, m). The compound was hydrolyzed by a procedure similar to that described above to give **19c** (70% overall yield): mp 140-143 °C (recrystallized from benzene and hexane); $[\alpha]^{25}_D$ +287 (*c* 0.53, THF); ^{1}H NMR δ 1.4-1.6 (4H, m), 1.72 (4H, m), 4.0-4.1 (2H, m), 4.22-4.53 (2H, m), 5.31 (2H, br s), 6.72 (2H, d, *J* = 8.6 Hz), 7.32 (2H, m), 7.36 (2H, d, *J* = 8.6 Hz), 7.42 (4H, m), 7.59 (4H, m); ^{13}C NMR δ 24.3, 25.8, 67.6, 104.8, 110.4, 121.3, 126.8, 128.3, 129.2, 131.1, 137.8, 151.4, 157.4; IR (KBr disk) 3510 (br), 1095, 1055, 780, 755, 695 cm^{-1}; MS m/z (relative intensity) 452 (M$^+$, 100), 370 (18), 352 (6); HRMS: Calcd for $C_{30}H_{28}O_4$: 452.1988, found 452.1993. Anal. Calcd for $C_{30}H_{28}O_4$: C, 79.62; H, 6.24. Found: C, 79.20; H, 6.32.

(*S*)-3,3'-Bis(*tert*-butyldimethylsilyl)-6,6'-butylenedioxy-2,2'-biphenyldiol (20a). To a solution of **17b** (66.5 mg, 0.155 mmol) and imidazole (31.6 mg, 0.464 mmol) in DMF (1.6 mL) at rt was

added *t*-butylchlorodimethylsilane (73.4 mg, 0.487 mmol). After being stirred for 24 h, the mixture was poured into water and extracted twice with ether. The dried organic layers were concentrated in vacuo. Purification of the residue by flash chromatography (20% ethyl acetate in hexane) gave 59.5 mg (58%) of (*S*)-3,3'-dibromo-6,6'-butylenedioxy-2,2'-bis(*tert*-butyldimethylsilyloxy)biphenyl: ^{1}H NMR δ -0.65 (6H, s), 0.92 (6H, s), 0.903 (18H, s), 1.7-1.95 (4H, m), 4.15-4.3 (2H, m), 6.56 (2H, d, *J* = 9.1 Hz), 7.42 (2H, d, *J* = 9.1 Hz).

To a solution of the bis(TBS) ether (15.5 mg, 0.024 mmol) in THF (0.4 mL) at 0 °C under Ar was added *t*-BuLi (1.7 M in pentane, 0.059 mL, 0.084 mmol). After being stirred for 1 h at rt, the mixture was poured into aq NH_4Cl and extracted twice with ether. The dried organic layers were concentrated in vacuo. The residue was purified by silica gel flash chromatography (30% EtOAc in hexane) to give 8.9 mg (74%) of **20a**: $[\alpha]^{25}_D$ + 139 (*c* 0.125, THF); ^{1}H NMR δ 0.28 (12H, s), 0.90 (18H, s), 1.5-1.9 (4H, m), 4.15-4.35 (4H, m), 5.14 (2H, s), 6.70 (2H, d, *J* = 8.8 Hz), 7.35 (2H, d, *J* = 8.8 Hz); ^{13}C NMR δ -4.6, -4.8, 17.6, 26.1, 26.9, 70.5, 108.2, 108.9, 115.9, 137.3, 158.6, 159.7; IR (KBr disk) 3340 (br), 1585, 1560, 1240, 1050, 835 cm-1; MS m/z (relative intensity) 500 (M^+, 5), 469 (5), 443 (32), 427 (100); HRMS: Calcd for $C_{28}H_{44}O_4Si_2$: 500.2778, found 500.2784.

(*S*)-6,6'-Pentylenedioxy-3,3'-bis(trimethylsilyl)-2,2'-biphenyldiol (20b). To a solution of **17a** (44.2 mg, 0.10 mmol) and imidazole (21.0 mg, 0.30 mmol) in CH_2Cl_2 (1.0 mL) at rt was added chlorotrimethylsilane (0.04 mL, 0.32 mmol). After being stirred for 24 h, the mixture was poured into water and extracted twice with ether. The dried organic layers were concentrated in vacuo. To a THF (1.5 mL) solution of the residue at 0 °C under Ar was added *t*-BuLi (1.7 M in pentane, 0.180 mL, 0.31 mmol). After being stirred for 1 h, the mixture was poured into aq NH_4Cl and extracted twice with ether. The dried organic layers were concentrated in vacuo. The residue was purified by silica gel flash chromatography (20% EtOAc in hexane) to give 24.6 mg (62%) of **20b**: $[\alpha]^{25}_D$ + 184 (*c* 0.780, THF); ^{1}H NMR δ 0.29 (18H, s), 1.50-1.62 (2H, m), 1.62-1.85 (4H, m), 4.05 (2H, ddd, *J* = 4.2, 5.2, and 10.8 Hz), 4.33 (2H, ddd, *J* = 4.2, 6.6, and 10.8 Hz), 5.13 (2H, s), 6.62 (2H, d, *J* = 8.4 Hz), 7.36 (2H, d, *J* = 8.4 Hz); IR (KBr disk) 3540, 3400 (br) 1585, 1560, 1240, 1190, 840, cm^{-1}; MS m/z (relative intensity) 430 (M^+, 70), 359 (16), 329 (10), 143 (34); HRMS: Calcd for $C_{23}H_{34}O_4Si_2$: 430.1955, found 430.2002.

Acknowledgment: This work was supported partially by a Grant-in-Aid from the Ministry of Education, Science, and Culture, Japan.

References and Notes

(1) For a review, see: (a) Kagan, H. B.; Riant, O. *Chem. Rev.* **1992**, *92*, 1007. (b) Narasaka, K. *Synthesis* **1991**, 1.

(2) (a) For leading references, see Bao, J.; Wulff, W. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **1993**, *115*, 3814 and references cited therein. (b) Kelly, T. R; Whiting, A.; Chandrakumar, N. S.; *J. Am. Chem. Soc.* **1986**, *108*, 3510. (c) Maruoka, K.; Itoh, T.; Shirasaka, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 310. (d) Maruoka, K.; Concepcion, A. B.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 3501. (e) Maruoka, K.; Murase, N.; Yamamoto, H. *J. Org. Chem.* **1993**, *58*, 2938.

(3) (a) Mikami, K.; Motoyama, Y.; Terada, M. *Inorg. Chim. Acta* **1994**, *222*, 71. (b) Harada, T.; Takeuchi, M.; Hatsuda, M.; Ueda, S.; Oku, A. *Tetrahedron: Asymmetry* **1996**, 7, 2479.

(4) For the asymmetric synthesis of axially chiral biaryls, see: (a) Review: Bringmann, G.; Walter, R. : Weirich, R. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 977. (b) Review: Bringmann, G.; Walter, R.; Weirich, R. *Methods of Organic Chemistry (Houben-Weyl)*; Helmchen, G.; Hoffmann, R. W. ; Mulzer, J.; Schumann, E., Ed.; Georg Thieme Verlag: Stuttgart, 1995; Vol. E21a, p 567. (c) Hattori, T.; Hotta, H.; Suzuki, T.; Miyano, S. *J. Chem. Soc., Chem. Commun.* **1991**, 1375. (d) Hattori, T.; Hotta, H.; Suzuki, T.; Miyano, S. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 613. (e) Miyano, S.; Koike, N.; Hattori, T.

Tetrahedron: Asymmetry **1994**, *5*, 1899. (f) Moorlag, H.; Meyers, A. I. *Tetrahedron Lett.* **1993**, *34*, 6989. (g) Moorlag, H.; Meyers, A. I. *Tetrahedron Lett.* **1993**, *34*, 6993. (h) Nelson, T. D.; Meyers, A. I. *J. Org. Chem.* **1994**, *59*, 2655. (i) Nelson, T. D.; Meyers, A. I. *Tetrahedron Lett.* **1994**, *35*, 3259. (j) Meyers, A. I.; McKennon, M. J. *Tetrahedron Lett.* **1995**, *36*, 5869. (k) Meyers, A. I.; Meir, A.; Rawson, D. J. *Tetrahedron Lett.* **1992**, *33*, 853. (l) Shindo, M.; Koga, K.; Tomioka, K. *J. Am. Chem. Soc.* **1992**, *114*, 8732. (m) Harada, T.; Yoshida, T.; Inoue, A.; Takeuchi, M.; Oku, A. *Synlett* **1995**, 283. (n) Uemura, M.; Kamikawa, K. *J. Chem. Soc., Chem. Commun.* **1994**, 2697. (o) Kamikawa, K.; Watanabe, T.; Uemura, M. *Synlett* **1995**, 1040. (p) Watanabe, T.; Kamikawa, K.; Uemura, M. *Tetrahedron Lett.* **1995**, *37*, 6695. (q) Osa, T.; Kashiwagi, Y. ;Yanagisawa, Y.; Bobbitt, J. M. *J. Chem. Soc., Chem. Commun.* **1994**, 2535. (r) Lipshutz, B. H.; Kayser, F.; Liu, Z.-P. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1842. (s) Lipshutz, B. H.; Li, Z.-P.; Kayser, F. *Tetrahedron Lett.* **1994**, *35*, 5567. (t) Lipshutz, B. H.; James, B.; Vance, S.; Carrico, I. *Tetrahedron Lett.* **1997**, *38*, 1997. (u) Rawal, V. H.; Florjancicn, A. S.; Singh, S. P. *Tetrahedron Lett.* **1994**, *35*, 8985. (v) Hayashi, T.; Niizuma, S.; Kamikawa, T.; Suzuki, N.; Uozumi, Y. *J. Am. Chem. Soc.* **1995**, *117*, 9101. (w) Itoh, T.; Chika, J.; Shirakami, S.; Ito, H.; Yoshida, T.; Kubo, Y.; Uenishi, J. *J. Org. Chem.* **1996**, *61*, 3700.

(5) (a) Ward, R. S. *Chem. Soc. Rev.* **1990**, *19*, 1. (b) Harada, T.; Oku, A. *Synlett* **1994**, 95. (c) Gais, H. -J. *Methods of Organic Chemistry (Houben-Weyl)*; Helmchen, G.; Hoffmann, R. W. ; Mulzer, J.; Schumann, E., Ed.; Georg Thieme Verlag: Stuttgart, 1995; Vol. E21a, p 589. (d) Vedejs, E.; Daugulis, O.; Diver, S. T. *J. Org. Chem.* **1996**, *61*, 430 and references cited therein.

(6) Preliminary communication of this work has appeared: Harada, T.; Ueda, S.; Yoshida, T.; Inoue, A, Takeuchi, M.; Ogawa, N.; Oku, A.; Shiro, M. *J. Org. Chem.* **1994**, *59*, 7575.

(7) (a) Harada, T.; Hayashiya, T.; Wada, I.; Iwa-ake, N.; Oku, A. *J. Am. Chem. Soc.* **1987**, *109*, 527. (b) Harada, T.; Sakamoto, K.; Ikemura, Y.; Oku, A. *Tetrahedron Lett.* **1988**, *29*, 3097. (c) Harada, T.; Wada, I.; Oku, A. *J. Org. Chem.* **1989**, *54*, 2599.

(8) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1357.

(9) Harada, T.; Tanaka, S. Oku, A. *Tetrahedron* **1992**, *48*, 8621.

(10) The authors have deposited atomic coordinates for **5a** and **6c** with the Cambridge Crystallographic Data Centre.

(11) Harada, T.; Kurokawa, H.; Kagamihara, Y. Tanaka, S.; Inoue, A.; Oku, A. *J. Org. Chem.* **1992**, *57*, 1412.

(12) Allinger, N. L.; Yuh, Y. H.; Lii, J.-H. *J. Am. Chem. Soc.* **1989**, *111*, 8551.

(13) Barton, D. H. R.; Finet, J.-P.; Khamsi, J.; Pichon, C. *Tetrahedron Lett.* **1986**, *27*, 3619.

(14) Simpson, J. E.; Daub, G. H.; Hayes, F. N. *J. Org. Chem.* **1973**, *38*, 4428.

(15) The mechanism of racemization is still unclear. Although acid catalyzed racemization of BINOL at 100 °C has been reported previously,[16] a separate experiment showed that **13a** did not racemize under acidic conditions at rt.

(16) Kyba, E. O.; Gokel, G. W.; de Jong, F.; Koga, K.; Sousa, R. L.; Siegel, M. G.; Kaplan, R. J.; Sogah, G. D. Y.; Cram, D. J. *J. Org. Chem.*, **1977**, *42*, 4173.

(17) Cox, P. J.; Wang, W.; Snieckus, V. *Tetrahedron Lett.* **1992**, *33*, 2253.

(18) Snieckus, V. *Chem. Rev.* **1990**, 90, 879.

(19) Pearson, D. E.; Wysong, R. D.; Breder, C. V. *J. Org. Chem.* **1967**, *32*, 2359.

(20) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.

(21) Maruoka, K.; Itoh, T.; Araki, Y.; Shirasaka, T.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 2975.

(22) Lindsten, G.; Wennerstorm, O.; Isaksson, R. *J. Org. Chem.* **1987**, *52*, 547.

(23) Delogu, G.; Fabbri, D. *Tetrahedron: Asymmetry* **1997**, *8*, 759.

(*Received in Japan* 6 *August* 1997; *accepted* 17 *September* 1997)