A General Method for the Preparation of Enantiomerically Pure 2-Substituted Glycerol Derivatives by Utilizing *l*-Menthone as a Chiral Template

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A general method for preparation of a variety of enantiomerically pure 2-substituted glycerol derivatives **1** was developed by utilizing *l*-menthone as a chiral template. Spiroacetals **6** derived formally from 2-substituted 2-(trimethylsiloxy)-1,3-propanediols and *l*-menthone were prepared with high stereoselectivity (>95% de) either by Grignard reactions of oxospiroacetal **4** or by epoxidation of methylenespiroacetal **5** followed by ring opening with higher order cuprates. Highly stereoselective ring-cleavage reaction of **6** with acetophenone enol trimethylsilyl ether and $TiCl_4$ followed by protection of the resulting diol **10** and subsequent removal of the chiral auxiliary gave 2-substituted glycerol derivatives of high enantiomeric purity.

Enantiomerically pure derivatives of glycerol and their 2-substituted homologues are versatile chiral building blocks which can be incorporated into target structures possessing secondary or tertiary asymmetric alcohol carbons.[1] The utility of these compounds has been demonstrated by the frequent use of 1,2-acetonide derivatives **1a** (R = H)[2] and **1b** (R = Me)[3] in natural product syntheses. Homologues of **1a,b** with an arbitrary substituent R at the 2 position should be useful as tailor-made chiral building blocks for specific target molecules. We wish to report here a general method for the preparation of enantiomerically pure 2-substituted glycerol derivative **1** by utilizing *l*-menthone as a chiral template.

Results and Discussion

Based on our recent finding that titanium tetrachloride-promoted ring cleavage of a variety of spiroacetals derived from *l*-menthone proceeds in a highly stereoselective manner,[4] we envisaged spiroacetal **3** as an ideal precursor of chiral acetonide **1**. Thus, **1** might be obtained by selective ring cleavage of spiroacetal **3**, followed by protection of the resulting diol **2** and subsequent removal of the chiral auxiliary (Scheme I). Two approaches for stereoselective preparation of key intermediate **3** were examined: (i) Grignard reactions of oxospiroacetal **4** and (ii) epoxidation of methylenespiroacetal **5** followed by ring opening.

Bis-silylation of commercially available 2-methylene-1,3-propanediol followed by reaction with *l*-menthone in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf)[5] gave methylenespiroacetal **5** in high yield.[4e]

Scheme I

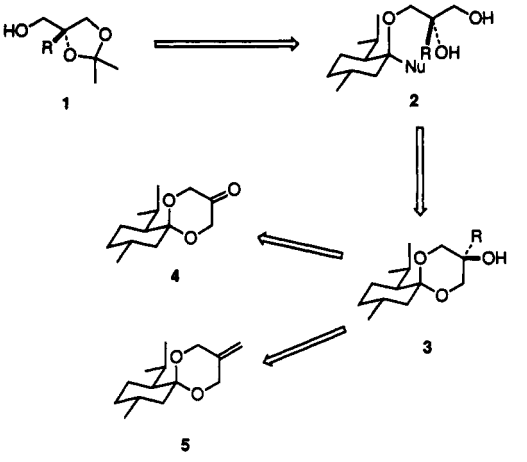


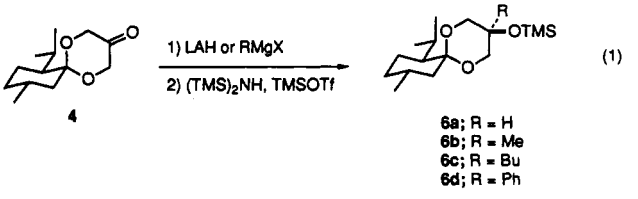
Table I. Stereoselective Preparation of Trimethylsiloxy Spiroacetals 6a–d

	preparation of 3a–d				trimethylsilation	
entry	reagent	product	yield (%)	stereoselectivity	product	yield (%)
1	$LiAlH_4$	**3a**	78	7.7:1	**6a**	83
2	DIBALH	**3a**		16:1	**6a**	69[a]
3	MeMgI	**3b**	72	>25:1	**6b**	94
4	BuMgCl	**3c**	73[b]	>25:1	**6c**	84
5	PhMgBr	**3d**	78	>25:1	**6d**	92

[a] Overall yield from **4**. [b] A small amount (8%) of the reduction product **3a** was also obtained.

Oxospiroacetal **4** was prepared by ozonolysis of **5** in 94% yield.

Oxospiroacetal **4** underwent highly diastereofacial Grignard addition reactions to give exclusively equatorial alcohols **3b–d** which were isolated as trimethylsilyl ethers **6b–d** after treatment with hexamethyldisilazane (eq 1, entries 3–5 in Table I). While $LiAlH_4$ reduction of **4**



(1)

proceeded with somewhat lower selectivity to give a mixture of **3a** (R = H) and the alternate diastereomer *epi*-**3a**

(1) (a) Scott, J. W. In *Asymmetric Synthesis*; Morrison, J. D., Scott, J. W., Eds.; Academic Press: New York, 1984; Vol. 4, Chapter 1. (b) Hanessian, S. *Total Synthesis of Natural Products: The 'Chiron' Approach*; Pergamon Press: Oxford, 1983.

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

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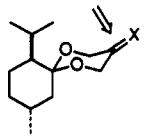
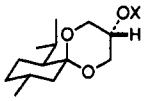


4; X = O
5; X = CH_2

	axial : equatorial attack
RMgX	>25:1
DIBALH	16:1
$LiAlH_4$	7.7:1
NBS	>25:1
9-BBN	14:1
MCPBA	2.3:1

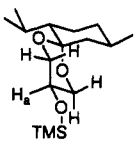
Figure 1.

(entry 1), higher selectivity (16:1) was observed when DIBALH was employed in the reduction (entry 2).

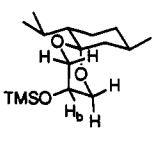


epi-3a; R = H
epi-6a; R = TMS

Spiroacetals derived from *l*-menthone and 1,3-diols adopt a rigid double chair conformation.[4c] The stereochemistry of **6a** and *epi*-**6a** obtained by hydride reduction of **4** and subsequent silylation was unambiguously determined by analysis of the vicinal coupling constants between the protons attached to the conformationally fixed 1,3-dioxane ring: The axial ring proton H_a in **6a** (see conformational formula **6A**) appears as a broad triplet ($J_{ax,ax}$ = 8.9 Hz) at δ 3.53 while the equatorial ring proton H_b in *epi*-**6a** (*epi*-**6A**) resonates as a broad triplet ($J_{eq,ax}$ = 2.0 Hz) at δ 3.00. The structures of **6b–d** are assigned tentatively by assuming similar diastereofacial selectivity in the Grignard reactions.

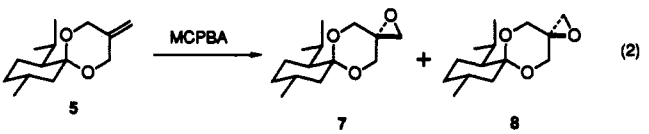


6A

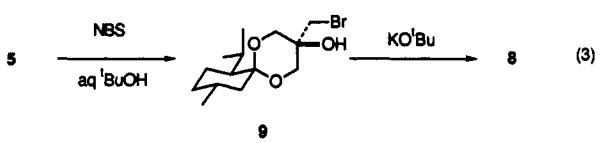


epi-**6A**

Epoxidation of methylene spiroacetal **5** with *m*-CPBA proceeded with moderate diastereofacial selectivity to give a 2:1 mixture of α-epoxide **7** (53%) and β-epoxide **8** (27%) (eq 2). In contrast, reaction of **5** with *N*-bromosuccinimide



(2)



(3)

9

(NBS) in aqueous *t*-BuOH afforded bromohydrin **9** without formation of the diastereomer and the successive treatment of **9** with *t*-BuOK in *t*-BuOH afforded β-epoxide **8** in 60% overall yield from **5** (eq 3). It should be noted that preferential axial attack on **5** was observed in reactions with both *m*-CPBA and NBS.

Reaction of epoxyspiroacetal **8** with higher order cuprate $(Ph)_2Cu(CN)Li_2$[6] proceeded cleanly to give equatorial alcohol **3e** (R = $PhCH_2$) which was isolated as trimethylsilyl ether **6e** in 68% overall yield (eq 4). Similarly, reaction

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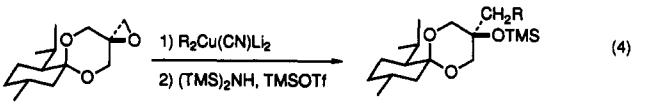
Table II. Conversion of Spiroacetals 6 into Chiral Glycerol Derivatives 1

	ring-cleavage reaction		removal of chiral auxiliary		
entry	product	yield (%)	product	yield (%)	$[\alpha]^{25}_D$ (solvent)
1	**10a**	85			
2	**10b**	87	**1b**	63	+5.35° (CH_2Cl_2)[a]
3	**10c**	75	**1c**	81	+3.20° ($CHCl_3$)
4	**10d**	84	**1d**	76	+4.54° ($CHCl_3$)
5	**10e**	86	**1e**	90	−6.54° ($CHCl_3$)
6[b]	**10f**		**1f**	58[c]	−1.04° ($CHCl_3$)

[a] Lit.[3a] $[\alpha]^{25}_D$ +5.25° (CH_2Cl_2). [b] Crude mixture of the ring-cleavage product **10f** was converted into **1f** without purification. [c] Overall yield from **10f**.

of **8** with $(CH_2{=}CH)_2Cu(CN)Li_2$ followed by trimethylsilation of the resulting alcohol gave **6f** (R = $CH_2{=}CH$) in 70% yield.

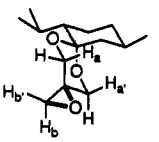


(4)

8

6e; R = Ph
6f; R = $CH{=}CH_2$

In the ^1H NMR spectrum of epoxyspiroacetal **8**, the signals from the axial protons H_a and $H_{a'}$ (see conformational formula **8A**) appear at δ 3.77 (dd, J = 0.6 and 12.0 Hz) and 3.97 (dd, J = 0.9 and 11.4 Hz). The small coupling constants can be attributed to a long-range W-type coupling[7] between H_a ($H_{a'}$) and the oxirane ring proton H_b ($H_{b'}$). Molecular models indicate that such W-type coupling is possible only if the epoxide possesses the stereochemistry shown in **8A**.[8] Indeed, in the ^1H NMR spectrum of diastereomer **7**, the axial protons on the 1,3-dioxane ring give rise to simple doublets (J = 12.6 and 12.6 Hz) at δ 3.83 and 4.09. The stereochemical assignments were further confirmed by $LiAlH_4$ reduction of **8** to give **3b** (R = Me, 76% yield) which was identical with the compound obtained by the reaction of oxospiroacetal **4** with MeMgI.

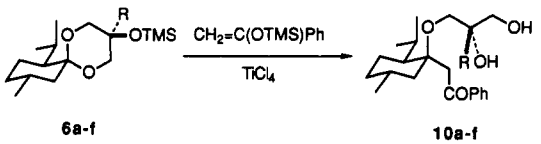


8A

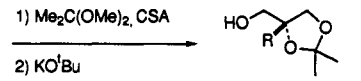
As we anticipated, ring-cleavage reaction of **6a–f** with acetophenone enol trimethylsilyl ether and titanium tetrachloride proceeded in a highly stereoselective manner at the equatorial carbon–oxygen bond of the substrate to give exclusively **10a–f** (eq 5). Protection of the vicinal diols of **10b–f** as acetonides ($Me_2C(OMe)_2$, camphorsulfonic acid (CSA)) followed by treatment with *t*-BuOK in *t*-BuOH[4] gave chiral derivatives **1b–f** in high yields (Table II).

Since ring-cleavage products **10** were diastereomerically pure according to 200- or 300-MHz ^1H NMR analysis, chiral acetonides **1b–f** obtained by the present method should be of high enantiomeric purity. Indeed, **1b** prepared by the present method showed a reasonable specific rotation (entry 2). Moreover, the enantiomeric excess of **1c** was determined to be >95% by converting it into the

(7) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; Pergamon Press: New York, 1969; pp 222, 234.
(8) Piers, E.; Gavai, A. V. *J. Org. Chem.* **1990**, *55*, 2380.



6a-f 10a-f (5)



1b; R = Me
1c; R = Bu
1d; R = Ph
1e; R = CH_2Ph
1f; R = $CH_2CH{=}CH_2$

corresponding (−)-camphanyl ester.[3c] The absolute configuration of (*R*)-**1b** was determined by optical rotation measurement.[3a,c] The absolute configurations of **1c–f** are tentatively assigned by assuming similar selectivities in the reaction sequences.

The high levels of stereoselectivity observed in the reaction of oxospiroacetal **4** and methylenespiroacetal **5** are worthy of note. In this connection, we previously reported that hydroboration of **5** with 9-BBN also proceeded in a diastereofacial manner (14:1) from the axial direction.[4e] Preferential attack from the axial direction on the conformationally fixed 1,3-dioxane rings was generally observed both in the nucleophilic addition to **4** and in the electrophilic addition to **5** (Figure 1).

Houk and Wu reported that 2-phenyl-1,3-diox-5-one is attacked by $LiAlH_4$ and MeMgI with high axial selectivity.[9] The selectivity was rationalized by them in terms of unfavorable torsional strain in the transition state for the alternative equatorial attack.[9] The explanation is equally adaptable to the present nucleophilic additions to spiroacetal **4**. Moreover, the observed axial attack of the electrophilic reagents on methylenespiroacetal **5** may also be rationalized in terms of similar unfavorable torsional strain in the analogous staggered transition state[10] for equatorial attack.

Experimental Section

GC analyses were performed by using PEG-20M (20 m) and OV-1 (30 m) capillary columns. Flash chromatography was performed by using silica gel (Wakogel C-300) as an adsorbent. All extracts were dried over Na_2SO_4 unless otherwise specified. *l*-Menthone was purchased from Norse Laboratories Inc. Ether and THF were distilled from sodium/benzophenone ketyl. CH_2Cl_2, DMF, and *t*-BuOH were distilled from CaH_2. Methylenespiroacetal **5** was prepared as described previously in 87% yield.[4e] *J* values are given in Hz.

(7*S*,10*R*)-10-Methyl-7-(1-methylethyl)-1,5-dioxaspiro[5.5]undecan-3-one (4). O_3 was introduced into a stirred solution of **5** (3.0 g, 13.4 mmol) in 270 mL of MeOH at −80 °C until the blue color persisted for more than 2 min. The excess O_3 was removed by allowing O_2 to bubble through the solution at −80 °C. Then, 5.0 g of dimethyl sulfide was added dropwise and the mixture was allowed to stir and to warm to 25 °C over 3 h. After concentration of the mixture in vacuo, the residue was purified by flash chromatography (2–10% ether in hexane) to give 2.84 g (94% yield) of **4**. Attempted purification of **4** by distillation (124 °C (23 mmHg), Kugelrohr) caused slight decomposition to menthone. **4**: $[\alpha]^{20}_D$ −7.6 (*c* 1.05, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (1 H, m), 0.91 (3 H, d, *J* = 7.0), 0.92 (3 H, d, *J* = 6.6), 0.93 (3 H, d, *J* = 7.0), 1.01 (1 H, t, *J* = 12.9), 1.36–1.48 (2 H, m), 1.50–1.65 (2 H, m), 1.76 (1 H, m), 2.22 (1 H, ddd, *J* = 2.0, 3.4, 13.7), 2.37 (1 H, d sept, *J* = 1.2, 7.1), 4.23 (1 H, d, *J* = 18.2), 4.283 (1 H, d, *J* = 18.2), 4.353 (2 H, s); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 18.56, 22.02, 22.31, 23.67, 24.47, 29.57, 34.53, 40.12, 51.21, 67.81, 68.58, 101.38, 207.41; IR (liquid film) 1740 (s), 1120 (s) cm^{-1}; MS *m/z* (relative intensity) 226 (M^+, 13), 211 (10), 169 (34), 141 (100); HRMS calcd for $C_{13}H_{22}O_3$ 226.1570, found 226.1578.

(3*S*,7*S*,10*R*)-3,10-Dimethyl-7-(1-methylethyl)-3-(trimethylsiloxy)-1,5-dioxaspiro[5.5]undecane (6b) (General Procedure). To a solution of MeMgI (8.85 mmol) in ether (34 mL) was added an ether solution (4 mL) of **4** (401 mg, 1.77 mmol) at −80 °C, and the mixture was stirred for 1 h at 0 °C before it was quenched by the addition of aq NH_4Cl. After extraction with AcOEt, the organic layers were washed with aq $NaHCO_3$, dried, and concentrated to give the crude product which was purified by flash chromatography (10–15% AcOEt in hexane) to give 308 mg (72% yield) of the hydroxyspiroacetal **3b**; ^1H NMR (200 MHz, C_6D_6) δ 0.60 (1 H, t, *J* = 12.8), 0.80 (1 H, m), 0.82 (3 H, d, *J* = 6.4), 1.04 (3 H, d, *J* = 7.2), 1.15 (3 H, d, *J* = 7.2), 1.30 (3 H, s), 1.27–1.75 (6 H, m), 2.70 (1 H, br d, *J* = ca. 13), 2.79 (1 H, br sept, *J* = 7.2), 3.30 (1 H, dd, *J* = 2.4, 10.4), 3.36 (1 H, dd, *J* = 2.4, 10.4), 3.49 (1 H, d, *J* = 10.4), 3.72 (1 H, d, *J* = 10.4).

To a solution of **3b** (308 mg, 1.27 mmol) and hexamethyldisilazane (0.27 mL, 1.3 mmol) in THF (1.3 mL) was added 0.025 mL (0.13 mmol) of TMSOTf at 25 °C, and the mixture was stirred for 5 h. After dilution with hexane, the reaction mixture was washed twice with ice-cooled water, dried, and concentrated in vacuo. The crude product was purified by flash chromatography (1% ethyl acetate/hexane) to give 375 mg (94% yield) of **6b**: ^1H NMR (200 MHz, C_6D_6) δ 0.10 (9 H, s), 0.64 (1 H, t, *J* = 12.8), 0.81 (3 H, d, *J* = 6.4), 0.82 (1 H, m), 1.08 (3 H, d, *J* = 7.2), 1.20 (3 H, d, *J* = 7.2), 1.35–1.74 (8 H, m, including s (3 H) at 1.54), 2.76 (1 H, ddd, *J* = 1.6, 3.0, 13.0), 2.86 (1 H, d sept, *J* = 1.6, 7.2), 3.50 (1 H, dd, *J* = 2.4, 10.4), 3.56 (1 H, dd, *J* = 2.4, 10.4), 3.76 (1 H, d, *J* = 10.4), 3.98 (1 H, d, *J* = 10.4); IR (liquid film) 1160 (s) 1110 (s) 840 (s) cm^{-1}; MS *m/z* (relative intensity) 314 (M^+, 19), 299 (16), 229 (33), 143 (100); HRMS calcd for $C_{17}H_{34}SiO_3$ 314.2278, found 314.2270.

(3*S*,7*S*,10*R*)-3-Butyl-10-methyl-7-(1-methylethyl)-3-(trimethylsiloxy)-1,5-dioxaspiro[5.5]undecane (6c). By a similar procedure, **6c** was prepared from **4** via **3c**. **3c**: ^1H NMR (200 MHz, C_6D_6) δ 0.64 (1 H, d, *J* = 11.2), 0.81 (1 H, m), 0.83 (3 H, d, *J* = 6.4), 0.93 (3 H, t, *J* = 6.4), 1.04 (3 H, d, *J* = 7.2), 1.16 (3 H, d, *J* = 7.2), 1.22–1.93 (12 H, m), 2.70 (1 H, ddd, *J* = 2.0, 4.4, 14.0), 2.81 (1 H, d sept, *J* = 1.6, 7.2), 3.43 (1 H, d, *J* = 10.8), 3.51 (1 H, dd, *J* = 2.4, 10.8), 3.53 (1 H, dd, 2.4, 10.8), 3.69 (1 H, d, *J* = 10.8); IR (liquid film) 3400 (br), 1130 (s) cm^{-1}. **6c**: ^1H NMR (200 MHz, C_6D_6) δ 0.07 (9 H, s), 0.67 (1 H, t, *J* = 13.0), 0.80 (1 H, m), 0.84 (3 H, d, *J* = 7.2), 0.96 (3 H, t, *J* = 7.2), 1.05 (3 H, d, *J* = 7.2), 1.19 (3 H, d, *J* = 7.2), 1.35–1.71 (9 H, m), 1.83–1.95 (1 H, m), 1.98–2.09 (1 H, m), 2.75–2.91 (2 H, m), 3.69 (3 H, m), 3.95 (1 H, d, *J* = 10.2); IR (liquid film) 1155 (s), 1115 (s), 1100 (s), 875 (s) 840 (s) cm^{-1}; MS *m/z* (relative intensity) 356 (M^+, 20), 341 (13), 299 (22), 130 (100); HRMS calcd for $C_{20}H_{40}SiO_3$ 356.2748, found 356.2730.

(3*S*,7*S*,10*R*)-10-Methyl-7-(1-methylethyl)-3-phenyl-3-(trimethylsiloxy)-1,5-dioxaspiro[5.5]undecane (6d). By a similar procedure, **6d** was prepared from **4** via **3d**. **3d**: ^1H NMR (200 MHz, C_6D_6) δ 0.62 (1 H, t, *J* = 12.8), 0.76 (1 H, m), 0.80 (3 H, d, *J* = 6.8), 0.87 (3 H, d, *J* = 7.0), 0.89 (3 H, d, *J* = 7.2), 1.16–1.70 (6 H, m), 2.48 (1 H, d sept, *J* = 1.6, 7.2), 2.72 (1 H, ddd, *J* = 1.6, 3.1, 13.6), 3.80 (1 H, d, *J* = 11.2), 3.92 (1 H, dd, *J* = 1.6, 11.2), 4.00 (2 H, m), 7.01–7.30 (3 H, m), 7.60–7.74 (2 H, m). **6d**: ^1H NMR (200 MHz, C_6D_6) δ −0.16 (9 H, s), 0.64 (1 H, dd, *J* = 12.8, 13.6), 0.65 (10 H, m, including d (3 H, *J* = 7.6) at 0.76, d (3 H, *J* = 6.4) at 0.78, and d (3 H, *J* = 6.4) at 0.84), 1.10–1.68 (5 H, m), 2.37 (1 H, d sept, *J* = 1.6, 7.2), 2.82 (1 H, ddd, *J* = 1.6, 3.2, 13.6), 3.97 (1 H, d, *J* = 11.2), 4.15 (1 H, dd, *J* = 2.4, 11.2), 4.19 (1 H, d, *J* = 11.2), 4.27 (1 H, dd, *J* = 2.4, 11.2), 7.01–7.28 (3 H, m), 7.60–7.74 (2 H, m); IR (liquid film) 1110 (s), 880 (s) 840 (s) cm^{-1}; MS *m/z* (relative intensity 376 (M^+, 12), 205 (44), 192 (100); HRMS calcd for $C_{22}H_{36}SiO_3$ 376.2435, found 376.2427.

(3*S*,7*S*,10*R*)-10-Methyl-7-(1-methylethyl)-3-(trimethylsiloxy)-1,5-dioxaspiro[5.5]undecane (6a) and (3*R*,7*S*,10*R*)-10-Methyl-7-(1-methylethyl)-3-(trimethylsiloxy)-1,5-dioxaspiro[5.5]undecane (*epi*-6a). To a solution of **4** (104.1 mg, 0.460 mmol) in 2.8 mL of THF was added 35 mg (0.92 mmol) of $LiAlH_4$ at 0 °C, and the mixture was stirred for 0.5 h

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(10) Houk, K. N.; Rondan, N. G.; Wu, Y-D.; Metz, J. T.; Paddon-Row, M. N. *Tetrahedron* **1984**, *40*, 2257.

at 25 °C before it was quenched with aq NH_4Cl at 0 °C. The mixture was extracted twice with AcOEt. The organic layers were dried, concentrated in vacuo, and purified by flash chromatography (5–10% AcOEt in hexane) to give a 7.7:1 mixture of **3a** and *epi*-**3a** (82 mg, 78% yield). **3a**: ^1H NMR (200 MHz, C_6D_6) δ 0.65 (1 H, t, J = 12.8), 0.84 (1 H, m), 0.86 (3 H, d, J = 6.4), 1.09 (3 H, d, J = 7.2), 1.17 (3 H, d, J = 7.2), 1.30–1.74 (6 H, m), 2.58–2.88 (2 H, m), 3.52–3.83 (5 H, m); IR (liquid film) 3370 (br), 1090 (s) cm^{-1}.

The mixture of **3a** and *epi*-**3a** (69 mg, 0.102 mmol) was converted into the trimethylsilyl ethers by a procedure similar to that described for the preparation of **6b**. Flash chromatography (1% AcOEt in hexane) of the crude products gave in the order of elution 66.4 mg (83% yield) of **6a** and 12.7 mg (13% yield) of *epi*-**6a**. **6a**: ^1H NMR (300 MHz, C_6D_6) δ −0.10 (9 H, s), 0.59 (1 H, t, J = 12.6), 0.71 (1 H, m), 0.75 (3 H, d, J = 6.6), 1.02 (3 H, d, J = 7.1), 1.13 (3 H, d, J = 7.0), 1.32–1.64 (5 H, m), 2.67 (1 H, ddd, J = 1.8, 3.4, 13.4), 2.77 (1 H, d sept, J = 2.0, 7.0), 3.53 (1 H, br t, J = 8.9), 3.72–3.86 (4 H, m); IR (liquid film) 1110 (s), 880 (s), 840 (s) cm^{-1}; MS m/z (relative intensity) 300 (M^+, 16), 285 (29), 243 (46), 215 (73), 129 (100); HRMS calcd for $C_{16}H_{32}SiO_3$ 300.2122, found 300.2124. *epi*-**6a**: ^1H NMR (300 MHz, C_6D_6) δ 0.036 (9 H, s), 0.64 (1 H, t, J = 13.2), 0.87 (1 H, m), 0.84 (3 H, d, J = 6.6), 1.21 (3 H, d, J = 7.1), 1.21 (3 H, d, J = 6.9), 1.33 (1 H, ddd, J = 2.1, 3.6, 12.3), 1.42–1.68 (4 H, m), 2.42 (1 H, ddd, J = 1.8, 3.3, 13.4), 2.89 (1 H, d sept, J = 2.3, 7.1), 3.00 (1 H, br t, J = 2.0), 3.42–3.53 (2 H, m), 3.61 (1 H, t, d, J = 2.2, 12.1), 3.74 (1 H, d, J = 2.2, 12.1); MS m/z (relative intensity) 300 (M^+, 16), 285 (28), 243 (42), 215 (82), 129 (100); HRMS calcd for $C_{16}H_{32}SiO_3$ 200.2122, found 300.2122.

To a solution of 101.3 mg (0.448 mmol) of **4** in THF (4.5 mL) was added at −80 °C 0.60 mL (0.90 mol) of DIBALH (1.5 M in toluene), and the mixture was stirred for 3 h while warming to rt. After addition of water (5 mL), the mixture was extracted twice with AcOEt. The organic layers were washed successively with aq NH_4Cl and aq $NaHCO_3$, dried, and concentrated in vacuo. The residue was purified by flash chromatography (1% AcOEt in hexane) to give a mixture of **3a** and *epi*-**3a** (0.371 mg, 83% yield) whose ratio was determined to be 15.6:1 by capillary GC analysis of the trimethylsilyl ether derivatives prepared by the procedure described above.

Epoxyspiroacetals 7 and 8. To a solution of **5** (112 mg, 0.50 mmol) in $CHCl_3$ (14 mL) was added 216 mg (1.25 mmol) of *m*-CPBA at 0 °C and the mixture was stirred for 19 h at 25 °C. The mixture was poured into aq $NaHCO_3$ and extracted twice with AcOEt. The organic layers were washed with aq $NaHSO_3$, dried, and concentrated in vacuo. The crude product was purified by flash chromatography (5–10% AcOEt in hexane) to give, in the order of elution, 32.0 mg (27% yield) of epoxide **8** and 63 mg (53% yield) of epoxide **7**. **8**: $[\alpha]^{20}_D$ −28.2 (*c* 1.10, $CHCl_3$); ^1H NMR (300 MHz, C_6D_6) δ 0.64 (1 H, t, J = 12.6), 0.74 (1 H, m), 0.76 (3 H, d, J = 6.6), 1.01 (3 H, d, J = 7.1), 1.20 (3 H, d, J = 7.0), 1.30–1.62 (5 H, m), 2.16 (2 H, m), 2.52 (1 H, ddd, J = 1.9, 3.4, 13.6), 2.68 (1 H, d sept, J = 2.1, 7.0), 3.20 (1 H, dd, J = 1.3, 11.8), 3.28 (1 H, dd, J = 1.3, 11.7), 3.77 (1 H, dd, J = 0.6, 12.0), 3.97 (1 H, dd, J = 0.9, 11.4); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 18.84, 22.18, 22.38, 23.72, 24.57, 29.26, 34.76, 37.52, 50.96, 52.78, 55.11, 62.97, 63.39, 100.90; IR (KBr disk) 1115 (s), 1105 (s), 940 (s), 855 (s), 780 (s) cm^{-1}; MS m/z (relative intensity) 240 (M^+, 10), 225 (24), 183 (42), 155 (100); HRMS calcd for $C_{14}H_{24}O_3$ 240.1726, found 240.1730. **7**: $[\alpha]^{20}_D$ −31.2 (*c* 1.00, $CHCl_3$); ^1H NMR (300 MHz, C_6D_6) δ 0.76 (1 H, dd, J = 12.7, 13.1), 0.87 (1 H, m), 0.95 (3 H, d, J = 7.4), 1.14 (3 H, d, J = 7.1), 1.27 (3 H, d, J = 6.9), 1.44–1.61 (5 H, m), 2.00 (2 H, s), 2.52 (1 H, ddd, J = 1.8, 3.5, 13.5), 2.97 (1 H, d sept, J = 2.2, 7.2), 3.17 (1 H, dd, J = 2.4, 12.6), 3.25 (1 H, dd, J = 2.4, 12.6), 3.83 (1 H, d, J = 12.6), 4.09 (1 H, d, J = 12.6); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 18.92, 22.22, 22.24, 23.68, 24.59, 29.12, 34.82, 36.59, 47.12, 51.08, 53.84, 63.74, 64.02, 100.45; IR (liquid film) 1110 (s), 925 (s), 845 (s), 750 (s) cm^{-1}; MS m/z (relative intensity) 240 (M^+, 10), 225 (21), 183 (48), 155 (100); HRMS calcd for $C_{14}H_{24}O_3$ 240.1726, found 240.1714.

Stereoselective Preparation of Epoxyspiroacetal 8 via Bromohydrin 9. To a solution of **5** (324 mg, 1.0 mmol) in *t*-BuOH (3 mL) and pH 7.5 phosphate buffer (2.4 mL) was added 320 mg (1.8 mmol) of NBS at 25 °C, and the mixture was stirred for 5 h at the same temperature. The mixture was poured into aq $NaHCO_3$ and extracted twice with AcOEt. The organic layers were washed successively with aq $NaHSO_3$ and aq $NaHCO_3$, dried, and concentrated in vacuo. The crude product was purified by flash chromatography (5–10% AcOEt in hexane) to give 210 mg (65% yield) of bromohydrin **9**: $[\alpha]^{20}_D$ −25.4 (*c* 0.95, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.73 (1 H, t, J = 14.2), 0.87 (1 H, m), 0.90 (3 H, d, J = 6.5), 0.92 (3 H, d, J = 7.0), 0.91 (3 H, d, J = 6.5) 1.27 (1 H, m), 1.38–1.59 (4 H, m), 1.73 (1 H, m), 2.54 (1 H, ddd, J = 1.6, 3.2, 13.6), 2.68 (1 H, d sept, J = 1.6, 7.0), 3.72 (2 H, s), 3.86–4.00 (3 H, m), 4.14 (1 H, d, J = 13.4); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 18.42, 21.70, 22.15, 23.71, 23.98, 29.01, 34.71, 35.77, 50.75, 64.10, 64.41 (2C), 65.37, 101.22; IR (liquid film) 3450 (br), 1165 (s), 1145 (s), 1115 (s), 1090 (s) cm^{-1}; MS m/z (relative intensity) 322, 320 (M^+, 8), 305, 307 (20), 265, 263 (35), 69 (100). HRMS calcd for $C_{14}H_{25}O_3{}^{79}Br$ 320.0988, found 320.0985, calcd for $C_{14}H_{25}O_3{}^{81}Br$ 322.0968, found 322.0978.

To a solution of *t*-BuOK (96 mg, 0.86 mmol) in *t*-BuOH (4.6 mL) was added 184 mg (0.573 mmol) of **9** at 25 °C, and the mixture was stirred for 0.5 h before it was quenched by the addition of water. After extraction twice with water, the organic layers were washed with brine, dried, and concentrated in vacuo. The crude product was purified by flash chromatography (5–10% AcOEt in hexane) to give 127 mg (92% yield) of **8**.

(3*S*,7*S*,10*R*)-10-Methyl-7-(1-methylethyl)-3-(phenylmethyl)-3-(trimethylsiloxy)-1,5-dioxaspiro[5.5]undecane (6e). To a suspension of CuCN (100 mg, 1.1 mmol) in THF (2 mL) was added phenyllithium (1.8 M in cyclohexane and ether) (1.1 mL) at −85 °C, and the mixture was allowed to warm to −25 °C in 2.5 h before it was recooled to −85 °C. To the resulting brown solution was added a THF (1 mL) solution of epoxide **8** (102 mg, 0.424 mmol). The mixture was gradually warmed to 25 °C and stirred further for 2 h before the reaction was quenched by the addition of brine and diluted with ether. After filtration through a pad of Celite, the filtrate was washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The residue was purified by flash chromatography (5–20% AcOEt in hexane) to give 109 mg (81% yield) of spiroacetal **3e**: ^1H NMR (300 MHz, C_6D_6) δ 0.54 (1 H, dd, J = 12.6, 13.5), 0.73 (1 H, m), 0.75 (3 H, d, J = 6.6), 1.03 (3 H, d, J = 7.1), 1.19 (3 H, d, J = 7.0), 1.33–1.62 (6 H, m), 2.59 (1 H, ddd, J = 1.7, 3.3, 13.6), 2.88 (1 H, d sept, J = 1.3, 7.0), 3.05 (2 H, s), 3.37 (1 H, d, J = 10.8), 3.43 (1 H, dd, J = 2.3, 10.8), 3.47 (1 H, dd, J = 2.3, 10.8), 3.62 (1 H, d, J = 10.8), 7.00–7.13 (3 H, m), 7.23–7.28 (2 H, m); IR (liquid film) 3325 (br), 1110 (s), 1075 (s), 725 (s), 695 (s) cm^{-1}; MS m/z (relative intensity) 318 (M^+, 40); 303 (32), 261 (58), 233 (72), 129 (100); HRMS calcd for $C_{20}H_{30}O_3$ 318.2196, found 318.2192.

Trimethylsilylation of **3e** by the procedure described above gave spiroacetal **6e** in 84% yield. **6e**: ^1H NMR (300 MHz, C_6D_6) δ 0.38 (9 H, s), 0.76 (1 H, t, J = 12.6), 0.87 (1 H, m), 0.90 (3 H, d, J = 6.6), 1.15 (3 H, d, J = 7.1), 1.32 (3 H, d, J = 7.0), 1.45–1.78 (5 H, m), 2.83 (1 H, br d, = 13.3), 3.03 (1 H, br sept, J = 7.0), 3.26 (1 H, d, J = 13.4), 3.31 (1 H, d, J = 13.4), 3.74 (3 H, m), 3.90 (1 H, d, J = 10.8), 7.00–7.14 (3 H, m), 7.23–7.28 (2 H, m); IR (liquid film) 1245 (s), 1105 (s), 835 (s) cm^{-1}; MS m/z (relative intensity) 390 (M^+, 18), 375 (8), 299 (32), 129 (40), 73 (100); HRMS calcd for $C_{23}H_{38}SiO_3$ 390.2591, found 390.2595.

(3*S*,7*S*,10*R*)-10-Methyl-7-(1-methylethyl)-3-(2-propenyl)-3-(trimethylsiloxy)-1,5-dioxaspiro[5.5]undecane (6f). By a similar procedure, reaction of epoxide **8** (985 mg, 4.10 mmol) with $(CH_2{=}CH)_2Cu(CN)Li_2$[6,11] gave 1.05 g (96% yield) of spiroacetal **3f**: ^1H NMR (300 MHz, C_6D_6) δ 0.65 (1 H, dd, J = 12.8, 13.5), 0.83 (1 H, m), 0.81 (3 H, d, J = 6.6), 1.07 (3 H, d, J = 7.1), 1.19 (3 H, d, J = 7.0), 1.38–1.64 (6 H, m), 2.51–2.67 (2 H, m), 2.70 (1 H, ddd, J = 1.8, 5.2, 13.5), 2.83 (1 H, d sept, J = 1.4, 7.0), 3.51–3.57 (3 H, m), 3.76 (1 H, d, J = 11.0), 5.08–5.20 (2 H, m), 5.84 (1 H, t, d, J = 7.6, 9.7, 17.3); IR (liquid film) 3420 (br), 1110 (s), 915 (s), 845 (s) cm^{-1}.

Trimethylsilation of **3f** by the procedure described above gave spiroacetal **6f** in 77% yield. **6f**: ^1H NNR (300 MHz, C_6D_6) δ 0.02 (9 H, s), 0.62 (1 H, t, J = 13.4), 0.77 (1 H, m), 0.78 (3 H, d, J = 6.6), 1.00 (3 H, d, J = 7.0), 1.13 (3 H, d, J = 7.0), 1.31–1.63 (5 H, m), 2.61 (1 H, dd, J = 6.7, 14.3), 2.71 (1 H, ddd, J = 1.8, 3.2, 13.6), 2.78 (2 H, m), 3.64 (2 H, s), 3.66 (1 H, d, J = 10.4), 3.89 (1 H, d,

(11) Vinyllithium was prepared by the reaction of tetravinyltin with BuLi. Seyferth, D.; Weiner, M. A. *J. Am. Chem. Soc.* **1961**, *83*, 3583.

J = 10.4), 5.12–5.29 (2 H, m), 5.97 (1 H, tdd, J = 7.6, 9.9, 17.0); IR (liquid film) 3100 (s), 1100 (s), 850 (s), 770 (s) cm^{-1}; MS m/z (relative intensity) 340 (M^+, 10), 325 (8), 299 (7), 283 (12), 255 (14) 73 (100); HRMS calcd for $C_{19}H_{36}SiO_3$ 340.2435, found 340.2432.

Reduction of Epoxide 8 with $LiAlH_4$. To a suspension of $LiAlH_4$ (14.8 mg, 0.391 mmol) in THF (1.3 mL) was added a THF (0.2 mL) solution of 8 (78.3 mg, 0.326 mmol) at 0 °C. After being stirred for 15 min at the same temperature, the reaction was quenched by the addition of AcOEt and 1 N HCl. The mixture was extracted twice with AcOEt. The organic layers were dried and concentrated, and the residue was purified by flash chromatography (5–10% AcOEt in hexane) to give 59.9 mg (76% yield) of **3b** whose ^1H NMR spectrum was identical with that of **3b** prepared by the reaction of 4 with MeMgI.

General Procedure for the Ring-Cleavage Reaction of Spiroacetals 6a–f. To a solution of the spiroacetal (1.00 mmol) and acetophenone enol trimethylsilyl ether (1.05 mmol) in CH_2Cl_2 (30 mL) was added $TiCl_4$ (1.05 mmol, 1 M solution in CH_2Cl_2) at −85 °C, and the resulting yellow solution was stirred at the same temperature for 1 h before it was quenched by the addition of pyridine (0.1 mL). The mixture was diluted with hexane, poured into aq NH_4F, and extracted twice with AcOEt. The organic layers were washed with aq $NaHCO_3$, dried, and concentrated in vacuo. The resulting crude products were dissolved in MeOH (5 mL) containing 0.2 mL of saturated aq $NaHCO_3$, and the mixture was stirred 5–10 h at a room temperature. After removal of solvents in vacuo followed by the addition of water, the mixture was extracted twice with AcOEt. The organic layers were dried and concentrated in vacuo to give an oil from which ring-cleaved product **10** was isolated by flash chromatography (10–50% AcOEt in hexane). In the reaction of **6f**, the crude ring-cleavage product **10f** was used for the further transformation without purification by flash chromatography.

Ring-cleavage product 10a: ^1H NMR (200 MHz, C_6D_6) δ 0.78–0.99 (1 H, m), 0.83 (6 H, d, J = 6.8), 1.01 (3 H, d, J = 6.8), 1.22–2.08 (8 H, m), 2.50 (2 H, brs), 2.86 (1 H, d, J = 16.0), 3.22 (1 H, d, J = 16.0), 3.25 (2 H, m), 3.63 (2 H, br s), 3.72 (1 H, br), 7.02–7.18 (3 H, m), 7.86–7.92 (2 H, m).

Ring-cleavage product 10b: ^1H NMR (200 MHz, C_6D_6) δ 0.73 (3 H, d, J = 6.4), 0.77 (3 H, d, J = 5.6), 0.90 (3 H, d, J = 6.4), 1.11 (3 H, s), 1.28–1.96 (9 H, m), 2.15 (1 H, br t, J = 6.4), 2.49 (1 H, s), 2.82 (1 H, d, J = 16.0), 3.09 (1 H, d, J = 16.0), 3.13 (1 H, d, J = 8.0), 3.21 (1 H, d, J = 8.0), 3.36 (1 H, dd, J = 5.2, 11.2), 3.59 (1 H, dd, J = 5.2, 11.2), 6.94–7.10 (3 H, m), 7.78–7.86 (2 H, m); IR (liquid film) 3420 (br), 1680 (s), 1070 (s), 755 (s), 690 (s) cm^{-1}.

Ring-cleavage product 10c: $[\alpha]^{20}_D$ −5.4 (c 0.84, $CHCl_3$); ^1H NMR (200 MHz, C_6D_6) δ 0.80 (3 H, d, J = 6.4), 0.87 (3 H, d, J = 5.6), 0.95 (3 H, t, J = 7.2), 0.99 (3 H, d, J = 6.4), 1.22–2.06 (13 H, m), 2.40 (1 H, br s), 2.59 (1 H, br s), 2.98 (1 H, d, J = 16.0), 3.22 (1 H, d, J = 16.0), 3.31 (1 H, d, J = 8.0), 3.38 (1 H, d, J = 8.0), 3.52 (1 H, br d, J = ca. 10), 3.75 (1 H, br d, J = ca. 10), 7.02–7.16 (3 H, m), 7.88–8.00 (2 H, m); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 14.01, 18.42, 20.81, 22.19, 23.34, 25.12, 27.06, 28.04, 34.53, 34.83, 42.34, 43.17, 48.14, 64.00, 66.80, 73.75, 80.84, 127.98, 128.63, 133.08, 138.13, 198.93; IR (liquid film) 3420 (br), 1675 (s), 1070 (s), 750 (s) 690 (s) cm^{-1}.

Ring-cleavage product 10d: $[\alpha]^{20}_D$ −0.3 (c 1.00, $CHCl_3$); ^1H NMR (200 MHz, C_6D_6) δ 0.68 (3 H, d, J = 6.6), 0.77 (3 H, d, J = 6.0), 0.82 (3 H, d, J = 6.8), 1.15–1.87 (8 H, m), 2.17 (1 H, t, J = 6.4), 2.64 (1 H, d, J = 16.0), 3.01 (1 H, d, J = 16.0), 3.39 (1 H, s), 3.45 (1 H, d, J = 8.8), 3.66 (1 H, d, J = 8.8), 3.70 (1 H, dd, J = 6.4, 11.2), 3.88 (1 H, dd, J = 6.4, 11.2), 6.94–7.24 (6 H, m), 7.48–7.58 (2 H, m), 7.68–7.70 (2 H, m); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 18.29, 20.63, 22.22, 23.28, 26.92, 27.97, 34.79, 42.15, 42.94, 47.56, 66.10, 68.09, 76.16, 80.96, 125.35, 127.42, 127.88, 128.28, 128.57, 133.04, 137.95, 142.12, 198.45; IR (KBr) 3430 (br), 1680 (s), 1060 (s), 755 (s), 700 (s), 690 (s) cm^{-1}.

Ring-cleavage product 10e: ^1H NMR (300 MHz, $CDCl_3$) δ 0.75 (3 H, d, J = 6.9), 0.82 (3 H, d, J = 6.2), 0.93 (3 H, d, J = 6.8), 1.36–1.98 (11 H, m), 2.88 (2 H, br s), 3.16 (1 H, d, J = 15.9), 3.28 (1 H, d, J = 8.7), 3.35 (1 H, d, J = 15.9), 3.39 (1 H, d, J = 8.7), 3.50 (1 H, d, J = 11.2), 3.69 (1 H, d, J = 11.2), 7.25–7.60 (5 H, m), 7.92 (2 H, m); IR (liquid film) 3460 (br), 1690 (s), 1060 (s) 760 (s), 710 (s) cm^{-1}.

General Procedure for Preparation of Glycerol Derivatives 1b–f. To a solution of **10b–f** (1.00 mmol) in 2,2-dimethoxypropane (1 mL) was added 0.05–0.1 mmol of 10-camphorsulfonic acid at 25 °C, and the mixture was stirred at the same temperature for 0.5 h. After dilution with AcOEt, the mixture was washed with aq $NaHCO_3$, dried, and concentrated in vacuo. Flash chromatography (5–10% AcOEt in hexane) of the residue gave the corresponding acetonide, which was then treated with a 0.5 N solution of t-BuOK (3 equiv) in t-BuOH at 60 °C for 2 h. The mixture was poured into brine and extracted twice with AcOEt. The organic layers were dried, concentrated in vacuo, and purified by flash chromatography (10–20% AcOEt in hexane) to give **1b–f**.

(*R*)-2,2,4-Trimethyl-1,3-dioxolane-4-methanol (1b): $[\alpha]^{25}_D$ +5.35° (c 0.28, CH_2Cl_2) (lit.[3a] $[\alpha]^{25}_D$ +5.25° (c 0.30, CH_2Cl_2)); ^1H NMR (300 MHz, C_6D_6) δ 1.06 (3 H, s), 1.30 (3 H, s), 1.31 (3 H, s), 1.80 (1 H, br), 3.16–3.36 (2 H, m), 3.40 (1 H, d, J = 8.4), 3.80 (1 H, d, J = 8.4); IR (liquid film) 3420 (br), 1050 (s) cm^{-1}.

(*R*)-2-Butyl-2,2-dimethyl-1,3-dioxolane-4-methanol (1c): $[\alpha]^{25}_D$ +3.20° (c 2.03, $CHCl_3$); ^1H NMR (300 MHz, C_6D_6) δ 0.83 (3 H, t, J = 6.9), 1.03–1.30 (5 H, m), 1.314 (3 H, s), 1.33 (3 H, s), 1.50 (2 H, m), 3.30 (1 H, dd, J = 0.9, 11.1), 3.48 (1 H, dd, J = 0.9, 11.1), 3.52 (1 H, d, J = 8.5), 3.76 (1 H, d, J = 8.5); IR (liquid film) 3450 (br), 1050 (s) cm^{-1}. Anal. Calcd for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71. Found: C, 63,76; H, 10.94.

(*R*)-2,2-Dimethyl-4-phenyl-1,3-dioxolane-4-methanol (1d): bp 157 °C (17 mmHg); $[\alpha]^{25}_D$ +4.54° (c 2.51, $CHCl_3$); ^1H NMR (200 MHz, C_6D_6) δ 1.17 (3 H, s), 1.49 (3 H, s), 3.64 (1 H, d, J = 8.8), 4.11 (1 H, d, J = 8.8), 4.14 (1 H, d, J = 11.6), 4.24 (1 H, d, J = 8.8), 6.94–7.14 (3 H, m), 7.16–7.28 (2 H, m); IR (liquid film) 3480 (br), 1060 (s), 765 (s) 705 (s) cm^{-1}; MS m/z (relative intensity) 177 (M^+ − CH_2OH, 70), 119 (65), 91 (100). Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.08; H, 7.94.

(*R*)-2,2-Dimethyl-4-(phenylmethyl)-1,3-dioxolane-4-methanol (1e): $[\alpha]^{25}_D$ −6.56° (c 1.34, $CHCl_3$); ^1H NMR (300 MHz, C_6D_6) δ 1.15 (3 H, s), 1.23 (3 H, s), 2.72 (1 H, d, J = 13.7), 2.78 (1 H, d, J = 13.7), 3.17 (1 H, dd, J = 4.2, 10.7), 3.26 (1 H, dd, J = 5.7, 10.7), 3.60 (1 H, d, J = 8.7), 3.66 (1 H, d, J = 8.7), 7.00–7.14 (5 H, m); IR (liquid film) 3480 (br), 1070 (s), 765 (s), 710 (s) cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.29; H, 8.39.

(*R*)-2,2-Dimethyl-4-(2-propenyl)-1,3-dioxolane-4-methanol (1f): bp 127 °C (28 mmHg); $[\alpha]^{25}_D$ −1.04° (c 1.52, $CHCl_3$); ^1H NMR (300 MHz, C_6D_6) δ 0.35 (3 H, s), 1.37 (3 H, s), 1.72 (1 H, br), 2.32 (2 H, m), 3.35 (1 H, dd, J = 5.5, 11.1), 3.44 (1 H, dd, J = 5.5, 11.1), 3.63 (1 H, d, J = 8.6) 3.80 (1 H, d, J = 8.6) 4.98–5.04 (2 H, m), 5.80 (1 H, tdd, J = 7.3, 10.5, 16.4); IR (liquid film) cm^{-1}; MS m/z (relative intensity) 157 (M^+ − CH_3, 13), 141 (38), 131 (38), 78 (59), 43 (100); exact mass (Cl) calcd for $C_9H_{17}O_3$ (M^+ + H) 173.1178, found 173.1172. Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.52; H, 9.63. The enantiomeric purity of **1c** was estimated by ^1H NMR after conversion to the corresponding (*S*)-(−)-camphanyl ester by the procedure described in ref 3c. Racemic **1c** was prepared by the reaction of 2-butylglycerol with 2,2-dimethoxypropane in the presence of CSA and converted into the corresponding diastereomeric mixture of camphanyl esters. (*S*)-Camphanyl ester of (*R*)-**1c**: ^1H NMR (300 MHz, D_6D_6), δ 0.69 (3 H, s), 0.82 (3 H, s), 0.83 (3 H, s), 0.81 (3 H, t, J = ca. 6), 1.07–1.36 (12 H, including s (3 H) at 1.28 and s (3 H) at 1.39), 1.52 (2 H, m), 1.70 (1 H, ddd, J = 5.1, 8.7, 14.0), 2.06 (1 H, ddd, J = 6.0, 9.0, 13.2), 3.51 (1 H, d, J = 9.0), 3.77 (1 H, d, J = 9.0), 4.01 (1 H, d, J = 11.1), 4.25 (1 H, d, J = 11.1). (*S*)-(−)-Camphanyl ester of racemic **1c**: ^1H NMR (300 MHz, C_6D_6) δ 0.69 (3 H, s), 0.80–0.86 (9 H, m), 1.10–1.34 (9 H, m, including s at 1.28), 1.38 and 1.39 (3 H, s), 1.47 (2 H, m), 1.70 (1 H, m), 2.07 (1 H, m), 3.50 and 3.51 (1 H, d, J = 9.0), 3.78 (1 H, d, J = 9.0), 3.96 and 4.01 (1 H, d, J = 11.1), 4.246 and 4.253 (1 H, d, J = 11.1).

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Supplementary Material Available: High-field ^1H NMR spectra for **6a–f**, *epi*-**6a**, **7**, **8**, **10a–e**, and (−)-campanyl ester of (*R*)-**1c** (16 pages). Ordering information is given on any current masthead page.