(C-13), 50.98 (C-14), 21.95 (C-15), 35.73 (C-16), 223.13 (C-17), 13.68 (C-18).

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Registry No. 1, 53875-00-6; 2, 76251-10-0; 4 (epimer 1), 76251-11-1; 4 (epimer 2), 76251-12-2; 5 (epimer 1), 76251-13-3; 5 (epimer 2), 76251-14-4; 8, 76251-15-5; 10, 76251-16-6; 12, 38522-00-8; 13, 76251-17-7; estrone, 53-16-7.

Preparation of (*R*)-(+)- and (*S*)-(-)-4-Iodo-1,2-epoxybutane [(*R*)- and (*S*)-(2-Iodoethyl)oxirane], Useful Chiral Synthons

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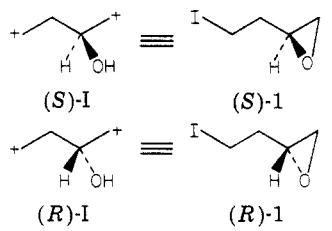
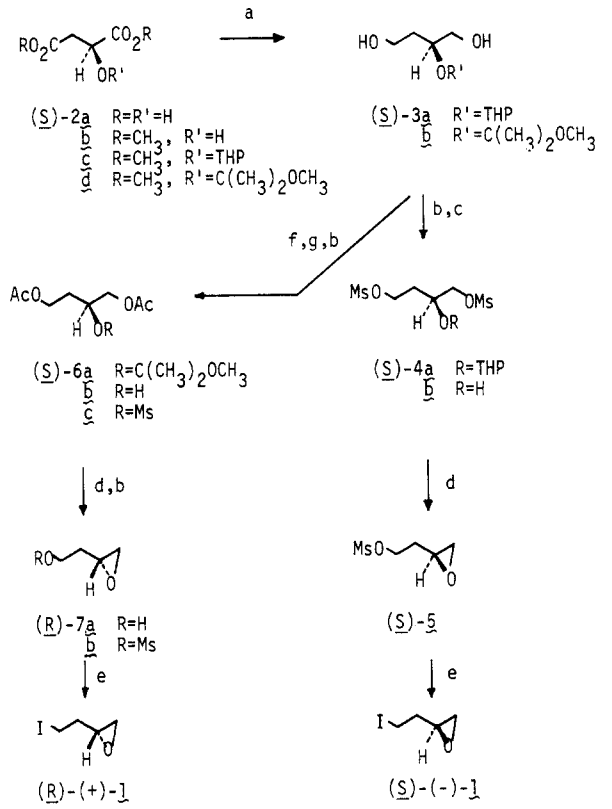
In the course of studies involving the total synthesis and conclusive determination of the absolute configuration of certain optically active natural products, we required synthetic equivalents of the chiral 4-carbon synthons (*R*)-I and (*S*)-I possessing *different* electrophilic centers at each



terminus.[1] The different level of reactivity exhibited by primary iodides and terminal oxiranes (epoxides) suggested that the use of the iodo epoxides (*R*)- and (*S*)-4-iodo-1,2-epoxybutane (1) [(*R*)- and (*S*)-(2-iodoethyl)oxirane] would allow sufficient selectivity for the introduction of two different, though similarly reactive, nucleophiles. Herein, we describe convenient and high-yielding preparations of both (*R*)- and (*S*)-I from readily available (*S*)-(-)-malic acid (**2a**, natural form), Scheme I.[2]

Scheme I[a]



[a] Reagents and conditions: a, $LiAlH_4$, THF, reflux; b, CH_3SO_2Cl, Et_3N, CH_2Cl_2, -20 to -15 °C; c, cat. CH_3SO_3H, EtOH, 50 °C; d, K_2CO_3, MeOH-THF, 25 °C; e, NaI, acetone, 25 °C; f, Ac_2O, pyridine, THF, cat. DMAP, 25 °C; g, 5% aqueous HCl wash.

Lithium aluminum hydride reduction of the THP-protected dimethyl ester of (*S*)-(-)-malic acid [(*S*)-**2c**] to give (*S*)-**3a**[1c] followed by immediate mesylation[3] afforded (*S*)-**4a** (65–70% overall).[1c] Acid-catalyzed hydrolysis of the THP ether (74%) and subsequent mild base treatment of the crystalline dimesylate alcohol (*S*)-**4b** afforded (*S*)-**5** (98%). Treatment of (*S*)-**5** with sodium iodide (2.0 equiv, acetone, 25 °C, 48 h, 81%)[4] gave (*S*)-(-)-4-iodo-1,2-epoxybutane [(*S*)-(-)-**1**], $[\alpha]^{24}_D$ -13.52° (*c* 5.00, CH_2Cl_2).[4]

The preparation of (*R*)-(+)-**1** from (*S*)-(-)-malic acid (**2a**) requires inversion of the chirality about the hydroxyl center and is detailed below. Lithium aluminum hydride reduction of (*S*)-**2d** as described previously gave the labile, protected triol (*S*)-**3b**.[1d] Immediate acetylation in the

(1) For related and recent preparations of small chiral fragments and their incorporation into chiral syntheses, see: (a) Seebach, D.; Kalinowski, H. O. *Nachr. Chem. Tech.* **1976**, *24*, 415; (b) [(*S*)-(2-bromoethyl)oxirane, (*S*)-ethyloxirane, (*S*)-methyloxirane, (*S*)-1-iodo-3-butanol] Seebach, D.; Seuring, B. *Helv. Chim. Acta* **1977**, *60*, 1175; [(*S,S*)-vermiculin] Seebach, D.; Seuring, B.; Kalinowski, H. O.; Lubosch, W.; Renger, B. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 264; [(*R*)-recifeiolide] Gerlach, H.; Oertle, K.; Thalmann, A. *Helv. Chim. Acta* **1976**, *59*, 755; (c) [(*S*)-1,2,4-butanetriol 1,4-bis(methanesulfonate)] Feit, P. W.; Nielsen, O. T. *J. Med. Chem.* **1966**, *9*, 416; (d) [(*S*)-1,2,4-butanetriol 1,2-acetonide for (*S*)-HETE] Corey, E. J.; Niwa, H.; Knolle, J. *J. Am. Chem. Soc.* **1978**, *100*, 1942; (e) [(*S*)-4-bromo-1,2-butanediol 1,2-acetonide for (*S*)-dihydroxypentyluracil] Hayashi, H.; Nakanishi, K.; Brandon, C.; Marmur, J. *Ibid.* **1973**, *95*, 8749; (f) [(*R*)-methyloxirane] Price, C. C.; Osgan, M. *J. Am. Chem. Soc.* **1956**, *78*, 4787; Levene, P. A.; Walti, A. *J. Biol. Chem.* **1926**, *68*, 415; [its use in the synthesis of (*R*)-recifeiolide] Utimoto, K.; Uchida, K.; Yamaya, M.; Nozaki, H. *Tetrahedron Lett.* **1977**, 3641; [(*S*)-methyloxirane] Gombos, J.; Haslinger, E.; Schmidt, U. *Chem. Ber.* **1976**, *109*, 2645; [for nonactin] Schmidt, U.; Gombos, J.; Haslinger, E.; Zak, H. *Ibid.* **1976**, *109*, 2628; (g) [(*R*)- and (*S*)-epichlorohydrin] Baldwin, J. J.; Raab, A. W.; Mensler, K.; Arison, B. H.; McClure, D. E. *J. Org. Chem.* **1978**, *43*, 4876; McClure, D. E.; Arison, B. H.; Baldwin, J. J. *J. Am. Chem. Soc.* **1979**, *101*, 3666; (h) [(*R*)- and (*S*)-glycidol and derivatives] McClure, D. E.; Engelhardt, E. L.; Mensler, K.; King, S.; Saari, W. S.; Huff, J. R.; Baldwin, J. J. *J. Org. Chem.* **1979**, *44*, 1826; Schmidt, U.; Talbiersky, J.; Bartkowiak, F.; Wild, J. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 198.

(2) (*R*)-, (*S*)-, and racemic 4-iodo-1,2-epoxybutane [(2-iodoethyl)oxirane] have not been previously described. Racemic and (*S*)-4-bromo-1,2-epoxybutane [(2-bromoethyl)oxirane] and their use have been described; see ref 1b and: Cruickshank, P. A.; Fishman, M. *J. Org. Chem.* **1969**, *34*, 4060.

(3) Crossland, R. K.; Servis, K. L. *J. Org. Chem.* **1970**, *35*, 3195.

(4) The conditions for the mesylate displacement employing sodium iodide–acetone represent optimized conditions. The use of less sodium iodide (1.0 equiv) or shorter reaction times (24 h) results in significant amounts of recovered starting material, whereas the use of more sodium iodide (4.0 equiv) but not longer reaction times affords varying amounts of 1,4-diiodo-2-butanol. The optical rotations of impure samples of (*R*)- and (*S*)-4-iodo-1,2-epoxybutane were *higher* than those of purified material. The chiral purity of each enantiomer could be determined by ^{1}H NMR, using the chiral shift reagent tris[3-[(trifluoromethyl)hydroxymethylene]-*d*-camphorato]europium(III) [Eu(tfc)$_3$]. In the presence of 0.1–0.3 molar equiv of [Eu(tfc)$_3$], (*S*)-**1** and (*R*)-**1** were determined to be 99 ± 1% and 98 ± 2% enantiomerically pure, respectively; cf. ref 1b and 1g.

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presence of catalytic 4-(dimethylamino)pyridine[5] yielded (*S*)-**6a** and removal of the labile ketal afforded (*S*)-1,2,4-butanetriol 1,4-diacetate [(*S*)-**6b**, 45–55% from (*S*)-(−)-malic acid]. Mesylation[3] of (*S*)-**6b** to give (*S*)-**6c** (99%) and mild base-catalyzed methanolysis effected hydrolysis of both acetates with concomitant intramolecular displacement of the mesylate, affording (*R*)-4-hydroxy-1,2-epoxybutane [(*R*)-**7a**, (*R*)-(2-hydroxyethyl)oxirane, 80–90%]. Mesylation[3] of the primary alcohol gave the mesylate epoxide (*R*)-**7b** and iodide displacement (2.0 equiv of sodium iodide, acetone, 25 °C, 48 h)[4] afforded (*R*)-(+)-4-iodo-1,2-epoxybutane [(*R*)-(+)-**1**, 70–80%], $[\alpha]^{24}_D$ +13.36° (*c* 5.00, CH_2Cl_2).[4]

The ease with which both (*S*)-(−)- and (*R*)-(+)-4-iodo-1,2-epoxybutane may be prepared from commercially inexpensive (*S*)-(−)-malic acid should make them useful chiral synthons for the preparation of optically active compounds of synthetic and medicinal interest.[1,6] Such applications are currently underway in our laboratories.

Experimental Section

Dimethyl (*S*)-(−)-Malate [(*S*)-2b]. Esterification of (*S*)-malic acid (5.0 g, 37.3 mmol), $[\alpha]^{24}_D$ −31.70° (*c* 1.10, pyridine), in absolute MeOH (60 mL) containing 3 drops of concentrated HCl (4 days, 25 °C) followed by the addition of a small amount of Ag_2O,[1c] filtration through Celite, concentration in vacuo, and chromatography (SiO_2 plug, 50% ethyl acetate–hexane eluant) afforded 5.54 g (91%) of pure (*S*)-**2b**[7] as a colorless oil, $[\alpha]^{25}_D$ −7.57° (neat) (lit.[7] $[\alpha]^{20}_D$ −6.85° neat)).

(*S*)-Dimethyl 2-*O*-(2-Tetrahydropyranyl)malate [(*S*)-2c]. Dihydropyran (24 mmol, 1.48 g, 1.6 mL, 1.5 equiv) was added to a solution of (*S*)-**2b** (2.6 g, 16 mmol) in 110 mL of CH_2Cl_2 (25 °C) containing pyridinium *p*-toluenesulfonate (400 mg, 1.6 mmol, 0.1 equiv).[8] After 4.0 h (25 °C) the reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with half-saturated brine (2 × 50 mL), dried ($MgSO_4$), and concentrated in vacuo. Chromatography (SiO_2, 25% ether–hexane eluant) afforded pure (*S*)-**2c** (3.77 g, 96%) as a colorless oil: $[\alpha]^{23}_D$ −59.00° (*c* 6.00, acetone); ^1H NMR ($CDCl_3$) δ 4.78 (1 H, m, OCHO), 4.62 (1 H, m, CHO), 3.78 and 3.70 (6 H, 2 s, CO_2CH_3), 2.78 (2 H, m, CH_2), 1.66 (8 H, br m, THP CH_2's); IR (film) ν_{max} 2840, 1742 (C=O), 1390, 773 cm^{-1}; mass spectrum, *m/e* (relative intensity) 246 (M^+, 0.3), 187 (2), 146 (9), 131 (6), 118 (36), 115 (36), 103 (54), 101 (15), 84 (base), 83 (45), 71 (34), 65 (37). Anal. Calcd for $C_{11}H_{18}O_6$: C, 53.65; H, 7.37. Found: C, 53.98; H, 7.39.

(*S*)-1,2,4-Butanetriol 1,4-Bis(methanesulfonate) [(*S*)-4b]. A suspension of lithium aluminum hydride (30 mmol, 1.14 g) in 30 mL of THF under N_2 was warmed at 55 °C for 1 h. (*S*)-**2c** (15.45 mmol, 3.90 g) in 15 mL of THF was added dropwise and the resulting mixture was warmed at 55 °C for 18 h before cautious, sequential addition of water (1.14 mL), 10% aqueous NaOH (2.28 mL), and water (3.42 mL). After filtration (ether wash), the filtrate was dried ($MgSO_4$) and concentrated in vacuo, affording 2.72 g of crude (*S*)-**3a**[1b,c] [lit.[1b,c] $[\alpha]^{20}_D$ −41.7° (*c* 6.00, acetone), −14.4° (*c* 1.4, $CHCl_3$)].

A solution of (*S*)-**3a** (2.72 g, 14.3 mmol) in 55 mL of CH_2Cl_2 cooled to −15 °C was treated sequentially with Et_3N (51.5 mmol, 7.1 mL, 5.2 g, 1.8 equiv) and methanesulfonyl chloride[3] (42.9 mmol, 3.32 mL, 4.9 g, 1.5 equiv). After 45 min at −15 °C the reaction mixture was poured onto crushed ice and stirred for 5 min before the organic layer was washed with 5% HCl, saturated $NaHCO_3$, and water, dried (Na_2SO_4), and concentrated in vacuo. Chromatography (SiO_2, ether eluant) afforded 3.56 g of pure (*S*)-**4a**[1c] (63% from (*S*)-**2b**) as a colorless oil: ^1H NMR ($CDCl_3$) δ 4.7 (1 H, br s, OCHO), 4.35 (5 H, m, CH_2OMs and CHOTHP), 3.08 and 3.02 (6 H, 2 s, CH_3SO_3), 2.15 (2 H, q, *J* = 6 Hz, CH_2), 1.66 (8 H, m, THP CH_2's); IR (film) ν_{max} 2940, 2860, 1440, 1325, 1150, 1055, 1010 cm^{-1}.

A solution of (*S*)-**4a** (2.75 g, 7.9 mmol) in 15 mL of absolute EtOH containing 0.2 mL of methanesulfonic acid was warmed at 50 °C for 1 h. The cooled mixture was stored at 0 °C for 10 h and filtered (EtOH wash, 10–15 mL), affording 1.38 g of pure (*S*)-**4b** as white needles. Concentration of the mother liquor to ca. 5 mL afforded an additional 180 mg of material: 1.56 g total (74%) of pure (*S*)-**4b**; mp 67–68.5 °C (lit.[1c] mp 68–70 °C); $[\alpha]^{24}_D$ −16.13° (*c* 6.00, acetone); [lit.[1c] $[\alpha]^{25}_D$ −16.5° (*c* 6, acetone)]; ^1H NMR ($CDCl_3$) δ 4.28 (5 H, m, 2 CH_2OMs and CHOH), 3.09 and 3.05 (6 H, 2 s, CH_3SO_3), 1.95 (2 H, m, CH_2); IR (KBr pellet) ν_{max} 3530, 2930, 1325, 1155, 828 cm^{-1}.

(*S*)-(2-Hydroxyethyl)oxirane Methanesulfonate [(*S*)-5]. Anhydrous K_2CO_3 (2.75 mmol, 380 mg, 1.1 equiv) was added to a solution of (*S*)-**4b** (665 mg, 2.5 mmol) in 30 mL of 50% MeOH–THF. After 10 h (25 °C) the mixture was partitioned between CH_2Cl_2 (35 mL)–water (20 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 15 mL) and the combined organic layers were dried ($MgSO_4$) and concentrated in vacuo. Chromatography (SiO_2, ether eluant) afforded 408 mg (98%) of pure (*S*)-**5** as a colorless oil: $[\alpha]^{25}_D$ −21.54° (*c* 5.00, acetone); ^1H NMR ($CDCl_3$) δ 4.29 (2 H, t, *J* = 6 Hz, CH_2OMs), 3.07 (3 H, s, CH_3SO_3), 2.95 (1 H, m, epoxide CHO), 2.78 (1 H, t, *J* = 4 Hz) and 2.49 (1 H, dd, *J* = 4, 2 Hz) for epoxide CH_2O, 1.98 (2 H, q, *J* = 6 Hz, CH_2); IR (film) ν_{max} 2960, 1400, 1325, 1155, 775 cm^{-1}; mass spectrum, *m/e* (relative intensity) 166 (M^+, 10), 151 (4), 97 (33), 79 (55), 71 (78), 57 (base), 55 (55). Anal. Calcd for $C_5H_{10}O_4S$: C, 36.13; H, 6.02. Found: C, 36.50; H, 6.10.

(*S*)-4-Iodo-1,2-epoxybutane [(*S*)-1, (*S*)-(2-Iodoethyl)oxirane]. A solution of (*S*)-**5** (482 mg, 2.90 mmol) in 16 mL of acetone cooled to 0–5 °C was treated with anhydrous K_2CO_3 (40 mg, 0.1 equiv) and NaI (865 mg, 5.8 mmol, 2.0 equiv). The resulting reaction mixture was allowed to slowly warm to 25 °C (ca. 3.0 h) where it was stirred for 48 h before being partitioned between ether–water (1:1). The organic phase was washed with saturated NaCl and dried ($MgSO_4$), and the solvent was removed at aspirator pressure (<30 °C). Chromatography (SiO_2, 70% ether–hexane eluant) afforded 466 mg (81%) of pure (*S*)-**1**: $[\alpha]^{24}_D$ −13.52° (*c* 5.00, CH_2Cl_2);[4] ^1H NMR ($CDCl_3$) δ 3.25 (2 H, t, *J* = 6 Hz, CH_2I), 3.05–2.84 (1 H, m, epoxide CHO), 2.80 (1 H, t, *J* = 4 Hz) and 2.56 (1 H, dd, *J* = 4, 2 Hz) for the epoxide CH_2O, 2.22–1.86 (2 H, m, CH_2); IR (film) ν_{max} 2980, 2950, 1400, 1223, 1150, 875, 810 cm^{-1}; mass spectrum, *m/e* (relative intensity) 198 (M^+, 1.7), 71 (80), 57 (base), 55 (60). Anal. Calcd for C_4H_7IO: C, 24.24; H, 3.53. Found: C, 24.10; H, 3.78.

(*S*)-1,2,4-Butanetriol 1,4-Diacetate [(*S*)-6b]. A solution of (*S*)-**2b** (7.9 g, 48.0 mmol) in 120 mL of CH_2Cl_2 cooled to 0 °C was treated sequentially with 2-methoxypropene[9] (10.4 g, 134 mmol, 3.0 equiv) and phosphorus oxychloride[10] (6 drops) and stirring was continued for 4 h (25 °C). Addition of a small amount of powdered Ag_2O,[1c] filtration through Celite, and concentration in vacuo afforded 11.23 g (99%) of crude (*S*)-**2d** as a light yellow oil. Labile ketal (*S*)-**2d** was used immediately without purification: ^1H NMR ($CDCl_3$) δ 4.61 (1 H, t, *J* = 6 Hz, CHO), 3.69 and 3.64 (6 H, 2 s, CO_2CH_3), 3.15 (3 H, s, OCH_3), 2.72 (2 H, d, *J* = 6 Hz, CH_2), 1.36 and 1.12 (6 H, 2 s, CH_3); IR (film) ν_{max} 2978, 2930, 1730 (C=O), 1410, 1350 cm^{-1}.

A suspension of lithium aluminum hydride (3.65 g, 96 mmol) in 100 mL of THF under nitrogen was warmed at 55 °C for 1 h. (*S*)-**2d** (11.23 g, 48 mmol) in 25 mL of THF was added dropwise and the resulting solution was warmed at 50 °C for 8–12 h. After cautious, sequential addition of water (3.65 mL), 10% aqueous NaOH (7.12 mL), and water (10.95 mL) and filtration (ether wash), the filtrate was dried ($MgSO_4$) and concentrated in vacuo, affording 7.83 g of crude, labile[11] (*S*)-**3b**[1b] as a yellow oil which was used immediately without purification: ^1H NMR ($CDCl_3$) δ 4.10 (1 H, m, CHO), 3.70 (4 H, m, 2 CH_2O), 3.22 (3 H, s, OCH_3), 1.80

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(11) Exposure of (*S*)-diol ketal **3b** to mild acid results in the formation of (*S*)-1,2,4-butanetriol 1,2-acetonide; see ref 1d.

(2 H, q, J = 6 Hz, CH_2), 1.41 (6 H, br s, CH_3's).

A solution of crude (*S*)-**3b** (7.83 g) in 70 mL of THF cooled to 0 °C under nitrogen was treated sequentially with acetic anhydride (132 mmol, 12.46 mL, 13.46 g, 3.0 equiv), pyridine (154 mmol, 12.43 mL, 12.16 g, 3.5 equiv), and 4-(dimethylamino)-pyridine[5] (5 mg). The reaction mixture was allowed to warm to 25 °C (ca. 3 h) where it was stirred for 20 h before being poured onto crushed ice. The crude product was extracted into CH_2Cl_2 (4 × 25 mL) and the organic phase was washed with 5% aqueous HCl (10 × 25 mL, which effected removal of pyridine and hydrolysis of the ketal-protecting group), saturated aqueous $NaHCO_3$, and water and dried ($MgSO_4$). The acid layer was reextracted with CH_2Cl_2 (5 × 25 mL) to recover additional alcohol. Chromatography (SiO_2, 80% ether–hexane eluant) gave 3.85 g [46% from (*S*)-**2b**] of pure (*S*)-**6b** as a colorless oil: $[\alpha]^{24}_D$ −16.79° (neat); ^1H NMR ($CDCl_3$) δ 4.20 (1 H, m, CHO), 4.15 (2 H, t, J = 6 Hz, CH_2OAc), 4.00 (2 H, d, J = 6 Hz, CH_2OAc), 2.08 and 2.00 (6 H, 2 s, CH_3CO_2), 1.78 (2 H, q, J = 6 Hz, CH_2); IR (film) ν_{max} 3435 (OH), 2950, 1720 (C=O), 1350, 1220, 1120 cm^{-1}; mass spectrum, m/e (relative intensity) 172 (0.03, loss of H_2O), 117 (2), 104 (0.8), 100 (3), 86 (0.2), 70 (3), 57 (11), 43 (51), 31 (base). Anal. Calcd for $C_8H_{14}O_5$: C, 50.52; H, 7.42. Found: C, 50.14; H, 7.50.

(*S*)-1,2,4-Butanetriol 1,4-Diacetate 2-Methanesulfonate [(*S*)-6c]. A solution of (*S*)-**6b** (7.0 g, 36.8 mmol) in 70 mL of CH_2Cl_2 cooled to −15 °C under argon was treated sequentially with Et_3N (9.23 mL, 6.70 g, 66 mmol, 1.8 equiv) and methanesulfonyl chloride[3] (4.27 mL, 6.32 g, 55 mmol, 1.5 equiv) and the resulting mixture was stirred for 1 h at −15 °C before being poured onto crushed ice. The organic layer was washed with 5% aqueous HCl, saturated $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated in vacuo. Chromatography (SiO_2, ether eluant) afforded 9.86 g (100%) of pure (*S*)-**6c** as a colorless oil: $[\alpha]^{24}_D$ −8.68° (*c* 5.00, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 5.0 (1 H, m, CHOMs), 4.38–4.08 (4 H, m, CH_2OAc), 3.05 (3 H, s, CH_3SO_3), 2.10 and 2.05 (6 H, 2 s, CH_3CO_2), 2.2–1.91 (2 H, m, CH_2); IR (film) ν_{max} 1725 (C=O), 1330, 1215, 1160, 1030, 890 cm^{-1}; mass spectrum m/e (relative intensity) 268 (M^+, 2), 195 (6), 134 (20), 85 (55), 83 (base), 78 (36), 49 (63). Anal. Calcd for $C_9H_{16}O_7S$: C, 40.28; H, 5.96. Found: C, 40.00; H, 5.90.

(*R*)-4-Hydroxy-1,2-epoxybutane [(*R*)-7a, (*R*)-(2-Hydroxyethyl)oxirane]. A solution of (*S*)-**6c** (9.86 g, 36.8 mmol) in 250 mL of 50% MeOH–THF containing anhydrous K_2CO_3 (11.20 g, 80 mmol, 2.2 equiv) was stirred at 25 °C for 10 h. Removal of the solvent in vacuo and chromatography (SiO_2, ether eluant) gave 2.73 g (85%) of pure (*R*)-**7a** as a colorless oil: $[\alpha]^{23}_D$ +16.64° (*c* 5.00, acetone), +23.42° (*c* 5.00, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 3.72 (2 H, t, J = 6 Hz, CH_2OH), 3.00 (1 H, m, CHO), 2.70 (1 H, t, J = 4 Hz) and 2.52 (2 H, dd, J = 4, 2 Hz) for epoxide CH_2O, 1.78 (3 H, m, CH_2, OH); IR (film) ν_{max} 3350 (OH), 2900, 1460, 1380, 1220, 1010, 850, 785 cm^{-1}; mass spectrum, m/e (relative intensity) 88 (M^+, 0.5%), 87 (5), 70 (3), 58 (16), 57 (45), 31 (base). Anal. Calcd for C_4H_8O: C, 54.53; H, 9.15. Found: C, 54.33; H, 9.18.

(*R*)-(2-Hydroxyethyl)oxirane Methanesulfonate [(*R*)-7b]. A solution of (*R*)-**7a** (2.5 g, 28.0 mmol) in 30 mL of CH_2Cl_2 cooled to −20 °C was treated sequentially with Et_3N (7.02 mL, 5.1 g, 50.0 mmol, 1.8 equiv) and methanesulfonyl chloride[3] (3.25 mL, 4.81 g, 42.0 mmol, 1.5 equiv) and the resulting reaction mixture was stirred for 1 h (−20 °C) before being poured onto crushed ice. The organic layer was washed with 5% aqueous HCl, saturated $NaHCO_3$, and water, dried ($MgSO_4$), and concentrated in vacuo. Chromatography (SiO_2, 75% ether–hexane eluant) afforded 3.61 g (78%) of pure (*R*)-**7b** as a colorless oil: $[\alpha]^{25}_D$ +20.04° (*c* 5.00, acetone); ^1H NMR ($CDCl_3$) δ 4.29 (2 H, t, J = 6 Hz, CH_2OMs), 3.07 (3 H, s, CH_3SO_3), 2.95 (1 H, m, epoxide CHO), 2.78 (1 H, t, J = 4 Hz) and 2.49 (1 H, dd, J = 4, 2 Hz) for epoxide CH_2O, 1.98 (2 H, q, J = 6 Hz, CH_2); IR (film) ν_{max} 2960, 1400, 1325, 1155, 775 cm^{-1}; mass spectrum, m/e (relative intensity) 166 (M^+, 10), 151 (4), 97 (33), 79 (55), 71 (78), 57 (base), 55 (55). Anal. Calcd for $C_5H_{10}O_4S$: C, 36.13; H, 6.02. Found: C, 35.98; H, 5.80.

(*R*)-4-Iodo-1,2-epoxybutane [(*R*)-1, (*R*)-(2-Iodoethyl)oxirane)]. A solution of (*R*)-**7b** (3.61 g, 22 mmol) in 110 mL of acetone cooled to 0–5 °C was treated sequentially with anhydrous K_2CO_3 (304 mg, 0.1 equiv) and NaI (6.59 g, 44.0 mmol, 2.0 equiv) and the resulting mixture was allowed to warm slowly to 25 °C (ca. 3 h) where it was stirred for 48 h. The reaction mixture was partitioned between ether–water (1:1), the organic phase was washed with saturated NaCl and dried ($MgSO_4$), and the solvent was removed at aspirator pressure (<30 °C). Chromatography (SiO_2, 70% ether–hexane eluant) afforded 2.80 g (71%) of pure (*R*)-1: $[\alpha]^{25}_D$ +13.36° (*c* 5.00, CH_2Cl_2);[4] ^1H NMR ($CDCl_3$) δ 3.25 (2 H, t, J = 6 Hz, CH_2I), 3.09–2.84 (1 H, m, epoxide CHO), 2.80 (1 H, t, J = 4 Hz) and 2.56 (1 H, dd, J = 4, 2 Hz) for epoxide CH_2O, 2.22–1.86 (2 H, m, CH_2); IR (film) ν_{max} 2980, 2950, 1400, 1223, 1150, 875, 810 cm^{-1}; mass spectrum, m/e (relative intensity) 198 (M^+, 2), 71 (80), 57 (base). Anal. Calcd for C_4H_4IO: C, 24.24; H, 3.53. Found: C, 24.16; H, 3.46.

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Registry No. (*S*)-**1**, 76282-41-2; (*R*)-**1**, 76282-42-3; (*S*)-**2a**, 97-67-6; (*S*)-**2b**, 617-55-0; (*S*)-**2c**, 76332-79-1; (*S*)-**2d**, 76282-43-4; (*S*)-**3a**, 5055-09-4; (*S*)-**3b**, 66348-33-2; (*S*)-**4a**, 76282-44-5; (*S*)-**4b**, 5055-10-7; (*S*)-**5**, 76282-45-6; (*S*)-**6b**, 76282-46-7; (*S*)-**6c**, 76282-47-8; (*R*)-**7a**, 76282-48-9; (*R*)-**7b**, 76282-49-0; 2-methoxypropene, 116-11-0.

Synthesis and Properties of Two Dioxadioxoparacyclophanes

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Considerable current interest centers on macrocycles with lipophilic cavities.[1,2] These molecules may serve as models for enzyme active sites,[2] as ring moieties in rotaxanes and catenanes,[3] or as hosts for inclusion complexes.[4] This report deals with two such macrocycles which have functional groups on opposite sides of the ring.

14,34-Dioxa-4,24-dioxo[7.1.7.1]paracyclophane[5] (**3**) and 12,30-dioxa-3,21-dioxo[5.1.5.1]paracyclophane (**4**) were made from diesters by the Dieckmann condensation. Reactions at high dilution were necessary to preclude complete formation of polymers. Even with dilution, yields of the diphenyl ether derivatives, **3** and **4**, were low. The corresponding monoketones were not formed. The C–O–C bond angle and the bond lengths are evidently sufficient to prevent formation of the smaller rings in this reaction that involves a nucleophilic addition of one end of the chain to the other end of the chain. Lüttringhaus found that a chain of over eight atoms was required to connect the 4 and 4′ positions of diphenyl ether in a nucleophilic substitution reaction,[6] although the 4 and 4′ positions of

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