Stereoselective Synthesis of *cis*-2,5-Disubstituted Tetrahydrofurans Using Oxabicyclo[3.2.1]heptanone Platforms. Building Blocks for Natural Product Synthesis

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Received August 2, 1994

Versatile syntheses of *cis*-2,5-disubstituted tetrahydrofurans represent an important challenge because of the presence of this structural unit in polyoxygenated terpenes such as eurylene (**1**),[1] polyether antibiotic ionophores such as ionomycin (**2**),[2] and other natural products (Figure 1). Methods which allow the stereoselective introduction of functionality contiguous to C-2 and C-5 (i.e., at C-1′ and C-1″) are particularly attractive because such fragments (e.g., **3**) are potentially useful building blocks in natural product synthesis. Among the numerous approaches to this class of compound, perhaps the most successful are those which utilize 1,5-dienes or substituted pentenols as starting materials.[3] These methods are limited by the availability of suitable alkene precursors. Consequently, development of new synthetic methods for the preparation of tetrahydrofurans continues to attract attention.[4]

Methods in which oxabicyclic systems are used as a stereochemical scaffold to prepare functionalized tetrahydrofurans provide an attractive alternative route to these important ring systems.[5] We recently described highly diastereoselective, Lewis acid catalyzed, [3 + 4] and [3 + 5] annulation procedures in which 1,4- and 1,5-dicarbonyl compounds reacted with bis(trimethylsilyl) enol ether **5** to provide oxabicyclo[3.2.1]octanones and oxabicyclo[3.3.1]nonanones, respectively.[6] We envisaged that the stereoselective manipulation of **6** (Scheme 1), prepared using the [3 + 4] annulation of **4** and **5**, could lead to a highly versatile tetrahydrofuran synthesis. Bicyclic ether **6** contains two of the four stereocenters present in fragment **3**, and we reasoned that the other two stereocenters, corresponding to C-2 and C-4 in **6**, could be introduced through the selective manipulation of the β-keto ester functionality present in **6**. Our results describing the successful accomplishment of these goals are described below.

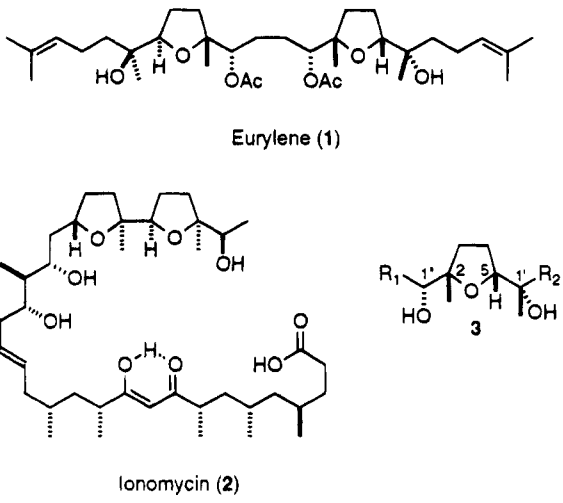
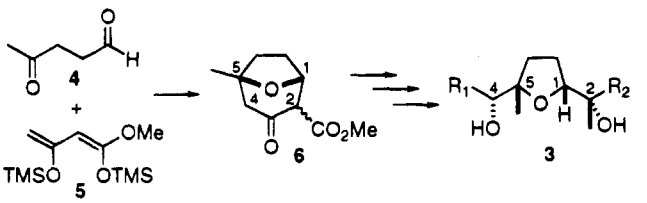


Figure 1. Representative examples of tetrahydrofuran-containing natural products.

Scheme 1



Results and Discussion

Bicyclic ether **6** was prepared (55%) according to the published procedure (Scheme 2).[6] Stereoselective alkylation of the derived β-keto ester enolate afforded keto ester **7** (92%) as the only isolated product. Baeyer–Villiger oxidation of **7** initially proved troublesome. Treatment with *m*-CPBA at room temperature for 24 h led to only 8% conversion of the starting material. The use of elevated temperature and a radical scavenger gave the desired lactone **8** in 49% yield after 86 h.[7] Trifluoroperacetic acid prepared using urea hydrogen peroxide as an anhydrous source of peroxide also failed to give the product in an acceptable yield.[8] The rate enhancement of Baeyer–Villiger oxidations by $NaHCO_3$ has been reported previously,[9] and treatment of **7** with *m*-CPBA and $NaHCO_3$ led to a faster, regioselective reaction in which lactone **8** was obtained in 67% yield (89% based on recovered starting material) after 72 h. Subsequent hydroxylation using Davis's protocol[10] afforded the α-hydroxy lactone **10** as a single diastereoisomer (48%) along with a number of byproducts including the bislactone **9**

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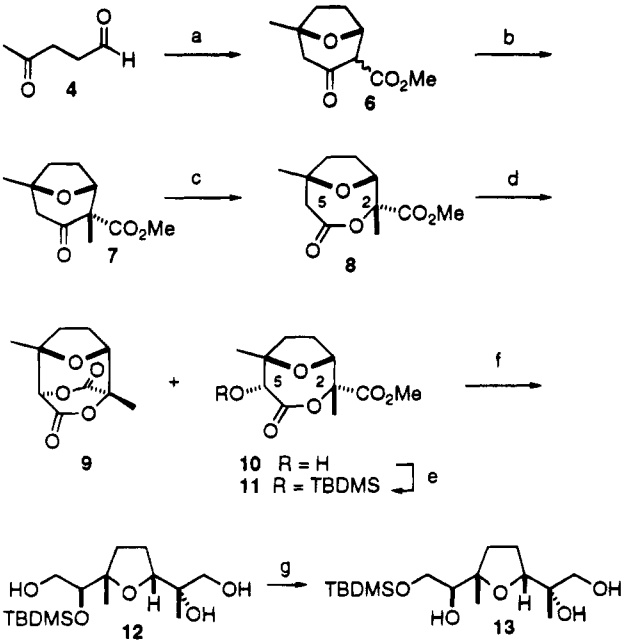
Scheme 2[a]

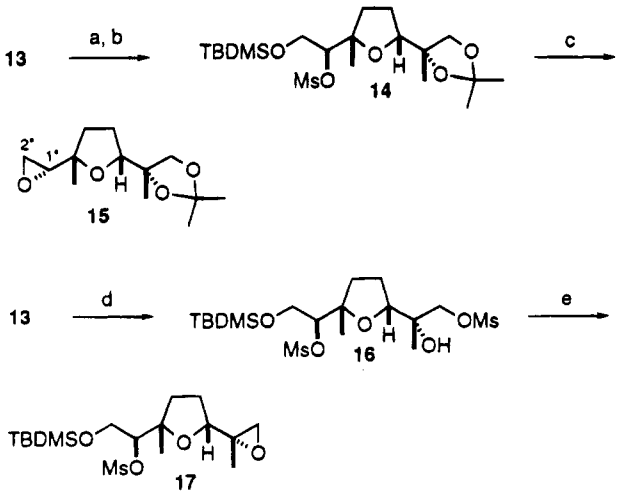


[a] Key: (a) cat. TMSOTf, **5**, CH_2Cl_2, −78 °C; (b) NaH, MeI, THF, −10 °C; (c) *m*-CPBA, $NaHCO_3$, $(CH_2Cl)_2$; (d) KHMDS, *trans*-benzenesulfonyl)-3-phenyloxaziridine, THF, −78 °C; (e) TBDMSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C to rt; (f) DIBALH, THF, −78 °C to rt; (g) DBU, CH_2Cl_2.

(10%). The α-orientation of the hydroxyl group in **10** was readily determined by X-ray analysis.[17] An examination of models[11] suggested that the *si* face of the enolate, derived from **8**, would be blocked by the presence of the β-methyl group at C-2 and that enolate oxidation would occur predominantly from the *re* face. Stereoelectronic effects may also contribute to the high diastereoselectivity observed.[12] Attempts to oxidize the enolate derived from **8** using MoO_5·Py·DMPU[13] as the oxidizing agent gave only recovered starting material. Protection of the alcohol **10** as its TBDMS ether **11** (99%) followed by treatment with DIBALH afforded monoprotected tetrol **12** (73%). DBU-catalyzed migration of the TBDMS protecting group from the secondary to the adjacent primary hydroxyl gave the key intermediate **13** (82%, 98% based on recovered starting material).[14]

Both **12** and **13** possess the four stereocenters in the core tetrahydrofuran unit required in the synthesis of several natural product fragments, and all four hydroxyl groups in **12** can be readily differentiated using standard synthetic methods and converted to versatile intermediates for further elaboration. Perhaps most importantly, both ends of the tetrahydrofuran core can be selectively activated by conversion into epoxides **15** and **17**, which are ideally suited for the sequential introduction of suitably functionalized side chains. Thus, protection of the 1,2-diol in **13** as the acetonide (96%) followed by mesylation of the remaining unprotected hydroxyl group afforded **14** (92%) (Scheme 3). Desilylation and *in situ* treatment with K_2CO_3 afforded epoxide **15** (98%). In this way C-2″ is activated toward nucleophilic attack and the

Scheme 3[a]



[a] Key: (a) $Me_2C(OMe)_2$, cat. PPTS, CH_2Cl_2; (b) MsCl, cat. DMAP, pyridine; (c) Bu_4NF, THF, K_2CO_3; (d) MsCl, cat. DMAP, pyridine; (e) K_2CO_3, MeOH.

desired stereochemistry at C-1″ is incorporated. Dimesylation of triol **13** afforded alcohol **16** (91%) which was readily converted to the epoxide **17** (97%) upon treatment with K_2CO_3 in MeOh, thereby activating C-2′ for nucleophilic attack.

Not only are epoxides **15** and **17** synthetically useful but the potential to vary substituents at C-2 and C-5 in **10** by use of alternative electrophiles in the two enolate anion reactions make this a desirable approach to tetrahydrofuran synthesis. The ability to introduce substituents stereoselectively within the tetrahydrofuran ring using substituted 1,4-dicarbonyl compounds (c.f., **4**) is also attractive.[6]

Experimental Section

Reagents. THF was distilled immediately prior to use from sodium benzophenone ketyl under argon. CH_2Cl_2 was distilled from CaH_2 and stored over 4-Å molecular sieves. *m*-CPBA was purified according to the literature procedure.[15] Standard benchtop techniques were employed for handling air-sensitive reagents.[16]

(1*R,2*S**,5*S**)-2,5-Dimethyl-2-(methoxycarbonyl)-8-oxabicyclo[3.2.1]octan-3-one (7).** Sodium hydride (58 mg of a 60% suspension in mineral oil, 1.45 mmol) was washed under argon with dry hexanes, suspended in THF (2 mL) at rt, and treated dropwise with a solution of **6** (260 mg, 1.31 mmol) in THF (4 mL). After 20 min the solution was cooled to −10 °C and methyl iodide (340 mg, 2.40 mmol) was added dropwise. After 3 h the solution was concentrated *in vacuo* and the residue was dissolved in ether and filtered through Celite. Concentration *in vacuo* followed by flash chromatography (7:3 hexanes/ethyl acetate) and Kugelrohr distillation provided **7** as a white solid (251 mg, 90%): mp 43−45 °C; bp 80−85 °C/0.3 mmHg; ^1H NMR (300 MHz, $CDCl_3$) δ 4.38 (dd, *J* = 6, 3 Hz, 1H), 3.71 (s, 3H), 2.63 (dd, *J* = 16, 2 Hz, 1H), 2.25 (d, *J* = 16 Hz, 1H), 2.15 (m, 2H), 1.85−1.60 (m, 2H), 1.56 (s, 3H), 1.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.6, 171.3, 82.3, 80.8, 61.9, 52.2, 51.2, 35.3, 28.4, 25.7, 21.1; IR (neat) 1730, 1716 cm^{-1}; HRMS calcd for $C_{11}H_{16}O_4$ 212.1049, found 212.106; LRMS (EI) *m/z* 212. Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25, H, 7.60. Found: C, 62.18; H, 7.54.

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(1*R,2*S**,6*S**)-2,6-Dimethyl-2-(methoxycarbonyl)-3,9-dioxabicyclo[4.2.1]nonan-4-one (8).** A stirred solution of **7** (5.0 g, 23.6 mmol) in $ClCH_2CH_2Cl$ (35 mL) was treated with $NaHCO_3$ (2.9 g, 35.4 mmol) and *m*-CPBA (6.0 g, 35.4 mmol) and stirred at rt for 24 h. More $NaHCO_3$ (2.9 g, 35.4 mmol) and *m*-CPBA (6.0 g, 35.4 mmol) were added, and the mixture was stirred for a further 48 h. The solution was diluted with CH_2Cl_2 and treated with a 10% solution of Na_2SO_3 followed by vigorous stirring for 15 min. The aqueous phase was extracted with CH_2Cl_2, and the combined organic phase was washed with saturated $NaHCO_3$ and brine and dried over $MgSO_4$. Concentration *in vacuo* followed by flash chromatography (3:1 hexanes/ethyl acetate) afforded starting material (0.9 g, 18%) and **8** as a white solid (3.605 g, 67%): mp 96–97 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 4.59 (d, J = 8.5 Hz, 1H), 3.76 (d, J = 1 Hz, 3H), 2.94 (d, J = 16 Hz, 1H), 2.82 (d, J = 16 Hz, 1H), 2.20–1.90 (m, 3H), 1.80–1.70 (m, 1H), 1.73 (d, J = 1 Hz, 3H), 1.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 170.2, 86.1, 81.6, 80.8, 53.1, 51.2, 34.7, 27.1, 26.3, 21.6; IR ($CHCl_3$) 1729 cm^{-1}; HRMS calcd for $C_{11}H_{16}O_5$: 228.0998, found 228.0989; LRMS (EI) *m/z* 228. Anal. Calcd for $C_{11}H_{16}O_5$: C, 57.91; H, 7.07; Found: C, 57.75; H, 7.01.

(1*R,2*S**,5*S**,6*S**)-1,5-Dimethyl-9-oxo-8,10,11-trioxatricyclo-[4.2.2.1^{2,5}]undecan-7-one (9) and (1*R**,2*S**,5*S**,6*S**)-2,6-Dimethyl-5-hydroxy-2-(methoxycarbonyl)-3,9-dioxabicyclo-[4.2.1]nonan-4-one (10).** A solution of KHMDS (2.61 g, 13.1 mmol) in THF (325 mL) at −78 °C under argon was treated dropwise with a solution of **8** (2.0 g, 8.77 mmol) in THF (25 mL). After 20 min the solution was treated with *trans*-(benzenesulfonyl)-3-phenyloxaziridine (3.57 g, 13.8 mmol) in THF (260 mL) and stirred for a further 30 min. Camphorsulfonic acid (3.04 g, 13.1 mmol) in dry THF (30 mL) was added, and the solution was stirred for 30 min before being warmed to room temperature. Water was added, and the aqueous phase was extracted with ethyl acetate. The combined organic phase was washed with water, saturated $NaHCO_3$, and brine and dried over $MgSO_4$. Concentration *in vacuo* followed by flash chromatography (4:1 hexanes/ethyl acetate) afforded **9** as a white solid (190 mg, 10%) [mp 106–107 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 4.68 (s, 1H), 4.12 (d, J = 7 Hz, 1H), 2.28 (m, 2H), 1.87 (m, 1H), 1.72 (m, 1H), 1.54 (s, 3H), 1.53 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.5, 164.2, 85.1, 82.9, 82.4, 79.9, 29.9, 27.8, 22.9, 20.2; IR (neat) 1770 cm^{-1}; HRMS calcd for $C_{10}H_{12}O_5$ 212.0685, found 212.0683; LRMS (EI) *m/z* 212. Anal. Calcd for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70. Found: C, 56.38; H, 5.73] followed, after recrystallization from ethyl acetate, by **10** as a white solid (1.02 g, 48%): mp 121–122 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 4.59 (dd, J = 9, 2 Hz, 1H), 4.06 (t, J = 2 Hz, 1H), 3.77 (s, 3H), 3.68 (d, J = 2 Hz, 1H), 2.25–1.80 (m, 3H), 1.71 (s, 3H), 1.50–1.65 (m, 1H), 1.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.7, 170.1, 88.0, 83.9, 80.8, 76.6, 53.2, 31.5, 25.6, 24.0, 21.7; IR (neat) 3697, 1771, 1715 cm^{-1}; HRMS calcd for $C_{11}H_{16}O_6$ 244.0947, found 244.0948; LRMS (EI) *m/z* 244. Anal. Calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 54.12; H, 6.68.

(1*R,2*S**,5*S**,6*S**)-5-[(*tert*-Butyldimethylsilyl)oxy]-2,6-dimethyl-2-(methoxycarbonyl)-3,9-dioxabicyclo[4.2.1]-nonan-4-one (11).** A stirred solution of **10** (100 mg, 0.41 mmol) in CH_2Cl_2 (2 mL) at 0 °C under argon was treated with TBDMSOTf (102 mg, 0.46 mmol) followed by 2,6-lutidine (49 mg, 0.46 mmol). After 2 h the solution was diluted with CH_2Cl_2 and a saturated $NaHCO_3$ solution was added. The aqueous phase was extracted with CH_2Cl_2, and the combined organic phase was washed with cold 1% HCl, saturated $NaHCO_3$, and brine and dried over $MgSO_4$. Concentration *in vacuo* followed by flash chromatography (9:1 hexanes/ethyl acetate) afforded **11** as a white solid (146 mg, 99%): mp 51–52.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 4.57 (dd, J = 8.5, 2.5 Hz, 1H), 4.04 (d, J = 1.2 Hz, 1H), 3.76 (s, 3H), 2.20–1.80 (m, 3H), 1.69 (s, 3H), 1.65–1.50 (m, 1H), 1.39 (s, 3H), 0.89 (s, 9H), 0.13 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.1, 171.0, 86.1, 84.7, 81.1, 79.9, 53.0, 32.1, 26.0, 25.8, 25.2, 22.3, 18.4, −4.5, −5.8; IR (neat) 1738 cm^{-1}; HRMS calcd for $C_{17}H_{30}SiO_6$ 358.1824, found 358.1812; LRMS (EI) *m/z* 358. Anal. Calcd for $C_{17}H_{30}SiO_6$: C, 56.95; H, 8.44. Found: C, 56.88; H, 8.29.

(1″*R,1′*R**,2*S**,5*R**)-5-(1′,2′-Dihydroxy-1′-methylethyl)-5-methyl-2-[1″-[(*tert*-butyldimethylsilyl)oxy]-2″-hydroxyethyl]tetrahydrofuran (12).** A stirred solution of **11** (109 mg, 0.302 mmol) in THF (4 mL) at −78 °C under argon was treated with DIBALH (0.241 g, 1.508 mmol) and allowed to warm to rt. After 2 h a saturated solution of Rochelle's salts was added and the solution was diluted with ethyl acetate and stirred vigorously overnight. The aqueous phase was extracted with ethyl acetate, and the combined organic phase was dried over $MgSO_4$. Concentration *in vacuo* followed by flash chromatography (1:2 hexanes/ethyl acetate) afforded **12** as a white solid (74 mg, 73%): mp 75–76 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.96 (t, J = 7.8 Hz, 1H), 3.76 (dd, J = 11.7, 3.7 Hz, 1H), 3.67 (dd, J = 11.7, 4.4 Hz, 1H), 3.64 (d, J = 11.5 Hz, 1H), 3.58 (t, J = 3.9 Hz, 1H), 3.35 (d, J = 11.5 Hz, 1H), 3.11 (bs, 1H), 2.66 (bs, 2H), 2.05 (m, 1H), 1.90 (m, 2H), 1.59 (m, 1H), 1.20 (s, 3H), 1.12 (s, 3H), 0.91 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 85.9, 83.5, 77.1, 73.0, 67.2, 64.1, 34.0, 26.5, 25.8, 24.1, 21.6, 18.1, −4.5, −4.7; IR (neat) 3396 cm^{-1}; HRMS calcd for $C_{16}H_{34}SiO_5$ + H 335.2254, found 335.2250; LRMS (EI) *m/z* 335. Anal. Calcd for $C_{16}H_{34}SiO_5$: C, 57.44; H, 10.24; Found: C, 57.31; H, 10.20.

(1″*R,1′*R**,2*S**,5*R**)-5-(1′,2′-Dihydroxy-1′-methylethyl)-5-methyl-2-[2″-[(*tert*-butyldimethylsilyl)oxy]-1″-hydroxyethyl]tetrahydrofuran (13).** A solution of the triol **12** (450 mg, 1.35 mmol) in CH_2Cl_2 (40 mL) was treated with DBU (205 mg, 1.35 mmol) and stirred at rt overnight under argon. Saturated NH_4Cl solution was added, and the mixture was extracted with CH_2Cl_2. The organic phase was washed with brine and dried over $MgSO_4$. Concentration *in vacuo* followed by flash chromatography (3:1 hexanes/acetone) afforded recovered starting material (70 mg, 16%) and **13** as a colorless oil (370 mg, 82%): ^1H NMR (300 MHz, $CDCl_3$) δ 3.98 (t, J = 7.3 Hz, 1H), 3.73 (dd, J = 9, 2.9 Hz, 1H), 3.67 (d, J = 11.5 Hz, 1H), 3.60 (t, J = 9 Hz, 1H), 3.54 (dd, J = 9, 2.9 Hz, 1H), 3.31 (d, J = 11.5 Hz, 1H), 3.3–3.0 (bs, 3H), 2.23 (m, 1H), 1.90 (m, 2H), 1.62 (m, 1H), 1.11 (s, 3H), 1.09 (s, 3H), 0.87 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 85.1, 83.0, 76.2, 73.2, 67.1, 63.5, 35.3, 26.8, 25.8, 22.7, 21.9, 18.2, −5.5; IR (neat) 3416 cm^{-1}; HRMS calcd for $C_{16}H_{34}SiO_5$ + H 335.2254, found 335.2261; LRMS (CI) *m/z* 335.

(1″*R,1′*R**,2*S**,5*R**)-5-[(1-Methylethylidene)dioxy]-1′-methylethyl]-5-methyl-2-[2″-[(*tert*-butyldimethylsilyl)oxy]-1″-hydroxyethyl]tetrahydrofuran.** A solution of **13** (197 mg, 0.59 mmol), $Me_2C(OMe)_2$ (1.3 mL), and PPTS (20 mg) in CH_2Cl_2 (10 mL) was stirred at rt under argon for 4 h. Saturated $NaHCO_3$ solution was added, the mixture was extracted with CH_2Cl_2, and the organic phase was dried over $MgSO_4$. Concentration *in vacuo* followed by flash chromatography (4:1 hexanes/ethyl acetate) afforded the acetonide as a colorless oil (212 mg, 96%): ^1H NMR (300 MHz, $CDCl_3$) δ 3.97 (d, J = 8.5 Hz, 1H), 3.93 (t, J = 7.8 Hz, 1H), 3.69 (d, J = 8.5 Hz, 1H), 3.68 (dd, J = 6.8, 5.1 Hz, 1H), 3.59 (dd, J = 10, 6.8 Hz, 1H), 3.49 (dd, J = 6.8, 5.1 Hz, 1H), 2.85 (bs, 1H), 2.08 (m, 1H), 1.94 (m, 1H), 1.80 (m, 1H), 1.60 (dt, J = 12.2, 8.1 Hz, 1H), 1.39 (s, 3H), 1.37 (s, 3H), 1.26 (s, 3H), 1.16 (s, 3H), 0.87 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.6, 84.5, 82.3, 82.1, 72.3, 64.1, 34.8, 27.0, 26.7, 25.8, 22.1, 21.5, 18.2, −5.4, −5.5; IR (neat) 3490 cm^{-1}; HRMS calcd for $C_{19}H_{38}SiO_5$ + H 375.2567, found 375.2543; LRMS (CI) *m/z* 375. Anal. Calcd for $C_{19}H_{38}O_5Si$: C, 60.92; H, 10.22. Found: C, 60.74; H, 10.35.

(1″*R,1′*R**,2*S**,5*R**)-5-[1′,2′-[(1-Methylethylidene)dioxy]-1′-methylethyl]-5-methyl-2-[2″-[(*tert*-butyldimethylsilyl)-oxy]-1″-(methanesulfonyloxy)ethyl]tetrahydrofuran (14).** A solution of the acetonide (210 mg, 0.56 mmol), MsCl (332 mg, 2.8 mmol), and DMAP (1 mg) in pyridine (4 mL) was stirred overnight under argon. The solution was poured into water and extracted with ether. The organic phase was washed with 10% HCl, saturated $NaHCO_3$, and brine and dried over $MgSO_4$. Concentration *in vacuo* followed by flash chromatography (9:1 hexanes/ethyl acetate) afforded **14** as a colorless oil (230 mg, 91%): ^1H NMR (300 MHz, $CDCl_3$) δ 4.54 (dd, J = 7.3, 3.2 Hz, 1H), 3.97 (d, J = 8.5 Hz, 1H), 3.76–3.94 (m, 3H), 3.67 (d, J = 8.5 Hz, 1H), 3.09 (s, 3H), 2.75–2.10 (m, 3H), 1.65 (m, 1H), 1.35 (s, 6H), 1.22 (s, 3H), 1.21 (s, 3H), 0.87 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.5, 89.5, 83.3, 82.0, 81.9, 72.3, 62.9, 38.9, 35.1, 26.9, 26.9, 26.8, 25.8, 22.8, 20.9, 18.3, −5.5, −5.6; HRMS calcd for $C_{20}H_{40}O_7SSi - CH_3$ 437.2029, found 437.2012; LRMS (CI) *m/z* 470, 453. Anal. Calcd for $C_{20}H_{40}O_7SSi$: C, 53.06; H, 8.91. Found: C, 52.89; H, 9.20.

(1″*R,1′*R**,2*S**,5*R**)-5-[1′,2′-[(1-Methylethylidene)dioxy]-1′-methylethyl]-5-methyl-2-(1″,2″-epoxyethyl)tetrahydrofuran (15).** A stirred solution of **14** (183 mg, 0.40 mmol) in THF (4 mL) was treated with Bu_4NF (0.45 mL of a 1.0 M solution in THF, 0.45 mmol). After 45 min solid K_2CO_3 (700 mg) was added

and the mixture was stirred for a further 7 h. Water was added, and the aqueous phase was extracted with ethyl acetate. The organic phase was washed with brine and dried over Na_2SO_4. Concentration *in vacuo* followed by flash chromatography (4:1 hexanes/ethyl acetate) afforded **15** as a colorless oil (96 mg, 98%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.02 (d, J = 8.5 Hz, 1H), 3.95 (t, J = 6.6 Hz, 1H), 3.70 (d, J = 8.5 Hz, 1H), 3.00 (dd, J = 4.1, 2.7 Hz, 1H), 2.70 (t, J = 4.6 Hz, 1H), 2.56 (dd, J = 4.9, 2.7 Hz, 1H), 1.93 (m, 1H), 1.70–1.86 (m, 2H), 1.52 (m, 1H), 1.36 (s, 6H), 1.23 (s, 3H), 1.18 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 109.4, 82.2, 82.1, 81.9, 72.9, 56.6, 44.3, 32.8, 26.9, 26.8, 23.1, 20.0; HRMS calcd for $C_{13}H_{22}O_4 - CH_3$ 227.1283, found 227.1284; LRMS (CI) *m/z* 260. Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.43, H, 9.15. Found: C, 64.08; H, 9.03.

(1″*R,1′*R**,2*S**,5*R**)-5-[1′-Hydroxy-2′-(methanesulfonyloxy)-1′-methylethyl]-5-methyl-2-[2″-[(*tert*-butyldimethylsilyl)oxy]-1″-(methanesulfonyloxy)ethyl]tetrahydrofuran (16).** A solution of **13** (240 mg, 0.72 mmol), MsCl (183 mg, 1.58 mmol), and DMAP (1 mg) in pyridine (5 mL) was stirred overnight under argon. The solution was poured into water and extracted with ether. The organic phase was washed with 10% HCl, saturated $NaHCO_3$, and brine and dried over $MgSO_4$. Concentration *in vacuo* followed by flash chromatography (7:3 hexanes/ethyl acetate) afforded **16** as a colorless oil (300 mg, 85%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.53 (t, J = 5.6 Hz, 1H), 4.11 (d, J = 10.5 Hz, 1H), 4.03 (d, J = 10.5 Hz, 1H), 3.93 (t, J = 7.1 Hz, 1H), 3.72 (d, J = 5.6 Hz, 2H), 3.10 (bs, 1H), 3.08 (s, 3H), 3.04 (s, 3H), 1.97 (m, 3H), 1.73 (m, 1H), 1.27 (s, 3H), 1.18 (s, 3H), 0.86 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 89.3, 82.3, 81.9, 73.8, 71.8, 62.8, 39.0, 37.2, 35.7, 25.9, 25.8, 21.8, 21.5, 18.2, −5.5, −5.6; IR (neat) 3500 cm^{-1}; HRMS calcd for $C_{18}H_{38}S_2SiO_9$ + H 491.1805, found 491.1804; LRMS (CI) *m/z* 491.

(1″*R,1′*R**,2*S**,5*R**)-5-(1′,2′-Epoxy-1′-methylethyl)-5-methyl-2-[2″-[(*tert*-butyldimethylsilyl)oxy]-1″-(methanesulfonyloxy)ethyl]tetrahydrofuran (17).** A mixture of **16** (250 mg, 0.51 mmol) and K_2CO_3 (300 mg, 2.17 mmol) in methanol (10 mL) was stirred at rt for 1.5 h. Water was added, and the solution was extracted with ether. The combined organic phase was washed with brine and dried over Na_2SO_4. Concentration *in vacuo* followed by flash chromatography (85:15 hexanes/ethyl acetate) afforded **16** as a colorless oil (195 mg, 97%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.54 (dd, J = 7.6, 3.7 Hz, 1H), 3.92–3.74 (m, 3H), 3.12 (s, 3H), 2.75 (d, J = 4.9 Hz, 1H), 2.56 (d, J = 4.9 Hz, 1H), 2.14–1.62 (m, 4H), 1.31 (s, 3H), 1.22 (s, 3H), 0.87 (s, 9H), 0.06 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 89.2, 83.5, 80.0, 62.8, 57.2, 51.9, 38.9, 35.2, 27.7, 25.8, 22.8, 18.3, 17.7, −5.5, −5.6; HRMS calcd for $C_{17}H_{34}O_6SSi$ 395.1923, found 395.1928; LRMS (CI) *m/z* 395. Anal. Calcd for $C_{17}H_{34}O_6SSi$: C, 51.74, H, 8.68. Found: C, 52.07; H, 8.81.

Acknowledgment. The authors thank the National Institutes of Health for their generous support of this research and the Science and Engineering Research Council–NATO for a postdoctoral fellowship (to S.S.).

Supplementary Material Available: ^{1}H and ^{13}C NMR spectra of compounds for which no elemental analysis was obtained (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.