5,13,21,29-Tetrabromo-8,16,24,32-tetrahydroxy[2.2.2.2]metacyclophane (17). To a mixture of 160 mg (0.33 mmol) of **2b** and 200 mg of Fe powder in 50 mL of $CHCl_3$ was added a solution of 422 mg (2.6 mmol) of Br_2 in 20 mL of $CHCl_3$. After the reaction mixture was stirred at room temperature for 12 h, it was poured into ice–water and extracted with $CHCl_3$. The extract was washed with water, dried over $MgSO_4$, and evaporated in vacuo to give 230 mg (87%) of **17**·C_6H_6, colorless needles (benzene), mp >350 °C: IR (KBr) ν(OH) 3220 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.71 (16 H, br s), 6.93 (8 H, s), 7.74 (4 H, br s, exchanged with D_2O); MS m/z 792, 794, 796, 798, 800 (M^+). Anal. Calcd for $C_{32}H_{28}O_4Br_4 \cdot C_6H_6$: C, 52.20; H, 3.92. Found: C, 51.90; H, 3.97.

[2.2.2.2]Metacyclo-1,4-benzoquinonophane (19). After a mixture of 100 mg (0.26 mmol) of **2b** and 4 mL of 0.88 M solution of $Tl(OCOCF_3)_3$ in CF_3CO_2H was stirred at room temperature for 13 h in the dark, it was poured into ice–water and extracted with $CHCl_3$. The extract was washed with water, dried over $MgSO_4$, and concentrated in vacuo to leave a residue, which was subjected to preparative TLC (precoated plates with concentrating zone, 20 × 20 cm, kiesel gel 60F_{254}S) using ether as an eluant. The fraction of R_f = 0.45 afforded 8 mg (5%) of **19**·$3H_2O$ as orange prisms (CCl_4), mp 129–132 °C: IR (KBr) ν 1650 cm^{-1}; ^1H NMR δ 2.62 (16 H, s), 6.48 (8 H, s); MS m/z 536 (M^+). Anal. Calcd for $C_{32}H_{24}O_8 \cdot 3H_2O$: C, 65.08; H, 5.08. Found: C, 65.57; H, 5.17.

5,8,13,16,21,24,28,32-Octaacetoxy[2.2.2.2]metacyclophane (20). A mixture of 10 mg (0.017 mmol) of **19**·$3H_2O$, 500 mg of zinc powder, and a few drops of concentrated hydrochloric acid in 10 mL of acetic acid and 10 mL of acetic anhydride was refluxed for 10 min, poured into water, and extracted with $CHCl_3$. The extract was washed with water, dried over $MgSO_4$, and evaporated in vacuo to give 9 mg (59%) of **20** as colorless needles (CCl_4), mp 350 °C: IR (KBr) ν 1750 cm^{-1}; ^1H NMR δ 1.30 (6 H, s), 1.69 (6 H, s), 2.17 (12 H, s), 2.65 (16 H, br s), 6.85 (8 H, s); MS m/z 880 (M^+). Anal. Calcd for $C_{48}H_{48}O_{16} \cdot 0.5H_2O$: C, 64.79; H, 5.54. Found: C, 65.03; H, 5.62.

Registry No. **1a**, 125685-43-0; **1b**, 76447-59-1; **1c**, 125666-21-9; **2a**, 125666-22-0; **2b**, 125666-23-1; **2c**, 125666-24-2; **3a**, 125666-19-5; **3b**, 76447-58-0; **3c**, 125666-20-8; **4a**, 125665-97-6; **4b**, 76447-56-8; **4c**, 125665-98-7; **5a**, 125665-99-8; **5b**, 125666-00-4; **5c**, 125666-01-5; **6a**, 125666-02-6; **6b**, 125666-03-7; **6c**, 125666-04-8; **7a**, 125666-14-0; **7b**, 125666-17-3; **7c**, 125666-18-4; **9**, 125666-05-9; **10**, 125666-06-0; **11**, 125666-07-1; **12**, 125666-08-2; **13**, 125666-09-3; **14**, 125666-10-6; **15**, 125666-11-7; **16**, 125666-12-8; **17**, 125666-13-9; **19**, 125666-15-1; **20**, 125666-16-2; **21**, 98085-84-8; 5,5′-di-*tert*-butyl-2,2′-dihydroxydiphenylmethane, 799-13-3; 1,3-bis(5-*tert*-butyl-2-methoxyphenyl)propane, 108656-63-9.

Approaches to Avermectin Assembly: A Concise Stereospecific Synthesis of the Hexahydrobenzofuran Entity

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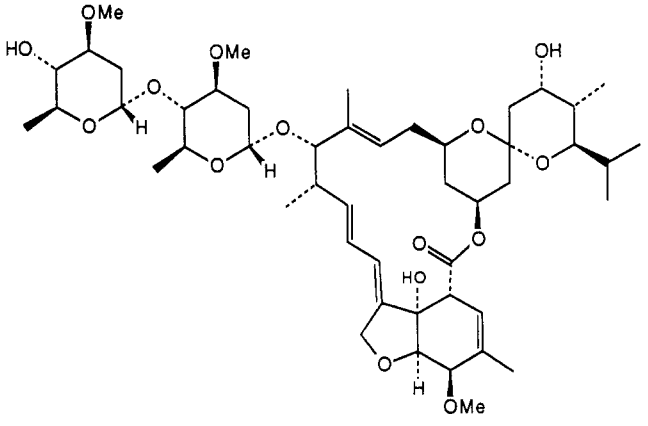
Received October 30, 1989

Epoxy ketone **18** was prepared in racemic form via the Diels–Alder reaction of 1-acetoxy-1,3-pentadiene with acrylic acid, subsequent iodolactonization, ortho ester protection, and oxidation. Reaction of **18** with 4-[(*tert*-butyldiphenylsilyl)oxy]-2-lithio-1-(lithiooxy)-(*Z*)-2-butene, which was prepared from stannane **19** and butyllithium, gave the bicyclic avermectin fragment **21**.

Introduction

The avermectins[1] and milbemycins[2] are potent parasiticidal and anthelmintic agents isolated from *Streptomyces avermitilis* and *S. hygroscopicus* subsp. *aureolacrimosus*, respectively. These molecules, for example, avermectin A_{2b} (**1**), are attractive synthetic targets on account of their significant biological activities and challenging molecular architecture. Several total syntheses of milbemycin β_3,[3] milbemycin β_1 and E,[4] and avermectin A_{1a}[5] have recently been published. In addition, many synthetic studies of spiroketals and of the "southern" hexahydrobenzofuran ring system have been described.[6] In spite of all these



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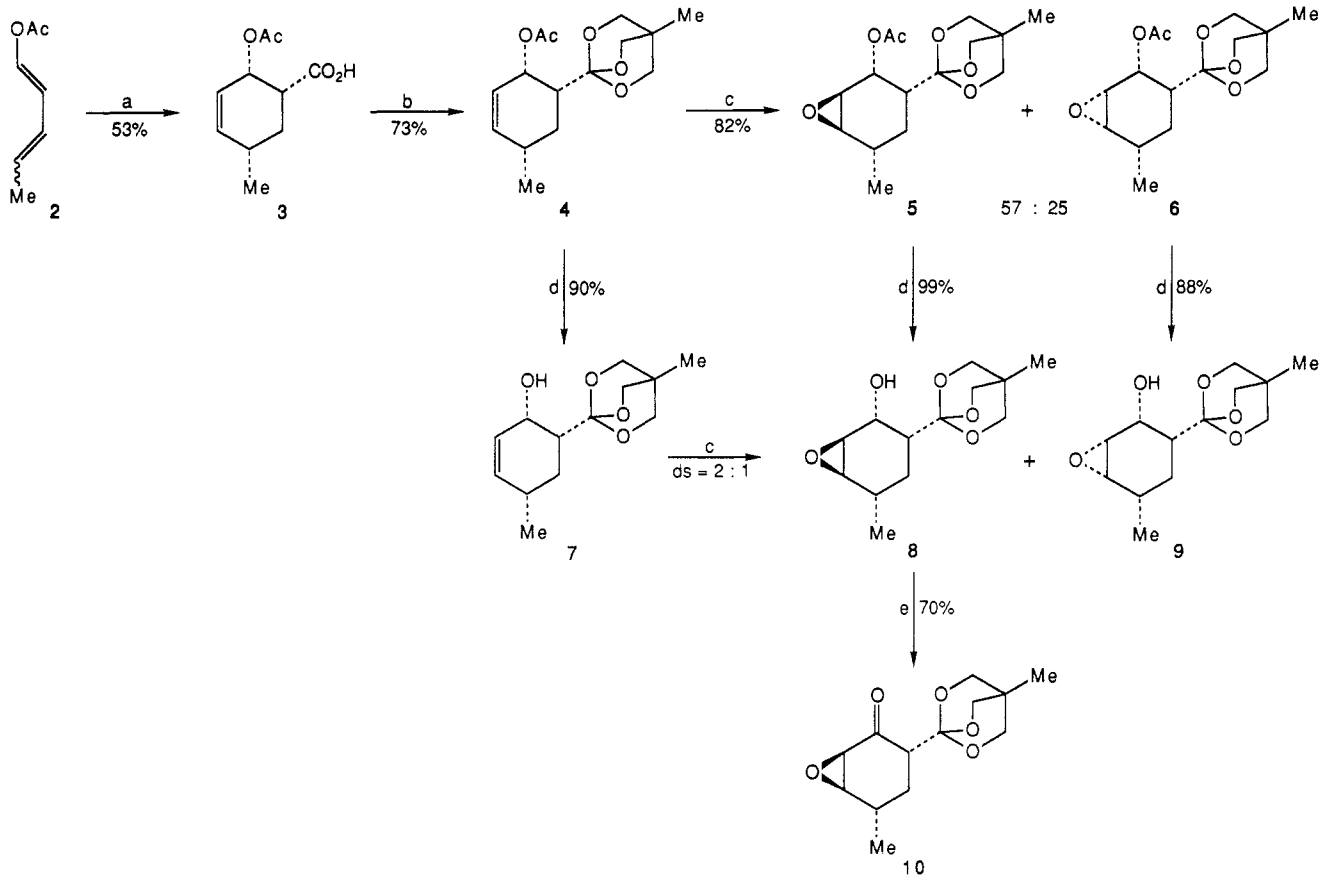
Scheme I[a]



[a] Reagents: (a) CH_2=$CHCO_2H$, BH_3·THF, I_2, CH_2Cl_2; (b) $(COCl)_2$, DMF, MeCN; pyridine, $HOCH_2\overline{C(Me)CH_2OCH_2}$; BF_3·OEt_2, CH_2Cl_2; (c) $NaHCO_3$, MCPBA, CH_2Cl_2; (d) NaOMe, MeOH; (e) DMSO, TFAA, CH_2Cl_2, -78 °C; Et_3N.

studies, there is still a need to develop a concise stereospecific method to elaborate the southern zone.[7] Recently we reported a simple method to prepare cis-fused octahydrobenzofurans from the reaction of 4-[(*tert*-butyldiphenylsilyl)oxy]-2-lithio-1-(lithiooxy)-(*Z*)-2-butene with epoxy ketones.[8] We now describe the application of this chemistry in the avermectin milbemycin area.

Results and Discussion

The acetoxy dienes **2** were prepared by the copper(II) acetate and 4-toluenesulfonic acid catalyzed acetylation of 2-pentenal using isopropenyl acetate.[9] Distillation gave **2** as a mixture of the 1*E*,3*Z* and 1*E*,3*E* isomers (5:4). However, this stereochemically inauspicious start is of no consequence. Thus, the Diels–Alder reaction of dienes **2** with acrylic acid gave the crystalline cyclohexenecarboxylic acid derivative **3** (53%) (Scheme I). This cycloaddition is noteworthy since it was carried out using *dual catalysis by diborane and iodine.* The iodine isomerized the major unwanted 1*E*,3*Z* isomer of **2** to the more reactive 1*E*,3*E* isomer. Additionally, diborane catalyzed the cycloaddition via the (acryloxy)borane.[10] Recently Yamamoto has reported that Diels–Alder reactions may be dramatically accelerated using α,β-unsaturated (acyloxy)boranes as dienophiles and this elegant methodology is clearly pivotal in the preparation of the cyclohexene derivative **3**.

Carboxylic acid **3** was converted into the bicyclic ortho ester **4** by esterification with 3-methyloxetane-3-methanol and rearrangement using boron trifluoride etherate according to the Corey protocol.[11] Epoxidation of the allylic acetate **4** using 3-chloroperoxybenzoic acid gave two isomeric epoxy acetates **5** (57%) and **6** (25%). The stereochemical assignments of these compounds were determined by subsequent transformations. Zemplen methanolysis of each ester **5** and **6** gave the corresponding epoxy alcohols **8** and **9**. These same two alcohols were obtained via methanolysis of the acetate **4** and 3-chloroperoxybenzoic acid mediated epoxidation of the resultant allylic alcohol **7**. Much to our surprise this epoxidation also provided the trans isomer **8** as the major product (2:1). Clearly, hydrogen bonding between the peracid and the alcohol **7** is of little consequence in directing the stereochemistry of epoxidation. Finally, Swern oxidation[12] of epoxide **8** smoothly gave the corresponding epoxy ketone **10**.

The stereochemical assignments in this chemistry are based upon an X-ray crystallographic study of the minor epoxy alcohol **9** (Figure 1, Table I). The final ORTEP drawing clearly shows that the bulky ortho ester substituent is pseudoequatorial and that all ring substituents are cis.

(7) The major problem with existing strategies is the facile isomerization of Δ^3 to Δ^2 (avermectin numbering) and inefficient C-2 epimerization on deconjugation.

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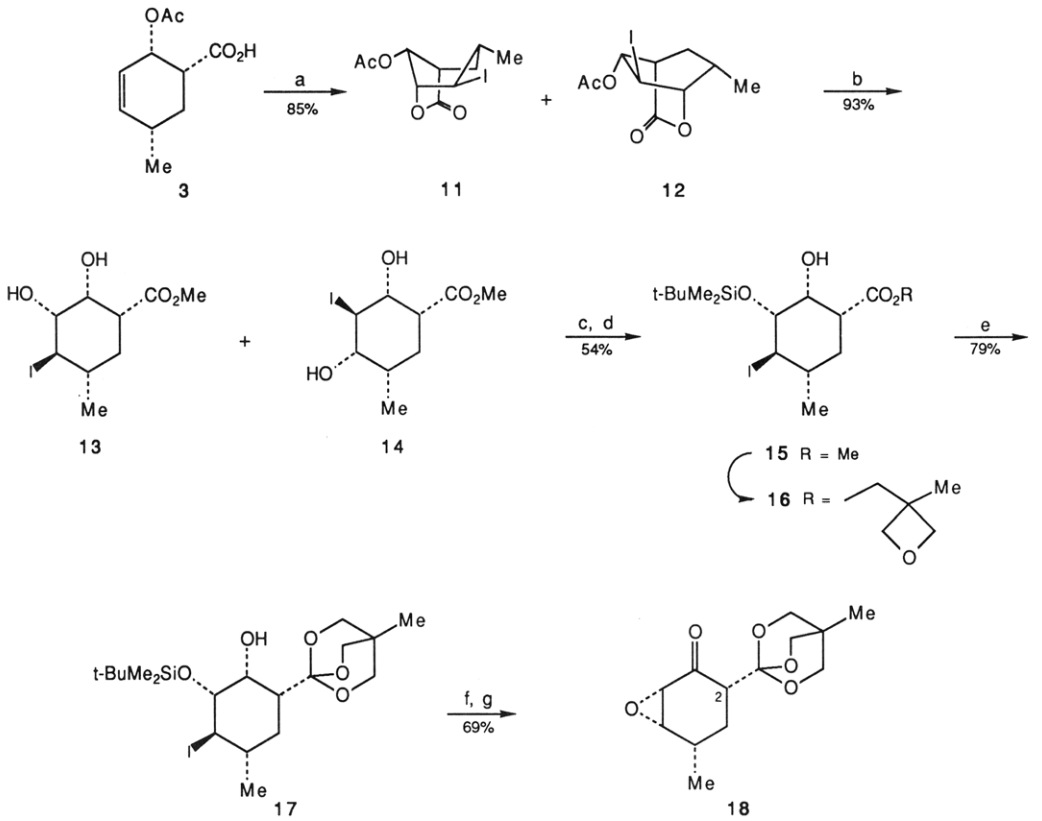
Scheme II[a]



[a] Reagents: (a) NIS, THF, reflux, $NaHCO_3$; (b) MeOH, AcCl, reflux; (c) *t*-$BuMe_2SiCl$, imidazole, DMF, DMAP; (d) $Ti(O\text{-}i\text{-}Pr)_4$ (0.3 equiv), $HOCH_2\overline{C(Me)CH_2OCH_2}$ (20 equiv), 80 °C; (e) $BF_3{\cdot}OEt_2$, CH_2Cl_2, 0 °C; Et_3N, Et_2O, −78 °C; (f) Bu_4NF, THF; (g) DMSO, TFAA, CH_2Cl_2, −78 °C; Et_3N, *i*-PrOH.

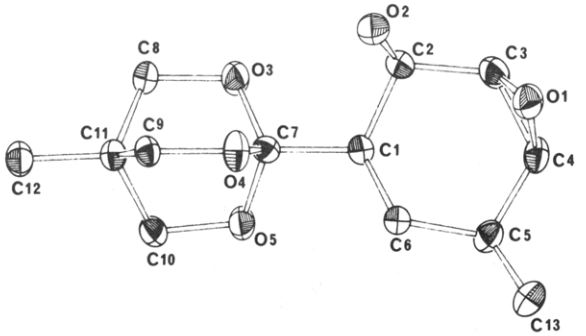


Figure 1. ORTEP drawing of (1*S**,2*R**,3*R**,5*S**,6*S**)-2-hydroxy-5-methyl-3-(2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-7-oxabicyclo-[4.1.0]heptane (**9**). Thermal elipsoids are drawn at 50% probability level.

Since the direct epoxidation of either **4** or **7** proceeded with poor stereochemical control, we decided to examine an iodolactonization strategy[13] to prepare the required epoxy alcohol **9** (Scheme II). Iodolactonization of acid **3** gave a 3.3:1 mixture of isomeric lactones **11** and **12** and these were smoothly methanolyzed, under acidic conditions, to yield the methyl esters **13** and **14**. Although the major ester **13** did not undergo titanium tetraisopropoxide catalyzed transesterification,[14] the derived equatorial mono silyl ether **15** was easily converted into the oxetane ester **16**. Presumably, chelation of titanium(IV) by the cis diol unit in ester **13** resulted in suppression of the exchange catalysis. It is interesting to note that the oxetane ester, iodo substituent, and the silyl ether survived the titanium(IV)-mediated transesterification reaction. The oxetane ester **16** was rearranged[11] in the presence of boron trifluoride etherate to reveal the ortho ester. Again, it is appropriate to comment on chemoselectivity. Both the silyl ether and iodo substituents were unchanged during the rearrangement reaction. Finally, fluoride-mediated epoxide closure and Swern oxidation[12] gave the target epoxy β-keto ortho ester **18**. In contrast to the preparation of the isomer **10**, both the Swern oxidation and isolation of the epoxy ketone **18** were problematic. Thus, 2-propanol was added to quench the excess oxidant and the product

Table I. Summary of the Crystal Structure Data

formula	$C_{13}H_{18}O_5$
M_r	254.28
cryst. size, mm	0.36 × 0.32 × 0.25
cryst. system	orthorhombic
space group	$P2_12_12_1$ (No. 19)
a, Å	5.693 (2)
b, Å	7.820 (1)
c, Å	27.323 (3)
V, Å^3	1216.4 (7)
Z	4
d_{calcd}, g cm^{-3}	1.39
radiation	graphite-monochromated Mo Kα (λ = 0.71069 Å)
scan type	ω
2θ range, deg	4–55
scan width, deg	0.90 + 0.35 tau θ
unique data	1683
unique data with $I > 3\sigma(I)$	1307
no. of parameters	244
$R(F)$	0.036
$R_w(F)$	0.043
GOF	1.26

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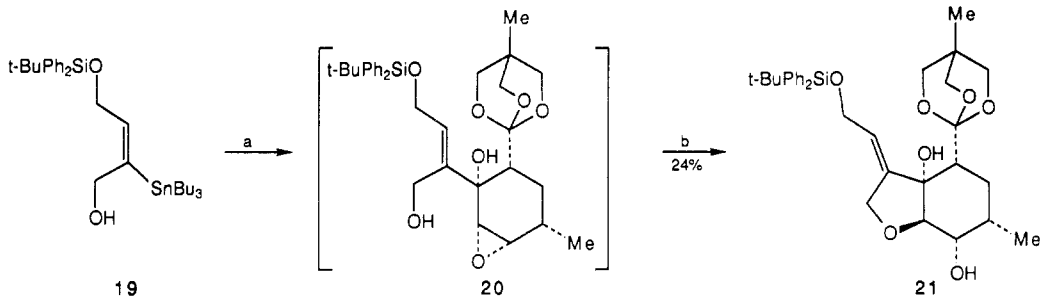
Scheme III[a]



[a] Reagents: (a) BuLi (2.1 equiv), THF, −78 to −35 °C; **18**, THF, −78 °C; NH_4Cl, H_2O; (b) *t*-BuOK, THF.

18 was isolated by recrystallization, not chromatography. Without these precautions, extensive decomposition of **18** was observed.

We anticipated that the masked β-keto ester **18** should readily react with nucleophiles, since the acidity of the C-2 proton is suppressed by the ortho ester residue. Much to our delight, this expectation is correct (Scheme III). Thus, sequential reaction of the stannane **19**[8] with *n*-butyllithium and ketone **18** gave an adduct, presumably **20**. This substance was not isolated but was reacted further under basic conditions to produce the bicyclic southern fragment **21**. Although the ring annulation proceeded in only modest yield (24% overall), the strategy herein described has several major advantages. First, the sequence is experimentally concise and remarkable in that every single compound with the sole exception of **21** is crystalline. Second, the strategy directly incorporates Δ^8 (avermectin numbering) with the required *E* geometry. Finally, the C-1 substituent is introduced at the correct carboxylic acid oxidation level. Unwanted side reactions are suppressed by ortho ester protection. Further application of this chemistry will be reported in due course.

Experimental Section

Melting points were determined on a Reichert hot stage apparatus and are uncorrected. Infrared spectra were recorded as KBr disks or films on a Sargent Welch SP3-100, Perkin-Elmer 283, or Nicolet 7199 FT instrument. ^1H NMR spectra were recorded on a JEOL FX270, Varian VXR-300, or Varian XL-400 spectrometer using tetramethylsilane as internal standard. Mass spectra were recorded on a VG7070F or VG70-250SE mass spectrometer. Microanalyses were determined at G.D. Searle and Company, Skokie, IL.

Hexane, diethyl ether, and ethyl acetate were purified by distillation. THF was dried by distillation under nitrogen from sodium benzophenone ketyl. DMF and CH_2Cl_2 were freshly distilled from CaH_2. All reactions were carried out under dry nitrogen. Silica gel for chromatography refers to the Merck product kieselgel 60 (Art. 9385). Thin-layer chromatography was performed on Merck kieselgel 60 F254 (Art. 5715).

1-Acetoxy-1,3-pentadiene (2). Pentenal (20 g) was added dropwise to a reluxing solution of TsOH (0.5 g) and copper(II) acetate (0.10 g) in isopropenyl acetate (48 g) over 40 min. After an additional 40 min, Me_2CO and excess isopropenyl acetate were slowly removed by distillation. Further distillation at reduced pressure, followed by fractional redistillation, gave **2** (14.7 g, 50%) as a colorless oil containing two isomers (1*E*,3*Z*/1*E*,3*E* = 5:4): bp 30–33 °C (1.0 mmHg); IR (film) 3050, 2940, 1765, 1375, 1225, 1115 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, 0.56 H, *J* = 14 Hz), 7.28 (d, 0.44 H, *J* = 14 Hz), 6.32 (app t, 0.56 H, *J* = 14 Hz), 5.95 (m, 1.44 H), 5.68, 5.54 (2 m, 1 H), 2.15 (s, 1.67 H), 2.13 (s, 1.33 H), 1.76 (d, *J* = 6.8 Hz), 1.73 (dd, *J* = 7.2, 1.6 Hz), 1.76–1.73 (3 H); MS (EI) *m/e* 126 ($M^{+\cdot}$), 115, 93, 84, 69, 55; high resolution MS (EI) calcd for $C_7H_{10}O_2$ ($M^{+\cdot}$) 126.0681, found ($M^{+\cdot}$) 126.0691.

(1*R,2*S**,5*S**)-2-Acetoxy-5-methyl-3-cyclohexene-1-carboxylic Acid (3).** To a solution of acrylic acid (2.8 mL) in CH_2Cl_2 (100 mL) at 0 °C was added 1 M diborane in THF (10.3 mL). After 30 min, 1-acetoxy-1,3-pentadiene (**2**) (13.0 g) and iodine (2–3 crystals) were added. Further acrylic acid (11.3 mL) in CH_2Cl_2 (10 mL) was added slowly via syringe pump over 36 h. After a total of 67 h, the solution was washed with aqueous sodium bisulfite and H_2O (2×), dried, and evaporated in vacuo. Recrystallation from Et_2O/hexanes gave the pure acid **3** (10.8 g, 53%): mp 92–93 °C; R_f 0.5 (Et_2O/hexanes/HOAc = 50:50:1); IR (KBr) 3040 (br), 2990, 1740, 1705, 1240, 965 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.86 (m, 2 H), 5.53 (m, 1 H), 2.76 and 2.73 (m, 1 H), 2.23 (m, 1 H), 2.05 (m, 1 H), 2.02 (s, 3 H), 1.53 (app q, 1 H, *J* = 12.8 Hz), 1.09 (d, 3 H, *J* = 7.2 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.8, 170.4, 139.8, 122.7, 66.0, 43.7, 31.0, 27.5, 21.0, 20.8; MS (EI) *m/e* 199 (MH^+), 155, 139, 93. Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.53; H, 7.19.

(1*R,2*S**,5*S**)-2-Acetoxy-5-methyl-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-3-cyclohexene (4).** To a solution of DMF (2.3 mL) in MeCN (20 mL) at 0 °C was added oxalyl chloride (2.1 mL) dropwise with stirring over 10 min. After an additional 10 min, carboxylic acid **3** (3.96 g) in MeCN (10 mL) was added. The solution was allowed to stand for 20 min; then pyridine (8 mL) and 3-methyl-3-oxetanemethanol (2.8 mL) were added simultaneously. The mixture was warmed to room temperature and allowed to stand for 23 h, diluted with Et_2O, washed with H_2O and aqueous $CuSO_4$ (2×), dried, and evaporated in vacuo. Chromatography of the residue (silica, 1:1 Et_2O/hexanes) gave (1*R**,2*S**,5*S**)-(3-methyl-3-oxetanyl)methyl 2-acetoxy-5-methyl-3-cyclohexenecarboxylate (5.27 g, 93%), which was used directly in the next step.

To a solution of the ester (5.3 g) in CH_2Cl_2 (40 mL) at 0 °C was added BF_3·OEt_2 (0.46 mL). After 6 h, the solution was cooled to −78 °C and Et_3N (2.6 mL) in Et_2O (150 mL) was added. The suspension was allowed to warm up to room temperature and filtered. Evaporation of the solvent in vacuo and chromatography (silica pretreated with 1% Et_3N in hexanes; Et_2O/hexanes 1:1) gave **4** (4.18 g, 78%): mp 107–108 °C (Et_2O, hexanes); R_f 0.62 (Et_2O); IR (KBr) 2985, 1740, 1250, 990 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.74 (m, 2 H), 5.55 (m, 1 H), 3.86 (s, 6 H), 2.20 (m, 1 H), 2.03 (s, 3 H), 1.96 (m, 1 H), 1.89 (m, 1 H), 1.40 (app q, 1 H, *J* = 12 Hz), 1.04 (d, 3 H, *J* = 6.8 Hz), 0.79 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 139.1, 123.7, 108.8, 72.5, 64.2, 44.6, 32.1, 30.4, 26.8, 21.4, 20.9, 14.5; MS (EI) *m/e* 282 ($M^{+\cdot}$), 239, 137, 93, 55, 43. Anal. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.86. Found: C, 63.76; H, 8.04.

(1*R,2*R**,3*R**,5*S**,6*R**)-2-Acetoxy-5-methyl-3-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-7-oxabicyclo[4.1.0]heptane (5) and the 1*S**,2*R**,3*R**,5*S**,6*S** Isomer (6).** To a solution of the allylic acetate **4** (1.0 g) in CH_2Cl_2 (5 mL) at room temperature were added $NaHCO_3$ (1.2 g) and *m*-chloroperbenzoic acid (1.2 g). Stirring was continued for 6 h, and the solution was washed with H_2O, aqueous sodium bisulfite, and aqueous sodium bicarbonate, dried, and evaporated in vacuo. Chromatography of the residue (silica, 2:1 hexanes/Et_2O) gave the less polar isomer **5** (0.66 g, 57%): mp 115–116 °C (CH_2Cl_2, hexanes); R_f 0.65 (Et_2O); IR (KBr) 2990, 2890, 1750, 1315, 1240, 1010 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.79 (br s, 1 H), 3.82 (s, 6 H), 3.11 (m, 1 H), 2.87 (d, 1 H, *J* = 3.6 Hz), 2.07 (s, 3 H), 2.01 (m, 2 H), 1.64 (m, 1 H), 1.26 (app q, 1 H, *J* = 11.6 Hz), 1.10 (d, 3 H, *J* = 7.2 Hz), 0.78 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2, 108.8, 72.4, 65.7, 57.1, 53.4, 39.6, 30.4, 28.7, 25.0, 21.2, 19.6, 14.4; MS (EI) *m/e* 298 ($M^{+\cdot}$), 268, 197, 110, 81, 55. Anal. Calcd for $C_{15}H_{22}O_6$: C, 60.39; H, 7.43.

Found: C, 60.13; H, 7.49. Further elution of the column gave **6** (0.26 g, 25%): mp 106–108 °C (CH_2Cl_2, hexanes); R_f 0.52 (Et_2O); IR (KBr) 2995, 2895, 1725, 1265, 1005 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.44 (br t, 1 H, J = 4.4 Hz), 3.83 (s, 6 H), 3.42 (dd, 1 H, J = 3.6, 5.2 Hz), 3.08 (d, 1 H, J = 3.2 Hz), 2.11 (s, 3 H), 1.88 (m, 1 H), 1.71 (m, 1 H) 1.50 (m, 1 H), 1.34 (app q, 1 H, J = 13.2 Hz), 1.14 (d, 3 H, J = 7.2 Hz), 0.78 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.6, 108.5, 72.5, 64.4, 57.4, 52.6, 44.9, 31.6, 30.4, 22.6, 21.0, 18.3, 14.4; MS (EI) m/e 298 ($M^{+\cdot}$), 268, 197, 137, 110, 81, 55, 43. Anal. Calcd for $C_{15}H_{22}O_6$: C, 60.39; H, 7.43. Found: C, 60.15; H, 4.50.

(1*R,2*R**,3*R**,5*S**,6*R**)-2-Hydroxy-5-methyl-3-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-7-oxabicyclo-[4.1.0]heptane (8).** To a solution of sodium (0.01 g) in MeOH (1.5 mL) was added epoxy acetate **5** (0.1 g). The solution was allowed to stand at room temperature for 1.5 h, diluted with CH_2Cl_2, washed with H_2O, dried, and evaporated in vacuo to give **8** (86 mg, 99%): mp 130–132 °C (Et_2O, hexanes); R_f 0.63 (Et_2O); IR (KBr) 3560, 2990, 1410, 1075, 1005 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.56 (br s, 1 H), 3.92 (s, 6 H), 3.45 (s, 1 H), 3.22 (t, 1 H, J = 2.8 Hz), 2.88 (d, 1 H, 2.8 Hz), 2.0 (m, 1 H), 1.92 (m, 1 H), 1.55 (m, 1 H), 1.24 (app q, 1 H, J = 11.6 Hz), 1.10 (d, 3 H, J = 7.2 Hz), 0.82 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 109.6, 72.5, 64.3, 57.2, 55.6, 40.4, 30.3, 29.0, 23.7, 19.7, 14.4; MS (EI) m/e 256 ($M^{+\cdot}$), 226, 157, 144, 101, 73, 55. Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.92; H, 7.96.

(1*S,2*R**,3*R**,5*S**,6*S**)-2-Hydroxy-5-methyl-3-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-7-oxabicyclo-[4.1.0]heptane (9).** Epoxy acetate **6** (0.1 g) was hydrolyzed in the same way to give **9** (0.076 g, 88%): mp 141–143 °C (CH_2Cl_2, hexanes); R_f 0.24 (Et_2O); IR (KBr) 3505, 2980, 1280, 1000, 850 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.44 (m, 1 H), 3.91 (s, 6 H), 3.37 (dd, 1 H, J = 4.4, 4.8 Hz), 3.11 (br d, 1 H, J = 3.2 Hz), 3.07 (d, 1 H, J = 3.6 Hz), 1.88 (m, 1 H), 1.60 (m, 1 H), 1.44 (m, 1 H), 1.30 (app q, 1 H, J = 12 Hz), 1.14 (d, 3 H, J = 6.8 Hz), 0.81 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 109.0, 72.5, 62.6, 57.9, 54.4, 45.9, 31.9, 30.3, 21.7, 18.4, 14.4; MS (EI) m/e 257 (MH^+) 226, 157, 137, 109, 93, 81, 55. Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.66; H, 7.94.

(1*R,2*S**,5*S**)-2-Hydroxy-5-methyl-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-3-cyclohexene (7).** To a solution of Na (0.137 g) in MeOH (20 mL) was added the allylic acetate **4** (1.4 g). The solution was allowed to stand at room temperature for 16 h; then it was diluted with H_2O and extracted with Et_2O (3×). The combined extracts were washed with H_2O, dried, and evaporated in vacuo. Chromatography (silica, 1:1 Et_2O/hexanes) gave **7** (1.07 g, 90%): mp 80–82 °C (Et_2O, hexanes); R_f 0.37 (Et_2O); IR (KBr) 3580, 2990, 1410, 1000 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.80 (m, 1 H), 5.68 (d, 1 H, J = 9.6 Hz), 4.39 (m, 1 H), 3.95 (s, 6 H), 3.22 (s, 1 H), 2.18 (m, 1 H), 1.86 (dt, 1 H, J = 3.2, 13.6 Hz), 1.79 (m, 1 H), 1.40 (app q, 1 H, J = 11.2 Hz), 1.03 (d, 1 H, J = 6.8 Hz), 0.83 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.1, 126.7, 109.5, 72.5, 62.5, 45.5, 32.3, 30.3, 25.7, 21.1, 14.5; MS (EI) m/e 240 ($M^{+\cdot}$), 210, 157, 137, 94, 85, 55. Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.97; H, 8.39. Found: C, 64.85; H, 8.58.

Epoxidation of Allylic Alcohol 7. To a solution of **7** (0.24 g) in CH_2Cl_2 (5 mL) at room temperature was added *m*-chloroperbenzoic acid (0.32 g) and saturated aqueous $NaHCO_3$ (2 mL). The solution was allowed to stand for 3.5 h, washed with H_2O, aqueous sodium bisulfite, and aqueous sodium bicarbonate, dried, and evaporated in vacuo to give a crude mixture of epoxy alcohols **8** and **9** (0.235 g) (2:1; ^1H NMR).

(1*R,3*R**,5*S**,6*R**)-5-Methyl-3-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-7-oxabicyclo[4.1.0]heptan-2-one (10).** To a solution of DMSO (50 μL) in CH_2Cl_2 (3 mL) at −78 °C was added trifluoroacetic anhydride (0.1 mL). After 10 min, the epoxy alcohol **8** (60 mg) in CH_2Cl_2 (0.5 mL) was added and stirring was continued for an additional 30 min, when Et_3N (0.36 mL) was added. After 5 min the mixture was allowed to warm up to 0 °C. The solution was washed with aqueous $NaHCO_3$, dried, and evaporated in vacuo. Chromatography (silica, hexane/Et_2O 1:1) gave **10** (42 mg, 70%): mp 145 °C (sublimes) (CH_2Cl_2, hexanes); R_f 0.50 (Et_2O); IR (KBr) 2980, 1730, 1470, 1000, 830 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.92 (s, 6 H), 3.23 (m, 3 H), 2.40 (m, 1 H), 2.27 (m, 1 H), 1.57 (app dt, 1 H, J = 10.4, 10.8 Hz), 1.12 (d, 3 H, J = 7.2 Hz), 0.81 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 203.0, 107.8, 72.3, 64.8, 56.7, 47.3, 35.0, 30.4, 28.6, 18.7, 14.5; MS (EI) m/e 254 ($M^{+\cdot}$), 224, 199, 153, 126, 107, 55. Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.40; H, 7.13. Found: C, 61.38; H, 7.27.

(1*R,3*S**,4*R**,5*R**,8*R**)-8-Acetoxy-4-iodo-3-methyl-6-oxabicyclo[3.2.1]octan-7-one (11) and (1*S**,4*R**,5*R**,6*S**,7*S**)-5-Acetoxy-6-iodo-7-methyl-2-oxabicyclo[2.2.2]octan-3-one (12).** To a solution of the acid **3** (1.98 g) in THF (30 mL) were added $NaHCO_3$ (1.01 g) and *N*-iodosuccinimide (5.0 g). The solution was heated to reflux for 18 h, cooled, diluted with Et_2O (100 mL), washed with aqueous $Na_2S_2O_3$ and aqueous $NaHCO_3$, dried, and evaporated in vacuo. Chromatography of the residue (silica; Et_2O/hexanes 1:3) gave **11** and **12** (3.3:1) (2.75 g, 85%). The product was used directly in the next step. Careful chromatography of a small sample (silica, Et_3O/hexanes 1:6) gave the less polar isomer **11**: mp 72–73 °C (Et_2O, hexanes); R_f 0.50 (3:1 hexanes/Et_2O developed 3×); IR (KBr) 3040, 1795, 1745, 1370, 1230, 1160, 1020, 910, 695 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.69 (s, 1 H), 4.90 (m, 1 H), 4.27 (m, 1 H), 2.75 (m, 1 H), 2.49 (m, 1 H), 2.40 (m, 1 H), 2.12 (s, 3 H), 1.82 (m, 1 H), 1.23 (d, 3 H, J = 7.6 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.7, 170.0, 84.9, 76.1, 41.6, 36.5, 29.9, 27.2, 23.5, 20.9; MS (EI) m/e 324 ($M^{+\cdot}$), 253, 197, 155, 137, 111, 93, 81, 46. Anal. Calcd for $C_{10}H_{13}IO_4$: C, 37.06; H, 4.04. Found: C, 37.06; H, 4.04. Further elution gave the more polar isomer **12**: mp 114–115 °C (Et_2O, hexanes); R_f 0.43 (3:1 hexane/Et_2O, developed 3×); IR (KBr) 2995, 1765, 1745, 1360, 1245, 1025 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.25 (dd, 1 H, J = 0.8, 3.2 Hz), 4.41 (d, 1 H, J = 3.6 Hz), 4.23 (t, 1 H, J = 4 Hz), 2.80 (m, 1 H), 2.70 (m, 1 H), 2.27 (m, 1 H), 2.10 (s, 3 H), 1.48 (dt, 1 H, J = 14.4, 3.6 Hz), 1.15 (d, 3 H, J = 7.2 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4, 169.6, 83.5, 79.3, 41.5, 28.0, 26.4, 21.7, 20.7, 19.4; MS (EI) m/e 324 ($M^{+\cdot}$), 264, 220, 155, 137, 111, 93. Anal. Calcd for $C_{10}H_{13}IO_4$: C, 37.06; H, 4.04. Found: C, 37.05; H, 4.06.

(1*R,2*R**,3*R**,4*R**,5*S**)-Methyl 2,3-Dihydroxy-4-iodo-5-methylcyclohexanecarboxylate (13) and (1*R**,2*R**,3*R**,4*S**,5*S**)-Methyl 2,4-Dihydroxy-3-iodo-5-methylcyclohexanecarboxylate (14).** To a solution of acetyl chloride (0.5 mL) in dry MeOH (15 mL) was added a mixture of **11** and **12** (2.6:1, 1.37 g). The solution was heated to reflux for 3 h. After cooling, the solution was concentrated in vacuo, diluted with aqueous $NaHCO_3$ and $Na_2S_2O_3$, and extracted with CH_2Cl_2 (5×). The combined CH_2Cl_2 extracts were dried and evaporated in vacuo. Chromatography (silica, Et_2O/hexanes 1:1) gave the less polar isomer **14** (0.35 g, 27%): mp 127–128 °C (Et_2O, hexanes); R_f 0.70 (Et_2O); IR (KBr) 3490, 3420, 1725, 1430, 1270, 1205, 1160, 1080, 980, 960 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.64 (t, 1 H, J = 2.4 Hz), 4.45 (br s, 1 H), 4.10 (d, 1 H, J = 4 Hz), 3.84 (m, 1 H), 3.75 (s, 3 H), 3.43 (d, 1 H, J = 9.2 Hz), 3.29 (m, 1 H), 2.44 (m, 1 H), 1.81 (app q, 1 H, J = 13.2 Hz), 1.68 (m, 1 H), 1.04 (d, 3 H, J = 6.8 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.6, 75.5, 72.3, 52.2, 41.7, 29.9, 25.0, 18.0, 5.6; MS (EI) m/e 314 ($M^{+\cdot}$), 296, 264, 194, 169, 137, 109, 81, 55. Anal. Calcd for $C_9H_{15}IO_4$: C, 34.41; H, 4.81. Found: C, 34.32, H, 4.82. Further chromatography gave the more polar isomer **13** (0.845 g, 66%): mp 140–142 °C ($CHCl_3$, hexanes); R_f 0.40 (Et_2O); IR (KBr) 3500, 2990, 1710, 1440, 1280, 1220, 1140, 1080, 1040, 895 cm^{-1}; ^1H NMR (400 MHz, CD_2Cl_2) δ 4.27 (br s, 1 H), 4.03 (app t, 1 H, J = 10.4 Hz), 3.70 (s, 3 H), 2.84 (d, 1 H, J = 2 Hz), 2.75 (d, 1 H, J = 6 Hz), 2.56 (dq, 1 H, J = 2.4, 12.8 Hz), 1.90 (m, 1 H), 1.79 (m, 1 H), 1.68 (app q, 1 H, J = 12.4 Hz), 1.21 (d, 3 H, J = 6.4 Hz); ^{13}C NMR (101 MHz, CD_2Cl_2) δ 173.6, 77.7, 69.7, 52.4, 48.5, 45.3, 39.6, 29.8, 24.3; MS (EI) m/e 314 ($M^{+\cdot}$), 265, 187, 169, 155, 137, 109, 81, 55. Anal. Calcd for $C_9H_{15}IO_4$: C, 34.41; H, 4.81. Found: C, 34.25; H, 4.86.

(1*R,2*R**,3*R**,4*R**,5*S**)-Methyl 3-[(*tert*-Butyldimethylsilyl)oxy]-2-hydroxy-4-iodo-5-methylcyclohexanecarboxylate (15).** To a solution of diol **13** (0.15 g) in DMF (2 mL) were added imidazole (0.1 g), 4-(dimethylamino)pyridine (10 mg), and *tert*-butyldimethylsilyl chloride (0.19 g). The solution was allowed to stand at room temperature for 21 h; then it was diluted with Et_2O, washed with dilute hydrochloric acid, aqueous sodium bicarbonate, and H_2O, dried, and evaporated in vacuo. Chromatography (silica, hexanes/Et_2O 2:1) gave **15** (0.2 g, 97%): mp 59–60 °C (hexanes); R_f 0.60 (hexanes/Et_2O 1:1); IR (KBr) 3520, 3440, 2980, 1745, 1205, 1110, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.01 (br s, 1 H), 3.81 (t, 1 H, J = 10.4 Hz), 3.73 (dd, 1 H, J = 3.2, 10.4 Hz), 3.64 (s, 3 H), 2.43 (m, 1 H), 2.37 (s, 1 H), 1.74 (m, 1 H), 1.66 (m, 1 H), 1.13 (d, 3 H, J = 6.4 Hz), 0.86 (s, 9 H), 0.19

(s, 3 H), 0.08 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 78.9, 70.6, 52.0, 45.0, 44.9, 39.1, 28.8, 25.9, 24.5, 18.1, -4.0, -4.1; MS (EI) m/e 371, 353, 339, 311, 279, 151, 93, 75. Anal. Calcd for $C_{15}H_{29}IO_4Si$: C, 42.06; H, 6.80. Found: C, 41.89; H, 6.86.

(1*R,2*R**,3*R**,4*R**,5*S**)-(3-Methyl-3-oxetanyl)methyl 3-[(*tert*-Butyldimethylsilyl)oxy]-2-hydroxy-4-iodo-5-methylcyclohexanecarboxylate (16).** To a solution of methyl ester **15** (8.8 g) in 3-methyl-3-oxetanemethanol (42.3 g) at 80 °C was added titanium tetraisopropoxide (1.8 mL). The solution was stirred at 80 °C for 2.75 h; it was cooled, diluted with 1 M HCl, and extracted with Et_2O (3×). The combined Et_2O extracts were washed with aqueous $NaHCO_3$ and H_2O, dried, and evaporated in vacuo. Chromatography (silica, hexane/Et_2O 1:1) gave **16** (8.3 g, 80%): mp 85–86 °C (hexanes, Et_2O); R_f 0.68 (Et_2O); IR (KBr) 3450, 2985, 1745, 1260, 1180, 1110, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.54 (t, 2 H, J = 5.6 Hz), 4.39 (m, 2 H), 4.32 (d, 1 H, J = 10 Hz), 4.16 (br s, 1 H), 4.11 (d, 1 H, J = 10 Hz), 3.91 (t, 1 H, J = 10.4 Hz), 3.83 (m, 1 H), 2.59 (m, 1 H), 2.55 (s, 1 H), 1.85 (m, 1 H), 1.78 (m, 1 H), 1.33 (s, 3 H), 1.23 (d, 3 H, J = 6.2 Hz), 0.95 (s, 9 H), 0.28 (s, 3 H), 0.17 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 79.4, 78.9, 70.7, 68.5, 45.0, 44.9, 39.3, 39.1, 28.6, 25.9, 24.5, 21.1, 18.2, -4.17, -4.31; MS (EI) m/e 441, 321, 85, 75. Anal. Calcd for $C_{19}H_{35}IO_5Si$: C, 45.78, H, 7.08. Found: C, 45.68; H, 7.06.

(1*R,2*R**,3*R**,4*R**,5*S**)-3-[(*tert*-Butyldimethylsilyl)oxy]-2-hydroxy-4-iodo-5-methyl-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)cyclohexane (17).** To a solution of the oxetane ester **16** (1.49 g) in dry CH_2Cl_2 (5 mL) at 0 °C was added $BF_3{\cdot}OEt_2$ (74 μL). The solution was allowed to stand at 0 °C for 6 h, cooled to -78 °C, and carefully quenched with a solution of Et_3N (0.84 mL) in dry Et_2O (50 mL). The resultant suspension was filtered and the filtrate evaporated in vacuo. Chromatography (silica, hexane/Et_2O 1:1) gave **17** (1.18 g, 79%): mp 98–99 °C (hexanes); R_f 0.72 (Et_2O); IR (KBr) 3520, 2980, 1460, 1400, 1260, 1155, 1090, 1050, 1010, 835 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.11 (br s, 1 H), 4.05 (t, 1 H, J = 10.4 Hz), 3.92 (s, 6 H), 3.66 (dd, 1 H, J = 2.8, 10.4 Hz), 2.85 (s, 1 H), 1.8 (m, 2 H), 1.63 (m, 1 H), 1.55 (m, 1 H), 1.19 (d, 3 H, J = 6.4 Hz), 0.96 (s, 9 H), 0.82 (s, 3 H), 0.23 (s, 3 H), 0.16 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 108.8, 79.5, 72.6, 69.1, 47.2, 45.5, 40.0, 30.3, 27.5, 26.1, 24.5, 14.4, -4.07, -4.12; MS (EI) m/e 483, 441, 75. Anal. Calcd for $C_{19}H_{35}IO_5Si$: C, 45.78; H, 7.08. Found: C, 45.78; H, 7.06.

(1*S,2*R**,3*R**,5*S**,6*S**)-2-Hydroxy-5-methyl-3-(2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-7-oxabicyclo[4.1.0]heptane (9).** To a solution of iodide **17** (1.0 g) in THF (5 mL) was added 1.0 M tetrabutylammonium fluoride in THF (4.0 mL). The solution was allowed to stand for 4 h, diluted with CH_2Cl_2, washed with H_2O, dried, and evaporated in vacuo. Chromatography (silica, pretreated with Et_3N, Et_2O) gave **9** (0.45 g, 88%), identical with the previously prepared sample.

In several experiments it was necessary to treat the crude product with MeONa/MeOH to complete epoxide formation.

(1*S,3*R**,5*S**,6*S**)-5-Methyl-3-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-7-oxabicyclo[4.1.0]heptan-2-one (18).** To a solution of DMSO (1.12 mL) in CH_2Cl_2 (16 mL) at -78 °C was added trifluoroacetic anhydride (1.9 mL). After 10 min the epoxy alcohol **9** (1.24 g) in CH_2Cl_2 (2 mL) was added. Stirring was continued for an additional 30 min and Et_3N (15.0 mL) was added. The resulting solution was allowed to warm to 0 °C over 10 min. Isopropyl alcohol (1 mL) was added and the mixture warmed to room temperature. The solution was washed with H_2O and aqueous bicarbonate, dried, and evaporated in vacuo. Crystallization from Et_2O gave **18** (0.95 g, 77%): mp 133–135 °C (CH_2Cl_2, hexanes); R_f 0.31 (Et_2O); IR (KBr) 2980, 2890, 1710, 1230, 1075, 1040, 1010, 985, 890, 850 cm^{-1}, ^1H NMR (400 MHz, $CDCl_3$) δ 3.91 (s, 6 H), 3.37 (d, 1 H, J = 4.4 Hz), 3.32 (d, 1 H, J = 4.4 Hz), 2.49 (dd, 1 H, J = 7.2, 12 Hz), 2.07 (m, 1 H), 1.93 (app q, 1 H, J = 12.8 Hz), 1.73 (m, 1 H), 1.23 (d, 3 H, J = 6.8 Hz), 0.79 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.8, 108.7, 72.8, 60.2, 57.4, 51.5, 30.4, 28.4, 25.2, 19.0, 14.4; MS (EI) m/e 224, 153, 126, 111, 97, 82, 71, 55. Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.40; H, 7.13. Found: C, 61.15, H, 7.06.

(1*S,2*R**,4*S**,5*S**,6*R**)-9(*E*)-[2-[(*tert*-Butyldiphenylsilyl)oxy]-1-ethylidene]-1,5-dihydroxy-4-methyl-2-(4-methyl-2,6,7-trioxabicyclo[2.2.2]oct-1-yl)-7-oxabicyclo-[4.3.0]nonane (21).** To a solution of vinylstannane **19** (2.15 g) in THF (30 mL) was added 1.8 M *n*-BuLi in hexanes (4.8 mL) dropwise, maintaining a temperature of -78 (±2 °C). The solution was warmed to -35 °C, stirred for 1.5 h, and recooled to -78 °C. The epoxy ketone **18** (0.66 g) in THF (4 mL) was added and the mixture was stirred at -78 °C for 30 min and at -45 °C for an additional 1.5 h. The solution was diluted with aqueous NH_4Cl and extracted with CH_2Cl_2 (3×). The combined CH_2Cl_2 extracts were dried and evaporated in vacuo. The crude oil was redissolved in THF (30 mL) and 1.0 M *t*-BuOK in THF (5.2 mL) was added. The mixture was stirred at room temperature for 1 h, quenched with pH 7.0 phosphate buffer, and extracted with Et_2O (×3). The combined Et_2O extracts were washed with H_2O, dried, and evaporated in vacuo. Chromatography of the residue (silica, CH_2Cl_2/Et_2O 40:1) gave **21** (0.35 g, 24%) as a white foam: R_f 0.29 (Et_2O/hexanes 2:1); IR (film) 3480, 2980, 1465, 1430, 1400, 1380, 1280, 1200, 1115, 1055, 1000, 740, 710 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (m, 4 H), 7.40 (m, 6 H), 5.53 (m, 1 H), 4.92 (s, 1 H), 4.32, 4.22 (AB q, 2 H, J = 12 Hz), 4.17 (d, 2 H, J = 6.4 Hz), 3.82 (s, 6 H), 3.78 (m, 1 H), 3.58 (d, 1 H, J = 2.8 Hz), 2.68 (d, 1 H, J = 10 Hz), 2.03 (dd, 1 H, J = 3.2, 12.8 Hz), 1.79 (m, 1 H), 1.64 (m, 1 H), 1.57 (app q, 1 H, J = 13.2 Hz), 1.05 (s, 9 H), 1.03 (d, 3 H), 0.78 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.3, 135.6 (×2), 133.8, 133.5, 129.7, 129.6, 127.7, 127.6, 120.2, 110.4, 81.5, 77.4, 72.1, 70.6, 67.6, 61.8, 44.7, 32.1, 30.0, 26.8, 23.3, 19.1, 17.4, 14.3; MS (FAB) m/e 581 (MH^+), 523, 325, 199; HRMS (FAB) calcd for $C_{33}H_{44}O_7Si$ ($MH^{+\bullet}$) 581.2934, found ($MH^{+\bullet}$) 581.2994. Anal. Calcd for $C_{33}H_{44}O_7Si{\cdot}0.5H_2O$: C, 67.18; H, 7.70. Found: C, 66.98; H, 7.60.

X-ray Data Collection and Structure Determination. A crystal of dimensions 0.36 × 0.32 × 0.25 mm was mounted on a glass fiber and transferred to a N_2 cold stream (-120 °C) of an Enraf-Nonius CAD4 diffractometer. All measurements were carried out by using Mo Kα radiation (λ = 0.71069 Å). Lattice parameters were determined by the least-squares refinement of the setting angles for 25 high angle reflections. Intensities of four standard reflections were measured every 3 h of X-ray exposure, showing no significant changes. All calculations were performed on a MicroVAX 3600 computer with the TEXSAN 4.0 crystallographic software.[15] The structure was solved by direct methods (MITHRIL).[16] Full-matrix least-squares refinement with anisotropic thermal displacement parameters for all non-hydrogen atoms yielded the final R of 0.036 (R = 0.043). All hydrogen atoms were found in Fourier difference maps and were refined with isotropic temperature factors. The goodness of fit was 1.26. The highest peak in the final difference map was 0.23 e/Å^3 high. The refinement of the enantiomer with inverted coordinates yields the same values of the R factors and goodness of fit.

Acknowledgment. We thank the National Institutes of Health for support of this program (AI-20644 and IF32GM-11749) and for funding a 400-MHz NMR spectrometer (RR02314) and a high resolution mass spectrometer (RR03245). Additionally we thank Dr. Tony Raynham for helpful discussions.

Supplementary Material Available: Tables of crystal data, positional parameters, bond distances, and bond angles for **9** (7 pages); a listing of structure factors (9 pages). Ordering information is given on any current masthead page.

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