sample remained homogeneous throughout the experiment.

In another experiment, 1.0 mmol of ^{10}B labeled 2-MeB_5H_8 in a large excess of 2,6-lutidine reached equilibrium in 3 h.

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Registry No. B_5H_9, 19624-22-7; B_2H_6, 19287-45-7; MeB_2H_5, 23777-55-1; K[1-MeB_5H_7], 56009-96-2; $^{10}B_2H_6$, 19465-29-3; Me_2O, 115-10-6; 2,6-lutidine, 108-48-5.

The Convergent Synthesis of Polyether Ionophore Antibiotics: The Synthesis of the Monensin Spiroketal[1]

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Abstract: The monensin spiroketal **2**, a versatile intermediate for the synthesis of polyether ionophore antibiotics, is prepared from D-fructose. Key steps include the ester enolate Claisen rearrangement of a glycal propionate, expansion of a furanoid to a pyranoid ring, and the acid-catalyzed equilibration of a bicyclic ketal to a spiroketal. An alternative approach, entailing the hetero-Diels–Alder condensation of the exocyclic enol ether **15** with acrolein, is thwarted by facile isomerization to the endocyclic enol ether **18**.

The complex chemistry and potent biological activity of the polyether antibiotics have engaged widespread interest.[4] As ionophores, these compounds possess a striking ability to perturb ionic gradients by catalytically transporting cations across lipid barriers.[5] While optimal membrane and ion selectivity remain elusive goals, the commercial use of monensin for control of poultry coccidiosis[6] and enhancement of ruminant feed utilization[6] have encouraged intensive efforts in the isolation and study of these compounds. Several have demonstrated potential in human medicine, particularly as cardiovascular agents.[7] In addition to their diverse biological activity, these antibiotics display a formidable molecular complexity, and the attendant challenge of total synthesis has been taken up by numerous research groups.[8] Structurally, most of the polyether ionophores feature linear chains of substituted tetrahydropyran and tetrahydrofuran rings. Comparison reveals that nearly all these rings recur with high frequency, often in stereochemically indistinguishable sequences. The unified biosynthetic pathway proposed by Cane, Celmer, and Westley underscores the structural identities and combinatorial diversity of these antibiotics.[9]

We have recently developed a versatile, building-block approach to the polyethers in which prefabricated tetrahydrofuran and tetrahydrogen rings are joined via the ester enolate Claisen rearrangement. This work has culminated in the total synthesis of lasalocid A[8b] and its enantiomer[10] from readily available carbohydrates. In this and the following two papers in this issue, we report the preparation of several additional subunits for the synthesis of naturally occurring polyethers and potentially informative analogues.

Serving as rigid bands in the polyether backbone, spiroketals play a critical role in establishing the coordination geometry necessary for ion complexation.[11] Since one of the spiro oxygens usually acts as a ligand as well, spiroketals are prominent features of the polyether class.[12] Monensin's[13] spiroketal is a particularly attractive synthetic target, as it occurs in at least eight other ionophores. Disconnection of the C2,3 and C12,13 bonds of monensin generates the common structural subunit **2**, and the results of an aldol and ester enolate Claisen transform are shown in Scheme I.

Our synthetic plan for this polyether building block developed out of model studies which demonstrated the value of the hetero-Diels–Alder condensation in the construction of spiroketals (Scheme II).[14] Although the rigidity of the spiroketal system itself can mediate control of relative stereochemistry,[15] in this

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(3) National Science Foundation Research Fellow, 1981-1984.

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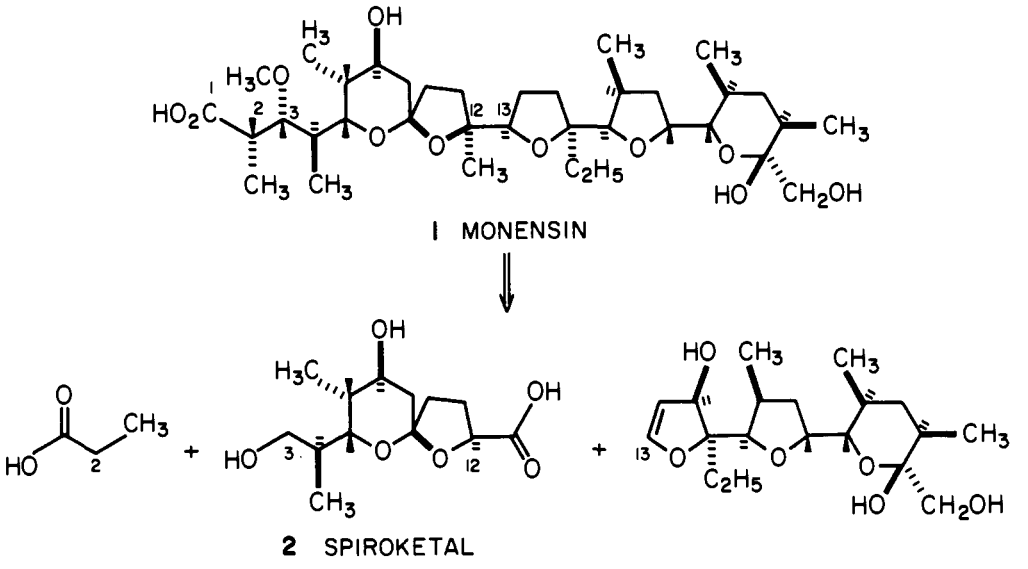
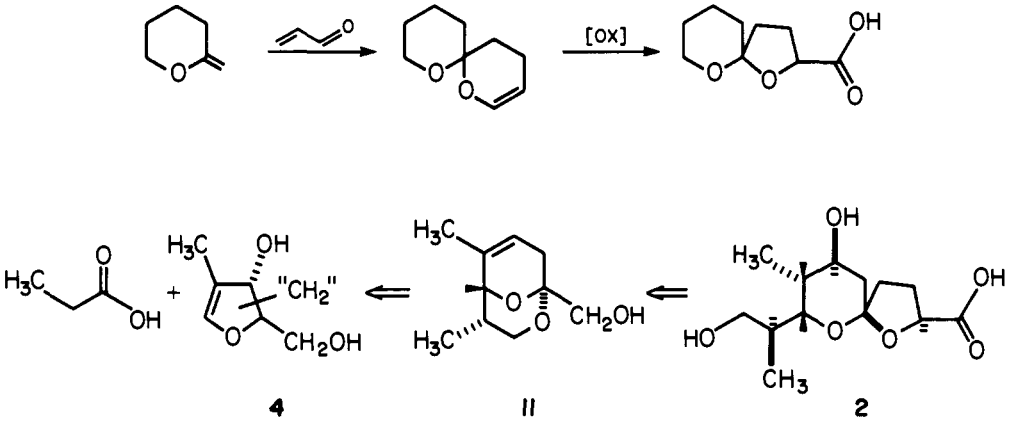
Scheme I. Retrosynthetic Analysis for Monensin



Scheme II. Basic Design for the Syntheis of the Spiroketal 2



instance we planned to use the bicyclic ketal **11** for this purpose. Conceptually, a 2,4-dideoxy-2-methyl pyranoid glycal is an appealing starting material for this modified *C*-glycoside.[16] However, the problems associated with deoxygenating a hexopyranose at the 4 position[17] and the rarity of branched carbohydrates[18] prompted us to take a more subtle tack using the furanoid glycal **4** as a pyranoid equivalent.

Available on large scale by treatment of invert sugar with aqueous calcium hydroxide, the branched chain carbohydrate α-D-glucosaccharinic acid, γ-lactone (**3**),[19] has been converted previously to the required glycal **4**[20] (Scheme III). Application of the ester enolate Claisen rearrangement to the corresponding propionate provided a diastereomeric mixture of the esters **5** and **6**. As described earlier,[21] either isomer could be made to predominate by choice of enolization conditions (LDA/THF, **5**:**6**/20%:80%; LDA/THF, 23% HMPA, **5**:**6**/80%:20%. Ample precedent[22] allowed us to predict that rearrangement of the *Z* silyl ketene acetal through a preferred boatlike transition state would deliver the *R* configuration at C4,[23] and thus the major product obtained from enolization in the presence of HMPA was identified as the desired diastereomer and separated by chromatography.

Having attached the side chain at C5,[23] we now confronted three problems: expansion of a furanoid to a pyranoid ring; stereoselective oxygenation of the carbon backbone at C7;[23] and introduction of the ketone oxidation state at C9.[23] Reduction of the ester **5**, iodoetherification, and then elimination of HI overcame the latter problem and neatly set the stage for solving the remaining two. While the acid sensitivity[24] of the furanoid glycal **7** precluded Simmons–Smith cyclopropanation,[25] the incipient "4-deoxypyranose" carbon was introduced without complication by phase transfer catalyzed dichlorocyclopropanation[26] followed by hydrodehalogenation.[27,28] When purification was carried out only at this point, the cyclopropane **9** was reproducibly obtained

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(24) On the standing in chloroform, **7** was quantitatively converted to the corresponding furan.

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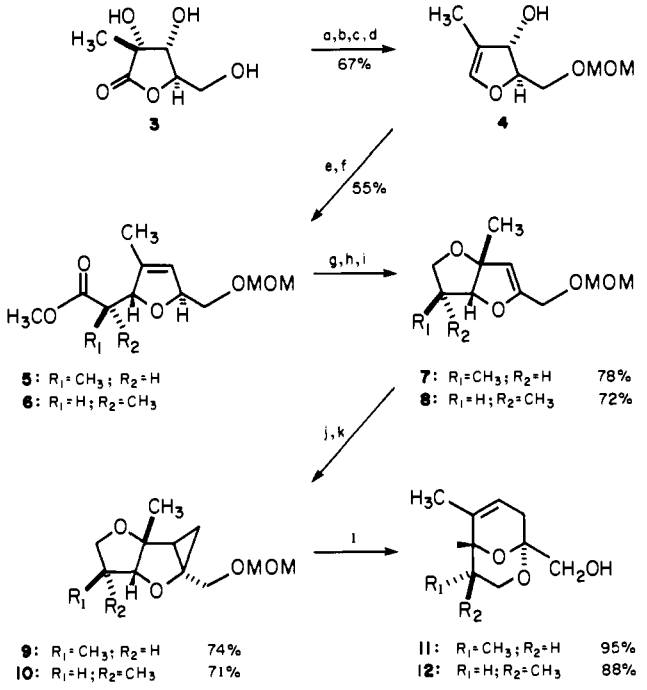
(28) Cyclopropanes **9** and **10** were both obtained as a single diastereomer; carbene addition presumably occurred from the conex face of bicyclooctenes **7** and **8**.

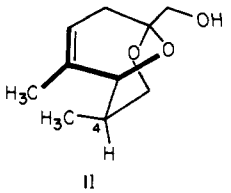
Scheme III. Synthesis of the Bicyclic Ketal **11**[a]



[a] (a) H_2SO_4, $(CH_3)_2CO$; (b) KH, $ClCH_2OCH_3$, THF; (c) DIBAL, Et_2O, −78 °C; (d) $P(NMe_2)_3$, CCl_4, THF; Li, NH_3; NH_4Cl; (e) *n*-BuLi, n-C_2H_5COCl, THF; LDA, THF/HMPA; Me_3SiCl; OH^-; (f) CH_2N_2, Et_2O; (g) LAH, Et_2O; (h) I_2, Na_2CO_3, CH_3CN; (i) DBU, C_6H_6; (j) 50% aqueous NaOH, $CHCl_3$, TEBAC; (k) LAH, Et_2O; (l) **11**, 62% $HClO_4$, CH_3CN; **12**, 10% HCl, THF.

in 85% overall yield from the methyl ester **5**. Acid-catalyzed rearrangement of this cyclopropyl ether[29] to the bicyclic ketal **11** completed the furanoid to pyranoid ring conversion and restored a double bond between C6 and C7[23] for future oxygenation.

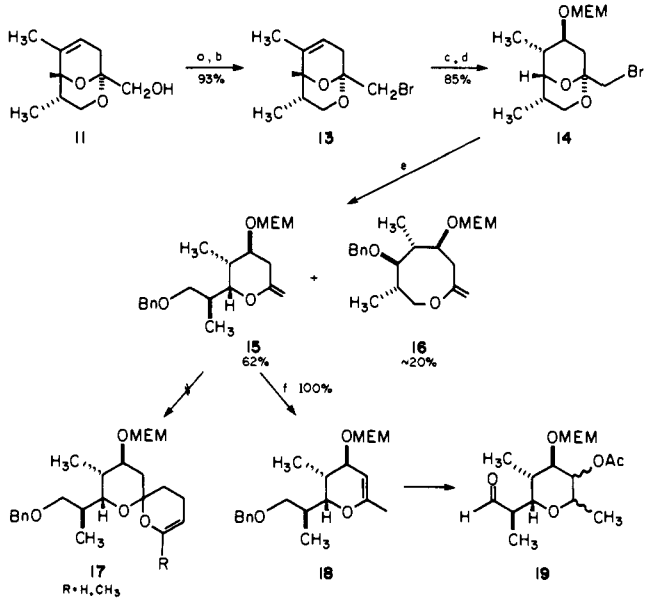
The diastereomeric cyclopropanes **9** and **10** showed disparate reactivity in this transformation. Heating the α-methyl epimer **10** in 1:4 10% HCl/THF at 55 °C for 17 h induced rearrangement to the bicyclic ketal **12** in 88% yield. With the β-methyl epimer **9**, these conditions merely removed the MOM group to give the corresponding cyclopropyl carbinol. At higher temperatures and extended reaction times, TLC indicated that the bicyclic ketal **11** decomposed nearly as rapidly as it formed. Although the reason for the difference in rearrangement rate is not entirely clear, models show that the difference in product stabilities is a result of the severe steric congestion encountered by the C6[23] methyl group in bicyclic ketal **11**.[30] Choice of both solvent and acid



11

proved to be crucial to the success of this reaction. While modest yields were obtained with 2 equiv of $TiCl_4$ in benzene at 7 °C,

Scheme IV. Hetero-Diels-Alder Approach to the Spiroketal **2**[a]



[a] (a) $(CF_3SO_2)_2O$, C_5H_5N, CH_2Cl_2; (b) $(n\text{-}Bu)_4NBr$, HMPA; (c) BH_3, THF; 10% NaOH, 30% H_2O_2; (d) $CH_3OCH_2CH_2OCH_2Cl$, $(i\text{-}Pr)_2NEt$, CH_2Cl_2; (e) *n*-BuLi, THF; BnBr, HMPA; (f) H^+.

consideration of the ionic character of the transition state suggested that use of a more polar solvent might facilitate the rearrangement. To our delight, concentrated perchloric acid in acetonitrile at room temperature gave the bicyclic ketal **11** in 95% yield.[31]

Conversion of this intermediate to an exocyclic enol ether required deoxygenation at a neopentyl center with *two* α oxygens (Scheme IV). Although S_N2 displacement at this center was expected to be difficult,[32] the triflate ester[33] of **11**, recovered quantitatively from excess lithium bromide in refluxing THF, was seemingly indestructible under S_N2 conditions. The surprising ease with which the triflate succumbed to tetra-*n*-butylammonium bromide in HMPA suggests changeover to an S_N1 mechanism with anchimeric assistance from a ketal oxygen.[34] Hydroboration of the resulting bromoolefin **13** occurred with complete regio- and stereoselectivity from the convex face of the bicyclic ketal, which, having served its intended architectural role, was now expendable. Stereoelectronic considerations[35] led us to predict that the desired methylene pyran **15**, resulting from the fragmentation of an axial carbon–carbon bond, rather than its eight-membered ring analogue **16**, should be the major product of a reductive elimination across C9 and C10.[23] An obstacle before, the steric hindrance about C10[23] now permitted clean metal–halogen exchange with *n*-butyllithium at −78 °C. After the reaction was quenched with benzyl bromide, the protected methylene pyran **15** was reproducibly obtained in 62% yield after chromatography on alumina.[36]

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(30) The conformation of the bicyclic ketal **11** depicted is supported by 90-MHz NMR. While the C4[23] hydrogen occurs in the expected 2.1–2.4 ppm range as a multiplet, the C4 methyl group occurs as a doublet at 0.75 ppm. We attribute this upfield shift to shielding by the olefin. The effect is more dramatic in the C4 epimer **12**. Here the C4 methyl group has the same chemical shift as the C4 hydrogen and occurs as a singlet at 1.37 ppm.

(31) Concentrated perchloric acid (62%) is essentially a trihydrate, and the minimal amount of water present in the reaction no doubt enhances the effective acidity. Although ring expansion actually occurs faster than MOM removal under these conditions, the protecting group must be hydrolyzed prior to rearrangement by treatment with aqueous HCl in acetonitrile. Attempts to do so afterward resulted in decomposition. The presence of a nonnucleophilic counterion also appeared to be essential, as concentrated HCl in acetonitrile caused degradation.

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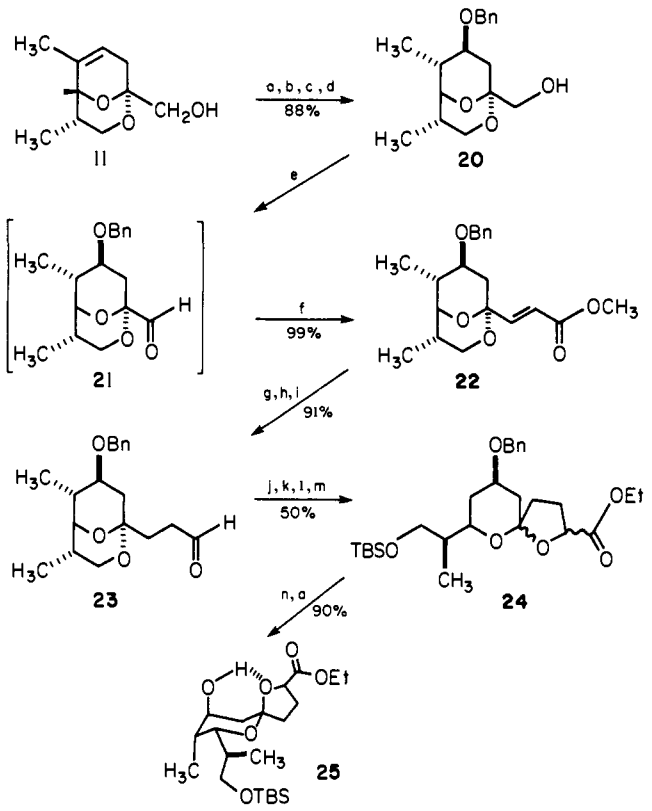
(36) The structure of **15** was confirmed by conversion to the aldehydes **19** via isomerization, hydroboration, acetylation, debenylation, and Swern oxidation. All compounds had satisfactory spectra and combustion analyses. Although the isomeric exocyclic enol ether **16** could not be consistently isolated, NMR analysis of the crude reaction mixture indicated a 3:1 mixture of **15** and **16**.

Scheme V. Thermodynamic Equilibration to the Monensin Spiroketal[a]



[a] (a) TBSCl, C_6H_5N, CH_2Cl_2; (b) BH_3, THF; 10% NaOH, 30% H_2O_2; (c) *t*-BuOK, BnBr, THF; (d) $(n\text{-Bu})_4NF$, THF; (e) $(COCl)_2$, Me_2SO, CH_2Cl_2; Et_3N; (f) Ph_3PCHCO_2Me; (g) H_2, 5% Rh/C, $n\text{-}C_5H_{12}$; (h) LAH, Et_2O; (i) $(COCl)_2$, Me_2SO, CH_2Cl_2; Et_3N; (j) $CH_2C(OEt)Li$; (k) O_3, CH_2Cl_2, MeOH; Me_2S; (l) $C_6H_5NH^+\cdot p\text{-}TsO^-$, $CHCl_3$; (m) TBSCl, C_6H_5N, CH_2Cl_2; (n) H_2, 10% Pd/C, EtOH: (o) $C_6H_5NH^+\cdot p\text{-}TsO^-$, $CHCl_3$.

Two factors conspired to thwart the hetero-Diels–Alder reaction we had envisioned. First, isomerization to the endocyclic olefin **18** was incredibly facile, with a half-life of no more than 10 min in THF at 55 °C in base-washed glassware. Although no isomerization was detected at this temperature after several hours when either pyridine or triethylamine were used as a solvent, these and even the hindered base 4-hydroxy-2,2,6,6-tetramethylpiperidine polymerized acrolein at room temperature.[37] Furthermore, although good yields of adduct were obtained by allowing 2-methylenetetrahydropyran to stand at room temperature with 1 equiv of acrolein for a few days,[14] the use of acrolein as *solvent* for the functionalized methylene pyran **15** led only to slow isomerization. It was this second factor, lack of reactivity, which finally forced us to abandon this route. For despite the fact that methyl vinyl ketone could be heated to reflux as a 1:1 mixture with either pyridine or triethylamine without undue polymerization, no adduct with the methylene pyran **15** could be detected at reaction temperatures below 70 °C. At higher temperatures, isomerization was complete in a few hours.

Recognizing that the extremely severe steric congestion created by hydroboration of the bicyclic ketal **11** is relieved by cleavage of the axial carbon–oxygen bond, we envisioned an alternative, thermodynamic entry to the spiroketal system via acid-catalyzed equilibration with an appropriately functionalized side chain. Fortunately, this new strategy could be implemented with an advanced intermediate in the hetero-Diels–Alder route (Scheme V).

Hydroboration of the silyl ether of olefin **11** was again completely selective, and a protection–deprotection[38] sequence gave the neopentyl alcohol **20**[39] in 88% overall yield from the bicyclic ketal. In light of our previous difficulties, this initially appeared to be an unlikely site for appending the spiroketal side chain. However, the extreme steric demands of a pentagonal transition state are attenuated in the corresponding conversion from trigonal to tetrahedral hybridization, and the inductive effect of the ketal oxygens should activate an adjacent electrophilic center. In fact, special reaction conditions were required to overcome the propensity of the neopentyl aldehyde **21** toward hydration and decomposition. The Swern oxidation[40] is both mildly basic and completely anhydrous, and addition of methyl (triphenylphosphoranylidene)acetate to the crude reaction mixture provided the unsaturated ester **22** in nearly quantitative yield. After adjustment of the side chain oxidation state, the spiroketal carboxylate carbon was introduced by ozonization of the adduct with lithiated ethyl vinyl ether.[41]

Complete equilibration from the bicyclic to spirocyclic ketal system was smoothly promoted by pyridinium *p*-toluenesulfonate, and protection[42] of the liberated primary hydroxyl group gave the four spiroketal diastereomers **24**[43] in an overall yield of 50% from the aldehyde **23**.[44] Easily separated by chromatography, each epimer at the carboethoxy center[43] gave a single spiroisomer **25** when debenzylated and subjected to equilibration with pyridinium *p*-toluenesulfonate. A sharp absorption at 3560 cm^{-1} in the IR spectrum confirmed the presence of an intramolecular hydrogen bond between the $C7^{23}$ hydroxyl and axial spiroketal oxygen. Since the asymmetry at the carboethoxy center will be lost during enolization in the Claisen rearranement joining this subunit to the polyether backbone, each of the four diastereomers can, in principle, by converted to the thermodynamic[45] monensin spiroketal.

Experimental Section

Melting points are uncorrected. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded at 90 MHz except where designated "500 MHz". Data are reported as follows: chemical shift (multiplicity, integrated intensity, coupling constants, assigment). Optical rotations were measured in 1-dm cells of 1-mL capacity; chloroform, when used as a solvent for optical rotations, was filtered through neutral alumina (Activity I) immediately prior to use. Reaction solvents and liquid reagents were purified by distillation or drying shortly before use. Reactions were run under an argon atmosphere arranged with a mercury bubbler so that the system could be alternately evacuated and filled with argon and left under a positive pressure. Reported temperatures were measured externally. Syringes and reaction flasks were dried at least 12 h in an over (120–140 °C) and cooled in a dessicator over anhydrous $CaSO_4$ prior to use. If feasible, reaction flasks were also flame-dried in vacuo.

Methyl 2(*R*)- and 2(*S*)-[2,5-Dihydro-5(*S*)-([(methoxymethyl)oxy]methyl)-3-methyl-2(*R*)-furyl]propanoate (5 and 6). To a stirred solution of 2.65 g (15.2 mmol) of the glycal **4**[20] in 50 mL of THF at −78 °C was added 6.43 mL (15.2 mmol) of a 2.36 M solution of *n*-butyllithium in hexane, and then after 5 min, 1.37 mL (15.8 mmol) of propionyl chloride was added. After 10 min at 0 °C, the solution was recooled to −78 °C and added dropwise to a stirred solution of 17.5 mmol of LDA in 27 mL of THF and 11 mL of HMPA at −78 °C. After 10 min, the reaction

(37) Smith, C. W., Ed. "Acrolein"; Wiley: New York, 1962.

(38) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

(39) That the $C7^{23}$ hydrogen of bicyclic ketal **20** is indeed axial was confirmed by 500-MHz NMR, which showed a 6-Hz and 9-Hz coupling of this proton to the $C8^{23}$ methylene hydrogens and a 10-Hz coupling to the $C6^{23}$ hydrogen.

(40) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651–1660.

(41) Baldwin, J. E.; Höfle, G. A.; Lever, O. W. *J. Am. Chem. Soc.* **1974**, *96*, 7125–7127. Chavdarian, C. G.; Heathcock, C. H. *J. Am. Chem. Soc.* **1975**, *97*, 3822–3823. Pappas, J. J.; Keaveny, W. P. *Tetrahedron Lett.* **1966**, 4273–4278.

(42) Silylation under these conditions is selective for primary alcohols. Chaudhary, S. K.; Hernandez, O. *Tetrahedron Lett.* **1979**, 99–102.

(43) In order of increasing polarity, the spiroketals were obtained in a ratio of 7.4:4.0:2.1:1.0. As expected on the basis of these ratios, the most and least polar compounds were shown to bear the same configuration at the carboethoxy center by equilibration of the spiroketal center with pyridinium *p*-toluenesulfonate in chloroform. The spiroketals of intermediate polarity were also interconvertible.

(44) For a similar equilibration, see: Grieco, P. A.; Williams, E.; Ken-Ichi, K. In "Organic Synthesis: Today and Tomorrow"; Trost, B. M., Hutchinson, C. R., Eds.; Pergamon Press: New York, 1981; pp 187–196.

(45) Reference 8c.

mixture was treated with 4.57 mL (26.3 mmol of Me_3SiCl) of the supernatant centrifugate from a 3:1 mixture of trimethylchlorosilane and triethyamine. After 3 h at room temperature, the reaction mixture was diluted with 70 mL of 1 N aqueous NaOH and stirred for 15 min. The THF was evaporated at reduced pressure, and the aqueous solution was then washed with 100 mL of ether. The organic phase was counterextracted with five 20-mL portions of 1 N aqueous sodium hydroxide, and then the combined aqueous base phases were washed with two 40-mL portions of ether, acidified to pH 2 with concentrated aqueous HCl, and then extracted with six 50-mL portions of ether. The combined ethereal extracts were washed with 50 mL of saturated aqueous NaCl, dried ($MgSO_4$), concentrated to 100 mL, and then treated with excess ethereal diazomethane. The solvent was removed under reduced pressure, and medium-pressure liquid chromatography of the residue with 24:76 ethyl acetate/cyclohexane afforded first 408 mg (11%) of the ester **6** as a colorless oil: R_f = 0.26 (silica gel, 1:1 ether/petroleum ether); evaporative distillation 80–90 °C (0.005 mmHg); $[\alpha]^{23}_D$–137° (*c* 1.66, $CHCl_3$); IR ($CHCl_3$) 2990, 1740, 1475, 1455, 1170, 1130, 1100, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.14 (d, 3 H, *J* = 8 Hz, CH_3CH), 1.67 (br s, 3 H, $CH_3C{=}CH$), 3.33 (s, 3 H, OCH_3), 3.67 (s, 3 H, CO_2CH_3), 4.60 (s, 2 H, OCH_2O), 5.47 (br s, 1 H, $CH_3C{=}CH$).

There was then eluted 1.64 g (44%) of the ester **5** as a colorless oil: R_f = 0.20 (silica gel, 1:1 ether/petroleum ether); evaporative distillation 80–90 °C (0.005 mmHg); $[\alpha]^{23}_D$ –87.3° (*c* 1.53, $CHCl_3$); IR ($CHCl_3$) 2990, 1740, 1455, 1145, 1130, 1100, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (d, 3 H, *J* = 7 Hz, CH_3CH), 1.67 (br s, 3 H, $CH_3C{=}CH$), 3.33 (s, 3 H, OCH_3), 3.70 (s, 3 H, CO_2CH_3), 4.49 (s, 2 H, OCH_2O), 5.50 (br s, 1 H, $CH_3C{=}CH$). Anal. Calcd for $C_{12}H_{20}O_5$ (mixture of **5** and **6**): C, 59.00; H, 8.25. Found: C, 58.91; H, 8.23.

2(*S*)-[2,5-Dihydro-5(*S*)-([(methoxymethyl)oxy]methyl)-3-methyl-2-(*R*)-furyl]propan-1-ol. To a stirred solution of 439 mg (1.80 mmol) of the methyl ester **5** in 12 mL of ether at 0 °C was added 68 mg (1.80 mmol) of lithium tetrahydridoaluminate. After 1 h at room temperature, the mixture was cautiously treated with 70 μL of water, 70 μL of 15% aqueous NaOH, and then 210 μL of water. The mixture was filtered and then concentrated under reduced pressure. Chromatography of the residue on 20 g of silica gel with ether afforded 373 mg (96%) of the alcohol as a colorless oil: R_f = 0.23 (silica gel, 9:1 ether/petroleum ether); $[\alpha]^{22}_D$ –94° (*c* 1.33, $CHCl_3$); IR ($CHCl_3$) 3645, 3500, 1680, 1440, 1155, 1120, 1085, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.81 (d, 3 H, *J* = 7 Hz, CH_3CH); 1.67 (br s, 3 H, $CH_3C{=}CH$), 3.33 (s, 3 H, OCH_3), 4.60 (s, 2 H, OCH_2O), 5.41 (br s, 1 H, $CH_3C{=}CH$). Anal. Calcd for $C_{11}H_{20}O_4$: C, 61.09; H, 9.32. Found: C, 60.80; H, 9.30.

2(*R*)-[2,5-Dihydro-5(*S*)-([(methoxymethyl)oxy]methyl)-3-methyl-2-(*R*)-furyl]propan-1-ol. By the procedure described for the above alcohol, 3.87 g (15.8 mmol) of the methyl ester **6** and 0.6 g (15.8 mmol) of lithium tetrahydridoaluminate in 100 mL of ether afforded, after flash chromatography on 150 g of silica gel with ether, 3.25 g (95%) of the alcohol as a colorless oil: R_f = 0.24 (silica gel, 9:1 ether/petroleum ether); evaporative distillation 70–80 °C (0.004 mmHg); IR ($CHCl_3$) 3630, 3480, 1670, 1445, 1145, 1110, 1020, 915 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (d, 3 H, *J* = 7 Hz, CH_3CH), 1.75 (br s, 3 H, $CH_3C{=}CH$), 3.33 (s, 3 H, OCH_3), 4.62 (s, 2 H, OCH_2O), 5.45 (br s, 1 H, $CH_3C{=}CH$). Anal. Calcd for $C_{11}H_{20}O_4$: C, 61.09; H, 9.32. Found: C, 61.16; H, 9.34.

(5*R*,1*S*,4*S*)-1,4-Dimethyl-8(*S*)-iodo-7(*R*)-([(methoxymethyl)oxy]methyl)-2,6-dioxabicyclo[3.3.0]octane. To a stirred solution of 509 mg (2.35 mmol) of the above alcohol (derived from ester **5**) in 26 mL of dry acetonitrile was added 2.49 g (23.5 mmol) of anhydrous sodium carbonate and 2.99 g (11.8 mmol) of iodine. The mixture was stirred in the dark for 2 h at room temperature, diluted with 80 mL of ether, and then treated with 40 mL of 10% aqueous Na_2SO_3. The organic layer was separated, washed with 50 mL of saturated aqueous NaCl, and dried ($MgSO_4$). Removal of the solvent under reduced pressure and chromatography of the residue on 30 g of silica gel with 3:7 ether/petroleum ether afforded 732 mg (93%) of the iodoether as a light yellow oil: R_f = 0.20 (silica gel, 3:7 ether/petroleum ether); evaporative distillation 65–75 °C (0.001 mmHg); $[\alpha]^{22.5}_D$ +36.2 (*c* 1.64, $CHCl_3$); IR ($CHCl_3$) 1480, 1405, 1165, 1125, 1100, 1055, 938 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (d, 3 H, *J* = 7.5 Hz, CH_3CH), 1.70 (s, 3 H, CH_3), 3.37 (s, 3 H, OCH_3), 4.40 (d, 1 H, *J* = 4 Hz, CHI), 4.63 (s, OCH_2O, 2 H). Anal. Calcd for $C_{11}H_{19}IO_4$: C, 38.61; H, 5.60. Found: C, 38.62; H, 5.56.

(5*R*,1*S*,4*R*)-1,4-Dimethyl-8(*S*)-iodo-7(*R*)-([(methoxymethyl)oxy]methyl)-2,6-dioxabicyclo[3.3.0]octane. By the procedure described for the preparation of the above iodoether, 3.25 g (15.0 mmol) of the above alcohol (derived from the ester **6**), 19.07 g (75.1 mmol) of iodine, and 15.93 g (150 mmol) of anhydrous sodium carbonate in 150 mL of acetonitrile afforded, after flash chromatography on 150 g of silica gel with 3:7 ether/petroleum ether, 4.38 g (87%) of the iodoether as a light yellow oil: R_f = 0.26 (silica gel, 3:7 ether/petroleum ether); evaporative distillation 70–80 °C (0.005 mmHg); $[\alpha]^{25}_D$ +10.8° (*c* 1.14, $CHCl_3$); IR ($CHCl_3$) 1460, 1385, 1135, 1110, 1020, 985, cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 (d, 3 H, *J* = 7.5 Hz, CH_3CH), 1.67 (s, 3 H, CH_3C), 3.34 (s, 3 H, OCH_3), 4.40 (d, 1 H, *J* = 3 Hz, CHI), 4.62 (s, 2 H, OCH_2O). Anal. Calcd for $C_{11}H_{19}IO_4$: C, 38.61; H, 5.60. Found: C, 38.37; H, 5.35.

(5*R*,1*R*,4*S*)-1,4-Dimethyl-7-([(methoxymethyl)oxy]methyl)-2,6-dioxabicyclo[3.3.0]oct-7-ene (7). To a stirred solution of 5.90 g (17.6 mmol) of the above iodoether (derived from the ester 5) in 52 mL of benzene was added 11.85 mL (79.2 mmol) of 1,5-diazabicyclo[5.4.0]undec-5-ene. After 12 h at room temperature, the solution was heated to reflux for 2 h, allowed to cool, and then poured into 300 mL of ether. The resulting mixture was washed with three 100-mL portions of saturated aqueous NaCl and then drired (Na_2CO_3). Removal of the solvent under reduced pressure and flash chromatography of the residue on 50 g of silica gel with 4:6 ether/petroleum ether afforded 3.28 g (87%) of the olefin **7** as a colorless oil: R_f = 0.26 (silica gel, 4:6 ether/petroleum ether); evaporative distillation 60–65 °C (0.004 mmHg); $[\alpha]^{23}_D$ +0.014° (*c* 1.49, $CHCl_3$); IR ($CHCl_3$) 1675, 1470, 1385, 1150, 1105, 1040, 990, 960 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (d, 3 H, *J* = 7 Hz, CH_3CH), 1.51 (s, 3 H, CH_3C), 3.33 (s, 3 H, OCH_3), 4.07 (s, 2 H, CCH_2O), 4.63 (s, 2 H, OCH_2O), 4.90 (s, 1 H, C=CH). Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.49; H, 8.32.

(5*R*,1*R*,4*R*)-1,4-Dimethyl-7-([(methoxymethyl)oxy]methyl)-2,6-dioxabicyclo[3.3.0]oct-7-ene (8). By the procedure described above for the preparation of the olefin **7**, a solution of 4.37 g (13.1 mmol) of the above iodoether (derived from the ester **6**) and 8.96 g (58.8 mmol) of 1,5-diazabicyclo[5.4.0]undec-5-ene in 38 mL of benzene afforded, after flash chromatography on 50 g of silica gel with 3:7 ether/petroleum ether, 2.44 g (87%) of the olefin **8** as a colorless oil: R_f = 0.26 (silica gel, 3:7 ether/petroleum ether); evaporative distillation 55–65 °C (0.005 mmHg); $[\alpha]^{25}_D$ +11.8° (*c* 1.19, $CHCl_3$); IR ($CHCl_3$) 1670, 1460, 1380, 1150, 1030, 980, 950 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (d, 3 H, *J* = 7 Hz, CH_3CH), 1.42 (s, 3 H, CH_3C), 3.34 (s, 3 H, OCH_3), 4.07 (s, 2 H, CCH_2O), 4.63 (s, 2 H, OCH_2O), 4.84 (s, 1 H, CH=C). Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.54; H, 8.44.

(1*R*,5*R*)-4,4-Dichloro-6(*R*),9(*S*)-dimethyl-3(*R*)-([(methoxymethyl)oxy]methyl)-2,7-dioxatricyclo[4.3.0.0^{3,5}]nonane. To a stirred solution of 807 mg (3.76 mmol) of the olefin **7** in 16.5 mL of chloroform at 0 °C was added 16.5 mL of cold 50% aqueous NaOH and 17 mg (0.075 mmol) of benzyltriethylammonium chloride. The reaction mixture was vigorously sitrred for 6 h at 0 °C and was then diluted with 60 mL of cold water and 100 mL of ether. The resulting mixture was filtered through celite. The organic layer was separated, washed with 60 mL of saturated aqueous NaCl, and dried ($MgSO_4$). Removal of the solvent under reduced pressure and chromatography of the residue on 30 g of silica gel with 3:7 ether/petroleum ether afforded 997 mg (89%) of the dichlorocyclopropane as a colorless oil: R_f = 0.40 (1:1 ether/petroleum ether); evaporative distillation 90–100 °C (0.005 mmHg); $[\alpha]^{22}_D$ +90.4 (*c* 1.04, $CHCl_3$); IR ($CHCl_3$) 1465, 1390, 1150, 1105, 1038, 1000, 895, 845 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.99 (d, 3 H, *J* = 7 Hz, CH_3CH), 1.63 (s, 3 H, CH_3C), 2.24 (s, 1 H, Cl_2CCH), 3.40 (s, 3 H, OCH_3), 4.78 (s, OCH_2O, 2 H). Anal. Calcd for $C_{12}H_{18}Cl_2O_4$: C, 48.50; H, 6.11. Found: C, 47.31; H, 6.36.

(1*R*,5*R*)-4,4-Dichloro-6(*R*),9(*R*)-dimethyl-3(*R*)-([(methoxymethyl)oxy]methyl)-2,7-dioxatricyclo[4.3.0.0^{3,5}]nonane. By procedure described above for the dichlorocyclopropanation of the olefin **7**, 2.43 g (11.3 mmol) of the olefin **8**, 45 mL of chloroform, 45 mL of 50% aqueous NaOH, and 52 mg (0.226 mmol) of benzyltriethylammonium chloride afforded, after flash chromatography on 50 g of silica gel with 1:3 ether/petroleum ether, 3.05 g (91%) of the dichlorocyclopropane as a colorless oil: R_f = 0.19 (silica gel, 1:4 ether/petroleum ether); evaporative distillation 75–80 °C (0.005 mmHg); $[\alpha]^{24}_D$ +83.3 (*c* 1.12, $CHCl_3$); IR ($CHCl_3$) 1455, 1385, 1150, 1105, 1030, 1010, 875, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (d, 3 H, *J* = 7.5 Hz, CH_3CH), 1.52 (s, 3 H, CH_3C), 2.30 (s, 1 H, Cl_2CCH), 3.39 (s, 3 H, OCH_3), 4.70 (s, 2 H, OCH_2O). Anal. Calcd for $C_{12}H_{18}Cl_2O_4$: C, 48.50; H, 6.11. Found: C, 48.64; H, 6.25.

(1*R*,5*S*,6*R*,9*S*)-6,9-Dimethyl-3(*R*)-([(methoxymethyl)oxy]methyl)-2,7-dioxatricyclo[4.3.0.0^{3,5}]nonane (9). To a stirred solution of 994 mg (3.34 mmol) of the above dichlorocyclopropane (derived from the olefin **7**) in 38 mL of ether was added 380 mg (10 mmol) of lithium tetrahydridoaluminate. After 48 h at room temperature, the mixture was cautiously treated with 0.38 mL of water, 0.38 mL of 15% aqueous NaOH, and then 1.14 mL of water. The mixture was filtered and then concentrated under reduced pressure. Chromatography of the residue on 20 g of silica gel with 3:2 ether/petroleum ether afforded 630 mg (83%) of the cyclopropane **9** as a colorless oil: R_f = 0.23 (silica gel, 1:1 ether/petroleum ether); evaporative distillation 55–65 °C (0.005 mmHg); $[\alpha]^{22}_D$ +97.2 (*c* 1.05, $CHCl_3$); IR ($CHCl_3$) 1465, 1390, 1240, 1150, 1105, 1040, 925 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.6–0.8 (m, 2 H, cyclopropyl-CH_2), 1.00 (d, 3 H, *J* = 7.5 Hz, CH_3CH), 1.50 (s, 3 H, CH_3C), 3.37 (s, 3 H, OCH_3), 4.67 (s, 2 H, OCH_2O). Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.13;

H, 8.83. Found: C, 63.34; H, 9.09.

(1*R*,5*S*,6*R*,9*R*)-6,9-Dimethyl-3(*R*)-([(methoxymethyl)oxy]methyl)-2,3-dioxatricyclo[4.3.0.0^{3,5}]nonane (10). By the procedure described above for the preparation of the cyclopropane **9**, a solution of 528 mg (1.78 mmol) of the above dichlorocyclopropane (derived from the olefin **8**) and 202 mg (5.33 mmol) of lithium tetrahydriodoaluminate afforded, after chromatography on 20 g of silica gel with 2:3 ether/petroleum ether, 317 mg (78%) of the cyclopropane **10** as a colorless oil: R_f = 0.24 (silica gel, 1:1 ether/petroleum ether); evaporative distillation 55–65 °C (0.0056 mmHg); $[\alpha]^{22}_D$ +92.6° (*c* 1.01, $CHCl_3$); IR ($CHCl_3$) 1460, 1380, 1285, 1145, 1105, 1025, 1000, 915, 870 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.6–0.8 (m, 2 H, cyclopropyl-CH_2), 1.03 (d, 3 H, J = 7.5 Hz, CH_3CH), 1.40 (s, 3 H, CH_3C), 3.37 (s, 3 H, OCH_3), 4.67 (s, 2 H, OCH_2O). Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 63.21; H, 8.71.

(1*R*,2*R*,8*R*)-2,8-Dimethyl-5(*S*)-(hydroxymethyl)-6,9-dioxabicyclo[3.3.1]non-2-ene (12). To a stirred solution of 405 mg (1.77 mmol) of the cyclopropane **10** in 22.5 mL of THF at 55 °C was added 5.5 mL of 10% aqueous HCl. After 17 h, the cooled reaction mixture was diluted with 70 mL of ether. The organic layer was separated, washed with four 20-mL portions of saturated aqueous NaCl, and dried ($MgSO_4$). Removal of the solvent under reduced pressure and chromatography of the residue on 20 g of silica gel with 4:6 ether/petroleum ether afforded 288 mg (88%) of the alcohol **12** as a colorless oil: R_f = 0.12 (silica gel, 4:6 ether/petroleum ether); evaporative distillation 55–65 °C (0.008 mmHg); $[\alpha]^{23}_D$ −75.0° (*c* 0.955, $CHCl_3$); IR ($CHCl_3$) 3580, 3470, 1350, 1365, 1100, 1055, 1030, 990, 930 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.37 (s, 3 H, CH_3CH), 1.37 (m, 1 H, CH_3CH), 1.70, (d, 3 H, J = 2 Hz, CH_3C=CH), 3.48 (d, 2 H, J = 6 Hz, CH_2OH), 3.91 (s, 1 H, CHC*H*O), 4.22 (dd, 1 H, J = 12 Hz, J' = 3 Hz, CHC*H*HO), 5.67 (br s, 1 H, CH_3C=C*H*). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.24; H, 8.71.

(1*R*,2*S*,8*S*)-2,8-Dimethyl-5(*S*)-(hydroxymethyl)-6,9-dioxabicyclo[3.3.1]non-2-ene (11). To a stirred solution of 448 mg (1.97 mmol) of the cyclopropane **9** in 24 mL of acetonitrile at 55 °C was added 6 mL of 10% aqueous HCl. After 40 min, the reaction mixture was allowed to cool, diluted with 200 mL of ether, and then washed with 50 mL of saturated aqueous $NaHCO_3$. The organic phase was washed with 50 mL of saturated aqueous NaCl. The combined aqueous phases were extracted with four 70-mL portions of dichloromethane. The bombined organic phases were dried ($MgSO_4$) and then concentrated under reduced pressure. To a stirred solution of the residue in 18 mL of dry acetonitrile was added 0.45 mL of 62% aqueous $HClO_4$. After 30 min at room temperature, the reaction mixture was poured into 50 mL of saturated aqueous $NaHCO_3$ and extracted with 200 mL of ether and then three 30-mL portions of dichloromethane. The combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Chromatography of the residue on 15 g of silica gel with 7:3 ether/petroleum ether afforded 344 mg (95%) of the alcohol **11** as an oil: R_f = 0.36 (silica gel, ether); evaporative distillation 45–55 °C (0.005 mmHg); $[\alpha]^{24}_D$ −105° (*c* 1.69, $CHCl_3$); IR ($CHCl_3$) 3590, 3470, 1620, 1470, 1380, 1130, 1060, 940, 840 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.75 (d, 3 H, J = 7.5 Hz, CH_3CH), 1.77 (m, 3 H, CH_3C=CH), 3.43 (d, 2 H, J = 5.5 Hz, CH_2OH), 3.63, 3.70 (2 s, 2 H, $CHCH_2O$), 4.17 (d, 1 H, J = 5 Hz, CHC*H*O), 5.76 (br s, 1 H, CH_3C=C*H*). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.01; H, 8.92.

(1*R*,2*S*,8*S*)-2,8-Dimethyl-5(*S*)-[([(trifluoromethyl)sulfonyl]oxy)methyl]-6,9-dioxabicyclo[3.3.1]non-2-ene and (1*R*,2*S*,8*S*)-2,8-Dimethyl-5(*S*)-(bromomethyl)-6,9-dioxabicyclo[3.3.1]non-2-ene (13). To a stirred solution of 176 mg (0.955 mmol) of the alcohol **11** and 0.13 mL (1.62 mmol) of pyridine in 9.2 mL of dichloromethane at −20 °C was added 0.26 mL (1.53 mmol) of trifluoromethanesulfonic anhydride. After 1 h, the reaction was poured into 50 mL of ice-cold saturated aqueous $NaHCO_3$. The resulting mixture was extracted with 200 mL of dichloromethane and then washed with 20 mL of saturated aqueous $NaHCO_3$. The combined aqueous phases were extracted with three 20-mL portions of dichloromethane and dried over a mixture of K_2CO_3 and $MgSO_4$. The solvent was evaporated under reduced pressure to afford the triflate as a dark oil.

In a separate experiment, chromatography of the residue on silica gel with 1:9 ether/petroleum ether afforded the trilfate in 81% yield as a colorless oil: R_f = 0.23 (silica gel, 1:9 ether/petroleum ether); evaporative distillation 70–80 °C (0.005 mmHg); $[\alpha]^{21}_D$ −81.5° (*c* 1.209, $CHCl_3$); IR ($CHCl_3$) 1465, 1410, 1140, 1110, 1050, 1010, 985 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.75 (d, 3 H, J = 7.5 Hz, CH_3CH), 1.64 (m, 3 H, CH_3C=CH), 3.20. 4.12 (2 s, $CH_2OSO_2CF_3$), 3.48 (d, 1 H, J = 3 Hz, CHC*H*HO), 3.57 (s, 1 H, CHCH*H*O), 4.05 (d, 1 H, J = 5 Hz, CHC*H*O), 5.60 (br s, 1 H, CH_3C=C*H*). Anal. Calcd for $C_{11}H_{15}F_3O_3S$: C, 41.77; H, 4.78; S, 10.14. Found: C, 41.50; H, 5.08; S, 9.96.

To prepare the bromide **13**, to a stirred solution of the above crude triflate in 5.3 mL of HMPA was added 1.00 g (3.10 mmol) of tetra-*n*-butylammonium bromide. After the mixture was heated at 45 °C for 9 h, it was allowed to cool and then poured into 75 mL of water. The resulting mixture was extracted with one 200-mL portion and then four 25-mL portions of ether. The combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Chromatography of the residue on 20 g of silica gel with 35:46 ether/petroleum ether afforded 219 mg (93%) of the bromide **13** as a colorless white solid: mp 55–56 °C; R_f = 0.27 (silica gel, 1:9 ether/petroleum ether); evaporative distillation 50–60 °C (0.005 mmHg); $[\alpha]^{22}_D$ −92.9° (*c* 2.32, $CHCl_3$); IR ($CHCl_3$) 2960, 2925, 2880, 1450, 1240, 1130, 1190, 990 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.72 (d, 3 H, J = 7.5 Hz, CH_3CH), 1.77 (m, 3 H, CH_3C=CH), 3.37 (s, 3 H, CH_2Br), 3.63 (d, 1 H, J = 2.5 Hz, CHC*H*HO), 3.72 (s, 1 H, CHCH*H*O), 4.22 (d, 1 H, J = 5 Hz, CHC*H*O), 5.75 (br s, 1 H, CH_3C=C*H*). Anal. Calcd for $C_{10}H_{15}BrO_2$: C, 48.60; H, 6.12. Found: C, 48.61; H, 6.12.

(5*R*,4*S*,6*R*)-4,6-Dimethyl-7(*S*)-hydroxy-1(*S*)-(bromomethyl)-2,9-dioxabicyclo[3.3.1]nonane. To a stirred solution of the olefin **13** in 5 mL of THF at 0 °C was added 6.75 mL (6.75 mmol) of a 1 M solution of borane in THF. After 1 h at room temperature, the solution was recooled to 0 °C and cautiously treated with 0.5 mL of water. After the evolution of hydrogen ceased (ca. 15 min), 0.60 mL of 10% aqueous NaOH and 0.15 mL of 30% aqueous H_2O_2 were added to the reaction mixture. After 1 h at 55 °C, an additional 0.4 mL of 10% aqueous NaOH and 0.2 mL of 30% aqueous H_2O_2 were added. Heating was continued for 40 min, and then the cooled solution was poured into 40 mL of water and extracted with one 200-mL portion and three 35-mL portions of ether. The combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Chromatography of the residue on 35 g of silica gel with 1:1 ether/petroleum ether afforded 337 mg (94%) of the alcohol as a colorless oil: R_f = 0.15 (silica gel, 1:1 ether/petroleum ether); evaporative distillation 80–90 °C (0.001 mmHg); $[\alpha]^{24}_D$ +31.3° (*c* 1.76, $CHCl_3$); IR ($CHCl_3$) 3560, 3300, 2975, 2920, 1470, 1370, 1175, 1120, 990, 905 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.93, 1.27 (2 d, 6 H, J = 7.5 Hz, 2 CH_3CH), 3.32 (s, 2 H, CH_2Br), 3.58, 3.85 (2 d, 2 H, J = 12 Hz, $CHCH_2O$). Although an analytical sample of the bromide **13** decomposed on standing in a sealed tube at room temperature, the compound could be stored safely at −20 °C.

(5*R*,4*S*,6*R*)-4,6-Dimethyl-7(*S*)-([(2-methoxyethoxy)methyl]oxy)-1(*S*)-(bromomethyl)-2,9-dioxabicyclo[3.3.1]nonane (14). To a stirred solution of 303 mg (1.14 mmol) of the above alcohol in 6 mL of dichloromethane were added, every 2 h, 0.13 mL (1.14 mmol) of (2-methoxyethoxy)methyl chloride and 0.20 mL (1.14 mmol) of *N*,*N*-(diisopropylethyl)amine. After 10 h at room temperature, the reaction mixture was diluted with 200 mL of dichloromethane and was washed with 40 mL of saturated aqueous $NaHCO_3$ and then 20 mL of saturated aqueous NaCl. The organic phase was dried ($MgSO_4$) and then concentrated under reduced pressure. Chromatography of the residue on 35 g of silica gel with 1:1 ether/petroleum afforded 363 mg (90%) of the ether **14** as a colorless oil: R_f = 0.11 (silica gel, 4:6 ether/petroleum ether); evaporative distillation; 140–145 °C (0.001 mmHg); $[\alpha]^{23}_D$ +68° (*c* 0.50, $CHCl_3$); IR ($CHCl_3$) 2940, 2900, 1485, 1450, 1240, 1200, 1100, 1040, 910, 850 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.93, 1.13 (2 d, 6 H, J = 7 Hz, 2 CH_3CH), 3.33 (s, 2 H, CH_2Br), 3.38 (s, 3 H, OCH_3), 4.70, 4.83 (2 d, 2 H, J = 7 Hz, OCH_2O). Anal. Calcd for $C_{14}H_{25}BrO_5$: C, 47.60; H, 7.13. Found: C, 47.69; H, 7.09.

2(*R*)-[1-(Benzyloxy)-2(*S*)-propyl]-3(*R*)-methyl-4(*S*)-([(2-methoxyethoxy)methyl]oxy)-6-methylenetetrahydropyran (15). To a stirred solution of 263 mg (0.745 mmol) of the bromide **14** in 20 mL of THF at −78 °C was added 0.59 mL (1.40 mmol) of a 2.38 M solution of *n*-butyllithium in hexane. After 3.5 h at −78 °C, 0.4 mL (3.36 mmol) of benzyl bromide (purified by filtration through alumina) was added, and then the solution was allowed to warm to 0 °C. One milliliter of HMPA was added, and, after 3.5 h at room temperature, the solution was concentrated at reduced pressure. Chromatography of the residue on 30 g of alumina (Activity III) with 1:3 ether/petroleum ether afforded first 169 mg (62%) of the exocyclic enol ether **15** as colorless oil: R_f = 0.07, 0.30 (silica gel, 1:1 ether/petroleum ether. Silica gel causes isomerization to the endocyclic enol ether **18**. The more polar compound is presumably the hydrate); ^{1}H NMR (CCl_4) δ 0.97, 1.12 (2 d, 6 H, J = 6 Hz, 2CH_3CH), 1.67–2.07 (m, 2 H, 2CH_3CH), 2.33 (m, 2 H, CH_2C=CH_2), 3.28 (s, 3 H, OCH_3), 3.89, 4.22 (2 s, 2 H, OC=CH_2), 4.42 (s, 2 H, $C_6H_5CH_2$), 4.63 (s, 2 H, OCH_2O), 7.23 (s, 5 H, C_6H_5). There was then eluted 12 mg (4.4%) of the enol ether **16** as a colorless oil: R_f = 0.00, 0.19 (silica gel, 1:1 ether/petroleum ether); ^{1}H NMR (CCl_4) δ 1.05, 1.12 (2 d, 6 H, J = 6 Hz, 2CH_3CH), 3.28 (s, 3 H, OCH_3), 3.96, 4.25 (2 s, 2 H, OC=CH_2), 7.23 (s, 5 H, C_6H_5). In separate experiments, ^{1}H NMR analysis of the crude reaction mixture indicated a 3:1 mixture of **15** and **16**.

2(*R*)-[1-(Benzyloxy)-2(*S*)-propyl]-3(*R*)-methyl-4(*S*)-([(2-methoxyethoxy)methyl]oxy)-6-methyl-3,4-dihydro-2*H*-pyran (18). A solution of

169 mg (0.464 mmol) of the exocyclic enol ether **15** in 15 mL of THF was heated at 50 °C for 1 h. The cooled solution was then concentrated under reduced pressure, and chromatography of the residue on 20 g of alumina (Activity III) with 1:3 ether/petroleum ether afforded 169 mg (100%) of the endocyclic enol ether **18** as a colorless oil: R_f = 0.30 (silica gel, 1:1 ether/petroleum ether); evaporative distillation 145–155 °C (0.001 mmHg); $[\alpha]^{26}_D$ +142° (*c* 0.973, $CHCl_3$); IR ($CHCl_3$) 3000, 2925, 1660, 1450, 1090, 1030, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.77, 1.15 (2 d, 6 H, *J* = 7 Hz, $2CH_3CH$), 1.77 (s, 3 H, $CH_3C{=}CH$), 1.87–2.27 (m, 2 H, $2CH_3CH$), 3.37 (s, 3 H, OCH_3), 4.47 (s, 2 H, $C_6H_5CH_2$), 4.73 (s, 2 H, OCH_2O). Anal. Calcd for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85. Found: C, 69.07; H, 8.87.

(1*R*,2*S*,8*S*)-2,8-Dimethyl-5(*S*)-[([(1,1-dimethylethyl)dimethylsilyl]oxy)methyl]-6,9-dioxabicyclo[3.3.1]non-2-ene. To a stirred solution of 222 mg (1.21 mmol) of the alcohol **11** in 2.0 mL of dichloromethane were added 0.8 mL (9.64 mmol) of pyridine and 363 mg (2.41 mmol) of *tert*-butyldimethylchlorosilane. After 16 h at room temperature, the reaction mixture was poured into 50 mL of saturated aqueous NaCl and extracted with two 100-mL portions of ether. The combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Chromatography of the residue on 30 g of silica gel with 1:9 ether/petroleum ether afforded 360 mg (100%) of the silyl ether as a colorless oil: R_f = 0.30 (silica gel, 1:9 ether/petroleum ether); evaporative distillation 70–75 °C (0.005 mmHg); $[\alpha]^{21}_D$ −78.0° (*c* 1.75, $CHCl_3$); IR ($CHCl_3$) 2960, 2860, 1470, 1255, 1120, 1060, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.07 (s, 6 H, $(CH_3)_2Si$), 0.72 (d, 3 H, *J* = 7 Hz, CH_3CH), 0.90 (s, 9 H, $(CH_3)_3C$), 1.77 (br s, 3 H, $CH_3C{=}CH$), 3.52 (s, 2 H, CH_2OSi), 3.60, 3.68 (2 s, 2 H, $CHCH_2O$), 4.15 (d, 1 H, *J* = 5 Hz, CHC*H*O), 5.77 (br s, 1 H, $CH_3C{=}CH$). Anal. Calcd for $C_{16}H_{30}O_3Si$: C, 64.38; H, 10.13. Found: C, 64.47; H, 10.20.

(5*R*,4*S*,6*R*)-4,6-Dimethyl-7(*S*)-hydroxy-1(*S*)-[([(1,1-dimethylethyl)dimethylsilyl]oxy)methyl]-2,9-dioxabicyclo[3.3.1]nonane. To a stirred solution of 340 mg (1.14 mmol) of the above silyl ether in 5.7 mL of THF at 0 °C was added 5.7 mL (5.7 mmol) of a 1 M solution of borane in THF. After 1 h at room temperature, the solution was recooled to 0 °C and treated with 0.84 mL of 15% aqueous NaOH and then 0.25 mL of 30% aqueous H_2O_2. After 1 h at 55 °C, the cooled solution was poured into 50 mL of saturated aqueous NaCl and extracted with two 100-mL portions of ether. The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on 25 g of silica gel with 6:4 ether/petroleum ether afforded 332 mg (92%) of the alcohol as a white solid: mp 183 °C; R_f = 0.23 (silica gel, 1:1 ether/petroleum ether); $[\alpha]^{22}_D$ +26.4° (*c* 1.94, $CHCl_3$); IR ($CHCl_3$) 3620, 3450, 1460, 1390, 1255, 1120, 1020, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.07 (s, 6 H, $(CH_3)_2Si$), 0.90 (s, 9 H, $(CH_3)_3C$), 0.90 (d, 3 H, *J* = 7 Hz, CH_3CH), 1.17 (d, 3 H, *J* = 7 Hz, CH_3CH), 3.47 (s, 2 H, CH_2OSi). Anal. Calcd for $C_{16}H_{32}O_4Si$: C, 60.72; H, 10.19. Found: C, 60.81; H, 10.25.

(5*R*,4*S*,6*R*)-4,6-Dimethyl-7(*S*)-(benzyloxy)-1(*S*)-[([(1,1-dimethylethyl)dimethylsilyl]oxy)methyl]-2,9-dioxabicyclo[3.3.1]nonane. To a stirred solution of 62 mg (0.19 mmol) of the above alcohol in 4 mL of THF at 0 °C were added 90 μL (0.76 mmol) of benzyl bromide (purified by filtration through alumina) and then 43 mg (0.37 mmol) of potassium *tert*-butoxide. After 10 min, the reaction was poured into 30 mL of saturated aqueous NaCl and extracted with two 75-mL portions of ether. The combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Chromatography of the residue on 10 g of silica gel with 1:9 ether/petroleum ether afforded 77 mg (97%) of the benzyl ether as a colorless oil: R_f = 0.19 (silica gel, 1:9 ether/petroleum ether); evaporative distillation 145–150 °C (0.005 mmHg); $[\alpha]^{22}_D$ +75.0° (*c* 2.56, $CHCl_3$); IR ($CHCl_3$) 2950, 2920, 2860, 1470, 1460, 1120, 1110, 1000, 835 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.07 (s, 6 H, $(CH_3)_2Si$), 0.87 (d, 3 H, CH_3CH), 0.90 (s, 9 H, $(CH_3)_3C$), 1.12 (d, 3 H, *J* = 7 Hz, CH_3CH), 3.47 (s, 2 H, CH_2OSi), 4.43, 4.67 (2 d, 2 H, *J* = 12 Hz, $C_6H_5CH_2$), 7.31 (s, 5 H, C_6H_5). Anal. Calcd for $C_{23}H_{38}O_4Si$: C, 67.94; H, 9.42. Found: C, 68.08; H, 9.39.

(5*R*,4*S*,6*R*)-4,6-Dimethyl-7(*S*)-(benzyloxy)-1(*S*)-(hydroxymethyl)-2,9-dioxabicyclo[3.3.1]nonane (20). To a stirred solution of 166 mg (0.407 mmol) of the above silyl ether in 4.0 mL of THF was added 1.0 mL (1.0 mmol) of a 1 M solution of tetra-*n*-butylammonium fluoride in THF. After 2 h at room temperature, the solution was poured into 50 mL of 50% saturated aqueous NaCl and extracted with two 75-mL portions of ether. The combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Chromatography of the residue on 25 g of silica gel with ether afforded 118 mg (99%) of the alcohol **20** as a colorless oil: R_f = 0.30 (silica gel, ether); evaporative distillation 145–150 °C (0.005 mmHg); $[\alpha]^{22}_D$ +98° (*c* 0.59, $CHCl_3$); IR ($CHCl_3$) 3580, 3500, 3000, 2920, 1475, 1190, 1130, 1065, 1005, 910 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.90 (d, 3 H, *J* = 7 Hz, CH_3CH), 1.16 (d, 3 H, *J* = 7 Hz, CH_3CH), 1.83 (dd, 1 H, *J* = 13 Hz, *J'* = 9 Hz, C(8)−βH), 2.05 (dd, 1 H, *J* = 8, *J'* = 5 Hz, CH_2OH), 2.27 (m, 1 H, CH_3CH), 2.36 (dd, 1 H, *J* = 13, *J'* = 6 Hz, C(8)−αH), 2.53 (m, 1 H, CH_3CH), 3.43 (dd, 1 H, *J* = 11, *J'* = 8 Hz, CHHOH), 3.49 (dd, 1 H, *J* = 11, *J'* = 5 Hz), 3.64 (dd, 1 H, *J* = 12, *J'* = 12 Hz, CHCHHO), 3.84 (dd, 1 H, *J* = 12, *J'* = 6 Hz, CHCHHO), 3.99 (dd, 1 H, *J* = 5, *J'* = 5 Hz, CHCHO), 4.02 (ddd, 1 H, *J* = 10, *J'* = 9, *J''* = 6 Hz, $CH_2CHCHCH_2$), 4.47, 4.68 (2 d, 2 H, *J* = 12 Hz, $C_6H_5CH_2$). Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27. Found: C, 69.75; H, 8.18.

Methyl 3-[(5*R*,4*S*,6*R*)-4,6-Dimethyl-7(*S*)-(benzyloxy)-2,9-dioxabicyclo[3.3.1]nonan-1-yl]-*cis*- and *trans*-propenoate (22). To a stirred solution of 42 μL (0.49 mmol) of oxalyl chloride in 4.0 mL of dichloromethane at −60 °C was added 69 μL (0.97 mmol) of dimethyl sulfoxide. After 10 min, a solution of 118 mg (0.404 mmol) of the alcohol **20** in 3 mL of dichloromethane was added to the reaction mixture. After 15 min, the reaction mixture was treated with 0.28 mL (2.0 mmol) of triethylamine and then allowed to warm to 0 °C. Methyl (triphenylphosphoranylidene) acetate (405 mg, 1.21 mmol) was then added, and after 10 min at room temperature, the reaction mixture was poured into 40 mL of saturated aqueous NaCl and extracted with two 100 mL portions of dichloromethane. The combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Chromatography of the residue on 25 g of silica gel with 1:1 ether/petroleum ether afforded 138 mg (99%) of a 95:5 trans/cis mixture (^1H NMR) of α,β-unsaturated esters as a colorless oil: R_f = 0.67 (trans), 0.63 (cis) (silica gel, ether). The trans isomer had the following physical properties: evaporative distillation 165–170 °C (0.005 mmHg); $[\alpha]^{21}_D$ +92.9 (*c* 1.47, $CHCl_3$); IR ($CHCl_3$) 3000, 2950, 2885, 1715, 1430, 1305, 1275, 1125, 1070, 1000, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90, 1.15 (2 d, 6 H, *J* = 7 Hz, 2 CH_3CH), 1.75 (dd, 1 H, *J* = 14, *J'* = 9 Hz, CCHHCH), 2.42 (dd, H, *J* = 14, *J'* = 6 Hz, CCHHCH), 3.70 (s, 3 H, OCH_3), 4.43, 4.65 (2 d, 2 H, *J* = 12 Hz, $C_6H_5CH_2$), 6.10, 6.77 (2 d, 2 H, *J* = 16 Hz, CH=CH), 7.31 (s, 5 H, C_6H_5). Anal. Calcd for $C_{20}H_{26}O_5$: C, 69.34; H, 7.56. Found: C, 69.29; H, 7.50. ^1H NMR (cis isomer, $CDCl_3$) δ 0.88, 1.14 (2 d, 6 H, *J* = 7 Hz, $2CH_3CH$), 3.37 (s, 3 H, OCH_3), 5.83 (s, 2 H, *cH*=CH), 7.32 (s, 5 H, C_6H_5).

Methyl 3-[(5*R*,4*S*,6*R*)-4,6-Dimethyl-7(*S*)-(benzyloxy)-2,9-dioxabicyclo[3.3.1]nonan-1-yl]propanoate. To a stirred solution of 131 mg (0.378 mmol) of the above olefins **22** in 5 mL of *n*-pentane was added 35 mg of 5% rhodium on carbon. The reaction mixture was stirred at room temperature under a hydrogen atmosphere for 5 h. The catalyst was then removed by filtration and washed with three 10-mL portions of ethyl acetate. Removal of the solvent from the combined filtrates and chromatography of the residue on 25 g of silica gel with 4:6 ether/petroleum ether afforded 124 mg (94%) of the alkane as a colorless oil: R_f = 0.28 (silica gel, 4:6 ether/petroleum ether); evaporative distillation 165–170 °C (0.005 mmHg); $[\alpha]^{21}_D$ +87.1° (*c* 2.03, $CHCl_3$); IR ($CHCl_3$) 3000, 2950, 1730, 1435, 1190, 1125, 1065, 1005, 960 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88, 1.13 (2 d, 6 H, *J* = 7 Hz, $2CH_3CH$), 3.68 (s, 3 H, OCH_3), 4.48, 4.72 (2 d, 2 H, *J* = 12 Hz, $C_6H_5CH_2$), 7.34 (s, 5 H, C_6H_5). Anal. Calcd for $C_{20}H_{28}O_5$: C, 68.94; H, 8.10. Found: C, 68.80; H, 8.02.

3-[(5*R*,4*S*,6*R*)-4,6-Dimethyl-7(*S*)-(benzyloxy)-2,9-dioxabicyclo-[3.3.1]nonan-1-yl]propan-1-ol. To a stirred solution of 115 mg (0.331 mmol) of the above methyl ester in 5 mL of ether at 0 °C was added 36 mg (0.95 mmol) of lithium tetrahydridoaluminate. After 1 h, the reaction mixture was cautiously treated with 36 μL of water, 36 μL of 15% aqueous NaOH, and then 108 μL of water. The reaction mixture was filtered and then concentrated under reduced pressure. Chromatography of the residue on 10 g of silica gel with ether afforded 106 mg (100%) of the alcohol as a colorless oil: R_f = 0.21 (silica gel, ether); evaporative distillation 175 °C (0.001 mmHg); $[\alpha]^{21}_D$ +95.7° (*c* 2.03, $CHCl_3$); IR ($CHCl_3$) 3440, 3000, 2960, 2890, 1450, 1370, 1190, 1065, 1000, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87, 1.13 (2 d, 6 H, *J* = 7 Hz, $2CH_3CH$), 4.43, 4.67 (2 d, 2 H, *J* = 12 Hz, $C_6H_5CH_2$), 7.33 (s, 5 H, C_6H_5). Anal. Calcd for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81. Found: C, 71.25; H, 8.75.

3-[(5*R*,4*S*,6*R*)-4,6-Dimethyl-7(*S*)-(benzyloxy)-2,9-dioxabicyclo-[3.3.1]nonan-1-yl]propanol (23). To a stirred solution of 29 μL (0.33 mmol) of oxalyl chloride in 3 mL of dichloromethane at −60 °C was added 47 μL (0.66 mmol) of dimethyl sulfoxide. After 10 min, a solution of 88 mg (0.27 mmol) of the above alcohol in 2 mL of dichloromethane was added to the reaction mixture. After 15 min, the reaction mixture was treated with 0.19 mL (1.4 mmol) of triethylamine, allowed to warm to room temperature, and then poured into 20 mL of brine. The resulting mixture was extracted with two 50-mL portions of ether. The combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Chromatography of the residue on 25 g of silica gel with 4:6 ether/petroleum ether afforded 86 mg (97%) of the aldehyde **23** as a colorless oil: R_f = 0.30 (silica gel, 1:1 ether/petroleum ether); evaporative distillation 170 °C (0.005 mmHg); $[\alpha]^{21}_D$ +89.7° (*c* 1.76, $CHCl_3$); IR ($CHCl_3$) 3000, 2960, 1720, 1450, 1370, 1190, 1090, 1080, 1010, 910 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85, 1.12 (2 d, 6 H, *J* = 7 Hz,

2CH_3CH), 4.40, 4.63 (2 d, 2 H, J = 12 Hz, $C_6H_5CH_2$), 7.32 (s, 5 H, C_6H_5), 9.73 (t, 1 H, J = 1.5 Hz, C(0)H). Anal. Calcd for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.57; H, 8.29.

Ethyl 4-[(5*R*,4*S*,6*R*)-4,6-Dimethyl-7(*S*)-(benzyloxy)-2,9-dioxabicyclo[3.3.1]nonan-1-yl]-2(*R*)- and 2(*S*)-hydroxybutanoate. To a stirred solution of 0.25 mL (2.6 mmol) of ethyl vinyl ether in 2.5 mL of THF at −78 °C was added 1.36 mL (1.63 mmol) of a 1.2 M solution of *tert*-butyllithium in pentane. The resulting mixture was placed in an ice bath, and after 10 min, 1.5 mL (~0.6 mmol) of the pale yellow solution was added all at once to a solution of 93 mg (0.29 mmol) of the aldehyde **23** in 4 mL of THF at −78 °C. After 10 min, the solution was allowed to warm to 0 °C and was then poured into 25 mL of a saturated aqueous solution of NH_4Cl buffered to pH 8 with concentrated aqueous ammonia. The resulting mixture was extracted with two 50-mL portions of ether. The combined organic extracts were dried and then concentrated under reduced pressure. To a solution of the residue in 4 mL of dichloromethane at −78 °C was added 1 mL of methanol. A stream of ozone was passed through this solution until the light blue color persisted (1 min). The solution was purged with a stream of nitrogen, and then 0.4 mL of dimethyl sulfide was added to the reaction mixture. After 1 h at room temperature, the solvent was removed under reduced pressure. Chromatography of the residue on 10 g of silica gel with 7:3 ether/petroleum ether afforded 71 mg (62%) of a ~1:1 mixture of ethyl esters as a colorless oil: R_f = 0.26 (silica gel, 7:3 ether/petroleum ether); evaporative distillation 190 °C (0.005 mmHg); IR ($CHCl_3$) 3530, 3400, 3000, 2980, 1725, 1450, 1385, 1365, 1205, 1190, 1065, 1005 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88, 1.13, (2 d, 6 H, J = 7 Hz, 2CH_3CH), 1.30 (t, 3 H, J = 7 Hz, CH_3CH$_2$), 4.18 (q, 2 H, J = 7 Hz, CH$_3$CH_2), 4.43, 4.67 (2 d, 2 H, J = 12 Hz, $C_6H_5CH_2$), 7.33 (s, 5 H, C_6H_5). Anal. Calcd for $C_{22}H_{32}O_6$: C, 67.32; H, 8.22. Found: C, 67.40; H, 8.29.

(6*S*,2*R*)- and (6*R*,2*R*)-2-(1-Hydroxy-2(*S*)-propyl)-3(*R*)-methyl-4-(*S*)-(benzyloxy)-8(*R*)- and 8(*S*)-carboethoxy-1,7-dioxaspiro[5.4]decane. To a solution of 56 mg (0.14 mmol) of the above alcohol in 1.0 mL of $CDCl_3$ in an NMR tube was added 19 mg (0.077 mmol) of pyridinium *p*-toluenesulfonate. The progress of the equilibrium was monitored by the disappearance of the doublet (CH_3CH) at 1.13 ppm. After 20 h, the reaction mixture was concentrated under reduced pressure. Chromatography of the residue on 10 g of silica gel with ether afforded 48 mg (85%) of an unseparated mixture of spiroketals as a colorless oil: R_f = 0.48, 0.41, 0.36 (silica gel, ether); evaporative distillation 190–195 °C (0.005 mmHg); IR ($CHCl_3$) 3450, 3000, 2930, 1735, 1450, 1375, 1350, 1215, 1195, 1095, 1065, 1055, 1025 cm^{-1}. Anal. Calcd for $C_{22}H_{32}O_6$: C, 67.32; H, 8.22. Found: C, 67.27; H, 8.18.

(6*S*,2*R*)- and (6*R*,2*R*)-2-[1-([(1,1-Dimethylethyl)dimethylsilyl]oxy)-2(*S*)-propyl]-3(*R*)-methyl-4(*S*)-(benzyloxy)-8(*R*)- and 8(*S*)-carboethoxy-1,7-dioxaspiro[5.4]decane (24). To a stirred solution of 34 mg (0.087 mmol) of the above alcohols in 2.0 mL of dichloromethane were added 0.5 mL of pyridine and 50 mg (0.33 mmol) of *tert*-butyldimethylchlorosilane. After 4 h at room temperature, the reaction mixture was poured into 20 mL of saturated aqueous NaCl and extracted with 75 mL of ether. The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue on 10 g of silica gel with 2:8 ether/petroleum ether afforded first 19.9 mg (45%) of a spiroketal as a colorless oil: R_f = 0.26 (silica gel, 2:8 ether/petroleum ether); evaporative distillation 195 °C (0.001 mmHg); IR ($CHCl_3$) 3000, 2960, 2930, 2860, 1740, 1460, 1380, 1350, 1250, 1100, 1050, 1030, 1010, 840 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.02 (s, 6 H, $(CH_3)_2$Si), 0.87 (s, 9 H, $(CH_3)_3$C), 0.88, 0.95 (2 d, 6 H, J = 7 Hz, 2CH_3CH), 1.26 (t, 3 H, J = 7 Hz, CH_3CH$_2$), 1.68–1.80 (m, 2 H), 1.89 (dd, 1 H, J = 15, J' = 4 Hz, CHHCHO), 1.89–1.98 (m, 3 H), 2.12 (dd, 1 H, J = 15, J' = 1 Hz, CHHCHO), 2.42 (m, 1 H, CH$_3$CH), 3.35 (dd, 1 H, J = 10, J' = 6.5 Hz, CHCHHOSi), 3.47 (m, CH$_2$CHCH), 3.52 (dd, 1 H, J = 10, J' = 5 Hz, CHCHHOSi), 3.93 (dd, 1 H, J = 10, J' = 2 Hz, CHCHCH), 4.17 (q, 2 H, J = 7 Hz, CH$_3$CH_2), 4.54, 4.69 (2 d, 2 H, J = 12.5 Hz, $C_6H_5CH_2$), 4.59 (dd, 1 H, J = 9.5, J' = 3.5 Hz, CH$_2$CHCO$_2$Et). Anal. Calcd for $C_{28}H_{46}O_6Si$: C, 66.37; H, 9.15. Found: C, 66.45; H, 9.11.

There was then eluted 10.9 g (25%) of an isomeric spiroketal as a colorless oil: R_f = 0.16 (silica gel, 1:1 ether/petroleum ether); evaporative distillation 195 °C (0.001 mmHg); IR ($CHCl_3$) 3000, 2970, 2940, 2860, 1755, 1725, 1460, 1260, 1100, 1160, 840 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.00 (s, 6 H, $(CH_3)_2$Si), 0.85 (s, 9 H, $(CH_3)_3$C), 0.85, 0.89 (2 d, 6 H, J = 7 Hz, 2CH_3CH), 1.30 (t, 3 H, J = 7 Hz, CH_3CH$_2$), 1.64–1.73 (m, 2 H), 1.87 (dd, 1 H, J = 15, J' = 2.5 Hz, CHHCHO), 1.95 (dd, 1 H, J = 15, J' = 4 Hz, CHHCHO), 1.97–2.04 (m, 2 H), 2.17–2.32 (m, 2 H), 3.31 (dd, J = 10, J' = 6 Hz, CHCHHOSi), 3.45 (dd, J = 10, J' = Hz, CHCHHOSi), 3.50 (m, 1 H, CH$_2$CHCH), 4.13 (dd, 1 H, J = 10, J' = 2 Hz, CHCHCH). 4.13, 4.25 (2 dq, 2 H, J = 11, J' = 7 Hz, CH$_3$CH_2), 4.57, 4.64 (2 d, 2 H, J = 13 Hz, $C_6H_5CH_2$), 4.62 (dd, 1 H, J = 9.5, J' = 8 Hz, CH$_2$CHCO$_2$Et). Anal. Calcd for $C_{28}H_{46}O_6Si$: C, 66.37; H, 9.15. Found: C, 66.21; H, 9.16.

There was then eluted 8.5 mg (19%) of an isomeric spiroketal as a colorless oil: R_f = 0.12 (silica gel, 2:8 ether/petroleum ether); evaporative distillation 195 °C (0.001 mmHg); IR ($CHCl_3$) 3000, 2970, 2940, 2860, 1745, 1460, 1260, 1150, 1100, 1030, 1000, 840 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.02, 0.03 (2 s, 6 H, $(CH_3)_2$Si), 0.86 (s, 9 H, $(CH_3)_3$C), 0.98, 1.01 (2 d, 6 H, J = 7 Hz, 2CH_3CH), 1.28 (t, 3 H, J = 7.5 Hz, CH_3CH$_2$), 1.69 (m, 1 H), 1.80 (m, 1 H), 1.97–2.05 (m, 3 H), 2.20 (dd, 1 H, J = 15, J' = 3 Hz, CHHCHO), 2.37 (m, 1 H), 2.46 (m, 1 H), 3.49 (dd, 1 H, J = 11, J' = 5 Hz, CHCHHOSi), 3.51 (dd, 1 H, J = 11, J' = 5 Hz, CHCHHOSi), 3.64 (dd, 1 H, J = 6, J' = 3 Hz, CH$_2$CHCH), 3.69 (dd, 1 H, J = 9.5, J' = 2 Hz, CHCHCH), 4.19 (m, 2 H, CH$_3$CH_2), 4.52, 4.55 (2 d, 2 H, J = 12 Hz, $C_6H_5CH_2$), 4.68 (dd, 1 H, J = 9.5, 3 Hz, CH$_2$CHCO$_2$Et). Anal. Calcd for $C_{28}H_{46}O_6Si$: C, 66.37; H, 9.15. Found: C, 66.64; H, 9.15.

There was then eluted 2.7 mg (6%) of an isomeric spiroketal as a colorless oil: R_f = 0.09 (silica gel, 2:8 ether/petroleum ether); evaporative distillation 195 °C (0.001 mmHg); IR ($CHCl_3$) 2960, 2940, 2860, 1725, 1460, 1150, 1100, 1070, 1030, 1010, 840 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.02, 0.03 (2 s, 6 H, $(CH_3)_2$Si), 0.97, 0.98 (2 d, 6 H, J = 7 Hz, 2CH_3CH), 1.28 (t, 3 H, J = 7 Hz, CH_3CH$_2$), 1.67 (m, 1 H), 1.77 (m, 1 H), 1.83 (dd, 1 H, J = 14, J' = 2 Hz, CHHCHO), 1.98 (m, 1 H), 2.15 (dd, 1 H, J = 14, J' = 3 Hz, CHHCHO), 2.17–2.25 (m, 2 H), 2.53 (m, 1 H), 3.47 (d, 2 H, J = 4.5 Hz, CHCH_2OSi), 3.63 (ddd, 1 H, J = 6, J' = 3, J'' = 2 Hz, CH$_2$CHCH), 3.66 (dd, 1 H, J = 9.5, J' = 2 Hz, CHCHCH), 4.19, 4.25 (2 m, 2 H, CH$_3$CH_2), 4.48 (dd, 1 H, J = 8, J' = 8 Hz, CH$_2$CHCO$_2$Et), 4.49, 4.55 (2 d, 2 H, J = 12 Hz, $C_6H_5CH_2$). Anal. Calcd for $C_{28}H_{46}O_6Si$: C, 66.37; H, 9.15. Found: C, 66.26; H, 8.91.

The most and least polar of the spiroketal diastereomers were shown to bear the same configuration at the carboethoxy center by equilibration of the spiroketal center with pyridinium *p*-toluenesulfonate in chloroform. The spiroketals of intermediate polarity were also interconverted by acid-catalyzed equilibration.

(6*R*,2*R*)-2-[1-([(1,1-Dimethylethyl)dimethylsilyl]oxy)-2-(*S*)-propyl]-(3*R*,4*S*)-4-hydroxy-8-carboethoxy-1,7-dioxaspiro[5.4]decane (25). To a stirred solution of 5.0 mg (0.0098 mmol) of the spiroketal **24** (R_f = 0.16, silica gel, 2:8 ether/petroleum ether) in 2 mL of ethanol was added 10 mg of 10% palladium on carbon. The reaction mixture was stirred at room temperature under a hydrogen atmosphere for 22 h. The catalyst was then removed by filtration and washed with two 5-mL portions of ethyl acetate. The combined filtrates were concentrated under reduced pressure. To a solution of the residue in 0.5 mL of $CDCl_3$ was added 5 mg of pyridinium *p*-toluenesulfonate. After 24 h at room temperature, the solvent was removed under reduced pressure. Chromatography of the residue on 5 g of silica gel with 7:3 ether/petroleum ether afforded 3.7 mg (90%) of the alcohol **25** as a colorless oil: R_f = 0.25 (silica gel, 7:3 ether/petroleum ether); IR (CCl_4) 3560, 2960, 2940, 2860, 1760, 1740, 1465, 1375, 1255, 1100, 1060, 1035, 840 cm^{-1}; ^{1}H NMR (500 MHz, 9:1 CCl_4/C_6D_6) δ 0.03, 0.04 (2 s, 6 H, $(CH_3)_2$Si), 0.82, 0.89 (2 d, 6 H, J = 7 Hz, 2CH_3CH), 0.91 (s, 9 H, $(CH_3)_3$C), 1.22 (t, 3 H, J = 7 Hz, CH_3CH$_2$), 1.54 (m, 1 H), 1.56 (br d, 1 H, J = 12 Hz, CHHCHO), 1.69 (m, 1 H), 1.79 (m, 1 H), 1.94 (m, 1 H), 1.96 (d, 1 H, J = 12 Hz, CHHCHO), 2.07–2.22 (m, 2 H), 3.37 (dd, 1 H, J = 10, J' = 6 Hz, CHCHHOSi), 3.41 (dd, 1 H, J = 10, J' = 4 Hz, CHCHHOSi), 3.62 (br m, 1 H, CH$_2$CHCH), 4.05 (dd, 1 H, J = 10, J' = 2 Hz, CHCHCH), 4.06 (dq, 1 H, J = 11, J' = 7 Hz, CH$_3$CHH), 4.14 (dq, 1 H, J = 11, J' = 7 Hz, CH$_3$CHH), 4.43 (dd, 1 H, J = 8.5, J' = 8.5 Hz, CH$_2$CHCO$_2$Et).

By the procedure described above, a solution of 5.0 mg (0.0098 mmol) of the spiroketal **24** (R_f = 0.26, silica gel, 2:8 ether/petroleum ether) in 2 mL of ethanol with 10 mg of 10% palladium on carbon, and then 5 mg of pyridinium *p*-toluenesulfonate in 0.5 mL of $CDCl_3$, afforded, after chromatography on 5 g of silica gel with 7:3 ether/petroleum ether, 3.7 mg (90%) of the alcohol **25** as a colorless oil: R_f = 0.26 (silica gel, 7:3 ether/petroleum ether); evaporative distillation 190 °C (0.005 mmHg); IR (CCl_4) 3560, 2960, 2940, 2860, 1755, 1465, 1380, 1255, 1200, 1120, 1100, 1050, 1035, 840 cm^{-1}; ^{1}H NMR (500 MHz, 9:1 CCl_4/C_6D_6) δ 0.03, 0.04 (2 s, 6 H, $(CH_3)_2$Si), 0.83 (d, 3 H, J = 7 Hz, CH_3CH), 0.90 (s, 9 H, $(CH_3)_3$C), 0.96 (d, 3 H, J = 6.5 Hz, CH_3CH), 1.21 (t, 3 H, J = 7 Hz, CH_3CH$_2$), 1.63–1.74 (m, 2 H), 1.78 (dd, 1 H, J = 15, J' = 2 Hz, CHHCHO), 1.85–1.93 (m, 2 H), 1.96 (dd, 1 H, J = 15, J' = 3.5 Hz, CHHCHO), 2.24–2.33 (m, 2 H), 3.26 (br d, 1 H, J = 9 Hz, CHOH), 3.36 (dd, 1 H, J = 10, J' = 6 Hz, CHCHHOSi), 3.48 (dd, 1 H, J = 10, J' = 4 Hz), 3.65 (br m, 1 H, CH$_2$CHCH), 3.82 (dd, 1 H, J = 10, J' = 2 Hz, CHCHCH), 4.07, 4.08 (2 q, 2 H, J = 7 Hz, CH$_3$CH_2), 4.43 (dd, 1 H, J = 9, J' = 4 Hz, CH$_2$CHCO$_2$Et). Anal. Calcd for $C_{21}H_{40}O_6Si$: C, 60.54; H, 9.68. Found: C, 60.60; H, 9.57.