A Formal Total Synthesis of (+)-Tetronolide, the Aglycon of the Tetrocarcins: Enantio- and Diastereoselective Syntheses of the Octahydronaphthalene (Bottom-Half) and Spirotetronate (Top-Half) Fragments

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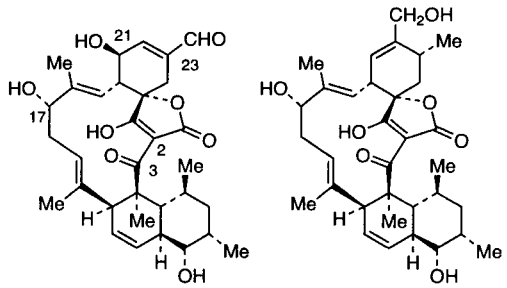
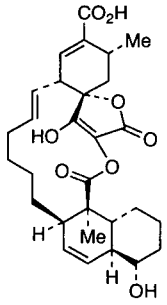
A formal total synthesis of (+)-tetronolide, the aglycon of the tetrocarcins, has been achieved by virtue of the development of highly diastereo- and enantioselective syntheses of the bottom- and top-half fragments **4** and **5** reported herein. These fragments previously served as key intermediates in Yoshii's pioneering total synthesis of (+)-tetronolide. The synthesis of the bottom-half octahydronaphthalene unit **4** features the intramolecular Diels−Alder reaction of tetraenal **20** and proceeds in 17 steps and 5−6% yield from D-glyceraldehyde pentylidene acetal **8**. The synthesis of the spirotetronate fragment **5** features the highly enantioselective exo selective Diels−Alder reaction of triene **37** and chiral dienophile **25b** and proceeds in 14 steps and 10% overall yield from *cis*-2-butene-1,4-diol (**38**). An enantioselective synthesis of Boeckman's top-half cyclohexene fragment **6** via the exo selective Diels−Alder reaction of diene **24** and dienophile **25a** was also developed, but this route was deemed too inefficient for use in a projected total synthesis of the natural product. The syntheses of **5** and **6** provide important information on the utility of chiral dienophiles **25a** and **25b** in organic synthesis.

Tetronolide (**1**) is the aglycon of the tetrocarcins, a group of structurally related spirotetronate antibiotics (e.g., tetrocarcins A−C, E1, E2, F, and F-1) isolated from the culture broth of *Micromonospora chaldea* KY 11091.[1−5] These antibiotics are complex glycosides, the full stereostructures of which have not been assigned. Tetrocarcins A, B, and C, which share a common nitro sugar (tetronose) as well as the deoxysugars L-amicetose and L-digitoxose, display activity against experimental tumors such as mouse sarcoma 180 and mouse leukemia P 388.[2] Tetronolide is structurally related to kijanolide (**2**)[6] and chlorothricolide (**3**),[7,8] the aglycons of kijanimicin and chlorothricin, which possess antibiotic activities.[9,10] The structure of tetronolide was assigned by an X-ray analysis,[1] and the absolute configuration was determined by Yoshii in his pioneering total synthesis.[11]

Because of its structural complexity and interesting biological activity, tetronolide has received considerable attention as a synthetic target. In 1991 Yoshii reported the first, and to date only, total synthesis[11] of **1** via the coupling of the bottom-half octahydronaphthalene fragment **4**[11,12] and the top-half spirotetronate subunit **5**.[13] Marshall[14,15] and Boeckman[16] have developed syntheses of bottom-half fragments related to **4**, while Boeckman





chlorothricolide (**3**)

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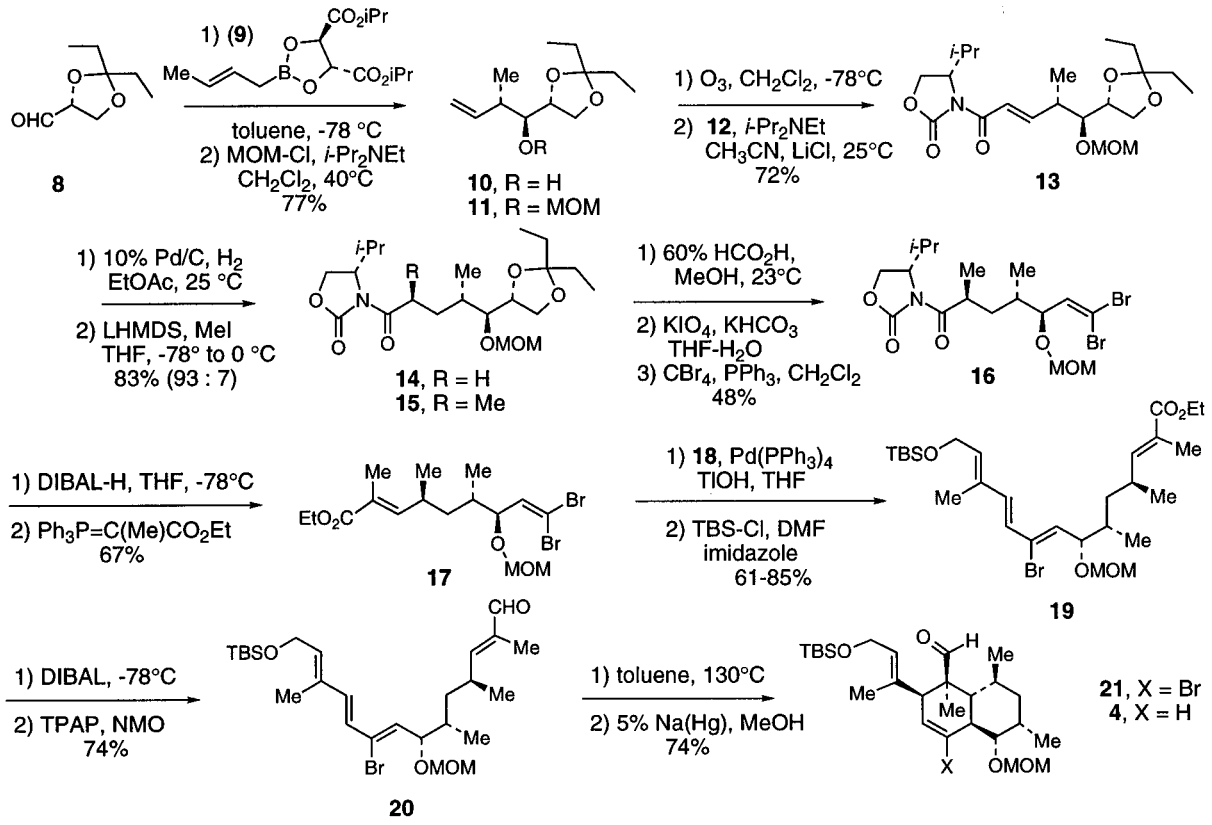
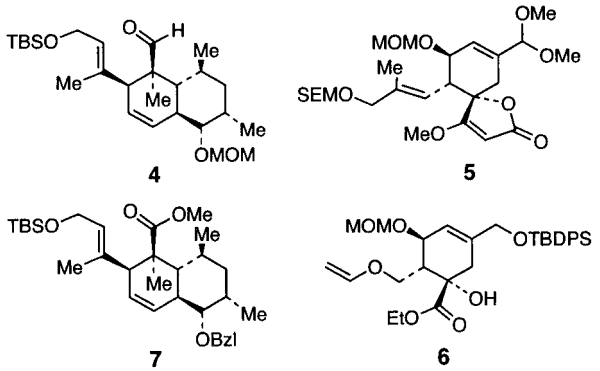
Scheme 1

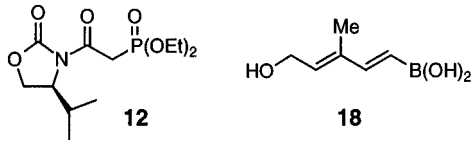


has described a synthesis of α-hydroxy ester **6** as a potential precursor to the top half of **1**.[17,18] We have reported syntheses of octahydronaphthalene **7**,[19] corresponding to the bottom halves of both kijanolide and tetronolide, as well as an enantioselective synthesis of spirotetronate (+)-**5**.[20] We report herein a highly diastereo- and enantioselective synthesis of Yoshii's bottom-half fragment **4**, as well as the full details of our enantioselective synthesis of the top-half fragment **5**. This work thus constitutes a formal total synthesis of tetronolide.



Enantio- and Diastereoselective Synthesis of the Bottom-Half Fragment 4. All previous syntheses of the octahydronaphthalene subunits of tetronolide (**1**) and kijanolide (**2**) have utilized intramolecular Diels–Alder reactions[21–24] as the key step.[11,12,15,16,19] In undertaking the synthesis of **4** reported here, we wished to avoid the introduction of a superfluous C(5)-hydroxyl group that complicated our earlier synthesis of **7**,[19] and we also wanted to avoid unwieldy protecting group switches which would have been necessary had we chosen to synthesize **4** from **7** or related series of intermediates.[19,25] Because our supplies of **7** had been virtually exhausted by the time we decided to initiate this synthesis of **4**, we developed the route summarized in Scheme 1.

D-Glyceraldehyde pentylidene ketal **8**[26] served as the starting material for this synthesis. This compound is much less prone to hydration and oligomerization than the corresponding acetonide[27] which we used in our earlier synthesis of **7**.[19] Thus, treatment of **8** with tartrate (*E*)-crotylboronate (*R*,*R*)-**9** provided homoallylic alcohol **10** as an 88:12 mixture of easily separated diastereomers.[28–30] Protection of the hydroxyl group of **10** as a MOM ether and ozonolysis of the terminal alkene provided the corresponding aldehyde, which was then treated with the known phosphonate reagent **12**[25] using Masamune's LiCl–*i*-Pr$_2$NEt conditions for the Wads-



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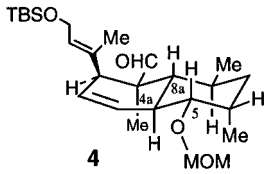
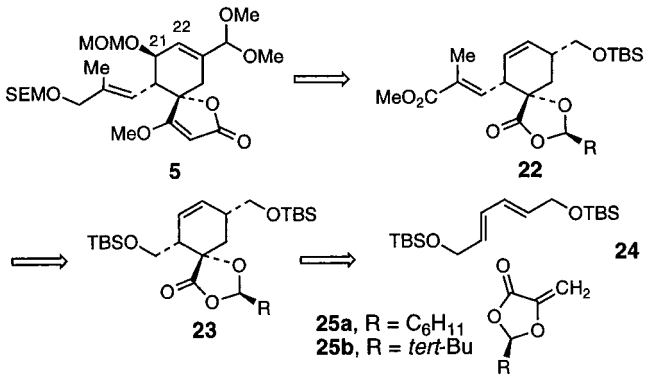
worth−Horner−Emmons reaction,[31] thereby giving **13** in 72% yield. Hydrogenation of **13** over 10% Pd/C provided **14**, the lithium enolate of which underwent a highly diastereoselective alkylation reaction with MeI (93:7 diastereoselectivity, 83% yield).[32] Removal of the pentylidene ketal was accomplished by treatment of **15** with 60% formic acid in MeOH. Oxidative cleavage of the resulting diol with KIO_4 and $KHCO_3$,[26] followed by Corey−Fuchs olefination of the intermediate aldehyde, provided dibromoolefin **16** in 48% overall yield.[33] Selective reduction of **16** with DIBAL in THF at −78 °C provided the corresponding aldehyde (79%) which was treated with (carbethoxyethylidene)triphenylphosphorane in toluene at 60 °C. This two-step sequence provided a 9:1 mixture of olefin isomers, from which **17** was obtained in 67% yield from **15**. Dibromoolefin **17** underwent cross coupling with vinylboronic acid **18** under Kishi's modified Suzuki cross-coupling conditions,[34,35] thereby providing tetraenoate **19** following protection of the primary hydroxyl as a TBS ether. Reduction of **19** with excess DIBAL and reoxidation of the intermediate allylic alcohol with TPAP and NMO[36] provided tetraenal **20** in 74% yield. A toluene solution of **20** was heated at 130 °C for 12 h to provide the desired cycloadduct **21** in 90% yield. Analysis of the ^{1}H NMR spectrum of the crude IMDA reaction mixture failed to reveal the presence of any diastereomeric cycloadducts, thereby indicating that the stereoselectivity of this reaction was ⩾98:⩽2. Finally, reductive removal of the C(9)-Br steric directing group[19,37] by using 5% Na(Hg) in MeOH provided the targeted tetronolide bottom half fragment **4** in 74% yield from **20**. The stereostructure of **4** was assigned initially by spectroscopic comparisons with **7**, especially in view of the characteristic coupling constants summarized below. Unambiguous verification of stereostructure was subsequently obtained by comparison of **4** ($[\alpha]^{20}_D$ −100° (*c* 0.6, $CHCl_3$)) with an authentic sample ($[\alpha]^{23}_D$ −101.2° (*c* 2.70, $CHCl_3$)) kindly provided by Professor Yoshii.[11]

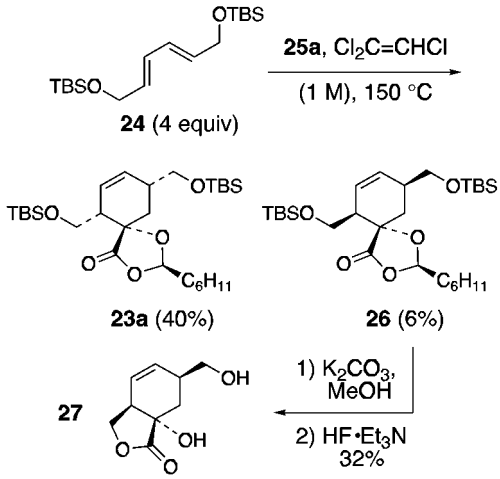


$J_{4a,8a}$ = 11.2 Hz
$J_{4a,5}$ = 10.8Hz
$J_{8,8a}$ = 10.0 Hz

Enantio- and Diastereoselective Synthesis of the Top-Half Spirotetronate Substructure. In contemplating a synthesis of a tetronolide top-half spirotetronate precursor such as **5**, we anticipated that the C(21) alkoxy group and the C(22−23) olefin could be introduced by a sequence involving either peroxidation or osmylation of **22** followed by oxidation of the primary hydroxymethyl group with concomitant elimination of the C(22) alkoxy substituent.[38] In turn, we anticipated that **22** could be prepared from spirolactone **23**, which we had already prepared via the Diels−Alder reaction of diene **24**[39] and the chiral dienophile **25a**.[40,41]



The Diels−Alder reaction of **24** and **25a** was performed by heating a mixture of 4 equiv of **24** and **25a** (1 M) in trichloroethylene at 150 °C for 42 h. Diene **24** proved to be substantially less reactive than the conjugated trienes used in our syntheses of the top halves of kijanolide[42,43] and chlorothricolide,[44,45] which necessitated that this reaction be performed at a higher temperature for longer reaction periods. Unfortunately, the instability of **25a** under these conditions limited the efficiency of the reaction. The combined yield of the exo and endo cycloadducts, **23a** and **26**, respectively, was only 10−15% when the reaction was performed with 1 equiv of **24** but increased to 46% (based on **25a**) when 4 equiv of the diene was used. Fortunately, the excess diene could be recovered efficiently (85% yield) at the conclusion of the reaction; on the basis of consumed diene the combined yield of cycloadducts was 75−80%.



The stereochemistry of the endo cycloadduct **26** was assigned following conversion to the cis-fused lactone **27**, mp 110−112 °C.[38,46] Under similar conditions, the major cycloadduct, **23a**, was converted to triol **28**, thereby confirming the assignment of **23a** as an exo cycloadduct (Scheme 2). Differentiation of the two primary hydroxymethyl groups was accomplished by treatment of **28** with benzaldehyde and $ZnCl_2$ in Et_2O, which provided a ca. 6−7:1 mixture of the diastereomeric benzylidene

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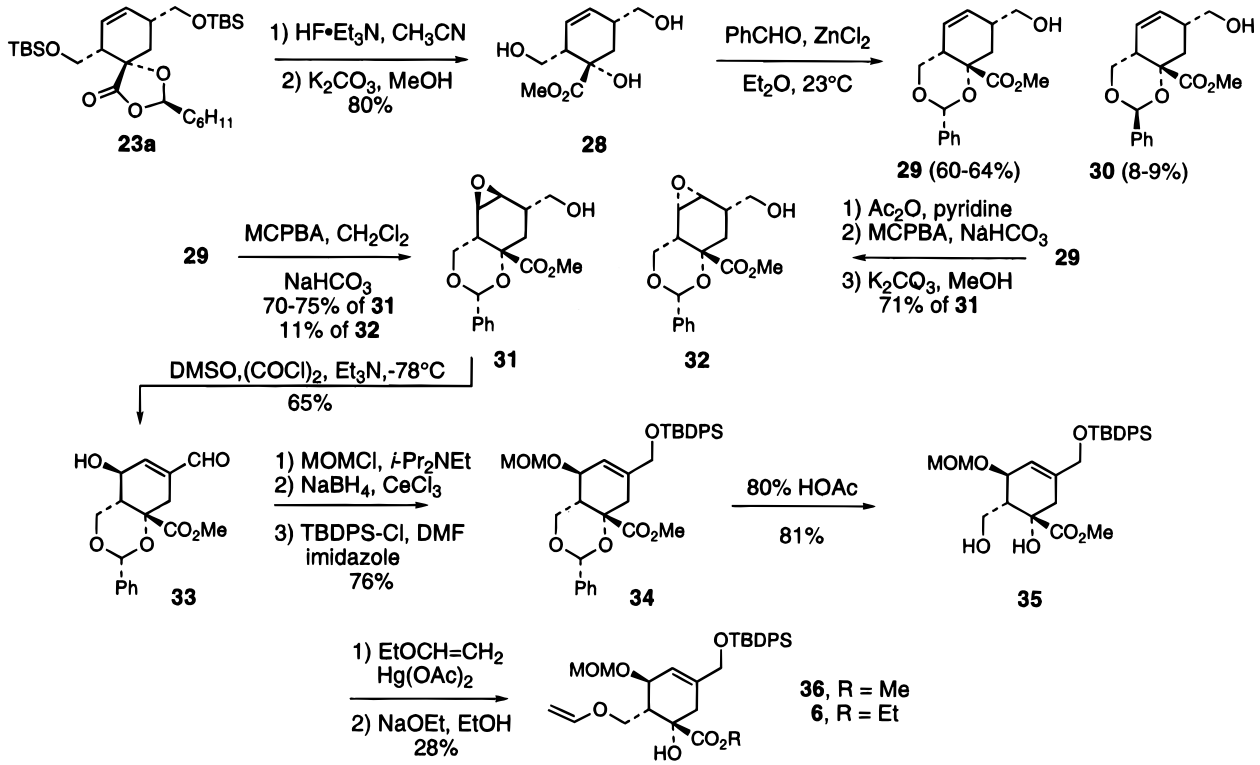
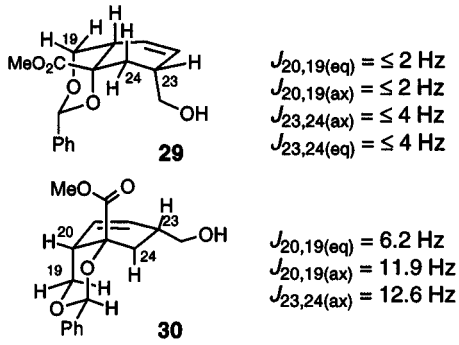
Scheme 2



acetals **29** (60−64%) and **30** (8−9%). Alternatively, when the benzylidene acetal was introduced by treatment of **28** with PhCHO and *p*-TsOH in benzene, acetal **30** was obtained as the major product, but in low yield (38%).

The stereochemistry of acetals **29** and **30** was assigned by NMR methods. Acetal **30** displayed large coupling constants between $H_{19(ax)}-H_{20}$ and between $H_{23}-H_{24}$, indicative of trans diaxial H/H relationships. These data require that **30** adopts the conformation indicated in the three-dimensional structure presented below. Although we did not make a conclusive assignment of the acetal center, examination of molecular models indicates that the phenyl group must occupy an equatorial position in **30** if the molecule is to adopt the conformation indicated by the *J* data. This conclusion allows us to assign the configuration of the acetal center in **29** as (*R*), since **29** and **30** are acetal epimers. Not surprisingly, the ^{1}H NMR data for **29**, specifically the small coupling constants $J_{20,19(ax)}$, $J_{20,19(eq)}$, $J_{23,24(ax)}$, and $J_{23,24(eq)}$ indicate that this intermediate adopts a different *cis*-decalin conformation than that of **30**. Because the β-face of the C(21−22) olefin of **29** appeared to be more exposed than that of **30**, we decided to use **29** to explore methods for introducing the C(21)-β-hydroxyl and the C(22−23) olefin in the spirotetronate unit of tetronolide.



Treatment of **29** with MCPBA in CH_2Cl_2 containing suspended $NaHCO_3$ provided a ca. 7:1 mixture of epoxide diastereomers **31** and **32** in 81−86% combined yield. We assumed that the major product derived from epoxidation of the more accessible β-face, although we recognized that the C(23)-hydroxymethyl group could have directed epoxidation to the α-face.[47] This possibility was probed and ultimately rejected as a significant contribution to the reaction stereoselectivity, by acylating the hydroxyl group prior to the epoxidation reaction. This three-step reaction sequence ((i) Ac_2O, pyridine, (ii) MCPBA, (iii) K_2CO_3, MeOH) provided **31** with excellent selectivity, as none of the unwanted α-epoxide **32** was detected. However, the yield of **31** was not improved (71%) relative to the direct epoxidation of **29**. As expected at the outset, Swern oxidation[48] of **31** led directly to the γ-hydroxy enal **33** via β-elimination of the intermediate β,γ-epoxy aldehyde.

While these studies were in progress, Boeckman's synthesis of racemic tetronolide top-half precursor **6** was published.[17] At this stage, therefore, we decided to converge with **6** as a means of verifying our stereochemical assignments. Accordingly, the free hydroxyl group of **33** was protected as a MOM ether; then the aldehyde was reduced under Luche conditions[49] and the resulting primary hydroxymethyl group was protected as a TBDPS ether, thereby providing **34** in 76% yield. The benzylidene acetal of **34** was removed by hydrolysis in 80% HOAc, giving diol **35** in 81% yield. Treatment of **35** with ethyl vinyl ether and $Hg(OAc)_2$ provided vinyl ether **36**, which was transesterified by exposure to NaOEt in EtOH to complete the synthesis of **6**. The identity of synthetic **6** was verified by comparison with ^{1}H NMR data kindly provided by Professor Boeckman. The optical rotation of our synthetic sample ($[\alpha]^{25}_D$ +41.3° (*c* 1.0, $CHCl_3$)) is also in reasonable agreement with the value subsequently reported by Boeckman ($[\alpha]^{25}_D$ +34.4° (*c* 2.9, CH_2Cl_2)).[18]

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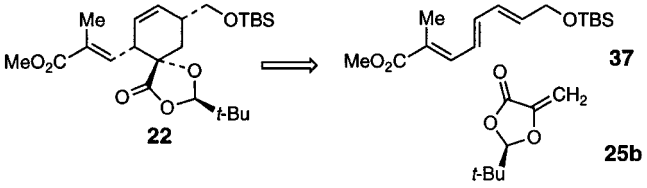
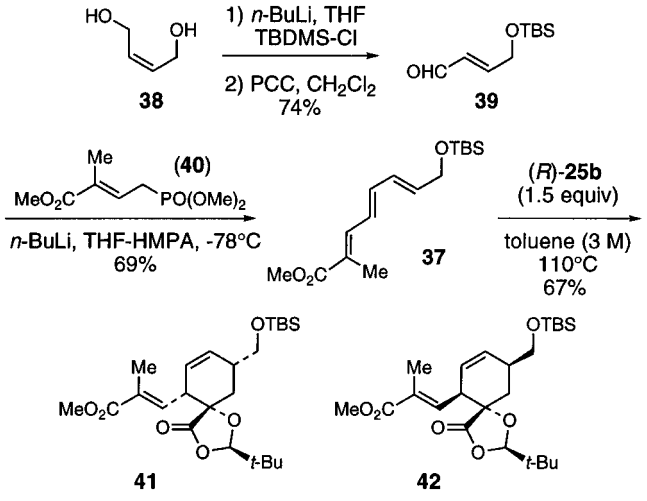
Although we had accomplished the first enantioselective synthesis of **6**, we were not pleased with the selectivity or efficiency of the route summarized in Scheme 2. Most problematic were the low efficiency of the Diels–Alder reaction of **24** and **25a** and the number of steps required to differentiate the two hydroxymethyl substituents of **28**. We also were not pleased with the low efficiency of the conversion of **35** to **36** (31%); however, no effort was made to optimize this sequence (e.g., by introduction of a bromoethyl acetal at the stage of **28**, by analogy to the work of Boeckman).[17] In view of the tremendous success we had achieved in the Diels–Alder reactions of dienophiles **25a** and **25b** with conjugated trienes in our syntheses of the top halves of kijanolide and chlorothricolide,[42–45] we decided to pursue instead a synthesis of Yoshii's top-half fragment **5** via the Diels–Alder reaction of **37** and dienophile **25b** (which typically exhibits higher diastereofacial selectivity than **25a**).[41,42]

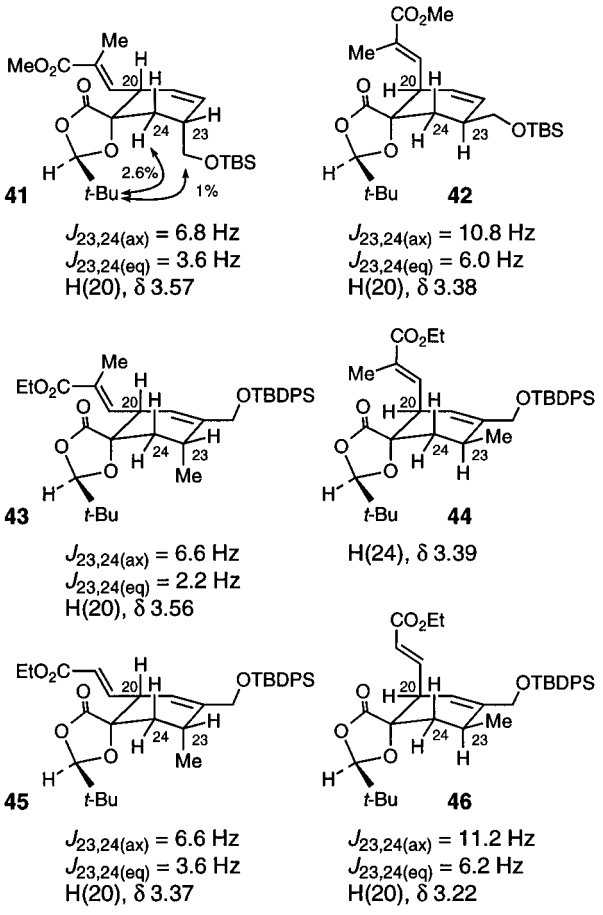


The synthesis of **37** originated from enal **39**, which was prepared in two steps from *cis*-2-butene-1,4-diol (**38**) by selective monosilylation[50–52] and then PCC oxidation of the resulting allylic alcohol.[53] Olefination of **39** by treatment with the lithium anion of methyl γ-(dimethylphosphono)tiglate **40**[54] (generated at −78 °C with *n*-BuLi) at −78 to 23 °C in a solvent system of THF containing 5 equiv of HMPA per equiv of **40** provided trienoate **37** in 69% yield. In contrast, the yield of **37** ranged from 24 to 41% when bases such as BuLi or NaH in Et_2O or THF were used in the absence of a polar aprotic solvent additive such as HMPA or DMPU. A significant competitive pathway under these conditions is the Michael addition of **40** to **39**. The yield of **37** was 58% when the reaction was performed in the presence of 5 equiv of DMPU rather than HMPA, and consequently the THF–HMPA solvent system is preferred.

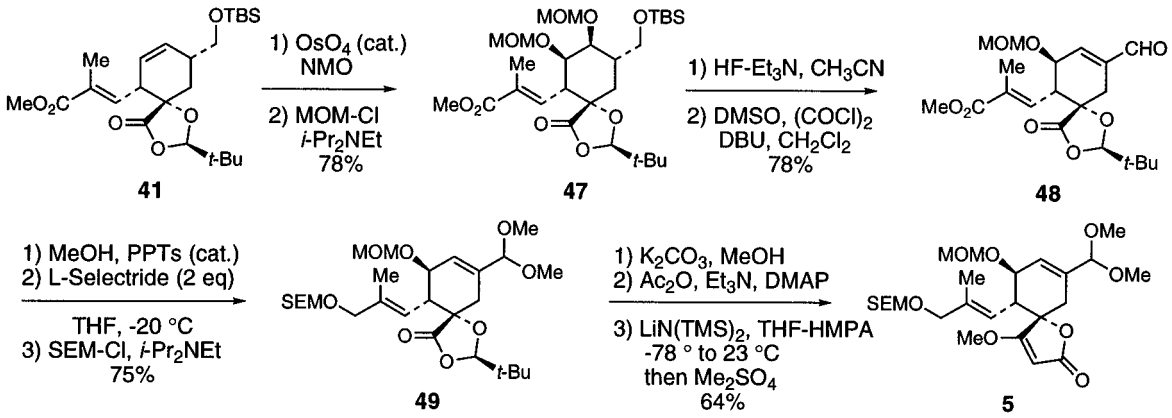


The key Diels–Alder reaction was performed by heating a mixture of **37** and 1.5 equiv of (*R*)-**25b** in toluene (3 M) at 110 °C for 90 h. Under these conditions, the desired exo cycloadduct **41** was obtained in 67% yield together with 7% of the endo isomer **42**. In addition, 14% of triene **37** was recovered, and 5% of a mixture of nonpolar products apparently resulting from the Diels–Alder dimerization of **37** was also obtained. The reaction is considerably faster at higher temperatures (150 °C, 20 h, 28% of **41**; 120 °C, 22 h, 48% yield), but the yield of **41** is diminished owing to the increased rate of dimerization of **37**. Interestingly, cycloadducts with reversed orientation of the diene and dienophile relative to that depicted in **41** and **42** were not detected. Although we were concerned at the outset that the regioselectivity of this reaction might be problematic,[55–58] the results suggest that the enoate substituent is a very powerful regiochemical directing element for this Diels–Alder reaction.

The stereochemistry of **41** and **42** was assigned by ^1H NMR methods. In particular, a NOE observed between the *tert*-butyl group and $H_{24\alpha}$ (2.6%) of **41** defines the stereochemistry of the acetal center relative to the cyclohexenyl unit and confirms that the diene added to the face of **25b** opposite to the bulky *tert*-butyl group.[41] Moreover, a weak NOE (1%) observed between the *tert*-butyl group and C(23)-CH_2OTBS unit requires that the C(23) substituent occupies a pseudoaxial position on the cyclohexenyl ring. This conclusion is supported by the relatively small coupling constants observed between H(23)–H(24_{ax}) ($J_{23,24(ax)}$ = 6.8 Hz) and H(23)–H(24_{eq}) ($J_{23,24(eq)}$ = 3.6 Hz). In contrast, the C(23)-CH_2OTBS substituent occupies a pseudoequatorial position in endo cycloadduct **42**, as indicated by $J_{23,24(ax)}$ = 10.8 Hz and $J_{23,24(eq)}$ = 6.0 Hz. Moreover, it is possible to assign the stereochemistry of C(20) on the basis of the chemical

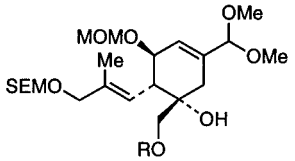


(50) Roush, W. R.; Blizzard, T. A. *J. Org. Chem.* **1984**, *49*, 1772. In particular, see ref 23 cited therein.



shifts of H(20) (δ 3.57 for **41** and δ 3.38 for **42**), since one would expect the equatorial H(20) of **42** to be shielded by adjacent carbonyl group.[59] These characteristic NMR data are very similar to those obtained for the exo and endo cycloadducts **43**−**44**[60] in the kijanolide series[42] and **45**−**46** in the chlorothricolide series.[44]

The synthesis of **5** proceeded by cis-dihydroxylation of **41** with catalytic OsO_4 and 1.0 equiv of *N*-methylmorpholine oxide (NMO).[61] Treatment of the resulting diol with MOM-Cl and *i*-Pr_2NEt in CH_2Cl_2 under standard conditions then provided **47** in 78% overall yield; no other isomers were detected. The primary TBS ether was cleaved upon exposure of **47** to HF−Et_3N in CH_3CN, and the alcohol was oxidized by using a modified Swern protocol.[48] When this oxidation was performed under standard conditions using Et_3N as the base, the β-alkoxy aldehyde was obtained as the major product with only minor amounts of enal **48**. However, by using the more basic DBU in place of Et_3N, enal **48** [$[\alpha]^{22}_D$ +93.5° (*c* 1.0, $CHCl_3$)] was obtained directly from the oxidation sequence in 78% yield overall from **47**. The stereochemistry of **48** was unambiguously verified by X-ray analysis.[62] After protection of the aldehyde as a dimethyl acetal (92% yield), the unsaturated ester was selectively reduced by treatment with 2.2 equiv of L-Selectride in THF at −20 °C (86% yield). Protection of the resulting allylic alcohol as a SEM ether then provided **49** in 75% yield for the three-step sequence from **48**. The enantiomeric purity of these intermediates was determined to be ⩾97% ee by Mosher ester analysis[18] of diol **50**.



50, R = H
51a, R = (*R*)-MTPA
51b, R = (*S*)-MTPA

The synthesis of spirotetronate **5** was completed by a sequence initiated by the methanolysis of **49** with K_2CO_3 in MeOH and acylation of the resulting 3°-hydroxy methyl ester with acetic anhydride (excess) in the presence of DMAP and Et_3N in CH_2Cl_2. The resulting α-acetoxy ester was treated with $LiN(TMS)_2$ (1 equiv) in a THF−HMPA mixture at −78 °C, and then the solution was allowed to warm to 23 °C to complete the Dieckmann cyclization.[63] Addition of Me_2SO_4 directly to the reaction mixture[42,44] then provided **5** ($[\alpha]^{24}_D$ +134.3° (*c* 2.80, $CHCl_3$)) in 64% overall yield. The spectroscopic properties of spirotetronate **5** were identical with those of an authentic sample ($[\alpha]^{23}_D$ +99.0° (*c* 3.02, $CHCl_3$)) kindly provided by Professor Yoshii.[11]

Summary. We have completed a formal total synthesis of (+)-tetronolide, the aglycon of the tetrocarcins, by virtue of our completion of highly diastereo- and enantioselective syntheses of the bottom- and top-half fragments **4** and **5** which served as key intermediates in Yoshii's pioneering total synthesis.[11] Our synthesis of the bottom-half octahydronaphthalene unit **4** proceeds in 17 steps and 5−6% yield from D-glyceraldehyde pentylidene acetal **8** and features the intramolecular Diels−Alder reaction of tetraenal **20**. Our synthesis of the spirotetronate fragment **5** proceeds in 14 steps and 10% overall yield from *cis*-2-butene-1,4-diol (**38**), and features the highly enantioselective exo selective Diels−Alder reaction of triene **37** and chiral dienophile **25b**. We also developed an enantioselective synthesis of Boeckman's top-half cyclohexene fragment **6** via the exo selective Diels−Alder reaction of diene **24** and dienophile **25a** (11 steps, 1.5% yield, from **24**), but in the final analysis this route was deemed too inefficient for use in a projected total synthesis of the natural product.

Work continues on the development of a workable strategy for completion of a tetronolide total synthesis (cf. ref 25), since the final stages of Yoshii's synthesis requires 15 steps from **4** and **5**.[11] Reports on these efforts will appear in due course.

Experimental Section[64]

(3*S*,4*S*,5*R*)-4-Hydroxy-5,6-(isopentylidenedioxy)-3-methylhex-1-ene (10). To a solution of (*R*,*R*)-diisopropyl tartrate (*E*)-crotylboronate (**9**)[30] (39.5 mL of a 0.75 M stock

(51) Roush, W. R.; Gillis, H. R.; Essenfeld, A. P. *J. Org. Chem.* **1984**, *49*, 4674. See, in particular, the procedures for the syntheses of **49**-**51** therein.
(52) McDougal, P. G.; Rico, J. G.; Oh, Y.-I.; Condon, B. D. *J. Org. Chem.* **1986**, *51*, 3388.
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(55) Corey, E. J.; Snider, B. B. *J. Am. Chem. Soc.* **1972**, *94*, 2549.
(56) Stork, G.; Nakahara, Y.; Nakahara, Y.; Greenlee, W. J. *J. Am. Chem. Soc.* **1978**, *100*, 7775.
(57) Vedejs, E.; Campbell, J. B., Jr.; Gadwood, R. C.; Rodgers, J. D.; Spear, K. L.; Watanabe, Y. *J. Org. Chem.* **1982**, *47*, 1534.
(58) Okumura, K.; Okazaki, K.; Takeda, K.; Yoshii, E. *Tetrahedron Lett.* **1989**, *30*, 2233.
(59) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, 2nd ed.; Pergamon Press: Oxford, 1969.
(60) H_{24ax} and H_{24eq} of **43** partially overlap with the resonance for the vinylic-Me group and are not fully resolved.
(61) VanRheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.
(62) Details of the X-ray strcture analysis of enal **48** are provided in Report No. 92118 of the Indiana University Molecular Structure Center. Final residuals are $R(F) = 0.0256$ and $R_w(F) = 0.0279$. We thank Dr. John C. Huffman for performing this analysis.
(63) Ireland, R. E.; Thompson, W. J. *J. Org. Chem.* **1979**, *44*, 3041.
(64) For general experimental details, see: Roush, W. R.; Brown, B. B. *J. Am. Chem. Soc.* **1993**, *115*, 2268 or Roush, W. R.; Brown, B. B. *J. Org. Chem.* **1993**, *58*, 2151. Unless otherwise noted, all compounds purified by chromatography are sufficiently pure (>95% by ^1H NMR analysis) for use in subsequent reactions.

solution, 29.6 mmol) and 4 Å molecular sieves in toluene at −78 °C was slowly added a solution of D-glyceraldehyde pentylidene ketal **8**[26] (2.0 g, 12.6 mmol) in 30 mL of toluene. The reaction mixture was allowed to stir at −78 °C for 4 h and then was allowed to warm to room temperature overnight. The white slurry (at 0 °C) was diluted with 0.5 N NaOH (60 mL) and was stirred for 3 h at room temperature. The toluene layer was separated and washed with a saturated $NaHCO_3$ solution (50 mL), dried ($MgSO_4$), and concentrated in vacuo. The aqueous phase was extracted with Et_2O (3 × 50 mL). The combined ethereal extracts were dried ($MgSO_4$), concentrated in vacuo, and combined with the toluene extracts. ^{1}H NMR analysis revealed that the crude product consisted of an 88:12 mixture of **10** and the (3*R*,4*R*,5*R*)-diastereomer. Purification of the crude product by silica gel chromatography (19:1 hexane−ether) provided 2.3 g (85% based on **8**) of alcohol **10** as a colorless oil: R_f 0.26 (4:1 hexanes−ethyl acetate); $[\alpha]^{21}_D$ +15.1° (*c* 1.0, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85 (m, 1 H), 5.12 (m, 2 H), 4.03 (m, 2 H), 3.86 (m, 1 H), 3.63 (dd, J = 9.4, 5.1 Hz, 1 H), 2.40 (ddq, J = 6.9, 7.7, 6.4 Hz, 1 H), 1.90 (d, J = 4.3 Hz, 1 H), 1.64 (m, 4 H), 1.00 (d, J = 6.9 Hz, 3 H), 0.90 (dd, J = 14.5, 7.2 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.2, 116.9, 113.1, 77.7, 75.3, 66.3, 40.6, 29.7, 29.3, 16.7, 8.2, 8.0; IR (neat) 3470, 1635 cm^{-1}; high-resolution mass spectrum, calcd for $C_{12}H_{23}O_3$ (M^+ + 1) 215.1647, found 215.1644.

(3*S*,4*S*,5*R*)-4-(Methoxymethyl)-5,6-(isopentylidenedioxy)-3-methylhex-1-ene (11). To a solution of **10** (2.3 g, 10.7 mmol) in CH_2Cl_2 (20 mL) were added *i*-Pr_2NEt (2.05 mL, 11.8 mmol) and chloromethyl methyl ether (0.813 mL, 10.7 mmol). The solution was warmed to reflux for 10 h. The yellow solution was cooled to room temperature and then washed with a saturated NH_4Cl solution (30 mL). The aqueous phase was extracted with EtOAc (3 × 30 mL). The combined organic extracts were then dried ($MgSO_4$), filtered, and concentrated in vacuo. Purification of the crude product by silica gel chromatography (6:1 hexanes−ethyl acetate) provided 2.5 g (90%) of **11** as a colorless liquid: R_f 0.54 (4:1 hexanes−ethyl acetate); $[\alpha]^{21}_D$ +12.0° (*c* 1.5, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (m, 1 H), 5.02, (m, 2 H), 4.74 (A of AB, J_{AB} = 6.8 Hz, 1 H), 4.67 (B of AB, J_{BA} = 6.8 Hz, 1 H), 4.02 (m, 2 H), 3.80 (m, 1 H), 3.61 (dd, J = 5.4, 3.5 Hz, 1 H), 3.38 (s, 3 H), 2.53 (m, 1 H), 1.60 (m, 4 H), 1.10 (d, J = 7.0 Hz, 3 H), 0.82 (dd, J = 14.2, 7.5 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 115.1, 112.2, 97.8, 82.2, 66.9, 55.8, 40.6, 29.7, 29.0, 16.8, 8.2, 8.0; IR (neat) 3070, 1670, 1462 cm^{-1}; high-resolution mass spectrum, calcd for $C_{14}H_{27}O_4$ (M^+ + 1) 259.1909, found 259.1920. Anal. Calcd for $C_{14}H_{26}O_4$: C, 65.09; H, 10.14. Found: C, 65.02; H, 9.93.

(2′*E*,4*S*,4′*R*,5′*S*,6′*R*)-3-[5′-[(Methoxymethyl)oxy]-6′,7′-*O*-isopentylidene-4′-methylhept-2′-enoyl]-4-isopropyl-1,3-oxazolidin-2-one (13). A −78 °C solution of homoallylic ether **11** (1.7 g, 6.6 mmol) in 1:1 MeOH−CH_2Cl_2 (20 mL) was treated with a stream of ozone in O_2 until the solution turned blue. The solution was then purged with nitrogen for 5 min. Triphenylphosphine (8.4 g, 32 mmol) was added to the reaction mixture, and the solution was allowed to warm to room temperature and stir overnight. The solvents were removed in vacuo. Purification of the crude product by silica gel chromatography (9:1 hexane−Et_2O) provided 1.4 g (82%) of the corresponding aldehyde as a colorless oil: R_f 0.38 (4:1 hexanes−ethyl acetate); $[\alpha]^{20}_D$ −6.7° (*c* 1.0, toluene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.69 (s, 1 H), 4.69 (A of AB, J_{AB} = 7.0 Hz, 1 H), 4.66 (B of AB, J_{AB} = 7.0 Hz, 1 H), 4.14 (m, 2 H), 3.98 (m, 1 H), 3.80 (m, 1 H), 3.36 (s, 3 H), 2.76 (m, 1 H), 1.59 (m, 4 H), 1.21 (d, J = 7.0 Hz, 3 H), 0.86 (t, J = 7.5 Hz, 3 H), 0.85 (t, J = 7.5 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.8, 113.5, 96.5, 79.3, 74.8, 68.0, 55.8, 48.6, 29.5, 28.6, 8.8, 8.1, 8.0; IR (neat) 2970, 1725 cm^{-1}; high-resolution mass spectrum, calcd for $C_{13}H_{25}O_5$ (M^+ + 1) 261.1702, found 261.1712.

To a solution of flame-dried LiCl (5.78 g, 136 mmol) in CH_3CN (60 mL) were added the phosphonate reagent **12**[25] (5.0 g, 16.2 mmol) and *i*-Pr_2NEt (6.03 mL, 34.6 mmol). The solution stirred at room temperature for 1 h; then a solution of the above aldehyde (3.6 g, 13.8 mmol; combined from several runs) in 20 mL of CH_3CN was added. The resulting solution was stirred at room temperature for 2 d. The solution was quenched with pH 7 phosphate buffer (100 mL) and diluted with EtOAc (100 mL). The organic layer was separated and washed with a saturated solution of NaCl (50 mL). The combined aqueous extracts were extracted with EtOAc (5 × 50 mL) and then were dried ($MgSO_4$) and concentrated in vacuo. Purification of the crude product by silica gel chromatography (9:1 hexanes−ethyl acetate) provided 5.0 g (87%) of the α,β-unsaturated oxazolidinone **13** as a colorless oil: R_f 0.85 (5:1 hexanes−ethyl ether); $[\alpha]^{20}_D$ +37.2° (*c* 0.9, toluene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 15.5 Hz, 1 H), 7.19 (dd, J = 15.5, 8.1 Hz, 1 H), 4.71 (A of AB, J_{AB} = 7.0 Hz, 1 H), 4.64 (B of AB, J_{BA} = 7.0 Hz, 1 H), 4.48 (m, 1 H), 4.26 (t, J = 9.1 Hz, 1 H), 4.20 (dd, J = 8.9, 3.2 Hz, 1 H), 4.02 (m, 2 H), 3.79 (m 1 H), 3.66 (dd, J = 5.6, 3.5 Hz, 1 H), 3.36 (s, 3 H), 2.79 (m, 1 H), 2.39 (m, 1 H), 1.59 (m, 4 H), 1.17 (d, J = 7.0 Hz, 3 H), 0.90 (d, J = 6.9 Hz, 3 H), 0.86 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 153.9, 152.1, 120.6, 112.6, 97.7, 82.1, 76.5, 67.1, 63.2, 58.4, 55.9, 39.5, 29.6, 29.0, 28.4, 17.9, 16.0, 14.5, 8.1, 8.0; IR (neat) 1751, 1659, 1631 cm^{-1}; high-resolution mass spectrum, calcd for $C_{21}H_{36}NO_7$ (M^+ + 1) 414.2492, found 414.2480. Anal. Calcd for $C_{21}H_{35}NO_7$: C, 61.00; H, 8.53; N, 3.39. Found: C, 61.19; H, 8.75; N, 3.38.

(4*S*,4′*S*,5′*S*,6′*R*)-3-[5′-[(Methoxymethyl)oxy]-6′,7′-*O*-isopentylidene-4′-methylheptanoyl]-4-isopropyl-1,3-oxazolidin-2-one (14). A stream of H_2 was bubbled through a solution of **13** (2.3 g, 5.57 mmol) in EtOAc (30 mL). To this solution was added 120 mg of 10% Pd on carbon. H_2 gas was bubbled through the solution for an additional 10 min; then the solution was allowed to stir under H_2 for 4 h at room temperature. The solution was filtered through a plug of Celite, dried ($MgSO_4$), and concentrated in vacuo. Purification of the crude product by silica gel chromatography (5:1 hexanes−ethyl acetate) provided **14** (2.20 g, 95%) as a colorless oil: R_f 0.89 (hexanes−ethyl ether); $[\alpha]^{20}_D$ +78.7° (*c* 1.4, THF); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.70 (A of AB, J_{AB} = 6.7 Hz, 1 H), 4.65 (B of AB, J_{BA} = 6.7 Hz, 1 H), 4.42 (m, 1 H) 4.22 (m, 2 H), 4.12 (m, 1 H), 4.05 (dd, J = 7.8, 6.1 Hz, 1 H), 3.82 (t, J = 7.8 Hz, 1 H), 3.60 (dd, J = 5.9, 4.0 Hz, 1 H), 3.38, (s, 3 H), 2.97 (m, 2 H), 2.36 (m, 1 H), 1.97−1.78 (m, 2 H), 1.60 (m, 5 H), 0.99 (d, J = 7.0 Hz, 3 H), 0.89 (m, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 112.5, 97.4, 82.0, 76.0, 67.2, 63.3, 58.4, 55.9, 35.0, 33.5, 29.7, 29.1, 28.4, 26.9, 18.0, 15.6, 14.6, 8.2, 8.1; IR (neat) 1760, 1700 cm^{-1}; high-resolution mass spectrum, calcd for $C_{21}H_{38}NO_7$ (M^+ + 1) 416.2648, found 416.2629. Anal. Calcd for $C_{21}H_{37}NO_7$: C, 60.70; H, 8.98; N, 3.37. Found: C, 60.76; H, 9.03; N, 3.41.

(2′*S*,4*S*,4′*S*,5′*S*,6′*R*)-3-[5′-[(Methoxymethyl)oxy]-6′,7′-*O*-isopentylidene-4′-methylhept-2′-enoyl]-4-isopropyl-1,3-oxazolidin-2-one (15). To a 0 °C solution of *n*-BuLi (7.5 mL 1.6 M in hexanes, 12 mmol) in THF (20 mL) was slowly added $NH(TMS)_2$ (3.9 mL, 19 mmol). The solution was stirred at 0 °C for 45 min, before being cooled to −78 °C and transferred via cannula into a −78 °C solution of **14** (4.8 g, 11.6 mmol) and MeI (7.0 mL, 112 mmol) in THF (110 mL). The reaction mixture was warmed slowly to 0 °C and stirred for 2 h. The reaction was then quenched by addition of a cold saturated NaCl solution (10 mL). The organic layer was separated and washed with saturated brine (2 × 100 mL). The combined aqueous extracts were washed with EtOAc (5 × 100 mL), dried ($MgSO_4$), and concentrated in vacuo. ^{1}H NMR analysis of the crude reaction mixture revealed **15** as the major product of a 93:7 mixture (86% de). Purification of the crude product by silica gel chromatography (9:1 hexane−Et_2O) provided **15** (4.3 g, 87%) as a colorless oil: R_f 0.90 (5:1 hexanes−ethyl ether); $[\alpha]^{20}_D$ +9.6° (*c* 1.1, toluene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.64 (A of AB, J_{AB} = 6.7 Hz, 1 H), 4.61 (B of AB, J_{BA} = 6.7 Hz, 1 H), 4.42 (m, 1 H), 4.25 (m, 1 H), 4.18 (dd, J = 8.8, 2.9 Hz, 1 H), 4.06 (m, 2 H), 3.92 (m, 1 H), 3.79 (m, 1 H), 3.54 (dd, J = 6.4, 3.5 Hz, 1 H), 3.34 (s, 3 H), 2.36 (m, 1 H), 1.86 (m, 1 H), 1.62 (m, 6 H), 1.18 (d, J = 6.7 Hz, 3 H) 0.96 (d, J = 7.0 Hz, 3 H), 0.89 (m, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 153.6, 112.6, 97.2, 82.0, 75.7, 67.8, 63.2, 58.5, 55.8, 35.3, 35.2, 33.0, 29.7, 29.1, 28.5, 18.0, 17.6, 15.7, 14.7, 8.2, 8.1; IR (neat) 2960, 2922, 1775, 1700, 1461, 1382, 1261 cm^{-1}; high-resolution mass spectrum, calcd for $C_{21}H_{36}NO_6$ ($M - OCH_3$)$^+$ 398.2542, found 398.2493. Anal. Calcd for $C_{22}H_{39}NO_7$: C, 61.52; H, 9.15; N, 3.26. Found: C, 61.34; H, 9.28; N, 3.11.

(2′*S*,4*S*,4′*S*,5′*S*)-3-[5′-[(Methoxymethyl)oxy]-7′,7′-dibromo-2′,4′-dimethylhept-6′-enoyl]-4-isopropyl-1,3-oxazolidin-2-one (16). A mixture of oxazolidinone **15** (1.15 g, 2.68 mmol) in 60% formic acid−MeOH (20 mL) was stirred at room temperature for 2 h. The solvent was then removed in vacuo, and the resulting oil was run through a column of silica gel (1:1 hexanes−EtOAc) to yield 750 mg (77%) of the diol as a colorless oil: R_f 0.65 (EtOAc); $[\alpha]^{20}_D$ +3.7° (*c* 0.1, $CDCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.72 (A of AB, J_{AB} = 6.7 Hz, 1 H), 4.59 (B of AB, J_{BA} = 6.7 Hz, 1 H), 4.42 (m, 1 H), 4.26 (m, 1 H), 4.19 (dd, *J* = 9.1, 3.2 Hz, 1 H), 3.85 (m, 1 H), 3.69 (m, 3 H), 3.42 (s, 3 H), 3.35 (m, 1 H), 2.90 (br s, 2 H), 2.32 (m, 1 H), 1.82−1.48 (m, 3 H), 1.18 (d, *J* = 6.7 Hz, 3 H), 0.95 (d, *J* = 6.7 Hz, 3 H), 0.90 (d, *J* = 7.2 Hz, 3 H), 0.86 (d, *J* = 6.9 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 153.6, 99.0, 87.9, 71.1, 63.2, 63.1, 58.5, 56.1, 35.6, 35.4, 32.6, 28.4, 17.9, 17.4, 16.4, 14.7; IR (neat) 3450, 1770, 1695 cm^{-1}; high-resolution mass spectrum, calcd for $C_{16}H_{28}NO_6$ ($M^+ - OCH_3$) 330.1916, found 330.1904. Anal. Calcd for $C_{17}H_{31}NO_7$: C, 56.49; H, 8.65; N, 3.88. Found: C, 56.52; H, 8.44; N, 3.61.

To a slurry of KIO_4 (834 mg, 3.62 mmol) and $KHCO_3$ (33 mg, 0.33 mmol) in 25% aqueous THF (33 mL) at 0 °C was added a solution of the above diol (750 mg, 2.08 mmol) in 5 mL of THF. The reaction mixture was allowed to warm to room temperature and stirred overnight. The mixture was filtered through Celite. The aqueous layer was separated and washed with EtOAc (5 × 5 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. Purification of the resulting oil by silica gel chromatography (9:1 hexanes−EtOAc) provided 0.60 g (88%) of the desired aldehyde as a colorless oil: R_f 0.62 (4:1 hexanes−EtOAc); $[\alpha]^{20}_D$ +119.3° (*c* 1.0, acetone); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (d, *J* = 1.9 Hz, 1 H), 4.72 (A of AB, J_{AB} = 6.7 Hz, 1 H), 4.65 (B of AB, J_{BA} = 6.7 Hz, 1 H), 4.42 (m, 1 H), 4.29 (m, 1 H), 4.19 (dd, *J* = 8.8, 3.0 Hz, 1 H), 3.76 (m, 1 H), 3.69 (dd, *J* = 4.5, 1.8 Hz, 1 H), 3.40 (s, 3 H), 2.30 (m, 1 H), 2.07 (m, 1 H), 1.69 (m, 1 H), 1.55 (m, 1 H), 1.17 (d, *J* = 6.7 Hz, 3 H), 1.08 (d, *J* = 6.7 Hz, 3 H), 0.90 (d, *J* = 6.9 Hz, 3 H), 0.86 (d, *J* = 6.9 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.8, 176.8, 153.7, 97.3, 86.5, 63.4, 58.6, 56.1, 35.5, 34.9, 32.9, 28.5, 17.9, 17.7, 16.4, 14.8; IR (neat) 2961, 1780, 1758, 1692 cm^{-1}; high-resolution mass spectrum, calcd for $C_{15}H_{26}NO_5$ (M^+ − CHO) 300.1811, found 300.1804.

A solution of triphenylphosphine (5.05 g, 19.3 mmol) and CBr_4 (3.19 g, 9.62 mmol) in CH_2Cl_2 (12 mL) was stirred at 0 °C for 30 min. A solution of the aldehyde generated above (434 mg, 1.32 mmol) in 3 mL of CH_2Cl_2 was slowly added to the reaction mixture. The mixture was stirred at 0 °C for 10 min and then was diluted with EtOAc. The solvents were removed in vacuo, and the resulting crude product was purified via silica gel chromatography (4:1 hexane−EtOAc) to yield 453 mg (71%) of the desired dibromoolefin **16** as a colorless oil: R_f 0.51 (4:1 hexanes−EtOAc); $[\alpha]^{20}_D$ +15.0° (*c* 9.5, $CDCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.37 (d, *J* = 8.9 Hz, 1 H), 4.64 (A of AB, J_{AB} = 6.7 Hz, 1 H), 4.52 (B of AB, J_{BA} = 6.7 Hz, 1 H), 4.45 (m, 1 H), 4.27 (m, 1 H), 4.20 (dd, *J* = 9.1, 2.9 Hz, 1 H), 4.12 (dd, *J* = 8.6, 6.1 Hz, 1 H), 3.90 (m, 1 H), 3.38 (s, 3 H), 2.35 (m, 1 H), 1.80 (m, 1 H), 1.54−1.70 (m, 2 H), 1.19 (d, *J* = 6.7 Hz, 3 H), 0.91 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 153.6, 137.8, 94.7, 92.1, 80.4, 63.2, 58.5, 55.9, 35.5, 35.5, 35.2, 28.4, 18.0, 17.6, 15.4, 14.7; IR ($CDCl_3$) 1775, 1695 cm^{-1}; high-resolution mass spectrum, calcd for $C_{17}H_{28}NO_5{}^{79}Br^{81}Br$ (M^+ + 1) 486.0313, found 486.0337. Anal. Calcd for $C_{17}H_{27}NO_5Br_2$: C, 42.08; H, 5.61; N, 2.89. Found: C, 42.20; H, 5.76; N, 2.87.

Ethyl (*E*)-(4*S*,6*S*,7*S*)-7-[(Methoxymethyl)oxy]-8,8-dibromo-1,3,5-trimethylnona-2,8-dienoate (17). To a −78 °C solution of **16** (1.6 g, 3.3 mmol) in CH_2Cl_2 (15 mL) was slowly added a −78 °C solution of DIBAL (8.8 mL, 1.0 M in CH_2Cl_2, 8.8 mmol). The reaction mixture was stirred for 1 h and then was quenched by addition of MeOH (4 mL) and warmed to room temperature. A saturated solution of Rochelle's salt (10 mL) was added, and the mixture was stirred for 30 min. The white slurry was then filtered through a fritted glass funnel. The aqueous layer was washed (5 × 30 mL) with EtOAc; then the combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. Purification of the crude product by silica gel chromatography (6:1 hexanes−EtOAc) provided 912 mg (77%) of the desired aldehyde: R_f 0.45 (4:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −48.1° (*c* 1.0, toluene); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.61 (d, *J* = 1.6 Hz, 1 H), 6.35 (d, *J* = 8.9 Hz, 1 H), 4.63 (A of AB, J_{AB} = 6.7 Hz, 1 H), 4.52 (B of AB, J_{BA} = 6.7 Hz, 1 H), 4.14 (dd, *J* = 8.8, 6.4 Hz, 1 H), 3.37 (s, 3 H), 2.45 (m, 1 H), 1.84 (m, 1 H), 1.56 (m, 2 H), 1.09 (d, *J* = 7.0 Hz, 3 H), 0.99 (d, *J* = 7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.6, 137.4, 94.5, 92.5, 80.1, 55.9, 44.1, 34.9, 32.7, 14.9, 13.1; IR (neat) 2960, 2935, 1750, 1622, 1459 cm^{-1}; high-resolution mass spectrum, calcd for $C_{11}H_{19}O_3{}^{79}Br^{81}Br$ (M^+ + 1) 358.9680, found 358.9652.

A solution of the above aldehyde (125 mg, 0.35 mmol) and (carbethoxyethylidene)triphenylphosphorane (500 mg, 1.4 mmol) in 7 mL of toluene was heated to 60 °C for 30 h. The solution was cooled, and the solvents were removed in vacuo. Purification of the crude product by silica gel chromatography (9:1 hexanes−EtOAc) provided 135 mg (88%) of enoate **17**: R_f 0.20 (4:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −10.3° (*c* 0.7, $CDCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (dq, *J* = 10.0, 1.2 Hz, 1 H), 6.38 (d, *J* = 9.2 Hz, 1 H), 4.65 (A of AB, J_{AB} = 6.8 Hz, 1 H), 4.52 (B of AB, J_{BA} = 6.8 Hz, 1 H), 4.10−4.28 (m, 3 H), 3.38 (s, 3 H), 2.61 (m, 1 H), 1.86 (s, 3 H), 1.80 (m, 1 H), 1.50 (m, 1 H), 1.30 (m, 3 H), 1.17 (m, 1 H), 0.98 (d, *J* = 6.8 Hz, 3 H), 0.95 (d, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 147.6, 137.0, 126.3, 94.4, 92.3, 79.4, 60.5, 55.7, 39.4, 35.3, 31.0, 19.6, 15.4, 14.3, 12.5; IR (neat) 2959, 2910, 1720, 1645, 1460, 1362 cm^{-1}; high-resolution mass spectrum (FAB), calcd for $C_{16}H_{26}O_4{}^{79}Br_2$-Na ($M + Na$)$^+$ 463.0094, found 463.0042.

(*E*,*Z*,*E*,*E*)-(4*S*,5*S*,6*S*,7*S*)-7-[(Methoxymethyl)oxy]-14-[(*tert*-butyldimethylsilyl)oxy]-9-bromo-2,4,6,12-tetramethyltetradeca-2,8,10,12-tetraenoate (19). A solution of dibromoolefin **17** (250 mg, 0.57 mmol) and $Pd(PPh_3)_4$ (50 mg, 0.04 mmol) in degassed THF (4 mL) was stirred at room temperature for 30 min before being transferred to a degassed solution of vinylboronic acid **18**[19] (300 mg, 2.1 mmol) in 1.5 mL of a 0.53 M aqueous thallium hydroxide (TlOH) solution (0.79 mmol). The reaction mixture was stirred for 1 h at ambient temperature; then the solution was diluted with EtOAc and filtered through Celite. The aqueous layer was separated and washed with EtOAc (3 × 15 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. Purification of the crude product by silica gel chromatography (4:1 hexanes−EtOAc) provided 170 mg (65%) of tetraenoate alcohol. When performed on a smaller scale (ca. 50 mg of **17**), the yield of this intermediate was 91%: R_f 0.10 (5:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −6.6° (*c* 0.6, CH_3CN); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.80 (d, *J* = 14.8 Hz, 1 H), 6.46 (dq, *J* = 10.0, 1.6 Hz, 1 H), 6.22 (d, *J* = 14.8 Hz, 1 H), 5.90 (d, *J* = 8.8 Hz, 1 H), 5.84 (t, *J* = 6.8 Hz, 1 H), 4.63 (A of AB, J_{AB} = 6.8 Hz, 1 H), 4.53 (dd, *J* = 8.8, 5.6 Hz, 1 H), 4.50 (B of AB, J_{BA} = 6.8 Hz, 1 H), 4.32 (d, *J* = 6.8 Hz, 2 H), 4.18 (q, *J* = 7.2 Hz, 2 H), 3.40 (s, 3 H), 2.65 (m, 1 H), 1.86 (s, 3 H), 1.82 (s, 3 H), 1.80 (m, 1 H), 1.58 (m, 1 H), 1.30 (t, *J* = 7.2 Hz, 3 H), 1.20 (m, 1 H), 0.99 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 147.8, 138.7, 135.0, 133.4, 131.7, 128.0, 126.7, 126.1, 94.3, 78.6, 60.4, 59.4, 55.6, 39.4, 35.7, 31.0, 19.5, 15.6, 14.2, 12.9, 12.4; IR ($CDCl_3$) 3420, 1700, 1642 cm^{-1}; high-resolution mass spectrum, calcd for $C_{22}H_{34}O_4{}^{79}Br$ (M^+ − OH) 441.1640, found 441.1674.

A solution of tetraenoate alcohol (400 mg, 0.87 mmol), imidazole (350 mg, 5.2 mmol), and *tert*-butyldimethylchlorosilane (390 mg, 2.6 mmol) in DMF (17.4 mL) was stirred under N_2 at room temperature for 30 min, at which point TLC analysis showed the reaction to be complete. The reaction mixture was diluted with 1:1 H_2O−brine and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. This produced a yellow oil which was purified by silica gel chromatography (12:1 hexane/EtOAc) to yield 465 mg (93%) of **19**: $[\alpha]^{20}_D$ −2.7° (*c* 0.9, $CDCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 (d, *J* = 15.2 Hz, 1 H), 6.55 (dd, *J* = 10.0, 1.6 Hz, 1 H), 6.17 (d, *J* = 14.8 Hz, 1 H), 5.87 (d, *J* = 9.2 Hz, 1 H), 5.77 (t, *J* = 6.4 Hz, 1 H), 4.63 (A of AB, J_{AB} = 6.8 Hz, 1 H), 4.54 (m, 1 H), 4.50 (B of AB, J_{BA} = 6.8 Hz, 1 H), 4.35 (d, *J* = 6.8 Hz, 2 H), 4.18 (q, *J* = 7.2 Hz, 2 H), 3.39 (s, 3 H), 2.69 (m, 1 H), 1.87 (s, 3 H), 1.79 (s, 3 H), 1.53 (m, 1 H), 1.29 (t, *J* = 7.2 Hz, 3 H), 1.27 (m, 1 H), 1.17 (m, 1 H), 0.97 (d, *J* = 6.8 Hz, 3 H), 0.94 (d, *J* = 7.2 Hz, 3 H), 0.90 (s, 9 H), 0.10 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 147.9, 139.1, 135.2, 133.0, 131.2, 128.3, 126.2, 125.9, 94.3, 78.6, 76.7, 60.4, 60.3, 55.7, 39.5, 35.7, 31.0, 25.9, 19.6, 18.4, 15.6,

14.3, 13.0, 12.5, −5.1; IR (benzene-d_6) 2950, 2920, 1705, 1645, 1620, 1435 cm^{-1}; high-resolution mass spectrum, calcd for $C_{24}H_{40}O_5{}^{79}BrSi$ ($M^+ - t$-Bu) 515.1828, found 519.1858.

(*E*,*Z*,*E*,*E*)-(4*S*,5*S*,6*S*,7*S*)-7-[(Methoxymethyl)oxy]-14-[(*tert*-butyldimethylsilyl)oxy]-9-bromo-2,4,6,12-tetramethyltetradeca-2,8,10,12-tetraen-1-al (20). A solution of tetraenoate **19** (421 mg, 0.73 mmol) in 5 mL of CH_2Cl_2 was cooled to −78 °C. DIBAL (2.9 mL, 1.0 M in CH_2Cl_2) was added slowly, and the resulting solution was stirred for 1 h. The solution was then quenched with MeOH and was allowed to stand at room temperature for 30 min. The solution was diluted with a saturated solution of Rochelle's salt (2 mL), and the layers were separated. The aqueous layer was extracted with EtOAc (3 × 5 mL), and then the combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo to give the crude allylic alcohol: R_f 0.35 (4:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −34.0° (*c* 2.7, $CDCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 (d, J = 14.8 Hz, 1 H), 6.18 (d, J = 14.8 Hz, 1 H), 5.89 (d, J = 8.8 Hz, 1 H), 5.76 (t, J = 6.0 Hz, 1 H), 5.20 (d, J = 9.6 Hz, 1 H), 4.64 (A of AB, J_{AB} = 6.8 Hz, 1 H), 4.55 (dd, J = 9.2, 5.6 Hz, 1 H), 4.52 (B of AB, J_{BA} = 6.8 Hz, 1 H), 4.36 (d, J = 6.0 Hz, 2 H), 3.99 (s, 2 H), 3.37 (s, 3 H), 2.58 (m, 1 H), 1.87 (m, 1 H), 1.79 (s, 3 H), 1.72 (s, 3 H), 1.50 (m, 1 H), 1.42 (m, 1 H), 1.10 (m, 1 H), 0.84−0.96 (m, 15 H), 0.07 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 135.1, 133.1, 132.9, 132.7, 131.1, 128.2, 125.9, 94.5, 78.6, 69.0, 60.3, 55.6, 40.1, 35.5, 29.6, 25.9, 20.6, 18.3, 15.5, 13.8, 13.0, −5.1; IR (neat) 3430 (br), 2960, 2930, 1460, 1380 cm^{-1}.

The crude allylic alcohol from the preceding experiment (theoretically 0.74 mmol) was added to a solution of TPAP (12 mg, 0.036 mmol), *N*-methylmorpholine *N*-oxide (129 mg, 1.09 mmol), and 4 Å molecular sieves (366 mg) in 4 mL of CH_2Cl_2. The solution was stirred for 10 min and then was concentrated in vacuo. Purification of the crude product by silica gel chromatography provided 288 mg (74%) of tetraenal **20** as a colorless oil: $[\alpha]^{20}_D$ −26.6° (*c* 0.01, $CDCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.40 (s, 1 H), 6.68 (d, J = 15.2 Hz, 1 H), 6.28 (dd, J = 1.2, 10.0 Hz, 1 H), 6.18 (d, J = 14.8 Hz, 1 H), 5.87 (d, J = 8.8 Hz, 1 H), 5.77 (t, 6.0 Hz, 1 H), 4.62 (A of AB, J_{AB} = 6.8, 1 H), 4.55 (dd, J = 8.8, 5.6, 1 H), 4.50 (B of AB, J_{BA} = 6.8, 1 H), 4.35, (d, J = 6.0 Hz, 2 H), 3.35 (s, 3 H), 2.90 (m, 1 H), 1.79 (m, 6 H), 1.60 (m, 2 H), 1.20 (m, 1 H), 1.04 (d, J = 6.8 Hz, 3 H), 0.95 (d, J = 6.5 Hz, 3 H), 0.84 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.6, 160.4, 139.2, 137.7, 135.3, 132.9, 130.9, 128.5, 125.7, 94.3, 78.6, 77.1, 60.3, 55.7, 39.4, 35.7, 31.4, 25.9, 19.4, 15.6, 13.0, 9.3, −5.1; IR ($CDCl_3$) 3020, 3000, 2955, 2911, 1759 cm^{-1}; high-resolution mass spectrum, calcd for $C_{26}H_{46}O_4{}^{79}BrSi$ (M^+ + 1) 529.2348, found 529.2351.

2*β*-[(*E*)-3-[(*tert*-Butyldimethylsilyl)oxy]-1-methylprop-1-enyl]-5α-[(methoxymethyl)oxy]-4-bromo-1α,6α,8*β*-trimethyl-1,2,4aα,5,6,7α,8,8a*β*-octahydronaphthalene-1*β*-carboxaldehyde (21). A solution of tetraenal **20** (30 mg, 0.057 mmol), one crystal of BHT, and one drop of bis(trimethylsilyl)acetamide in degassed toluene (2 mL) was heated to 130 °C in a sealed tube for 12 h. The tube was cooled; then the contents were removed and concentrated in vacuo. ^{1}H NMR analysis of the crude product failed to reveal the presence of any cycloadducts other than **21**. Purification of the crude product by silica gel chromatography (12:1 hexanes−EtOAc) provided 27 mg (90%) of **21** as a colorless oil: R_f 0.76 (4:1 hexanes−ethyl acetate); $[\alpha]^{20}_D$ −19.4° (*c* 0.4, $CDCl_3$); ^{1}H NMR (400 MHz, toluene-d_8) δ 9.33 (s, 1 H), 5.82 (dq, J = 6.0, 0.8 Hz, 1 H), 5.50 (t, J = 6.0 Hz, 1 H), 4.81 (A of AB, J_{AB} = 6.8 Hz, 1 H), 4.67 (B of AB, J_{BA} = 6.8 Hz, 1 H), 4.04−4.16, (m, 2 H), 3.80 (dd, J = 9.6, 4.4 Hz, 1 H), 3.28 (s, 3 H), 2.40 (m, 1 H), 2.10 (m, 2 H) 1.80 (m, 1 H), 1.40 (s, 3 H), 1.25 (m, 2 H), 1.10 (m, 1 H), 1.07 (m, 6 H), 0.98 (s, 9 H), 0.43 (d, J = 6.8 Hz, 3 H), 0.05 (s, 6 H); ^{13}C NMR (100 MHz, toluene-d_8) δ 205.5, 133.1, 131.7, 124.0, 96.9, 84.7, 82.7, 61.4, 60.0, 56.8, 55.3, 50.8, 47.0, 43.8, 40.4, 33.3, 29.7, 25.7, 18.2, 15.0, 13.8, −5.3; IR ($CDCl_3$) 3019, 2950, 2920, 1728, 1537 cm^{-1}; high-resolution mass spectrum, calcd for $C_{22}H_{36}{}^{79}BrO_4Si$ ($M^+ - t$-Bu) 471.1566, found 471.1547.

2*β*-[(*E*)-3-([*tert*-Butyldimethylsilyl)oxy]-1-methylprop-1-enyl]-5α-[(methoxymethyl)oxy]-1α,6α,8*β*-trimethyl-1,2,4aα,5,6,7α,8,8a*β*-octahydronaphthalene-1*β*-carboxaldehyde (4). A solution of hydronaphthalene **21** (23 mg, 0.043 mmol) and 5% Na(Hg) (425 mg) in MeOH (2 mL) was stirred overnight at room temperature. The reaction mixture was decanted away from insoluble material, and then K_2CO_3 (2 mg) was added. The resulting solution was stirred for 2 h at ambient temperature. The solution was diluted with EtOAc (5 mL) and extracted with H_2O (2 × 2 mL). The aqueous extracts were washed with EtOAc (3 × 2 mL), and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated in vacuo. Purification of the crude product by silica gel chromatography (12:1 hexanes−EtOAc) provided aldehyde **4** (16 mg, 82%) as a colorless oil: R_f 0.50 (4:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −100° (*c* 0.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.43 (s, 1 H), 6.01 (d, J = 10.2 Hz, 1 H), 5.44 (m, 2 H), 4.77 (AB, J_{AB} = 6.7 Hz, 1 H), 4.65 (B of AB, J_{AB} = 6.7 Hz, 1 H), 4.20 (m, 2 H), 3.45 (dd, J = 11.0, 5.1 Hz, 1 H), 3.42 (s, 3 H), 2.37 (bs, 1 H), 2.31 (m, 1 H), 2.13 (t, J = 9.5 Hz, 1 H), 1.73−1.53 (m, 6 H) 1.43 (m, 1 H), 1.09 (s, 3 H), 1.02 (d, J = 7.2 Hz, 3 H), 0.89 (s, 9 H), 0.69 (d, J = 6.1 Hz, 3 H), 0.06 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.9, 133.3, 132.3, 126.8, 126.2, 95.4, 80.7, 60.4, 55.9, 54.5, 50.9, 43.9, 41.6, 36.0, 31.7, 28.5, 25.9, 21.0, 18.3, 15.2, 13.1, −5.0, −5.1; IR (neat) 2979, 2948, 2910, 2875, 1725, 1540, 1391, 1265, 1155, 1111, 1050 cm^{-1}; high-resolution mass spectrum, calcd for $C_{26}H_{47}O_4Si$ (M^+ + 1) 451.3244, found 451.3231.

The identity of synthetic **4** was verified by comparison with an authentic sample of **4** ($[\alpha]^{23}_D$ −101.2° (*c* 2.70, $CHCl_3$)) kindly provided by Professor Yoshii.[11]

2,4-Hexadiyne-1,6-diol. To a solution of 4.10 g (41 mmol) of cuprous chloride in 300 mL of acetone was added 6.3 mL of TMEDA (42 mmol). Oxygen was bubbled through the solution for 30 min; then propargyl alcohol (50 mL, 0.86 mol) was added dropwise at 35−40 °C. The reaction mixture was stirred at room temperature overnight (20 h) and then was diluted with Et_2O (500 mL) and washed sequentially with saturated NH_4Cl and brine. The organic extracts were dried over $MgSO_4$, filtered, and concentrated to give a yellow white solid. The crude product was recrystallized from ethyl acetate−benzene to give 42.2 g (89%) of the known[65−67] diyne as a white solid: mp 113−114 °C; lit.[67] mp 113−115 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 4.44 (t, J = 6.0 Hz, 2 H), 4.30 (d, J = 6.0 Hz, 4 H).

(2*E*,4*E*)-2,4-Hexadiene-1,6-diol. To a 0 °C solution of Red-Al (53 mL of a 3.4 M solution in toluene, 180 mmol) in 100 mL of THF was added 3.3 g (30 mmol) of the above diyne in 200 mL of THF. The reaction mixture was stirred at room temperature for 12 h and then was cooled to 0 °C and transferred via cannula to a flask containing 300 mL of aqueous saturated Rochelle's salt. The aqueous layer was extracted with ethyl acetate. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated to give a yellow solid. The crude product was recrystallized from ethyl acetate/benzene to give 3.18 g (93%) of the known diene:[38,65] mp 104−105 °C; lit.[65] mp 105.5−106.5 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 6.27 (m, 2H), 5.81 (m, 2 H), 4.11 (t, J = 5.3 Hz, 4 H), 3.80 (t, J = 5.3 Hz, 2 H); high-resolution mass spectrum, calcd for $C_6H_{10}O_2$ 114.0680, found 114.0678.

1,6-Bis[(*tert*-butyldimethylsilyl)oxy]-(2*E*,4*E*)-hexadiene (24). To a solution of (2*E*,4*E*)-2,4-hexadiene-1,6-diol (2.00 g, 17.5 mmol) in DMF (40 mL) at room temperature were added imidazole (3.56 g, 52.3 mmol) and *tert*-butyldimethylsilyl chloride (5.80 g, 38.5 mmol). This solution was stirred for 48 h and then was diluted with 1:1 Et_2O−hexane (400 mL) and washed with 1:1 H_2O−brine (200 mL). The organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified via silica gel chromatography (19:1 hexane/Et_2O) to yield 5.72 g (95%) of the known[39] diene **24** as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.20 (m, 2 H), 5.70 (m, 2 H), 4.18 (d, J = 4.4 Hz, 4 H), 0.87 (s, 18 H), 0.04 (s, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.1, 129.2, 63.4, 25.9, 18.3, −5.2; IR ($CHCl_3$) 3000, 2955, 2930, 2859, 1471, 1452

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cm^{-1}; high-resolution mass spectrum calcd for $C_{14}H_{29}O_2Si_2$ ($M^+ - C_4H_9$) 285.1706, found 285.1689.

(2′*R*,3*S*,4*S*,6*R*)-Spiro[3,6-bis[[(*tert*-butyldimethylsilyl)oxy]methyl]-1-cyclohexene-[4,5′]-2′-cyclohexyl-1′,3′-dioxolan-4′-one] (23a) (Diels−Alder Reaction of 24 and 25a). A Carius tube was soaked in a 2-propanol−KOH bath for 12 h. The tube was emptied, washed repeatedly with distilled water, and dried in a 120 °C oven. The tube was then treated with 250 μL of bis(trimethylsilyl)acetamide and sealed. The contents were heated to reflux for 30 min; then the tube was cooled to room temperature and rinsed with hexanes. A solution of diene **24** (3.00 g, 8.75 mmol) and dienophile **25a**[41] (402 mg, 2.21 mmol) in trichloroethylene (2.2 mL) was then added to the Carius tube. Two crystals of BHT were added, and the solution was degassed with a stream of nitrogen. The tube was sealed and immersed in a 150 °C oil bath for 42 h. The tube was then cooled, and the contents were concentrated in vacuo to yield a crude solid. This material was purified by silica gel chromatography (100% hexane−19:1 hexane/Et_2O) to yield 408 mg (35%, based on **25a**) of the desired exo adduct **23a** and 78 mg (6.7%) of the endo isomer **26**; 2.56 g (85%) of diene **24** was also recovered.

Data for 23a: $[\alpha]^{23}_D$ −13.9° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.82 (ddd, J = 10.0, 4.0, 3.0 Hz, 1 H), 5.35 (d, J = 4.8 Hz, 1H), 5.31 (dt, J = 10.4, 2.0 Hz, 1 H), 3.60 (m, 4 H), 2.80 (m, 1 H), 2.50 (m, 1 H), 1.97 (m, 2 H), 1.65 (m, 5 H), 1.15 (m, 6 H), 0.86 (s, 18 H), 0.01 (s, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 129.1, 123.9, 106.9, 65.8, 63.0, 44.0, 42.2, 37.1, 32.2, 26.3, 26.2, 26.0, 25.9, 25.8, 25.6, 18.2, 18.1, −5.4, −5.7; IR ($CHCl_3$) 1785 cm^{-1}; high-resolution mass spectrum, calcd for $C_{24}H_{43}O_5Si_2$ ($M^+ - C_4H_9$) 467.2649, found 467.2680. Anal. Calcd for $C_{28}H_{52}O_5Si_2$: C, 64.07; H, 9.99. Found: C, 64.26; H, 10.26.

Data for 26: $[\alpha]^{23}_D$ 48.6° (*c* 1.03, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.81 (d, J = 10.4 Hz, 1 H), 5.63 (ddd, J = 10.0, 3.6, 2.0 Hz, 1 H), 5.33 (d, J = 4.0 Hz, 1 H), 3.64 (dd, J = 10.0, 7.2 Hz, 1 H), 3.50 (m, 3 H), 2.50 (m, 2 H), 1.79 (m, 6 H), 1.30 (m, 7 H), 0.90 (s, 18 H), 0.00 (s, 12 H); IR (neat) 1789 cm^{-1}; high-resolution mass spectrum, calcd for $C_{28}H_{53}O_5Si_2$ (M^+ + 1) 525.3431, found 525.3449.

(3a*S*,6*S*,7a*S*)-7a-Hydroxy-6-(hydroxymethyl)-3a,6,7,7a-tetrahydro-3*H*-isobenzofuran-1-one (27). A 0 °C solution of K_2CO_3 (60 mg, 0.43 mmol) and endo cycloadduct **26** (112 mg, 0.21 mmol) in MeOH (4 mL) was stirred for 1 h. The reaction mixture was then diluted with ethyl acetate, washed with NH_4Cl (aq) and brine, dried with $MgSO_4$, and concentrated. The crude product was purified via silica gel chromatography (1:9 Et_2O−hexane to 1:4 Et_2O−hexane) to yield 89 mg (94%) of the desired methyl ester: ^1H NMR (400 MHz, $CDCl_3$) δ 5.78 (d, J = 10.0 Hz, 1 H), 5.56 (ddd, J = 10.0, 4.4, 2.4 Hz, 1 H), 3.73 (s, 3 H), 3.50 (m, 4 H), 3.05 (m, 1 H), 2.49 (m, 1 H), 2.33 (m, 1 H), 1.80 (m, 2 H), 0.93 (m, 18 H), 0.03 (m, 12 H); IR ($CHCl_3$) 3010, 2950, 1725 cm^{-1}; high-resolution mass spectrum, calcd for $C_{18}H_{35}O_5Si_2$ ($M^+ - C_4H_9$) 387.2023, found 387.1946.

A 40 °C solution of the above ester (84 mg, 0.19 mmol) in CH_3CN (2.0 mL) was then treated with $Et_3N{\cdot}HF$ (92 mg, 0.75 mmol). The solution was stirred for 15 h and then was diluted with ethyl acetate and washed with saturated NH_4Cl (aq) and brine. The organic extracts were dried with $MgSO_4$ and concentrated to yield 13 mg (37%) of the known[38] lactone **27** as a white solid: mp 110−112 °C; lit.[38] mp 112−113 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 5.90 (d, J = 10.4 Hz, 1 H), 5.71 (ddd, J = 10.0, 3.2, 2.8 Hz, 1 H), 4.52 (t, J = 8.8 Hz, 1 H), 3.78 (t, J = 9.6 Hz, 1 H), 3.66 (m, 2 H), 3.01 (m, 1 H), 2.78 (m, 1 H), 2.66 (m, 1 H), 1.88 (m, 1 H), 1.60 (m, 2 H); IR ($CHCl_3$) 3440 (br), 1755 cm^{-1}; high-resolution mass spectrum, calcd for $C_9H_{13}O_4$ (M^+ + 1) 185.0821, found 185.0808.

Methyl (1*S*,2*S*,5*R*)-1-Hydroxy-2,5-bis(hydroxymethyl)-cyclohex-3-ene-1-carboxylate (28). A solution of exo cycloadduct **23a** (1.07 g, 2.04 mmol) and $Et_3N{\cdot}HF$ (870 mg, 7.2 mmol) in CH_3CN (10 mL) was heated at 40 °C for 42 h. After being cooled to room temperature, the solution was diluted with ethyl acetate and washed sequentially with NH_4Cl (aq) and brine. The organic extracts were dried with Na_2SO_4 and concentrated in vacuo. The crude product was then purified via silica gel chromatography (1:1 Et_2O−hexane to 100% Et_2O) to yield the 532 mg (88%) of the desired diol: $[\alpha]^{23}_D$ +14.8 (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 5.84 (dt, J = 10.2, 3.2 Hz, 1 H), 5.46 (m, J = 4.5 Hz, 2 H), 3.75 (dd, J = 11.2, 4.8 Hz, 1 H), 3.67 (m, 3 H), 2.84 (m, 1 H), 2.66 (br s, 1 H), 2.13 (dd, J = 14.0, 7.6 Hz, 1 H), 1.90 (m, 3 H), 1.78 (m, 4 H), 1.67 (m, 2 H), 1.16 (m, 5 H); IR ($CHCl_3$) 3470, 1785 cm^{-1}; high-resolution mass spectrum calcd for $C_{16}H_{23}O_4$ (M^+ − OH) 279.1596, found 279.1612.

To a solution of the above diol (532 mg, 1.80 mmol) in MeOH (16 mL) was added K_2CO_3 (500 mg, 3.6 mmol). The solution was stirred at room temperature for 1 h and then was diluted with ethyl acetate and washed with NH_4Cl (aq). The aqueous layer was extracted with ethyl acetate, and the combined organic extracts were further washed with brine, dried ($MgSO_4$), and concentrated in vacuo. The crude oil was then triturated with hexane to yield 358 mg (91%) of **28** as a white solid: mp 95−97 °C; $[\alpha]^{24}_D$ +23.2° (*c* 1.12, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.74 (d, J = 10.0 Hz, 1 H), 5.58 (d, J = 10.4 Hz, 1 H), 3.75 (s, 3 H), 3.70 (m, 3 H), 3.57 (m, 1 H), 2.83 (m, 1 H), 2.52 (m, 1 H), 2.34 (m, 1 H), 1.87 (d, J = 14.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 128.4, 126.9, 77.1, 73.6, 65.5, 63.1, 52.8, 42.8, 36.1; IR ($CHCl_3$) 3400 (br), 1723 cm^{-1}; high-resolution mass spectrum, calcd for $C_{10}H_{17}O_5$ (M^+ + 1) 217.1076, found 217.1092. Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.55; H, 7.46. Found: C, 55.40; H, 7.36.

Methyl (2*R*,4a*S*,7*R*,8a*R*)-7-(Hydroxymethyl)-2-phenyl-4,4a,7,8-tetrahydrobenzo[1,3]dioxine-8a-carboxylate (29) and Methyl (2*S*,4a*S*,7*R*,8a*R*)-7-(Hydroxymethyl)-2-phenyl-4,4a,7,8-tetrahydrobenzo[1,3]dioxine-8a-carboxylate (30). To a solution of triol **28** (325 mg, 1.50 mmol) in benzaldehyde (6.6 mL) was added a 1 M solution of $ZnCl_2$ in Et_2O (1.8 mL, 1.8 mmol). The solution was stirred at room temperature for 1 h and then was diluted with ethyl acetate, washed with aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated in vacuo. The crude mixture was then purified via silica gel chromatography (100% Et_2O) to yield 294 mg (64%) of the α-isomer (**29**; kinetic) and 41 mg (9%) of the β-isomer (**30**; thermodynamic).

Data for 29: $[\alpha]^{20}_D$ +14.4° (*c* 1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.45−7.29 (m, 5 H), 5.96 (m, 1 H), 5.75 (dt, J = 10.0, 2.0 Hz, 1 H), 5.57 (s, 1 H), 4.13 (dd, J = 11.8, 1.4 Hz, 1 H), 4.05 (dd, J = 11.8, 3.0 Hz, 1 H), 3.86 (s, 3 H), 3.68 (dd, J = 10.8, 5.8 Hz, 1 H), 3.60 (dd, J = 10.8, 4.4 Hz, 1 H), 2.82 (br s, 1 H), 2.48 (m, 1 H), 2.09 (m, 2 H), 1.60 (m, 1 H); IR ($CHCl_3$) 3450 (br), 1730 cm^{-1}; high-resolution mass spectrum, calcd for $C_{17}H_{20}O_5$ (M^+) 304.1311, found 304.1338. Anal. Calcd for $C_{17}H_{20}O_5$: C, 67.09; H, 6.62. Found: C, 66.86; H, 6.75.

Data for 30: $[\alpha]^{20}_D$ +5.6 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.52−7.33 (m, 5 H), 5.80 (s, 1 H), 5.66 (m, 2 H), 4.24 (dd, J = 11.4, 5.8 Hz, 1 H), 3.77 (s, 3 H), 3.71 (m, 2 H), 3.63 (dd, J = 10.4, 4.8 Hz, 1 H), 3.27 (m, 1 H), 2.50 (m, 1 H), 2.44 (dd, J = 10.8, 10.8 Hz, 1H), 2.20 (dd, J = 10.8, 5.2 Hz, 1 H), 1.28 (m, 1 H); IR ($CHCl_3$) 3450 (br), 1739 cm^{-1}; high-resolution mass spectrum, calcd for $C_{17}H_{20}O_5$ (M^+) 304.1310, found 304.1324.

Methyl (2*R*,4a*S*,5*R*,6*S*,7*R*,8a*R*)-5,6-Epoxy-7-(hydroxymethyl)-2-phenyl-4,4a,7,8-tetrahydrobenzo[1,3]dioxine-8a-carboxylate (31) and Methyl (2*R*,4a*S*,5*S*,6*R*,7*R*,8a*R*)-5,6-Epoxy-7-(hydroxymethyl)-2-phenyl-4,4a,7,8-tetrahydrobenzo[1,3]-dioxine-8a-carboxylate (32). To a solution of **29** (150 mg, 0.49 mmol) in pyridine (3 mL) was added Ac_2O (71 μL, 0.75 mmol). The solution was stirred at room temperature for 20 h and then was diluted with ethyl acetate and washed with 1 N HCl. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated. The crude mixture was purified via silica gel chromatography (5:1 Et_2O−hexane) to yield 162 mg (95%) of the desired acetate: R_f 0.89 (5:1 Et_2O−hexane); ^1H NMR (400 MHz, $CDCl_3$) δ 7.49−7.31 (m, 5 H), 5.96 (m, 1 H), 5.77 (m, 1 H), 5.55 (s, 1 H), 4.24 (dd, 1 H), 4.09 (m, 3 H), 3.86 (s, 3 H), 2.84 (m, 1 H), 2.55 (m, 1 H), 2.04−1.93 (m, 2 H), 2.03 (s, 3 H); IR ($CHCl_3$) 1735 cm^{-1}; high-resolution mass spectrum, calcd for $C_{19}H_{22}O_6$ (M^+) 346.1416, found 346.1389.

To a solution of the above methyl ester obtained (162 mg, 0.47 mmol) in $CHCl_3$ (14 mL) were added $NaHCO_3$ (60 mg, 0.7 mmol) and 80% MCPBA (106 mg, 0.5 mmol). This solution was stirred at room temperature for 18 h and then was diluted

with ethyl acetate and washed with aqueous $NaHCO_3$ and brine. The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo to yield 173 mg of crude epoxide, which was used in the next step without further purification: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.36 (m, 5 H), 5.55 (s, 1 H), 4.38 (dd, 1 H), 4.28 (m, 2 H), 4.08 (m, 1 H), 3.82 (s, 3 H), 3.37 (m, 2 H), 2.54 (m, 1 H), 2.04 (s, 3 H), 2.03 (m, 1 H), 1.85 (m, 1 H), 1.23 (m, 1 H); IR ($CHCl_3$) 1735 cm^{-1}; high-resolution mass spectrum, calcd for $C_{19}H_{22}O_7$ (M^+) 362.1366, found 362.1375.

To a 0 °C solution of the crude epoxide (173 mg, 0.47 mmol theoretically) in MeOH (5 mL) was added K_2CO_3 (103 mg, 0.75 mmol). This solution was stirred at 0 °C for 1.5 h and then was warmed to room temperature, diluted with ethyl acetate, and washed with aqueous NH_4Cl. The aqueous extracts were extracted with additional ethyl acetate. The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated. The crude product was purified via silica gel chromatography (9:1 Et_2O/hexane) to yield 112 mg (71% over three steps) of the desired β-epoxy alcohol **31**: $[\alpha]^{24}_D$ +13.8° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.37 (m, 5 H), 5.59 (s, 1 H), 4.33 (dd, J = 12.2, 1.0 Hz, 1 H), 4.08 (dd, J = 12.2, 2.6 Hz, 1 H), 3.85 (s, 3 H), 3.81 (d, J = 5.6 Hz, 2 H), 3.42 (A of AB, J_{AB} = 4.0 Hz, 1 H), 3.38 (B or AB, J_{AB} = 4.0 Hz, 1 H), 2.55 (m, 1 H), 2.47 (dd, J = 6.0, 1.6 Hz, 1 H), 1.89 (m, 2 H); IR ($CHCl_3$) 3150 (br), 1763 cm^{-1}; high-resolution mass spectrum, calcd for $C_{17}H_{20}O_6$ (M^+) 320.1260, found 320.1229.

Direct epoxidation of **29** with MCPBA provided β-epoxide **31** in 70−75% yield, along with 11% of the α-epoxide **32**: $[\alpha]^{20}_D$ +14.0° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50−7.33 (m, 5 H), 5.56 (s, 1 H), 4.25 (dd, J = 11.4, 5.8 Hz, 1 H), 4.14 (dd, J = 11.6, 4.0 Hz, 1 H), 3.90 (dd, J = 10.4, 8.0 Hz, 1 H), 3.89 (s, 3 H), 3.69 (dd, J = 10.0, 6.0 Hz, 1 H), 3.35 (m, 2 H), 2.84 (m, 1 H), 2.32 (m, 1 H), 1.87 (dd, J = 10, 6 Hz, 1 H), 1.78 (dd, J = 10, 7 Hz, 1 H); IR ($CHCl_3$) 3440 (br), 1728 cm^{-1}; high-resolution mass spectrum, calcd for $C_{17}H_{20}O_6$ (M^+) 320.1260, found 320.1264.

Methyl (2*R*,4a*S*,5*S*,8a*R*)-7-Formyl-5-hydroxy-2-phenyl-4,4a,5,8-tetrahydrobenzo[1,3]dioxine-8a-carboxylate (33). To a −78 °C solution of $(COCl)_2$ (40 μL, 0.46 mmol) in CH_2Cl_2 (2.0 mL) was added DMSO (64 μL, 0.9 mmol) followed, 10 min later, by a −78 °C solution of alcohol **31** (110 mg, 0.34 mmol) in CH_2Cl_2. The solution became white and was stirred for 30 min. Et_3N (300 μL, 2.1 mmol) was then added, and the cooling bath was removed. The reaction was stirred at room temperature for 1 h and then was diluted with ethyl acetate and extracted with $NaHCO_3$ (aq) and brine. The crude product was purified via silica gel chromatography (90% Et_2O in hexane) to yield 71 mg (65%) of α,β-unsaturated aldehyde **33**: $[\alpha]^{24}_D$ −16.5° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.47 (s, 1 H), 7.44−7.32 (m, 5 H), 6.75 (s, 1 H), 5.65 (s, 1 H), 5.08 (dd, J = 9.2, 2.4 Hz, 1 H), 4.39 (A of AB, J_{AB}=12.0 Hz, 1 H), 4.02 (B of AB, J_{BA}=12.0 Hz, 1 H), 3.86 (s, 3 H), 2.69 (d, J = 19.2 Hz, 1 H), 2.54 (m, 1 H), 2.23 (d, J = 9.2 Hz, 1 H), 1.23 (s, 1 H); IR ($CHCl_3$) 3400 (br), 1734, 1687 cm^{-1}; high-resolution mass spectrum, calcd for $C_{17}H_{18}O_6$ (M^+) 318.1103, found 318.1096. Anal. Calcd for $C_{17}H_{18}O_6$: C, 64.14; H, 5.70. Found: C, 63.94; H, 5.79.

Methyl (2*R*,4a*S*,5*S*,8a*R*)-7-[[(*tert*-Butyldiphenylsilyl)-oxy]methyl]-5-(methoxymethoxy)-2-phenyl-4,4a,5,8-tetrahydrobenzo[1,3]dioxine-8a-carboxylate (34). A solution of alcohol **33** (87 mg, 0.27 mmol), *i*-Pr_2NEt (480 μL, 2.7 mmol), and MOM-Cl (210 μL, 2.8 mmol) in CH_2Cl_2 (4 mL) was stirred at room temperature for 16 h. The solution was then diluted with Et_2O, washed with NH_4Cl (aq) and brine, dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified via silica gel chromatography (3:1 to 7:1 Et_2O−hexane) to yield 91 mg (91%) of the MOM ether: $[\alpha]^{24}_D$ −8.0° (*c* 1.0, $CHCl_3$);^{1}H NMR (400 MHz, $CDCl_3$) δ 9.51 (s, 1 H), 7.46−7.36 (m, 5 H), 6.92 (s, 1 H), 5.67 (s, 1 H), 5.00 (m, 1 H), 4.89 (dd, J = 10.2, 7.0 Hz, 2 H), 4.29 (m, 1 H), 4.04 (m, 1 H), 3.88 (s, 3 H), 3.49 (s, 3 H), 2.67 (m, 1 H), 2.57 (m, 1 H), 2.37 (m, 1 H); IR ($CHCl_3$) 1740, 1695 cm^{-1}; high-resolution mass spectrum, calcd for $C_{19}H_{22}O_7$ (M^+) 362.1366, found 362.1359.

To a 0 °C solution of the above aldehyde (90 mg, 0.25 mmol) in 5 mL of MeOH were added $CeCl_3 \cdot 7H_2O$ (94 mg, 0.25 mmol) and $NaBH_4$ (10 mg, 0.25 mmol). This solution stirred at 0 °C for 30 min and then was diluted with ethyl acetate, washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified via silica gel chromatography (30% ethyl acetate−hexane to 100% ethyl acetate) to yield 82 mg (91%) of the corresponding allylic alcohol: $[\alpha]^{25}_D$ +29.3° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.32 (m, 5 H), 5.89 (s, 1 H), 5.63 (s, 1 H), 4.85 (A of AB, J_{AB} = 7.0 Hz, 1 H), 4.80 (B of AB, J_{AB} = 7.0 Hz, 1 H), 4.76 (m, 1 H), 4.28 (d, J = 12.0 Hz, 1 H), 3.99 (m, 3 H), 3.85 (s, 3 H), 3.44 (s, 3 H), 2.48 (d, J = 18.4 Hz, 1 H), 2.34 (d, J = 18.4 Hz, 1 H), 2.29 (dd, J = 9.2, 1.8 Hz, 1 H), 1.74 (br s, 1 H); IR ($CHCl_3$) 3400 (br), 1736 cm^{-1}; high-resolution mass spectrum, calcd for $C_{19}H_{24}O_7$ (M^+) 364.1522, found 364.1506. Anal. Calcd for $C_{19}H_{24}O_7$: C, 62.63; H, 6.64. Found: C, 62.62; H, 6.57.

To solution of the above allylic alcohol (70 mg, 0.19 mmol) in DMF (0.5 mL) were added TBDPS-Cl (65 μL, 0.25 mmol) and imidazole (17 mg, 0.25 mmol). This solution was stirred for 12 h at room temperature and then was diluted with Et_2O, washed with aqueous NH_4Cl and brine, dried (Na_2SO_4), and concentrated in vacuo. The crude product was then purified via silica gel chromatography (1:10 to 2:3 Et_2O−hexane) to yield 107 mg (92%) of **34**: $[\alpha]^{25}_D$ +14.8° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67−7.36 (m, 15 H), 5.99 (s, 1 H), 5.64 (s, 1 H), 4.85 (A of AB, J_{AB} = 7.2 Hz, 1 H), 4.82 (B of AB, J_{AB} = 7.2 Hz, 1 H), 4.76 (dd, J = 8.6, 1.8 Hz, 1 H), 4.29 (d, J = 11.8 Hz, 1 H), 4.06 (m, 2 H), 3.98 (d, J = 11.8 Hz, 1 H), 3.85 (s, 3 H), 3.44 (s, 3 H), 2.41 (d, J = 18.4 Hz, 1 H), 2.31 (d, J = 8.8 Hz, 1 H), 2.27 (d, J = 18.4 Hz, 1 H), 1.06 (s, 9 H); IR ($CHCl_3$) 1733 cm^{-1}; high-resolution mass spectrum, calcd for $C_{31}H_{33}O_7Si$ ($M^+ - C_4H_9$) 545.1996, found 545.1976.

Methyl (1*R*,5*S*,6*R*)-1-Hydroxy-3-[[(*tert*-butyldiphenylsilyl)oxy]methyl]-6-(hydroxymethyl)-5-(methoxymethoxy)cyclohex-3-enecarboxylate (35). A solution of **34** (89 mg, 0.15 mmol) in 80% HOAc (3 mL) was heated to 80 °C for 1 h. The solution was then cooled to room temperature, diluted with ethyl acetate, washed with aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude product via silica gel chromatography (1:1 Et_2O−hexane to 100% Et_2O) yielded 62 mg (81%) of diol **35**: $[\alpha]^{25}_D$ +45.0° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67−7.37 (m, 10 H), 5.93 (s, 1 H), 4.79 (A of AB, J_{AB} = 6.8 Hz, 1 H), 4.75 (B of AB, J_{AB} = 6.8 Hz, 1 H), 4.44 (br d, J = 9.2 Hz, 1 H), 4.06 (s, 2 H), 3.91 (dd, J = 11.6, 4.4 Hz, 1 H), 3.80 (s, 3 H), 3.77 (dd, J = 11.6, 3.0 Hz, 1 H), 3.41 (s, 3 H), 2.59 (d, J = 17.6 Hz, 1 H), 2.18 (m, 1 H), 2.01 (d, J = 17.6 Hz, 1 H), 1.05 (s, 9 H); IR ($CHCl_3$) 3490 (br), 1729 cm^{-1}; high-resolution mass spectrum, calcd for $C_{24}H_{29}O_7Si$ ($M^+ - C_4H_9$) 457.1682, found 457.1674. Anal. Calcd for $C_{28}H_{38}O_7Si$: C, 65.34; H, 7.44. Found: C, 65.82; 7.03.

Methyl (1*R*,5*S*,6*R*)-1-Hydroxy-3-[[(*tert*-butyldiphenylsilyl)oxy]methyl]-5-(methoxymethoxy)-6-[(vinyloxy)-methyl]cyclohex-3-enecarboxylate (36). To a solution of diol **35** (46 mg, 0.089 mmol) in ethyl vinyl ether (1 mL) was added $Hg(OAc)_2$ (3.0 mg, 0.009 mmol). This solution was stirred at room temperature for 19 h and then was diluted with ethyl acetate, washed with aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. Purification of the crude product via silica gel chromatography (1:1 Et_2O−hexane) yielded 15 mg (31%) of the desired vinyl ether **36**: $[\alpha]^{25}_D$ +42.6° (*c* 0.98, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72−7.35 (m, 10 H), 6.37 (dd, J = 14.0, 6.8 Hz, 1 H), 5.93 (s, 1 H), 4.74 (d, J = 6.8 Hz, 1 H), 4.68 (d, J = 7.2 Hz, 1 H), 4.20 (dd, J = 14.4, 2.0 Hz, 1 H), 4.18 (m, 1 H), 4.07 (br s, 1 H), 4.02 (dd, J = 6.8, 2.0 Hz, 1 H), 3.93 (dd, J = 10.2, 7.4 Hz, 1 H), 3.85 (dd, J = 10.4, 2.8 Hz, 1 H), 3.77 (s, 3 H), 3.59 (s, 1 H), 3.39 (s, 3 H), 2.62 (d, J = 17.2 Hz, 1 H), 2.43 (m, 1 H), 2.20 (s, 1 H), 2.02 (d, J = 17.2 Hz, 1 H), 1.07 (s, 9 H); IR ($CHCl_3$) 3510 (br), 1729 cm^{-1}; high-resolution mass spectrum, calcd for $C_{26}H_{31}O_7Si$ ($M^+ - C_4H_9$) 483.1839, found 483.1864.

Ethyl (1*R*,5*S*,6*R*)-1-Hydroxy-3-[[(*tert*-butyldiphenylsilyl)oxy]methyl]-5-(methoxymethoxy)-6-[(vinyloxy)methyl]cyclohex-3-enecarboxylate (6). A solution of **36** (14 mg, 0.026 mmol) in EtOH (0.4 mL) was added to a solution of NaOEt (38 mg, 0.56 mmol) in 1 mL of EtOH. This solution was stirred for 3 h at room temperature and then was diluted with ethyl acetate, washed with aqueous NH_4Cl and brine, dried (Na_2SO_4), and concentrated in vacuo. Purification of the crude product by silica gel chromatography (5% to 20% Et_2O−

hexane) yielded 13 mg (90%) of the known[17,18] ethyl ester **6**: $[\alpha]^{25}_D$ +41.3° (*c* 1.0, $CHCl_3$); lit.[18] $[\alpha]^{25}_D$ +34.4° (*c* 2.9, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60−7.32 (m, 10 H), 6.38 (dd, *J* = 14.6, 6.8 Hz, 1 H), 5.93 (br s, 1 H), 4.79 (d, *J* = 6.8 Hz, 1 H), 4.69 (d, *J* = 6.8 Hz, 1 H), 4.1−4.3 (m, 4 H), 4.07 (br s, 2 H), 4.03 (dd, *J* = 6.8, 2.2 Hz, 1 H), 3.98 (dd, *J* = 10.0, 7.2 Hz, 1 H), 3.85 (dd, *J* = 10.2, 3.0 Hz, 1 H), 3.61 (s, 1 H), 3.40 (s, 3 H), 2.62 (br d, *J* = 17.2 Hz, 1 H), 2.44 (m, 1 H), 2.01 (d, *J* = 17.2 Hz, 1 H), 1.29 (t, *J* = 7.0 Hz, 3 H), 1.05 (s, 9 H); IR ($CHCl_3$) 3520 (br), 1726 cm^{-1}; high-resolution mass spectrum, calcd for $C_{27}H_{33}O_7Si$ ($M^+ - C_4H_9$) 497.1995, found 497.2018.

The ^{1}H NMR spectrum of **6** was in excellent agreement with NMR data kindly provided by Professor Boeckman.[17,18]

4-[(*tert*-Butyldimethylsilyl)oxy]-2(*E*)-buten-1-al (39). *n*-Butyllithium (4.4 mL, 2.7 M in hexane, 11.9 mmol) was added dropwise to a −78 °C solution of *cis*-2-butene-1,4-diol (1.0 mL, 12.2 mmol) in 19 mL of THF. The solution was stirred for 5 min; then a solution of TBDMS-Cl (1.72 g, 11.4 mmol) in 5 mL of THF was added. The reaction mixture was allowed to warm to ambient temperature over a 2 h period and then was heated just below reflux for 3 h. The solution was concentrated in vacuo, hexane−ether (7:1, 25 mL) was added, and the solution was filtered through a short plug of silica gel. Concentration of the filtrate in vacuo provided a 97:3 mixture of the mono-TBS ether and the bis-TBS ether (^{1}H NMR analysis). Separation of this mixture by chromatography over silica gel (10 g; 5:1 hexane−Et_2O) yielded the desired mono-TBS ether (2.14 g, 87% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.67 (m, 2 H), 4.23 (d, *J* = 4.3 Hz, 2 H), 4.18 (dd, *J* = 5.3, 5.3 Hz, 2 H), 2.03 (br d, *J* = 4.9 Hz, −OH), 0.89 (s, 9 H), 0.06 (s, 6 H); IR ($CHCl_3$) 3615, 1463 cm^{-1}; mass spectrum, *m*/*e* 189 ($M^+ - CH_3 + H_2$). Anal. Calcd for $C_{10}H_{22}O_2Si$: C, 59.35; H, 10.96. Found: C, 59.05; H, 10.99.

A solution of the mono-TBS ether (1.00 g, 4.94 mmol) in dry CH_2Cl_2 (5 mL) was added to a suspension of pyridinium chlorochromate (1.70 g, 7.89 mmol) and Celite (2.00 g) in dry CH_2Cl_2 at 23 °C. The mixture was stirred for 3 h and then was diluted with Et_2O and filtered through a layer of Celite. The filtrate and ether washings were combined. Removal of the solvent in vacuo gave an oily residue, which was purified by silica gel chromatography (10% ether−hexane as eluent) to afford the known enal **39** as a pale yellow oil (838 mg, 85%): R_f 0.45 (2:5 ether−hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60 (d, *J* = 8.0 Hz, 1 H), 6.88 (dt, *J* = 15.6, 3.2 Hz, 1 H), 6.40 (ddt, *J* = 15.6, 8.0, 2.2 Hz, 1 H), 4.45 (dd, *J* = 3.2, 2.2 Hz, 2 H), 0.93 (s, 9 H), 0.10 (s, 6 H); IR ($CHCl_3$) 2960, 1685 cm^{-1}; high-resolution mass spectrum, calcd for $C_{10}H_{20}O_2Si$ (M^+), 200.1233, found 200.1236.

Methyl 8-[(*tert*-Butyldimethylsilyl)oxy]-2-methyl-2(*E*),4(*E*),6(*E*)-octatrienoate (37). A solution of *n*-BuLi in hexane (1.30 mL, 2.5 M, 3.25 mmol) was added slowly to a −78 °C solution of methyl γ-(dimethylphosphono)tiglate **40**[54] (725 mg, 3.26 mmol) in anhydrous THF (18 mL). The mixture was stirred for 15 min at −78 °C; then HMPA (2.9 mL, 16.7 mmol) was added. The mixture was stirred for an additional 15 min; then a solution of enal **39** (540 mg, 2.70 mmol) in anhydrous THF (4 mL) was added. The reaction mixture was stirred for 15 min at −78 °C and then was allowed to warm to 23 °C and stirred for an additional 30 min. The reaction mixture was diluted with Et_2O and poured into saturated aqueous NH_4Cl. The aqueous layer was separated and extracted with Et_2O. The combined ethereal layers were dried over Na_2SO_4 and concentrated in vacuo. Purification of the crude mixture by silica gel chromatography (10% ether−hexane as eluent) provided trienoate **37** as a white solid (551 mg, 69%): mp 47−49 °C; R_f 0.60 (2:5 ether−hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (dd, *J* = 10.8, 1.2 Hz, 1 H), 6.35−6.60 (m, 3 H), 5.95 (dt, *J* = 15.6, 4.4 Hz, 1 H), 4.28 (dd, *J* = 4.4, 1.2 Hz, 2 H), 3.76 (s, 3 H), 1.96 (d, *J* = 1.2 Hz, 3 H), 0.92 (s, 9 H), 0.09 (s, 6 H); IR ($CHCl_3$) 2960, 2860, 1700, 1615 cm^{-1}; high-resolution mass spectrum, calcd for $C_{16}H_{28}O_3Si$ (M^+), 296.1808, found 296.1815.

(2′*R*,3*S*,4*S*,6*R*)-Spiro[3-[2-(methoxycarbonyl)-1(*E*)-propen-1-yl]-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]-1-cyclohexene-[4,5′]-2′-*tert*-butyl-1′,3′-dioxolan-4′-one] (41). A mixture of triene **37** (508 mg, 1.71 mmol), freshly prepared dienophile (*R*)-**25b**[41] (401 mg, 2.57 mmol), and BHT (10 mg) in toluene (0.57 mL, 3 M) was heated in sealed Carius tube at 110 °C for 90 h. Evaporation of the solvent in vacuo afforded an oily residue which consisted of a 7:1 mixture of **41** (exo) and **42** (endo), along with recovered triene **37**, as determined by ^{1}H NMR analysis. This mixture was purified by silica gel chromatography. Elution of the column with 8% ether−hexane afforded recovered **37** (73 mg, 14%), and further elution with 10% ether−hexane afforded the exocycloadduct **41** as a white solid (516 mg, 67%): mp 102−104 °C; R_f 0.40 (1:5 ether−hexane); $[\alpha]^{24}_D$ −91.3° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.64 (dd, *J* = 10.8, 1.6 Hz, 1 H), 5.88 (ddd, *J* = 10.0, 3.2, 2.8 Hz, 1 H), 5.42 (td, *J* = 10.8, 2.8 Hz, 1 H), 5.07 (s, 1 H), 3.75 (s, 3 H), 3.60−3.70 (m, 2 H), 3.57 (ddd, *J* = 10.8, 2.8, 2.4 Hz, 1 H), 2.60−2.65 (m, 1 H), 2.09 (dd, *J* = 14.4, 3.6 Hz, 1 H), 2.03 (dd, *J* = 14.4, 6.8 Hz, 1 H), 1.88 (d, *J* = 1.6 Hz, 3 H), 0.94 (s, 9 H), 0.88 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 174.7, 168.1, 137.7, 130.7, 129.2, 124.8, 109.7, 79.3, 65.5, 52.0, 40.9, 36.7, 34.9, 30.2, 25.8, 23.3, 18.2, −5.4; IR ($CHCl_3$) 2960, 1785, 1715 cm^{-1}; high-resolution mass spectrum, calcd for $C_{24}H_{40}O_6Si$ (M^+) 452.2594, found 452.2621. Anal. Calcd for $C_{24}H_{40}O_6Si$: C, 63.68; H, 8.91. Found: C, 63.68; H, 8.91.

Further elution of the column with 12% ether−hexane afforded an inseparable oily mixture containing the endo adduct **42** (95 mg). This mixture was treated with HF·NEt_3 (52 mg, 0.45 mmol) in CH_3CN (2 mL) at 40 °C for 16 h. Purification of the crude mixture by silica gel chromatography gave desilylated endo adduct (46 mg) as a colorless oil. Treatment of this compound (46 mg, 0.14 mmol) with TBDMS-Cl (26 mg, 0.16 mmol) and imidazole (12 mg, 0.18 mmol) in anhydrous DMF (1 mL) at 23 °C for 16 h afforded endo cycloadduct **42** (59 mg, 7% from **37**) as a colorless oil: R_f 0.35 (1:5 ether−hexane); $[\alpha]^{24}_D$ +153.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.53 (ddd, *J* = 10.4, 3.2, 1.6 Hz, 1 H), 5.80 (d, *J* = 10.4, Hz, 1 H), 5.48 (ddd, *J* = 10.4, 4.8, 2.4 Hz, 1 H), 5.28 (s, 1 H), 3.72 (s, 3 H), 3.50−3.65 (m, 2 H), 3.38 (ddt, *J* = 10.4, 4.8, 1.6 Hz, 1 H), 2.50−2.60 (m, 1 H), 1.90 (dd, *J* = 13.6, 10.8 Hz, 1 H), 1.88 (d, *J* = 1.2 Hz, 3 H), 1.83 (dd, *J* = 13.6, 6.0 Hz, 1 H), 0.96 (s, 9 H), 0.90 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 172.9, 167.9, 137.4, 129.7, 128.7, 124.0, 107.7, 79.2, 66.0, 51.9, 39.3, 35.4, 34.5, 29.3, 25.8, 23.3, 18.2, 12.7, −5.4; IR ($CHCl_3$) 2950, 1785, 1710 cm^{-1}; high-resolution mass spectrum, calcd for $C_{24}H_{40}O_6Si$ (M^+) 452.2594, found 452.2606. Anal. Calcd for $C_{24}H_{40}O_6Si$: C, 63.68; H, 8.91. Found: C, 63.66; H, 8.90.

(1*S*,2*R*,2′*R*,3*S*,4*S*,6*R*)-Spiro[1,2-bis(methoxymethoxy)-3-[2-(methoxycarbonyl)-1(*E*)-propen-1-yl]-6-[[(*tert*-butyldimethylsilyl)oxy]methyl]cyclohexane-[4,5′]-2′-*tert*-butyl-1′,3′-dioxolan-4′-one (47). A 2.5% solution of OsO_4 in *t*-BuOH (0.63 mL, 0.06 mmol) was added to a suspension of **41** (513 mg, 1.13 mmol) and *N*-methylmorpholine *N*-oxide monohydrate (153 mg, 1.13 mmol) in 2:1 acetone−water (10 mL), and the solution was stirred for 7 h at 23 °C. The resultant clear solution was diluted with EtOAc and brine. The aqueous layer was separated and extracted with EtOAc. The combined organic layers were washed with brine and dried over Na_2SO_4. Removal of the solvent i*n vacuo* gave a solid residue, which was purified by silica gel chromatography (80% ether−hexane as eluent) to afford the cis-β-diol as a white solid (451 mg, 82%). An analytical sample was recrystallized from EtOAc−hexane: mp 86−88 °C; R_f 0.76 (5:1 ether−hexane); $[\alpha]^{24}_D$ +8.3° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.69 (dd, *J* = 10.8, 1.6 Hz, 1 H), 5.11 (s, 1 H), 4.16 (t, *J* = 3.2 Hz, 1 H), 3.91 (br d, *J* = 10.8 Hz, 1 H), 3.77 (s, 3 H), 3.60−3.80 (m, 2 H), 3.30 (t, *J* = 10.8 Hz, 1 H), 2.25−2.40 (m, 3 H), 1.90 (d, *J* = 1.6 Hz, 3 H), 0.93 (s, 9 H), 0.89 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 173.6, 167.8, 135.6, 134.3, 110.2, 82.5, 69.1, 68.7, 63.7, 52.1, 43.7, 42.2, 35.0, 29.9, 25.8, 23.3, 18.2, 13.2, −5.5; IR ($CHCl_3$) 3560, 3440, 1785, 1710 cm^{-1}; high-resolution mass spectrum, calcd for $C_{24}H_{42}O_8Si$ (M^+), 486.2649; found 486.2647. Anal. Calcd for $C_{24}H_{42}O_8Si$: C, 59.23; H, 8.70. Found: C, 59.41; H, 8.64.

A mixture of methoxymethyl chloride (990 μL, 13.0 mmol), the diol prepared above (418 mg, 0.86 mmol), and *N*,*N*-diisopropylethylamine (2.3 mL, 13.2 mmol) in anhydrous CH_2Cl_2 (5 mL) was stirred for 22 h at 23 °C. The reaction mixture was diluted with Et_2O and poured into brine. The aqueous layer was separated and extracted with Et_2O. The combined ethereal layers were washed with 0.5 N HCl and brine and

dried over Na_2SO_4. Removal of the solvent in vacuo gave an oily residue, which was purified by silica gel chromatography (40% ether−hexane as eluent) to give **47** as a colorless oil (470 mg, 95%): R_f 0.62 (2:1 ether−hexane); $[\alpha]^{22}_D$ +17.8° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 (dd, J = 10.8, 1.6 Hz, 1 H), 5.09 (s, 1 H), 4.74 (s, 2 H), 4.66 (d, J = 7.2 Hz, 1 H), 4.49 (d, J = 7.2 Hz, 1 H), 4.15 (br s, 1 H), 3.92 (dd, J = 11.2, 2.8 Hz, 1 H), 3.78 (t, J = 10.8 Hz, 1 H), 3.74 (s, 3 H), 3.63 (dd, J = 10.8, 6.0 Hz, 1 H), 3.47 (t, J = 11.2 Hz, 1 H), 3.39 (s, 3 H), 3.31 (s, 3 H), 2.3−2.4 (m, 1 H), 2.32 (dd, J = 14.0, 6.4 Hz, 1 H), 1.89 (d, J = 1.6 Hz, 3 H), 1.66 (d, J = 14.0 Hz, 1 H), 0.93 (s, 9 H), 0.89 (s, 9 H), 0.05 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 173.3, 167.9, 137.0, 132.8, 110.3, 96.3, 95.0, 83.2, 73.0, 72.3, 63.3, 55.7, 55.4, 51.9, 42.8, 42.1, 35.0, 30.2, 25.8, 23.4, 18.1, 13.2, −5.5; IR ($CHCl_3$) 3015, 2950, 1785, 1710 cm^{-1}; high-resolution mass spectrum, calcd for $C_{27}H_{47}O_9Si$ ($M^+ - OCH_3$) 543.2989, found 543.2990. Anal. Calcd for $C_{28}H_{50}O_{10}Si$: C, 58.51; H, 8.77. Found: C, 58.69; H, 8.76.

(2′*R*,3*S*,4*S*,5*S*)-Spiro[1-formyl-3-(methoxymethoxy)-4-[2-(methoxycarbonyl)-1(*E*)-propen-1-yl]-1-cyclohexene-[5,5′]-2′-*tert*-butyl-1′,3′-dioxolan-4′-one] (48). $Et_3N{\cdot}HF$ (189 mg, 1.56 mmol) was added to a 23 °C solution of **47** (443 mg, 0.77 mmol) in anhydrous CH_3CN (8 mL). The reaction mixture was heated at 40 °C for 16 h. At this point, the reaction mixture was diluted with EtOAc and poured into brine. The aqueous layer was separated and extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude mixture by silica gel chromatography (80% Et_2O−hexane as eluent) afforded the primary alcohol as a colorless oil (326 mg, 92%): R_f 0.41 (ether); $[\alpha]^{22}_D$ +26.5° (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.67 (dd, J = 10.8, 1.6 Hz, 1 H), 5.10 (s, 1 H), 4.75 (s, 2 H), 4.70 (d, J = 7.0 Hz, 1 H), 4.49 (d, J = 7.0 Hz, 1 H), 4.13 (t, J = 2.7 Hz, 1 H), 3.97 (dd, J = 10.8, 2.7 Hz, 1 H), 3.75 (s, 3 H), 3.60−3.80 (m, 2 H), 3.47 (t, J = 10.8 Hz, 1 H), 3.40 (s, 3 H), 3.31 (s, 3 H), 2.30−2.40 (m, 3 H), 1.89 (d, J = 1.6 Hz, 3 H), 0.93 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 173.1, 167.9, 136.8, 132.9, 110.2, 96.4, 95.0, 83.0, 73.2, 72.7, 63.2, 55.7, 55.5, 51.9, 42.6, 41.8, 34.9, 30.3, 23.3, 13.1; IR ($CHCl_3$) 3420, 2950, 1785, 1710, 1345, 1280, 1100, 1050, 920 cm^{-1}; high-resolution mass spectrum, calcd for $C_{21}H_{33}O_9$ ($M^+ - OCH_3$) 429.2124, found 429.2134. Anal. Calcd for $C_{22}H_{36}O_{10}$: C, 57.38; H, 7.88 Found: C, 57.03; H, 7.54.

A solution of the above primary alcohol (306 mg, 0.66 mmol) in anhydrous CH_2Cl_2 (4 mL) was added to a −78 °C solution of oxalyl chloride (83 μL, 0.95 mmol) and DMSO (130 μL, 1.83 mmol) in anhydrous CH_2Cl_2 (6 mL). The reaction mixture was stirred for 30 min at −78 °C; then DBU (670 μL, 4.48 mmol) was added, and the mixture was allowed to warm to 23 °C. The reaction mixture was stirred for 30 min and then was diluted with Et_2O and poured into brine. The aqueous layer was separated and extracted with Et_2O. The combined ethereal layers were washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. Purification of the crude product by silica gel chromatography (40% ether−hexane as eluent) afforded enal **48** as a white solid (224 mg, 85%). An analytical sample was recrystallized from EtOAc−hexane: mp 137−139 °C; R_f 0.61 (5:1 ether−hexane); $[\alpha]^{22}_D$ +93.5° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.55 (s, 1 H), 6.83 (br s, 1 H), 6.71 (dd, J = 10.8, 1.6 Hz, 1 H), 5.22 (s, 1 H), 4.76 (d, J = 7.0 Hz, 1 H), 4.66 (br d, J = 7.0 Hz, 1 H), 4.61 (dd, J = 10.8, 2.8 Hz, 1 H), 3.78 (s, 3 H), 3.37 (s, 3 H), 3.16 (t, J = 10.8 Hz, 1 H), 2.77 (dt, J = 18.4, 2.8 Hz, 1 H), 2.62 (d, J = 18.4 Hz, 1 H), 1.89 (d, J = 1.6 Hz, 3 H), 0.92 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 192.2, 172.2, 167.6, 146.9, 137.1, 135.1, 134.4, 110.9, 96.3, 81.4, 74.3, 55.8, 52.1, 45.6, 35.0, 31.4, 23.2, 13.2; IR ($CHCl_3$) 2980, 1790, 1715, 1685, 1245, 1135, 1035 cm^{-1}; high-resolution mass spectrum, calcd for $C_{20}H_{28}O_8$ (M^+) 396.1784, found 396.1805. Anal. Calcd for $C_{20}H_{28}O_8$: C, 60.59; H, 7.12. Found: C, 60.32; H, 7.13.

The stereostructure of **48** was unambiguously verified by X-ray analysis.[62]

(2′*R*,3*S*,4*S*,5*S*)-Spiro[1-(dimethoxymethyl)-3-(methoxymethoxy)-4-[2-methyl-3-[[2-(trimethylsilyl)ethoxy]methoxy]-1(*E*)-propen-1-yl]-1-cyclohexene-[5,5′]-2′-*tert*-butyl-1′,3′-dioxolan-4′-one (49). A mixture of enal **48** (201 mg, 0.51 mmol) and pyridinium *p*-toluenesulfonate (10 mg, 0.04 mmol) in anhydrous MeOH (3 mL) was stirred for 3 h at 23 °C. The reaction mixture was diluted with Et_2O and washed with saturated aqueous $NaHCO_3$ and brine; the combined extracts were dried over Na_2SO_4. Removal of the solvent in vacuo afforded a solid residue, which was purified by silica gel chromatography (30% Et_2O−hexane as eluent) to give the corresponding dimethyl acetal as a white solid (207 mg, 92%). An analytical sample was recrystallized from EtOAc−hexane: mp 120−122 °C; R_f 0.67 (5:1 ether−hexane); $[\alpha]^{20}_D$ +61.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.72 (dd, J = 10.8, 1.6 Hz, 1 H), 6.00 (br s, 1 H), 5.21 (s, 1 H), 4.71 (d, J = 7.3 Hz, 1 H), 4.61 (s, 1 H), 4.58 (d, J = 7.3 Hz, 1 H), 4.43 (br d, J = 10.8 Hz, 1 H), 3.76 (s, 3 H), 3.31 (s, 6 H), 3.30 (s, 3 H), 3.11 (t, J = 10.8 Hz, 1 H), 2.66 (dt, J = 18.0, 2.8 Hz, 1 H), 2.32 (d, J = 18.0 Hz, 1 H), 1.89 (d, J = 1.6 Hz, 3 H), 0.92 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 172.7, 167.7, 136.4, 133.7, 132.4, 125.9, 110.6, 103.7, 95.6, 82.2, 74.2, 55.5, 53.2, 52.7, 51.9, 45.7, 35.0, 33.1, 23.3, 13.2; IR ($CHCl_3$) 2960, 2930, 1790 cm^{-1}; high-resolution mass spectrum, calcd for $C_{22}H_{34}O_9$ (M^+) 442.2203, found 442.2158. Anal. Calcd for $C_{22}H_{34}O_9$: C, 59.71; H, 7.74. Found: C, 59.83; H, 7.48.

A 1.0 M solution of L-Selectride in THF (1.0 mL, 1.0 mmol) was added dropwise to a −20 °C solution of the above acetal (203 mg, 0.46 mmol) in anhydrous THF (4.6 mL). After being stirred for 4 h at −20 °C, the reaction mixture was diluted with Et_2O and poured into brine. The aqueous layer was separated and extracted with Et_2O. The combined ethereal layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude mixture by silica gel chromatography (80% ether−hexane as eluent) afforded the corresponding primary allylic alcohol as a white solid (164 mg, 86%). An analytical sample was recrystallized from EtOAc−hexane: mp 85−87 °C; R_f 0.29 (5:1 ether−hexane); $[\alpha]^{24}_D$ +82.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98 (br s, 1 H), 5.48 (dd, J = 10.4, 1.6 Hz, 1 H), 5.23 (s, 1 H), 4.71 (d, J = 7.0 Hz, 1 H), 4.63 (d, J = 7.0 Hz, 1 H), 4.60 (s, 1 H), 4.33 (br d, J = 10.4 Hz, 1 H), 4.04 (s, 2 H), 3.35 (s, 3 H), 3.30 (s, 3 H), 3.29 (s, 3 H), 3.03 (t, J = 10.4 Hz, 1 H), 2.64 (dt, J = 18.0, 2.8 Hz, 1 H), 2.29 (d, J = 18.0 Hz, 1 H), 1.67 (d, J = 1.6 Hz, 3 H), 0.92 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 173.4, 142.0, 132.4, 126.6, 119.4, 110.7, 103.8, 95.9, 82.9, 75.0, 67.6, 55.5, 53.3, 52.7, 44.8, 35.0, 33.2, 23.4, 14.5; IR ($CHCl_3$) 3440, 2960, 1785 cm^{-1}; high-resolution mass spectrum, calcd for $C_{21}H_{34}O_8$ (M^+) 414.2254, found 414.2231. Anal. Calcd for $C_{21}H_{34}O_8$: C, 60.85; H, 8.27. Found: C, 60.61; H, 8.28.

A mixture of the allylic alcohol prepared above (157 mg, 0.38 mmol), *N*,*N*-diisopropylethylamine (86 μL, 0.49 mmol), and [2-(trimethylsilyl)ethoxy]methyl chloride (81 μL, 0.46 mmol) in anhydrous CH_2Cl_2 (4 mL) was stirred for 4 h at 23 °C. The reaction mixture was diluted with Et_2O and poured into brine. The aqueous layer was separated and extracted with Et_2O. The combined ethereal layers were washed with brine and dried over Na_2SO_4. Removal of the solvent in vacuo gave an oily residue, which was purified by silica gel chromatography (30% ether−hexane as eluent) to give SEM ether **49** as a colorless oil (197 mg, 95%): R_f 0.67 (2:1 ether−hexane); $[\alpha]^{23}_D$ +48.1° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.97 (br s, 1 H), 5.46 (dd, J = 10.2, 1.2 Hz, 1 H), 5.22 (s, 1 H), 4.70 (d, J = 7.0 Hz, 1 H), 4.62 (s, 2 H), 4.61 (d, J = 7.0 Hz, 1 H), 4.33 (br d, J = 10.2 Hz, 1 H), 3.96 (s, 2 H), 3.61 (t, J = 8.4 Hz, 2 H), 3.59 (t, J = 8.6 Hz, 1 H), 3.34 (s, 3 H), 3.30 (s, 3 H), 3.28 (s, 3 H), 3.02 (t, J = 10.2 Hz, 1 H), 2.64 (dt, J = 18.0, 2.8 Hz, 1 H), 2.27 (d, J = 18.0 Hz, 1 H), 1.67 (d, J = 1.2 Hz, 3 H), 0.93 (t, J = 8.3 Hz, 2 H), 0.91 (s, 9 H), 0.01 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 173.5, 139.0, 132.3, 126.5, 122.2, 110.6, 103.8, 95.9, 93.3, 82.9, 74.7, 71.9, 65.1, 55.5, 53.3, 52.7, 44.9, 35.0, 33.2, 23.4, 18.1, 14.8, −1.4; IR ($CHCl_3$) 2950, 1785 cm^{-1}; high-resolution mass spectrum, calcd for $C_{27}H_{48}O_9Si$ (M^+) 544.3068, found 544.3052. Anal. Calcd for $C_{27}H_{48}O_9Si$: C, 59.53; H, 8.88. Found: C, 59.39; H, 8.57.

Enantiomeric Purity Determination. A 1.0 M solution of DIBAL-H in THF (0.46 mL, 0.46 mmol) was slowly added to a 0 °C solution of **49** (56 mg, 0.10 mmol) in anhydrous CH_2Cl_2 (1 mL). This mixture was allowed to warm to 23 °C and stirred for 1 h. The reaction mixture was diluted with Et_2O and poured into brine. The aqueous layer was separated and extracted with Et_2O. The combined ethereal layers were dried

over Na_2SO_4 and concentrated in vacuo. Purification of the crude mixture by silica gel chromatography (ether as eluent) produced **50** as a colorless oil (43 mg, 90%): R_f 0.33 (ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93 (d, J = 1.6 Hz, 1 H), 5.48 (dd, J = 10.8, 1.6 Hz, 1 H), 4.67 (d, J = 7.0 Hz, 1 H), 4.66 (s, 2 H), 4.61 (d, J = 7.0 Hz, 1 H), 4.57 (s, 1 H), 4.14 (br d, J = 7.0 Hz, 1 H), 4.01 (d, J = 11.6 Hz, 1 H), 3.94 (d, J = 11.6 Hz, 1 H), 3.5−3.7 (m, 4 H), 3.40 (dd, J = 11.2, 6.4 Hz, 1 H), 3.33 (s, 3 H), 3.29 (s, 6 H), 2.72 (dd, J = 10.4, 1.6 Hz, 1 H), 2.65 (s, 1 H), 2.16 (d, J = 18.4 Hz, 1 H), 2.08 (d, J = 18.4 Hz, 1 H), 1.73 (d, J = 1.6 Hz, 3 H), 0.92 (t, J = 10.0 Hz, 2 H), 0.01 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 136.8, 134.6, 125.2, 152.1, 104.7, 96.0, 94.2, 75.6, 74.1, 73.4, 68.5, 65.4, 55.4, 53.4, 53.3, 45.0, 33.4, 18.0, 14.8, −1.5; IR ($CHCl_3$) 3450, 2950 cm^{-1}; high-resolution mass spectrum, calcd for $C_{21}H_{39}O_7Si$ ($M^+ - CH_3O$) 431.2465, found 431.2494.

To a solution of this diol (20 mg, 0.04 mmol) in anhydrous CH_2Cl_2 (0.5 mL) were added either (*S*)-(−)-MTPA-Cl or (*R*)-(+)-MTPA-Cl (13 μL, 0.06 mmol), Et_3N (18 μL, 0.13 mmol), and catalytic DMAP. These reaction mixtures were stirred for 12 h at ambient temperature. The mixtures were diluted with Et_2O, washed with brine, and dried over Na_2SO_4. Concentration of the ethereal layers in vacuo yielded the crude Mosher ester derivatives that were purified by silica gel chromatography (60% ether−hexane as eluent, the diastereomeric MTPA derivatives do not separate) to give (*S*)-(−)-MTPA derivative (28 mg, 95%) and (*R*)-(+)-MTPA derivative (27 mg, 92%), respectively. The purified esters were examined by high-field ^{1}HNMR analysis. The (*S*)-(−)-MTPA derivative **51b** showed characteristic signals at δ 4.28 and 4.35 (d, J = 11.2 Hz, each 1 H, CH_2OMTPA), 4.62 (s, 2 H, CH_3OCH_2O). The (*R*)-(+)-MTPA derivative **51a**, however, showed characteristic signals at δ 4.22 and 4.41 (d, J = 11.2 Hz, each 1 H, CH_2OMTPA), 4.52 and 4.58 (d, J = 7.2 Hz, each 1 H, CH_3OCH_2O). In this way, the enantiomeric purity of **50** was determined to be >97% ee.

(5*S*,6*S*,7*S*)-4-Methoxy-6-[2-methyl-3-[[2-(trimethylsilyl)ethoxy]methoxy]-1(*E*)-propen-1-yl]-7-(methoxymethoxy)-9-(dimethoxymethyl)-1-oxaspiro[4.5]deca-3,8-dien-2-one (5). Anhydrous K_2CO_3 (95 mg, 0.69 mmol) was added to a solution of **49** (188 mg, 0.35 mmol) in anhydrous MeOH (3.5 mL). The mixture was stirred for 20 h at 23 °C and then was diluted with Et_2O and poured into brine. The aqueous layer was separated and extracted with Et_2O. The combined ethereal layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude product by silica gel chromatography (50% ether−hexane as eluent) afforded the corresponding tertiary α-hydroxy methyl ester as a colorless oil (140 mg, 83%): R_f 0.44 (5:1 ether−hexane); $[\alpha]^{24}_D$ +58.3° (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.97 (br s, 1 H), 5.43 (dd, J = 10.4, 1.2 Hz, 1 H), 4.66 (d, J = 6.8 Hz, 1 H), 4.58 (s, 3 H), 4.57 (d, J = 6.8 Hz, 1 H), 4.24 (br d, J = 10.4 Hz, 1 H), 3.91 (s, 2 H), 3.70 (s, 3 H), 3.59 (t, J = 8.4 Hz, 2 H), 3.35 (s, 1 H), 3.31 (s, 6 H), 3.29 (s, 3 H), 2.95 (t, J = 10.4 Hz, 1 H), 2.60 (dt, J = 18.0, 2.8 Hz, 1 H), 2.16 (d, J = 18.0 Hz, 1 H), 1.65 (d, J = 1.2 Hz, 3 H), 0.92 (t, J = 8.4 Hz, 2 H), 0.01 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 175.7, 137.0, 132.5, 126.7, 123.6, 104.8, 96.1, 93.4, 76.8, 74.9, 72.6, 65.0, 55.3, 53.4, 53.3, 52.8, 45.0, 34.6, 18.1, 14.4, −1.5; IR ($CHCl_3$) 3515, 2950, 1730 cm^{-1}; high-resolution mass spectrum, calcd for $C_{23}H_{42}O_9Si$ (M^+) 490.2598, found 490.2588. Anal. Calcd for $C_{23}H_{42}O_9Si$: C, 56.30; H, 8.63. Found: C, 56.06; H, 8.34.

A solution of the above α-hydroxy ester (65 mg, 0.13 mmol), acetic anhydride (75 μL, 0.79 mmol), Et_3N (220 μL, 1.58 mmol), and DMAP (2 mg, 0.02 mmol) in anhydrous CH_2Cl_2 (2 mL) was stirred for 48 h at 23 °C. The reaction mixture was diluted with Et_2O and poured into brine. The aqueous layer was separated and extracted with Et_2O. The combined ethereal extracts were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The crude product was purified by silica gel chromatography (50% ether−hexane as eluent) to give the corresponding acetate as a colorless oil (65 mg, 92%): R_f 0.47 (5:1 ether−hexane); $[\alpha]^{23}_D$ +54.2° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.94 (br s, 1 H), 5.41 (dd, J = 10.4, 1.6 Hz, 1 H), 4.55−4.65 (m, 5 H), 4.19 (br d, J = 7.2 Hz, 1 H), 3.94 (s, 2 H), 3.63 (s, 3 H), 3.61 (t, J = 8.4 Hz, 2 H), 3.34 (s, 3 H), 3.29 (s, 3 H), 3.27 (s, 3 H), 3.03 (dd, J = 10.4, 7.2 Hz, 1 H), 3.00 (dt, J = 18.4, 2.4 Hz, 1 H), 2.85 (d, J = 18.4 Hz, 1 H), 2.03 (s, 3 H), 1.66 (d, J = 1.6 Hz, 3 H), 0.93 (t, J = 8.4 Hz, 2 H), 0.01 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 170.4, 169.7, 136.9, 133.9, 124.2, 123.0, 103.7, 95.7, 93.6, 82.6, 74.2, 72.6, 65.1, 55.5, 53.1, 52.9, 52.2, 45.2, 29.4, 21.2, 18.1, 14.5, −1.5; IR ($CHCl_3$) 2950, 2885, 1750 (sh), 1735 cm^{-1}; high-resolution mass spectrum, calcd for $C_{25}H_{44}O_{10}Si$ (M^+) 532.2704, found 532.2686. Anal. Calcd for $C_{25}H_{44}O_{10}Si$: C, 56.37; H, 8.33. Found: C, 56.07; H, 8.03.

A 1.0 M solution of lithium hexamethyldisilazide (220 μL, 0.22 mmol) was slowly added to a −78 °C solution of the α-acetoxy methyl ester (51 mg, 0.096 mmol) in a mixture of HMPA (350 μL, 2.01 mmol) and anhydrous THF (1 mL). This reaction mixture was stirred for 30 min at −78 °C and then allowed to warm to 23 °C over a 1 h period. The mixture was stirred for 15 min at 23 °C and then was treated with $(MeO)_2SO_4$ (23 μL, 0.24 mmol). This mixture was stirred for 2 h before being diluted with Et_2O and poured into brine. The aqueous layer was separated and extracted with Et_2O. The combined ethereal layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude material by silica gel chromatography (80% ether−hexane as eluent) produced **5** as a white solid (42 mg, 85%). An analytical sample was recrystallized from EtOAc-hexane: mp 65−66 °C; R_f 0.36 (5:1 ether−hexane); $[\alpha]^{23}_D$ +134.3° (*c* 2.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98 (br s, 1 H), 5.22 (dd, J = 10.0, 1.2 Hz, 1 H), 4.98 (1 H, s), 4.66 (d, J = 7.0 Hz, 1 H), 4.57 (s, 3 H), 4.56 (d, J = 7.0 Hz, 1 H), 4.31 (br d, J = 10.0 Hz, 1 H), 3.90 (d, J = 12.4 Hz, 1 H), 3.86 (d, J = 12.4 Hz, 1 H), 3.78 (s, 3 H), 3.57 (t, J = 8.4 Hz, 2 H), 3.30 (s, 6 H), 3.28 (s, 3 H), 2.92 (t, J = 10.0 Hz, 1 H), 2.64 (dt, J = 18.0, 2.8 Hz, 1 H), 2.10 (d, J = 18.0 Hz, 1 H), 1.64 (d, J = 1.2 Hz, 3 H), 0.91 (t, J = 8.4 Hz, 2 H), 0.01 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 183.2, 171.6, 137.8, 132.1, 126.9, 121.7, 104.4, 96.2, 93.6, 88.9, 85.6, 75.0, 72.5, 65.1, 59.2, 55.4, 53.4, 53.3, 42.8, 32.5, 18.0, 14.4, −1.5; IR ($CHCl_3$) 2950, 1745, 1635 cm^{-1}; high-resolution mass spectrum, calcd for $C_{25}H_{42}O_9Si$ (M^+) 514.2598, found 514.2601. Anal. Calcd for $C_{25}H_{42}O_9Si$: C, 58.34; H, 8.23. Found: C, 58.57; H, 8.44.

The spectroscopic properties of spirotetronate **5** were identical with those of an authentic sample ($[\alpha]^{23}_D$ +99.0° (*c* 3.02, $CHCl_3$)) kindly provided by Professor Yoshii.[11]

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Supporting Information Available: ^{1}H NMR spectra of **4**−**6** (synthetic and authentic), **10**, **17**, **19**, **20**, **21**, **26**, **30**, **31**, **32**, **34**, **36**, **39**, and **37** (19 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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