Acid-Mediated Conversion of Methylene-Interrupted Bisepoxides to Tetrahydrofurans: A Biomimetic Transformation

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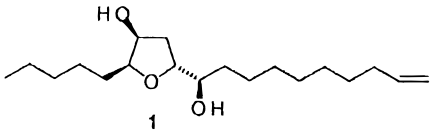
The acid-mediated transformation of syn and anti methylene interrupted cis,cis and cis,trans bisepoxides to tetrahydrofurans is high yielding, and demonstrates both regioselectivity and stereoselectivity. Trans,trans methylene interrupted bisepoxides do not yield tetrahydrofurans under the same conditions.

Substituted tetrahydrofurans feature in many biologically potent natural products, such as the polyether antibiotics and annonaceous acetogenins. The latter is an emerging class of bioactive natural products which exhibit a host of promising biological properties including antitumor, antimalarial, antimicrobial, immunosuppressant, antifeedant, and pesticidal activity.[1] To fully exploit the opportunities offered by these compounds requires access to synthetic methodology capable of targeting chiral substituted tetrahydrofurans.[2] While early efforts in this direction focused on the purely synthetic option, more recent contributions have emphasized the value of biomimic solutions. The polyepoxide cyclization cascade, for example, has been recognized as an efficient biomimetic route to complex chiral tetrahydrofuranyl systems.[3] Although ethylene-interrupted bisepoxides have been acknowledged as biosynthetic and biomimetic precursors to tetrahydrofurans, the potential of methylene-interrupted bisepoxides has received less attention.



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Our interest in this field came about during investigations into the chemistry of the southern Australian marine brown alga *Notheia anomala*, which yielded an array of novel epoxylipids,[4−7] exemplified by the dihydroxytetrahydrofuran **1** and accompanying methylene-interrupted bisepoxides, trisepoxides and tetraepoxides. In this regard a natural methylene-interrupted bisepoxide cometabolite appeared to be a potential biosynthetic precursor to the tetrahydrofuran **1** and related metabolites—proceeding via a somewhat truncated version of the polyepoxide cyclization cascade mentioned above. Our attempts to unravel the relative stereochemistry of these epoxylipids led to a detailed study of the biomimetic transformation of methylene-interrupted bisepoxides into tetrahydrofurans. The prospects that this methodology might return an efficient route to a large array of synthetic tetrahydrofuran analogues was especially attractive, given the discovery that epoxylipids from *Notheia anomala* exhibited potent in vitro anthelmintic activity.[8] This report details the results of our investigations into the acid-mediated transformation of methylene-interrupted bisepoxides into tetrahydrofurans, culminating in a mechanistic model that satisfies the observed regiochemical and stereochemical outcomes.

Results and Discussion

Syn and Anti Methylene Interrupted Cis,Cis Bisepoxides. The model system chosen for these studies was prepared as shown in Scheme 1. Commercially available 1-heptyne (**2**) was lithiated with *n*-butyllithium to afford the acetylide which was immediately reacted with solid paraformaldehyde to yield 2-octyn-1-ol (**3**) (94%). Hydrogenation of **3** with Lindlar catalyst returned the allylic alcohol **4** (90%), which was converted to the volatile chloride **5** (75%) via treatment of an intermediate tosylate with LiCl. The methylene-interrupted C_{15} enyne **6** was formed (82%) by coupling **5** with 1 equiv of **2** using conditions similar to those described by Jeffery.[9] Epoxidation of **6** with freshly purified *m*-CPBA provided the propargylic epoxide **7** (88%), which was selectively reduced with Lindlar catalyst to the allylic epoxide **8** (72%). Treatment of **8** with *m*-CPBA yielded a mixture (1:1.2) of the methylene-interrupted bisepoxides **9** and **10** (82%), which were resolved by normal phase silica HPLC and distinguished by spectroscopic analysis. The ^{1}H NMR multiplicity for 8-H_2 proved diagnostic in distinguishing between the syn **9** (AB: δ 1.73, ddd, 14.4, 5.9, 5.9 Hz and δ 1.81, ddd, 14.4, 6.8, 6.8 Hz) versus anti **10** (A_2: δ 1.73, t, 16.2 Hz) diastereomers. The two diastereomers **9** and **10** were used as model compounds to investigate the acid-

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(1) Rupprecht, J. K.; Hui, Y.-H.; McLaughlin, J. L. *J. Nat. Prod.* **1990**, *53*, 237.
(2) Boivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309.
(3) O'Hagan, D. *Nat. Prod. Rep.* **1989**, *6*, 205.
(4) Warren, R. G.; Wells, R. J.; Blount, J. F. *Aust. J. Chem.* **1980**, *33*, 891.
(5) Barrow, R. A.; Capon, R. J. *Aust. J. Chem.* **1990**, *43*, 895.
(6) Murray, L. M.; Barrow, R. A.; Capon, R. J. *Aust. J. Chem.* **1991**, *44*, 843.
(7) Rochfort, S.; Murray, L. M.; Capon, R. J. *J. Nat. Prod.* **1992**, *55*, 1332.

(8) Some 30+ natural and 80+ synthetic and semisynthetic epoxylipids have been evaluated for in vitro anthelmintic activity. Selected compounds have also been subjected to in vivo screening in both laboratory animal models, as well as commercial and domestic livestock. The SAR analysis of these studies will be published elsewhere.[12]

(9) Jeffery, T. *Tetrahedron Lett.* **1989**, *30*, 2225.

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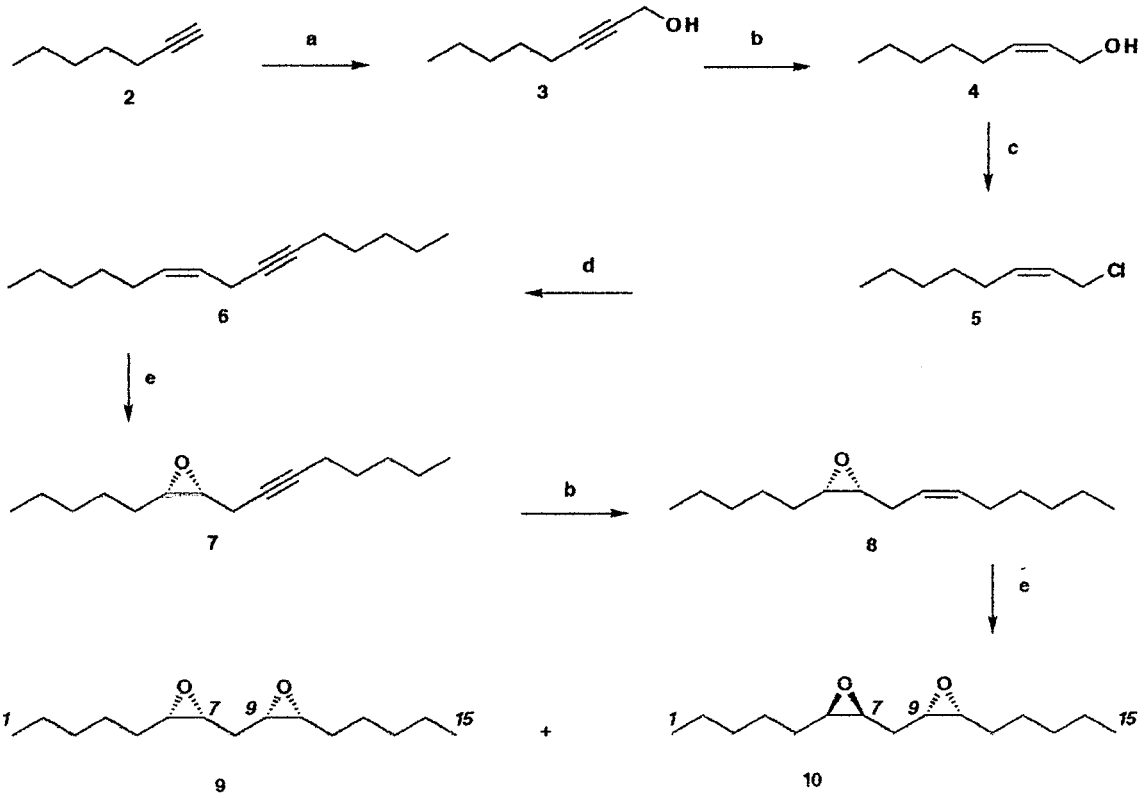
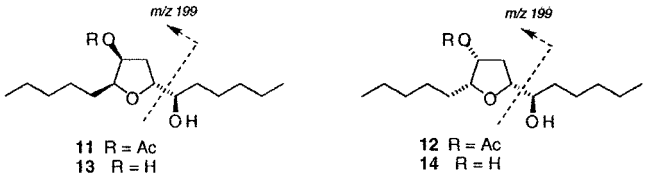
Scheme 1. Synthesis of Cis,Cis Bisepoxide Model Compounds[a]



2 3 4 5 6 7 8 9 10

[a] (a) (i) n-BuLi, Et_2O; (ii) $(CH_2O)_n$, THF; (b) H_2, Lindlar catalyst, EtOH, quinoline (cat.); (c) (i) n-BuLi, Et_2O/HMPA (3:1); (ii) *p*-TsCl; (iii) LiCl; (d) 1-heptyne, K_2CO_3, TBAC, CuI, DMF; (e) *m*-CPBA, CH_2Cl_2. Note: **7**−**10** are racemic.



11 R = Ac
13 R = H

12 R = Ac
14 R = H

Figure 1. Products from the cyclization of syn and anti cis,cis bisepoxides (note: **11**−**14** are racemic).

mediated rearrangement of methylene interrupted cis,cis bisepoxides to dihydroxytetrahydrofurans.

Treatment of the syn isomer **9** at 90 °C overnight (15 h) in glacial AcOH followed by aqueous workup yielded as major and minor products the trans tetrahydrofuran acetate **11** (69%) and the cis tetrahydrofuran acetate **12** (19%) respectively (Figure 1). Identical treatment of the anti isomer **10** yielded as major and minor products the cis tetrahydrofuran acetate **12** (66%) and the trans tetrahydrofuran acetate **11** (22%). Characteristic fragment ions in the EI mass spectra of **11** and **12** (C-9/C-10 cleavage, *m*/*z* 199) confirmed placement of the acetate functionality on the tetrahydrofuran ring. Treatment of the acetates with methanolic ammonium hydroxide returned a quantitative yield of the respective dihydroxytetrahydrofurans **13** and **14**. The relative stereochemistry in **13** was determined by spectroscopic comparison with the natural product **1** which had previously been confirmed by X-ray analysis.[4] The relative stereochemistry for **14** was determined by NOE measurements and consideration of the proposed mechanistic pathway (Figure 2), which accounts for both major and minor cyclization products. In this mechanistic proposal the initial nucleophilic attack is biased in favor of endo (75−80%) versus exo (20−25%) epoxy carbons (endo and exo terminology is used to differentiate between C-7/C-9 and C-6/C-10 epoxy carbons, respectively). While the intermediate derived from endo attack undergoes cyclization to yield tetrahydrofurans directly, that derived from exo attack undergoes intramolecular transesterification of the acetate moiety to the adjacent alcohol followed by cyclization. The result of this latter process is that exo nucleophilic attack on the syn cis,cis bisepoxide **9** leads to the same product as that derived from endo attack on the anti cis,cis bisepoxide **10** while exo nucleophilic attack on the anti cis,cis -bisepoxide **10** leads to the same product as that derived from endo attack on the syn cis,cis bisepoxide **9**.

Syn and Anti Methylene-Interrupted Cis,Trans Bisepoxides. The model system chosen for these studies was prepared as shown in Scheme 2. The propargylic alcohol **3** prepared as described above was reduced with lithium aluminum hydride to the trans allylic alcohol **15** (85%) and sequentially transformed as per the methodology described in Scheme 2 to **16** (76%), **17** (79%), **18** (86%), **19** (88%), and finally to a mixture (1:1.3) of **20** and **21** (81%). The syn and anti diastereomeric cis,trans bisepoxides **20** and **21** were resolved by normal phase silica HPLC and distinguished by spectroscopic analysis. As with **9** and **10**, the ^1H NMR multiplicity for 8-H_2 proved diagnostic in distinguishing between the syn **20** (AB: δ 1.70, ddd, 14.5, 6.8, 5.1 Hz and δ 1.77, ddd, 14.5, 7.3, 4.6 Hz) versus anti **21** (A_2: δ 1.82, bt, 5.1 Hz) diastereomers.

Treatment of the syn isomer **20** at 100 °C overnight (24 h) in glacial AcOH followed by aqueous workup yielded as major and minor products the trans tetrahydrofuran acetate **22** (70%) and the cis tetrahydrofuran

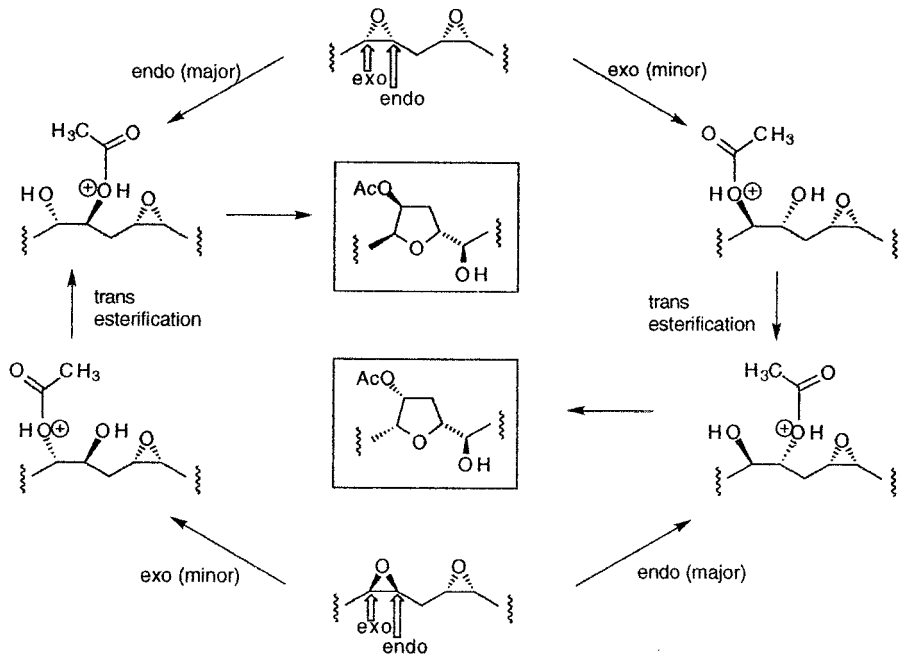
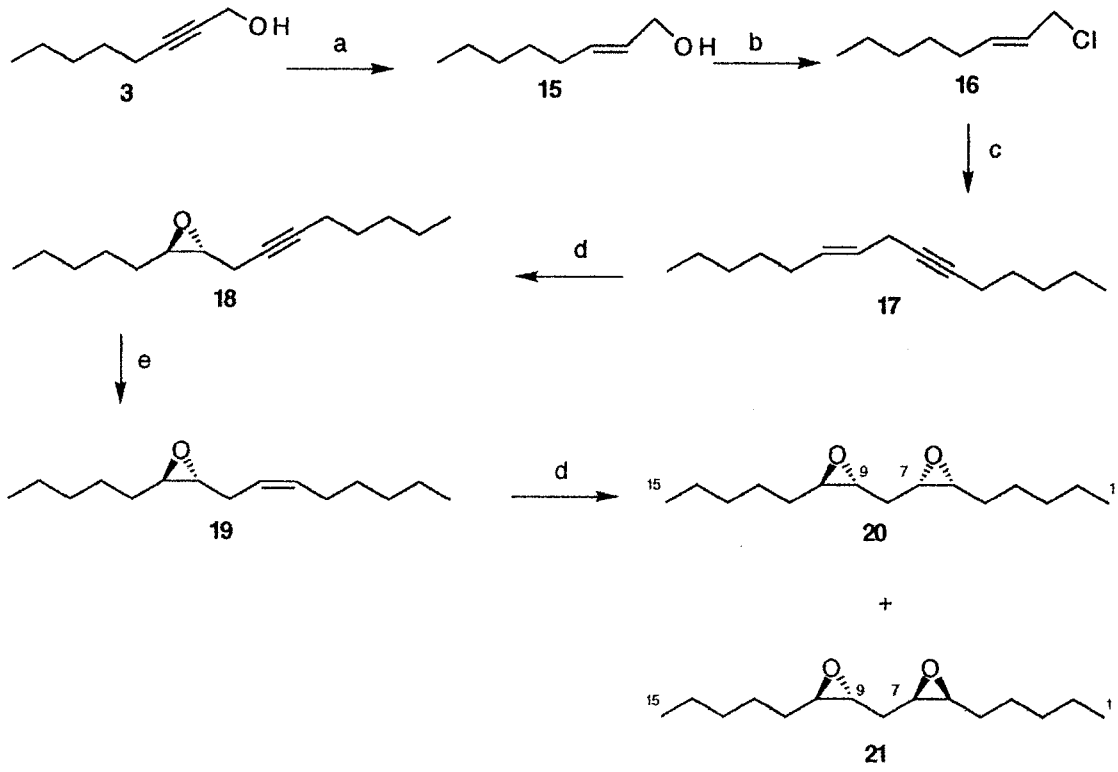


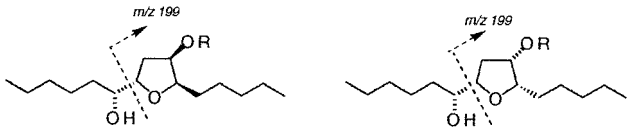
Figure 2. Proposed mechanism for cyclization of syn and anti cis,cis bisepoxides.

Scheme 2. Synthesis of Cis,Trans Bisepoxide Model Compounds[a]



[a] (a) $LiAlH_4$, THF; (b) (i) n-BuLi, Et_2O/HMPA (3:1); (ii) *p*-TsCl; (iii) LiCl; (c) 1-heptyne, K_2CO_3, TBAC, CuI, DMF; (d) *m*-CPBA, CH_2Cl_2; (e) H_2, Lindlar catalyst, EtOH, quinoline (cat.). Note: **18**−**21** are racemic.

acetate **23** (20%) respectively (Figure 3). Identical treatment of the anti isomer **21** yielded as major and minor products the cis tetrahydrofuran acetate **23** (68%) and the trans tetrahydrofuran acetate **22** (19%). Characteristic fragment ions in the EI mass spectra of both **22** and **23** (C-9/C-10 cleavage, *m*/*z* 199) confirmed placement of the acetate functionality on the tetrahydrofuran ring. Not withstanding the potential for intramolecular transesterification to influence the product distribution, nucleophilic attack at either endo or exo carbons of both cis and trans epoxides can generate four isomeric tetrahydrofuran products. The observation of only two products in each reaction suggests that nucleophilic attack on **20** and **21** was more regioselective than that observed for **9** and **10**. Treatment of the acetates **22** and **23** with methanolic ammonium hydroxide returned a quantitative yield of the respective dihydroxytetrahydrofurans **24** and **25**. The relative stereochemistry for **24** was indicated by NOE



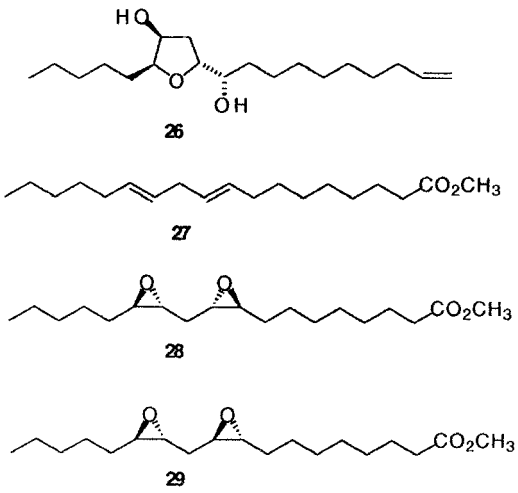
22 R = Ac
24 R = H

23 R = Ac
25 R = H

Figure 3. Products from the cyclization of syn and anti cis,trans bisepoxides (note: **22**−**25** are racemic).

difference experiments and spectroscopic comparison to **26**, prepared by selective epimerisation of the natural product **1**[4] (oxidation to the 10-oxo analogue followed by reduction to yield C-10 epimers separable by HPLC). The relative stereochemistry for **25** was apparent from NOE measurements that confirmed 6-H, 7-H, and 9-H as residing on the same face of the tetrahydrofuran ring, and through consideration of the proposed mechanism (Figure 4), which accounts for both major and minor cyclization products. In this mechanistic proposal the initial nucleophilic attack is totally selective for the cis rather than trans epoxide. Furthermore, as detailed above for cis,cis bisepoxides, initial nucleophilic attack is biased in favor of endo (C-7) (78−79%) versus exo (C-6) (21−22%) epoxy carbons, with the intermediate derived from endo attack undergoing cyclization to yield tetrahydrofurans directly, and that from exo attack proceeding via intramolecular transesterification to tetrahydrofurans.

Syn and Anti Methylene-Interrupted Trans,Trans Bisepoxides. The transformation described above was successfully extended to the syn and anti bisepoxides derived from cis,cis-linoleic acid in a biomimetic synthesis of *N. anomala* metabolites and subsequent SAR investigations.[8] Consequently the model system selected to study the reaction of syn and anti trans,trans bisepoxides was that derived from the commercially available trans,trans-methyl linoleate (**27**). Epoxidation of **27** with *m*-CPBA yielded a mixture of two trans,trans bisepoxides **28** and **29** (100%). Although inseparable by HPLC, spectroscopic data was consistent with the formation of



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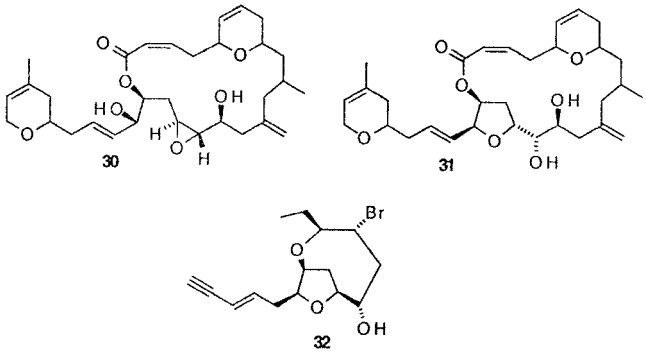
(Note : **28-29** are racemic)

bisepoxides, and discrete ^{1}H NMR resonances for 8-H_2 could be observed consistent with a 1:1 mixture of both syn and anti isomers. This product distribution was confirmed by GC analysis. Treatment of this mixture under the acid conditions described above resulted in consumption of starting material to yield a complex mixture of "acetates" for which spectroscopic analysis failed to reveal any evidence of tetrahydrofurans.

Although literature precedent suggests that acid treatment of methylene interrupted bisepoxides lacks specificity and leads to a complex array of products,[10] the current study reveals this not to be the case. Acid treatment (glacial AcOH, 15 h, 90 °C) of both syn and anti methylene interrupted cis,cis and cis,trans bisepoxides results in high yields of tetrahydrofurans (isolable >85%) with no trace of nontetrahydrofuran byproducts. This acid-mediated transformation displays both regioselectivity and stereoselectivity. In all cases initial nucleophilic attack takes place predominantly (75−80%) at the endo carbon of a cis epoxide, with a minor product (20−25%) arising from attack at the exo carbon. While endo attack intermediates proceed directly to tetrahydrofurans, the intermediates derived from exo attack undergo intramolecular transesterification prior to cyclization to tetrahydrofurans. Trans,trans methylene interrupted bisepoxides do not undergo acid-mediated conversion to tetrahydrofurans under these conditions. The reaction pathway from bisepoxides to tetrahydrofurans as described in this report has potential application in the synthesis of key functional units in important bioactive molecules. To illustrate this potential, we have successfully applied this methodology to the biomimetic synthesis of novel epoxylipids from the southern Australian marine brown alga *Notheia anomala*,[11] and to the preparation of a large number of synthetic analogues for SAR studies.[12] Further to the marine theme, this process is also descriptive of the possible intramolecular transformation between the sponges metabolites fijianolide A (**30**) and B (**31**)[13] (a stepwise intramolecular nucleophilic addition to the cis epoxide of a methylene interrupted cis,trans bisepoxide precursor), and of the possible biosynthetic origins of the red algal oxylipid (**32**)[14] (intramolecular nucleophilic addition to a methylene interrupted cis,cis bisepoxide precursor). This investigation clearly demonstrates the potential of methylene interrupted bisepoxides as biosynthetic and biomimetic precursors to chiral substituted tetrahydrofurans.



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(10) Kuranova, I. L.; Gordienko, S. L.; Korskaya, G. N.; Filonova, E. B. *Zh. Org. Khim.* **1976**, *12*, 1699.
(11) Capon, R. J.; Barrow, R. A.; Skene, C.; Rochfort, S. *Tetrahedron Lett.* **1997**, *37*, in press.
(12) Capon, R. J.; Barrow, R. A.; Rochfort, S.; Jobling, M. F.; Skene, C.; Lacey, E.; Friedel, T.; Wadsworth, D. *Tetrahedron* **1997**, submitted.
(13) Quinoa, E.; Kakou, Y.; Crews, P. *J. Org. Chem.* **1988**, *53*, 3642.
(14) Furusaki, A.; Kurosawa, E.; Fukusawa, A.; Irie, T. *Tetrahedron Lett.* **1973**, *14*, 4579.

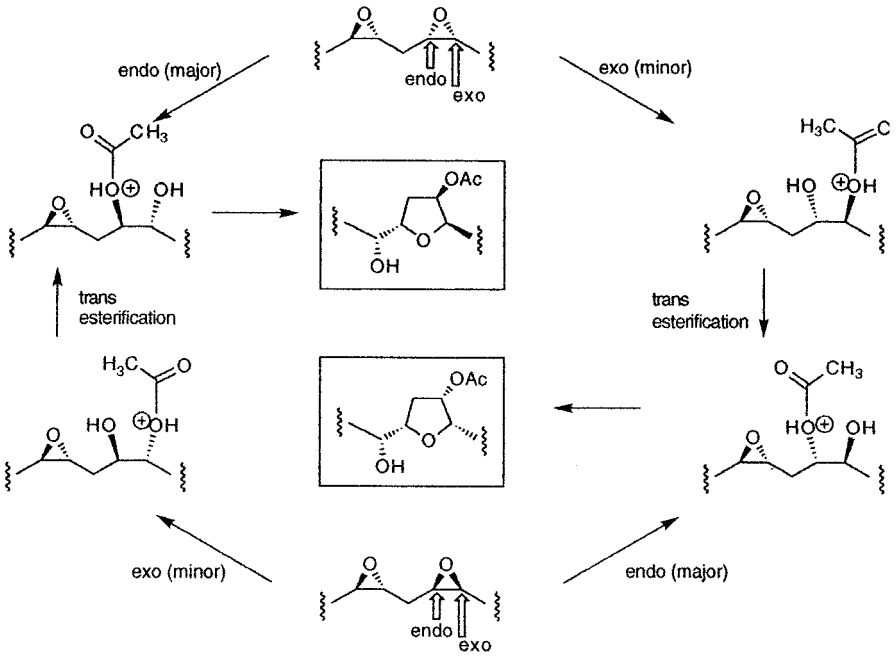

Figure 4. Proposed mechanism for cyclization of syn and anti cis,trans bisepoxides to tetrahydrofurans.

Experimental Section

General Methods. See ref 15. **2-Octyn-1-ol (3).** 1-Heptyne **(2)** (13.8 mL, 0.1 mol) was added slowly to a stirred solution of Et_2O (80 mL) and *n*-BuLi (45 mL as a 2.34 M solution in hexanes, 0.1 mol) under anhydrous conditions at −10 °C. To the resultant acetylide was added a suspension of paraformaldehyde (3.6 g, excess) in THF (100 mL), and the gelantinous mixture allowed to stir at ∼0 °C for 45 min after which time it was heated to reflux for a further 90 min. The reaction mixture was then cooled to room temperature, poured into ice/water (300 mL), and extracted with Et_2O (2 × 150 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, and the solvent was removed in vacuo to give a yellow oil which was distilled to yield **3** as a colorless mobile oil (12.3 g, 94%): bp 75−76 °C/12 mmHg; IR (film) ν_{max} 3330, 2285 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.1 Hz, 8-H_3), 1.25−1.40 (bm, 6-H_2 and 7-H_2), 1.49 (tt, J = 7.1, 7.1 Hz, 5-H_2), 1.86 (bs, OH), 2.19 (tt, J = 7.1, 2.4 Hz, 4-H_2), 4.23 (dt, J = 6.8, 2.4 Hz, 1-H_2); ^{13}C NMR (100 MHz, $CDCl_3$) 13.8 (C-8), 18.6 (C-4), 22.1 (C-7), 28.2 (C-5), 30.9 (C-6), 51.1 (C-1), 78.2 (C-2), 86.3 (C-3) ppm; EIMS (70 eV, *m*/*z*, %) 111 ($M^+ - CH_3$), 97 (14), 95 (100), 83 (52), 71 (15), 69 (33), 57 (17), 55 (71), 43 (24); CIMS (isobutane, 20 eV, *m*/*z*, %) 127 (M + H, 2), 109 (100), 95 (18); HRMS found 111.0810 ($C_8H_{14}O$ ($M^+ - CH_3$) requires 111.0809).

(*Z*)-2-Octen-1-ol (4). A solution of **3** (2.4 g, 0.02 mol) in a pleated flask with EtOH (30 mL), quinoline (0.25 mL), and Lindlar's catalyst (400 mg, 17% w/w) was stirred vigorously under an atmosphere of H_2. After consumption of 1 mol equiv of H_2 the mixture was filtered through a plug of silica to remove the catalyst and purified by MPLC (silica, 10% EtOAc/hexane) to yield **4** (2.2 g, 90%) as a colorless mobile oil: IR (film) ν_{max} 3384, 1598 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.0 Hz, 8-H_3), 1.3−1.45 (bm, 5, 6, 7-H_2), 1.65 (bs, OH), 2.05 (dt, J = 7.3, 6.4 Hz, 4-H_2), 4.18 (bd, J = 6.1 Hz, 1-H_2), 5.54 (dt, J = 11.0, 7.3 Hz, 3-H), 5.59 (dt, J = 11.0, 6.1 Hz, 2-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0 (C-8), 22.4 (C-7), 27.3, 29.2 (C-5, C-6), 31.3 (C-4), 58.4 (C-1), 128.3 (C-2), 132.9 (C-3) ppm.

(*Z*)-1-Chloro-2-octene (5). To a stirred solution of **4** (530 mg, 4.1 mmol) in Et_2O/HMPA (3:1, 40 mL) under a nitrogen atmosphere at 0 °C was added *n*-BuLi (1.75 mL as a 2.4 M solution in hexane, 4.1 mmol). The initially colorless solution developed a clear red color which dissipated upon addition of *p*-toluenesulfonyl chloride (790 mg, 4.1 mmol) to return a clear pale yellow solution. LiCl (800 mg, excess) was added and the reaction mixture allowed to stir for a further 40 h after which time it was diluted with Et_2O (50 mL) and washed with dilute aqueous HCl (50 mL, 1 M) followed by H_2O (3 × 50 mL) and the organic layer dried over anhydrous $MgSO_4$ and concentrated in vacuo to yield starting material **4** (238 mg, 45%) and **5** (250 mg, 75%*) as a mobile, volatile, colorless oil: (* yield based on reaction proceeding to 55% completion.): ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 7.1 Hz, 8-H_3), 1.2−1.4 (bm, 6, 7-H_2), 1.39 (tt, J = 7.1, 7.1 Hz, 5-H_2), 2.11 (dt, J = 6.8, 7.1 Hz, 4-H_2), 4.10 (d, J = 6.8 Hz, 1-H_2), 5.63 (m, 2-H and 3-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0 (C-8), 22.5 (C-7), 27.0 (C-4), 29.0 (C-5), 31.4 (C-6), 39.5 (C-1), 125.0 (C-2), 135.6 (C-3) ppm; EIMS (70 eV, *m*/*z*, %) 148 (M^+, ^{37}Cl, 4), 146 (M^+, ^{35}Cl, 12), 113 (4), 111 (11), 97 (16), 95 (13), 81 (31), 71 (26), 70 (56), 69 (56), 68 (30), 67 (34), 56 (58), 55 (50), 54 (100).

(*Z*)-6-Pentadecen-9-yne (6). To stirred solution of freshly distilled DMF (2 mL) at room temperature under an atmosphere of N_2 were added in order 1-heptyne **(2)** (123 μL, 0.94 mmol), K_2CO_3 (160 mg, 1.16 mmol), tetrabutylammonium chloride (TBAC) (30 mg, 0.11 mmol), and CuI (8 mg, 0.04 mmol). The resulting mixture was stirred for 10 min and then treated with **5** (120 mg, 0.82 mmol) as a solution in DMF (0.5 mL) after which it was warmed to 40 °C and allowed to stir for a further 48 h. After this time the reaction mixture was cooled to room temperature and diluted with Et_2O (50 mL) and the organic layer washed with H_2O (2 × 50 mL), dilute aqueous HCl (50 mL, 1 M), brine (50 mL), and finally H_2O (50 mL). The ethereal extract was dried over anhydrous $MgSO_4$ and concentrated in vacuo to return a pale yellow oil that was purified by elution through a silica Sep-pak using hexane as the eluent to yield **6** (138 mg, 82%) as a colorless mobile oil: IR (film) ν_{max} 1640 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 and 0.89 (2t, J = 6.8 Hz, 1 and 15-H_3), 1.25−1.55 (bm, 2, 3, 4, 12, 13, 14-H_2), 2.03 (dt, J = 7.6, 6.6 Hz, 5-H_2), 2.14 (tt. J = 7.1, 2.4 Hz, 11-H_2), 2.90 (dt, J = 5.1, 2.4 Hz, 8-H_2), 5.42 (m, 6 and 7-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0, 14.1 (C-1 and C-15), 17.1 (C-8), 18.8 (C-11), 22.2, 22.5 (C-2 and C-14), 27.1 (C-5), 28.7, 29.1 (C-4 and C-12), 31.1, 31.5 (C-3 and C-13), 78.4 (C-9), 80.1 (C-10), 125.0 (C-7), 131.4 (C-6) ppm; EIMS (70 eV, *m*/*z*, %) 206 (M^+, 2), 191 (1), 177 (4), 163 (5), 149 (19), 135 (16), 121 (25), 110 (30), 109 (9), 107 (38), 95 (31), 93 (92), 79

(15) Murray, L. M.; Lim, T. K.; Currie, G.; Capon, R. J. *Aust. J. Chem.* **1995**, *48*, 1253.

(100), 71 (28), 67 (57), 53 (64), 53 (30); HRMS found 206.2034 ($C_{15}H_{26}$ requires 206.2036).

(6*S,7*R**)-6,7-Epoxypentadec-9-yne (7).** To a stirred solution of **6** (85 mg, 0.41 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added freshly prepared *m*-CPBA (99%, 80 mg, 0.46 mmol). The reaction mixture was allowed to warm to room temperature where it was stirred for 24 h before being diluted with Et_2O (50 mL) and washed with saturated $NaHCO_3$ solution (2 × 40 mL), dilute aqueous KOH (30 mL, 1 M), and finally brine (20 mL). The organic layer was dried over anhydrous $MgSO_4$ and the solvent removed in vacuo to return a mobile yellow oil which was purified by elution through a silica Sep-pak using hexane as the eluant to yield **7** (81 mg, 88%) as a colorless oil: IR (film) ν_{max} 2260 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 and 0.90 (t, J = 7.1 Hz, 1 and 15-H_3), 1.25−1.55 (bm, 2, 3, 4, 5, 12, 13, 14-H_2), 2.15 (tt, J = 7.1, 2.4 Hz, 11-H_2), 2.24 (ddt, J = 16.8, 7.3, 2.4 Hz, 8-H_A), 2.56 (ddt, J = 16.8, 5.4, 2.4 Hz, 8-H_B), 2.95 (ddd, J = 6.1, 5.9, 4.2 Hz, 6-H), 3.11 (ddd, J = 7.3, 5.4, 4.2 Hz, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0 (C-1 and C-15), 18.7 (C-8), 18.8 (C-11), 22.2, 22.6 (C-2 and C-14), 26.1, 27.5, 28.6 (C-4, C-5 and C-12), 31.1, 31.7 (C-3 and C-13), 55.5, 57.1 (C-6 and C-7), 74.8, 82.5 (C-9 and C-10) ppm; EIMS (70 eV, *m*/*z*, %) 222 (M^+, 1), 221 ($M^+ - 1$, 2), 207 (2), 193 (3), 179 (26), 165 (35), 151 (63), 133 (56), 123 (18), 109 (36), 105 (20), 99 (29), 95 (48), 93 (23), 91 (21), 81 (90), 67 (100), 54 (92); HRMS found 221.1905 ($C_{15}H_{25}O$ requires: 221.1904).

(6S*,7R*, 9Z)-6,7-epoxy-9-pentadecene (8): A solution of **7** (80 mg, 0.36 mmol) in EtOH (10 mL) with quinoline (50 μL) and Lindlar's catalyst (20 mg, 25% w/w) was stirred vigorously under an atmosphere of H_2 until uptake ceased (30 min), after which the reaction mixture was diluted with hexane (20 mL), filtered through a pad of silica and concentrated in vacuo to yield **8** (58 mg, 72%) as a colorless mobile oil: IR (film) ν_{max} 1453 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 and 0.90 (2t, J = 7.1 Hz, 1 and 15-H_3), 1.2−1.6 (bm, 2, 3, 4, 5, 12, 13, 14-H_2), 2.04 (dt, J = 7.1, 7.1 Hz, 11-H_2), 2.18 (bddd, J = 15.0, 7.3, 5.9 Hz, 8-H_A), 2.37 (bddd, J = 15.0, 7.3, 5.9 Hz, 8-H_B), 2.93 (bm, 6-H and 7-H), 5.41 (ddt, J = 10.7, 7.3, 1.5 Hz, 9-H), 5.52 (ddt, J = 10.7, 7.3, 1.5 Hz, 10-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.1, 14.1 (C-1 and C-15), 22.6, 22.6 (C-2 and C-14), 26.2, 26.3, 27.4, 27.7, 29.2, 31.5, 31.7 (C-3, C-4, C-5, C-8, C-11, C-12 and C-13), 56.6, 57.2 (C-6 and C-7), 123.8, 132.7 (C-9 and C-10) ppm; EIMS (70 eV, *m*/*z*, %) 224 (M^+, 1), 206 (1), 193 (3), 181 (2), 167 (3), 153 (10), 139 (5), 124 (6), 113 (24), 111 (11), 110 (21), 109 (10), 99 (11), 97 (15), 96 (15), 95 (31), 93 (10), 84 (17), 81 (56), 69 (72), 68 (54), 67 (71), 56 (28), 54 (100); HRMS found 224.2140 ($C_{15}H_{28}O$ requires 224.2141).

Bisepoxides 9 and 10. To a stirred solution of **8** (32 mg, 0.14 mmol) at 0 °C was added *m*-CPBA (99%, 28 mg, 0.016 mmol) and the reaction mixture warmed to room temperature. After 24 h the reaction mixture was diluted with Et_2O (50 mL), washed with saturated $NaHCO_3$ solution (2 × 30 mL), dilute aqueous KOH (15 mL, 2 M), and H_2O (30 mL), and the ethereal layer was dried over anhydrous $MgSO_4$ and concentrated in vacuo to return a crude mixture of the bisepoxides **9** and **10**. Chromatographic purification by HPLC (silica, 5% EtOAc/hexane) yielded the two bisepoxide diastereomers, with the syn diastereomer **9** (13 mg, 38%) eluting first followed by the anti diastereomer **10** (15 mg, 44%): **(6*S**,7*R**,9*S**,10*R**)-6,7:9,10-bis(epoxy)pentadecane (9)**: a colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, J = 7.2 Hz, 1 and 15-H_3), 1.34−1.52 (bm, 2, 3, 4, 12, 13, 14-H_2), 1.55 (m, 5 and 11-H_2), 1.73 (ddd, J = 14.4, 5.9, 5.9 Hz, 8-H_A), 1.81 (ddd, J = 14.4, 6.8, 6.8 Hz, 8-H_B), 2.97 (dt, J = 4.4, 6.0 Hz, 6 and 10-H), 3.08 (ddd, J = 6.8, 5.9, 4.4 Hz, 7 and 9-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0 (C-1 and C-15), 22.6 (C-2 and C-14), 26.2, 27.8 (C-4, C-5, C-11 and C-12), 26.9 (C-8), 31.7 (C-3 and C-13), 54.2 (C-7 and C-9), 56.8 (C-6 and C-10) ppm; EIMS (70 eV, *m*/*z*, %) 199 (2), 194 (11), 187 (20), 131 (33), 127 (5), 117 (30), 113 (12), 91 (54), 83 (49), 69 (70), 54 (100); HRMS found 127.1123 ($C_8H_{15}O$ requires 127.1122), 113.0966 ($C_7H_{13}O$ requires 113.0966). **(6*S**,7R*,9*R**,10*S**)-6,7:9,10-Bis(epoxy)pentadecane (10)**: a waxy solid; mp 41−43 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, J = 7.2 Hz, 1 and 15-H_3), 1.33−1.5 (bm, 2, 3, 4, 12, 13, 14-H_2), 1.52 (m, 5 and 11-H_2), 1.73 (t, J = 6.2 Hz, 8-H_2), 2.98 (dt, J = 4.2, 6.3 Hz, 6 and 10-H), 3.12 (dt, J = 4.2, 6.2 Hz, 7 and 9-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0 (C-1 and C-15), 22.5 (C-2 and C-14), 26.1, 27.9 (C-4, C-5, C-11 and C-12), 27.2 (C-8), 31.7 (C-3 and C-13), 54.4 (C-7 and C-9), 57.0 (C-6 and C-10) ppm; EIMS (70 eV, *m*/*z*, %) 183 (1), 175 (2), 169 (2), 165 (5), 157 (7), 139 (8), 127 (4), 123 (5), 113 (14), 96 (30), 84 (39), 83 (46), 81 (24), 69 (65), 54 (100); HRMS found 127.1123 ($C_8H_{15}O$ requires 127.1122), 113.0966 ($C_7H_{13}O$ requires 113.0966).

Cyclization of (6*S,7*R**,9*S**,10*R**)-6,7:9,10-Bis(epoxy) pentadecane (9).** A sample of the syn bisepoxide **9** (8.0 mg, 0.033 mmol) in glacial acetic acid (3 mL) was stirred at 90 °C for 15 h after which the reaction mixture was diluted with Et_2O (40 mL) and washed with H_2O (3 × 40 mL), saturated $NaHCO_3$ solution (20 mL), and H_2O (40 mL). The organic layer was collected, dried over anhydrous $MgSO_4$, and concentrated in vacuo to return a colorless oil (9.2 mg). Chromatographic purification by HPLC (silica, 40% EtOAc/hexane and then 20% EtOAc/hexane) yielded the trans tetrahydrofuran acetate **11** (6.8 mg, 69%) and cis tetrahydrofuran acetate **12** (1.9 mg, 19%), with the trans isomer being slightly less polar than the cis isomer.

(6*S,7*S**,9*R**,10*R**)-6,9-Epoxypentadecane-7,10-diol 7-acetate (11):** a colorless oil; IR (film) ν_{max} 3468, 1740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 and 0.89 (2t, J = 7.0 Hz, 1 and 15-H_3), 1.3−1.6 (bm, 2, 3, 4, 5, 11, 12, 13, 14-H_2), 1.99 (ddd, J = 13.5, 8.9, 4.5 Hz, 8-H_A), 2.03 (ddd, J = 13.5, 6.9, 1.5 Hz, 8-H_B), 2.25 (bs, OH), 3.39 (m, 10-H), 3.89 (ddd, J = 7.6, 5.9, 3.2 Hz, 6-H), 3.99 (ddd, J = 8.9, 6.9, 6.3 Hz, 9-H), 5.31 (m, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0, 14.1 (C-1 and C-15), 21.0 ($COCH_3$), 22.5, 22.6 (C-2 and C-14), 25.3, 25.9, 29.0, 31.9, 31.9, 33.3 (C-3, C-4, C-5, C-11, C-12 and C-13), 35.6 (C-8), 73.9 (C-10), 75.5 (C-7), 80.4 (C-9), 81.3 (C-6), 170.5 ($COCH_3$) ppm; EIMS (70 eV, *m*/*z*, %) 199 (7), 140 (20), 139 (100), 113 (4), 99 (27), 84 (10).

(6*S,7*S**,9*S**,10*S**)-6,9-Epoxypentadecane-7,10-diol 7-acetate (12):** a colorless oil; IR (film) ν_{max} 3465, 1740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 and 0.89 (2t, J = 6.8 Hz, 1 and 15-H_3), 1.3−1.6 (bm, 2, 3, 4, 5, 11, 12, 13, 14-H_2), 1.74 (ddd, J = 14.4, 6.4, 2.0 Hz, 8-H_A), 2.06 ($COCH_3$), 2.38 (ddd, J = 14.4, 8.3, 6.6 Hz, 8-H_B), 3.47 (ddd, J = 7.9, 6.0, 4.2 Hz, 10-H), 3.73 (ddd, J = 7.8, 5.9, 3.9 Hz, 6-H), 3.76 (ddd, J = 8.3, 6.4, 6.0 Hz, 9-H), 5.22 (ddd, J = 6.6, 3.9, 2.2 Hz, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0, 14.1 (C-1 and C-15), 21.1 ($COCH_3$), 22.5, 22.6 (C-2 and C-14), 25.4, 25.9, 28.7, 31.8, 31.8, 33.6 (C-3, C-4, C-5, C-11, C-12 and C-13), 35.9 (C-8), 73.8 (C-10), 74.7 (C-7), 80.4 (C-9), 81.8 (C-6), 170.6 ($COCH_3$) ppm; EIMS (70 eV, *m*/*z*, %) 199 (5), 140 (18), 139 (100), 113 (6), 99 (40), 95 (10), 84 (10).

Cyclization of (6*S,7*R**,9*R**,10*S**)-6,7:9,10-Bis(epoxy)-pentadecane (10):** A sample of the anti bisepoxide **10** (7.0 mg, 0.029 mmol) in glacial acetic acid (3 mL) was stirred at 90 °C for 15 h after which the reaction mixture was diluted with Et_2O (40 mL) and washed with H_2O (3 × 40 mL), saturated $NaHCO_3$ solution (20 mL), and H_2O (40 mL). The organic layer was collected, dried over anhydrous $MgSO_4$, and concentrated in vacuo to return a colorless oil (7.9 mg). Chromatographic purification by HPLC (silica, 40% EtOAc/hexane and then 20% EtOAc/hexane) yielded the cis tetrahydrofuran acetate **12** (5.7 mg, 66%) and trans tetrahydrofuran acetate **11** (1.9 mg, 22%).

(6*S,7*S**,9*R**,10*R**)-6,9-Epoxypentadecane-7,10-diol (13):** A solution of **11** (4.0 mg, 0.013 mmol) in MeOH (2 mL) and NH_4OH (33% aq solution, 1 mL) was stirred for 5 h at room temperature after which it was concentrated in vacuo to yield the trans tetrahydrofuran **13** (3.4 mg, 100%) as a colorless oil: IR (film) ν_{max} 3413 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 and 0.90 (2t, J = 7.1 Hz, 1 and 15-H_3), 1.3−1.6 (methylene envelope, 2, 3, 4, 5, 11, 12, 13, 14-H_2), 1.87 (ddd, J = 13.4, 9.0, 4.4 Hz, 8-H_A), 2.01 (ddd, J = 13.4, 6.6, 1.0 Hz, 8-H_B), 3.39 (m, 10-H), 3.75 (dt, J = 2.7, 6.8 Hz, 6-H), 4.02 (ddd, J = 9.0, 6.8, 6.6 Hz, 9-H), 4.25 (bdd, J = 4.4, 2.7 Hz, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0, 14.0 (C-1 and C-15), 22.5, 22.6 (C-2 and C-14), 25.3, 26.0, 28.8, 31.9, 32.0, 33.1 (C-3, C-4, C-5, C-11, C-12 and C-13), 37.9 (C-8), 73.5 (C-7), 74.1 (C-10), 80.2 (C-9), 82.4 (C-6) ppm; EIMS (70 eV, *m*/*z*, %) 258 (M^+, 1), 240

(1), 222 (1), 201 (2), 187 (3), 169 (3), 157 (57), 139 (34), 121 (12), 114 (21), 113 (69), 95 (65), 83 (28); HRMS found 258.2183 ($C_{15}H_{30}O_3$ (M^+) requires 258.2195).

(6*S,7*S**,9*S**,10*S**)-6,9-Epoxypentadecane-7,10-diol (14).** A solution of **12** (3.8 mg, 0.013 mmol) in MeOH (2 mL) and NH_4OH (33% aq solution, 1 mL) was stirred for 5 h at room temperature after which it was concentrated in vacuo to yield the cis tetrahydrofuran **14** (3.3 mg, 100%) as a colorless oil: IR (film) ν_{max} 3400 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 and 0.89 (2t, J = 7.2 Hz, 1 and 15-H_3), 1.3−1.6 (methylene envelope, 2, 3, 4, 5, 11, 12, 13, 14-H_2), 1.84 (dd, J = 13.9, 3.6 Hz, 8-H_A), 2.38 (ddd, J = 13.9, 9.9, 5.6 Hz, 8-H_B), 3.48 (ddd, J = 7.8, 5.3, 2.4 Hz, 10-H), 3.62 (dt, J = 2.7, 6.8 Hz, 6-H), 3.96 (ddd, J = 9.9, 3.6, 2.4 Hz, 9-H), 4.04 (dd, J = 5.6, 2.7 Hz, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0 (C-1 and C-15), 22.6 (C-2 and C-14), 25.7, 25.9, 28.8, 31.7, 32.0, 34.4 (C-3, C-4, C-5, C-11, C-12 and C-13), 38.8 (C-8), 71.6 (C-7), 74.0 (C-10), 79.0 (C-9), 84.4 (C-6) ppm; EIMS (70 eV, *m*/*z*, %) 258 (M^+, 1), 240 (1), 201 (2), 187 (4), 169 (3), 157 (84), 139 (28), 121 (20), 114 (221), 113 (69), 99 (100), 95 (47), 83 (43); HRMS found 258.2188 ($C_{15}H_{30}O_3$ (M^+) requires 258.2195).

(*E*)-2-Octen-1-ol (15). The propargylic alcohol **3** (1.4 g, 11 mmol) in THF (5 mL) was added dropwise over 15 min to an anhydrous suspension of lithium aluminum hydride (640 mg, 17 mmol) in THF (20 mL) at 0 °C. The resulting suspension was warmed to 67 °C and stirred for 24 h after which the reaction mixture was cooled to room temperature and excess $LiAlH_4$ destroyed by careful addition of dilute aqueous HCl (2 M)(CAUTION!). The resulting solution was then extracted into Et_2O (100 mL), and the organic phase washed with dilute aqueous HCl (50 mL, 2 M), H_2O (2 × 50 mL), and brine (100 mL) and then dried over anhydrous $MgSO_4$ and concentrated in vacuo to return a yellow oil that was purified by MPLC (silica, 40% EtOAc/hexane) to yield **15** (1.2 g, 85%) as a colorless mobile oil: IR (film) ν_{max} 3385, 1598 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, J = 7.1 Hz, 8-H_3), 1.2−1.4 (bm, J = 5, 6, 7-H_2), 1.78 (bs, OH), 2.03 (dt, J = 7.1, 6.8 Hz, 4-H_2), 4.08 (bd, J = 6.3 Hz, 1-H_2), 5.66 (bm, 2 and 3-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0 (C-8), 22.5 (C-7), 28.8 (C-5), 31.3 (C-6), 32.1 (C-4), 63.7 (C-1), 128.8 (C-2), 133.4 (C-3) ppm; EIMS (70 eV, *m*/*z*, %) 128 (M^+, 2), 110 (9), 97 (4), 83 (4), 57 (8), 56 (100).

(*E*)-1-Chloro-2-octene (16). To a stirred solution of **15** (800 mg, 6.25 mmol) in Et_2O/HMPA (3:1, 20 mL) under a nitrogen atmosphere at 0 °C was added *n*-BuLi (2.6 mL as a 2.4 M solution in hexane, 0.25 mmol). Addition made the initally colorless solution turn a deep orange/red color which dissipated upon addition of *p*-toluenesulfonyl chloride (1.2 g, 6.3 mmol). The reaction mixture was stirred for 15 min and then LiCl (700 mg, 21.3 mmol) added and stirring maintained at room temperature for 10 h after which the reaction mixture was diluted with Et_2O (30 mL), washed with dilute aqueous HCl (30 mL, 2 M) and H_2O (3 × 30 mL), and the organic phase dried over anhydrous $MgSO_4$ and concentrated in vacuo to return a yellow oil that was purified by MPLC (silica, 20% EtOAc/hexane) to yield **16** (690 mg, 76%) as a volatile colorless oil: IR (film) ν_{max} 1666 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, J = 7.0 Hz, 8-H_3), 1.2−1.4 (bm, 5, 6, 7-H_2), 2.05 (dt, J = 6.8, 6.6 Hz, 4-H_2), 4.03 (dd, J = 7.1, 1.0 Hz, 1-H_2), 5.60 (dtt, J = 15.1, 7.1, 1.5 Hz, 2-H), 5.75 (dtt, J = 15.1, 6.6, 1.0 Hz, 3-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0 (C-8), 22.5 (C-7), 28.5 (C-5), 31.3 (C-4), 32.0 (C-6), 45.6 (C-1), 125.8 (C-2), 136.3 (C-3) ppm.

(*E*)-6-Pentadecen-9-yne (17). To a suspension of 1-heptyne (73 mg, 0.76 mmol), K_2CO_3 (145 mg, 1.1 mmol), TBAC (19 mg, 0.07 mmol), and CuI (6.7 mg, 0.035 mmol) in DMF (2 mL) under a nitrogen atmosphere was added **16** (100 mg, 0.7 mmol), and the resulting mixture stirred at 40 °C for 12 h. The reaction was then diluted with Et_2O (80 mL) and washed with H_2O (3 × 50 mL), brine (50 mL), and H_2O (50 mL), before the organic phase was dried over anhydrous $MgSO_4$ and then concentrated in vacuo to return a mobile oil that was purified by HPLC (silica, hexane) to yield **17** (115 mg, 79%) as a colorless mobile oil: IR (film) ν_{max} 2360, 2341, 1639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 and 0.89 (2t, J = 7.1 Hz, 1 and 15-H_3), 1.2−1.4 (bm, 2, 3, 4, 13, 14-H_2), 1.49 (m, 12-H_2), 2.01 (ddt, J = 6.8, 6.6, 1.5 Hz, 5-H_2), 2.17 (tt, J = 7.1, 2.4, 11-H_2), 2.87 (ddt, J = 5.5, 2.4, 1.5 Hz, 8-H_2), 5.39 (ddt, J = 15.1, 5.5, 1.5 Hz, 7-H), 5.66 (ddt, J = 15.1, 6.8, 1.5 Hz, 6-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0 and 14.1 (C-1 and C-15), 18.8 (C-11), 22.0 (C-8), 22.2, 22.5 (C-2 and C-14), 28.8, 29.0 (C-4 and C-12), 31.1, 31.4 (C-3 and C-13), 32.2 (C-5), 77.6 (C-9), 82.1 (C-10), 124.7 (C-7), 131.8 (C-6) ppm; EIMS (70 eV, *m*/*z*, %) 206 (M^+, <1), 205 (M^+ − 1, 1), 177 (4), 163 (4), 149 (22), 135 (23), 121 (30), 110 (33), 107 (42), 93 (88), 81 (57), 79 (100), 67 (58), 54 (63); HRMS found 205.1956 ($C_{15}H_{25}$ (M^+ − 1) requires 205.1959).

(6*R,7*R**)-6,7-Epoxy-9-pentadecyne (18).** To a solution of **17** (34 mg, 0.17 mmol) in CH_2Cl_2 (2 mL) was added freshly prepared *m*-CPBA (34.5 mg, 1 equiv) and the mixture stirred at room temperature for 3 h after which it was extracted into Et_2O (25 mL) and washed with a saturated solution of $NaHCO_3$ (3 × 25 mL), brine, (25 mL), and H_2O (25 mL). The organic phase was collected, dried over anhydrous $MgSO_4$, and concentrated in vacuo to return a viscous oil (37 mg) that was purified by HPLC (silica, 5% EtOAc/hexane) to yield **18** (32 mg, 86%) as a colorless oil: IR (film) ν_{max} 2363 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, J = 7.1 Hz, 1 and 15-H_3), 1.2−1.6 (bm, 2, 3, 4, 5, 12, 13, 14-H_2), 2.14 (tt, J = 7.1, 2.4 Hz, 11-H_2), 2.36 (ddt, J = 17.1, 5.1, 2.4 Hz, 8-H_A), 2.57 (ddt, J = 17.1, 4.2, 2.4 Hz, 8-H_B), 2.83 (m, 6 and 7-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0 (C-1 and C-15), 18.7 (C-11), 22.3 (C-8), 22.2, 22.6 (C-2 and C-14), 25.6, 28.6, 31.0, 31.5, 31.6 (C-3, C-4, C-5, C-12 and C-13), 56.6, 58.5 (C-6 and C-7), 74.4, 82.6 (C-9 and C-10) ppm; EIMS (70 eV, *m*/*z*, %) 222 (M^+, 2), 221 (M^+ − 1, 6), 207 (2), 193 (3), 179 (19), 165 (33), 151 (63), 156 (30), 139 (25), 127 (5), 113 (7), 109 (31), 99 (40), 95 (54), 81 (78), 71 (39), 69 (46), 67 (93), 54 (100); HRMS found 221.1905 ($C_{15}H_{21}O$ (M^+ − 1) requires 221.1904).

(6*R,7*R**,9*Z*)-6,7-Epoxy-9-pentadecene (19).** To a solution of **18** (32 mg, 0.14 mmol) in EtOH (10 mL) were added quinoline (50 μL) and Lindlar's catalyst (15 mg, 47% w/w) and the resulting mixture vigorously stirred under an atmosphere of H_2 until approximately 1 equiv of H_2 had been consumed (~6 h). The reaction mixture was then diluted with hexane (20 mL) and filtered through a pad of silica to return a crude product that was purified by HPLC (silica, 5% EtOAc/hexane) to yield **19** (30 mg, 88%) as a colorless oil: IR (film) ν_{max} 1465 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 and 0.89 (2t, J = 7.0 Hz, 1 and 15-H_3), 1.2−1.55 (bm, 2, 3, 4, 5, 12, 13, 14-H_2), 2.02 (dt, J = 6.1, 7.2 Hz, 11-H_2), 2.21 (bddd, J = 14.8, 7.4, 7.1 Hz, 8-H_A), 2.39 (bddd, J = 14.8, 7.4, 7.3 Hz, 8-H_B), 2.69 (m, 6 and 7-H), 5.38 (dtt, J = 10.9, 7.3, 1.5, 9-H), 5.51 (dtt, J = 10.9, 7.3, 1.5 Hz, 10-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0, 14.0 (C-1 and C-15), 22.5, 22.6 (C-2 and C-14), 30.0 (C-8), 25.7, 27.3, 29.2, 31.4, 31.6, 31.9 (C-3, C-4, C-5, C-11, C-12, and C-13), 58.1, 58.5 (C-6 and C-7), 123.3 (C-9), 132.9 (C-10) ppm; EIMS (70 eV, *m*/*z*, %) 224 (M^+, 1), 206 (1), 195 (1), 181 (2), 167 (2), 153 (9), 139 (4), 135 (5), 127 (3), 124 (11), 113 (33), 110 (29), 96 (21), 95 (32), 83 (35), 82 (30), 81 (54), 71 (14), 69 (78), 67 (58), 54 (100); HRMS found 224.2140 ($C_{15}H_{28}O$ requires 224.2137).

Epoxidation of (6*R,7*R**,9*Z*)-6,7-Epoxy-9-pentadecene (19).** To a solution of the homoallylic epoxide **19** (28 mg, 0.13 mmol) in CH_2Cl_2 (3 mL) at 0 °C was added *m*-CPBA (99%, 30 mg, 0.17 mmol). The reaction mixture was then warmed to room temperature and stirred for 20 h before extraction into Et_2O (25 mL). The organic phase was washed with a saturated $NaHCO_3$ solution (3 × 20 mL) followed by H_2O (25 mL) and then dried over anhydrous $MgSO_4$ and concentrated in vacuo to return a colorless oil (26 mg) that was purified by HPLC (silica, 20% EtOAc/hexane) to yield the diastereomeric bis-epoxides **20** (11 mg, 35%) and **21** (14.5 mg, 35%) as colorless oils that readily solidified at low temperature (<0 °C): **(6*R**,7*R**,9*S**,10R*)-6,7:9,10-Bis(epoxy)pentadecane (20):** ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 and 0.89 (2t, J = 7.2 Hz, 1 and 15-H_3), 1.3−1.6 (bm, 2, 3, 4, 5, 11, 12, 13, 14-H_2), 1.70 (ddd, J = 14.5, 6.8, 5.1 Hz, 8-H_A), 1.77 (ddd, J = 14.5, 7.3, 4.6 Hz, 8-H_B), 2.74 (dt, J = 2.2, 5.6 Hz, 6-H), 2.86 (ddd, J = 6.8, 4.6, 2.2 Hz, 7-H), 2.97 (dt, J = 4.4, 6.2 Hz, 10-H), 3.10 (ddd, J = 7.3, 5.1, 4.4 Hz, 9-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0 (C-1 and C-15), 22.6 (C-2 and C-14), 25.6, 26.1, 27.8, 31.6, 31.6, 31.9 (C-3, C-4, C-5, C-11, C-12 and C-13), 31.3 (C-8), 54.0

(C-6), 56.0 (C-7), 56.9 (C-10), 58.8 (C-9) ppm; EIMS (70 eV, *m/z*, %) 183 ($M^+ - C_4H_9$, 1), 169 (1), 156 (2), 140 (2), 127 (1), 113 (4), 111 (6), 96 (32), 84 (59), 69 (79), 54 (100); HRMS found 183.1385 ($C_{11}H_{19}O_2$ requires 183.1386), 54.0469 (C_4H_6 requires 54.0469).

(6*R,7*R**,9*R**,10*S**)-6,7:9,10-Bis(epoxy)pentadecane (21):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 and 0.90 (2t, J = 7.1 Hz, 1 and 15-H_3), 1.25−1.6 (bm, 2, 3, 4, 5, 11, 12, 13, 14-H_2), 1.81 (d, J = 5.1 Hz, 8-H_A), 1.83 (dd, J = 5.1, 1.2 Hz, 8-H_B), 2.82 (dt, J = 2.2, 5.4 Hz, 6-H), 2.85 (ddd, J = 5.1, 5.1, 2.2 Hz, 7-H), 2.94 (dt, J = 4.2, 5.9 Hz, 10-H), 3.10 (ddd, J = 6.1, 5.9, 4.2 Hz, 9-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0 (C-1 and C-15), 22.6 (C-2 and C-14), 25.7, 26.2, 27.9, 31.6, 31.7, 31.9 (C-3, C-4, C-5, C-11, C-12 and C-13), 30.4 (C-8), 53.3 (C-9), 55.8 (C-7), 56.5 (C-10), 58.2 (C-6) ppm; EIMS (70 eV, *m/z*, %) 183 ($M^+ - C_4H_9$, 1), 169 (1), 157 (1), 140 (4), 139 (9), 127 (7), 113 (19), 111 (7), 96 (27), 84 (41), 69 (65), 54 (100). HRMS found 183.1385 ($C_{11}H_{19}O_2$ requires 183.1386).

Cyclization of (6*R,7*R**,9*S**,10*R**)-6,7:9,10-Bis(epoxy)-pentadecane (20).** The bisepoxide **20** (10 mg, 0.042 mmol) in glacial acetic acid (2 mL) was stirred at 100 °C for 24 h after which the solution was cooled to room temperature and diluted with Et_2O (30 mL) and the organic phase washed with H_2O (3 × 30 mL), saturated $NaHCO_3$ solution (30 mL), and H_2O (20 mL). The organic phase was dried over anhydrous $MgSO_4$ and concentrated in vacuo to return a pale yellow oil (12 mg) which was purified by HPLC (silica, 40% EtOAc/hexane) to yield the trans tetrahydrofuran acetate **22** (8.8 mg, 70%) and the cis tetrahydrofuran acetate **23** (2.5 mg, 20%) as colorless oils: **(6*R**,7*R**,9*S**,10*R**)-6,9-epoxypentadecane-7,10-diol 7-acetate (22):** IR (film) ν_{max} 3465, 1740 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 and 0.89 (2t, J = 6.8 Hz, 1 and 15-H_3), 1.25−1.6 (bm, 2, 3, 4, 5, 11, 12, 13, 14-H_2), 1.88 (ddd, J = 13.7, 6.1, 1.0 Hz, 8-H_A), 2.09 (s, $COCH_3$), 2.20 (ddd, J = 13.7, 10.0, 4.6 Hz, 8-H_B), 3.85 (dt, J = 3.6, 6.9 Hz, 10-H), 3.97 (ddd, J = 7.6, 5.9, 3.6 Hz, 6-H), 4.10 (ddd, J = 10.0, 6.1, 3.6 Hz, 9-H), 5.34 (bdd, J = 4.6, 3.6 Hz, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0, 14.0 (C-1 and C-15), 21.1 ($COCH_3$), 22.5, 22.5 (C-2 and C-14), 25.6, 25.9, 29.4, 31.8, 31.9, 32.2 (C-3, C-4, C-5, C-11, C-12, and C-13), 32.0 (C-8), 71.8 (C-10), 75.4 (C-7), 80.3 (C-9), 82.1 (C-10), 170.5 ($COCH_3$) ppm; EIMS (70 eV, *m/z*, %) 240 (M^+ − HOAc, 1), 199 ($M^+ - C_6H_{13}O$, 8), 140 (18), 139 (100), 113 (4), 95 (6), 84 (7), 69 (7), 67 (4), 54 (15); HRMS found 199.1334 ($C_{11}H_{19}O_3$ requires 199.1332), 139.1123 ($C_9H_{15}O$ requires 139.1123).

(6*S,7*S**,9*S**,10*R**)-6,9-Epoxypentadecane-7,10-diol 7-acetate (23):** IR (film) ν_{max} 3468, 1739 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 1 and 15-H_3), 1.3−1.6 (bm, 2, 3, 4, 5, 11, 12, 13, 14-H_2), 1.95 (ddd, J = 14.4, 6.3, 1.7 Hz, 8-H_A), 2.06 (s, $COCH_3$), 2.23 (ddd, J = 14.4, 8.1, 6.6 Hz, 8-H_B), 3.79 (ddd, J = 7.7, 5.7, 3.7 Hz, 6-H), 3.86 (bm, 10-H and 9-H), 5.21 (ddd, J = 6.6, 3.7, 1.7 Hz, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0, 14.0 (C-1 and C-15), 21.1 ($COCH_3$), 22.5, 22.6 (C-2 and C-14), 25.5, 25.9, 28.5, 31.8, 31.9, 32.6 (C-3, C-4, C-5, C-11, C-12, and C-13), 32.2 (C-8), 71.0 (C-10), 74.5 (C-7), 80.4 (C-9), 81.7 (C-6), 170.6 ($COCH_3$) ppm; EIMS (70 eV, *m/z*, %) 199 ($M^+ - C_6H_{13}O$, 5), 175 (2), 140 (26), 139 (100), 113 (3), 91 (23), 84 (13), 69 (10), 54 (21); HRMS found 199.1334 ($C_{11}H_{19}O_3$ requires 199.1332), 139.1121 ($C_9H_{15}O$ requires 139.1123).

Cyclization of (6*R,7*R**,9*R**,10*S**)-6,7:9,10-Bis(epoxy)-pentadecane (21).** The bisepoxide **21** (10 mg, 0.042 mmol) in glacial acetic acid (2 mL) was stirred at 100 °C for 24 h after which the solution was cooled to room temperature and diluted with Et_2O (30 mL), and the organic phase was washed with H_2O (3 × 30 mL), saturated $NaHCO_3$ solution (30 mL), and H_2O (20 mL). The organic phase was dried over anhydrous $MgSO_4$ and concentrated in vacuo to return a pale yellow oil (12 mg) which was purified by HPLC (silica, 40% EtOAc/hexane) to yield the trans tetrahydrofuran acetate **22** (1.9 mg, 19%) and the cis tetrahydrofuran acetate **23** (6.8 mg, 68%) as colorless oils.

(6*R,7*R**,9*S**,10*R**)-6,9-Epoxypentadecane-7,10-diol (24).** A solution of **22** (5.2 mg, 0.017 mmol) in MeOH (2 mL) and NH_4OH (33% aq solution, 0.5 mL) was stirred at room temperature for 5 h after which it was concentrated in vacuo to yield the trans tetrahydrofuran **24** (4.5 mg, 100%) as a colorless amorphous solid: mp 93−95°; IR (film) ν_{max} 3355 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 and 0.89 (2t, J = 6.6 Hz, 1 and 15-H_3), 1.3−1.6 (bm, 2, 3, 4, 5, 11, 12, 13, 14-H_2), 1.85 (dd, J = 13.2, 6.1 Hz, 8-H_A), 2.12 (ddd, J = 13.2, 10.2, 4.4 Hz, 8-H_B), 3.84 (dt, J = 2.9, 6.8 Hz, 6-H), 3.86 (m, 10-H), 4.17 (ddd, J = 10.2, 6.1, 3.4 Hz, 9-H), 4.29 (dd, J = 4.4, 2.9 Hz, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0 (C-1 and C-15), 22.6, 22.6 (C-2 and C-14), 26.0, 26.0, 29.2, 31.8, 32.0, 32.2 (C-3, C-4, C-5, C-11, C-12, and C-13), 34.2 (C-8), 72.1 (C-10), 73.3 (C-7), 80.0 (C-9), 83.6 (C-6) ppm; EIMS (70 eV, *m/z*, %) 258 (M^+, 1), 240 (1), 214 (1), 201 (1), 187 (1), 169 (1), 157 (78), 139 (29), 121 (20), 114 (21), 113 (100), 101 (15), 96 (18), 95 (69), 83 (31), 69 (39), 57 (33), 56 (44), 54 (72); HRMS found 258.2195 ($C_{15}H_{30}O_3$ requires 258.2193).

(6*S,7*S**,9*S**,10*R**)-6,9-Epoxypentadecane-7,10-diol (25).** A solution of **23** (4.9 mg, 0.016 mmol) in MeOH (3 mL) and NH_4OH (33% aq solution, 1 mL) was stirred at room temperature for 5 h after which it was concentrated in vacuo to yield the cis tetrahydrofuran **25** (4.2 mg, 100%) as a colorless oil: IR (film) ν_{max} 3355 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, J = 6.7 Hz, 1 and 15-H_3), 1.3−1.65 (bm, 2, 3, 4, 5, 11, 12, 13, 14-H_2), 1.91 (ddd, J = 14.2, 3.4, 1.7 Hz, 8-H_A), 2.19 (ddd, J = 14.2, 10.0, 5.4 Hz, 8-H_B), 3.59 (dt, J = 2.7, 6.8 Hz, 6-H), 3.84 (ddd, J = 7.4, 5.1, 2.2 Hz, 10-H), 4.00 (ddd, J = 10.0, 3.4, 2.2 Hz, 9-H), 4.03 (ddd, J = 5.4, 2.7, 1.7 Hz, 7-H); ^{13}C NMR (100 MHz, $CDCl_3$) 14.0, 14.0 (C-1 and C-15), 22.5, 22.6 (C-2 and C-14), 25.6, 26.0, 28.8, 31.7, 32.1, 33.3 (C-3, C-4, C-5, C-11, C-12 and C-13), 34.3 (C-8), 71.2 (C-7), 72.1 (C-10), 79.9 (C-9), 83.9 (C-6) ppm; EIMS (70 eV, *m/z*, %) 258 (M^+, 2), 240 (1), 214 (1), 201 (3), 187 (2), 169 (2), 157 (93), 140 (17), 139 (44), 121 (21), 114 (36), 113 (100), 101 (29), 96 (30), 95 (67), 84 (21), 83 (47), 69 (45), 57 (51), 56 (49), 54 (83); HRMS found 258.2199 ($C_{15}H_{30}O_3$ requires 258.2195).

10-Epimer (26) of the Natural Dihydroxytetrahydrofuran 1. To a solution of the natural product **1** (87 mg, 0.28 mmol) in CH_2Cl_2 (5 mL) was added pyridinium dichromate (160 mg, 0.42 mmol) and the reaction mixture stirred at room temperature for 48 h, after which it was filtered through a plug of Celite and the filtrate concentrated in vacuo to return a crude mixture of products that were resolved by HPLC (silica, 30% EtOAc/hexane) to yield, in decreasing order of polarity, **(6*S*,7*S*,9*R*)-7-hydroxy-6,9-epoxynonadec-18-en-10-one** (29 mg, 33%): an unstable colorless oil; $[\alpha]_D$ +20.4 (*c* = 1.0, $CHCl_3$); IR (film) ν_{max} 3445, 1715, 1640 cm^{-1}; ^{1}H NMR (100 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 1-H_3), 1.2−1.6 (methylene envelope, 2, 3, 4, 5, 12, 13, 14, 15, 16-H_2), 2.01 (dt, J = 6.8, 6.8 Hz, 17-H_2), 2.09 (ddd, J = 13.7, 8.3, 4.8 Hz, 8-H_A), 2.22 (ddd, J = 13.7, 8.3, 0.7 Hz, 8-H_B), 2.48 (dt, J = 17.6, 7.4 Hz, 11-H_A), 2.54 (dt, J = 17.6, 7.4 Hz, 11-H_B), 3.75 (dt, J = 2.9, 7.0 Hz, 6-H), 4.22 (dd, J = 4.8, 2.9 Hz, 7-H), 4.55 (dd, J = 8.3, 8.3 Hz, 9-H), 4.93 (ddt, J = 10.3, 2.2, 1.3 Hz, 19-H_{cis}), 4.99 (ddt, J = 17.1, 2.2, 1.5 Hz, 19-H_{trans}), 5.80 (ddt, J = 17.1, 10.3, 6.8 Hz, 18-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 (C-1), 22.5 (C-2), 23.2 (C-4), 25.9 (C-12), 28.6, 28.8, 28.9, 29.1, 29.2, 29.2 (C-5, C-11, C-13, C-14 and C-16), 31.9 (C-3), 33.7 (C-17), 38.3 (C-8), 72.5 (C-7), 81.0 (C-6), 84.1 (C-9), 114.2 (C-19), 139.1 (C-18), 212.5 (C-10) ppm; EIMS (70 eV, *m/z*, %) 310 (M^+, 2), 157 (100), 139 (17), 121 (14), 113 (60), 95 (42), 69 (33), 55 (38), 43 (34); HRMS found 310.2508 ($C_{19}H_{34}O_3$ requires 310.2507). **(6*S*,9*R*,10*R*)-10-hydroxy-6,9-epoxynonadec-18-en-7-one** (14 mg, 16%): a stable colorless oil; $[\alpha]_D$ +33.2 (*c* = 1.0, $CHCl_3$); IR (film) ν_{max} 3460, 1755, 1640 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 1-H_3), 1.2−1.6 (methylene envelope, 2, 3, 4, 5, 11, 12, 13, 14, 15, 16-H_2), 2.03 (dt, J = 6.8, 6.8 Hz, 17-H_2), 2.25 (bs, OH), 2.42 (ddd, J=18.3, 7.1, 0.9 Hz, 8-H_A), 2.52 (dd, J = 18.3, 7.1 Hz, 8-H_B), 3.54 (bm, 10-H), 3.98 (dd, J = 8.1, 4.6 Hz, 6-H), 4.18 (ddd, J = 7.1, 7.1, 5.4 Hz, 9-H), 4.92 (ddt, J = 10.3, 2.2, 1.2 Hz, 19-H_{cis}), 4.99 (ddt, J = 17.1, 2.2, 1.5 Hz, 19-H_{trans}), 5.81 (ddt, J=17.1, 10.3, 6.8 Hz, 18-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 (C-1), 22.4 (C-2), 24.9 (C-4), 25.5 (C-12), 28.9, 29.0, 29.3, 29.5 (C-13, C-14, C-15 and C-16), 31.0 (C-5), 31.5 (C-3), 33.2 (C-11), 33.8 (C-17), 38.9 (C-8), 73.6 (C-10), 77.8 (C-6), 79.8 (C-9), 114.1 (C-19), 139.1 (C-18), 215.8 (C-7) ppm; EIMS (70 eV, *m/z*, %) 310 (M^+, 24), 240

(2), 157 (20), 156 (18), 155 (12), 128 (16), 127 (17), 101 (30), 99 (78), 57 (100); HRMS found 310.2507 ($C_{19}H_{34}O_3$ requires 310.2508). **(6*S*,9*R*)-6,9-epoxynonadec-18-ene-7,10-dione** (42 mg, 48%): a moderately stable colorless oil; $[\alpha]_D$ −35.9 (c = 1.0, $CHCl_3$); IR (film) ν_{max} 1760, 1720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 1-H_3), 1.3−1.7 (methylene envelope, 2, 3, 4, 5, 12, 13, 14, 15, 16-H_2), 2.04 (dt, J = 6.8, 6.8 Hz, 17-H_2), 2.60 (t, J = 7.4 Hz, 11-H_2), 2.62 (dd, J = 18.3, 8.8 Hz, 8-H_A), 2.72 (dd, J = 18.3, 5.4 Hz, 8-H_B), 3.90 (dd, J = 7.8, 4.5 Hz, 6-H), 4.74 (dd, J = 8.8, 5.4 Hz, 9-H), 4.92 (ddt, J = 10.3, 2.2, 1.2 Hz, 19-H_{cis}), 4.99 (ddt, J = 17.1, 2.2, 1.5 Hz, 19-H_{trans}), 5.81 (ddt, J = 17.1, 10.3, 6.8 Hz, 18-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 (C-1), 22.4 (C-2), 23.1 (C-4), 24.8 (C-12), 28.8, 28.9, 29.1, 29.2, 30.8 (C-5, C-13, C-14, C-15, and C-16), 31.3 (C-3), 33.7 (C-17), 37.5 (C-11), 38.7 (C-8), 78.7 (C-6), 79.7 (C-9), 114.2 (C-19), 139.1 (C-18), 209.7 (C-10), 213.7 (C-7) ppm; EIMS (70 eV, m/z, %) 308 (M^+, 2), 266 (2), 237 (1), 209 (8), 181 (29), 151 (52), 135 (39), 127 (71), 111 (47), 99 (23), 83 (81), 69 (57), 55 (100), 43 (40), 41 (63); HRMS found 308.2351 ($C_{19}H_{32}O_3$ requires: 308.2351).

(6*S*,7*S*,9*R*,10*S*)-6,9-Epoxynonadec-18-ene-7,10-diol (26). A sample of (6*S*,7*S*,90*R*)-7-hydroxy-6,9-epoxynonadec-18-en-10-one (25 mg, 0.08 mmol) in MeOH (10 mL) was treated with $NaBH_4$ (60 mg, excess) and the mixture stirred at room temperature for 2 h, after which it was concentrated in vacuo to return a colorless waxy solid which was extracted into Et_2O (30 mL). The ethereal extract was washed with H_2O (30 mL), saturated $NaHCO_3$ solution (20 mL), and dilute aqueous HCl (20 mL, 2M), dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo to yield a waxy solid (24.5 mg, 97%) that was resolved by HPLC (silica, 40% EtOAc/hexane) into a 1.2:1 ratio of the natural dihydroxy tetrahydrofuran **1** and the 10-epimer **26**: a stable colorless crystalline solid; mp 98−99 °C (from hexane); $[\alpha]_D$ +9.2° (c = 0.25, $CHCl_3$); IR (film) ν_{max} 3375, 3325, 1640 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, J = 6.8 Hz, 1-H_3), 1.3−1.6 (methylene envelope, 2, 3, 4, 5, 11, 12, 13, 14, 15, 16-H_2), 1.85 (bdd, J = 13.2, 6.1 Hz, 8-H_A), 1.96 (bs, OH), 2.03 (bdt, J = 6.8, 7.1 Hz, 17-H_2), 2.12 (ddd, J = 13.2, 10.3, 4.4 Hz, 8-H_B), 3.84 (dt, J = 2.9, 7.1 Hz, 6-H), 3.86 (m, 10-H), 4.16 (ddd, J = 10.3, 6.1, 3.5 Hz, 9-H), 4.29 (bs, 7-H), 4.94 (ddt, J = 10.1, 2.2, 1.2 Hz, 19-H_{cis}), 4.99 (ddt, J = 17.1, 2.2, 1.5 Hz, 19-H_{trans}), 5.81 (ddt, J = 17.1, 10.1, 6.8 Hz, 18-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0 (C-1), 22.6 (C-2), 25.9, 26.0, 28.9, 29.0, 29.2, 29.4, 29.6 (C-4, C-5, C-12, C-13, C-14, C-15 and C-16), 32.0 (C-3), 32.3 (C-11), 33.8 (C-17), 34.3 (C-8), 72.1 (C-10), 73.3 (C-7), 80.1 (C-9), 83.5 (C-6), 114.1 (C-19), 139.2 (C-18) ppm; EIMS (70 eV, m/z, %) 312 (M^+, 1), 276 (2), 157 (76), 139 (38), 121 (37), 113 (100), 95 (87), 81 (44), 69 (56), 57 (63), 55 (90); HRMS found 312.2666 ($C_{19}H_{36}O_3$ requires 312.2664).

Bisepoxides 28 and 29 of *trans,trans*-Methyl Linoleate (27). To a solution of trans,trans-methyl linoleate (50 mg, 0.17 mmol) in CH_2Cl_2 (10 mL) was added *m*-CPBA (73 mg, 0.42 mmol) and the reaction stirred at room temperature for 18 h, after which the reaction mixture was added to H_2O (30 mL) and extracted with Et_2O (3 × 30 mL). The combined ethereal extract was washed with NaOH (2 M, 3 × 15 mL) and H_2O (30 mL) and then dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo to return a light yellow oil (60 mg, 100%). This material proved to be an inseparable mixture of stereoisomeric bisepoxides for which NMR analysis revealed both syn and anti diastereomers.

Cyclization of Bisepoxides 28 and 29. A solution of **28** and **29** (60 mg, 0.2 mmol) in glacial acetic acid (5 mL) was stirred at 100 °C for 24 h, after which the reaction mixture was added to H_2O (30 mL) and extracted with Et_2O (3 × 30 mL). The combined ethereal extract was washed with NaOH (2 M, 3 × 15 mL) and H_2O (30 mL) and then dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo to return a light yellow oil (40 mg). NMR analysis revealed no trace of resonances consistent with either the starting material or cyclized products, but instead was dominated by multiple acetate resonances suggestive of a mixture of acyclic diol diacetate isomers.

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Supporting Information Available: Figures showing ^{13}C NMR spectra for **3**−**26**, ^1H NMR for **9**, **12**, and **26**, and HETCOR data for **9** and **12** are provided (30 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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