Cyclopropane-Containing Eicosanoids of Marine Origin. Biomimetic Synthesis of Constanolactones A and B from the Alga *Constantinea simplex*

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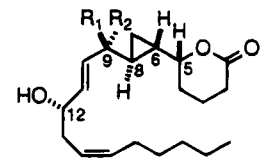
Abstract: Asymmetric syntheses of **7**, a substance isolated from incubation of arachidonic acid with an acetone powder of the coral *Plexaura homomalla*, and of constanolactones A (**9**) and B (**10**), metabolites of the red alga *Constantinea simplex*, are described. The key step involves stannic chloride-mediated cyclization of the oxirane derived from Sharpless epoxidation of 10-hydroxy-5,8-decadienoates, and is shown to yield a *trans* disubstituted cyclopropane linked to a δ-lactone. Both (*R*) and (*S*) configurations at C5 of the lactone are produced in the cyclization, the ratio being independent of olefin geometry in the acyclic precursor. Elaboration of the cyclization products via Nozaki−Kishi coupling of the derived aldehydes **26** and **37** with the appropriate (1*E*,5*Z*)-1-iodo-1,5-undecadiene led to **7**, **9**, and **10**, thereby establishing the relative configuration of **7** and confirming the absolute configuration of **9** and **10**.

In 1987 Corey put forward a general pathway for marine prostanoid biosynthesis (Scheme 1) in which arachidonic acid (**1**) is oxidized by a lipoxygenase enzyme to (8*R*)-8-hydroperoxyeicosatetraenoic acid (8*R*-HPETE, **2**). The latter is then converted enzymatically to the allene oxide **3**.[1] It was suggested that prostanoids, such as preclavulone (**5**), originate by closure of the derived cation **4** at C12 of the eicosanoid.[2] Subsequently, Brash was able to isolate and characterize Corey's proposed allene oxide by incubation of **2** with an acetone powder from the coral *Plexaura homomalla*.[3] Similar incubation of arachidonic acid itself was found to give, in addition to **5**, a novel eicosanoid **7** containing a cyclopropane.[4] This finding has led to an extension of Corey's biogenetic hypothesis that includes an alternative pathway from cation **4** involving participation by the $\Delta^{5,6}$ bond (Scheme 1). Rearrangement of **4** to the cyclopropyl carbocation **6** followed by hydrolysis and relocation of the $\Delta^{11,12}$ bond into conjugation with the C9 ketone would lead to **7**. This δ-hydroxy acid was found to undergo facile lactonization to **8** in which the cyclopropane substituents were shown to be *trans*. Surprisingly, the circular dichroism spectrum of **7** was reported to be featureless,[4] suggesting that this substance is racemic. However, attempts to resolve enantiomers by chiral phase high-pressure liquid chromatography were fruitless.[5]

More recently, substances closely related to **8** have been isolated from the red alga *Constantinea simplex* harvested off the Oregon coast.[6] Two of these, constanolactones A and B, were shown to possess structures **9** and **10**, respectively, by a combination of degradative and spectroscopic methods.[7] The constanolactones can be accommodated within the biogenetic framework that includes **7**, and their presence in a different marine species from that giving rise to **7** lends credence to the view[8] that cyclopropanoid oxylipins are characteristic of a general pathway in marine (as opposed to mammalian) systems.



9, R_1 = H, R_2 = OH
10, R_1 = OH, R_2 = H

No direct test of the Corey−Brash hypothesis outlined in Scheme 1 has been made, but the intriguing possibility that **7**, **9**, and **10** arise in nature via a cyclization cascade triggered by epoxide opening clearly invited mimicry. Although exchange of an epoxide for a cyclopropane would seem to be a rare event,[9] it appeared reasonable that a precursor akin to **3** could be induced to undergo *chemical* conversion to the functionalized cyclopropane structure present in the C1−C9 segment of these eicosanoids. A plan was therefore devised which, while eschewing the labile allene oxide **3**, incorporated the key features of the biogenesis depicted in Scheme 1. This has resulted in a synthesis of **7**, which has established its relative configuration as shown.[10] In addition, an extension of this approach to synthesis of constanolactones A (**9**) and B (**10**) has permitted confirmation of the structures and absolute configurations of these substances reached on the basis of circular dichroism and chemical degradation.[7]

A guiding principle of our synthetic plan was that there should be a unidirectional cyclization cascade in the pivotal step. This was achieved by placing a hydroxyl group at the epoxide terminus of the acyclic precursor. The hydroxyl function was intended to serve not only as a locus for attaching an electrophile

[⊗] Abstract published in *Advance ACS Abstracts,* June 1, 1995.

(1) Corey, E. J.; Matsuda, S. P. T. *Tetrahedron Lett.* **1987**, *28*, 4247.

(2) Corey, E. J.; d'Alarcao, M.; Matsuda, S. P. T.; Lansbury, P. T., Jr.; Yamada, Y. *J. Am. Chem. Soc.* **1987**, *109*, 289.

(3) Brash, A. R. *J. Am. Chem. Soc.* **1989**, *111*, 1891.

(4) Baertschi, S. W.; Brash, A. R.; Harris, T. M. *J. Am. Chem. Soc.* **1989**, *111*, 5003.

(5) This finding must be viewed in the context of the very small quantity of natural material that was isolated.

(6) Nagle, D. G.; Gerwick, W. H. *Tetrahedron Lett.* **1990**, *31*, 2995.

(7) Nagle, D. G.; Gerwick, W. H. *J. Org. Chem.* **1994**, *59*, 7227.

(8) Gerwick, W. H. *Chem. Rev.* **1993**, *93*, 1807.

(9) For an interesting and unexpected example, see: Shirahama, H.; Hayano, K.; Kanemoto, Y.; Misumi, S.; Ohtsuka, T.; Hashiba, N.; Furusaki, A.; Murata, S.; Noyori, R.; Matsumoto, T. *Tetrahedron Lett.* **1980**, *21*, 4835.

(10) Preliminary communication: White, J. D.; Jensen, M. S. *J. Am. Chem. Soc.* **1993**, *115*, 2970.

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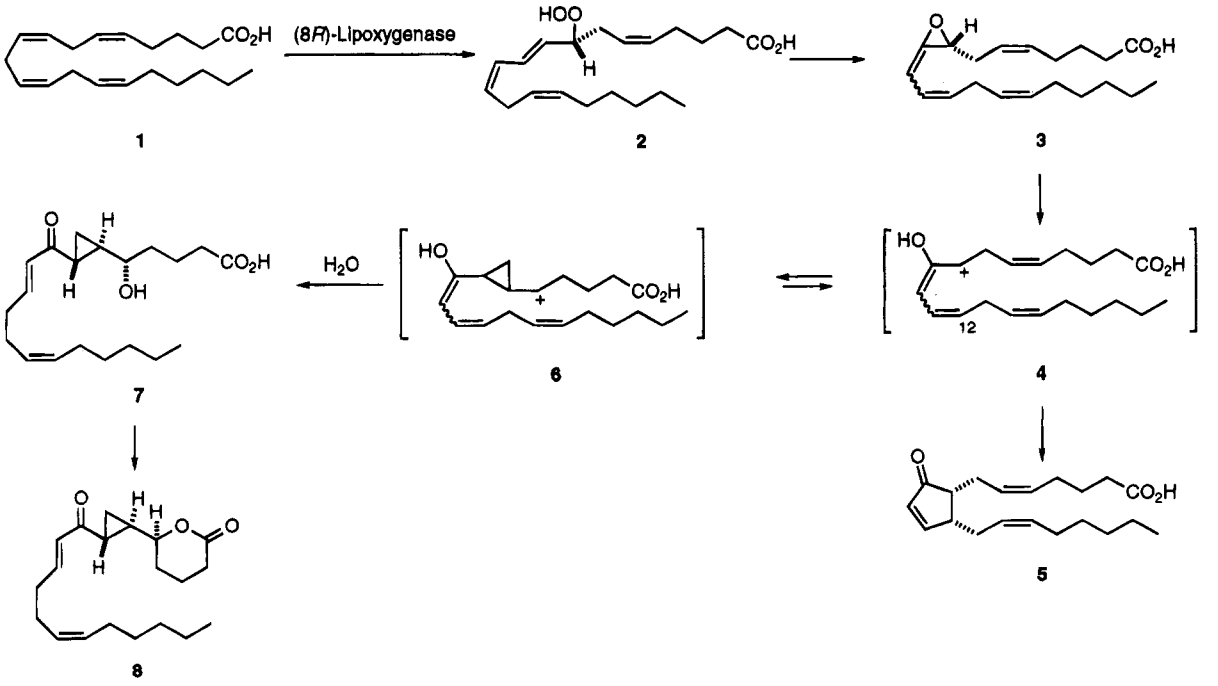
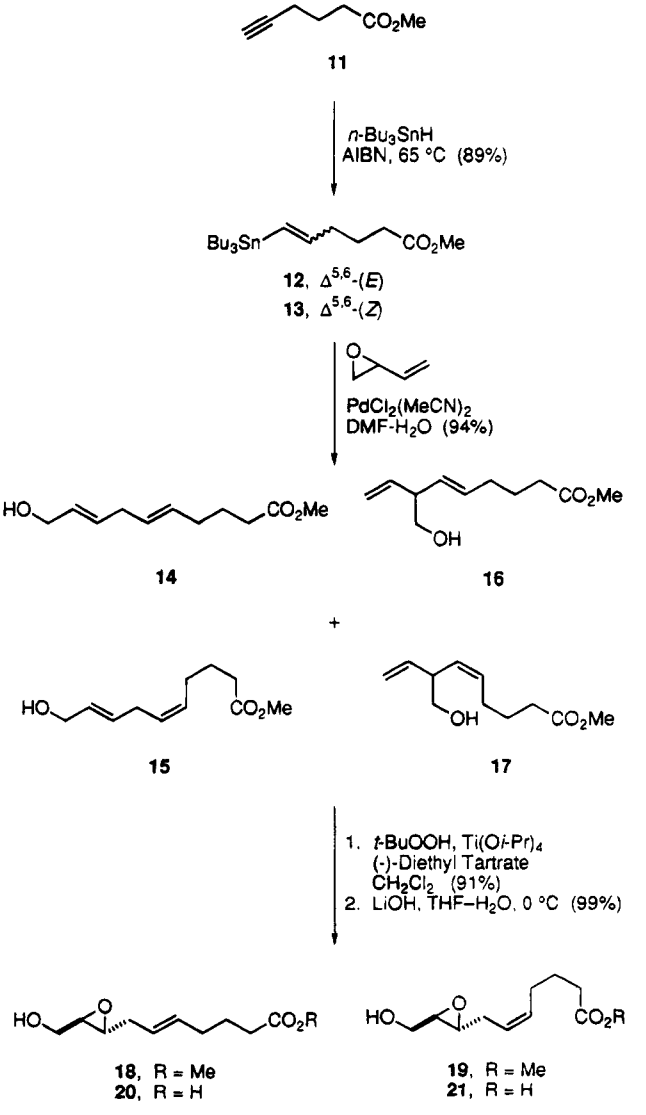
Scheme 1



to trigger epoxide opening but also as a handle for connecting the C11−C20 chain of **7** and **10**. A carboxyl group terminates cyclization by trapping the putative cyclopropyl carbinyl cation analogous to **6** as a δ-lactone. In simplest terms, this biomimetic strategy reduces to a cyclization precursor which is the 8,9-oxirane derived from 10-hydroxydeca-5,8-dienoic acid.

Hydrostannylation of methyl 5-hexynoate (**11**) afforded a mixture of (*E*) and (*Z*) stannanes, **12** and **13**, in the ratio 4:1, respectively.[11] These substances proved difficult to separate, and the mixture of isomers was therefore subjected to reaction with butadiene monoepoxide in the presence of a catalytic quantity of the bis(acetonitrile) complex of palladium(II) chloride.[12] A 4:1 mixture of 1,4- and 1,2-addition products was obtained, each as a (5*E*,*Z*) mixture of olefin isomers. As expected, only the allylic alcohols **14** and **15** in this mixture underwent asymmetric epoxidation.[13] The unreacted alcohols **16** and **17** were removed by column chromatography, and further chromatographic separation on silica impregnated with silver nitrate yielded the pure (*E*) and (*Z*) isomers **18** and **19** of (8*R*,9*R*) configuration. The choice of (*S*)-(−)-tartrate as the chiral adjuvant for Sharpless epoxidation of **14** and **15** was influenced by the fact that **3** is known to possess (*R*) configuration,[3] and even though the asymmetry of **7** was in question,[4] it was assumed that this substance, **9**, and **10** were all produced in vivo via the same biogenetic pathway involving **3**. As seen below, this assumption is probably incorrect.

Saponification of **18** and **19** gave (*E*) and (*Z*) carboxylic acids **20** and **21**, respectively. These were reacted with a wide range of Lewis and Bronsted acids in the hope of effecting cyclization. However, only stannic chloride in cold nitromethane led to identifiable products.[14] It was found that under these conditions **20** and **21** yielded the same 1.5:1 mixture of steoisomeric lactones **22** and **23** in yields which ranged from 44% to 64%. The variability in yield is due to the instability of the diol products which could not be chromatographed or stored (even at −20 °C) without substantial decomposition.

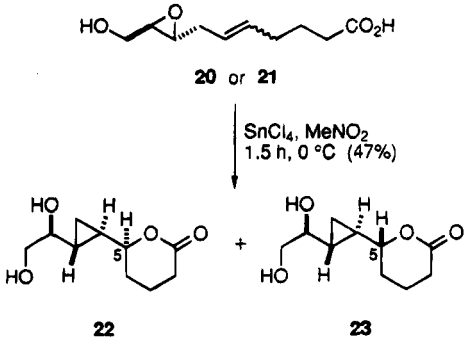


(11) Leusink, A. J.; Budding, H. A.; Drenth, W. *J. Organomet. Chem.* **1968**, *11*, 541 and preceding papers.

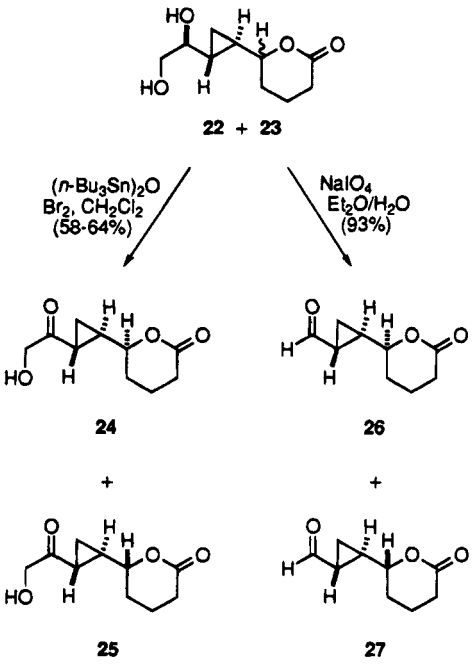
(12) Echavarren, A. M.; Tueting, D. R.; Stille, J. K. *J. Am. Chem. Soc.* **1988**, *110*, 4039.

(13) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.

(14) This observation conforms to previous results obtained in the course of studies on the cyclization of squalene oxide and related systems. See: (a) van Tamelen, E. E. *Acc. Chem. Res.* **1975**, *8*, 152. (b) van Tamelen, E. E. *Acc. Chem. Res.* **1968**, *1*, 111.

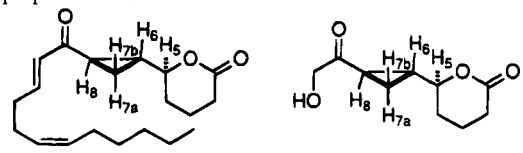


Treatment of the mixture of **22** and **23** with bromine and hexa-*n*-butylstannoxane[15] resulted in selective oxidation of the secondary alcohol to α-hydroxy ketones **24** and **25**. Not only



were these materials less labile than their diol precursors but **24** could be cleanly separated from its isomer by radial chromatography. The availability of pure **24** enabled a detailed analysis of its ^{1}H NMR spectrum to be carried out which established that it possesses *trans* configuration at the cyclopropane. Direct measurement of the coupling between H_6 and H_8 in **24** was not possible, but application of the phase-sensitive COSY technique[16] permitted assignment of the complete set of chemical shifts and coupling constants for the four cyclopropane protons. Data are shown in Table 1, along with the analogous proton chemical shifts and coupling constants of natural **8** for comparison. Resonances due to H_{7a} and H_{7b} were sufficiently dispersed from other signals to allow unequivocal assignment, and from a correlation of each of these protons with H_6 and H_8, it was deduced that each member of the latter pair is *cis* to a different proton.[17] This analysis stipulates that H_6 and H_8 are *trans* to each other. Examination of coupling constants of the minor isomer **25** by means of one-dimensional NMR experiments confirmed that the cyclopropane in this structure is also *trans*. Since the absolute configuration of **18** and **19** is known from their method of preparation and since opening of these epoxides can be assumed to occur with inversion at C8,[18] the absolute configuration of **22** and **23** is defined as (6*R*,8*R*,9*S*).

Table 1. Chemical Shifts and Coupling Constants of Cyclopropanone Protons in 8 and 24

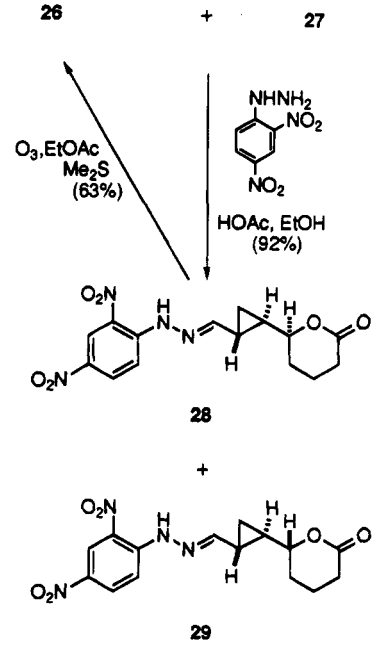


8 **24**

compd	proton	chemical shift (ppm)	coupling constant (Hz)
24	H_6	2.05	H_6, H_{7a} = 4.6; H_6, H_{7b} = 8.3
24	H_{7a}	1.11	H_{7a}, H_{7b} = 4.3; H_{7a}, H_8 = 9.2
24	H_{7b}	1.41	H_{7b}, H_8 = 6.5
24	H_8	1.90	
8[a]	H_6	1.64−1.74	H_6, H_{7a} = 6.1
8[a]	H_{7a}	0.91−1.00	H_{7a}, H_{7b} = 3.8; H_{7a}, H_8 = 8.2
8[a]	H_{7b}	1.22−1.31	
8[a]	H_8	2.25−2.33	

[a] Data from ref 4.

The configuration at C5 of **24** and **25** could not be ascertained from the available NMR data, and for this purpose, resort was made to X-ray crystallography. Since neither of the hydroxy ketones **24** and **25** nor their parent diols yielded a suitable crystalline derivative, the mixture of **22** and **23** was oxidized with sodium periodate[19] to afford aldehydes **26** and **27**. Both aldehydes readily formed (2,4-dinitrophenyl)hydrazones which were cleanly separable by medium-pressure liquid chromatography. Of the two hydrazones, **28** and **29**, only the latter,



prepared from the aldehyde **27** originating in the minor cyclization product **23**, afforded crystals suitable for X-ray analysis. A crystal structure (Figure 1) revealed the configuration at C5 of this derivative as (*R*).

The observation that cyclization of either **20** or **21** affords the same 1.5:1 mixture of **22** and **23**, differing only in configuration at C5, suggests that the reaction proceeds through discrete cyclopropyl carbinyl cations as shown in Scheme 2. These cations could be formed in either of two conformations **32** and/or **33** by geometrically distinct pathways emanating from

(15) Ueno, Y.; Okawara, M. *Tetrahedron Lett.* **1976**, 4597.
(16) Derome, A. E. In *Modern NMR Techniques for Chemistry Research*; Pergamon Press: Oxford, U.K., 1987; pp 209−220.
(17) Inouye, Y.; Sugita, T.; Walborsky, H. M. *Tetrahedron* **1964**, *20*, 1695.
(18) Smith, J. G. *Synthesis* **1984**, 629.
(19) Perlin, A. S. In *Oxidation*; Augustine, R. L., Ed.; Marcel Dekker: New York, 1969; Vol. 1, pp 189−212.

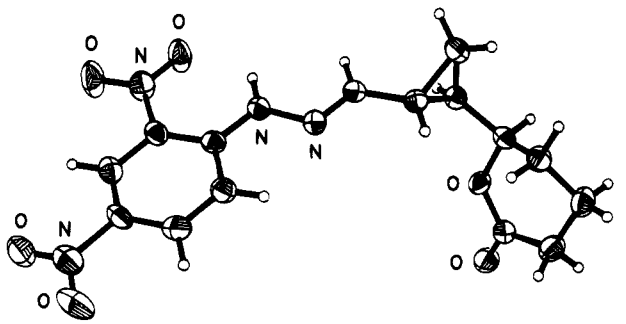


Figure 1. ORTEP representation of the X-ray crystal structure of **29**. Thermal ellipsoids are drawn at the 50% probability level.

Table 2. Chemical Shifts of C5 Protons of Natural and Synthetic δ-Lactones

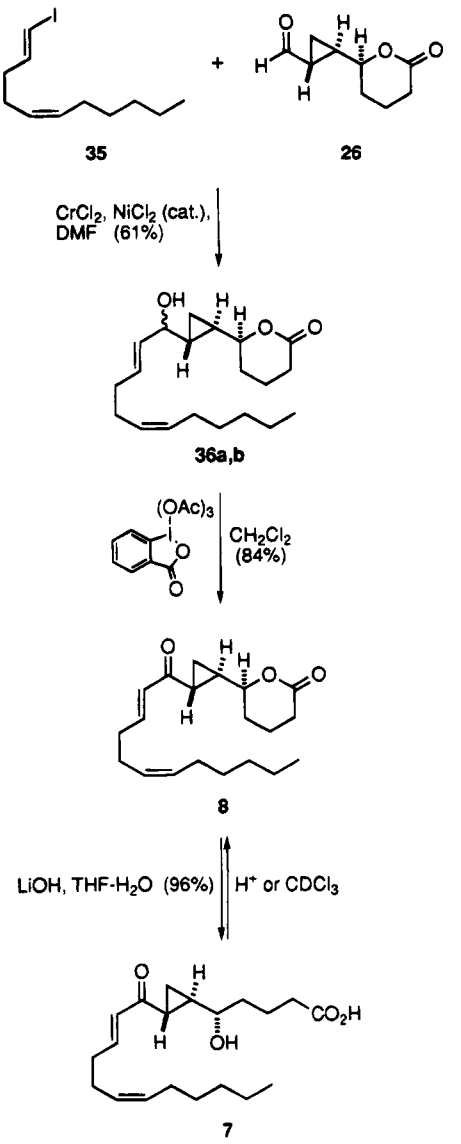
natural lactones		synthetic lactones			
		(5*S*) diastereomers		(5*R*) diastereomers	
compd	chemical shift (ppm)	compd	chemical shift (ppm)	compd	chemical shift (ppm)
8[a]	3.81	**24**	3.85	**25**	4.21
9[b]	3.72	**26**	3.91	**27**	4.21
10[b]	3.73	**28**	3.90	**29**	4.06

[a] Data from ref 4. [b] Data from ref 6.

(*E*) and (*Z*) complexed epoxides **30** and **31**, respectively. Although bisected carbocations **32** and **33** can each derive stabilization by σ delocalization from the cyclopropane into the empty p orbital,[20] their rapid interconversion by bond rotation is clearly possible. In this event, the proportion of **22** to **23** corresponds to a thermodynamic distribution. Alternatively, the ratio may reflect a modest kinetic preference for closure of the carboxyl terminus at the sterically less hindered top face of carbocations **32** and **33**.

At this juncture it was unclear whether a diastereomer of the (5*R*) or (5*S*) series represented the correct precursor for advancing the synthesis toward **7**. However, comparison of chemical shift data for **24**−**29** with those for **8**, **9**, and **10** (Table 2) showed a pattern in which the C5 proton consistently appears upfield in the series **24**, **26**, and **28** relative to the set of stereoisomers **25**, **27**, and **29**. The C5 proton in lactone **8**, as well as in constanolactones A (**9**) and B (**10**), displays a chemical shift in close accord with that of lactones **24**, **25**, and **28**, and on this basis, the major diol **22** from cyclization of **18** and **19** was carried forward. Initial efforts focused on **24** in the hope that it would be possible to elaborate this α-hydroxy ketone to a phosphorane suitable for Wittig coupling with 4-decenal (**34**). This plan was thwarted by the instability of the α-chloro ketone from **24**, and the more tractable aldehyde **26** was employed instead. The latter was most conveniently obtained in pure form by ozonolysis of its (2,4-dinitrophenyl)-hydrazone **28**.

The coupling partner for **26**, (1*E*,5*Z*)-1-iodo-1,5-undecadiene (**35**), was prepared from (4*Z*)-4-decenal (**34**) using the homologation method of Takai.[21] Treatment of **35** with chromium(II) chloride,[22] followed by addition of **26**, afforded a 1:1 mixture of stereoisomeric alcohols **36** which was directly oxidized with Dess−Martin periodinane.[23] The resulting ketone possessed ^1H and ^{13}C NMR spectra identical with those recorded for **8** and thus completes the assignment of relative configuration to this



eicosanoid. Saponification of synthetic (−)-**8** afforded the hydroxy acid **7**, which rapidly relactonized in the presence of mineral acid or upon standing in $CDCl_3$.

In contrast to **7**, the constanolactones are optically active. Although the relative configurations at C5, C6, and C8 of **9** and **10** correspond to those of **8**, the absolute configuration at these stereogenic centers has been assigned as (5*R*,6*S*,8*S*), i.e. the reverse of the foregoing synthetic intermediates. Extrapolation of our biomimetic strategy applied to **7** toward **9** and **10** therefore required a tactical revision in which the pathway to (−)-**26** was modified in order to enter the antipodal series. A further change was mandated by the presence of a hydroxyl group at C12 in the constanolactones. This necessitated a more elaborate synthesis plan for the C10−C20 coupling partner which would accommodate (*S*) configuration at this center.

The chirality of the sequence leading to (−)-**26** was easily reversed by using (*R*,*R*)-(+)-diisopropyl tartrate in place of its enantiomer as the chiral adjuvant in Katsuki−Sharpless epoxidation of **14**−**17**. A series antipodal to that proceeding via **18**, **20**, **22**, and **28**, then led to (+)-**37**, the enantiomer of **26**. Synthesis of (3*S*,1*E*,5*Z*)-3-hydroxy-1-iodo-1,5-undecadiene (**48**), the coupling partner for **37**, began from D-arabinose (**38**) and was patterned after a route to (2*S*,4*Z*)-2-hydroxy-4-decenal

(20) Wiberg, K. B.; Shobe, D.; Nelson, G. L. *J. Am. Chem. Soc.* **1993**, *115*, 10645.

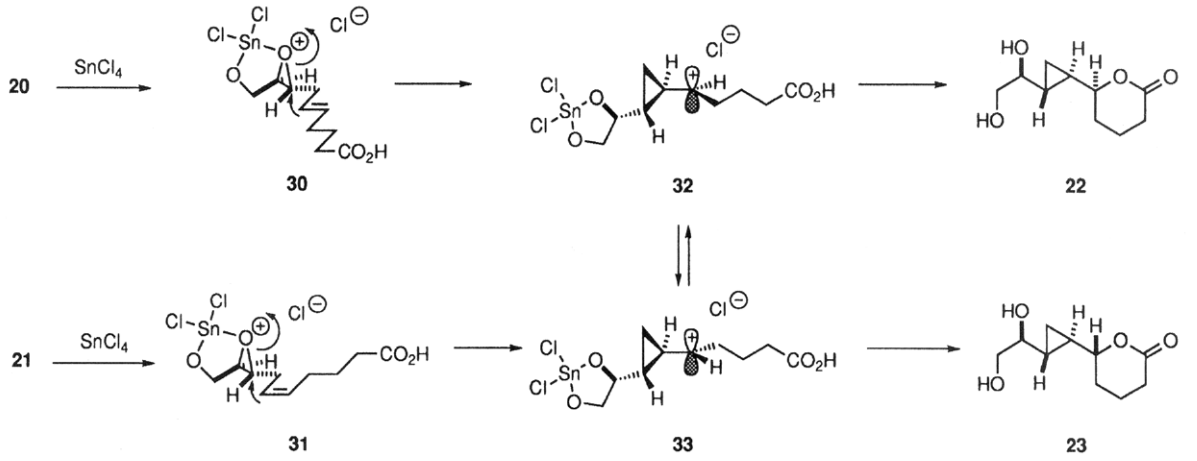
(21) Takai, K.; Nitta, K.; Utimoto, K. *J. Am. Chem. Soc.* **1986**, *108*, 7408.

(22) Jin, H.; Uenishi, J.; Christ, W. J.; Kishi, Y. *J. Am. Chem. Soc.* **1986**, *108*, 5644.

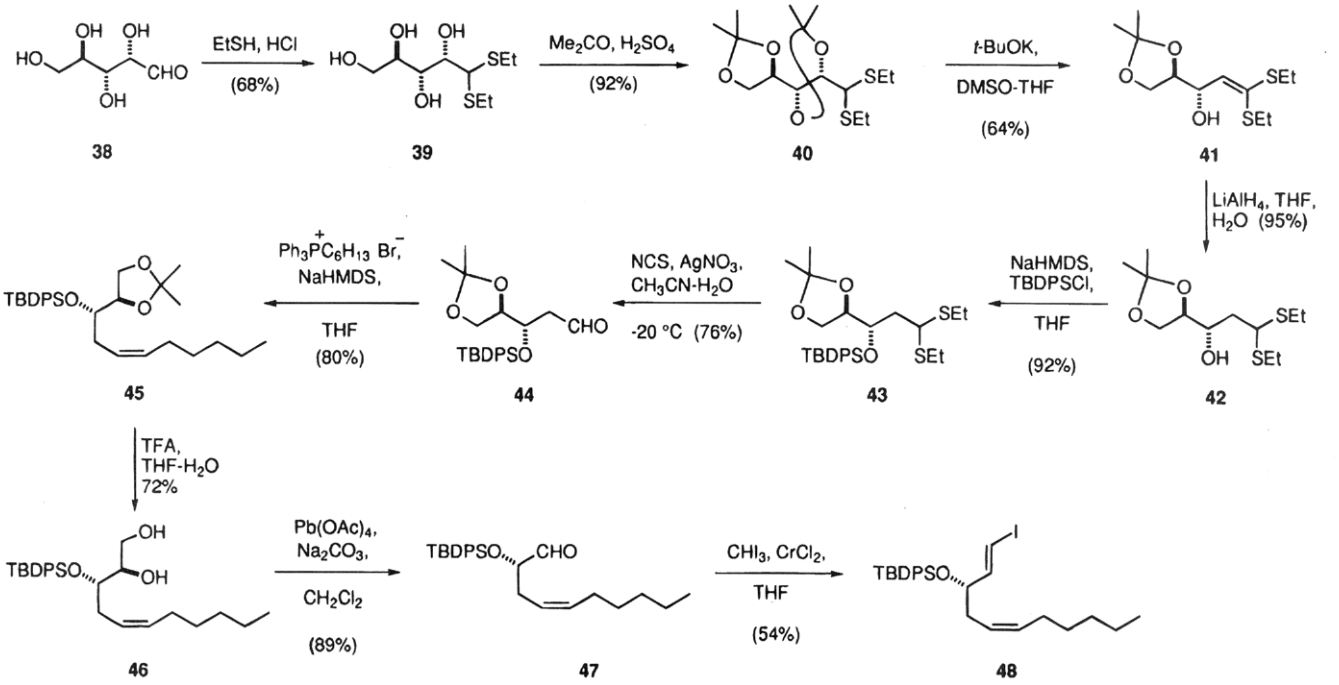
(23) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277.

(24) (a) Leblanc, Y.; Fitzsimmons, B. J.; Adams, J.; Perez, F.; Rokach, J. *J. Org. Chem.* **1986**, *51*, 789. (b) Zamboni, R.; Rokach, J. *Tetrahedron Lett.* **1982**, *23*, 2631. (c) Adams, J.; Leblanc, Y.; Rokach, J. *Tetrahedron Lett.* **1984**, *25*, 1227.

Scheme 2

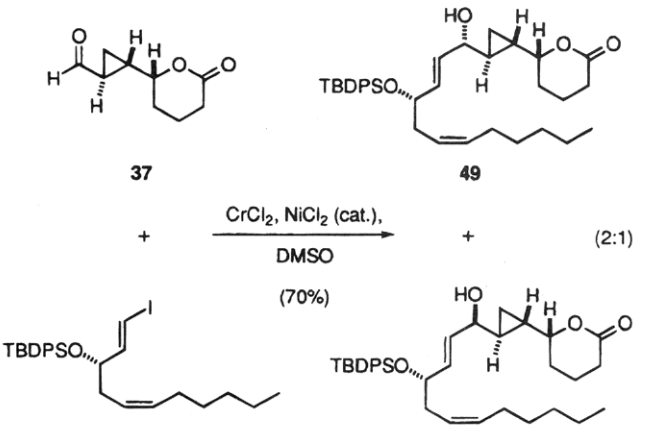


Scheme 3



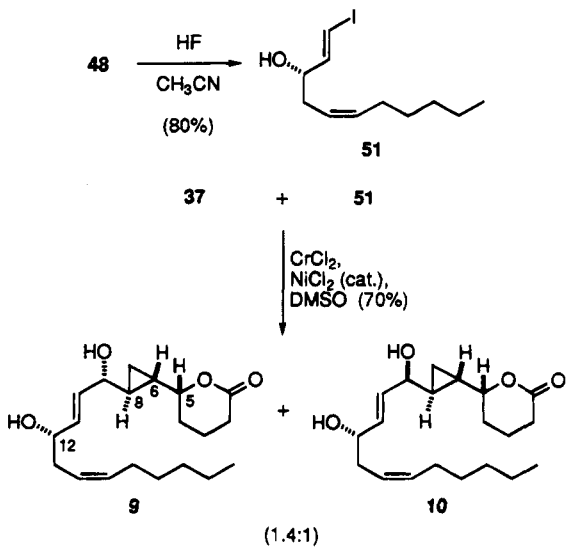
reported from the Merck Frosst laboratories (Scheme 3).[24] The route employs chemistry initially developed by Gray[25] to reach **44** and involves conversion of arabinose to its thioacetal **39**, which was protected as the bis(acetonide) **40**. Base-promoted elimination led to thioketene acetal **41**, the hydroxyl group of which directed a hydride reduction to give the deoxy sugar derivative **42**.[26] The latter was protected as its *tert*-butyldiphenylsilyl (TBDPS) ether **43**, using sodium bis(trimethylsilyl)amide as a base, and the thioacetal was removed with *N*-chlorosuccinimide and silver(I) nitrate[27] to afford **44**. A Wittig olefination of this aldehyde with the ylide prepared from *n*-hexyltriphenylphosphonium bromide yielded (*Z*) alkene **45**, from which the acetonide was removed by acidic hydrolysis. Oxidative cleavage of the resulting diol **46** furnished the protected decenal **47**, which upon Takai olefination[21] produced **48**.

Steric considerations suggest that the aldehyde carbonyl of **37** should undergo nucleophilic attack preferentially from the *si* face since, in the more favorable bisected conformation, access to this side of the C=O bond is opposed only by the methylene hydrogens of the cyclopropane. In the event, treatment of **48** with chromium(II) chloride and a catalytic quantity of nickel(II) chloride[22] followed by **37** yielded a 2:1 mixture of two alcohols which were separated by high-pressure liquid chromatography. The major alcohol **49** showed ^{1}H NMR spectral characteristics similar to those of constanolactone A (**9**), suggesting that this isomer possessed (9*S*) configuration, whereas the minor alcohol **50** corresponded more closely to constano-



(25) Wong, M. Y. H.; Gray, G. R. *J. Am. Chem. Soc.* **1978**, *100*, 3548.
(26) Micovic, V. M.; Mihailovic, M. L. J. *J. Org. Chem.* **1953**, *18*, 1190.
(27) Corey, E. J.; Erickson, B. W. *J. Org. Chem.* **1971**, *36*, 3553.

lactone B (**10**). However, the final, seemingly trivial task of removing the silyl protecting group from **49** and **50** proved to be insuperable, all conventional reagents for this purpose affording products from decomposition of the sensitive cyclopropane-containing structures. The problem was conveniently solved by removing the *tert*-butyldiphenylsilyl blocking group from **48** and using **51** in a Nozaki–Kishi coupling[22] with **37**.



In this case, a 1.4:1 mixture of constanolactones A and B were produced which, after separation by high-pressure liquid chromatography, exhibited chromatographic behavior as well as infrared, ^{1}H NMR, and ^{13}C NMR spectra in excellent agreement with those of the natural materials. Comparison of optical rotations of synthetic and natural **9** and **10** left no doubt that constanolactones A and B are correctly represented in the absolute configuration shown. However, **9** was found to exhibit mutarotation in methanol, and examination of this process revealed that the δ-lactone undergoes facile methanolysis to yield the hydroxy ester in this solvent.

In conclusion, the synthesis of constanolactones A and B confirms that these eicosanoids possess (5*R*,6*S*,8*S*,12*S*) absolute configuration and differ only with respect to the configuration at C9. The biomimetic cyclization exploited successfully en route to **7**, **9**, and **10** lends credence to the Corey–Brash hypothesis outlined in Scheme 1 but raises a troubling issue with regard to stereochemistry. It appears that in vivo cyclization of (8*R*)-**3** would lead to a cyclopropane with absolute configuration at C6 and C8 opposite to that found in the constanolactones. On the other hand, **9** and **10** could originate from the (8*S*) enantiomer of **3**, thus requiring a further extension of the original Corey proposal.

Experimental Section

Starting materials and reagents purchased from commercial suppliers were generally used without further purification. Solvents were dried by distillation from the appropriate drying agent immediately prior to use. Tetrahydrofuran was distilled from sodium and benzophenone under an argon atmosphere. Diisopropylamine, triethylamine, dimethyl sulfoxide, and dichloromethane were distilled from calcium hydride under argon. Nitromethane was distilled and stored under argon over anhydrous calcium chloride. All solvents used for routine isolation of products and chromatography were reagent grade and glass distilled. Air- and moisture-sensitive reactions were performed under an argon atmosphere.

Concentration under reduced pressure refers to the use of a rotary evaporator at water aspirator pressures. Residual solvent was removed under high vacuum at less than 1 Torr. Reaction flasks were flame dried under a stream of argon. Syringes were oven dried at 190 °C and cooled in a desicator over anhydrous calcium sulfate.

Analytical thin-layer chromatography was performed using precoated aluminum TLC plates (0.2 mm layer thickness of silica gel 60 F-254). Column chromatography was carried out using silica gel 60 (230–400 mesh ASTM). For radial chromatography a Harrison Associates 7924T chromatotron was used.

Melting points were measured on a Büchi melting point apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer 243 polarimeter at ambient temperature using a 1 dm cell of 1 mL capacity. Infrared spectra were recorded on a Nicolet 5DXB FT-IR spectrometer. Carbon and proton nuclear magnetic resonance spectra were recorded on either a Bruker AC-300 or Bruker AM-400 spectrometer. Chemical shifts are reported in parts per million downfield from tetramethylsilane on the δ scale. ^{1}H NMR data are reported in the order of chemical shift, number of protons, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad, etc.), and coupling constant in hertz (Hz). Electron impact (EI) mass spectra were determined on a Varian MAT 311 spectrometer, chemical ionization (CI) mass spectra were obtained with a Finnigan 4023 spectrometer, and fast atom bombardment (FAB) mass spectra were measured on a Kratos MS-50 RFTC mass spectrometer. The X-ray crystal structure of **29** was determined with a Siemens P-4 diffractometer. Elemental analyses were performed by Desert Analytics, Tucson, AZ.

Methyl 5-Hexynoate (11). To a solution of 5-hexynoic acid (0.501 g, 4.47 mmol) in anhydrous ether (5 mL) was added dropwise an ethereal solution of diazomethane until a yellow color persisted. The solvent was removed to yield 0.533 g (95%) of **11** as a colorless oil: bp 98–100 °C (70 mmHg); IR (neat) 3296, 2954, 2114, 1739, 1250, 642 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.84 (2H, pent, J = 7 Hz), 1.97 (1H, t, J = 3 Hz), 2.26 (2H, dt, J = 3, 7 Hz), 2.46 (2H, t, J = 7 Hz), 3.67 (3H, s); ^{13}C NMR ($CDCl_3$) δ 17.8, 23.5, 32.6, 51.5, 69.1, 83.2, 173.5. Anal. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.36; H, 7.93.

(*E*)-Methyl 6-(Tri-*n*-butylstannyl)-5-hexenoate (12) and (*Z*)-Methyl 6-(Tri-*n*-butystannyl)-5-hexenoate (13). A mixture of tri-*n*-butyltin hydride (7.31 g, 25.13 mmol), **11** (3.17 g, 25.13 mmol), and azobis(isobutyronitrile) (0.10 g, 0.63 mmol) was heated slowly to 65 °C and kept at that temperature for 2 h. The cooled mixture was purified by chromatography on silica, using 10% ethyl acetate in hexane as eluant, to yield 9.36 g (89%) of a 4:1 mixture of **12** and **13**, respectively, as a colorless oil: bp 150–153 °C (0.52 mmHg); IR (neat) 2957, 2927, 2850, 1744, 1599, 1460, 1199 cm^{-1}; ^{1}H NMR ($CDCl_3$) (*E* isomer) δ 0.88 (15H, m), 1.31 (6H, m), 1.46 (6H, m), 1.73 (2H, m, J = 8 Hz), 2.16 (2H, m), 2.30 (2H, t, J = 8 Hz), 3.66 (3H, s), 5.90 (2H, m); (*Z* isomer) 0.88 (15H, m),1.31 (6H, m), 1.46 (6H, m), 1.73 (2H, m), 2.05 (2H, dt, J = 7, 7 Hz), 2.31 (2H, t, J = 8 Hz), 3.65 (3H, s), 5.82 (1H, d, J = 12 Hz), 6.46 (1H, dt, J = 12, 7 Hz); ^{13}C NMR ($CDCl_3$) (*E* isomer) δ 9.4, 13.7, 24.0, 27.3, 29.1, 33.3, 37.0, 51.4, 128.7, 148.0, 174.2; MS (EI) m/z 361 ($M^+ - C_4H_9$), 327, 305, 213, 177, 151; HRMS m/z 361.1191 (calcd for $C_{15}H_{29}O_2Sn$ ($M^+ - C_4H_9$) 361.1190). Anal. Calcd for $C_{19}H_{38}O_2Sn$: C, 54.70; H, 9.39. Found: C, 54.89; H, 9.39.

(5*E*,8*E*)-Methyl 10-Hydroxy-5,8-decadienoate (14), (5*Z*,8*E*)-Methyl 10-Hydroxy-5,8-decadienoate (15), (*E*)-Methyl 7-(Hydroxymethyl)-5,8-nonadienoate (16), and (*Z*)-Methyl 7-(Hydroxymethyl)-5,8-nonadienoate (17). To a solution containing a mixture of **12** and **13** (1.25 g, 3.0 mmol) in dimethylformamide (20 mL) were added water (0.54 mL, 30.0 mmol), butadiene monoepoxide (0.24 mL, 3.0 mmol), and palladium dichloride acetonitrile complex (78 mg, 0.30 mmol). The yellow solution was stirred at room temperature for 0.5 h, and the dimethylformamide was removed under high vacuum. The black residue was purified by chromatography on silica, using 50% ethyl acetate in hexane as the eluant, to give 0.557 g (94%) of a 4:1 mixture of **14**, **15** and **16**, **17**, respectively, as a colorless oil. The pairs of geometrical isomers were separated by chromatography on silica, using 5% methanol in dichloromethane as eluant.

14, **15**: IR (neat) 3413, 3004, 2952, 1743, 1671, 1438, 1220, 971 cm^{-1}; ^{1}H NMR (**14**) ($CDCl_3$) δ 1.26 (1H, t, J = 7 Hz), 1.70 (2H, m, J = 7 Hz), 2.05 (2H, m), 2.31 (2H, dt, J = 7, 3 Hz), 2.74 (2H, m), 3.67 (3H, s), 4.11 (2H, b), 5.41 (2H, m), 5.66 (2H, m); ^{13}C NMR (**14**) ($CDCl_3$) δ 24.5, 31.8, 33.3, 35.1, 51.5, 63.5, 128.7, 129.5, 130.3, 131.2,

174.3; MS (EI) *m/z* 180 ($M^+ - H_2O$), 148, 120, 106, 84; HRMS *m/z* 180.1150 (calcd for $C_{11}H_{16}O_2$ ($M^+ - H_2O$) 180.1151).

16, 17: IR (neat) 3427, 2997, 2952, 1738, 1637, 1438, 1217 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.56 (1H, t, J = 6 Hz), 1.72 (2H, m, J = 7 Hz), 2.08 (2H, q, J = 7 Hz), 2.31 (2H, t, J = 7 Hz), 2.91 (1H, m, J = 7 Hz), 3.52 (2H, t, J = 6 Hz), 3.67 (3H, s), 5.11 (1H, d, J = 7 Hz), 5.15 (1H, s), 5.35 (1H, dd, J = 15, 7 Hz), 5.53 (1H, m), 5.72 (1H, m); ^{13}C NMR ($CDCl_3$) δ 24.4, 32.0, 33.3, 49.7, 51.5, 65.2, 116.7, 129.7, 132.1, 137.8, 174.0; MS (EI) *m/z* 182, 168, 136, 121, 107, 93, 79; HRMS *m/z* 168.1149 (calcd for $C_{10}H_{16}O_2$ ($M^+ - CH_2O$) 168.1150).

(8*R*,9*R*)-(*E*)-Methyl 8,9-Epoxy-10-hydroxy-5-decenoate (18) and (8*R*,9*R*)-(*Z*)-Methyl 8,9-Epoxy-10-hydroxy-5-decenoate (19). To a stirred solution of titanium tetraisopropoxide (0.55 mL, 1.85 mmol) in dichloromethane (7 mL) at −70 °C was added (−)-diethyl tartrate (0.39 mL, 2.28 mmol) followed by a solution containing a mixture of **14** and **15** (470 mg, 2.37 mmol) in dichloromethane (8 mL). After 15 min, *tert*-butyl hydroperoxide (0.68 mL of a 7.3 M solution in isooctane, 5.00 mmol) was added dropwise and the resulting mixture was allowed to warm to 0 °C during 2 h. A solution containing ferrous sulfate (1.50 g) and tartaric acid (0.60 g) in water (6 mL) was added, and the two-phase mixture was extracted with ether (2 × 25 mL). The combined extracts were dried (sodium sulfate), and the solvent was evaporated. The residue was purified by chromatography on silica, using 33% ethyl acetate in hexane as eluant, to give 462 mg (91%) of **18** and **19** as a 4:1 mixture, respectively. These were separated by radial chromatography, using gradient elution from 20% to 100% ethyl acetate in hexane and a rotor coated with silica impregnated with 4% silver nitrate.

18: $[\alpha]^{23}_D$ +12.8° (*c* 2.62, $CHCl_3$); IR (neat) 3400, 2949, 2872, 2850, 1737, 1438, 1203 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.68 (2H, m), 2.06 (3H, m), 2.29 (4H, m), 2.93 (1H, dt, J = 4, 2 Hz), 2.98 (1H, dt, J = 5, 2 Hz), 3.64 (3H, s), 3.88 (1H, ddd, J = 13, 5, 3 Hz), 5.45 (2H, m); ^{13}C NMR ($CDCl_3$) δ 24.3, 31.8, 33.3, 34.4, 51.5, 55.1, 57.9, 61.6, 125.1, 132.5, 174.0; MS (EI) *m/z* 214 (M^+), 154, 140, 105, 94, 80; HRMS *m/z* 214.1204 (calcd for $C_{11}H_{18}O_4$ (M^+) 214.1205). Anal. Calcd for $C_{11}H_{18}O_3$: C, 61.66; H, 8.47. Found: C, 61.40; H, 8.63.

19: $[\alpha]^{23}_D$ +10.0° (*c* 0.25, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.69 (2H, m), 1.84 (1H, b), 2.08 (2H, q), 2.31 (4H, m), 2.98 (2H, m), 3.63 (1H, m), 3.66 (3H, s), 3.90 (1H, ddd, J = 13, 5, 3 Hz), 5.47 (2H, m); ^{13}C NMR ($CDCl_3$) δ 24.6, 26.6, 29.2, 33.3, 51.5, 55.1, 57.8, 61.5, 124.1, 131.8, 174.0; MS (EI) *m/z* 197 ($M^+ - OH$), 183 ($M^+ - OCH_3$), 165, 154, 140, 123, 105, 94, 80; HRMS *m/z* 183.1022 (calcd for $C_{10}H_{15}O_3$ ($M^+ - OCH_3$) 183.1022).

(8*R*,9*R*)-(*E*)-8,9-Epoxy-10-hydroxy-5-decenoic Acid (20). A stirred solution of **18** (71.8 mg, 0.34 mmol) in 50% aqueous tetrahydrofuran (10 mL) was cooled to 0 °C, and lithium hydroxide (139 mg, 3.4 mmol) was added in one portion. After 1 h, the solution was acidified with 1% aqueous hydrochloric acid (12 mL) and the mixture was extracted with ethyl acetate (6 × 20 mL). The combined extracts were dried (sodium sulfate), and the solvent was evaporated. The residue was purified by radial chromatography, using a 1 mm silica-coated rotor with 1% formic acid and 10% methanol in chloroform as eluant, to give 66.2 mg (99%) of **20** as a colorless, waxy solid: $[\alpha]^{23}_D$ +15.6° (*c* 1.78, MeOH); IR (neat) 3400, 3077, 2996, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.70 (2H, m), 2.07 (2H, m), 2.33 (4H, m), 2.97 (1H, m), 3.02 (1H, m), 3.77 (2H, ddd, J = 7, 9, 3 Hz), 5.47 (2H, m), 6.13 (1H, b); ^{13}C NMR ($CDCl_3$) δ 24.0, 31.8, 33.2, 34.4, 55.4, 58.2, 61.5, 125.1, 132.5, 179.0; MS (CI) *m/z* 201 (M^+ + 1), 183, 165, 147, 137, 123, 119, 81; HRMS *m/z* 201.1126 (calcd for $C_{10}H_{17}O_4$ (M^+ + 1) 201.1127).

(8*R*,9*R*)-(*E*)-8,9-Epoxy-10-hydroxy-5-decenoic Acid (21). A stirred solution of **19** (29.1 mg, 0.14 mmol) in 50% aqueous tetrahydrofuran (5 mL) was cooled to 0 °C, and lithium hydroxide (56.5 mg, 1.36 mmol) was added in one portion. After 1 h, the solution was acidified with 1% aqueous hydrochloric acid (7 mL) and the mixture was extracted with ethyl acetate (7 × 10 mL). The combined extracts were dried (sodium sulfate), and the solvent was evaporated. The residue was purified by radial chromatography, using a 1 mm silica-coated rotor with 1% formic acid and 10% methanol in chloroform as eluant, to give 26.8 mg (99%) of **21** as a colorless, waxy solid: $[\alpha]^{23}_D$ +11.5° (*c* 0.58, $CHCl_3$); IR (neat) 3400, 2936, 2877, 1710, 1237, 1023 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.71 (2H, tt, J = 7, 7 Hz), 2.11 (2H, q, J = 7 Hz), 2.36 (4H, m), 3.00 (2H, m), 3.63 (1H, dd, J = 13, 4 Hz), 3.90 (1H, dd, J = 13, 3 Hz), 5.48 (2H, m); ^{13}C NMR ($CDCl_3$) δ 24.3, 26.5, 29.2, 33.1, 55.3, 58.1, 61.6, 124.3, 131.8, 178.4; MS (CI) *m/z* 201 (M^+ + 1), 183, 165, 147, 137, 123, 119, 81; HRMS *m/z* 201.1128 (calcd for $C_{10}H_{17}O_4$ (M^+ + 1) 201.1127).

[1α(*S*),2β(*S*)]-6-[2-(1,2-Dihydroxyethyl)cyclopropyl]tetrahydro-2*H*-pyran-2-one (22) and [1α(*R*),2β(*S*)]-6-[2-(1,2-Dihydroxyethyl)-cyclopropyl]tetrahydro-2*H*-pyran-2-one (23). To a solution of a 4:1 mixture of **18** and **19** (65.9 mg, 0.33 mmol) in nitromethane (20 mL) at 0 °C was added stannic chloride (96.3 mL, 0.82 mmol) dropwise. The solution was stirred for 1.5 h, and 10% aqueous sodium carbonate (10 mL) was added. The mixture was extracted with ether (1 × 20 mL) and with ethyl acetate (6 × 20 mL), and the combined extracts were dried (sodium sulfate). The solvent was evaporated to give 41.9 mg (64%) of a 1.5:1 mixture of **22** and **23** as a colorless oil: IR (neat) 3400, 2926, 1727, 1245, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.61 (0.5H, m), 0.76 (1H, m), 1.03 (1.5H, m), 1.87−1.73 (1H, m), 2.07−1.91 (3H, m), 2.50 (2H, m), 3.19 (1H, m), 3.66 (2H, m), 3.77 (1H, m); ^{13}C NMR ($CDCl_3$) (major diastereomer) δ 7.0, 18.3, 19.8, 20.3, 27.8, 29.4, 66.2, 74.6, 84.4, 172.2. This material decomposed upon standing for several hours or upon chromatography.

[1α(*S*),2β]-Tetrahydro-6-[2-(hydroxyacetyl)cyclopropyl]-2*H*-pyran-2-one (24) and [1α(*R*),2β]-Tetrahydro-6-[2-(hydroxyacetyl)-cyclopropyl]-2*H*-pyran-2-one (25). To a stirred solution of a freshly prepared mixture of **22** and **23** (77.5 mg, 0.39 mmol) and hexa-*n*-butyldistannoxane (289 mg, 0.50 mmol) in dichloromethane (30 mL) was added bromine (80.4 mL, 0.50 mmol) dropwise. After 15 min, the solvent was removed and the residue was purified by chromatography on silica, using ether followed by 10% methanol in ether as eluant, to yield 43.6 mg (57%) of a mixture of **24** and **25** as a colorless oil. Separation of the mixture by radial chromatography on a 1 mm silica-coated rotor, using a gradient of 3% to 10% methanol in ether as eluant, gave 5.3 mg of pure **24** followed by 33.0 mg of a mixed fraction containing **24** and **25**.

24: $[\alpha]^{23}_D$ −88.4° (*c* 0.38, $CHCl_3$); IR (neat) 3400, 2956, 2922, 1731, 1715, 1247, 1044 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.11 (1H, ddd, J = 8, 7, 4 Hz), 1.41 (1H, ddd, J = 10, 5, 4 Hz), 1.61−1.78 (2H, m), 1.79−1.90 (2H, m), 1.98 (1H, m), 2.03 (2H, m), 2.33−2.64 (2H, m), 3.85 (1H, ddd, J = 11, 7, 3 Hz), 4.46 (2H, ABq, J = 19 Hz); ^{13}C NMR ($CDCl_3$) δ 14.3, 18.4, 22.1, 28.0, 28.8, 29.5, 68.7, 81.3, 170.8, 208.0; MS (EI) *m/z* 198, 177, 167, 135, 119, 88, 83.

Hydrazones 28 and 29. To a solution of a freshly prepared mixture of **22** and **23** (126.2 mg, 0.63 mmol) in ether (40 mL) at 0 °C were added sodium metaperiodate (148 mg, 0.69 mmol) and water (3 mL). After 15 min, the layers were separated and the aqueous phase was extracted with ethyl acetate (2 × 20 mL). The combined extracts were evaporated to yield 99.1 mg (93%) of a mixture of **26** and **27** as a yellow oil. This mixture was used without further purification.

To a solution of **26** and **27** (54.4 mg, 0.32 mmol) in ethanol (5 mL) were added (2,4-dinitrophenyl)hydrazine (70.5 mg, 0.36 mmol) and acetic acid (20 mL). The mixture was stirred for 16.5 h, during which the orange suspension became yellow and a flocculent precipitate was formed. The solvent was evaporated, and the residual orange solid was purified by radial chromatography on a 1 mm silica-coated rotor, using a gradient from 50% ethyl acetate in hexane to 100% ethyl acetate as eluant, to give 104 mg (92%) of a 1.5:1 mixture of **28** and **29**, respectively, as a pale yellow solid. These diastereomers were separated by medium-pressure liquid chromatography on silica (1.5 × 30 cm, 85 psi, 27 mg of sample in dichloromethane (1 mL) for each run, 0.1% acetic acid and 50% ethyl acetate in hexane as eluant, UV detection at 300 nm).

28: mp 209−210 °C; $[\alpha]^{23}_D$ + 90.1° (*c* 0.94, $CHCl_3$); IR (neat) 3295, 1730, 1664, 1619, 1588, 1514, 1334 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.12 (1H, ddd, J = 9, 6, 6 Hz), 1.19 (1H, ddd, J = 9, 6, 5 Hz), 1.57 (1H, m), 1.76 (1H, m), 1.86 (1H, m), 1.98 (2H, m), 2.06 (1H, m), 2.56 (2H, m), 3.90 (1H, ddd, J = 11, 8, 3 Hz), 7.28 (1H, d, J = 7 Hz), 7.88 (1H, d, J = 10 Hz), 8.29 (1H, dd, J = 10, 3 Hz), 9.11 (1H, d, J = 3 Hz), 11.04 (1H, s); ^{13}C NMR ($CDCl_3$) δ 11.2, 18.5, 19.0, 25.9, 27.9, 29.5, 82.1, 116.4, 123.5, 128.8, 130.0, 137.8, 144.8, 152.5, 170.9; MS (EI) *m/z* 348 (M^+), 331, 302, 261, 214; HRMS *m/z* 348.1070 (calcd for $C_{15}H_{16}N_4O_6$ (M^+) 348.1070). Anal. Calcd for $C_{15}H_{16}N_4O_6$: C, 51.72; H, 4.63; N, 16.09. Found: C, 51.72; H, 4.49; N, 15.87.

29: mp 191−193 °C; $[\alpha]^{23}_D$ +95.8° (*c* 1.20, $CHCl_3$); IR (neat) 3294, 3016, 2954, 1729, 1665, 1618, 1589, 1514, 1333 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17 (1H, ddd, J = 9, 5, 3 Hz), 1.25 (1H, ddd, J = 9, 6, 5

Hz), 1.57 (1H, m), 1.70 (1H, m), 2.03−1.77 (3H, m), 2.07 (1H, m), 2.55 (2H, m), 4.06 (1H, ddd, J = 10, 7, 3 Hz), 7.23 (1H, d, J = 7 Hz), 7.88 (1H, d, J = 9, 2 Hz), 8.31 (1H, dd, J = 9, 2 Hz), 9.12 (1H, d, J = 2 Hz),11.05 (1H, s); ^{13}C NMR ($CDCl_3$) δ 11.2, 18.5, 19.0, 25.9, 27.9, 29.5, 82.1, 116.4, 123.5, 128.8, 129.9, 137.8, 144.8, 152.6,170.9; MS (EI) m/z 348 (M^+), 331, 302, 261, 214, 80; HRMS m/z 348.1070 (calcd for $C_{15}H_{16}N_4O_6$ (M^+) 348.1070). Compound **29** crystallized in the orthorhombic space group $P2(1)2(1)2(1)$ with a = 5.887 (2) Å, b = 12.967 (3) Å, c = 20.954 (4) Å, V = 1599.6(7) Å^3, Z = 4, and D_{calcd} = 1.446 g/cm^3. All 1244 nonequivalent reflections in the range of 3.5° < 2Θ < 95° were measured with graphite-monochromated Cu Kα radiation (λ = 1.54178 Å). The structure was solved by direct methods (SHELXTL) using 1031 unique reflections with $F > 4\sigma(F)$. Full matrix least squares refinement with anisotropic temperature factors for all non-hydrogen atoms and calculated hydrogen atom positions led to the final discrepancy indixes of R = 0.0321 and $_wR$ = 0.0283.

2-(Tetrahydro-6-oxo-2*H*-pyran-2-yl)-[1α,2β(*S*)]-cyclopropanecarboxaldehyde (26). A solution of **28** (49.3 mg, 0.14 mmol) in ethyl acetate (20 mL) was cooled to −78 °C, and ozone was bubbled through the orange solution until it turned blue-green. Dimethyl sulfide (0.5 mL) was added to the solution which was slowly warmed to room temperature. The solvent was removed, and the resulting oily residue was purified by radial chromatography on a 1 mm silica-coated rotor, with 25% ethyl acetate in hexane as eluant, to yield 15 mg (63%) of **26** as an oil: $[\alpha]^{23}_D$ −43.5° (c 2.39, $CHCl_3$); IR (neat) 2956, 1734, 1706, 1241, 1042 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.12 (1H, ddd, J = 8, 6, 5 Hz), 1.35 (1H, ddd, J = 9, 5, 5 Hz), 1.89−1.64 (3H, m), 1.93 (1H, m), 2.00 (1H, m), 2.07 (1H, m), 2.51 (2H, m), 3.91 (1H, ddd, J = 10, 7, 3 Hz), 9.35 (1H, d, J = 4 Hz); ^{13}C NMR ($CDCl_3$) δ 11.7, 18.3, 26.6, 26.9, 27.9, 29.4, 80.8, 170.7, 199.7; MS (EI) m/z 168 (M^+), 150, 140, 112, 95, 81; HRMS m/z 168.0786 (M^+, calcd for $C_9H_{12}O_3$ 168.0786).

(1*E*,5*Z*)-Iodo-1,5-undecadiene (35). A suspension of chromous chloride (0.74 g, 6.0 mmol) in tetrahydrofuran (10 mL) was cooled to 0 °C, and a solution of (*Z*)-4-decenal (**34**, 154 mg, 1.0 mmol) and iodoform (790 mg, 2.0 mmol) in tetrahydrofuran (5 mL) was added dropwise. After 3 h, the red suspension was poured into water (25 mL) and the mixture was extracted with ether (3 × 10 mL). The combined extracts were dried (magnesium sulfate) and concentrated to leave a brown oil. This was purified by chromatography on silica, with pentane as eluant, to give a purple oil which was taken up in pentane (3 mL) and cooled to −78 °C. A yellow precipitate of iodoform was deposited, and the supernatant was decanted. Evaporation of the supernatant gave 264 mg (95%) of **35** as an oil: IR (neat) 3007, 2956, 2926, 2871, 2856, 1465, 1457, 941 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (3H, t), 1.30 (6H, m), 2.00 (2H, m), 2.11 (2H, m), 2.18 (2H, m), 5.32 (1H, m), 5.40 (1H, m), 6.01 (1H, d, J = 15 Hz), 6.51 (1H, dt, J = 14, 7 Hz); ^{13}C NMR ($CDCl_3$) δ 14.1, 22.6, 26.1, 27.2, 29.3, 31.5, 36.0, 74.8, 127.7, 131.3, 146.0; MS m/z 278 (M^+), 207, 167, 151, 109, 95, 81, 69; HRMS m/z 278.0527 (calcd for $C_{11}H_{19}I$ 278.0531).

[1α(*S*),2β(1*R*,2*E*,6*Z*)]-Tetrahydro-6-[2-(1-hydroxy-2,6-dodecadienyl)cyclopropyl]-2*H*-pyran-2-one (36a) and [1α(*S*),2β(1*S*,2*E*,6*Z*)]-Tetrahydro-6-[2-(1-hydroxy-2,6-dodecadienyl)cyclopropyl]-2*H*-pyran-2-one (36b). To a mixture of **26** (14.2 mg, 0.08 mmol) and **35** (141 mg, 0.51 mmol) which had been thoroughly dried by addition of benzene, followed by azeotropic distillation, were added (in a glovebox under nitrogen) degassed dimethylformamide (4 mL), chromium(II) chloride (63 mg, 0.51 mmol), and nickel(II) chloride (0.5 mg, 0.003 mmol). The green solution was stirred at room temperature for 18 h and was poured into saturated, aqueous ammonium chloride. The resulting mixture was extracted with ether (3 × 15 mL), the combined extracts were dried (sodium sulfate), and the solvent was evaporated. The residue was purified by radial chromatography on a 1 mm silica-coated rotor, with gradient elution from 50% ethyl acetate in hexane to 100% ethyl acetate, to give 16.5 mg (61%) of **36a,b** as a colorless oil. This material was a 1:1 mixture of diastereomers at C9: IR (neat) 3430, 3005, 2955, 2925, 2855, 1730, 1242, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.57 (1.5H, m), 0.68 (0.5H, ddd, J = 9, 5, 5 Hz), 0.88 (3H, t, J = 7 Hz), 1.18−0.99 (2H, m), 1.29 (6H, m), 1.73−1.57 (2H, m), 1.85−1.74 (1H, m), 2.04−1.86 (4H, m), 2.11 (4H, m), 2.61−2.38 (2H, m), 3.62 (0.5H, t, J = 7 Hz), 3.79 (1.5H, m), 5.37 (2H, m), 5.52 (1H, dt, J = 16, 6 Hz), 5.69 (1H, m); ^{13}C NMR ($CDCl_3$) δ 6.3 (0.5), 6.5 (0.5), 14.0, 18.3, 19.8 (0.5), 21.2 (0.5), 22.5, 22.76 (0.5), 23.3 (0.5), 26.7, 27.1, 27.8, 29.3, 29.4, 31.4, 32.2, 73.8 (0.5), 74.8 (0.5), 82.8 (0.5), 83.0 (0.5), 128.6, 130.5, 130.9 (0.5), 131.1 (0.5), 131.9 (0.5), 132.0 (0.5), 171.4; MS (EI) m/z 320, 302, 193, 175, 83; HRMS m/z 320.2351 (calcd for $C_{20}H_{32}O_3$ 320.2351). The isomeric mixture was used in the following reaction.

[1α(*S*),2β(2*E*,6*Z*)]-Tetrahydro-6-[2-(1-oxo-2,6-dodecadienyl)cyclopropyl]-2*H*-pyran-2-one (8). To a solution of **36a,b** (8.0 mg, 0.025 mmol) in dichloromethane (1 mL) was added Dess−Martin periodinane (15.8 mg, 0.037 mmol), and the suspension was stirred at room temperature for 2 h. Ether (4 mL) was added, followed by 10% aqueous sodium sulfate (1.5 mL) and saturated, aqueous ammonium chloride (1.5 mL). After 5 min, the layers were partitioned and the separated aqueous layer was extracted with ether (3 × 4 mL). The combined extracts were dried (sodium sulfate), and the solvent was evaporated. The residue was purified by radial chromatography on a 1 mm silica-coated rotor, with 50% ethyl acetate in hexane as eluant, to yield 6.7 mg (84%) of **8** as a colorless oil: $[\alpha]^{23}_D$ −27.4° (c 0.46, $CHCl_3$); IR (neat) 3007, 2956, 2928, 2892, 2872, 2857, 1737, 1683, 1660, 1625, 1238, 1038 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (3H, t, J = 7 Hz), 0.98 (1H, ddd, J = 8, 6, 4 Hz), 1.29 (7H, m), 1.73 (2H, m), 1.83 (1H, m), 1.95 (1H, m), 2.02 (3H, m), 2.24 (2H, m), 2.29 (3H, m), 2.47 (1H, m), 2.57 (1H, m), 3.88 (1H, ddd, J = 10, 8, 3 Hz), 5.35 (1H, dt, J = 11, 7 Hz), 5.43 (1H, dt, J = 11, 7 Hz), 6.25 (1H, dt, J = 16, 1 Hz), 6.94 (1H, dt, J = 16, 7 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0, 14.1, 18.4, 22.6, 23.6, 25.8, 27.2, 28.1, 28.3, 29.3, 29.5, 31.5, 32.7, 81.8, 127.7, 130.6, 131.4, 147.2, 171.1, 198.2; MS (EI) m/z 318, 300, 247, 231, 208, 191, 149, 135, 121, 107, 95, 69; HRMS m/z 318.2194 (calcd for $C_{20}H_{30}O_3$ 318.2195).

Hydroxy Acid 7. A solution of **8** (3.3 mg, 0.010 mmol) in 50% aqueous tetrahydrofuran (1 mL) was cooled to 0 °C, and lithium hydroxide (4.2 mg, 0.10 mmol) was added. The solution was stirred for 1 h and was diluted with 1 M aqueous sodium bisulfate (0.5 mL). The mixture was extracted with ether (20 mL), and the extract was dried (sodium sulfate) and evaporated to yield 3.2 mg (96%) of pure **7** as a colorless oil: IR (neat) 3400 (br), 3008, 2956, 2926, 2857, 1711, 1656, 1623, 1457, 1407, 1243, 1205, 1170, 1112, 1081 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.89 (4H, m), 1.31 (8H, m), 1.59−1.68 (3H, m), 1.71−1.89 (2H, m), 2.02 (2H, q, J = 7 Hz), 2.16−2.35 (4H, m), 2.41 (3H, t, J = 7 Hz), 3.23 (1H, dt, J = 7, 5 Hz), 5.39 (2H, m), 6.24 (1H, dt, J = 16, 1 Hz), 6.93 (1H, dt, J = 16, 7 Hz). This substance underwent lactonization to **8** upon standing.

2-(Tetrahydro-6-oxo-2*H*-pyran-2-yl)-[1α,2β(*R*)]-(+)-cyclopropanecarboxaldehyde (37). Aldehyde **37** was prepared from **14**−**17** in the same manner described for its enantiomer **26** using (+)-diisopropyl tartrate: $[\alpha]^{23}_D$ +41.5° (c 0.83, $CHCl_3$).

D-Arabinose Diethyl Dithioacetal (39). To a solution of D-arabinose (**38**, 50.00 g, 0.33 mol) in 6 M hydrochloric acid (500 mL) was added dropwise ethyl mercaptan (41.38 g, 0.67 mol) over 20 min. After being stirred for 2.5 h the mixture was cooled to 0 °C and filtered. The collected solid was washed with cold water (500 mL) and air-dried to give 58.05 g (68%) of **39** as colorless plates: mp 125−127 °C (lit.[24] 124−126 °C); ^{1}H NMR (CD_3OD) δ 2.22 (6H, m), 2.59−2.76 (4H, m), 3.58 (1H, dd, J = 11, 6 Hz), 3.65 (1H, m), 3.77 (1H, dd, J = 11, 3 Hz), 3.82 (1H, dd, J = 10, 1 Hz), 3.95 (1H, dd, J = 8, 1 Hz), 4.03 (1H, dd, J = 9 Hz); ^{13}C NMR (CD_3OD) δ 14.8 (×2), 25.4 (×2), 56.2, 65.1, 72.0, 72.8, 73.1; MS m/z 256 (M^+), 177, 135, 105, 75; HRMS m/z 256.0803 (calcd for $C_9H_{20}O_4S_2$ (M^+) 256.0803).

2,3:4,5-Di-*O*-isopropylidene-D-arabinose Diethyl Dithioacetal (40). To a suspension of **39** (10.81 g, 42.17 mmol) in acetone (125 mL) at 0 °C was added concentrated sulfuric acid (1.5 mL). The resulting tan solution was warmed to room temperature and was stirred for 16 h. The acidic mixture was neutralized by addition of calcium hydroxide (4.0 g), and the precipitated solid was removed by filtration. The filtrate was evaporated, and the residual oil was chromatographed on neutral alumina, using benzene as eluant, to afford 12.98 g (92%) of **40** as a colorless oil: $[\alpha]^{23}_D$ +84.1° (c 1.39, MeOH) [lit[24] +83.3° (c 1.4, MeOH)]; IR (neat) 2986, 2931, 2875, 1453, 1376, 1239, 1216, 1156, 1097, 1062, 883 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (6H, q, J = 8 Hz), 1.34 (3H, s), 1.37 (3H, s), 1.41 (3H, s), 1.45 (3H, s), 2.73 (4H, m), 3.97 (1H, m), 4.04 (1H, d, J = 3 Hz), 4.08 (2H, d, J = 5 Hz), 4.13 (1H, dt, J = 8, 6 Hz), 4.30 (1H, dd, J = 7, 3 Hz); ^{13}C NMR ($CDCl_3$) δ 14.2, 14.3, 24.8, 25.1, 25.2, 26.5, 27.0, 27.2, 52.3, 67.6, 79.0, 84.3,

109.6, 110.1; MS m/z 336, 321, 217, 203, 177, 159, 143, 135; HRMS *m/z* 336.1428 (calcd for $C_{15}H_{28}O_4S_2$ 336.1429).

2-Deoxy-4,5-*O*-isopropylidene-D-*erythro*-pent-1-enose Diethyl Dithioacetal (41). To a solution of potassium *tert*-butoxide (5.00g, 44.6 mmol) in tetrahydrofuran (250 mL) and dimethyl sulfoxide (85 mL) at 23 °C was added dropwise over 15 min a solution of **40** (10.00 g, 29.7 mmol) in tetrahydrofuran (100 mL). The mixture was stirred for 1 h and was poured on to ice (500 g). The aqueous mixture was extracted with chloroform (3 × 250 mL), and the combined extracts were washed with cold water and dried (sodium sulfate). Removal of the solvent in vacuo and chromatography of the residual oil on neutral alumina, using 20% ethyl acetate in hexane as eluant, gave 5.29 g (64%) of **41** as a pale yellow oil: $[\alpha]^{23}_D$ +77.1° (*c* 0.89, $CHCl_3$) [lit.[24] +49.2° (*c* 0.9, $CHCl_3$)]; IR (neat) 3441, 2981 2928, 2875, 1584, 1452, 1376, 1259, 1214, 1067 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 (3H, t, J = 7 Hz), 1.26 (3H, t, J = 7 Hz), 1.36 (3H, s), 1.44 (3H, s), 2.32 (1H, d, J = 3 Hz), 2.94−2.69 (4H, m), 3.88 (1H, dd, J = 8, 8 Hz), 3.99 (1H, dd, J = 8, 7 Hz), 4.17 (1H, dt, J = 7, 4 Hz), 4.90 (1H, ddd, J = 8, 4, 4 Hz), 5.92 (1H, d, J = 8 Hz); ^{13}C NMR ($CDCl_3$) δ 13.8, 15.0, 25.2, 26.3, 27.0, 27.5, 65.0, 69.5, 77.9, 109.3, 133.0, 135.5; MS *m/z* 278.1, 263.1, 217.1, 203.1, 177.0; HRMS *m/z* 278.1010 (calcd for $C_{12}H_{22}O_3S_2$ 278.1010).

2-Deoxy-4,5-*O*-isopropylidene-D-*erythro*-pentose Diethyl Dithioacetal (42). To a stirred suspension of lithium aluminum hydride (2.41 g, 63.50 mmol) in tetrahydrofuran (250 mL) at 0 °C was added a solution of **41** (4.42 g, 15.88 mmol) in tetrahydrofuran (80 mL) over 20 min. After the addition was complete the mixture was allowed to warm to room temperature and was stirred for a further 3.5 h. Residual lithium aluminum hydride was quenched by sequential addition of water (2 mL), 15% aqueous sodium hydroxide (2 mL), and water (7 mL). The resulting mixture was filtered through Celite, and the collected solid was washed with ether (2 × 100 mL). The filtrate was washed with brine and dried (sodium sulfate), and the solvent was removed in vacuo to leave 4.22 g (95%) of **42** as a colorless oil: $[\alpha]^{23}_D$ −4.2° (*c* 1.49, $CHCl_3$) [lit.[24] −7.8° (*c* 1.3, $CHCl_3$)]; IR (neat) 3443, 2969, 2929, 2874, 1453, 1374, 1261, 1216, 1156, 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (3H, t, J = 7 Hz), 1.28 (3H, t, J = 8 Hz), 1.36 (3H, s), 1.42 (3H, s), 1.86 (1H, ddd, J = 15, 9, 5 Hz), 2.01 (1H, ddd, J = 15, 9, 2 Hz), 2.55 (1H, bs), 2.76−2.59 (4H, m), 4.09−3.90 (5H, m); ^{13}C NMR ($CDCl_3$) δ 13.8, 14.3, 14.4, 23.7, 24.3, 25.1, 26.5, 48.1, 65.5, 69.7, 78.3, 109.2; MS *m/z* 280, 265, 247, 221, 177, 162, 143, 117, 89, 75; HRMS *m/z* 280.1166 (calcd for $C_{12}H_{24}O_3S_2$ 280.1167).

3-*O*-(*tert*-Butyldiphenylsilyl)-2-deoxy-4,5-*O*-isopropylidene-D-*erythro*-pentose Diethyl Dithioacetal (43). To a solution of **42** (3.00 g, 10.69 mmol) in tetrahydrofuran (100 mL) at −78 °C was added dropwise a solution of sodium bis(trimethylsilyl)amide (11.2 mL of a 1.0 M solution in tetrahydrofuran, 11.2 mmol). The mixture was stirred for 0.5 h, and a solution of *tert*-butylchlorodiphenylsilane (3.53 g, 12.83 mmol) in tetrahydrofuran (10 mL) was added dropwise. The solution was allowed to warm to 15 °C over 6 h and was stirred for 16 h. The solvent was removed, and the residual oil was purified by chromatography on silica, using 5% ethyl acetate in hexane as eluant, to yield 5.12 g (92%) of **43** as a colorless oil: $[\alpha]^{23}_D$ +16.4° (*c* 2.62, $CHCl_3$); IR (neat) 2963, 2931, 2893, 2860, 1428, 1375, 1261, 1213, 1110, 1074, 740, 705, 610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05 (9H, s), 1.10 (3H, t, J = 8 Hz), 1.12 (3H, t, J = 7 Hz), 1.27 (3H, s), 1.31 (3H, s), 2.02 (2H, m), 2.42 (4H, m), 3.59 (1H, dd, J = 8, 6 Hz), 3.84 (1H, dd, J = 8, 6 Hz), 3.90 (1H, dd, J = 9, 6 Hz), 4.10 (2H, m), 7.40 (6H, m), 7.72 (4H, m); ^{13}C NMR ($CDCl_3$) δ 14.2, 14.3, 19.4, 22.9, 23.8, 25.2, 26.3, 26.9, 40.6, 47.8, 66.8, 72.0, 79.0, 109.1, 127.5, 127.6, 129.7, 133.4, 133.6, 135.9, 136.0; MS *m/z* 518 ($M^+ - C_4H_9$), 503, 461, 403, 341, 199, 135, 103, 75; HRMS *m/z* 518.2344 (calcd for $C_{28}H_{42}O_3S_2Si$ 518.2345).

3-*O*-(*tert*-Butyldiphenylsilyl)-2-deoxy-4,5-*O*-isopropylidene-D-*erythro*-pentose (44). To a stirred mixture of water (5 mL) and acetonitrile (25 mL) at −20 °C was added *N*-chlorosuccinimide (0.95 g, 7.14 mmol) and silver nitrate (1.23 g, 7.27 mmol), followed by a solution of **43** (1.07 g, 2.07 mmol) in acetonitrile (6 mL). After 10 min, dimethyl sulfoxide (0.60 mL) was added, and after an additional 10 min, a 25% aqueous solution of sodium acetate (12 mL) was added. The stirred suspension was allowed to warm to 0 °C and was filtered through Celite. The collected solid was washed with water (3 mL) and with dichloromethane (15 mL), and the filtrate was partitioned. The aqueous layer was extracted with dichloromethane (3 × 15 mL), and the combined extracts were dried (sodium sulfate). Removal of the solvent left a yellow oil which was purified by chromatography on silica, using 20% ethyl acetate in hexane as eluant, to give 0.65 g (76%) of **44** as a colorless oil: $[\alpha]^{23}_D$ −3.6° (*c* 3.78, $CHCl_3$) [lit.[23] −6.9° (*c* 0.54, $CHCl_3$)]; IR (neat) 3072, 3051, 2986, 2958, 2934, 2892, 2859, 1726, 1470, 1428, 1376, 1214, 1110, 1073, 705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 (9H, s), 1.26 (3H, s), 1.28 (3H, s), 2.56 (2H, m), 3.59 (1H, m), 3.93 (1H, m), 4.13 (2H, m), 7.42 (6H, m), 7.67 (4H, m), 9.62 (1H, t, J = 2 Hz); ^{13}C NMR ($CDCl_3$) δ 19.2, 25.0, 26.2, 26.5, 26.8, 47.9, 67.1, 70.5, 78.6, 109.5, 127.6, 127.7, 127.8, 129.5, 129.9, 130.0, 133.0, 134.7, 135.8, 200.4; MS *m/z* 355 ($M^+ - C_4H_9$), 297, 267, 253, 225, 219, 199, 181; HRMS *m/z* 355.1355 (calcd for $C_{20}H_{23}O_4Si$ 355.1356).

(2*R*,3*S*)-(*Z*)-3-*O*-(*tert*-Butyldiphenylsilyl)-1,2-*O*-isopropylidene-5-undecene-1,2,3-triol (45). To a solution of *n*-hexyltriphenylphosphonium bromide (2.03 g, 4.75 mmol) in tetrahydrofuran (50 mL) was added sodium bis(trimethylsilyl)amine (4.75 mL of a 1.0 M solution in tetrahydrofuran, 4.75 mmol), and the resulting orange solution was stirred at room temperature for 15 min. The solution was cooled to −78 °C, and a solution of **44** (653 mg, 1.58 mmol) in tetrahydrofuran (20 mL) was added dropwise. After stirring at −78 °C for 2 h the orange solution was allowed to warm to room temperature and was stirred for 16 h. To this solution was added 25% aqueous ammonium acetate (20 mL), the layers were separated, and the aqueous phase was extracted with ether (3 × 25 mL). The combined extracts were washed with brine and dried (sodium sulfate). The solvent was removed, and the residue was chromatographed on silica, using gradient elution from hexane to 20% ethyl acetate in hexane, to yield 610 mg (80%) of **45** as a colorless oil: $[\alpha]^{23}_D$ +39.6° (*c* 1.12, $CHCl_3$) (lit.[23] +36.2° (*c* 1.5, $CHCl_3$)]; IR (neat) 3070, 3050, 2958, 2896, 2859, 1465, 1214, 1107, 1073, 738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (3H, t, J = 7 Hz), 1.06 (9H, s), 1.24 (6H, m), 1.30 (3H, s), 1.33 (3H, s), 1.80 (2H, q, J = 7 Hz), 2.05 (1H, ddd, J = 14, 7, 7 Hz), 2.14 (1H, ddd, 14, 6, 4 Hz), 3.80 (1H, t, J = 7 Hz), 3.90 (2H, m), 4.06 (1H, m), 5.34 (2H, m), 7.39 (6H, m), 7.70 (4H, m); ^{13}C NMR ($CDCl_3$) δ 14.0, 19.4, 22.5, 25.3, 26.5, 27.0, 27.2, 29.1, 31.5, 32.1, 66.0, 73.2, 77.8, 108.7, 124.1, 127.4, 127.5, 129.6, 132.4, 133.6, 134.1, 135.9, 136.0; MS *m/z* 423 ($M^+ - C_4H_9$), 365 , 345 , 311, 267, 251, 225.

(2*R*,3*S*)-(*Z*)-3-*O*-(*tert*-Butyldiphenylsilyl)-5-undecene-1,2,3-triol (46). A solution of **45** (300 mg, 0.62 mmol) in tetrahydrofuran (4 mL), water (1 mL), and trifluoroacetic acid (0.25 mL) was warmed to 70 °C for 10 h. The solution was neutralized by addition of concentrated ammonium hydroxide, and the tetrahydrofuran was removed under reduced pressure. The residue was diluted with water (5 mL), and the resulting mixture was extracted with dichloromethane (3 × 20 mL). The combined organic extracts were dried (sodium sulfate), and the solvent was evaporated. Radial chromatography on a 2 mm silica-coated rotor, using 20% ethyl acetate in hexane as eluant, yielded 197 mg (72%) of **46** as a viscous, colorless oil: $[\alpha]^{23}_D$ +44.3° (*c* 1.93, $CHCl_3$) [lit.[23] +39.4° (*c* 1.8, $CHCl_3$)]; IR (neat) 3392, 2960, 2930, 2858, 1428, 1111, 1080, 737, 705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.86 (3H, t, J = 7 Hz), 1.07 (9H, s), 1.21 (6H, m), 1.77 (2H, q, J = 7 Hz), 2.22 (2H, m), 2.35 (2H, bs), 3.65 (2H, m), 3.77 (1H, m), 3.91 (1H, ddd, J = 8, 5, 4 Hz), 5.19 (1H, dt, J = 11, 7 Hz), 5.34 (1H, dt, J = 11, 7 Hz), 7.41 (6H, m), 7.69 (4H, m); ^{13}C NMR ($CDCl_3$) δ 14.0, 19.3, 22.5, 27.0, 27.2, 29.0, 31.3, 31.4, 63.0, 73.4, 75.5, 123.8, 127.6, 127.8, 129.8, 129.9, 132.7, 133.0, 133.5, 135.9; MS *m/z* 378, 364, 305, 199, 181, 149, 135.

(2*S*)-(*Z*)-2-*O*-((*tert*-Butyldiphenylsilyl)oxy)-4-decenal (47). To a suspension of **46** (147 mg, 0.33 mmol) and sodium carbonate (114 mg, 1.07 mmol) in dichloromethane (3 mL) at −78 °C was added freshly recrystallized lead tetraacetate (223 mg, 0.50 mmol) in one portion. The suspension was stirred for 15 min and was applied directly to a 1.5 × 14 cm chromatography column packed with silica in hexane. The column was eluted with 20% ethyl acetate in hexane to give 121.8 mg (89%) of **47** as a colorless oil: $[\alpha]^{23}_D$ +17.8° (*c* 2.52, $CHCl_3$); IR (neat) 2958, 2931, 2858, 1737, 1428, 1112, 628 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (3H, t, J = 7 Hz), 1.11 (9H, s), 1.26 (6H, m), 1.91 (2H, m), 2.39 (2H, m), 4.06 (1H, dt, J = 6, 2 Hz), 5.41 (2H, m), 7.43 (6H, m), 7.65 (4H, m), 9.56 (1H, d, J = 2 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0, 19.3, 22.5, 26.9, 27.3, 29.1, 31.1, 31.4, 77.8, 122.6, 127.7, 127.8, 129.9, 130.0, 133.0, 133.1, 133.4, 135.8, 203.3.

(3*S*)-(1*E*,5*Z*)-3-*O*-((*tert*-Butyldiphenylsilyl)oxy)-1-iodo-1,5-undecadiene (48). To a stirred suspension of chromium(II) chloride (520 mg, 4.23 mmol) in tetrahydrofuran (20 mL) was added dropwise a solution

of **47** (278.3 mg, 0.70 mmol) and iodoform (553.6 mg, 1.41 mmol) in tetrahydrofuran (10 mL). The mixture was stirred for 18 h at 0 °C and was quenched with water (10 mL) and extracted with ether (3 × 25 mL). The combined extracts were dried (sodium sulfate), and the solvent was evaporated. The residual oil was purified by chromatography on silica, using hexane as eluant, to yield 211.6 mg (57%) of **48** as a colorless oil: $[\alpha]^{23}_D$ −37.2° (*c* 2.9,$CHCl_3$); IR (neat) 3071, 3014, 2957, 2900, 2857, 1469, 1109, 1086, 792 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.87 (3H, t, *J* = 7 Hz), 1.06 (9H, s), 1.24 (6H, m), 1.83 (2H, m), 2.20 (2H, m), 4.09 (1H, ddt, *J* = 7, 6, 1 Hz), 5.24 (1H, dt, *J* = 11, 7 Hz), 5.40 (1H, dt, *J* = 11, 7 Hz), 5.96 (1H, dd, *J* = 14, 1 Hz), 6.47 (1H, dd, *J* = 15, 6 Hz), 7.40 (6H, m), 7.65 (4H, m); ^{13}C NMR ($CDCl_3$) δ 14.1, 19.3, 22.6, 27.0, 27.3, 29.2, 31.5, 35.2, 75.7, 123.6, 129.7, 132.8, 133.5, 133.8, 135.9, 147.9; MS (EI) *m/z* 475 ($M^+ - C_4H_9$), 421, 309, 237, 199, 135; HRMS *m/z* 475.0954 (calcd for $C_{27}H_{37}IOSi$ ($M^+ - C_4H_9$) 475.0954).

12-*O*-(*tert*-Butyldiphenylsilyl)constanolactone A (49) and 12-*O*-(*tert*-Butyldiphenylsilyl)constanolactone B (50). A mixture of **37** (7.0 mg, 0.042 mmol) and **48** (31.5 mg, 0.059 mmol) was thoroughly dried by azeotropic removal of water with benzene (twice). To the mixture were added degassed dimethyl sulfoxide (3 mL), chromium(II) chloride (31 mg, 0.25 mmol), and nickel(II) chloride (0.5 mg). The green solution was stirred at room temperature for 24 h and was poured into saturated, aqueous ammonium chloride. The resulting mixture was extracted with ethyl acetate (3 × 10 mL), and the combined extracts were dried (magnesium sulfate). The solvent was removed, and the residue was purified by radial chromatography on a 1 mm silica-coated rotor, using gradient elution from 10% to 50% ethyl acetate in hexane, to give 16.7 mg (70%) of a 2:1 mixture of **49** and **50**. These isomers were separated by HPLC (10μ Maxsil, 500 × 10 mm, 50% ethyl acetate in hexane, 4.0 mL/min, UV detection at 256 nm).

49: $[\alpha]^{23}_D$ +1.2° (*c* 0.9, $CHCl_3$); IR (neat) 3400, 2958, 2929, 2895, 2857, 1733, 1109, 1044 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.48 (1H, ddd, *J* = 11, 8, 5 Hz), 0.56 (1H, ddd, *J* = 11, 8, 5 Hz), 0.87 (3H, t, *J* = 7 Hz), 0.97 (2H, dt, *J* = 10, 6 Hz), 1.06 (9H, s), 1.26 (6H, m), 1.58 (2H, m), 1.79 (1H, m), 1.87 (3H, m), 1.91 (1H, m), 2.22 (1H, m), 2.35 (1H, m), 2.42 (1H, m), 2.54 (1H, m), 3.80 (2H, m), 4.22 (1H, q, *J* = 6 Hz), 5.29−5.44 (3H, m), 5.67 (1H, ddd, *J* = 15, 7, 1 Hz), 7.34−7.42 (6H, m), 7.67 (4H, m); ^{13}C NMR ($CDCl_3$) δ 5.8, 14.1, 18.4, 19.3, 19.4, 22.0, 22.6, 27.0 (×3), 27.3, 27.7, 29.2, 29.5, 31.5, 35.9, 72.0, 73.5, 82.5, 124.6, 127.4 (×2), 127.5 (×2), 129.5, 129.6, 131.1, 132.0, 133.6, 134.2, 134.5, 135.9 (×2), 136.0 (×2), 171.4; MS (CI) *m/z* 557, 518, 497, 479, 463, 417, 319, 301, 199, 179; HRMS *m/z* 518.2850 (calcd for $C_{32}H_{42}O_4Si$ ($M^+ - C_4H_9$) 518.2852).

50: $[\alpha]^{23}_D$ +3.5° (*c* 0.3, $CHCl_3$); IR (neat) 3400, 2957, 2932, 2857, 1732, 1109, 1044 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.47 (2H, m), 0.87 (3H, t, *J* = 6 Hz), 0.97 (1H, m), 1.06 (9H, s), 1.25 (8H, m), 1.62 (1H, m), 1.74−1.99 (5H, m), 2.21 (1H, m), 2.31 (1H, m), 2.39−2.59 (2H, m), 3.48 (1H, dd, *J* = 7, 6 Hz), 3.77 (1H, ddd, *J* = 10, 7, 3 Hz), 4.19 (1H, dt, *J* = 7, 6 Hz), 5.28−5.42 (3H, m), 5.60 (1H, dd, *J* = 16, 6 Hz), 7.38 (6H, m), 7.67 (4H, m); ^{13}C NMR ($CDCl_3$) δ 6.0, 14.1, 18.4, 19.3, 21.2, 22.6 (×2), 27.0 (×3), 27.4, 27.8, 29.2, 29.5, 31.5, 35.9, 73.7, 74.3, 82.6, 124.6, 127.4 (×2), 127.5 (×2), 129.5, 129.6, 130.9, 132.0, 134.0, 134.2, 134.5, 135.9 (×2), 136.0 (×2), 171.4.

(3*S*)-(1*E*,5*Z*)-3-Hydroxy-1-iodo-1,5-undecadiene (51). A solution of **48** (211.6 mg, 0.40 mmol) in 5% hydrofluoric acid in acetonitrile (15 mL) was stirred for 18 h at room temperature. The solution was neutralized with aqueous sodium carbonate and was extracted with chloroform (3 × 25 mL). The combined extracts were dried (sodium sulfate), and the solvent was evaporated. The resulting yellow oil was purified by chromatography on silica, using gradient elution from 10% to 33% ethyl acetate in hexane, to furnish 93.7 mg (80%) of **51** as a colorless oil: $[\alpha]^{23}_D$ −22.5° (*c* 1.35, $CHCl_3$); IR (neat) 3400, 2956, 2926, 2856, 1608, 1461, 1035, 945 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (3H, t, *J* = 7 Hz), 1.32 (6H, m), 1.72 (1H, bd, *J* = 4 Hz), 2.04 (2H, q, *J* = 7 Hz), 2.32 (2H, t, *J* = 7 Hz), 4.14 (1H, bm), 5.35 (1H, dt, *J* = 11, 8 Hz), 5.61 (1H, dt, *J* = 11, 7 Hz), 6.37 (1H, dd, *J* = 14, 1 Hz), 6.60 (1H, dd, *J* = 14, 6 Hz); ^{13}C NMR ($CDCl_3$) δ 14.0, 22.5, 27.4, 29.2, 31.5, 34.6, 73.9, 77.2, 123.2, 134.6, 147.8; MS (EI) *m/z* 183 ($M^+ - C_8H_{15}$) 167, 112; HRMS *m/z* 182.9309 (calcd for C_3H_4IO ($M^+ - C_8H_{15}$) 182.9307).

Constanolactones A (9) and B (10). A mixture of **37** (15 mg, 0.09 mmol) and **51** (79 mg, 0.27 mmol) was thoroughly dried by azeotropic removal of water with benzene (twice). To the mixture was added degassed dimethyl sulfoxide (5 mL), chromium(II) chloride (66 mg, 0.54 mmol), and nickel(II) chloride (0.5 mg). The green solution was stirred at room temperature for 18 h, and the solution was poured into saturated, aqueous ammonium chloride. The resulting mixture was extracted with ethyl acetate (4 × 15 mL), and the combined extracts were dried (sodium sulfate). The solvent was evaporated, and the residue was purified by radial chromatography on a 1 mm silica-coated rotor, using ethyl acetate as eluant, to give 23.4 mg (78%) of a 1.4:1 mixture of **9** and **10**. Constanolactones A and B were separated by HPLC (10μ Maxsil, 500 × 10 mm, 20% isopropyl alcohol in hexane, 5.0 mL/min, refractive index detection).

9: IR (neat) 3315, 3230, 2957, 2924, 2857, 1710, 1463, 1256, 1099, 1029 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.61 (1H, dt, *J* = 9, 5 Hz), 0.75 (1H, dt, *J* = 9, 5 Hz), 0.88 (3H, t, *J* = 7 Hz), 1.00 (1H, m), 1.15 (1H, m), 1.31 (6H, m), 1.67 (1H, ddd, *J* = 13, 10, 5 Hz), 1.79 (1H, m), 1.94 (1H, m), 1.99 (1H, m), 2.04 (2H, m), 2.14 (2H, bs), 2.31 (2H, q, *J* = 6 Hz), 2.44 (1H, ddd, *J* = 18, 8, 7 Hz), 2.55 (1H, dt, *J* = 18, 7 Hz), 3.73 (2H, m), 4.17 (1H, dt, *J* = 6, 3 Hz), 5.39 (1H, dt, *J* = 11, 7 Hz), 5.54 (1H, dt, *J* = 11, 7 Hz), 5.78 (2H, m); ^{13}C NMR ($CDCl_3$) δ 7.5, 14.0, 18.3, 20.4, 22.5, 23.4, 27.4, 27.7, 29.3, 29.5, 31.5, 35.0, 71.6, 74.2, 83.8, 124.5, 131.6, 133.3, 133.7, 171.6; MS (CI) *m/z* 337 (M^+ + 1), 319 (M^+ − OH), 301, 225, 207; HRMS *m/z* 319.2273 (calcd for $C_{20}H_{31}O_3$ (M^+ − OH) 319.2273).

10: IR (neat) 3403, 2956, 2926, 2858, 1722, 1245, 1042 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.58 (1H, dt, *J* = 9, 5 Hz), 0.63 (1H, dt, *J* = 9, 5 Hz), 0.88 (3H, t, *J* = 7 Hz), 1.29 (2H, m), 1.29 (4H, m), 1.35 (2H, m), 1.70 (1H, m), 1.95−1.80 (4H, m), 2.01 (1H, m), 2.04 (2H, m), 2.31 (2H, q, *J* = 7 Hz), 2.45 (1H, dt, *J* = 18, 8 Hz), 2.58 (1H, dt, *J* = 18, 6 Hz), 3.68 (1H, m), 3.73 (1H, ddd, *J* = 10, 8, 3 Hz), 4.16 (1H, m), 5.38 (1H, dt, *J* = 11, 7 Hz), 5.56 (1H, dt, *J* = 11, 8 Hz), 5.78 (2H, m); ^{13}C NMR ($CDCl_3$) δ 6.6, 14.0, 18.4, 21.2, 22.5, 23.4, 27.4, 27.8, 29.3, 29.5, 31.5, 35.2, 71.6, 73.9, 83.5, 124.3, 131.6, 133.3, 133.6, 171.6; MS (CI) *m/z* 337 (M^+ + 1), 319 (M^+ − OH), 301, 225, 207; HRMS *m/z* 319.2273 (calcd for $C_{20}H_{31}O_3$ (M^+ − OH) 319.2273).

Both **9** and **10** undergo mutarotation in methanol. After 10 h, **9** was converted completely to its hydroxy methyl ester: $[\alpha]^{23}_D$ +26.6° (*c* 0.95, MeOH).

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Supplementary Material Available: X-ray crystallographic data for **29**, including atomic coordinates, bond lengths, and bond angles (7 pages); observed and calculated structure factors (16 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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