Total Synthesis of Uvaricin

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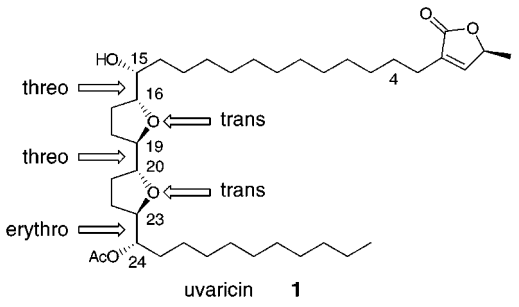
The first total synthesis of naturally occurring (+)-uvaricin was achieved using three consecutive Sharpless asymmetric dihydroxylation (AD) reactions to place the necessary oxygen functions on a "naked" carbon skeleton in a regio- and enantioselectively controlled manner. The appropriate bis-THF ring system was constructed using a Williamson type etherification reaction on a functionalized bis-mesylate intermediate.

Introduction

The diverse bioactivities of the Annonaceous acetogenins as antitumor, immunosuppressive, pesticidal, antiprotozoal, antifeedant, anthelmintic, and antimicrobial agents have attracted increasing interest.[1] The past few years have witnessed an explosion of activity in the isolation (approximately 300 different Annonaceous acetogenins have already been isolated from about 30 plants of the *Annonaceae*), structural elucidation, and synthesis of these long chain fatty acid derivatives.[2,3] We have shown that many acetogenins of the mono-THF,[4] the bis-THF,[5] as well as the newly discovered tris-THF[6] subgroups can be efficiently synthesized either by a convergent approach or via the "naked" carbon skeleton strategy,[7,8] thus unequivocally confirming their absolute configuration.

Uvaricin, **1**, an adjacent bis-THF acetogenin which was isolated in 1982 from *Uvari accuminata*, is of special historical value because it was the first Annonaceous acetogenin discovered.[9] Uvaricin demonstrated antitumor properties in the in vivo PS system (P-388 lymphocytic leukemia in mice).[10] The synthesis of (15,16,19,20,23,24)-*hexepi*-uvaricin by Hoye,[11] which was accomplished at the time when the absolute configuration of **1** was still unknown,[12] represents the only reported attempt to synthesize this molecule. That synthetic work, together with subsequent NMR studies,[13] suggested that the absolute configuration of the bis-THF portion of **1** is 15*R*,16*R*,19*R*,20*R*,23*R*,24*S*. Herein we report on the first total synthesis of the naturally occurring isomer, **1**.



uvaricin **1**

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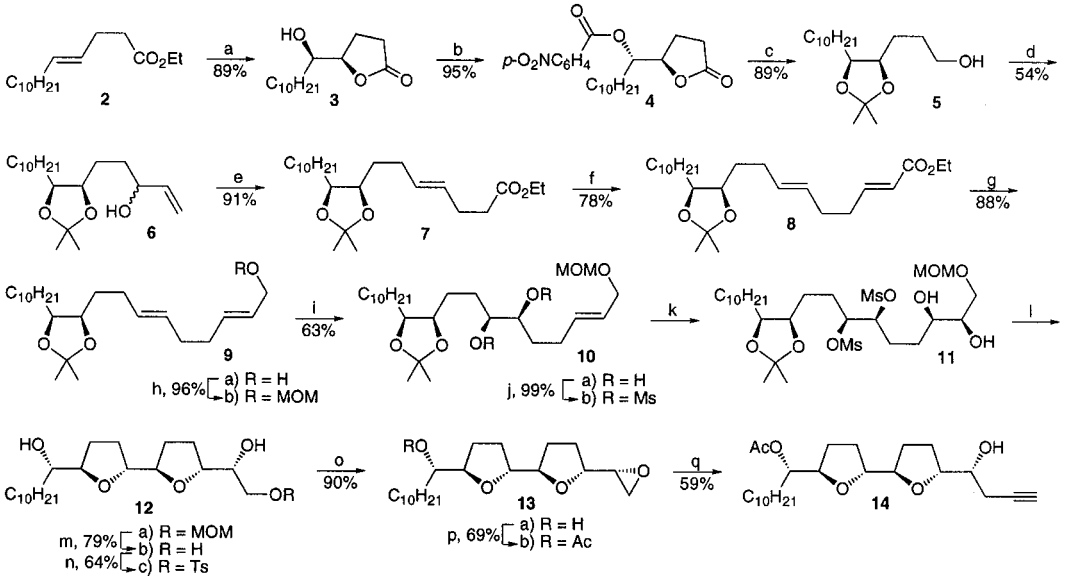
Scheme 1. Synthesis of 14[a]



[a] Reagents and conditions: (A) i. AD-mix-β, $MeSO_2NH_2$, butanol:water (1:1), 0 °C, 16 h. ii. 3 N KOH then 3 N HCl; iii. TsOH (5%), CH_2Cl_2, 0.5 h. (B) *p*-nitrobenzoic Acid, PPh_3, DEAD, C_6H_6, 16 h. (C) i. LAH, Et_2O−THF, 0 °C to reflux, 2 h; ii. hexane, acetone, TsOH (cat.), reflux 16 h. (D) i. PCC, CH_2Cl_2, 25 °C, 2 h; ii. Vinylmagnesium bromide, −30 °C, 0.5 h. (E) Triethyl orthoacetate, xylene, propionic acid (cat.). (F) DIBAL-H, toluene, −78 °C, then triethylphosphonoacetate/ NaH, THF, −78 °C to 25 °C, 16 h. (G) DIBAL-H, THF, −78 °C, 1 h. (H) MOMCl, CH_2Cl_2, diisopropylethylamine, 25 °C, 16 h. (I) AD-mix-α, $MeSO_2NH_2$, butanol:water (1:1), 0 °C, 16 h. (J) MsCl, Et_3N, CH_2Cl_2, 0 °C, 1 h. (K) AD-mix-β, $MeSO_2NH_2$, butanol:water (1:1), 0 °C, 16 h. (L) i. MeOH, TsOH, 16 h; ii. Pyridine, 140 °C, 4 h: **12a** (48%), **12b** (13%). (M) $BF_3{\cdot}Et_2O$, DMS, CH_2Cl_2, 0 °C, 51% yield from **10b** to **12b**. (N) TsCl, pyridine, 0 °C, 3.5 h. (O) K_2CO_3, MeOH, 16 h. (P) Pyridine, acetic anhydride, 25 °C, 16 h. (Q) I. (trimethylsilyl)acetylene, THF, *n*-BuLi, −78 °C to −30 °C, 0.5 H, then **13b**, $BF_3{\cdot}Et_2O$ (2 equiv), −78 °C to −30 °C, 10 h; ii. TBAF, THF, 0 °C, 0.5 h.

Results and Discussion

Clearly, the C15−C24 fragment, which contains the bis-THF structure, represented the main challenge in the total synthesis of **1**. In addition to the requirement of synthesizing six asymmetric carbinol centers in this fragment, there was a need to selectively acetylate one of two nearly identical secondary alcohols at positions 15 and 24. Interestingly, **1** was the only naturally acetylated Annonaceous acetogenin reported to date. We decided to employ here some of the principles of our "naked" carbon skeleton strategy.[7,8] Thus, an unsaturated carbon skeleton of the molecule was first constructed and then hydroxylated in a regio- and enantioselective manner using the Sharpless asymmetric dihydroxylation (AD) reaction.[14] All six asymmetric centers of the C15−C24 fragment were introduced by three AD steps as shown herein.

The synthesis started with ethyl pentadec-4-enoate, **2**, which was produced in two steps from undecanal (first, reaction with vinylmagnesium bromide and then, Claisen−Johnson rearrangement with triethyl orthoacetate and propionic acid). An AD reaction using AD-mix-β produced the *threo* hydroxy lactone **3** (Scheme 1). As the two asymmetric centers in **3** were destined to become positions 23 and 24 in the target molecule, inversion of the configuration at the latter carbinol center was necessary. Thus, Mitsunobu reaction of **3** with *p*-nitrobenzoic acid, triphenylphosphine, and diethyl azodicarboxylate (DEAD) afforded the *erythro* lactone ester, **4**. LAH reduction of these functions afforded the corresponding triol which was protected in the form of the acetonide **5**. Oxidation of the free alcohol using PCC followed by treatment of the resultant aldehyde with vinylmagnesium bromide afforded allylic alcohols **6**. Treatment of the latter with triethyl orthoacetate and propionic acid resulted in the Claisen−Johnson rearrangement product, **7**. Reduction of the ester to the aldehyde using DIBAL-H in toluene followed by a Wittig−Horner reaction afforded the (*E*)-unsaturated ester **8**. Reduction of the ester to the allylic alcohol **9a** followed by protection with MOM chloride produced **9b**. Playing a key role in the synthetic scheme, diene **9b** was designed to undergo two consecutive AD reactions to incorporate stereochemical features necessary for synthesis of **1**. Using AD-mix-α, the more electron-rich double bond was regioselectively dihydroxylated to produce diol **10a**. The regioselectivity of this dihydroxylation was complete, as the only byproduct observed was the tetrol obtained from overoxidation of **9b**. Diol **10a** was converted to the bis-mesylate **10b** before undergoing the second AD reaction, now with AD-mix-β, at the slightly less reactive double bond to give **11**. Hydrolysis of the acetonide group followed by heating under reflux in pyridine produced primarily the desired bis-THF fragment **12a** accompanied by small amounts of the deprotected alcohol, **12b**. Deprotection of **12a** was performed using BF_3-Et_2O and Me_2S in CH_2Cl_2. Conversion of the primary alcohol in **12b** to the corresponding tosylate, **12c**, set the stage for a ring closure reaction with K_2CO_3 in methanol to give epoxide **13a**. The epoxide group served two purposes: (a) protection of the secondary alcohol that was destined to be the free alcohol at C15 in **1**, and (b) activation of the primary position toward the C−C bond formation upon reaction with a carbon nucleophile. Acetylation using pyridine and acetic anhydride gave **13b**, a key intermediate possessing correct absolute configurations for synthesis of **1**, and is enantiomeric to the intermediate used by Hoye to prepare

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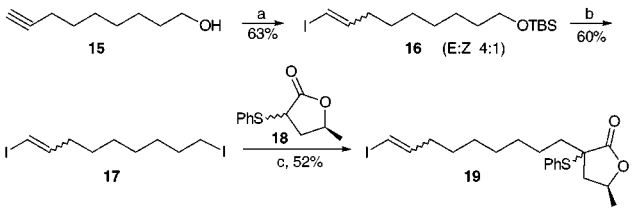
Scheme 2. Synthesis of 21[a]



[a] Reagents and conditions: (A) i. *tert*-butyldimethylsilyl chloride (1.1 equiv), imidazole, DMF, rt, 16 h; ii. tributyltin hydride (1.43 equiv), 1,1-azobis(cyclohexanecarbonitrile) (0.0086 equiv), 130 °C, 2H, then I_2, ether. (B) i. Bu_4NF, THF, 0 °C, 3 h; ii. TsCl (1.1 equiv), pyridine, 0 °C to room temperature, 5 h; iii. NaI (5 equiv), acetone, rt, 3 h. (C) $(Me_3Si)_2NK$ (1 equiv), (3*RS*,5*S*)-5-methyl-3-(phenylsulfenyl)tetrahydrofuran-2-one (1 equiv), THF, 0 °C to room temperature, 2 h.

hexepi-uvaricin.[11] Further reaction with lithium (trimethylsilyl)acetylide followed by desilation produces alkyne **14**.

The butenolide portion of the target molecule was prepared according to the method described by Hoye (Scheme 2),[11] with slight modifications. Thus, non-8-yn-1-ol was protected as its *tert*-butyldimethylsilyl (TBS) ether, **15**. The terminal acetylene was converted into vinyl iodide **16** via hydrostannation with tributyltin hydride followed by iodolysis of the resultant vinylstannane.[15] The primary alcohol was deprotected and converted to the corresponding tosylate, and the latter was reacted with iodide to produce diiodide **17**. Selective nucleophilic substitution of the aliphatic iodide by the enolate of (3*RS*,5*S*)-5-methyl-3-(phenylsulfenyl)tetrahydrofuran-2-one produced **19**.[11,15]

The final steps of this convergent synthesis were based on the cross-coupling of key intermediates **14** and **19** (Scheme 3) following the same strategy reported earlier.[11,15] Thus, Pd(0)- and CuI-catalyzed cross-coupling reaction of the terminal acetylene **14** with vinyl iodide **19** afforded the eneyne intermediate, **20**, which was hydrogenated over Wilkinson's catalyst to give **21**. Finally, oxidation of the thioether to the corresponding sulfoxide followed by thermal elimination afforded **1**.

In conclusion, the first total synthesis of naturally occurring (+)-uvaricin, **1** has been achieved using (a) Sharpless AD reactions to incorporate necessary stereochemical features in a regio- and enantioselectively controlled manner, and (b) a Williamson type etherification reaction on an appropriately functionalized bismesylate intermediate for construction of the bis-THF ring system.

Experimental Section

General Methods. ^1H and ^{13}C NMR spectra were measured in $CDCl_3$ at 400 and 100 MHz, respectively. Positive ion mass spectra, using the fast ion bombardment (FIB) technique, were obtained on a VG ZAB-VSE double focusing, high-resolution mass spectrometer equipped with either a cesium or sodium ion gun. Negative mass spectra were obtained with Sciex API 100. Optical rotations were measured in a one decimeter (1.3 mL) cell using an Autopol III automatic polarimeter. TLC was performed on glass sheets precoated with silica gel (Merck, Kieselgel 60, F254, Art. 5715). Column chromatographic separations were performed on silica gel (Merck, Kieselgel 60, 230−400 mesh, Art. 9385) under pressure. THF and diethyl ether were dried and distilled over sodium ketyl. AD-mix-α (#39,275-8) and AD-mix-β (#39,276-6) were purchased from Aldrich.

(*trans*)-Ethyl Pentadec-4-enoate, 2. Vinylmagnesium bromide (1 M, 100 mL, 0.1 mol) was added to a solution of undecanal (15.3 g, 0.09 mol) in THF (150 mL) at 0 °C, and the mixture was stirred for 0.5 h and then worked up with ether and saturated aqueous NH_4Cl. Removal of solvents followed by filtration over silica gel (hexanes−ethyl acetate, 4:1) afforded tridec-1-en-3-ol (16.7 g, 94%). ^1H NMR: δ 5.81 (m, 1H), 5.18 (dq, J = 18.5, 1.3 Hz, 1H), 5.07 (dq, J = 10.4, 1.3 Hz, 1H), 4.06 (q, J = 5.9 Hz, 1H), 1.75 (br s, 1H), 1.60−1.20 (m and br s, 18H), 0.85 (t, J = 7.2 Hz, 3H); ^{13}C NMR: δ 141.3, 114.4, 73.3, 37.0, 31.9, 29.5, 29.4, 29.1, 25.3, 22.7, 14.1 ppm; MS: ($C_{13}H_{26}O$ = 198) found 181 $(MH - H_2O)^+$.

The above-mentioned alcohol (65.12 g, 0.33 mol), triethyl orthoacetate (106.7 g, 0.67 mol), and propionic acid (0.23 g, 3.1 mmol) were dissolved in xylene (130 mL), and the mixture was refluxed for 2 h. Solvents were removed under reduced pressure, and the residue was distilled (kugelrohr, 130 °C/ 0.5 mmHg) to give *trans*-ethyl pentadec-4-enoate (71.36 g, 81%). ^1H NMR: δ 5.39 (m, 2H), 4.08 (q, J = 7.2 Hz, 2H), 2.29 (m, 4H), 1.93 (q, J = 6.8 Hz, 2H), 1.25 (m and br s, 16H), 1.23 (t, J = 7.0 Hz, 3H), 0.85 (t, J = 6.8 Hz, 3H); ^{13}C NMR: 173.2, 131.7, 127.8, 60.2, 34.4, 32.4, 31.9, 29.7, 29.5, 29.4, 29.2, 29.1, 27.9, 22.7, 14.2, 14.1 ppm. MS: ($C_{17}H_{32}O_2$ = 268) found 269 (MH^+), 291 (MNa^+).

(4*R*,5*R*)-5-Hydroxypentadecan-1,4-olide, 3. Compound **2** (20.26 g, 75.6 mmol) was added to a cold (0 °C) solution of AD-mix-β (106 g) and $MeSO_2NH_2$ (7.16 g, 75.4 mmol) in *tert*-butyl alcohol−water (1:1, 750 mL), and the mixture was stirred at 0 °C for 16 h and then quenched by the addition of sodium metabisulfite (113 g). The mixture was worked-up with ethyl acetate and water, solvents were removed under reduced pressure, and the residue was dissolved in methanol (80 mL). Aqueous KOH (3 N, 80 mL) was added, and the mixture was stirred at 60 °C for 2 h and then cooled to 0 °C, acidified with 3 N HCl, and extracted with ethyl acetate. Solvents were removed under reduced pressure, and the residue was dissolved in CH_2Cl_2. *p*-Toluenesulfonic acid (TsOH, 0.2 g) was added, and the mixture was stirred at room temperature for 1 h, worked up with saturated aqueous $NaHCO_3$ and CH_2Cl_2, and purified by column chromatography (silica gel, hexanes−ethyl acetate, 1:1) to give lactone **3** (17.2 g, 89%) in the form of white crystals. Mp 64−65°; $[\alpha]_D$ −25.3 (c = 2.1, $CHCl_3$); ^1H NMR: 4.40 (td, J = 7.4, 4.6 Hz, 1H), 3.55 (m, 1H), 2.61 (ddd, J = 17.8, 9.9, 5.0 Hz, 1H), 2.53 (dd, J = 17.8, 9.5 Hz, 1H), 2.28−2.19 (m, 1H), 2.16−2.06 (m, 1H), 1.86 (d, J = 5.4 Hz, 1H), 1.60−1.20 (m and br s, 18H), 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR: 177.3, 83.0, 73.6, 32.9, 31.9, 29.5, 29.3, 28.7, 25.4, 24.1, 22.7, 14.1 ppm; MS: ($C_{15}H_{28}O_3$ = 256) found 257 (MH^+), 279 (MNa^+).

(4*R*,5*S*)-5-(4-Nitrobenzoyloxy)pentadecan-1,4-olide, 4. DEAD (5.71 g, 32.8 mmol) was added to a solution of **3** (7.0 g, 27.3 mmol), PPh_3 (8.6 g, 32.8 mmol), and 4-nitrobenzoic acid (5.48 g, 32.8 mmol) in dry benzene (70 mL), and the mixture was stirred at room temperature for 16 h and then worked up by chromatography over a double layer column (neutral active alumina over silica gel, hexanes−ethyl acetate, 9:1−3:1) to give the crude nitrobenzoate ester **4** (10.53 g, 95%). ^1H NMR: 8.24 (d, J = 8.8 Hz, 2H), 8.14 (d, J = 8.8 Hz, 2H), 5.35 (dt, J = 8.7, 4.4 Hz, 1H), 4.65 (td, J = 7.4, 4.4 Hz, 1H), 2.54 (m, 2H), 2.34 (m, 1H), 2.20 (m, 1H), 1.73 (m, 2H), 1.40−1.16 (m and br s, 16H), 0.80 (t, J = 6.8 Hz, 3H); ^{13}C NMR: δ 176.2 164.0, 150.7, 135.1, 130.7, 123.6, 79.9, 75.2, 31.9, 31.8, 29.8, 29.5, 29.4, 29.3, 29.2, 28.0, 25.2, 23.1, 22.6, 14.1 ppm; MS analysis ($C_{22}H_{31}NO_6$ = 405) found 406 (MH^+), 428 (MNa^+).

(4*R*,5*S*)-(Isopropylidenedioxy)pentadecan-1-ol, 5. Lithium aluminum hydride (4.94 g, 0.13 mol) was slowly added to a solution of **4** (10.53 g, 26.0 mmol) in dry ether (100 mL) at 0 °C. The mixture was stirred at 0 °C for 0.5 h and then refluxed for another 2 h, cooled, diluted with ether, and quenched with water. The mixture was filtered through Celite, and solvents were removed to afford crude 1,4,5-trihydroxypentadecane (8.89 g, >100%) which was taken to

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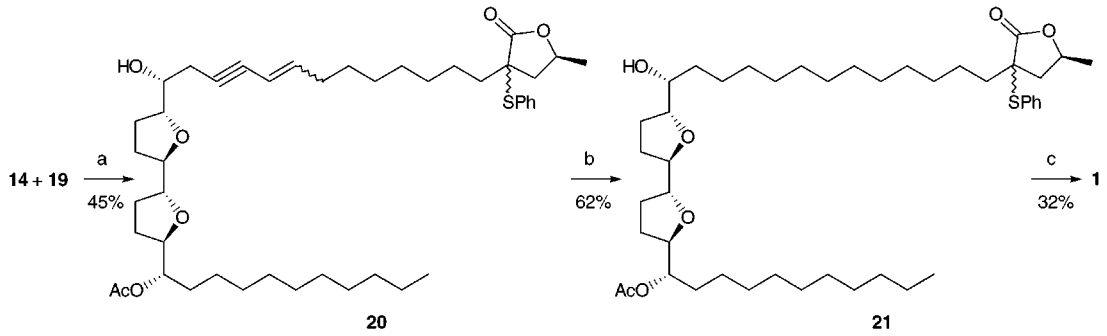
Scheme 3. Synthesis of 1[a]



[a] Reagents and conditions: (A) CuI (cat.), $Pd(PPh_3)_4$ (cat), Et_3N, rt, 22 h. (B) $RhCl(PPh_3)_3$ (cat.), H_2, MeOH−benzene, 1:1, 24 h. (C) i. *m*-CPBA, CH_2Cl_2, 0 °C, 20 min; ii. toluene, reflux, 1 h.

the next step without further purification. Physical data of a purified sample: $[\alpha]_D$ −3.76 (*c* = 1.01, MeOH); ^{1}H NMR: δ 3.76−3.59 (m, 4H), 1.92 (br s, 3H), 1.80−1.60 (m, 3H), 1.60−1.40 (m, 4H), 1.40−1.20 (m, 15H), 0.86 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR: δ 74.7, 74.3, 63.0, 33.6, 31,9, 30.8, 29.6, 29.3, 29.0, 25.6, 22.7, 14.1 ppm; MS: ($C_{15}H_{32}O_3$ = 260) found 283 (MNa^+).

The above-mentioned triol (8.89 g) was dissolved in a mixture of acetone (90 mL) and hexane (180 mL) together with TsOH (0.9 g), and the solution was refluxed for 16 h and then worked-up with saturated aqueous $NaHCO_3$ and hexane followed by column chromatography (silica gel, hexanes−ethyl acetate, 7:3) to give **5** (6.94 g, 89%) in the form of a colorless oil. $[\alpha]_D$ +1.9 (*c* = 1.96, MeOH); ^{1}H NMR: δ 4.01 (m, 2H), 3.64 (m, 2H), 2.23 (br s, 1H), 1.69 (m, 2H), 1.52 (m, 4H), 1.41 (s, 3H), 1.31 (s, 3H), 1.24 (m and br s, 16H), 0.84 (t, *J* = 6.4 Hz, 3H); ^{13}C NMR: δ 107.5, 78.1, 78.0, 62.7, 31.9, 29.8, 29.7, 29.6, 29.5, 29.3, 28.5, 26.7, 26.2, 25.9, 22.6, 14.1 ppm; MS: ($C_{18}H_{36}O_3$ = 300) found 301 (MH^+), 323 (MNa^+).

(3*RS*,6*R*,7*S*)-6,7-(Isopropylidenedioxy)heptadec-1-en-3-ol, 6. Celite (12.5 g) and PCC (12.5 g, 58 mmol) were added to a solution of **5** (8.71 g, 29.0 mmol) in CH_2Cl_2 (90 mL), and the mixture was stirred at room temperature for 2 h, monitored by TLC (hexanes−ethyl acetate, 4:1), and then filtered through silica gel. Removal of the solvent afforded the corresponding aldehyde (6.46 g, 75%), which was immediately used in the next step without further purification.

Vinylmagnesium bromide (1 M in THF, 26 mL, 26 mmol) was added to the solution of the above-mentioned aldehyde (6.46 g, 21.6 mmol) in ether (65 mL) at −30 °C. The mixture was stirred at the same temperature for 0.5 h and then worked up with saturated aqueous NH_4Cl and ether. Purification by column chromatography (silica gel, hexanes−ethyl acetate, 4:1) afforded **6** (5.1 g, 72%). ^{1}H NMR (300 MHz): δ 5.84 (ddd, *J* = 17.2, 10.4, 3.9 Hz, 1H), 5.14 (dq, *J* = 17.2, 1,5 Hz, 1H), 5.08 (dq, *J* = 10.4, 1.5 Hz, 1H), 4.10 (m, 1H), 4.01 (m, 2H), 2.10 (br s, 1H), 1.41 (s, 3H), 1.35 (s, 3H), 1.80−1.15 (m and br s, 22H), 0.85 (t, *J* = 6.9 Hz, 3H); MS: ($C_{20}H_{38}O_3$ = 326) found 349 (MNa^+).

(*trans*,8*R*,9*S*)-Ethyl 8,9-(Isopropylidenedioxy)nonadec-4-enoate, 7. A solution of **6** (5.1 g, 15.6 mmol), triethyl orthoacetate (5.03 g, 31 mmol), and propionic acid (114 mg, 1.5 mmol) in xylene (25 mL) was refluxed for 2 h. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel, hexanes−ethyl acetate 9:1) to give **7** (5.62 g, 91%) in the form of a colorless oil. ^{1}H NMR: δ 5.43 (m, 2H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.96 (m, 2H), 2.30 (m, 4H), 2.15 (m, 1H), 1.98 (m, 1H), 1.54−1.20 (m and br s, 20H), 1.36 (s, 3H), 1.33 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H), 0.84 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR: δ 173.2, 130.8, 128.6, 107.3, 78.0, 77.3, 60.2, 34.3, 31.9, 29.7, 29.6, 29.5, 29.3, 29.0, 28.6, 27.9, 26.2, 26.0, 22.7, 14.2, 14.1 ppm; MS: ($C_{24}H_{44}O_4$ = 396) found 419 (MNa^+).

(*trans*,*trans*,10*R*,11*S*)-Ethyl 10,11-(Isopropylidenedioxy)heneicosa-2,6-dienoate, 8. DIBAL-H (1 M in toluene, 15.6 mL, 15.6 mmol) was added to a solution of **7** (5.62 g, 14.2 mmol) in dry toluene (56 mL) at −78 °C, and the mixture was stirred at the same temperature for 2 h. In a separate flask, a mixture of NaH (60% in mineral oil, 0.68 g, 17.0 mmol) in dry THF (30 mL) was cooled to 0 °C, triethyl phosphonoacetate (3.81 g, 17.0 mmol) was added dropwise, the mixture was stirred at 0 °C for 0.5 h, and then the whole mixture was added dropwise to the first at −78 °C. The combined mixture was stirred at room temperature for 16 h, water (6 mL) was added, followed by Celite (6 g), diluted with ether (30 mL), and the mixture was stirred at 0 °C for 0.5 h. Filtration over Celite and removal of the solvent followed by column chromatography (silica gel, hexanes−ethyl acetate, 95:5) yielded **8** (4.67 g, 78%) in the form of a colorless oil. $[\alpha]_D$ = +1.4 (*c* = 1.94, $CHCl_3$); ^{1}H NMR: δ 6.91 (dt, *J* = 15.6, 6.7 Hz, 1H), 5.78 (d, *J* = 15.6 Hz, 1H), 5.41 (m, 2H), 4.12 (q, *J* = 7.2 Hz, 2H), 3.96 (m, 2H), 2.30−1.95 (m, 6H), 1.45−1.18 (m and br s, 20H), 1.37 (s, 3H), 1.30 (s, 3H), 1.25 (t, *J* = 6.6 Hz, 3H), 0.83 (t, *J* = 7.8 Hz, 3H). ^{13}C NMR: δ 166.6, 148.5, 130.8, 129.0, 121.5, 107.3, 78.0, 77.9, 60.1, 32.1, 31.9, 31.6, 30.9, 29.7, 29.6, 29.5, 29.3, 29.0, 28.6, 26.2, 26.0, 22.6, 14.2, 14.1 ppm; MS: ($C_{26}H_{46}O_4$ = 422) found 445 (MNa^+).

(*trans*,*trans*,10*R*,11*S*)-10,11-(Isopropylidenedioxy)-heneicosa-2,6-dien-1-ol, 9a. Compound **8** (4.67 g, 11.06 mmol) was dissolved in dry THF (46 mL) and cooled to −78 °C, DIBAL-H (1 M in toluene, 28 mL, 28 mmol) was added, and the mixture was stirred at −78 °C for 1 h. Water (10 mL) was added, followed by Celite (10 g), diluted with ether (50 mL), and the mixture was stirred at 0 °C for 0.5 h. Filtration through Celite and removal of the solvent followed by column chromatography (silica gel, hexanes−ethyl acetate, 7:3) afforded **9a** (3.68 g, 88%) in the form of a colorless oil. $[\alpha]_D$ = +0.7 (*c* = 2.2, $CHCl_3$); ^{1}H NMR: δ 5.62 (m, 2H), 5.41 (m, 2H), 4.04 (d, *J* = 4.4 Hz, 2H), 3.97 (m, 2H), 2.22−1.95 (m, 6H), 1.69−1.20 (m and br s, 21H), 1.40 (s, 3H), 1.32 (s, 3H), 0.85 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR: δ 132.5, 130.0, 129.3, 107.3, 78.0, 77.3, 63.6, 32.2, 32.1, 31.9, 29.7, 29.6, 29.5, 29.3, 29.0, 28.6, 26.2, 26.1, 26.0, 22.7, 14.1 ppm; MS: ($C_{24}H_{44}O_3$ = 380) found 381 (MH^+), 403 (MNa^+).

(*trans*,*trans*,10*R*,11*S*)-1-(Methoxymethoxy)-10,11-(isopropylidenedioxy)heneicosa-2,6-diene, 9b. Diisopropylethylamine (3 mL, 17.2 mmol) was added to a solution of **9a** (3.68 g, 9.7 mmol) in dry CH_2Cl_2 (35 mL) at 0 °C followed by the addition of chloromethyl methyl ether (1.17 g, 14.52 mmol). The mixture was stirred overnight at room temperature and then worked up with water and CH_2Cl_2. Purification by column chromatography (silica gel, hexanes−ethyl acetate, 9:1) afforded **9b** (3.96 g, 96%) in the form of a colorless oil. $[\alpha]_D$ = +1.29 (*c* = 2.08, $CHCl_3$); ^{1}H NMR: δ 5.69 (dtd, *J* = 15.4, 6.4, 0.8 Hz, 1H), 5.53 (dtd, *J* = 15.6, 6.4, 0.6 Hz, 1H), 5.42 (m, 2H), 4.6 (d, *J* = 0.8 Hz, 2H), 3.98 (m, 4H), 3.34 (s, 3H), 2.25−1.95 (m, 6H), 1.60−1.15 (m and br s, 20H), 1.40 (s, 3H), 1.31 (s, 3H), 0.82 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR: δ 134.4, 130.0, 126.0, 107.3, 95.3, 78.0, 77.3, 67.9, 55.2, 32.3, 32.1, 31.9, 29.7, 29.6, 29.5, 29.3, 29.1, 28.6, 26.2, 26.0, 22.7, 14.1 ppm. MS: ($C_{26}H_{48}O_4$ = 424) found 447 (MNa^+).

(*trans*,6*S*,7*S*,10*R*,11*S*)-1-(Methoxymethoxy)-6,7-dihydroxy-10,11-(isopropylidenedioxy)heneicos-2-ene, 10a.

Methanesulfonamide (0.27 g) and **9b** (1.23 g, 2.9 mmol) were added to a two-phase mixture of AD-mix-α (4.1 g) in *tert*-butyl alcohol−water (1:1, 29 mL). The mixture was stirred at 0 °C for 16 h and then worked up by slow addition of sodium metabisulfite (4.5 g) and extraction with ethyl acetate. Purification by column chromatography (silica gel, hexanes−ethyl acetate, 3:7) afforded **10a** (0.84 g, 63%). $[\alpha]_D = -9.22$ (c = 1.94, $CHCl_3$); ^{1}H NMR: δ 5.72 (dt, J = 15.4, 6.2 Hz, 1H), 5.58 (dt, J = 15.4, 6.2 Hz, 1H), 4.61 (s, 2H), 4.02 (m, 2H), 3.98 (d, J = 6.2 Hz, 2H), 3.41 (m, 2H), 3.34 (s, 3H), 2.43 (br s, 2H), 2.23 (m, 1H), 2.14 (m, 1H), 1.75−1.20 (m and br s, 24H), 1.41 (s, 3H), 1.31 (s, 3H), 0.85 (t, J = 6.8 Hz, 3H). ^{13}C NMR: δ 134.2, 126.5, 107.5, 95.5, 78.1, 74.2, 74.0, 67.9, 55.2, 32.7, 31.9, 30.6, 29.8, 29.7, 29.6, 29.5, 29.3, 28.6, 28.5, 26.3, 26.0, 25.9, 25.8, 22.7, 14.1 ppm. MS: ($C_{26}H_{50}O_6$ = 458) found 481 (MNa^+).

(*trans*,6*S*,7*S*,10*R*,11*S*)-1-(Methoxymethoxy)-6,7-bis-(mesyloxy)-10,11-(isopropylidenedioxy)heneicos-2-ene, 10b. Methanesulfonyl chloride (2.31 g, 20.2 mmol) was added dropwise to a solution of **10a** (2.32 g, 5.1 mmol) in dry CH_2Cl_2 (24 mL) and triethylamine (5 mL) at −30 °C. The mixture was warmed to 0 °C, kept at this temperature for an additional 1 h, and then quenched with water and extracted with CH_2Cl_2. Solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel, hexanes−ethyl acetate, 1:1) to give **10b** (3.07 g, 5.0 mmol, 99%). ^{1}H NMR: δ 5.68 (m, 2H), 4.87 (m, 1H), 4.82 (m, 1H), 4.63 (s, 2H), 4.08 (m, 1H), 4.01 (d, J = 4.4 Hz, 2H), 4.00 (m, 1H), 3.36 (s, 3H), 3.10 (s, 6H), 2.24 (m, 2H), 2.15−1.20 (m and br s, 24H), 1.42 (s, 3H), 1.32 (s, 3H), 0.87 (t, J = 6.0 Hz, 3H). ^{13}C NMR: δ 132.0, 127.7, 95.4, 80.7, 80.0, 77.8, 77.4, 67.5, 51.0, 38.6, 31.8, 31.0, 29.6, 29.5, 29.2, 28.4, 27.3, 26.2, 25.7, 25.4, 22.6, 14.1 ppm. MS: ($C_{28}H_{54}O_{10}S_2$ = 614) found 637 (MNa^+).

(2*R*,3*R*,6*S*,7*S*,10*R*,11*S*)-1-(Methoxymethoxy)-6,7-bis-(mesyloxy)-10,11-(isopropylidenedioxy)heneicosane-2,3-diol, 11. Compound **10b** (3.07 g, 5.0 mmol) was added to a cold (0 °C) mixture of AD-mix-β (7.0 g) and methanesulfonamide (0.475 g, 5 mmol) in *tert*-butyl alcohol−water (3:2, 50 mL). The mixture was stirred at 0 °C for 16 h and then worked up by slow addition of sodium metabisulfite (7.5 g) followed by extraction with ethyl acetate. Solvent was removed, and the resultant crude **11** (3.4 g) was used in the next reaction without further purification. ^{1}H NMR: δ 4.85 (m, 2H), 4.63 (s, 2H), 4.04 (m, 1H), 3.98 (m, 1H), 3.69 (m, 1H), 3.62 (m, 3H), 3.37 (s, 3H), 3.11 (s, 3H), 3.10 (s, 3H), 2.07 (m, 2H), 1.84−1.20 (m and br s, 26H), 1.40 (s, 3H), 1.30 (s, 3H), 0.85 (t, J = 7.0 Hz, 3H). ^{13}C NMR: δ 107.6, 97.0, 80.9, 77.8, 77.4, 72.5, 71.5, 70.5, 55.4, 53.3, 43.2, 38.7, 31.8, 29.5, 29.4, 29.2, 28.4, 28.3, 27.3, 26.7, 26.2, 25.7, 25.4, 22.5, 14.0 ppm. MS: ($C_{28}H_{56}O_{12}S_2$ = 648) found 781 (MCs^+).

(2*R*,3*R*,6*R*,7*R*,10*R*,11*S*)-1-(Methoxymethoxy)-3,6:7,10-dioxydoheneicosane-2,11-diol, 12a. TsOH (1.0 g) was added to a solution of the above-mentioned diol (3.4 g) in methanol (50 mL), and the mixture was stirred at room temperature for 16 h and then washed with saturated aqueous $NaHCO_3$ and extracted with ethyl acetate. Solvent was removed under reduced pressure, the residue was dissolved in pyridine (10 mL), and the mixture was heated to 140 °C for 4 h. The solvent was removed again, worked-up with water and ethyl acetate, and purified over silica gel to give **12a** (1.0 g, 48%) and **12b** (0.25 g, 13%). Physical data of **12a**: ^{1}H NMR: δ 4.62 (AB quartet, 6.8 Hz, 2H), 3.96 (dt, J = 8.5, 5.9 Hz, 1H), 3.90 (m, 2H), 3.84 (m, 2H), 3.67−3.50 (m, 3H), 3.33 (s, 3H), 2.75 (br, 1H), 1.96 (m, 4H), 1.91 (m, 2H), 1.77 (m, 2H), 1.56 (br s, 1H), 1.21 (m and br s, 20H), 0.84 (t, J = 7.1 Hz, 1H). ^{13}C NMR: δ 96.8, 82.8, 82.5, 82.4, 80.2, 73.1, 71.2, 69.5, 55.3, 32.3, 31.9, 29.7, 29.6, 29.5, 29.3, 28.9, 28.8, 28.2, 26.0, 24.4, 22.7, 14.1 ppm. MS: ($C_{23}H_{44}O_6$ = 416) found 439 (MNa^+).

(2*R*,3*R*,6*R*,7*R*,10*R*,11*S*)-1,2,11-Trihydroxy-3,6:7,10-dioxidoheneicosane, 12b. Compound **12a** (1.0 g, 2.4 mmol) was dissolved in dimethyl sulfide (4 mL) and dry CH_2Cl_2 (2 mL) and cooled to 0 °C. Boron trifluoride etherate (0.89 mL, 7.2 mmol) was added dropwise, and the mixture was stirred for additional 5 min then quenched with saturated aqueous $NaHCO_3$ and extracted with ethyl acetate. Removal of the solvent and column chromatography (silica gel, hexanes−ethyl acetate, 3:7) afforded **12b** (0.705 g, 79%) in the form of a colorless oil. $[\alpha]_D$ +0.6 (c = 2.05, $CHCl_3$); ^{1}H NMR: δ 4.01 (dt, J = 8.3, 5.8 Hz, 1H), 3.95−3.82 (m, 4H), 3.68 (dd, J = 11.5, 3.4 Hz, 1H), 3.60 (dd, J = 11.5, 5.3 Hz, 1H), 3.53 (td, J = 5.3, 3.8 Hz, 1H), 2.50 (br s, 3H), 1.93−1.20 (m and br s, 26H), 0.85 (t, J = 7.2 Hz, 3H); ^{13}C NMR: δ 82.8, 82.7, 82.5, 80.5, 73.6, 71.3, 64.2, 32.3, 31.9, 29.7, 29.6, 29.5, 29.3, 29.0, 28.7, 28.1, 26.1, 24.4, 22.7, 14.1 ppm. MS: ($C_{21}H_{40}O_5$ = 372) found 395 (MNa^+).

(2*R*,3*R*,6*R*,7*R*,10*R*,11*S*)-1-(Tosyloxy)-3,6:7,10-dioxidoheneicosane-2,11-diol, 12c. Tosyl chloride (0.558 g, 2.93 mmol) was added in small portions to a solution of **12b** (0.91 g, 2.44 mmol) in pyridine (5 mL) at 0 °C, and the mixture was stirred for additional 3.5 h and then worked up with water and CH_2Cl_2. Solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel, ethyl acetate) to give **12c** (0.66 g, 51%) and recovered **12b** (0.18 g, 20%). Physical properties of **12c**: ^{1}H NMR: δ 7.76 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 4.06−3.98 (m, 2H), 3.94 (dt, J = 8.5, 5.7 Hz, 1H), 3.92−3.74 (m, 4H), 3.66 (q, J = 5.3 Hz, 1H), 2.42 (s, 3H), 2.05−1.16 (m and br s, 26H), 0.84 (t, J = 7.2 Hz, 3H); ^{13}C NMR: δ 144.9, 132.7, 129.9, 128.0, 127.9, 82.8, 82.5, 79.3, 71.5, 71.2, 71.1, 31.9, 29.7, 29.6, 29.5, 29.3, 28.9, 28.7, 28.1, 26.0, 24.4, 22.7, 21.6, 14.1 ppm. MS: ($C_{28}H_{46}O_7S$ = 526) found 527 (MH^+).

(2*R*,3*R*,6*R*,7*R*,10*R*,11*S*)-11-Hydroxy-1,2-epoxy-3,6:7,10-dioxidoheneicosane, 13a. Potassium carbonate (0.345 g, 2.5 mmol) was added to a solution of **12c** (0.66 g, 1.25 mmol) in methanol (10 mL), and the mixture was stirred at room-temperature overnight, worked up with water and ethyl acetate, and purified by column chromatography (silica gel, ethyl acetate) to give **13a** (398 mg, 90%). $[\alpha]_D$ +4.4 (c = 1.44, $CHCl_3$); ^{1}H NMR: δ 3.96 (td, J = 7.0, 4.4 Hz, 1H), 3.93−3.80 (m, 4H), 2.96 (q, J = 3.5 Hz, 1H), 2.72 (d, J = 3.5 Hz, 2H), 2.12−1.20 (m and br s, 26H), 0.84 (t, J = 7.0 Hz, 3H); ^{13}C NMR: δ 82.8, 82.6, 82.3, 78.5, 71.2, 54.2, 44.1, 32.4, 31.9, 29.7, 29.6, 29.5, 29.3, 28.8, 28.2, 26.0, 24.5, 22.7, 14.1 ppm. MS: ($C_{21}H_{38}O_4$ = 354) found 377 (MNa^+); 393 (MK^+).

(2*R*,3*R*,6*R*,7*R*,10*R*,11*S*)-11-Acetoxy-1,2-epoxy-3,6:7,10-dioxidoheneicosane, 13b. Pyridine (1 mL) and acetic anhydride (0.5 mL) were mixed with **13a** (375 mg, 1.06 mmol). The mixture was stirred at room temperature for 16 h, worked up with water and ethyl acetate, and purified by column chromatography (silica gel, hexanes−ethyl acetate, 1:1) to give **13b** (291 mg, 69%). ^{1}H NMR: δ 4.88 (m, 1H), 3.96 (m, 1H), 3.95−3.82 (m, 3H), 2.93 (m, 1H), 2.68 (m, 2H), 2.15−1.20 (m and br s, 26H), 1.90 (s, 3H), 0.87 (t, J = 7.2 Hz, 3H). MS: ($C_{23}H_{40}O_5$ = 396): 397 (MH^+), 419 (MNa^+).

(4*R*,5*R*,8*R*,9*R*,12*R*,13*S*)-13-Acetoxy-4-hydroxy-3,6:7,10-dioxidotricos-1-yne, 14. A solution of *n*-BuLi (1.6 M in THF, 0.32 mL, 0.51 mmol) was added to a solution of (trimethylsilyl)-acetylene (50.6 mg, 0.51 mmol) in THF (1 mL) at −78 °C. The mixture was warmed to −30 °C, stirred at this temperature for 0.5 h, and then cooled again to −78 °C. Boron trifluoride (72.54 mg, 0.51 mmol) was added, the mixture was stirred for 0.5 h, epoxide **13b** (98 mg, 0.25 mmol) was added, and the mixture was stirred between −78 °C and −30 °C for 10 h. Saturated aqueous ammonium chloride was added, the mixture was extracted with ethyl acetate, and the solvent was removed under reduced pressure. The residue (102 mg) was dissolved in THF (2 mL) and cooled to 0 °C, tetrabutylammonuim fluoride (1 M solution in THF, 0.25 mL) was added, and the mixture was stirred for 2 h and then quenched with saturated aqueous ammonium chloride. Extraction with ethyl acetate and purification by column chromatography (silica gel, hexanes−ethyl acetate, 7:3) afforded **14** (41 mg, 39%) and recovered **13b** (33 mg, 35%). $[\alpha]_D = -14.6$ (c = 0.84, $CHCl_3$); ^{1}H NMR: δ 4.92 (m, 1H), 3.99 (m, 2H), 3.87 (m, 2H), 3.59 (q, J = 5.7 Hz, 1 H,), 2.62 (br s, 1H), 2.41 (m, 2H), 2.03 (s, 3H), 2.05−1.85 (m, 4H), 1.80−1.45 (m, 6H), 1.22 (m and br s, 16H), 0.86 (t, J = 6.8 Hz, 3H). ^{13}C NMR: δ 82.1, 82.0, 81.3, 80.6, 75.3, 71.9, 70.1, 31.9, 31.0, 29.6, 29.5, 29.3, 28.7, 28.3, 27.5, 25.4, 23.9, 22.7, 21.2, 14.1 ppm. MS: ($C_{25}H_{42}O_5$ = 422) found 445 (MNa^+).

(*E,Z*)-8-(*tert*-Butyldimethylsilyloxy)-1-iodonon-1-ene, 16. To a solution of non-8-yn-1-ol[11] (2.03 g, 14.5 mmol) in DMF (30 mL) were added imidazole (2.44 g, 35.9 mmol) and *tert*-butyldimethylchlorosilane (2.36 g, 15.6 mmol). The mixture was stirred at room temperature overnight and worked-up with ether and water, and the residue was purified by column chromatography (silica gel, hexanes−ethyl acetate, 7:3) to give 9-(*tert*-butyldimethylsilyloxy)non-1-yne (3.6 g, 98%). ^{1}H NMR: δ 3.59 (t, J = 6.8 Hz, 2H), 2.17 (td, J = 7.6, 4.8 Hz, 2H), 1.93 (t, J = 2.8 Hz, 1H), 1.66−0.82 (m, 10H), 0.88 (s, 9H), 0.04 (s, 6H).

Tributyltin hydride (6.56 g, 22.6 mmol) was added to a mixture of the above-mentioned silyl ether (3.6 g, 14.1 mmol) and 1,1 azobis(cyclohexanecarbonitrile) (30 mg, 0.12 mmol). The mixture was heated at 130 °C for 2 h and then cooled to room temperature. Excess tributyltin hydride was removed by distillation under reduced pressure. The residue was dissolved in ether (10 mL), iodine (4.0 g, 15.75 mmol) was slowly added, and the solution was stirred at room temperature for 2 h. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel, hexanes−EtOAc) to give **16** (3.45 g, 64%). ^{1}H NMR: δ 6.48 (dt, J = 14.3, 7.2 Hz 0.8H), 6.15 (m, 0.4H), 5.94 (dt, J = 14.3, 1.4 Hz, 0.8H), 3.58 (two t, J = 6.6 Hz each, 0.4 and 1.6H), 2.10 (qd, J = 5.7, 2.6 Hz 0.4H), 2.03 (qd, J = 7.4, 1.4 Hz, 1.6H), 1.52−1.25 (m, 10H), 0.88 (s, 9H), 0.03 (s, 6H). MS: ($C_{15}H_{31}$-IOSi = 382) found 381 $[M - H]^-$.

(*E,Z*)-1,9-Diiodonon-1-ene, 17. To an ice-cold solution of **16** (3.45 g, 9.0 mmol) in dry THF (34 mL) was added tetrabutylammonium fluoride (1 M in THF, 10 mL), and the mixture was stirred at 0 °C for 3 h and then worked up with ether and water. The solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel, hexanes−EtOAc, 7:3) to give the corresponding alcohol (1.81 g, 75%). MS: 291 ($M + Na^+$). ^{1}H NMR: δ 6.48 (dt, J = 14.3, 7.2 Hz, 0.8H), 6.15 (m, 0.4H), 5.95 (dt, J = 14.3, 1.2 Hz, 0.8H), 3.17 (t, J = 7.0 Hz, 0.4H), 3.16 (t, J = 7.0 Hz, 1.6H), 2.11 (q, J = 6.7 Hz, 0.4H), 2.02 (q, J = 7.1 Hz, 1.6H), 1.77 (m, 2H), 1.45−1.22 (m, 8H).

To an ice-cooled solution of the above-described alcohol (1.81 g, 6.76 mmol) in pyridine (30 mL) was added TsCl (1.68 g, 8.8 mmol). The mixture was stirred for 1 h at 0 °C and 3 h at room temperature and then was diluted with ether, washed with 1 N HCl, and with water. Solvent was removed under reduced pressure, and the residue was dissolved in acetone (20 mL). NaI (2.99 g, 19.9 mmol) was added, and the mixture was stirred for 3 h, filtered, and concentrated. The residue was purified by column chromatography (silica gel, hexanes−EtOAc) to give **17** (2.0 g, 78%). ^{1}H NMR: δ 6.47 (m, 1H), 5.95 (dt, J = 14.4, 1.2 Hz, 1H), 3.5 (t, J = 6.8, t Hz, 1H), 3.16 (t, J = 8.0 Hz, 1H), 2.02 (q, J = 6.8 Hz, 2H), 1.76 (m, 3H), 1.32 (m, 7H); ^{13}C NMR: δ 146.56, 141.26, 74.54, 45.12, 35.99, 32.55, 30.36, 28.73, 28.68, 28.62, 28.22, 26.75.

(*E,Z*,3*RS*,5*S*)-3-(9-Iodonon-8-enyl)-5-methyl-3-(phenylsulfenyl)-tetrahydrofuran-2-one, 19. Sodium bis(trimethylsilyl)amide (0.5 M in toluene, 3 mL, 1.5 mmol) was added to a cold (0 °C) solution of (3*RS*,5*S*)-5-methyl-2-(phenylsulfenyl)-tetrahydrofuran-2-one, **18**[16] (0.312 g, 1.5 mmol), in THF (7 mL), and the mixture was stirred at 0 °C for 0.5 h. A solution of **17** (0.567 g, 1.5 mmol) in HMPA (3 mL) was added, and the mixture was warmed to room temperature and heated under reflux for 2 h. The mixture was worked up with ether and saturated aqueous NH_4Cl, the solvent was removed under reduced pressure, and the residue was purified by column chromatography (silica gel, hexanes−EtOAc, 4:1) to give **19** in the form of a 4:1 mixture of two diastereomers (0.361 g, 52%). ^{1}H NMR: δ 7.53 (m, 2H), 7.35 (m, 3H), 6.47 (dt, J = 14.3, 7.2 Hz, 0.8H), 6.14 (m, 0.4H), 5.94 (dt, J = 14.3, 1.2 Hz, 0.8H), 4.58 (m, 0.2H), 4.47 (m, 0.8H), 2.49 (dd, J = 14.0, 7.6 Hz, 0.8H), 2.31 (dd, J = 13.8, 5.4 Hz, 0.2H), 2.11 (m, 0.4H), 2.01 (qd, J = 7.4, 1.4 Hz, 1.6H), 1.94 (dd, J = 14.0, 6.8 Hz, 1H), 1.76 (m, 2H), 1.35 (d, J = 6.2 Hz, 0.6H), 1.62−1.20 (m and br s, 10H), 1.16 (d, J = 6.4 Hz, 2.4H); MS: ($C_{20}H_{27}IO_2S$ = 458) found 459 (MH^+), 481 (MNa^+).

3-(Phenylthio)-11,12,13,13,14,14-hexadehydrouvaricin, 20. Copper(I) iodide (3 mg, 0.015 mmol) and $Pd(PPh_3)_4$ (4 mg, 0.0034 mmol) were added to a solution of **14** (14 mg, 0.033 mmol) and **19** (30.3 mg, 0.066 mmol) in Et_3N (0.5 mL). The mixture was stirred at room temperature for 22 h, washed by saturated aqueous ammonium chloride, and extracted with ether, and the crude product was purified by column chromatography (silica gel, hexanes−ethyl acetate, 1:1) to give **20** (11.2 mg, 45%). ^{1}H NMR: δ 7.49−7.54 (m, 2H), 7.31−7.39 (m, 3H), 6.04 (dt, J = 15.8, 7.0 Hz, 1H), 5.42 (d, J = 15.8 Hz, 1H), 4.92 (m, 1H), 4.47 (m, 1H), 3.99 (q, J = 6.4 Hz, 2H), 3.87 (m, 2H), 3.57 (q, J = 5.7 Hz, 1H), 2.49 (m, 4H), 2.10−1.85 (m, 6H), 2.03 (s, 3H), 1.75−1.40 (m, 10H), 1.37−1.20 (m, 24H), 1.17 (d, J = 6.2 Hz, 3H), 0.85 (t, J = 7.1 Hz, 3H). MS: ($C_{45}H_{68}O_7S$ = 752) found 885 (MCs^+).

3-(Phenylthio)uvaricin, 21. A solution of **20** (10 mg, 0.013 mmol) in benzene−methanol (1:1, 2 mL) was purged with argon and then hydrogenated (1 atm H_2) over chlorotris-(triphenylphosphine)rhodium (10 mg, 0.01 mmol) for 16 h. Column chromatography (silica gel, hexanes−ethyl acetate, 1:1) afforded **21** (6 mg, 62%). ^{1}H NMR: δ 7.49−7.55 (m, 2H), 7.31−7.40 (m, 3H), 4.92 (ddd, J = 9.0, 4.8, 4.2 Hz, 1H), 4.47 (m, 1H), 4.00 (td, J = 7.5, 5.6 Hz, 1H), 3.86 (m, 2H), 3.80 (td, J = 7.6, 6.4 Hz, 1H), 3.36 (m, 1H), 2.50 (dd, J = 13.9, 7.6 Hz, 2H), 2.04 (s, 3H), 1.95 (m, 4H), 1.80−1.15 (m and br s, 47H), 1.17 (d, J = 6.3, 3H), 0.85 (t, J = 7.0 Hz, 3H); MS: ($C_{45}H_{74}O_7S$ = 758) found 781 (MNa^+).

Uvaricin, 1. m-CPBA (2 mg) was added to a solution of the above-described product (6 mg, 0.008 mmol) in CH_2Cl_2 (2 mL) at 0 °C, and the mixture was stirred at this temperature for 20 min and then filtered through a silica gel column using CH_2Cl_2. Solvent was removed under reduced pressure, and the residue was refluxed in toluene (1 mL) for 1 h. Solvent was removed again, and the residue was purified by column chromatography (silica gel, hexanes−ethyl acetate, 1:1) to give **1** (2 mg, 32%). $[\alpha]_D$ +11.6 (c = 0.09, MeOH), lit.[9] 11.3 (MeOH); ^{1}H NMR and ^{13}C NMR data were found to be identical to the reported spectral data.[9] HRMS: ($C_{39}H_{68}O_7Cs$ = 781.4019) found 781.4044 (MCs^+).

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Supporting Information Available: Copies of ^{1}H NMR spectra of compounds **1, 3, 4, 7, 8, 9a, 10a, 11, 12a, 13a, 14, 19, 20,** and **21**, ^{13}C NMR spectra of compounds **3, 4, 7, 8, 9a, 10a, 11, 12a, 13a, 14,** and **19** (25 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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