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Syntheses of Two Possible Diastereoisomers of the Epoxy Lactone Proposed for an Annonaceous Acetogenin, Epoxyrollin A[1)]

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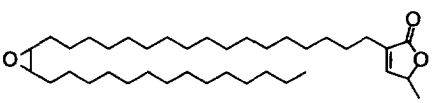
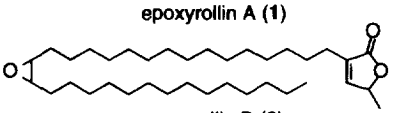
Abstract: Syntheses of two possible diastereoisomers (5*S*, 18'*S*, 19'*R*)- and (5*S*, 18'*R*, 19'*S*)-**1** corresponding to the epoxy lactone that has been proposed for epoxyrollin A, a structural representative of biosynthetic precursors of tetrahydrofuran annonaceous acetogenins, are described. The ^{13}C-NMR and tandem mass spectral data of the synthetic samples were not in accord with those recorded for natural epoxyrollin A. Consequently, the structure of epoxyrollin A needs to be revised. Copyright © 1996 Elsevier Science Ltd

The Annonaceous acetogenins, that are endemic to certain plants of the *Annonaceae*, are of much interest especially due to their unique structural features and their significant cytotoxic, antitumor, pesticidal, antiinfective and antifeedant activities.[2)] More than 160 compounds belonging to this family have been isolated to date, and most of them possess one or more tetrahydrofuran rings, together with a terminal α,β-unsaturated γ-lactone unit on a C-35 or C-37 long carbon chain. In addition to this major group of acetogenins, there are several congeners bearing an epoxide group in place of the tetrahydrofuran ring, which can be assumed to be intermediary precursors in the biosynthesis of tetrahydrofuran ring-containing annonaceous acetogenins from polyunsaturated fatty acids.[3,4)] A. Cavé and co-workers isolated epoxyrollins A and B from *Rollinia urei* in 1990 as an inseparable mixture, and proposed structures **1** and **2** for them, respectively.[5)] Both compounds have the even-numbered carbon atoms of 38 and 36 unlike almost all other acetogenins. In connection with our ongoing synthetic work on annonaceous acetogenins, this prompted us to synthesize these substances. The absolute stereochemistry of **1** and **2** has not yet been reported. However, because the epoxide ring stereo-



epoxyrollin A (**1**)



epoxyrollin B (**2**)

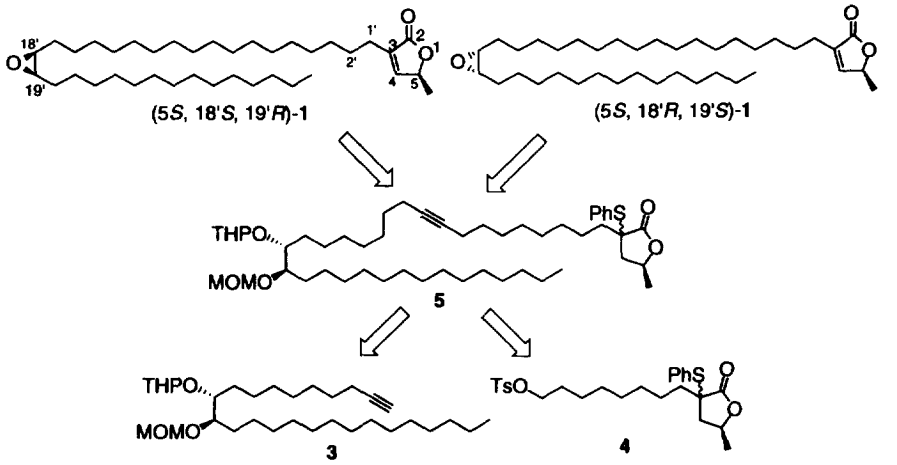
Fig. 1

chemistry of **1** and **2** has been determined to be *cis* on the basis of ^{1}H-NMR data and the *S* configuration of the secondary methyl group of the lactone moiety is well-known, it follows that their absolute stereostructures are (5*S*, 18'*S*, 19'*R*) or (5*S*, 18'*R*, 19'*S*) for **1**, and (5*S*, 16'*S*, 17'*R*) or (5*S*, 16'*R*, 17'*S*) for **2**. Here, we describe total syntheses of two possible diastereoiomers (5*S*, 18'*S*, 19'*R*)- and (5*S*, 18'*R*, 19'*S*)-**1** corresponding to the epoxy lactone **1** that has been proposed for epoxyrollin A.[6] And we also report that the structure of epoxyrollin A should be revised.

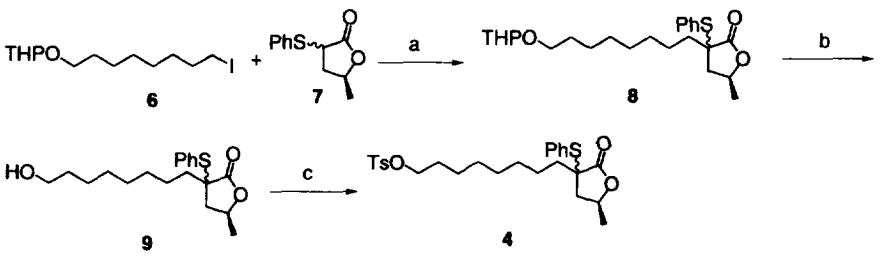
Our first synthetic strategy is outlined in Scheme 1. This route involves a coupling reaction between the lithium salt of **3** and lactonic tosylate **4**.[7]

Firstly, lactonic tosylate **4** was constructed by the method shown in Scheme 2. Alkylation[8] of the sodium enolate of lactone **7**[9] with iodide **6** afforded **8** in 72 % yield. Removal of the tetrahydropyranyl (THP) group of **8** with *p*-toluenesulfonic acid (*p*-TsOH) gave **9**, which was then treated with *p*-toluenesulfonyl chloride (*p*-TsCl) in pyridine to yield **4**.

Next, protected dihydroxy synthon **3** was obtained as depicted in Scheme 3. Base-promoted alkylation of 2-propyn-1-ol with myristyl bromide afforded acetylenic alcohol **11**, which on lithium aluminum hydride reduction gave (*E*)-allylic alcohol **12**. The hydroxy group of **12** was protected as a *tert*-butyldimethylsilyl (TBS) ether to provide **13**, which was then submitted to asymmetric dihydroxylation with AD-mix β[10] to furnish waxy (2*R*, 3*R*) diol **14**. Protection of **14** as an acetonide and subsequent deprotection of the TBS group of **15** with tetrabutylammonium fluoride (TBAF) afforded primary alcohol **16**, which on successive treatment with *p*-TsCl in pyridine, acidic methanol and excess potassium hydroxide in methanol led to epoxy



Scheme 1

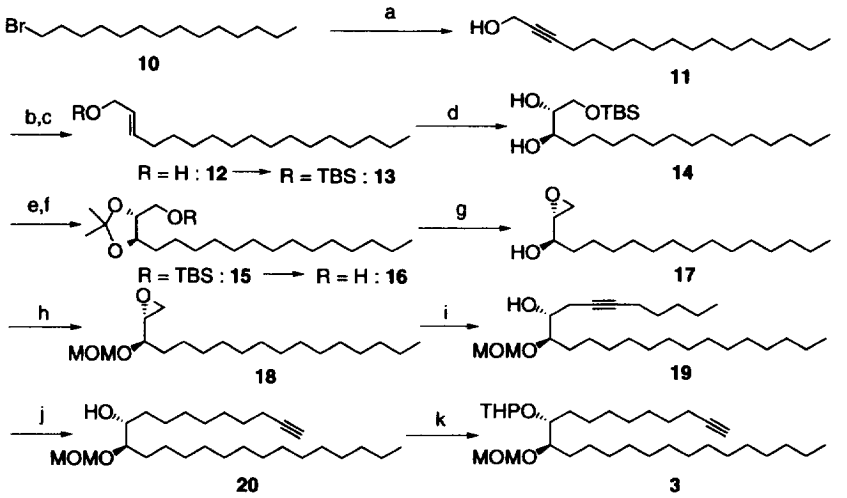


Scheme 2

Reagents and conditions : a) NaHMDS, HMPA, THF, 71%. b) *p*-TsOH, MeOH, 83%, c) *p*-TsCl, pyridine, 92%.

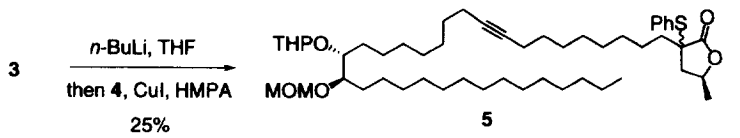
alcohol **17** in 89% yield. At this stage, the enantiomeric purity of **17** was proved to be 94% ee by a ^{1}H-NMR analysis of the corresponding Mosher ester derivative. Recrystallization of this sample from hexane gave enantiomerically pure **17**. The secondary hydroxyl group of **17** was protected as a methoxymethyl (MOM) ether to yield **18**, which was then subjected to the coupling reaction with 1-octynyllithium in the presence of boron trifluoride etherate[11] to afford **19**. Acetylene zipper reaction[12] of **19** with potassium 3-aminopropyl-amide (KAPA) furnished terminal alkyne **20**, of which the hydroxyl group was then protected as a THP ether to give the requisite synthon **3**.

Finally, the reaction between the organocopper reagent derived from **3** and **4** provided coupling product **5** having the full carbon skeleton of the target molecule, but in only poor yield (Scheme 4).



Scheme 3

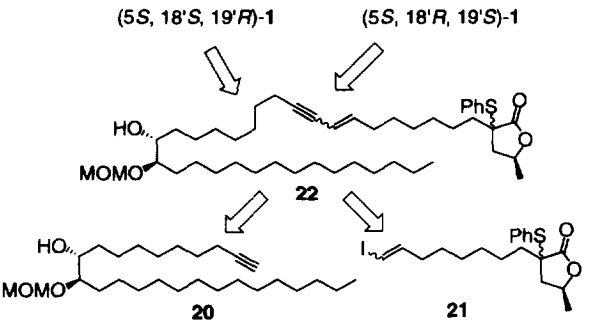
Reagents and conditions : a) 2-propyn-1-ol, $LiNH_2$, HMPA, 83%. b) $LiAlH_4$, THF, reflux, 95%. c) TBDMSCl, imidazole, DMF, 98%. d) AD-mix β, *t*-BuOH, H_2O, 99%. e) 2,2-dimethoxy-propane, acetone, 89%. f) TBAF,THF, 92%. g) i: *p*-TsCl, pyridine; ii : HCl, $MeOH$,; iii : KOH, MeOH, 89% (94% ee); iv : recrystallization,75% (>98% ee). h) MOMCl, *i*-Pr_2NEt,CH_2Cl_2,85%. i) 1-octyne, *n*-BuLi, BF_3-Et_2O, THF, 97%. j) Li,1,3-diaminopropane, *t*-BuOK, 89%. k) DHP, *p*-TsOH, CH_2Cl_2, 78%.



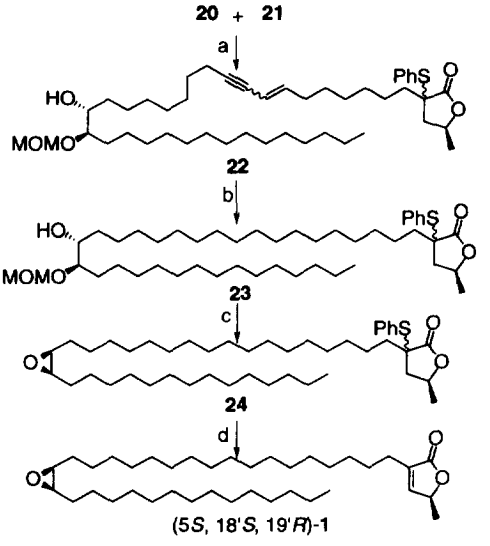
Scheme 4

In the second synthetic approach involving a palladium-catalyzed cross-coupling reaction, we selected vinyl iodide **21** that had been reported earlier[8] as a coupling partner with ternimal acetylene synthon **20** (Scheme 5).

Completion of the carbon skeleton leading to **22** was achieved by the Alami method[13] consisting of a mild treatment with $Pd(Ph_3P)_4$, CuI and organic base (Scheme 6). Catalytic homogeneous hydrogenation of **22**, using the Wilkinson catalyst, afforded saturated product **23**, which after successive treatment with methane-sulfonyl chloride (MsCl), methanolic HCl and KOH in tetrahydrofuran, furnished **24** in 70% overall yield. Oxidation of **24** with *m*-chloroperbenzoic acid (*m*-CPBA) and subsequent thermal elimination afforded (5*S*, 18'*S*, 19'*R*)-**1**.



Scheme 5

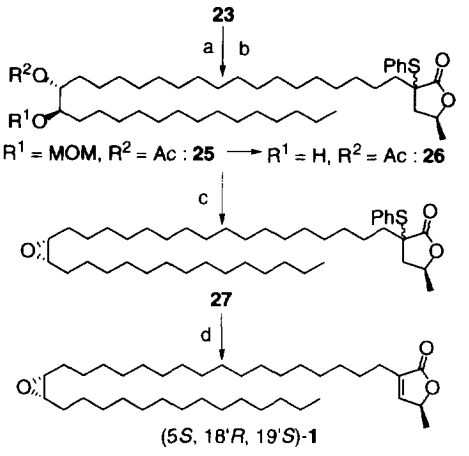


Scheme 6

Reagents and conditions : a) $Pd(PPh_3)_4$, pyrrolidine, CuI, 84%. b) H_2, $Rh(PPh_3)_3Cl$, benzene, 90%. c) i : MsCl, Et_3N, pyridine; ii : HCl, MeOH. THF; iii : KOH, 81%. d) i : *m*-CPBA, CH_2Cl_2; ii : toluene reflux, 85%.

Transformation of **23** into (5*S*, 18'*R*, 19'*S*)-**1** was carried out as shown in Scheme **7**. After protecting the hydroxyl group of **23** as an acetate, the MOM ether was deprotected with a catalytic amount of pyridinium *p*-toluenesulfonate (PPTS) in dichloromethane-methanol (4 : 1) to yield hydroxy acetate **26**. Treating **26** with MsCl and subsequent epoxy ring closure with potassium hydroxide resulted in the formation of compound **27**. Finally, the oxidation-elimination sequence similar to that described above afforded (5*S*, 18'*R*, 19'*S*)-**1**.

While the ^{1}H-NMR and IR spectral data for synthetic (5*S*, 18'*S*, 19'*R*)- and (5*S*, 18'*R*, 19'*S*)-**1** were almost consistent with those reported for natural epoxyrollin A, their ^{13}C-NMR and tandem mass spectral data were considerably different from each other. The comparative ^{13}C-NMR data for synthetic (5*S*, 18'*S*, 19'*R*)- or (5*S*, 18'*R*, 19'*S*)-**1** and natural epoxyrollin A are shown in Fig. 2, in which considerable chemical shift differences were observed primarily at the four carbon atoms on and around the oxirane ring. As illustrated in Fig. 3, the tandem mass spectral data of synthetic (5*S*, 18'*S*, 19'*R*)-**1** exhibited a simple fragmentation pattern in contrast to those of natural epoxyrollin A. These results, in conjunction with the unusual carbon numbers (C-38) of epoxyrollin A, strongly suggested that the structure of natural product should be revised.



Scheme 7

Reagents and conditions : a) Ac_2O, DMAP, 92%. b) PPTS, MeOH, CH_2Cl_2, 45%. c) i : MsCl, Et_3N, pyridine; ii : KOH, MeOH, 85 %. d) i : *m*-CPBA, CH_2Cl_2 ii : toluene reflux, 90%.

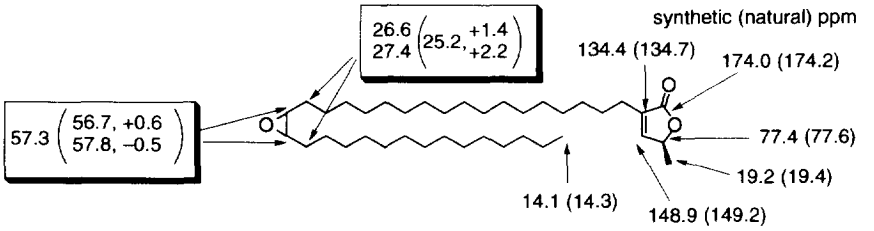


Fig. 2

Fig. 3

EXPERIMENTAL

All melting point (mp) data are uncorrected. Optical rotations were measured with a JASCO DIP-4 spectrometer. IR spectra were taken with a JASCO IR-810 infrared spectrometer. ^{1}H- and ^{13}C-NMR spectra were measured with JEOL GSX-270 and GSX-400 spectrometer. Mass spectra were recorded with JEOL JMS-DX-300, JMS-DX-303, and JMS-AX-500 instruments.

(3*RS*,5*S*)-3-[8'-(Tetrahydropyranyl-2''-oxy)octyl]-5-methyl-3-(phenylsulfanyl)tetrahydrofuran-2-one (8) To an ice-cooled solution of lactone 7 (5.00 g, 24.0 mmol) in THF (50 ml) was added sodium bis(trimethylsilyl)amide (1.0 M in THF, 24 ml). After the mixture had been stirred at 0℃ for 30 min, iodide **6** (12.2 g, 36.0 mmol) in HMPA (5 ml) was added to it and the whole was allowed to warm to room temperature. The reaction mixture was then poured into saturated aqueous NH_4Cl and extracted with

ether (150 ml). Drying the ethereal solution over $MgSO_4$ and subsequent concentration gave the crude lactone, which was chromatographed over silica gel (hexane : AcOEt = 4:1) to give pure lactone **8** (7.10 g, 17.0 mmol, 71%) as a yellow oil. IR (film) ν_{max} cm^{-1} : 2920, 2850, 1760, 1440, 1340, 1180, 1120, 1080, 1030, 750, 690. ^{1}H-NMR (CDCl$_3$, 270 MHz) δ: 1.10-2.10 (21H, m), 1.19 (3H, d, J = 6.4Hz, CH_3CH), 2.35-2.55 (1H, m, CHHCHCH$_3$), 3.37 (1H, m), 3.50 (1H, m), 3.72 (1H, m), 3.88 (1H, m), 4.40-4.55 (1H, m, CH$_2$CHCH$_3$), 4.57 (1H, m, OCHO), 7.38 (3H, m, aromatic-H), 7.54 (2H, m, aromatic-H). HREIMS (m / z) : (M^+-C_3H_6) Calcd. for $C_{21}H_{30}O_4S$, 378.1855; Found, 378.1865.

(3*RS*,5*S*)-3-(8'-Hydroxyoctyl)-5-methyl-3-(phenylsulfanyl)tetrahydrofuran-2-one (9) To an ice-cooled solution of lactone **8** (2.00 g, 4.75 mmol) in MeOH (20 ml) was added *p*-TsOH (10 mg) at 0℃. After being stirred at room temperature for 3 h, the reaction mixture was quenched with saturated aqueous NaHCO$_3$ (20 ml), and the MeOH was evaporated. The residual solution was extracted with AcOEt, the organic layer being washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Silica gel column chromatography of the residue (hexane : AcOEt = 4:1) gave pure alcohol **9** (1.39 g, 3.94 mmol, 83%) as a colorless oil. IR (film) ν_{max} cm^{-1} : 3450, 2920, 2850, 1760, 1440, 1340, 1180, 750, 690. ^{1}H-NMR (CDCl$_3$, 270 MHz) δ: 1.10-2.10 (16H, m), 1.19 (3H, d, J = 6.4 Hz, CHCH_3), 2.35-2.55 (1H, m), 3.64 (2H, t, J = 6.6 Hz, CH_2OH), 4.40-4.55 (1H, m, CHCH$_3$), 7.38 (3H, m, aromatic-H), 7.54 (2H, m, aromatic-H). *Anal.* Calcd. for $C_{19}H_{28}O_3S$: C, 67.82; H, 8.39. Found: C, 67.45; H, 8.24%.

(3*RS*,5*S*)-3-(8'-*p*-Toluenesulfonyloxyoctyl)-5-methyl-3-(phenylsulfanyl)tetrahydrofuran-2-one (4) To an ice-cooled solution of alcohol **9** (50 mg, 0.140 mmol) in pyridine (5 ml) was added *p*-TsCl (30 mg, 0.158 mmol). After being stirred in an ice-bath for 1 h and then at room temperature for 10 h, the mixture was extracted with AcOEt (60 ml). The extract was dried over $MgSO_4$ and concentrated *in vacuo* to give the crude tosylate (74 mg, 0.145 mmol, 92%) as a colorless oil, which was used in the next step without further purification. IR (film) ν_{max} cm^{-1} : 2920, 2850, 1760, 1440, 1340, 1180, 1020. ^{1}H-NMR (CDCl$_3$, 270 MHz) δ: 1.10-2.20 (15H, m), 1.19 (3H, d, J = 6.4 Hz, CHCH_3), 2.35-2.55 (1H, m, CHHCHCH$_3$), 2.62 (3H, s, CH_3C$_6$H$_4$), 3.53 (2H, t, J = 6.8 Hz, TsOCH_2), 4.45-4.65 (1H, m, CHCH$_3$), 7.30-7.80 (9H, m, aromatic-H).

2-Heptadecyn-1-ol (11) To a $LiNH_2$ solution, which had been prepared from Li (10.8 g, 1.44 mol) and liq. NH_3 (1.5 l), was added gradually a solution of 2-propyn-1-ol (40.4 g, 0.720 mol) in ether (50 ml) over 30 min. After stirring for 2 h, a solution of myristyl bromide **11** (100 g, 0.360 mol) in ether (200 ml) was added to the solution over 1 h, dry HMPA (50 ml) was then added, and the ammonia was allowed to evaporate overnight. The residue was diluted with H_2O and extracted with ether (1.5 l). Drying over $MgSO_4$ and concentration gave the crude alcohol, which was purified by silica gel column chromatography, eluted with hexane-AcOEt (4:1) to give acetylene alcohol **11** (75.4 g, 0.30 mol, 83%) as a wax, mp 52 ℃. IR (film) ν_{max} cm^{-1} : 3320, 3180, 2920, 2850, 2340, 1465, 1020, 720. ^{1}H-NMR (CDCl$_3$, 270 MHz) δ: 0.88 (3H, t, J = 6.8 Hz, CH$_3$), 1.10-1.60 (25H, m), 2.21 (2H, tt, J = 6.8, 2.7 Hz, HOCH$_2$C≡CCH_2), 4.25 (2H, dt, J = 5.8, 2.7 Hz, C≡CCH_2OH). *Anal.* Calcd. for $C_{17}H_{32}O$: C, 80.88; H, 12.78. Found: C, 80.28; H, 12.26%.

(*E*)-2-Heptadecen-1-ol (12) To a suspension of $LiAlH_4$ (4.39 g, 130 mmol) in THF (300 ml) was added a solution of alcohol **11** (31.4 g, 124 mmol) in THF (200 ml) at 0℃. The reaction mixture was then stirred at reflux for 3 h, and excess $LiAlH_4$ was hydrolyzed by dropwise addition of H_2O (100 ml). The white precipitate was filtered off with ether (1000 ml), and the combined filtrates were dried over $MgSO_4$ and concentrated *in vacuo*. Silica gel column chromatography of the residue (hexane:AcOEt = 4:1) gave allyl alcohol **12** (30.0 g, 110 mmol, 95 %) as a wax, m.p. 41-42℃. IR (film) ν_{max} cm^{-1} : 3200, 2920, 2850, 1460, 1080, 960, 720. ^{1}H-NMR (CDCl$_3$, 27 0MHz) δ: 0.88 (3H, t, J = 6.8 Hz, CH$_3$), 1.10-1.60 (25H, m), 2.04 (2H, dt, J = 5.1, 6.4 Hz, H OCH$_2$C=CCH_2), 4.09 (2H, t, J = 5.1 Hz, C=CCH_2OH), 5.62 (1H, dt, J = 15.4, 5.1 Hz, HOCH$_2$CH=CH), 5.71 (1H, dt, J = 15.34, 5.1 Hz, HOCH$_2$CH=CH). *Anal.* Calcd. for $C_{17}H_{34}O$: C, 80.24; H, 13.47. Found : C, 79.90; H, 13.61%.

(*E*)-1-*tert*-Butyldimethylsilyloxy-2-heptadecene (13) To a solution of allylic alcohol **12** (31.6 g, 0.124 mol) in DMF (200 ml) were added imidazole (16.9 g, 0.25 mol) and *tert*-butyldimethylchlorosilane (22.3 g, 0.149 mol). After the mixture had been stirred for 10 h, it was diluted with ether (600 ml) and washed with H_2O (200 ml) and brine (200 ml). Drying ($MgSO_4$) and concentration gave crude silyl ether, which was purified by silica gel column chromatagraphy, eluted with hexane-AcOEt (10:1) to give silyl ether **13** (45.1 g, 0.122 mol, 98%) as a colorless oil. IR (film) ν_{max} cm^{-1} : 2925, 2850, 1460, 1250, 1100, 1060, 960, 840, 775. ^{1}H-NMR (CDCl$_3$, 270 MHz) δ: 0.07 [6H, s, Si(CH$_3$)$_2$], 0.88 (3H, t, J = 6.8 Hz, CH$_2$CH_3), 0.91 [9H, s, SiC(CH$_3$)$_3$], 1.20-1.40 (24H, m), 2.02 (2H, dt, J = 6.4, 6.8 Hz, CH_2C=CCH$_2$OH), 4.12 (2H, dd, J = 4.9, 1.2 Hz, CH_2OH), 5.52 (1H, dt, J = 15.1, 4.9 Hz, C H=CHCH$_2$OH), 5.64 (1H, dt, J = 15.1, 6.4 Hz, CH=CHCH$_2$OH). *Anal.* Calcd. for $C_{23}H_{48}OSi$: C, 74.93; H, 13.12. Found : C, 75.02; H, 12.79%.

(2*R*, 3*R*)-1-*tert*-Butyldimethylsilyloxy-2,3-heptadecanediol (14) To a solution of AD-mix β (50.0 g) in 1:1 *tert*-butyl alcohol / H_2O (400 ml) was added $CH_3SO_2NH_2$ (3.41 g, 35.9 mmol) and the resulting solution was stirred for 15 min. It was cooled to 0℃and silyl ether **13** (13.3 g, 35.9 mmol) was added to the mixture, which after being stirred for a further 24 h, was treated with Na_2CO_3 (20.0 g) and extracted with AcOEt (900 ml). The extract was dried ($MgSO_4$) and concentrated to give the crude diol, which was purified by

silica gel column chromatography, eluted with hexane-AcOEt (2 :1) to give diol **14** (14.23 g, 35.4 mmol, 99%) as a wax, mp 31-32 ℃. $[\alpha]_D^{22}$+1.6 (*c* 1.13, MeOH). IR (film) ν_{max} cm^{-1}: 3350, 2950, 2850, 1460, 1250, 1100, 840, 775, 720, 660. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.09 [6H, s, $Si(CH_3)_2$], 0.88 (3H, t, *J* = 6.8 Hz, CH_3CH_2), 0.91 [9H, s, $SiC(CH_3)_3$], 1.10-1.60 (26H, m), 2.61 (1H, d, *J* = 6.3 Hz, 2-OH), 2.71 (1H, d, *J* = 4.2 Hz, 3-OH), 3.48 (1H, m, 2-H), 3.65 (1H, m, 3-H), 3.70 (1H, dd, *J* = 5.1, 10.3 Hz, CHHOSi), 3.78 (1H, dd, *J* = 3.7, 10.3 Hz, CHHOSi). *Anal.* Calcd. for $C_{23}H_{50}O_3Si$: C, 68.60; H, 12.52. Found : C, 68.60; H, 12.55%.

(2*R*,3*R*)-1-*tert*-Butyldimethylsilyloxy-2,3-methylethylidenedioxyheptadecane (15) To an ice-cooled solution of diol **14** (4.51 g, 11.2 mmol) and 2,2-dimethoxypropane in acetone (20 ml) were added *p*-TsOH (10 mg). After the mixture had been stirred for 10 h, it was diluted with ether (150 ml) and washed with saturated aqueous $NaHCO_3$ (100 ml) and brine (100 ml). Drying ($MgSO_4$) and concentration gave crude acetal, which was purified by silica gel column chromatography, eluted with hexane-AcOEt (6:1) to give acetal **15** (4.39 g, 9.93 mmol, 89%) as a colorless oil. $[\alpha]_D^{22}$+8.43 (*c* 1.36, MeOH). IR (film) ν_{max} cm^{-1}: 2920, 2850, 1460, 1250, 1080, 840, 775. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.07 [6H, s, $Si(CH_3)_2$], 0.88 (3H, t, *J* = 6.8 Hz, CH_3CH_2), 0.90 [9H, s, $SiC(CH_3)_3$], 1.20-1.70 (26H, m), 1.38 (3H, m, $CH_3C(CH_3)$], 1.40 [3H, m, $CH_3C(CH_3)$], 3.60-3.80 (3H, m), 3.88 (1H, dt, *J* = 4.4, 7.3 Hz). *Anal.* Calcd. for $C_{26}H_{54}O_3Si$: C, 70.54; H, 12.42. Found : C, 70.53, H, 12.12%.

(2*R*,3*R*)-2,3-Methylethylidenedioxy-1-heptadecanol (16) To an ice-cooled solution of acetal **15** (4.39 g, 9.93 mmol) in THF (50 ml) was added Bu_4NF (1.0M in THF, 11.9 ml). The mixture was allowed to warm to room temperature and then stirred for a further 10 h. After completion of the reaction, the mixture was diluted with ether (150 ml) and washed with H_2O (100 ml) and brine (100 ml). Drying ($MgSO_4$) and concentration afforded the crude alcohol, which was chromatographed over silica gel (hexane : AcOEt = 4:1) to afford pure alcohol **16** (2.99 g, 9.14 mmol, 92%), mp 38-39℃. $[\alpha]_D^{22}$ +14.5 (*c* 0.51, MeOH). IR (film) ν_{max} cm^{-1} : 3510, 2920, 2840, 1465, 1375, 1240, 1220, 1160, 1100, 1040, 840, 715. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ : 0.88 (3H, t, *J* = 6.8 Hz, CH_3CH_2), 1.15-1.70 (26H, m), 1.41 [3H, s, $CH_3C(CH_3)$], 1.42 [3H, s, $CH_3C(CH_3)$], 1.90 (1H, m, OH), 3.61 (1H, m, 3-H), 3.73 (1H, ddd, *J* = 0.7, 3.9, 8.1 Hz, CHHOH), 3.78 (1H, m, 2-H), 3.87 (1H, ddd, *J* = 12.6, 3.9, 8.1 Hz, CHHOH). *Anal.* Calcd. for $C_{20}H_{40}O_3$: C, 73.12; H, 12.27. Found : C, 72.84; H, 12.35%.

(2*R*,3*R*)-1,2-Epoxy-3-heptadecanol (17) To an ice-cooled solution of alcohol **16** (2.99 g, 9.14 mmol) in pyridine (20 ml) was added *p*-TsCl (2.08 g, 11.0 mmol). After being stirred in an ice-bath for 1 h and then at room temperature for 5 h, the mixture was extracted with AcOEt (150 ml). The extract was dried and concentrated to give the crude tosylate as a colorless oil, which was then dissolved in MeOH (20 ml) and conc. HCl (3 drops) was added to the solution. After being stirred at room temperature for 10 h, the mixture was extracted with AcOEt (150 ml). The extract was dried and concentrated to give the crude diol as a colorless oil, which was then dissolved in MeOH (30 ml) and KOH (2.00 g) was added to the solution. After being stirred at room temperature for 1 h, the mixture was diluted with H_2O and extracted with AcOEt (150 ml). Drying ($MgSO_4$) and subsequent concentration gave the crude epoxy alcohol, which was chromatographed over silica gel (hexane : AcOEt = 4:1) to give pure epoxy alcohol **17** [2.20 g, 8.15 mmol, 89%, 94 %ee from (*R*)-(+)-MTPA ester]. Two recrystalization from hexane gave a sample of >99 %ee (1.65 g, 6.11 mmol, 75%), mp. 54-57℃. $[\alpha]_D^{22}$ +4.9 (*c* 1.00, MeOH). IR (film) ν_{max} cm^{-1}: 3150, 2920, 2845, 1460, 1250, 1120, 965, 895, 865, 720. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.88 (3H, t, *J* = 6.8 Hz, CH_3CH_2), 1.10-1.60 (26H, m), 1.82 (1H, d, *J* = 5.9 Hz, OH), 2.72 (1H, dd, *J* = 2.7, 4.9 Hz, CHHOCH), 2.83 (1H, dd, *J* = 4.2, 4.9 Hz, CHHOCH), 2.98 (1H, ddd. *J* = 2.7, 4.2, 4.9 Hz, CH_2OCH), 3.44 (1H, m, CHOH). *Anal.* Calcd. for $C_{17}H_{34}O_2$: C, 75.50; H, 12.67. Found : C, 75.22; H, 12.67%.

(2*R*,3*R*)-1,2-Epoxy-3-methoxymethoxyheptadecane (18) An ice-cooled mixture of epoxy alcohol **17** (1.00 g, 3.70 mmol) and chloromethyl methyl ether **(CAUTION)** (450 mg, 5.56 mmol) in CH_2Cl_2 (10 ml) was treated with *i*-Pr_2NEt (1.43 g, 11.1 mmol), and the resultant mixture was warmed to room temperature and stirred for 30 hr. After completion of the reaction, the reaction mixture was cooled to 0℃ and diluted with H_2O (10 ml), the mixture being extracted with CH_2Cl_2 (60 ml). The extract was dried ($MgSO_4$) and concentrated to give crude MOM ether, which was purified by silica gel column chromatography, eluted with hexane-AcOEt (6:1) to give MOM ether **18** (980 mg, 3.11 mmol, 84%) as a colorless oil. $[\alpha]_D^{22}$ +30.8 (*c* 1.07, MeOH). IR (film) ν_{max} cm^{-1}: 2920, 2850, 1460, 1150, 1090, 1030, 920, 840, 720. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.88 (3H, t, *J* = 6.8 Hz, CH_3CH_2), 1.10-1.70 (26H, m), 2.54 (1H, dd, *J* = 4.9, 2.7 Hz, CHHOCH), 2.78 (1H, dd, *J* = 4.9, 4.4 Hz, HHOCH), 2.98 (1H, ddd, *J* = 2.7, 4.4, 6.8 Hz, CH(H)OCH), 3.26 (1H, m, CHOMOM), 3.40 (3H, s, CH_3O), 4.69 (1H, d, *J* = 6.6 Hz, CH_3OCHH), 4.89 (1H, d, *J* = 6.6 Hz, CH_3OCHH). *Anal.* Calcd. for $C_{19}H_{38}O_3$: C, 72.56; H, 12.18. Found : C, 72.13, H; 12.30%.

(10*R*,11*R*)-11-Methoxymethoxy-7-pentacosyn-10-ol (19) Under a nitrogen atomosphere, a solution of *n*-butyllithium (1.6M in hexane, 0.80 ml) was added to a THF solution (10 ml) of 1-octyne (140 mg, 1.27 mmol) at -40℃, and the mixture was stirred for 2 h. Then, boron trifluoride etherate (145 mg, 1.27 mmol) was added to the solution and stirring was continued for 30 min at -78℃. Finally, a THF solution of MOM ether **18** (200 mg, 0.635 mmol) was added, and after stirring for 2 h at -78℃, the reaction was quenched by adding aqueous NH_4Cl. The aqueous solution was extracted with ether, the ethereal solution being dried over $MgSO_4$. After removal of the solvent, acetylene alcohol **19** (261 mg, 0.614 mmol, 97 %) was obtained by silica gel column chromatography

(hexane-AcOEt = 6:1) as a colorless oil. $[\alpha]_D^{22}$ -1.6 (*c* 1.01, MeOH). IR (film) ν_{max} cm^{-1} : 3425, 2920, 2850, 1460, 1375, 1205, 1140, 1090, 1035, 920, 720. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.88 (3H, t, *J* = 6.8 Hz, $CH_3(CH_2)_{13}$], 0.89 [3H, t, *J* = 6.3 Hz, $CH_3(CH_2)_6$], 1.20-1.80 (34H, m), 2.22 (2H, tt, *J* = 2.2, 7.1 Hz, $CH_2C{\equiv}CCH_2CHOH$), 2.42 (2H, dt, *J* = 5.6, 2.2 Hz, $CH_2C{\equiv}CCH_2CHOH$), 2.79 (1H, d, *J* = 5.4 Hz, OH), 3.42 (3H, s, CH_3O), 3.59 (1H, m, C*H*OH), 3.65 (1H, m, C*H*OMOM), 4.70 (1H, d, *J* = 6.6 Hz, CH_3OCHH), 4.73 (1H, d, *J* = 6.6 Hz, CH_3OCHH). HREIMS (m / z) : (M^+) Calcd. for $C_{27}H_{52}O_3$, 424.3916; Found, 424.3930.

(10*R*,11*R*)-11-Methoxymethoxy-1-pentacosyn-10-ol (20) A mixture of Li (100 mg, 14.7 mmol) and 1,3-diaminopropane (15 ml) was stirred at room temperature for 30 min. and then heated at 70℃ for 3 h. The reaction mixture was cooled to room temperature, and potassium *tert*-butoxide (1.10 g, 9.82 mmol) was added, the mixture being stirred for a further 20 min. Acetylene alcohol **19** (837 mg, 1.97 mmol) was added and the mixture was stirred for 2 h. Then, after quenching the reaction with H_2O (100 ml), the solution was extracted with hexane, the organic layer being dried over $MgSO_4$. After removal of the solvent, terminal acetylene **20** (710 mg, 1.65 mmol, 84 %) was obtained by silica gel column chromatography (hexane : AcOEt = 6:1) as a colorless oil. $[\alpha]_D^{22}$ +10.9 (*c* 1.00, MeOH). IR (film) ν_{max} cm^{-1} : 3460, 3310, 2920, 2850, 2110, 1460, 1378, 1235, 1145, 1090, 1035, 720, 620. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.88 (3H, t, *J* = 6.8 Hz, CH_3CH_2), 1.20-1.80 (38H, m), 1.94 (1H, t, *J* = 2.7 Hz, C≡C*H*), 2.18 (2H, dt, *J* = 2.7, 7.1 Hz, $CH_2C{\equiv}CH$), 2.73 (1H, d, *J* = 4.4 Hz, OH), 3.34 (1H, m, C*H*OH), 3.41 (3H, s, CH_3O), 3.49 (1H, m, C*H*OMOM), 4.68 (1H, d, *J* = 6.83 Hz, CH_3OCHH), 4.71 (1H, d, *J* = 6.8 Hz, CH_3OCHH). *Anal.* Calcd. for $C_{27}H_{52}O_3$: C, 76.34; H, 12.34. Found : C, 76.15; H, 12.46%.

(10*R*,11*R*)-11-Methoxymethoxy-10-(tetrahydropyranyl-2'-oxy)-1-pentacosyne (3) To an ice-cooled solution of terminal acetylene **21** (194 mg, 0.456 mmol) in CH_2Cl_2 (2 ml) were added 3,4-dihydro-2*H*-pyran (46 mg, 0.547 mmol) and *p*-TsOH (3 mg) and the mixture was stirred for 10 h. After the reaction mixture was poured to H_2O, it was extracted with CH_2Cl_2 (20 ml). Drying over $MgSO_4$ and concentration *in vacuo* gave crude THP ether, which was purified by silica gel column chromatography, eluted with hexane-AcOEt (4:1) to give compound **3** (180 mg, 0.354 mmol, 78 %) as a colorless oil. IR (film) ν_{max} cm^{-1} : 3300, 2920, 2850, 1460, 1040. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.88 (3H, t, *J* = 6.8 Hz, CH_3CH_2), 1.10-1.90 (44H, m), 1.93 (1H, t, *J* = 2.7 Hz, C≡C*H*), 2.17 (2H, dt, *J* = 2.7, 7.1 Hz, $CH_2C{\equiv}CH$), 3.38 (3H, s, CH_3O), 3.51 (2H, m), 3.67 (1H, m), 3.91 (1H, m), 4.68 (2H, m, CH_3OCH_2O), 4.96 (1H, m, OCHO). HREIMS (m / z) : (M^+-$C_6H_{11}O_2$) Calcd. for $C_{26}H_{47}O_2$, 391.3576; Found, 391.3575.

(3RS,5*S*,18'*R*,19'*R*)-3-[19'-Methoxymethoxy-18'-(tetrahydropyranyl-2''-oxy)-9'-tritriacontynyl]-5-methyl-3-(phenylsulfanyl)tetrahydrofuran-2-one (5) Under a nitrogen atmosphere, a solution of *n*-butyllithium (1.6M in hexane, 0.06 ml) was added to an ether solution (1 ml) of THP ether **3** (50 mg, 0.098 mmol) at -40℃, and the mixture was stirred for 2 h. Then, copper iodide (18.6 mg, 0.098 mmol) and tosylate **4** (50 mg, 0.102 mol) was added to the solution at 0℃. After stirring for 15 min, HMPA (200 mg) was added. After stirring at room temperature for 3 h, the reaction was quenched by adding saturated aqueous NH_4Cl (10 ml). The aqueous solution was extracted with ether (90 ml), the ethereal layer being dried over $MgSO_4$ and concentrated *in vacuo* to give the crude acetylene, which was purified by silica gel column chromatography, eluted with hexane-AcOEt (3:1) to give acetylene **5** (20 mg, 0.025 mmol, 25%) as a colorless oil. IR (film) ν_{max} cm^{-1} : 2920, 2850, 1760, 1600, 1460, 1360, 1170, 1040. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.88 (3H, t, *J* = 6.8 Hz, CH_3CH_2), 1.19 (3H, d, *J* = 6.4 Hz, CH_3CH_2), 1.10-2.10 (59H, m), 2.25 (4H, m, $CH_2C{\equiv}CCH_2$), 2.35-2.55 (1H, m), 3.38 (3H, s, CH_3O), 3.51 (2H, m), 3.67 (1H, m), 3.91 (1H, m), 4.40-4.55 (1H, m), 4.68 (2H, m, CH_3OCH_2O), 4.96 (1H, m, OCHO), 7.38 (3H, m, aromatic-H), 7.54 (2H, m, aromatic-H). ESIMS (m / z) : 826(M^+), 804, 708, 492, 443, 317, 281, 239, 119, 103.

(*EZ*,3*RS*,5*S*,18'*R*,19'*R*)-3-(18'-Hydroxy-19'-methoxymethoxy-7'-tritriaconten-9'-ynyl)-5-methyl-3-(phenylsulfanyl)tetrahtdrofuran-2-one (22) To a solution of vinyl iodide **21** (1.78 g, 4.01 mmol) in pyrrolidine (10 ml) was added $Pd(PPh_3)_4$ (232 mg) and the resulting solution was stirred for 45 min. Acetylene **20** (1.70 g, 4.01 mmol) and copper iodide (50 mg) were then added to the mixture, which, after being stirred for a further 3 h, was treated with saturated aqueous NH_4Cl (2 ml) and extracted with AcOEt (100 ml). The extract was dried ($MgSO_4$) and concentrated to give the crude enyne, which was purified by silica gel column chromatography, eluted with hexane-AcOEt (3:1) to give enyne **22** (2.50 g, 3.37 mmol, 84%) as a colorless oil. IR (film) ν_{max} cm^{-1} : 3470, 2920, 2845, 1760, 1460, 1435, 1375, 1340, 1180, 1145, 1095, 1035, 950, 915, 740, 690. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ : 0.88 (3H, t, *J* = 6.8 Hz, CH_3CH_2), 1.10-2.11 (51H, m), 1.19 (3H, d, *J* = 6.6 Hz, CH_3CH), 2.20-2.56 (3H, m), 2.72 (1H, d, *J* = 4.1 Hz, OH), 3.35 (1H, m, C*H*OMOM), 3.41 (3H, s, CH_3O), 3.49 (1H, m, C*H*OH), 4.48 (1H, m, CH_3CH), 4.68 (1H, d, *J* = 7.1 Hz, CH_3OCHH), 4.71 (1H, d, *J* = 7.1 Hz, CH_3OCHH), 5.44 (1H, m, $C{\equiv}CCH{=}CH$), 6.02 (1H, m, $C{\equiv}CCH{=}CH$), 7.38 (3H, m, aromatic-H), 7.54 (2H, m, aromatic-H). EIMS (m / z) : 708(M^+-C_2H_4O), 662, 632, 600, 581, 554, 543, 523, 469, 451, 356, 343, 248, 208, 110.

(3*RS*,5*S*,18'*R*,19'*R*)-3-(18'-Hydroxy-19'-methoxymethoxytritriacontyl)-5-methyl-3-(phenylsulfanyl)tetrahydrofuran-2-one (23) A solution of enyne **22** (1.00 g, 1.35 mmol) in benzene (20 ml) was hydrogenated over chlorotris(triphenylphosphine)rhodium (50 mg) for 3 hr. Filtration and evaporation of the solvent provided an oil, which was purified by silica gel chromatography (hexane :

AcOEt = 4:1) to give **23** (900 mg, 1.22 mmol, 90%) as a wax. IR (film) ν_{max} cm^{-1} : 3480, 2920, 2850, 1760, 1460, 1380, 1340, 1270, 1180, 1145, 1100, 1040, 960, 920, 745, 720, 690. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.88 (3H, t, J = 6.8 Hz, C*H*$_3$CH$_2$), 1.00-2.10 (64H, m), 2.30-2.55 (1H, m, CH$_3$CHC*H*H), 2.72 (1H, m, OH), 3.34 (1H, m, C*H*OMOM), 3.41 (3H, s, CH$_3$O), 3.50 (1H, m, C*H*OH), 4.44-4.64 (1H, m, CH$_3$C*H*), 4.68 (1H, d, J = 7.1 Hz, CH$_3$OC*H*H), 4.71 (1H, d, J = 7.1 Hz, CH$_3$OCH*H*), 7.37 (3H, m, aromatic-H), 7.54 (2H, m, aromatic-H). EIMS (m / z) : 742 (M$^+$-CH$_2$), 711, 682, 665, 637, 604, 574, 521, 501, 475, 455, 367, 208.

(3*RS*,5*S*,18'*S*,19'*R*)-3-(18',19'-Epoxytritriacontyl)-5-methyl-3-(phenylsulfanyl)tetrahydrofuran-2-one (24) To an ice-cooled solution of **23** (200 mg, 0.27 mmol) and Et$_3$N (100 mg) in pyridine (2 ml) was added MsCl (40 mg, 0.35 mmol). After being stirred in an ice-bath for 1 h and then at room temperature for 5 h, the mixture was diluted with H_2O and extracted with AcOEt (10 ml). The extract was dried and concentrated to give crude mesylate as a colorless oil, which was then dissolved in MeOH (2 ml) and conc. HCl (1 drop) was added to the solution. After being stirred at room temperature for 10 h, the mixture was extracted with AcOEt. The extract was dried and concentrated to give the crude alcohol as a colorless oil, which was then dissolved in THF (2 ml) and KOH (50 mg) was added to the solution. After being stirred at room temperature for 1 h, the mixture was diluted with H_2O and extracted with AcOEt. Drying ($MgSO_4$) and subsequent concentration gave the crude product, which was chromatographed over silica gel (hexane : AcOEt = 3:1) to give pure **24** (152 mg, 0.220 mmol, 81%). IR (KBr) ν_{max} cm^{-1} : 2920, 2850, 1760, 1460, 1340, 1190, 840, 750, 720. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.88 (3H, t, J = 6.8 Hz, C*H*$_3$CH$_2$), 1.10-2.04 (64H, m), 2.28-2.57 (1H, m, CH$_3$CHC*H*H), 2.92 (2H, m, CH$_2$C*H*OC*H*CH$_2$), 4.41-4.66 (1H, m, CH$_3$C*H*), 7.36 (3H, m, aromatic-H), 7.54 (2H, m, aromatic-H). HREIMS (m / z) : (M$^+$) Calcd. for $C_{44}H_{76}O_3S$, 684.5515; Found, 684.5519.

(5*S*,18'*S*,19'*R*)-3-(18',19'-Epoxytritriacontyl)-5-methyl-2,5-dihydrofuran-2-one [(5*S*,18'*S*,19'*R*)-1] To a solution of **24** (72 mg, 0.105 mmol) in MeOH (5 ml) was added *m*-CPBA (40 mg, 0.234 mmol) at 0℃. After the mixture had been stirred at this temperature for 15 min, it was poured to aqueous $Na_2S_2O_3$ / $NaHCO_3$ (1:1) and extracted with AcOEt. Drying and concentrating afforded a white solid, which was used in the next step without further purification. The solid was dissolved in toluene (5 ml) and the solution was refluxed for 1 h. After completion of the reaction, evaporation of the solvent gave crude **1**, which upon recrystallization (hexane) gave pure compound (5*S*, 18'*S*, 19'*R*)-**1** (47 mg, 0.089 mmol, 85%) as a white solid, mp 77-78℃. $[\alpha]_D^{22}$ +7.64 (*c* 1.10, $CHCl_3$). IR (KBr) ν_{max} cm^{-1} : 2920, 2850, 1740, 1485, 1330, 1080, 840, 720. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.88 (3H, t, J = 6.8 Hz, C*H*$_3$CH$_2$), 1.10-1.70 (58H, m), 1.40 (3H, d, J = 6.8 Hz, C*H*$_3$CH), 2.26 (2H, ddt, J = 1.7, 1.7, 7.1 Hz, C*H*$_2$CH=CH), 2.90 (2H, m, CH$_2$C*H*OC*H*CH$_2$), 4.99 (1H, dtq, J = 1.7, 1.7, 6.6 Hz. CH=C*H*CH), 6.98 (1H, dt, J = 1.7, 1.7 Hz, CH$_3$C*H*). ^{13}C-NMR ($CDCl_3$, 66.7 MHz) δ: 14.1 (CH_3), 19.2, 22.7, 25.2, 26.6 (CH$_2$CHOCHC*H*$_2$), 27.4 (*C*H$_2$CHOCHCH$_2$), 27.8-29.7, 31.9, 57.3 (*C*HOCH), 77.4 (*C*H$_3$CH), 134.4 (CH=*C*HC=O), 148.9 (*C*H=CHC=O), 174.0 (*C*=O). FABMS (m/z): 597 (M$^+$+Na), 567, 553, 539, 525, 511, 497, 483, 469, 455, 441, 427, 413, 399, 387, 371, 357, 343, 329, 315, 301, 287, 273, 259, 245, 231, 217, 203, 189, 175, 161, 147, 134, 120. FABMS / MS (CID spectrum of the m/z 576 ion): 547, 529, 489, 461, 447, 440, 391, 378, 335, 321, 308, 293, 279, 265, 250, 237, 223, 208, 195, 181, 167, 152, 135, 109, 95, 81, 54, 41, 26. HREIMS (m / z) : (M$^+$) Calcd. for $C_{38}H_{70}O_3$ 574.5325; Found, 574.5356.

(3*RS*,5*R*,18'*R*,19'*R*)-3-(18'-Acetoxy-19'-methoxymethoxytritriacontyl)-5-methyl-3-(phenylsulfanyl)tetrahydrofuran-2-one (25) To an ice-cooled solution of **23** (215 mg, 0.289 mmol) in pyridine (5 ml) were added acetic anhydride (24 mg, 0.578 mmol) and 4-dimethylaminopyridine (20 mg). After the mixture had been stirred for 10 h, it was diluted with AcOEt and washed with H_2O and brine. Drying over $MgSO_4$ and evaporating the solvent *in vacuo* gave crude **26**, which was purified by silica gel column chromatography, eluted with hexane - AcOEt (3:1) to give MOM acetate **26** (210 mg, 0.266 mmol, 92%) as a colorless oil. IR (film) ν_{max} cm^{-1} : 2920, 2850, 1760 , 1740, 1460, 1240, 1040. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 0.88 (3H, d, J = 6.8 Hz, C*H*$_3$CH$_2$), 1.10-2.02 (64H, m), 2.08 (3H, s, CH$_3$C=O), 2.30 (0.2H, dt, J = 13.9, 7.3 Hz, CH$_3$CHC*H*H), 2.51 (0.8H, dt, J = 13.9, 5.5 Hz, CH$_3$CHC*H*H), 3.39 (3H, s, CH$_3$O), 3.55 (1H, dt, J = 4.4, 6.1 Hz, C*H*OMOM), 4.48 (0.8H, m, CH$_3$C*H*), 4.59 (0.2H, m, CH$_3$C*H*), 4.67 (1H, d, J = 7.0 Hz, CH$_3$OC*H*H), 4.69 (1H, d, J = 7.0 Hz, CH$_3$OCH*H*), 4.98 (1H, ddd, J = 4.4, 4.4, 8.8 Hz, AcOC*H*), 7.38 (2H, m, aromatic-H), 7.54 (3H, m, aromatic-H). FABMS (m / z) : 789 (MH$^+$), 727, 685, 667, 575, 475, 208, 154, 137, 113.

(3*RS*,5*R*,18*R*',19*R*')-3-(18'-Acetoxy-19'-hydroxytritriacontyl)-5-methyl-3-(phenylsulfanyl)tetrahydrofuran-2-one (26) To an ice-cooled solution of MOM acetate **25** (189 mg, 0.240 mmol) in MeOH (5 ml) was added PPTS (10 mg) at 0℃. After stirring at room temperature for 96 h, H_2O (5 ml) was added, and the MeOH was evaporated. The aqueous solution was extracted with AcOEt, the organic layer being washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. Silica gel column chromatography of the residue (hexane : AcOEt = 2:1) gave acetate **26** (80 mg, 0.108 mmol, 45 %) as a colorless oil. IR (film) ν_{max} cm^{-1} : 3250, 2920, 2850, 1760, 1740, 1480, 1240. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.88 (3H, t, J = 6.8 Hz, C*H*$_3$CH$_2$), 1.10-2.08 (66H, m), 2.09 (3H, s, CH$_3$C=O), 3.50-3.70 (1H, m), 4.41-4.66 (1H, m), 4.82 (1H, m), 7.36 (3H, m, aromatic-H), 7.54 (2H, m, aromatic-H). FABMS (m / z) : 746 (MH$^+$), 725, 683, 665, 639, 611, 573, 551, 523, 475, 459, 429, 413, 401, 369, 313.

(3*RS*,5*R*,18'*R*,19'*S*)-3-(18',19'-Epoxytritriacontyl)-5-methyl-3-(phenylsulfanyl)tetrahydrofuran-2-one (27) To an ice-cooled solution of acetate **26** (64 mg, 0.086 mmol) and Et$_3$N (100mg) in pyridine (3 ml) was added MsCl (20 mg, 0.172 mmol). After

stirring in an ice-bath for 1 h and then at room temperature for 5 h, H_2O was added and the mixture was extracted with AcOEt (30 ml). The extract was dried and concentrated to give crude mesylate, which was then dissolved in THF (1 ml) and KOH (5 mg, 0.086 mmol) was added to the solution. After being stirred at room temperature for 1 h, the mixture was diluted with H_2O and extracted with AcOEt. Drying over $MgSO_4$ and subsequent concentrating gave crude **27**, which was chromatographed over silica gel (hexane : AcOEt = 2:1) to give pure epoxy lactone **27** (50 mg, 0.073 mmol, 85%) as a wax, mp 53-54℃. IR (KBr) ν_{max} cm^{-1}: 2920, 2850, 1760, 1460, 1340, 1190, 840, 750, 720. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.88 (3H, t, J = 6.8 Hz, CH_3CH_2), 1.10-2.04 (64 H, m), 2.28-2.57 (1H, m, CH_3CHCHH), 2.92 (2H, m, $CHOCH$), 4.41-4.66 (1H, m, CH_3CH), 7.36 (3H, m, aromatic-H), 7.54 (2H, m, aromatic-H). HREIMS (m / z) : (M^+) Calcd. for $C_{44}H_{76}O_3S$, 684.5526; Found, 684.5515.

(5*S*,18'*R*,19'*S*)-2-(18',19'-Epoxytritriacontyl)-5-methyl-2,5-dihydrofuran-2-one [(5*S*,18'*R*,19'*S*)-1] To a solution of epoxy lactone **27** (33 mg, 0.049 mmol) in MeOH (2 ml) was added *m*-CPBA (17 mg, 0.098 mmol) at 0℃. After the mixture had been stirred at this temperature for 15 min, an aqueous $Na_2S_2O_3$ / $NaHCO_3$ (1:1) solution was added and the solution was extracted with AcOEt. The extract was dried and concentrated to afford a white solid, which was used in the next step without further purification. The solid was dissolved in toluene (2 ml) and the solution was refluxed for 1 h. After completion of the reaction, concentration of the mixture gave crude compound (5*S*, 18'*R*, 19'*S*)-**1**, which upon recrystallization gave pure compound (5*S*, 18'*R*, 19'*S*)-**1** (25 mg, 0.044 mmol, 90%) as a white solid, mp 77-78℃. $[\alpha]_D^{22}$ +9.28 (*c* 0.60, $CHCl_3$). IR (KBr) ν_{max} cm^{-1}: 2920, 2850, 1740, 1485, 1330, 1080, 840, 720. ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 0.88 (3H, t, J = 6.8 Hz, CH_3CH_2), 1.10-1.70 (58H, m), 1.40 (3H, d, J = 6.8 Hz, CH_3CH), 2.26 [2H, ddt, J = 1.7, 1.7, 7.1 Hz, CH_2CH=CH)], 2.90 (2H, m, CHOCH), 4.99 (1H, dtq, J = 1.7, 1.7, 6.6 Hz, CH_3CHCH), 6.98 (1H, dt, J = 1.7, 1.7 Hz, CH_3CHCH). ^{13}C-NMR ($CDCl_3$, 66.7 MHz) δ: 14.1 (CH_3), 19.2, 22.7, 25.2, 26.6 ($CH_2CHOCHCH_2$), 27.4 ($CH_2CHOCHCH_2$), 27.8-29.7, 31.9, 57.3 (CHOCH), 77.4 (CH_3CH), 134.4 (CH=*C*HC=O), 148.9 (*C*H=CHC=O), 174.0 (C=O). HREIMS (m / z) : (M^+) Calcd. for $C_{38}H_{70}O_3$, 574.5325; Found, 574.5347.

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