TOTAL SYNTHESIS OF (8'R)- AND (8'S)-COROSSOLINE

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Abstract - A convergent stereoselective total synthesis of (8'R)- and (8'S)-
corossoline (1) has been performed via a multi-step process. Comparison of the
mp, [α]D, ir and nmr data of both synthetic materials with those reported for
natural corossoline did not allow for the strict determination of the configuration
at the C-8' hydroxyl group of 1. However, a slight chemical shift difference at the
C-8' methine proton was observed in the 1H-nmr spectra of the corresponding
tris-MTPA esters of synthetic (8'R)- and (8'S)-1, indicating that if the tris-MTPA
ester of natural 1 is available, the stereochemistry at the C-8' hydroxyl group of
corossoline will be established.

The Annonaceous acetogenins, that have been isolated from a number of plants of the Annonaceae, have
attracted much attention due to potent cytotoxic, antitumor, pesticidal, antifeedant, antiparasitic,
immunosuppressive activities. More than 200 compounds belonging to this family have been reported
since isolation of the first in 1982. Most of them possess one or more tetrahydrofuran rings, together
with an α, β-unsaturated γ-lactone part on a C-35 or C-37 carbon chain. Their unique structural features
and their broad spectrum of potent biological activities make them an attractive target for total synthesis.
Corossoline (1), a monotetrahydrofuranyl acetogenin was isolated from the seeds of Annona muricata in
1991. Its absolute stereochemistry except for the C-8' position was deduced by applying new Mosher's
methodology to the monotetrahydrofuranyl annonaceous acetogenin analogs such as reticulatacin6 and by
a total synthesis of (8'RS)-corossoline by Chinese group. Thus, the absolute configuration of corossoline is (5S, 8'R, 13'R, 14'R, 17'R, 18'R) or (5S, 8'S, 13'R, 14'R, 17'R, 18'R). Here, we report a total synthesis of two possible diastereoisomers (8'R)- and (8'S)-1 to confirm the stereochemistry at the C-8' hydroxyl group. Our synthetic strategy is outlined in Scheme 1.

As shown in Scheme 2, the tetrahydrofuran part 18 of 1 was constructed via a multi-step process starting from 1-iodododecane (2) and 5-(tetrahydro-2-pyranoxy)pentyne (3). Base-promoted alkylation of 3 with 2 gave 4, which on reduction with Na in liquid ammonia led to (E)-olefinic ether (5). After removal of the tetrahydropyranyl (THP) group of 5 with p-TsOH and subsequent Swern oxidation, the resultant aldehyde (7) underwent Horner-Emmons reaction with triethyl phosphonoacetate to the chain-extended ester (8), which was then submitted to reduction with diisobutylaluminum hydride (DIBALH) to afford
(E)-allylic alcohol (9). At this stage, four asymmetric centers were introduced by a consecutive sequence consisting of Sharpless asymmetric epoxidation and dihydroxylation procedures. Asymmetric epoxidation\(^9\) of compound (9) with \(L-(-)-\)diethyl tartrate gave epoxy alcohol (10), which showed a 96% ee by a \(^1\)H-nmr analysis of the corresponding Mosher ester derivative. Recrystallization of this sample from hexane gave enantiomerically pure 10. Asymmetric dihydroxylation with AD-mix\(\beta\) \(^10\) and subsequent acid-catalyzed cyclization with camphorsulfonic acid (CSA) resulted in tetrahydrofuran ring-containing building block (11). The diastereomeric purity of this material proved to be a 96% de based on a \(^1\)H-nmr analysis of the corresponding Mosher ester after conversion of 11 to acetonide (12). Recrystallization of 11 from AcOEt gave diastereomerically pure 11. The secondary hydroxyl moiety of 12 was protected as a methoxymethyl (MOM) ether to afford 13. Selective deprotection of the acetonide group of 13 with 60% AcOH was followed by silylation of the primary hydroxyl group of 14 to 15 with \(t\)-butyldimethylchlorosilane (TBSCI), Et$_3$N, and 4-dimethylaminopyridine (DMAP). Successive treatment with methanesulfonyl chloride (MsCl), tetrabutylammonium fluoride (TBAF) and 15% aq. NaOH furnished terminal
epoxide (16). Coupling reaction with lithium (trimethylsilyl)acetylide in the presence of boron trifluoride etherate and subsequent treatment with TBAF afforded alkyne (18), after protection of the resulting hydroxyl group of 17 as a MOM ether.

As shown in Scheme 3, the $\gamma$-lactone parts (28) and (30) of (8S)- and (8'R)-1 were constructed as follows.

Reagents and conditions: a) i: p-TsCl, pyridine ii: Nal, NaHCO$_3$, acetone, 67%. b) 21, n-BuLi, THF-HMPA, 59%. c) H$_2$, 10%Pd-C, AcOEt, 96%. d) i: p-TsCl, pyridine ii: Nal, NaHCO$_3$, acetone, 91%. e) NaHMDS, THF-HMPA, 88%. f) p-TsOH, MeOH, 99%. g) i: p-TsCl, pyridine ii: powdered KOH, THF, 69%. h) TBSCI, Et$_3$N, DMAP, CH$_2$Cl$_2$, 82%. i) i: MsCl, Et$_3$N, CH$_2$Cl$_2$ ii: HF MeCN, iii: NaH, THF, 47%.

The substituted $\gamma$-lactone (19) was prepared by White's method, starting from (S)-(−)-ethyl lactate. The synthon (25) corresponding to terminal epoxide part of 28 and 30 was prepared from 5-benzyloxy-1-pentyne (22) and (S)-[3,4-(1-ethylpropylidene)dioxyl]-1-iodobutane (21), which had been derived from alcohol (20) via a two-step process. Thus, base-promoted alkylation of 22 with 21 afforded 23, which
on hydrogenation over 10% Pd-C underwent saturation of the triple bond and hydrogenolysis of the benzyl group to give 24. Transformation of 24 into iodide (25) was effected in two steps through tosylate. Iodide (25) thus obtained was then subjected to alkylation with the sodium enolate of 19 to afford 26 in good yield. The following three-step reactions leading to the requisite terminal epoxide (28) was effected via hydrolysis of the acetonide group of 26, selective tosylation of the primary hydroxyl group of 27 and oxirane ring closure with powdered KOH. Transformation of 27 into another target molecule (30) was carried out as follows. Selective protection of the primary hydroxyl group of 27 with TBSCl was followed by formation of the sulfonate with MsCl, desilylation with aq. HF and epoxy ring closure with NaH to 30.

As shown in Scheme 4, completion of the carbon skeleton to give the coupled products (31) and (32) was achieved by the application of Wu’s method. Coupling reaction between the lithium salt of 18 and 28 (or 30) in the presence of boron trifluoride etherate afforded 31 (or 32), which was converted to saturated product 33 (or 34) by catalytic hydrogenation of 31 (or 32) using Wilkinson’s catalyst. Oxidation with
mCPBA followed by thermal elimination afforded 35 (or 36). Finally, deprotection of the MOM group with boron trifluoride etherate in the presence of dimethyl sulfide\textsuperscript{15} gave (8'S)- and (8'R)-1. Their ir and \textsuperscript{1}H-nmr spectral data were almost consistent with those reported for natural 1 by French group, and the optical rotation values (+22.2° and +21.0°) of (8'S)-and (8'R)-1 were also very close to that of natural 1 (+19°), whereas the melting point data [56.5-58°C for (8'S)-1 and 66-69°C for (8'R)-1] were considerably different from that (45-50°C) of natural 1. Very recently, C.-J. Chang \textit{et al.} isolated corossoline possessing the mp of 62°C and the [\(\alpha\)]D of +64° from \textit{Goniothalamus amuyon}.\textsuperscript{15} This indicated the difficulty of strictly determining the stereochemistry at the C-8' position of natural corossoline by comparison of the data accessible from natural and synthetic 1. However, the \textsuperscript{1}H-nmr spectra of the corresponding tris-(S)-MTPA esters of synthetic (8'R)- and (8'S)-1 showed a slight chemical shift difference for the C-8' methine proton. Thus, the C-8' proton of 8'R ester resonated at higher field (0.04ppm) relative to that of 8'S ester. This indicated that if the tris-(S)-MTPA ester of natural 1 is available, the stereochemistry of corossoline will be established.

**EXPERIMENTAL**

All melting points (mp) are uncorrected. Optical rotation was measured with a JASCO DIP-4 spectrometer. Ir spectra were taken with a JASCO ir-810 infrared spectrophotometer. \textsuperscript{1}H- and \textsuperscript{13}C-nmr spectra were measured with JEOL GSX-270 (270 MHz) and GSX-400 (400 MHz) spectrometers. Ms spectra were recorded with a JEOL JMS-HX-105 and JMS-DX-303 instruments.

\textbf{1-(Tetrahydro-2-pyranlyoxy)-4-heptadecyne (4).} To a solution of 5-(tetrahydro-2-pyranlyoxy)-4-pentyne (3) (3.34 g, 20 mmol) in THF (20 ml) was added \textit{n}-BuLi (1.56 M solution in hexane, 12.8 ml) at -40°C. After stirring for 40 min at 0°C, 1-iodododecane (2) (6.51 g, 22 mmol) in HMPA (10 ml) was added to the mixture over 1 h. The mixture was stirred for 1 h at 0°C and then for 1 h at room temperature. The reaction mixture was quenched with sat. aq. NH\textsubscript{4}Cl and extracted with ether. The extract was washed with brine and dried over MgSO\textsubscript{4}. After removal of the solvents, the residue was purified by silica gel column chromatography, eluted with hexane-AcOEt (20:1) to give compound (4) (4.57 g, 68%) as a colorless oil. Ir (film) \(v_{\text{max}}\) cm\textsuperscript{-1}: 2930, 2850, 1470, 1460, 1205, 1120, 1140, 1040. \textsuperscript{1}H-Nmr (CDCl\textsubscript{3}) \(\delta\): 0.88 (3H, t, \(J = 6.6\) Hz), 1.25-1.90 (28H, m), 2.13 (2H, tt, \(J = 7.0, 2.2\) Hz), 2.27 (2H, tt,
\( J = 7.0, 2.2 \text{ Hz})\), 3.50 (2H, m), 3.82 (2H, m), 4.60 (1H, dd, \( J = 3.9, 2.7 \text{ Hz})\). Anal. Calcd for \( \text{C}_{22}\text{H}_{40}\text{O}_{2}\): C, 78.51; H, 11.98. Found: C, 78.21; H, 11.75.

**(E)-1-(Tetrahydro-2-pyranoyloxy)-4-heptadecene (5).** Anhydrous liq. ammonia (100 ml) was condensed in a 300 ml four-necked flask. Sodium metal (1.5 g, 65 mmol) was added, producing a deep blue color. THF (20 ml) and dry \( t\)-BuOH (6 ml) followed by a solution of 4 (3.7 g, 11 mmol) in THF (10 ml) were added. After being stirred for 8 h at -40\(^\circ\)C, the reaction mixture was quenched with \( \text{NH}_4\text{Cl}\). The mixture was extracted with ether and the extract was washed with brine. Drying over MgSO\(_4\) and concentration gave crude 5, which was purified by silica gel chromatography, eluted with hexane-AcOEt (20:1) to give compound (5) (3.50 g, 94%) as a colorless oil. \( \text{Ir} \) (film) \( \nu_{\text{max}} \text{ cm}^{-1}: \) 3020, 2930, 2850, 1465, 1455, 1200, 1140, 1120, 1035, 965. \(^1\)H-Nmr (CDCl\(_3\)) \( \delta: \) 0.88 (3H, t, \( J = 6.7 \text{ Hz})\), 1.25-1.90 (28H, m), 1.97 (2H, m), 2.05 (2H, m), 3.37 (1H, m), 3.40 (1H, m), 3.72 (1H, m), 3.87 (1H, m), 4.58 (1H, dd, \( J = 2.9, 2.9 \text{ Hz})\), 5.41 (2H, m). Anal. Calcd for \( \text{C}_{22}\text{H}_{42}\text{O}_{2}\): C, 78.04; H, 12.50. Found: C, 77.82; H, 12.04.

**(E)-4-Heptadecen-1-ol (6).** To a solution of 5 (3.00 g, 8.9 mmol) in MeOH (20 ml) was added \( p\)-TsOH (10 mg). After the mixture had been stirred for 6 h, the solvent was evaporated and the crude product was chromatographed over silica gel with hexane-AcOEt (10:1 – 5:1) as eluent to give compound (6) (2.13 g, 94%) as a colorless oil. \( \text{Ir} \) (film) \( \nu_{\text{max}} \text{ cm}^{-1}: \) 3350, 3020, 2930, 2850, 1465, 1460, 1060, 965. \(^1\)H-Nmr (CDCl\(_3\)) \( \delta: \) 0.88 (3H, t, \( J = 6.7 \text{ Hz})\), 1.20-1.40 (21H, m), 1.62 (2H, m), 1.97 (2H, m), 2.07 (2H, m), 3.66 (2H, dt, \( J = 5.4, 6.6 \text{ Hz})\), 5.43 (2H, m). Anal. Calcd for \( \text{C}_{17}\text{H}_{34}\text{O}\): C, 80.24; H, 13.47. Found: C, 79.86; H, 13.68.

**(E)-4-Heptadecenal (7).** A solution of alcohol 6 (1.27 g, 5.0 mmol) in CH\(_2\)Cl\(_2\) (15 ml) was added dropwise to a mixture of oxalyl chloride (0.87 ml, 10 ml) and DMSO (0.94 ml, 13.3 mmol) in CH\(_2\)Cl\(_2\) (20 ml) at -78\(^\circ\)C over 30 min. After 40 min, Et\(_3\)N (5.21 ml, 36.5 mmol) was added slowly and the temperature was raised to 0\(^\circ\)C. The reaction mixture was quenched with sat. aq. \( \text{NH}_4\text{Cl}\) and extracted with ether. Drying over MgSO\(_4\) and evaporation of the solvent gave crude aldehyde (7) (1.01 g, 80%), which was taken to the next step without purification. \( \text{Ir} \) (film) \( \nu_{\text{max}} \text{ cm}^{-1}: \) 3020, 2930, 2850, 2720, 1730, 1460, 970. \(^1\)H-Nmr (CDCl\(_3\)) \( \delta: \) 0.88 (3H, t, \( J = 6.9 \text{ Hz})\), 1.20-1.40 (20H, m), 1.96 (2H, m), 2.34 (2H, m), 5.43 (2H, m).
(2E,6E)-Ethyl Nonadeca-2,6-dienoate (8). To a suspension of NaH (60% in mineral oil, 400 mg, 10 mmol) in THF (20 ml) was added triethyl phosphonoacetate (2.24 g, 10 mmol) at 0°C. The mixture was stirred for 30 min at 0°C and then for 1 h at room temperature. The mixture was cooled to -78°C, and a solution of aldehyde (7) (1.51 g, 6 mmol) in THF (5 ml) was then added. After being stirred for 2 h, the reaction mixture was quenched with sat. aq. NH₄Cl. The mixture was extracted with ether, the ethereal solution being washed with brine and dried over MgSO₄ and concentrated. Silica gel column chromatography of the residue (hexane-AcOEt = 20:1) gave 8 (1.67 g, 86%) as a colorless oil. IR (film) ν cm⁻¹: 2930, 2850, 1725, 1655, 1260, 1145, 970. ¹H-Nmr (CDCl₃) δ: 0.88 (3H, t, J = 6.7 Hz), 1.20-1.40 (23H, m), 1.97 (2H, m), 2.16 (2H, m), 2.25 (2H, m), 4.17 (2H, q, J = 7.1 Hz), 5.40 (2H, m), 5.82 (1H, dt, J = 15.6, 1.5 Hz), 6.96 (1H, dt, J = 15.6, 6.7 Hz). Anal. Calcd for C₂₁H₃₈O₂: C, 78.20; H, 11.88. Found: C, 78.47; H, 12.13.

(2E,6E)-Nonadeca-2,6-dien-1-ol (9). To a solution of 8 (650 mg, 2.0 mmol) in CH₂Cl₂ (6 ml) cooled to -78°C was added DIBALH (1.0 M solution in hexane, 4 ml). After being stirred for 1 h at this temperature, the reaction mixture was quenched with MeOH (2 ml) and warmed to room temperature. The mixture was filtered through a Celite pad and the filtrate was concentrated. Silica gel column chromatography of the residue (hexane-AcOEt = 10:1 ~ 5:1) gave 9 (0.53 g, 95%) as a colorless solid, mp 34~36°C. IR (KBr) ν cm⁻¹: 3350, 3020, 2930, 2850, 1465, 1455, 1165, 965. ¹H-Nmr (CDCl₃) δ: 0.88 (3H, t, J = 6.6 Hz), 1.21 (1H, br OH), 1.22-1.40 (20H, m), 1.97 (2H, m), 2.10 (4H, m), 4.09 (2H, m), 5.40 (2H, m), 5.67 (2H, m). Anal. Calcd for C₁₉H₃₆O: C, 81.36; H, 12.94. Found: C, 81.00; H, 12.95.

(2S,3S,6E)-2,3-Epoxynonadec-6-en-1-ol (10). To a suspension of Ti(Oi-Pr)₄ (2.12 g, 7.5 mmol) and 4A molecular sieves in CH₂Cl₂ (30 ml) were added L-(+)-diethyl tartrate (1.55 g, 7.5 mmol) at -25°C. After stirring for 10 min, a solution of allyl alcohol (9) (1.90 g, 6.8 mmol) in CH₂Cl₂ (5 ml) and t-butyl hydroperoxide (5.2 M solution in toluene, 2.86 ml) were added to the mixture at the same temperature, stirring being continued for 20 h. The mixture was quenched with a 10% aq. solution of tartaric acid (17 ml), and allowed to warm to room temperature. The mixture was extracted with CH₂Cl₂, the organic layer being washed with water and concentrated. The residue was dissolved in ether (50 ml) and to this solution
was added 1M NaOH (22 ml) at 0°C. After vigorous stirring for 30 min, the mixture was extracted with ether, the ethereal solution being washed with brine and dried over MgSO₄ and concentrated. Silica gel column chromatography of the residue (hexane-AcOEt = 6:1) gave 10 as a colorless solid [2.00 g, 94%, 96% ee by a ¹H-nmr analysis of the ester derived from (R)-(−)-MTPA chloride], which upon recrystallization from hexane gave optically pure 10 (>99% ee) as colorless needles (1.70 g, 80%), mp 69–70°C. [α]D²³ -20.0° (c 1.14, CHCl₃). IR (KBr) νmax cm⁻¹: 3300, 3150, 2920, 2850, 1460, 960, 870. ¹H-Nmr (CDCl₃) δ: (3H, t, J = 6.6 Hz), 1.20-1.40 (20H, m), 1.60 (1H, br, OH), 1.62 (2H, m), 1.98 (2H, m), 2.15 (2H, m), 2.95 (2H, m), 3.58-3.67 (1H, ddd, J = 12.5, 7.3, 4.2 Hz), 3.87-3.95 (1H, ddd, J = 12.5, 5.6, 2.4 Hz), 5.41-5.52 (2H, m). Anal. Calcd for C₁₉H₃₉O₂: C, 76.97; H, 12.94. Found: C, 76.72; H, 12.17.

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**(2R,5R,1'S,1''R)-2-(1',2'-Dihydroxyethyl)-5-(1''-hydroxytridecyi)tetrahydrofuran (11).** A solution of 10 (1.49 g, 5.0 mmol) in t-BuOH/H₂O (20 ml, 1:1) was added to a mixture of AD-mix β (8.50 g) and methanesulfonamide (0.30 g, 3.2 mmol) in t-BuOH/H₂O (50 ml, 1:1) at 0°C. The resulting heterogeneous mixture was stirred for 24 h at 0°C. This reaction mixture was directly extracted with three 50 ml portions of AcOEt. The combined organic extract was washed with half-saturated aq. Na₂SO₃ and dried with MgSO₄. Subsequent concentration of the extract gave a colorless solid, which was dissolved in CH₂Cl₂ (30 ml) and to the solution was added camphorsulfonic acid (50 mg) at 0°C. After the mixture had been stirred for 2 h at this temperature, it was treated with sat. aq. NaHCO₃ and extracted with AcOEt. The extract was dried with MgSO₄ and concentrated to afford crude 11 as a colorless solid [1.45 g, 96% de by a ¹H-nmr analysis of the ester derived from (R)-(−)-MTPA chloride after conversion to acetonide (12)], which upon recrystallization from AcOEt gave optically pure 11 (>99% de) as colorless needles (1.34 g, 85%), mp 108–109°C. [α]D²⁴ +11.0° (c 0.20, EtOH). IR (KBr) νmax cm⁻¹: 3400, 2930, 2850, 1460, 1120, 1030, 880. ¹H-Nmr (CDCl₃) δ: 0.88 (3H, t, J = 6.7 Hz), 1.20-1.70 (22H, m), 1.80-2.10 (4H, m), 2.00 (1H, br OH), 2.26 (1H, br OH), 2.36 (1H, br OH), 3.39 (1H, m), 3.60-4.00 (5H, m). Anal. Calcd for C₁₉H₃₈O₄: C, 69.04; H, 11.59. Found: C, 69.08; H, 11.86.

**(2R,5R,1'S,1''R)-2-[1',2'-((1-Methyethylidene)dioxy]-5-(1''-hydroxytridecyi)tetrahydrofuran (12).** To a solution of compound (11) (140 mg, 0.45 mmol) and 2,2-dimethoxypropane (1.0 ml) was added p-TsOH (10 mg). After the mixture had been stirred for 2 h, it was diluted with ether and washed with sat.
aq. NaHCO₃ and brine. Drying with MgSO₄ and concentration gave crude 12, which was purified by silica gel column chromatography, eluted with hexane-AcOEt (5:1) to give 12 (156 mg, 95%) as a colorless oil. [α]D²⁴+3.5° (c 1.00, CHCl₃). ¹H-Nmr (CDCl₃) δ: 0.88 (3H, t, J = 6.6 Hz), 1.20-1.60 (22H, m), 1.35 (3H, s), 1.41 (3H, s), 1.60-2.20 (4H, m), 2.27 (1H, d, J = 3.9 Hz, OH), 3.36 (1H, m), 3.77-4.12 (5H, m). Anal. Calcd for C₂₂H₄₂O₄: C, 71.30; H, 11.42. Found: C, 71.31; H, 11.52.

(2⁵R,5⁵R,1'S,1''R)-2-[1',2'-(1-Methylethylidene)dioxyl-5-(1''-methoxymethoxytridecyl)tetrahydrofuran (13). An ice-cooled mixture of 12 (4.64 g, 12.6 mmol) and chloromethyl methyl ether (CAUTION; carcinogen) (1.84 ml, 24 mmol) in CH₂Cl₂ (20 ml) was treated with i-Pr₂NEt (4.52 ml, 26 mmol) and the resultant mixture was warmed to room temperature and stirred for 24 h. After completion of the reaction, the reaction mixture was cooled to 0°C and sat. aq. NH₄Cl (10 ml) was added to it. The mixture was extracted with ether and the organic layer was washed with brine. The extract was dried over MgSO₄ and concentrated to give crude 13, which was purified by silica gel column chromatography, eluted with hexane-AcOEt (15:1), to give 13 (5.18 g, 99%) as a colorless oil. [α]D²⁴+16.9° (c 1.00, CHCl₃). ¹H-Nmr (CDCl₃) δ: 0.88 (3H, t, J = 6.5 Hz), 1.20-1.50 (22H, m), 1.35 (3H, s), 1.40 (3H, s), 1.60-2.10 (4H, m), 3.39 (3H, s), 3.45 (1H, m), 3.81-4.11 (5H, m), 4.67 (1H, d, J = 6.8 Hz), 4.80 (1H, d, J = 6.8 Hz). Anal. Calcd for C₂₄H₄₆O₅: C, 69.52; H, 11.18. Found: C, 69.62; H, 11.17.

(2⁵R,5⁵R,1'S,1''R)-2-[2'-(tert-Butyldimethylsilyl)nxy-1'-hydroxyethyl]-5-(1''-methoxymethoxytridecyl)tetrahydrofuran (14). A solution of compound (13) (1.64 g, 3.96 mmol) in 60% aq. AcOH (20 ml) was stirred at 60°C. After the mixture had been stirred for 6 h, the solvent was evaporated and the crude product was chromatographed over silica gel with hexane-AcOEt (2:1) as eluent to give compound (14) (1.42 g, 96%) as colorless needles, mp 61-61.5°C. [α]D²⁴+24.1° (c 1.00, CHCl₃). ¹H-Nmr (CDCl₃) δ: 0.88 (3H, t, J = 6.7 Hz), 1.20-1.50 (22H, m), 1.35 (3H, s), 1.40 (3H, s), 1.60-2.24 (4H, m), 2.29 (1H, br OH), 2.43 (1H, br OH), 3.40 (3H, s), 3.42-4.06 (6H, m), 4.68 (1H, d, J = 6.8 Hz), 4.79 (1H, d, J = 6.8 Hz). Anal. Calcd for C₂₄H₄₆O₅: C, 69.62; H, 11.17. Found: C, 67.06; H, 11.17.
decyl)tetrahydrofuran (15). To a mixture of 14 (265 mg, 0.70 mmol) and Et3N (0.12 ml, 0.85 mmol) and DMAP (20 mg) was added t-butyldimethylchlorosilane (128 mg, 0.80 mmol). After the mixture had been stirred for 12 h, it was diluted with ether and washed with sat. aq. NaHCO3, sat. aq. NH4Cl and brine. Drying with MgSO4 and concentration gave crude 15, which was chromatographed over silica gel, eluted with hexane-AcOEt (10:1), to give compound (15) (330 mg, 97%) as a colorless oil. \[\alpha\]D24 +16.9° (c 1.00, CHCl3). Ir (film) νmax cm⁻¹: 3470, 2920, 2850, 1460, 1250, 1100, 1040, 840, 780. 1H-Nmr (CDCl3) δ: 0.07 (6H, s), 0.90 (12H, br.), 1.20-1.60 (22H, m), 1.60-2.05 (4H, m), 2.45 (IH, d, J = 4.2 Hz, OH), 3.40 (3H, s), 3.41-4.01 (6H, m), 4.68 (1H, d, J = 6.8 Hz), 4.80 (1H, d, J = 6.8 Hz). Anal. Calcd for C27H56OSSi: C, 66.34; H, 11.55. Found: C, 66.31; H, 11.26.

(2R,5R,1'R,1''R)-2-(1',2'-Epoxyethyl)-5-(1''-methoxymethoxytridecyl)tetrahydrofuran (16). To a mixture of 15 (330 mg, 0.68 mmol) and Et3N (0.18 ml, 1.28 mmol) in CH2Cl2 (3 ml) was added methanesulfonyl chloride (0.075 ml, 0.97 mmol) at -10°C. After the reaction had been completed, the mixture was diluted with ether and washed with 0.1 M HCl and brine. Drying with MgSO4 and evaporation provided an oil, which was dissolved in THF (3 ml) and treated with n-Bu4NF (1.0 M solution in THF, 0.75 ml) at 0°C. After the mixture had been stirred for 12 h, 15% aq. NaOH (0.6 ml) was added to it at 0°C. After being stirred in an ice-bath for 30 min and then at room temperature for 5 h, the mixture was diluted with ether and washed with water and brine. Drying with MgSO4 and concentration gave crude 16. Purification by silica gel column chromatography (hexane-AcOEt = 7:1) gave 16 (205 mg, 85%) as a colorless wax, mp 39-41°C. [α]D24+20.9° (c 2.48, CHCl3). Ir (film) νmax cm⁻¹: 2920, 2850, 1460, 1145, 1100, 1040, 910. 1H-Nmr (CDCl3) δ: 0.88 (3H, t, J = 6.6 Hz), 1.20-1.55 (22H, m), 1.60-2.10 (4H, m), 2.71 (1H, dd, J = 5.1, 2.6 Hz), 2.75 (1H, dd, J = 5.1, 4.2 Hz), 3.00 (1H, ddd, J = 6.8, 4.2, 2.6 Hz), 3.40 (3H, s), 3.45 (1H, m), 3.92 (1H, m), 4.05 (1H, m), 4.68 (1H, d, J = 6.8 Hz), 4.79 (1H, d, J = 6.8 Hz). Anal. Calcd for C21H40O4: C, 70.74; H, 11.31. Found: C, 70.30; H, 11.19.

(2R,5R,1'R,1''R)-2-(1'-Hydroxy-3'-butynyl)-5-(1''-methoxymethoxytridecyl)tetrahydrofuran (17). To a solution of trimethylsilylacetylene (1.46 ml, 15 mmol) in THF (15 ml) was added a solution of n-BuLi (1.56 M solution in hexane, 9.6 ml) at -78°C. After the mixture had been stirred for 20 min, boron trifluoride etherate (1.84 ml, 15 mol) was added at this temperature and stirred for 30 min. The resulting
mixture was treated with epoxide 16 (2.40 g, 6.7 mmol), then stirred for 2 h, and then quenched by addition of sat. aq. NH₄Cl. The mixture was stirred for 5 min, warmed to room temperature, and extracted with ether. The organic extract was washed with brine, dried with MgSO₄ and concentrated in vacuo. The residue was dissolved in THF (15 ml) and treated with n-Bu₄NF (1.0 M solution in THF, 6.9 ml) at 0°C. The mixture was allowed to warm to room temperature and stirred for a further 5 h. After completion of the reaction, the mixture was diluted with ether (50 ml) and washed with water and brine. Drying (MgSO₄) and evaporation of the solvent afforded crude 17, which was chromatographed over silica gel (hexane:AcOEt = 6:1) to afford pure 17 (2.41 g, 85%) as a colorless oil. [α]D²⁴+12.9° (c 1.10, CHCl₃). Ir (film) ν, cm⁻¹: 3450, 3320, 2930, 2850, 2120, 1640, 1150, 1100, 1040, 920. 'H-Nmr (CDCl₃) δ: 0.88 (3H, t, J = 7.0 Hz), 1.20-2.00 (26H, m), 2.01 (1H, t, J = 2.6 Hz), 2.43 (2H, dd, J = 6.2, 2.6 Hz), 2.53 (1H, d, J = 5.5 Hz, OH), 3.41 (3H, s), 3.51 (1H, m), 3.63 (1H, m), 4.00 (2H, m), 4.70 (1H, d, J = 7.0 Hz), 4.80 (1H, d, J = 6.6 Hz). Anal. Calcd for C₂₃H₄₂O₄: C, 72.21; H, 11.06. Found: C, 71.91; H, 11.08.

(2R,5R,1'R,1''R)-2-(1'-Methoxymethoxy-3'-butynyl)-5-(1''-methoxymethoxytridecyl)tetrahydrofuran (18). An ice-cooled mixture of alcohol (17) (2.16 g, 5.65 mmol) and chloromethyl methyl ether (CAUTION; carcinogen) (0.92 ml, 12.0 mmol) in CH₂Cl₂ (20 ml) was treated with i-Pr₂NEt (2.26 ml, 13.0 mmol) and the resulting mixture was allowed to warm to room temperature and stirred for 25 h. After completion of the reaction, the reaction mixture was cooled to 0°C and sat. aq. NH₄Cl was added to it. The mixture was extracted with ether and the extract was washed with brine, dried with MgSO₄ and concentrated. The residue was purified by silica gel column chromatography (hexane-AcOEt = 15:1) afforded 18 (2.55 g, 96%) as a colorless oil. [α]D²⁴+20.9° (c 1.02, CHCl₃). Ir (film) ν, cm⁻¹: 3320, 2930, 2850, 2130, 1470, 1150, 1100, 1040, 920. 'H-Nmr (CDCl₃) δ: 0.88 (3H, t, J = 6.7 Hz), 1.20-1.60 (22H, m), 1.61-1.80 (2H, m), 1.92-2.05 (2H, m), 1.98 (1H, t, J = 2.7 Hz), 2.38-2.60 (2H, ddd, J = 17.2, 6.0, 2.7 Hz), 3.40 (3H, s), 3.42 (3H, s), 3.47 (1H, m), 3.66 (1H, m), 4.00 (1H, m), 4.16 (1H, m), 4.67 (1H, d, J = 6.6 Hz), 4.78 (2H, s), 4.84 (1H, d, J = 6.6 Hz). Anal. Calcd for C₂₅H₄₆O₅: C, 70.38; H, 10.87. Found: C, 70.24; H, 11.22.

(S)-1-Iodo-[3,4-(1-ethylpropyldene)dioxy]butane (21). To an ice-cooled solution of (S)-3,4-(1-ethylpropyldene)dioxybutan-1-ol (20) (5.8 g, 33.3 mmol) in pyridine (20 ml) was added p-TsCl (7.6 g, 39.9
mmol). After being stirred in an ice-bath for 1 h and then at room temperature for 5 h, the mixture was extracted with ether. The extract was washed 0.1 N HCl (50 ml) and brine, dried over MgSO₄, and concentrated in vacuo. The residue was dissolved in acetone (50 ml), and NaHCO₃ (13.0 g, 155 mmol) and NaI (12.5 g, 83.4 mmol) were added to the solution. After being stirred for 6 h, the mixture was extracted with ether. The extract was washed with sat. aq. Na₂S₂O₃, brine, dried over MgSO₄, and concentrated in vacuo. The residue was purified by silica gel column chromatography (hexane-AcOEt = 20:1) to give 21 (8.26 g, 87%) as a colorless oil. [α]D²² -20.6° (c 4.61, CHCl₃). IR (film) νmax cm⁻¹: 2975, 2940, 1460, 1350, 1200, 1170, 1080, 920, 770. ¹H-Nmr (CDCl₃) δ: 0.89 (3H, t, J = 6.7 Hz), 0.90 (3H, t, J = 6.7 Hz), 1.62 (4H, m), 2.08 (2H, m), 3.26 (2H, m), 3.52 (1H, dd, J = 7.5, 7.5 Hz), 4.10 (1H, dd, J = 7.5, 7.5 Hz), 4.15 (1H, m). Anal. Calcd for C₁₁H₁₇I : C, 38.04; H, 6.03. Found : C, 38.23; H, 5.89.

(5)-8,9-(1-Ethylpropylidene)dioxynonan-1-o(24). To a solution of 23 (5.46 g, 16.6 mmol) in AcOEt (50 ml) was added 10% Pd-C (540 mg) at room temperature, and the suspension was vigorously stirred under a hydrogen atmosphere. After being stirred for 12 h, the reaction mixture was filtered through a Celite pad and concentrated in vacuo. Silica gel column chromatography of the residue (hexane-AcOEt = 5:1) gave 24 (3.90 g, 96%) as a colorless oil. [α]D²⁴+13.8° (c 1.00, CHCl₃). IR (film) νmax cm⁻¹: 3400, 2970, 2930, 2850, 1460, 1350, 1200, 1170, 1075, 920. ¹H-Nmr (CDCl₃) δ: 0.89 (3H, t, J = 7.5 Hz), 0.90 (3H,
t, \(J = 7.5\) Hz), 1.24 (1H, br OH), 1.30-1.68 (16H, m), 3.45 (1H, m), 3.63 (2H, m), 4.06 (2H, m). Anal. Calcd for C\(_{14}\)H\(_{26}\)O\(_3\) : C, 68.81; H, 11.55. Found : C, 69.24; H, 11.40.

(5S)-1-Iodo-8,9-(1-ethylpropylidene)dioxynonane (25). To an ice-cooled of 24 (2.65 g, 10.8 mmol) in pyridine (15 ml) was added p-TsCl (2.54 g, 13.0 mmol). After being stirred for 1 h at 0°C and then for 5 h at room temperature, the mixture was diluted with ether and washed with water, 0.1 N HCl and brine. Drying over MgSO\(_4\) and subsequent concentration gave an oil, which was dissolved in acetone (15 ml) and treated with NaHCO\(_3\) (4.0 g, 47.6 mmol) and NaI (4.0 g, 25.5 mmol). After being stirred for 8 h, the mixture was extracted with ether and the extract was washed with water, sat. aq. Na\(_2\)S\(_2\)O\(_3\), brine, and dried over MgSO\(_4\). Removal of the solvent and silica gel column chromatography (hexane-AcOEt = 20:1) afforded 25 (3.51 g, 91%) as a colorless oil, \([\alpha]_D^{22}+9.2^\circ\) (c 1.68, CHCl\(_3\)). Ir (film) \(\nu_{\text{max}}\) cm\(^{-1}\): 2980, 2940, 2860, 2850, 1460, 1080, 920. \(^1\)H-Nmr (CDCl\(_3\)) \(\delta\): 0.89 (3H, \(t, J = 7.5\) Hz), 0.90 (3H, \(t, J = 7.5\) Hz), 1.20-1.87 (16H, m), 3.19 (2H, \(t, J = 7.1\) Hz), 3.45 (1H, m), 4.04 (2H, m). Anal. Calcd for C\(_{14}\)H\(_{27}\)O\(_2\)I : C, 47.47; H, 7.68. Found : C, 47.83; H, 7.77.

(3RS,5S,8'S)-3-[8',9'-([1-ethylpropylidene]dioxynonyl]-5-methyl-3-(phenylsulfanyl)tetrhydrofuran-2-one (26). To an ice-cooled solution of lactone (19)(1.80 g, 8.97 mmol) in THF (20 ml) was added NaHMDS (0.6 M solution in toluene, 15 ml). After the mixture had been stirred at 0°C for 30 min, 25 (3.18 g, 8.97 mmol) in HMPA (10 ml) was added to it and the whole was allowed to warm to room temperature. The reaction mixture was quenched by addition of sat. aq. NH\(_4\)Cl and extracted with ether. Drying over MgSO\(_4\) and subsequent concentration gave crude 26, which was chromatographed over silica gel (hexane-AcOEt = 10:1) to afford pure 26 (3.42 g, 88%) as a colorless oil. Ir (film) \(\nu_{\text{max}}\) cm\(^{-1}\): 3050, 2970, 2930, 2850, 1765, 1460, 1440, 1340, 1180, 1175, 920, 750, 695. \(^1\)H-Nmr (CDCl\(_3\)) \(\delta\): 0.89 (3H, \(t, J = 6.5\) Hz), 0.90 (3H, \(t, J = 6.5\) Hz), 1.19 (2.4H, d, \(J = 6.2\) Hz), 1.38 (0.6H, d, \(J = 6.2\) Hz), 1.23-1.83 (18H, m), 1.98 (1H, m), 2.35 (0.2H, dd, \(J = 13.9, 5.5\) Hz), 2.45 (1H, m), 2.50 (0.8H, dd, \(J = 13.9, 7.7\) Hz), 4.05 (2H, m), 4.48 (0.8H, m), 4.52 (0.2H, m), 7.35 (3H, m), 7.54 (2H, m). Anal. Calcd for C\(_{25}\)H\(_{38}\)O\(_4\)S: C, 69.09; H, 8.81. Found: C, 69.22; H, 8.58.

(3RS,5S,8'S)-3-(8',9'-Dihydroxy)nonyl-5-methyl-3-(phenylsulfanyl)tetrhydrofuran-2-one (27).
To a solution of 26 (900 mg, 2.07 mmol) in MeOH (10 ml) was added p-TsOH (50 mg). After the mixture had been stirred for 48 h, the solvent was evaporated. The residue was purified by silica gel column chromatography (hexane-AcOEt = 2:1~1:1) to afford 27 (721 mg, 99%) as a colorless oil. Ir (film) ν_{max} \text{cm}^{-1} : 3400, 3060, 2940, 2850, 1760, 1460, 1440, 1340, 1190, 1070, 750, 695. \text{^1H-Nmr} (\text{CDCl}_3) \delta : 1.19 (2.4H, d, J = 6.2 Hz), 1.37 (0.6H, d, J = 6.2 Hz), 1.25-1.81 (14H, m), 1.98 (1H, m), 1.90 (1H, br OH), 2.01 (1H, br OH), 2.35 (0.2H, dd, J = 13.8, 5.5 Hz), 2.50 (0.8H, dd, J = 13.9, 7.6 Hz), 3.43 (1H, m), 3.63 (2H, m), 4.47 (0.8H, m), 4.57 (0.2H, m), 7.35 (3H, m), 7.54 (2H, m). HREIms (M^+). Found: 366.1848. Calcd for C_{20}H_{30}O_{3}S: 366.1865.

\((3RS,5S,8'S)-3-(8',9'-\text{Epoxynonyl})-5\text{-methyl-3-(phenylsulfanyl)tetrahydrofuran-2-one} (28)\). To an ice-cooled solution of 27 (1.00 g, 2.74 mmol) in pyridine (10 ml) was added p-TsCl (574 mg, 3.01 mmol). After being stirred in an ice-bath for 1 h and then at room temperature for 5 h, the mixture was extracted with ether. The extract was washed with water, brine, dried over MgSO_4, and concentrated in vacuo. The residue was dissolved in dry THF (20 ml) and treated with powdered KOH (230 mg, 4.1 mmol) at 0°C. After being stirred for 2 h, the mixture was diluted with ether. The organic layer was washed with water, brine, dried over MgSO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (hexane-AcOEt = 8:1) to give 28 (663 mg, 69%) as a colorless oil. Ir (film) ν_{max} \text{cm}^{-1} : 3050, 2980, 2850, 1765, 1440, 1340, 1185, 1110, 750, 695. \text{^1H-Nmr} (\text{CDCl}_3) \delta : 1.19 (2.4H, d, J = 6.2 Hz), 1.38 (0.6H, d, J = 6.2 Hz), 1.30-1.83 (14H, m), 1.98 (1H, m), 2.35 (0.2H, dd, J = 13.9, 5.5 Hz), 2.46 (1H, dd, J = 4.9, 2.7 Hz), 2.50 (0.8H, dd, J = 13.9, 7.7 Hz), 2.75 (1H, dd, J = 4.9, 4.0 Hz), 2.90 (1H, m), 4.47 (0.8H, m), 4.60 (0.2H, m), 7.38 (3H, m), 7.54 (2H, m). Anal. Calcd for C_{20}H_{28}O_{3}S: C, 68.93; H, 8.10. Found: C, 68.64; H, 7.99.

\((3RS,5S,8'S)-3-(9'-\text{tst-Butyldimethylsilyloxy-8'-hydroxynonyl})-5\text{-methyl-3-(phenylsulfanyl)tetrahydrofuran-2-one} (29)\). To a mixture of 27 (500 mg, 1.37 mmol) in CH_2Cl_2 (10 ml), Et_3N (0.24 ml, 1.70 mmol) and DMAP (50 mg) was added t-butyldimethylchlorosilane (256 mg, 1.60 mmol). After the mixture had been stirred for 12 h, it was diluted with ether and washed with sat. aq. NaHCO_3, sat. aq. NH_4Cl, and brine. Drying over MgSO_4 and subsequent concentration gave crude 29, which was purified by silica gel column chromatography to give 29 (538 mg, 82%) as a colorless oil. Ir (film) ν_{max} \text{cm}^{-1} : 3500,
3150, 2930, 2855, 1765, 1250, 1190, 1100, 840.\textsuperscript{1}H-Nmr (CDCl\textsubscript{3}) \(\delta\): 0.08 (6H, s), 0.90 (9H, s), 1.19 (2.4H, d, \(J = 6.2\) Hz), 1.38 (0.6H, d, \(J = 6.2\) Hz), 1.20-1.81 (14H, m), 1.98 (1H, m), 2.32 (0.2H, dd, \(J = 13.9, 5.5\) Hz), 2.43 (1H, d, \(J = 3.3\) Hz, OH), 2.50 (0.8H, dd, \(J = 13.9, 7.7\) Hz), 3.39 (1H, m), 3.62 (2H, m). Anal. Calcd for C\textsubscript{26}H\textsubscript{44}O\textsubscript{4}SSi: C, 64.95; H, 9.22. Found: C, 64.96; H, 9.22.

(3RS,5S,8'R)-3-(8',9'-Epoxy)nonyl-5-methyl-3-(phenylsulfanyl)tetrahydrofuran-2-one (30). To a mixture of 29 (200 mg, 0.42 mmol) and Et\textsubscript{3}N (0.1 ml, 0.71 mmol) was added MsCl (0.05 ml, 0.65 mmol) at -10°C. After the reaction had been completed, the mixture was diluted with ether and washed with 0.1 N HCl and brine. Drying over MgSO\textsubscript{4} and evaporation of the solvent gave an oil, which was dissolved in MeCN (0.41 ml) and treated with 55% aq. HF (21 \mu l, 0.58 mmol) at 0°C. After being stirred for 3 h at room temperature, the reaction mixture was quenched with sat. aq. NaHCO\textsubscript{3}. The mixture was extracted with ether and the organic layer was washed with brine. Drying over MgSO\textsubscript{4} and concentration gave an oil, which was purified by silica gel column chromatography (hexane-AcOEt = 8:1) to afford 30 (69 mg, 47%) as a colorless oil. The ir and \textsuperscript{1}H-nmr spectra were similar to those of 28. Anal. Calcd for C\textsubscript{26}H\textsubscript{44}O\textsubscript{4}SSi: C, 64.93; H, 9.22. Found: C, 64.96; H, 9.22.

(3RS,5S,8'S,13'R,2''R,5''R,1''R)-3-(8'-Hydroxy-13'-methoxymethoxy-13'-[5''-(1'''-methoxymethoxytridecyl)tetrahydrofuran-2''-yl]tridec-10'-ynyl)-5-methyl-3-(phenylsulfanyl)tetrahydrofuran-2-one (31). To a solution of 18 (2.55 g, 5.4 mmol) in THF (30 ml) was added a solution of n-BuLi (1.6 M solution in hexane, 3.4 ml) at -78°C. After the mixture had been stirred for 30 min, boron trifluoride etherate (0.66 ml, 5.4 mmol) was added to the mixture and stirring was continued for further 20 min. Finally, a solution of 28 (0.94 g, 2.7 mmol) was added to the mixture. After the mixture had been stirred for 1 h, the reaction was quenched with sat. aq. NH\textsubscript{4}Cl. The organic materials were extracted with ether and the extract was washed with brine. Drying over MgSO\textsubscript{4} and evaporation of the solvent gave an oil, which was chromatographed over silica gel (hexane-AcOEt = 3:1) to give 31 (1.93 g, 92%) as a colorless oil. Ir (film) \(v_{\text{max}}\) cm\textsuperscript{-1}: 3480, 3120, 2930, 2850, 1765, 1465, 1440, 1180, 1150,
(3RS,5S,8'R,13'R,2''R,5''R,1''''R)-3-{8'-Hydroxy-13'-methoxymethoxy-13'-[5''-(1''''-methoxymethoxytridecyl)tetrahydrofuran-2''-yl]tridec-10'-ynyl}-5-methyl-3-(phenylsulfanyl)tetrahydrofuran-2-one (32). In the same manner as just described, 30 (115 mg, 0.33 mmol) and 18 (306 mg, 0.65 mmol) afforded 32 (253 mg, 99%) as a colorless oil. The IR spectrum was similar to that of 31. 

\[ \text{Anal. Calcd for C}_{45}\text{H}_{74}\text{O}_{8}\text{S}: \text{C, 69.73; H, 9.62. Found: C, 69.42; H, 9.18.} \]

(3RS,5S,8'S,13'R,2''R,5''R,1''''R)-3-{8'-Hydroxy-13'-methoxymethoxy-13'-[5''-(1''''-methoxymethoxytridecyl)tetrahydrofuran-2''-yl]tridecyl}-5-methyl-3-(phenylsulfanyl)tetrahydrofuran-2-one (33). A solution of 31 (523 mg, 0.67 mmol) in benzene (5 ml) was hydrogenated over chlorotris(triphenylphosphine)rhodium (150 mg, 0.16 mmol) for 5 h. Filtration and concentration afforded an oil, which was purified by silica gel column chromatography (hexane-AcOEt = 3:1) to give 33 (480 mg, 92%) as a colorless oil. IR (film) \( v_{\text{max}} \) cm\(^{-1}\): 3500, 3050, 2930, 2850, 1765, 1460, 1440, 1340, 1180, 1150, 1100, 1030, 920, 750, 695. 

\[ \text{Anal. Calcd for C}_{45}\text{H}_{78}\text{O}_{8}\text{Na}_{1}\text{S}: \text{801.5315.} \]
In the same manner as just described above, 32 (16 mg, 0.021 mmol) afforded 34 (16 mg, 99%) as a colorless oil. The ir and $^1$H-nmr spectra were similar to those of 33. HRFABms (M+Na$^+$). Found: 801.5335. Calcd for C$_{43}$H$_{78}$O$_8$NaS: 801.5315.

(3RS,5S,8'S,13'R,2''R,5''R,1''''R)-3-[(8'-Hydroxy-13'-methoxymethoxy-13'-[5''-(1''''-methoxymethoxytridecyl)tetrahydrofuran-2''-yl]tridecyl]-5-methyl-2,5-dihydrofuran-2-one (35). To a solution of 33 (19 mg, 0.024 mmol) in CH$_2$Cl$_2$ (0.5 ml) was added mCPBA (80%, 5.2 mg, 0.024 mmol) at 0°C. After the mixture had been stirred at this temperature for 10 min, aq. Na$_2$S$_2$O$_3$/NaHCO$_3$ (1:1, 1.0 ml) was added. After stirring at room temperature for 1 h, the mixture was extracted with ether and the extract was washed with brine. Drying over MgSO$_4$ and subsequent concentration gave an oil, which was dissolved in toluene (2.0 ml) and the solution was refluxed for 1 h. After completion of the reaction, concentration of the mixture gave an oil, which was purified by silica gel column chromatography (hexane-AcOEt = 2:1) to afford 35 (14 mg, 87%) as a colorless oil. [$\alpha$]$_D^{22}+31.4'$ (c 0.14, CHCl$_3$). Ir (film) $\nu_{\max}$ cm$^{-1}$: 3500, 2920, 2850, 1755, 1455, 1315, 1145, 1100, 1030, 920. $^1$H-Nmr (CDCl$_3$) $\delta$: 0.88 (3H, t, $J = 7.0$ Hz), 1.40 (3H, d, $J = 7.0$ Hz), 1.20-1.63 (45H, m), 1.92 (2H, m), 1.95 (1H, br OH), 2.26 (2H, t, $J = 7.7$ Hz), 3.39 (6H, s), 3.46 (2H, m), 3.57 (1H, m), 3.97 (2H, m), 4.66 (2H, d, $J = 7.0$ Hz), 4.83 (1H, d, $J = 7.0$ Hz), 4.84 (1H, d, $J = 7.0$ Hz), 4.99 (1H, dq, $J = 1.5$, 6.6 Hz), 6.98 (1H, d, $J = 1.5$ Hz). HRFABms (M+Na$^+$). Found: 691.5130. Calcd for C$_{39}$H$_{72}$O$_8$Na: 691.5125.

(3RS,5S,8'S,13'R,2''R,5''R,1''''R)-3-[(8'-Hydroxy-13'-methoxymethoxy-13'-[5''-(1''''-methoxymethoxytridecyl)tetrahydrofuran-2''-yl]tridecyl]-5-methyl-2,5-dihydrofuran-2-one (36). In the same manner as just described above, 34 (16 mg, 0.021 mmol) afforded 36 (12 mg, 87%) as a colorless oil. [$\alpha$]$_D^{22}+32.5'$ (c 0.16, CHCl$_3$). The ir and $^1$H-nmr spectra were similar to those of 35. HRFABms (M+Na$^+$). Found: 691.5146. Calcd for C$_{39}$H$_{72}$O$_8$Na: 691.5125.

(8'S)-Corossoline [(8'S)-1]. Boron trifluoride etherate (0.1 ml, 0.8 mmol) was added dropwise to a solution of 35 (14 mg, 0.021 mmol) in dimethylsulfide (0.7 ml) at 0°C, and the mixture was stirred for 5 min at this temperature. The reaction mixture was quenched with sat. aq. NaHCO$_3$ and diluted with AcOEt. The mixture was washed with water and brine. Drying over MgSO$_4$ and evaporation of the
solvent gave a colorless solid, which was purified by preparative tlc (AcOEt) to give (8'S)-1 (12 mg, 98\%) as a colorless solid, mp 56.5–58°C. \([\alpha]_D^{22} +22.2^\circ\) (c 0.18, MeOH). Ir (KBr) \(\nu_{\text{max}}\) cm\(^{-1}\): 3400, 2920, 2850, 1750, 1465, 1380, 1320, 1190, 1080. \(^1^H\)-Nmr (CDCl\(_3\)) \(\delta\): 0.88 (3H, t, \(J = 6.8\) Hz), 1.20–1.80 (45H, m), 1.40 (3H, d, \(J = 6.6\) Hz), 2.27 (2H, t, \(J = 7.3\) Hz), 2.32 (1H, br OH), 2.36 (1H, br OH), 3.40 (2H, m), 3.59 (1H, m), 3.81 (2H, m), 5.00 (1H, dq, \(J = 1.5, 6.6\) Hz), 6.98 (1H, d, \(J = 1.5\) Hz). \(^{13}C\)-Nmr (CDCl\(_3\), 100 MHz) \(\delta\): 173.87, 148.89, 134.24, 82.68, 82.62, 77.41, 74.03, 73.84, 71.67, 37.44, 37.32, 33.42, 33.27, 31.89, 29.69–28.73, 27.35, 25.56, 25.53, 25.47, 25.13, 22.66, 19.18, 14.08. HREIms (M\(^+\)). Found: 580.4734. Calcd for C\(_{35}\)H\(_{64}\)O\(_6\): 580.4703.

(8'R)-Corossoline [(8'R)-1]. In the same manner as just described, 36 (12 mg, 0.018 mmol) afforded (8'R)-1 (10 mg, 98\%) as a colorless solid, mp 66–69°C. \([\alpha]_D^{22} +21.0^\circ\) (c 0.20, MeOH). The ir, \(^1\)H-nmr and \(^{13}C\)-nmr spectra were similar to those of (8'S)-1. HRFABms (M+Na\(^+\)). Found: 603.4601. Calcd for C\(_{35}\)H\(_{64}\)O\(_6\)Na: 603.4601.

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