Alkylated Levoglucosan in Organic Synthesis. A Formal Total Synthesis of Elaiophylin

Hideo NAKAMURA,[a] Kazushi ARATA,[a] Takeshi WAKAMATSU,*[,b,1)] Yoshio BAN,[b] and Masakatsu SHIBASAKI*[,b]

Hokkaido University of Education,[a] Hachiman-cho, Hakodate 040, Japan and Faculty of Pharmaceutical Sciences, Hokkaido University,[b] Sapporo 060, Japan. *Received March 7, 1990*

Levoglucosan (8) has been found to be a useful material for the synthesis of chiral compounds having five contiguous chiral centers (14). Conversion of 8 to 14 involves two *trans*-diaxial openings of epoxides by nucleophilic reagents. Among 14, 14c was successfully transformed into the intermediate 5 for the total synthesis of elaiophylin (1). Efficient lactonization of the carboxylic acid 33 has been achieved by use of Yamaguchi's method.

Keywords corn starch; levoglucosan; epoxide; *trans*-diaxial opening; nucleophile; lactonization; chiral synthesis

Several 16-membered ring macrodiolides with C_2 symmetry have been isolated: pyrenophorin, vermiculine, conglobatin, and elaiophylin (**1**).[2)] Of these, the latter presents the greatest challenge as a synthetic target. Elaiophylin (**1**) was isolated, originally, from cultures of *Streptomyces melanosporus*[2a)] and exhibits activity against gram-positive bacteria. Compounds that ultimately proved to be identical with elaiophylin were subsequently isolated from other strains of *Streptomyces*.[2b-d)] The constitution of elaiophylin was first elucidated in 1981[3)] and subsequently the relative and absolute configuration were determined by X-ray analysis and nuclear magnetic resonance (NMR) studies.[4)]

The first total synthesis of **1** was achieved by Kinoshita and his coworkers in 1986.[5,6)] They used aldol condensation of the ethyl-ketone **4** with the aldehyde **6**, derived from **5**, as a key step. Independently we have also pursued our studies on a total synthesis of **1**.[7)] In this paper we report an efficient synthesis of Kinoshita's intermediate **5** starting with levoglucosan (**8**),[8)] which is readily obtainable in large quantities from corn starch *via* pyrolysis.

Manipulation of Levoglucosan It was envisioned that levoglucosan (**8**) would be a reasonable chiral source for the synthesis of **1** in the naturally occurring form. The utility of levolglucosan (**8**) in organic synthesis stems from its abnormal $^1C_4$ conformation[8)] with three axial hydroxy groups caused by the 1,6-anhydro-ring. Levoglucosan (**8**) is readily converted to **9**, and by using various nucleophilic reagents (allylmagnesium chloride/a catalytic amount of cuprous iodide and methylmagnesium chloride/cuprous bromide–dimethyl sulfide) **9** can be transformed into **10** *via* stereo- and regiocontrolled *trans*-diaxial ring opening.[9)] Moreover, levoglucosan (**8**) can also be converted to **12** *via* the epoxide **11**.[10)] In order to synthesize the intermediate **5** for the synthesis of elaiophylin (**1**) and further to enhance the synthetic utility of levolglucosan (**8**) in organic synthesis, regio- and stereocontrolled conversion of **8** to **14** was investigated in detail.

First of all, the epoxy-tosylate **9** was converted to a variety of hydroxy-tosylates **10**, which were treated with sodium

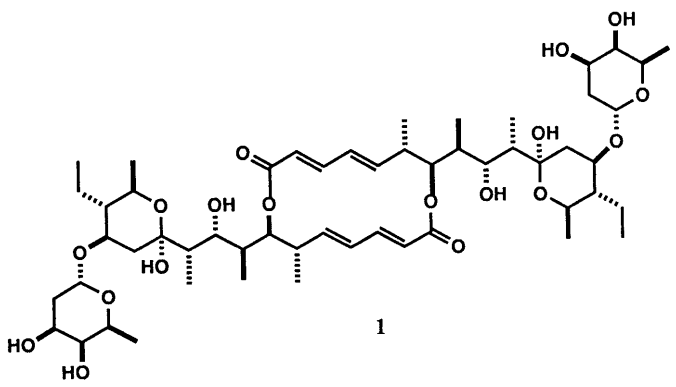


Fig. 1

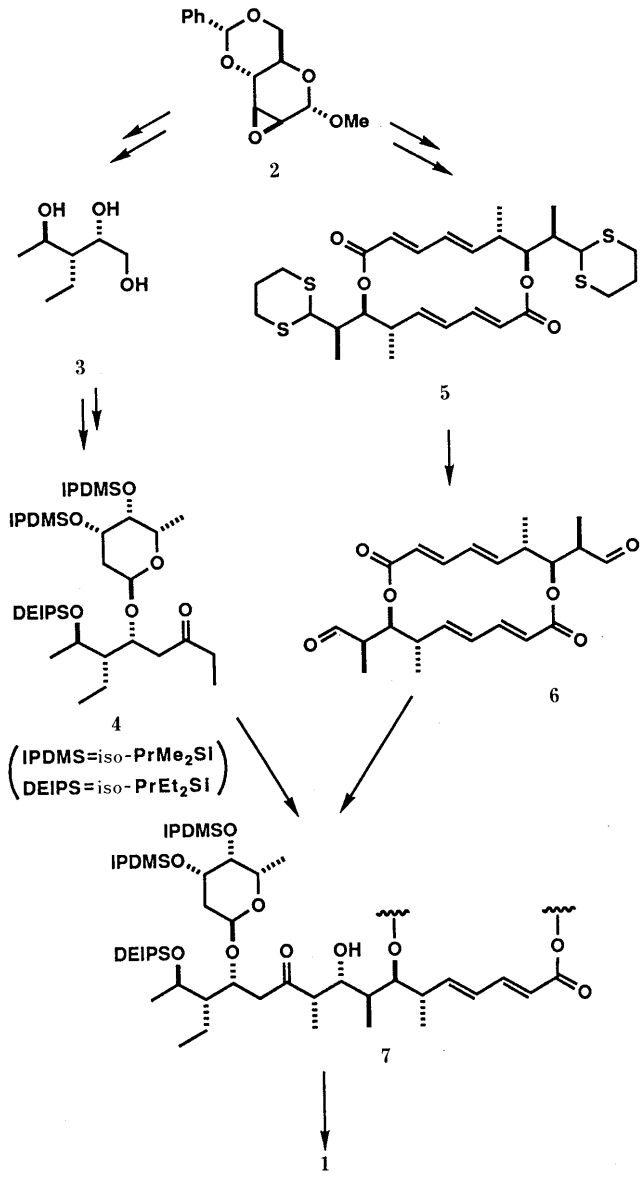


Chart 1

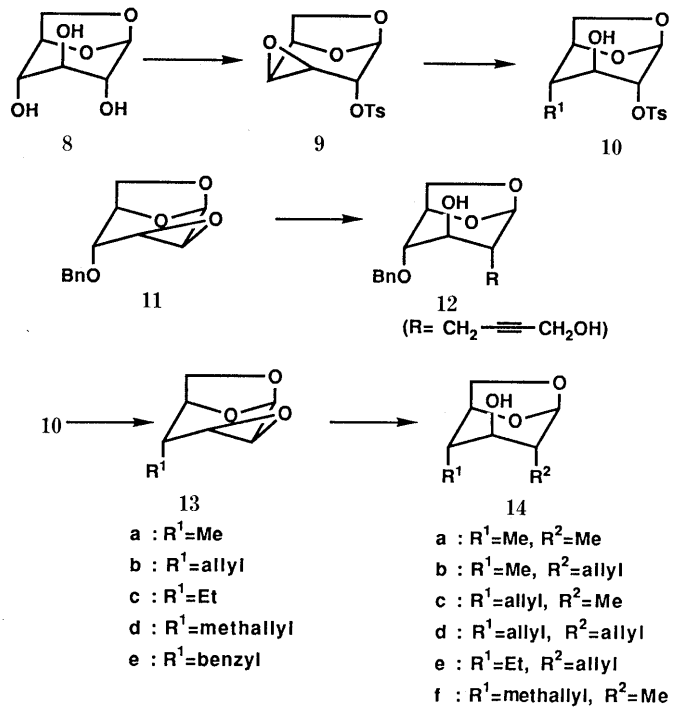


Chart 2

Table I. Conversion of **9** to **13**

	R_1	Yield (%) (**9**→**10**[a])	Yield (%) (**10**→**13**[b])
a	Me	62	86
b	Allyl	96	Quant.
c	Et	75	Quant.
d	Methallyl	82	Quant.
e	Benzyl	62	90

a) Treatment with excess of R_1MgCl–CuI or –CuBr in THF–ether at 0 °C or room temperature. *b*) Treatment with *ca.* 2 eq of NaH in THF at room temperature.

hydride, giving **13**. The results are summarized in Table I. The structures of the epoxides **13** were unequivocally determined from the NMR spectra.

Secondly, the epoxides **13** were transformed into **14** by treatment with various nucleophilic reagents as shown in Table II. The structures of the alcohols **14** were also determined from the NMR spectra. In this way, levoglucosan (**8**) was found to be an extremely useful chiral source for the synthesis of optically active compounds having five contiguous chiral centers.

Synthesis of the Intermediate 5 for Elaiophylin With **14c** available in large quantities, conversion of **14c** to the synthetic intermediate **5** for elaiophylin (**1**) was pursued. The alcohol **14c** was protected as a benzyl ether by treatment with sodium hydride/benzyl bromide (quantitative yield). Isomerization of the benzyl ether **15** with rhodium(III) chloride/potassium carbonate afforded **16** as a mixture of the *cis* and *trans* isomers (quantitative yield). Ozonolysis followed by treatment with dimethyl sulfide gave a complex mixture. However, direct reduction of the ozonolysis product with sodium borohydride in methanol gave the alcohol **17** in 95% yield. After protection as a benzyl ether (96%), **18** was treated with 1,3-propanedithiol in the

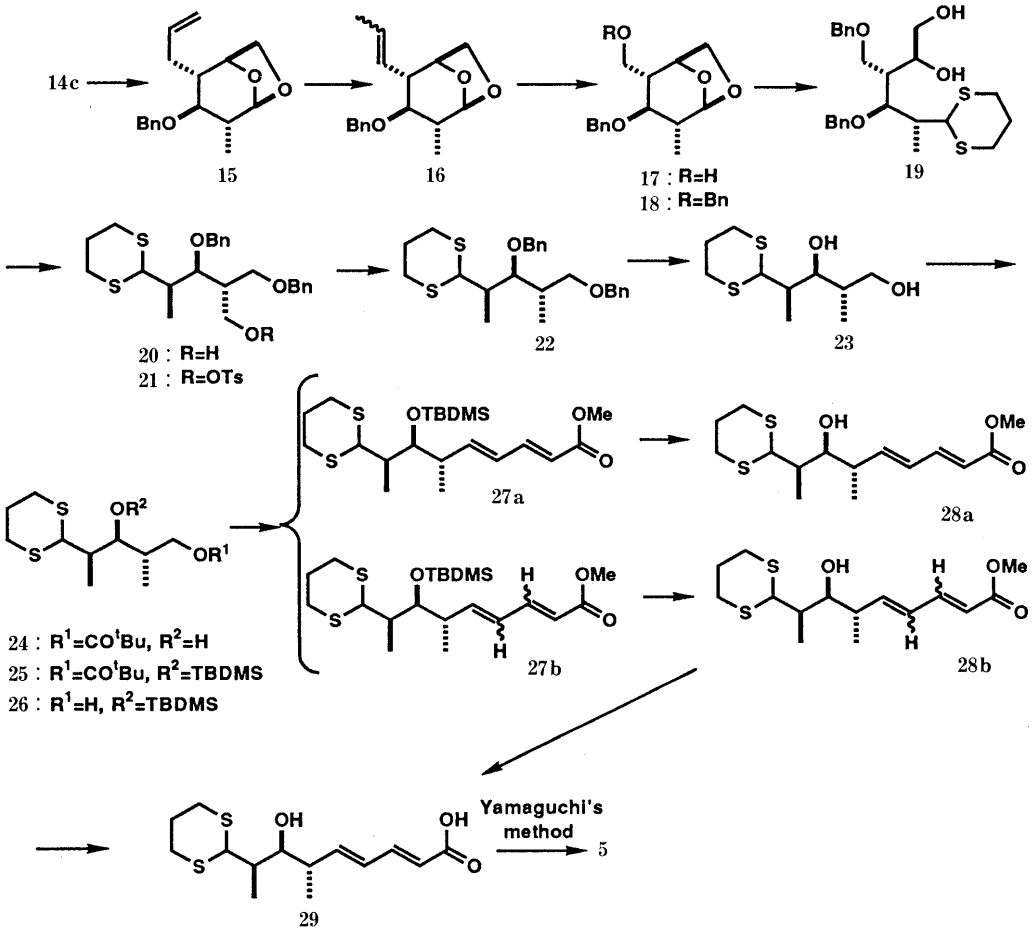
Table II. Conversion of **13** to **14**[a]

	R^1	Reagent	Yield (%)
a	Me	Me_2CuLi	41
b	Me	AllylMgCl–CuI	47
	Me	AllylMgBr–CuI	71
c	Allyl	Me_2CuLi	70
	Allyl	MeMgI–CuI	55
d	Allyl	AllylMgCl–CuI	56
e	Et	AllylMgCl–CuI	41
	Et	AllylMgBr–CuI	55
f	Methallyl	MeMgBr–CuI	45

a) Treatment with excess of reagent (6—20 eq) in THF–ether at 0 °C or room temperature.

presence of boron trifluoride etherate to provide **19** in 78% yield. Oxidative cleavage of the diol **19** by lead tetraacetate followed by reduction with sodium borohydride in methanol gave **20** in 77% yield. The alcohol **20** was then converted to the tosylate **21**, which, without purification, was reduced (lithium triethylborohydride) to furnish **22** in 92% yield. Deprotection of **22** by treatment with 1,3-propanedithiol in the presence of boron trifluoride etherate[11] gave the diol **23** in 87% yield. A three-step sequence of reactions (1. pivaloyl chloride, 2. *tert*-butyldimethylsilyl trifluoromethanesulfonate, 3. lithium aluminum hydride) afforded **26** in 70% overall yield. Swern oxidation of **26** gave the aldehyde, which was then treated with [(2*E*)-3-methoxycarbonyl-2-propenylidene]triphenylphosphorane[12] to furnish **27a** (59%) together with the isomer **27b** (a mixture of the *ZZ*, *EZ* and *ZE* isomers) (23%). Exposure of **27a** to tetrabutylammonium fluoride in the presence of benzoic acid[13] provided **28a** in 77% yield. Likewise, **27b** was converted to **28b** (75%), and according to the procedure developed by Kinoshita *et al.*,[5] **28b** was isomerized to give **28a** and **28b** in a ratio of 3 : 2. The ester **28a** was hydrolyzed with lithium hydroxide in aqueous tetrahydrofuran (THF) to produce the hydroxy-carboxylic acid **29** (quantitative yield). Lactonization of **29** by use of Yamaguchi's method[14] provided the desired lactone **5**. The yield, however, was low (trace) and the reaction was not reproducible.[5] Furthermore, lactonization by use of the mixed phosphoric anhydride method[15] did not produce **5**, giving only **30** (10%) after treatment with methanol. Finally, an efficient lactonization has been achieved as follows.. Hydrolysis of **27a** with lithium hydroxide in aqueous THF gave the carboxylic acid **31** (quantitative yield), which was then condensed with **28a** by use of Yamaguchi's method to afford **32** in quantitative yield. Treatment of **32** with tetrabutylammonium fluoride in the presence of benzoic acid[13] furnished the hydroxy-ester **30** in 66% yield. After highly chemoselective hydrolysis of **30**, the resulting hydroxy-carboxylic acid **33** underwent lactonization *via* Yamaguchi's method to give, in quantitative yield, the key intermediate **5**, whose spectral data were in accord with those of an authentic sample.[5,16]

In this way we have achieved a synthesis of the key intermediate **5** for the total synthesis of elaiophylin (**1**). The synthesis has succeeded in demonstrating that levoglucosan (**8**) is a useful chiral source for the synthesis of complex molecules.



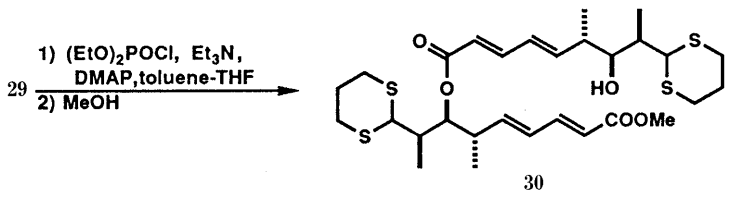


Chart 3

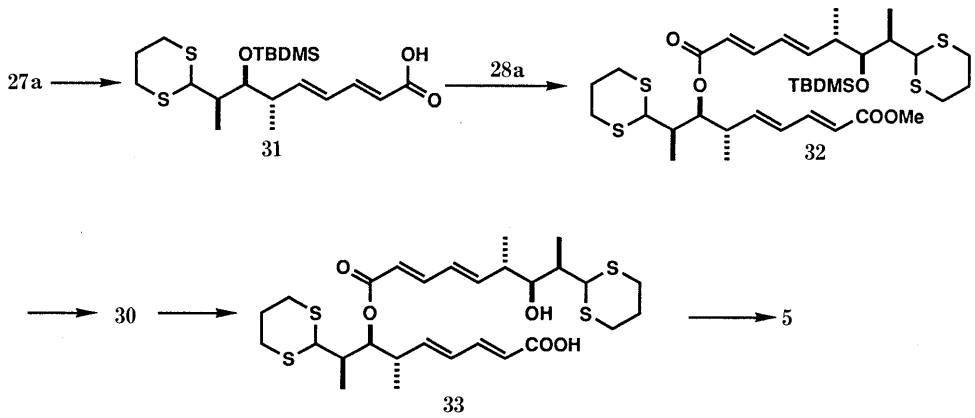


Chart 4

Experimental

Infrared (IR) spectra were measured on a JASCO A-300 diffraction grating infrared spectrophotometer. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded with a JEOL JNM-FX-100 NMR spectrometer or a JEOL JNM-GX-270 NMR spectrometer with tetramethylsilane as an internal standard. Mass spectra (MS) were obtained from a JEOL JMS-DX303, a JEOL JMS-D300 or a JEOL JMS-HX100 instrument. Optical rotation was measured on a JASCO DIP-370 polarimeter. In general, reactions were carried out in dry solvents under an argon atmosphere unless otherwise mentioned. Solvent were distilled before use as follows: THF and ether from benzophenone ketyl; dichloromethane and dimethyl sulfoxide (DMSO) from calcium hydride,

benzene, toluene and hexane from sodium. Satisfactory IR, ^{1}H-NMR, and MS data were obtained on all intermediates described herein using chromatographically homogeneous samples.

Compounds **10a, b** were prepared according to Kelly and Roberts.[9a]

(1*S*,2*S*,3*S*,4*R*,5*R*)-2-Ethyl-4-(*p*-toluenesulfonyl)oxy-6,8-dioxabicyclo-[3.2.1]octan-3-ol (10c) **9** (1.0 g, 3.4 mmol) was converted by treatment with ethylmagnesium chloride (20 mmol) and CuBr (287 mg, 2 mmol) in ether (20 ml)–THF (45 ml) at 0 °C for 11 h to **10c** (686 mg, 62% yield) as colorless crystals. IR (neat): 3350, 1600 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.97 (t, J=7.3 Hz, 3H), 1.54 (dd, J=2.5, 9.0 Hz, 2H), 1.66 (dq, J=7.3 Hz, 2H), 2.55 (s, 3H), 3.65—3.68 (m, 2H), 4.01 (d, J=1.7 Hz, 1H), 4.18 (s, 1H), 4.41 (d, J=4.9 Hz, 1H), 5.26 (s, 1H), 7.37 (d, J=8.3 Hz, 2H), 7.82 (d, J=8.3 Hz, 2H), MS m/z: 329 (MH^+). *Anal.* Calcd for $C_{15}H_{20}O_6S$: C, 54.86; H, 6.14; S, 9.76. Found: C, 54.72; H, 6.10; S, 9.52. $[\alpha]_D^{27}$ −55.8° (c=1.33, $CHCl_3$).

(1*S*,2*S*,3*S*,4*R*,5*R*)-2-(2-Methyl-2-propenyl)-4-(*p*-toluenesulfonyl)oxy-6,8-dioxabicyclo[3.2.1]octan-3-ol (10d) **9** (1.04 g, 3.49 mmol) was converted by treatment with methallylmagnesium chloride (61 mmol) and CuI (1.1 g, 6 mmol) in THF (220 ml) at 0 °C for 24 h to **10d** (1.01 g, 82% yield). IR (neat): 3350, 1065 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.72 (s, 3H), 1.75—1.95 (m, 1H), 2.32 (d, J=7.8 Hz, 2H), 2.46 (s, 3H), 3.70 (dd, J=5.1, 7.1 Hz, 1H), 4.08 (dd, J=0.8, 7.1 Hz, 1H), 4.18 (s, 1H), 4.38 (d, J=4.2 Hz, 1H), 4.77—4.87 (m, 2H), 5.29 (d, J=1.7 Hz, 1H), 7.36 (d, J=8.1 Hz, 2H), 7.82 (d, J=8.3 Hz, 2H). MS m/z: 299 ($M^+ - CH_2=CMeCH_2$), 199 (M^+ −Ts), 155. HR-MS m/z: 199.0977 (Calcd for $C_{10}H_{15}O_4$, 199.0971, M^+ −Ts). $[\alpha]_D^{20}$ −56.0° (c=0.35, $CHCl_3$).

(1*S*,2*S*,3*S*,4*R*,5*R*)-2-Benzyl-4-*p*-toluenesulfonyloxy-6,8-dioxabicyclo-[3.2.1]octan-3-ol (10e) **9** (1.01 g, 3.3 mmol) was converted by treatment with benzylmagnesium chloride (26 mmol) and CuI (0.6 g, 3 mmol) in THF (41 ml) at 0 °C for 14 h to **10e** (1.01 g, 82% yield). IR (neat): 3430, 1595, 1495, 1450 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.75—2.45 (m, 2H), 2.45 (s, 3H), 2.90 (d, J=6.3 Hz, 2H), 3.61—3.74 (m, 2H), 3.95 (d, J=6.6 Hz, 1H), 4.18 (s, 1H), 4.43 (d, J=4.8 Hz, 1H), 5.31 (s, 1H), 7.21—7.88 (m, 7H). MS m/z: 299 (M^+ −Bn), 235 (M^+ −Ts), 155, 91 (bp). HR-MS m/z: 235.0977 (Calcd for $C_{13}H_{15}O_4$, 235.0979, M^+ −Ts). $[\alpha]_D^{23}$ −72.1° (c=0.21, $CHCl_3$).

(1*S*,2*S*,3*S*,4*S*,5*R*)-2-Methyl-3,4-epoxy-6,8-dioxabicyclo[3.2.1]octan-3-ol (13a) A solution of **10a** (248 mg, 0.76 mmol) in THF (10 ml) was added to a suspension of 60% NaH in oil (60 mg, 1.1 mmol) in THF (2 ml) at 0 °C. The reaction mixture was stirred at room temperature for 3 h, and then quenched by the addition of saturated NH_4Cl followed by extraction with ethyl acetate. The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate to give **13a** (120 mg, quantitative yield) as a colorless oil. IR (neat): 1150, 1250 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.24 (d, J=7.4 Hz, 3H), 2.15 (q, J=7.4 Hz, 1H), 2.88 (dd, J=0.9, 4.1 Hz, 1H), 3.36 (t, J=3.2 Hz, 1H), 3.71—3.76 (m, 2H), 4.09—4.13 (m, 1H), 5.69 (d, J=3.9 Hz, 1H). MS m/z: 242 (M^+), 112 (M^+ −Me), 41 (bp). HR-MS m/z: 142.0633 (Calcd for $C_7H_{10}O_3$, 142.0630, M^+). $[\alpha]_D^{20}$ −21.3° (c=0.95, $CHCl_3$).

(1*S*,2*S*,3*S*,4*S*,5*R*)-2-Allyl-3,4-epoxy-6,8-dioxabicyclo[3.2.1]octan-3-ol (13b) **10b** (1.95 g, 6.2 mmol) was converted to **13b** (757 mg, 86%) as a colorless oil by treatment with 60% NaH in oil (400 mg, 10 mmol) in THF (40 ml) for 23 h at room temperature. IR (neat): 1645, 1130 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.04 (t, J=7.4 Hz, 1H), 2.35 (t, J=7.4 Hz, 2H), 2.97 (d, J=3.9 Hz, 1H), 3.38 (t, J=3.2, 4.0 Hz, 1H), 3.73—3.78 (m, 2H), 4.26 (t, J=3.7 Hz, 1H), 5.1—5.2 (m, 2H), 5.68 (d, J=3.2 Hz, 1H), 5.74—5.96 (m, 1H). MS m/z: 168 (M^+), 49 (bp). HR-MS m/z: 168.0801 (Calcd for $C_9H_{12}O_3$, 168,0786, M^+). $[\alpha]_D^{22}$ −27.0° (c=0.73, $CHCl_3$).

(1*S*,2*S*,3*S*,4*S*,5*R*)-2-Ethyl-3,4-epoxy-6,8-dioxabicyclo[3.2.1]octan-3-ol (13c) **10c** (10.7 g, 62.5 mmol) was converted to **13c** (4.98 g, quantitative yield) as a colorless oil by treatment with 60% NaH in oil (3.75 g, 0.94 mol) in THF (130 ml) for 23 h at room temperature. IR (neat): 1465, 1425, 1350 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.83 (t, J=6.8 Hz, 3H), 1.49—1.93 (m, 3H), 2.95 (dd, J=3.9, 1.0 Hz, 1H), 3.37 (t, J=3.2 Hz, 1H), 3.72—3.77 (m, 2H), 4.26 (d, J=3.9 Hz, 1H), 5.67 (d, J=3.2 Hz, 1H). MS m/z: 156 (M^+), 127 (M^+ −Et). HR-MS m/z: 156.0816 (Calcd for $C_8H_{12}O_3$, 156.0787, M^+). $[\alpha]_D^{22}$ −31.3° (c=0.55, $CHCl_3$).

(1*S*,2*S*,3*S*,4*S*,5*R*)-2-(2-Methyl-2-propenyl)-3,4-epoxy-6,8-dioxabicyclo-[3.2.1]octan-3-ol (13d) **10d** (260 mg, 0.73 mmol) was converted to **13d** (134 mg, quantitative yield) as a colorless oil by treatment with 60% NaH in oil (44 mg, 1.1 mmol) in THF (4 ml) for 11 h at room temperature. IR (neat): 1605, 1585, 1500, 1455 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.78 (s, 3H), 2.05—2.46 (m, 3H), 2.95 (dd, J=4.2, 1.2 Hz, 1H), 3.37 (t, J=3.4 Hz, 1H), 3.75—3.80 (m, 2H), 4.13—4.18 (m, 1H), 4.76—4.85 (m, 2H), 5.68 (d, J=2.6 Hz, 1H). MS m/z: 182 (M^+), 81. HR-MS m/z: 182.0949 (Calcd for $C_{10}H_{14}O_3$, 182.0943, M^+). $[\alpha]_D^{22}$ −27.4° (c=0.73, $CHCl_3$).

(1*S*,2*S*,3*S*,4*S*,5*R*)-2-Benzyl-3,4-epoxy-6,8-dioxabicyclo[3.2.1]octan-3-ol (13e) **10e** (98 mg, 0.29 mmol) was converted to **13e** (44 mg, 90%) as a colorless oil by treatment with 60% NaH in oil (18 mg, 0.43 mmol) in THF (3 ml) for 20 h at room temperature. IR (neat): 1650 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 2.27 (t, J=8.1 Hz, 1H), 2.88 (d, J=7.9 Hz, 2H), 2.98 (dd, J=1.0, 3.8 Hz, 1H), 3.40 (dt, J=0.7, 2.8 Hz, 1H), 3.57—3.76 (m, 2H), 4.13—4.17 (m, 1H), 5.70 (d, J=2.9 Hz, 1H), 7.29 (s, 5H). MS m/z: 218 (M^+), 91 (bp). HR-MS m/z: 218.0972 (Calcd for $C_{13}H_{14}O_3$, 218.0955, M^+). $[\alpha]_D^{25}$ −34.3° (c=0.60, $CHCl_3$).

(1*S*,2*S*,3*S*,4*R*,5*R*)-2,4-Dimethyl-6,8-dioxabicyclo[3.2.1]octan-3-ol (14a) A 1.4 M solution of methyllithium in ether (33 ml, 45 mmol) was added to a suspension of CuI (4.3 g, 22.8 mmol) in THF (20 ml) at −10 °C and the mixture was stirred for 10 min at 0 °C. A solution of **13a** (810 mg, 5.7 mmol) in THF (6 ml) was added at 0 °C. The mixture was stirred at 0 °C for 40 min and then at room temperature for an additional 16 h. The reaction was quenched by the addition of saturated NH_4Cl at 0 °C followed by extraction with ether. The combined extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (1 : 1) to afford **14a** (365 mg, 41% yield) as a colorless oil. IR (neat): 3350 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.07 (d, J=7.6 Hz, 3H), 1.19 (d, J=7.6 Hz, 3H), 1.58 (s, 1H), 1.71—1.94 (m, 2H), 1.79 (t, J=7.6 Hz, 2H), 2.49 (br s, 1H), 3.27 (br s, 1H), 3.85 (dd, J=5.1, 6.8 Hz, 1H), 4.08 (d, J=7.1 Hz, 1H), 4.19 (d, J=4.9 Hz, 1H), 5.28 (s, 1H). MS m/z: 158 (M^+). HR-MS m/z: 158.0961 (Calcd for $C_8H_{14}O_3$, 158.0943, M^+). $[\alpha]_D^{22}$ −65.1° (c=1.8, $CHCl_3$).

(1*S*,2*S*,3*S*,4*R*,5*R*)-4-Allyl-2-methyl-6,8-dioxabicyclo[3.2.1]octan-3-ol (14b) **13a** (1.3 g, 5.4 mmol) was treated with allylmagnesium bromide (54 mmol) and CuI (1.03 g, 54 mmol) in ether–THF at room temperature for 17.5 h to afford **14b** (1.12 g, 71% yeild) as a colorless oil. IR (neat): 3550, 3450, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.22 (d, J=7.3 Hz, 3H), 1.73—1.94 (m, 2H), 2.15—2.31 (m, 2H), 3.45 (s, 1H), 3.74 (dd, J=5.0, 6.9 Hz, 2H), 4.17 (dd, J=5.0, 6.9 Hz, 1H), 4.28 (d, J=4.9 Hz, 1H), 4.65—5.04 (m, 1H), 5.12—5.17 (m, 1H), 5.42 (s, 1H), 5.60—6.01 (m, 1H). MS m/z: 184 (M^+), 166 ($M^+ - H_2O$), 55 (bp). HR-MS m/z: 184.1085 (Calcd for $C_{10}H_{16}O_3$, 184.1100, M^+). $[\alpha]_D^{22}$ −42.3° (c=0.38, $CHCl_3$).

(1*S*,2*S*,3*S*,4*R*,5*R*)-2-Allyl-4-methyl-6,8-dioxabicyclo[3.2.1]octan-3-ol (14c) **13b** (5.2 g, 31 mmol) was treated with methylmagnesium chloride (0.3 mol) and CuI (3.7 g, 20 mmol) in ether–THF at room temperature for 4 h and then at 0 °C for an additional 12 h to afford **14c** (4.01 g, 70% yield) as a colorless oil. IR (neat): 3450, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.09 (d, J=7.3 Hz, 3H), 1.7—2.0 (m, 2H), 2.2—2.5 (m, 2H), 3.45 (s, 1H), 3.76 (dd, J=7.0, 5.1 Hz, 1H), 4.16 (dd, J=0.7, 7.0 Hz, 1H), 4.40 (d, J=5.5 Hz, 1H), 5.07—5.15 (m, 2H), 5.35 (s, 1H), 5.72—5.85 (m, 1H). MS m/z: 184 (M^+). HR-MS m/z: 184.1111 (Calcd for $C_{10}H_{16}O_3$, 184.1100, M^+). $[\alpha]_D^{15}$ −17.1° (c=1.5, $CHCl_3$).

(1*S*,2*S*,3*S*,4*R*,5*R*)-2,4-Diallyl-6,8-dioxabicyclo[3.2.1]octan-3-ol (14d) **13b** (655 mg, 3.9 mmol) was treated with allylmagnesium chloride (25 mmol) and CuI (2.1 g, 11 mmol) in ether–THF at 0 °C for 13 h to afford **14d** (462 mg, 56% yield) as a colorless oil. IR (neat): 3450, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.7—2.0 (m, 2H), 2.11—2.40 (m, 4H), 3.50 (t, J=1.2 Hz, 1H), 3.74 (dd, J=5.1, 7.1 Hz, 1H), 4.13 (dd, J=6.4, 0.7 Hz, 1H), 4.38 (d, J=4.9 Hz, 1H), 4.97—5.21 (m, 4H), 5.40 (s, 1H), 5.59—6.00 (m, 2H). MS m/z: 210 (M^+). HR-MS m/z: 210.1294 (Calcd for $C_{12}H_{18}O_3$, 210.1257, M^+). $[\alpha]_D^{22}$ −47.5° (c=1.69, $CHCl_3$).

(1*S*,2*S*,3*S*,4*R*,5*R*)-4-Allyl-2-ethyl-6,8-dioxabicyclo[3.2.1]octan-3-ol (14e) **13c** (90 mg, 0.58 mmol) was treated with allylmagnesium bromide (5.8 mmol) and CuI (600 mg, 3.1 mmol) in ether–THF at 0 °C for 16 h to afford **14e** (63 mg, 55% yield) as a colorless oil. IR (neat): 3450, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.00 (t, J=7.1 Hz, 3H), 3.50 (s, 1H), 3.75 (dd, J=5.1, 6.8 Hz, 1H), 4.19 (dd, J=6.3, 0.3 Hz, 1H), 4.40 (d, J=5.1 Hz, 1H), 4.96—5.18 (m, 2H), 5.40 (s, 1H), 5.59—6.00 (m, 1H). MS m/z: 198 (M^+). HR-MS m/z: 198.1269 (Calcd for $C_{11}H_{18}O_3$, 128.1256, M^+). $[\alpha]_D^{21}$ −29.0° (c=0.53, $CHCl_3$).

(1*S*,2*S*,3*S*,4*R*,5*R*)-4-Methyl-2-(2-methyl-2-propenyl)6,8-dioxabicyclo[3.2.1]octan-3-ol (14f) **13d** (288 mg, 1.58 mmol) was treated with methylmagnesium bromide (8.0 mmol) and CuI (1.5 g, 8 mmol) in THF at 0 °C for 39 h to afford **14f** (141 mg, 45% yield) as a colorless oil. IR (neat): 3430, 3160, 1645, 890 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.08 (d, J=7.6 Hz, 3H), 1.75 (s, 3H), 1.9—2.1 (m, 2H), 2.2—2.6 (m, 2H), 3.42 (s, 1H), 3.76 (dd, J=5.1, 6.8 Hz, 1H), 4.17 (d, J=6.8 Hz, 1H), 4.37 (d, J=4.8 Hz, 1H), 4.78—4.86 (m, 2H), 5.35 (s, 1H). MS m/z: 198 (M^+), 167, 152, 142, 95, 58. HR-MS m/z: 198.1262 (Calcd for $C_{11}H_{18}O_3$, 198.1256, M^+). $[\alpha]_D^{22}$ −93.9° (c=0.48, $CHCl_3$).

(1*S*,2*S*,3*S*,4*R*,5*R*)-2-Allyl-3-*O*-benzyl-4-methyl-6,8-dioxabicyclo-

[3.2.1]octan-3-ol (15) NaH in oil (60%, 300 mg, 7.6 mmol) was added to a solution of **14c** (700 mg, 3.8 mmol) in THF (10 ml) at 0 °C. The mixture was stirred for 15 min and then benzyl bromide (0.7 ml, 5.8 mmol) and Bu_4NI (10 mg) were added. The mixture was stirred for an additional 17 h at room temperature, poured into ice-water, and extracted with ether. The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (4:1) to give **15** (1.04 g, quantitative yield) as a colorless oil. IR (neat): 1640 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.04 (d, J=7.6 Hz, 3H), 1.73—2.09 (m, 2H), 2.15—2.43 (m, 2H), 3.15 (s, 1H), 3.77 (t, J=6.1 Hz, 1H), 4.23 (d, J=6.1 Hz, 1H), 4.37 (d, J=6.1 Hz, 1H), 4.49 (d, J=1.2 Hz, 2H), 4.97—5.15 (m, 2H), 5.29 (s, 1H), 5.55—5.96 (m, 1H), 7.32 (s, 5H). MS *m/z*: 274 (M^+), 91. HR-MS *m/z*: 274.1540 (Calcd for $C_{17}H_{22}O_3$, 274.1569, M^+). $[\alpha]_D^{15}$ −17.1° (c=1.5, $CHCl_3$).

(1*S*,2*S*,3*S*,4*R*,5*R*)-3-*O*-Benzyl-4-methyl-2-(1-propenyl)-6,8-dioxabicyclo-[3.2.1]octan-3-ol (16) $RhCl_3 \cdot 3H_2O$ (150 mg, 0.57 mmol) was added to a solution of **15** (1.65 g, 6.0 mmol) and K_2CO_3 (150 mg, 1.08 mmol) in ethanol (50 ml) at room temperature. The mixture was stirred under reflux for 1 h, allowed to recool to room temperature, and then filtered. The filtrate was concentrated, then brine and ethyl acetate were added and the organic layer was separated. The aqueous layer was extracted with ethyl acetate. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (6:1) to give **16** (1.65 g, quantitative yield). IR (neat): 1610, 1590, 1500, 1465, 1555, 740, 705 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.01 (d, J=7.8 Hz, 3H), 1.05—1.72 (m, 3H), 1.91—2.28 (m, 1H), 2.43—2.77 (m, 1H), 3.12—3.18 (m, 1H), 3.7—3.8 (m, 1H), 4.16—4.48 (m, 2H), 4.53 (s, 2H), 5.30 (s, 1H), 5.44—5.84 (m, 2H), 7.32 (s, 5H). MS *m/z*: 274 (M^+), 148, 91. HR-MS *m/z*: 274.1574 (Calcd for $C_{17}H_{22}O_3$, 274.1569, M^+). $[\alpha]_D^{25}$ −75.2° (c=6.16, $CHCl_3$).

(1*S*,2*S*,3*S*,4*R*,5*R*)-3-*O*-Benzyl-2-hydroxymethyl-4-methyl-6,8-dioxa-bicyclo[3.2.1]octan-3-ol (17) Ozone gas was passed into a solution of **16** (3.61 g, 13.2 mmol) in dichloromethane (30 ml) at −78 °C until the solution became blue. The solution was then allowed to warm to room temperature. When the blue color of the solution disappeared, the solution was recooled to 0 °C. Methanol (10 ml) and $NaBH_4$ (2 g) were added and the mixture was stirred for 1 h. After addition of water, the mixture was extracted with dichloromethane. The extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated to afford **17** (3.31 g, 95% yield). IR (neat): 3450, 1610, 1585, 1500 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 0.99 (d, J=7.6 Hz, 3H), 1.86—2.18 (m, 2H), 3.16 (t, J=1.1 Hz, 1H), 3.57—3.94 (m, 4H), 4.22 (dd, J=6.6, 1 Hz, 1H), 4.52 (s, 2H), 5.28 (br s, 1H), 7.32 (s, 5H). MS *m/z*: 264 (M^+), 246 ($M^+ - H_2O$). HR-MS *m/z*: 264.1334 (Calcd for $C_{15}H_{20}O_4$, 264.1361, M^+). $[\alpha]_D^{24}$ −49.9° (c=1.35, $CHCl_3$).

(1*S*,2*S*,3*S*,4*R*,5*R*)-3-*O*-Benzyl-2-benzyloxymethyl-4-methyl-6,8-dioxabicyclo[3.2.1]octan-3-ol (18) NaH in oil (60%, 3 g, 75 mmol) was added portionwise to a solution of crude **17** (3.31 g, 12.5 mmol) in THF (30 ml) at −30 °C. The solution was stirred at 0 °C for 15 min and benzyl bromide (5 ml, 41.8 mmol) and Bu_4NI (100 mg) were added. The reaction mixture was stirred for 48 h at room temperature, poured into ice-water, and extracted with ethyl acetate. The extracts were dried over $MgSO_4$, filtered, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (20:1—4:1) to give **18** (7.7 g, 96% yield). IR (neat): 1600, 1590 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 0.91 (d, J=7.8 Hz, 3H), 1.99—2.22 (m, 2H), 3.16 (s, 1H), 3.38—3.84 (m, 4H), 4.21 (dd, J=0.7, 4.6 Hz, 1H), 4.38—4.65 (m, 4H), 5.27 (s, 1H), 7.30 (s, 5H), 7.31 (s, 5H). MS *m/z*: 263 ($M^+ - CH_2C_6H_5$), 91. HR-MS *m/z*: 263.1286 (Calcd for $C_{15}H_{19}O_4$, 263.1283, $M^+ - CH_2C_6H_5$). $[\alpha]_D^{26}$ −32.8° (c=0.99, $CHCl_3$).

(2*S*,3*R*,4*S*,5*R*)-4-*O*-Benzyl-3-benzyloxymethyl-5-(1,3-dithian-2-yl)-1,2,4-hexanetriol (19) $BF_3 \cdot Et_2O$ (2 ml) was added dropwise to a solution of **18** (881 mg, 2.5 mmol), 1,3-propanedithiol (0.25 ml, 2.5 mmol) and trifluoroacetic acid (6 ml) in dichloromethane (10 ml) at −30 °C. After completion of the reaction, the solution was poured into cold saturated $NaHCO_3$ and extracted with dichloromethane. The extracts were dried over $MgSO_4$, filtered, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (1:1) to afford **19** (897 mg, 78% yield). IR (neat): 3420 (OH), 1600, 1595, 1580, 1450 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.23 (d, J=6.8 Hz, 3H), 1.7—2.3 (m, 4H), 2.76—2.87 (m, 6H), 3.61 (dd, J=6.6, 14.6 Hz, 1H), 3.70—3.82 (m, 4H), 4.06—4.15 (m, 2H), 4.47 (s, 2H), 4.65 (s, 2H), 7.30 (s, 5H), 7.32 (s, 5H). MS *m/z*: 431 ($M^+ - CH_2OH$), 354, 263, 119, 91. HR-MS *m/z*: 431.1731 (Calcd for $C_{24}H_{31}O_3S_2$, 431.1715, $M^+ - CH_2OH$). $[\alpha]_D^{26}$ +3.1° (c=3.7, CH_3OH).

(2*S*,3*S*,4*R*)-3-*O*-Benzyl-2-benzyloxymethyl-4-(1,3-dithian-2-yl)-1,3-pentanediol (20) Lead tetraacetate (400 mg, 0.9 mmol) was added portionwise to a solution of **19** (137 mg, 0.3 mmol) in benzene (10 ml) and hexane (1 ml) at 0 °C until **19** was no longer detectable. After the addition of ethyleneglycol (1 ml), the mixture was diluted with ether (20 ml). The solution was passed through a silica gel pad with ether and the ether eluate was concentrated. The residue was treated with $NaBH_4$ (1 g) and methanol (10 ml) for 1 h at 0 °C. The reaction was quenched by the addition of water and the mixture was extracted with dichloromethane. The extracts were dried over $MgSO_4$, filtered, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (2:1) to give **20** (99 mg, 77% yield). IR (neat): 3470, 1610, 1590, 1500, 1460 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.18 (d, J=6.8 Hz, 3H), 2.37 (br s, 1H), 2.01—2.37 (m, 4H), 2.76—2.82 (m, 4H), 3.72—3.81 (m, 4H), 4.02—4.13 (m, 1H), 4.06 (d, J=6.8 Hz, 1H), 4.51 (s, 2H), 4.63 (AB type, J=11.2 Hz, 2H), 7.31—7.33 (m, 10H). MS *m/z*: 341 ($M^+ - CH_2C_6H_5$), 119, 91. HR-MS *m/z*: 341.1267 (Calcd for $C_{17}H_{25}O_3S_2$, 341.1245, $M^+ - CH_2C_6H_5$). $[\alpha]_D^{27}$ −4.5° (c=1.9, $CHCl_3$).

(2*R*,3*S*,4*R*)-1,3-*O*-Dibenzyl-2-(*p*-toluenesulfonyloxy)methyl-4-(1,3-dithian-2-yl)-1,3-pentanediol (21) *p*-TsCl (1.4 g, 7.31 mmol) and *N*,*N*-dimethylaminopyridine (DMAP) (100 mg) were added to a solution of **20** (1.58 g, 3.65 mmol) in pyridine (3 ml) and dichloromethane (15 ml) at 0 °C. The solution was stirred at room temperature for 40 h, diluted with ether, washed with 10% H_2SO_4, water, saturated $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (6:1—1:1) to give crude **21** as an oil. IR (neat): 1595, 1495, 1450, 1420 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.12 (d, J=6.8 Hz, 3H), 1.9—2.2 (m, 4H), 2.40 (s, 3H), 2.71—2.86 (m, 4H), 3.41—3.72 (m, 2H), 3.87—4.02 (m, 3H), 4.13 (d, J=5.9 Hz, 1H), 4.39 (s, 2H), 4.52 (AB type, J=11.2 Hz, 2H), 7.32—7.83 (m, 10H), 7.78 (d, J=8.3 Hz, 2H). MS *m/z*: 478 ($M^+ - BnOH$), 416 ($M^+ - OTs$). HR-MS *m/z*: 478.1296 (Calcd for $C_{24}H_{30}O_4S_3$, 478.1307, $M^+ - BnOH$). $[\alpha]_D^{28}$ −7.2° (c=2.78, $CHCl_3$).

(2*S*,3*S*,4*R*)-1,3-*O*-Dibenzyl-2-methyl-4-(1,3-dithian-2-yl)-1,3-pentanediol (22) A 1 M solution of lithium triethylborohydride in THF (6.4 ml, 6.4 mmol) was added dropwise to a solution of **21** in THF (5 ml) at 0 °C, and the mixture was stirred at room temperature for 20 h. The reaction was quenched by the addition of water and the mixture was extracted with dichloromethane. The extracts were dried over $MgSO_4$, filtered, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (6:1) to give **22** (1.40 g, 92% yield). IR (neat) 1600, 1590 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 1.02 (d, J=6.8 Hz, 3H), 1.15 (d, J=6.8 Hz, 3H), 1.7—2.2 (m, 4H), 2.69—2.91 (m, 4H), 3.48 (dd, J=5.4, 8.8 Hz, 1H), 3.59 (dd, J=4.6, 8.8 Hz, 1H), 3.81 (dd, J=3.4, 7.6 Hz, 1H), 4.06 (d, J=7.6 Hz, 1H), 4.50 (s, 2H), 4.65 (AB type, J=11.5 Hz, 2H), 7.31 (s, 5H), 7.33 (s, 5H). MS *m/z*: 416 (M^+), 308, 217, 119, 91. HR-MS *m/z*: 416.1859 (Calcd for $C_{24}H_{32}O_2S_2$, 416.1845, M^+). $[\alpha]_D^{21}$ +1.8° (c=0.42, $CHCl_3$).

(2*S*,3*S*,4*R*)-2-Methyl-4-(1,3-dithian-2-yl)-1,3-pentanediol (23) $BF_3 \cdot Et_2O$ (2 ml) was added dropwise to a solution of **22** (285 mg, 0.69 mmol) and 1,3-propanedithiol (1.5 ml) in dichloromethane (5 ml) at 0 °C. The solution was stirred at room temperature for 24 h, and saturated $NaHCO_3$ and ethyl acetate were added. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. The combined extracts were dried over $MgSO_4$, filtered, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (1:1) to give **23** (140 mg, 87% yield). IR (neat): 3450 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 0.80 (d, J=6.8 Hz, 3H), 1.13 (d, J=6.8 Hz, 3H), 1.7—2.3 (m, 4H), 2.40 (br s, 1H), 2.84—2.96 (m, 4H), 3.66 (d, J=5.7 Hz, 2H), 3.94 (dd, J=2.1, 8.4 Hz, 1H), 4.17 (d, J=6.8 Hz, 1H). MS *m/z*: 236 (M^+), 218.119. HR-MS *m/z*: 236.0911 (Calcd for $C_{10}H_{20}O_2S_2$, 236.0905, M^+). $[\alpha]_D^{25}$ +23.4° (c=3.18, $CHCl_3$).

(2*S*,3*S*,4*R*)-1-*O*-(2,2-Dimethylpropanoyl)-4-(1,3-dithian-2-yl)-2-methyl-1,3-pentanediol (24) Pivaloyl chloride (0.11 ml, 0.93 mmol) was added dropwise to a solution of **23** (220 mg, 0.93 mmol) in dichloromethane (3 ml) and pyridine (1 ml) at 0 °C, and the mixture was stirred for 30 min then diluted with ether. The solution was washed with 5% HCl, water, saturated $NaHCO_3$, and brine, dried over Na_2SO_4, filtered, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (2:1) to give **24** (300 mg) as a colorless oil. IR (neat): 3480, 1735 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 0.91 (d, J=6.8 Hz, 3H), 1.10 (d, J=6.8 Hz, 3H), 1.22 (s, 9H), 1.7—2.2 (m, 4H), 2.83—2.93 (m, 4H), 3.81 (dd, J=2.0, 9.5 Hz, 1H), 4.09 (dd, J=3.4, 11.0 Hz, 1H), 4.17 (d, J=7.8 Hz, 1H), 4.35 (dd, J=5.1, 11.0 Hz, 1H). MS *m/z*: 320 (M^+), 263, 119. HR-MS *m/z*: 320.1491 (Calcd for $C_{15}H_{28}O_3S_2$, 320.1480, M^+). $[\alpha]_D^{21}$ +31.3° (c=0.62, $CHCl_3$).

(2*S*,3*S*,4*R*)-2-Methyl-1-*O*-(2,2-dimethylpropanoyl)-3-*O*-(*tert*-butyldimethylsilyl)-4-(1,3-dithian-2-yl)-1,3-pentanediol (25) *tert*-Butyldimethyl-

silyl trifluoromethanesulfonate (0.3 ml) was added dropwise to a solution of **24** and 2,6-lutidine (0.3 ml) in dichloromethane (2 ml) at 0 °C. The mixture was stirred for 30 min. The reaction was quenched with saturated NH_4Cl followed by extraction with ethyl acetate. The extracts were dried over Na_2SO_4, filtered, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (6 : 1) to give **25**. IR (neat): 1730 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.09 (s, 3H), 0.14 (s, 3H), 0.91 (s, 9H), 0.9—1.0 (m, 3H), 1.08 (d, J=6.8 Hz, 3H), 1.21 (s, 9H), 1.8—2.1 (m, 4H), 2.79—2.90 (m, 4H), 3.81—4.29 (m, 4H). MS m/z: 434 (M^+), 377. HR-MS m/z: 434.2318 (Calcd for $C_{21}H_{42}O_3S_2Si$, 434.2345, M^+). $[\alpha]_D^{22}$ +25.3° (c=0.88, $CHCl_3$).

(2*S*,3*S*,4*R*)-2-Methyl-3-*O*-(*tert*-butyldimethylsilyl)-4-(1,3-dithian-2-yl)-1,3-pentanediol (26) A 1 M solution of lithium triethylborohydride in THF (6 ml, 6 mmol) was added to a solution of **25** in THF at −78 °C, and the mixture was stirred for 5 min. Saturated NH_4Cl was added and the mixture was extracted with ethyl acetate. The extracts were dried over Na_2SO_4, filtered, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (4 : 1) to afford **26** (227 mg, 70% yield) as a colorless oil. IR (neat): 3370 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.13, 0.15 (s, each 3H), 0.92 (s, 9H), 0.96 (d, J=7.8 Hz, 3H), 1.11 (d, J=6.8 Hz, 3H), 1.76—2.19 (m, 4H), 2.80—2.90 (m, 4H), 3.62 (d, J=5.6 Hz, 2H), 4.00 (dd, J=5.45, 3.9 Hz, 1H), 4.03 (d, J=6.8 Hz, 1H). MS m/z: 350 (M^+), 293 (M^+ − *tert*-Bu), 119. HR-MS m/z: 350.1779 (Calcd for $C_{16}H_{34}O_2S_2Si$, 350.1770, M^+). $[\alpha]_D^{23}$ +20.6° (c=0.24, $CHCl_3$).

Methyl (2*E*,4*E*,6*S*,7*S*,8*R*)-6-Methyl-7-[(*tert*-butyldimethylsilyl)oxy]-8-(1,3-dithian-2-yl)-2,4-nonadienoate (27a) A solution of oxalyl chloride (0.6 ml) in dichloromethane (2 ml) was added dropwise to DMSO (1.0 ml) in dichloromethane (4 ml) at −78 °C. The solution was stirred for 20 min and a solution of **26** (130 mg, 0.37 mmol) in dichlorometane (3 ml) was added. The mixture was stirred for 20 min, then triethylamine (2 ml) was added. The solution was allowed to warm to room temperature. Ether and water were added and the organic layer was separated. The organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (4 : 1) to afford the aldehyde (130 mg, quantitative yield). This aldehyde was carried on to the next step without purification. A mixture of the aldehyde and [(2*E*)-3-methoxycarbonyl-2-propenylidene]triphenylphosphorane (2 g, 5.5 mmol) in toluene (10 ml) was stirred at 80 °C for 1 h. After removal of the solvent, the residue was chromatographed on a silica gel column with hexane–ethyl acetate (19 : 1) to afford **27a** (94 mg, 59% yield) and crude **27b** (37 mg, 23% yield), **27a**: IR (neat): 1715, 1635, 1610 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 3H), 0.11 (s, 3H), 0.89 (s, 9H), 1.05 (d, J=6.8 Hz, 3H), 1.06 (d, J=6.8 Hz, 3H), 1.7—2.1 (m, 3H), 2.4—2.6 (m, 1H), 2.77—2.85 (m, 4H), 3.74 (s, 3H), 3.97 (d, J=7.3 Hz, 1H), 3.92—4.04 (m, 1H), 5.81 (d, J=15.4 Hz, 1H), 6.14—6.35 (m, 2H), 7.15—7.49 (m, 1H). MS m/z: 430 (M^+), 373, 119. HR-MS m/z: 430.2013 (Calcd for $C_{21}H_{38}O_3S_2Si$, 430.2034, M^+). $[\alpha]_D^{21}$ −11.7° (c=0.68, $CHCl_3$).

Methyl (2*E*,4*E*,6*S*,7*S*,8*R*)-7-Hydroxy-6-methyl-8-(1,3-dithian-2-yl)-2,4-nonadienoate (28a) A 1 M solution of Bu_4NF in THF was added dropwise to a mixture of **27a** (96 mg, 0.11 mmol) and benzoic acid (260 mg, 2.1 mmol) at room temperature. The solution was stirred for 24 h under reflux and allowed to cool to room temperature. After addition of 2 N K_2CO_3 and ethyl acetate, the organic layer was separated and passed through a short silica gel pad. The eluate was concentrated. The residue was chromatographed on a silica gel column with dichloromethane–ethyl acetate (19 : 1—5 : 1) to afford **28a** (34 mg, 77% yield) as a colorless oil. IR (neat): 3350, 1700, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.02 (d, J=7.0 Hz, 3H), 1.12 (d, J=7.0 Hz, 3H), 1.81—2.17 (m, 4H), 2.42—2.50 (m, 1H), 2.83—2.90 (m, 4H), 3.74 (s, 3H), 3.70—3.82 (m, 1H), 4.17 (d, J=7.0 Hz, 1H), 5.84 (d, J=15.4, 1H), 6.13 (dd, J=15.4, 8.1 Hz, 1H), 6.27 (dd, J=15.4, 10.6 Hz, 1H), 7.23—7.33 (m, 1H). MS m/z: 316 (M^+), 285, 119. HR-MS m/z: 316.1177 (Calcd for $C_{15}H_{24}O_3S_2Si$, 316.1168, M^+). $[\alpha]_D^{22}$ −20.1° (c=1.5, $CHCl_3$).

(2*E*,4*E*,6*S*,7*S*,8*R*)-6-Methyl-7-[(*tert*-butyldimethylsilyl)oxy]-8-(1,3-dithian-2-yl)-2,4-nonadienoic Acid (31) A solution of 0.4 N LiOH (2 ml) was added to a solution of **27a** (38 mg, 0.09 mmol) in THF (2 ml) at 0 °C and the mixture was stirred at room temperature for 21 h. After neutralization with Dowex 50W-X8 and filtration, the filtrate was extracted with ethyl acetate. The extracts were washed with brine and concentrated. The residue was chromatographed on a silica gel column with ethyl acetate to give **31** (28 mg, quantitative yield) as a colorless oil. IR ($CHCl_3$): 3500, 3350, 1700, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 3H), 0.12 (s, 3H), 0.90 (s, 9H), 1.05 (d, J=7.0 Hz, 3H), 1.07 (d, J=7.0 Hz, 3H), 1.7—1.9 (m, 2H), 2.05—2.12 (m, 1H), 2.50—2.57 (m, 1H), 2.77—2.87 (m, 4H), 3.98 (d, J=7.3 Hz, 1H), 3.96—4.03 (m, 2H), 5.82 (d, J=15.4 Hz, 1H), 6.16—6.25 (m, 2H), 7.35 (dd, J=15.4, 5.5 Hz, 1H). MS m/z: 416 (M^+). HR-MS m/z: 416.1863 (Calcd for $C_{20}H_{36}O_3S_2Si$, 416.1896, M^+). $[\alpha]_D^{21}$ −25.5° (c=1.5, $CHCl_3$).

(1*E*,3*E*,5*S*,6*S*,7*R*)-1-Carbomethoxy-5-methyl-8-(1,3-dithian-2-yl)-1,3-octadien-6-yl (2*E*,4*E*,6*S*,7*S*,8*R*)-6-Methyl-7-[(*tert*-butyldimethylsilyl)-oxy]-8-(1,3-dithian-2-yl)-2,4-nonadienoate (32) 1,3,5-Trichlorobenzoyl chloride (20 mg, 0.08 mmol) and triethylamine (0.3 ml) was added to a solution of **31** (8 mg, 0.025 mmol) in THF (0.2 ml) at room temperature under an argon atmosphere. The mixture was stirred for 2 h. A solution of **28a** (15 mg, 0.035 mmol) in benzene (0.3 ml) was added, followed by addition of DMAP (300 mg). The mixture was stirred for 2 h and then diluted with ether. The solution was filtered through a short silica gel pad and the filtrate was concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (4 : 1) to afford **32** (18 mg, quantitative yield). IR ($CHCl_3$): 1700, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 3H), 0.11 (s, 3H), 0.89 (s, 9H), 1.03—1.28 (m, 12H), 2.7—2.9 (m, 8H), 3.73 (s, 3H), 3.97—4.08 (m, 3H), 5.24 (t, J=5.5 Hz, 1H), 5.80 (d, J=15.1 Hz, 1H), 5.81 (d, J=15.4 Hz, 1H), 6.11—6.23 (m, 4H), 7.17—7.35 (m, 2H). MS m/z: 714 (M^+), 119. HR-MS m/z: 714.2940 (Calcd for $C_{35}H_{58}O_5S_4Si$, 714.2936, M^+). $[\alpha]_D^{21}$ −14.5° (c=0.32, $CHCl_3$).

(1*E*,3*E*,5*S*,6*S*,7*R*)-1-Carbomethoxy-5-methyl-8-(1,3-dithian-2-yl)-1,3-octadien-6-yl (2*E*,4*E*,6*S*,7*S*,8*R*)-7-Hydroxy-6-methyl-8-(1,3-dithian-2-yl)-2,4-nonadienoate (30) **32** (18 mg, 0.025 mmol) and benzoic acid (60 mg, 0.5 mmol) were dissolved in THF (0.1 ml). A 1 M solution of Bu_4NF in THF (0.2 ml, 0.2 mmol) was added and the mixture was stirred for 9 h under reflux. Then 2 N K_2CO_3 and ethyl acetate were added and the organic layer was separated. The organic layer was passed through a short silica gel pad and the eluate was concentrated. The residue was chromatographed on a silica gel column with dichloromethane–ethyl acetate (19 : 1—5 : 1) to give **30** (10 mg, 66% yield) as a colorless oil. IR ($CHCl_3$): 3350, 1700, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.92 (d, J=7.0 Hz, 3H), 0.96 (d, J=6.6 Hz, 3H), 1.01 (d, J=7.0 Hz, 3H), 1.02 (d, J=7.0 Hz, 3H), 1.71—1.83 (m, 4H), 1.89—2.06 (m, 4H), 2.31—2.40 (m, 1H), 2.54—2.61 (m, 1H), 2.71—2.80 (m, 8H), 3.64 (s, 3H), 3.70 (dd, J=8.1, 5.5 Hz, 1H), 3.99 (d, J=5.1 Hz, 1H), 4.07 (d, J=6.6 Hz, 1H), 5.13 (dt, J=5.5, 0.4 Hz, 1H), 5.71 (d, J=15.4 Hz, 2H), 5.93—6.20 (m, 4H), 7.08—7.14 (m, 2H). MS m/z: 600 (M^+). HR-MS m/z: 600.2072 (Calcd for $C_{29}H_{44}O_5S_4$, 600.2109, M^+). $[\alpha]_D^{22}$ −10.5° (c=0.22, $CHCl_3$).

(3*E*,5*E*,7*S*,8*S*,11*E*,13*E*,15*S*,16*S*)-7,15-Dimethyl-8,16-bis[(1*R*)-1-(1,3-dithian-2-yl)ethyl]-1,9-dioxa-3,5,11,13-cyclohexadecatetraene-2,10-dione (5) A 0.4 N LiOH solution (0.5 ml) was added to a solution of **30** (3 mg, 0.005 mmol) in THF (0.5 ml) at room temperature. The mixture was stirred at room temperature for 12 h. After neutralization with 5% HCl and then saturation with NaCl, the solution was extracted with ethyl acetate. The extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was azeotroped with toluene and dissolved in THF (0.5 ml). 1,3,5-Trichlorobenzoyl chloride (10 mg, 0.04 mmol) and triethylamine (0.01 ml) were added at room temperature and the mixture was stirred for 1 h, and then diluted with toluene (10 ml), followed by the addition of DMAP (200 mg). The mixture was stirred at room temperature for 3 h, diluted with ether, washed with 5% HCl, saturated $NaHCO_3$, water, and brine, dried over Na_2SO_4, filtered, and concentrated. The residue was chromatographed on a silica gel column with hexane–ethyl acetate (1 : 1) to give **5** (3 mg, quantitative yield) as colorless crystals. IR (KBr): 1710, 1640 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.07 (d, J=6.6 Hz, 3H × 2), 1.19 (d, J=7.3 Hz, 3H × 2), 2.39—2.49 (m, 1H × 2), 2.79—2.90 (m, 4H × 2), 4.02 (d, J=7.7 Hz, 1H × 2), 5.18 (dd, J=10.3, 1.1 Hz, 1H × 2), 5.616 (dd, J=10.6, 1.1 Hz, 1H × 2), 5.618 (d, J=15.0 Hz, 1H × 2), 6.01 (dd, J=11.4, 15.0 Hz, 1H × 2), 6.96 (dd, J=11.4, 15.2 Hz, 1H × 2). MS m/z: 568 (M^+). HR-MS m/z: 568.1817 (Calcd for $C_{28}H_{41}O_4S_4$, 568.1810, M^+). $[\alpha]_D^{22}$ +76.2° (c=0.3, $CHCl_3$).

References and Notes

1) Present address: *Tsumura Institute of Biology and Chemistry, Yoshihara 3586, Ami-cho, Inashiki-gun, Ibaragi 300-01, Japan.*
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