Total Synthesis of Elaiophylin (Azalomycin B)

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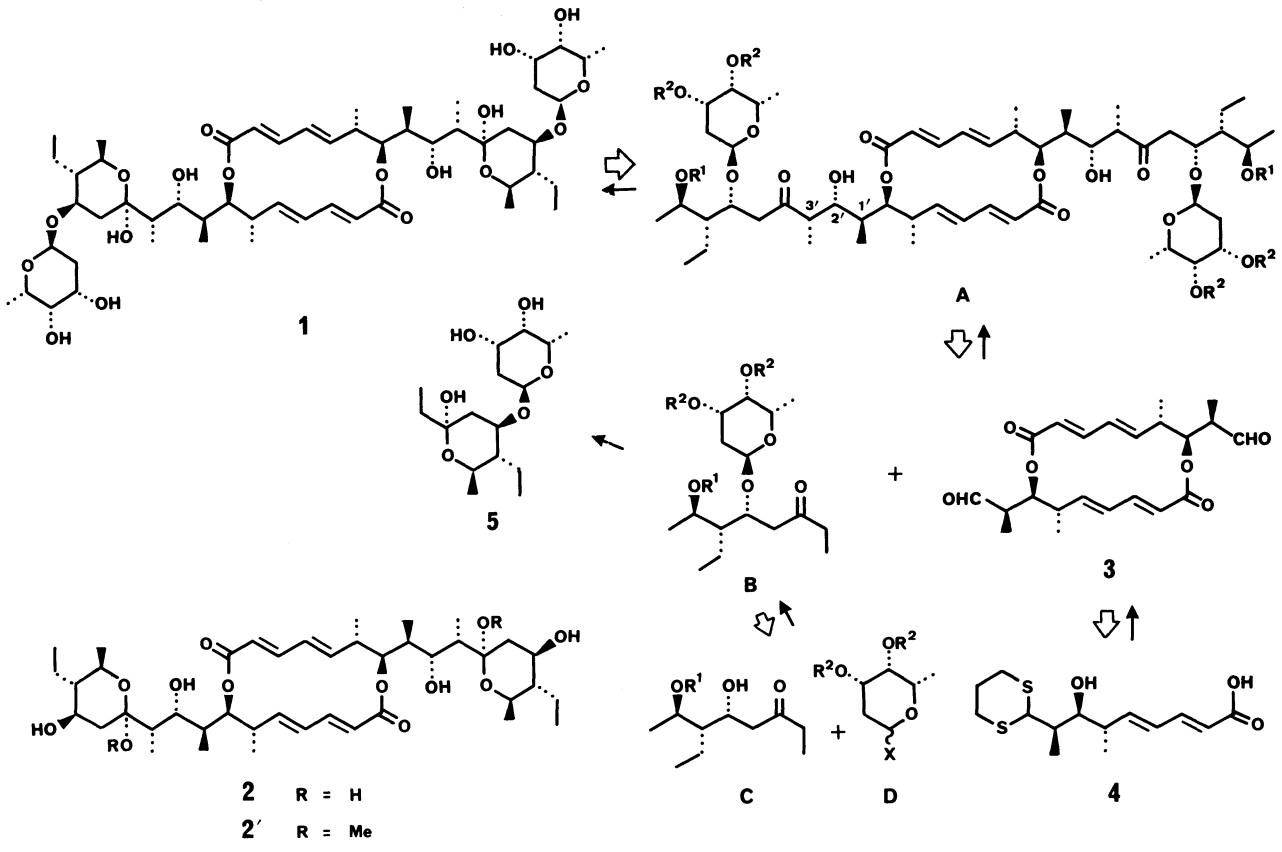
Antibiotic elaiophylin (**1**) has been first synthesized by a convergent route involving aldol coupling of (5*R*,6*R*,7*R*)-5-*O*-[2-deoxy-3,4-bis-*O*-(isopropyldimethylsilyl)-α-L-fucopyranosyl]-6-ethyl-7-*O*-(diethylisopropylsilyl)-5,7-dihydroxy-3-octanone (**25f**) and (7*S*,8*S*,15*S*,16*S*:3*E*,5*E*,11*E*,13*E*)-8,16-bis[(1*R*)-1-formylethyl]-7,15-dimethyl-1,9-dioxa-3,5,11,13-cyclohexadecatetraene-2,10-dione (**3**), followed by desilylation. The appropriately O-protected segment **25f** and the macrocyclic dialdehyde **3** were synthesized from D-glucose and 2-deoxy-L-fucose.

The anti-Gram-positive bacterial antibiotic elaiophylin (**1**) was first isolated in 1959 by Arcamone et al.[1] and then isolated as azalomycin B in 1960 by Arai.[2] The chemical structure was elucidated partially by Takahashi et al.[3–5] and fully by Kaiser and Keller-Schierlein,[6] and the absolute configuration was established by X-ray crystallography.[7,8] Elaiophylin (**1**) belongs to a group of C_2-symmetrical 16-membered macrodiolides.[9] Of this class of natural products, the molecule of **1** has the most complex side chain with a glycosidated β-hydroxy hemiacetal structure. The similar side chain structure has also been found in other class of macrolide antibiotics such as concanamycins.[10] The isolation of the cyclic methyl acetal aglycon derivative **2′** from the methanolysis products of **1** and the total synthesis of **2′** from chiral carbon sources other than carbohydrate have been reported in 1985 by Seebach et al.[11,12] Other synthetic efforts toward **1** have been made by Wakamatsu et al.[13] As a synthetic challenge, we have been interested in **1** which is so sensitive to acid and base that its free aglycon **2** has never been isolated.[4–6,12] Herein we wish to describe, in full,[14] the total synthesis of elaiophylin (**1**) (azalomycin B), which makes use of carbohydrates as chiral source.

The retrosynthetic analysis of **1** is shown in Scheme 1 along with our synthesis plan. The synthesis of **1** through the glycosidation of free aglycon **2** would be impossible because of the extraordinary instability of **2**,[12] whereas it would be possible to synthesize an

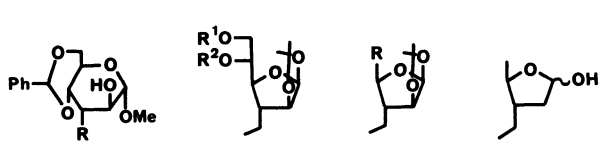


Scheme 1.

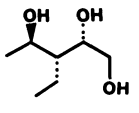
appropriately protected segment **B** from a more stable β-hydroxy ketone **C** and a sugar derivative **D**. The aldol coupling of **B** with the macrocyclic dialdehyde **3** which is obtainable through the dimerization of **4** would give a key intermediate **A**. The target compound **1** then will be obtainable, if the deprotection of **A** followed by the hemiacetalization produced smoothly without any decomposition of **1** formed. In this case, **B** (a synthetic segment of **A**) should have appositely chosen protecting groups (R^1 and R^2) to afford effectively the hemiacetal compound **5** by its deprotection under conditions in which **1** is stable. The conversion of **A** into **1** is presumably achieved under almost the same conditions as used in the deprotection of **B**. Thus it would be required to find the ideal protective groups for the segment **B** to make a success of the elaiophylin synthesis by our plan. Furthermore, it would be a formidable[15] but challenging task to realize the highly stereocontrolled aldol coupling of **B** and **3** in the penultimate step to the aforesaid deprotection.

Preparation of the Segment B. The starting material **6**[16] was obtainable in large scale by the reaction of methyl 2,3-anhydro-4,5-*O*-benzylidene-α-D-mannopyranoside[17] and ethylmagnesium chloride in ether. The reaction product was once recrystallized from ethyl acetate–hexane to afford a 7:1 mixture of **6** and the by-product **6′**.[16] The yields of **6** and **6′** from the starting 2,3-anhydro sugar derivative were assumed to be ca. 64 and 9%, respectively. The complete isolation of **6** from **6′** by further recrystallization or column chromatography was impracticable at this stage. The facile one-step conversion of the crude **6** into the furanose derivative **7** was well-achieved by the direct treatment of **6** with a catalytic amount of boron trifluoride etherate in acetone; an 80% yield of the pure **7** was obtained after chromatography. Selective 5,6-de-*O*-isopropylidenation of **7** with 75% aqueous acetic acid afforded **8** in 85% yield. The periodate oxidation of **8** followed by sodium borohydride reduction of the resulting aldehyde **9** gave **10** in 97% yield. The alcohol **10** was converted into the mesylate **11** by the usual way, which was immediatelly reduced with lithium aluminium hydride (LAH) in ether to afford **12** in 72.5% yield from **10**. Hydrolysis of **12** with 50% aqueous acetic acid gave the free sugar **13** in 82% yield, which was treated with LAH in THF to afford **14** in 95% yield. The triol **14** was directly subjected to the one-step epoxidation[18] of vicinal diol with triphenylphosphine, diethyl azodicarboxylate (DEAD), and 3A Molecular Sieves in refluxed benzene to yield **15**. The crude sample of **15** isolated through a short silica-gel column was contaminated with a considerable amount of *N,N*-bis(ethoxycarbonyl)hydrazine. Since further chromatographic purification of this sample was not practicable, the crude **15** was *t*-butyldimethylsilylated to obtain the pure sample of **16a** in 57% overall yield from **14**. The reaction of **16a** with 5 equivalents of 2-ethyl-2-lithio-1,3-dithiane in THF afforded a 90% yield of essentially pure **17a**. The dithioacetal group of **17a** was cleaved with a 1:1 mixture of $HgCl_2$ and HgO to generate the ethyl ketone **18a** in 93% yield.

We have now in our hand the segment **C** in which R^1 is *t*-butyldimethylsilyl (TBS), a most useful silyl protective group. In our preliminary deprotection experiments for the TBS group of **18a**, it was found that **18a** was smoothly deprotected by tetrabutylammonium fluoride[19] (TBAF) in THF to give the hemiacetal **19**, but the tetrahydropyranyl (THP) derivative **20**, which was prepared from **18a** by the usual way, afforded under the similar desilylation conditions the unsaturated ketone **21** in 48% yield instead of the expected **22**. It was also observed that the mild acidic hydrolysis (3:1:3 AcOH–H_2O–THF,[20] 0 °C, 3 h or 22 °C, 2.5 h) of **20** yielded **19** (20%), **22** (16%), and considerable amounts of **18a** and **21**. These results suggested that the 5-*O*-glycosidation of **18a** may lead to a β-eliminated desilylation product under the basic conditions (TBAF in THF), furthermore, under the acidic conditions (3:1:3 AcOH–H_2O–



6 R = Et
6′ R = H
7 R^1,R^2 = Me_2C
8 $R^1=R^2$ = H
9 R = CHO
10 R = CH_2OH
11 R = CH_2OMs
12 R = Me
13



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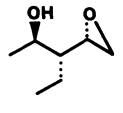

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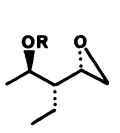
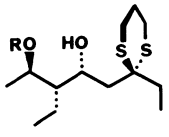
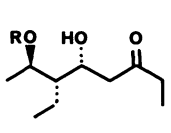


16a~f



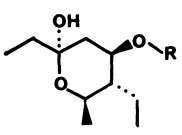
17a~f



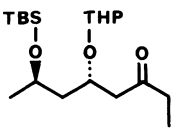
18a~f

R	a	b	c	d	e	f
	TBS	TES	IPDMS	IPDPS	DIPMS	DEIPS

TBS = *t*-$BuMe_2Si$- , TES = Et_3Si- , IPDMS = *i*-$PrMe_2Si$-
IPDPS = *i*-Pr(*n*-Pr)$_2$Si-, DIPMS = (*i*-Pr)$_2$MeSi- , DEIPS = *i*-$PrEt_2Si$-



19 R = H
22 R = THP



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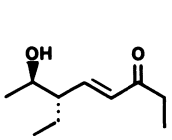

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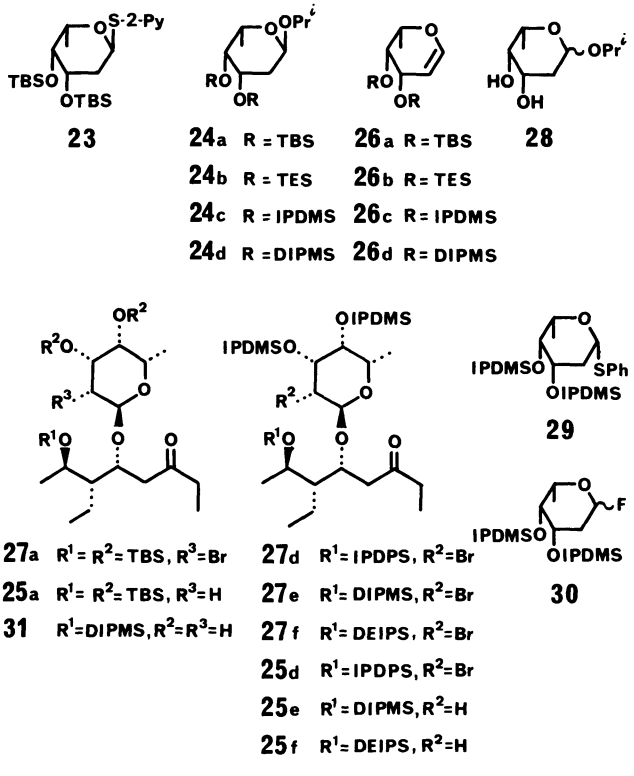
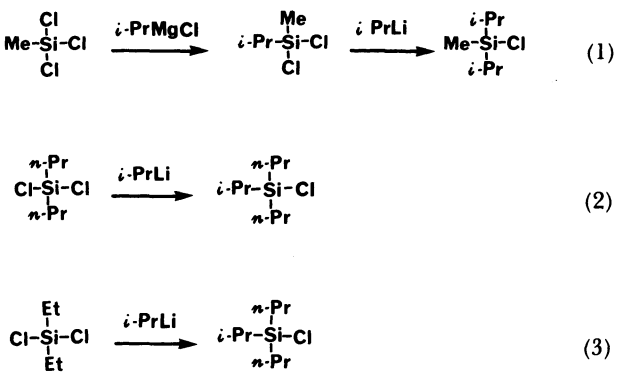
THF), the rate of hydrolytic cleavage of the TBS ether linkage may be rather slower than that of the cleavage of the glycosidic linkage with the 2-deoxysugar moiety. In this respect, it was noteworthy that azalomycin B[21] (**1**) was immediately decomposed by TBAF in THF even at lower temperature, but it was hardly affected by 3:1:3 AcOH–H_2O–THF, recovering the unchanged **1** after evaporation of the resulting mixture and subsequent silica-gel column chromatography. Although the TBS group thus seemed to be not apposite as the protective group (R^1) of the segment **C**, we first pursued the 5-*O*-glycosidation of **18a** with a 3,4-di-*O*-protected 2-deoxy-L-fucose derivative. Treatment of 2-deoxy-D-fucose with di-2-pyridyl disulfide and tributylphosphine[22] followed by silylation[23] with TBS triflate and 2,6-lutidine in DMF afforded the α-thioglycoside **23** along with the minor β-anomer. 2-Propanol reacted with **23** in acetonitrile in the presence of *N*-bromosuccinimide (NBS) and 4A Molecular Sieves[24] to give only the α-glycoside **24a** in 55% yield. However, the reaction of **18a** and **23** provided no glycoside **25a** under the similar conditions or with $Pb(ClO_4)_2$ in acetonitrile, recovering **18a** in 71% yield. Desilylation of **24a** in an acidic conditions (6.9% aqueous 46% HF in acetonitrile,[25] 20 °C, 16 h) failed, resulting in only the cleavage of glycosidic bond of **24a**. We next pursued the glycosidation of **18a** with the glycal derivative **26a** which was obtained by the silylation[23] of L-fucal[26] in 52% yield. The glycosidation of **18a** with **26a** was first accomplished by the method[27] which was previously developed in our laboratories. The reaction of **18a** and **26a** in the presence of NBS afforded a ca. 3:1 mixture of α- and β-anomeric bromo derivative, which was chromatographed on silica gel to separate the desired α-anomer **27a** in 65% yield. Debromination of **27a** with tributylstannane and α,α'-azobisisobutyronitrile (AIBN) in benzene afforded **25a** in 73% yield (47.5% overall yield from **18a**). The synthetic route to segment **B** (R^1=R^2=TBS) was thus confirmed. However, as had been predicted by the desilylation experiment for **20** and **24a**, **25a** was decomposed with TBAF in THF at 20 °C to give no deprotected hemiacetal **5** (Scheme 1), while **25a** was hardly affected with 3:1:3 AcOH–H_2O–THF at 25 °C for 7 h.

Our selection of the ideal silyl protective group for the segment **B** was aided by the classical reasoning that the rate of acidic hydrolysis of alkylsilyl ether should be subtly influenced by steric effects of alkylsilyl ligands on silicon.[28] We examined the alkylsilyl groups less hindered than TBS, such as triethylsilyl (TES), isopropyldimethylsilyl (IPDMS), diisopropylmethylsilyl (DIPMS), isopropyldipropylsilyl (IPDPS), and diethylisopropylsilyl (DEIPS). The silylating agents, DIPMS-Cl[29] and unknown reagents, IPDPS-Cl and DEIPS-Cl, were prepared from the appropriate chlorosilanes according to the reactions (1,2,3) shown in Scheme 2, respectively. The silylation of the crude **15** using TES-Cl, IPDMS-Cl,[30] IPDPS-Cl, DIPMS-Cl, and DEIPS-Cl with imidazole in dichloromethane afforded **16b**, **16c**, **16d**, **16e**, and **16f**, respectively, which were converted into the corresponding dithiane derivatives, **17b**, **17c**, **17d**, **17e**, and **17f** in good yields. Among them **17d**, **17e**, and **17f** were smoothly dedithioacetalized with $HgCl_2$–H_2O to give **18d**, **18e**, and **18f** in 91, 80, and 79% yields, respectively, whereas **17b** and **17c** afforded **18b** (58%) and **18c** (44%) together with hemiacetal **19** (30 and 46%), respectively. From a preparative point of view, the silyl derivatives, **18d**, **18e**, and **18f**, were more suitable for the segment **C**.

The glycal derivatives, **26b**, **26c**, and **26d**, were prepared by treatment of L-fucal with the corresponding silylating agents and imidazole in DMF. The model glycosides (**24b**, **24c**, **24d**) were then prepared





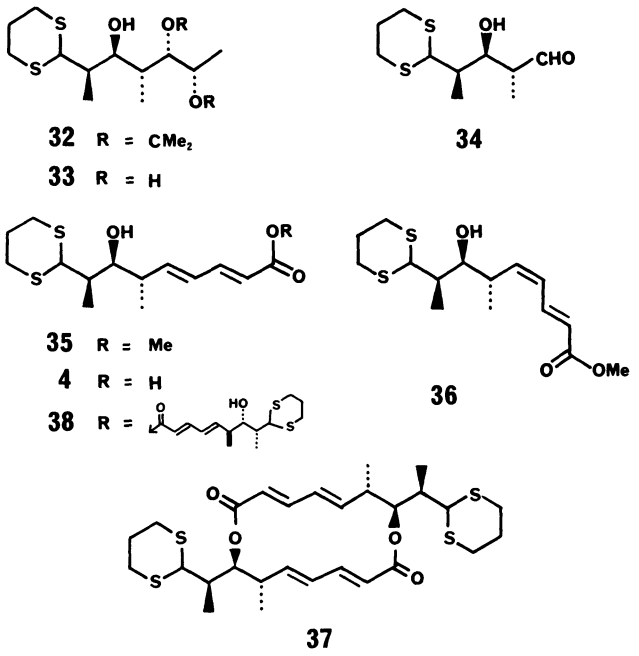
Scheme 2.

from the corresponding glycals and 2-propanol by the procedure described in the preparation of **25a**. Based on the facilities in the formation of the desilylation products **28** from **24b**, **24c**, and **24d** under the acidic conditions (8:1:8 AcOH-H_2O-THF, 30 °C, 24 h),[31] the most apposite protective group for the sugar moiety of **B** was assumed to be IPDMS, therefore **26c** became the most promising glycal derivative.

Each of the selected ketone derivatives, **18d**, **18e**, and **18f**, were subjected to glycosidation with **26c** followed by debromination to afford the glycosides, **25d** (24% via **27d**), **25e** (38% via **27e**), and **25f** (30% via **27f**), respectively. The glycosidation of **18f** with fluoride **30** did not proceed because the thioglycoside **29**, a precursor of **30**, was completely deprotected under the conditions of its fluoridation with (dimethylamino)-sulfur trifluoride (DAST) and NBS.[24,32] However, we found that the treatment of **18f** (1 equiv) with the glycal **26c** (3.5 equiv) and *dl*-10-camphorsulfonic acid (CSA) (0.36 equiv) in dichloromethane containing 4A Molecular Sieves[33] by modification of the Wakamatsu's methods[13a] afforded **25f** as a sole anomer in 80% yield.

Finally, thus obtained **25d**, **25e**, and **25f** were subjected to a deprotection test to determine the most favorable compound for the segment **B**. Exposure of **25d** to 2:1:2 AcOH-H_2O-THF (28 °C, 6 h) or 2:1:2 AcOH-aq 0.46% HF-THF (28 °C, 4 h) afforded mainly **5** accompanied by a small amount of partially deprotected product and 2-deoxy-L-fucose, which were detectable on TLC. Treatment of **25e** with 3:1:3 AcOH-H_2O-THF (25 °C, 20 h) or 2:1:2 AcOH-aq 0.46% HF-THF (26 °C, 6 h) gave mainly **5** and the same Kind of by-products. Exposure of **25e** to 8:1:8 AcOH-H_2O-THF (26 °C, 11 h) yielded mainly **31** in 45% yield. Treatment of **25f** with 2:1:2 AcOH-H_2O-THF (24—26 °C, 12—18 h) also afforded **5** as major product. In view of the minimal formation of by-products observed in the deprotection test, **25f** was considered to be the most promising segment **B**. In fact, **25f** provided a 64% yield of **5** on treatment with 3:1:4 AcOH-aq 1% HF·KF-THF (30 °C, 14 h). Under this conditions, natural azalomycin **B** was confirmed to be stable. The synthesis of the segment **B** was accomplished.

Preparation of the Segment 3. The synthesis of the second segment **3**[11,12] started from **32** which was previously prepared from D-glucose in our laboratories.[34] Deisopropylidenation of **32** with 50% aqueous acetic acid afforded the crystalline triol **33** in 90% yield. Treatment of **33** with lead tetraacetate[35] gave the aldehyde **34** (ca. 95% yield) which was allowed to react with [(2*E*)-3-methoxycarbonyl-2-propenyliden]triphenylphosphorane[36] in toluene at 80 °C to yield (2*E*,4*E*)-dienoic ester **35** and its (4*Z*)-isomer **36** in 51 and 21% overall yields from **33**, respectively, after chromatographic separation. The (4*Z*)→(4*E*) isomerization of **36** proceeded in benzene



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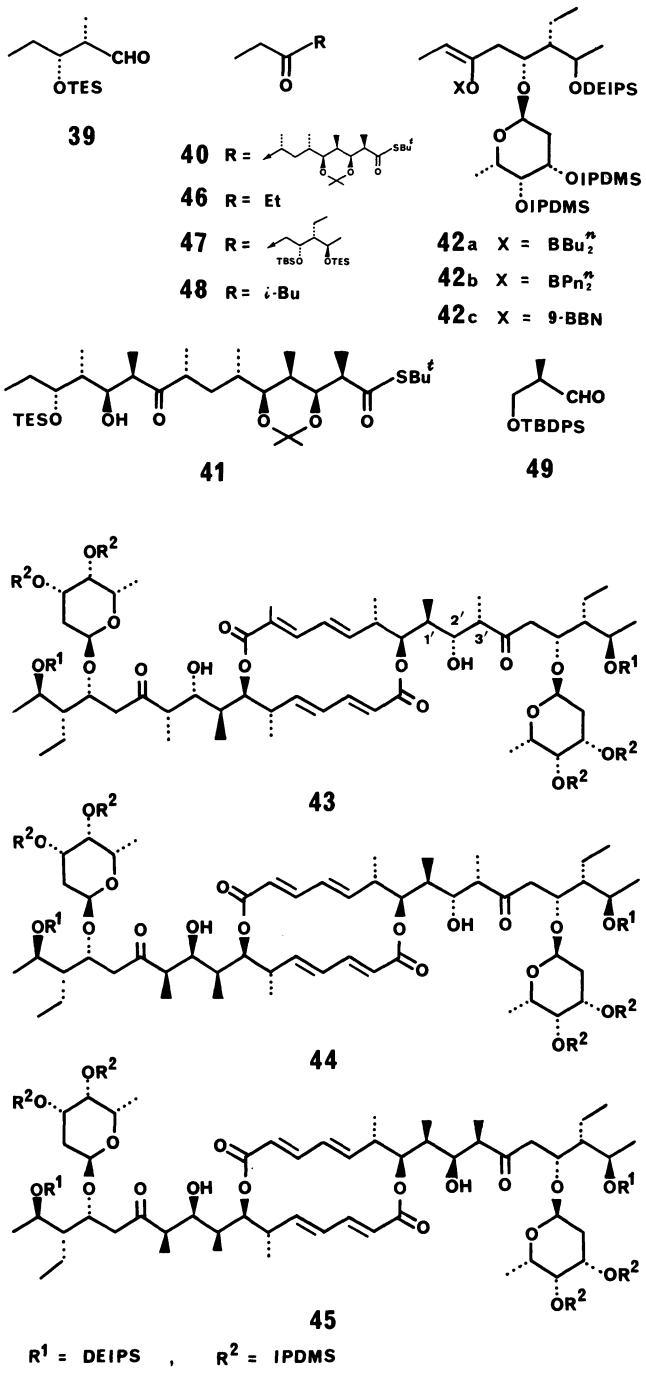
with a catalytic amount of iodine[37] at 25 °C for 1 m to afford **35** and **36** in 37.4 and 27% isolated yields, respectively. Saponification of **35** with lithium hydroxide gave the hydroxy dienoic acid **4** in quantitative yield. The dimerization of **4** was best effected by the Yamaguchi's method[38,39] to afford the crystalline diolide **37** in 31% yield. It was found that the reaction of **4** with 1-chloro-2-methylpyridinium iodide and triethylamine according to the Mukaiyama's method[40] gave the anhydride **38** in 85.5% yield, which was treated with 4-(dimethylamino)pyridine (DMAP) in acetonitrile to afford the diolide **37** in 9.4% overall yield from **4**. Dedithioacetalization of **37** with 1:1 $HgCl_2$-HgO (red) was carried out with irradiation in the water bath of an ultrasound laboratory cleaner to give the crystalline dialdehyde **3** in 70% yield.

Aldol Coupling of 25f and 3, and Synthesis of Elaiophylin. In the synthesis of 6-deoxyerythronolide B, Masamune et al.[41] have found that the aldol coupling of chiral aldehyde **39** and (*Z*)-lithium enolate prepared from ethyl ketone **40** with lithium bis-(trimethylsilyl)amide (LBTMSA) give the anti-Cram-syn aldol **41** in 88% yield and 94% diastereomeric purity. The aldol coupling of **25f** and **3** was first pursued according to this procedure. The lithium enolate was prepared by treatment of **25f** (2.4 equiv) with LBTMSA (2.4 equiv) in THF at −78 °C for 0.5 h. This was added slowly to a THF solution of **3** (1 equiv) at −78 °C and the resulting colorless mixture was stirred at −78 °C for 2 h. By careful chromatographic purification of the reaction products, three diastereomeric aldols, **43** (5.2%), **44** (8.9%), and **45** (6.3%), could be obtained in low yields. The minor aldol **43** proved to be the desired precursor **A** to elaiophylin **1** as will be described in the next paragraph. When inversely was added the aldehyde **3**

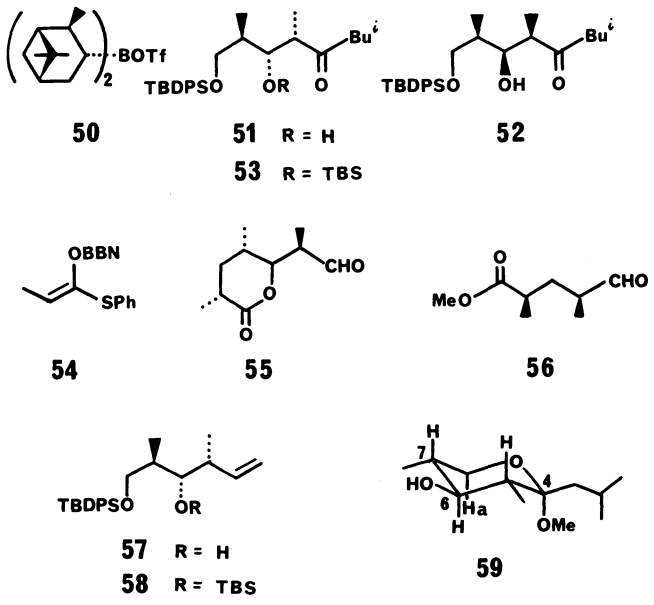


to the lithium enolate solution at −78 °C, the resulted red-colored reaction mixture afforded only poor yields of the aldol products. It was revealed that **3** was very sensitive to the strong base such as lithium enolate.

It has also been known that dibutylboryl triflate[42] reacts with ethyl ketones such as **46** and **47**[11,12] in the presence of weak base *i*-Pr_2NEt to give with high stereoselectivity the (*Z*)-boron enolates[43] which add to aldehydes to provide syn aldols.[12,42-44] The coupling of **25f** and **3** was next carried out by this procedure using dialkylboryl triflates. The (*Z*)-boron enolate **42a** was prepared under the standard conditions[43] (*n*-Bu_2BOTf, *i*-Pr_2NEt, ether, −78 °C, 0.5 h). The reaction was performed by addition of an etherial solution of **42a** (4 equiv) to an etherial solution of **3** (1 equiv) at −78 °C under argon. It was allowed to warm to −10 °C and stirred for 2 h. Quenching with a phosphate buffer (pH 7) (25 °C, 3 min)[45] followed by chromatographic isolation afforded the three aldols, **43**, **44**, and **45** in 13, 24, and 26% yields, respectively. The ^1H NMR examination of these products revealed that **43** and **45** were C_2 symmetric, while **44** was unsymmetric (see Experimental). Upon treatments of these products with 3:1:3 AcOH–1% aqueous HF·KF–THF at 30 °C for 18 h, only **43** gave a 22% yields of **1**. The TLC behavior of **1** was coincidental with azalomycin B, and after two recrystallizations from ethyl acetate there was obtained colorless needles, mp 179—182 °C, $[\alpha]_D$ −53° which compared well with natural material. Comparison of ^1H NMR spectra at 400 MHz showed both materials to be identical. Unexpectedly, we could not obtain the diastereomers[46] of **1** from the aldol diastereomers **44** and **45** under the same deprotection conditions. Having thus assigned **43** as the bis(1′,2′-anti-2′,3′-syn)-product, **45** and **44** were assumed to be the bis(1′,2′-syn-2′3′-syn)- and (1′,2′-anti-2′,3′-syn:1″,2″-syn-2″,3″-syn)-products, respectively.

The reaction of **3** with other (*Z*)-boron enolates **42b** and **42c** which were prepared from **25f** and the corresponding boryl triflates were carried out by the procedure described above to afford **43** (12 and 5%), **44** (25.5 and 16.5%), and **45** (19 and 39%), respectively. The reaction of **3** with **42a** in the presence of $ZnCl_2$ in THF gave **43** (14%), **44** (31%), and **45** (21%). Moreover, the Mukaiyama's aldol reaction of **3** with **25f** via divalent tin enolate[47] gave **43** (6.5%), **44** (21%), and **45** (28%).

With the goal of obtaining the desired anti-Cram (1′,2′-anti) product **43** in high yield, we also examined the aldol reaction with the boron enolate of **25f** with chiral ligands attached to boron. A model coupling reaction of **48** and **49** using the chiral boryl triflate **50**[48,49] was carried out under the Paterson's conditions[49] (*i*-Pr_2NEt, ether, 0 °C) to afford a 2:1 mixture of **51** (anti-Cram product[51]) and **52** (Cram product[51]) in 30% yield. While the coupling using achiral boryl triflates, *n*-Bu_2BOTf and 9-BBNOTf, gave 2.3:1 and 1.2:1 mixture of **51** and **52** in 59 and 93% yields, respectively. The (−)-diisopinocampheylboron enolate of **48** showed to be of little help for enhancement of the expected *si*-face selectivity[50] in direction of the inherent 1,2-asymmetric induction on addition of achiral boron enolates to the α-chiral aldehyde **49**. Furthermore, on the reaction of **49** and **25f** using **50**, there could not be obtained any aldol products. The enolization of the large ethyl ketone **25f** with the bulky boryl triflate **50** seemed to be quite difficult. An extensive study by Masamune[52] revealed that Cram/anti-Cram selectivity in the coupling of boron enolate



50 51 R = H 52

53 R = TBS

54 55 56

57 R = H

58 R = TBS

59

54 with chiral aldehydes depended on the aldehydes employed: the reaction of **54** with lactone aldehyde **55** afforded the Cram product in a 1.9—2.5:1 selectivity, whereas the reaction with linear aldehyde **39** or **56** gave the anti-Cram product in a 1.5:1 or 55:45 selectivity, respectively. The Cram selectivity observed in the coupling of **3** with **42c** and the anti-Cram selectivity in the reaction of **49** with 9-BBN enolate of **48** appeared to be in line with the Masamune's observation. The rationalization for these results is now not available.

Although the closing stages of this total synthesis of **1** were sullied by the minor preponderance of the unwanted Cram (1′2′-syn) product **45** over the anti-Cram (1′2′-anti) product **43** in the aldol reaction step, the synthesis of elaiophylin (**1**) which was sensitive to acid and base was first achieved via **43** by using the appropriate O-protecting groups such as DEIPS and DMIPS.

Experimental

Melting points were determined on a micro hot-stage Yanaco MP-S3 and were uncrrected. Optical rotations were measured with a Carl Zeiss photoelectric polarimeter or a JAS.CO DIP-360 photoelectric polarimeter in chloroform unless otherwise stated. IR spectra were recorded on a Hitachi Perkin-Elmer 225 spectrometer, UV spectra on a JAS.CO UVIDEC-1 spectrometer, and ^{1}H NMR spectra on a Varian EM-390, a Bruker WM 250, or a JEOL GX-400 spectrometer in $CDCl_3$ using TMS as internal standard unless otherwise stated. Mass spectra were measured with a Hitachi M-80 mass spectrometer or a Hitachi RMU-6M mass spectrometer. TLC was carried out on Merck TLC plates (60F-254, 0.25 mm). Column chromatography was performed on silica gel, Wakogel C-200 and Merck Kiesel gel 60 (230—400 mesh) for "Flash Chromatography". In general, organic solvents were purified and dried by the appropriate procedure, and evaporation and concentration were carried out under reduced pressure below 35 °C, unless otherwise noted.

3-Deoxy-3-*C*-ethyl-1,2:5,6-di-*O*-isopropylidene-β-D-altrofranose (7). To a solution of the crude sample of **6** (32.2 g) containing ca. 12.5% of **6′** in dry acetone (1.29 l) was added $BF_3 \cdot Et_2O$ (6.04 ml, 65.4 mmol) under ice-cooling. After being kept at room temperature for 15 h, the reaction mixture was neutralized with Et_3N under ice-cooling and then concentrated to afford a yellow syrup, which was chromatographed on silica gel (2 kg) with 6:1 toluene–ethyl acetate to give **7** (21.3 g, 80% based on **6**) as colorless needles. R_f=0.41 (9:1 toluene–ethyl acetate); mp 63—64 °C; $[\alpha]_D^{22}$ +16° (*c* 1.07); ^{1}H NMR (90 MHz) δ=1.00 (3H, t, 3-$CH_2C\underline{H}_3$, *J*=6.6 Hz), 1.30, 1.35, 1.40, and 1.53 (each 3H, each s, CMe_2×2), 1.2—1.8 (2H, m, 3-$C\underline{H}_2CH_3$), 2.37 (1H, dt, H-3, *J*=2.4, 7.5 Hz), 3.6—4.4 (4H, m, H-4, 5, 6, 6′), 4.43 (1H, d, H-2, *J*=4.5 Hz), and 5.77 (1H, d, H-1, *J*=4.5 Hz).

Found: C, 61.74; H, 8.88%. Calcd for $C_{14}H_{24}O_5$: C, 61.63; H, 8.71%.

3-Deoxy-3-*C*-ethyl-1,2-*O*-isopropylidene-β-D-altrofuranose (8). A solution of **7** (671 mg, 2.46 mmol) in aqueous 75% acetic acid (13.4 ml) was stirred at 30 °C for 4 h and then concentrated to give a crude syrup (684 mg) which was chromatographed on silica gel (21 g) with 1:1 toluene–ethyl acetate to afford **8** (487 mg, 85%) as a colorless surup: R_f=0.12 (3:2 toluene–ethyl acetate); $[\alpha]_D^{28}$ +13° (*c* 1.18); ^{1}H NMR (90 MHz) δ=1.00 (3H, t, 3-$CH_2C\underline{H}_3$, *J*=6.3 Hz), 1.30 and 1.53 (each 3H, each s, CM_2), 1.2—1.8 (2H, m, 3-$C\underline{H}_2CH_3$), 2.25—2.7 (2H, m, H-3 and OH), 2.87 (1H, d like, OH), 3.65—4.15 (4H, m, H-4.5, 6, 6′), 4.43 (1H, d, H-2, *J*=3.9 Hz), and 5.80 (1H, d, H-1, *J*=3.9 Hz).

Found: C, 56.71; H, 8.32%. Calcd for $C_{11}H_{20}O_5$: C, 56.88; H, 8.68%.

3-Deoxy-3-*C*-ethyl-1,2-*O*-isopropylidene-β-D-arabinofuranose (10). To an ice-cooled solution of **8** (4.55 g, 19.5 mmol) in acetone (45.5 ml) was slowly added a solution of $NaIO_4$ (8.35 g, 39.1 mmol) in water (83.5 ml). After being stirred at room temperature for 30 min, the mixture was concentrated to remove the acetone. The residue was diluted with water (100 ml), extracted with ethyl acetate (50 ml×3), and the extracts were washed with saturated aqueous NaCl (50 ml), dried and concentrated to afford a crude sample of **9** (4.35 g) as pale yellow needles, which was used without further purification. Powdered $NaBH_4$ (1.64 g, 43.5 mmol) was slowly added to a stirred ice-cooled solution of the crude sample of **9** (4.35 g) in methanol (43.5 ml), and then the mixture was stirred at room temperature for 10 min. The reaction mixture was neutralized with CO_2 (solid) and concentrated. The residue was triturated with chloroform, and the chloroform solutions were evaporated to give a pale yellow syrup, which was chromatographed on silica gel (110 g) with 1:1 toluene–ethyl acetate to afford **10** (3.83 g, 97% from **8**) as a colorless syrup. R_f=0.46 (1:1 toluene–ethyl acetate); $[\alpha]_D^{27}$ +11° (*c* 0.90); ^{1}H NMR (90 MHz) δ=1.00 (3H, t, 3-$CH_2C\underline{H}_3$, *J*=6.6 Hz), 1.30 and 1.53 (each 3H, each s, CMe_2), 1.25—1.55 (2H, m, 3-$C\underline{H}_2CH_3$), 1.9—2.2 (1H, m, H-3), 2.2—2.45 (1H, br, OH), 3.55—4.1 (3H, m, H-4,5,5′), 4.42 (1H, dd, H-2, *J*=1.5, 4.5 Hz), and 5.81 (1H, d, H-1, *J*=4.5 Hz).

Found: C, 59.71; H, 8.88%. Calcd for $C_{10}H_{18}O_4$: C, 59.39; H, 8.97%.

3-Deoxy-3-*C*-ethyl-1,2-*O*-isopropylidene-5-*O*-methylsulfonyl-β-D-arabinofuranose (11). To a solution of **10** (4.50 g, 22.2 mmol) in dry pyridine (45.0 ml) was added methanesulfonyl chloride (2.07 ml, 26.7 mmol) under ice-cooling. After being stirred at room temperature for 0.5 h, the reaction mixture was poured into cold water (50 ml), extracted with ethyl acetate (20 ml×3), washed with saturated aqueous NaCl (30 ml), dried, and concentrated to afford a crude sample of **11** (6.40 g) as yellow needles which was suitable for the next synthesis. Analytical sample was obtained after silica-gel column chromatography with 3:1 benzene–ethyl acetate. R_f=0.40 (3:1 toluene–ethyl acetate); mp 69.5—70 °C (ethyl acetate–hexane); $[\alpha]_D^{33}$ +25° (*c* 0.88); ^{1}H NMR (90 MHz) δ=1.00 (3H, t, 3-$CH_2C\underline{H}_3$, *J*=6.6 Hz), 1.30 and 1.58 (each 3H, each s, CMe_2), 1.25—1.7 (2H, m, 3-$C\underline{H}_2CH_3$), 2.10 (1H, dt, H-3, *J*=3.0, 1.5 Hz), 3.10 (3H, s, OMs), 4.0—4.75 (4H, m, H-2,4,5,5′), and 5.83 (1H, d, H-1, *J*=3.3 Hz).

Found: C, 46.92; H, 7.00%. Calcd for $C_{11}H_{20}O_6S$: C, 47.13; H, 7.19%.

3,5-Dideoxy-3-*C*-ethyl-1,2-*O*-isopropylidene-β-D-arabinofuranose (12). To an ice-cooled solution of the crude sample of **11** (6.40 g) in dry ether (96.0 ml) was slowly added powdered $LiAlH_4$ (2.60 g, 68.5 mmol) under stirring. The stirring was continued at room temperature for 5 h and to the reaction mixture were successively added dropwise water (2.60 ml), aqueous 15% NaOH (2.60 ml) and water (7.80 ml) under ice-cooling. The resulting mixture was then filtered, and the filter cake was washed with chloroform. The filtlate and washings were combined, and concentrated (10 °C, 40 mmHg; 1 mmHg≈133.322 Pa) to give a syrup (15.8 g) which was chromatographed on silica gel (790 g) with 10:1 hexane–acetone to afford **15** (3.00 g, 72.5% from **10**) as a colorless syrup. Analytical sample was obtained by distillation [bp_5 78—80 °C (bath temp)]. R_f=0.63 (5:1 toluene–ethyl acetate); $[\alpha]_D^{25}$ 0°, $[\alpha]_{365}$ +4.2° (*c* 1.19); ^{1}H NMR (90 MHz) δ=1.00 (3H, t, 3-$CH_2C\underline{H}_3$, *J*=6.6 Hz), 1.25—1.55 (2H, m, 3-$C\underline{H}_2CH_3$), 1.30 and 1.53 (each 3H, each s, CMe_2), 1.37 (3H, d, 4-Me, *J*=7.5 Hz), 1.75—2.1 (1H, m, H-3), 3.87 (1H, dq, H-4, *J*=7.5, 1.5 Hz), 4.37 (1H, dd, H-2, *J*=4.5, 1.5 Hz), and 5.72 (1H, d, H-1, *J*=4.5 Hz).

Found: C, 64.64; H, 9.52%. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74%.

3,5-Dideoxy-3-*C*-ethyl-β-D-arabinofuranose (13). A solution of **12** (9.90 g, 53.2 mmol) in aqueous 50% acetic acid (9.90 ml) was stirred at 100 °C for 0.5 h and then concentrated to give a syrup (8.20 g) which was subsequently chromatographed on silica gel (390 g) with 3:2 hexane–acetone to afford **13** (6.41 g, 82%) as a colorless syrup. Analytical sample was obtained by distillation [bp_2 100—110 °C (bath temp)]. R_f=0.33 (3:2 hexane–acetone); $[\alpha]_D^{29}$ −44° (*c* 1.41, after 2 d); ^{1}H NMR (90 MHz) δ=1.00 and 1.02 (3H, each t, 3-$CH_2C\underline{H}_3$ of α and β anomers, each *J*=6.6 Hz), 1.31 and 1.33 (3H, each d, 4-Me of α and β anomers, each *J*=6.3 Hz), 1.3—1.85 (3H, m, 3-$C\underline{H}_2CH_3$, H-3), 2.83 (2H, br s, OH×2), 3.45—4.15 (2H, m, H-2,4), 5.19 and 5.27 (1H, each d, H-1 of α and β anomers, *J*=4.5, 2.0 Hz).

Found: C, 57.30; H, 9.36%. Calcd for $C_7H_{14}O_3$: C, 57.51; H, 9.65%.

(2*S*,3*R*,4*R*)-3-Ethyl-1,2,4-pentanetriol (14). To an ice-cooled solution of **13** (6.41 g, 43.8 mmol) in dry THF (256 ml) was slowly added powdered $LiAlH_4$ (3.33 g, 87.6 mmol) under stirring. The stirring was continued at 70 °C for 2 h and to the reaction mixture were added dropwise water (3.3 ml), aqueous 10% NaOH (3.3 ml) and water (9.9 ml) successively under ice-cooling. The resulting mixture was then filtered, and filter cake was washed with chloroform. The filtrate and washings were combined, and concentrated to give a crude syrup (8.64 g) which was chromatographed on silica gel (400 g) with 11:1 chloroform–methanol to afford **14** (6.18 g, 95%) as a colorless syrup. R_f=0.32 (11:1 chloroform–methanol); $[\alpha]_D^{26}$ −4.4° (*c* 1.00, CH_3OH); ^{1}H NMR (90 MHz) δ=0.97 (3H, br t, 3-$CH_2C\underline{H}_3$), 1.28 (3H, d, H-5, *J*=6.6 Hz), 1.15—1.85 (3H, m, 3-$C\underline{H}_2CH_3$, H-3), and 3.4—4.45 (7H, m, H-1,1′,2,4, OH×3).

Found: C, 56.43; H, 10.60%. Calcd for $C_7H_{16}O_3$: C, 56.73; 10.88%.

(2*R*,3*R*,4*S*)-2-*O*-(*t*-Butyldimethylsilyl)-4,5-epoxy-3-ethyl-2-pentanol (16a). According to the procedure described by Achab and Das,[18] **14** (331 mg, 2.23 mmol) was directly epoxidated with triphenylphosphine (644 mg, 2.45 mmol) and DEAD (0.387 ml, 2.45 mmol) in refluxing benzene containing 3A Molecular Sieves (0.9 g) to afford the crude epoxide **15** (347 mg) which was contaminated by a considerable amount of *N*,*N*-bis(ethoxycarbonyl)hydrazine. To a solution of the crude sample of **15** (347 mg) and imidazole (219 mg, 3.21 mmol) in dry CH_2Cl_2 (2.46 ml) was added *t*-butyldimethylsilyl chloride (456 mg, 3.02 mmol) under ice-cooling. The reaction mixture was stirred at room temperature for 9 h, and then poured into cold water (10 ml) and extracted with CH_2Cl_2 (8 ml×3). The extracts were washed with saturated aqueous NaCl (8 ml), dried, and concentrated. The residue was chromatographed on silica gel (40 g) with benzene to afford a pure sample of **16a** (329 mg, 57% from **14**) as a colorless syrup. R_f=0.55 (benzene); $[\alpha]_D^{20}$ −14.3° (*c* 0.95); ^{1}H NMR (90 MHz) δ=0.87 (9H, s, *t*-Bu), 0.97 (3H, t, 3-$CH_2C\underline{H}_3$, *J*=7.2 Hz), 1.16 (3H, d, H-1, *J*=6.0 Hz), 1.1—1.3 (1H, m, H-3), 1.57 (2H, dq, 3-$C\underline{H}_2CH_3$, *J*=7.2, 1.0 Hz), 2.45—2.55 (1H, m, H-4), 2.7—3.0 (2H, m, H-5,5′), and 3.93 (1H, q, H-2, *J*=6.0, 2.3 Hz).

Found: C, 63.92; H, 11.28%. Calcd for $C_{13}H_{28}O_2Si$: C, 63.88; H, 11.54%.

(2*R*,3*R*,4*S*)-4,5-Epoxy-3-ethyl-2-*O*-(diethylisopropylsilyl)-2-pentanol (16f). By the procedure described in the preparation of **16a**, the crude sample of **15** (1.42 g) was silylated with DEIPS-Cl (1.63 ml, 8.82 mmol) and imidazole (651 mg, 9.56 mmol) to give a pure sample of **16f** (1.37 g, 72% from **14**) as a colorless syrup. R_f=0.53 (10:1 hexane–ethyl acetate); $[\alpha]_D^{20}$ −9° (*c* 1.10); ^{1}H NMR (90 MHz) δ=0.5—0.8 (4H, m, $Si(C\underline{H}_2CH_3)_2$), 0.8—1.15 (16H, m, *i*-Pr$Si(CH_2C\underline{H}_3)_2$, 3-$CH_2C\underline{H}_3$).

Found: *m*/*z* 229.1622. Calcd for $C_{12}H_{25}O_2Si$: M−Et, 229.1622.

2-[(2*R*,3*R*,4*R*)-4-*O*-(*t*-Butyldimethylsilyl)-3-ethyl-2,4-dihydroxypentyl]-2-ethyl-1,3-dithiane (17a). A solution of 2-ethyl-1,3-dithiane (997 mg, 6.73 mmol) in dry THF (9.97 ml) was cooled to −40 °C under argon. A solution of 1.42 M butyllithium (1 M=1 mol dm^{-3}) in hexane (4.74 ml, 6.73 mmol) was added to the solution dropwise under stirring. After being stirred for an additional 2 h at −20 °C, the mixture was again cooled to −50 °C. A solution of **16a** (329 mg, 1.35 mmol) in dry THF (0.99 ml) was then added dropwise to this solution, and stirring was continued at −50 °C→−20 °C for 4 h. The reaction mixture was poured into cold water (20 ml) and extracted with chloroform

(10 ml×3). The extracts were washed with saturated aqueous NaCl (10 ml), dried, and concentrated. The residual syrup (1.40 g) was chromatographed on silica gel (210 g) with benzene to afford **17a** (474 mg, 90%) as a colorless syrup. R_f=0.43 (benzene); ^{1}H NMR (90 MHz) δ=0.87 (9H, s, *t*-Bu), 0.88 (3H, t, 2-$CH_2C\underline{H}_3$, J=7.2 Hz), 1.07 (3H, t, 3'-$CH_2C\underline{H}_3$, J=7.5 Hz), 1.30 (3H, d, H-5', J=6.0 Hz), 1.15—1.35 (1H, m, H-3'), 1.4—1.8 (2H, m, 3'-$C\underline{H}_2CH_3$), 1.75—2.35 (6H, m, 2-$CH_2C\underline{H}_3$, H-1', $SCH_2C\underline{H}_2$), 2.75—2.95 (4H, m, $SC\underline{H}_2CH_2C\underline{H}_2S$), 3.47 (1H, s, OH), 4.10 (1H, dq, H-4', J=7.5, 3.0 Hz), and 4.3—4.7 (1H, m, H-3').

(5*R*,6*R*,7*R*)-7-*O*-(*t*-Butyldimethylsilyl)-6-ethyl-5,7-dihydroxy-3-octanone (18a). To a mixture of **17a** (23.4 mg, 0.0596 mmol), mercury(II) oxide (56.8 mg, 0.262 mmol) and 80% aqueous acetone (1.64 ml) was added mercury(II) chloride (71.2 mg, 0.262 mmol) under ice-cooling with efficient stirring. The reaction mixture was stirred under ice-cooling for 0.5 h and filtered through a Celite. The filter cake was washed with acetone, and then the filtrate and the washings were combined. After removal of the acetone under reduced pressure (0 °C), to the aqueous residue was added aqueous 10% KI until orange color was disappeared. The mixture was then extracted with chloroform (7 ml×3) and the extracts were washed with saturated aqueous NaCl (10 ml), dried, and concentrated to give a crude syrup (22.6 mg) which was chromatographed on silica gel (2 g) with 8:1 hexane–ethyl acetate to afford a pure sample of **18a** (16.7 mg, 93%) as a colorless syrup. R_f=0.30 (benzene); $[\alpha]_D^{29}$ −2.9° (*c* 1.18); IR ($CHCl_3$) 1710 cm^{-1}; ^{1}H NMR (90 MHz) δ=0.89 (9H, s, *t*-Bu), 0.93 (3H, t, H-1, J=6.0 Hz), 1.03 (3H, t, 6-$CH_2C\underline{H}_3$, J=7.2 Hz), 1.30 (3H, d, H-8, J=6.0 Hz), 1.40 (2H, q, 6-$C\underline{H}_2CH_3$, J=7.2 Hz), 1.2—1.4 (1H, m, H-6), 2.2—2.95 (4H, m, H-2,2',4,4'), 3.63 (1H, br s, OH), 4.17 (1H, dq, H-7, J=3.0, 6.0 Hz), and 4.5—4.85 (1H, m, H-5).

Found: C, 63.75; H, 11.10%. Calcd for $C_{16}H_{34}O_3Si$: C, 63.52; H, 11.33%.

2-Pyridinyl 3,4-Bis-*O*-(*t*-butyldimethylsilyl)-2-deoxy-1-thio-α-L-fucoside (23) and β-Anomer (23-β). To a solution of 2-deoxy-L-fucose[26] (35.2 mg, 0.238 mmol) in dry THF (0.70 ml) was added *n*-Bu_3P (88.8 µl, 0.357 mmol) dropwise and PySSPy (38.5 mg, 0.357 mmol) under ice-cooling. After being stirred under ice-cooling for 2 h, *n*-Bu_3P (29.6 µl, 0.119 mmol) and PySSPy (26.2 mg, 0.119 mmol) was added to the reaction mixture and stirred at room temperature (25 °C) for 1 h. The resulting mixture was concentrated to a crude syrup (0.3 g) which was chromatographed on silica gel (27 g) with 2:1 chloroform–acetone to afford a pale yellow syrup (39 mg). To an ice-cold solution of this sample (0.495 g, 2.15 mmol) in dry CH_2Cl_2 (4.95 ml) was added successively 2,6-lutidine (1.57 ml, 8.20 mmol) and TBDMSOTf (1.27 ml, 10.9 mmol) and the mixture was stirred under ice-cooling for 0.5 h. The reaction mixture was dilluted with ethyl acetate (20 ml) and water (10 ml) and extracted with saturated aqueous NaCl (20 ml), dried, and concentrated to give a crude syrup (1.6 g) which was chromatographed on silica gel (80 g) with 10:1 hexane–acetone to afford **23** (0.773 g, 80%) and **23-β** (0.173 g, 18%) as pale yellow syrup.

23: R_f=0.54 (10:1 hexane–acetone); ^{1}H NMR (90 MHz) δ=0.93 and 0.97 (each 9H, each s, *t*-Bu×2), 1.17 (3H, d, 5-Me, J=6.2 Hz), 1.82 (1H, ddd, H-2_{eq}, J=13.0, 4.5, 1.5 Hz), 2.58 (1H, ddd, H-2_{ax}, J=15.0, 13.0, 6.0 Hz), 3.63 (1H, br, H-4), 3.85—4.30 (2H, m, H-3,5), 6.27 (1H, dd, H-1, J=6.0, 1.5 Hz), 6.9—7.15 (1H, m), 7.2—7.7 (2H, m), and 8.4—8.7 (1H, m).

23-β: R_f=0.54 (10:1 hexane–acetone); ^{1}H NMR (90 MHz) δ=0.93 and 0.97 (each 9H, each s, *t*-Bu×2), 1.28 (3H, d, 5-Me, J=6.2 Hz), 1.7—1.95 (1H, m, H-2_{eq}), 2.05—2.25 (1H, m, H-2_{ax}), 3.55—4.15 (3H, m, H-3,4,5), 5.35 (1H, dd, H-1, J=12.6, 2.3 Hz), 6.6—6.9 (1H, m), 7.0—7.35 (1H, m), 7.35—7.75 (1H, m), and 7.95—8.15 (1H, m).

3,4-Bis-*O*-(*t*-butyldimethylsilyl)-L-fucal (26a). To a solution of L-fucal (48.4 mg, 0.372 mmol) and 2,6-lutidine (0.173 ml, 1.49 mmol) in dry CH_2Cl_2 (0.484 ml) was added TBDMSOTf (0.216 ml, 1.12 mmol) under ice-cooling. The resulting suspension was stirred at the same temperature for 20 min, and then the reaction mixture was poured into cold water (5 ml) and extracted with ethyl acetate (5 ml×3). The extracts were washed with saturated aqueous NaCl (10 ml), dried, and concentrated to a crude syrup (200 mg). The syrup was chromatographed on silica gel (10 g) with 70:1 hexane–ethyl acetate to afford **26a** (68.8 mg, 51.6%) as a colorless syrup. R_f=0.65 (50:1 hexane–ethyl acetate); $[\alpha]_D^{25}$ +31° (*c* 1.00); ^{1}H NMR (90 MHz) δ=0.90 (18H, s, *t*-Bu×2), 1.30 (3H, d, 5-CH_3, J=6.0 Hz), 3.75—3.9 (1H, m, H-4), 4.07 (1H, dq, H-5, J=6.0, 1.5 Hz), 4.25—4.35 (1H, m, H-3), 4.57 (1H, dd, H-2, $J_{1,2}$=6.3, $J_{2,3}$=2.0 Hz), and 6.20 (1H, dd, H-1, $J_{1,2}$=6.3, $J_{1,3}$=1.5 Hz).

Found: C, 60.49; H, 10.56%. Calcd for $C_{18}H_{38}O_3Si_2$: C, 60.28; H, 10.68%.

(5*R*,6*R*,7*R*)-5-*O*-[2-*C*-Bromo-3,4-bis-*O*-(*t*-butyldimethylsilyl)-2-deoxy-α-L-fucosyl]-7-*O*-(*t*-butyldimethylsilyl)-6-ethyl-5,7-dihydroxy-3-octanone (27a). To a mixture of **18a** (46.0 mg, 0.156 mmol) and **26a** (273 mg, 0.760 mmol) in dry CH_3CN (0.273 ml) was added NBS (135 mg, 0.760 mmol) under ice-cooling. The reaction mixture was stirred under ice-cooling for 0.5 h and then stirred at room temperature (25 °C) for 2 h. The solution was poured into cold saturated aqueous $NaHCO_3$ (5 ml) and extracted with ethyl acetate (5 ml×3). The extracts were washed with saturated aqueous NaCl (7 ml), dried, and concentrated to give a syrup (509 mg) which was chromatographed on silica gel (80 g) with 12:1 hexane–ethyl acetate to afford **27a** (72.9 mg, 65%) and **27a-β** (23.0 mg, 16%) as a colorless syrup, respectively.

27a: R_f=0.53 (10:1 hexane–ethyl acetate); ^{1}H NMR (90 MHz) δ=0.87 and 0.97 (30H, m, *t*-Bu×3, 6-$CH_2C\underline{H}_3$), 1.01, 1.15, and 1.24 (each, 3H, each d, H-1,8, 5'-Me, each J=6.0 Hz), 1.0—1.65 (3H, m, H-6, 6-$C\underline{H}_2CH_3$), 2.3—3.15 (4H, m, H-2,4), 3.35—3.4 (1H, m, H-4'), 3.8—4.15 (3H, m, H-2',3',5'), 4.15—4.55 (2H, m, H-5,7), and 5.02 (1H, d, H-1', J=2.8 Hz).

27a-β: R_f=0.42 (10:1 hexane–ethyl acetate); ^{1}H NMR (90 MHz) δ=0.8—1.7 (42H, m, *t*-Bu×3, H-1,8,6, 5-CH_2CH_3), 2.3—3.2 (4H, m, H-2,2',4,4'), and 3.3—4.7 (7H, m, H-5,7,1',2',3',4',5').

(5*R*,6*R*,7*R*)-5-*O*-(*t*-Butyldimethylsilyl)-[3,4-bis-*O*-(*t*-butyldimethylsilyl)-2-deoxy-α-L-fucosyl]-6-ethyl-5,7-dihydroxy-3-octanone (25a). To a solution of **27a** (53.4 mg, 0.0722 mmol) in dry benzene (0.379 ml) was added *n*-Bu_3SnH (46.5 µl, 0.173 mmol) and AIBN (1.42 mg, 0.00866 mmol) and then stirred at 60 °C for 1 h under argon. The solution was cooled and concentrated to give a syrup which was chromatographed on silica gel (16 g) with 12:1:0.6 hexane–ethyl acetate–chloroform to afford **25a** (34.9 mg, 73% from **18a**) as a colorless syrup. R_f=0.30 (12:1:0.6 hexane–ethyl acetate–chloroform); $[\alpha]_D^{20}$ −46° (*c* 1.36); IR ($CHCl_3$) 1710 cm^{-1}; ^{1}H NMR (90 MHz) δ=0.75—1.7 (42H,

m, *t*-BuX3, H-1,6,8,6-CH_2CH_3, 5'-Me), 1.7—3.0 (6H, m, H-2,4,2'), 3.2—3.25 (1H, m, H-4'), 3.6—4.6 (4H, m, H-5,7,3',5'), and 4.97 (1H, m, H-1').

Found: C, 61.61; H, 10.77%. Calcd for $C_{34}H_{72}O_6Si_3$: C, 61.76; H, 10.98%.

(5*R*,6*R*,7*R*)-6-Ethyl-7-*O*-(diethylisopropylsilyl)-5,7-dihydroxy-3-octanone (18f). By the procedure described in the preparation of **18a** from **16a** via **17a**, a sample of **16f** (1.60 g, 6.19 mmol) was converted into crude **17f** (2.66 g) which was dedithioacetalized and worked up to afford a crude syrup of **18f** (1.84 g) which was chromatographed on silica gel (180 g) with 6:1 hexane–ethyl acetate to afford a pure sample of **18f** (1.54 g, 79% from **16f**) as a colorless syrup. R_f=0.16 (8:1 hexane–ethyl acetate); IR ($CHCl_3$) 1710 cm^{-1}; $[\alpha]_D^{26}$ 0°, $[\alpha]_{435}$ +3.8°, $[\alpha]_{365}$ +19.8° (*c* 1.01); ^1H NMR (90 MHz) δ=0.6—0.85 (4H, m, Si(CH_2CH_3)$_2$), 0.9—1.15 (16H, m, *i*-PrSi(CH_2CH_3)$_2$, 6-CH_2CH_3), 1.30 (3H, d, H-8, *J*=6.0 Hz), 1.2—1.75 (3H, m, H-6, 6-CH_2CH_3), 2.2—2.9 (4H, m, H-2,2',4,4'), 3.63 (1H, s, OH), 4.0—4.35 (1H, m, H-7), and 4.6—4.75 (1H, m, H-5).

Found: *m/z* 273.1856. Calcd for $C_{14}H_{29}O_3Si$: M−*i*-Pr, 273.1884. Found: *m/z* 287.2010. Calcd for $C_{15}H_{31}O_3Si$: M−Et, 287.2040.

3,4-Bis-*O*-(isopropyldimethylsilyl)-L-fucal (26c). To a solution of L-fucal (500 mg, 3.84 mmol) and imidazole (654 mg, 9.60 mmol) in dry DMF (7.5 ml) was added IPDMS-Cl (1.42 ml, 9.60 mmol) under ice-cooling. The resulting homogeneous solution was kept at room temperature for 2 h, and then the reaction mixture was poured into cold water (10 ml) and extracted with ethyl acetate (10 mlX3). The extracts were washed with saturated aqueous NaCl (15 ml), dried, and concentrated to a crude syrup (1.92 g). The syrup was chromatographed on silica gel (96 g) with 40:1 hexane–ethyl acetate to afford **26c** (820 mg, 65%) as a colorless syrup. R_f=0.57 (30:1 hexane–ethyl acetate); $[\alpha]_D^{26}$ +31° (*c* 1.07, acetone); ^1H NMR (90 MHz) δ=0.97 (14H, s, *i*-PrX2), 1.28 (3H, d, 5-Me, *J*=6.3 Hz), 3.70 (1H, ddd, H-4, $J_{4,2}$=2.0, $J_{4,3}$=3.6, $J_{4,5}$=2.0 Hz), 4.02 (1H, dq, H-5, *J*=6.3, 2.0 Hz), 4.3—4.5 (1H, m, H-3), 4.50 (1H, ddd, H-2, $J_{2,1}$=6.3, $J_{2,3}$=2.0, 2.0 Hz), and 6.23 (1H, dd, H-1, $J_{1,3}$=1.5 Hz).

Found: *m/z* 330.2018. Calcd for $C_{16}H_{34}O_3Si_2$: M, 330.2044.

(5*R*,6*R*,7*R*)-5-*O*-[2-Deoxy-3,4-bis-*O*-(isopropyldimethylsilyl)-α-L-fucosyl]-6-ethyl-7-*O*-(diethylisopropylsilyl)-5,7-dihydroxy-3-octanone (25f). Method A: By the procedure described in the preparation of **27a**, glycosidation of **18f** (1.04 g, 3.29 mmol) with **26c** (3.80 g, 11.5 mmol) and NBS (2.05 g, 11.5 mmol) afforded a crude sample of **27f** (983 mg) which was contaminated by a considerable amount of by-product, and a pure sample of the β-anomer of **27f** (501 mg, 21%) as colorless syrup. To a solution of the crude sample of **27f** (938 mg) in dry benzene (9.38 ml) was added *n*-Bu_3SnH (834 μl, 3.10 mmol) and AIBN (25.4 mg, 0.155 mmol) and then stirred at 60 °C for 0.5 h under argon. The solution was cooled and concentrated to give a syrup (2.04 g) which was chromatographed on silica gel (300 g) with 3:1:0.1 hexane–chloroform–ethyl acetate to afford **25f** (630 mg, 30% from **18f**) as a colorless syrup. R_f=0.39 (10:1 hexane–ethyl acetate); $[\alpha]_D^{20}$ −46° (*c* 1.36); IR ($CHCl_3$) 1710 cm^{-1}; ^1H NMR (250 MHz) δ=0.04, 0.05, 0.055, 0.07 (each 3H, each s, SiMeX4), 0.55—0.7 (4H, m, Si(CH_2CH_3)$_2$), 0.8—1.3 (7H, m, 6-CH_2CH_3, H-6, Me), 1.13 (3H, d, Me, *J*=6.8 Hz), 1.23 (3H, d, Me, *J*=6.5 Hz), 1.35—1.55 (3H, m, 6-CH_2CH_3, H-2'$_{eq}$), 1.99 (1H, ddd, H-2'$_{ax}$, *J*=12.8, 11.5, 3.8 Hz), 2.43 (2H, dq, H-2X2, *J*=7.5 and 2.3 Hz), 2.54 (1H, dd, H-4$_{AorB}$, *J*=16.0, 4.5 Hz), 2.82 (1H, dd, H-4$_{AorB}$, *J*=16.0, 8.8 Hz), 3.5—3.55 (1H, m, H-4'), 3.84 (1H, dq, H-5', *J*=6.5, 0.3 Hz), 3.93 (1H, ddd, H-3', *J*=12.5, 4.5, 2.5 Hz), 4.01 (1H, dq, H-7, *J*=7.3, 3.3 Hz), 4.18 (1H, ddd, H-5, *J*=4.5, 4.3, 8.8 Hz), and 4.94 (1H, dd, H-1', *J*=3.3, 1.2 Hz).

Found: C, 61.55; H, 10.61%. Calcd for $C_{33}H_{70}O_6Si_3$: C, 61.25; H, 10.90%.

Method B: To a mixture of **18f** (498 mg, 1.57 mmol), **26c** (1.82 g, 4.71 mmol), 4A Molecular Sieves (0.91 g), and dry CH_2Cl_2 (28.1 ml) was added *dl*-10-camphorsulfonic acid (128 mg, 0.471 mmol) under ice-cooling. After being stirred under ice-cooling for 1 h, *dl*-10-camphorsulfonic acid (25.6 mg, 0.0942 mmol) was added to the reaction mixture and stirred at the same temperature for 1 h. To the reaction mixture was then added dropwise triethylamine (76.8 μl) and water (30 ml) and then the mixture was extracted with ethyl acetate (30 mlX1 and 15 mlX2). The combined extracts were washed with saturated aqueous NaCl (30 ml), dried, and concentrated to give a crude syrup (2.45 g) which was chromatographed on silica gel (270 g) with 3:1:0.1 hexane–chloroform–ethyl acetate to afford **25f** (819 mg, 80%) as a colorless syrup.

(2*S*,4*R*,5*R*,6*R*)-4-*O*-(2-Deoxy-α-L-fucosyl)-2,5-diethyl-3,4,5,6-tetrahydro-2,4-hydroxy-6-methyl-2*H*-pyran (5). A solution of **25f** (63.4 mg, 0.0979 mmol) in 3:1:3 acetic acid–aqueous 1% HF·KF–THF (1.9 ml) was stirred at 30 °C for 14 h. The reaction mixture was concentrated to afford crude syrup which was chromatographed on silica gel (9 g) with 6:1 chloroform–methanol to afford **5** (19.9 mg, 64%) as colorless crystals. R_f=0.30 (6:1 chloroform–methanol); mp 55—62 °C (dichloromethane–hexane); $[\alpha]_D^{32}$ −96.1° (*c* 1.30); ^1H NMR (250 MHz) δ=0.88 (3H, t, 2-CH_2CH_3, *J*=7.5 Hz), 0.95 (3H, t, 5-CH_2CH_3, *J*=7.3 Hz), 1.15—1.3 (1H, m, H-5), 1.19 (3H, d, Me, *J*=6.3 Hz), 1.27 (3H, d, Me, *J*=6.5 Hz), 1.35—1.55 (2H, m, 5-CH_2CH_3), 1.55—1.70 (1H, m, H-2'$_{eq}$), 1.63 (2H, q, 2-CH_2CH_3, *J*=7.5 Hz), 1.75—1.9 (2H, m, H-3$_{AorB}$, H-2'$_{ax}$), 2.18 (1H, dd, H-3$_{AorB}$, *J*=12.5, 5.0 Hz), 3.6—3.7 (1H, br, H-4'), 3.8—4.1 (4H, m, H-4,6,3',5'), and 5.06 (1H, dd, H-1', *J*=2.8, 2.5 Hz).

Found: C, 60.07; H, 9.23%. Calcd for $C_{16}H_{30}O_6$: C, 60.36; H, 9.50%.

Preparation of DEIPS-Cl. To a solution of Li (1.90 g) in petroleum ether (130 ml) was added slowly a solution of *i*-PrCl (11.9 ml, 130 mmol) in dry petroleum ether (38 ml). The mixture was irradiated in the sonicator (65 W, 48 kHz) at 30—50 °C for 45 min to afford about 0.53 M *i*-PrLi–petroleum ether. To this 0.53 M *i*-PrLi–petroleum ether (120 ml) was added Et_2SiCl_2 (9.91 ml, 63.1 mmol) and stirred at 50 °C for 1 h. The reaction mixture was cooled to room temperature and LiCl was filtered off under argon. The filtrate was distilled at atmospheric pressure to remove solvent and then the residue distilled to give DEIPS-Cl (8.14 g, 92%) as a colorless liquid. Bp_{32} 73—74.5 °C.

Preparation of DPIPS-Cl. This experiment was carried out under the conditions described in the preparation DEIPS-Cl. DPIPS-Cl (3.12 g, 75%) was obtained as a colorless liquid from *n*-Pr_2SiCl_2 (4.14 ml). Bp_{26} 96.5—97.0 °C.

Preparation of DIPMS-Cl. To a suspension of Mg (3.97 g, 0.164 mmol) in dry THF (127 ml) was added dropwise $MeSiCl_3$ (30.0 ml, 0.256 mol) and *i*-PrCl (11.6 ml,

0.128 mol) and the reaction mixture was then refluxed for 14 h. The mixture was cooled to room temperature and the solvent was removed by distillation under atmospheric pressure. To the residue was added dry ether (150 ml), and $MgCl_2$ was filtered off under argon. The filtrate was distilled to give *i*-Pr(Me)$SiCl_2$ (5.17 g, bp 88—90 °C) as a colorless liquid. Next experiment to introduce the *i*-Pr group to this sample was carried out under the conditions described in the preparation DEIPS-Cl. DIPMS-Cl (2.99 g, 11%) was given as a colorless liquid. Bp 141—143 °C.

(2*R*,3*R*,4*S*,5*S*,6*R*)-4-Methyl-6-(1,3-dithian-2-yl)-2,3,5-heptanetriol (33). A solution of **32** (416 mg, 1.30 mmol) in aqueous 50% acetic acid (8.31 ml) was stirred at 50 °C for 1 h and then concentrated to give a syrup which was chromatographed on silica gel (20 g) with 10:1 chloroform–methanol to afford **33** (327 mg, 90%) as colorless needles. R_f=0.43 (10:1 chloroform–methanol); mp 134.9—135.2 °C (acetone–hexane); $[\alpha]_D^{21}$ 0°, $[\alpha]_{405}$ +1.9°, $[\alpha]_{315}$ +3.7°, (*c* 0.67); ^{1}H NMR (90 MHz, CD_3OD) δ=0.83 and 1.03 (each 3H, each d, Me×2, each *J*=7.2 Hz), 1.05—1.2 (3H, m, Me), 1.45—2.35 (4H, m, H-4,6, $SCH_2C\underline{H}_2$), 2.65—3.0 (4H, m, $SC\underline{H}_2CH_2C\underline{H}_2S$), 3.55—4.1 (3H, m, H-2,3,5), and 4.17 (1H, d, H-2′, *J*=8.4 Hz).

Found: C, 51.60; H, 8.41; S, 22.99%. Calcd for $C_{12}H_{24}O_3S_2$: C, 51.39; H, 8.63; S, 22.87%.

Methyl (6*S*,7*S*,8*R*)-(2*E*,4*E*)-7-Hydroxy-6-methyl-8-(1,3-dithian-2-yl)-2,4-nonadienoate (35) and (4*Z*)-Isomer (36). To a suspension of **33** (263 mg, 9.38 mmol) and potassium acetate (463 mg, 4.69 mmol) in dry CH_3CN (21.8 ml) was added lead tetraacetate (462 mg, 0.938 mmol) at −25 °C and then stirred for 3 min. The resulting mixture was chromatographed on Florisil (10 g) with ether to afford a crude sample of **34** (208 mg) which was suitable for the next synthesis. A mixture of the crude sample of **34** (319 mg) and [(2*E*)-3-methoxycarbonyl-2-propenylidene]triphenylphosphorane (980 mg, 2.72 mmol) in dry toluene (15.9 ml) was stirred at 80 °C for 0.5 h. The reaction mixture was concentrated and the residue (1.42 g) was chromatographed on silica gel (210 g) with 9:1 dichloromethane–ethyl acetate to afford **35** (232 mg, 51% from **33**) and **36** (93.4 mg, 21% from **33**) as colorless syrups.

35: R_f=0.51 (8:1 dichloromethane–ethyl acetate); $[\alpha]_D^{22}$ −22° (*c* 1.06); IR ($CHCl_3$) 1705 cm^{-1}; UV (EtOH) λ_{max} nm (log ε) 261 (4.39); ^{1}H NMR (90 MHz) δ=1.03 and 1.13 (each 3H, each d, Me×2, each *J*=7.2 Hz), 1.85—2.25 (4H, m, H-8, $SCH_2C\underline{H}_2$, OH), 2.30—2.65 (1H, m, H-6), 2.7—3.05 (4H, m, $SC\underline{H}_2CH_2C\underline{H}_2S$), 3.65—3.95 (1H, m, H-7), 3.77 (3H, s, COOMe), 4.17 (1H, d, H-2′, *J*=7.5 Hz), 5.83 (1H, d, H-2, *J*=15.3 Hz), 6.1—6.35 (2H, m, H-4,5), and 7.15—7.50 (1H, m, H-3).

Found: C, 56.71; H, 7.55; S, 20.08%. Calcd for $C_{15}H_{24}O_3S_2$: C, 56.93; H, 7.64; S, 20.26%.

36: R_f=0.56 (8:1 dichloromethane–ethyl acetate); ^{1}H NMR (90 MHz) δ=1.02 and 1.17 (each 3H, each d, Me×2, each *J*=7.2 Hz), 1.7—2.65 (5H, m, H-6,8, $SCH_2C\underline{H}_2$, OH), 2.7—3.05 (4H, m, $SC\underline{H}_2CH_2C\underline{H}_2S$), 3.75 (3H, s, COOMe), 4.05—4.3 (2H, m, H-8,2′), 5.7—6.45 (2H, m, H-4,5), 5.91 (1H, d, H-2, *J*=15.3 Hz), and 7.65 (1H, dd, H-3, $J_{2,3}$=15.3 and $J_{3,4}$=12.0 Hz).

Isomerisation of 36 to 35. A solution of **36** (2.11 g, 6.67 mmol) and iodine (8.4 mg) in dry benzene (51.3 ml) was stirred at room temperature (25 °C) in daylight for about a month. The reaction mixture was then washed with a saturated aqueous sodium thiosulfate solution (50 ml) and extracted with ethyl acetate (30 ml×3). The extracts were washed with saturated aqueous NaCl (40 ml), dried, and then concentrated to a crude syrup which was chromatographed on silica gel (300 g) with 9:1 dichloromethane–ethyl acetate to afford the (*E*,*E*)-diene **35** (790 mg, 37.4%) and the starting diene **36** (570 mg, 27%).

(6*S*,7*S*,8*R*)-7-Hydroxy-6-methyl-8-(1,3-dithian-2-yl)-2,4-nonadienoic Acid (4). To a solution of the methyl ester **35** (232 mg, 0.733 mmol) in 50% THF–H_2O (8.81 ml) was added 0.2 M LiOH/50% THF–H_2O (6.41 ml, 1.28 mmol) and the mixture was kept at 24 °C for 7 h. The solution was then neutralized with CG-50 resin (H^+ type) under ice-cooling, and filtered. The filterate and methanolic washings were combined and concentrated to give a crude syrup (0.5 g) which was chromatographed on silica gel (20 g) with 10:1:0.2 chloroform–acetone–acetic acid to afford **4** (220 mg, 100%) as a white form. R_f=0.26 (10:1:0.1 chloroform–acetone–acetic acid); $[\alpha]_D^{20}$ −31° (*c* 1.04); IR ($CHCl_3$) 1640 and 1685 cm^{-1}; UV (EtOH) λ_{max} nm (log ε) 254 (4.28); ^{1}H NMR (90 MHz) δ=1.03 and 1.12 (each 3H, each d, Me×2, each *J*=7.2 Hz), 1.75—2.2 (3H, m, H-8, $SCH_2C\underline{H}_2$), 2.3—2.65 (1H, m, H-6), 2.7—3.0 (4H, m, $SC\underline{H}_2CH_2C\underline{H}_2S$), 3.87 (1H, dd, H-7, *J*=8.4, 2.8 Hz), 4.18 (1H, d, H-2′, *J*=7.5 Hz), 5.85 (1H, d, H-2, *J*=15.3 Hz), 6.1—6.4 (2H, m, H-4,5), 6.4—6.95 (2H, br, OH, COOH), and 7.15—7.55 (1H, m, H-3).

Found: C, 55.86; H, 7.23; S, 20.96%. Calcd for $C_{14}H_{22}O_3S_2$: C, 55.60; H, 7.33; S, 21.20%.

(7*S*,8*S*,15*S*,16*S*:3*E*,5*E*,11*E*,13*E*)-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 (37). Method A: A solution of **4** (208 mg, 0.688 mmol) in THF (2.98 ml) was treated with triethylamine (115 μl, 0.826 mmol) and 2,4,6-trichlorobenzoyl chloride (185 mg, 0.757 mmol) and the mixture was then stirred at room temperature for 2 h. The triethylamine hydrochloride was then filtered off and the filtrate diluted with dry toluene (344 ml). This solution was then added at 35 °C over a period of 2 h to a solution of 4-(dimethylamino)pyridine (505 mg, 4.13 mmol) in dry toluene (68.8 ml). After the addition had completed, the mixture was stirred at 35 °C for an additional 2.5 h, and then diluted with ether (300 ml). The mixture was washed with saturated aqueous citric acid (300 ml), saturated aqueous $NaHCO_3$ (300 ml), and finally saturated aqueous NaCl (300 ml). The organic layer was dried and concentrated to a syrup (290 mg) which was chromatographed on silica gel (43 g) with 5:1 dichloromethane–ethyl acetate to afford a pure sample of **37** (57.9 mg, 31%) as colorless crystals. R_f=0.44 (2:1 hexane–acetone); mp 262.0—263.5 °C (dichloromethane–hexane); $[\alpha]_D^{30}$ +75° (*c* 1.16); IR (KBr) 1640 and 1710 cm^{-1}; ^{1}H NMR (250 MHz) δ=1.07 and 1.19 (each 3H×2, each d, 7-Me, 15-Me, 1′-Me×2, each *J*=7.2 Hz), 1.86 (1H×2, ddq, H-1′×2, $J_{1',Me}=J_{1',2'}$=7.2 and $J_{1',8\text{or}16}$=10.6 Hz), 2.0—2.3 (2H×2, m, $SCH_2C\underline{H}_2$×2), 2.44 (1H×2, ddq, H-7,15, *J*=7.2, 1.1, 11.4 Hz), 2.75—2.95 (4H×2, m, $SC\underline{H}_2CH_2$-$C\underline{H}_2S$×2), 4.02 (1H×2, d, H-2″×2, *J*=7.2 Hz), 5.18 (1H×2, dd, H-8,16, *J*=10.6, 1.1 Hz), 5.60 (1H×2, d, H-3,11, *J*=15.2 Hz), 5.62 (1H×2, dd, H-6,14, *J*=9.5, 15.0 Hz), 6.00 (1H×2, dd, H-5,13, *J*=15.0, 11.4 Hz), and 6.98 (1H×2, dd, H-4,12, *J*=11.4, 15.2 Hz); MS *m/z* 568 (M^+).

Found: C, 58.83; H, 6.82; S, 22.80%. Calcd for $C_{28}H_{40}O_4S_4$:

C, 59.12; H, 7.09; S, 22.55%.

Method B: To a solution of **4** (48.2 mg, 0.159 mmol) in dry CH_3CN (12.7 ml) was added triethylamine (0.176 ml, 1.28 mmol) and the mixture was added to a solution of 2-chloro-1-methylpyridinium iodide (163 mg, 0.638 mmol) in dry CH_3CN (16 ml) for 15 min. After being stirred at 25 °C, the reaction mixture was concentrated to give a syrup which was subsequently chromatographed on silica gel (20 g) with 2:1 hexane–acetone to afford **38** (40.0 mg, 85.5%) as a colorless syrup. R_f=0.30 (2:1 hexane–acetone); IR (CH_3Cl_3) 1710 and 1765 cm^{-1}; To a solution of **38** (9.60 mg, 0.0164 mmol) in dry CH_3CN (0.192 ml) was added 4-(dimethylamino)pyridine (5.20 mg, 0.00425 mmol) and the reaction mixture was stirred at room temperature (26 °C) for 30 min. Then the mixture was poured into cold water (1 ml) and extracted with ethyl acetate (0.5 ml×3) and the combined extracts were washed with saturated aqueous NaCl (1 ml), dried, and concentrated. The residue was chromatographed on silica gel (1 g) with 3:1 hexane–acetone to afford **37** (0.5 mg, 11% from **38**).

(7*S*,9*S*,15*S*,16*S*:3*E*,5*E*,11*E*,13*E*)-8,16-Bis[(1*R*)-1-formylethyl]-7,15-dimethyl-1,9-dioxa-3,5,11,13-cyclohexadecatetraene-2,10-dione (3). To a mixture of **37** (30.6 mg, 0.159 mmol) and mercury(II) oxide (51.7 mg, 2.39 mmol) in 4:7 CH_2Cl_2–80% aqueous acetone was added mercury(II) chloride (64.9 mg, 2.39 mmol) at room temperature. The mixture was ultrasonificated in the sonicator (65 W, 48 kHz) at 30—50 °C for 8 h, cooled, and filtered through a Celite. The filter cake was washed with acetone, and the filtrate and the washing were combined. After the subsequent removal of the acetone by concentration, to the aqueous residue was added aqueous 10% KI until orange color disappeared and extracted with chloroform (30 ml×3). The extracts were washed with saturated aqueous NaCl (20 ml), dried, and concentrated to give crude crystals which was chromatographed on silica gel (10 g) with 5:1 chloroform–ethyl acetate to afford the pure sample of **3** (43.1 mg, 70%) as colorless crystals. R_f=0.19 (10:1 chloroform–ethyl acetate); mp 152—156 °C (dichloromethane–hexane); $[\alpha]_D^{25}$ +46.8° (*c* 0.35, MeOH after 45 min); IR (KBr) 1710 cm^{-1}; UV (EtOH) λ_{max} nm (log ε) 253 (4.74); ^1H NMR (90 MHz) δ=1.10 and 1.19 (each 3H×2, each d, 7-Me, 15-Me, 2′-Me×2, each *J*=7.2 Hz), 2.3—2.9 (2H×2, m, H-7,15,2′×2), 5.39 (1H×2, dd, H-8, 16, *J*=10.8, 2.8 Hz), 5.56 (1H×2, d, H-3,11, *J*=15.6 Hz), 6.07 (1H×2, dd, H-5,13, *J*=15.0, 10.8 Hz), 6.98 (1H×2, dd, H-4,12, *J*=15.6, 10.8 Hz), and 9.69 (1H×2, s, CHO×2).

Found: C, 67.06; H, 7.30%. Calcd for $C_{22}H_{28}O_6 \cdot 1/4H_2O$: C, 67.24; H, 7.31%.

After drying the crystalline **3** over CaH_2 at 65 °C for 14 h gave an anhydrous sample of **3** as an orange-red colored solid whose ^1H NMR spectra was superimposesable to that of the crystalline sample of **3** except for the signals ascribed to water.

Found: C, 67.98; H, 7.35%. Calcd for $C_{22}H_{28}O_6$: C, 68.02; H, 7.26%.

(7*S*,8*S*,15*S*,16*S*:3*E*,5*E*,11*E*,13*E*)-8,16-Bis[(1*S*,2*R*,3*S*,6*R*,7*R*,8*R*)-6-*O*-[2-deoxy-3,4-bis-*O*-(isopropyldimethylsilyl)-α-L-fucosyl]-7-ethyl-8-*O*-(diethylisopropylsilyl)-2,6,8-trihydroxy-1,3-dimethyl-4-oxononyl]-7,15-dimethyl-1,9-dioxa-3,5,11,13-cyclohexadecatetraene-2,10-dione (43), Isomers 44 and 45. (A) With *n*-Bu_2BOTf: To a solution of *n*-Bu_2OTf (24.1 μl, 0.0958 mmol) and *N*,*N*-diisopropylethylamine (16.7 μl, 0.0958 mmol) in dry ether (0.192 mmol) was added dropwise a solution of **25f** (61.4 mg, 0.0958 mmol) in dry ether (0.012 ml) at −78 °C under argon with stirring. After being stirred for 30 min, the mixture was added dropwise to a solution of **3** (9.30 mg, 0.0239 mmol) in dry THF (0.186 ml) at −30 °C with stirring and then stirred at −10 °C for 2 h. To the reaction mixture was added pH 7 phosphate buffer[47] (0.5 ml) at −10 °C, and the mixture was stirred at 25 °C for 3 min, and then extracted with ether (0.5 ml×3). The extracts were washed with saturated aqueous NaCl (1.5 ml), dried, and concentrated to give a syrup (80.0 mg) which was purified by flash chlomatography on silica gel (20 g) with 6:1 benzene–ethyl acetate and then 3.5:1 benzene–ethyl acetate to afford **43** (5.1 mg, 12.7%), **44** (9.8 mg, 24.3%), and **45** (10.6 mg, 26.3%) as a colorless glassy solid respectively and recovered **25f** (22.1 mg, 36.0%). **43**: R_f=0.10 (6:1 benzene–ethyl acetate); $[\alpha]_D^{20}$ −9.3° (*c* 0.41); ^1H NMR (400 MHz) δ=0.03 (6H, s, SiMe×2), 0.035 (6H, s, SiMe×2), 0.04 (6H, s, SiMe×2), 0.06 (6H, s, SiMe×2), 0.55—0.70 (8H, m, $Si(C\underline{H}_2CH_3)_2$×2), 0.80—1.30 (62H, m, $Si(CH_2C\underline{H}_3)_2$×2, *i*-Pr Si×6,7′-$CH_2C\underline{H}_3$×2, H-7′×2), 0.87 (6H, d, Me×2, *J*=7.2 Hz), 1.04 (6H, d, Me×2, *J*=7.2 Hz), 1.11 (6H, d, Me×2, *J*=6.8 Hz), 1.12 (6H, d, Me×2, *J*=6.8 Hz), 1.26 (6H, d, Me×2, *J*=6.4 Hz), 1.35—1.45 (4H, m, 7′-$C\underline{H}_2CH_3$), 1.45—1.55 (2H, m, H-2″$_{eq}$×2), 1.85—1.95 (2H, m, H-1′×2), 1.97 (2H, ddd, H-2′$_{ax}$×2, *J*=12.8, 12.0, 3.8 Hz), 2.45—2.65 (6H, m, H-5′$_{AorB}$×2, H-3′×2, H-7,15), 2.99 (2H, dd, H-5′$_{AorB}$×2, *J*=16.4, 8.8 Hz), 3.36 (2H, d, OH×2, *J*=3.2 Hz), 3.50—3.55 (2H, br, H-4″×2), 3.72 (2H, ddd, H-2′×2, *J*=9.2, 3.2, 3.2 Hz), 3.38 (2H, q, H-5″×2, *J*=6.2 Hz), 3.90 (2H, ddd, H-3″×2, *J*=12.0, 4.0, 2.0 Hz), 4.00 (2H, dq, H-8′, *J*=6.8, 3.6 Hz), 4.15—4.25 (2H, m, H-6′×2), 4.91 (2H, dd, H-1″×2, *J*=3.6, 0.8 Hz), 5.04 (2H, dd, H-8,16, *J*=10.4, 1.2 Hz), 5.62 (2H, d, H-3,11, *J*=15.6 Hz), 5.65 (2H, dd, H-6,14, *J*=9.5, 15.0 Hz), 6.07 (2H, dd, H-5,13, *J*=15.0, 11.4 Hz), 6.97 (2H, dd, H-4,12, *J*=11.4, 15.6 Hz). **44:** R_f=0.31 (6:1 benzene–ethyl acetate); $[\alpha]_D^{20}$ −13.3° (*c* 1.05); ^1H NMR (400 MHz) δ=0.021 (3H, s, SiMe), 0.027 (3H, s, SiMe), 0.028 (3H, s, SiMe), 0.035 (6H, s, SiMe×2), 0.04 (6H, s, SiMe×2), 0.06 (3H, s, SiMe), 0.55—0.70 (8H, m, $Si(C\underline{H}_2CH_3)_2$×2), 0.80—1.30 (71H, m, $Si(CH_2C\underline{H}_3)_2$, *i*-Pr Si×6, Me×3, 7′-$CH_2C\underline{H}_3$×2, H-7′×2), 0.86 (3H, d, Me, *J*=7.2 Hz), 1.03 (3H, d, Me, *J*=7.2 Hz), 1.05—1.15 (9H, m, Me×3), 1.19 (3H, d, Me, *J*=6.4 Hz), 1.26 (3H, d, Me, *J*=6.4 Hz), 1.35—1.55 (6H, m, 7′-$C\underline{H}_2CH_3$×2, H-2″$_{eq}$×2), 1.85—2.05 (4H, m, H-1′×2, H-2″$_{ax}$×2), 2.45—2.65 (4H, m, H-5′$_{(16)AorB}$, H-7, 15, H-3′$_{(16)}$), 2.66 (1H, dd, H-5′$_{(8)AorB}$, *J*=16.4, 3.6 Hz), 2.82 (1H, dd, H-5′$_{(8)AorB}$, *J*=16.4, 8.8 Hz), 2.96 (1H, d, OH$_{(8)}$, *J*=3.2 Hz), 3.00 (1H, dd, H-5′$_{(16)AorB}$, *J*=16.4, 8.8 Hz), 3.05 (1H, dq, H-3′$_{(8)}$, *J*=7.2, 1.6 Hz), 3.32 (1H, d, OH$_{(16)}$, *J*=3.2 Hz), 3.45—3.50 (1H, br, H-4″$_{(8)}$), 3.50—3.55 (1H, br, H-4″$_{(16)}$), 3.65—3.75 (2H, m, H-2′$_{(8)\text{ and }(16)}$), 3.75—3.85 (2H, m, H-5″$_{(8)\text{ and }(16)}$), 3.85—3.95 (2H, m, H-3″$_{(8)\text{ and }(16)}$), 3.95—4.05 (2H, m, H-8′$_{(8)\text{ and }(16)}$), 4.15—4.25 (2H, m, H-6′$_{(8)\text{ and }(16)}$), 4.69 (1H, dd, H-8, *J*=10.4, 1.2 Hz), 4.82 (1H, dd, H-1″$_{(8)}$, *J*=3.0, 0.8 Hz), 4.92 (1H, dd, H-1″$_{(16)}$, *J*=3.0, 0.8 Hz), 5.09 (1H, dd, H-16, *J*=10.4, 1.2 Hz), 5.59 (1H, d, H-3, *J*=16.0 Hz), 5.60 (1H, dd, H-6, *J*=15.2, 9.5 Hz), 5.62 (1H, d, H-11, *J*=15.6 Hz), 5.64 (1H, dd, H-14, *J*=15.0, 9.5 Hz), 6.044 (1H, dd, H-5, *J*=15.2, 12.0 Hz), 6.047 (1H, dd, H-13, *J*=15.0, 11.6 Hz), 6.91 (1H, dd, H-4, 16.0, 12.0 Hz), 6.95 (1H, dd, H-12, *J*=15.0, 11.6 Hz).

Found: C, 62.91; H, 9.70%. Calcd for $C_{88}H_{168}O_{18}Si_6$: C,

62.81; H, 10.06%.

45: R_f=0.46 (6:1 benzene–ethyl acetate); $[\alpha]_D^{20}$ −22.4° (*c* 0.98); ^{1}H NMR (400 MHz) δ=0.01 (6H, s, SiMe×2), 0.02 (6H, s, SiMe×2), 0.035 (6H, s, SiMe×2), 0.04 (6H, s, SiMe×2), 0.55—0.70 (8H, m, Si(CH_2CH_3)$_2$×2), 0.80—1.30 (74H, m, Si(CH_2CH_3)$_2$×2, *i*-PrSi×6, Me×4, 7′-CH_2CH_3×2, H-7′×2), 1.11 (12H, d, Me×4, *J*=6.8 Hz), 1.19 (6H, d, Me×2, *J*=6.4 Hz), 1.35—1.55 (6H, m, 7′-CH_2CH_3×2, H-2″$_{eq}$×2), 1.90—2.00 (2H, m, H-1′), 1.92 (2H, ddd, H-2″$_{ax}$×2, *J*=12.8, 12.0, 3.8 Hz), 2.45—2.60 (2H, m, H-7,15), 2.66 (2H, dd, H-5′$_{AorB}$×2), 2.82 (2H, dd, H-5′$_{AorB}$×2), 2.94 (2H, d, OH×2, *J*=3.2 Hz), 3.05 (2H, dq, H-3′×2, *J*=7.2, 1.6 Hz), 3.45—3.50 (2H, br, H-4″×2), 3.73 (2H, ddd, H-2′×2, *J*=9.2, 3.2, 3.2 Hz), 3.79 (2H, q, H-5″×2, *J*=6.8 Hz), 3.88 (2H, ddd, H-3″×2, *J*=12.0, 4.0, 2.0 Hz), 3.99 (2H, dq, H-8′×2, *J*=6.8, 3.6 Hz), 4.20—4.25 (2H, m, H-6′×2), 4.72 (2H, dd, H-8,16, *J*=10.4, 1.2 Hz), 4.83 (2H, dd, H-1″×2, *J*=3.0, 0.8 Hz), 5.59 (2H, d, H-3,11, *J*=16.0 Hz), 5.60 (2H, dd, H-6,14, *J*=15.2, 10.0 Hz), 6.04 (2H, dd, H-5,13, *J*=15.2, 12.0 Hz), 6.91 (2H, dd, H-4,12, *J*=16.0, 12.0 Hz).

Found: C, 63.10; H, 9.99%. Calcd for $C_{88}H_{168}O_{18}Si_6$: C, 62.81; H, 10.06%.

In the case of the aldol coupling of **25f** and **3** in the presence of $ZnCl_2$, 4 molar equivalents of $ZnCl_2$ was first added to the THF solution of **3** and then to this mixture was added the ethereal boron enolate mixture prepared from **25f** with *n*-Bu_2BOTf by the aforesaid procedure.

(B) With Sn(OTf)$_2$: To a suspension of Sn(OTf)$_2$ (25.8 mg, 0.0618 mmol) and 1-ethylpiperidine (0.0093 ml, 0.060 mmol) in dry CH_2Cl_2 (0.124 ml) was added dropwise **25f** (39.6 mg, 0.0618 mmol) in CH_2Cl_2 (0.124 ml) at −78 °C under argon with stirring. After the mixture was stirred for 30 min, the solution was added dropwise to a solution of **3** (6.0 mg, 0.0155 mmol) in dry CH_2Cl_2 (0.060 ml) at −78 °C and then stirred at −78 °C for 30 min and at −78 °C→−10 °C for 2.5 h. To the reaction mixture was added pH 7 posphate buffer (0.5 ml) at −10 °C and then stirred at room temperature for 3 min, and extracted with CH_2Cl_2 (0.5 ml×3). The extracts were washed with saturated aqueous NaCl (1 ml), dried, and concentrated to give a crude syrup which was purified by flash chromatography on silica gel (10 g) with 6:1 benzene–ethyl acetate and 3.5:1 benzene–ethyl acetate to afford **43** (1.7 mg, 6.5%), **44** (5.4 mg, 20.8%), and **45** (7.2 mg, 27.7%) and recoverd **25f** (17.6 mg, 44.4%).

(C) With LiN(TMS)$_2$: To a solution of **25f** (24.6 mg, 0.0383 mmol) in dry THF (0.0766 ml) was added dropwise 1 M LiN(TMS)$_2$–THF (0.0383 ml, 0.0383 mmol) at −78 °C under argon with stirring. After the mixture was stirred for 30 min, the solution was added dropwise to a solution of **3** (6.2 mg, 0.0160 mmol) in dry THF (0.124 ml) at −78 °C and then stirred for 2 h at the same temperature. To the reaction mixture was added saturated aqueous NH_4Cl (0.4 ml), warmed to room temperature and extracted with ether (0.5 ml×3). The extracts were washed with saturated aqueous NaCl (1 ml), dried, and concentrated to give a crude syrup (30 mg) which was chromatographed on silica gel (10 g) with 4:1 benzene–ethyl acetate to afford fraction A (**25f**, **44**, **45**, 12.4 mg), fraction B (**43**, **3**, 2.0 mg), and **3** (1.7 mg, 6.3%). Further, fraction A was purified by flash chromatography on silica gel (2.5 g) with benzene–ethyl acetate to afford **25f** (8.3 mg, 33.7%), **45** (2.4 mg, 8.9%), and **44** (1.7 mg, 6.3%). Fraction B was purified by flash chromatography on silica gel (1 g) with 3:1 benzene–ethyl acetate to afford **43** (1.4 mg, 5.2%).

Elaiophylin (1). A solution of **43** (9.5 mg, 0.00565 mmol) in 3:1:3 acetic acid–aqueous 1% HF·KF–THF (0.380 ml) was stirred at 30 °C for 18 h. To the reaction mixture was added water (0.5 ml) and chloroform (0.5 ml) and then extracted with chloroform (0.5 ml×3). The extracts were washed with saturated aqueous NaCl (1 ml), dried, and concentrated to crude crystals (10.0 mg) which were purified by flash chlomatography on silica gel (2.5 g) with 6:1 chloroform–methanol to afford **1** (1.3 mg, 22.4%) as colorless crystals. R_f=0.31 (6:1 chloroform–methanol); $[\alpha]_D^{20}$ −53° (*c* 0.26, MeOH); mp 179—182 °C (AcOEt); mixture mp 179—182 °C; The ^{1}H NMR spectra (400 MHz, 5:1 $CDCl_3$–CD_3OD) was identical with that of the authentic sample of azalomycin B.

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