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An Efficient Synthesis of Sulfobacin A (Flavocristamide B), Sulfobacin B, and Flavocristamide A

Takayuki Shioiri* and Naoko Irako

Faculty of Pharmaceutical Sciences, Nagoya City University, Tanabe-dori, Mizuho-ku, Nagoya 467-8603, Japan

Dedicated to Professor Paul J. Scheuer, a great pioneer of marine natural product chemistry, on the occasion of his 85th birthday

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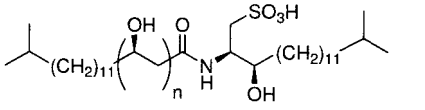
Abstract—Sulfobacin A (flavocristamide B, **1**), sulfobacin B (**2**), and flavocristamide A (**3**), biologically active sulfonolipids, have been efficiently synthesized utilizing the asymmetric aldol reaction of the Schiff base **8** derived from glycine ester and (+)-2-hydroxy-3-pinanone (HyPN).

Introduction

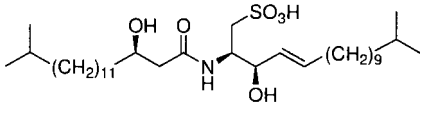
Sulfobacins A (**1**) and B (**2**) were isolated by Kamiyama and co-workers[1] from the culture broth of *Chryseobacterium* sp. (*Flavobacterium* sp.) NR 2993 in a soil sample collected at Iriomote Island, Okinawa Prefecture, Japan. Biological activities of these compounds were revealed to inhibit the binding of von Willebrand factor to the GPIb/IX receptors in a competitive manner with IC_{50s} of 0.47 μM for sulfobacin A (**1**) and 2.2 μM for sulfobacin B (**2**), respectively.[1a] Sulfobacin A (named as flavocristamide B) and flavocristamide A (**3**) were also isolated by Kobayashi and co-workers[2] from *Flavobacterium* sp. in the marine bivalve *Cristaria plicata* collected in Ishikari Bay, Hokkaido, Japan. Both flavocristamides B (**1**) and A (**3**) have been found to exhibit inhibitory activity against DNA polymerase α. The structures of these compounds **1**–**3** are related to sulfonolipids having an aminosulfonic acid moiety and are analogous to sphingosine, as shown in Fig. 1. Their structural uniqueness as well as intriguing biological activities led us to synthesize them in a suitable manner for large scale production. We now wish to report the details of the efficient stereoselective synthesis of sulfobacins (**1** and **2**)[3] and flavocristamide A (**3**). Mori, Takikawa, and co-workers also accomplished their synthesis by a different approach.[4]

Synthetic strategy

Scheme 1 shows our synthetic strategy for **1**, **2** and **3**. The sulfonic acid part of these compounds would be prepared by the oxidation of the corresponding thioacetate **4**. Bisection of **4** at the amide linkage into the left carboxylic acid **5** and the right aminodiol **6** is obvious from the retrosynthetic point of view, and the amide coupling would be attained by use of diethylphosphorocyanidate (DEPC, $(C_2H_5O)_2P(O)CN$).[5] The left fragment **5** of sulfobacin A (**1**) and flavocristamide A (**3**) could be prepared by the asymmetric reduction of the corresponding β-keto ester **7**, while the right fragment **6** would be constructed by the asymmetric aldol reaction[6] utilizing the Schiff base **8** derived from (+)-2-hydroxy-3-pinanone ((+)-HyPN).[7]



Sulfobacin A (1, Flavocristamide B) : n=1
Sulfobacin B (2) : n=0



Flavocristamide A (3)

Figure 1.

Preparation of the side chain

In the synthesis of topostins, DNA topoisomerase I inhibitors,[8] we have already synthesized 13-methyl-1-tetradecanol (**14a**) and 13-methyltetradecanoic acid (**16**) starting from 1,10-decanediol (**9a**) in a straight forward manner, as outlined in Scheme 2. Analogously, 10-methyl-1-undecanol (**14b**) was efficiently synthesized from 1,9-nonanediol (**9b**) through monobenzylation, oxidation, Wittig reaction, and catalytic hydrogenation. Both alcohols **14a** and **14b** were

Keywords: sulfonolipids; asymmetric aldol reaction; 2-hydroxy-3-pinanone; oxidation.

* Corresponding author. Tel.: +81-52-836-3439; fax: +81-52-834-4172; e-mail: shioiri@phar.nagoya-cu.ac.jp

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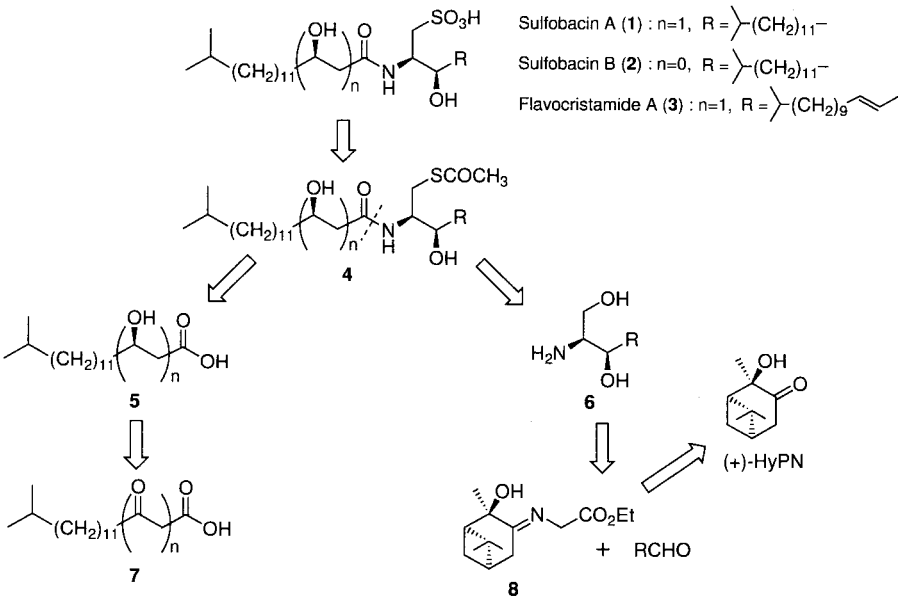
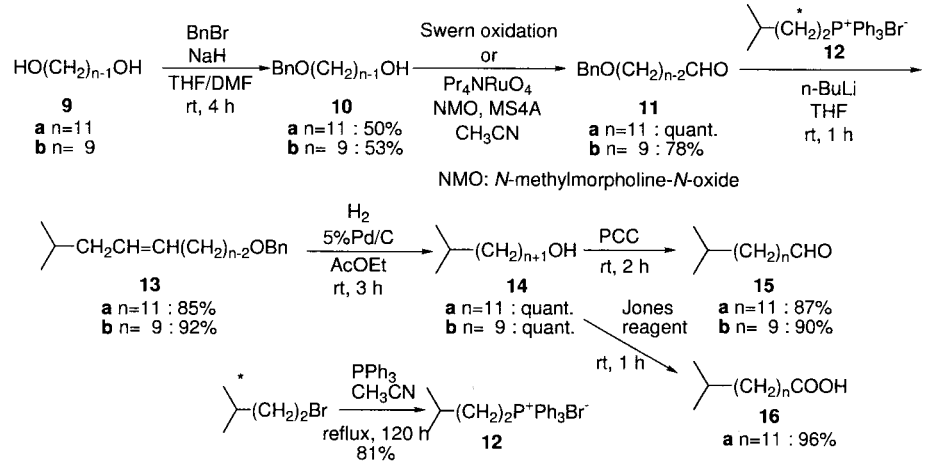


Scheme 1.



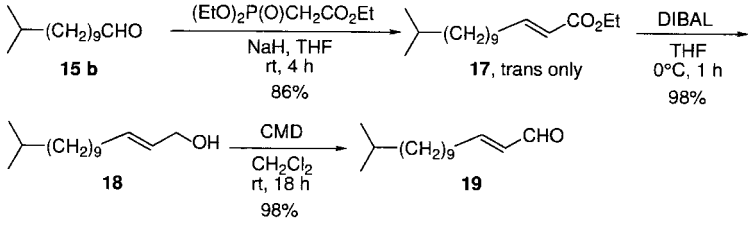
Scheme 2.

respectively oxidized with pyridinium chlorochromate (PCC) to give the aldehydes **15a** and **15b**, which were respectively utilized for the synthesis of sulfobacins A and B (**1** and **2**).

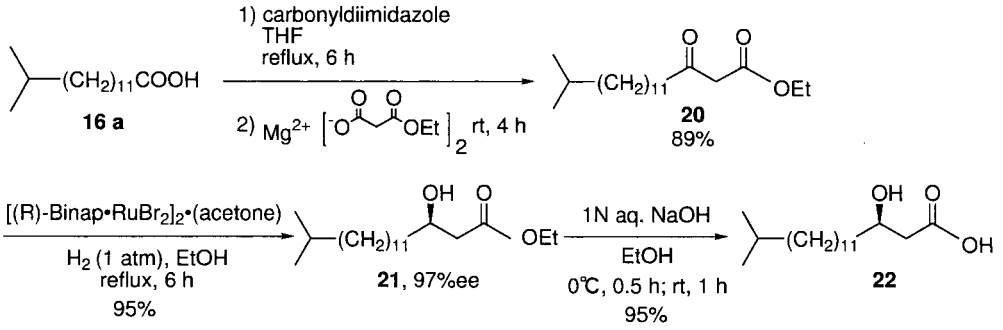
The aldehyde **19** required for the construction of flavocristamide A (**3**) was prepared from the aldehyde **15b** by three step operations; Horner–Wadsworth–Emmons reaction, DIBAL (Bu^i_2AlH) reduction, and then CMD (chemical manganese dioxide)[9] oxidation, as summarized in Scheme 3.

Synthesis of the left fragment of sulfobacin A (1) and flavocristamide A (3)

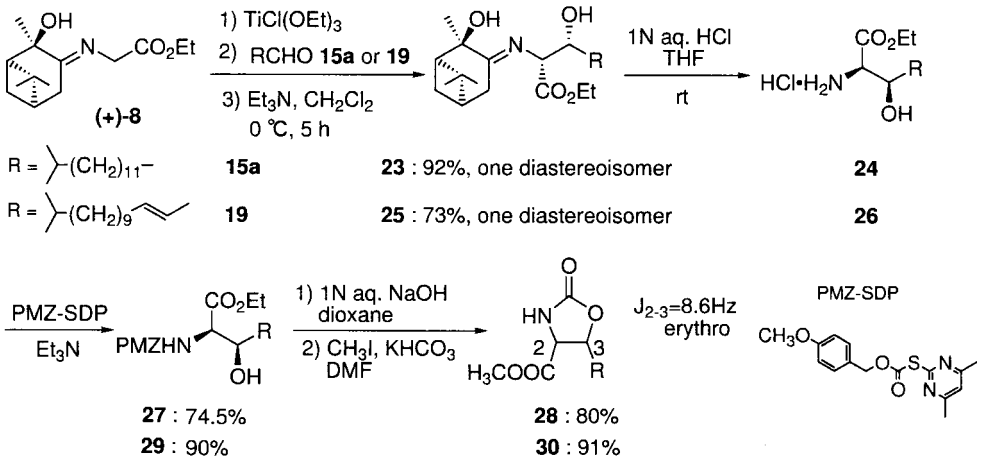
15-Methyl-3-hydroxyhexadecanoic acid (**22**), the left fragment of sulfobacin (**1**) and flavocristamide A (**3**), was also prepared from **16a** in our topostin synthesis,[8] the key steps



Scheme 3.



Scheme 4.



Scheme 5.

of which were the addition of acetate unit followed by the asymmetric reduction of the β-keto ester **20**, as summarized in Scheme 4.

Asymmetric aldol reaction for the right fragment

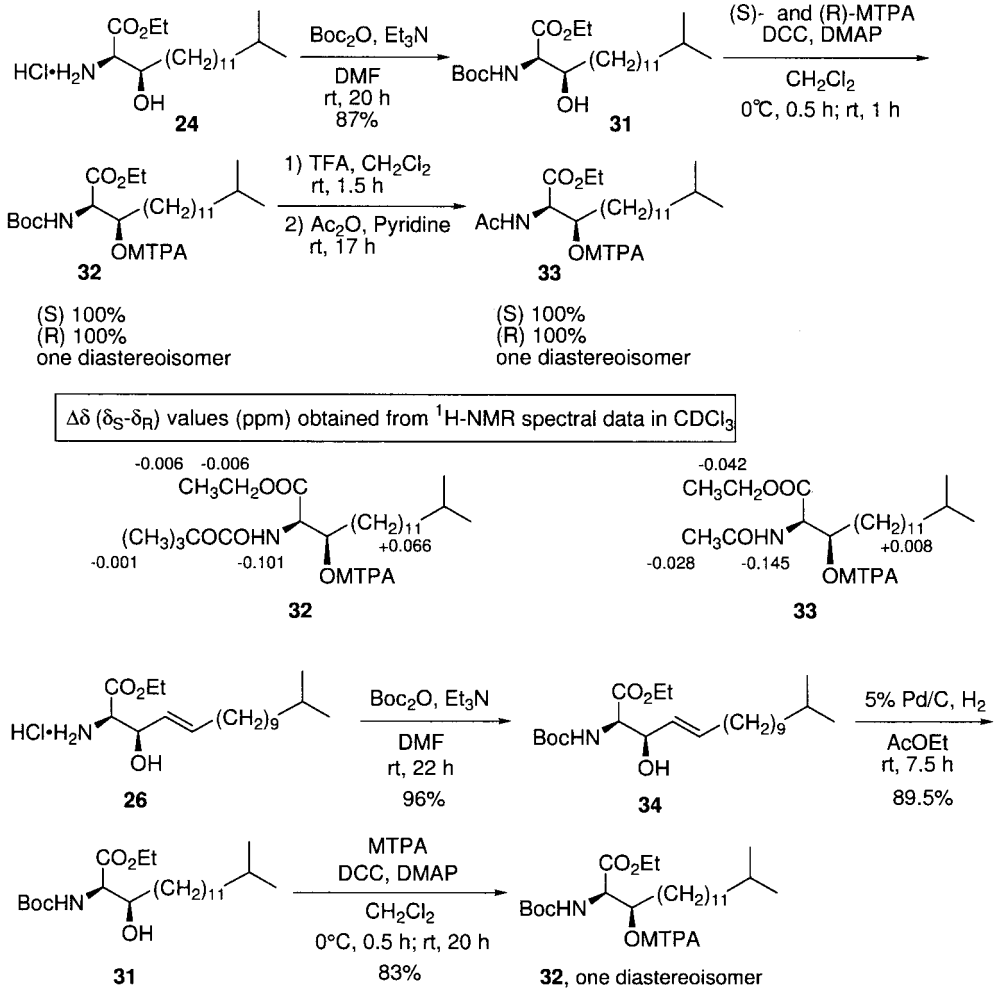
We have already developed optically active 2-hydroxy-3-pinane (HyPN) as an efficient chiral auxiliary for the synthesis of optically active amines and amino acids by asymmetric alkylation.[7] Solladié-Cavallo and co-workers[6] extended the utility of HyPN to the asymmetric aldol reaction, which we adopted for the synthesis of the right fragment of **1**, **2** and **3**, as shown in Scheme 5. Thus the aldehyde **15a** was allowed to react with the titanium enolate generated from the Schiff base (+)-**8** derived from (+)-HyPN[7] and titanium chlorotriethoxide to give the erythro aldol adduct **23** in an efficient and completely stereoselective manner. Removal of the chiral auxiliary was easily carried out under acidic conditions to give the right fragment **24** of **1** and **2**. Analogously, the right fragment **26** of **3** was prepared from the aldehyde **19**. Unambiguous proof for the erythro configuration of these aldol adducts **24** and **26** were obtained by their respective conversion to the oxazolidines **28** and **30** and their ^{1}H NMR analysis, shown in Scheme 5.

The absolute configuration of **24** was determined by the modified Moshers method[10] through its conversion to the MTPA esters **32** and **33**, while that of **26** was established by its conversion to **31** as well as the MTPA ester **32**, as shown in Scheme 6.

With the required right and left fragments in hand, we constructed the full carbon skeletons of **1**, **2** and **3**.

Synthesis of sulfobacin B (2)

The amino alcohol **24** obtained from the aldol adduct **23** was smoothly condensed with the carboxylic acid **16a** by use of DEPC to give the amide **35**, as shown in Scheme 7. After protection of its hydroxyl group with *tert*-butyldimethylsilyl chloride (TBSCl), the resulting ester **36** was reduced with $NaBH_4$–LiCl to give the alcohol **37**. Initial attempts to convert the hydroxyl group to the sulfonic acid via the bromide were failed. Furthermore, replacement of the hydroxyl group with the *O*-mesyl (*O*-Ms) one, followed by treatment with potassium thioacetate afforded the aziridine **39** as the major product and the desired thioacetate **38** was obtained in only 10% yield. However, the Mitsunobu reaction[11] of the alcohol **37** with thioacetic acid smoothly proceeded to give the thioacetate **38** in almost quantitative yield. Oxidation of **38** with peroxytrifluoroacetic acid afforded sulfobacin B (**2**). Alternatively, the thioacetate was first reduced with $LiAlH_4$ to give the thiol **40**, which was oxidized with peroxytrifluoroacetic acid to produce **2**. The synthetic sulfobacin B (**2**) ($[\alpha]_D^{18}=-18.7$ (*c* 0.14, MeOH)) was indistinguishable from the natural one by comparison of $[\alpha]_D^{24}=-19$ (*c* 0.14, MeOH),[1a] IR and ^{1}H NMR spectra, and TLC.



Scheme 6.

Synthesis of sulfobacin A (1)

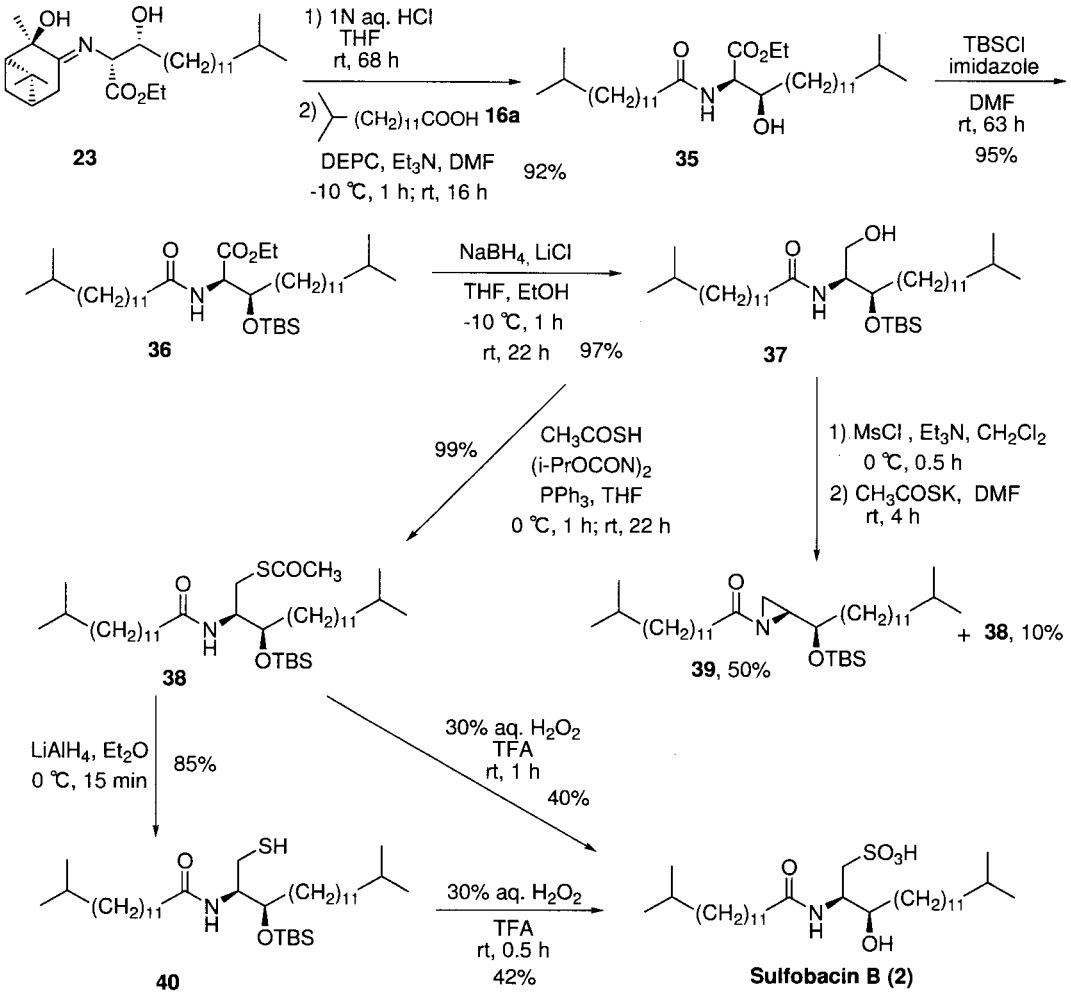
The above synthetic route used for the synthesis of sulfobacin B (**2**) was applied to the synthesis of sulfobacin A (**1**). The aldol adduct **24** was smoothly condensed with the carboxylic acid **22** with DEPC to give the amide **41**. After treatment with TBSCl, the reduction with $NaBH_4$–LiCl afforded the desired alcohol **42** in only 37% yield accompanied with the diol which was produced by the deprotection of the TBS group of the left part, shown in Scheme 8.

This unsatisfactory result led us to investigate another route, summarized in Scheme 9. After acidic removal of the chiral auxiliary, the amino group was protected with di-*tert*-butyl dicarbonate (Boc_2O) and then the hydroxyl group was protected with TBSCl. The resulting ester **43** was reduced with $NaBH_4$–LiCl to give the primary alcohol **44** in quantitative yield. Mesylation of **44** followed by treatment with potassium thioacetate quantitatively afforded the thioacetate **45**. After removal of the Boc group, condensation with the carboxylic acid **22** smoothly gave the amide **46**. Direct oxidation of **46** or the reduction followed by the oxidation produced sulfobacin A (**1**), $[\alpha]_D^{18}=-31.6$ (*c* 0.14, MeOH), which was identical with the natural one ($[\alpha]^{24}=-35$ (*c* 0.14, MeOH))[1a] in every respect (IR, ^{1}H NMR and ^{13}C NMR spectra, and TLC).

Synthesis of flavocristamide A (3)

The synthesis of flavocristamide A (**3**) was carried out analogously to the synthesis of sulfobacin A (**2**), as shown in Scheme 10. The Boc derivative **34** obtained from **26** was successively treated with TBSCl, $NaBH_4$–LiCl, MsCl, and potassium thioacetate afforded the thioacetate **50**, which underwent the acidic deprotection of the Boc group followed by condensation with the carboxylic acid **22** to give the amide **51**. It is known that the oxidation of the double bond having various oxygen substituents in the allylic position generally proceeds slowly, but the free hydroxyl substituent in the allyl group facilitates the oxidation because of the formation of the hydrogen bond between the hydroxyl group and peroxyacid oxygen.[12] Thus the hydroxyl group of **51** was first protected as the acetyl one, and then the resulting acetate **52** was oxidized with potassium monoperoxysulfate (OXONE®) and treated with potassium carbonate in aqueous methanol. After neutralization, flavocristamide A (**3**) was obtained in quantitative yield. The synthetic flavocristamide A, $[\alpha]_D^{26}=-18.7$ (*c* 0.27, MeOH), was identified with the natural one, $[\alpha]_D^{26}=-17$ (*c* 0.27, MeOH),[2] by spectral (IR, ^{1}H NMR, and ^{13}C NMR) comparisons and TLC.

Thus we have completed the total synthesis of sulfobacin A

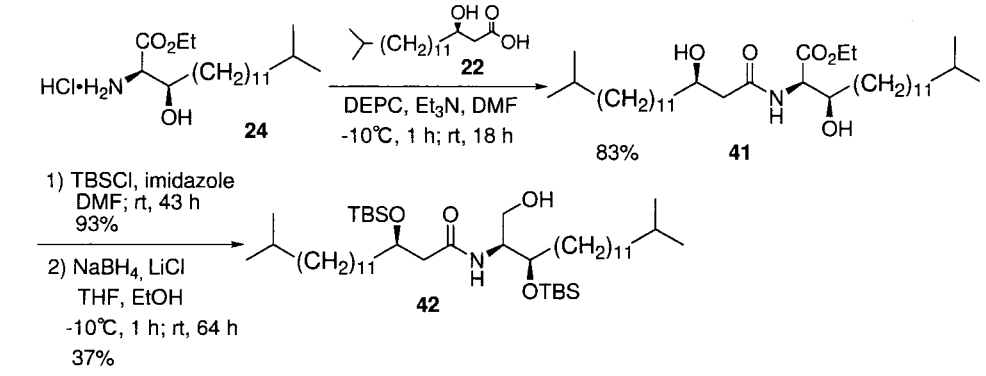


Scheme 7.

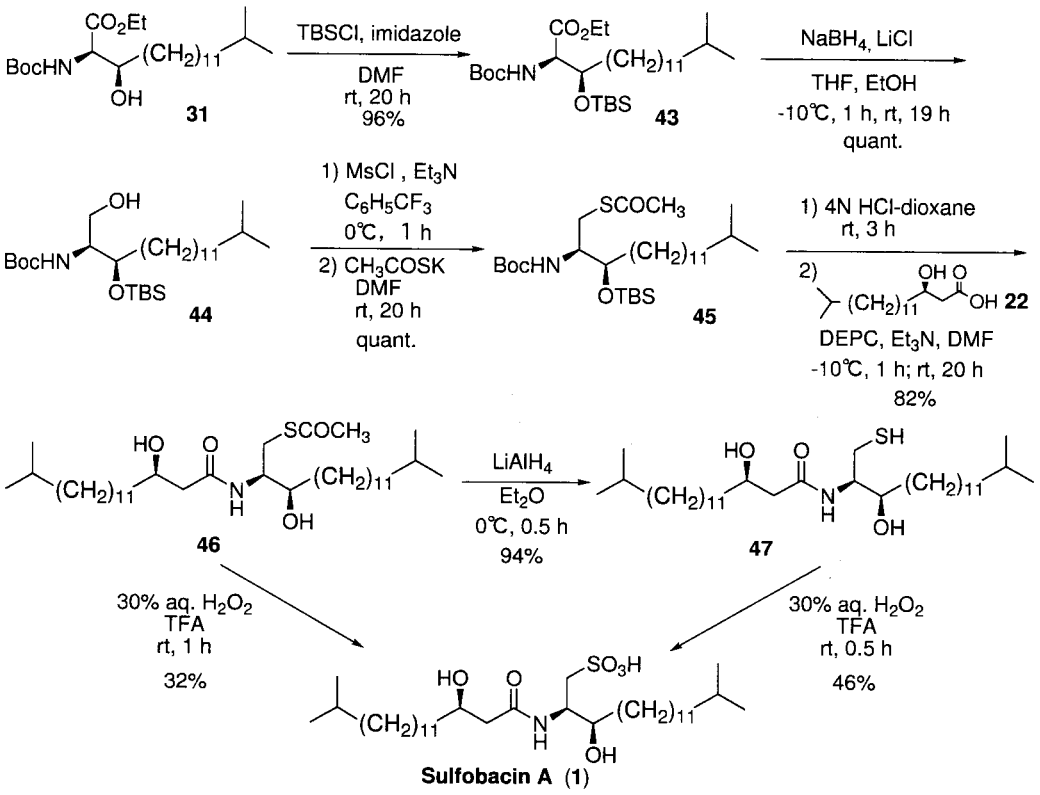
(**1**, flavocristamide B), sulfobacin B (**2**), and flavocristamide A (**3**) in an efficient manner. The method employed here showed have a broader applicability in synthesis.

Experimental

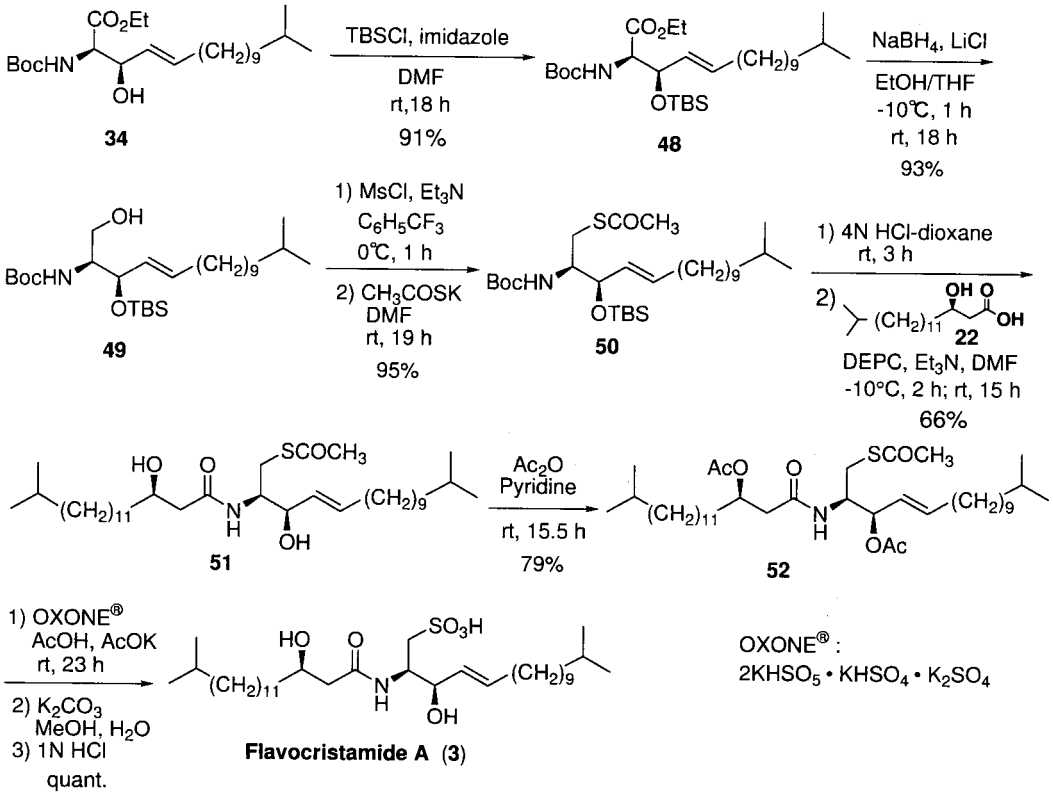
Melting points were determined on a YANAGIMOTO micro melting point apparatus (hot plate). Distillation was carried out by a Kugelrohr apparatus. Infrared (IR) spectra were measured with a SHIMADZU FT IR-8100 spectrometer. All melting and boiling points were uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL EX-270 or α-500 spectrometer with tetramethylsilane (TMS) or $CHCl_3$ as an internal standard. Mass spectra were obtained on a JEOL SX 102A or AX 505HA spectrometer. Optical rotations were measured with a JASCO DIP-1000 digital polarimeter. Silica gel (BW-820MH or BW-200) purchased from Fuji Silysia Chemical Co. Ltd. was used for column chromatography. Tetrahydrofuran (THF) was



Scheme 8.



Scheme 9.



Scheme 10.

dried by distillation from benzophenone ketyl. Diethyl ether (Et_2O) was dried by distillation from lithium aluminum hydride. Other solvents were distilled and stored over molecular sieves (4 Å).

3-Methyltetradecanoic acid (16a). Prepared from 1,10-decanediol (**9a**) according to the literature.[8]

The compounds 10b–14b. Prepared from 1,9-nonanediol (**9b**) analogously to the preparation of **14a**.[8]

8-Benzyloxy-1-octanol (10b). Bp 160°C/5 mmHg. IR ν_{max} (film): 3374, 2930, 1497, 1455, 1364, 1206, 1100, 753 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.33 (brs, 8H), 1.53–1.64 (m, 5H, 1H disappeared with D_2O), 3.46 (t, 2H, J=6.6 Hz), 3.63 (t, 2H, J=6.6 Hz), 4.50 (s, 2H), 7.26–7.35 (m, 5H). HRMS Calcd for $C_{15}H_{24}O_2$: 236.1776. Found: 236.1760.

8-Benzyloxy-1-decanal (11b). IR ν_{max} (film): 2932, 1725, 1455, 1364, 1102, 737, 698 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 1.335 and 1.62 (brs and brs, 10H), 2.42 (dt, 2H, J=1.7, 7.3 Hz), 3.46 (t, 2H, J=6.6 Hz), 4.50 (s, 2H), 7.24–7.38 (m, 5H), 9.76 (t, 1H, J=1.7 Hz).

12-Benzyloxy-2-methyl-4-dodecene (13b). Bp 170–175°C/5 mmHg. IR ν_{max} (film): 2928, 1470, 1464, 1455, 1366, 1113, 1103, 1028, 733 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.889 (d, 6H, J=6.6 Hz), 1.31 (brs, 8H), 1.52–1.64 (m, 3H), 1.86–2.02 (m, 4H), 3.46 (t, 2H, J=6.6 Hz), 4.50 (s, 2H), 5.31–5.44 (m, 2H), 7.26–7.35 (m, 5H). Anal. Calcd for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.10; H, 10.98.

11-Methyl-1-dodecanol (14b). Bp 120°C/5 mmHg. IR ν_{max} (film): 3328, 2926, 1468, 1383, 1057, 722 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.862 (d, 6H, J=6.6 Hz), 1.14–1.37 (m, 17H), 1.47–1.59 (m, 3H, 1H disappeared with D_2O), 3.64 (br, 2H, t, J=6.6 Hz with D_2O). Anal. Calcd for $C_{13}H_{28}O$: C, 77.93; H, 14.08. Found: C, 77.62; H, 14.02.

13-Methyl-1-tetradecanal (15a). To a stirred suspension of PCC (1.58 g, 7.18 mmol) in CH_2Cl_2 (20 ml) was added dropwise a solution of alcohol **14a** (1.00 g, 4.38 mmol) in CH_2Cl_2 at room temperature, and the reaction mixture was stirred for 2 h. After hexane (40 ml) was added, the mixture was allowed to settle and then passed through a short pad of silica gel. Removal of the solvent under reduced pressure afforded a crude aldehyde **15a**, which was purified by silica gel column chromatography with hexane–AcOEt (10:1) to give the aldehyde **15a** (858 mg, 87%) as a colorless oil, IR ν_{max} (film): 2926, 2855, 1728, 1468, 1410, 1385, 1366, 722 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.861 (d, 6H, J=6.6 Hz), 1.26 (br, 18H), 1.43–1.66 (m, 3H), 2.42 (dt, 2H, J=2.0, 7.3 Hz), 9.77 (t, 1H, J=2.0 Hz).

11-Methyl-1-dodecanal (15b). Prepared analogously from alcohol **14b**. IR ν_{max} (film): 2924, 2714, 1728, 1468 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.862 (d, 6H, J=6.6 Hz), 1.26 (br, 16H), 1.47–1.63 (m, 1H), 2.42 (dt, 2H, J=2.0, 7.3 Hz), 9.77 (d, 1H, J=1.7 Hz).

Ethyl 13-methyl-2-tetradecenoate (17). To suspension of NaH (60%, 480 mg, 12.0 mmol) in anhydrous THF (10 ml) under argon was added dropwise at 0°C triethyl phosphonoacetate (2.4 ml, 12.1 mmol). After 15 min of stirring at room temperature, **15b** (1.90 g, 9.56 mmol) in THF (4 ml) was added dropwise at 0°C. The mixture was stirred at room temperature for 4 h. Water (40 ml) was added, and the mixture was extracted with Et_2O (2×60 ml) and AcOEt (60 ml). The organic extracts were washed with saturated aqueous NaCl, and dried over $MgSO_4$. Concentration in vacuo gave a colorless oil, which was purified by silica gel column chromatography with hexane–AcOEt (20:1) to give **17** (2.21 g, 86%) as a colorless oil. IR ν_{max} (film): 2926, 1725, 1655, 1466, 1266, 1179, 1046, 982 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.861 (d, 6H, J=6.6 Hz), 1.16–1.30 and 1.26 (m and brs, 17H), 1.31–1.55 (m, 3H), 2.19 (q, 2H, t, J=6.9 Hz), 4.18 (q, 2H, J=6.9 Hz), 5.18 (d, 1H, J=15.8 Hz), 6.95 (dt, 1H, J=6.9, 15.5 Hz). Anal. Calcd for $C_{17}H_{32}O_2$: C, 76.06; H, 12.02. Found: C, 75.78; H, 12.26.

13-Methyl-2-tetradecenol (18). To a solution of **17** (1.97 g, 7.34 mmol) in THF (18 ml) under argon at −15°C was added dropwise a solution of DIBAL (1.01 M in toluene, 18 ml, 18.2 mmol). The reaction mixture was stirred at 0°C for 1 h, and 1N aqueous $KHSO_4$ (40 ml) was added dropwise. The mixture was filtered though the pad of celite and washed with Et_2O (100 ml). The filtrate was extracted with AcOEt (2×100 ml). The extracts were dried over $MgSO_4$. Concentration in vacuo gave the residue, which was purified by silica gel column chromatography with hexane–AcOEt (2:1) to give **18** (1.63 g, 98%) as a colorless oil. IR ν_{max} (film): 3326, 2924, 1466, 1366, 1089, 1005, 968 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.862 (d, 6H, J=6.6 Hz), 1.16–1.39 and 1.26 (m and brs, 16H), 1.49–1.56 (m, 2H, 1H disappeared with D_2O), 2.00–2.07 (m, 2H), 4.09 (br, 2H, d, J=5.0 Hz, disappeared with D_2O), 5.58–5.76 (m, 2H). Anal. Calcd for $C_{15}H_{30}O$: C, 79.58; H, 13.36. Found: C, 79.28; H, 13.52.

13-Methyl-2-tetradecenal (19). To a solution of **18** (122 mg, 0.495 mmol) in CH_2Cl_2 (5 ml) at room temperature was added CMD[9] (440 mg, 5.06 mmol). After stirring for 18 h at room temperature, the mixture was filtered through the pad of celite and washed with $CHCl_3$ (40 ml). The filtrate was concentrated in vacuo to give a colorless oil, which was purified by silica gel column chromatography with hexane–Et_2O (10:1) to furnish **19** (109 mg, 98.2%) as a colorless oil. IR ν_{max} (film): 2926, 1696, 1468, 1385, 1366, 1140, 974 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.862 (d, 6H, J=6.6 Hz), 1.14–1.27 and 1.26 (m and brs, 16H), 1.43–1.56 (m, 1H), 2.29–2.37 (m, 2H), 6.12 (dd, 1H, J=7.9, 5.8 Hz), 6.85 (dt, 1H, J=6.6, 15.8 Hz), 9.51 (d, 1H, J=7.9 Hz).

(3*R*)-Ethyl-3-hydroxy-15-methylhexadecanoate (22). Prepared from **16a** according to the literature.[8]

***N*-(+)-(1*R*,2*R*,5*R*)-2-Hydroxy-3-pinanylidene-(2*R*,3*R*)-2-ethoxycarbonyl-3-hydroxy-14-methylpentadecylamine (23).** To a solution of the iminoglycinate (+)-**8**[7a] (649 mg, 2.56 mmol) in CH_2Cl_2 (1.5 ml) at 0°C was dropwise added a solution of $ClTi(OEt)_3$ (1.28 g, 5.86 mmol) in CH_2Cl_2 (2.25 ml), a solution of the aldehyde **15a** (650 mg, 2.88 mmol) in CH_2Cl_2 (1.25 ml), and Et_3N (1.51 ml, 10.8 mmol). After stirring at 0°C for 5 h, cold saturated aqueous NaCl (50 ml) and AcOEt (60 ml) were added. The mixture was filtered though the pad of celite and the filtrate was extracted with AcOEt (60 ml). The extracts

were dried over $MgSO_4$. Concentration in vacuo gave the residue, which was purified by silica gel column chromatography with hexane–Et_2O (1:2) to give **23** (1.13 g, 92%) as a pale yellow oil, $[\alpha]_D^{27}=+62.6$ (*c* 1.04, $CHCl_3$). IR ν_{max} (film): 3385, 2924, 1733, 1657, 1468, 1397, 1183, 1161, 1105, 1084, 911, 735 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.861 (d, 6H, *J*=6.6 Hz), 0.84–0.87 (m, 3H), 1.25 (brs, 25H), 1.33 and 1.51 and 1.43–1.63 (s and s and m, 9H), 2.04–2.11 (m, 2H), 2.34–2.38 (m, 1H), 2.56–2.63 (m, 2H), 4.08–4.15 and 4.19 (m and q, 4H, *J*=7.0 Hz). HRMS Calcd for $C_{29}H_{53}O_4N$: 479.3974. Found: 479.3968.

(2*R*,3*R*)-3-Hydroxy-2-ethoxycarbonyl-15-methylpentadecylammonium chloride (24). To a solution of the Schiff base **23** (1.33 g, 2.78 mmol) in THF (4 ml) at room temperature was added dropwise 1N aqueous HCl (25 ml). The reaction mixture was stirred at room temperature for 68 h. Removal of the solvent under reduced pressure afforded the crude **24** as a white solid, which was used for the next reactions.

***N*-(+)-(1*R*,2*R*,5*R*)-2-Hydroxy-3-pinanylidene-(2*R*,3*R*)-2-ethoxycarbonyl-3-hydroxy-14-methyl-3-pentadecenylamine (25).** Prepared analogously from 13-methyl-2-tetradecenal (**19**). $[\alpha]_D^{22}=+45.2$ (*c* 1.05, $CHCl_3$). IR ν_{max} (film): 3347, 1742, 1659, 1438, 1368, 1179, 1161, 1020, 970, 924 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.861 and 0.873 (d and s, 9H, *J*=6.6 Hz), 1.15–1.38 and 1.22 and 1.33 (m and brs and s, 23H), 1.43–1.52 and 1.50 (m and s, 4H), 1.98–2.10 (m, 4H), 2.30–2.36 (m, 1H), 2.39 (br, 1H, disappeared with D_2O), 2.54 (brs, 2H), 3.11 (br, 1H, disappeared with D_2O), 4.15–4.22 (m, 3H), 4.56 (t, 1H, *J*=6.6 Hz), 5.46 (dd, 1H, *J*=7.3, 15.5 Hz), 5.73–5.84 (m, 1H). Anal. Calcd for $C_{29}H_{51}NO_4$: C, 72.91; H, 10.76; N, 2.93. Found: C, 72.64; H, 10.91; N, 2.89.

Ethyl (2*R*,3*R*)-4-methoxybenzyloxycarbonyl)amino-3-hydroxy-15-methylhexadecanoate (27). To a stirred solution of the above crude **24** (200 mg, 0.493 mmol) in Et_3N (10 ml) was added PMZ-SDP (300 mg, 0.986 mmol). The reaction mixture was stirred at 0°C for 0.5 h and then at room temperature for 16.5 h. Removal of the solvent under reduced pressure afforded the residue, which was purified by silica gel column chromatography with hexane–Et_2O (1:1) to give **27** (183 mg, 75%) as a white solid, IR ν_{max} (nujol): 3407, 2917, 1738, 1680, 1514, 1466, 1258, 1204, 1076, 1026, 818 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.861 (d, 6H, *J*=6.6 Hz), 1.25 and 1.13–2.17 (brs and m, 26H), 2.56 (br, 1H, disappeared with D_2O), 3.81 (s, 3H), 3.80–3.90 (m, 1H), 4.23 (q, 2H, *J*=5.3 Hz), 4.43 (br, 1H), 5.05 (s, 2H), 5.63 (br, 1H), 6.89 (d, 2H, *J*=8.6 Hz), 7.30 (d, 2H, *J*=8.6 Hz).

2-Methoxycarbonyl-3-(12-methyltridecanyl)oxazolidin-5-one (28). To a stirred solution of **27** (176 mg, 0.357 mmol) in dioxane (6 ml) was added dropwise 1N NaOH at 0°C. After stirring at room temperature for 21 h, water (20 ml) was added. The aqueous layer was washed with Et_2O (40 ml), and acidified with 1N HCl and extracted with AcOEt (40 ml). The extracts were dried over $MgSO_4$ and concentration in vacuo gave the oxazolidone as a white solid. To a stirred solution of the above oxazolidone in DMF (1.5 ml) was added $KHCO_3$ (65 mg, 0.65 mmol) and then CH_3I (0.06 ml, 0.96 mmol). After stirring at room temperature for 20 h, water (40 ml) was added, and the mixture was extracted with benzene–AcOEt (1:2, 60 ml). The extracts were dried over Na_2SO_4. Concentration in vacuo gave the residue, which was purified by silica gel column chromatography with hexane–Et_2O (1:3→0:1) to give the methyl ester **28** (88 mg, 80%) as a pale orange solid, IR ν_{max} (nujol): 3270, 2914, 1767, 1744, 1470, 1217, 1117, 972, 953 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.862 (d, 6H, *J*=6.6 Hz), 1.26 (brs, 20H), 1.43–1.61 (m, 3H), 3.81 (s, 3H), 4.39 (dd, 1H, *J*=2.0, 8.6 Hz), 4.76 (dd, 1H, *J*=4.3, 8.6 Hz), 5.32 (br, 1H).

Ethyl (2*R*,3*R*)-(4-methoxybenzyloxycarbonyl)amino-3-hydroxy-15-methyl-4-hexadecenoate (29). Prepared analogously from **26**. IR ν_{max} (film): 3434, 2926, 1723, 1615, 1586, 1516, 1466, 1248, 1175, 1051, 920, 824 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.883 (d, 6H, *J*=6.6 Hz), 1.27 and 1.15–1.32 (brs and m, 19H), 1.49–1.59 (m, 1H), 2.12–2.18 (m, 2H), 3.2–3.4 (br, 1H), 3.83 and 3.72–3.84 (s and m, 4H), 4.23 (q, 2H, *J*=7.3 Hz), 4.51 (br, 1H), 5.07 (s, 2H), 5.44 (dd, 1H, *J*=6.3, 15.5 Hz), 5.61 (br, 1H), 5.71–5.79 (m, 1H), 6.90 (d, 2H, *J*=8.6 Hz), 7.32 (d, 2H, *J*=8.6 Hz).

2-Methoxycarbonyl-3-(12-methyl-1-tridecenyl)oxazolidin-5-one (30). Prepared analogously from **29**. IR ν_{max} (film): 3342, 2926, 1767, 1464, 1366, 1217, 1121, 972, 914, 878 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.856 (d, 6H, *J*=6.6 Hz), 1.25 and 1.15–1.53 (brs and m, 19H), 2.04–2.07 (m, 2H), 3.74 (s, 3H), 4.75 (d, 1H, *J*=8.6 Hz), 5.17 (t, 1H, *J*=8.2 Hz), 5.36 (dd, 1H, *J*=8.0, 15.2 Hz), 5.68 (brs, 1H), 5.94 (dt, 1H, *J*=6.9, 15.2 Hz).

Ethyl (2*R*,3*R*)-2-*tert*-butoxycarbonylamino-3-hydroxy-15-methylhexadecanoate (31). (i) From **24**. To a suspension of the above crude **24** (2.78 mmol) in DMF (10 ml) at 0°C was added dropwise Et_3N (3.00 ml, 21.5 mmol) and Boc_2O (1.28 g, 5.84 mmol) in DMF (10 ml). After the mixture was stirred at room temperature for 20 h, water (100 ml) was added, and extracted with Et_2O (150 ml). The extracts were washed with saturated aqueous NaCl (50 ml), and dried over Na_2SO_4. Concentration in vacuo gave the residue, which was purified by silica gel column chromatography with hexane–AcOEt (5:1) to give **31** (1.04 g, 87%) as a colorless oil, $[\alpha]_D^{16}=-17.3$ (*c* 1.00, $CHCl_3$). IR ν_{max} (film): 3432, 2926, 1722, 1699, 1505, 1468, 1368, 1252, 1167, 1028 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.861 (d, 6H, *J*=6.6 Hz), 1.25 (brs, 21H), 1.45 and 1.40–1.68 (s and m, 14H), 2.72 (d, 1H, *J*=5.9 Hz, disappeared with D_2O), 3.89 (br, 1H), 4.18–4.30 (m, 2H), 4.37 (br, 1H), 5.46 (br, 1H). Anal. Calcd for $C_{24}H_{47}NO_5$: C, 67.09; H, 11.03; N, 3.26. Found: C, 66.86; H, 10.97; N, 3.21.

(ii) From **34**. A mixture of **34** (105 mg, 0.25 mmol) and 5% Pd–C (40 mg) in AcOEt (5 ml) under an atmosphere of H_2 was stirred at room temperature for 7.5 h. The mixture was filtered though the pad of celite and the filtrate was concentration in vacuo to give a colorless oil, which was purified by silica gel column chromatography with hexane–AcOEt (5:1) and then AcOEt only to give **31** (94 mg, 89.5%) as a colorless oil. $[\alpha]_D^{25}=-16.6$ (*c* 1.00, $CHCl_3$). IR ν_{max} (film): 3437, 2926, 1722, 1700, 1505, 1468, 1368, 1256, 1167,

1028 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.860 (d, 6H, J=6.6 Hz), 1.25 (brs, 21H), 1.45 and 1.40–1.55 (s and m, 14H), 2.70 (brs, 1H), 3.90 (br, 1H), 4.19–4.28 (m, 2H), 4.35 (br, 1H), 5.43 (br, 1H). These data were identical with that of **31** from **24**.

Ethyl (2*R*,3*R*)-2-*tert*-butoxycarbonylamino-3-(α-methoxy-α-trifluoromethylphenylacetoxy)-15-methylhexadecanoate (32). To a solution of **31** (45 mg, 0.105 mmol) in CH_2Cl_2 (1 ml) at 0°C was added MTPA (45 mg, 0.192 mmol), DCC (44 mg, 0.21 mmol) and DMAP (10 mg, 0.082 mmol). The reaction mixture was stirred at 0°C for 0.5 h and at room temperature for 1 h. After addition of Et_2O (10 ml), the mixture was filtered though the pad of celite and the filtrate was successively washed with 10% aqueous citric acid, water, saturated aqueous $NaHCO_3$, water, saturated aqueous NaCl, and dried over Na_2SO_4. Concentration in vacuo gave the residue, which was purified by silica gel column chromatography with hexane–AcOEt (8:1) to give the MTPA ester **32** (68 mg, quant.) as a colorless oil, IR ν_{max} (film): 3474, 3374, 2926, 1750, 1717, 1499, 1368, 1252, 1169, 1021, 718 cm^{-1}. For (−)-(*S*)-MTPA ester **32**, ^1H NMR ($CDCl_3$) δ: 0.863 (d, 6H, J=6.1 Hz), 1.22 and 1.25 (t and brs, 21H, J=7.3 Hz), 1.44 (s, 9H), 1.71–1.78 (m, 5H), 3.52 (s, 3H), 4.13 (q, 2H, J=7.3 Hz), 4.59–4.60 (m, 1H), 5.10 (d, 1H, J=8.5 Hz), 5.34–5.37 (m, 1H), 7.41–7.42 (m, 3H), 7.41–7.54 (m, 2H). For (+)-(*R*)-MTPA ester **32**, ^1H NMR ($CDCl_3$) δ: 0.865 (d, 6H, J=6.7 Hz), 1.23–1.25 and 1.25 (m and brs, 21H), 1.44 (s, 9H), 1.59–1.71 (m, 5H), 3.54 (s, 3H), 4.18 (q, 2H, J=7.3 Hz), 4.63–4.64 (m, 1H), 5.20 (d, 1H, J=7.9 Hz), 5.30–5.40 (m, 1H), 7.39–7.41 (m, 3H), 7.41–7.54 (m, 2H).

Ethyl (2*R*,3*R*)-2-acetylamino-3-(α-methoxy-α-trifluoromethylphenylacetoxy)-15-methylhexadecanoate (33). To a stirred solution of **32** (35 mg, 0.054 mmol) in CH_2Cl_2 (0.9 ml) at room temperature was added dropwise TFA (0.2 ml, 2.60 mmol). The reaction mixture was stirred at room temperature for 1.5 h. Removal of the solvent under reduced pressure afforded a colorless oil. To a stirred solution of the above colorless oil in pyridine (5 ml) was added Ac_2O (1 ml) at room temperature. The reaction mixture was stirred at room temperature for 17 h. After removal of the volatiles, AcOEt (30 ml) was added. The mixture was washed with 0.5N HCl, water, saturated aqueous $NaHCO_3$, saturated aqueous NaCl, and dried over Na_2SO_4. Concentration in vacuo gave the residue, which was purified by silica gel column chromatography with hexane–AcOEt (2:1) to give the acetate **33** (32 mg, quant.) as a colorless oil, IR ν_{max} (film): 3297, 2926, 1750, 1665, 1541, 1466, 1375, 1271, 1170, 1021, 720 cm^{-1}. For (−)-(*S*)-MTPA ester **33**, ^1H NMR ($CDCl_3$) δ: 0.863 (d, 6H, J=6.6 Hz), 1.25 (brs, 21H), 1.41–1.92 (m, 5H), 1.96 (s, 3H), 3.51 (s, 3H), 4.16 (q, 2H, J=7.1 Hz), 4.88 (dd, 1H, J=3.0, 7.3 Hz), 5.27 (dt, 1H, J=6.3, 3.0 Hz), 6.05 (d, 1H, J=7.9 Hz), 7.41–7.71 (m, 5H). For (+)-(*R*)-MTPA ester **33**, ^1H NMR ($CDCl_3$) δ: 0.863 (d, 6H, J=6.6 Hz), 1.25 (brs, 21H), 1.26–1.64 (m, 5H), 1.98 (s, 3H), 3.52 (s, 3H), 4.20 (q, 2H, J=7.3 Hz), 4.89 (dd, 1H, J=2.6, 7.9 Hz), 5.32 (dt, 1H, J=5.3, 3.0 Hz), 6.19 (d, 1H, J=7.9 Hz), 7.23–7.40 (m, 5H).

Ethyl (2*R*,3*R*)-2-*tert*-butoxycarbonylamino-3-hydroxy-15-methyl-4-hexadecenoate (34). Prepared analogously from **26**. $[\alpha]_D^{24}$=−30.1 (*c* 1.19, $CHCl_3$). IR ν_{max} (film): 3441, 2926, 1721, 1505, 1468, 1368, 1252, 1167, 1057, 1028, 970, 864 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.862 (d, 6H, J=6.6 Hz), 1.26 and 1.25–1.31 (brs and m, 19H), 1.45 (s, 9H), 1.49–1.57 (m, 1H), 2.01–2.04 (m, 1H), 3.10 (brs, 1H), 4.17–4.26 (m, 3H), 4.45 (br, 2H), 5.38–5.46 (m, 2H), 5.69–5.77 (m, 1H).

Ethyl (2*R*,3*R*)-3-hydroxy-2-(13-methyltetradecanamido)-15-methylhexadecanoate (35). To a solution of the above crude **24** (4.23 mmol) and the carboxylic acid **16a** (450 mg, 1.86 mmol) in DMF (7 ml) at −10°C was dropwise added DEPC (0.31 ml, 2.04 mmol) and then Et_3N (0.64 ml, 4.59 mmol). Then reaction mixture was stirred at −10°C for 1 h, and then at room temperature for 16 h. After dilution with AcOEt–benzene (2:1, 120 ml), the whole was successively washed with saturated aqueous $NaHCO_3$, water, saturated aqueous NaCl, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography with hexane–Et_2O (1:1) to give **35** (949 mg, 92%) as a white solid, mp 57.5–59°C (hexane–Et_2O), $[\alpha]_D^{28}$=−23.6 (*c* 1.0, $CHCl_3$). IR ν_{max} (nujol): 3303, 2918, 1736, 1651, 1543, 1377, 1202, 1121, 720 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.86 (d, 12H, J=6.6 Hz), 1.25 and 1.20–1.65 (br and m, 47H), 2.27 (t, 2H, J=7.3 Hz), 3.33 (d, 1H, J=7.3 Hz, disappeared with D_2O), 3.94 (brs, 1H), 4.20–4.29 (m, 2H), 4.67 (dd, 1H, J=6.6, 3.0 Hz), 6.42 (d, 1H, J=6.9 Hz). Anal. Calcd for $C_{34}H_{67}NO_4$: C, 73.73; H, 12.19; N, 2.53. Found: C, 73.23; H, 12.15; N, 2.80.

Ethyl (2*R*,3*R*)-3-*tert*-butyldimethylsiloxy-2-(13-methyltetradecanamido)-15-methylhexadecanoate (36). To a stirred solution of **35** (493 mg, 0.891 mmol) in DMF (3.5 ml) was added imidazole (340 mg, 4.99 mmol) and TBSCl (537 ml, 3.56 mmol). The mixture was stirred at room temperature for 63 h, and quenched with 1 M aqueous $KHSO_4$ (40 ml). After extraction with Et_2O (120 ml), the extracts were washed with saturated aqueous NaCl (40 ml), dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography with hexane–AcOEt (10:1) to give the protected compound **36** (566 mg, 95%) as a colorless oil, $[\alpha]_D^{27}$=−25.3 (*c* 1.51, $CHCl_3$). IR ν_{max} (film): 3434, 3306, 2926, 1742, 1651, 1466, 1256, 1190, 1107, 837, 777 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.040 and 0.051 (s×2, 6H), 0.859 and 0.870 (d and s, 21H, J=5.6 Hz), 1.26 (brs, 43H), 1.44–1.66 (m, 4H), 2.22 (t, 2H, J=7.9 Hz), 3.90 (dt, 1H, J=6.9, 2.6 Hz), 4.15–4.28 (m, 2H), 4.63 (dd, 1H, J=2.6, 7.9 Hz), 6.21 (d, 1H, J=7.6 Hz). Anal. Calcd for $C_{40}H_{81}NO_4Si$: C, 71.90; H, 12.22; N, 2.10. Found: C, 71.93; H, 12.14; N, 1.91.

***N*-[(1′*R*,2′*R*)-1′-Hydroxymethyl-2′-*tert*-butyldimethylsiloxy-14-methylpentadecanyl]-13-methyltetradecanamide (37).** To a stirred solution of the above compound **36** (350 mg, 0.524 mmol) in THF (1 ml) at −10°C was added LiCl (105 mg, 2.47 mmol), $NaBH_4$ (96 mg, 2.54 mmol), followed by dropwise addition of EtOH (2 ml). The reaction mixture was stirred at −10°C for 1 h, and then at room temperature for 22 h. Citric acid (10%, 20 ml) was added, and the mixture was extracted with AcOEt (40 ml). The extracts were dried over Na_2SO_4. Concentration in vacuo gave the residue, which was purified by silica gel column

chromatography with hexane–AcOEt (5:1→3:1→2:1) to give the alcohol **37** (312 mg, 97%) as a colorless oil $[\alpha]_D^{27}=-11.8$ (*c* 1.02, $CHCl_3$). IR ν_{max} (film): 3299, 2926, 1644, 1549, 1468, 1256, 1086, 837, 776 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.083 and 0.087 (s×2, 6H), 0.861 and 0.900 (d and s, 21H, *J*=6.6 Hz), 1.25 (brs, 38H), 1.47–1.59 (m, 6H), 2.08 (br, 1H), 2.22 (t, 2H, *J*=7.3 Hz), 3.58 (dd, 1H, *J*=2.6, 11.6 Hz), 3.89–3.97 (m, 2H), 4.05 (dd, 1H, *J*=3.0, 11.6 Hz), 6.32 (d, 1H, *J*=2.5 Hz). Anal. Calcd for $C_{38}H_{79}NO_3Si$: C, 72.89; H, 12.72; N, 2.24. Found: C, 72.74; H, 12.67; N, 2.28.

S-(2*R*,3*R*)-3-*tert*-Butyldimethylsiloxy-2-(13-methyltetradecanamido)-15-methylhexadecanyl thioacetate (38). To a stirred solution of PPh_3 (225 mg, 0.858 mmol) in THF (2 ml) at 0°C under argon was added dropwise $(i\text{-PrOCON})_2$ (0.165 ml, 0.838 mmol). After the mixture was stirred at 0°C for 5 h, a solution of the alcohol **37** (259 mg, 0.414 mmol) and thioacetic acid (0.065 ml, 0.909 mmol) in THF (1 ml) was added. The reaction mixture was stirred at 0°C for 1 h, and then at room temperature for 22 h. After dilution with AcOEt (80 ml), the whole was washed with saturated aqueous $NaHCO_3$, water, saturated aqueous NaCl, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by silica gel column chromatography with benzene–hexane–Et_2O (40:21:1→8:5:1) to give the thioacetate **38** (281 mg, 99%) as a colorless oil. This compound was unstable, so it was used for the next reaction immediately. IR ν_{max} (film): 3303, 2926, 1698, 1648, 1466, 1119, 837 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.060 and 0.067 (s×2, 6H), 0.859 and 0.931 (d and s, 15H, *J*=6.6 Hz), 1.251 and 1.16–1.25 (s and m, 38H), 1.43–1.56 (m, 6H), 2.09 (td, 2H, *J*=2.3, 7.0 Hz), 2.33 (s, 3H), 2.98 (dd, 1H, *J*=3.6, 14.2 Hz), 3.14 (dd, 1H, *J*=10.9, 14.2 Hz), 3.77–3.78 (m, 1H), 4.07–4.11 (m, 1H), 5.74 (d, 1H, *J*=8.6 Hz).

(2*R*)-1-(13-Methyltetradecanoyl)-2-((*R*)-1-*tert*-butyldimethylsiloxy-13-methyltetradecanyl)aziridine (39). To a solution of the alcohol **37** (52 mg, 0.083 mmol) in CH_2Cl_2 (0.3 ml) at 0°C was added Et_3N (0.025 ml, 0.179 mmol) and MsCl (0.015 ml, 0.194 mmol). The mixture was stirred at 0°C for 0.5 h. After dilution with AcOEt (30 ml), the whole was washed with water, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel short column chromatography with hexane–AcOEt (3:1) to give the mesylate (50 mg, 86%) as a pale yellow oil. This compound was unstable, so it was used for the next reaction immediately. For the mesylate, IR ν_{max} (film): 3287, 2926, 1740, 1667, 1466, 1374, 1252, 1177, 1042, 837, 777 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.075 (s, 6H), 0.860 and 0.901 (d and s, 21H, *J*=6.6 Hz), 1.25 and 1.16–1.26 (s and m, 38H), 1.46–1.56 (m, 6H), 2.18 (t, 2H, *J*=7.3 Hz), 3.02 (s, 3H), 3.82–3.84 (m, 1H), 4.29–4.40 (m, 3H), 5.68 (d, 1H, *J*=8.6 Hz).

The above material was dissolved in DMF (0.5 ml). CH_3COSK (50 mg, 0.438 mmol) was added at room temperature. After stirring at room temperature for 4 h, water (10 ml) was added, and the mixture was extracted with AcOEt (30 ml). The extracts were washed with saturated aqueous NaCl, and dried over Na_2SO_4. Concentration in vacuo gave the residue, which was purified by silica gel column chromatography with hexane–Et_2O (5:1) and then AcOEt only to give the aziridine **39** (24 mg, 50%) as a colorless oil and the thioacetate **38** (5 mg, 10%) as a colorless oil. The aziridine **39**; $[\alpha]_D^{23}=+14.9$ (*c* 0.505, $CHCl_3$). IR ν_{max} (film): 2926, 1673, 1468, 1256, 1115, 837, 776 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.022 and 0.049 (s×2, 6H), 0.857 and 0.860 (s and d, 21H, *J*=6.6 Hz), 1.25 and 1.16–1.26 (s and m, 38H), 1.43–1.56 (m, 6H), 2.22 (t, 2H, *J*=7.0 Hz), 3.86–3.88 (m, 1H), 4.11 (d, 2H, *J*=4.9 Hz), 4.20–4.26 (m, 1H). Anal. Calcd for $C_{38}H_{70}NO_2Si$: C, 75.05; H, 12.76; N, 2.30. Found: C, 74.92; H, 12.55; N, 2.17.

***N*-[(1′*R*,2′*R*)-1′-Mercaptomethyl-2′-*tert*-butyldimethylsiloxy-14-methylpentadecanyl]-13-methyltetradecanamide (40).** To a solution of the thioacetate **38** (70 mg, 0.102 mmol) in Et_2O (0.5 ml) was added $LiAlH_4$ (7 mg, 0.148 mmol) at 0°C. The reaction mixture was stirred at 0°C for 15 min. HCl (3N, 5 ml) was added, the mixture was extracted with AcOEt (40 ml). The extracts were dried over $MgSO_4$. Concentration in vacuo gave a colorless oil **40** (56 mg, 85%), which was used for the next reaction directly. ^1H NMR ($CDCl_3$) δ: 0.065 (s, 6H), 0.859 and 0.897 (d and s, 21H, *J*=6.6 Hz), 0.912–1.25 and 1.252 (m and brs, 38H), 1.28–1.64 (m, 6H), 2.09 (s, 1H), 2.20 (t, 2H, *J*=7.6 Hz), 2.69–2.79 (m, 1H), 3.80–3.82 (m, 1H), 4.08–4.10 (m, 1H), 5.71 (d, 1H, *J*=8.9 Hz).

Sulfobacin B (2). *Method A:*
To a stirred solution of the thioacetate **38** (95 mg, 0.139 mmol) in TFA (0.35 ml) was added dropwise 30% aqueous H_2O_2 (0.12 ml). The reaction mixture was stirred at room temperature for 1 h. Removal of the solvent under reduced pressure afforded the residue, which was purified by silica gel column chromatography with $CHCl_3$–MeOH–H_2O (65:10:1→65:25:3) to give sulfobacin B (**2**) (32 mg, 40%) as a white solid, mp 218–220°C, $[\alpha]_D^{18}=-18.7$ (*c* 0.14, MeOH) [lit.[1] $[\alpha]_D^{24}=-19$ (*c* 0.14, MeOH)] IR ν_{max} ($CHCl_3$): 3291, 2920, 1651, 1547, 1468, 1184, 1060 cm^{-1}. [lit.[1] IR ν_{max} (KBr): 3300, 2925, 1655, 1550, 1470, 1220, 1060 cm^{-1}.] ^1H NMR (DMSO-d^6/500 MHz) δ: 0.841 (d, 12H, *J*=6.7 Hz), 1.09–1.16 (m, 4H), 1.22 (brs, 36H), 1.36–1.53 (m, 4H), 2.02 (t, 2H, *J*=7.3 Hz), 2.65 (dd, 1H, *J*=4.3, 14.0 Hz), 2.78 (dd, 1H, *J*=6.1, 14.0 Hz), 3.51 (br, 1H), 3.84–3.87 (m, 1H), 4.83 (d, 1H, *J*=5.5 Hz), 7.61 (d, 1H, *J*=8.5 Hz). [lit.[1] ^1H NMR (DMSO-d^6/400 MHz) δ: 0.84 (d, 12H, *J*=6.8 Hz), 1.14 (m, 4H), 1.23 (brs, 36H), 1.40–1.48 (m, 4H), 2.02 (t, 2H, *J*=7.3 Hz), 2.62 (dd, 1H, *J*=4.4, 14.2 Hz), 2.79 (dd, 1H, *J*=5.9, 14.2 Hz), 3.51 (m, 1H), 3.84 (m, 1H), 4.83 (d, 1H, *J*=5.4 Hz), 7.58 (d, 1H, *J*=8.3 Hz).] TLC (R_f value): 0.22 (solvent: the low layer of $CHCl_3$–MeOH–H_2O (65:25:10) [lit.[1] TLC (R_f value): 0.22 (solvent: the lower layer of $CHCl_3$–MeOH–H_2O (65:25:10)]

Method B:
To a stirred solution of the crude thiol **40** (50 mg, 0.078 mmol) in TFA (1 ml) was added dropwise 30% aqueous H_2O_2 (0.1 ml). The reaction mixture was stirred at room temperature of 0.5 h. Removal of the solvent under reduced pressure afforded the residue, which was purified by silica gel column chromatography with $CHCl_3$–MeOH–H_2O (65:10:1→65:25:3) to give sulfobacin B (**2**) (19 mg, 42%) as a white solid.

Ethyl (2*R*,3*R*)-3-hydroxy-2-[(*R*)-3-hydroxy-15-methylhexadecanamido]-15-methylhexadecanoate (41). To a

solution of the crude **24** (1.20 mmol) and the carboxylic acid **22** (344 mg, 1.20 mmol) in DMF (5 ml) at −10°C was added dropwise DEPC (0.20 ml, 1.32 mmol) and then Et_3N (0.42 ml, 3.01 mmol). The reaction mixture was stirred at −10°C for 1 h, and then at room temperature for 18 h. After dilution with AcOEt–benzene (2:1, 75 ml), the whole was washed with saturated aqueous $NaHCO_3$, water, saturated aqueous NaCl, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography with hexane–AcOEt (2:1) to give **41** (598 mg, 83%) as a white solid, mp 64.5–66°C. $[\alpha]_D^{23}=-26.5$ (*c* 1.0, $CHCl_3$). IR ν_{max} (nujol): 3299, 2920, 1736, 1726, 1644, 1619, 1545, 1377, 1200, 1080, 1026, 720 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.861 (d, 12H, *J*=6.6 Hz), 1.16–1.33 and 1.25 (m and brs, 43H), 1.47–1.64 (m, 6H), 2.38 (dd, 1H, *J*=8.9, 15.2 Hz), 2.46 (dd, 1H, *J*=3.0, 15.2 Hz), 3.03 (brs, 1H, disappeared with D_2O), 3.38 (brs, 1H, disappeared with D_2O), 3.95–3.96 (m, 2H), 4.20–4.30 (m, 2H), 4.66 (dd, 1H, *J*=3.3, 7.3 Hz), 6.82 (d, 1H, *J*=7.3 Hz) Anal. Calcd for $C_{36}H_{71}NO_5$: C, 72.31; H, 11.97; N, 2.34. Found: C, 72.09; H, 11:87; N, 2.66.

Ethyl (2*R*,3*R*)-3-*tert*-butyldimethylsiloxy-2-[(*R*)-3-hydroxy-15-methylhexadecanamido]-15-methylhexadecanoate. To a stirred solution of the diol **41** (200 mg, 0.335 mmol) in DMF (1.5 ml) was added imidazole (194 mg, 2.85 mmol) and TBSCl (303 mg, 2.01 mmol). The mixture was stirred at room temperature for 43 h, and quenched with 1 M aqueous $KHSO_4$ (30 ml). After extraction with Et_2O (50 ml), the extracts were washed with saturated aqueous NaCl (30 ml), dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography with hexane–AcOEt (10:1) to give the protected compound of hydroxy group (257 mg, 93%) as a colorless oil, $[\alpha]_D^{23}=-19.0$ (*c* 1.03, $CHCl_3$). IR ν_{max} (film): 3374, 2926, 1715, 1682, 1505, 1464, 1383, 1256, 1192, 1103, 839, 777 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.048 and 0.055 and 0.064 and 0.076 (s×4, 12H), 0.858 and 0.867 and 0.884 (d and s×2, 30H, *J*=6.3 Hz), 1.16–1.30 and 1.25 (m and brs, 43H), 1.46–1.59 (m, 6H), 2.32 (dd, 1H, *J*=5.6, 14.9 Hz), 2.46 (dd, 1H, *J*=4.6, 14.9 Hz), 3.95–4.05 (m, 1H), 4.11–4.13 (m, 1H), 4.18 (q, 2H, *J*=7.3 Hz), 4.69 (dd, 1H, *J*=3.3, 7.9 Hz), 6.80 (d, 1H, *J*=7.3 Hz) Anal. Calcd for $C_{48}H_{99}NO_5Si_2$: C, 69.76; H, 12.07; N, 1.69. Found: C, 69.73; H, 11.81; N, 1.72.

***N*-[(1′*R*,2′*R*)-1′-Hydroxymethyl-2′-*tert*-butyldimethylsiloxy-14-methylpentadecanyl]-(*R*)-3-hydroxy-15-methylhexadecanamide (42).** To a stirred solution of the above compound (250 mg, 0.303 mmol) in THF (1 ml) at −10°C was added LiCl (65 mg, 1.53 mmol) and $NaBH_4$ (58 mg, 1.53 mmol), followed by the dropwise addition of EtOH (2 ml). The reaction mixture was stirred at −10°C for 1 h, and then at room temperature for 64 h. Citric acid (10%, 10 ml) was added, and the mixture was extracted with AcOEt (40 ml). The extracts were dried over Na_2SO_4. Concentration in vacuo gave the residue, which was purified by silica gel column chromatography with hexane–AcOEt (5:1) to give the alcohol **42** (85 mg, 37%) as a colorless oil, $[\alpha]_D^{23}=-11.5$ (*c* 0.501, $CHCl_3$). IR ν_{max} (film): 3362, 2926, 1650, 1464, 1366, 1256, 1055, 837, 777 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.051 and 0.076 and 0.097 (s×3, 12H), 0.848–0.912 (m, 30H), 1.16–1.28 and 1.25 (m and brs, 43H), 1.46–1.58 (m, 6H), 2.28 (dd, 1H, *J*=6.6, 14.2 Hz), 2.37 (dd, 1H, *J*=4.6, 14.5 Hz), 3.44 (br, 1H), 3.57 (br, 1H), 3.86–4.00 (m, 2H), 4.08–4.10 (m, 1H), 6.55 (d, 1H, *J*=6.9 Hz) Anal. Calcd for $C_{49}H_{97}NO_4Si_2$: C, 70.43; H, 12.46; N, 1.79. Found: C, 70.29; H, 12.41; N, 1.95.

The corresponding diol was obtained as a white amorphous solid. IR ν_{max} (film): 3347, 2926, 1744, 1666, 1466, 1374, 1240, 1048, 837, 777 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.091 and 0.097 (s×2, 6H), 0.859 and 0.849–0.912 (d and m, 20H, *J*=6.6 Hz), 1.13–1.25 and 1.25 (m and brs, 38H), 1.44–1.56 (m, 10H, 2H disappeared with D_2O), 2.35 (dd, 1H, *J*=5.0, 14.9 Hz), 2.50 (dd, 1H, *J*=4.3, 14.9 Hz), 3.71–3.83 (m, 2H), 3.96–4.07 (m, 3H), 7.02 (d, 1H, *J*=7.3 Hz).

Ethyl (2*R*,3*R*)-2-*tert*-butoxycarbonylamino-3-*tert*-butyldimethylsiloxy-15-metylhexadecanoate (43). To a stirred solution of the alcohol **31** (545 mg, 1.27 mmol) in DMF (3 ml) was added imidazole (251 mg, 3.69 mmol) and TBSCl (475 mg, 3.15 mmol). The mixture was stirred at room temperature for 18 h. After dilution with Et_2O (100 ml), the whole was washed with 1N $KHSO_4$, water, saturated aqueous NaCl, and dried over Na_2SO_4. Concentration in vacuo gave the residue, which was purified by silica gel column chromatography with hexane–AcOEt (10:1) to give **43** (663 mg, 96%) as a colorless oil, $[\alpha]_D^{16}=-21.1$ (*c* 1.02, $CHCl_3$). IR ν_{max} (film): 3447, 2928, 1744, 1717, 1497, 1368, 1256, 1165, 1059, 1030, 837, 776 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.047 and 0.075 (s×2, 6H), 0.861 and 0.872 (d and s, 15H, *J*=6.0 Hz), 1.26 (brs, 21H), 1.44 (s, 9H), 1.47–2.04 (m, 5H), 3.90 (brs, 1H), 4.08–4.27 (m, 2H), 4.32 (d, 1H, *J*=6.3 Hz), 5.28 (d, 1H, *J*=7.3 Hz). Anal. Calcd for $C_{30}H_{61}NO_5Si$: C, 66.25; H, 11.30; N, 2.58. Found: C, 66.10; H, 11.43; N, 2.39.

(2*R*,3*R*)-2-*tert*-Butoxycarbonylamino-3-*tert*-butyldimethylsiloxy-15-metylhexadecanol (44). To a stirred solution of the ester **43** (563 mg, 1.04 mmol) in THF (1 ml) at −10°C was added LiCl (275 mg, 6.46 mmol) and $NaBH_4$ (237 mg, 6.27 mmol), followed by the dropwise addition of EtOH (3 ml). The reaction mixture was stirred at −10°C for 1 h, and then at room temperature for 19 h. Citric acid (10%, 30 ml) was added at 0°C, and the mixture was extracted with $CHCl_3$ (100 ml). The extracts were dried over Na_2SO_4. Concentration in vacuo gave the residue, which was purified by silica gel column chromatography with hexane–AcOEt (5:1) to give the alcohol **44** (543 mg, quant.) as a colorless oil, $[\alpha]_D^{16}=-13.7$ (*c* 1.02, $CHCl_3$). IR ν_{max} (film): 3451, 2928, 1700, 1499, 1464, 1366, 1255, 1173, 1055, 837, 776 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.078 and 0.102 (s×2, 6H), 0.859 and 0.894 (d and s, 15H, *J*=6.6 Hz), 1.25 (brs, 18H), 1.45 (s, 9H), 1.45–1.59 (m, 5H), 3.10 (d, 1H, *J*=10.2 Hz, disappeared with D_2O), 3.56–3.59 (m, 1H), 3.63–3.64 (m, 1H), 3.95–3.99 (m, 1H), 4.04–4.08 (m, 1H), 5.34 (d, 1H, *J*=8.6 Hz). Anal. Calcd for $C_{28}H_{59}NO_4Si$: C, 67.01; H, 11.85; N, 2.79. Found: C, 66.68; H, 11.79; N, 2.54.

***S*-(2*R*,3*R*)-2-*tert*-Butoxycarbonylamino-3-*tert*-butyldimethylsiloxy-15-metylhexadecanyl thioacetate (45).** To a solution of the alcohol **44** (100 mg, 0.199 mmol) in benzotrifluoride (0.5 ml) at 0°C was added Et_3N (0.06 ml, 0.43 mmol), followed by the dropwise addition of MsCl

(0.03 ml, 0.388 mmol). The mixture was stirred at 0°C for 1 h. After dilution with AcOEt (60 ml), the whole was washed with water, 5% aqueous $NaHCO_3$, and dried over Na_2SO_4. Concentration in vacuo gave the residue, which was purified by silica gel column chromatography with hexane–Et_2O (10:1) to give the mesylate (116 mg, 100%) as a colorless oil which was unstable, and used for the next reaction immediately, IR ν_{max} (film): 3389, 2928, 1713, 1366, 1254, 1177, 1053, 837, 777 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.067 and 0.082 (s×2, 6H), 0.861 and 0.893 (d and s, 15H, J=6.6 Hz), 0.949–1.23 and 1.25 (m and brs, 18H), 1.44 (s, 9H), 1.45–1.55 (m, 5H), 3.03 (s, 3H), 3.80–3.82 (m, 1H), 3.91–3.93 (m, 1H), 4.25 (dd, 1H, J=10.2, 6.6 Hz), 4.37 (dd, 1H, J=4.3, 10.6 Hz), 4.76 (d, 1H, J=9.6 Hz).

The above material was dissolved in DMF (1 ml). CH_3COSK (130 mg, 1.14 mmol) was added at room temperature. After the mixture was stirred at room temperature for 20 h, water (20 ml) was added, and the mixture was extracted with AcOEt (60 ml). The extracts were washed with saturated aqueous NaCl (20 ml), and dried over Na_2SO_4. Concentration in vacuo gave the crude thioacetate **45** (119 mg, quantitative) as a yellow oil which was directly used for the next reaction. IR ν_{max} (film): 3374, 2906, 1716, 1698, 1499, 1366, 1252, 1171, 1113, 837, 776 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.059 and 0.081 (s×2, 6H), 0.861 and 0.914 (d and s, 15H, J=6.6 Hz), 1.16–1.26 and 1.256 (m and s, 18H), 1.42–1.55 and 1.43 (m and s, 14H), 2.34 (s, 3H), 2.98–2.99 (m, 1H), 3.11 (dd, 1H, J=3.3, 14.0 Hz), 3.60–3.85 (m, 2H), 4.70 (d, 1H, J=8.6 Hz).

***S*-(2*R*,3*R*)-3-Hydroxy-2-[(*R*)-3-hydroxy-15-methylhexadecanamido]-15-methylhexadecanyl thioacetate (46).** The thioacetate **45** (77 mg, 0.128 mmol) was treated with 4N HCl–dioxane at room temperature for 3 h. Removal of the solvent under reduced pressure afforded the crude hydrochloride salt as a pale yellow solid. To a solution of the above crude solid and β-hydroxycarboxylic acid **22** (30 mg, 0.106 mmol) in DMF (1 ml) at −10°C was added dropwise DEPC (0.02 ml, 0.132 mmol) and then Et_3N (0.055 ml, 0.395 mmol). The reaction mixture was stirred at −10°C for 1 h, and then at room temperature for 20 h. After dilution with AcOEt–benzene (2:1, 60 ml), the whole was washed with saturated aqueous $NaHCO_3$, water, saturated aqueous NaCl, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography with hexane–AcOEt (1:1) to give **46** (53 mg, 82%) as a white solid, mp 85–87°C, $[\alpha]_D^{17}$=−1.61 (c 0.3, $CHCl_3$). IR ν_{max} (nujol): 3291, 2922, 1694, 1643, 1539, 1377, 1134, 1036 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.860 (d, 12H, J=6.6 Hz), 1.16–1.25 and 1.253 (m and brs, 40H), 1.43–1.57 (m, 6H), 2.21 (dd, 1H, J=8.9, 15.2 Hz), 2.366 and 2.370 (dd and s, 4H, J=2.6, 14.9 Hz), 2.57 (brs, 1H, disappeared with D_2O), 3.05 (dd, 1H, J=3.6, 14.5 Hz), 3.19 (dd, 1H, J=9.2, 14.5 Hz), 3.32 (brs, 1H, disappeared with D_2O), 3.64 (br, 1H), 3.96–4.07 (m, 2H), 6.21 (d, 1H, J=8.9 Hz). HRMS Calcd for $C_{36}H_{67}NO_2S$ (M^+-$2H_2O$): 577.4892. Found: 577.4900. HRMS Calcd for $C_{34}H_{68}NO_3S$ (M^+-$SCOCH_3$): 570.4920. Found: 570.4933.

***N*-[(1′*R*,2′*R*)-1′-Mercaptomethyl-2′-hydroxy-14-methylpentadecanyl]-(*R*)-3-hydroxy-15-methylhexadecanamide (47).** To a suspension of the thioacetate **46** (105 mg, 0.171 mmol) in Et_2O (1 ml) was added $LiAlH_4$ (15 mg, 0.316 mmol) at 0°C. The reaction mixture was stirred at 0°C for 0.5 h. HCl (3N, 10 ml) was added, and the mixture was extracted with AcOEt (30 ml). The extracts were dried over Na_2SO_4. Concentration in vacuo gave the thiol **47** (92 mg, 94%) as a pale yellow oil which was directly used for the next reaction. IR ν_{max} (film): 3304, 2923, 1647, 1541, 1377, 1080, 722 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.859 (d, 12H, J=6.6 Hz), 1.16–1.25 and 1.25 (m and brs, 40H), 1.43–1.59 (m, 6H), 2.04–2.08 (m, 1H), 2.32 (dd, 1H, J=9.2, 15.0 Hz), 2.45 (d, 1H, J=14.8 Hz), 2.76–2.82 (m, 2H), 3.72 (brs, 1H), 4.01 (br, 2H), 6.41 (d, 1H, J=8.6 Hz).

Sulfobacin A (1). *Method A:*
To a stirred solution of the thiol **47** (68 mg, 0.119 mmol) in TFA (0.5 ml) was added dropwise 30% aqueous H_2O_2 (0.05 ml). The reaction mixture was stirred at room temperature for 0.5 h. Removal of the solvent under reduced pressure afforded the residue, which was purified by silica gel column chromatography with $CHCl_3$–MeOH–H_2O (65:10:1→65:25:3) to give sulfobacin **A** (**1**) (34 mg, 46%) as a white solid, mp 220–222°C, $[\alpha]_D^{18}$=−31.6 (c 0.14, MeOH). [lit.[1] $[\alpha]_D^{24}$=−35 (c 0.14, MeOH)] IR ν_{max} ($CHCl_3$): 3291, 2922, 1647, 1553, 1466, 1168, 1059 cm^{-1}. [lit.[1] IR ν_{max} (KBr): 3350, 2945, 2860, 1660, 1560, 1480, 1200, 1070 cm^{-1}.] ^1H NMR (DMSO-d^6/500 MHz) δ: 0.841 (d, 12H, J=6.7 Hz), 1.04–1.14 (m, 4H), 1.23 and 1.234–1.47 (s and m, 40H), 1.48–1.53 (m, 2H), 2.08–2.17 (m, 2H), 2.74 (d, 2H, J=5.5 Hz), 3.35–3.43 (m, 1H), 3.63–3.75 (m, 1H), 3.90–3.96 (m, 1H), 4.67 (d, 1H, J=4.3 Hz), 4.80 (d, 1H, J=5.5 Hz), 7.70 (d, 1H, J=8.9 Hz). [lit.[1] ^1H NMR (DMSO-d^6/400 MHz) δ: 0.84 (d, 12H, J=6.8 Hz), 1.14 (m, 4H), 1.22 (m, 38H), 1.37 (m, 2H), 1.49 (m, 2H), 2.11 and 2.13 (dd and dd, 2H, J=5.9, 10.8 Hz and J=5.4, 10.8 Hz), 2.73 (d, 2H, J=8.3 Hz), 3.46 (m, 1H), 3.76 (m, 1H), 3.92 (m, 1H), 4.66 (d, 1H, J=4.4 Hz), 4.80 (d, 1H, J=5.4 Hz), 7.68 (d, 1H, J=8.3 Hz).] ^{13}C NMR (DMSO-d^6) δ: 22.4 (q), 25.1 (t), 25.3 (t), 26.7 (t), 27.3 (d), 28.9–29.3 (m), 33.2 (t), 36.5 (t), 38.4 (t), 44.6 (t), 51.0 (d), 51.7 (t), 67.4 (t), 71.8 (d), 170.2 (s). [lit.[1] ^{13}C NMR (DMSO-d^6) δ: 22.6 (q×2), 25.2 (t), 25.5 (t), 26.9 (t), 27.4 (d), 29.2–29.4 (t×4), 33.4 (t), 36.6 (t), 38.5 (t), 44.8 (t), 51.1 (d), 51.8 (t), 67.6 (d), 72.0 (d), 170.2 (s).] TLC (R_f value): 0.26 (solvent: the low layer of $CHCl_3$–MeOH–H_2O (65:25:10) [lit.[1] TLC (R_f value): 0.26 (solvent: the low layer of $CHCl_3$–MeOH–H_2O (65:25:10)]

Method B:
To a stirred solution of the thioacetate **46** (25 mg, 0.041 mmol) in TFA (0.1 ml) was added dropwise 30% aqueous H_2O_2 (0.025 ml). After being stirred at room temperature for 1 h, removal of the solvent under reduced pressure afforded the residue, which was purified by silica gel column chromatography with $CHCl_3$–MeOH–H_2O (65:10:1→65:25;3) to given sulfobacin **A** (**1**) (8 mg, 32%) as a white solid.

Ethyl (2*R*,3*R*)-2-*tert*-butoxycarbonylamino-3-*tert*-butyldimethylsiloxy-15-metyl-4-hexadecenoate (48). Prepared from **34** in a similar manner as **43**. $[\alpha]_D^{24}$=−25.8 (c 1.09, $CHCl_3$). IR ν_{max} (film): 3447, 2927, 1725, 1497, 1471, 1368, 1252, 1169, 837 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.0099 and 0.0429 (s×2, 6H), 0.857 and 0.867 (d and s, 15H,

J=6.0 Hz), 1.25 and 1.25–1.30 (brs and m, 21H), 1.44 (s, 9H), 1.49–1.55 (m, 1H), 2.00–2.03 (m, 2H), 4.18 and 4.21–4.27 and 4.30–4.37 (dd, J=3.0, 7.0 Hz, and m and m, 4H), 5.14 (brs, 1H), 5.43 (dd, 1H, J=15.5, 6.6 Hz), 5.62–5.70 (m, 1H). Anal. Calcd for $C_{30}H_{59}NO_5Si$: C, 66.50; H, 10.97; N, 2.58. Found: C, 66.60; H, 11.31; N, 2.50.

(2*R*,3*R*)-2-*tert*-Butoxycarbonylamino-3-*tert*-butyldimethylsiloxy-15-metyl-4-hexadecenol (49). Prepared from **48** in a similar manner as **44**. $[\alpha]_D^{24}=-14.5$ (c 1.13, $CHCl_3$). IR ν_{max} (film): 3451, 2927, 1698, 1501, 1366, 1252, 1173, 837 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.0331 and 0.0746 (s×2, 6H), 0.861 and 0.900 (d and s, 15H, J=6.6 Hz), 1.26 (brs, 16H), 1.45 and 1.49–1.60 (s and m, 11H, 1H disappeared with D_2O), 2.00–2.04 (m, 2H), 3.40–3.50 (m, 1H), 3.57 (dd, 1H, J=3.3, 11.2 Hz), 4.03 (d, 1H, J=9.3 Hz), 4.48 (br, 1H), 5.53 (br, 1H), 5.54 (dd, 1H, J=6.3, 15.5 Hz), 5.49–5.77 (m, 1H). Anal. Calcd for $C_{28}H_{57}NO_4Si$: C, 67.28; H, 11.49; N, 2.80. Found: C, 67.43; H, 11.78; N, 2.79.

***S*-(2*R*,3*R*)-2-*tert*-Butoxycarbonylamino-3-*tert*-butyldimethylsiloxy-15-metyl-4-hexadecenyl thioacetate (50).** Prepared from **49** in a similar manner as **45**. $[\alpha]_D^{18}=-14.9$ (c 1.01, $CHCl_3$). IR ν_{max} (film): 3368, 2926, 1721, 1698, 1505, 1470, 1366, 1254, 1173, 1113, 967, 837 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.011 and 0.055 (s×2, 6H), 0.859 and 0.916 (d and s, 15H, J=6.6 Hz), 1.25 and 1.42 and 1.46–1.54 (brs and s and m, 26H), 2.01–2.33 (m, 1H), 2.52 (s, 3H), 3.04–3.12 (m, 2H), 3.65 (br, 1H), 4.23 (br, 1H), 4.17 (d, 1H, J=8.2 Hz), 5.39 (dd, 1H, J=6.3, 15.5 Hz), 5.62–5.73 (m, 1H). Anal. Calcd for $C_{30}H_{59}NO_4SSi$: C, 64.58; H, 10.66; N, 2.51. Found: C, 64.67; H, 10.72; N, 2.21.

***S*-(2*R*,3*R*)-3-Hydroxy-2-[(*R*)-3-hydroxy-15-methylhexadecanamido]-15-methyl-4-hexadecenyl thioacetate (51).** Prepared from **50** and **22** in a similar manner as **46**. A white solid: mp 89–90°C, $[\alpha]_D^{25}=-13.1$ (c 0.52, $CHCl_3$). IR ν_{max} (nujol): 3293, 1694, 1644, 1539, 1134, 1034, 961 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.861 (d, 12H, J=6.6 Hz), 1.16–1.25 and 1.26 and 1.38–1.54 (m and brs and m, 40H), 2.02–2.12 (m, 2H), 2.20 (dd, 1H, J=8.9, 15.2 Hz), 2.35 and 2.36 (dd and s, 4H, J=2.6, 15.2 Hz), 2.68 (brs, 1H, disappeared with D_2O), 3.02 (dd, 1H, J=3.6, 14.2 Hz). 3.16 (dd, 1H, J=9.2, 14.2 Hz), 3.33 (brs, 1H, disappeared with D_2O), 3.92–3.94 (m, 1H), 4.08–4.15 (m, 2H), 5.48 (dd, 1H, J=6.3, 15.5 Hz), 5.71–5.82 (m, 1H), 6.16 (d, 1H, J=7.3 Hz). Anal. Calcd for $C_{36}H_{69}NO_4S$: C, 70.65; H, 11.36; N, 2.29. Found: C, 70.56; H, 11.30; N, 2.11.

***S*-(2*R*,3*R*)-3-Acetoxy-2-[(*R*)-3-acetoxy-15-methylhexadecanamido]-15-methyl-4-hexadecenyl thioacetate (52).** To a solution of **51** (40 mg, 0.065 mmol) in pyridine (0.5 ml) at room temperature was added Ac_2O (0.025 ml). After stirring for 15.5 h at room temperature, ice water (20 ml) was added, and the mixture was extracted with Et_2O (30 ml). The organic extracts were washed with 1N aqueous $KHSO_4$ (20 ml), water (20 ml), and saturated aqueous $NaHCO_3$ (20 ml), and dried over Na_2SO_4. Concentration in vacuo gave the residue, which was purified by silica gel column chromatography with hexane–AcOEt (2:1) to give **52** (36 mg, 79%) as a white solid, mp 45–46°C, $[\alpha]_D^{24}=-7.95$ (c 0.35, $CHCl_3$). IR ν_{max} (nujol): 3314, 2926, 1738, 1700, 1651, 1545, 1468, 1372, 1235, 1028, 965 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 0.861 (d, 12H, J=6.6 Hz), 1.25 and 1.16–1.36 (brs and m, 40H), 1.39–1.62 (m, 4H), 2.05–2.11 and 2.07 and 2.09 (m and s, 8H), 2.35 and 2.41 (s and d, 5H, J=6.3 Hz), 2.99–3.15 (m, 2H), 4.29–4.31 (m, 1H), 5.06–5.11 (m, 1H), 5.28–5.29 (m, 1H), 5.40 (dd, 1H, J=7.3, 15.5 Hz), 5.76–5.82 (m, 1H), 5.94 (d, 1H, J=8.9 Hz). Anal. Calcd for 1.5 $C_{40}H_{73}NO_6S\cdot CH_3COOC_2H_5$: C, 67.89; H, 10.46; N, 1.86. Found: C, 68.06; H, 10.38; N, 1.79.

Flavocristamide A (3). To a solution of **52** (82 mg, 0.118 mmol) in AcOH (3 ml) was added AcOK (375 mg, 3.82 mmol) and then OXONE® (160 mg, 0.260 mmol). The reaction mixture was stirred at room temperature for 23 h. Removal of the solvent under reduced pressure afforded the residue, to which was added water (50 ml). The mixture was extracted with AcOEt (4×50 ml). The extracts were washed saturated aqueous $NaHCO_3$ (50 ml), and dried over Na_2SO_4. Concentration in vacuo gave a colorless oil (93 mg) which was directly used for the next reaction. The above material was dissolved in methanol (4 ml) and H_2O (1 ml). K_2CO_3 (199 mg, 1.43 mmol) was added at room temperature. After being stirred for 19 h at room temperature, 1N aqueous HCl was added. The mixture was extracted with AcOEt (2×100 ml). The extracts were dried over Na_2SO_4. Concentration in vacuo gave the residue, which was purified by silica gel column chromatography with $CHCl_3$–MeOH–H_2O (65:25:10 low layer) to give flavocristamide A (**3**) (73 mg, quant.) as a white solid, mp 216–218°C, $[\alpha]_D^{26}=-18.7$ (c 0.27, MeOH). [lit.[2] $[\alpha]_D^{20}=-17$ (c 0.27, MeOH)] IR ν_{max} (nujol): 3308, 2922, 1634, 1553, 1202, 1051, 965, 826, 722 cm^{-1}. [lit.[2] IR ν_{max} (KBr): 3450, 1640, 1560, 1200, 1060 cm^{-1}.] ^1H NMR (CD_3OD/500 MHz) δ: 0.876 (d, 12H, J=6.6 Hz), 1.15–1.29 and 1.29 (m and br, 36H), 1.37–1.45 (m, 2H), 1.48–1.55 (m, 2H), 2.01–2.07 (m, 2H), 2.28–2.31 (m, 2H), 2.97 (dd, 1H, J=9.1, 14.3 Hz), 3.13 (dd, 1H, J=3.2, 14.3 Hz), 3.96 (br, 1H), 4.14 (t, 1H, J=6.6 Hz), 4.32–4.36 (m, 1H), 5.47 (dd, 1H, J=15.4, 6.9 Hz), 5.70–5.76 (m, 1H). [lit.[2] ^1H NMR (CD_3OD/500 MHz) δ: 0.92 (d, 12H, J=6.7 Hz), 1.1–1.4 (m, 32H), 1.21 (m, 4H), 1.50 (m, 2H), 1.55 (m, 2H), 2.09 (m, 2H), 2.35 (m, 2H), 3.05 (dd, 1H, J=8.8, 14.4 Hz), 3.16 (dd, 1H, J=3.2, 14.4 Hz), 4.00 (m, 1H), 4.23 (m, 1H), 4.37 (m, 1H), 5.52 (dd, 1H, J=15.5, 7.1 Hz), 5.78 (dt, 1H, J=15.5, 6.8 Hz).] ^{13}C NMR (CD_3OD) δ: 23.10 (q), 26.74 (t), 28.59 (t), 28.62 (t), 29.20 (d), 30.45, 30.50, 30.78, 30.85, 30.87, 30.93, 31.10, 31.13, 33.54 (t), 38.16 (t), 40.29 (t), 40.31 (t), 45.43 (t), 51.84 (t), 52.60 (d), 69.81 (d), 75.15 (d), 130.57 (d), 134.98 (d), 173.99 (C=O). [lit.[2] ^{13}C NMR (CD_3OD) δ: 23.1 (q), 26.7 (t), 28.6 (t), 29.2 (d), 30.4, 30.5, 30.7, 30.8 (t), 30.9, 31.1, 33.5 (t), 38.1 (t), 40.3 (t), 45.6 (t), 51.7 (t), 52.7 (d), 69.8 (d), 75.0 (d), 130.5 (d), 134.9 (d).]

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