Synthesis of sphingosine relatives. Part 19.[1] Synthesis of penaresidin A and B, azetidine alkaloids with actomyosin ATPase-activating properties

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Three stereoisomers of penaresidin A 1 and two stereoisomers of penaresidin B 2′ (Scheme 5), azetidine alkaloids isolated from the Okinawan marine sponge *Penares* sp., have been synthesized. In the course of our synthetic study, the correct structure of penaresidin B has been shown to be not 2 but 2′. Natural penaresidin A is either (2*S*,3*R*,4*S*,15*S*,16*S*)- or (2*S*,3*R*,4*S*,15*R*,16*R*)-1 and natural penaresidin B is either (2*S*,3*R*,4*S*,15*S*)- or (2*S*,3*R*,4*S*,15*R*)-2′.

In 1991, penaresidin A **1** and B **2**, actomyosin ATPase activators, were isolated by Kobayashi *et al.*[2] from the Okinawan marine sponge *Penares* sp., and characterized as a mixture of the corresponding tetraacetyl derivatives. Because nothing was known about the absolute configuration of penaresidin A and B, **1** and **2**, we attempted the synthesis of the enantiomerically pure stereoisomers of **1** and **2** so as to determine the absolute configurations of the natural products. We have already reported the synthesis of penaresidin A as a preliminary communication[3] and the synthesis[1] of a similar azetidine alkaloid penazetidine A.[4] A synthesis of a simple model compound of **1** was also reported by Hiraki *et al.*[5] Herein we describe our synthesis of penaresidin A and B in detail.

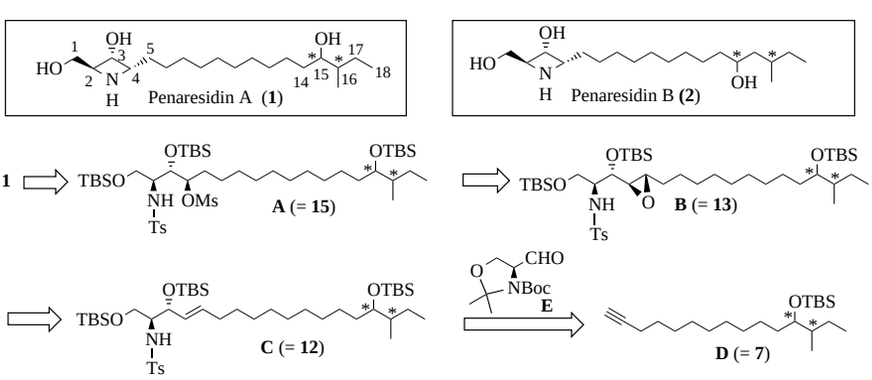
Results and discussion

Synthetic plan for penaresidins

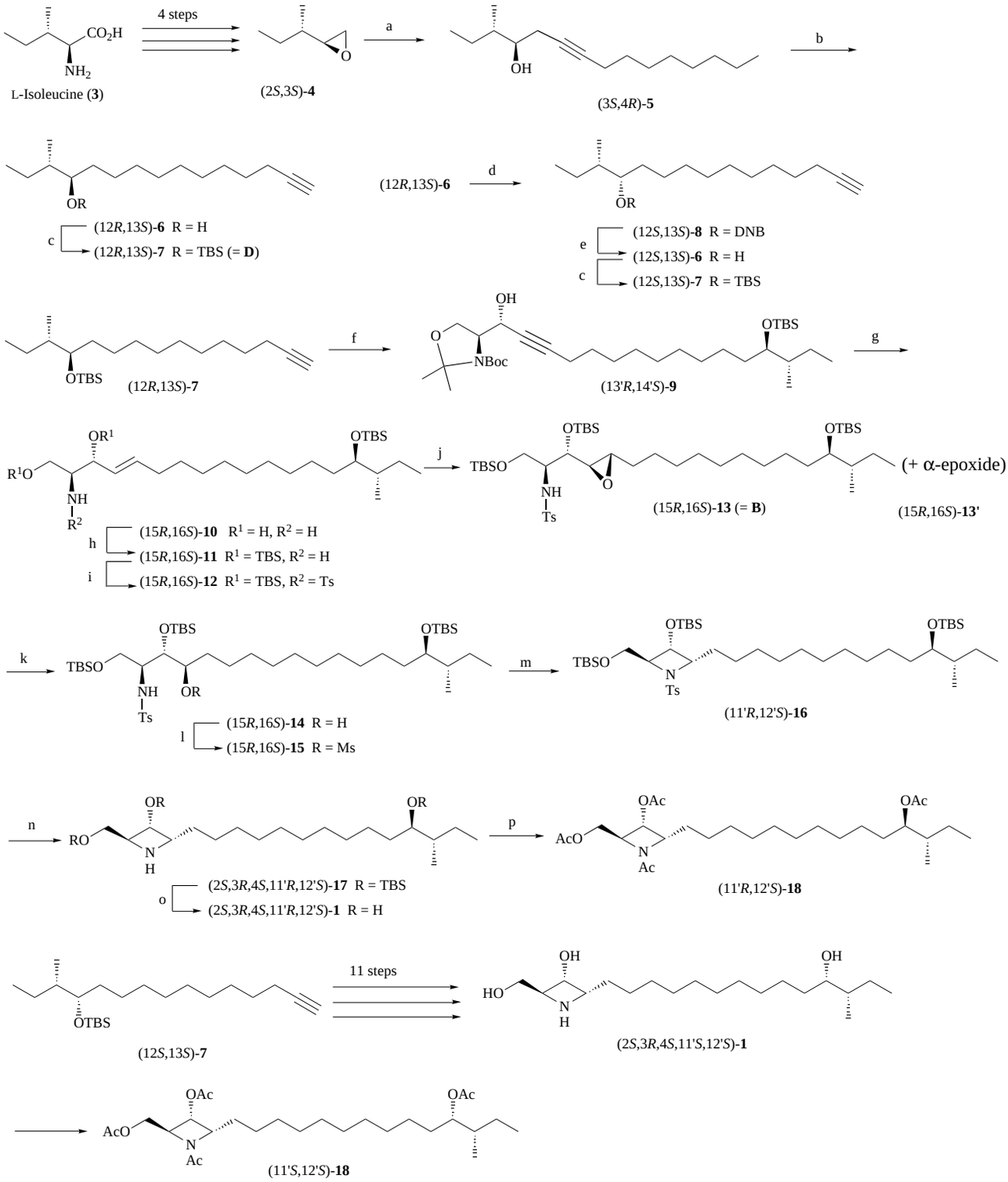
We assumed the absolute configuration of the azetidine portion of penaresidins to be 2*S*,3*R*,4*S*, considering the possible biogenetic relationship between penaresidins and the natural phytosphingosines. We first attempted the synthesis of penaresidin A **1**, because it was reported to be the major component.[2] There are two contiguous stereogenic centres in the side-chain of **1**. We therefore planned to synthesize 15,16 *syn*- and *anti*-isomers, respectively, to determine the relative stereochemistry of the natural product. We could then synthesize an additional stereoisomer with the correct relative stereochemistry for the chiral centres in the side-chain. Once we had synthesized **1**, we could turn our attention to the synthesis of penaresidin B **2**, which is reported to be the minor component. Scheme 1 shows the synthetic plan for **1**. According to this synthetic plan, our target molecule **1** can be prepared from a phytosphingosine derivative **A**. Intermediate **A** can be obtained by regioselective reduction of **B**, itself derived from **C**. We planned to prepare the sphingosine analogue **C** from **D** and **E** employing Garner's general method of sphingosine synthesis.[6] Stereoisomers of **D** could then be obtained from L-isoleucine in the usual manner. The basic strategy of this plan is also applicable to the synthesis of penaresidin B.

Preparation of the key intermediate B

The alkynes, (12*R*,13*S*)- and (12*S*,13*S*)-**7** (= **D**), were prepared and converted into the key intermediates **12** (= **C**) as shown in Scheme 2. The epoxide (2*S*,3*S*)-**4** was prepared from L-isoleucine **3** in 4 steps.[7] Regioselective cleavage of the epoxy ring of (2*S*,3*S*)-**4** with the anion derived from dec-1-yne gave the alcohol (3*S*,4*R*)-**5** (53%), which was submitted to an acetylene-zipper reaction[8] to give (12*R*,13*S*)-**6** in 73% yield. The hydroxy group of (12*R*,13*S*)-**6** was protected as a *tert*-butyldimethylsilyl (TBS) ether to give (12*R*,13*S*)-**7** (= **D**) in 99% yield. Together with this, Mitsunobu inversion[9] of (12*R*,13*S*)-**6** gave the inverted 3,5-dinitrobenzoate (12*S*,13*S*)-**8** in 71% yield. After the



Scheme 1 Structure of penaresidins, and the synthetic plan for penaresidin A

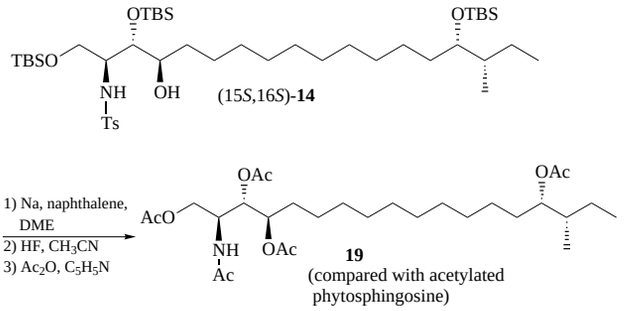


Scheme 2 Synthesis of (15*R*,16*S*)- and (15*S*,16*S*)-penaresidin A. *Reagents, conditions and yields:* (a) dec-1-yne, BuLi, BF_3·OEt_2, THF (53%); (b) Li, Bu^tOK, $H_2N(CH_2)_3NH_2$ (73%); (c) TBSCl, imidazole, DMF (99% or 96%); (d) 3,5-DNB acid, DEAD, Ph_3P, THF (71%); (e) aq. KOH, THF–MeOH (86%); (f) BuLi, THF, then Garner's aldehyde **E** (94%); (g) Li, $EtNH_2$ (quant.); (h) TBSOTf, 2,6-dimethylpyridine, CH_2Cl_2 (84% in 2 steps); (i) TsCl, C_5H_5N (95%); (j) *m*-CPBA, $NaHCO_3$, hexane (39% of **13** and 60% of **13**′); (k) DIBAL, toluene (84%); (l) MsCl, C_5H_5N (quant.); (m) NaH, THF (88% in 2 steps); (n) Na, naphthalene, DME (88%); (o) aq. HF, CH_3CN (81%); (p) Ac_2O, C_5H_5N (95%).

hydrolysis of (12*S*,13*S*)-**8** with aq. KOH, the resulting alcohol (12*S*,13*S*)-**6** was converted into the corresponding TBS ether (12*S*,13*S*)-**7** (= **D**) (83% in 2 steps). The anion derived from (12*R*,13*S*)-**7** by treatment with BuLi was coupled with the aldehyde **E**[5] diastereoselectively to give the *erythro*-isomer (13′*R*,14′*S*)-**9** in 94% yield. It was then reduced with lithium in ethylamine to furnish the crude amino diol (15*R*,16*S*)-**10**. The hydroxy groups and amino group of (15*R*,16*S*)-**10** were protected as TBS ethers and as a toluene-*p*-sulfonamide (Ts amide) respectively to give the key intermediate, the fully protected sphingosine analogue, (15*R*,16*S*)-**12** (= **C**) (80% in 3 steps). Similarly, (12*S*,13*S*)-**7** was converted into (15*S*,16*S*)-**12** (= **C**) (64% in 4 steps).

Synthesis of (2*S*,3*R*,4*S*,15*R*,16*S*)- and (2*S*,3*R*,4*S*,15*S*,16*S*)-penaresidin A

Epoxidation of (15*R*,16*S*)-**12** with *m*-chloroperbenzoic acid (*m*-CPBA) in hexane yielded (15*R*,16*S*)-**13** in only 39% yield, the



Scheme 3 Determination of the structure of **14**

major isomer being the undesired α-epoxide (15*R*,16*S*)-**13**′. Although various reagents were examined under different conditions for the epoxidation of **12**, we were unable to improve the diastereoselectivity; the optimum ratio of **13**:**13**′ was *ca*. 4:6. The reductive opening of the epoxy ring of (15*R*,16*S*)-**13** with diisobutylaluminium hydride (DIBAL) took place regioselectively to give the alcohol (15*R*,16*S*)-**14** in 84% yield.

To confirm the depicted stereochemistry of the alcohol **14**, the alcohol (15*S*,16*S*)-**14** was converted into **19** in the conventional manner as follows: (i) Na and naphthalene in DME, (ii) aq. HF in MeCN and (iii) Ac_2O in pyridine (Scheme 3). The ^{1}H NMR data of **19** were then compared with the published data of acetylated phytosphingosine[10] and found to be same with regard to the signals for the protons at C-1 to C-4.

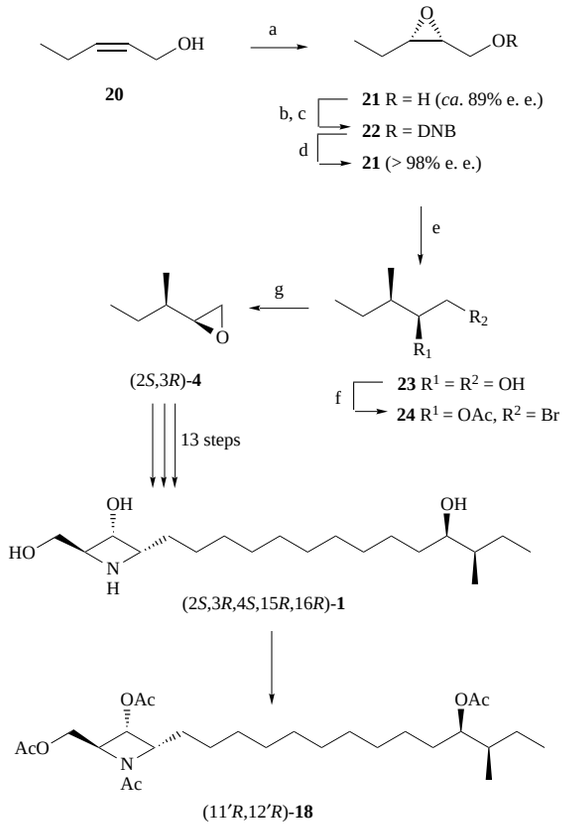
Treatment of (15*R*,16*S*)-**14** with methanesulfonyl chloride (MsCl) gave the mesylate (methanesulfonate) (15*R*,16*S*)-**15** in quantitative yield and this upon treatment with sodium hydride in tetrahydrofuran (THF) underwent smooth ring-closure to furnish the azetidine (11′*R*,12′*S*)-**16** (88% in 2 steps). After the removal of the *N*-Ts group by treatment with sodium naphthalenide (88%), the TBS groups of (11′*R*,12′*S*)-**17** were cleaved by treatment with hydrofluoric acid (HF) in acetonitrile to give (2*S*,3*R*,4*S*,15*R*,16*S*)-penaresidin A **1** in 81% yield. The overall yield was 5.9% in 13 steps based on the epoxide (2*S*,3*S*)-**4**. For comparison with the naturally occurring product, (2*S*,3*R*,4*S*,15*R*,16*S*)-**1** was converted into the corresponding tetraacetyl derivative (2*S*,3*R*,4*S*,11′*R*,12′*S*)-**18**. It was dextrorotatory, $[\alpha]_D^{27}$ = +45 ($CHCl_3$). The synthesis of (2*S*,3*R*,4*S*,15*S*,16*S*)-**1** was achieved by a similar procedure starting from the intermediate (15*S*,16*S*)-**12**. The overall yield was 3.4% in 15 steps based on the epoxide (2*S*,3*S*)-**4**. The product (2*S*,3*R*,4*S*,15*S*,16*S*)-**1** was also acetylated to give the tetraacetyl derivative (2*S*,3*R*,4*S*,11′*S*,12′*S*)-**18**, $[\alpha]_D^{27}$ = +38.0 ($CHCl_3$).‡

We then carefully compared the highfield ^{1}H and ^{13}C NMR spectra of the mixture of the tetraacetyl derivatives derived from natural penaresidins A and B[2] with those of the synthetic stereoisomers of **18**. The spectra were very similar to each other. In the ^{1}H NMR spectrum of the naturally derived materials, however, the signal due to the proton at C-11′ appeared at δ = 4.84, while that of (2*S*,3*R*,4*S*,11′*R*,12′*S*)-**18** appeared at δ = 4.79. (2*S*,3*R*,4*S*,11′*S*,12′*S*)-**18** showed its NMR signal due to the C-11′ proton at δ = 4.86. Accordingly, the 11′,12′-*syn* isomer must be the natural penaresidin A.

Synthesis of (2*S*,3*R*,4*S*,15*R*,16*R*)-penaresidin A and speculation on stereochemistry of penaresidin A

Since we have already shown that the 15,16-*syn* isomer corresponds to natural penaresidin A, we therefore synthesized the alternative 15,16-*syn* isomer (2*S*,3*R*,4*S*,15*R*,16*R*)-**1**, as shown in Scheme 4. (*Z*)-Pent-2-en-1-ol **20** was subjected to Sharpless asymmetric epoxidation[11] to give the epoxy alcohol **21** (*ca*. 89% ee; 60% yield). This alcohol was purified by recrystallization of the corresponding 3,5-dinitrobenzoate **22** to afford enantiomerically enriched **21** (> 98% ee; 42% yield) after hydrolysis of

‡ $[\alpha]_D$ Values are quoted in units of 10^{-1} deg cm^2 g^{-1} throughout.



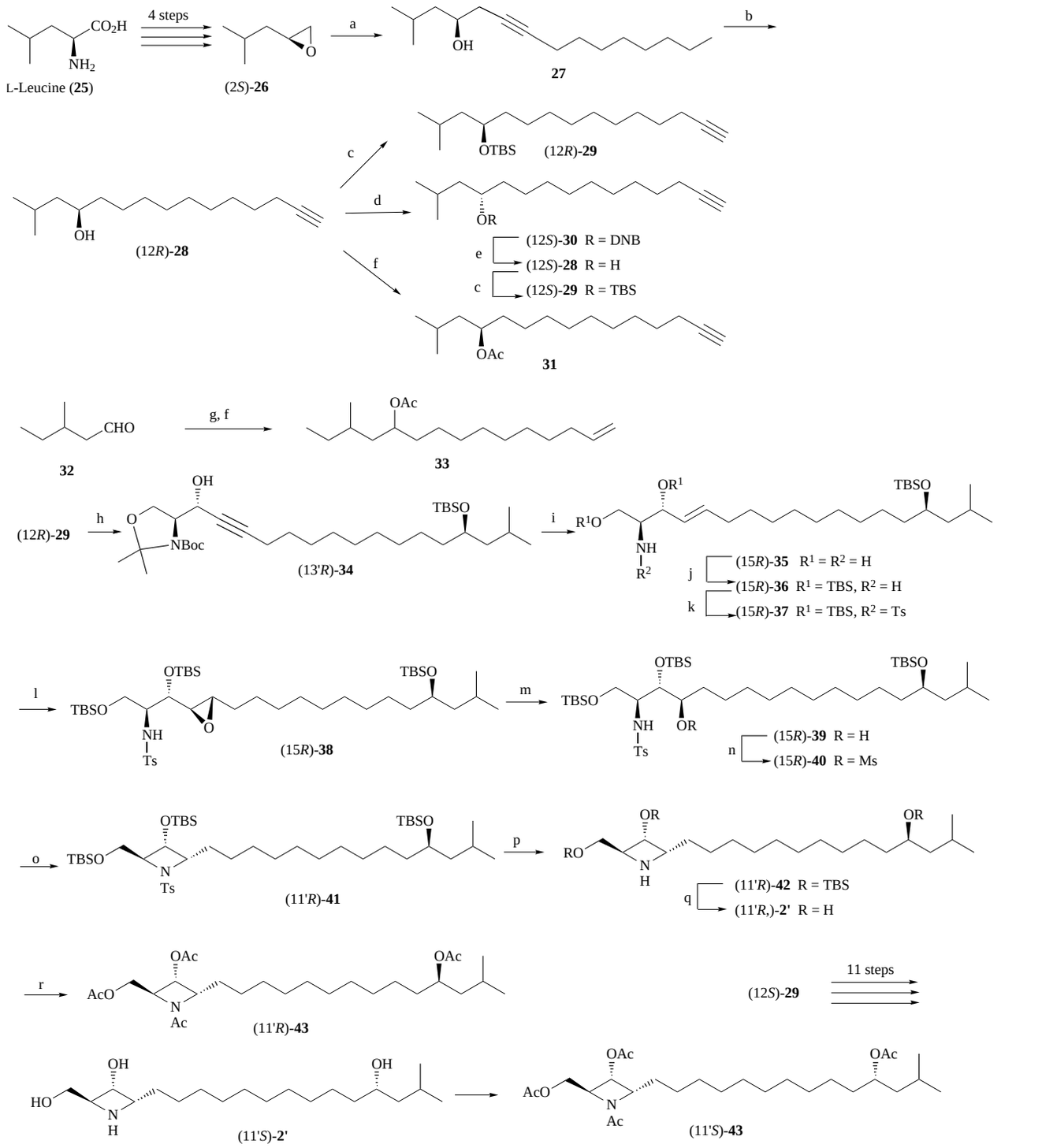
Scheme 4 Synthesis of (15*R*,16*R*)-penaresidin A. *Reagents, conditions and yields:* (a) TBHP, (−)-DIPT, $Ti(OPr^i)_4$, 4 Å molecular sieves, CH_2Cl_2 (60%); (b) 3,5-DNBCl, C_5H_5N, CH_2Cl_2; (c) recrystallization (from hexane–benzene, 5:1) (55%); (d) aq. KOH, THF–MeOH (77%); (e) Me_3Al, BuLi, pentane (50%); (f) HBr, AcOH (quant.); (g) NaOMe, MeOH (79% in 2 steps).

22. Conversion of **21** into the epoxide (2*S*,3*R*)-**4** was brought about by our previously described method:[7d] treatment with (i) trimethylaluminium and BuLi–pentane, (ii) HBr–AcOH and (iii) NaOMe–MeOH (40% in 3 steps). By a similar procedure to that used earlier, the epoxide (2*S*,3*R*)-**4** was finally converted into (2*S*,3*R*,4*S*,15*R*,16*R*)-**1**. The overall yield was 4.5% in 13 steps based on the epoxide (2*S*,3*R*)-**4** or 0.5% in 19 steps based on **20**. The corresponding tetraacetyl derivative (2*S*,3*R*,4*S*,11′*R*,12′*R*)-**18** was also synthesized, and shown to be dextrorotatory, $[\alpha]_D^{27}$ = +42 ($CHCl_3$).

The optical rotational values of all three synthetic stereoisomers of **18** were dextrorotatory. Since the mixture of the tetraacetyl derivatives derived from the natural penaresidins A and B was reported to be dextrorotatory, $[\alpha]_D^{23}$ = +47.9 ($CHCl_3$), the stereochemistry of the azetidine ring of the natural **1** must be 2*S*,3*R*,4*S* as we assumed initially. Because of the considerable distance between the azetidine portion of **18** and the contiguous stereogenic centres at C-11′ and C-12′, (2*S*,3*R*,4*S*,11′*R*,12′*R*)-**18** and its (11′*S*,12′*S*)-isomer showed indistinguishable ^{1}H and ^{13}C NMR spectra. We were, therefore, unable to determine the absolute configuration of the side-chain part of the natural product.[13]

Revised structure of penaresidin B

Following the synthesis of penaresidin A we then synthesized penaresidin B. After a careful study of the reported ^{13}C NMR data for the tetraacetyl derivative of natural penaresidin B we concluded that the proposed structure of penaresidin B **2** might be in error. As mentioned earlier, the natural penaresidins were isolated and characterized as a mixture of their corresponding tetraacetyl derivatives. A structure determination of the natural penaresidins was, therefore, difficult. Completion of the synthesis of penaresidin A, however, made it pos-

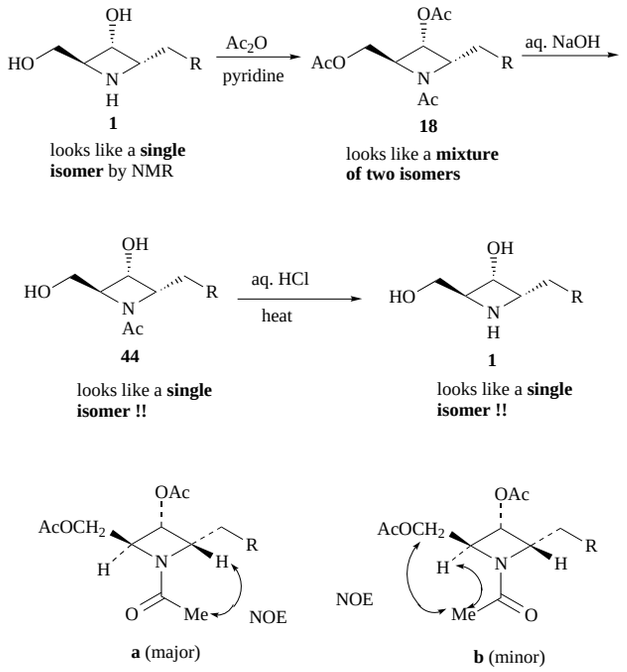


Scheme 5 Synthesis of penaresidin B. *Reagents, conditions and yields:* (a) dec-1-yne, BuLi, $BF_3{\cdot}OEt_2$, THF (65%); (b) Li, Bu^{t}OK, $H_2N(CH_2)_3NH_2$ (59%); (c) TBSCl, imidazole, DMF (93% or 96%); (d) 3,5-DNB acid, DEAD, Ph_3P, THF (83%); (e) aq. KOH, THF–MeOH (93%); (f) Ac_2O, C_5H_5N; (g) $CH_2{=}CH(CH_2)_8MgBr$, THF; (h) BuLi, THF, then Garner's aldehyde **E** (80%); (i) Li, $EtNH_2$ (quant.); (j) TBSOTf, 2,6-dimethylpyridine, CH_2Cl_2 (70% in 2 steps); (k) TsCl, C_5H_5N (90%); (l) *m*-CPBA, $NaHCO_3$, hexane (38%); (m) DIBAL, toluene (82%); (n) MsCl, C_5H_5N (quant.); (o) NaH, THF (72% in 2 steps); (p) Na, naphthalene, DME (87%); (q) aq. HF, CH_3CN (86%); (r) Ac_2O, C_5H_5N (82%).

sible for us to detect some signals arising from the tetraacetyl derivative of the natural penaresidin B from the ^{13}C NMR spectrum of the acetylated natural penaresidins. There were some signals which could not be assigned as arising from the acetylated penaresidin A. In other words, these signals could arise from the acetylated penaresidin B. These signals appeared at δ = 23.1, 24.6, 34.7, 43.3 and 72.7 (ppm), and their chemical-shift values led us to propose the revised structure **2′** as shown in Scheme 5.

Clarification of the structure of penaresidin B by its synthesis

We started with a synthesis of the compound corresponding to the revised structure of penaresidin B (**2′**). The synthetic route was almost the same as that of penaresidin A except for the starting material. For penaresidin B, we used L-leucine **25** as the starting material instead of L-isoleucine for penaresidin A. The epoxide **26**, which was prepared from L-leucine in the usual manner,[7] was converted into the enantiomers of the TBS ether (12*R*)- and (12*S*)-**29**. Apart from the main stream of the syn-



Scheme 6 Rotational isomers of penaresidin tetraacetyl derivatives

thesis, we synthesized the acetates **31** and **33**, to clarify the structure of the side-chain part of penaresidin B. We compared the ^{13}C NMR spectra of **31** and **33** with that of the acetylated natural penaresidin B and found that the former fitted more closely to the natural one than the latter. We therefore became convinced that **2′** should be penaresidin B and continued the synthesis.

In the same manner as described for the synthesis of penaresidin A, both the enantiomers (12*R*)- and (12*S*)-**27** were converted into (2*S*,3*R*,4*S*,15*R*)- and (2*S*,3*R*,4*S*,15*S*)-penaresidin B **2′**, respectively. The overall yields of (2*S*,3*R*,4*S*,15*R*)- and (2*S*,3*R*,4*S*,15*S*)-**2′** were 3.1% in 13 steps and 3.2% in 15 steps based on the epoxide **26**, respectively. For a comparison with the naturally occurring product, (2*S*,3*R*,4*S*,15*R*)- and (2*S*,3*R*,4*S*,15*S*)-**2′** were converted into the corresponding tetraacetyl derivatives (2*S*,3*R*,4*S*,11′*R*)- and (2*S*,3*R*,4*S*,11′*S*)-**43**. These were dextrorotatory, (2*S*,3*R*,4*S*,11′*R*)-**43**: $[\alpha]_D^{27}$ = +35 ($CHCl_3$); (2*S*,3*R*,4*S*,11′*S*)-**43**: $[\alpha]_D^{27}$ = +47 ($CHCl_3$). Because the mixture of the tetraacetyl derivatives derived from the natural penaresidins A and B was reported to be dextrorotatory, $[\alpha]_D^{23}$ = +47.9 ($CHCl_3$), the stereochemistry of the azetidine ring of the natural compound **2′** must also be 2*S*,3*R*,4*S* as we assumed at the beginning. Due to the long distance between the azetidine portion of **43** and the stereogenic centre at C−11′, (2*S*,3*R*,4*S*,11′*R*)-**43** and its (11′*S*)-isomer showed indistinguishable ^{1}H and ^{13}C NMR spectra. As for the side-chain portion, we therefore could not clarify the absolute configuration of the natural product.[13]

Existence of two rotational isomers of acetylated penaresidins

In the course of ^{1}H and ^{13}C NMR analyses of the stereoisomers of acetylated penaresidins (**18** and **43**), we found that each of them exists as a mixture of two rotational isomers (**a** and **b**, shown in Scheme 6) about the N−Ac bond. Indeed **18**, which has ^{1}H and ^{13}C NMR spectra like a mixture of two isomers as in the case reported by Kobayashi *et al.*[2] and Hiraki *et al.*,[5] gave back the starting single isomer of **1** upon hydrolysis with aq. NaOH followed by hot aq. HCl. In the ^{1}H NMR study (NOESY) of **18**, the interaction between N−CO*Me* and the proton at C−4 of **a** as well as that between N−CO*Me* and the proton at C−1 and C−2 of **b** could be observed. The present interpretation of the NMR properties of **18** and **43** is different from that proposed by Hiraki *et al.*[5] A similar example of rotational isomerism about an N−Ac bond was reported earlier for methyl 5-acetamido-5-deoxy-2,3,4-tri-*O*-methyl-α-D-xylopyranoside.[12] In cooperation with Dr T. Nukada (The Institute of Physical and Chemical Research), we employed computational chemistry to clarify the existence of rotational isomers. The details concerning the computational study will be described separately.

In conclusion, we have synthesized three stereoisomers of penaresidin A **1** and two stereoisomers of penaresidin B **2′**. In the course of our synthetic study, the correct structure of penaresidin B was shown to be **2′**. In view of this result, natural penaresidin A must be either (2*S*,3*R*,4*S*,15*S*,16*S*)- or (2*S*,3*R*,4*S*,15*R*,16*R*)-**1**, and natural penaresidin B must be either (2*S*,3*R*,4*S*,15*S*)- or (2*S*,3*R*,4*S*,15*R*)-**2′**. Due to the long distance between the azetidine portion and the stereogenic centres at C-15 and C-16, we could not clarify the absolute configuration of the side-chain portion. For an unambiguous determination of the stereochemistry of penaresidin A, we must await the re-isolation of pure material so that we are able to compare its chiroptical and biological properties with those of our synthetic samples.[13]

Experimental

All bps and mps are uncorrected. IR spectra were measured as films for oils or as KBr disks for solids on a Perkin-Elmer 1640 spectrometer. ^{1}H NMR spectra were recorded at 60 MHz on a Hitachi R-24B spectrometer, at 270 MHz on a JEOL JNM EX 270L spectrometer, at 500 MHz on a JEOL JNM A500 spectrometer or at 600 MHz on a JEOL JNM A600 instrument. The peak for TMS or solvent ($CHCl_3$: δ 7.26, CD_2HOD: δ 3.30) was used as the internal standard. *J* Values are given in Hz. ^{13}C NMR spectra were recorded at 67.8 MHz on a JEOL JNM EX 270L spectrometer, at 125 MHz on a JEOL JNM A500 spectrometer or at 150 MHz on a JEOL JNM A600. Solvent peak ($CDCl_3$: δ 77.0, CD_3OD: δ 49.0) was used as the internal standard. Optical rotations were measured on a Jasco DIP-1000 polarimeter. Mass spectra were recorded on a JEOL JMS-SX102A mass spectrometer. Refractive indexes were measured on an ATAGO Abbe refractometer 1T.

3-Methylpentadec-6-yn-4-ol 5

(3*S*,4*R*)-Isomer. BuLi (1.71 mol dm^{-3} in hexane; 96.5 cm^3, 165 mmol) was added dropwise to a solution of dec-1-yne (22.8 cm^3, 165 mmol) in dry THF (300 cm^3) at −20 °C under Ar, and the mixture was stirred for 30 min at −10 °C. After this the solution was re-cooled to −78 °C, and treated with BF_3·OEt_2 (20.3 cm^3, 165 mmol), added dropwise. The mixture was then stirred for 10 min after which a solution of the epoxide (2*S*,3*S*)-**4** (11.2 g, 112 mmol) in dry THF (60 cm^3) was added to it. This reaction mixture was allowed to warm to room temperature with stirring during 1 h after which it was quenched with saturated aq. NH_4Cl and then extracted with diethyl ether. The extract was washed successively with water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *alcohol* (3*S*,4*R*)-**5** (14.0 g, 53%) as a colourless oil, n_D^{26} 1.4579 (Found: C, 80.57; H, 12.72. $C_{16}H_{30}O$ requires C, 80.61; H, 12.68%); $[\alpha]_D^{28}$ −11.5 (*c* 0.99 in MeOH); ν_{max}(film)/cm^{-1} 3450m (OH), 1050m (CO); δ_H(270 MHz; $CDCl_3$) 0.89 (9 H, m, Me), 1.10–1.70 (15 H, m, 2, 3, 9, 10, 11, 12, 13, 14-H), 2.00 (1 H, d, *J* 5, OH), 2.16 (2 H, m, 8-H), 2.27 (1 H, ddt, *J* 16, 8 and 2, 5-Ha), 2.40 (1 H, ddt, *J* 16, 4 and 2, 5-Hb) and 3.48 (1 H, m, 4-H).

13-Methylpentadec-1-yn-12-ol 6

(12*R*,13*S*)-Isomer. Li wire (1.63 g, 235 mmol) was added to freshly distilled 1,3-diaminopropane (140 cm^3) under Ar. This mixture was heated and stirred at 70 °C for 2 h until the blue

colour was discharged, and a milky white suspension of the lithium salt was obtained. After the mixture had cooled to room temperature, Bu^{t}OK (14.8 g, 130 mmol) was added to it and the stirring was continued for 15 min. Upon addition of the alcohol (3*S*,4*R*)-**5** (6.89 g, 28.9 mmol) to the reaction mixture it turned dark red. After being stirred for 2.5 h, the reaction mixture was quenched with saturated aq. NH_4Cl, and extracted with diethyl ether. The extract was washed with dil. aq. HCl, water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *alcohol* (12*R*,13*S*)-**6** (5.50 g, 73%), a colourless oil, n_D^{25} 1.4608 (Found: C, 80.55; H, 12.70. $C_{16}H_{30}O$ requires C, 80.61; H, 12.68%); $[\alpha]_D^{28}$ +8.1 (*c* 0.94 in MeOH); ν_{max}(film)/cm^{-1} 3380m (OH), 3310m (HC≡C), 2120w (C≡C) and 1055m (CO); δ_H(60 MHz; $CDCl_3$) 0.92 (6 H, m, Me), 1.30 (20 H, br s, 4, 5, 6, 7, 8, 9, 10, 11, 13, 14-H, OH), 1.90 (1 H, t, *J* 3, 1-H), 2.17 (2 H, m, 3-H) and 3.43 (1 H, m, 12-H).

13-Methylpentadec-1-yn-12-yl 3,5-dinitrobenzoate 8

(12*S*,13*S*)-Isomer. Ph_3P (13.7 g, 52.2 mmol) and 3,5-dinitrobenzoic acid (11.1 g, 52.3 mmol) were added portionwise to a solution of the alcohol (12*R*,13*S*)-**6** (5.00 g, 21.0 mmol) in THF (100 cm^3) at room temperature under Ar. A solution of DEAD (9.14 g, 52.5 mmol) in THF (30 cm^3) was added dropwise to this solution, and the stirring was continued overnight. The reaction mixture was then filtered through Celite, and the filtrate was concentrated under reduced pressure. The residue was diluted with hexane–EtOAc (1:1) to precipitate Ph_3PO which was removed by filtration through SiO_2. After evaporation of the filtrate under reduced pressure, the residue was chromatographed over SiO_2 to give the *benzoate* (12*S*,13*S*)-**8** (6.41 g, 71%), a pale yellow oil, n_D^{26} 1.5176 (Found: C, 63.68; H, 7.20; N, 6.38. $C_{23}H_{32}O_6N_2$ requires C, 63.87; H, 7.46; N, 6.48%); $[\alpha]_D^{28}$ −5.83 (*c* 1.49 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3305m (HC≡C), 3105m (aromatic), 2115w (C≡C), 1730s (C=O), 1660m (aromatic) and 1550m (nitro); δ_H(60 MHz; $CDCl_3$) 1.02 (6 H, m, Me), 1.29 (19 H, br s, 4, 5, 6, 7, 8, 9, 10, 11, 13, 14-H), 1.90 (1 H, t, *J* 3, 1-H), 2.15 (2 H, m, 3-H), 5.20 (1 H, m, 12-H) and 9.10 (3 H, m, aromatic).

13-Methylpentadec-1-yn-12-ol 6

(12*S*,13*S*)-Isomer. To a solution of the 3,5-dinitrobenzoate (12*S*,13*S*)-**8** (5.75 g, 13.6 mmol) in THF–MeOH (2:1; 60 cm^3), aq. KOH (1.0 mol dm^{-3}; 16 cm^3, 16 mmol) was added at 0 °C. After removal of the cooling bath, the mixture was stirred for 5 h and then poured into water and extracted with diethyl ether. The extract was washed with water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *alcohol* (12*S*,13*S*)-**6** (2.79 g, 86%), a colourless oil, n_D^{25} 1.4611 (Found: C, 80.59; H, 12.79. $C_{16}H_{30}O$ requires C, 80.61; H, 12.68%); $[\alpha]_D^{28}$ −14.1 (*c* 1.22 in MeOH); ν_{max}(film)/cm^{-1} 3380m (OH), 3310m (HC≡C) and 2120w (C≡C); δ_H(60 MHz; $CDCl_3$) 0.92 (6 H, m, Me), 1.30 (20 H, br s, 4, 5, 6, 7, 8, 9, 10, 11, 13, 14-H, OH), 1.91 (1 H, t, *J* 3, 1-H), 2.17 (2 H, m, 3-H) and 3.48 (1 H, m, 12-H).

Diastereoisomeric purity of the alcohol 6

(12*R*,13*S*)-**6** was converted into the corresponding 3,5-dinitrobenzoate (12*R*,13*S*)-**8** in the conventional manner. This isomer and its stereoisomer (12*S*,13*S*)-**8** which was obtained by Mitsunobu inversion, were analysed by HPLC to determine their diastereoisomeric purities. HPLC analysis [column, Senshu Pak Silica 1251-N (4.6 i.d. × 250 mm); solvent, hexane–EtOAc (150:1); flow, 1.2 cm^3 min^{-1}; detect, at 254 nm] (i) (12*R*,13*S*)-**8**; R_t/min 27.3 [~1.5%, (12*S*,13*S*)-**8**], 28.8 [~98.5%, (12*R*,13*S*)-**8**]. The diastereoisomeric purity was determined as *ca*. 97% de (ii) (12*S*,13*S*)-**8**; R_t/min 27.2 [~98.5%, (12*S*,13*S*)-**8**], 28.9 [~1.5%, (12*R*,13*S*)-**8**]. The diastereoisomeric purity was determined as *ca*. 97% de.

12-*tert*-Butyldimethylsilyloxy-13-methylpentadec-1-yne 7

(12*R*,13*S*)-Isomer. To a solution of (12*R*,13*S*)-**6** (4.57 g, 19.2 mmol) in dry DMF (20 cm^3), imidazole (3.27 g, 48.0 mmol) and TBSCl (4.32 g, 28.7 mmol) were added portionwise. This mixture was stirred at room temperature overnight and then quenched with MeOH. After this it was poured into water and extracted with diethyl ether. The extract was washed with water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *TBS ether* (12*R*,13*S*)-**7** (6.70 g, 99%), a colourless oil, n_D^{25} 1.4527 (Found: C, 74.72; H, 12.54. $C_{22}H_{44}OSi$ requires C, 74.92; H, 12.58%); $[\alpha]_D^{28}$ +12 (*c* 0.98, in hexane); ν_{max}(film)/cm^{-1} 3315m (HC≡C), 2120w (C≡C) and 1255s (SiMe); δ_H(60 MHz; $CDCl_3$) 0.01 (6 H, s, SiMe), 0.70–1.00 (6 H, m, 13-Me, 15-H), 0.87 (9 H, s, Bu^t), 1.28 (19 H, br s, 4, 5, 6, 7, 8, 9, 10, 11, 13, 14-H), 1.89 (1 H, t, *J* 3, 1-H), 2.15 (2 H, m, 3-H) and 3.50 (1 H, m, 12-H).

(12*S*,13*S*)-Isomer. In a manner similar to that described above, (12*S*,13*S*)-**6** (3.18 g, 13.3 mmol) was converted into the *TBS ether* (12*S*,13*S*)-**7** (4.50 g, 96%), n_D^{27} 1.4493 (Found: C, 74.94; H, 12.60. $C_{22}H_{44}OSi$ requires C, 74.92; H, 12.58%); $[\alpha]_D^{26}$ −0.59 (*c* 0.97 in hexane); ν_{max}(film)/cm^{-1} 3315m (HC≡C), 2120w (C≡C) and 1255s (SiMe); δ_H(60 MHz; $CDCl_3$) 0.01 (6 H, s, SiMe), 0.70–1.00 (6 H, m, 13-Me, 15-H), 0.87 (9 H, s, Bu^t), 1.28 (19 H, br s, 4, 5, 6, 7, 8, 9, 10, 11, 13, 14-H), 1.89 (1 H, t, *J* 3, 1-H), 2.15 (2 H, m, 3-H) and 3.50 (1 H, m, 12-H).

tert-Butyl (4*S*)-4-[(1′*R*)-13′-*tert*-butyldimethylsilyloxy-1′-hydroxy-14′-methylhexadec-2′-ynyl]-2,2-dimethyloxazolidine-3-carboxylate 9

(13′*R*,14′*S*)-Isomer. To a solution of (12*R*,13*S*)-**7** (2.00 g, 5.67 mmol) in dry THF (30 cm^3), BuLi (1.71 mol dm^{-3} in hexane; 4.0 cm^3, 6.8 mmol) was added dropwise at −10 °C under Ar. After being stirred for 30 min, the mixture was treated with a solution of Garner's aldehyde (1.56 g, 6.80 mmol) in dry THF (5 cm^3), added dropwise at −78 °C. The reaction mixture was then stirred and allowed to warm gradually to −40 °C during 1.5 h. After this it was quenched with saturated aqueous NH_4Cl and extracted with diethyl ether. The extract was washed with water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give recovered **7** (0.30 g, 15%) and the *title compound* (13′*R*,14′*S*)-**9** (2.64 g, 94% based on consumed **7**), a colourless oil, n_D^{26} 1.4619 (Found: C, 67.65; H, 10.79; N, 2.58. $C_{33}H_{63}NO_5Si$ requires C, 68.11; H, 10.91; N, 2.41%); $[\alpha]_D^{28}$ −21.6 (*c* 1.23 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3445m (OH), 1700s (C=O) and 1255s (SiMe); δ_H(270 MHz; $CDCl_3$) 0.00 and 0.02 (6 H, each s, SiMe), 0.83 (3 H, d, *J* 6.9, 14′-Me), 0.87 (3 H, t, *J* 7.3, 16′−H), 0.88 (9 H, s, Bu^t), 1.00–1.70 (19 H, m, 5′, 6′, 7′, 8′, 9′, 10′, 11′, 12′, 14′, 15′-H), 1.50 (9 H, br s, Bu^t), 1.59 (6 H, br s, 2-Me), 2.19 (2 H, br t, *J* 5.4, 4′-H), 3.51 (1 H, m, 13′-H), 3.90 (1 H, br s, OH), 4.10 (2 H, m, 5-H), 4.52 (1 H, m, 1′-H) and 4.78 (1 H, m, 4-H).

(13′*S*,14′*S*)-Isomer. In a manner similar to that described above, (12*S*,13*S*)-**7** (4.48 g, 12.7 mmol) was converted into the *title compound* (13′*S*,14′*S*)-**9** (5.79 g, 94% based on consumed **7**; 0.76 g, 17% of **7** recovered), n_D^{26} 1.4649 (Found: C, 67.68; H, 10.84; N, 2.59. $C_{33}H_{63}NO_5Si$ requires C, 68.11; H, 10.91; N, 2.41%); $[\alpha]_D^{26}$ −30.3 (*c* 1.11 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3450m (OH), 1695s (C=O) and 1255s (SiMe); δ_H(270 MHz; $CDCl_3$) 0.02 and 0.03 (6 H, each s, SiMe), 0.80 (3 H, d, *J* 6.9, 14′-Me), 0.87 (3 H, t, *J* 7.3, 16′-H), 0.88 (9 H, s, Bu^t), 1.00–1.70 (19 H, m, 5′, 6′, 7′, 8′, 9′, 10′, 11′, 12′, 14′, 15′-H), 1.50 (9 H, br s, Bu^t), 1.58 (6 H, br s, 2-Me), 2.20 (2 H, br t, *J* 5.4, 4′-H), 3.51 (1 H, m, 13′-H), 3.90 (1 H, br s, OH), 4.10 (2 H, m, 5-H), 4.52 (1 H, m, 1′-H) and 4.78 (1 H, m, 4-H).

(2*S*,3*R*,4*E*)-2-Amino-15-*tert*-butyldimethylsilyloxy-16-methyloctadec-4-ene-1,3-diol 10

(15*R*,16*S*)-Isomer. Under a stream of N_2, Li wire (1.31 g, 189

mmol) was added to ethylamine (165 cm^3) at −78 °C. After the stirring had been continued for 2 h < −50 °C, a solution of (13′*R*,14′*S*)-**9** (7.32 g, 12.6 mmol) in dry THF (35 cm^3) was added dropwise to the mixture which was then stirred overnight whilst being allowed to warm to room temperature; it was then quenched with NH_4Cl (*ca*. 20 g, 0.37 mol). After removal of ethylamine by evaporation, the mixture was diluted with saturated aq. NH_4Cl and extracted with CH_2Cl_2. The extract was washed with water and brine, dried (Na_2SO_4) and concentrated under reduced pressure to give the crude amine (15*R*,16*S*)-**10** (6.77 g, quant.); ν_{max}(film)/cm^{-1} 3355m and 3300m (OH or NH), 1250m (SiMe) and 1050s (CO). This compound was directly used for the next step without purification.

(15*S*,16*S*)-Isomer. In a manner similar to that described above, (13′*S*,14′*S*)-**9** (5.73 g, 9.85 mmol) was converted into the crude amine (15*S*,16*S*)-**10** (5.03 g, quant.); ν_{max}(film)/cm^{-1} 3360m and 3300m (OH or NH), 1250m (SiMe) and 1055s (CO). This compound was directly used for the next step without purification.

(2*S*,3*R*,4*E*)-2-Amino-1,3,15-tris-*tert*-butyldimethylsilyloxy-16-methyloctadec-4-ene 11

(15*R*,16*S*)-Isomer. To the solution of (15*R*,16*S*)-**10** (5.58 g) and 2,6-dimethylpyridine (7.3 cm^3, 63 mmol) in CH_2Cl_2 (55 cm^3), TBSOTf (11.5 cm^3, 50.1 mmol) was added at 0 °C under Ar. The reaction mixture was stirred for 1 h at room temperature and then quenched with MeOH. After this it was poured into water and extracted with diethyl ether. The extract was washed with water, saturated aq. $NaHCO_3$ and brine, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *compound* (15*R*,16*S*)-**11** (7.12 g, 84% based on **9**), an oil, n_D^{26} 1.4569 (Found: C, 66.06; H, 12.23; N, 2.07. $C_{37}H_{81}NO_3Si_3$ requires C, 66.10; H, 12.14; N, 2.08%); $[\alpha]_D^{26}$ +4.77 (*c* 1.19 in MeOH); ν_{max}(film)/cm^{-1} 3385w (NH) and 1255m (SiMe); δ_H(60 MHz; $CDCl_3$) 0.00 (18 H, br s, SiMe), 0.87 (33 H, br s, CMe), 1.25 (21 H, br s, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17-H, NH_2), 2.00 (2 H, m, 6-H), 2.75 (1 H, m, 2-H), 3.55 (3 H, m, 1, 15-H), 4.00 (1 H, m, 3-H) and 5.50 (2 H, m, 4, 5-H).

(15*S*,16*S*)-Isomer. In a manner similar to that described above, (15*S*,16*S*)-**10** (5.03 g) was converted into the compound (15*S*,16*S*)-**11** (5.13 g, 77% based on **9**), n_D^{23} 1.4582 (Found: C, 66.07; H, 12.26; N, 2.12. $C_{37}H_{81}NO_3Si_3$ requires C, 66.10; H, 12.14; N, 2.08%); $[\alpha]_D^{27}$ −0.74 (*c* 0.92 in MeOH); ν_{max}(film)/cm^{-1} 3385w (NH) and 1255m (SiMe); δ_H(60 MHz; $CDCl_3$) 0.00 (18 H, br s, SiMe), 0.87 (33 H, br s, CMe), 1.25 (21 H, br s, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17-H, NH_2), 2.00 (2 H, m, 6-H), 2.75 (1 H, m, 2-H), 3.55 (3 H, m, 1, 15-H), 4.00 (1 H, m, 3-H) and 5.50 (2 H, m, 4, 5-H).

(2*S*,3*R*,4*E*)-1,3,15-Tris-*tert*-butyldimethylsilyloxy-16-methyl-2-*p*-tolylsulfonylaminooctadec-4-ene 12

(15*R*,16*S*)-Isomer. To an ice-cooled solution of (15*R*,16*S*)-**11** (5.74 g, 8.54 mmol) in dry pyridine (50 cm^3), TsCl (2.44 g, 12.8 mmol) was added, and the stirring was continued for 3 h at room temperature. The reaction mixture was then poured into dil. HCl and extracted with diethyl ether. The extract was washed with water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *compound* (15*R*,16*S*)-**12** (6.73 g, 95%), a colourless oil, n_D^{23} 1.4817 (Found: C, 63.95; H, 10.63; N, 1.75. $C_{44}H_{87}NO_5SSi_3$ requires C, 63.94; H, 10.61; N, 1.70%); $[\alpha]_D^{27}$ +3.44 (*c* 1.19 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3285m (NH), 1600w (aromatic), 1335m (SO_2), 1255m (SiMe) and 1165s (SO_2); δ_H(270 MHz; $CDCl_3$) −0.07, −0.05, −0.02, 0.00 and 0.03 (total 18 H, each s, SiMe), 0.80 (9 H, s, Bu^t), 0.85 (9 H, s, Bu^t), 0.88 (9 H, s, Bu^t), 0.80–0.92 (6 H, m, 16-Me, 18-H), 1.02–1.60 (19 H, m, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17-H), 1.95 (2 H, m, 6-H), 2.41 (3 H, s, Ar-*Me*), 3.13 (1 H, m, 2-H), 3.45 (1 H, dd, *J* 10.2 and 5.9, 1-Ha), 3.52 (1 H, m, 15-H), 3.80 (1 H, dd, *J* 10.2 and 4.0, 1-Hb), 4.23 (1 H, br t, *J* 6.3, 3-H), 4.64 (1 H, d, *J* 6.9, NH), 5.22 (1 H, dd, *J* 15.2 and 7.0, 4-H), 5.57 (1 H, dt, *J* 15.2 and 6.8, 5-H), 7.28 (2 H, d, *J* 8.3, *m*-Ar) and 7.73 (2 H, d, *J* 8.3, *o*-Ar).

(15*S*,16*S*)-Isomer. In a manner similar to that described above, (15*S*,16*S*)-**11** (5.10 g, 7.59 mmol) was converted into the *compound* (15*S*,16*S*)-**12** (5.54 g, 88%), n_D^{23} 1.4811 (Found: C, 64.12; H, 10.55; N, 1.66. $C_{44}H_{87}NO_5SSi_3$ requires C, 63.94; H, 10.61; N, 1.70%); $[\alpha]_D^{27}$ +2.36 (*c* 1.37 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3285m (NH), 1600w (aromatic), 1335m (SO_2), 1255m (SiMe) and 1165s (SO_2); δ_H(270 MHz; $CDCl_3$) −0.07, −0.05, −0.03, 0.00, 0.02 and 0.03 (total 18 H, each s, SiMe), 0.80 (9 H, s, Bu^t), 0.85 (9 H, s, Bu^t), 0.88 (9 H, s, Bu^t), 0.78–0.92 (6 H, m, 16–Me, 18-H), 1.02–1.60 (19 H, m, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17-H), 1.95 (2 H, m, 6-H), 2.41 (3 H, s, Ar-*Me*), 3.11 (1 H, m, 2-H), 3.45 (1 H, dd, *J* 10.2 and 5.9, 1-Ha), 3.52 (1 H, m, 15-H), 3.80 (1 H, dd, *J* 10.2 and 4.0, 1-Hb), 4.23 (1 H, br t, *J* 6.3, 3-H), 4.64 (1 H, d, *J* 6.9 Hz, NH), 5.22 (1 H, dd, *J* 15.5 and 7.3, 4-H), 5.57 (1 H, dt, *J* 15.5 and 6.6, 5-H), 7.28 (2 H, d, *J* 8.6, *m*-Ar) and 7.73 (2 H, d, *J* 8.6, *o*-Ar).

(2*S*,3*S*,4*R*,5*S*)-1,3,15-Tris-*tert*-butyldimethylsilyloxy-4,5-epoxy-16-methyl-2-*p*-tolylsulfonylaminooctadecane 13

(15*R*,16*S*)-Isomer. To an ice-cooled suspension of (15*R*,16*S*)-**12** (7.93 g, 9.59 mmol) and $NaHCO_3$ (4.14 g, 19.2 mmol) in dry hexane (100 cm^3), *m*-CPBA (*ca*. 80%; 4.14 g, 19.2 mmol) was added, and the stirring was continued for 32 h at room temperature. After this saturated aq. $Na_2S_2O_3$ and saturated aq. $NaHCO_3$ were added to the reaction mixture to destroy the excess of *m*-CPBA. It was then stirred for 1 h and extracted with diethyl ether. The extract was washed with water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the undesired α-epoxide (15*R*,16*S*)-**13**′ (4.84 g, 60%) and the *desired epoxide* (15*R*,16*S*)-**13** (3.13 g, 39%), a colourless oil, n_D^{27} 1.4789 (Found: C, 62.58; H, 10.46; N, 1.66. $C_{44}H_{87}NO_6SSi_3$ requires C, 62.73; H, 10.41; N, 1.66%); $[\alpha]_D^{28}$ −12.8 (*c* 1.01 in MeOH); ν_{max}(film)/cm^{-1} 3285m (NH), 1600w (aromatic), 1335m (SO_2), 1255m (SiMe) and 1165s (SO_2); δ_H(270 MHz; $CDCl_3$) −0.05, −0.02, 0.03, 0.04 and 0.05 (total 18 H, each s, SiMe), 0.82 (9 H, s, Bu^t), 0.84 (9 H, s, Bu^t), 0.88 (9 H, s, Bu^t), 0.80–0.92 (6 H, m, 16-Me, 18-H), 1.00–1.60 (21 H, m, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17-H), 2.41 (3 H, s, Ar-*Me*), 2.67 (1 H, dd, *J* 5.0 and 2.0, 4-H), 2.78 (1 H, m, 5-H), 3.26 (1 H, m, 2-H), 3.52 (1 H, m, 15-H), 3.55 (1 H, dd, *J* 10.2 and 5.0, 1-Ha), 3.71 (1 H, dd, *J* 10.2 and 5.0, 1-Hb), 3.77 (1 H, br t, *J* 5.0, 3-H), 4.76 (1 H, d, *J* 6.9, NH), 7.28 (2 H, d, *J* 8.6, *m*-Ar) and 7.76 (2 H, d, *J* 8.6, *o*-Ar).

(15*S*,16*S*)-Isomer. In a manner similar to that described above, (15*S*,16*S*)-**12** (5.48 g, 6.63 mmol) was converted into the undesired α-epoxide (3.15 g, 56%) and the *desired epoxide* (15*S*,16*S*)-**13** (2.37 g, 42%), n_D^{24} 1.4790 (Found: C, 62.92; H, 10.34; N, 1.62. $C_{44}H_{87}NO_6SSi_3$ requires C, 62.73; H, 10.41; N, 1.66%); $[\alpha]_D^{26}$ −20 (*c* 0.81 in MeOH); ν_{max}(film)/cm^{-1} 3285m (NH), 1600w (aromatic), 1335m (SO_2), 1255m (SiMe) and 1165s (SO_2); δ_H(270 MHz; $CDCl_3$) −0.05, −0.02, 0.01, 0.03, 0.04 and 0.05 (total 18 H, each s, SiMe), 0.82 (9 H, s, Bu^t), 0.85 (9 H, s, Bu^t), 0.88 (9 H, s, Bu^t), 0.78–0.92 (6 H, m, 16-Me, 18-H), 1.00–1.60 (21 H, m, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17-H), 2.41 (3 H, s, Ar-*Me*), 2.67 (1 H, dd, *J* 5.0 and 2.0, 4-H), 2.78 (1 H, m, 5-H), 3.27 (1 H, m, 2-H), 3.52 (1 H, m, 15-H), 3.55 (1 H, dd, *J* 10.5 and 5.0, 1-Ha), 3.71 (1 H, dd, *J* 10.5 and 5.0, 1-Hb), 3.78 (1 H, br t, *J* 5.0, 3-H), 4.76 (1 H, d, *J* 6.6, NH), 7.28 (2 H, d, *J* 8.3, *m*-Ar) and 7.76 (2 H, d, *J* 8.3, *o*-Ar).

(2*S*,3*S*,4*R*)-1,3,15-Tris-*tert*-butyldimethylsilyloxy-16-methyl-2-*p*-tolylsulfonylaminooctadecan-4-ol 14

(15*R*,16*S*)-Isomer. To a stirred and cooled solution of (15*R*,16*S*)-**13** (2.62 g, 3.11 mmol) in dry toluene (15 cm^3), DIBAL (1.01 mol dm^{-1} in toluene; 9.2 cm^3, 9.3 mmol) was added dropwise at −78 °C under Ar. This mixture was then

warmed gradually to room temperature with stirring during 4 h after which it was quenched with MeOH. After stirring had been continued for 1 h, the mixture was filtered through Celite and the filter cake was washed with diethyl ether. The combined filtrate and washings were concentrated under reduced pressure and the residue was chromatographed over SiO_2 to give the *alcohol* (15*R*,16*S*)-**14** (2.34 g, 84%), a colourless oil, n_D^{23} 1.4807 (Found: C, 62.56; H, 10.65; N, 1.63. $C_{44}H_{89}NO_6SSi_3$ requires C, 62.58; H, 10.62; N, 1.66%); $[\alpha]_D^{28}$ −3.31 (*c* 1.06 in MeOH); ν_{max}(film)/cm^{-1} 3530m (OH), 3315m (NH), 1600w (aromatic), 1255m (SiMe), 835m, 780m and 665s; δ_H(270 MHz; $CDCl_3$) −0.05, −0.02, 0.02, 0.03, 0.09 and 0.12 (total 18 H, each s, SiMe), 0.82 (9 H, s, Bu^t), 0.88 (18 H, s, Bu^t), 0.80–0.95 (6 H, m, 16-Me, 18-H), 1.00–1.60 (23 H, m, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17-H), 2.42 (3 H, s, Ar-*Me*), 2.57 (1 H, d, *J* 5.3, OH), 3.42 (1 H, m, 4-H), 3.48–3.60 (2 H, m, 2, 15-H), 3.58 (1 H, dd, *J* 10.2 and 5.6, 1-Ha), 3.69 (1 H, dd, *J* 10.2 and 6.3, 1-Hb), 3.81 (1 H, dd, *J* 4.8 and 3.0, 3-H), 4.82 (1 H, d, *J* 6.9, NH), 7.28 (2 H, d, *J* 8.3, *m*-Ar) and 7.74 (2 H, d, *J* 8.3, *o*-Ar).

(15*S*,16*S*)-Isomer. In a manner similar to that described above, (15*S*,16*S*)-**13** (2.33 g, 2.77 mmol) was converted into the *alcohol* (15*S*,16*S*)-**14** (2.05 g, 88%), n_D^{24} 1.4810 (Found: C, 62.56; H, 10.68; N, 1.66. $C_{44}H_{89}NO_6SSi_3$ requires C, 62.58; H, 10.62; N, 1.66%); $[\alpha]_D^{25}$ −12 (*c* 0.73 in MeOH); ν_{max}(film)/cm^{-1} 3540m (OH), 3320m (NH), 1600w (aromatic), 1255m (SiMe), 1090s, 835m, 775m and 665s; δ_H(270 MHz; $CDCl_3$) −0.05, −0.02, 0.02, 0.03, 0.09 and 0.12 (total 18 H, each s, SiMe), 0.82 (9 H, s, Bu^{t}Si), 0.88 (18 H, s, Bu^t), 0.78–0.95 (6 H, m, 16-Me, 18-H), 1.00–1.60 (23 H, m, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17-H), 2.42 (3 H, s, Ar-*Me*), 2.57 (1 H, d, *J* 5.3, OH), 3.42 (1 H, m, 4-H), 3.48–3.60 (2 H, m, 2, 15-H), 3.58 (1 H, dd, *J* 10.2 and 5.6, 1-Ha), 3.69 (1 H, dd, *J* 10.2 and 6.6, 1-Hb), 3.81 (1 H, dd, *J* 4.8 and 3.0, 3-H), 4.82 (1 H, d, *J* 6.9, NH), 7.28 (2 H, d, *J* 8.3, *m*-Ar) and 7.74 (2 H, d, *J* 8.3, *o*-Ar).

(2*S*,3*R*,4*S*)-3-*tert*-Butyldimethylsilyloxy-2-*tert*-butyldimethylsilyloxymethyl-4-(11′-*tert*-butyldimethylsilyloxy-12′-methyltetradecyl)-*N*-*p*-tolylsulfonylazetidine 16

(11′*R*,12′*S*)-Isomer. MsCl (0.33 cm^3, 4.3 mmol) was added to an ice-cooled solution of (15*R*,16*S*)-**14** (2.26 g, 2.68 mmol) in dry pyridine (12 cm^3), and the reaction mixture was stirred at 0 °C overnight. After having been quenched with water, the mixture was extracted with diethyl ether. The extract was washed with dil. HCl, water and brine, dried ($MgSO_4$) and concentrated under reduced pressure to gave the crude mesylate (15*R*,16*S*)-**15** (2.47 g, quant.); ν_{max}(film)/cm^{-1} 3300m (NH), 1360s (SO_2) and 1255s (SO_2). Mesylate (15*R*,16*S*)-**15** (2.47 g, ~2.68 mmol) was dissolved in dry THF (40 cm^3) and NaH (*ca.* 60% in mineral oil; 0.32 g, 8.0 mmol) was added to this solution at 0 °C under Ar. The reaction mixture was stirred for 24 h at room temperature and then quenched with water. After neutralization with dil. HCl, the mixture was extracted with diethyl ether. The extract was washed with water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *cyclized compound* (11′*R*,12′*S*)-**16** (1.95 g, 88%), a colourless oil, n_D^{27} 1.4745 (Found: C, 63.84; H, 10.61; N, 1.70. $C_{44}H_{87}NO_5SSi_3$ requires C, 63.94; H, 10.61; N, 1.70%); $[\alpha]_D^{28}$ +40.5 (*c* 1.16 in $CHCl_3$); ν_{max}(film)/cm^{-1} 1600w (aromatic), 1345m (SO_2), 1255m (SiMe) and 1160s (SO_2); δ_H(270 MHz; $CDCl_3$) 0.01, 0.03 and 0.04 (total 18 H, each s, SiMe), 0.84 (9 H, s, Bu^t), 0.87 (9 H, s, Bu^t), 0.88 (9 H, s, Bu^t), 0.80–0.92 (6 H, m, 12′-Me, 14′-H), 1.00–1.60 (21 H, m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 10′, 12′, 13′-H), 1.75 (2 H, m, 1′-H), 2.41 (3 H, s, Ar-*Me*), 3.52 (1 H, m, 11′-H), 3.80 (1 H, dd, *J* 11.2 and 3.2, 2- C*H*H-OTBS), 3.86 (1 H, dd, *J* 11.2 and 4.6, 2-CH*H*-OTBS), 3.97 (1 H, q-like, *J* 3.6, 4-H), 4.22 (1 H, m, 2-H), 4.41 (1 H, dd, *J* 6.3 and 3.0, 3-H), 7.26 (2 H, d, *J* 8.3, *m*-Ar) and 7.71 (2 H, d, *J* 8.3, *o*-Ar).

(11′*S*,12′*S*)-Isomer. In a manner similar to that described above, (15*R*,16*S*)-**14** (2.01 g, 2.38 mmol) was converted into the *cyclized compound* (11′*S*,12′*S*)-**16** (1.59 g, 81%), n_D^{26} 1.4795 (Found: C, 63.80; H, 10.69; N, 1.70. $C_{44}H_{87}NO_5SSi_3$ requires C, 63.94; H, 10.61; N, 1.70%); $[\alpha]_D^{24}$ +37.2 (*c* 1.18 in $CHCl_3$); ν_{max}(film)/cm^{-1} 1600w (aromatic), 1345m (SO_2), 1255m (SiMe), 1160s (SO_2), 1090s, 835m, 775m and 665s; δ_H(270 MHz; $CDCl_3$) 0.01, 0.02, 0.03 and 0.04 (total 18 H, each s, SiMe), 0.84 (9 H, s, Bu^t), 0.87 (9 H, s, Bu^t), 0.88 (9 H, s, Bu^t), 0.78–0.90 (6 H, m, 12′-Me, 14′-H), 1.00–1.60 (21 H, m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 10′, 12′, 13′-H), 1.76 (2 H, m, 1′-H), 2.41 (3 H, s, Ar-*Me*), 3.52 (1 H, m, 11′-H), 3.80 (1 H, dd, *J* 11.2 and 3.2, 2-C*H*H-OTBS), 3.86 (1 H, dd, *J* 11.2 and 4.6, 2-CH*H*-OTBS), 3.97 (1 H, q-like, *J* 3.6, 4-H), 4.22 (1 H, m, 2-H), 4.41 (1 H, dd, *J* 6.3 and 3.0, 3-H), 7.26 (2 H, d, *J* 8.5, *m*-Ar) and 7.71 (2 H, d, *J* 8.5, *o*-Ar).

(2*S*,3*R*,4*S*)-3-*tert*-Butyldimethylsilyloxy-2-*tert*-butyldimethylsilyloxymethyl-4-(11′-*tert*-butyldimethylsilyloxy-12′-methyltetradecyl)azetidine 17

(11′*R*,12′*S*)-Isomer. Sodium naphthalenide was prepared from naphthalene (2.73 g, 21.3 mmol) and Na (0.39 g, 17 mmol) in dry DME (15 cm^3) in the usual manner. To a solution of (11′*R*,12′*S*)-**16** (1.76 g, 2.13 mmol) in dry DME (25 cm^3), the prepared sodium naphthalenide solution was added dropwise at −78 °C under Ar. The reaction mixture was stirred for 40 min and then quenched with water. After being stirred for 30 min, the mixture was extracted with $CHCl_3$. The extract was washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *amine* (11′*R*,12′*S*)-**17** (1.26 g, 88%), a colourless oil, n_D^{22} 1.4622 (Found: C, 66.27; H, 11.96; N, 2.00. $C_{37}H_{81}NO_3Si_3$ requires C, 66.10; H, 12.14; N, 2.08%); $[\alpha]_D^{26}$ +1.82 (*c* 1.09 in MeOH); ν_{max}(film)/cm^{-1} 1255m (SiMe), 1070w, 835s and 775m; δ_H(270 MHz; $CDCl_3$) 0.02, 0.065 and 0.07 (total 18 H, each s, SiMe), 0.83 (3 H, d, *J* 6.9, 12′-Me), 0.89 and 0.92 (27 H, each s, Bu^t), 0.85–0.90 (3 H, m, 14′-H), 1.00–1.50 (21 H, m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 10′, 12′, 13′-H), 1.60 (3 H, m, 1′-H, NH), 3.48–3.67 (5 H, m, 2-CH_2OTBS, 2, 4, 11′-H) and 4.43 (1 H, dd, *J* 7.3 and 5.3, 3-H).

(11′*S*,12′*S*)-Isomer. In a manner similar to that described above, (11′*R*,12′*S*)-**16** (1.43 g, 1.73 mmol) was converted into the *amine* (11′*S*,12′*S*)-**17** (972 mg, 84%), n_D^{26} 1.4602 (Found: C, 66.11; H, 12.01; N, 2.02. $C_{37}H_{81}NO_3Si_3$ requires C, 66.10; H, 12.14; N, 2.08%); $[\alpha]_D^{23}$ −7.9 (*c* 0.98 in MeOH); ν_{max}(film)/cm^{-1} 1255m (SiMe), 1060w, 835s and 775m; δ_H(270 MHz; $CDCl_3$) 0.01, 0.02, 0.06 and 0.07 (total 18 H, each s, SiMe), 0.80 (3 H, d, *J* 6.6, 12′-Me), 0.87 (3 H, t, *J* 7.6, 14′-H), 0.875, 0.88 and 0.91 (27 H, each s, Bu^t), 1.00–1.53 (21 H, m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 10′, 12′, 13′-H), 1.53–1.73 (2 H, m, 1′-H) and 1.79 (1 H, br s, NH), 3.48–3.67 (5 H, m, 2-CH_2OTBS, 2, 4, 11′-H) and 4.43 (1 H, dd, *J* 7.3 and 5.3, 3-H).

(2*S*,3*R*,4*S*)-3-Hydroxy-2-hydroxymethyl-4-(11′-hydroxy-12′-methyltetradecyl)azetidine 1

(11′*R*,12′*S*)-Isomer, [(15*R*,16*S*)-penaresidin A]. To a solution of (11′*R*,12′*S*)-**17** (1.16 g, 1.73 mmol) in CH_3CN (30 cm^3), aq. HF (46%; 0.7 cm^3, 0.02 mol) was added. After being stirred for 12 h at room temperature, the mixture was neutralized with an excess of $NaHCO_3$ and concentrated under reduced pressure. The residue was filtered through Celite and the filter cake was washed with CH_2Cl_2. The combined filtrate and washings were evaporated under reduced pressure. The residue was chromatographed over SiO_2 several times to give the *penaresidin* (11′*R*,12′*S*)-**1** (460 mg, 81%), a hygroscopic solid, mp 71–73 °C [Found: (HRFAB-MS) M + 1, 330.2999. $C_{19}H_{40}NO_3$ requires *m*/*z*, 330.3008]; $[\alpha]_D^{25}$ −30 (*c* 0.38 in MeOH); ν_{max}(KBr)/cm^{-1} 3388s (OH), 2919s (CH), 1558w, 1469m, 1304w and 1112m; δ_H(600 MHz; CD_3OD) 0.87 (3 H, d, *J* 6.8, 12′-Me), 0.90 (3 H, t, *J* 7.3, 14′-H), 1.12 (1 H, m, 13′-Ha), 1.32 and ~1.60 (20 H, br s and m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 10′, 12′-H, 13-Hb), 1.90 (2 H,

m, 1′-H), 3.35 (1 H, m, 11′-H), 3.83 (1 H, dd, *J* 12.7 and 3.4, 2-CH*H*-OH), 3.86 (1 H, dd, *J* 12.7 and 4.6, 2-C*H*H-OH), 4.11 (1 H, ddd, *J* 4.9, 4.6 and 3.4, 2-H), 4.26 (1 H, dt, *J* 7.3 and 7.3, 4-H) and 4.54 (1 H, dd, *J* 7.3 and 4.9, 3-H); δ_C(150 MHz; CD_3OD) 12.11, 15.23, 25.85, 26.13, 27.22, 27.64, 30.36, 30.49, 30.59, 30.67, 30.73, 30.85, 34.25, 41.95, 59.59, 65.36, 66.30, 69.99 and 76.32.

(11′*S*,12′*S*)-Isomer, [(15*S*,16*S*)-penaresidin A]. In a similar manner to that described above, (11′*S*,12′*S*)-**17** (949 mg, 1.41 mmol) was converted into a crude product. This was chromatographed over SiO_2 and then over Sephadex LH-20 (CH_2Cl_2–MeOH, 1:1) to give the *penaresidin* (11′*S*,12′*S*)-**1** (AcOH salt; 510 mg, 93%), a slightly yellow oil, n_D^{26} 1.4840 [Found: (HRFAB-MS) M + 1 330.2997. $C_{19}H_{40}NO_3$ requires *m*/*z*, 330.3008]; $[\alpha]_D^{26}$ −17 (*c* 0.34 in MeOH); ν_{max}(film)/cm^{-1} 3270s (OH), 2926s (CH), 2854s (CH), 1566m, 1556m, 1415m, 1124m and 653m; δ_H(600 MHz; CD_3OD) 0.86 (3 H, d, *J* 6.8, 12′-Me), 0.91 (3 H, t, *J* 7.3, 14′-H), 1.17 (1 H, m, 13′-Ha), 1.32 and ~1.54 (20 H, br s and m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 10′, 12′-H, 13′-Hb), 1.80–1.96 (2 H, m, 1′-H), 1.92 (3 H, s, Ac), 3.43 (1 H, m, 11′-H), 3.81 (1 H, dd, *J* 12.7 and 3.9, 2-CH*H*-OH), 3.84 (1 H, dd, *J* 12.7 and 4.4, 2-C*H*H-OH), 4.06 (1 H, ddd, *J* 4.9, 4.4 and 3.9, 2-H), 4.21 (1 H, dt, *J* 8.3 and 6.8, 4-H) and 4.51 (1 H, dd, *J* 6.8 and 4.9, 3-H); δ_C(150 MHz; CD_3OD) 12.22, 13.91, 23.99, 26.21, 27.07, 27.43, 27.89, 30.42, 30.52, 30.62, 30.68, 30.75, 30.83, 35.35, 41.48, 59.90, 64.98, 66.56, 69.79, 75.43 and 180.5.

(2*S*,3*R*,4*S*)-3-Acetoxy-2-acetoxymethyl-4-(11′-acetoxy-12′-methyltetradecyl)-*N*-acetylazetidine 18

(11′*R*,12′*S*)-Isomer, [(15*R*,16*S*)-penaresidin A tetraacetyl derivative]. To a solution of (11′*R*,12′*S*)-**1** (167 mg, 506 μmol) in dry pyridine (10 cm^3), Ac_2O (1.0 cm^3, 11 mmol) was added and the stirring was continued at room temperature overnight. After removal of volatile materials from the mixture by evaporation, the residue was chromatographed over SiO_2 to give the *tetraacetyl derivative* (11′*R*,12′*S*)-**18** (239 mg, 95%), colourless oil, n_D^{27} 1.4671 (Found: C, 65.12; H, 9.50; N, 2.78. $C_{27}H_{47}NO_7$ requires C, 65.16; H, 9.52; N, 2.81%); $[\alpha]_D^{27}$ +45 (*c* 0.38 in $CHCl_3$); ν_{max}(film)/cm^{-1} 2927s (CH), 2855s (CH), 1748s (ester), 1658s (amide), 1413m, 1376m, 1241s and 1043w; δ_H(600 MHz; $CDCl_3$) 0.86 (3 H, d, *J* 6.8, 12′-Me), 0.89 (3 H, t, *J* 7.3, 14′-H), 1.10 (1 H, m, 13′-Ha), 1.25 (16 H, br s, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′-H), 1.41 (1 H, m, 13′-Hb), 1.48 (2 H, m, 10′-H), 1.60 (1 H, m, 12′-H), 1.67–1.78 (1 H, m, 1′-Ha, 1′-Ha*), 1.89 (6/5 H, s, NAc*), 1.92 (9/5 H, s, NAc), ~2.00 (3/5 H, m, 1′-Hb), 2.05 (3 H, s, 11′-OAc), 2.08 (9/5 H, s, 2-CH_2-O*Ac*), 2.11 (6/5 H, s, 2-CH_2-O*Ac**), 2.12 (9/5 H, s, 3-OAc), 2.13 (6/5 H, s, 3-OAc*), ~2.19 (2/5 H, m 1′-Hb*), 4.29 (2/5 H, dd, *J* 12.2 and 2.9, 2-CH*H*-OAc*), 4.33 (2/5 H, m, 2-H*), 4.36–4.38 (3/5 H, m, 2-H), 4.39 (3/5 H, dd, *J* 12.2 and 2.5, 2-CH*H*-OAc), 4.44 (1 H, m, 4-H, 4-H*), 4.59 (2/5 H, dd, *J* 12.2 and 3.4, 2-C*H*H-OAc*), 4.69 (3/5 H, dd, *J* 12.2 and 4.4, 2-C*H*H-OAc), 4.79 (1 H, m, 11′-H), 5.14 (2/5 H, dd, *J* 7.1 and 3.2, 3-H*), 5.28 (3/5 H, dd, *J* 7.1 and 4.2, 3-H). This compound exists as a mixture of two rotational isomers (*ca*. 3:2). The asterisked ^{1}H NMR signals arise from the minor isomer; δ_C(150 MHz; $CDCl_3$) 11.55, 14.53, 20.57, 20.64, 20.67, 20.70, 20.80, 20.95, 21.18, 24.84, 25.16, 25.51, 25.56, 26.84, 29.03, 29.37, 29.49, 29.54, 29.59, 30.27, 37.88, 60.97, 62.25, 63.18, 64.79, 65.03, 66.41, 66.61, 67.40, 77.70, 77.74, 169.99, 170.05, 170.15, 170.33, 170.40, 170.44 and 170.95.

(11′*S*,12′*S*)-Isomer, [(15*S*,16*S*)-penaresidin A tetraacetyl derivative]. In a manner similar to that described above, (11′*S*,12′*S*)-**1** (AcOH salt; 288 mg, 739 μmol) was converted into the *tetraacetyl derivative* (11′*S*,12′*S*)-**18** (413 mg, 83%), n_D^{24} 1.4648 (Found: C, 65.33; H, 9.63; N, 2.80. $C_{27}H_{47}NO_7$ requires C, 65.16; H, 9.52; N, 2.81%); $[\alpha]_D^{27}$ +38.0 (*c* 0.378 in $CHCl_3$); ν_{max}(film)/cm^{-1} 2927s (CH), 2855s (CH), 1747s (ester), 1658s (amide), 1413w, 1376m, 1241s and 1042w; δ_H(600 MHz; $CDCl_3$) 0.88 (3 H, d, *J* 6.4, 12′-Me), 0.89 (3 H, t, *J* 7.3, 14′-H), 1.14 (1 H, m, 13′-Ha), 1.26 (16 H, br s, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′-H), 1.40 (1 H, m, 13′-Hb), 1.45–1.57 (3 H, m, 10′, 12′-H), 1.68–1.81 (1 H, m, 1′-Ha, 1′-Ha*), 1.89 (6/5 H, s, NAc*), 1.92 (9/5 H, s, NAc), ~2.00 (3/5 H, m, 1′-Hb), 2.04 (3 H, s, 11′-OAc), 2.08 (9/5 H, s, 2-CH_2O*Ac*), 2.11 (6/5 H, s, 2-CH_2O*Ac**), 2.12 (9/5 H, s, 3-OAc), 2.13 (6/5 H, s, 3-OAc*), ~2.20 (2/5 H, m, 1′-Hb), 4.29 (2/5 H, dd, *J* 12.2 and 2.9, 2-CH*H*-OAc*), 4.33 (2/5 H, m, 2-H*), 4.35–4.38 (3/5 H, m, 2-H), 4.38 (3/5 H, dd, *J* 12.2 and 2.4, 2-CH*H*-OAc), 4.45 (1 H, m, 4-H, 4-H*), 4.59 (2/5 H, dd, *J* 12.2 and 3.4, 2-C*H*H-OAc*), 4.69 (3/5 H, dd, *J* 12.2 and 4.4, 2-C*H*H-OAc), 4.86 (1 H, m, 11′-H), 5.14 (2/5 H, dd, *J* 6.8 and 3.4, 3-H*) and 5.26 (3/5 H, dd, *J* 7.3 and 3.9, 3-H). This compound exists as a mixture of two rotational isomers (*ca*. 3:2). The asterisked ^{1}H NMR signals arise from the minor isomer; δ_C(150 MHz; $CDCl_3$) 11.69, 13.90, 20.57, 20.64, 20.67, 20.70, 20.80, 20.96, 21.12, 25.16, 25.51, 25.67, 26.85, 29.03, 29.37, 29.49, 29.59, 31.35, 37.95, 60.97, 62.26, 63.18, 64.79, 65.03, 66.41, 66.60, 67.40, 76.94, 169.96, 170.04, 170.12, 170.33, 170.38, 170.43 and 170.97.

Determination of the relative stereochemistry of 14

To assign the stereochemistry of **14**, the alcohol (15*S*,16*S*)-**14** was converted into the corresponding pentaacetyl derivative **19** in 3 steps as follows. In a manner similar to that described before, (15*S*,16*S*)-**14** (6.9 mg, 8.2 μmol) was treated with sodium naphthalenide to give the amino alcohol, which was treated with aq. HF in CH_3CN to give the phytosphingosine analogue. Acetylation of this compound afforded (11′*S*,12′*S*)-**19** (4.5 mg, quant.); δ_H(270 MHz; $CDCl_3$) 0.87 (3 H, d, *J* 6.9, 16-Me), 0.89 (3 H, t, *J* 7.6, 18-H), 1.00–1.80 (23 H, m, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17-H), 2.03, 2.047, 2.050, 2.08 (total 15 H, each s, COMe), 4.00 (1 H, dd, *J* 11.6 and 3.0, 1-Ha), 4.29 (1 H, dd, *J* 11.6 and 4.8, 1-Hb), 4.48 (1 H, m, 2-H), 4.85 (1 H, dt, *J* 4.6 and 8.3, 15-H), 4.93 (1 H, dt, *J* 8.6 and 3.6, 4-H), 5.11 (1 H, dd, *J* 8.6 and 3.0, 3-H) and 6.02 (1 H, d, *J* 9.5, NH).

The reported peracetylphytosphingosine;[10a] δ_H(360 MHz; $CDCl_3$) 0.88 (3 H, t, *J* 6.8), 1.25 (24 H, s-like), 1.65 (2 H, m), 2.03 (3 H, s), 2.05 (6 H, s), 2.08 (3 H, s), 4.00 (1 H, dd, *J* 11.7 and 3.0, 1-Ha), 4.29 (1 H, dd, *J* 11.7 and 4.8, 1-Hb), 4.47 (1 H, m, 2-H), 4.85 (1 H, dt, *J* 4.6 and 8.3, 15-H), 4.93 (1 H, dt, *J* 9.6 and 3.3, 4-H), 5.11 (1 H, dd, *J* 8.3 and 3.0, 3-H) and 6.02 (1 H, d, *J* 9.4, NH).

The ^{1}H NMR signals of **19** arising from C-1 to C-4 were almost identical with those of the reported acetylated phytosphingosine.[10a]

(2*R*,3*S*)-2,3-Epoxypentan-1-ol 21

To a stirred suspension of $Ti(OPr^i)_4$ (113 cm^3, 383 mmol), (−)-DIPT (97.8 g, 417 mmol) and 4 Å molecular sieves (*ca*. 210 g) in dry CH_2Cl_2 (2.7 dm^3), **20** (30.0 g, 348 mmol) and TBHP (4.5 mol dm^{-3} in CH_2Cl_2; 155 cm^3, 698 mmol) were added dropwise successively at −20 °C under Ar. This reaction mixture was stirred < −20 °C for 2 days and then quenched with aq. tartaric acid (*ca*. 10%; 0.9 dm^3). After removal of the cooling-bath, this mixture was stirred for 1.5 h and then filtered through Celite. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer and extracts were washed with water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 to give the *epoxy alcohol* **21** (21.3 g, 60%), ν_{max}(film)/cm^{-1} 3400s (OH) and 1040s (CO). This compound was employed for the next step immediately.

(2′*R*,3′*S*)-2′,3′-Epoxypentyl 3,5-dinitrobenzoate 22

To an ice-cooled solution of **21** (21.3 g, 209 mmol) and pyridine (50 cm^3, 0.62 mol) in dry CH_2Cl_2 (200 cm^3), 3,5-DNBCl (62.6 g, 272 mmol) was added and stirring was continued at 0 °C for 20 min. After being quenched with water, the mixture was poured into water and extracted with diethyl ether. The extract was

washed with saturated aq. $CuSO_4$, water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated under reduced pressure to give the crude ester **22** (49.0 g). This crude compound, shown to have an 89% ee by HPLC analysis, was purified by recrystallization (from hexane–benzene = 4:1; × 3) to give the *enantiomerically enriched* **22** (34.0 g, 55%), slightly yellow needles, mp 71–72 °C (Found: C, 48.42; H, 3.95; N, 9.45. $C_{12}H_{12}N_2O_7$ requires C, 48.66; H, 4.08; N, 9.46%); ν_{max}(KBr)/cm^{-1} 1725s (CO_2R), 1630m (aromatic) and 1545s (nitro); δ_H(60 MHz; $CDCl_3$) 1.20 (3 H, t, *J* 7, Me), 1.40–2.00 (2 H, m, 4′-H), 2.90–3.60 (2 H, m, 2′, 3′-H), 4.40 (1 H, dd, *J* 13 and 7, 1′-Ha), 4.80 (1 H, dd, *J* 13 and 4, 1′-Hb) and 9.10 (3 H, br s, aromatic); HPLC analysis [column, Chiralcel OB–H® (4.6 i.d. × 250 mm); solvent, hexane–Pr^iOH (6:1); flow, 0.5 cm^3 min^{-1}; detect, 254 nm] R_t/min 94.6 (~0.9%, antipode of **22**), 97.9 (~99.1%, **22**); The enantiomeric purity was determined to be > 98% ee.

(2*R*,3*S*)-2,3-Epoxypentan-1-ol 21

To a solution of **22** (27.5 g, 92.8 mmol) in THF–MeOH (1:1; 400 cm^3), aq. KOH (1.0 mol dm^{-3}; 94 cm^3, 94 mmol) was added dropwise at 0 °C. After stirring had been continued at 0 °C for 1 h, the mixture was poured into water and extracted with diethyl ether. The extract was washed with water and brine, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 and distilled to give the *enriched alcohol* **21** (7.30 g, 77%), a colourless oil, bp 91–92 °C/24 mmHg [Found: (HRFAB-MS) M + 1, 103.0747. $C_5H_{10}O_2$ requires *m*/*z* 103.0760]; n_D^{25} 1.4321; $[\alpha]_D^{25}$ +12.0 (*c* 0.930 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3415s (OH) and 1045s (CO); δ_H(60 MHz; $CDCl_3$) 1.10 (3 H, t, *J* 7, Me), 1.20–1.80 (2 H, m, 4-H), 2.45 (1 H, m, OH), 2.80–3.30 (2 H, m, 2, 3-H) and 3.40–4.20 (2 H, m, 1-H).

(2*S*,3*R*)-3-Methylpentane-1,2-diol 23

To a solution of **22** (7.30 g, 71.5 mmol) in dry pentane (150 cm^3), Me_3Al (1.07 mol dm^{-3} in hexane; 140 cm^3, 150 mmol) and BuLi (1.64 mol dm^{-3}; 10.9 cm^3, 17.9 mmol) were added dropwise successively at −50 °C under Ar. The mixture was stirred for 2 days and then allowed to warm gradually to room temperature. It was then quenched by the addition of dil. HCl (2.0 mol dm^{-3}; 190 cm^3) at −50 °C and extracted with diethyl ether. The extract was washed with saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed over SiO_2 and distilled to give the *diol* **23** (4.19 g, 50%), a colourless oil, bp 93 °C/5 mmHg (Found: C, 60.68; H, 11.64. $C_6H_{14}O_2$ requires C, 60.98; H, 11.94%); n_D^{23} 1.4466; $[\alpha]_D^{24}$ +9.78 (*c* 1.03 in MeOH); ν_{max}(film)/cm^{-1} 3355vs (OH); δ_H(60 MHz; $CDCl_3$) 0.95 (6 H, m, Me), 1.00–1.80 (3 H, m, 3, 4-H), 2.70 (2 H, br s, OH) and 3.55 (3 H, br s, 1, 2-H).

(2*S*,3*R*)-1,2-Epoxy-3-methylpentane 4

(2*S*,3*R*)-Isomer. HBr (33% in AcOH; 19 cm^3, 106 mol) was added dropwise to stirred and neat **23** (4.14 g, 35.0 mmol) at −5 °C. After the cooling-bath had been removed, the stirring was continued for 1 h. The mixture was then diluted with ice–water, neutralized with Na_2CO_3 and extracted with diethyl ether. The extract was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure to give crude **24** (8.02 g, quant.), ν_{max}(film)/cm^{-1} 1745s (CO_2R), 1370m and 1235s. This compound was employed for the next step without further purification. To an ice-cooled NaOMe solution (3.7 mol dm^{-3} in MeOH; 15 cm^3, 56 mmol), **24** (8.02 g) was added dropwise. After removal of the cooling-bath, the mixture was stirred for 1 h, diluted with water and extracted with pentane. The extract was washed with water and brine, dried ($MgSO_4$) and concentrated. The residue was distilled to give the *epoxide* **4** (2.76 g, 79%), a colourless oil, bp ~108 °C/760 mmHg; δ_H(60 MHz; $CDCl_3$) 0.95 (6 H, m, Me), 1.10–1.70 (3 H, m, 3, 4-H) and 2.40–2.80 (3 H, m, 1, 2-H). The high volatility of this epoxide made its purification difficult so that it was employed immediately in the next step.

(3*R*,4*R*)-3-Methylpentadec-6-yn-4-ol 5

(3*R*,4*R*)-Isomer. In a similar manner to that described for the preparation of (3*S*,4*R*)-**5**, the epoxide (2*R*,3*R*)-**4** (2.35 g, 23.5 mmol) was converted into the *alcohol* (3*R*,4*R*)-**5** (3.45 g, 62%), a colourless oil, n_D^{21} 1.4563 (Found: C, 80.80; H, 12.73. $C_{16}H_{30}O$ requires C, 80.61; H, 12.68%); $[\alpha]_D^{28}$ +8.45 (*c* 1.10 in MeOH); ν_{max}(film)/cm^{-1} 3400m (OH) and 1055m (CO); δ_H(270 MHz; $CDCl_3$) 0.89 (9 H, m, Me), 1.10–1.65 (15 H, m, 2, 3, 9, 10, 11, 12, 13, 14-H), 1.87 (1 H, d, *J* 4, OH), 2.16 (2 H, m, 8-H), 2.32–2.37 (2 H, m, 5-H) and 3.59 (1 H, m, 4-H).

(12*R*,13*R*)-13-Methylpentadec-1-yn-12-ol 6

(12*R*,13*R*)-Isomer. In a manner similar to that described for the preparation of (12*R*,13*S*)-**6**, compound (3*R*,4*R*)-**5** (3.35 g, 14.05 mmol) was converted into the *alcohol* (12*R*,13*R*)-**6** (2.24 g, 66%), a colourless oil, n_D^{21} 1.4591 (Found: C, 80.22; H, 12.70. $C_{16}H_{30}O$ requires C, 80.61; H, 12.68%); $[\alpha]_D^{28}$ +14.7 (*c* 1.67 in MeOH). The IR and ^1H NMR spectra of (12*R*,13*R*)-**6** were identical with those of (12*S*,13*S*)-**6**.

12-*tert*-Butyldimethylsilyloxy-13-methylpentadec-1-yne 7

(12*R*,13*R*)-Isomer. In a manner similar to that described for the preparation of (12*R*,13*S*)-**7**, compound (12*R*,13*R*)-**6** (2.19 g, 9.19 mmol) was converted into the *TBS ether* (12*R*,13*R*)-**7** (2.87 g, 89%), a colourless oil, n_D^{21} 1.4521 (Found: C, 74.89; H, 12.51. $C_{22}H_{44}OSi$ requires C, 74.92; H, 12.58%); $[\alpha]_D^{28}$ +1.1 (*c* 1.1, in hexane). The IR and ^1H NMR spectra of (12*R*,13*R*)-**7** were identical with those of (12*S*,13*S*)-**7**.

***tert*-Butyl (4*S*)-4-[(1′*R*)-13′-*tert*-butyldimethylsilyloxy-1′-hydroxy-14′-methylhexadec-2′-ynyl]-2,2-dimethyloxazolidine-3-carboxylate 9**

(13′*R*,14′*R*)-Isomer. In a manner similar to that described for the preparation of (13′*R*,14′*S*)-**9**, compound (12*R*,13*R*)-**7** (2.80 g, 7.94 mmol) was converted into the *title compound* (13′*R*,14′*R*)-**9** (3.63 g, 83% based on consumed **7**; 0.14 g, 5% of **7** recovered), a colourless oil, n_D^{25} 1.4640 (Found: C, 67.89; H, 10.33; N, 2.41. $C_{33}H_{63}NO_5Si$ requires C, 68.11; H, 10.91; N, 2.41%); $[\alpha]_D^{27}$ −29.0 (*c* 1.11 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3400m (OH), 1700s (C=O), 1255m (SiMe); δ_H(270 MHz; $CDCl_3$) 0.01 and 0.02 (6 H, each s, SiMe), 0.80 (3 H, d, *J* 6.9, 14′-Me), 0.866 (3 H, t, *J* 7.3, 16′-H), 0.873 (9 H, s, Bu^t), 1.00–1.70 (19 H, m, 5′, 6′, 7′, 8′, 9′, 10′, 11′, 12′, 14′, 15′-H), 1.50 (9 H, br s, Bu^t), 1.58 (6 H, br s, 2-Me), 2.19 (2 H, br t, *J* 5.4, 4′-H), 3.51 (1 H, m, 13′-H), 3.90 (1 H, br s, OH), 4.10 (2 H, m, 5-H), 4.51 (1 H, m, 1′-H) and 4.76 (1 H, m, 4-H).

(2*S*,3*R*,4*E*)-2-Amino-15-*tert*-butyldimethylsilyloxy-16-methyloctadec-4-ene-1,3-diol 10

(15*R*,16*R*)-Isomer. In a manner similar to that described for the preparation of (15*R*,16*S*)-**10**, compound (13′*R*,14′*R*)-**9** (2.40 g, 4.12 mmol) was converted into the crude amine (15*R*,16*R*)-**10** (2.02 g, quant.), ν_{max}(film)/cm^{-1} 3355m and 3300m (OH or NH), 1255m (SiMe) and 1055s (CO). This compound was directly used for the next step without purification.

(2*S*,3*R*,4*E*)-2-Amino-1,3,15-tris-*tert*-butyldimethylsilyloxy-16-methyloctadec-4-ene 11

(15*R*,16*R*)-Isomer. In a manner similar to that described for the preparation of (15*R*,16*S*)-**11**, compound (15*R*,16*R*)-**10** (2.02 g) was converted into the *compound* (15*R*,16*R*)-**11** (2.30 g, 83% based on **9**), an oil, n_D^{25} 1.4569 (Found: C, 65.87; H, 12.09; N, 2.05. $C_{37}H_{81}NO_3Si_3$ requires C, 66.10; H, 12.14; N, 2.08%); $[\alpha]_D^{26}$ +2.50 (*c* 1.01 in MeOH); ν_{max}(film)/cm^{-1} 3385w (NH), 1255m (SiMe) and 835s; δ_H(60 MHz; $CDCl_3$) 0.00 (18 H, br s, SiMe), 0.87 (33 H, br s, CMe), 1.25 (21 H, br s, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17-H, NH_2), 2.00 (2 H, m, 6-H), 2.75 (1 H, m, 2-H), 3.55 (3 H, m, 1, 15-H), 4.00 (1 H, m, 3-H) and 5.50 (2 H, m, 4, 5-H).

(2*S*,3*R*,4*E*)-1,3,15-Tris-*tert*-butyldimethylsilyloxy-16-methyl-2-*p*-tolylsulfonylaminooctadec-4-ene 12

(15*R*,16*R*)-Isomer. In a manner similar to that described for the preparation of (15*R*,16*S*)-**12**, compound (15*R*,16*R*)-**11** (2.17 g, 3.23 mmol) was converted into *compound* (15*R*,16*R*)-**12** (2.30 g, 86%), a colourless oil, n_D^{26} 1.4780 (Found: C, 63.86; H, 10.54; N, 1.65. $C_{44}H_{87}NO_5SSi_3$ requires C, 63.94; H, 10.61; N, 1.70%); $[\alpha]_D^{26}$ −0.33 (*c* 1.06 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3290m (NH), 1600w (aromatic), 1335m (SO_2), 1255m (SiMe), 1165s (SO_2) and 835s; δ_H(270 MHz; $CDCl_3$) −0.06, −0.05, −0.02, 0.00, 0.02 and 0.03 (total 18 H, each s, SiMe), 0.79 (9 H, s, Bu^t), 0.84 (9 H, s, Bu^t), 0.87 (9 H, s, Bu^t), 0.78–0.92 (6 H, m, 16-Me, 18-H), 1.02–1.60 (19 H, m, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17-H), 1.94 (2 H, m, 6-H), 2.41 (3 H, s, ArMe), 3.11 (1 H, m, 2-H), 3.45 (1 H, dd, *J* 10.2 and 5.9, 1-Ha), 3.52 (1 H, m, 15-H), 3.80 (1 H, dd, *J* 10.2 and 4.0, 1-Hb), 4.23 (1 H, br t, *J* 6.3, 3-H), 4.64 (1 H, d, *J* 6.9, NH), 5.22 (1 H, dd, *J* 15.5 and 7.3, 4-H), 5.57 (1 H, dt, *J* 15.5 and 6.6, 5-H), 7.28 (2 H, d, *J* 8.6, *m*-Ar) and 7.73 (2 H, d, *J* 8.6, *o*-Ar).

(2*S*,3*S*,4*R*,5*S*)-1,3,15-Tris-*tert*-butyldimethylsilyloxy-4,5-epoxy-16-methyl-2-*p*-tolylsulfonylaminooctadecane 13

(15*R*,16*R*)-Isomer. In a manner similar to that described for the preparation of (15*R*,16*S*)-**13**, compound (15*R*,16*R*)-**12** (2.28 g, 2.76 mmol) was converted into the unwanted α-epoxide (15*R*,16*S*)-**13′** (1.35 g, 58%) and the *desired epoxide* (15*R*,16*R*)-**13** (967 mg, 42%), a colourless oil, n_D^{26} 1.4787 (Found: C, 62.66; H, 10.61; N, 1.64. $C_{44}H_{87}NO_6SSi_3$ requires C, 62.73; H, 10.41; N, 1.66%); $[\alpha]_D^{27}$ +15.3 (*c* 1.00 in MeOH); ν_{max}(film)/cm^{-1} 3290m (NH), 1600w (aromatic), 1340m (SO_2), 1255m (SiMe) and 1165s (SO_2); δ_H(270 MHz; $CDCl_3$) −0.05, −0.02, 0.01, 0.03, 0.04 and 0.05 (total 18 H, each s, SiMe), 0.82 (9 H, s, Bu^t), 0.84 (9 H, s, Bu^t), 0.88 (9 H, s, Bu^t), 0.78–0.92 (6 H, m, 16-Me, 18-H), 1.00–1.60 (21 H, m, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17-H), 2.41 (3 H, s, Ar*Me*), 2.67 (1 H, dd, *J* 5.0 and 2.0, 4-H), 2.78 (1 H, m, 5-H), 3.27 (1 H, m, 2-H), 3.52 (1 H, m, 15-H), 3.55 (1 H, dd, *J* 10.5 and 5.0, 1-Ha), 3.71 (1 H, dd, *J* 10.5 and 5.0, 1-Hb), 3.78 (1 H, br t, *J* 5.0, 3-H), 4.76 (1 H, d, *J* 6.6, NH), 7.28 (2 H, d, *J* 8.3, *m*-Ar) and 7.76 (2 H, d, *J* 8.3, *o*-Ar).

(2*S*,3*S*,4*R*)-1,3,15-Tris-*tert*-butyldimethylsilyloxy-16-methyl-2-*p*-tolylsulfonylaminooctadecan-4-ol 14

(15*R*,16*R*)-Isomer. In a manner similar to that described for the preparation of (15*R*,16*S*)-**14**, compound (15*R*,16*R*)-**13** (952 mg, 1.13 mmol) was converted into the *alcohol* (15*R*,16*R*)-**14** (779 mg, 82%), a colourless oil, n_D^{26} 1.4811 (Found: C, 62.75; H, 10.83; N, 1.62. $C_{44}H_{89}NO_6SSi_3$ requires C, 62.58; H, 10.62; N, 1.66%); $[\alpha]_D^{27}$ −7.8 (*c* 0.75 in MeOH); ν_{max}(film)/cm^{-1} 3545m (OH), 3325m (NH), 1600w (aromatic), 1255m (SiMe), 1165s (SO_2), 1095s, 835s and 780m; δ_H(270 MHz; $CDCl_3$) −0.05, −0.02, 0.02, 0.03, 0.09 and 0.12 (total 18 H, each s, SiMe), 0.82 (9 H, s, Bu^{t}Si), 0.88 (18 H, s, Bu^t), 0.78–0.95 (6 H, m, 16-Me, 18-H), 1.00–1.60 (23 H, m, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17-H), 2.42 (3 H, s, Ar*Me*), 2.57 (1 H, d, *J* 5.3, OH), 3.42 (1 H, m, 4-H), 3.48–3.60 (2 H, m, 2, 15-H), 3.58 (1 H, dd, *J* 10.2 and 5.6, 1-Ha), 3.69 (1 H, dd, *J* 10.2 and 6.6, 1-Hb), 3.81 (1 H, dd, *J* 4.8 and 3.0, 3-H), 4.82 (1 H, d, *J* 6.9, NH), 7.28 (2 H, d, *J* 8.3, *m*-Ar) and 7.74 (2 H, d, *J* 8.3, *o*-Ar).

(2*S*,3*R*,4*S*)-3-*tert*-Butyldimethylsilyloxy-2-*tert*-butyldimethylsilyloxymethyl-4-(11′-*tert*-butyldimethylsilyloxy-12′-methyltetradecyl)-*N*-*p*-tolylsulfonylazetidine 16

(11′*R*,12′*R*)-Isomer. In a manner similar to that described for the preparation of (11′*R*,12′*S*)-**16**, compound (15*R*,16*R*)-**14** (762 mg, 902 μmol) was converted into the *cyclized compound* (11′*R*,12′*R*)-**16** (578 mg, 78%), a colourless oil, n_D^{25} 1.4799 (Found: C, 63.67; H, 10.50; N, 1.65. $C_{44}H_{87}NO_5SSi_3$ requires C, 63.94; H, 10.61; N, 1.70%); $[\alpha]_D^{26}$ +36.3 (*c* 1.02 in $CHCl_3$); ν_{max}(film)/cm^{-1} 1600w (aromatic), 1255m (SiMe), 1160s (SO_2), 1095m, 835s, 775m and 670s; δ_H(270 MHz; $CDCl_3$) 0.01, 0.02, 0.03 and 0.04 (total 18 H, each s, SiMe), 0.84 (9 H, s, Bu^t), 0.87 (9 H, s, Bu^t), 0.88 (9 H, s, Bu^t), 0.78–0.90 (6 H, m, 12′-Me, 14′-H), 1.00–1.60 (21 H, m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 10′, 12′, 13′-H), 1.76 (2 H, m, 1′-H), 2.41 (3 H, s, Ar*Me*), 3.52 (1 H, m, 11′-H), 3.80 (1 H, dd, *J* 11.2 and 3.2, 2-C*H*H-OTBS), 3.86 (1 H, dd, *J* 11.2 and 4.6, 2-CH*H*−OTBS), 3.97 (1 H, q-like, *J* 3.6, 4-H), 4.22 (1 H, m, 2-H), 4.41 (1 H, dd, *J* 6.3 and 3.0, 3-H), 7.26 (2 H, d, *J* 8.5, *m*-Ar) and 7.71 (2 H, d, *J* 8.5, *o*-Ar).

(2*S*,3*R*,4*S*)-3-*tert*-Butyldimethylsilyloxy-2-*tert*-butyldimethylsilyloxymethyl-4-(11′-*tert*-butyldimethylsilyloxy-12′-methyltetradecyl)azetidine 17

(11′*R*,12′*R*)-Isomer. In a manner similar to that described for the preparation of (11′*R*,12′*S*)-**17**, compound (11′*R*,12′*R*)-**16** (565 mg, 684 μmol) was converted into the *amine* (11′*R*,12′*R*)-**17** (416 mg, 91%), a colourless oil, n_D^{25} 1.4619 (Found: C, 66.52; H, 12.08; N, 1.69. $C_{35}H_{75}NSi_2O_2$ requires C, 66.10; H, 12.14; N, 2.08%); $[\alpha]_D^{26}$ −1.79 (*c* 1.11 in MeOH); ν_{max}(film)/cm^{-1} 1255m (SiMe), 1060w, 835s and 775m; δ_H(270 MHz; $CDCl_3$) 0.01, 0.02, 0.06 and 0.07 (total 18 H, each s, SiMe), 0.80 (3 H, d, *J* 6.6, 12′-Me), 0.87 (3 H, t, *J* 7.6, 14′-H), 0.875, 0.88 and 0.91 (27 H, each s, Bu^t), 1.00–1.53 (21 H, m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 10′, 12′, 13′-H), 1.53–1.73 (2 H, m, 1′-H), 1.79 (1 H, br s, NH), 3.48–3.67 (5 H, m, 2-CH_2OTBS, 2, 4, 11′-H) and 4.43 (1 H, dd, *J* 7.3 and 5.3, 3-H).

(2*S*,3*R*,4*S*)-3-Hydroxy-2-hydroxymethyl-4-(11′-hydroxy-12′-methyltetradecyl)azetidine 1

(11′*R*,12′*R*)-Isomer, [(15*R*,16*R*)-penaresidin A]. In a manner similar to that described for the preparation of (11′*S*,12′*S*)-**1**, compound (11′*R*,12′*R*)-**17** (404 mg, 601 μmol) was converted into the *penaresidin* (11′*S*,12′*S*)-**1** (AcOH salt; 199 mg, 85%), a slightly yellow oil, n_D^{27} 1.4810 [Found: (HRFAB-MS) M + 1, 330.3001. $C_{19}H_{40}NO_3$ requires *m*/*z* 330.3008]; $[\alpha]_D^{26}$ −0.4 (*c* 0.36 in MeOH); ν_{max}(film)/cm^{-1} 3270s (OH), 2926s (CH), 2854s (CH), 1566m, 1556m, 1415m, 1122m and 653m; δ_H(500 MHz; CD_3OD) 0.86 (3 H, d, *J* 6.8, 12′-Me), 0.91 (3 H, t, *J* 7.3, 14′-H), 1.17 (1 H, m, 13′-Ha), 1.32 and ~1.54 (20 H, br s and m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 10′, 12′-H, 13-Hb), 1.80–1.96 (2 H, m, 1′-H), 1.91 (3 H, s, Ac), 3.43 (1 H, m, 11′-H), 3.81 (1 H, dd, *J* 12.7 and 3.9, 2-CH*H*-OH), 3.84 (1 H, dd, *J* 12.7 and 4.4, 2-C*H*H-OH), 4.06 (1 H, ddd, *J* 4.9, 4.4 and 3.9, 2-H), 4.22 (1 H, dt, *J* 8.3 and 6.8, 4-H), 4.51 (1 H, dd, *J* 6.8 and 4.9, 3-H); δ_C(125 MHz; CD_3OD) 12.23, 13.90, 23.85, 26.19, 27.09, 27.44, 27.81, 30.43, 30.53, 30.65, 30.71, 30.76, 30.85, 35.35, 41.50, 59.76, 65.12, 66.46, 69.85 and 75.41.

(2*S*,3*R*,4*S*)-3-Acetoxy-2-acetoxymethyl-4-(11′-acetoxy-12′-methyltetradecyl)-*N*-acetylazetidine 18

(11′*R*,12′*R*)-isomer, [(15*R*,16*R*)-penaresidin A tetraacetyl derivative]. In a manner similar to that described for the preparation of (11′*R*,12′*S*)-**18**, compound (11′*R*,12′*R*)-**1** (AcOH salt; 24 mg, 61 μmol) was converted into the *tetraacetyl derivative* (11′*R*,12′*R*)-**18** (29 mg, 95%), a colourless oil, n_D^{27} 1.4653 (Found: C, 64.87; H, 9.44; N, 2.81. $C_{27}H_{47}NO_7$ requires C, 65.16; H, 9.52; N, 2.81%); $[\alpha]_D^{27}$ +42 (*c* 0.41 in $CHCl_3$); ν_{max}(film)/cm^{-1} 2928s (CH), 2855s (CH), 1746s (ester), 1657s (amide), 1458m, 1414w, 1376m, 1241s, 1042w, 1022w and 952w; δ_H(500 MHz; $CDCl_3$) 0.88 (3 H, d, *J* 6.4, 12′-Me), 0.89 (3 H, t, *J* 7.3, 14′-H), 1.14 (1 H, m, 13′-Ha), 1.26 (16 H, br s, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′-H), 1.40 (1 H, m, 13′-Hb), 1.45–1.57 (3 H, m, 10′, 12′-H), 1.68–1.81 (1 H, m, 1′-Ha, 1′-Ha*), 1.89 (6/5 H, s, NAc*), 1.92 (9/5 H, s, NAc), ~2.00 (3/5 H, m, 1′-Hb), 2.04 (3 H, s, 11′-OAc), 2.08 (9/5 H, s, 2-CH_2O*Ac*), 2.11 (6/5 H, s, 2-CH_2-O*Ac**), 2.12 (9/5 H, s, 3-OAc), 2.13 (6/5 H, s, 3-OAc*), ~2.20 (2/5 H, m, 1′-Hb*), 4.29 (2/5 H, dd, *J* 12.2 and 2.9, 2-CH*H*-OAc*), 4.33 (2/5 H, m, 2-H*), 4.35–4.38 (3/5 H, m, 2-H), 4.38 (3/5 H, dd, *J* 12.2 and 2.4, 2-CH*H*-OAc), 4.45 (1 H, m, 4-H, 4-H*), 4.59 (2/5 H, dd, *J* 12.2 and 3.4, 2-C*H*H-OAc*), 4.69 (3/5 H, dd, *J* 12.2 and 4.4, 2-C*H*H-OAc),

4.86 (1 H, m, 11′-H), 5.14 (2/5 H, dd, *J* 6.8 and 3.4, 3-H*) and 5.26 (3/5 H, dd, *J* 7.3 and 3.9, 3-H). This compound exists as a mixture of two rotational isomers (*ca*. 3:2). The asterisked ^{1}H NMR signals are due to the minor isomer; δ_C(125 MHz; $CDCl_3$) 11.69, 13.90, 20.57, 20.67, 20.79, 20.95, 21.13, 25.15, 25.55, 25.66, 26.82, 29.01, 29.47, 31.32, 37.93, 60.94, 62.24, 63.16, 64.76, 65.00, 66.38, 66.59, 67.37, 76.91, 169.97, 170.05, 170.12, 170.37 and 170.96.

(4*S*)-2-Methylpentadec-6-yn-4-ol 27

In a manner similar to that described for the preparation of (3*S*,4*R*)-**5**, the epoxide **26** (2.00 g, 20.0 mmol) was converted into the *alcohol* **27** (3.10 g, 65%), a colourless oil, n_D^{25} 1.4485 (Found: C, 80.58; H, 12.48. $C_{16}H_{30}O$ requires C, 80.61; H, 12.68%); $[\alpha]_D^{24}$ −18.6 (*c* 1.32 in MeOH); ν_{max}(film)/cm^{-1} 3400m (OH), 3315m (HC≡C); δ_H(60 MHz; $CDCl_3$) 0.70–1.00 (9 H, m, Me), 1.10–1.70 (15 H, m, 2, 3, 9, 10, 11, 12, 13, 14-H), 1.87 (1 H, d, *J* 5, OH), 2.00–2.40 (4 H, m, 5, 8-H) and 3.65 (1 H, m, 4-H).

14-Methylpentadec-1-yn-12-ol 28

(12*R*)-Isomer. In a manner similar to that described for the preparation of (12*R*,13*S*)-**6**, compound **27** (8.86 g, 37.2 mmol) was converted into the *alcohol* (12*R*)-**28** (5.19 g, 59%), a colourless oil, n_D^{25} 1.4561 (Found: C, 80.52; H, 12.39. $C_{16}H_{30}O$ requires C, 80.61; H, 12.68%); $[\alpha]_D^{27}$ −6.14 (*c* 1.15 in MeOH); ν_{max}(film)/cm^{-1} 3400m (OH), 3315m (CH≡C); δ_H(60 MHz; $CDCl_3$) 0.91 (6 H, d, *J* 5, Me), 1.10–1.70 (20 H, m, 4, 5, 6, 7, 8, 9, 10, 11, 13, 14-H, OH), 1.70–2.40 (3 H, m, 1, 3-H) and 3.65 (1 H, m, 12-H).

(12*S*)-14-Methylpentadec-1-yn-12-yl 3,5-dinitrobenzoate 30

In a manner similar to that described for the preparation of (12*S*,13*S*)-**8**, compound (12*R*)-**28** (4.14 g, 17.4 mmol) was converted into the 3,5-dinitrobenzoate **30** (6.24 g, 83%), a pale yellow solid, mp 41–43 °C (Found: C, 64.06; H, 7.45; N, 6.46. $C_{23}H_{32}O_6N_2$ requires C, 63.87; H, 7.46; N, 6.48%); $[\alpha]_D^{26}$ +4.67 (*c* 1.07 in $CHCl_3$); ν_{max}(CCl_4)/cm^{-1} 3315w (HC≡C), 3100w (aromatic), 1730s (C=O) and 1550m (nitro); δ_H(60 MHz; $CDCl_3$) 0.95 (6 H, d, *J* 5, Me), 1.30 (19 H, br s, 4, 5, 6, 7, 8, 9, 10, 11, 13, 14-H), 1.90 (1 H, t, *J* 3, 1-H), 2.15 (2 H, m, 3-H), 5.25 (1 H, m, 12-H) and 9.10 (3 H, m, aromatic).

14-Methylpentadec-1-yn-12-ol 28

(12*S*)-Isomer. In a manner similar to that described for the preparation of (12*S*,13*S*)-**6**, compound **30** (6.00 g, 13.9 mmol) was converted into the *alcohol* (12*S*)-**28** (3.09 g, 93%), a colourless oil, n_D^{26} 1.4570 (Found: C, 80.31; H, 12.55. $C_{16}H_{30}O$ requires C, 80.61; H, 12.68%); $[\alpha]_D^{26}$ +6.34 (*c* 1.10 in MeOH). The IR and ^{1}H NMR spectra of (12*S*)-**28** were identical with those of (12*R*)-**28**.

Enantiomeric purity of the alcohol 28

The alcohol (12*R*)-**28** was converted into the corresponding 3,5-dinitrobenzoate (12*R*)-**30** in the conventional manner. This enantiomer and the antipode, (12*S*)-**30** which was yielded by Mitsunobu inversion, were analysed by HPLC to determine their enantiomeric purities.

HPLC analysis [column, Chiralcel OD-H® (4.6 i.d. × 250 mm); solvent, hexane–Pr^{i}OH (100:1); flow, 0.3 cm^3 min^{-1}; detect, 254 nm].

(i) (12*R*)-**30**; R_t/min 36.2 [>99.5%, (12*R*)-**30**], ~40 [<0.5%, (12*S*)-**30**]. The enantiomeric purity was determined to be >99% ee. (ii) (12*S*)-**30**; R_t/min^{-1} 36.7 [< 1%, (12*S*,13*S*)-**8**], 40.4 [>99%, (12*R*,13*S*)-**8**]. The enantiomeric purity was determined to be >98% ee.

12-*tert*-Butyldimethylsilyloxy-14-methylpentadec-1-yne 29

(12*R*)-Isomer. In a manner similar to that described for the preparation of (12*R*,13*S*)-**7**, compound (12*R*)-**28** (5.12 g, 21.5 mmol) was converted into the *TBS ether* (12*R*)-**29** (7.08 g, 93%), a colourless oil, n_D^{25} 1.4484 (Found: C, 75.09; H, 12.37. $C_{22}H_{44}OSi$ requires C, 74.92; H, 12.58%); $[\alpha]_D^{26}$ −6.80 (*c* 1.05, in hexane); ν_{max}(film)/cm^{-1} 3315m (CH≡C) and 1255m (SiMe); δ_H(60 MHz; $CDCl_3$) 0.01 (6 H, s, SiMe), 0.88 (9 H, s, Bu^t), 0.88 (6 H, d, *J* 5, C-Me), 1.25 (19 H, br s, 4, 5, 6, 7, 8, 9, 10, 11, 13, 14-H), 1.70–2.40 (3 H, m, 1, 3-H) and 3.65 (1 H, m, 12-H).

(12*S*)-Isomer. In a manner similar to that described for the preparation of (12*R*,13*S*)-**7**, compound (12*S*)-**28** (3.03 g, 12.7 mmol) was converted into the *TBS ether* (12*S*)-**29** (4.30 g, 96%), a colourless oil, n_D^{24} 1.4494 (Found: C, 74.79; H, 12.65. $C_{22}H_{44}OSi$ requires C, 74.92; H, 12.58%); $[\alpha]_D^{26}$ +6.46 (*c* 1.15, in hexane). The IR and ^{1}H NMR spectra of (12*S*)-**29** were identical with those of (12*R*)-**29**.

(*R*)-12-Acetoxy-14-methylpentadec-1-yne 31

In the conventional manner, (12*R*)-**28** (36 mg, 0.15 mmol) was converted into the corresponding *acetate* (40 mg, 94%); δ_H(270 MHz; $CDCl_3$) 0.89 (3 H, d, *J* 6.6, 14–Me or 15-H), 0.90 (3 H, d, *J* 6.3, 14-Me or 15-H), 1.20–1.70 (19 H, m, 4, 5, 6, 7, 8, 9, 10, 11, 13, 14-H), 1.78 and 1.94 (total 1 H, each t, *J* 2.6, 1-H), 2.03 (3 H, s, Ac), 2.18 (2 H, dt, *J* 2.6 and 6.9, 3-H) and 4.96 (1 H, m, 12-H); δ_C(67.8 MHz; $CDCl_3$) 18.40, 21.31, 22.23, 23.20, 24.67, 25.25, 28.48, 28.73, 29.07, 29.42, 29.47, 29.52, 34.79, 43.38, 68.07, 72.76, 84.80 and 170.92.

11-Acetoxy-13-methylpentadec-1-ene 33

In the conventional manner, 3-methylpentanal **32** (0.40 g, 4.0 mmol) was treated with dec-9-enylmagnesium bromide to give 13-methylpentadec-1-en-11-ol, which was converted into the corresponding *acetate* **33** (0.70 g, 62%), a diastereoisomeric mixture; δ_H(270 MHz; $CDCl_3$) 0.82–0.90 (6 H, m, 13-Me, 14-Me), 1.05–1.70 (19 H, m, 4, 5, 6, 7, 8, 9, 10, 12, 13, 14-H), 2.00–2.15 (2 H, m, 3-H), 2.030 and 2.033 (total 3 H, each s, Ac), 4.90–5.05 (3 H, m, 1, 11-H) and 5.81 (1 H, ddt, *J* 16.8, 10.2, 6.6, 2-H); δ_C(67.8 MHz; $CDCl_3$) 11.04, 11.22, 18.92, 19.48, 21.24, 21.30, 23.60, 25.16, 25.27, 28.88, 28.99, 29.06, 29.36, 29.44, 29.49, 29.98, 30.82, 31.04, 33.77, 34.41, 35.02, 38.23, 41.04, 41.26, 72.47, 72.83, 114.07, 139.16, 170.82 and 170.87.

***tert*-Butyl (4*S*)-4-[(1′*R*)-13′-*tert*-butyldimethylsilyloxy-1′-hydroxy-15′-methylhexadec-2′-ynyl]-2,2-dimethyl oxazolidine-3-carboxylate 34**

(13′*R*)-Isomer. In a manner similar to that described for the preparation of (13′*R*,14′*S*)-**9**, compound (12*R*)-**29** (7.06 g, 20.0 mmol) was converted into the *title compound* (13′*R*)-**34** (8.91 g, 80% based on consumed **29**; 0.3 g, 5% of **29** recovered), a colourless oil, n_D^{25} 1.4611 (Found: C, 68.27; H, 10.55; N, 2.64. $C_{33}H_{63}NO_5Si$ requires C, 68.11; H, 10.91; N, 2.41%); $[\alpha]_D^{26}$ −34.1 (*c* 1.04 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3450m (OH), 1705s (C=O), 1390s and 1255m (SiMe); δ_H(270 MHz; $CDCl_3$) 0.04 (6 H, s, SiMe), 0.86–0.89 (6 H, m, 16′-H, 15′-Me), 0.88 (9 H, s, Bu^t), 1.15–1.70 (19 H, m, 5′, 6′, 7′, 8′, 9′, 10′, 11′, 12′, 14′, 15′-H), 1.50 (9 H, br s, Bu^t), 1.59 (6 H, br s, 2-Me), 2.19 (2 H, br t, *J* 5.3, 4′-H), 3.68 (1 H, m, 13′-H), 3.90 (1 H, br s, OH), 4.10 (2 H, m, 5-H), 4.51 (1 H, m, 1′-H) and 4.76 (1 H, m, 4-H).

(13′*S*)-Isomer. In a manner similar to that described for the preparation of (13′*R*,14′*S*)-**9**, compound (12*S*)-**29** (4.25 g, 12.05 mmol) was converted into the *title compound* (13′*S*)-**34** (4.73 g, 95% based on consumed **29**; 1.22 g, 29% of **29** recovered), a colourless oil, n_D^{26} 1.4609 (Found: C, 67.56; H, 10.50; N, 2.57. $C_{33}H_{63}NO_5Si$ requires C, 68.11; H, 10.91; N, 2.41%); $[\alpha]_D^{26}$ −22.3 (*c* 1.07 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3445m (OH), 1705s (C=O), 1390s and 1255m (SiMe); δ_H(60 MHz; $CDCl_3$) 0.04 (6 H, s, SiMe), 0.87 (6 H, d, *J* 5, 16′-H, 15′-Me), 0.88 (9 H, s, Bu^t), 1.15–1.70 (19 H, m, 5′, 6′, 7′, 8′, 9′, 10′, 11′, 12′, 14′, 15′-H), 1.50 (9 H, br s, Bu^t), 1.59 (6 H, br s, 2-Me), 2.19 (2 H, m, 4′-H), 3.68 (1 H, m, 13′-H), 3.90–4.15 (3 H, m, 5-H, OH) and 4.60 (1 H, m, 1′-H, 4-H).

(2*S*,3*R*,4*E*)-2-Amino-15-*tert*-butyldimethylsilyloxy-17-methyloctadec-4-ene-1,3-diol 35

(15*R*)-Isomer. In a manner similar to that described for the preparation of (15*R*,16*S*)-**10**, compound (13′*R*)-**34** (8.69 g, 14.9 mmol) was converted into the *crude amine* (15*R*)-**35** (8.30 g, quant.), ν_{max}(film)/cm^{-1} 3365m (OH and NH) and 1255m (SiMe). This compound was used directly for the next step without purification.

(15*S*)-Isomer. In a manner similar to that described for the preparation of (15*R*,16*S*)-**10**, compound (13′*S*)-**34** (5.16 g, 8.87 mmol) was converted into the *crude amine* (15*S*)-**35** (3.85 g, 98%), ν_{max}(film)/cm^{-1} 3360m and 3300m (OH and NH) and 1255m (SiMe). This compound was used directly for the next step without purification.

(2*S*,3*R*,4*E*)-2-Amino-1,3,15-tris-*tert*-butyldimethylsilyloxy-17-methyloctadec-4-ene 36

(15*R*)-Isomer. In a manner similar to that described for the preparation of (15*R*,16*S*)-**11**, compound (15*R*)-**35** (8.30 g) was converted into the *compound* (15*R*)-**36** (7.02 g, 70% based on **34**), an oil, n_D^{25} 1.4572 (Found: C, 65.80; H, 11.84; N, 2.13. $C_{37}H_{81}NO_3Si_3$ requires C, 66.10; H, 12.14; N, 2.08%); $[\alpha]_D^{27}$ −1.43 (*c* 1.02 in MeOH); ν_{max}(film)/cm^{-1} ~3300w (NH), 1255m (SiMe) and 835s; δ_H(60 MHz; $CDCl_3$) 0.00 (18 H, br s, SiMe), 0.87 (33 H, br s, CMe), 1.25 (21 H, br s, 7, 8, 9, 10, 11, 12, 13, 14, 16, 17-H, NH_2), 2.00 (2 H, m, 6-H), 2.75 (1 H, m, 2-H), 3.55 (3 H, m, 1, 15-H), 4.00 (1 H, m, 3-H) and 5.50 (2 H, m, 4, 5-H).

(15*S*)-Isomer. In a manner similar to that described for the preparation of (15*R*,16*S*)-**11**, compound (15*S*)-**35** (3.85 g) was converted into the *compound* (15*S*)-**36** (4.12 g, 69% based on **34**), an oil, n_D^{26} 1.4562 (Found: C, 66.03; H, 12.16; N, 1.73. $C_{37}H_{81}NO_3Si_3$ requires C, 66.10; H, 12.14; N, 2.08%); $[\alpha]_D^{26}$ +2.91 (*c* 1.04 in MeOH); ν_{max}(film)/cm^{-1} ~3300w (NH), 1255m (SiMe) and 835s; δ_H(60 MHz; $CDCl_3$) 0.00 (18 H, br s, SiMe), 0.87 (33 H, br s, CMe), 1.25 (21 H, br s, 7, 8, 9, 10, 11, 12, 14, 16, 17-H, NH_2), 2.00 (2 H, m, 6-H), 2.75 (1 H, m, 2-H), 3.55 (3 H, m, 1, 15-H), 4.00 (1 H, m, 3-H) and 5.50 (2 H, m, 4, 5-H).

(2*S*,3*R*,4*E*)-1,3,15-Tris-*tert*-butyldimethylsilyloxy-17-methyl-2-*p*-tolylsulfonylaminooctadec-4-ene 37

(15*R*)-Isomer. In a manner similar to that described for the preparation of (15*R*,16*S*)-**12**, compound (15*R*)-**36** (7.00 g, 10.4 mmol) was converted into the *compound* (15*R*)-**37** (8.61 g, 90%), a colourless oil, n_D^{26} 1.4788 (Found: C, 63.80; H, 10.85; N, 1.69. $C_{44}H_{87}NO_5SSi_3$ requires C, 63.94; H, 10.61; N, 1.70%); $[\alpha]_D^{26}$ −4.78 (*c* 1.02 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3290m (NH), 1600w (aromatic), 1335m (SO_2), 1255m (SiMe), 1165s (SO_2) and 835s; δ_H(270 MHz; $CDCl_3$) −0.06, −0.05, −0.02, 0.00 and 0.04 (total 18 H, each s, SiMe), 0.79 (9 H, s, Bu^t), 0.84 (9 H, s, Bu^t), 0.87 (9 H, s, Bu^t), 0.78–0.92 (6 H, m, 17-Me, 18-H), 1.15–1.50 (18 H, m, 7, 8, 9, 10, 11, 12, 13, 14, 16-H), 1.65 (1 H, m, 17-H), 1.94 (2 H, m, 6-H), 2.41 (3 H, s, Ar*Me*), 3.11 (1 H, m, 2-H), 3.45 (1 H, dd, *J* 10.2 and 5.9, 1-Ha), 3.68 (1 H, m, 15-H), 3.80 (1 H, dd, *J* 10.2 and 4.0, 1-Hb), 4.23 (1 H, br t, *J* 6.3, 3-H), 4.64 (1 H, d, *J* 6.9, NH), 5.22 (1 H, dd, *J* 15.5 and 7.3, 4-H), 5.57 (1 H, dt, *J* 15.5 and 6.6, 5-H), 7.28 (2 H, d, *J* 8.6, *m*-Ar) and 7.73 (2 H, d, *J* 8.6, *o*-Ar).

(15*S*)-Isomer. In a manner similar to that described for the preparation of (15*R*,16*S*)-**12**, compound (15*S*)-**36** (4.08 g, 6.07 mmol) was converted into the *compound* (15*S*)-**37** (4.29 g, 86%), a colourless oil, n_D^{26} 1.4783 (Found: C, 63.67; H, 10.44; N, 1.74. $C_{44}H_{87}NO_5SSi_3$ requires C, 63.94; H, 10.61; N, 1.70%); $[\alpha]_D^{22}$ +1.37 (*c* 1.05 in $CHCl_3$); ν_{max}(film)/cm^{-1} 3290m (NH), 1600w (aromatic), 1335m (SO_2), 1255m (SiMe), 1165s (SO_2) and 835s; δ_H(270 MHz; $CDCl_3$) −0.06, −0.05, −0.02, 0.00 and 0.04 (total 18 H, each s, SiMe), 0.79 (9 H, s, Bu^t), 0.84 (9 H, s, Bu^t), 0.87 (9 H, s, Bu^t), 0.78–0.92 (6 H, m, 17-Me, 18-H), 1.15–1.50 (18 H, m, 7, 8, 9, 10, 11, 12, 13, 14, 16-H), 1.65 (1 H, m, 17-H), 1.94 (2 H, m, 6-H), 2.41 (3 H, s, Ar*Me*), 3.11 (1 H, m, 2-H), 3.45 (1 H, dd, *J* 10.2 and 5.9, 1-Ha), 3.68 (1 H, m, 15-H), 3.80 (1 H, dd, *J* 10.2 and 4.0, 1-Hb), 4.23 (1 H, br t, *J* 6.3, 3-H), 4.64 (1 H, d, *J* 6.9, NH), 5.22 (1 H, dd, *J* 15.5 and 7.3, 4-H), 5.57 (1 H, dt, *J* 15.5 and 6.6, 5-H), 7.28 (2 H, d, *J* 8.6, *m*-Ar) and 7.73 (2 H, d, *J* 8.6, *o*-Ar).

(2*S*,3*S*,4*R*,5*S*)-1,3,15-Tris-*tert*-butyldimethylsilyloxy-4,5-epoxy-17-methyl-2-*p*-tolylsulfonylaminooctadecane 38

(15*R*)-Isomer. In a manner similar to that described for the preparation of (15*R*,16*S*)-**13**, compound (15*R*)-**37** (7.66 g, 9.27 mmol) was converted into the unwanted α-epoxide (15*R*)-**38′** (4.28 g, 55%) and the *desired epoxide* (15*R*)-**38** (3.06 g, 39%), a colourless oil, n_D^{29} 1.4770 (Found: C, 62.55; H, 10.86; N, 1.66. $C_{44}H_{87}NO_6SSi_3$ requires C, 62.73; H, 10.41; N, 1.66%); $[\alpha]_D^{27}$ −20.5 (*c* 1.03 in MeOH); ν_{max}(film)/cm^{-1} 3285m (NH), 1600w (aromatic), 1335m (SO_2), 1255m (SiMe) and 1165s (SO_2); δ_H(270 MHz; $CDCl_3$) −0.05, −0.02, 0.04 and 0.05 (total 18 H, each s, SiMe), 0.82 (9 H, s, Bu^t), 0.84 (9 H, s, Bu^t), 0.88 (9 H, s, Bu^t), 0.82–0.90 (6 H, m, 17-Me, 18-H), 1.15–1.60 (20 H, m, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16-H), 1.65 (1 H, m, 17-H), 2.41 (3 H, s, Ar*Me*), 2.67 (1 H, dd, *J* 5.0 and 2.0, 4-H), 2.78 (1 H, m, 5-H), 3.27 (1 H, m, 2-H), 3.55 (1 H, dd, *J* 10.5 and 5.0, 1-Ha), 3.68 (1 H, m, 15-H), 3.71 (1 H, dd, *J* 10.5 and 5.0, 1-Hb), 3.78 (1 H, br t, *J* 5.0, 3-H), 4.76 (1 H, d, *J* 6.6, NH), 7.28 (2 H, d, *J* 8.3, *m*-Ar) and 7.76 (2 H, d, *J* 8.3, *o*-Ar).

(15*S*)-Isomer. In a manner similar to that described for the preparation of (15*R*,16*S*)-**13**, compound (15*S*)-**37** (4.28 g, 5.18 mmol) was converted into the unwanted α-epoxide (15*S*)-**38′** (2.37 g, 54%) and the *desired epoxide* (15*S*)-**38** (1.73 g, 40%), a colourless oil, n_D^{24} 1.4790 (Found: C, 63.22; H, 10.86; N, 1.77. $C_{44}H_{87}NO_6SSi_3$ requires C, 62.73; H, 10.41; N, 1.66%); $[\alpha]_D^{27}$ −14.7 (*c* 1.10 in MeOH); ν_{max}(film)/cm^{-1} 3290m (NH), 1600w (aromatic), 1335m (SO_2), 1255m (SiMe) and 1165s (SO_2); δ_H(270 MHz; $CDCl_3$) −0.05, −0.02, 0.04 and 0.05 (total 18 H, each s, SiMe), 0.82 (9 H, s, Bu^t), 0.84 (9 H, s, Bu^t), 0.88 (9 H, s, Bu^t), 0.82–0.90 (6 H, m, 17-Me, 18-H), 1.15–1.60 (20 H, m, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16-H), 1.65 (1 H, m, 17-H), 2.41 (3 H, s, Ar*Me*), 2.67 (1 H, dd, *J* 5.0 and 2.0, 4-H), 2.78 (1 H, m, 5-H), 3.27 (1 H, m, 2-H), 3.55 (1 H, dd, *J* 10.5 and 5.0, 1-Ha), 3.68 (1 H, m, 15-H), 3.71 (1 H, dd, *J* 10.5 and 5.0, 1-Hb), 3.78 (1 H, br t, *J* 5.0, 3-H), 4.76 (1 H, d, *J* 6.6, NH), 7.28 (2 H, d, *J* 8.3, *m*-Ar) and 7.76 (2 H, d, *J* 8.3, *o*-Ar).

(2*S*,3*S*,4*R*)-1,3,15-Tris-*tert*-butyldimethylsilyloxy-17-methyl-2-*p*-tolylsulfonylaminooctadecan-4-ol 39

(15*R*)-Isomer. In a manner similar to that described for the preparation of (15*R*,16*S*)-**14**, compound (15*R*)-**38** (2.55 g, 3.03 mmol) was converted into the *alcohol* (15*R*)-**39** (2.09 g, 82%), a colourless oil, n_D^{25} 1.4788 (Found: C, 62.51; H, 10.99; N, 1.66. $C_{44}H_{89}NO_6SSi_3$ requires C, 62.58; H, 10.62; N, 1.66%); $[\alpha]_D^{27}$ −11.8 (*c* 1.00 in MeOH); ν_{max}(film)/cm^{-1} 3545m (OH), 3325m (NH), 1600w (aromatic), 1255m (SiMe), 1090s, 835s and 775m; δ_H(270 MHz; $CDCl_3$) −0.05, −0.02, 0.04, 0.09 and 0.12 (total 18 H, each s, SiMe), 0.82 (9 H, s, Bu^t), 0.88 (18 H, s, Bu^t), 0.82–0.95 (6 H, m, 17-Me, 18-H), 1.17–1.55 (22 H, m, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16-H), 1.65 (1 H, m, 17-H), 2.42 (3 H, s, Ar*Me*), 2.58 (1 H, d, *J* 5.3, OH), 3.42 (1 H, m, 4-H), 3.48–3.60 (2 H, m, 1-Ha, 2-H), 3.62–3.75 (2 H, m, 1-Hb, 15-H), 3.81 (1 H, dd, *J* 4.8 and 3.0, 3-H), 4.82 (1 H, d, *J* 6.9, NH), 7.28 (2 H, d, *J* 8.3, *m*-Ar) and 7.74 (2 H, d, *J* 8.3, *o*-Ar).

(15*S*)-Isomer. In a manner similar to that described for the preparation of (15*R*,16*S*)-**14**, compound (15*S*)-**38** (120 mg, 142 μmol) was converted into the *alcohol* (15*S*)-**39** (99 mg, 82%), a colourless oil, n_D^{24} 1.4790 (Found: C, 63.04; H, 10.62; N, 1.71. $C_{44}H_{89}NO_6SSi_3$ requires C, 62.58; H, 10.62; N, 1.66%); $[\alpha]_D^{26}$ −6.69 (*c* 1.08 in MeOH); ν_{max}(film)/cm^{-1} 3545m (OH), 3325m (NH), 1600w (aromatic), 1255m (SiMe), 1090s, 835s and 775m; δ_H(270 MHz; $CDCl_3$) −0.05, −0.02, 0.04, 0.09 and 0.12 (total 18 H, each s, SiMe), 0.82 (9 H, s, Bu^t), 0.88 (18 H, s, Bu^t), 0.82–0.95 (6 H, m, 17-Me, 18-H), 1.17–1.55 (22 H, m, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 16-H), 1.65 (1 H, m, 17-H), 2.42 (3 H, s,

Ar*Me*), 2.58 (1 H, d, *J* 5.3, OH), 3.42 (1 H, m, 4-H), 3.48–3.60 (2 H, m, 1-Ha, 2-H), 3.62–3.75 (2 H, m, 1-Hb, 15-H), 3.81 (1 H, dd, *J* 4.8 and 3.0, 3-H), 4.82 (1 H, d, *J* 6.9, NH), 7.28 (2 H, d, *J* 8.3, *m*-Ar) and 7.74 (2 H, d, *J* 8.3, *o*-Ar).

(2*S*,3*R*,4*S*)-3-*tert*-Butyldimethylsilyloxy-2-*tert*-butyldimethylsilyloxymethyl-4-(11′-*tert*-butyldimethylsilyloxy-13′-methyltetradecyl)-*N*-*p*-tolylsulfonylazetidine 41

(11′*R*)-Isomer. In a manner similar to that described for the preparation of (11′*R*,12′*S*)-**16**, compound (15*R*)-**39** (2.03 g, 2.40 mmol) was converted into the *cyclized compound* (11′*R*)-**41** (1.43 g, 72%), a colourless oil, n_D^{25} 1.4775 (Found: C, 64.11; H, 10.47; N, 1.63. $C_{44}H_{87}NO_5SSi_3$ requires C, 63.94; H, 10.61; N, 1.70%); $[\alpha]_D^{28}$ +34.6 (*c* 1.01 in $CHCl_3$); ν_{max}(film)/cm^{-1} 1600w (aromatic), 1255m (SiMe), 1160s (SO_2), 835s, 775m and 670s; δ_H(270 MHz; $CDCl_3$) 0.01, 0.02, 0.03 and 0.04 (total 18 H, each s, SiMe), 0.84 (9 H, s, Bu^t), 0.87 (9 H, s, Bu^t), 0.88 (9 H, s, Bu^t), 0.85–0.90 (6 H, m, 13′-Me, 14′-H), 1.05–1.55 (20 H, m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 10′, 12′-H), 1.65 (1 H, m, 13′-H), 1.76 (2 H, m, 1′-H), 2.41 (3 H, s, Ar*Me*), 3.68 (1 H, m, 11′-H), 3.80 (1 H, dd, *J* 11.2 and 3.2, 2-C*H*H-OTBS), 3.86 (1 H, dd, *J* 11.2 and 4.6, 2-CH*H*-OTBS), 3.97 (1 H, q-like, *J* 3.6, 4-H), 4.22 (1 H, m, 2-H), 4.41 (1 H, dd, *J* 6.3 and 3.0, 3-H), 7.26 (2 H, d, *J* 8.5, *m*-Ar) and 7.71 (2 H, d, *J* 8.5, *o*-Ar).

(11′*S*)-Isomer. In a manner similar to that described for the preparation of (11′*R*,12′*S*)-**16**, compound (15*S*)-**39** (834 mg, 988 μmol) was converted into the *cyclized compound* (11′*S*)-**41** (613 mg, 75%), a colourless oil, n_D^{26} 1.4790 (Found: C, 63.45; H, 10.45; N, 1.58. $C_{44}H_{87}NO_5SSi_3$ requires C, 63.94; H, 10.61; N, 1.70%); $[\alpha]_D^{28}$ +36.4 (*c* 1.02 in $CHCl_3$); ν_{max}(film)/cm^{-1} 1600w (aromatic), 1255m (SiMe), 1160s (SO_2), 835s, 775m and 670s; δ_H(270 MHz; $CDCl_3$) 0.01, 0.02, 0.03 and 0.04 (total 18 H, each s, SiMe), 0.84 (9 H, s, Bu^t), 0.87 (9 H, s, Bu^t), 0.88 (9 H, s, Bu^t), 0.85–0.90 (6 H, m, 13′-Me, 14′-H), 1.05–1.55 (20 H, m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 10′, 12′-H), 1.65 (1 H, m, 13′-H), 1.76 (2 H, m, 1′-H), 2.41 (3 H, s, Ar*Me*), 3.68 (1 H, m, 11′-H), 3.80 (1 H, dd, *J* 11.2, 3.2, 2-C*H*H-OTBS), 3.86 (1 H, dd, *J* 11.2, 4.6, 2-CH*H*-OTBS), 3.97 (1 H, q-like, *J* 3.6, 4-H), 4.22 (1 H, m, 2-H), 4.41 (1 H, dd, *J* 6.3, 3.0, 3-H), 7.26 (2 H, d, *J* 8.5, *m*-Ar) and 7.71 (2 H, d, *J* 8.5, *o*-Ar).

(2*S*,3*R*,4*S*)-3-*tert*-Butyldimethylsilyloxy-2-*tert*-butyldimethylsilyloxymethyl-4-(11′-*tert*-butyldimethylsilyloxy-13′-methyltetradecyl)azetidine 42

(11′*R*)-Isomer. In a manner similar to that described for the preparation of (11′*R*,12′*S*)-**17**, compound (11′*R*)-**41** (1.34 g, 1.62 mmol) was converted into the *amine* (11′*R*)-**42** (942 mg, 87%), a colourless oil, n_D^{25} 1.4580 (Found: C, 65.70; H, 11.77; N, 2.14. $C_{35}H_{75}NSi_2O_2$ requires C, 66.10; H, 12.14; N, 2.08%); $[\alpha]_D^{28}$ −7.84 (*c* 1.02 in MeOH); ν_{max}(film)/cm^{-1} 1255m (SiMe), 1060w, 835s and 775m; δ_H(270 MHz; $CDCl_3$) 0.02, 0.04 and 0.07 (total 18 H, each s, SiMe), 0.85–0.90 (6 H, m, 13′-Me, 14′-H), 0.875, 0.88 and 0.91 (27 H, each s, Bu^t), 1.15–1.50 (20 H, m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 10′, 12′-H), 1.58–1.85 (4 H, m, 1′, 13′-H, NH), 3.48–3.73 (5 H, m, 2-CH_2-OTBS, 2, 4, 11′-H) and 4.43 (1 H, dd, *J* 7.3 and 5.3, 3-H).

(11′*S*)-Isomer. In a manner similar to that described for the preparation of (11′*R*,12′*S*)-**17**, compound (11′*S*)-**41** (599 mg, 725 μmol) was converted into the *amine* (11′*S*)-**42** (435 mg, 89%), a colourless oil, n_D^{25} 1.4593 (Found: C, 65.70; H, 11.77; N, 2.14. $C_{35}H_{75}NSi_2O_2$ requires C, 66.20; H, 11.73; N, 1.88%); $[\alpha]_D^{26}$ −2.00 (*c* 1.04 in MeOH); ν_{max}(film)/cm^{-1} 1255m (SiMe), 1060w, 835s and 775m; δ_H(270 MHz; $CDCl_3$) 0.02, 0.04 and 0.07 (total 18 H, each s, SiMe), 0.85–0.90 (6 H, m, 13′−Me, 14′-H), 0.875, 0.88 and 0.91 (27 H, each s, Bu^t), 1.15–1.50 (20 H, m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 10′, 12′-H), 1.58–1.85 (4 H, m, 1′, 13′-H, NH), 3.48–3.73 (5 H, m, 2-CH_2-OTBS, 2, 4, 11′-H) and 4.43 (1 H, dd, *J* 7.3 and 5.3, 3-H).

(2*S*,3*R*,4*S*)-3-Hydroxy-2-hydroxymethyl-4-(11′-hydroxy-13′-methyltetradecyl)azetidine 2′

(11′*R*)-Isomer, [(15*R*)-penaresidin B]. In a manner similar to that described for the preparation of (11′*S*,12′*S*)-**1**, compound (11′*R*)-**42** (853 mg, 1.27 mmol) was converted into the *penaresidin* (11′*S*)-**2′** (AcOH salt; 494 mg, 86%), a slightly yellow oil, n_D^{26} 1.4744 [Found: (HRFAB-MS) M + 1 330.3011. $C_{19}H_{40}NO_3$ requires *m*/*z* 330.3008]; $[\alpha]_D^{26}$ −13.7 (*c* 0.39 in MeOH); ν_{max}(film)/cm^{-1} 3331s (OH), 2926s (CH), 2854s (CH), 1556m, 1467m, 1415m, 1048m, 757w and 654m; δ_H(500 MHz; CD_3OD) 0.89 and 0.91 (total 6 H, each d, *J* 5.4, 14′-H, 13′-Me), 1.18 (1 H, ddd, *J* 13.2, 8.8 and 4.2, 12′-Ha), 1.31 and ~1.48 (19 H, br s and m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 10′, 13′-H, 12′-Hb), 1.72–1.97 (2 H, m, 1′-H), 1.91 (3 H, s, Ac), 3.58 (1 H, m, 11′-H), 3.81 (1 H, dd, *J* 12.7 and 3.9, 2-CH*H*-OH), 3.84 (1 H, dd, *J* 12.7 and 4.4, 2-C*H*H-OH), 4.08 (1 H, br q, *J* 4.3, 2-H), 4.24 (1 H, br q, *J* 8.0, 4-H) and 4.52 (1 H, dd, *J* 6.8 and 4.9, 3-H); δ_C(125 MHz; CD_3OD) 22.43, 23.85, 23.93, 25.65, 26.15, 26.78, 27.71, 30.40, 30.51, 30.67, 30.84, 39.04, 47.87, 59.66, 65.16, 66.38, 69.88 and 70.34.

(11′*S*)-Isomer, [(15*S*)-penaresidin B]. In a manner similar to that described for the preparation of (11′*S*,12′*S*)-**1**, compound (11′*S*)-**42** (425 mg, 632 μmol) was converted into the *penaresidin* (11′*S*)-**2′** (AcOH salt; 224 mg, 91%), a slightly yellow oil, n_D^{25} 1.4692 [Found: (HRFAB-MS) M + 1 330.2983. $C_{19}H_{40}NO_3$ requires *m*/*z* 330.3008]; $[\alpha]_D^{25}$ −6.8 (*c* 0.35 in MeOH); ν_{max}(film)/cm^{-1} 3258s (OH), 2925s (CH), 2854s (CH), 1564m, 1556m, 1467m, 1415m, 1367w, 1121m, 1048m, 839w, 720w and 654m; δ_H(500 MHz; CD_3OD) 0.89 and 0.91 (total 6 H, each d, *J* 5.4, 14′-H, 13′-Me), 1.18 (1 H, ddd, *J* 13.2, 8.8 and 4.2, 12′-Ha), 1.31 and ~1.48 (19 H, br s and m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 10′, 13′-H, 12′-Hb), 1.72–1.97 (2 H, m, 1′-H), 1.90 (3 H, s, Ac), 3.58 (1 H, m, 11′-H), 3.81 (1 H, dd, *J* 12.7 and 3.9, 2-CH*H*-OH), 3.84 (1 H, dd, *J* 12.7 and 4.4, 2-C*H*H-OH), 4.08 (1 H, br q, *J* 4.3, 2-H), 4.23 (1 H, br q, *J* 8.0, 4-H) and 4.52 (1 H, dd, *J* 6.8 and 4.9, 3-H); δ_C(125 MHz; CD_3OD) 22.43, 23.34, 23.94, 25.66, 26.16, 26.79, 27.67, 30.41, 30.53, 30.71, 30.84, 39.06, 47.88, 59.60, 65.22, 66.35, 69.93 and 70.34.

(2*S*,3*R*,4*S*)-3-Acetoxy-2-acetoxymethyl-4-(11′-acetoxy-13′-methyltetradecyl)-*N*-acetylazetidine 43

(11′*R*)-Isomer, [(15*R*)-penaresidin B tetraacetyl derivative]. In a manner similar to that described for the preparation of (11′*R*,12′*S*)-**18**, compound (11′*R*)-**2′** (AcOH salt; 62 mg, 0.19 mmol) was converted into the *tetraacetyl derivative* (11′*R*)-**43** (57 mg, 82%), a colourless oil, n_D^{26} 1.4631 (Found: C, 65.20; H, 9.44; N, 2.74. $C_{27}H_{47}NO_7$ requires C, 65.16; H, 9.52; N, 2.81%); $[\alpha]_D^{27}$ +35 (*c* 0.41 in $CHCl_3$); ν_{max}(film)/cm^{-1} 2928s (CH), 2855s (CH), 1746s (CO_2R), 1658s, 1454w, 1415m, 1376m, 1240s, 1169w, 1141w, 1119w, 1045m, 1123w, 953w and 722w; δ_H(500 MHz; $CDCl_3$) 0.89 and 0.90 (total 6 H, each d, *J* 5.4, 14′-H, 13′-Me), 1.20–1.39 (17 H, m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 13′-H), 1.45–1.63 (4 H, m, 10′, 12′-H), 1.68–1.81 (1 H, m, 1′-Ha, 1′-Ha*), 1.89 (6/5 H, s, NAc*), 1.92 (9/5 H, s, NAc), ~2.00 (3/5 H, m, 1′-Hb), 2.03 (3 H, s, 11′-OAc), 2.08 (9/5 H, s, 2-CH_2-O*Ac*), 2.11 (6/5 H, s, 2-CH_2-O*Ac**), 2.12 (9/5 H, s, 3-OAc), 2.13 (6/5 H, s, 3-OAc*), ~2.20 (2/5 H, m, 1′-Hb*), 4.29 (2/5 H, dd, *J* 12.2 and 2.9, 2-CH*H*-OAc*), 4.33 (2/5 H, m, 2-H*), 4.35–4.38 (3/5 H, m, 2-H), 4.38 (3/5 H, dd, *J* 12.2 and 2.4, 2-CH*H*-OAc), 4.45 (1 H, m, 4-H, 4-H*), 4.59 (2/5 H, dd, *J* 12.2 and 3.4, 2-C*H*H-OAc*), 4.69 (3/5 H, dd, *J* 12.2 and 4.4, 2-C*H*H-OAc), 4.96 (1 H, m, 11′-H), 5.14 (2/5 H, dd, *J* 6.8 and 3.4, 3-H*) and 5.26 (3/5 H, dd, *J* 7.3 and 3.9, 3-H). This compound exists as a mixture of two rotational isomers (*ca*. 3:2). The asterisked ^{1}H NMR signals arise from the minor isomer; δ_C(125 MHz; $CDCl_3$) 20.68, 20.79, 20.95, 21.25, 22.14, 23.13, 24.60, 25.19, 25.50, 26.82, 29.01, 29.47, 34.72, 43.31, 60.96, 62.24, 63.16, 64.78, 65.01, 66.38, 66.59, 67.37, 72.68, 170.00, 170.06, 170.17, 170.35, 170.40, 170.45 and 170.87.

(11′*S*)-Isomer, [(15*S*)-penaresidin B tetraacetyl derivative]. In a

manner similar to that described for the preparation of (11′*R*,12′*S*)-**18**, compound (11′*S*)-**2**′ (AcOH salt; 26 mg, 67 μmol) was converted into the *tetraacetyl derivative* (11′*S*)-**43** (32 mg, 96%), a colourless oil, n_D^{25} 1.4628 (Found: C, 65.10; H, 9.59; N, 2.83. $C_{27}H_{47}NO_7$ requires C, 65.16; H, 9.52; N, 2.81%); $[\alpha]_D^{25}$ +47 (*c* 0.42 in $CHCl_3$); ν_{max}(film)/cm^{-1} 2928s (CH), 2855s (CH), 1746s (CO_2R), 1658s, 1454w, 1415m, 1376m, 1240s, 1169w, 1141w, 1119w, 1045m, 1123w, 953w and 722w; δ_H(500 MHz; $CDCl_3$) 0.89 and 0.90 (total 6 H, each d, *J* 5.4, 14′-H, 13′-Me), 1.20–1.39 (17 H, m, 2′, 3′, 4′, 5′, 6′, 7′, 8′, 9′, 13′-H), 1.45–1.63 (4 H, m, 10′, 12′-H), 1.68–1.81 (1 H, m, 1′-Ha, 1′-Ha*), 1.89 (6/5 H, s, NAc*), 1.92 (9/5 H, s, NAc), ~2.00 (3/5 H, m, 1′-Hb), 2.03 (3 H, s, 11′-OAc), 2.08 (9/5 H, s, 2-CH_2-O*Ac*), 2.11 (6/5 H, s, 2-CH_2O*Ac**), 2.12 (9/5 H, s, 3-OAc), 2.13 (6/5 H, s, 3-OAc*), ~2.20 (2/5 H, m, 1′-Hb*), 4.29 (2/5 H, dd, *J* 12.2 and 2.9, 2-CH*H*-OAc*), 4.33 (2/5 H, m, 2-H*), 4.35–4.38 (3/5 H, m, 2-H), 4.38 (3/5 H, dd, *J* 12.2 and 2.4, 2-CH*H*-OAc), 4.45 (1 H, m, 4-H, 4-H*), 4.59 (2/5 H, dd, *J* 12.2 and 3.4, 2-C*H*H−OAc*), 4.69 (3/5 H, dd, *J* 12.2 and 4.4, 2-C*H*H-OAc), 4.96 (1 H, m, 11′-H), 5.14 (2/5 H, dd, *J* 6.8 and 3.4, 3-H*), 5.26 (3/5 H, dd, *J* 7.3 and 3.9, 3-H). This compound exists as a mixture of two rotational isomers (*ca*. 3:2). The asterisked ^{1}H NMR signals arise from the minor isomer; δ_C(125 MHz; $CDCl_3$) 20.66, 20.79, 20.95, 21.25, 22.15, 23.13, 24.60, 25.19, 25.50, 26.82, 29.01, 29.45, 34.72, 43.31, 60.94, 62.24, 63.16, 64.78, 65.00, 66.38, 66.59, 67.37, 72.66, 170.00, 170.06, 170.15, 170.35, 170.40, 170.45 and 170.86.

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13 **Note added in proof**. The absolute configuration of penaresidin A was established as 2*S*,3*R*,4*S*,15*S*,16*S* and that of penaresidin B as 2*S*,3*R*,4*S*,15*S*: see J. Kobayashi, M. Tsuda, J.-F. Cheng, M. Ishibashi, H. Takikawa and K. Mori, *Tetrahedron Lett.*, 1996, **37**, 6775.

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