Enantioselective total synthesis of vicenistatin, a novel 20-membered macrocyclic lactam antitumor antibiotic

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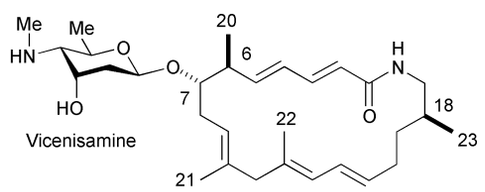
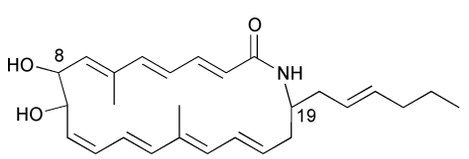
Enantioselective total synthesis of an antitumor antibiotic, vicenistatin, featuring a 20-membered macrocyclic lactam glycoside with the amino sugar vicenisamine, has been achieved. Key reactions in the synthesis of macrolactam aglycone involved Suzuki cross-coupling and Evans asymmetric aldol reaction. Penultimate glycosidation of the *O*-TMS-aglycone with appropriately protected 1-*O*-acetyl amino sugar and final deprotection allowed accomplishment of the total synthesis.

Vicenistatin (**1**), an antitumor antibiotic isolated from *Streptomyces* sp. HC-34, is interesting because of its novel structural features, including a 20-membered macrocyclic lactam aglycone and a new amino sugar (vicenisamine) as shown in Fig. 1.[1]



Vicenistatin (**1**)



BE-14106
(GT32-A)

Fig. 1 Structures of vicenistatin and BE-14106 (GT-32A).

A major biological characteristic is its significant inhibitory activity, especially against HL-60 (human leukaemia) and COLO205 (human colon carcinoma) *in vitro* and Co-3 (human colon carcinoma) *in vivo*.[1] The structure shown was determined mainly by extensive NMR spectral analysis[1] and the absolute stereochemistry of the aglycone part was determined by the synthetic approach.[2] So far, several kinds of macrocyclic lactam antibiotics have been reported including ansamycin antibiotics, hitachimycin[3] (stubomycin[4]) and BE-14106[5] (GT32-A[6]). In particular, BE-14106 should be noted here because of its 20-membered macrocyclic lactam structure. However, vicenistatin is distinct from those antibiotics by containing an amino sugar and by exhibiting intriguing antitumor activities. Recently, we have reported vicenistatin M, a neutral congener having D-mycarose instead of vicenisamine, and have determined its absolute structure by synthesis from synthetic D-mycarose and the naturally derived aglycone.[7] Interestingly, vicenistatin M showed no cytotoxicity, which strongly suggested that the vicenisamine amino sugar plays an important role in exerting the antitumor activity of vicenistatin.

To explore the chemical features essential to its biological activities, we have been engaged in synthetic studies of vicenistatin. Previously, we reported the synthesis of the aglycone part.[8] Furthermore, we have developed a new synthetic strategy for 2,6-dideoxyamino sugars, by which the synthesis of D-vicenisamine and L-kedarosamine was furnished.[9] Along these lines, we report herein the enantioselective total synthesis of vicenistatin.

Our convergent synthetic plan, which should be flexible in view of possible future structure modifications, is shown in Scheme 1. The final stage of the synthesis was to be glycosidation, however, a difficulty had already been found in that the free aglycone was extremely insoluble in most solvents.[7] Therefore, the aglycone part had to be prepared in a suitably protected form for glycosidation. Consequently, *O*-TMS (trimethylsilyl) protected aglycone **2** was envisaged as a glycosyl acceptor, and *N,O*-protected 1-*O*-acetyl sugar **3** was chosen as a glycosyl donor, because of the ease of preparation of the free 1-*O*-acetyl sugar and its usefulness in glycosidation with *O*-TMS-alcohol.[7,10] Accordingly, our previous synthetic strategy through the *N*-PMB (*p*-methoxybenzyl)-protected aglycone[8] was modified for the synthesis of *O*-TMS-aglycone **2**, especially about the time point of introduction of the nitrogen functional group. We further envisaged that lactam formation should be as the final macrocyclization for the aglycone. The crucial precursor **A** was expected to be synthesized from the triene-alcohol **B** by Evans asymmetric aldol reaction[11] and subsequent Wittig–Horner chain elongation, and the intermediate **B** seemed to be stereoselectively constructable by Suzuki cross-coupling[12] of **C** and **D**. The vinyl iodide **C** should be derived from cyclopropyl methyl ketone **4**, and the vinylboronate counterpart **D** could be derived from (*S*)-citronellol **5** *via* a corresponding acetylene **D′**.

Results and discussion

According to the above-mentioned strategy, our work started from the preparation of two components, **C** (≡ **11**) and **D′** (= **14**), which is depicted in Scheme 2. The homopropargyl alcohol **6**, which was obtained from cyclopropyl methyl ketone

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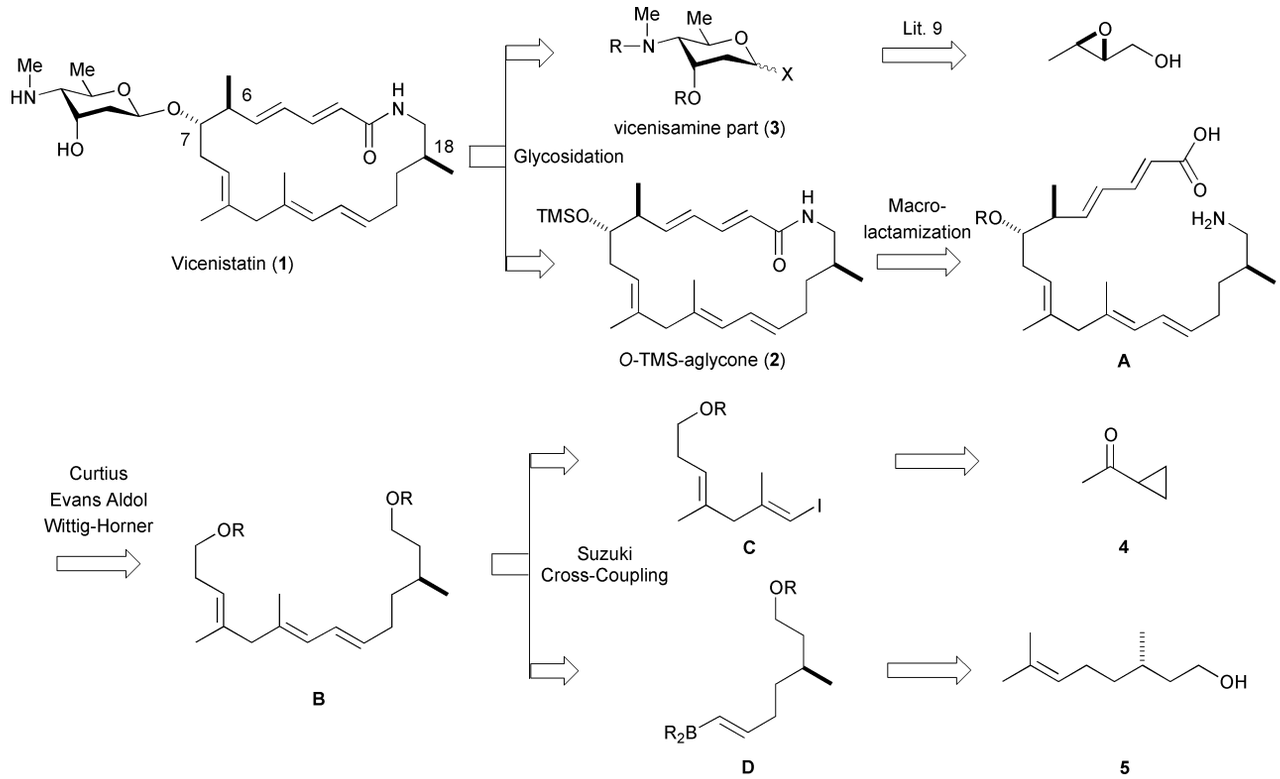
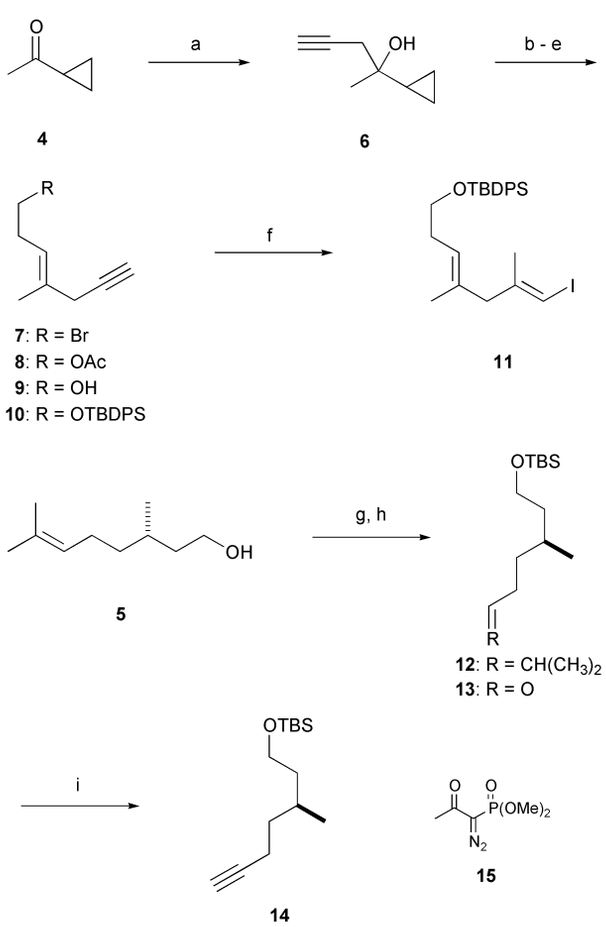


Scheme 1 Retrosynthetic analysis for vicenistatin.



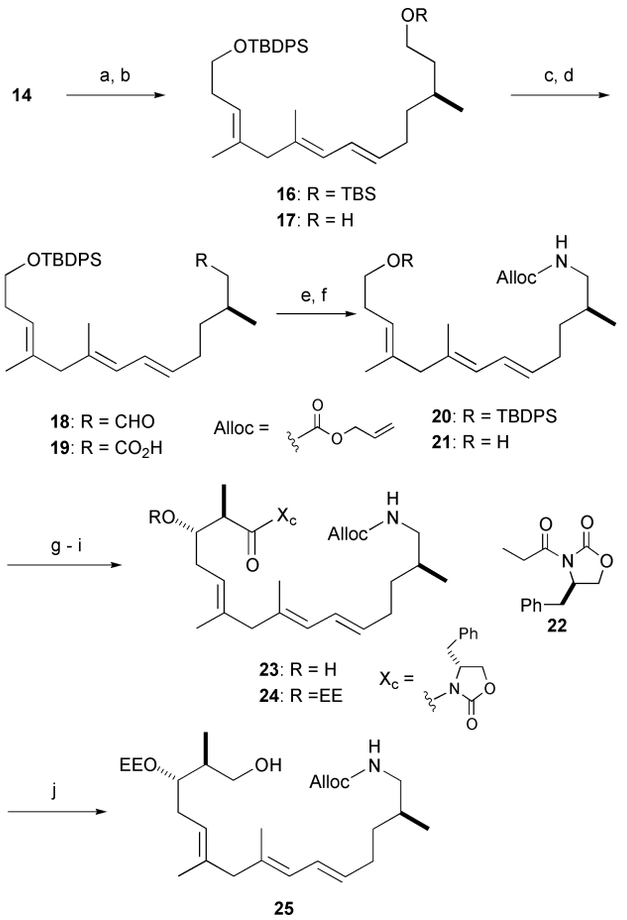
Scheme 2 Synthesis of coupling precursors (**11** and **14**). *Reagents, conditions and yields*: (a) propargyl bromide, Mg, cat. $HgCl_2$, Et_2O (87%); (b) 47% HBr; (c) CsOAc, DMF (79%, 2 steps); (d) KCN, EtOH (99%); (e) TBDPSCl, Imid., DMF (99%); (f) $AlMe_3$, cat. $ZrCl_2$; I_2, CH_2Cl_2 (88%); (g) TBSCl, Imid., DMF (quant.); (h) O_3, CH_2Cl_2, MeOH, Py.; Me_2S (94%); (i) Method A: (1) CBr_4, PPh_3, Py., CH_2Cl_2 (93%); (2) Bu^nLi, THF (88%); Method B: **15**, K_2CO_3, MeOH (80%).

4 by Grignard reaction, was stereoselectively converted to (*E*)-homoallylic bromide **7** (*E* : *Z* ≈ 14 : 1) with hydrobromic acid; the classical Julia method.[13] The bromide **7** was displaced with caesium acetate to introduce an oxygen functionality as acetate **8**.[14] After deprotection of the acetyl group of **8** under neutral conditions,[15] the hydroxy group of the resulting alcohol **9** was reprotected to give *tert*-butyldiphenylsilyl (TBDPS) ether **10**. Subsequently, the terminal acetylene **10** was converted to (*E*)-2-methylalk-1-enyl iodide **11** by Negishi's method.[16]

A vinylboronate counterpart **D** was synthesized from the corresponding acetylene. The starting (*S*)-citronellol TBS ether **12** was subjected to ozonolysis in MeOH to give aldehyde **13**, which was then transformed into the acetylenic compound **14** by the Corey–Fuchs method (82%, 2 steps).[17] The Ohira–Bestmann one-pot procedure[18] was also applicable to the aldehyde **13**. Thus, treatment of **13** in MeOH with dimethyl (1-diazo-2-oxopropyl)phosphonate **15** in the presence of potassium carbonate furnished the acetylene **14** in 80% yield.

The crucial Suzuki coupling[12] of these two components **11** and **14** and subsequent transformations were carried out as follows (Scheme 3). The vinylboronate **D**, prepared *in situ* by hydroboration of **14** with catecholborane, was treated with the vinyl iodide **11** in the presence of tetrakis(triphenylphosphine)palladium catalyst and NaOH as a base to give a coupling product **16** in moderate yield. The TBS protecting group of the resulting diene **16** was then selectively removed with aqueous acetic acid in THF to give alcohol **17**. This was then oxidized to aldehyde **18** by Swern oxidation[19] and the aldehyde **18** was further oxidized by sodium chlorite in a mixture of *tert*-butyl alcohol and phosphate buffer in the presence of 2-methylbut-2-ene as a scavenger[20] to afford carboxylic acid **19** in good yield. For the introduction of a nitrogen functional group, Curtius rearrangement[21] was carried out in refluxing benzene with diphenylphosphoryl azide and triethylamine in the presence of allyl alcohol to afford allyloxycarbonyl (Alloc)-protected amine **20** in 68% yield. Then, the remaining silyl protecting group of compound **20** was cleaved with hydrogen fluoride–pyridine[22] in THF to give alcohol **21**.

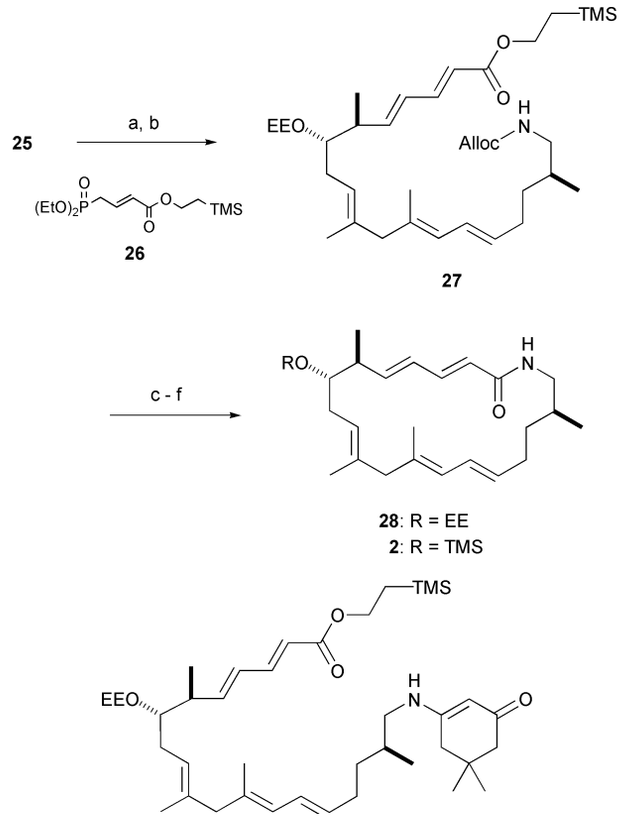
Subsequent key manipulations included construction of two contiguous chiral centers (C-6, -7) (Scheme 3), chain elongation



Scheme 3 Synthesis of *O*-TMS-aglycone (**2**)-1. *Reagents, conditions and yields*: (a) catecholborane, THF: **11**, cat. $Pd(PPh_3)_4$, 2 M NaOH, benzene (72% from **11**); (b) AcOH, H_2O, THF (60%); (c) $(COCl)_2$, DMSO; Et_3N, CH_2Cl_2 (82%); (d) $NaClO_2$, 2-methylbut-2-ene, NaH_2PO_4, Bu^tOH, H_2O (99%); (e) $(PhO)_2P(O)N_3$, Et_3N; allyl alcohol, benzene (68%); (f) HF·Py, THF (89%); (g) Dess–Martin periodinane, CH_2Cl_2; (h) **22**, Bu^n_2BOTf, Et_3N, CH_2Cl_2 (62%, 2 steps); (i) EVE, PPTS, CH_2Cl_2 (86%); (j) $LiBH_4$, MeOH, THF (74%).

(C-1–C-5) and the final macrolactamization (Scheme 4). Dess–Martin oxidation[23] of the alcohol **21** gave the corresponding aldehyde, but considerable decompostion was observed during the work-up and purification. Therefore, the highly unstable aldehyde had to be immediately subjected to Evans aldol reaction.[11] Thus, a reaction mixture of the oxidation was directly injected into a boron enolate solution, which previously had been prepared from chiral oxazolidinone **22**, to give an aldol product **23** in moderate yield. After protection of the resulting 7-hydroxy group as its 1-ethoxyethyl (EE) ether, compound **24** was reduced with lithium borohydride to give primary alcohol **25**. The alcohol **25** was then oxidized by Dess–Martin procedure to give the corresponding aldehyde, which in turn was subjected to Wittig–Horner chain elongation with phosphonate **26** to give (*E,E*)-diene ester **27**.

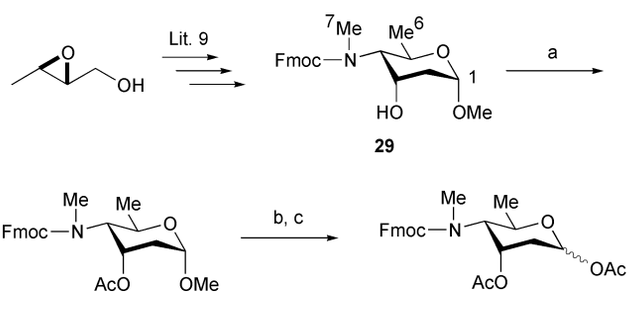
Removal of amino- and carboxy-protecting groups and subsequent macrolactamization were performed as follows. Initial palladium-catalyzed deprotection of the Alloc group of **27** was somewhat troublesome, *i.e.* the deprotected free amine happened to react with dimedone, which was the generally used allyl-transfer reagent, to form an enamine (*m/z* 669 $[M - H]^-$) as a by-product shown in Scheme 4.[24] Fortunately, this side reaction could be avoided by using 2-ethylhexanoic acid[25] or, more favorably, 1,3-dimethylbarbituric acid[26] as allyl-transfer reagent in the presence of tetrakis(triphenylphosphine)palladium to yield an intermediary seco-ester. The remaining TMS-ethyl protecting group of the seco-ester was immediately cleaved by tetra-*n*-butylammonium fluoride (TBAF) to give an



Scheme 4 Synthesis of *O*-TMS-aglycone (**2**)-2. *Reagents, conditions and yields*: (a) Dess–Martin periodinane, CH_2Cl_2; (b) **26**, $LiN(TMS)_2$, THF (58%, 2 steps); (c) $Pd(PPh_3)_4$, dimethylbarbituric acid, THF (65%); (d) TBAF, THF; (e) $(EtO)_2P(O)CN$, Et_3N, DMF (28%, 2 steps); (f) PPTS, MeOH; TMSCl, Et_3N, DMAP, CH_2Cl_2 (92%).

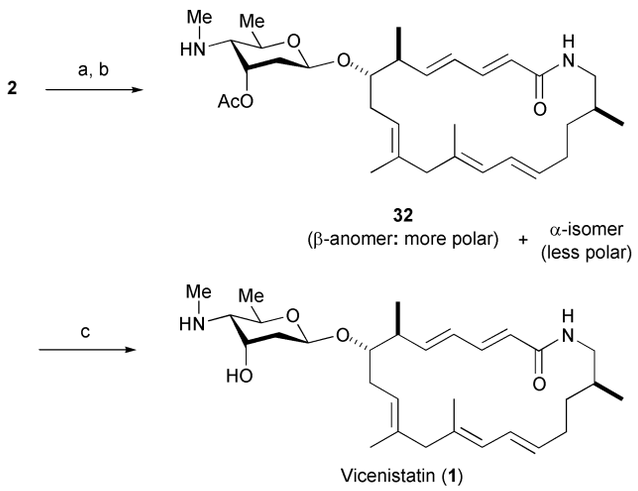
ω-amino carboxylic acid, the precursor for the macrolactamization. Subsequently, the final cyclization was successfully performed under high dilution (0.002 M) in DMF with diethyl cyanophosphonate and triethylamine at 0 °C (Shioiri's conditions for peptide synthesis[27]) to construct the macrolactam ring **28** (28%, 2 steps). The EE protecting group of **28** was finally removed by acid-catalyzed methanolysis and the resulting 7-hydroxy group was immediately reprotected to give the desired *O*-TMS-aglycone **2**. Its spectroscopic properties were identical with those of an authentic specimen, which was obtained from natural vicenistatin (**1**) in two steps, *i.e.* acidic solvolysis and *O*-TMS protection.[7] At this stage, we were successful in synthesizing the 20-membered macrocyclic lactam, *O*-TMS-aglycone (**2**) as the glycosyl acceptor.

The glycosyl donor was then prepared from *N*-Fmoc (fluoren-9-ylmethoxycarbonyl)-protected methyl α-vicenisaminide **29**, the synthesis of which was recently reported.[9] Thus, the C-3 hydroxy group of **29** was first protected as an acetate **30** (Scheme 5). After hydrolysis of **30** in aqueous acetic acid, the



Scheme 5 Synthesis of glycosyl donor. *Reagents, conditions and yield*: (a) Ac_2O, DMAP, Py. (89%); (b) AcOH, H_2O; (c) Ac_2O, DMAP, Py. (97%, 2 steps).

resulting free sugar was further acetylated to give the desired glycosyl donor 1,3-di-*O*-acetyl-*N*-Fmoc-vicenisamine **31**. It turned out that these *N*-Fmoc-protected compounds bore a slight disadvantage in that slow rotation around the urethane C–N bond resulted in complicated NMR spectra due to the presence of rotational isomers. However, the Fmoc protecting group was chosen because of its ease of removal in the final stage of the synthesis (See Scheme 6).



Scheme 6 Synthesis of vicenistatin (**1**). *Reagents, conditions and yields*: (a) $SnCl_4$, $AgClO_4$, **31** CH_2Cl_2, 0 °C (59% from **2**); (b) DBU, EtOAc: PLC separation (**32**: 46%; α-isomer: 46%); (c) conc KOH aq., MeOH, rt (83%).

Glycosidation of the *O*-TMS-aglycone **2** with **31** was achieved using Mukaiyama's protocol.[10] In the event, treatment of an ice-cooled solution of **2** and **31** in dry CH_2Cl_2 in the presence of $SnCl_4$–$AgClO_4$, followed by warming of the heterogeneous mixture, provided a inseparable anomeric mixture in 59% yield as shown in Scheme 6. The Fmoc proctective group of the mixture was subsequently cleaved with 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU)[28] to afford the desired β-glycoside **32** (1′-H: dd, J = 1.8, 9.8 Hz) and an α-anomer (1′-H: d, J = 4.2 Hz), which were separated by preparative thin-layer chromatography (PLC) (α : β ≈ 1 : 1). The 3′-*O*-acetyl group of the thus obtained β-glycoside **32** was deprotected by alkaline hydrolysis to afford vicenistatin (**1**). All the spectral data of the synthetic **1** were identical in every aspect to those of natural vicenistatin.

In conclusion, we were successful in enantioselectively synthesizing vicenistatin. The convergent synthetic strategy described above appears to be applicable to the synthesis of various vicenistatin derivatives.

Experimental

All mps are uncorrected. NMR spectra were recorded on a JEOL LA-300, or a Bruker DRX-500 spectrometer. ^{1}H-NMR and ^{13}C-NMR chemical shifts were reported in δ-values based on internal tetramethylsilane (δ_H = 0), or solvent signal ($CDCl_3$ δ_C = 77.0; pyridine-d_5 δ_H = 7.20, δ_C = 135.5) as reference. IR spectra were recorded on a Horiba FT-710 Fourier-transform infrared spectrometer. Optical rotations were measured on a JASCO DIP-360 polarimeter, and $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. Mass spectra were measured on a JEOL AX-505HA mass spectrometer. Silica gel column chromatography was carried out with Merck Kieselgel 60, Art. Nr. 7734, and flash column chromatography was carried out with Merck Kieselgel 60, Art. Nr. 9385.

2-Cyclopropylpent-4-yn-2-ol 6

To a suspension of magnesium turnings (2.66 g, 110 mmol) and mercury(II) chloride (24.2 mg, 8.91×10^{-2} mmol, 0.15 mol%) in dry Et_2O (80 cm^3) was added dropwise propargyl bromide (6.92 cm^3, 91.9 mmol) at a rate to maintain gentle reflux under Ar. To an ice-cooled solution of the resulting Grignard reagent was added dropwise a solution of cyclopropyl methyl ketone **4** (5.00 g, 59.4 mmol) in dry Et_2O (15 cm^3) and the reaction mixture was stirred at rt for 2 h. The reaction was quenched by addition of saturated aq. NH_4Cl at 0 °C, and the resulting mixture was extracted four times with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was vacuum-distilled at 80.5–81.0 °C (32 mmHg) to give compound **6** as a colorless oil (6.42 g, 87%) {HREIMS *m*/*z* 124.0842 [(M)$^+$; Calc. for $C_8H_{12}O$: *m*/*z*, 124.0888]}; ν_{max} (neat)/cm^{-1} 3423 (br), 3303, 3086, 2117, 1375 and 636; δ_H (300 MHz; $CDCl_3$) 0.33–0.48 (m, 4H), 0.99–1.09 (m, 1H), 1.24 (s, 3H), 2.09 (t, J = 2.2 Hz, 1H) and 2.38–2.51 (m, 2H); δ_C (75 MHz; $CDCl_3$) 0.03, 0.23, 19.9, 25.0, 32.7, 69.5, 70.5 and 80.4.

(*E*)-7-Acetoxy-4-methylhept-4-en-1-yne 8

To a solution of 47% aq. HBr (15 cm^3) was added dropwise the alcohol **6** (6.40 g, 51.5 mmol) at −24 °C. After the reaction mixture had been stirred for 3 hr at 0 °C, it was extracted four times with pentane. The combined extract was washed successively with saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residual crude bromide **7** (9.26 g, 96%) was immediately used for the next step without further purification.

To a solution of bromide **7** (9.26 g, ≈ 49.5 mmol) in dry DMF (20 cm^3) was added caesium acetate (15.0 g, 78.1 mmol) and the reaction mixture was stirred for 19 h at rt. The mixture was poured into water and extracted four times with Et_2O. The combined extract was washed successively with water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–EtOAc, 50 : 1 to 20 : 1) to give acetate **8** as a colorless oil (6.77 g, 79% in 2 steps) {HREIMS *m*/*z* 166.0966 [(M)$^+$; Calc. for $C_{10}H_{14}O_2$: *m*/*z*, 166.0994]}; ν_{max} (neat)/cm^{-1} 3284, 2117, 1739, 1245 and 1036; δ_H (300 MHz; $CDCl_3$) 1.72 (s, 3H), 2.05 (s, 3H), 2.09 (t, J = 2.2 Hz, 1H), 2.38 (q, J = 6.6 Hz, 2H), 2.91 (s, 2H), 4.07 (dt, J = 7.1, 2.5 Hz, 2H) and 5.43 (dt, J = 7.1, 1.2 Hz, 1H); δ_C (75 MHz; $CDCl_3$) 16.0, 20.9, 27.5, 28.5, 63.7, 70.4, 81.6, 120.9, 132.6 and 171.1.

(*E*)-4-Methylhept-3-en-6-yn-1-ol 9

A solution of acetate **8** (4.14 g, 24.5 mmol) and potassium cyanide (1.36 g, 20.0 mmol) in ethanol (83 cm^3) was stirred for 5 days at rt. The reaction was quenched by addition of water (30 cm^3), and the solvent was removed *in vacuo*. The residue was dissolved in water and extracted three times with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–EtOAc, 10 : 1 to 5 : 1) to give alcohol **9** as a colorless oil (3.07 g, 99%) {HREIMS *m*/*z* 124.0930 [(M)$^+$; Calc. for $C_8H_{12}O$: *m*/*z*, 124.0888]}; ν_{max} (neat)/cm^{-1} 3373 (br), 3298, 2117, 1421 and 1047; δ_H (300 MHz; $CDCl_3$) 1.73 (s, 3H), 2.13 (t, J = 2.4 Hz, 1H), 2.38 (q, J = 6.4 Hz, 2H), 2.92 (s, 2H), 3.65 (dt, J = 7.1, 2.5 Hz, 2H) and 5.46 (dt, J = 7.1, 1.2 Hz, 1H); δ_C (75 MHz; $CDCl_3$) 16.2, 28.5, 31.5, 62.2, 70.5, 81.7, 121.8 and 132.7.

(*E*)-7-(*tert*-Butyldiphenylsilyloxy)-4-methylhept-4-en-1-yne 10

To an ice-cooled solution of alcohol **9** (523.3 mg, 4.21 mmol) and imidazole (456 mg, 6.70 mmol) in DMF (5 cm^3) was added dropwise *tert*-butyldiphenylsilyl chloride (1.26 cm^3, 4.85 mmol) and the mixture was stirred for 0.5 h at 0 °C. The reaction mixture was poured into cold water and the mixture was extracted twice with pentane. The combined extract was washed successively with saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was

purified by column chromatography (hexane–Et_2O, 50 : 1) to give silyl ether **10** as a colorless oil (1.51 g, 99%) (Found: C, 79.37; H, 8.42. Calc. for $C_{24}H_{30}OSi$: C, 79.50; H, 8.34%); ν_{max} (neat)/cm^{-1} 3309, 2119, 1427, 1113, 823 and 702; δ_H (300 MHz; $CDCl_3$) 1.05 (s, 9H), 1.63 (s, 3H), 2.07 (t, J = 2.7 Hz, 1H), 2.30 (q, J = 6.8 Hz, 2H), 2.86 (s, 2H), 3.66 (t, J = 6.8 Hz, 2H), 5.46 (tt, J = 1.4, 7.3 Hz, 1H), 7.28–7.43 (m, 6H) and 7.66–7.69 (m, 4H); δ_C (75 MHz; $CDCl_3$) 16.0, 19.1, 26.8, 28.5, 31.5, 63.4, 70.3, 81.9, 122.4, 127.6, 129.5, 131.3, 134.0 and 135.6.

(1*E*,4*E*)-7-(*tert*-Butyldiphenylsilyloxy)-2,4-dimethyl-i1-odohepta-1,4-diene 11

To an ice-cooled suspension of dichlorobis(η_5-pentadienyl)-zirconium (156 mg, 5.34×10^{-1} mmol) in dry CH_2Cl_2 (2.5 cm^3) were added dropwise a solution of alkyne **10** (865 mg, 2.39 mmol) in dry CH_2Cl_2 (3.0 cm^3) and trimethylaluminium (2.50 cm^3, 2.0 M solution in toluene, 5.0 mmol) in that order under Ar. The resulting mixture was warmed to rt and stirred for an additional 5.5 h. To the mixture was added dropwise a solution of iodine (940 mg, 3.70 mmol) in THF (3 cm^3) at 0 °C and the mixture was stirred at the same temperature for 1 h. The reaction was carefully quenched by addition of cold water and the mixture was extracted twice with pentane. The combined extract was washed successively with 0.5 M HCl, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–EtOAc, 100 : 1) to give iodide **11** as a colorless oil (1.06 g, 88%) {HREIMS *m*/*z* 505.1389 [$(M)^+$; Calc. for $C_{25}H_{34}IOSi$: *m*/*z*, 505.1424]}; ν_{max} (neat)/cm^{-1} 3070, 1589, 1471, 1427, 1110 and 701; δ_H (300 MHz; $CDCl_3$) 1.04 (s, 9H), 1.47 (s, 3H), 1.73 (s, 3H), 2.28 (q, J = 7.3 Hz, 2H), 2.82 (s, 2H), 3.65 (t, J = 6.8 Hz, 2H), 5.21 (t, J = 7.3 Hz, 1H), 5.90 (s, 1H), 7.24–7.45 (m, 6H) and 7.65–7.69 (m, 4H); δ_C (75 MHz; $CDCl_3$) 15.5, 19.2, 23.3, 26.8, 31.6, 49.8, 63.5, 75.8, 123.8, 127.6, 129.5, 133.5, 134.0, 135.6 and 146.2.

(*S*)-8-*tert*-Butyldimethylsilyloxy-2,6-dimethyloct-2-ene [(*S*)-citronellol *tert*-butyldimethylsilyl ether] 12

To an ice-cooled solution of (*S*)-citronellol **5** (147.0 g, 941 mmol) and imidazole (96.1 g, 1.41 mol) in dry DMF (750 cm^3) was added portionwise *tert*-butyldimethylsilyl chloride (165.7 g, 1.10 mol). The mixture was stirred for 3 h at 0 °C. The reaction mixture was poured into water and the mixture was extracted three times with Et_2O. The combined extract was washed with brine, dried over ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–EtOAc, 50 : 1) to give silyl ether **12** as a colorless oil (266.9 g, quant.) (Found: C, 71.21; H, 12.72; Calc. for $C_{16}H_{34}OSi$: C, 71.04; H, 12.67%); $[\alpha]_D^{24}$ −1.42 (*c* 1.01, $CHCl_3$); ν_{max} (neat)/cm^{-1} 2956, 2857, 1471, 1255 and 1097; δ_H (300 MHz; $CDCl_3$) 0.05 (s, 6H), 0.89 (d, J = 10 Hz, 3H), 0.90 (s, 9H), 1.08–1.20 (m, 1H), 1.29–1.39 (m, 2H), 1.50–1.56 (m, 2H), 1.58 (s, 3H), 1.68 (s, 3H), 1.90–2.05 (m, 2H), 3.57–3.70 (m, 2H) and 5.10 (t, J = 7.3 Hz, 1H); δ_C (75 MHz; $CDCl_3$) −5.3, 17.5, 18.3, 19.6, 25.5, 25.7, 26.0, 29.1, 37.3, 40.0, 61.3, 125.0 and 130.7.

(*S*)-6-*tert*-Butyldimethylsilyloxy-4-methylhexanal 13

To a mixture of alkene **12** (35.2 g, 129 mmol), MeOH (120 cm^3), CH_2Cl_2 (120 cm^3), and pyridine (2 cm^3) was introduced ozone at −78 °C until the color of the resulting solution became pale blue. Excess ozone was purged with a stream of argon, and dimethyl sulfide (11.0 cm^3, 150 mmol) was added dropwise to the mixture at −78 °C. The solution was allowed to warm gradually to rt with stirring for 18 h. The mixture was concentrated *in vacuo* and the residue was purified by column chromatography (hexane–EtOAc, 20 : 1) to give aldehyde **13** as a colorless oil (29.9 g, 94%) (Found: C, 63.66; H, 11.64. Calc. for $C_{13}H_{28}O_2Si$: C, 63.88; H, 11.54%); $[\alpha]_D^{29}$ +5.38 (*c* 1.86, $CHCl_3$); ν_{max} (neat)/cm^{-1} 2713, 1728, 1471, 1463, 1255 and 1095; δ_H (300 MHz; $CDCl_3$) 0.05 (s, 6H), 0.89 (d, J = 10 Hz, 3H), 0.84 (s, 9H), 1.34–1.74 (m, 5H), 2.40–2.47 (m, 2H), 3.58–3.70 (m, 2H) and 9.78 (t, J = 1.7 Hz, 1H); δ_C (75 MHz; $CDCl_3$) −5.3, 17.5, 18.3, 19.6, 25.5, 25.7, 26.0, 29.1, 37.3, 40.0, 61.3, 125.0 and 130.7.

(*S*)-7-*tert*-Butyldimethylsilyloxy-5-methylhept-1-yne 14

Method A. To an ice-cooled solution of triphenylphosphine (86.1 g, 328 mmol) in CH_2Cl_2 (600 cm^3) and pyridine (16 cm^3) was added portionwise carbon tetrabromide (52.6 g, 159 mmol). After the mixture had been stirred for 10 min, a solution of aldehyde **13** (20.0 g, 81.8 mmol) in CH_2Cl_2 (20 cm^3) was added over a period of 10 min. The mixture was stirred for 2 h at 0 °C, and was then poured into a stirred mixture of hexane and saturated aq. $NaHCO_3$. The whole was extracted three times with hexane. The combined extract was washed twice with brine, dried ($MgSO_4$) and concentrated *in vacuo*. Insoluble material was filtered off when generated during the concentration. The residue was purified by column chromatography (hexane–EtOAc, 30 : 1) to give an intermediary dibromo olefin as a colorless oil (30.6 g, 93%) (Found: C, 42.24; H, 7.22. Calc. for $C_{14}H_{28}Br_2OSi$: C, 42.01; H, 7.05%); $[\alpha]_D^{25}$ −1.51 (*c* 1.27, $CHCl_3$); ν_{max} (neat)/cm^{-1} 2954, 2856, 1625, 1471, 1461, 1255 and 1095; δ_H (300 MHz; $CDCl_3$) 0.05 (s, 6H), 0.89 (s, 9H), 0.90 (d, J = 6.1 Hz, 3H), 1.20–1.65 (m, 5H), 2.02–2.18 (m, 2H), 3.60–3.69 (m, 2H) and 6.37 (t, J = 7.3 Hz, 1H); δ_C (75 MHz; $CDCl_3$) −5.3, 18.3, 19.4, 26.0, 29.0, 30.6, 34.9, 40.0, 61.1, 88.5 and 138.8.

To a solution of the dibromo olefin (21.47 g, 53.7 mmol) in THF (250 cm^3) was added dropwise *n*-butyllithium (87.5 cm^3; 1.53 M solution in hexane, 134 mmol) at −78 °C. The solution was then stirred for 1 h at −78 °C, and for 3.5 h at rt. Saturated aq. NH_4Cl (30 cm^3) was added slowly to the mixture. The solvent was removed *in vacuo*. The residue was diluted with Et_2O (40 cm^3) and water (50 cm^3). The aqueous layer was extracted three times with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–EtOAc, 50 : 1) to give alkyne **14** as a colorless oil (11.34 g, 88%) (Found: C, 69.67; H, 11.52. Calc. for $C_{14}H_{28}OSi$: C, 69.93; H, 11.74%); $[\alpha]_D^{26}$ −0.07 (*c* 1.19, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3315, 2119, 1255 and 1093; δ_H (300 MHz; $CDCl_3$) 0.01 (s, 6H), 0.84 (s, 9H), 0.85 (d, J = 4.4 Hz, 3H), 1.22–1.39 (m, 2H), 1.47–1.58 (m, 2H), 1.60–1.73 (m, 1H), 1.88 (t, J = 2.5 Hz, 1H), 2.12–2.21 (m, 2H) and 3.55–3.67 (m, 2H); δ_C (75 MHz; $CDCl_3$) −5.3, 16.1, 18.3, 19.1, 25.9, 28.8, 35.7, 39.5, 61.2, 68.0 and 84.7.

Method B. To a solution of aldehyde **13** (1.59 g, 6.50 mmol) and potassium carbonate (1.81 g, 13.1 mmol) in MeOH (98 cm^3) was added dimethyl (1-diazo-2-oxopropyl)phosphonate **15**[18] (1.52 g, 7.91 mmol). The reaction mixture was stirred for 5 h at rt. After the solvent had been removed *in vacuo*, the residue was suspended in water and extracted twice with Et_2O. The combined extract was washed successively with saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography (hexane) to afford alkyne **14** (1.26 g, 80%).

(3*E*,6*E*,8*E*,12*S*)-14-*tert*-Butyldimethylsilyloxy-1-*tert*-butyldiphenylsilyloxy-4,6,12-trimethyltetradeca-3,6,8-triene 16

To a solution of alkyne **14** (10.52 g, 43.78 mmol) in THF (120 cm^3) was added catecholborane (52.2 cm^3; 1.0 M solution in THF, 52 mmol) and the mixture was refluxed for 3 h. After the solvent had been removed *in vacuo*, the residue was dissolved in benzene (100 cm^3). To the solution were added the vinyl iodide **11** (20.08 g, 39.80 mmol), tetrakis(triphenylphosphine)palladium (1.45 g, 1.25 mmol, 3 mol%), and 2 M NaOH (43 cm^3) and the resulting mixture was refluxed for 10 h.

After the solution had been cooled to 0 °C, a mixture of 35% H_2O_2 (15 cm^3) and 2 M NaOH (22 cm^3) was added slowly. The solvent was then removed *in vacuo* and the residue was extracted three times with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography (hexane–EtOAc, 100 : 1) to give triene **16** as a colorless oil (17.86 g, 72% from **11**), which was used for the next reaction without further purification; ν_{max} (neat)/cm^{-1} 1471, 1255, 1110 and 701; δ_H (300 MHz; $CDCl_3$) 0.06 (s, 6H), 0.87–0.90 (m, 12H), 1.02 (s, 9H), 1.21–1.76 (m, 11H), 2.05–2.15 (m, 2H), 2.25–2.32 (m, 2H), 2.66 (s, 2H), 3.60–3.71 (m, 4H), 5.18 (dt, J = 7.1, 1.2 Hz, 1H), 5.57 (dt, J = 7.1, 15.1 Hz, 1H), 5.79 (d, J = 10.7 Hz, 1H), 6.23 (dd, J = 10.7, 15.1 Hz, 1H), 7.34–7.45 (m, 6H, aromatic) and 7.66–7.70 (m, 4H, aromatic); δ_C (75 MHz; $CDCl_3$) −5.2, 15.6, 15.9, 19.2, 19.6, 26.0, 26.8, 29.1, 30.4, 31.7, 36.9, 39.8, 50.4, 61.4, 63.7, 122.5, 126.2, 126.5, 127.6, 129.5, 132.8, 134.0, 134.4, 134.9 and 135.6.

(3*S*,6*E*,8*E*,11*E*)-14-*tert*-Butyldiphenylsilyloxy-3,9,11-trimethyltetradeca-6,8,11-trien-1-ol 17

A mixture of bis-silyl ether **16** (1.48 g, 2.38 mmol) in THF (9 cm^3), acetic acid (20 cm^3) and water (4 cm^3) was stirred for 40 h at rt. To the solution was added dropwise conc. aq. NaOH (13.9 g in 40 cm^3 of water) at 0 °C. The whole mixture was extracted four times with Et_2O. The combined extract was washed successively with saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography (hexane–EtOAc, 20 : 1 to 5 : 1) to give alcohol **17** as a colorless oil (722 mg, 60%) (Found: C, 78.31; H, 9.88. Calc. for $C_{33}H_{48}O_2Si$: C, 78.51; H, 9.58%); $[\alpha]_D^{26}$ −1.18 (*c* 1.50, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1471, 1255, 1110 and 701; δ_H (300 MHz; $CDCl_3$) 0.87 (d, J = 6.8 Hz, 3H), 1.04 (s, 9H), 1.17–1.66 (m, 11H), 2.05–2.15 (m, 2H), 2.29 (q, J = 7.1 Hz, 2H), 2.65 (s, 2H), 3.65 (t + overlapping signals, J = 7.0 Hz, 4H), 5.18 (dt, J = 7.3, 1.1 Hz, 1H), 5.55 (dt, J = 15.1, 7.3 Hz, 1H), 5.79 (d, J = 10.7 Hz, 1H), 6.23 (ddt, J = 10.7, 15.1, 1.5 Hz, 1H), 7.34–7.44 (m, 6H, aromatic) and 7.66–7.70 (m, 4H, aromatic); δ_C (75 MHz; $CDCl_3$) 15.6, 15.9, 19.1, 19.4, 26.8, 29.0, 30.3, 31.6, 36.8, 39.8, 50.3, 61.0, 63.7, 122.5, 126.2, 126.6, 127.5, 129.5, 132.6, 134.0, 134.5, 135.0 and 135.5.

(3*S*,6*E*,8*E*,11*E*)-14-*tert*-Butyldiphenylsilyloxy-3,9,11-trimethyltetradeca-6,8,11-trien-al 18

A solution of Swern reagent was prepared by dropwise addition of DMSO (2.00 cm^3, 28.2 mmol) to a stirred solution of oxalyl dichloride (7.34 cm^3; 2.0 M solution in CH_2Cl_2, 14.7 mmol) in CH_2Cl_2 (60 cm^3) at −78 °C under Ar and stirring was continued for 30 min. To the solution was added dropwise a solution of alcohol **17** (4.95 g, 9.78 mmol) in CH_2Cl_2 (20 cm^3) at −78 °C, and the mixture was stirred for 30 min. Triethylamine (5.40 cm^3, 38.7 mmol) was added to the mixture at −78 °C, and the temperature was allowed to rise gradually to rt over 2 h. The mixture was poured into water and extracted three times with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–EtOAc, 10 : 1) to give aldehyde **18** as a colorless oil (3.63 g, 82%) (Found: C, 78.71; H, 9.40. Calc. for $C_{33}H_{46}O_2Si$: C, 78.83; H, 9.22%); $[\alpha]_D^{25}$ −11.5 (*c* 1.60, $CHCl_3$); ν_{max} (neat)/cm^{-1} 2713, 1726, 1427 and 1110; δ_H (300 MHz; $CDCl_3$) 0.97 (d, J = 6.6 Hz, 3H), 1.04 (s, 9H), 1.27–1.69 (m, 9H), 2.11 (q, J = 6.8 Hz, 2H), 2.20–2.32 (m, 2H), 2.41 (ddd, J = 2.0, 3.8, 11.9 Hz, 2H), 2.66 (s, 2H), 3.65 (t, J = 6.9 Hz, 2H), 5.18 (d, J = 6.7 Hz, 1H), 5.54 (dt, J = 15.0, 6.8 Hz, 1H), 5.79 (d, J = 10.5 Hz, 1H), 6.24 (dd, J = 10.5, 15.0 Hz, 1H), 7.34–7.44 (m, 6H, aromatic), 7.66–7.70 (m, 4H, aromatic) and 9.75 (t, J = 2.3 Hz, 1H); δ_C (75 MHz; $CDCl_3$) 15.7, 16.0, 19.2, 26.8, 27.7, 30.3, 31.7, 36.6, 50.4, 51.0, 63.7, 122.6, 126.0, 127.1, 127.6, 129.5, 131.7, 134.0, 134.9, 135.6 and 202.9.

(3*S*,6*E*,8*E*,11*E*)-14-*tert*-Butyldiphenylsilyloxy-3,9,11-trimethyltetradeca-6,8,11-trienoic acid 19

To an ice-cooled solution of **18** (3.63 g, 7.22 mmol) in 2-methylbut-2-ene (40.0 cm^3, 376 mmol) and *tert*-butyl alcohol (55 cm^3) was added dropwise a solution of sodium chlorite (6.01 g, 665 mmol) and sodium dihydrogen phosphate dihydrate (7.83 g, 50.2 mmol) in water (65 cm^3). The mixture was stirred for 30 min and extracted three times with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–EtOAc, 2 : 1 to 1 : 1) to give acid **19** (3.74 g, 99%) as a colorless oil (Found: C, 76.15; H, 9.05. Calc. for $C_{33}H_{46}O_3Si$: C, 76.40; H, 8.94%); $[\alpha]_D^{25}$ −5.23 (*c* 1.03, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3089, 2857, 1709, 1427, 1110 and 823; δ_H (300 MHz; $CDCl_3$) 0.98 (d, J = 6.4 Hz, 3H), 1.05 (s, 9H), 1.26–1.34 (m, 1H), 1.47 (s, 3H), 1.62 (s, 3H), 1.96–2.40 (m, 8H), 2.65 (s, 2H), 3.65 (t, J = 6.9 Hz, 2H), 5.18 (t, J = 6.8 Hz, 1H), 5.55 (dt, J = 15.1, 6.9 Hz, 1H), 5.79 (d, J = 10.7 Hz, 1H), 6.24 (dd, J = 10.1, 15.1 Hz, 1H), 7.23–7.39 (m, 6H) and 7.66–7.69 (m, 4H); δ_C (75 MHz; $CDCl_3$) 15.7, 16.0, 19.2, 19.5, 26.8, 29.7, 30.3, 31.7, 36.4, 41.5, 50.4, 63.7, 122.6, 126.1, 127.0, 127.6, 129.5, 131.9, 134.0, 134.8, 135.0, 135.6 and 179.6.

(3*E*,6*E*,8*E*,12*S*)-13-Allyloxycarbonylamino-1-*tert*-butyldiphenylsilyloxy-4,6,12-trimethyltrideca-3,6,8-triene 20

A solution of acid **19** (3.73 g, 7.20 mmol), diphenylphosphoryl azide (1.87 cm^3, 10.1 mmol), and triethylamine (1.20 cm^3, 9.36 mmol) in benzene (60 cm^3) was refluxed for 3 h. After addition of allyl alcohol (2.55 cm^3, 39.6 mmol), the reaction mixture was refluxed again for another 24 h. The reaction was quenched by addition of water and the resulting mixture was extracted three times with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography (hexane–EtOAc, 30 : 1) to give carbamate **20** (2.81 g, 68%) as a colorless oil (Found: C, 75.20; H, 8.99; N, 2.53. Calc. for $C_{36}H_{51}NO_3$: C, 75.34; H, 8.96; N, 2.44%); $[\alpha]_D^{28}$ −1.63 (*c* 0.877, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3070, 2856, 1703, 1427, 1113 and 739; δ_H (75 MHz; $CDCl_3$) 0.90 (d, J = 6.4 Hz, 3H), 1.05 (s, 9H), 1.26–1.34 (m, 2H), 1.47 (s, 3H), 1.62 (s, 3H), 1.96–2.40 (m, 8H), 3.65 (t, J = 6.9 Hz, 2H), 4.55 (d, J = 5.6 Hz, 2H), 4.73 (br s, 1H), 5.18 (d, J = 6.8 Hz, 1H), 5.21 (dq, J = 10.4, 1.4 Hz, 1H), 5.30 (dq, J = 17.3, 1.4 Hz, 1H), 5.55 (dt, J = 15.1, 6.9 Hz, 1H), 5.79 (d, J = 10.1 Hz, 1H), 5.92 (ddt, J = 10.4, 17.3, 5.6 Hz, 1H), 6.23 (dd, J = 10.1, 15.1 Hz, 1H), 7.35–7.42 (m, 6H, aromatic) and 7.66–7.69 (m, 4H, aromatic); δ_C (75 MHz; $CDCl_3$) 15.6, 15.9, 17.3, 19.1, 26.8, 30.2, 31.6, 33.0, 33.9, 46.8, 50.3, 63.7, 65.4, 117.6, 122.5, 126.1, 126.9, 127.5, 129.5, 132.0, 133.0, 134.0, 134.8, 134.9, 135.5 and 156.4.

(3*E*,6*E*,8*E*,12*S*)-13-Allyloxycarbonylamino-4,6,12-trimethyltrideca-3,6,8-trien-1-ol 21

To a solution of silyl ether **20** (808 mg, 1.41 mol) in THF (15 cm^3) was added dropwise HF–pyridine (1.5 cm^3; ≈ 70% HF, 58 mmol) and the mixture was stirred for 6 h at rt before being carefully poured into saturated aq. $NaHCO_3$ and extracted twice with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–EtOAc, 5 : 1 to 2 : 1) to give alcohol **21** as a colorless oil (422 mg, 89%) (Found: C, 71.35; H, 10.08; N, 3.93. Calc. for $C_{20}H_{33}NO_3$: C, 71.60; H, 9.91; N, 4.18%); $[\alpha]_D^{29}$ −2.19 (c 0.42, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3344 (br), 3018, 2875, 1701, 1537, 1250 and 1047; δ_H (300 MHz; $CDCl_3$) 0.91 (d, J = 6.6 Hz, 3H), 1.15–1.51 (m, 3H), 1.57–1.68 (m, 9H), 2.02–2.19 (m, 2H), 2.32 (q, J = 6.8, 2H), 2.45 (s, 2H), 3.01 (quintet, J = 7.1 Hz, 1H), 3.63 (t, J = 6.3 Hz, 2H), 5.19 (d, J = 6.8 Hz, 1H), 5.21 (dq, J = 10.4, 1.4 Hz, 1H), 5.30 (dq, J = 17.3, 1.4 Hz, 1H), 5.57 (dt, J = 15.1, 6.9 Hz, 1H), 5.81 (d, J =

10.7 Hz, 1H), 5.93 (ddt, J = 10.4, 17.3, 5.6 Hz, 1H) and 6.24 (dd, J = 10.7, 15.1 Hz, 1H); δ_C (75 MHz; $CDCl_3$) 15.7, 15.9, 17.3, 30.1, 31.6, 33.0, 33.8, 46.8, 50.3, 62.3, 65.4, 117.5, 121.9, 126.2, 126.8, 132.2, 132.9, 134.3, 136.5 and 156.4.

(4*R*)-3-[(2*R*,3*S*,5*E*,8*E*,10*E*,14*S*)-15-Allyloxycarbonylamino-3-hydroxy-1,2,6,8,14-tetramethylpentadeca-5,8,10-trienoyl]-4-benzyloxazolidin-2-one 23

To a solution of alcohol **21** (1.58 g, 4.71 mmol) in CH_2Cl_2 (42 cm^3) was added Dess–Martin periodinane (2.82 g, 6.65 mmol). The mixture was stirred for 45 min at rt. The resulting aldehyde solution was kept at 0 °C until it was used for the next step.

To a solution of chiral oxazolidinone **22**[11] (1.57 g, 6.73 mmol) in CH_2Cl_2 (28 cm^3) were successively added dropwise di(*n*-butyl)boryl trifluoromethanesulfonate (7.65 cm^3; 1.0 M solution in CH_2Cl_2, 7.7 mmol) and triethylamine (1.19 cm^3, 8.54 mmol) at below −8 °C. To the resulting solution was added dropwise the above aldehyde solution at below −70 °C. The mixture was stirred for 50 min at −78 °C and then for 2 h at 0 °C. The reaction was quenched by addition of phosphate buffer (pH 7.4; 18.4 cm^3) and methanol (6.1 cm^3). To the mixture was added a 2 : 1 mixture of methanol–35% H_2O_2 (18.2 cm^3) at such a rate as to keep the internal temperature below 8 °C. After stirring for an additional 1 h, the mixture was evaporated *in vacuo*. The resulting slurry was extracted three times with Et_2O. The combined extract was washed successively with saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash chromatography (hexane–EtOAc, 2 : 1) to give alcohol **23** as a colorless oil (1.65 g, 62% from **21**) (Found: C, 69.64; H, 8.31; N, 4.97. Calc. for $C_{33}H_{46}N_2O_6$: C, 69.94; H, 8.18; N, 4.94%); $[\alpha]_D^{29}$ −42.7 (*c* 0.375, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3388 (br), 1782, 1722, 1242 and 704; δ_H (300 MHz; $CDCl_3$) 0.91 (d, J = 6.5 Hz, 3H), 1.28 (d, J = 6.8 Hz, 3H), 1.42–1.64 (m, 6H), 2.05–2.40 (m, 7H), 2.70 (s, 2H), 2.79 (dd, J = 9.5, 13.2 Hz, 1H), 2.97–3.15 (m, 2H), 3.25 (dd, J = 3.2, 13.2 Hz, 1H), 3.89 (dt, J = 3.2, 6.9 Hz, 1H), 4.00 (br s, 1H), 4.18–4.23 (m, 2H), 4.56 (br d, J = 5.6 Hz, 2H), 4.64–4.71 (m, 1H), 4.85 (br s, 1H), 5.18 (d, J = 6.8 Hz, 1H), 5.20 (dq, J = 10.4, 1.4 Hz, 1H), 5.29 (dq, J = 17.3, 1.4 Hz, 1H), 5.56 (dt, J = 15.1, 6.8 Hz, 1H), 5.80 (d, J = 10.7 Hz, 1H), 5.92 (ddt, J = 10.7, 17.3, 5.6 Hz, 1H), 6.23 (dd, J = 10.7, 15.1 Hz, 1H) and 7.20–7.34 (m, 5H, aromatic); δ_C (75 MHz; $CDCl_3$) 10.6, 15.8, 16.0, 17.3, 30.1, 32.6, 33.0, 33.9, 37.7, 41.5, 46.9, 50.4, 55.1, 65.4, 66.1, 71.5, 117.6, 121.6, 126.3, 126.9, 127.4, 129.0, 129.4, 132.2, 133.0, 134.5, 135.0, 136.5, 152.9, 156.4 and 177.3.

(4*R*)-3-[(2*R*,3*S*,5*E*,8*E*,10*E*,14*S*)-15-Allyloxycarbonylamino-3-(1-ethoxyethoxy)-2,6,8,14-tetramethylpentadeca-5,8,10-trienoyl]-4-benzyloxazolidin-2-one 24

To a solution of alcohol **23** (1.65 g, 2.91 mmol) in ethyl vinyl ether (EVE) (45 cm^3) and CH_2Cl_2 (25 cm^3) was added pyridinium toluene-*p*-sulfonate (PPTS, 160 mg, 6.37×10^{-1} mmol) at 0 °C. After being warmed to rt, the solution was stirred for 1.5 h. The reaction was quenched by addition of saturated aq. $NaHCO_3$ and the aqueous layer was extracted twice with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The reaction mixture was purified by flash chromatography (hexane–EtOAc, 10 : 1) to give the ether **24** as a colorless oil (1.77 g, 86%) (Found: C, 69.51; H, 8.70; N, 4.17. Calc. for $C_{37}H_{54}N_2O_7$: C, 69.56; H, 8.52; N, 4.39%); $[\alpha]_D^{29}$ −42.7 (*c* 0.375, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3388 (br), 1782, 1722, 1242 and 704; δ_H (300 MHz; $CDCl_3$) 0.91 (d, J = 6.8 Hz, 3H), 1.15–1.30 (m, 12H), 1.63 (s, 3H), 1.67 (s, 2H), 2.05–2.25 (m, 2H), 2.30–2.37 (m, 2H), 2.68 (s, 2H), 2.76 (ddd, J = 2.2, 9.9, 13.0 Hz, 1H), 2.90 (m, 2H), 3.29 (dq, J = 13.0, 3.6 Hz, 1H), 3.27–3.61 (m, 3H), 3.88–4.16 (m, 4H), 4.56 (br d, J = 5.6 Hz, 2H), 4.61 (br s, 1H), 4.73–4.77 (m, 1H), 5.18 (d, J = 6.8 Hz, 1H), 5.20 (dq, J = 10.4, 1.4 Hz, 1H), 5.29 (dq, J = 17.3, 1.4 Hz, 1H), 5.56 (dt, J = 15.1, 6.8 Hz, 1H), 5.80 (d, J = 10.7 Hz, 1H), 5.92 (ddt, J = 10.7, 17.3, 5.6 Hz, 1H), 6.23 (dd, J = 10.7, 15.1 Hz, 1H) and 7.20–7.34 (m, 5H, aromatic); δ_C (75 MHz; $CDCl_3$) 12.5, 12.7, 14.2, 15.2, 15.3, 15.4, 15.7, 17.3, 20.0, 20.5, 30.2, 31.3, 32.1, 33.1, 33.9, 37.8, 41.2, 46.9, 50.5, 55.7, 59.6, 60.4, 60.7, 65.4, 65.8, 66.0, 75.3, 98.6, 100.0, 117.6, 121.8, 122.2, 126.2, 126.3, 126.9, 127.3, 128.9, 129.4, 132.1, 133.0, 134.6, 134.7, 135.1, 135.3, 135.4, 152.7, 156.4, 175.1 and 175.4.

(2*S*,3*S*,5*E*,8*E*,10*E*,14*S*)-15-Allyloxycarbonylamino-3-(1-ethoxyethoxy)-2,6,8,14-tetramethylpentadeca-5,8,10-trien-1-ol 25

To an ice-cooled solution of amide **24** (335 mg, 5.24×10^{-1} mmol) in MeOH (0.46 cm^3) and THF (5.5 cm^3) was added dropwise a solution of lithium borohydride (2.80 cm^3; 2.0 M solution in THF, 5.6 mmol). After being stirred for 1 h, the reaction mixture was quenched by addtion of water. The solvent was removed *in vacuo*, and the resulting slurry was extracted three times with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*, and the residue was purified by flash chromatography (hexane–EtOAc, 3 : 1) to give alcohol **25** (90.8 mg, 37%) (R_f 0.34 [hexane–EtOAc 2 : 1]) and its diastereomer (90.3 mg, 37%) (R_f 0.23 [hexane–EtOAc 2 : 1]) as a colorless oil (Found: C, 69.43; H, 10.29; N, 3.22. Calc. for $C_{27}H_{47}NO_5$: C, 69.64; H, 10.17; N, 3.01%); $[\alpha]_D^{29}$ −2.2 (*c* 0.875, $CHCl_3$); δ_H (300 MHz; $CDCl_3$) (R_f 0.34) 0.82 (d, J = 7.1 Hz, 3H), 0.91 (d, J = 6.6 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H), 1.27 (d, J = 5.1 Hz, 3H), 1.31–1.66 (m, 8H), 1.83 (br s, 1H), 2.04–2.43 (m, 4H), 2.68 (m, 2H), 2.99–3.16 (m, 2H), 3.41–3.59 (m, 5H), 3.83 (dt, J = 6.9, 2.7 Hz, 1H), 4.56 (d, J = 5.6 Hz, 2H), 4.68 (q, J = 5.1 Hz, 1H), 4.76 (br s, 1H), 5.18 (d, J = 6.8 Hz, 1H), 5.20 (dq, J = 10.4, 1.4 Hz, 1H), 5.29 (dq, J = 17.3, 1.4 Hz, 1H), 5.56 (dt, J = 15.1, 6.8 Hz, 1H), 5.80 (d, J = 10.7 Hz, 1H), 5.93 (ddt, J = 10.7, 17.3, 5.6 Hz, 1H) and 6.24 (dd, J = 10.7, 15.1 Hz, 1H) and (R_f 0.23) 0.89 (d, J = 7.3 Hz, 3H), 0.91 (d, J = 7.3 Hz, 3H), 1.19 (t, J = 7.3 Hz, 3H), 1.32 (d, J = 5.4 Hz, 3H), 1.40–1.68 (m, 8H), 1.86–2.38 (m, 4H), 2.68 (s, 2H), 2.99–3.13 (m, 2H), 3.48–3.73 (m, 6H), 4.56 (d, J = 5.6 Hz, 2H), 4.72–4.81 (m, 2H), 5.19–5.33 (m, 3H), 5.56 (dt, J = 15.1, 6.8 Hz, 1H), 5.79 (d, J = 10.7 Hz, 1H), 5.93 (ddt, J = 10.7, 17.3, 5.6 Hz, 1H) and 6.24 (dd, J = 10.7, 15.1 Hz, 1H); δ_C (75 MHz; $CDCl_3$) (R_f 0.34) 9.9, 15.1, 15.8, 16.1, 17.3, 20.2, 30.1, 30.8, 33.1, 33.9, 46.8, 50.4, 61.5, 65.1, 65.4, 76.3, 100.1, 117.5, 122.3, 126.3, 126.8, 133.0, 134.4, 134.8 and 156.4; (R_f 0.23) 11.2, 15.2, 15.8, 16.0, 17.3, 20.3, 30.1, 30.2, 33.0, 33.9, 37.5, 46.8, 50.4, 60.4, 65.4, 65.6, 78.2, 99.5, 117.5, 122.6, 126.2, 126.9, 132.2, 133.0, 134.5, 134.8 and 156.4.

(2*R*,3*S*,5*E*,8*E*,10*E*,14*S*)-15-Allyloxycarbonylamino-3-(1-ethoxyethoxy)-2,6,8,14-tetramethylpentadeca-5,8,10-trienal

A solution of alcohol **25** (103 mg, 2.21×10^{-1} mmol) in CH_2Cl_2 (2.5 cm^3) was cooled to 0 °C and Dess–Martin periodinane (154 mg, 3.63×10^{-1} mmol) was added. The reaction mixture was stirred for 30 min at rt. The reaction was quenched by addition of 10% aq. $Na_2S_2O_3$. The mixture was then extracted twice with Et_2O. The combined extract was washed successively with saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (hexane–EtOAc, 3 : 1) to give title aldehyde as a colorless oil (61.7 mg, 60%); ν_{max} (neat)/cm^{-1} 3348 (br), 2721, 1728, 1703, 1533 and 1246; δ_H (300 MHz; $CDCl_3$) 0.91 (d, J = 6.8 Hz, 3H), 1.12 (d, J = 7.1 Hz, 3H), 1.18 (d, J = 6.8 Hz, 3H), 1.27 (d, J = 5.4 Hz, 3H), 1.40–1.67 (m, 8H), 2.04–2.51 (m, 4H), 2.74 (s, 2H), 2.97–3.17 (m, 2H), 3.36–3.65 (m, 3H), 4.08–4.13 (m, 1H), 4.55 (br d, J = 5.4 Hz, 2H), 4.75 (dq, J = 18.2, 5.4 Hz, 1H), 4.88 (br s, 1H), 5.15 (t, J = 6.8 Hz, 1H), 5.20 (dq, J = 10.4, 1.4 Hz, 1H), 5.30 (dq, J = 17.3, 1.4 Hz, 1H), 5.56 (dt, J = 15.1, 6.8 Hz, 1H), 5.79 (d, J = 10.7 Hz, 1H), 5.92 (ddt, J = 10.7, 17.3, 5.6 Hz, 1H), 6.23 (dd, J = 10.7, 15.1 Hz, 1H) and 9.75 (s, 1H); δ_C (75 MHz; $CDCl_3$) 7.7, 15.1, 15.2, 15.8, 16.0, 17.2, 20.1, 20.2,

30.1, 30.6, 31.5, 33.0, 33.8, 46.8, 49.5, 49.7, 59.7, 60.1, 65.3, 75.0, 75.5, 98.8, 99.7, 117.4, 121.2, 121.4, 126.3, 126.7, 132.3, 133.0, 134.1, 136.3, 156.3, 204.4 and 204.6.

2-Trimethylsilylethyl (2*E*,4*E*,6*S*,7*S*,9*E*,12*E*,14*E*,18*S*)-19-allyloxycarbonylamino-7-(1-ethoxyethoxy)-6,10,12,18-tetramethylnonadeca-2,4,9,12,14-pentaenoate 27

To a solution of Wittig–Horner reagent **26** (107 mg, 3.32×10^{-1} mmol) in THF (1.5 cm^3) was added dropwise lithium hexamethyldisilazide (0.31 cm^3; 1.0 M in THF, 3.1×10^{-1} mmol) at −78 °C. After stirring of this mixture for 10 min, a solution of the aldehyde (61 mg, 1.3×10^{-1} mmol) in THF (2 cm^3) was slowly added. The resulting mixture was warmed to −25 °C, and was stirred for an additional 40 min. Water (2 cm^3) was added to the reaction mixture to quench the reaction. The solvent was then removed *in vacuo*, and the aqueous layer was extracted three times with Et_2O. The combined extract was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash chromatography (hexane–EtOAc, 2 : 1) to give ester **27** (80 mg, 96%) as a colorless oil (Found: C, 68.30; H, 9.94; N, 2.12. Calc. for $C_{36}H_{61}NO_6Si$: C, 68.42; H, 9.73; N, 2.22%); $[\alpha]_D^{28}$ −24.1 (*c* 0.87, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3354 (br), 1730, 1712, 1250, 860 and 837; δ_H (300 MHz; $CDCl_3$) 0.05 (s, 9 H), 0.91 (d, *J* = 6.8 Hz, 3H), 1.02 (t, *J* = 8.6 Hz, 2H), 1.09 (d, *J* = 6.8 Hz, 3H), 1.15–1.26 (m, 8H), 1.28 (d, *J* = 5.1 Hz, 3H), 1.50 (s, 3H), 1.64 (s, 3H), 2.09–2.23 (m, 2H), 2.68 (s, 2H), 2.97–3.18 (m, 2H), 3.43–3.65 (q and m, *J* = 7.1 Hz, 4H), 4.24 (t, *J* = 8.6 Hz, 2H), 4.56 (d, *J* = 5.6 Hz, 2H), 4.75 (q, *J* = 5.1 Hz, 2H), 5.19 (d, *J* = 6.8 Hz, 1H), 5.21 (dq, *J* = 10.4, 1.4 Hz, 1H), 5.30 (dq, *J* = 17.3, 1.4 Hz, 1H), 5.56 (dt, *J* = 15.1, 6.8 Hz, 1H), 5.78 (d, *J* = 10.7 Hz, 1H), 5.78 (d, *J* = 14.7 Hz, 1H), 5.92 (ddt, *J* = 10.7, 17.3, 5.6 Hz, 1H), 6.15–6.18 (m, 2H), 6.24 (dd, *J* = 10.7, 15.1 Hz, 1H) and 7.24 (ddt, *J* = 7.8, 14.7, 2.0 Hz, 1H); δ_C (75 MHz; $CDCl_3$) −1.5, 14.1, 14.4, 15.0, 15.3, 15.8, 16.0, 17.3, 20.2, 20.4, 30.1, 30.3, 31.0, 33.1, 33.4, 40.1, 40.8, 46.8, 50.4, 59.7, 59.8, 60.3, 62.3, 65.3, 79.1, 80.1, 98.8, 99.8, 119.8, 119.9, 121.9, 122.3, 126.2, 126.3, 126.8, 127.9, 128.0, 132.2, 133.0, 134.4, 134.5, 134.9, 135.1, 144.7, 144.8, 146.3, 146.6, 156.3 and 167.3.

(6*S*,7*S*,18*S*)-20-Aza-6,10,12,18-tetramethyl-7-(1-ethoxyethoxy)cycloicosa-2,4,9,12,14-pentaenone (*O*-EE-aglycone) 28

To a solution of ester **27** (140.7 mg, 2.23×10^{-1} mmol) and 1,3-dimethylbarbituric acid (228 mg, 1.46 mmol) in THF (15 cm^3) was added tetrakis(triphenylphosphine)palladium (43.9 mg, 3.79×10^{-2} mmol, 17 mol%), and the resulting mixture was stirred at rt for 27 h. The mixture was then poured into saturated aq. $NaHCO_3$ and extracted four times with Et_2O. The combined extract was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by chromatography ($CHCl_3$–MeOH, 20 : 1 to 2 : 1) to give the corresponding free amino ester as a colorless oil (79.5 mg, 65%) {LRFABMS (NBA matrix) *m*/*z*, 548.3 $[(M + H)^+$; Calc. for $C_{32}H_{58}NO_4Si$: *m*/*z* 548.1]}; ν_{max} (neat)/cm^{-1} 2958, 1701, 1215 and 758; δ_H (300 MHz; $CDCl_3$) 0.05 (s, 9 H), 0.92 (d, *J* = 6.3 Hz, 3H), 0.99–1.10 (m, 8H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.28 (d, *J* = 5.1 Hz, 3H), 1.50 (s, 3H), 1.64 (s, 3H), 1.90 (br s, 2H), 2.10–2.25 (m, 3H), 2.48–2.74 (m, 4H), 3.46–3.64 (m, 3H), 4.23 (t, *J* = 8.5 Hz, 2H), 4.73 (dq, *J* = 5.3, 15.1 Hz, 1H), 5.58 (dt, *J* = 6.8, 15.1 Hz, 1H), 5.78 (d, *J* = 10.7 Hz, 1H), 5.78 (d, *J* = 10.7 Hz, 1H), 5.79 (d, *J* = 14.7 Hz, 1H), 6.12–6.18 (m, 2H), 6.25 (dd, *J* = 10.7, 15.1 Hz, 1H) and 7.24 (ddt, *J* = 14.7, 7.8, 2.0 Hz, 1H).

To an ice-cooled solution of the amino ester (79.5 mg, 1.45×10^{-1} mmol) in THF (10 cm^3) was added TBAF (0.40 cm^3 of 1.0 M THF solution, 4.0×10^{-1} mmol). After being stirred at rt for 24 h, the mixture was poured into water and extracted six times with $CHCl_3$. The combined extract was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was used for the next step without further purification.

The residue was dissolved in dry DMF (80 cm^3) and cooled in an ice–water-bath. To the ice-cooled solution were added dropwise diethyl cyanophosphonate (140 mm^3; 93% purity 8.59×10^{-1} mmol) and triethylamine (150 mm^3, 1.08 mmol). The reaction mixture was stirred for an additional 3 h at 0 °C. The mixture was then poured into water and extracted three times with Et_2O. The combined extract was washed successively with water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by PLC (hexane–EtOAc, 2 : 1) to give lactam **28** as a colorless solid (17.6 mg, 28%) {HRFABMS (NBA matrix) *m*/*z* 430.3366 $[(M + H)^+$; Calc. for $C_{27}H_{44}NO_3$: *m*/*z*, 430.3321]}; $[\alpha]_D^{26}$ + 65 (*c* 0.563, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2978, 2929, 1658, 1631, 1604, 1379, 1120, 1095, 1030 and 997; δ_H (300 MHz; $CDCl_3$) 0.95 (d, *J* = 7.1 Hz, 3H), 1.07–1.14 (m, 3H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.33 (d, *J* = 5.1 Hz, 3H), 1.50 (s, 3H), 1.71 (s, 3H), 2.07–2.42 (m, 6H), 2.71–2.92 (m, 2H), 3.14–3.32 (m, 2H), 3.40–3.72 (m, 4H), 4.72 (q, *J* = 5.4 Hz, 1H), 4.83 (q, *J* = 5.4 Hz, 1H), 5.14 (dt, *J* = 8.6, 17.3 Hz, 1H), 5.53–5.84 (m, 5H), 6.34 (dd, *J* = 10.7, 15.1 Hz, 1H) and 6.91 (dd, *J* = 11.2, 14.9 Hz, 1H).

(6*S*,7*S*,18*S*)-20-Aza-6,10,12,18-tetramethyl-7-(trimethylsilyloxy)cycloicosa-2,4,9,12,14-pentaenone (*O*-TMS-aglycone) 2

To a solution of compound **28** (21.1 mg, 4.91×10^{-2} mmol) in MeOH (10 cm^3) was added PPTS (8.0 mg, 3.2×10^{-2} mmol) at rt. The reaction mixture was stirred for 5 h. The mixture was treated with Et_3N (0.30 cm^3, 2.15 mmol) and concentrated *in vacuo*. To an ice-cooled mixture of the residue in CH_2Cl_2 (7 cm^3) containing DMAP (7.5 mg, 3.0×10^{-2} mmol) and Et_3N (1.00 cm^3, 7.17 mmol) was added dropwise TMSCl (0.30 cm^3, 2.36 mmol), and the reaction mixture was stirred for 45 min. The reaction was quenched by addition of ice–water and the resulting mixture was extracted twice with Et_2O. The combined extract was washed successively with saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography (hexane–EtOAc, 7 : 1 to 4 : 1) to afford title compound **2** (19.5 mg, 92%);

Methyl 3-*O*-acetyl-2,4,6-trideoxy-4-[fluoren-9-ylmethoxycarbonyl(methyl)amino]-α-D-*ribo*-hexopyranoside 30

To an ice-cooled solution of compound **29**[9] (128.5 mg, 3.23×10^{-1} mmol) and DMAP (65 mg, 5.3×10^{-1} mmol) in pyridine (4.0 cm^3) was added Ac_2O (0.50 cm^3, 5.30 mmol) and the mixture was stirred at rt for 1 h. The reaction was quenched by addition of ice–water at 0 °C and the resulting mixture was stirred for several minutes at rt, and extracted twice with Et_2O. The combined extract was washed successively with water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography (hexane–EtOAc, 5 : 1 to 2 : 1) to afford acetate **30** as a colorless, amorphous solid (126.3 mg, 89%) {HRFABMS (NBA matrix) *m*/*z* 440.2112 $[(M + H)^+$; Calc. for $C_{25}H_{30}NO_6$: *m*/*z*, 440.2073]}; mp 95.5–98.0 °C; $[\alpha]_D^{26}$ + 162 (*c* 0.585, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 1736, 1693, 1321, 1252, 1128 and 1066; δ_H (500 MHz; $CDCl_3$) 1.02 (d, *J* = 6.2 Hz, 3H, H-6), 1.17 (d, *J* = 6.3 Hz, 3H, H-6), 1.57 (ddd, *J* = 3.9, 3.9, 15.2 Hz, 1H, H-2_{ax}), 1.96 (ddd, *J* = 4.1, 4.1, 15.3 Hz, 1H, H-2_{ax}), 2.00 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.07 (dd, *J* = 2.2, 15.2 Hz, 1H, H-2_{eq}), 2.19 (dd, *J* = 2.3, 15.3 Hz, 1H, H-2_{eq}), 2.78 (s, 3H, NMe), 2.80 (s, 3H, NMe), 3.30 (s, 3H, OMe), 3.34 (s, 3H, OMe), 3.39 (dd, *J* = 2.7, 10.1 Hz, 1H, H-4), 4.03 (br s, 1H, H-4), 4.17–4.24 (m, 1H, H-5), 4.21–4.27 (m, 2H, Fmoc CH_2), 4.33 (br s, 1H, H-5), 4.47 (d, *J* = 6.7 Hz, 2H, Fmoc CH_2), 4.48–4.53 (m, 1H, Fmoc C*H*), 4.59 (d, *J* = 4.2 Hz, 1H, H-1), 4.61–4.67 (m, 2H, H-3 and Fmoc C*H*), 4.67 (d, *J* = 4.2 Hz, 1H, H-1), 5.08 (ddd, *J* = 2.2, 2.3, 4.1 Hz, 1H, H-3), 7.28–7.35, (m, 4H, Fmoc Ar), 7.36–7.42 (m, 4H, Fmoc Ar), 7.51–7.60 (m, 4H, Fmoc Ar) and 7.73–7.77 (m, 4H, Fmoc Ar); δ_C (126 MHz; $CDCl_3$) 18.2, 18.3, 21.4, 21.5, 31.1, 33.3, 33.5, 47.26, 47.32, 55.2, 57.7, 60.4, 60.6, 66.9, 67.3, 70.3,

97.1, 97.3, 119.8, 119.9, 124.5, 124.6, 124.8, 124.9, 126.96, 126.98, 127.0, 127.1, 127.6, 141.25, 141.27, 141.3, 143.8, 143.9, 156.1, 156.6, 170.16 and 170.25.

1,3-Di-*O*-acetyl-2,4,6-trideoxy-4-[fluoren-9-ylmethoxycarbonyl-(methyl)amino]-α-D-*ribo*-hexopyranose 31

A solution of glycoside **30** (122.5 mg, 2.79×10^{-1} mmol) in AcOH (8.2 cm^3) and water (1.7 cm^3) was heated at around 95 °C for 2.5 h. The reaction mixture was evaporated *in vacuo* with an aid of azeotropic distillation with toluene. To a solution of the obtained crude hemiacetal and DMAP (3.2 mg, 2.6×10^{-2} mmol) in pyridine (2.0 cm^3) was added Ac_2O (0.25 mm^3, 2.65 mmol) and the mixture was stirred at rt for 1 h. The reaction was quenched by addition of ice–water at 0 °C and the resulting mixture was stirred for several minutes at rt, and extracted twice with Et_2O. The combined extract was washed successively with water, saturated aq. $NaHCO_3$ and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography (hexane–EtOAc, 5 : 1 to 2 : 1) to afford diacetate **31** as a colorless powder (125.9 mg, 97%) {HRFABMS (NBA matrix) *m*/*z* 468.2026 $[(M + H)^+$; Calc. for $C_{26}H_{30}NO_7$: *m*/*z*, 468.2022]}; mp 50.0–55.0 °C; $[\alpha]_D^{26}$ +79 (*c* 0.530, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 1743, 1697, 1317, 1240 and 1066; δ_H (500 MHz; $CDCl_3$) 0.96 (d, *J* = 6.2 Hz, 3H, H-6), 1.06 (br d, *J* = 5.2 Hz, 3H, H-6), 1.16 (d, *J* = 6.2 Hz, 3H, H-6), 1.20 (d, *J* = 6.1 Hz, 3H, H-6), 1.55 (ddd, *J* = 3.0, 10.6, 13.8 Hz, 1H, H-2_{ax}), 1.55–1.61 (m, 1H, H-2), 1.91–1.98 (m, 1H, H-2), 1.93–1.98 (m, 1H, H-2), 2.01 (s, 3H, Ac), 2.04 (s, 6H, Ac), 2.076 (s, 3H, Ac), 2.078 (s, 3H, Ac), 2.09 (s, 3H, Ac), 2.10 (s, 3H, Ac), 2.11 (s, 3H, Ac), 2.03–2.12 (m, 2H, H-2 × 2), 2.07–2.13 (m, 1H, H-2), 2.22–2.27 (m, 1H, H-2), 2.73 (s, 3H, NMe × 2), 2.76 (s, 3H, NMe), 2.78 (s, 3H, NMe), 3.28 (dd, *J* = 2.5, 10.3 Hz, 1H, H-4), 3.35 (br d, *J* = 8.8 Hz, 1H, H-4), 4.01 (br s, 1H, H-4), 4.12 (br s, 2H, H-4 and H-5), 4.21–4.28 (m, 3H, Fmoc CH × 2 and H-5), 4.21–4.30 (m, 3H, Fmoc C*H*H × 2 and H-5), 4.40–4.47 (m, 1H, H-5), 4.46–4.52 (m, 4H, Fmoc CH × 2 and Fmoc C*H*H × 2), 4.52–4.59 (m, 1H, Fmoc C*H*H), 4.54–4.60 (m, 1H, Fmoc C*H*H), 4.55–4.60 (m, 1H, H-3), 4.65 (dd, *J* = 5.1, 10.7 Hz, 1H, Fmoc C*H*H), 4.70 (dd, *J* = 4.7, 10.7 Hz, 1H, Fmoc C*H*H), 4.82 (br s, 1H, H-3), 5.14 (br q, *J* = 2.2 Hz, 1H, H-3), 5.34 (br q, *J* = 2.8 Hz, 1H, H-3), 5.82 (br d, *J* = 10.0 Hz, 1H, H-1), 5.94 (dd, *J* = 2.1, 10.2 Hz, 1H, H-1), 6.00 (d, *J* = 4.0 Hz, 1H, H-1), 6.10 (d, *J* = 4.0 Hz, 1H, H-1), 7.29–7.36 (m, 8H, Fmoc Ar), 7.37–7.43 (m, 8H, Fmoc Ar), 7.51–7.59 (m, 8H, Fmoc Ar) and 7.74–7.79 (m, 8H, Fmoc Ar); δ_C (126 MHz; $CDCl_3$) 18.2, 18.4, 18.5, 21.02, 21.03, 21.06, 21.1, 21.2, 21.3, 30.8, 30.9, 32.4, 32.7, 34.9, 35.1, 47.26, 47.33, 47.4, 57.3, 57.7, 63.1, 63.3, 66.8, 67.1, 67.4, 68.6, 68.7, 69.8, 70.9, 71.1, 90.0, 90.2, 90.3, 90.4, 119.88, 119.90, 119.93, 119.95, 120.0, 124.36, 124.42, 124.45, 124.52, 124.81, 124.83, 127.00, 127.02, 127.08, 127.10, 127.2, 127.5, 127.65, 127.67, 127.73, 141.3, 141.4, 143.78, 143.81, 143.88, 143.90, 155.9, 156.0, 156.6, 169.17, 169.19, 169.3, 169.4, 169.56, 169.61 and 169.7.

Vicenistatin [(6*S*,7*S*,18*S*)-20-aza-6,10,12,18-tetramethyl-7-*O*-(2′,4′,6′-trideoxy-4′-methylamino-β-D-*ribo*-hexopyranosylcycloicosa-2,4,9,12,14-pentaenone] 1

To a suspension of $AgClO_4$ (7.0 mg, 3.4×10^{-2} mmol) in dry CH_2Cl_2 (5 cm^3) was added dropwise $SnCl_4$ (35 mm^3; 1 M in CH_2Cl_2, 3.5×10^{-2} mmol) at rt. The mixture was shielded from light and stirred for 1 h. To the ice-cooled mixture was added dropwise a solution of **31** (46.4 mg, 9.92×10^{-2} mmol) and **2** (19.5 mg, 4.53×10^{-2} mmol) in dry CH_2Cl_2 (2.4 cm^3), and the whole was stirred for 1 h. The mixture was treated with saturated aq. $NaHCO_3$ and extracted twice with Et_2O. The combined extract was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by PLC (hexane–EtOAc, 1 : 1) to afford 3′-*O*-acetyl-4′-*N*-Fmoc-vicenistatin (20.6 mg, 59%; mixture of α- and β-anomer), which was used for the next step without further purification.

To a solution of 3′-*O*-acetyl-4′-*N*-Fmoc-vicenistatin (12.3 mg, 1.60×10^{-2} mmol) in EtOAc (5 cm^3) was added DBU (20 mm^3, 1.3×10^{-1} mmol), and the mixture was stirred for 0.5 h at rt. The mixture was diluted with EtOAc and washed with saturated aq. $NaHCO_3$. The aqueous washings were extracted twice with EtOAc. The combined extract was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by PLC (benzene–acetone, 25 : 4) to afford 3′-*O*-acetyl-vicenistatin **32** (4.0 mg, 46%) and its α-anomer (4.0 mg, 46%); δ_H (500 MHz; $CDCl_3$) 0.95 (d, *J* = 6.9 Hz, 3H, H-23), 1.05 (d, *J* = 6.6 Hz, 3H, H-20), 1.32 (d, *J* = 6.2 Hz, 3H, H-6′), 1.41–1.47 (m, 2H, H-17), 1.54 (s, 3H, H-21), 1.65–1.75 (m, 1H, H-18), 1.74 (ddd, *J* = 2.9, 9.9, 14.2 Hz, 1H, H-2′), 1.77 (s, 3H, H-22), 2.01–2.10 (m, 1H, H-16), 2.12 (s, 3H, Ac), 2.14 (ddd, *J* = 2.1, 3.3, 14.2 Hz, 1H, H-2′), 2.21–2.28 (m, 2H, H-8 and H-16), 2.28 (dd, *J* = 3.0, 9.7 Hz, 1H, H-4′), 2.32–2.38 (m, 1H, H-6), 2.39 (s, 3H, NMe), 2.58 (d, *J* = 14.7 Hz, 1H, H-11), 2.66 (d, *J* = 14.7 Hz, 1H, H-11), 2.60–2.70 (m, 1H, H-8), 3.10 (ddd, *J* = 4.2, 8.3, 13.6 Hz, 1H, H-19), 3.26 (ddd, *J* = 1.6, 7.8, 9.3 Hz, 1H, H-7), 3.39 (ddd, *J* = 7.6, 9.8, 13.6 Hz, 1H, H-19), 3.65 (dq, *J* = 6.2, 9.7 Hz, 1H, H-5′), 4.74 (dd, *J* = 1.8, 9.8 Hz, 1H, H-1′), 5.09 (dd, *J* = 7.1, 7.1 Hz, 1H, H-9), 5.42 (ddd, *J* = 3.0, 3.0, 3.0 Hz, 1H, H-3′), 5.56 (ddd, *J* = 7.3, 7.3, 14.7 Hz, 1H, H-15), 5.62 (dd, *J* = 4.3, 7.1 Hz, 1H, NH-19), 5.69 (d, *J* = 15.2 Hz, 1H, H-2), 5.74 (d, *J* = 11.0 Hz, 1H, H-13), 5.75 (dd, *J* = 9.5, 15.2 Hz, 1H, H-5), 6.05 (dd, *J* = 10.9, 15.2 Hz, 1H, H-4), 6.33 (dd, *J* = 11.0, 15.1 Hz, 1H, H-14) and 6.95 (dd, *J* = 10.9, 15.1 Hz, 1H, H-3); δ_C (126 MHz; $CDCl_3$) 17.16, 17.19, 18.4, 18.7, 19.1, 21.1, 28.5, 33.3, 33.6, 34.0, 35.2, 36.2, 43.7, 45.0, 49.3, 62.8, 67.5, 70.9, 85.4, 99.7, 121.9, 123.8, 126.2, 128.0, 128.3, 132.5, 134.3, 134.7, 139.4, 142.5, 166.0 and 170.3.

To a solution of acetate **32** (4.3 mg, 7.9×10^{-3} mmol) in MeOH (5 cm^3) was added 5.0 M KOH (3.0 cm^3, 15 mmol) and the mixture was stirred at rt for 3 days. The reaction mixture was evaporated, and the residue was dissolved in a minimum amount of water and extracted three times with EtOAc. The combined extract was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by PLC ($CHCl_3$–MeOH, 3 : 1) to afford vicenistatin **1** (3.3 mg, 83%); {HRFABMS (NBA matrix) *m*/*z* 501.3698 $[(M + H)^+$; Calc. for $C_{30}H_{49}N_2O_4$: *m*/*z*, 501.3692]}; δ_H (500 MHz; pyridine-d_5) 0.84 (d, *J* = 6.9 Hz, 3H, H-23), 1.08 (d, *J* = 6.6 Hz, 3H, H-20), 1.42–1.50 (m, 1H, H-17), 1.51–1.63 (m, 1H, H-17), 1.52 (d, *J* = 6.2 Hz, 3H, H-6′), 1.70 (s, 3H, H-21), 1.80–1.88 (m, 1H, H-18), 1.91 (ddd, *J* = 3.0, 10.1, 13.1 Hz, 1H, H-2′$_{ax}$), 1.95 (s, 3H, H-22), 2.02–2.10 (m, 1H, H-16), 2.24 (dd, *J* = 2.9, 9.6 Hz, 1H, H-4′), 2.27 (ddd, *J* = 8.4, 8.4, 13.9 Hz, 1H, H-8), 2.33–2.43 (m, 1H, H-16), 2.37–2.45 (m, 1H, H-6), 2.41 (s, 3H, NMe), 2.38–2.48 (m, 1H, H-2′$_{eq}$), 2.62 (d, *J* = 15.1 Hz, 1H, H-11), 2.74 (d, *J* = 15.1 Hz, 1H, H-11), 3.03 (ddd, *J* = 2.8, 4.7, 13.4 Hz, 1H, H-19), 3.09 (dd, *J* = 8.3, 13.8 Hz, 1H, H-8), 3.37 (dd, *J* = 8.8, 8.8 Hz, 1H, H-7), 4.01 (dq, *J* 6.2, 9.7 Hz, 1H, H-5′), 3.98–4.07 (m, 1H, H-19), 4.39 (ddd, *J* = 2.9, 2.9, 2.9 Hz, 1H, H-3′), 5.20 (dd, *J* = 7.5, 7.5 Hz, 1H, H-9), 5.30 (dd, *J* = 1.7, 9.6 Hz, 1H, H-1′), 5.69 (ddd, *J* = 5.2, 9.3, 14.7 Hz, 1H, H-15), 5.86 (dd, *J* = 9.6, 15.1 Hz, 1H, H-5), 5.96 (d, *J* = 11.0 Hz, 1H, H-13), 6.21 (dd, *J* = 11.3, 15.2 Hz, 1H, H-4), 6.26 (d, *J* = 15.0 Hz, 1H, H-2), 6.80 (dd, *J* = 11.1, 14.9 Hz, 1H, H-14), 7.60 (dd, *J* = 11.2, 15.0 Hz, 1H, H-3), 8.49 (dd, *J* = 2.1, 9.2 Hz, 1H, NH); δ_C (126 MHz; pyridine-d_5) 17.3, 17.7, 17.9, 18.7, 19.5, 27.7, 32.7, 33.5, 34.0, 36.6, 39.4, 43.1, 46.3, 49.3, 63.2, 65.2, 70.5, 86.0, 100.8, 122.0, 124.6, 128.0, 128.4, 128.4, 132.6, 134.0, 135.1, 140.3, 143.3 and 166.3.

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