Formal Total Synthesis of Stevastelins B and B3

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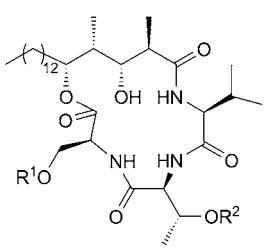
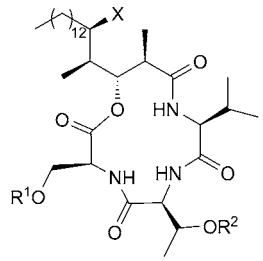
The formal total synthesis of stevastelins B and B3 (**2** and **4**, resp.) have been accomplished employing a highly enantiomerically controlled *Lewis* acid catalyzed non-aldol approach to obtain the *syn* aldol product and temperature controlled hydroboration oxidation reaction to construct four consecutive stereogenic centers. The other key reactions include *Sharpless* asymmetric epoxidation, macrolactonization, and macrolactamization towards building the core skeleton **2** and **4**.

Introduction. – In recent years, several new immunosuppressive agents have entered clinical trials, while cyclosporine A, calcinuerin, and FK506 have already been clinically used in organ transplantations. In 1994, the stevastelins A, B, A3, B3 and C3 (**1**–**5**, resp.) were isolated from a culture broth of penicillium sp. NK374186 [1] (*Fig.*). It has been reported that stevastelins show potent immunosuppressive activities by blocking human T-cell activation without affecting the phosphatase activity of calcineurin [2] and inhibiting dual specificity phosphatase, VHR [3]. With such a novel mode of action, stevastelins represent a new class of natural cyclic depsipeptides which differ from that of well-known immunosuppressant FK506 [4], cyclosporine A [5], and sanglifehrin A [6].

The structural study by spectroscopy, degradation, and synthetic considerations revealed that stevastelin B (**2**) consists of (2*S*,3*S*,4*S*,5*R*)-3,5-dihydroxy-2,4-dimethyloctadecanoic acid, *O*-acetyl-L-serine, L-threonine, and L-valine, and possesses a 15-membered ring structure [6]. Based on spectroscopic analyses of other stevastelins, it has been proposed that stevastelin B3 (**4**) is an isomer of stevastelin B (**2**) with a 13-



Stevastelin A (**1**) $R^1 = SO_3H$, R^2 = Ac
Stevastelin B (**2**) R^1 = H, R^2 = Ac



Stevastelin A3 (**3**) R^1 = Ac, $R^2 = SO_3H$, X = OH
Stevastelin B3 (**4**) R^1 = Ac, R^2 = H, X = OH
Stevastelin C3 (**5**) R^1 = H, R^2 = H, X = H

Figure. *Structures of stevastelins A, B, A3, B3, and C3* (**1**–**5**, resp.)

membered ring structure. The pronounced biological activities of stevastelins and their unique structures have attracted the attention of synthetic organic chemists, as evidenced by several contributions on the total synthesis of stevastelins B [7] and B3 [8] (**2** and **4**, resp.), along with other synthetic approaches [2][8c]. In continuation of our efforts on total synthesis of biologically active natural products [9], we herein describe our efforts for a formal total synthesis of **2** and **4** by employing a non-aldol approach for an aldol product to synthesize the key lipid fragment for the target synthesis.

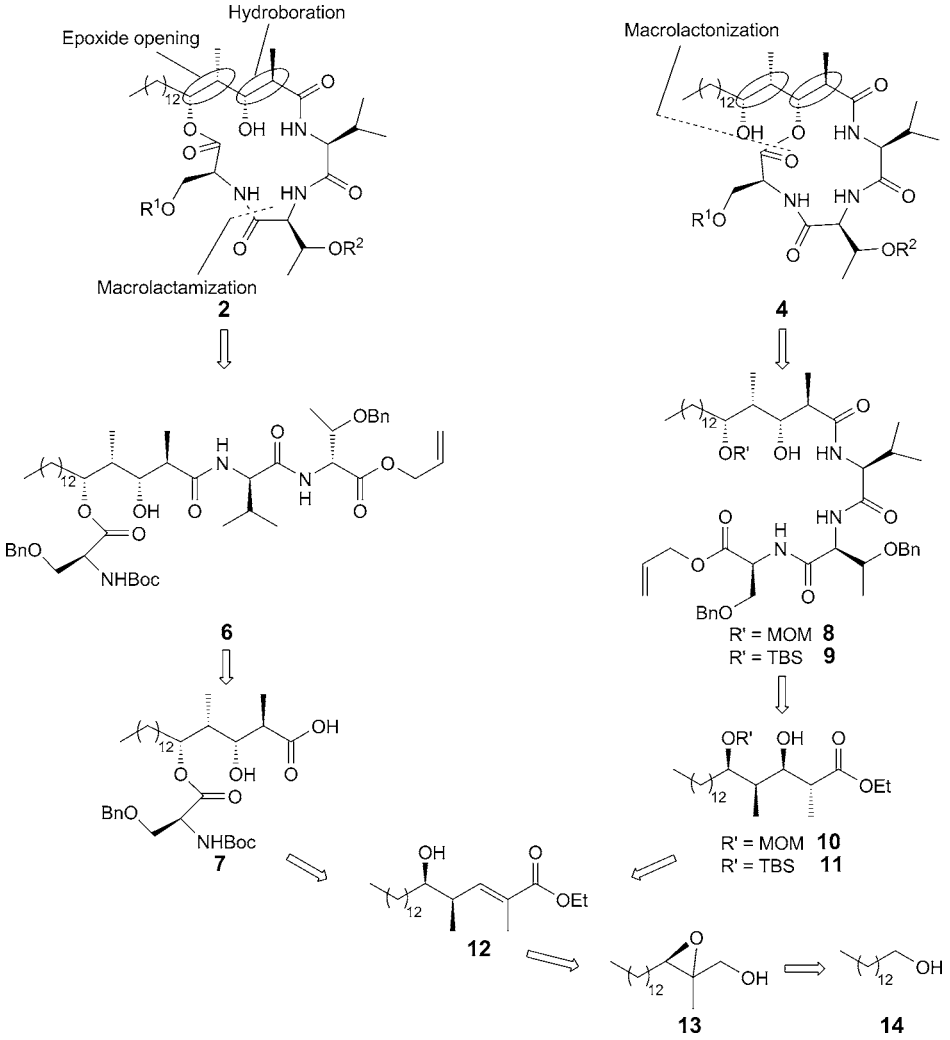
Results and Discussion. – Our retrosynthetic analysis suggested that stevastelin B (**2**), possessing a 15-membered ring structure, could be obtained by macrolactamization, followed by debenzylation and acetylation of the amino carboxylic acid obtained from **6** through allyl deprotection and Boc (^{t}BuOCO) deprotection (*Scheme 1*). The key intermediate **6** was envisioned to be synthesized by condensation of the peptide moiety with the fatty-acid precursor **7**. The synthesis by a macrolactonization-based strategy could lead to the 13-membered ring-containing stevastelin B3 (**4**) from the precursor **8** or **9**, respectively, after deallylation and cyclization. These two key intermediates, **8** and **9**, were envisioned to be obtained by condensation of the peptide moiety with the fatty-acid precursors **10** and **11**, respectively. While the precursor **12**, C(1)–C(18) fragment common to both stevastelin B and B3 (**2** and **4**, resp.) could be obtained using the non-aldol transformation from chiral epoxy alcohol **13**, generated through *Sharpless* asymmetric epoxidation from the readily available inexpensive starting material tetradecan-1-ol (**14**), the peptide chain could be easily prepared from commercially available protected serine, threonine, and valine derivatives (*Scheme 1*).

Our synthesis was initiated with the preparation of key intermediate **12**. Thus, we started with commercialy available tetradecan-1-ol (**14**) which was converted to epoxy alcohol **13**. *Swern* oxidation, followed by C_2-*Wittig* reaction of **14** provided α,β-unsaturated ester **15**. Compound **15** upon reduction with diisobutylaluminium hydride (DIBAL-H) [10], followed by *Sharpless* asymmetric epoxidation [11], provided **13**. Rearrangement of the epoxy alcohol on treatment with trimethylsilyl triflate (trimethylsilyl trifluoromethanesulfonate; TMSOTf) in the presence of *Hünig*'s base [12] afforded the *syn*-aldol product **16** as a single diastereoisomer in 89% yield (*Scheme 2*).

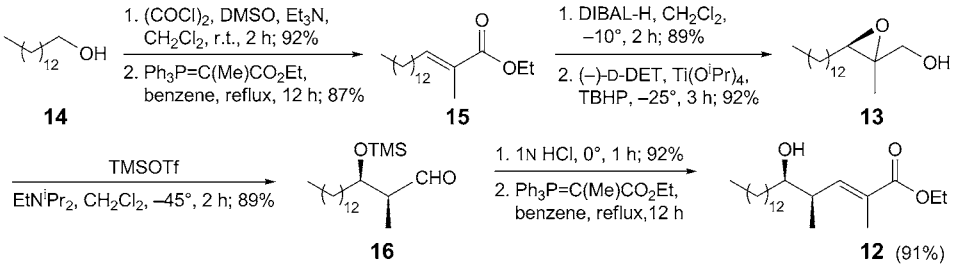
Deprotection of the silyl moiety with 1N HCl followed by *Wittig* reaction [10] with [1-(ethoxycarbonyl)ethylidene](triphenyl)phosphorane, provided an unseparable mixture of (*E*)- and (*Z*)-α,β-unsaturated hydroxy ester **12** (91.3%; *Scheme 2*).

Chemoselective reduction of the ester function in the presence of the C=C bond in **12** was achieved with DIBAL-H at $-10°$ to furnish the allylic alcohol **17** in 93% yield (*Scheme 3*). Hydroboration of **17** with borane dimethylsulfide ($BH_3 \cdot DMS$) [13] at $-10°$, followed by alkaline H_2O_2 workup, yielded the triol **18** along with its diasteroisomer **18a** in a minor amount (95:5). The spectroscopic data and specific rotation of **18** was in good agreement with the data reported in literature [3a]. The origin of the stereospecificity observed might be related to the conformational preference of allylic alcohol **17**, based on *Houk*'s transition-state model [14], which minimizes the allylic 1,3-strains. Therefore, hydroboration would take place preferentially from the sterically less hindered α-face to yield alcohol **18** as the major isomer. The configuration of the polyol chain of **18** was also confirmed based on the

Scheme 1. *Retrosynthetic Analysis for Stevastelins B and B3* (**2** and **4**, resp.)



Scheme 2. *Synthesis of the Key Intermediate* **12** ((−)-D-DET, (−)-D-diethyl tartrate; TBHP, ^{t}BuOOH)



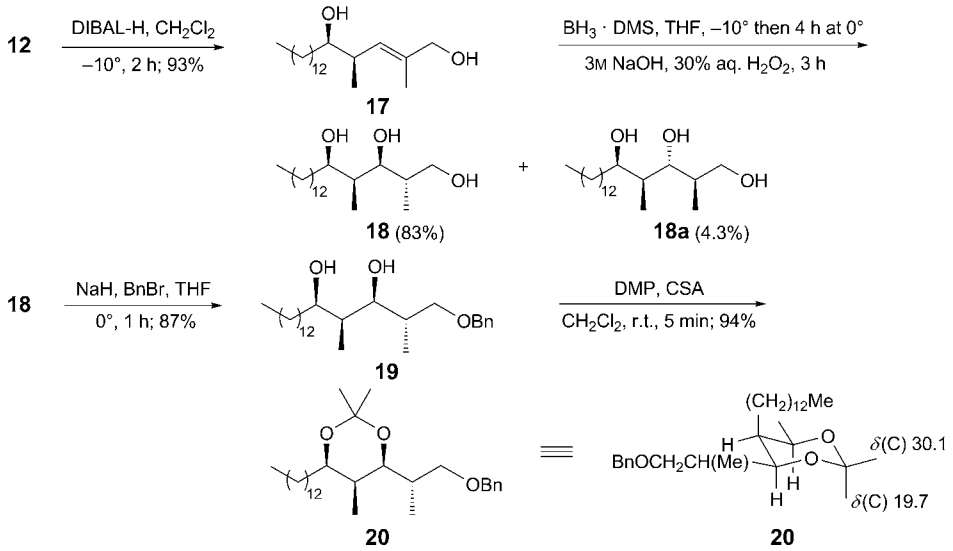
conformational property of 1,3-diol acetonide (*Scheme 3*). Towards this, the triol was subjected to primary-alcohol protection as the corresponding benzyl ether **19** and then to acetonide protection with with 2,2-dimethoxypropane (DMP) and a catalytic amount of camphorsulfonic acid (CSA) to yield **20** in 94% yield (*Scheme 3*). The ^{13}C-NMR spectrum of **20** displayed the Me signals at 19.4 and 30.1 ppm, confirming the *syn*-configuration for the 3,5-diol function [15].

Having established the route to advanced common precursor **18** for the synthesis of stevastelins, the total synthesis of stevastelin B (**2**), possessing a 15-membered cyclic depsipeptide structure, was first investigated. Compound **18** was treated with DMP in the presence of CSA [16] to afford the masked product **21** in 82% yield (*Scheme 4*). Initially, direct esterification of the alcohol with amino acid residue Boc-Val-Thr-Ser(Bzl) was attempted without any success [17]. The poor reactivity of the OH group in **21**, probably due to steric hindrance, led us to employ the stepwise introduction of the amino acid moiety. The condensation of **21** with Boc-Ser(Bn)–OH (**22**) using *N,N′*-dicyclohexylcarbodimide (DCC) [18] and 4-(dimethylamino)pyridine (DMAP) yielded the acylated product **23** in 73% yield. Acetonide deprotection with aqueous AcOH gave the diol **24** in 76% yield. The primary alcohol in **24** was selectively oxidized with (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) and [bis(acetoxy)iodo]benzene (BAIB) [19] to give the aldehyde which was further oxidized by $NaClO_2$ to afford the carboxylic acid **7** in 75% yield (*Scheme 4*).

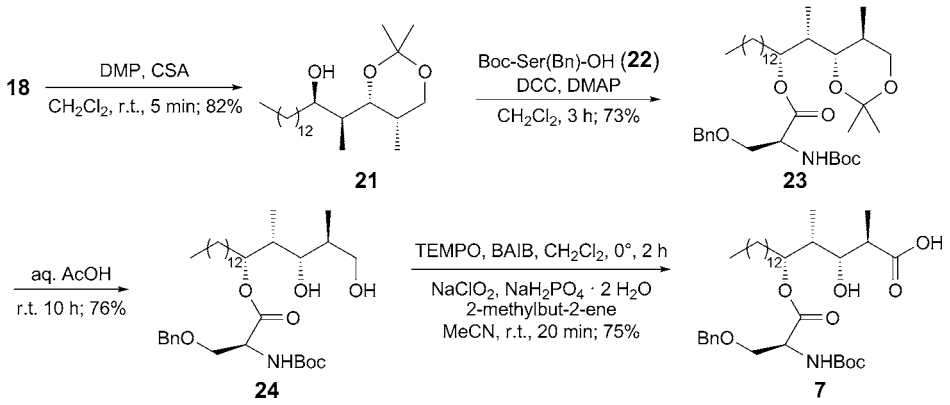
The synthesis of the peptide residue **26** (two amino acid residue) was achieved by a conventional method starting from the corresponding commercially available protected amino acid **25** in 83% yield (*Scheme 5*) [20].

The coupling of acid **7** with the amino salt (obtained after treating allyl-Thr-Val (**26**) with TFA) in the presence of 1-[3-(dimethylamino)propyl]-3-ethylcarbodimide hydrochloride (WSC · HCl) and 1-hydroxybenzotriazole (HOBt) provided the condensed

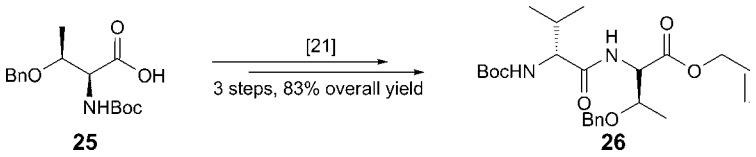
Scheme 3. *Synthesis of Triol* **18** *and Confirmation of* syn-*Geometry of 3,5-Diol*



Scheme 4. *Synthesis of the Fatty-Acid Precursor* **7**



Scheme 5. *Synthesis of the Peptide Fragment* **26**



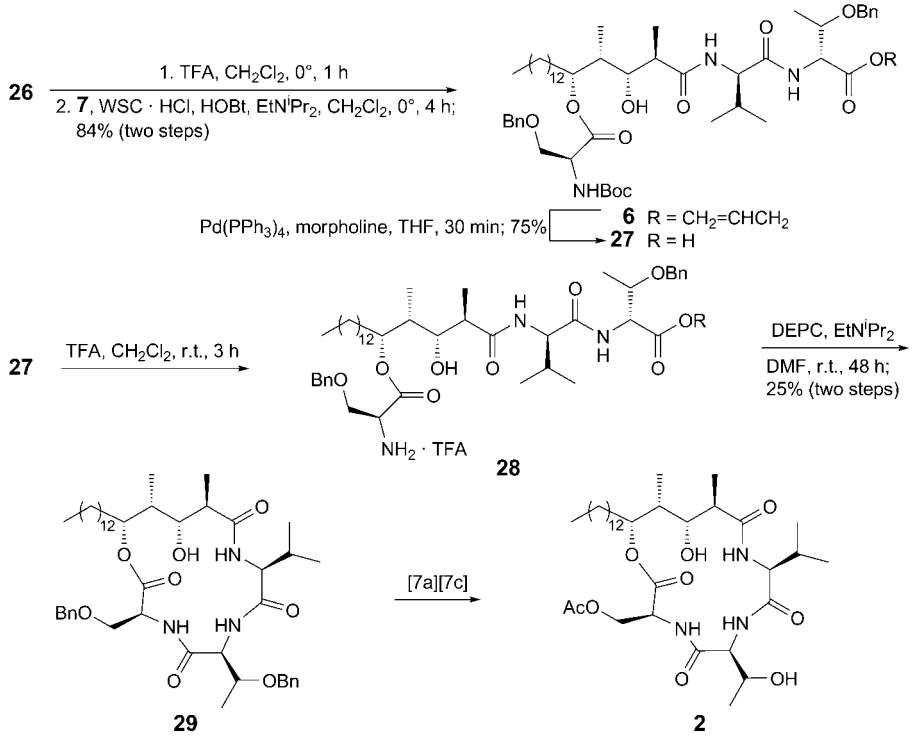
product **6** in 84% yield (*Scheme 6*). The allyl ester **6** was converted to the acid **27** with $Pd(PPh_3)_4$ and morpholine [21]. Treatment of **27** with CF_3COOH (TFA) provided the amino carboxylic acid as its corresponding TFA salt **28**. The crucial step, the macrolactamization, was successfully carried out according to the protocol of by *Shioiri et al.* [22] using diethylphosphoryl cyanide (DEPC) in DMF under high dilution condition (0.01M) to provide the 15-membered macrocycle **29** in 25% yield from **28**. Compound **29** was converted to stevastelin B (**2**) as reported in [7a][7c].

Synthesis of Stevastelin B3 (**4**). We then proceeded toward the synthesis of **4**, possessing a 13-membered cyclic depsipeptide, employing the macrolactonization strategy. Initially, keeping in mind the robustness of the methoxymethyl (MOM) moiety, we protected the free secondary alcohol **12** as the corresponding MOM ether **30** (*Scheme 7*). Chemoselective reduction of the ester functionality in the presence of the C=C bond in **30** was achieved with DIBAL-H to furnish allyl alcohol **32** in 93% yield. Hydroboration of **32** with $BH_3 \cdot DMS$ in THF, followed by alkaline H_2O_2 workup, yielded the alcohol **34** along with a small amount of its diastereoisomer **34a** that was easily separable by column chromatography. The primary alcohol group in **34** was selectively oxidized with TEMPO and BAIB to give the corresponding aldehyde, which was further oxidized with $NaClO_2$ to afford the carboxylic acid **10** (*Scheme 7*).

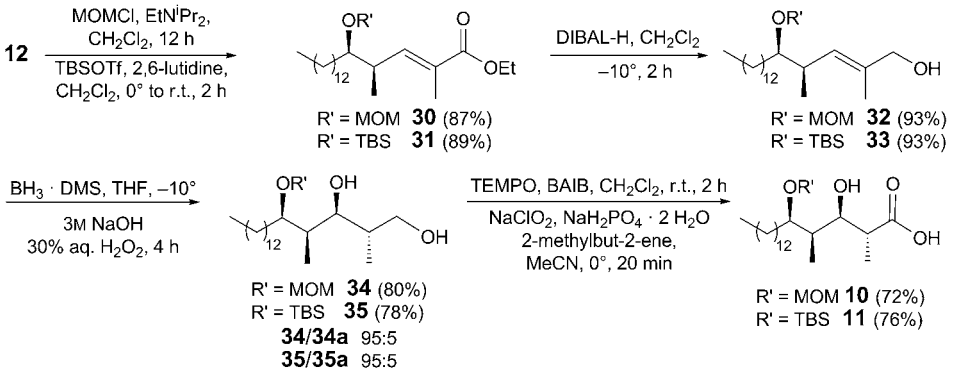
The peptide segment **36** was synthesized from commercially available protected amino acid **37** in three steps as reported in [7c](*Scheme 8*).

The peptide salt obtained after treatment of **36** with TFA was coupled with **10** in the presence of $WSC \cdot HCl$ and HOBt to furnish the amide **8** in 90% yield. The acid precursor for esterification the hydroxy acid **37** was obtained from the reaction of **8** with $Pd(PPh_3)_4$ in the presence of morpholine. The acid **37** was subjected to several

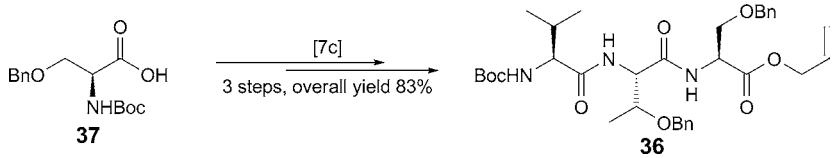
Scheme 6. *Formal Synthesis of Stevastelin B* (**2**)



Scheme 7. *Synthesis of the Lipid-Chain Precursor* **10** (TBS, ^{t}BuMe$_2$Si)



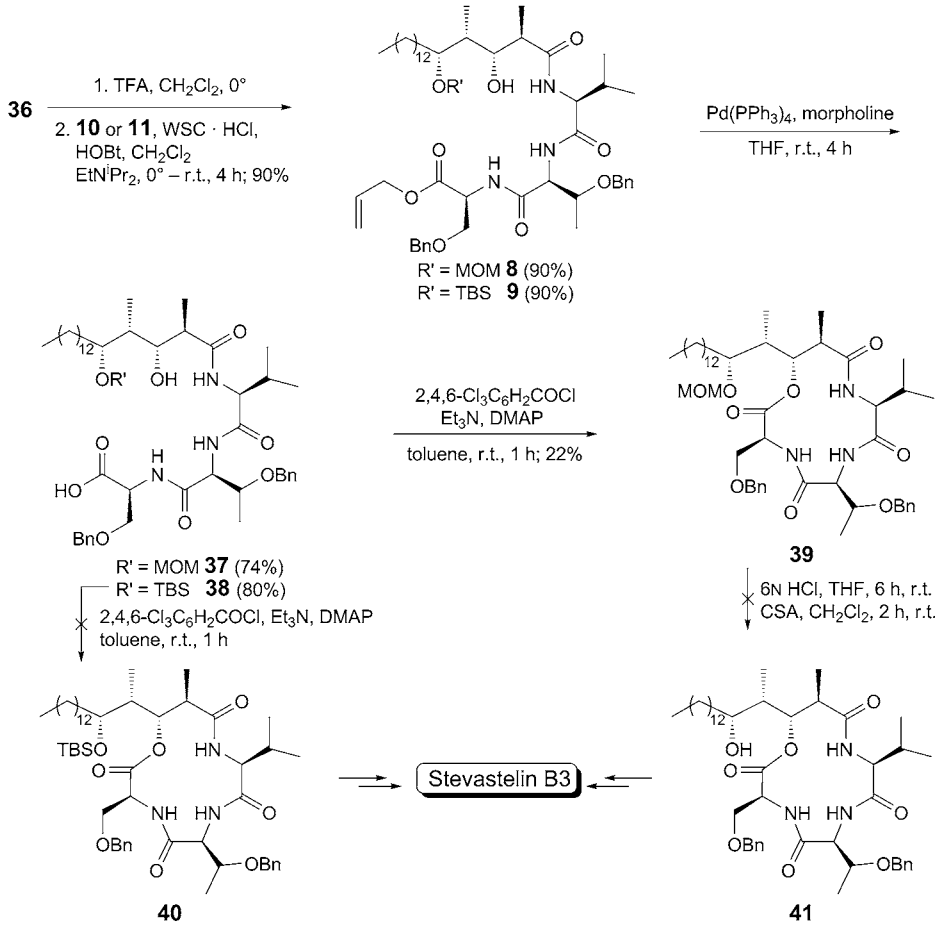
Scheme 8. *Synthesis of the Peptide Fragment* **36**



macrolactonization conditions, *e.g.*, *Yamaguchi* methodology, under high dilution conditions and also with a variety of coupling reagents [23], such as DEPC [24], diphenylphosphoryl azide (DPPA) [25], '1-ethyl-3-[3-(dimethylamino)propyl]carbodiimide' (EDCI)/HOBt, and pentafluorophenol/EDCI, in different solvents (CH_2Cl_2, THF, DMF, MeCN). All these attempts were not successfull. Finally, after several attempts, we succeeded in lactonization by applying conditions reported by *Yonemitsu* and co-workers [26] wherein the amino acid **37** underwent lactonization to yield the corresponding depsipeptide **39** (*Scheme 9*).

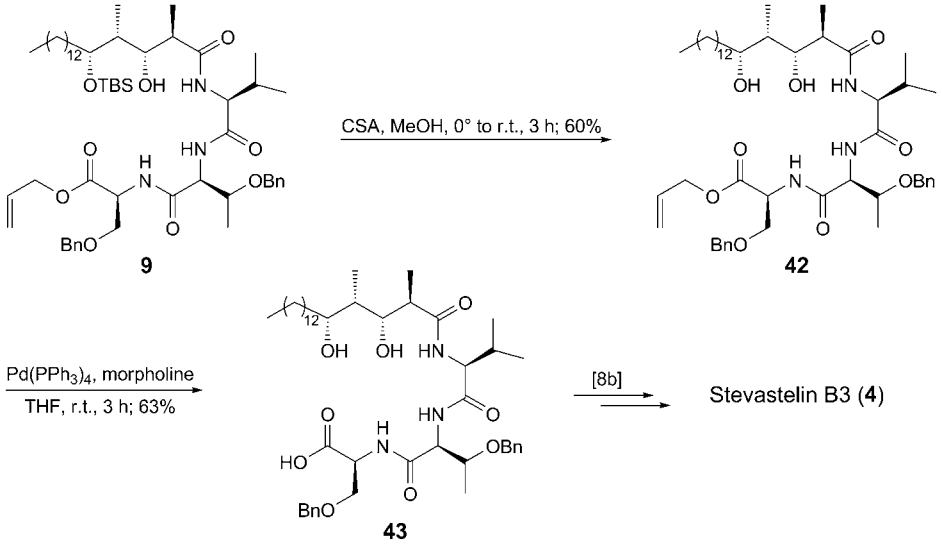
With the basic macrolide skeleton in hand after lactonization, we proceeded towards removal of the Bn and MOM moieties, and acetylation of the primary alcohol. Unfortunately, all our attempts to remove the MOM moiety under acidic conditions to provide **41** did not succeed and resulted in decomposition of the starting material. Thus, the best option left was to start the whole sequence by changing the protecting group that could be easily removed at the end stage. Hence, we chose a silyl protective group,

Scheme 9. *Synthesis of the Depsipeptide* **39**



^{t}BuMe$_2$Si in place of the MOM moiety. Compound **11** was synthesized starting from **12** *via* a similar set of reactions as performed for **10** (*Scheme 7*). Thus, **12** was protected as the corresponding TBS ether **31** and subjected to ester hydrolysis with DIBAL-H to obtain **33**. Hydroboration, followed by treatment with H_2O_2 under basic conditions, provided easily separable diastereoisomers **35** and **35a**, respectively. The primary OH group in **35** was oxidized to aldehyde and then to acid with TEMPO and BAIB, followed by *Pinnick* oxidation conditions, to furnish acid **11**. Compound **11** was then coupled with **36** to afford **9**, which, upon reaction with Pd(PPh$_3$)$_4$ in the presence of morpholine, gave acid **38** (*Scheme 9*). The acid **38** was subjected to macrolactonization to prepare **40** following *Yamaguchi*'s methodology under high-dilution conditions, or with a variety of coupling reagents in different solvents, but the reaction was not successful (*Scheme 9*). Reasoning this outcome due to bulkiness of the TBS moiety adjacent to the OH group, we opted to proceed further by removal of TBS moiety at this stage. Thus, compound **9** was converted to diol **42** by treating with CSA in MeOH, and then reacted with Pd(PPh$_3$)$_4$ in the presence of morpholine to give the known precursor **43**, which was utilized earlier for the total synthesis of stevastalin B3 (**4**) [8b] (*Scheme 10*).

Scheme 10. *Synthesis of the Key Precursor Diol* **43**



Conclusions. – In conclusion, we have accomplished the formal total synthesis of stevastelin B and B3 (**2** and **4**, resp.) in an enantioselective manner. The highlights of our synthesis include the preparation of the lipid chain through a 'non-aldol aldol' reaction, and employing *Sharpless* epoxidation, *Wittig* reaction, hydroboration/oxidation, macrolactonization, and macrolactamization as other key steps. Further investigations are currently under progress to accomplish the cyclization reaction and explore it further for the synthesis of several analogs for biological studies.

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Experimental Part

General. All reactions were carried out under Ar or N_2 using standard syringe, septa, and cannula techniques unless otherwise mentioned. Commercial reagents were used without further purification. All solvents were purified by standard techniques. Column chromatography (CC): silica gel (SiO_2, 60–120 mesh); elution with AcOEt/petroleum ether mixtures. Visualization of the spots on TLC plates was achieved either by exposure to I_2 vapor or UV light, or by dipping the plates to ethanolic anisaldehyde/H_2SO_4/AcOH or to phosphomolybdic acid/H_2SO_4 soln., and heating the plates at 120°. Optical rotations: *PerkinElmer 241* polarimeter in 1.0-dm and 1.0-ml cells. IR Spectra: *PerkinElmer 683* spectrometer using NaCl optics; $\tilde{\nu}$ in cm^{-1}; spectra were calibrated against the polystyrene absorption at 1610 cm^{-1}. Samples were scanned neat, in KBr wafers, or in $CHCl_3$ as a thin film. ^{1}H- and ^{13}C-NMR spectra: *Bruker 300* NMR spectrometer (^{13}C: 75 MHz); in $CDCl_3$; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz. MS: *Finnigan MAT1020B* or *micromass VG 70-70 H* spectrometer; at 70 eV using a direct inlet system; in *m*/*z*.

*Ethyl (2*E*)-2-Methylhexadec-2-enoate* (**15**). To the soln. of oxalyl chloride (8.1 ml, 93.3 mmol) in dry CH_2Cl_2 at −78° was slowly added a soln. of DMSO (13.3 ml, 186.6 mmol) in CH_2Cl_2 (80 ml). After stirring for 1 h at −78°, *tetradecan-1-ol* (**14**; 10.0 g, 46.6 mmol) in dry CH_2Cl_2 (100 ml) was slowly added. After 45 min., Et_3N (38.9 ml, 279.9 mmol) was introduced *via* a syringe. The mixture was then stirred at −78° for 10–15 min, and further at −50° for 20 min, prior to the addition of aq. sat. NH_4Cl (50.0 ml) soln. The org. phase was separated and then washed with CH_2Cl_2 (2 × 15 ml). The combined org. layer was dried (Na_2SO_4) and passed through a short pad of SiO_2. The filtrate was concentrated to give tetradecanal (9.11 g, 92%) as pale-yellow syrup, which was used as such for the next step without further purification. R_f (10% AcOEt/hexane) 0.8. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.88 (*t*, *J* = 6.8, 3 H); 1.20–1.38 (*m*, 20 H); 1.54–1.70 (*m*, 2 H); 2.28–2.45 (*m*, 2 H); 9.74 (*s*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 13.9; 21.9; 22.5; 24.6; 29.01; 29.2; 29.3; 29.4; 29.5 (2 C); 31.8; 33.8; 43.7; 202.2.

Tetradecanal (2.6 g, 12.3 mmol, 1.0 equiv.) was dissolved in benzene (25 ml), and to this soln. [1-(ethoxycarbonyl)ethylidene](triphenyl)phosphorane (6.67 g, 18.4 mmol, 1.5 equiv.) was added at r.t. The mixture was heated at reflux until the reaction was complete as judged by TLC (*ca.* 12 h). The solvents were removed by concentration under reduced pressure. The resulting crude residue was purified by CC (1% AcOEt/hexane) to give **15** (3.15 g, 87%) exclusively (LC/MS). Colorless liquid. R_f (2% AcOEt/hexane) 0.4. IR (neat): 1033, 1250, 1513, 1737, 2901, 3285. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.88 (*t*, *J* = 6.8, 3 H); 1.20–1.38 (*m*, 20 H); 1.30 (*t*, *J* = 6.8, 3 H); 1.38–1.50 (*m*, 2 H); 1.81 (*s*, 3 H); 2.15 (*q*, *J* = 7.6, 2 H); 4.17 (*q*, *J* = 7.6, 2 H); 6.70 (*t*, *J* = 7.6, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 12.2; 14.0; 14.2; 22.6; 28.5; 28.6; 29.3; 29.4; 29.5 (2 C); 29.6 (4 C); 31.8; 60.2; 127.5; 142.3; 168.1. ESI-MS: 297 ($[M+H]^+$). HR-ESI-MS: 296.2622 ($C_{19}H_{36}O_2^+$; calc. 296.2625).

*[(3*R*)-2-Methyl-3-tridecyloxiran-2-yl]methanol* (**13**). A soln. of **15** (4.6 g, 15.5 mmol) in 50 ml of CH_2Cl_2 was cooled to −10°. DIBAL-H (22.1 ml, 31.1 mmol; 20% soln. in toluene) was then added dropwise during 5 min. The resulting mixture was stirred for 2 h before quenching the reaction with sat aq. sodium potassium tartrate soln. (30 ml). The mixture was warmed to r.t. and stirred for 5 h. Org. layer was separated, and aq. layer was extracted with CH_2Cl_2 (2 × 15 ml). Combined org. layer was dried (Na_2SO_4) and evaporated. CC (SiO_2; AcOEt/hexane (8%)) of the crude product afforded the allyl alcohol (3.51 g, 89%). Colorless liquid. R_f (20% AcOEt/hexane) 0.7. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.88 (*t*, *J* = 6.8, 3 H); 1.20–1.38 (*m*, 22 H); 1.65 (*s*, 3 H); 2.01 (*q*, *J* = 6.8, 2 H); 3.95 (*s*, 2 H); 5.36 (*t*, *J* = 6.8, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 13.8; 14.0; 22.4; 28.3; 28.4; 29.1; 29.2; 29.3; 29.4; 31.7; 60.0; 127.3; 142.1. ESI-MS: 277 ($[M+Na]^+$).

Finely powdered activated molecular sieves (4 Å, 28.0 g) were placed in a 500-ml two-neck round-bottom flask equipped with a septum and N_2 inlet, and a magnetic bar. CH_2Cl_2 (120 ml) was cannulated, and the flask was then cooled to −25°. (−)-D-diethyl tartrate ((−)-D-DET; 1.8 ml, 10.5 mmol) and

$Ti(O^iPr)_4$ (2.5 ml, 8.4 mmol) were added sequentially, and resulting mixture was stirred for 30–40 min before adding a soln. of the above allyl alcohol (10.7 g, 42.12 mmol) in 40 ml of dry CH_2Cl_2. After stirring for another 50 min at $-25°$, ^{t}BuOOH (6.3M in toluene, 13.4 ml, 84.3 mmol) was added dropwise during 30 min period. The resulting mixture was stirred for 1.5 h, and the reaction was quenched with 50 ml H_2O. The resulting mixture was stirred for 30 min at r.t. After stirring 30 min at r.t., 12.5 g of NaOH (20% NaOH soln. in brine) was added at r.t. The mixture was stirred for another 4 h at r.t. The soln. was then filtered through a small pad of *Celite*, and the residue was washed with CH_2Cl_2 (at least 20 times). The combined CH_2Cl_2 layer was evaporated under reduced pressure. CC (SiO_2; AcOEt/hexane (10%) of the crude product afforded **13** (10.5 g, 92%; 94% ee by HPLC analysis). Colorless liquid. R_f (20% AcOEt/hexane) 0.4. $[\alpha]_D^{30} = +9.2$ ($c = 1.4$, $CHCl_3$). IR (neat): 1033, 1248, 1513, 1611, 2925, 3452. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.88 (t, $J = 6.8$, 3 H); 1.20–1.38 (m, 24 H); 1.44–1.61 (m, 2 H); 1.83–1.93 (m, 1 H); 2.97 (t, $J = 6.0$, 1 H); 3.51 (q, $J = 8.7$, 1 H); 3.63 (q, $J = 4.5$, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 13.9; 22.5; 26.3; 28.0; 29.2 (2 C); 29.3 (2 C); 29.4 (2 C); 29.5 (3 C); 31.8; 60.2; 61.0; 65.5. ESI-MS: 293 ($[M + Na]^+$). HR-ESI-MS: 293.2468 ($C_{17}H_{34}NaO_2^+$; calc. 293.2456).

(2S,3R)-2-Methyl-3-[(trimethylsilyl)oxy]hexadecanal (**16**). Finely powdered activated molecular sieves (4 Å; 8.0 g) were placed in a 50-ml two-neck round-bottom flask. The alcohol **13** (3.0 g, 11.1 mmol) in CH_2Cl_2 (30 ml) and EtN^iPr_2 (3.4 ml, 19.4 mmol) were added sequentially, and the mixture was stirred for 5–10 min. The resulting mixture was cooled to $-45°$ and treated with TMSOTf (2.9 ml, 16.1 mmol). The mixture was stirred at $-45°$ for 3 h, and then the reaction was quenched with H_2O (15 ml). Org. layer was separated, and the aq. layer was extracted with CH_2Cl_2 (2×5 ml). Combined org. layer was dried (Na_2SO_4) and evaporated. CC (SiO_2; AcOEt/hexane (4%) afforded **16** (3.4 g, 89%). Colorless liquid. R_f (10% AcOEt/hexane) 0.3. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.09 (s, 9 H); 0.88 (t, $J = 6.8$, 3 H); 1.06 (d, $J = 7.2$, 3 H); 1.20–1.37 (m, 23 H); 1.39–1.52 (m, 1 H); 2.31–2.42 (m, 1 H); 4.01–4.09 (m, 1 H); 9.70 (s, 1 H).

Ethyl (2E,4R,5R)-5-Hydroxy-2,4-dimethyloctadec-2-enoate (**12**). Compound **16** (3.2 g, 9.35 mmol) was dissolved in THF (30 ml), and 5 ml of 1N HCl were added at 0°. The mixture was stirred at r.t. for 30 min, and then the reaction was quenched with solid $NaHCO_3$ and filtered. The filtrate was concentrated in vacuum. CC (SiO_2; AcOEt/hexane (12%)) of the crude product gave the hydroxy aldehyde (2.32 g, 92%). Colorless oil. R_f (20% AcOEt/hexane) 0.4. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.88 (t, $J = 6.8$, 3 H); 1.14 (d, $J = 7.2$, 3 H); 1.20–1.38 (m, 23 H); 1.39–1.58 (m, 1 H); 2.36–2.47 (m, 1 H); 4.01–4.09 (m, 1 H); 9.70 (s, 1 H).

The hydroxy aldehyde obtained above (2.2 g, 8.1 mmol, 1.0 equiv.) was dissolved in benzene (25 ml), and [1-(ethoxycarbonyl)ethylidene](triphenyl)phosphorane (4.16 g, 11.5 mmol, 1.5 equiv.) was added at r.t. The mixture was heated at reflux until the reaction was complete as judged by TLC (*ca.* 12 h). The solvents were removed by concentration under reduced pressure. The resulting crude residue was purified by CC (SiO_2; AcOEt/hexane (5%)) to give **12** (2.63 g, 91.3%). Colorless liquid (in 95:5 ratio as determined by ^{1}H-NMR and LC/MS). R_f (10% AcOEt/hexane) 0.5. A small portion of the sample was purified to measure the optical rotation. $[\alpha]_D^{29} = +22.6$ ($c = 1.6$, $CHCl_3$). IR (neat): 1035, 1175, 1248, 1370, 1721, 2927. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.88 (t, $J = 6.8$, 3 H); 1.05 (d, $J = 6.8$, 3 H); 1.19–1.38 (m, 23 H); 1.31 (t, $J = 6.8$, 3 H); 1.39–1.51 (m, 1 H); 1.51–1.65 (br. s, OH); 1.85 (s, 3 H); 2.45–2.60 (m, 1 H); 3.39–3.52 (m, 1 H); 4.18 (q, $J = 6.8$, 2 H); 6.56 (d, $J = 9.8$, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 12.6; 14.0; 14.2; 15.2; 22.6; 25.9; 29.3; 29.6 (7 C); 31.9; 34.9; 39.6; 60.5; 75.2; 127.6; 144.0; 168.2. ESI-MS: 377 ($[M + Na]^+$). HR-ESI-MS: 377.3041 ($C_{22}H_{42}NaO_3^+$; calc. 377.3031).

(2E,4R,5R)-2,4-Dimethyloctadec-2-ene-1,5-diol (**17**). A soln. of **12** (2.0 g, 5.64 mmol) in 25 ml of CH_2Cl_2 was cooled to $-10°$. DIBAL-H (8.1 ml, 11.3 mmol; 20% soln. in toluene) was then added dropwise during 5 min. The resulting mixture was stirred for 2 h before quenching the reaction with sat. aq. $KNaC_4H_4O_6 \cdot 4\,H_2O$ soln. (15 ml). The mixture was warmed to r.t. and stirred for 5 h. Org. layer was separated, and aq. layer was extracted with CH_2Cl_2 (2×10 ml). Combined org. layer was dried (Na_2SO_4) and evaporated. CC (SiO_2; AcOEt/hexane (10%) of the crude product afforded **17** (1.64 g, 93%). Colorless liquid. R_f (20% AcOEt/hexane) 0.5. $[\alpha]_D^{30} = +19.2$ ($c = 1.4$, $CHCl_3$). IR (neat): 1246, 1513, 1615, 2853, 2925, 3256. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.88 (t, $J = 6.8$, 3 H); 0.97 (d, $J = 6.8$, 3 H); 1.22–1.33 (m, 23 H); 1.42–1.49 (m, 1 H); 1.68 (s, 3 H); 2.41–2.52 (m, 1 H); 3.35–3.42 (m, 1 H); 3.97 (s, 2 H); 5.26 (d,

$J = 10.2$, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 14.1; 15.7; 22.6; 26.1; 29.3; 29.6 (7 C); 31.9; 34.1; 37.9; 68.6; 75.8; 128.4; 135.1. ESI-MS: 335 ($[M+Na]$) $^+$. HR-ESI-MS: 335.2932 ($C_{20}H_{40}NaO_2^+$; calc. 335.2926).

*(2*S*,3*S*,4*S*,5*R*)-2,4-Dimethyloctadecane-1,3,5-triol* (**18**). To the soln. of **17** (3.0 g, 9.6 mmol) in dry THF (30 ml) was added $BH_3 \cdot DMS$ (1.36 ml, 14.4 mmol) during 15 min. maintaining the temp. at $-10°$. The mixture was then allowed to warm to 0° and stirred for 4 h. The soln. was cooled to $-10°$, and 3M NaOH (until the mixture was basic, maintaining the temp. at $-10°$.) and H_2O_2 (9 ml, 30% soln. in H_2O were added;) and then the mixture was further stirred for 3 h and diluted with AcOEt (20 ml). The org. layers were separated and washed with brine (1×15 ml), dried (Na_2SO_4), and evaporated to give the crude product, which was purified by CC (SiO_2; AcOEt/hexane (5%)) to give **18** (2.63 g, 83%) as a colorless liquid, along with minor diastereomer **18a** (0.136 g, 4.3%) as colorless liquid.

Data for **18**. R_f (30% AcOEt/hexane) 0.3. $[\alpha]_D^{30} = +9.2$ ($c = 1.4$, $CHCl_3$). IR (neat): 1078, 1461, 2385, 2922, 3251. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.75 (*d*, $J = 6.8$, 3 H); 0.88 (*t*, $J = 7.6$, 3 H); 0.92 (*d*, $J = 6.8$, 3 H); 1.16–1.35 (*m*, 23 H); 1.36–1.48 (*m*, 1 H); 1.55–1.66 (*m*, 1 H); 1.80–1.96 (*m*, 1 H); 3.60–3.87 (*m*, 3 H); 3.81–3.90 (*m*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 4.1; 13.1; 14.1; 22.7; 26.0; 29.3, 29.6 (7 C); 31.9; 35.4; 37.1; 37.7; 68.9; 77.6; 83.2. ESI-MS: 353 ($[M+Na]^+$). HR-ESI-MS: 353.3032 ($C_{20}H_{42}NaO_3^+$; calc. 353.3055).

*(2*S*,3*S*,4*S*,5*R*)-1-(Benzyloxy)-2,4-dimethyloctadecane-3,5-diol* (**19**). NaH (25 mg, 0.61 mmol) was slowly added in portions to a soln. of **18** (200 mg, 0.61 mmol) in anh. THF (5 ml) at 0°, and the mixture was stirred for 15 min. Then, BnBr (0.8 ml, 0.66 mmol) and cat. amount Bu_4NI were added at 0°, and the mixture was allowed to stir at r.t. for 4 h. After completion the reaction was quenched by slow addition of H_2O (5 ml), and the mixture was extracted with AcOEt (10 ml). The org. layer was separated, and washed with H_2O (5 ml) and brine (5 ml). The org. solvent was evaporated, and the crude product was purified by CC (SiO_2; AcOEt/hexane (15%)) to yield **19** (221 mg, 87%). Colorless liquid. R_f (30% AcOEt/hexane) 0.7. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.76 (*d*, $J = 7.0$, 3 H); 0.87 (*d*, $J = 7.0$, 3 H); 0.91 (*d*, $J = 7.0$, 3 H); 1.20–1.47 (*m*, 23 H); 1.49–1.70 (*m*, 2 H); 1.93–2.09 (*m*, 1 H); 3.47 (*t*, $J = 4.2$, 1 H); 3.61 (*dd*, $J = 5.1$, 9.4, 1 H); 3.72 (*dd*, $J = 2.1$, 9.4, 1 H); 3.80–3.87 (*m*, 1 H); 4.53 (*s*, 2 H); 7.28–7.41 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 4.2; 13.0; 14.1; 22.7; 26.2; 29.3; 29.6; 29.7 (6 C); 31.9; 35.1; 35.9; 38.1; 73.6; 76.8; 78.1; 82.9; 127.7; 128.0; 128.5; 137.4.

*(4*S*,5*S*,6*R*)-4-[(2*S*)-1-(Benzyloxy)propan-2-yl]-2,2,5-trimethyl-6-tridecyl-1,3-dioxane* (**20**). To a soln. of **19** (200 mg, 0.48 mmol) in CH_2Cl_2 (5 ml) at r.t. was added DMP (0.09 ml, 0.95 mmol), followed by CSA (12 mg), and the mixture was stirred at r.t. for 5 min. Solid $NaHCO_3$ was added at 0°, and the mixture was again stirred for 10 min. The mixture was filtered through a pad of neutral alumina, and the filtrate was concentrated in vacuum. CC (SiO_2; AcOEt/hexane (8%)) gave the acetonide-protected compound **20** (205.9 mg, 94%). Colorless liquid. R_f (20% AcOEt/hexane) 0.7. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.82 (*d*, $J = 6.8$, 3 H); 0.88 (*t*, $J = 7.0$, 3 H); 0.93 (*d*, $J = 7.0$, 3 H); 1.18–1.34 (*m*, 23 H); 1.37 (*s*, 3 H); 1.39–1.53 (*m*, 1 H); 1.56 (*s*, 3 H); 1.77–1.93 (*m*, 1 H); 3.45 (*dd*, $J = 6.0$, 8.9, 1 H); 3.55 (*dd*, $J = 3.0$, 8.9, 1 H); 3.69 (*dd*, $J = 1.9$, 10.0, 1 H); 3.77–3.85 (*m*, 1 H); 4.50 (*q*, $J = 12.1$, 2 H); 7.27–7.38 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 4.4; 12.6; 14.1; 19.7; 22.7; 25.4; 29.3; 29.7 (7 C); 30.1; 32.0; 32.3; 32.9; 35.3; 72.4; 73.2; 73.7; 74.0; 98.7; 127.3; 127.5; 128.2; 139.0.

*(2*S*,3*R*)-2-[(4*R*,5*S*)-2,2,5-Trimethyl-1,3-dioxan-4-yl]hexadecan-3-ol* (**21**). To a soln. of **18** (267 mg, 0.808 mmol) in CH_2Cl_2 (28 ml) at r.t. were added DMP (0.155 ml, 1.62 mmol) and CSA (19 mg, 0.081 mmol), and the mixture was stirred at r.t. for 5 min. To this mixture at 0° was added Et_3N (4 ml), and the mixture was diluted with AcOEt. The org. layer was washed with a sat. aq. $NaHCO_3$ soln. (5 ml) and brine (5 ml), and then dried (Na_2SO_4). Removal of the solvent left a residue, which was purified by CC (SiO_2; AcOEt/hexane (8%)) to give **21** (1.62 g, 82%). Colorless liquid. R_f (20% AcOEt/hexane) 0.7. $[\alpha]_D^{30} = +36.3$ ($c = 1.5$, $CHCl_3$). IR (neat): 1033, 1094, 1250, 1513, 1610, 2901, 3285, 3439. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.71(*d*, $J = 6.8$, 3 H); 0.88 (*t*, $J = 6.8$, 3 H); 0.91 (*d*, $J = 6.8$, 3 H), 1.21–1.32 (*m*, 23 H); 1.35 (*s*, 3 H); 1.46 (*s*, 3 H); 1.47–1.54 (*m*, 1 H); 1.59–1.65 (*m*, 1 H); 1.84–1.94 (*m*, 1 H); 3.08 (br. *s*, OH); 3.48 (*t*, $J = 11.6$, 1 H); 3.62–3.71 (*m*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 4.8; 12.0; 14.1; 19.2; 22.7; 26.2; 29.3; 29.6 (7 C); 29.7; 30.5; 31.9; 34.9; 36.8; 66.1; 76.7; 81.4; 98.2. ESI-MS: 393 ($[M+Na]^+$).

*(2*S*,3*R*)-2-[(4*S*,5*S*)-2,2,5-Trimethyl-1,3-dioxan-4-yl]hexadecan-3-yl (2*S*)-3-(Benzyloxy)-2-{[(*tert*-butoxy)carbonyl]amino}propanoate* (**23**). To a soln. of Boc-Ser(Bn)–OH **22** (1.43 g, 4.86 mmol) in CH_2Cl_2 (20 ml) were added *N*,*N*′-dicyclohexylcarbodimide (DCC; 2.51 g, 12.15 mmol) and 4-(dimethylamino)-

pyridine (DMAP; 99 mg, 0.81 mmol). After stirring for 30 min at 0°, under Ar at 0° a soln. of **21** (1.5 mg, 4.05 mmol) in CH_2Cl_2 (5 ml) was added under Ar at 0°, and the resulting mixture was further stirred at 0° for 2.5 h. To the mixture was added H_2O (10 ml) at 0°, and the products were extracted with CH_2Cl_2. The org. layer was washed with brine and then dried (Na_2SO_4). Removal of the solvent left a residue, which was purified by CC (SiO_2; AcOEt/hexane (8%)) to furnish **23** (1.91 g, 73%). Sticky colorless liquid. R_f (20% AcOEt/hexane) 0.7. $[\alpha]_D^{32} = -26.5$ ($c = 1.5$, $CHCl_3$). IR (neat): 1256, 1510, 1726, 2863, 2920, 3436. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.66 (*t*, *J* = 6.2, 3 H); 0.82–0.94 (*m*, 6 H); 1.21–1.29 (*m*, 23 H); 1.30 (*d*, *J* = 5.1, 3 H); 1.36 (*d*, *J* = 7.3, 3 H); 1.44 (*s*, 9 H); 1.47–1.56 (*m*, 1 H); 1.71–1.88 (*m*, 2 H); 3.36–3.48 (*m*, 1 H); 3.49–3.72 (*m*, 3 H); 3.81–3.92 (*m*, 1 H); 4.28–4.40 (*m*, 1 H); 4.50 (*s*, 2 H); 4.87–5.03 (*m*, 1 H); 5.29 (*t*, *J* = 9.9, 1 H); 7.11–7.33 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 9.1; 12.1; 14.1; 18.7; 22.6; 28.3; 29.3 (3 C); 29.4; 29.5; 29.6 (6 C); 30.5; 31.1; 31.9; 36.8; 54.2; 66.2; 70.3; 73.3; 74.3; 78.3; 79.7; 97.9; 127.6; 127.7 (2 C); 128.3 (2 C); 137.5; 155.3; 170.2. ESI-MS: 670 ($[M + Na]^+$). HR-ESI-MS: 670.4725 ($C_{38}H_{65}NaNO_7^+$; calc. 670.4732).

*(2S,3S,4R,5R)-1,3-Dihydroxy-2,4-dimethyloctadecan-5-yl (2S)-3-(Benzyloxy)-2-{[(*tert*-butoxy)carbonyl]amino}propanoate* (**24**). The soln. of **23** (1.8 g, 2.8 mmol) in AcOH (7.5 ml) and H_2O (2.5 ml) was stirred at r.t. for 10 h. The mixture was diluted with H_2O, and to this soln. was added solid $NaHCO_3$ (6.8 g) at 0°. The products were extracted with AcOEt, and the org. layer was washed with a sat. aq. $NaHCO_3$ soln. and brine, and then dried (Na_2SO_4). Removal of the solvent left a residue, which was purified by CC (SiO_2; AcOEt/hexane (30%)) to yield **24** (1.18 g, 76%). Colorless liquid. R_f (40% AcOEt/hexane) 0.4. $[\alpha]_D^{30} = -12.6$ ($c = 0.51$, $CHCl_3$). IR (neat): 1168, 1347, 1499, 1720, 2857, 2926, 3445. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.78 (*t*, *J* = 6.6, 3 H); 0.88 (*t*, *J* = 6.8, 3 H); 0.95 (*d*, *J* = 7.2, 3 H); 1.15–1.38 (*m*, 23 H); 1.44 (*s*, 9 H); 1.52–1.70 (*m*, 1 H); 1.71–1.85 (*m*, 1 H); 1.96–2.15 (*m*, 1 H); 3.45–3.73 (*m*, 4 H); 3.82–4.02 (*m*, 1 H); 4.23–4.40 (*m*, 1 H); 4.51 (*s*, 2 H); 4.96–5.11 (*m*, 1 H); 5.23–5.38 (*m*, 1 H); 7.17–7.37 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 6.8; 7.2; 14.0; 22.6; 25.3; 28.2; 29.3; 29.4; 29.6 (10 C); 31.8; 32.2; 32.5; 37.8; 38.4; 53.9; 68.1; 69.8; 73.4; 79.1; 79.6; 80.1; 127.6; 127.9 (2 C); 128.4 (2 C); 137.0; 155.6; 170.6. ESI-MS: 630 ($[M + Na]^+$). HR-ESI-MS: 630.4360 ($C_{35}H_{61}NaNO_7^+$; calc. 630.4345).

*(2R,3R,4R,5R)-5-[((2S)-3-(Benzyloxy)-2-{[(*tert*-butoxy)carbonyl]amino}propanoyl)oxy]-3-hydroxy-2,4-dimethyloctadecanoic Acid* (**7**). To the soln. of **24** (1.1 g, 1.81 mmol) in CH_2Cl_2 (12 ml) at 0° were added TEMPO (28.3 mg, 0.002 mmol), and BAIB (641.9 mg, 1.99 mmol). After stirring at 0° for 2 h, a 20% aq. $Na_2S_2O_3$ soln was added. The products were extracted with $CHCl_3$, and the org. layer was washed with a 20% aq. $Na_2S_2O_3$ soln. and then dried (Na_2SO_4). Removal of the solvent gave a crude aldehyde (1.12 g). The aldehyde was dissolved in MeCN (10 ml) and H_2O (2.5 ml). To this soln. were added 2-methylbut-2-ene (0.08 ml, 0.95 mmol), $NaH_2PO_4 \cdot 2\ H_2O$ (722 mg, 4.62 mmol), and $NaClO_2$ (333.2 mg, 3.70 mmol), and the mixture was stirred at r.t. for 20 min. To this mixture at 0° was added a 1M aq. citric acid soln., and the products were extracted with $CHCl_3$. The org. layer was washed with a 1M aq. citric acid soln. and then dried (Na_2SO_4). Removal of the solvent left a residue, which was purified by CC (SiO_2; AcOEt/hexane (40%)) gave **7** (860 mg, 75%). Colorless liquid. R_f (40% AcOEt/hexane) 0.2. IR (neat): 1036, 1248, 1372, 1731, 2924, 3445. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.88 (*t*, *J* = 7.7, 3 H); 0.94 (*t*, *J* = 6.8, 3 H); 1.01 (*t*, *J* = 7.7, 3 H); 1.19–1.32 (*m*, 23 H); 1.44 (*s*, 9 H); 1.51–1.70 (*m*, 1 H); 1.77–1.96 (*m*, 1 H); 2.60–2.83 (*m*, 1 H); 3.60–3.75 (*m*, 2 H); 3.82–3.98 (*m*, 1 H); 4.35–4.58 (*m*, 3 H); 5.01–5.17 (*m*, 1 H); 5.31–5.50 (*m*, 1 H); 7.20–7.40 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 9.0; 14.1; 16.1; 18.0; 22.6; 25.5; 28.2; 29.3; 29.5; 29.6 (6 C); 31.0; 32.2; 39.6; 43.1; 58.2; 69.8; 70.8; 73.3; 73.9; 74.7; 127.6; 127.8 (2 C); 128.4 (2 C); 137.6; 155.6; 169.8; 176.2. ESI-MS: 644 ($[M + Na]^+$).

*Prop-2-en-1-yl (2R)-3-(Benzyloxy)-2-[(2-{[(*tert*-butoxy)carbonyl]amino}-3-methylbutanoyl)amino]butanoate* (**26**). To a soln. of the Boc-Thr(allyl) (3.12 g, 8.95 mmol) in CH_2Cl_2 (15 ml) under Ar at 0° was added TFA (3.5 ml). After stirring at 0° for 1 h, the mixture was concentrated to give a crude amine, which was dissolved in CH_2Cl_2 (25 ml). To this soln. at 0° were added the 1-[3-(dimethylamino)propyl]-3-ethylcarbodimide hydrochloride (WSC · HCl; 2.15 g, 11.2 mmol), HOBt (1.0 g, 7.46 mmol), and Boc-Val (1.5 g, 7.46 mmol), and the mixture was stirred for 10 min. To this was added EtN^iPr_2 (until the mixture was basic, maintaining the temp. at 0°), and the whole mixture was further stirred at r.t. for 4 h. The mixture was diluted with CH_2Cl_2 and washed successively with a 1M aq. citric acid soln., a sat. aq. $NaHCO_3$ soln., and brine, and then dried (Na_2SO_4). Removal of the solvent left a residue, which was purified by CC (SiO_2; acetone/hexane (15%)) to provide **26** (3.07 g, 92%). Colorless liquid. R_f (30%

acetone/hexane) 0.6. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.91 (*d*, *J* = 6.8, 3 H); 0.96 (*d*, *J* = 6.8, 3 H); 1.22 (*d*, *J* = 6.4, 3 H); 1.42 (*s*, 9 H); 2.08–2.21 (*m*, 1 H); 3.60 (*dd*, *J* = 3.4, 9.4, 1 H); 3.88 (*dd*, *J* = 3.4, 9.4, 1 H); 4.10–4.24 (*m*, 1 H); 4.37 (*d*, *J* = 12.3, 1 H); 4.40 (*d*, *J* = 12.3, 1 H); 4.58–4.60 (*m*, 2 H); 5.07 (br. *d*, *J* = 7.9, 1 H); 5.17–5.35 (*m*, 2 H); 5.76–5.93 (*m*, 1 H); 6.89 (*bd*, *J* = 6.2, 1 H); 7.23–7.33 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 14.6; 17.6; 19.2; 28.2 (3 C); 31.0; 52.8; 59.9; 66.0; 69.3; 71.4; 74.2; 118.6; 127.5; 127.6 (2 C); 128.3 (2 C); 131.5; 137.9; 155.7; 169.2; 171.6. ESI-MS: 471 ($[M + Na]^+$).

*Prop-2-en-1-yl (6*S*,12*R*)-18-[(1*S*)-1-(Benzyloxy)ethyl]-6-[(benzyloxy)methyl]-11-hydroxy-2,2,10,12-tetramethyl-4,7,13,16-tetraoxo-15-(propan-2-yl)-9-tridecyl-3,8-dioxa-5,14,17-triazanonadecan-19-oate* (**6**). To a soln. of **26** (807 mg, 2.32 mmol) in CH_2Cl_2 (15 ml) under Ar at 0° was added TFA (1.1 ml). After stirring at 0° for 1 h, the mixture was concentrated to give a crude amino TFA salt, which was dissolved in CH_2Cl_2 (15 ml). To this soln. at 0° were added the WSC · HCl (370.5 mg, 1.93 mmol), HOBt (174 mg, 1.29 mmol), and acid compound **7** (800 mg, 1.29 mmol), and the mixture was stirred for 10 min. To this was added EtN^iPr_2 (until the mixture was basic, maintaining the temp. at 0°), and the whole mixture was further stirred at r.t. for 4 h. The mixture was diluted with CH_2Cl_2 and washed successively with a 1M aq. citric acid soln., a sat. aq. $NaHCO_3$ soln., and brine, and then dried (Na_2SO_4). Removal of the solvent left a residue, which was purified by CC (SiO_2; acetone/hexane (25%)) to give **6** (1.03 g, 84%). Colorless liquid. R_f (40% acetone/hexane) 0.6. $[\alpha]_D^{30} = -16.3$ (*c* = 1.0, $CHCl_3$). IR (neat): 745, 1166, 1456, 1662, 1734, 2856, 2925, 3439. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.87 (*t*, *J* = 7.2, 3 H); 0.89 (*d*, *J* = 6.0, 3 H); 0.96 (*t*, *J* = 7.2, 3 H); 0.98 (*d*, *J* = 6.0, 3 H), 1.11 (*d*, *J* = 7.2, 3 H); 1.18 (*d*, *J* = 6.8, 3 H); 1.20–1.32 (*m*, 23 H); 1.44 (*s*, 9 H); 1.53–1.66 (*m*, 1 H); 1.68–1.81 (*m*, 1 H); 2.08–2.23 (*m*, 1 H); 2.46–2.61 (*m*, 1 H); 3.33–3.53 (*m*, 2 H); 3.57–3.72 (*m*, 1 H); 3.79–3.93 (*m*, 1 H); 4.08–4.19 (*m*, 1 H); 4.23–4.40 (*m*, 2 H); 4.43–4.67 (*m*, 6 H); 5.01–5.13 (*m*, 1 H); 5.15–5.26 (*m*, 1 H); 5.27–5.36 (*m*, 1 H); 5.71–5.89 (*m*, 1 H); 6.55–6.72 (*m*, 2 H); 7.16–7.35 (*m*, 11 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 8.7; 14.1; 15.6; 16.1; 18.0; 19.2; 22.6; 25.5; 28.3(3 C); 29.3; 29.5; 29.6 (7 C); 31.0; 31.9; 32.2; 39.6; 40.1; 43.1; 43.5; 54.2; 56.7; 58.3; 66.1; 69.8; 70.8; 73.3; 73.9; 74.7; 77.3; 79.9; 119.0; 127.6; 127.7; 127.8 (2 C); 128.4 (2 C); 131.4; 137.2; 137.6; 155.6; 169.8; 170.5; 171.4; 176.2. ESI-MS: 974 ($[M + Na]^+$). HR-MS: 974.6102 ($C_{54}H_{85}NaN_3O_{11}^+$; calc. 974.6081).

*(6*S*,12*R*)-18-[(1*S*)-1-(Benzyloxy)ethyl]-6-[(benzyloxy)methyl]-11-hydroxy-2,2,10,12-tetramethyl-4,7,13,16-tetraoxo-15-(propan-2-yl)-9-tridecyl-3,8-dioxa-5,14,17-triazanonadecan-19-oic Acid* (**27**). To a soln. of **6** (950 mg, 0.99 mmol) in THF (10.0 ml) were added morpholine (0.44 ml, 4.5 mmol) and $Pd(PPh_3)_4$ (115.4 mg, 0.1 mmol) at 25°. After 30 min, the mixture was diluted with Et_2O and treated with a 0.5M aq. soln. of citric acid. Separation of both phases was followed by extraction of the aq. layer with Et_2O, and the combined org. extracts were washed with H_2O and brine, dried ($NaSO_4$), filtered, and concentrated under reduced pressure. The resulting crude residue was purified by CC (SiO_2; MeOH/$CHCl_3$ (10%)) to furnish **27** (693 mg, 75%). Colorless liquid. R_f (10% MeOH/$CHCl_3$) 0.8. $[\alpha]_D^{31} = -12.6$ (*c* = 1.6, $CHCl_3$). IR (neat): 1028, 1461, 1645, 1710, 1732, 3311. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.86 (*t*, *J* = 7.2, 3 H); 0.88 (*d*, *J* = 6.0, 3 H); 0.95 (*t*, *J* = 7.2, 3 H); 0.97 (*d*, *J* = 6.0, 3 H); 1.09 (*d*, *J* = 7.2, 3 H); 1.16 (*d*, *J* = 6.8, 3 H); 1.18–1.33 (*m*, 23 H); 1.42 (*s*, 9 H); 1.52–1.65 (*m*, 1 H); 1.67–1.79 (*m*, 1 H); 2.07–2.20 (*m*, 1 H); 2.44–2.58 (*m*, 1 H); 3.31–3.39 (*m*, 1 H); 3.57–3.68 (*m*, 1 H); 3.78–3.91 (*m*, 1 H); 4.08–4.18 (*m*, 1 H); 4.22–4.33 (*m*, 1 H); 4.42–4.61 (*m*, 6 H); 5.17 (*d*, *J* = 10.5, 1 H); 6.52–6.71 (*m*, 2 H); 7.15–7.34 (*m*, 11 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 9.5; 14.5; 16.0; 16.5; 18.4; 19.7; 23.1; 25.9; 28.7 (3 C); 29.7 (6 C); 29.9; 30.0; 31.4; 32.3; 32.7; 40.0; 40.5; 43.5; 44.0; 54.6; 57.1; 58.7; 70.3; 71.2; 73.8; 74.3; 75.2; 77.6; 80.3; 128.0; 128.1; 128.2; 128.4; 128.6 (2 C); 128.8 (2 C); 137.7; 138.0; 156.0; 170.3; 171.0; 171.8; 176.6. ESI-MS: 934 ($[M + Na]^+$). HR-ESI-MS: 934.5754 ($C_{51}H_{81}NaN_3O_{11}^+$; calc. 934.5768).

*(3*S*,6*S*,9*S*)-6-[1-(Benzyloxy)ethyl]-3-[(benzyloxy)methyl]-13-hydroxy-12,14-dimethyl-9-(propan-2-yl)-15-tridecyl-1-oxa-4,7,10-triazacyclopentadecane-2,5,8,11-tetrone* (**29**). To a soln. of **27** (85 mg, 0.09 mmol) in anh. CH_2Cl_2 (2 ml) was added TFA (1 ml) at 0°. The mixture was stirred for 3 h at r.t., then, the solvents were evaporated under reduced pressure, and the crude product was diluted with toluene (2 ml) and concentrated again, repeating this operation twice. The resulting salt **28** was used for the macrocyclization step without any further purification.

A soln. of the TFA salt **28** in DMF (400 ml, 2.4 mM) was treated with DEPC (0.07 ml, 0.47 mmol) at 25°, and, after 30 min, with EtN^iPr_2 (0.09 ml, 0.51 mmol). The mixture was allowed to react at this temp. for 48 h, after which DMF was removed by distillation under vacuum (0.5 mm Hg) at 50°. The crude mixture was purified by CC (SiO_2; AcOEt/hexane (10%)) to provide **29** (18.5 mg, 25%). Clear oil. R_f

(40% acetone/toluene) 0.5. IR (neat): 1074, 1214, 1441, 1646, 1738, 2853, 2924, 3457. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.85 (*d*, *J* = 8.3, 3 H); 0.88 (*d*, *J* = 9.8, 3 H); 0.90 (*d*, *J* = 9.8, 3 H); 1.03 (*d*, *J* = 6.8, 3 H); 1.09 (*d*, *J* = 6.0, 3 H); 1.18 (*d*, *J* = 6.0, 3 H); 1.20 – 1.37 (*m*, 23 H); 1.38 – 1.62 (*m*, 1 H); 1.90 – 2.04 (*m*, 1 H); 2.05 – 2.32 (*m*, 1 H); 2.41 – 2.61 (*m*, 1 H); 3.47 – 3.69 (*m*, 1 H); 3.71 – 3.90 (*m*, 2 H); 3.93 – 4.13 (*m*, 1 H); 4.35 (*d*, *J* = 11.3, 1 H); 4.43 (*d*, *J* = 11.3, 1 H); 4.50 – 4.65 (*m*, 3 H); 4.66 – 4.81 (*m*, 2 H); 5.10 – 5.24 (*m*, 1 H); 6.94 (br. *d*, *J* = 8.3, 1 H); 7.05 – 7.34 (*m*, 10 H); 7.53 (br. *d*, *J* = 7.6, 1 H); 7.72 (br. *d*, *J* = 8.3, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 14.1; 15.0; 16.1; 16.2; 16.6; 17.4; 17.9; 19.0; 22.6; 26.6; 29.1; 29.3; 29.4; 29.5; 29.6 (3 C); 31.9; 40.2; 44.0; 53.2; 56.7; 63.5; 68.2; 71.5; 72.0; 73.1; 74.3; 75.6; 81.0; 127.4; 127.5; 127.7; 127.8; 127.9; 128.1; 136.9; 137.7; 168.7; 169.8; 171.3; 178.2. ESI-MS: 816 ($[M+Na]^+$). HR-ESI-MS: 816.5118 ($C_{46}H_{71}N_3NaO_8^+$; calc. 816.5138).

*Ethyl (2*E*,4*R*,5*R*)-5-(Methoxymethoxy)-2,4-dimethyloctadec-2-enoate* (**30**). To **12** (2.6 g, 7.3 mmol) in anh. CH_2Cl_2 (30 ml) at 0° was added EtN^iPr_2 (7.7 ml, 44.0 mmol) and cat. amount of DMAP. After 15 min. chloromethyl methyl ether (MOMCl) (2.22 ml, 29.4 mmol) was added dropwise during 10 min, and stirring was continued for further 12 h. The mixture was diluted with H_2O (30 ml) and extracted with CH_2Cl_2 (2 × 15 ml). The combined org. extracts were washed with brine, dried (Na_2SO_4), and concentrated in vacuum. The obtained crude product was purified by CC (SiO_2; AcOEt/hexane (4%)) to afford **30** (2.54 g, 87%). Clear oil. R_f (10% AcOEt/hexane) 0.7. $[\alpha]_D^{31} = +23.2$ (*c* = 1.0, $CHCl_3$). IR (neat): 1035, 1248, 1514, 1734, 2934. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.88 (*t*, *J* = 6.8, 3 H); 1.02 (*d*, *J* = 6.8, 3 H); 1.21 – 1.36 (*m*, 23 H); 1.30 (*t*, *J* = 6.8, 3 H); 1.41 – 1.56 (*m*, 1 H); 1.48 (*s*, 3 H); 2.62 – 2.77 (*m*, 1 H); 3.35 (*s*, 3 H); 3.41 (*q*, *J* = 6.0, 1 H); 4.17 (*q*, *J* = 6.8, 1 H); 4.58 (*d*, *J* = 6.8, 1 H); 4.62 (*d*, *J* = 6.8, 1 H); 6.62 (*d*, *J* = 9.8, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 12.5; 14.1; 14.2; 15.3; 22.7; 25.3; 29.3; 29.5; 29.6 (5 C); 29.7; 31.8; 31.9; 36.7; 55.8; 60.4; 81.0; 96.1; 127.3; 144.1; 168.2. ESI-MS: 421 ($[M+Na]^+$). HR-ESI-MS: 421.3341 ($C_{24}H_{46}NaO_4^+$; calc. 421.3328).

*Ethyl (2*E*,4*R*,5*R*)-5-{[(*tert*-Butyl)(dimethyl)silyl]oxy}-2,4-dimethyloctadec-2-enoate* (**31**). To a stirred soln. of **12** (2.0 g, 5.65 mmol) in anh. CH_2Cl_2 (20 ml) and 2,6-lutidine (1.0 ml, 7.91 mmol) at 0° was added (*tert*-butyl)(dimethyl)silyl TBSOTf; (1.68 ml, 7.34 mmol) dropwise and stirred for 2 h at r.t. The reaction was quenched with H_2O, and the mixture was extracted with CH_2Cl_2 (3 × 5 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. CC (SiO_2; AcOEt/hexane (2%)) of the crude product afforded **31** (2.35 g, 89%). Colorless liquid. R_f (10% AcOEt/hexane) 0.7. $[\alpha]_D^{30} = +19.2$ (*c* = 1.4, $CHCl_3$). IR (neat): 1028, 1238, 1528, 1730, 2930, 3346. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.04 (*s*, 6 H); 0.87 – 0.94 (*m*, 12 H); 0.99 (*d*, *J* = 6.6, 3 H); 1.18 – 1.38 (*m*, 26 H); 1.39 – 1.54 (*m*, 1 H); 1.84 (*s*, 3 H); 2.49 – 2.67 (*m*, 1 H); 3.56 (*q*, *J* = 5.3, 1 H); 4.18 (*q*, *J* = 6.8, 2 H); 6.64 (*d*, *J* = 10.0, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): −4.2; −4.6; 12.5; 14.1; 14.3; 14.5; 18.1; 22.7; 24.8; 25.7; 25.9 (3 C); 29.3; 29.6 (5 C); 29.8; 31.9; 35.1; 37.9; 60.4; 75.1; 126.3; 145.6; 168.3. ESI-MS: 491 ($[M+Na]^+$). HR-ESI-MS: 491.3811 ($C_{28}H_{56}NaO_3Si^+$; calc. 491.3821).

*(2*E*,4*R*,5*R*)-5-(Methoxymethoxy)-2,4-dimethyloctadec-2-en-1-ol* (**32**). A soln. of **30** (2.32 g, 5.83 mmol) in 30 ml of CH_2Cl_2 was cooled to −10°. DIBAL-H (8.3 ml, 2.0 mmol; 20% soln. in toluene) was then added dropwise during 5 min. The resulting mixture was stirred for 2 h before quenching the reaction with sat. aq. $KNaC_4H_4O_6 \cdot 4\ H_2O$ soln. (10 ml). The mixture was warmed to r.t. and stirred for 5 h. Org. layer was separated, and aq. layer was extracted with CH_2Cl_2 (2 × 10 ml). Combined org. layer was dried (Na_2SO_4) and evaporated. CC (SiO_2; AcOEt/hexane (10%)) of the crude product afforded **32** (1.93 g, 93%). Colorless liquid. R_f (20% AcOEt/hexane) 0.4. $[\alpha]_D^{30} = +16.2$ (*c* = 1.5, $CHCl_3$). IR (neat): 1163, 1273, 1638, 2987, 3274, 3454. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.88 (*t*, *J* = 6.8, 3 H); 0.96 (*d*, *J* = 6.8, 3 H); 1.21 – 1.36 (*m*, 23 H); 1.40 – 1.51 (*m*, 1 H); 1.67 (*s*, 3 H); 2.53 – 2.66 (*m*, 1 H); 3.35 (*s*, 3 H); 3.30 – 3.40 (*m*, 1 H); 3.96 (*s*, 2 H); 5.29 (*d*, *J* = 9.8, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 13.9; 14.1; 16.4; 22.6; 25.4; 29.3; 29.6; 29.8; 31.6; 31.9; 35.5; 55.7; 68.8; 82.0; 96.1; 128.5; 134.6. ESI-MS: 379 ($[M+Na]^+$). HR-ESI-MS: 379.3243 ($C_{22}H_{44}NaO_3^+$; calc. 379.3251).

*(2*E*,4*R*,5*R*)-5-{[*tert*-Butyl(dimethyl)silyl]oxy}-2,4-dimethyloctadec-2-en-1-ol* (**33**). A soln. of unsaturated ester **31** (2.20 g, 4.7 mmol) in 10 ml of CH_2Cl_2 was cooled to −10°. DIBAL-H (8.4 ml, 11.75 mmol; 20% soln. in toluene) was then added dropwise during 5 min. The resulting mixture was stirred for 2 h before quenching the reaction with sat. aq. $KNaC_4H_4O_6 \cdot 4\ H_2O$ soln. (15 ml). The mixture was warmed to r.t. and stirred for 5 h. Org. layer was separated, and aq. layer was extracted with CH_2Cl_2 (2 × 10 ml). Combined org. layer was dried (Na_2SO_4) and evaporated. CC (SiO_2; AcOEt/hexane (8%))

of the crude product furnish **33** (1.86 g, 93%). Colorless liquid. R_f (20% AcOEt/hexane) 0.4. $[\alpha]_D^{30} = +18.2$ ($c = 1.5$, $CHCl_3$). IR (neat): 1166, 1284, 1652, 2980, 3253, 3447. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.02 (*s*, 6 H); 0.83 – 0.95 (*m*, 15 H); 1.18 – 1.33 (*m*, 23 H); 1.35 – 1.45 (*m*, 1 H); 1.66 (*s*, 3 H); 2.49 – 2.53 (*m*, 1 H); 3.47 (*q*, $J = 5.3$, 1 H); 3.95 (*s*, 2 H); 5.27 (*d*, $J = 8.7$, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): – 4.2; – 4.4; 13.8; 14.1; 15.9; 18.2; 22.7; 24.8; 25.9 (3 C); 29.3; 29.5; 29.6 (5 C); 29.7; 29.9; 31.9; 34.7; 69.1; 76.0; 130.1; 133.5. ESI-MS: 449 ($[M + Na]^+$).

*(2*S*,3*S*,4*R*,5*R*)-5-(Methoxymethoxy)-2,4-dimethyloctadecane-1,3-diol* (**34**). To the soln. of **32** (1.8 g, 5.05 mmol) in dry THF (20 ml) was added $BH_3 \cdot$ DMS (0.72 ml, 7.58 mmol) during 15 min, maintaining the temp. at – 10°. The mixture was then allowed to warm to 0° and stirred during 4 h. The soln. was cooled to – 10°, and 3N NaOH (until the mixture was basic, maintaining the temp. at – 10°.) and H_2O_2 (5 ml, 30% soln. in H_2O) were added, and the mixture was further stirred during 1 h and diluted with AcOEt (30 ml). The org. layers were separated and washed with brine (1 × 20 ml), dried (Na_2SO_4), and to give a crude product, which was purified by CC (SiO_2; AcOEt/hexane (5%)) to afford **34** (1.51 g, 80%). Colorless liquid. R_f (30% AcOEt/hexane) 0.5. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.78 (*d*, $J = 7.0$, 3 H); 0.88 (*t*, $J = 7.0$, 3 H); 0.95 (*d*, $J = 7.0$, 3 H); 1.16 – 1.39 (*m*, 23 H); 1.36 – 1.50 (*m*, 1 H); 1.51 – 1.63 (*m*, 1 H); 1.64 – 1.75 (*m*, 1 H); 1.82 (br. *s*, OH); 3.40 (*s*, 3 H); 3.49 – 4.04 (*m*, 4 H); 4.64 (*d*, $J = 6.4$, 1 H); 4.76 (*d*, $J = 6.4$, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 5.5; 13.7; 14.0; 22.6; 25.5; 29.3; 29.5; 29.6; 29.7 (5 C); 31.4; 31.9; 36.5; 37.4; 56.0; 68.7; 82.1; 83.4; 95.4. ESI-MS: 397 ($[M + Na]^+$). HR-ESI-MS: 397.3350 calc. ($C_{22}H_{46}NaO_4^+$; calc.397.3364).

*(2*S*,3*S*,4*R*,5*R*)-5-{[(*tert*-Butyl)(dimethyl)silyl]oxy}-2,4-dimethyloctadecane-1,3-diol* (**35**). To the soln. of **33** (1.7 g, 3.99 mmol) in dry THF (20 ml) was added $BH_3 \cdot$ DMS (0.57 ml, 5.98 mmol) during 15 min maintaining the temp. at 0°. The mixture was then allowed to warm to r.t. and stirred during 4 h. The soln. was cooled to 0°, and 3N NaOH (until the mixture was basic, maintaining the temp. at 0°.) and H_2O_2 (5 ml, 30% soln. in H_2O) were added, and the mixture was further stirred during 1 h and diluted with AcOEt (20 ml). The org. layers were separated and washed with brine (1 × 15 ml), dried (Na_2SO_4) and evaporated to give a crude product, which was purified by CC (SiO_2; AcOEt/hexane (5%)) to give **35** (1.38 g, 78%). Colorless liquid. R_f (30% AcOEt/hexane) 0.4. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.04 (*s*, 6 H); 0.70 (*d*, $J = 6.8$, 3 H); 0.74 – 0.88 (*m*, 15 H); 1.10 – 1.29 (*m*, 23 H); 1.34 – 1.55 (*m*, 1 H); 1.57 – 1.80 (*m*, 1 H); 1.71 – 1.86 (*m*, 1 H); 3.25 (br. *s*, OH); 3.41 – 3.65 (*m*, 3 H); 3.70 – 3.88 (*m*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): – 3.5; – 4.6; 4.7; 13.6; 14.1; 22.7; 25.4; 25.8 (3 C); 29.3; 29.5; 29.6 (6 C); 29.7; 31.9; 34.9; 36.2; 37.5; 68.9; 79.0; 82.7. ESI-MS: 467 ($[M + Na]^+$).

*(2*R*,3*R*,4*R*,5*R*)-3-Hydroxy-5-(methoxymethoxy)-2,4-dimethyloctadecanoic Acid* (**10**). To a soln. of **34** (1.4 g, 3.74 mmol) in CH_2Cl_2 (20 ml) at 0° were added (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO; 58.5 mg, 0.37 mmol) and bis(acetoxy)iodobenzene (BAIB; 1.32 g, 4.11 mmol). After stirring at 0° for 2 h, a 20% aq. $Na_2S_2O_3$ (5 ml) soln. was added. The products were extracted with $CHCl_3$, and the org. layer was washed with a 20% aq. $Na_2S_2O_3$ soln. and then dried (Na_2SO_4). Removal of the solvent under reduced pressure gave a crude aldehyde (1.4 g). The crude aldehyde was dissolved in MeCN (12 ml) and H_2O (4 ml). To this soln. were added 2-methylbut-2-ene (0.08 ml, 0.95 mmol), $NaH_2PO_4 \cdot 2\,H_2O$ (1.47 g, 9.4 mmol), and $NaClO_2$ (677 mg, 7.52 mmol), and the mixture was stirred at r.t. for 20 min. To the mixture at 0° was added a 1M aq. citric acid soln., and the products were extracted with $CHCl_3$. The org. layer was washed with a 1M aq. citric acid soln. and then dried. Removal of the solvent left a residue, which was purified by CC (SiO_2; AcOEt/hexane (30%)) to give **10** (1.05 g, 72%). Colorless liquid. R_f (40% AcOEt/hexane) 0.5. IR (neat): 1033, 1250, 1513, 1739, 3285, 3439. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.88 (*t*, $J = 7.0$, 3 H); 0.96 (*d*, $J = 7.2$, 3 H); 1.02 (*d*, $J = 7.2$, 3 H); 1.19 – 1.38 (*m*, 23 H); 1.40 – 1.84 (*m*, 2 H); 2.50 – 2.65 (*m*, 1 H); 3.39 (*s*, 3 H); 3.68 – 3.76 (*m*, 1 H); 3.94 (*dd*, $J = 1.9, 8.9$, 1 H); 4.64 (*d*, $J = 6.6$, 1 H); 4.74 (*d*, $J = 6.6$, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 6.0; 10.7; 14.1; 22.6; 25.6; 29.3; 29.5; 29.6 (7 C); 31.4; 31.9; 49.4; 56.0; 76.2; 82.8; 95.5; 205.6. ESI-MS: 411 ($[M + Na]^+$).

*(2*R*,3*R*,4*R*,5*R*)-5-{[*tert*-Butyl(dimethyl)silyl]oxy}-3-hydroxy-2,4-dimethyloctadecanoic Acid* (**11**). To a soln. of **35** (1.20 g, 2.7 mmol) in CH_2Cl_2 (15 ml) at 0° were added TEMPO (42.3 mg, 0.27 mmol) and BAIB (956.3 mg, 2.97 mmol). After stirring at 0° for 2 h, a 20% aq. $Na_2S_2O_3$ soln. was added. The products were extracted with $CHCl_3$, and the org. layer was washed with a 20% aq. $Na_2S_2O_3$ soln. and then dried (Na_2SO_4). Removal of the solvent gave a crude aldehyde (1.2 g).

The aldehyde was dissolved in MeCN (10 ml) and H_2O (2.5 ml). To this soln. were added 2-methylbut-2-ene (0.07 ml, 0.95 mmol), $NaH_2PO_4 \cdot 2\,H_2O$ (1.26 g, 8.06 mmol), and $NaClO_2$ (581 mg, 6.45 mmol), and the mixture was stirred at r.t. for 20 min. To the mixture at 0° was added a 1M aq. citric acid soln., and the products were extracted with $CHCl_3$. The org. layer was washed with a 1M aq. citric acid soln. and then dried (Na_2SO_4). Removal of the solvent left a residue, which was purified by CC (SiO_2; AcOEt/hexane (30%)) to furnish **11** (940 mg, 76%). Colorless liquid. R_f (30% AcOEt/hexane) 0.3. IR (neat): 1031, 1256, 1518, 1731, 3282, 3437. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.09 (*s*, 6 H); 0.87–0.93 (*m*, 15 H); 1.17 (*d*, *J* = 7.3, 3 H); 1.23–1.34 (*m*, 22 H); 1.43–1.63 (*m*, 2 H); 1.66–1.75 (*m*, 1 H); 2.57–2.67 (*m*, 1 H); 3.81–3.89 (*m*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): −3.7; −4.5; 5.7; 14.0; 14.1; 18.0; 22.7; 25.3; 25.8 (3 C); 29.3; 29.5; 29.6 (5 C); 29.7; 31.9; 34.6; 36.8; 43.1; 76.5; 77.3; 180.0. ESI-MS: 481 ($[M+Na]^+$).

*Prop-2-en-1-yl (6*S*)-9-[(1*R*)-1-(Benzyloxy)ethyl]-12-[(benzyloxy)methyl]-2,2-dimethyl-4,7,10-trioxo-6-(propan-2-yl)-3-oxa-5,8,11-triazatridecan-13-oate* (**36**). To a soln. of the Boc-Ser(allyl) (3.12 g, 8.95 mmol) obtained from **37** in CH_2Cl_2 (15 ml) under Ar at 0°, was added TFA (3.5 ml). After stirring at 0° for 1 h, the mixture was concentrated to give a crude amine, which was dissolved in CH_2Cl_2 (25 ml). To this soln. at 0° were added WSC·HCl (2.15g, 11.2 mmol), HOBt (1.0, 7.46 mmol), and Boc-Thr(Bzl)–OH (1.5 g, 7.46 mmol), and the mixture was stirred during of 10 min. To this was added EtN^iPr_2 (until the mixture was basic, maintaining the temp. at 0°), and the whole mixture was further stirred at r.t. for 4 h. The mixture was diluted with CH_2Cl_2 and washed successively with a 1M aq. citric acid soln., sat. aq. $NaHCO_3$ soln., and brine, and then dried (Na_2SO_4). Removal of the solvent left a residue, which was purified by CC (SiO_2; acetone/hexane (12%)) to afford compound Boc-Thr-Ser(allyl) (3.13 g, 92%). Colorless liquid. R_f (30% acetone/hexane) 0.5. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.24 (*d*, *J* = 6.4, 3 H); 1.45 (*s*, 9 H); 3.61 (*dd*, *J* = 3.2, 9.4, 1 H); 3.89 (*dd*, *J* = 3.2, 9.4, 1 H); 4.10–4.25 (*m*, 1 H); 4.30–4.49 (*m*, 3 H); 4.53–4.69 (*m*, 4 H); 4.70–4.84 (*m*, 1 H); 5.17–5.35 (*m*, 2 H); 5.52 (*bd*, *J* = 6.0, 1 H); 5.77–5.94 (*m*, 1 H); 7.13–7.37 (*m*, 10 H); 7.52 (*bd*, *J* = 7.7, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 15.0; 28.2 (3 C); 52.8; 57.3; 66.0; 69.4; 71.4; 73.1; 74.9; 80.0; 118.6; 127.5; 127.6; 127.7; 128.2; 128.3; 131.4; 137.3; 138.0; 155.6; 169.4; 169.8. ESI-MS: 549 ($[M+Na]^+$).

To a soln. of the Boc-Thr-Ser(allyl) (3.12 g, 7.16 mmol) in CH_2Cl_2 (25 ml) under Ar at 0° was added TFA (3.5 ml). After stirring at 0° for 1 h, the mixture was concentrated to give a crude salt, which was dissolved in CH_2Cl_2 (25 ml). To this soln. at 0° were added WSC·HCl (1.72 g, 8.95 mmol), HOBt (806.6 mg, 5.97 mmol), and Boc-Val (1.2 g, 5.97 mmol), and the mixture was stirred during of 10 min. To this was added EtN^iPr_2 (until the mixture was basic, maintaining the temp. at 0°), and the whole mixture was further stirred at r.t. for 4 h. The mixture was diluted with CH_2Cl_2 and washed successively with a 1M aq. citric acid soln., sat. aq. $NaHCO_3$ soln., and brine, and then dried (Na_2SO_4). Removal of the solvent left a residue, which was purified by CC (SiO_2; using acetone/hexane (10%)) to give **36** (3.36 g, 90%). Colorless liquid. R_f (30% acetone/hexane) 0.6. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.9 (*d*, *J* = 6.8, 3 H); 0.96 (*d*, *J* = 6.8, 3 H); 1.22 (*d*, *J* = 6.4, 3 H); 1.42 (*s*, 9 H); 2.06–2.22 (*m*, 1 H); 3.60 (*dd*, *J* = 3.4, 9.4, 1 H); 3.89 (*dd*, *J* = 3.4, 9.4, 1 H); 3.94–4.06 (*m*, 1 H); 4.10–4.23 (*m*, 1 H); 4.37 (*d*, *J* = 12.3, 1 H); 4.44 (*d*, *J* = 12.3, 1 H); 4.57–4.82 (*m*, 6 H); 5.06 (br. *d*, *J* = 7.9, 1 H); 5.17–5.35 (*m*, 2 H); 5.77–5.93 (*m*, 1 H); 6.89 (br. *d*, *J* = 6.2, 1 H); 7.13–7.40 (*m*, 10 H); 7.56 (br. *d*, *J* = 8.3, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 14.7; 17.6; 19.2; 28.2 (3 C); 30.9; 52.8; 55.8; 59.9; 66.0; 69.3; 71.4; 73.1; 73.8; 74.2; 79.8; 118.5; 127.5 (4 C); 127.6; 127.7; 128.3 (4 C); 131.5; 137.3; 137.9; 155.7; 169.2; 169.3; 171.6. ESI-MS: 648 ($[M+Na]^+$).

*Prop-2-en-1-yl (5*R*,6*R*,7*R*,8*R*,11*S*,14*S*,17*S*)-14-[1-(Benzyloxy)ethyl]-17-[(benzyloxy)methyl]-7-hydroxy-6,8-dimethyl-9,12,15-trioxo-11-(propan-2-yl)-5-tridecyl-2,4-dioxa-10,13,16-triazaoctadecan-18-oate* (**8**). To a soln. of **36** (1.46 g, 2.78 mmol) in CH_2Cl_2 (15 ml) under Ar at 0° was added TFA (1.5 ml). After stirring at 0° for 1 h, the mixture was concentrated to give a crude amine salt, which was dissolved in CH_2Cl_2 (1.9 ml). To this soln. at 0° were added the WSC·HCl (667 mg, 3.48 mmol), HOBt (313.4 mg, 2.78 mmol), and **10** (900 mg, 2.78 mmol), and the whole mixture was stirred at r.t. for 4 h. The mixture was diluted with CH_2Cl_2 and washed successively with a 1M aq. citric acid soln., sat. aq. $NaHCO_3$ soln., and brine, and then dried (Na_2SO_4). Removal of the solvent left a residue, which was purified by CC (SiO_2; acetone/hexane (20%)) to afford **8** (1.87 g, 90%). Colorless liquid. R_f (40% acetone/hexane) 0.5. $[\alpha]_D^{30} = -14.3$ (*c* = 1.0, $CHCl_3$). IR (neat): 1101, 1213, 1547, 1636, 1743, 2856, 2926, 3276. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.88 (*t*, *J* = 7.1, 3 H); 0.92 (*dd*, *J* = 2.4, 7.1, 3 H); 0.95 (*d*, *J* = 7.8, 3 H); 0.97 (*d*, *J* = 7.1, 3 H); 1.09 (*t*, *J* = 7.8, 3 H); 1.19 (*d*, *J* = 7.1, 3 H); 1.20–1.35 (*m*, 23 H); 1.38–1.51 (*m*, 1 H); 1.52–1.76 (*m*,

1 H); 2.11–2.26 (*m*, 1 H); 2.40–2.50 (*m*, 1 H); 3.34 (*s*, 3 H); 3.54–3.65 (*m*, 1 H); 3.67–3.77 (*m*, 2 H); 3.83–3.91 (*m*, 1 H); 4.08–4.20 (*m*, 1 H); 4.23–4.34 (*m*, 1 H); 4.38 (*d*, *J* = 11.7, 1 H); 4.46 (*d*, *J* = 11.7, 1 H); 4.51–4.78 (*m*, 8 H); 5.19 (*dd*, *J* = 5.5, 9.4, 1 H), 5.28 (*d*, *J* = 17.2, 1 H); 5.77–5.90 (*m*, 1 H); 6.61–6.67 (*m*, 1 H); 7.06 (*dd*, *J* = 7.8, 18.6, 1 H); 7.18–7.35 (*m*, 10 H); 7.48 (*dd*, *J* = 8.3, 18.6, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 6.5; 14.1; 14.8; 15.8; 17.8; 19.3; 22.6; 25.7; 29.0; 29.3; 29.6 (6 C); 29.8; 30.6; 31.4; 31.8; 37.2; 44.0; 52.7; 55.8; 56.2; 58.6; 66.0; 69.3; 71.4; 73.0; 74.2; 82.2; 95.5; 118.5; 127.5 (4 C); 127.6; 127.7; 128.3 (4 C); 131.5; 137.3; 137.8; 169.2; 171.3; 176.1; 176.3. ESI-MS: 918 ($[M+Na]^+$). HR-ESI-MS: 918.5790 ($C_{51}H_{81}N_3NaO_{10}^+$; calc. 918.5819).

*(5*R*,6*R*,7*R*,8*S*,11*S*,14*S*,17*S*)-14-[1-(Benzyloxy)ethyl]-17-[(benzyloxy)methyl]-7-hydroxy-6,8-dimethyl-9,12,15-trioxo-11-(propan-2-yl)-5-tridecyl-2,4-dioxa-10,13,16-triazaoctadecan-18-oic Acid* (**37**). To a soln. of **8** (250 mg, 0.28 mmol) in THF (10.0 ml) were added morpholine (0.02 ml, 0.28 mmol) and $Pd(PPh_3)_4$ (33 mg, 0.028 mmol) at 25°. After 3 h, the mixture was diluted with Et_2O and treated with a 0.5M aq. soln. of citric acid. Separation of both phases was followed by extraction of the aq. layer with Et_2O, and the combined org. extracts were washed with H_2O (8 ml) and brine (10 ml), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The resulting crude residue was purified by CC (SiO_2; acetone/hexane (50%)) to give **37** (176.7 mg, 74%). Colorless liquid. R_f (40% acetone/hexane) 0.2. $[\alpha]_D^{30} = -20.1$ ($c = 1.6$, $CHCl_3$). IR (neat): 1036, 1248, 1372, 1731, 2924, 3445. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.80–0.99 (*m*, 12 H); 1.07 (*t*, *J* = 5.7, 3 H); 1.18 (*d*, *J* = 6.2, 3 H); 1.20–1.35 (*m*, 23 H); 1.41–1.80 (*m*, 2 H); 1.96–2.17 (*m*, 1 H); 2.35–2.54 (*m*, 1 H); 3.35 (*s*, 3 H); 3.36–3.43 (*m*, 1 H); 3.60–3.74 (*m*, 2 H); 3.75–3.93 (*m*, 1 H); 4.02–4.20 (*m*, 1 H); 4.38–4.46 (*m*, 2 H); 4.47–4.78 (*m*, 7 H); 6.99 (*bd*, *J* = 8.1, 1 H); 7.14–7.36 (*m*, 10 H); 7.48 (*bd*, *J* = 7.6, 1 H); 7.60 (*bd*, *J* = 8.9, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 6.5; 11.4; 14.1; 14.8; 17.8; 19.3; 20.4; 22.6; 25.7; 29.0; 29.3; 29.6 (6 C); 30.8; 31.6 (2 C); 31.9; 37.2; 44.1; 52.8; 55.8; 58.7; 60.4; 69.3; 71.5; 73.1; 74.2; 82.4; 95.6; 127.5 (4 C); 127.6; 127.7; 128.3 (4 C); 137.4; 137.9; 169.2; 169.4; 171.3; 176.1. ESI-MS: 856 ($(M+H)^+$.

*(3*S*,6*S*,9*S*,12*R*,13*R*)-6-[1-(Benzyloxy)ethyl]-3-[(benzyloxy)methyl]-13-[(2*S*,3*R*)-3-(methoxymethoxy)hexadecan-2-yl]-12-methyl-9-(propan-2-yl)-1-oxa-4,7,10-triazacyclotridecane-2,5,8,11-tetrone* (**39**). A soln. of **37** (50 mg, 0.06 mmol) in toluene (2 ml) was treated at 0° with Et_3N (0.02 ml, 0.13 mmol) and 2,4,6-trichlorobenzoyl chloride (0.02 ml, 0.08 mmol). To this mixture under Ar at 0° was added a soln. of DMAP (16 mg, 0.13 mmol) in toluene (2 ml), and the resulting mixture was further stirred at 0° for 40 min. The mixture was allowed to warm to r.t. and stirred for 1 h. To the mixture was added 1M aq. citric acid soln. Then, Et_2O (10 ml) was added, and the resulting mixture was sequentially washed with H_2O (5 ml) and brine (5 ml), and the org. phase was separated, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. CC (SiO_2; acetone/hexane (10%)) of the crude product gave **39** (10.7 mg, 22%). Colorless liquid. R_f (40% acetone/hexane) 0.8. IR (neat): 1084, 1248, 1371, 1514, 1614, 1734, 2986, 3455. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.88 (*t*, *J* = 7.0, 3 H); 0.89 (*d*, *J* = 6.2, 3 H); 0.93 (*d*, *J* = 7.0, 3 H); 0.97 (*d*, *J* = 7.0, 3 H); 1.00 (*d*, *J* = 6.9, 3 H); 1.15 (*d*, *J* = 6.9, 3 H); 1.20–1.34 (*m*, 23 H); 1.51–1.66 (*m*, 1 H); 1.70–1.82 (*m*, 1 H); 1.99–2.30 (*m*, 1 H); 2.29–2.53 (*m*, 1 H); 3.36 (*s*, 3 H); 3.63–3.70 (*m*, 1 H); 3.76–3.83 (*m*, 1 H); 4.19 (*d*, *J* = 6.2, 1 H); 4.37–4.48 (*m*, 4 H); 4.50–4.59 (*m*, 4 H); 4.62 (*d*, *J* = 7.0, 1 H); 4.70 (*d*, *J* = 7.0, 1 H); 5.22 (*dd*, *J* = 2.2, 8.8, 1 H); 6.63 (*d*, *J* = 8.8, 1 H); 6.71 (*d*, *J* = 8.8, 1 H); 7.17–7.41 (*m*, 11 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 7.0; 14.2; 15.0; 16.5; 18.1; 19.3; 22.7; 25.8; 29.4; 29.6; 29.7 (2 C); 29.9 (4 C); 31.3; 31.6; 32.0; 37.5; 44.3; 52.2; 55.9; 58.4; 61.9; 71.4; 72.3; 74.7; 82.2; 95.6; 121.2; 127.5 (4 C); 127.6; 127.7 (4 C); 128.3; 133.1; 137.6; 137.7; 146.1; 156.4; 159.9; 171.4; 175.7. ESI-MS: 838 ($[M+H]$)$^+$.

*Prop-2-en-1-yl (5*S*,6*R*,7*R*,8*R*,11*S*,14*S*,17*S*)-14-[1-(Benzyloxy)ethyl]-17-[(benzyloxy)methyl]-7-hydroxy-2,2,3,3,6,8-hexamethyl-9,12,15-trioxo-11-(propan-2-yl)-5-tridecyl-4-oxa-10,13,16-triaza-3-silaoctadecan-18-oate* (**9**). To a soln. of **36** (1.24 g, 2.35 mmol) in CH_2Cl_2 (15 ml) under Ar at 0° was added TFA (1.5 ml). After stirring at 0° for 3 h, the mixture was concentrated to give a crude salt, which was dissolved in CH_2Cl_2 (5 ml). To this soln. at 0° were added the WSC·HCl (565.1 mg, 2.94 mmol), HOBt (264.8 mg, 1.96 mmol), and **11** (900 mg, 1.96 mmol), and the whole mixture was stirred at r.t. for 4 h. The mixture was diluted with CH_2Cl_2 and washed successively with 1M aq. citric acid soln., sat. aq. $NaHCO_3$ soln., and brine, and then dried (Na_2SO_4). Removal of the solvent left a residue, which was purified by CC (SiO_2; acetone/hexane (12%)) to furnish **9** (1.58 g, 90%). Colorless liquid. R_f (40% acetone/hexane) 0.5. $[\alpha]_D^{30} = -10.6$ ($c = 1.0$, $CHCl_3$). IR (neat): 1211, 1540, 1637, 1736, 2851, 2925, 3270. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.08 (*s*, 6 H); 0.88 (*s*, 9 H); 0.92 (*d*, *J* = 7.2, 3 H); 0.96 (*d*, *J* = 6.8, 3 H); 1.05 (*d*, *J* = 6.4,

3 H); 1.07 (*d*, *J* = 6.8, 3 H); 1.11 (*d*, *J* = 6.4, 3 H); 1.20 (*d*, *J* = 6.4, 3 H); 1.21 – 1.37 (*m*, 23 H); 1.41 – 1.58 (*m*, 1 H); 1.62 – 1.74 (*m*, 1 H); 2.12 – 2.27 (*m*, 1 H); 2.33 – 2.47 (*m*, 1 H); 3.58 (*dd*, *J* = 3.4, 9.4, 1 H); 3.65 – 3.77 (*m*, 2 H); 3.78 – 3.92 (*m*, 2 H); 4.06 – 4.21 (*m*, 1 H); 4.28 – 4.48 (*m*, 2 H); 4.53 – 4.66 (*m*, 5 H); 4.67 – 4.80 (*m*, 1 H); 5.19 (*dd*, *J* = 3.4, 10.2, 1 H); 5.28 (*d*, *J* = 17.4, 1 H); 5.74 – 5.92 (*m*, 1 H); 6.80 (*dd*, *J* = 8.3, 12.8, 1 H); 7.08 (*t*, *J* = 7.9, 1 H); 7.11 – 7.37 (*m*, 10 H); 7.52 (*dd*, *J* = 7.9, 8.3, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): – 4.7; – 3.7; 5.4; 14.0; 14.8; 15.8; 17.5; 17.9; 19.3; 22.6; 25.3; 25.7 (3 C); 29.3 (2 C); 29.5; 29.6 (4 C); 29.7; 30.7; 31.8; 34.7; 36.8; 44.0; 52.7; 55.8; 58.6; 66.0; 69.2; 71.4; 73.0; 74.2; 77.5; 118.4; 127.5 (4 C); 127.6; 127.7; 128.2 (4 C); 131.5; 137.3; 137.9; 169.3; 171.5; 176.0; 176.3. ESI-MS: 988 ($[M+Na]^+$). HR-ESI-MS: 988.6394 ($C_{55}H_{91}N_3NaO_9Si^+$; calc. 988.6422).

*(5*R*,6*R*,7*R*,8*S*,11*S*,14*S*,17*S*)-14-[1-(Benzyloxy)ethyl]-17-[(benzyloxy)methyl]-7-hydroxy-2,2,3,3,6,8-hexamethyl-9,12,15-trioxo-11-(propan-2-yl)-5-tridecyl-4-oxa-10,13,16-triaza-3-silaoctadecan-18-oic Acid* (**38**). To a soln. of **9** (300 mg, 0.31 mmol) in THF (8 ml) were added morpholine (0.03 ml, 0.31 mmol) and $Pd(PPh_3)_4$ (36 mg, 0.03 mmol) at 25°. After 4 h, the mixture was diluted with Et_2O (10 ml) and treated with a 0.5M aq. soln. of citric acid (4 ml). Separation of both phases was followed by extraction of the aq. layer with Et_2O (2 × 10 ml), and the combined org. extracts were washed with H_2O (8 ml) and brine (8 ml), dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The resulting crude residue was purified by CC (SiO_2; acetone/hexane (40%)) to yield **38** (230.3 mg, 80%). Colorless liquid. R_f (50% acetone/hexane) 0.3. $[\alpha]_D^{31} = -19.2$ ($c = 1.5$, $CHCl_3$). IR (neat): 1056, 1241, 1376, 1738, 2934, 3415. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.08 (*s*, 6 H); 0.80 – 0.98 (*m*, 21 H); 1.05 (*d*, *J* = 6.4, 3 H); 1.16 (*d*, *J* = 6.4, 3 H); 1.20 – 1.36 (*m*, 23 H); 1.40 – 1.58 (*m*, 1 H); 1.60 – 1.74 (*m*, 1 H); 2.04 – 2.22 (*m*, 1 H); 2.36 – 2.52 (*m*, 1 H); 3.66 (*d*, *J* = 8.8, 1 H); 3.75 (*d*, *J* = 7.6, 1 H); 3.79 – 3.91 (*m*, 2 H); 4.00 – 4.24 (*m*, 1 H); 4.40 (*s*, 2 H); 4.44 – 4.50 (*m*, 1 H); 4.52 (*d*, *J* = 4.9, 1 H); 4.58 (*d*, *J* = 6.6, 1 H); 4.62 – 4.77 (*m*, 2 H); 7.01 – 7.35 (*m*, 11 H); 7.43 (*dd*, *J* = 6.3, 17.2, 1 H); 7.64 (*dd*, *J* = 7.6, 17.0, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): – 4.7; – 3.6; 5.4; 14.0; 14.8; 15.8; 17.5; 17.9; 19.3; 22.6; 25.3; 25.7 (3 C); 29.3; 29.5; 29.6 (4 C); 29.7; 30.7; 31.8; 34.7; 36.8; 44.0; 52.7; 55.8; 58.6; 69.2; 71.4; 73.0; 74.2; 77.5; 127.5 (4 C); 127.6; 127.8; 128.2 (4 C); 137.3; 137.9; 169.3; 171.5; 171.6; 176.1. ESI-MS: 948 ($[M+Na]^+$). HR-ESI-MS: 948.6138 ($C_{52}H_{87}NaN_3O_9Si^+$; calc.948.6109).

*Prop-2-en-1-yl (2*S*)-3-(Benzyloxy)-2-{[(2*S*)-3-(benzyloxy)-2-{[(2*S*)-2-{[(2*R*,3*R*,4*S*,5*R*)-3,5-dihydroxy-2,4-dimethyloctadecanoyl]amino}-3-methylbutanoyl]amino}butanoyl]amino}propanoate* (**42**). To a soln. of **9** (400 mg, 0.42 mmol) in MeOH (5 ml) at 0° was added anh. CSA (52 mg, 0.21 mmol). The mixture was stirred at r.t. for 3 h, and then the reaction was quenched with solid $NaHCO_3$, and the mixture was filtered. The filtrate was concentrated in vacuum. CC (SiO_2; acetone/hexane (40%)) of the crude product gave **42** (211.6 mg, 60%). Colorless liquid. R_f (40% acetone/hexane) 0.2. $[\alpha]_D^{30} = -13.6$ ($c = 1.5$, $CHCl_3$). IR (neat): 1036, 1248, 1372, 1731, 2924, 3445. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.85 (*d*, *J* = 8.3, 3 H); 0.88 (*t*, *J* = 9.8, 3 H); 0.90 (*d*, *J* = 9.8, 3 H); 1.03 (*d*, *J* = 6.8, 3 H); 1.09 (*d*, *J* = 6.0, 3 H); 1.18 (*d*, *J* = 6.0, 3 H); 1.20 – 1.36 (*m*, 23 H); 1.38 – 1.60 (*m*, 1 H); 1.89 – 2.36 (*m*, 2 H); 2.40 – 2.60 (*m*, 1 H); 3.54 (*dd*, *J* = 3.0, 9.0, 1 H); 4.37 – 4.45 (*m*, 1 H); 3.59 – 3.69 (*m*, 1 H); 3.70 – 3.91 (*m*, 2 H); 3.93 – 4.13 (*m*, 1 H); 4.27 – 4.46 (*m*, 2 H); 4.49 – 4.64 (*m*, 5 H); 4.65 – 4.80 (*m*, 2 H); 5.17 (*d*, *J* = 10.6, 1 H); 5.27 (*d*, *J* = 16.6, 1 H); 5.73 – 5.90 (*m*, 1 H); 6.94 (*bd*, *J* = 8.3, 1 H); 7.06 – 7.35 (*m*, 10 H); 7.53 (*bd*, *J* = 7.6, 1 H); 7.72 (*bd*, *J* = 8.3, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 4.8; 12.2; 14.1; 14.5; 14.8; 19.3; 22.6; 26.1; 29.3; 29.5; 29.6 (4 C); 30.8; 31.9; 35.2; 36.9; 44.2; 52.8; 56.0; 58.9; 66.1; 69.3; 71.5; 74.3; 78.4; 118.6; 127.5 (4 C); 127.7; 127.8; 128.3 (4 C); 131.5; 137.4; 137.9; 169.3; 171.3; 173.8; 176.1. ESI-MS: 874 ($[M+Na]^+$). HR-ESI-MS: 874.5544 ($C_{49}H_{77}N_3NaO_9^+$; calc. 874.5557).

*(2*S*)-3-(Benzyloxy)-2-{[(2*S*)-3-(benzyloxy)-2-{[(2*S*)-2-{[(2*R*,3*R*,4*S*,5*R*)-3,5-dihydroxy-2,4-dimethyloctadecanoyl]amino}-3-methylbutanoyl]amino}butanoyl]amino}propanoic Acid* (**43**). To a soln. of **42** (180 mg, 0.21 mmol) in THF (5.0 ml) were added morpholine (0.09 ml, 1.06 mmol) and $Pd(PPh_3)_4$ (25 mg, 0.02 mmol) at r.t. After 3 h, the mixture was diluted with Et_2O (8 ml) and treated with a 0.5M aq. soln. of citric acid (5 ml). Separation of both phases was followed by extraction of the aq. layer with Et_2O, and the combined org. extracts were washed with H_2O and brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The resulting crude residue was purified by CC (SiO_2; acetone/hexane (40%)) to give **43** (108.5 mg, 63%). Colorless liquid. R_f (50% acetone/hexane) 0.2. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.87 (*d*, *J* = 7.0, 3 H); 0.88 (*t*, *J* = 7.0, 3 H); 0.92 (*dd*, *J* = 2.3, 7.0, 3 H), 0.96 (*dd*, *J* = 4.7, 7.0, 3 H), 1.09 (*t*, *J* = 7.8, 3 H); 1.19 (*d*, *J* = 6.2, 3 H); 1.21 – 1.35 (*m*, 23 H); 1.35 – 1.50 (*m*, 1 H); 1.53 – 1.77

(*m*, 1 H); 2.19 (*q*, *J* = 7.0, 1 H); 2.45 (*q*, *J* = 7.0, 1 H); 3.57 (*dd*, *J* = 3.1, 9.3, 1 H); 3.63 (*d*, *J* = 7.0, 1 H); 3.67–3.77 (*m*, 2 H); 3.87 (*dt*, *J* = 3.1, 9.3, 1 H); 4.37–4.45 (*m*, 1 H); 4.53–4.63 (*m*, 4 H); 4.64–4.68 (*m*, 1 H); 4.70–4.77 (*m*, 1 H); 6.60–6.67 (*m*, 1 H); 7.06 (*dd*, *J* = 7.8, 17.0, 1 H); 7.18–7.35 (*m*, 10 H); 7.48 (*dd*, *J* = 8.5, 17.0, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.1; 12.2; 14.1; 14.8; 18.0; 19.3; 22.6; 25.4; 29.3; 29.5; 29.6 (5 C) ; 30.8; 31.9; 35.2; 38.1; 44.2; 52.8;56.3; 58.9; 69.3; 71.5; 73.1; 74.3; 78.2; 127.5 (4 C); 127.7; 127.8; 128.3 (4 C); 137.4; 137.9; 169.3; 171.3; 176.1; 176.3. ESI-MS: 835 ($[M + Na]^+$).

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