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A stereoselective total synthesis of the HCl salts of mycestericins F, G and *ent*-F

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ABSTRACT

The total synthesis of the HCl salts of two natural sphingolipid-related amino acid derivatives, mycestericins F **4** and G **5** together with unnatural *ent*-**4**·**HCl**, starting from the four crucial scaffolds **6**, **8**, **9**, **11** and utilizing the Wittig reaction to build the C_{20} backbone, has been achieved. The selection of selective functional group interconversions accompanied with suitable protection–deprotection protocols in the coupling products **20** and **34** gave the desired structures.

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1. Introduction

Mycestericins (Fig. 1) are an interesting group of sphingolipid-related compounds which have been isolated from the culture broth of *Mycelia sterilia* (ATCC 20349) and fully characterized by Fujita et al.[1] It has been reported that the mycestericins possess a remarkable immuno suppressive activity in terms of suppressing the proliferation of lymphocytes in the mouse allogenic mixed lymphocyte reaction (MLR) with IC_{50} values in the nanomolar range[1] and have similar potential to that of myriocin.[2] Their structure showed the presence of the α-substituted serine scaffold,[3] which constitutes the common feature of all members of the mycestericin family.[1] Both the significant biological activity and the unique structure of the mycestericins continue to gain interest with regard to their total synthesis.

Recently, Chida et al.[4] reported the first total synthesis of mycestericin A **1** (Fig. 1) and its 14-epimer[4] from tartrates and also realized the degradation studies of the aforementioned compounds with the aim of confirming the proposed absolute structure of natural mycestericin A **1**.[1a] In their study, they employed the Overman rearrangement and the Negishi or Suzuki–Miyaura coupling as the key reactions. The synthesis of mycestericin D **2** by Node et al.[5] utilized the L-threonine aldolase-catalysed reaction of 4-benzyloxybutanal and glycine, followed by the selective hydroxymethylation of a more advanced oxazoline derivative for the formation of a quaternary stereocentre and a Wittig reaction to build the non-polar side chain. The total synthesis of mycestericin E **3** has been reported by two groups. Fujita et al.[6] applied the stereoselective acylation of an oxazolidine derived from D-serine for both; to generate the tetrasubstituted carbon and construct

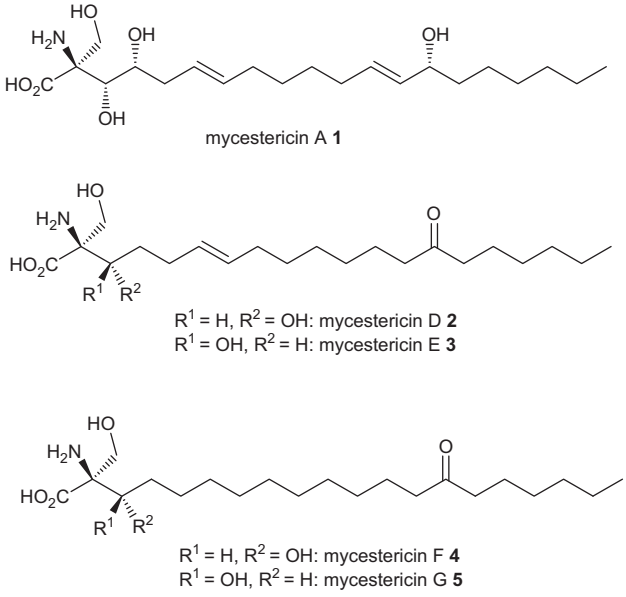

Figure 1. Some selected structures of the mycestericins.

the *E*-olefin. Hatakeyama et al.[7] employed an asymmetric Baylis–Hillman reaction of an achiral aldehyde and Lewis acid-promoted cyclization of an epoxytrichloroacetimidate as the key steps. Recently, two syntheses of mycestericin G **5** have been reported. Kumagai and Shibasaki[8] developed the catalytic asymmetric α-amination of a cyclic α-alkoxycarbonyl amide to incorporate the tetrasubstituted stereogenic centre, and utilized cross-metathesis to extend the side chain. They also succeeded in the total

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synthesis of mycestericin F **4** based on a diastereoselective reduction of the C=O group in the coupling product obtained. Carbery et al.[9] reported the synthesis of mycestericin G **5** and its enantiomer *ent*-**5** in which the Ireland–Claisen rearrangement of serine-derived oxazolidine enol ether substrates for the construction of a β,β′-dihydroxy α-amino acid scaffold and cross-metathesis to establish the requisite lipophilic chain were used. As part of our research aimed at the construction of the naturally occurring bioactive α-substituted α-amino acids as well as the advanced α-substituted serine frameworks,[10] we herein report our total synthesis of mycestericins **4·HCl**, **5·HCl** and *ent*-**4·HCl** according to the synthetic plan outlined in Scheme 1.

2. Results and discussion

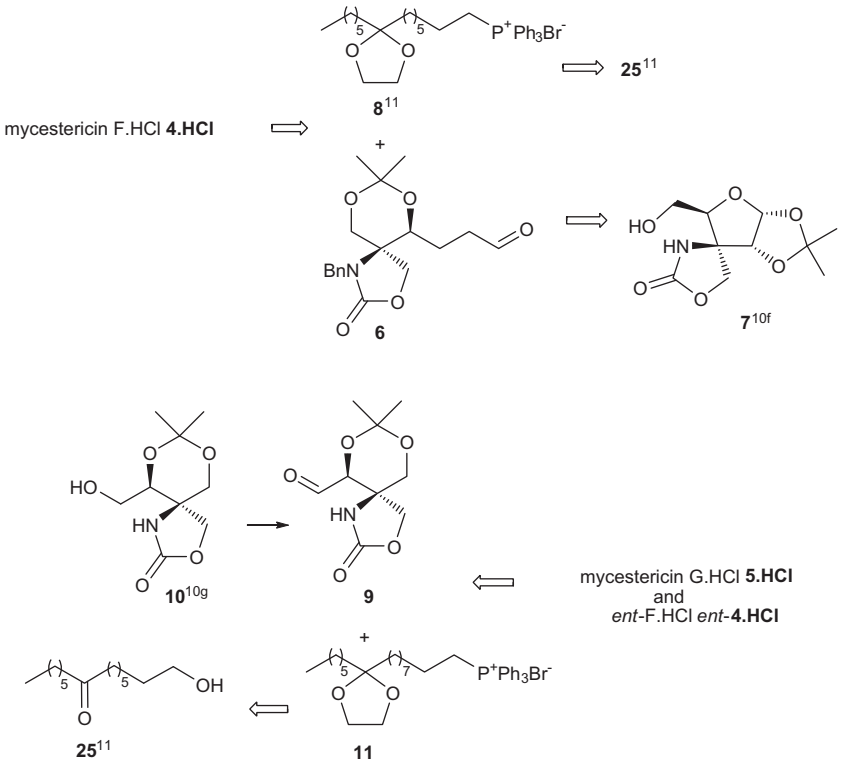
Retrosynthetically (Scheme 1), the carbon backbone of our target molecules **4·HCl**, **5·HCl** and *ent*-**4·HCl** could be disconnected into the highly functionalized polar scaffolds, aldehydes **6** and **9**, and the lipophilic frameworks, the corresponding phosphonium salts **8**[11] and **11**. Segments **6** and **9** could be derived from the known chiral oxazolidinones **7**[10f] and **10**,[10g] developed and prepared in our laboratory. On the other hand, the hydrophobic C_{14} and C_{16} counterparts **8**[11] and **11** were proposed to be synthesized from the known 14-hydroxytetradecan-7-one **25**.[11] The Wittig reaction of **6** and **9** with the corresponding phosphonium salts **8** and **11** was expected to complete the carbon backbone in these structures.

2.1. Preparation of mycestericin F·HCl 4·HCl

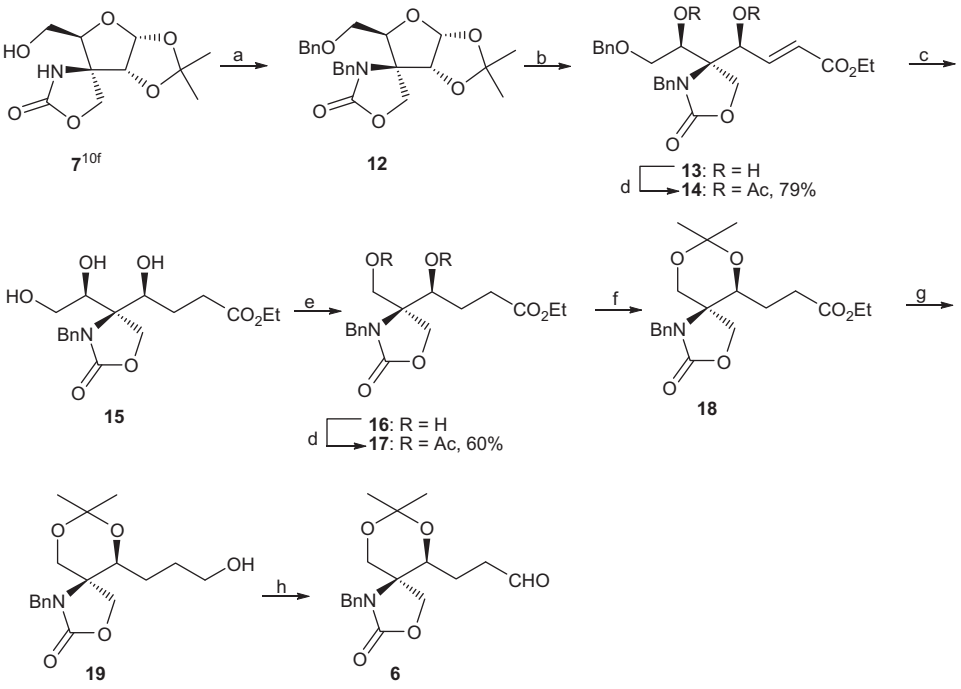
At first, we began with the synthesis of aldehyde **6** (Scheme 1), the key substrate for the Wittig reaction, starting with the 3-*C*-branched xylofuranose-oxazolidinone **7**,[10f] readily prepared on a large scale in our laboratory. Treatment with benzyl bromide in the presence of NaH and TBAI resulted in the formation of compound **12** in 98% yield (Scheme 2). Hydrolysis of the acetonide group in **12** with aqueous TFA followed by Wittig reaction ($Ph_3P{=}CHCO_2Et$, benzoic acid) afforded the corresponding α,β-unsaturated ester **13** as a single isomer in 70% overall yield from **12**. Due to the overlap of the proton signals in **13** in $CDCl_3$ and C_6D_6 solutions, it was not possible to find all values of the vicinal interaction constants and therefore ester **13** was fully characterized as its diacetate **14** (Ac_2O, pyridine DMAP, 79%, Scheme 2). The observed coupling constant in **14** (J = 15.6 Hz) clearly suggested the *trans*-configuration of the double bond. Hydrogenation of **13** under standard conditions (5% Pd/C, EtOH) removed both the double bond and *O*-benzyl protecting group to produce the corresponding derivative **15** (71%, Scheme 2). Its oxidative fragmentation with $NaIO_4$ in CH_3OH/H_2O followed by $NaBH_4$ treatment provided alcohol **16** in 81% yield after two steps. Analysis of its NMR spectra led to the same problems as those for compound **13**; therefore **16** was also transformed into diacetate **17** (Ac_2O, pyridine, DMAP). Isopropylidene protection of the 1,3-diol moiety in **16** with 2,2-dimethoxypropane in dry acetone, in the presence of CSA gave **18** in 83% yield (Scheme 2). To continue the synthesis, ethyl ester **18** was reduced with diisobutylaluminum hydride in THF at −15 °C, providing the corresponding alcohol **19** (68%). Its subsequent oxidation with IBX[12] in CH_3CN furnished the desired aldehyde **6** in 80% yield.

Having established the synthetic route to the segment **6**, which possessed the required functionalities, we were in a position to explore the Wittig reaction, which has been utilized to construct the C_{20} framework in our final molecules. The coupling of aldehyde **6** with a ylide derived from the known phosphonium salt **8**[11] produced an inseparable mixture of olefins **20** ($Z{:}E \approx 3.5{:}1$ ratio, determined by ^{1}H NMR analysis) in 81% yield (Scheme 3). Debenzylation of the *N*-benzyloxazolidinone fragment in **20** with Li in $EtNH_2$/*t*-BuOH[13] followed by reduction using Pearlman's catalyst[14] [$Pd(OH)_2/C$] produced the saturated derivative **21**.

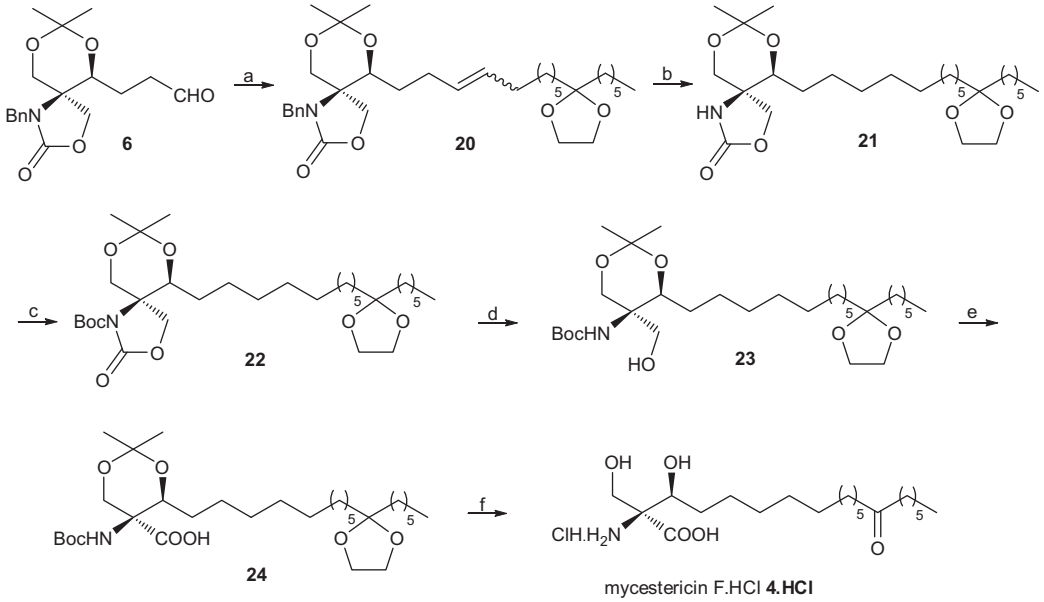
Protection of the carbamate nitrogen atom with a Boc group using Boc_2O and DMAP in CH_3CN afforded derivative **22** in 95% yield. Its exposure to mildly basic conditions (Cs_2CO_3, CH_3OH)[15]



Scheme 1. Synthetic plan.



Scheme 2. Synthesis of aldehyde **6**. Reagents and conditions: (a) BnBr, NaH, TBAI, DMF, 0 °C→rt, 98%; (b) (i) TFA/H_2O (8:2), rt, (ii) $Ph_3P{=}CHCO_2Et$, CH_2Cl_2, $PhCO_2H$, rt, 70% (over 2 steps); (c) H_2, 5% Pd/C, EtOH, rt, 71%; (d) Ac_2O, pyridine, DMAP, rt; (e) (i) $NaIO_4$, CH_3OH/H_2O (1:1), rt, (ii) $NaBH_4$, EtOH, 0 °C→rt, 81% (over 2 steps); (f) 2,2-DMP, acetone, CSA, rt, 83%; (g) DIBAl-H, CH_2Cl_2, −15 °C, 68%; (h) IBX, CH_3CN, reflux, 80%.



Scheme 3. Synthesis of the HCl salt of mycesterin F **4**. Reagents and conditions: (a) LHMDS, **8**,[11] THF, rt, 81%; (b) (i) Li, $EtNH_2$/*t*-BuOH, −78 °C → −20 °C, 77%, (ii) H_2, 20% $Pd(OH)_2$/C, EtOH, rt, 99%; (c) Boc_2O, DMAP, CH_3CN, rt, 95%; (d) Cs_2CO_3, CH_3OH, rt, 94%; (e) (i) PDC, DMF, rt, 87%, (ii) $NaClO_2$, CH_3CN/*t*-BuOH/2-methylbut-2-ene, 0 °C, 95%; (f) 6 M HCl, 100 °C, 87%.

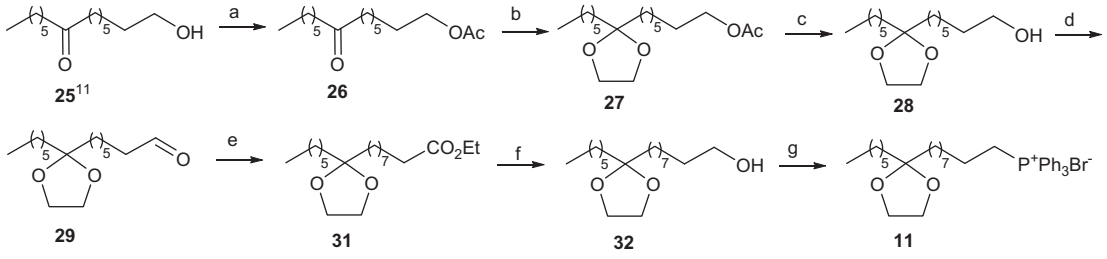
resulted in the formation of the corresponding amino alcohol **23** (94%, Scheme 3). The unprotected hydroxyl group in **23** was oxidized using pyridinium dichromate (PDC) in DMF to afford the aldehyde whose immediate treatment with $NaClO_2$ furnished amino acid **24**. Due to the relatively rapid decomposition of **24** in the standard NMR solvents (CD_3OD, $CDCl_3$ and C_6D_6), it was not possible to correctly determine its structure, therefore further attempted measurements were abandoned and this acid was directly subjected to the deprotection step. Finally, removal of the *N*-Boc, *O*-isopropylidene and ethyleneketal protecting groups in **24** upon acid hydrolysis (6 M HCl) provided the desired product, the HCl salt of mycestericin F·HCl **4·HCl** (87%, Scheme 3). The ^1H NMR data for derivative **4·HCl** matched the known values,[8] but the magnitude of the specific rotation was distinct from the value published[8] and in the ^{13}C NMR spectrum we found the quaternary carbon (C-2) at δ = 71.2 ppm together with C-3 (see Section 4).

2.2. Preparation of *ent*-4·HCl and mycestericin G·HCl 5·HCl

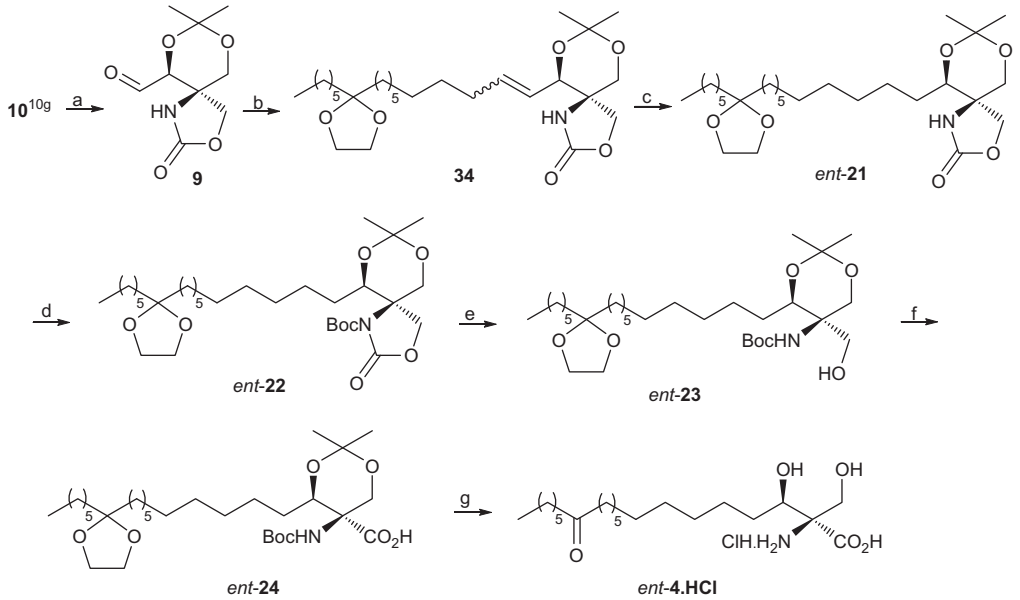
Having successfully completed the synthesis of mycestericin F·HCl, our next efforts were aimed at the preparation of *ent*-**4·HCl**, as shown in Scheme 1. Our first task was to realize the crucial coupling reaction between the aldehyde **9**, prepared on a large scale from **10**,[10g] and the C_{16} hydrophobic side chain **11**. The formation of the phosphonium salt **11** from the known 14-hydroxytetradecan-7-one **25**[11] proceeded without problems. Exposure of **25** to Ac_2O in pyridine produced acetate **26** in 98% yield (Scheme 4). Its ketalization with the freshly prepared $(TMSOCH_2)_2$ in the presence of TMSOTf[16] afforded compound **27** (99%). After removal of the acetyl group (K_2CO_3, CH_3OH, 99%), Swern oxidation of the resultant alcohol **28**[6,11a] led to the corresponding aldehyde **29**[6,17] (93%, Scheme 4). The Wittig reaction of **29** with a stabilized ylide ($Ph_3P{=}CHCO_2Et$) followed by the catalytic hydrogenation of **30** (93%), resulted in the formation of saturated ester **31** in 95% yield (Scheme 4). The $LiAlH_4$ mediated reduction of the ester function in **31** gave alcohol **32** (98%), whose hydroxy group was replaced with a bromide to produce **33** (86%). Finally, the resulting bromide **33** was converted into phosphonium salt **11** (76%) by treatment with Ph_3P in CH_3CN at reflux in the presence of anhydrous Na_2CO_3. Thus, the synthesis of **11** was accomplished in nine steps from **25** and with 51% overall yield.

With the C_{16} counterpart **11** in hand, we next carried out the synthesis of *ent*-**21**, the common substrate for the construction of *ent*-**4·HCl** and mycestericin G·HCl **5·HCl** as shown in Scheme 5. After several experiments, we found that the Wittig reaction of aldehyde **9** with a non-stabilized ylide, prepared from **11**, provided a moderate yield (58%) of the coupling product **34** (isolated as an inseparable mixture of alkenes, $Z{:}E \approx 4.5{:}1$, as determined by ^1H NMR analysis). A mixture of the geometrical isomers **34** obtained was subjected to hydrogenation under atmospheric pressure in EtOH containing 20% $Pd(OH)_2/C$ to furnish the saturated compound *ent*-**21** in 98% yield (Scheme 5). In order to obtain *ent*-**4·HCl**, derivative *ent*-**21** was converted into alcohol *ent*-**23** (87% from *ent*-**21**) by the same series of functional group manipulations as those used in Scheme 4. Stepwise oxidation of *ent*-**23** (DMSO, oxalyl chloride followed by $NaClO_2$) afforded acid *ent*-**24** whose treatment with 6 M HCl led to the formation of the HCl salt of *ent*-**4** in 64% yield (Scheme 5). The spectroscopic and specific rotation data were in good agreement with those reported for mycestericin F·HCl **4·HCl**.

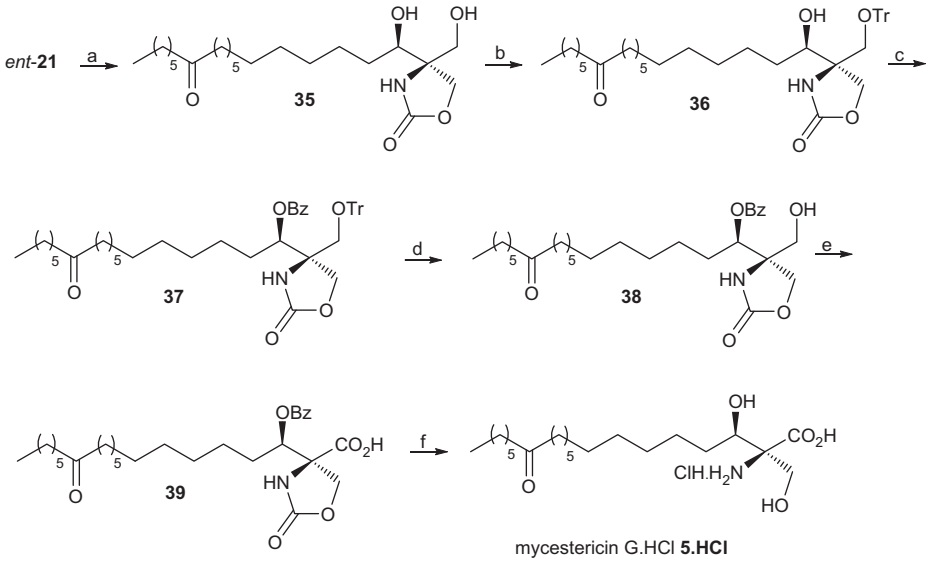
Having successfully accomplished the synthesis of *ent*-**4·HCl**, our next task was to establish a convenient synthetic protocol for the transformation of *ent*-**21** to mycestericin G·HCl **5·HCl**. Thus, the removal of the isopropylidene protection within *ent*-**21** by acid hydrolysis resulted in the production of diol **35** (79%, Scheme 6). After selective tritylation of **35** (TrCl, pyridine and DMAP), the



Scheme 4. Synthesis of phosphonium salt **11**. Reagents and conditions: (a) Ac_2O, pyridine, DMAP, rt, 98%; (b) $(TMSOCH_2)_2$, TMSOTf, CH_2Cl_2, 0 °C, 99%; (c) K_2CO_3, CH_3OH, 0 °C→rt, 99%; (d) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2, −78 °C, 93%; (e) (i) $Ph_3P{=}CHCO_2Et$, CH_2Cl_2, rt, **30**, 93%, (ii) H_2, $Pd(OH)_2/C$, rt, 95%; (f) $LiAlH_4$, Et_2O, 0 °C→rt, 98%; (g) (i) NBS, Ph_3P, DMF, 10 °C, **33**, 86%, (ii) Ph_3P, Na_2CO_3, CH_3CN, reflux, 76%.



Scheme 5. Synthesis of *ent*-**4·HCl**. Reagents and conditions: (a) IBX, CH_3CN reflux, 94%; (b) LHMDS, **11**, THF, 58%; (c) H_2, $Pd(OH)_2/C$, EtOH, 98%; (d) Boc_2O, DMAP, CH_3CN, 94%, rt; (e) Cs_2CO_3, CH_3OH, 92%, rt; (f) (i) DMSO, $(COCl)_2$, CH_2Cl_2, Et_3N, −78 °C, 93%, (ii) $NaClO_2$, CH_3CN/*t*-BuOH/2-methylbut-2-ene, 0 °C→rt, 88%; (g) 6 M HCl, 100 °C, 64%.



Scheme 6. Synthesis of mycestericin G·HCl **5·HCl**. Reagents and conditions: (a) AcOH/H_2O, 80 °C→40 °C, 79%; (b) TrCl, pyridine, DMAP, 60 °C, 88%; (c) BzCl, pyridine, DMAP, rt, 80%; (d) *p*-TsOH, CH_3OH/CH_2Cl_2, rt, 91%; (e) (i) IBX, CH_3CN, reflux, (ii) $NaClO_2$, CH_3CN/*t*-BuOH/2-methylbut-2-ene, 0 °C→rt, 84% (over 2 steps); (f) (i) 10% NaOH, CH_3OH, 80 °C, (ii) 6 M HCl, rt, 80 °C, 62%.

resulting unprotected secondary alcohol function in **36** was treated with BzCl in pyridine to deliver the corresponding benzoate ester **37** in 80% yield (Scheme 6). Exposure of **37** to *p*-TsOH in CH_3OH/CH_2Cl_2 afforded the requisite alcohol **38** (91%) with the liberated hydroxymethyl group, whose two-step oxidation (IBX followed by $NaClO_2$) furnished carboxylic acid **39** in 84% yield (Scheme 6). The fragmentation of the carbamate ring in **39** was realized with concomitant debenzoylation via exposure to 10% aqueous NaOH in CH_3OH at 80 °C, followed by treatment with 6 M HCl to give the final HCl salt of mycestericin G **5** in 62% yield (Scheme 6). The spectroscopic and specific rotation data were in excellent agreement with those reported.[8]

3. Conclusion

We have accomplished an efficient total synthesis of the HCl salts of two sphingolipid-related amino acid products, mycestericin F **4** and G **5** together with unnatural *ent*-F *ent*-**4·HCl**. For the construction of the carbon backbone of these molecules two pairs of important scaffolds **6**/**8** and **9**/**11** were used. Their coupling reaction together with the subsequent execution of suitably selective functional group manipulations accompanied by protection–deprotection protocols gave the final structures.

4. Experimental

4.1. General methods

All commercial reagents were used in the highest available purity from Aldrich, Fluka, Merck or Acros Organics without further purification. Solvents were dried and purified before use according to standard procedures. For flash column chromatography on silica gel, Kieselgel 60 (0.040–0.063 mm, 230–400 mesh, Merck) was used. Solvents for flash chromatography (hexane, ethyl acetate, methanol and dichloromethane) were distilled before using. Thin layer chromatography was run on Merck silica gel 60 F_{254} analytical plates; detection was carried out with either ultraviolet light (254 nm), or spraying with a solution of phosphomolybdic acid, a basic potassium permanganate solution or a solution of concentrated H_2SO_4, with subsequent heating. ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$, CD_3OD and C_6D_6 on a Varian Mercury Plus 400 FT NMR (400.13 MHz for ^1H and 100.6 MHz for ^{13}C) or on a Varian Premium Compact 600 (599.87 MHz for ^1H and 150.84 MHz for ^{13}C) spectrometers using TMS as the internal reference. For ^1H NMR, δ are given in parts per million (ppm) relative to TMS ($\delta = 0.0$) and for ^{13}C NMR are relative to $CDCl_3$ ($\delta = 77.0$), CD_3OD ($\delta = 49.05$) and C_6D_6 ($\delta = 128.02$). The multiplicity of the ^{13}C NMR signals concerning the ^{13}C–^1H coupling was determined by the DEPT method. Chemical shifts (in ppm) and coupling constants (in Hz) were obtained by first-order analysis; assignments were derived from COSY and H/C correlation spectra. Optical rotations were measured on a P-2000 Jasco polarimeter and reported as follows: $[\alpha]_D$ (*c* in grams per 100 mL, solvent). Melting points were recorded on a Kofler hot block and are uncorrected. Small quantities of reagents (μL) were measured with appropriate syringes (Hamilton). All reactions were performed under an atmosphere of nitrogen, unless otherwise noted.

4.2. (3a*R*,4′*S*,5*S*,6a*R*)-3′-Benzyl-5-[(benzyloxy)methyl]-2,2-dimethyldihydro-3a*H*-spiro[furo[2,3-*d*][1,3]dioxole-6,4′-oxazolidin]-2′-one 12

To a solution of **7**[10f] (5.81 g, 23.7 mmol) in DMF (58 mL), which was pre-cooled to 0 °C, was added NaH (2.88 g, 0.12 mol, 60% dispersion in mineral oil) and the resulting suspension was stirred for 15 min at 0 °C. Next, BnBr (6.80 mL, 56.8 mmol) and TBAI (0.17 g, 0.46 mmol) were added at 0 °C and the mixture was stirred for another 1.5 h at room temperature. The excess hydride was decomposed by the addition of CH_3OH (1 mL), after which the mixture was poured into ice water (58 mL) and extracted with Et_2O (3×180 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated and the residue was chromatographed on silica gel hexane/EtOAc (3:1) to afford 9.86 g (98%) of crystalline compound **12**. Mp 97.5–98 °C, $[\alpha]_D^{25} = +32.8$ (*c* 0.35, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 1.11 (3H, s, CH_3), 1.43 (3H, s, CH_3), 3.58 (1H, dd, $J_{5,H} = 6.9$ Hz, $J_{H,H} = 10.0$ Hz, CH_2O), 3.75 (1H, dd, $J_{5,H} = 5.4$ Hz, $J_{H,H} = 10.0$ Hz, CH_2O), 4.13 (1H, d, $J_{H,H} = 15.8$ Hz, NCH_2), 4.15 (1H, d, $J_{6a,3a} = 3.8$ Hz, H-3a), 4.17 (1H,

dd, $J_{5,H}$ = 5.4 Hz, $J_{5,H}$ = 6.9 Hz, H-5), 4.22 (1H, d, $J_{5',5'}$ = 9,7 Hz, H-5′), 4.53 (2H, s, OCH_2Ph), 4.55 (1H, d, $J_{5',5'}$ = 9.7 Hz, H-5′), 4.85 (1H, d, $J_{H,H}$ = 15.8 Hz, NCH_2), 5.65 (1H, d, $J_{6a,3a}$ = 3.8 Hz, H-6a), 7.28–7.39 (10H, m, 2 × Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.8 (CH_3), 26.3 (CH_3), 46.7 (NCH_2), 64.5 (C-5′), 66.7 (CH_2O), 70.4 (C-4′), 74.0 (OCH_2Ph), 80.7 (C-5), 83.4 (C-3a), 104.1 (C-6a), 112.3 (C-2), 127.6 (2 × CH_{Ph}), 127.9 (2 × CH_{Ph}), 128.0 (CH_{Ph}), 128.1 (CH_{Ph}), 128.5 (2 × CH_{Ph}), 128.8 (2 × CH_{Ph}), 137.2 (C_i), 137.4 (C_i), 158.7 (C-2′). Anal. Calcd for $C_{24}H_{27}NO_6$: C, 67.75; H, 6.40; N, 3.29. Found: C, 67.70; H, 6.35; N, 3.30.

4.3. Ethyl (4*S*,2*E*)-4-{(4′*R*)-3′-benzyl-4′-[(1″*S*)-2″-(benzyloxy)-1″-hydroxyethyl]-2′-oxooxazolidin-4′-yl}-4-hydroxybut-2-enoate 13

Compound **12** (9.80 g, 23.0 mmol) was treated with a mixture of 4:1 TFA/H_2O (194 mL). The resulting mixture was stirred for 3 h at room temperature and then concentrated. The residue was subjected to flash chromatography through a short column of silica gel hexane/EtOAc (1:1) to give 7.19 g (81%) of furanoses, which were used immediately in the next reaction. To a solution of the anomers obtained (7.10 g, 18.4 mmol) in dry CH_2Cl_2 (125 mL) were added stabilized ylide ($Ph_3P{=}CHCO_2Et$, 19.3 g, 55.4 mmol) and benzoic acid (225 mg, 1.84 mmol). After stirring for 26.5 h at room temperature, the solvent was removed, and the residue was chromatographed on silica gel hexane/EtOAc (3:2) to furnish 7.30 g (87%) of ester **13** as a colourless oil. $[\alpha]_D^{25} = +17.6$ (*c* 0.30, $CHCl_3$). Anal. Calcd for $C_{25}H_{29}NO_7$: C, 65.92; H, 6.42; N, 3.08. Found: C, 65.86; H, 6.49; N, 3.02. Compound **13** was fully characterized as its diacetate **14**.

4.4. Ethyl (4*S*,2*E*)-4-acetoxy-4-{(4′*R*)-4-[(1′*S*)-1″-acetoxy-2″-(benzyloxy)ethyl]-3′-benzyl-2′-oxooxazolidin-4′-yl}but-2-enoate 14

To a solution of **13** (50 mg, 0.11 mmol) in dry pyridine (0.8 mL) were successively added DMAP (1.33 mg, 11 μmol) and Ac_2O (16.0 μL, 0.17 mmol). The resulting mixture was stirred for 18 h at room temperature, then concentrated and coevaporated three times with toluene. The residue was purified by flash chromatography on silica gel hexane/EtOAc (2:1) to afford 47 mg (79%) of compound **14** as a colourless oil. $[\alpha]_D^{20} = +11.9$ (*c* 0.47, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.29 (3H, t, *J* = 7.1, CH_3), 1.91 (3H, s, CH_3), 2.10 (3H, s, CH_3), 3.35 (1H, dd, $J_{2'',1''}$ = 3.3 Hz, $J_{2'',2''}$ = 11.6 Hz, H-2″), 3.61 (1H, dd, $J_{2'',1''}$ = 3.1 Hz, $J_{2'',2''}$ = 11.6 Hz, H-2″), 4.09 (1H, d, $J_{5',5'}$ = 10.0 Hz, H-5′), 4.19 (2H, q, *J* = 7.1 Hz, CH_2), 4.37 (1H, d, $J_{H,H}$ = 11.8 Hz, OCH_2Ph), 4.41 (1H, d, $J_{H,H}$ = 11.8 Hz, OCH_2Ph), 4.47 (1H, d, $J_{H,H}$ = 15.6 Hz, NCH_2), 4.61 (1H, d, $J_{H,H}$ = 15.6 Hz, NCH_2), 4.63 (1H, d, $J_{5',5'}$ = 10.0 Hz, H-5′), 5.04 (1H, t, $J_{2'',1''}$ = 3.2 Hz, H-1″), 5.48 (1H, dd, $J_{4,2}$ = 1.3 Hz, $J_{4,3}$ = 6.3 Hz, H-4), 5.91 (1H, dd, $J_{4,2}$ = 1.3 Hz, $J_{3,2}$ = 15.6 Hz, H-2), 6.61 (1H, dd, $J_{4,3}$ = 6.2 Hz, $J_{3,2}$ = 15.6 Hz, H-3), 7.23–7.38 (10H, m, 2 × Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (CH_3), 20.8 (CH_3), 20.9 (CH_3), 46.1 (NCH_2), 61.0 (CH_2), 65.9 (C-5′), 67.4 (C-4′), 67.9 (C-2″), 70.7 (C-1″), 73.7 (OCH_2Ph), 74.0 (C-4), 127.3 (C-2), 127.7 (2 × CH_{Ph}), 127.9 (CH_{Ph}), 128.2 (CH_{Ph}), 128.4 (2 × CH_{Ph}), 128.6 (4 × CH_{Ph}), 136.7 (C_i), 137.2 (C_i, C-3), 158.7 (C-2′), 164.6 (C-1), 168.6 (C=O), 169.2 (C=O). Anal. Calcd for $C_{29}H_{33}NO_9$: C, 64.55; H, 6.16; N, 2.60. Found: C, 64.60; H, 6.10; N, 2.50.

4.5. Ethyl (4*S*)-4-{(4′*R*)-3′-benzyl-4′-[(1″*S*)-1″,2″-dihydroxyethyl]-2′-oxooxazolidin-4′-yl}-4-hydroxybutanoate 15

To a solution of ester **13** (7.20 g, 15.8 mmol) in dry EtOH (128 mL) was added 5% Pd/C (2.22 g). The resulting mixture was stirred under a hydrogen atmosphere for 19 h at room temperature, then filtered through a short pad of Celite. The filtrate was concentrated in vacuo, and the residue was chromatographed on silica gel hexane/EtOAc (1:2) to give 4.12 g (71%) of crystalline compound **15**. Mp 90–91 °C, $[\alpha]_D^{25} = -23.1$ (*c* 0.76, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26 (3H, t, *J* = 7.2 Hz, CH_3), 1.46–1.56 (1H, m, H-3), 1.84–1.91 (1H, m, H-3), 2.48 (2H, m, 2 × H-2), 2.74 (1H, br s, OH), 2.93 (1H, br s, OH), 3.10 (1H, br s, OH), 3.58 (1H, dd, $J_{2'',1''}$ = 6.2 Hz, $J_{2'',2''}$ = 11.4 Hz, H-2″), 3.72 (1H, dd, $J_{2'',1''}$ = 3.8 Hz, $J_{2'',2''}$ = 11.3 Hz, H-2″), 3.82–3.84 (1H, m, H-4), 4.01–4.04 (2H, m, H-5′, H-1″), 4.13 (2H, q, *J* = 7.1 Hz, CH_2), 4.18 (1H, d, $J_{5',5'}$ = 9.1 Hz, H-5′), 4.73 (2H, s, NCH_2), 7.27–7.37 (3H, m, Ph), 7.46–7.48 (2H, m, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (CH_3), 25.4 (C-3), 30.9 (C-2), 46.2 (NCH_2), 61.0 (CH_2), 62.3 (C-2″), 65.4 (C-5′), 69.4 (C-4′), 71.9 (C-1″), 72.0 (C-4), 128.1 (2 × CH_{Ph}), 128.2 (CH_{Ph}), 129.2 (2 × CH_{Ph}), 138.3 (C_i), 159.5 (C-2′), 174.5 (C-1). Anal. Calcd for $C_{18}H_{25}NO_7$: C, 58.84; H, 6.86; N, 3.81. Found: C, 58.80; H, 6.82; N, 3.85.

4.6. Ethyl (4*S*)-4-[(4′*R*)-3′-benzyl-4′-(hydroxymethyl)-2′-oxooxazolidin-4′-yl]-4-hydroxybutanoate 16

To a solution of **15** (4.0 g, 10.9 mmol) in CH_3OH (18 mL) was added $NaIO_4$ (2.80 g, 13.1 mmol) in water (18 mL). After stirring for 1 h at room temperature, CH_2Cl_2 (70 mL) was added, the solid was filtered off and the filtrate was concentrated in vacuo. Chromatography on silica gel hexane/EtOAc (1:2) afforded 3.61 g (99%) of aldehyde, which was used in the next reaction after a rapid ^{1}H NMR analysis. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.26 (3H, t, *J* = 7.1 Hz, CH_3), 1.57 (1H, m, H-3), 1.81 (1H, m, H-3), 2.50 (2H, m, 2 × H-2), 2.81 (1H, m, OH), 4.08 (1H, m, H-4), 4.14 (2H, q, *J* = 7.2 Hz, CH_2), 4.24 (1H, d, $J_{5',5'}$ = 9.7 Hz, H-5′), 4.28 (1H, d, $J_{5',5'}$ = 9.7 Hz, H-5′), 4.64 (1H, d, $J_{H,H}$ = 15.2 Hz, NCH_2), 4.72 (1H, d, $J_{H,H}$ = 15.2 Hz, NCH_2), 7.32–7.40 (3H, m, Ph), 7.43–7.49 (2H, m, Ph), 9.27 (1H, s, CHO). Anal. Calcd for $C_{17}H_{21}NO_6$: C, 60.89; H, 6.31; N, 4.18. Found: C, 60.92; H, 6.39; N, 4.20.

Sodium borohydride (0.47 g, 12.4 mmol) was added to a solution of the aldehyde obtained (3.5 g, 10.4 mmol) in EtOH (47 mL) that was pre-cooled to 0 °C. The resulting mixture was stirred for 10 min at 0 °C and then for a further 2 h at room temperature. After neutralization with Amberlite IR-120 (H^+ form), the insoluble materials were removed by filtration, and the filtrate was concentrated in vacuo. The residue was chromatographed on silica gel hexane/EtOAc (1:2) to give 2.85 g (81%) of diol **16** as white crystals. Mp 85–86.5 °C, $[\alpha]_D^{25} = -46.1$ (*c* 0.31, $CHCl_3$). Anal. Calcd for $C_{17}H_{23}NO_6$: C, 60.52; H, 6.87; N, 4.15. Found: C, 60.59; H, 6.80; N, 4.20. Compound **16** was fully characterized as its diacetate **17**.

4.7. Ethyl (4*S*)-4-acetoxy-4-[(4′*R*)-4′-(acetoxymethyl)-3′-benzyl-2′-oxooxazolidin-4′-yl]butanoate 17

According to the same procedure described for the preparation of **14**, compound **16** (0.10 g, 0.30 mmol), Ac_2O (85.0 μL, 0.90 mmol) and DMAP (7.3 mg, 60 μmol) in dry pyridine (2.2 mL) yielded after flash chromatography on silica gel hexane/EtOAc (1:1) 75 mg (60%) of derivative **17** as a colourless oil. $[\alpha]_D^{25} = -14.9$ (*c* 0.52, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.27 (3H, t, *J* = 7.1 Hz, CH_3), 1.67–1.78 (1H, m, H-3), 1.83 (3H, s, CH_3), 1.89–1.97 (1H, m, H-3), 2.12 (3H, s, CH_3), 2.29–2.39 (2H, m, H-2), 3.82 (1H, d, $J_{H,H}$ = 12.1 Hz, CH_2O), 3.92 (1H, d, $J_{H,H}$ = 12.1 Hz, CH_2O), 4.12–4.18 (3H, m, CH_2, H-5′), 4.19 (1H, d, $J_{H,H}$ = 15.8 Hz, NCH_2), 4.35 (1H, d, $J_{5',5'}$ = 9.2 Hz, H-5′), 4.79 (1H, d, $J_{H,H}$ = 15.8 Hz, NCH_2), 5.31 (1H, dd, $J_{4,3}$ = 2.4 Hz, $J_{4,3}$ = 10.9 Hz, H-4), 7.24–7.35 (5H, m, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (CH_3), 20.3 (CH_3), 20.6 (CH_3), 24.1 (C-3), 29.7 (C-2), 45.5 (NCH_2), 60.8 (CH_2), 63.3 (CH_2O), 65.3 (C-4′), 66.1 (C-5′), 71.2 (C-4), 127.8 (3 × CH_{Ph}), 128.5 (2 × CH_{Ph}), 137.3 (C_i), 158.4 (C-2′), 169.7 (C=O), 169.9 (C=O), 172.0 (C=O). Anal. Calcd for $C_{21}H_{27}NO_8$: C, 59.85; H, 6.46; N, 3.32. Found: C, 59.90; H, 6.30; N, 3.35.

4.8. Ethyl 3-[(5′*R*,6′*S*)-1′-benzyl-8′,8′-dimethyl-2′-oxo-3′,7′,9′-trioxa-1′-azaspiro[4′.5′]decan-6′-yl]propanoate 18

To a solution of **16** (2.7 g, 8.0 mmol) in dry acetone (10.4 mL) were successively added 2,2-dimethoxypropane (20.8 mL, 0.17 mol) and CSA (186 mg, 0.80 mmol). After stirring at room temperature for 4 h, the solvent was removed, and the residue was partitioned between CH_2Cl_2 (100 mL) and a saturated aqueous $NaHCO_3$ solution (28 mL). The organic layer was dried over Na_2SO_4, the solvent was evaporated in vacuo and the residue was chromatographed on silica gel hexane/EtOAc (2:1) providing 2.51 g (83%) of compound **18** as a colourless oil. $[\alpha]_D^{25} = -34.3$ (*c* 0.30, $CHCl_3$). ^{1}H NMR^{1}H NMR (400 MHz, $CDCl_3$): δ 1.27 (3H, t, J = 7.1 Hz, CH_3), 1.41 (3H, s, CH_3), 1.49 (3H, s, CH_3), 1.62–1.71 (1H, m, H-3), 1.94 (1H, m, H-3), 2.47 (2H, m, 2 × H-2), 3.69 (1H, d, $J_{4',4'}$ = 9.4 Hz, H-4′), 3.70 (1H, $J_{10',10'}$ = 12.4 Hz, H-10′), 3.74 (1H, $J_{10',10'}$ = 12.4 Hz, H-10′), 3.86 (1H, dd, $J_{6',3}$ = 1.9 Hz, $J_{6',3}$ = 10.6 Hz, H-6′), 4.03 (1H, d, $J_{4',4'}$ = 9.4 Hz, H-4′), 4.14 (2H, q, J = 7.1 Hz, CH_2), 4.74 (1H, d, $J_{H,H}$ = 15.3 Hz, NCH_2), 4.89 (1H, d, $J_{H,H}$ = 15.3 Hz, NCH_2), 7.26–7.34 (3H, m, Ph), 7.46–7.48 (2H, m, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.2 (CH_3), 18.5 (CH_3), 23.8 (C-3), 28.6 (CH_3), 29.2 (C-2), 47.1 (NCH_2), 58.1 (CH_2), 60.9 (C-10′), 65.9 (C-4′), 67.3 (C-5′), 75.0 (C-6′), 99.5 (C-8′), 127.4 (2 × CH_{Ph}), 128.0 (CH_{Ph}), 128.4 (2 × CH_{Ph}), 138.3 (C_i), 158.5 (C-2′), 173.1 (C-1). Anal. Calcd for $C_{20}H_{27}NO_6$: C, 63.64; H, 7.21; N, 3.71. Found: C, 63.67; H, 7.18; N, 3.75.

4.9. (5*R*,6*S*)-1-Benzyl-6-(3′-hydroxypropyl)-8,8-dimethyl-3,7,9-trioxa-1-azaspiro[4.5]decan-2-one 19

Diisobutylaluminum hydride (19.1 mL, a 1.0 M solution in THF) was added to a solution of **18** (2.40 g, 6.36 mmol) in dry CH_2Cl_2 (12.9 mL) that was pre-cooled to −15 °C, and the resulting mixture was stirred at −15 °C for 2 h. After decomposition of the excess hydride with CH_3OH (3 mL), a saturated aqueous NH_4Cl solution (17 mL) was added and the mixture was stirred for 30 min at room temperature. The solid parts were filtered off, the filtrate was diluted with EtOAc (45 mL) and the separated aqueous phase was extracted with further portions of EtOAc (2 × 45 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated in vacuo and the residue was chromatographed on silica gel hexane/EtOAc (1:2) to afford 1.45 g (68%) of compound **19** as a colourless oil. $[\alpha]_D^{25} = -11.8$ (*c* 0.55, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.44 (3H, s, CH_3), 1.46–1.51 (4H, m, CH_3, H-1′), 1.59–1.82 (3H, m, H-1′, 2 × H-2′), 3.62–3.65 (2H, m, 2 × H-3′), 3.67 (1H, d, $J_{4,4}$ = 9.4 Hz, H-4), 3.73 (2H, s, 2 × H-10), 3.79 (1H, dd, $J_{6,1'}$ = 1.3 Hz, $J_{6,1'}$ = 10.3 Hz, H-6), 3.94 (1H, d, $J_{4,4}$ = 9.4 Hz, H-4), 4.77 (1H, d, $J_{H,H}$ = 15.4 Hz, NCH_2), 4.87 (1H, d, $J_{H,H}$ = 15.4 Hz, NCH_2), 7.24–7.33 (3H, m, Ph), 7.45–7.47 (2H, m, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.6 (CH_3), 25.0 (C-1′), 28.5 (C-2′), 28.6 (CH_3), 47.1 (NCH_2), 58.2 (C-5), 62.0 (C-3′), 65.8 (C-10), 67.4 (C-4), 76.3 (C-6), 99.4 (C-8), 127.3 (CH_{Ph}), 127.9 (2 × CH_{Ph}), 128.3 (2 × CH_{Ph}), 138.3 (C_i), 158.6 (C-2). Anal. Calcd for $C_{18}H_{25}NO_5$: C, 64.46; H, 7.51; N, 4.18. Found: C, 64.50; H, 7.49; N, 4.20.

4.10. 3-[(5′*R*,6′*S*)-1′-Benzyl-8′,8′-dimethyl-2′-oxo-3′,7′,9′-trioxa-1′-azaspiro[4′.5′]decan-6′-yl]propanal 6

To a stirred solution of alcohol **19** (1.40 g, 4.17 mmol) in CH_3CN (37.5 mL) was added IBX (1.75 g, 6.25 mmol) at room temperature. After being heated at reflux for 30 min, the reaction mixture was allowed to cool to room temperature, the solid parts were filtered off, and the filtrate was evaporated in vacuo. The residue was purified by flash chromatography on silica gel hexane/EtOAc (2:1) to give 1.39 g (80%) of aldehyde **6** as a colourless oil. $[\alpha]_D^{25} = +61.6$ (*c* 0.35, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.39 (3H, s, CH_3), 1.48 (3H, s, CH_3), 1.61–1.70 (1H, m, H-3), 1.95–2.02 (1H, m, H-3), 2.48–2.68 (2H, m, 2 × H-2), 3.70 (1H, d, $J_{4',4'}$ = 9.4 Hz, H-4′), 3.71 (1H, d, $J_{10',10'}$ = 12.7 Hz, H-10′), 3.75 (1H, d, $J_{10',10'}$ = 12.7 Hz, H-10′), 3.82 (1H, d, $J_{6',3}$ = 2.0 Hz, $J_{6',3}$ = 10.6 Hz, H-6′), 4.06 (1H, d, $J_{4',4'}$ = 9.4 Hz, H-4′), 4.74 (1H, d, $J_{H,H}$ = 15.3 Hz, NCH_2), 4.89 (1H, d, $J_{H,H}$ = 15.3 Hz, NCH_2), 7.24–7.34 (3H, m, Ph), 7.46–7.48 (2H, m, Ph), 9.74 (1H, br s, H-1). ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.5 (CH_3), 21.3 (C-3), 28.6 (CH_3), 39.1 (C-2), 47.1 (NCH_2), 58.1 (C-5′), 65.8 (C-10′), 67.3 (C-4′), 75.1 (C-6′), 99.5 (C-8′), 127.4 (CH_{Ph}), 127.9 (2 × CH_{Ph}), 128.3 (2 × CH_{Ph}), 138.2 (C_i), 158.5 (C-2′), 201.4 (C-1). Anal. Calcd for $C_{18}H_{23}NO_5$: C, 64.85; H, 6.95; N, 4.20. Found: C, 64.90; H, 6.99; N, 4.18.

4.11. (5*R*,6*S*)-1-Benzyl-6-[(3′*E*)-10′-(2″-hexyl-1″,3″-dioxolan-2″-yl)dec-3′-en-1′-yl]-8,8-dimethyl-3,7,9-trioxa-1-azaspiro[4.5]decan-2-one (*E*)-20 and (5*R*,6*S*)-1-benzyl-6-[(3′*Z*)-10′-(2″-hexyl-1″,3″-dioxolan-2″-yl)dec-3′-en-1′-yl]-8,8-dimethyl-3,7,9-trioxa-1-azaspiro [4.5]-decan-2-one (*Z*)-20

To a solution of 1,1,1,3,3,3-hexamethyldisilazane (0.76 mL, 3.60 mmol) in dry THF (3.8 mL) was added *n*-BuLi (2.25 mL, 3.60 mmol, a 1.6 M solution in hexane) at room temperature. The solution of lithium hexamethyldisilazide (LHMDS) thus generated was treated with a solution of **8**[11] (2.51 g, 4.20 mmol) in dry THF (7.5 mL), and the resulting dark mixture was stirred for 5 min at room temperature. Next, aldehyde **6** (0.50 g, 1.50 mmol) dissolved in dry THF (3.8 mL) was added. After stirring for 30 min, the mixture was poured into a saturated aqueous NH_4Cl solution (26.7 mL) and extracted with EtOAc (3 × 45 mL). The combined organic layers were dried over Na_2SO_4, the solvent was removed, and the residue was purified by flash chromatography on silica gel hexane/EtOAc (3:1) to afford 0.69 g (81%) of an inseparable mixture of alkenes **20** as a colourless oil (*Z*:*E* ≈ 3.5:1 ratio, determined by ^{1}H NMR analysis). From the obtained ^{1}H NMR spectrum of **20**, we were able to find selected data for both geometrical isomers.

*Alkene (Z)-**20***: ^{1}H NMR (600 MHz, C_6D_6): δ 2.76 (1H, d, $J_{4,4}$ = 9.3 Hz, H-4), 2.94 (1H, d, $J_{10,10}$ = 12.6 Hz, H-10), 3.09 (1H, d, $J_{4,4}$ = 9.3 Hz, H-4), 3.25 (1H, d, $J_{6,1'}$ = 2.0 Hz, $J_{6,1'}$ = 10.4 Hz, H-6), 3.28 (1H, d, $J_{10,10}$ = 12.6 Hz, H-10), 4.74 (1H, d, $J_{H,H}$ = 15.1 Hz, NCH_2), 4.99 (1H, d, $J_{H,H}$ = 15.1 Hz, NCH_2), 5.21–5.27 (1H, m, H-3′), 5.41–5.48 (1H, m, H-4′).

*Alkene (E)-**20***: ^{1}H NMR (600 MHz, C_6D_6): δ 2.82 (1H, d, $J_{4,4}$ = 9.3 Hz, H-4), 2.97 (1H, d, $J_{10,10}$ = 12.6 Hz, H-10), 3.12 (1H, d, $J_{4,4}$ = 9.3 Hz, H-4), 3.28–3.30 (1H, m, H-6), 3.31 (1H, d, $J_{10,10}$ = 12.6 Hz, H-10), 4.73 (1H, d, $J_{H,H}$ = 15.1 Hz, NCH_2), 4.98 (1H, d, $J_{H,H}$ = 15.1 Hz, NCH_2), 5.21–5.27 (1H, m, H-3′), 5.41–5.48 (1H, m, H-4′).

4.12. (5*R*,6*S*)-6-[10′-(2″-Hexyl-1″,3″-dioxolan-2″-yl)decyl]-8,8-dimethyl-3,7,9-trioxa-1-azaspiro[4.5]decan-2-one 21

To a solution of **20** (0.69 g, 1.21 mmol) in *t*-BuOH (6.0 mL) which was pre-cooled to 0 °C was added liquid $EtNH_2$ (28.3 mL). Next, several pieces of lithium (0.18 g) were added at −78 °C to this solution. The resulting mixture was stirred for 15 min at −78 °C and then for a further 22 h at −20 °C. After this period, another portion of $EtNH_2$ (9.4 mL) and Li (0.18 g) was added at −78 °C and the mixture stirred for a further 22 h at −20 °C. The reaction was then quenched with a saturated aqueous NH_4Cl solution (40 mL) and the mixture was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried over Na_2SO_4, the solvent removed and the residue was chromatographed on silica gel hexane/EtOAc (2:1) to afford 0.45 g (77%) of an inseparable mixture of olefins as a colourless oil, which was used immediately in the next step.

To a solution of the alkenes obtained (0.45 g, 0.93 mmol) in dry EtOH (10.5 mL) was added 20% $Pd(OH)_2/C$ (32 mg). The resulting mixture was stirred for 2 h under an atmosphere of hydrogen and then filtered through a pad of Celite. The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel hexane/EtOAc (2:1) to afford 447 mg (99%) of compound **21** as a colourless oil. $[\alpha]_D^{22} = -16.2$ (*c* 0.52, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (3H, t, J = 6.8 Hz, CH_3), 1.27–1.36 (23H, m, 11 × CH_2, CH_2), 1.41 (3H, s, CH_3), 1.44 (3H, s, CH_3), 1.49–1.53 (3H, m, CH_2, CH_2), 1.57–1.61 (4H, m, 2 × CH_2), 3.64–3.67 (1H, m, H-6), 3.73 (1H, d, $J_{10,10}$ = 11.8 Hz, H-10), 3.82 (1H, d, $J_{4,4}$ = 9.3 Hz, H-4), 3.83 (1H, d, $J_{10,10}$ = 11.8 Hz, H-10), 3.93 (4H, s, 2 × H-4″, 2 × H-5″), 4.03 (1H, d, $J_{4,4}$ = 9.3 Hz, H-4), 5.84–5.86 (1H, m, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (C-6‴), 18.6 (CH_3), 22.6 (CH_2), 23.8 (CH_2), 23.8 (CH_2), 25.3 (CH_2), 28.3 (CH_2), 29.0 (CH_2), 29.4 (CH_3), 29.5 (3 × CH_2), 29.6 (2 × CH_2), 29.9 (CH_2), 31.8 (CH_2), 37.1 (C-10′, C-1‴), 57.0 (C-5), 64.8 (C-4″, C-5″), 67.8 (C-4), 67.9 (C-10), 74.0 (C-6), 99.4 (C-8), 111.9 (C-2″), 157.9 (C-2). Anal. Calcd for $C_{27}H_{49}NO_6$: C, 67.05; H, 10.21; N, 2.90. Found: C, 67.09; H, 10.25; N, 2.94.

4.13. *tert*-Butyl (5*R*,6*S*)-6-[10′-(2″-hexyl-1″,3″-dioxolan-2″-yl)decyl]-8,8-dimethyl-2-oxo-3,7,9-trioxa-1-azaspiro[4.5]decan-1-carboxylate 22

To a solution of **21** (0.17 g, 0.35 mmol) in dry CH_3CN (1 mL) were successively added Boc_2O (0.15 g, 0.69 mmol) and DMAP (42.8 mg, 0.35 mmol). The resulting mixture was stirred for 30 min at room temperature and then concentrated in vacuo. The residue was purified by flash chromatography on silica gel hexane/EtOAc (3:1) to provide 195 mg (95%) of compound **22** as a colourless oil. $[\alpha]_D^{21} = -7.9$ (*c* 0.62, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 0.87 (3H, t, J = 6.7 Hz, CH_3), 1.25 (24H, m, 12 × CH_2), 1.30 (3H, s, CH_3), 1.43 (3H, s, CH_3), 1.52–1.65 (15H, m, 3 × CH_3, 3 × CH_2), 3.46–3.48 (1H, m, H-6), 3.51 (1H, d, $J_{10,10}$ = 11.1 Hz, H-10), 3.79 (1H, dd, $J_{10,4}$ = 1.5 Hz, $J_{4,4}$ = 9.1 Hz, H-4), 3.91 (4H, s, 2 × H-4″, 2 × H-5″), 4.29 (1H, dd, $J_{10,4}$ = 1.5 Hz, $J_{10,10}$ = 11.0 Hz, H-10), 4.36 (1H, d, $J_{4,4}$ = 9.1 Hz, H-4). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (C-6‴), 22.6 (CH_2), 23.0 (CH_3), 23.8 (CH_2), 23.8 (CH_2), 24.3 (CH_3), 26.3 (CH_2), 27.4 (CH_2), 28.0 (3 × CH_3), 29.3 (CH_2), 29.4 (CH_2), 29.5 (2 × CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.9 (CH_2), 31.8 (CH_2), 37.1 (C-10′, C-1‴), 62.0 (C-10), 64.8 (C-4″, C-5″), 65.4 (C-5), 69.8 (C-4), 73.0 (C-6), 84.5 (C_q), 101.7 (C-8), 111.8 (C-2″), 149.6 (C=O), 152.7 (C-2). Anal. Calcd for $C_{32}H_{57}NO_8$: C, 65.83; H, 9.84; N, 2.40. Found: C, 65.87; H, 9.88; N, 2.44.

4.14. *tert*-Butyl {(4*S*,5*S*)-4-[10′-(2″-hexyl-1″,3″-dioxolan-2″-yl)decyl]-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxan-5-yl}carbamate 23

To a solution of **22** (0.19 g, 0.32 mmol) in dry CH_3OH (4.4 mL) was added Cs_2CO_3 (32.6 mg, 0.10 mmol). After being stirred at room temperature for 1.5 h, the solvent was removed, and the residue was subjected to flash chromatography through a short column of silica gel hexane/EtOAc (5:1) to give 0.17 g (94%) of compound **23** as a colourless oil. $[\alpha]_D^{22} = +22.2$ (*c* 0.52, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ 0.88 (3H, t, J = 6.8 Hz, CH_3), 1.26–1.39 (26H, m, 13 × CH_2), 1.43 (6H, br s, 2 × CH_3), 1.46 (9H, s, 3 × CH_3), 1.57–1.60 (4H, m, 2 × CH_2), 3.40–3.48 (1H, m, CH_2OH), 3.64–3.67 (1H, m, H-4), 3.77 (1H, d, $J_{6,6}$ = 12.3 Hz, H-6), 3.92–3.97 (5H, m, 2 × H-4″, 2 × H-5″, CH_2OH), 4.00 (1H, d, $J_{6,6}$ = 12.3 Hz, H-6), 4.79 (1H, dd, $J_{H,OH}$ = 2.9 Hz, $J_{H,OH}$ = 11.0 Hz, OH), 5.36 (1H, br s, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (C-6‴), 18.6 (CH_3), 22.6 (CH_2), 23.8 (CH_2), 23.8 (2 × CH_2), 25.5 (CH_2), 28.3 (3 × CH_3), 28.7 (CH_2), 29.3 (CH_3), 29.4 (CH_2), 29.5 (2 × CH_2), 29.6 (2 × CH_2), 29.9 (CH_2), 31.8 (CH_2), 37.1 (C-10′, C-1‴), 55.7 (C-5), 64.8 (C-4″, C-5″, CH_2OH), 65.0 (C-6), 74.7 (C-4), 80.3 (C_q), 98.8 (C-2), 111.9 (C-2″), 157.2 (C=O). Anal. Calcd for $C_{31}H_{59}NO_7$: C, 66.75; H, 10.66; N, 2.51. Found: C, 66.80; H, 10.61; N, 2.56.

4.15. (4*S*,5*S*)-5-[(*tert*-Butoxycarbonyl)amino]-4-[10′-(2″-hexyl-1″,3″-dioxolan-2″-yl)decyl]-2,2-dimethyl-1,3-dioxane-5-carboxylic acid 24

To a solution of **23** (0.16 g, 0.29 mmol) in dry DMF (2.7 mL) was added PDC (1.69 g, 4.49 mmol). After stirring at room temperature for 2 h, the reaction mixture was poured into ice water (22 mL) and extracted with Et_2O (3 × 45 mL). The combined organic layers were dried over Na_2SO_4, the solvent was removed, and the residue was chromatographed through a short column of silica gel hexane/EtOAc (9:1) to afford 138 mg (87%) of an aldehyde as a colourless oil which was used immediately in the next step. A solution of $NaClO_2$ (0.20 g, 2.21 mmol) and $NaH_2PO_4{\cdot}2H_2O$ (0.25 g, 1.60 mmol) in water (1.1 mL) was added to the aldehyde obtained (0.13 g, 0.23 mmol) in a 4:4:1 mixture of CH_3CN/*t*-BuOH/2-methylbut-2-ene (5.1 mL) at 0 °C. After being stirred at 0 °C for 30 min, the resulting mixture was poured into a saturated aqueous NaCl solution (3 mL) and extracted with EtOAc (2 × 10 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated in vacuo and the residue was purified by flash chromatography on silica gel hexane/EtOAc (9:1) providing 127 mg (95%) of compound **24** as a colourless oil which was used in the next step after a rapid ^1H NMR analysis. ^1H NMR (400 MHz, CD_3OD): δ 0.87 (3H, t, J = 7.0 Hz, CH_3), 1.25 (26H, m, 13 × CH_2), 1.35 (3H, s, CH_3), 1.41 (9H, s, 3 × CH_3), 1.43 (3H, s, CH_3), 1.51–1.55 (4H, m, 2 × CH_2), 3.87 (4H, s, 2 × H-4″, 2 × H-5″), 4.03 (1H, m, H-4), 4.10 (1H, d, $J_{6,6}$ = 11.9 Hz, H-6), 4.22 (1H, d, $J_{6,6}$ = 11.9 Hz, H-6).

4.16. (2*S*,3*S*)-2-Amino-3-hydroxy-2-(hydroxymethyl)-14-oxoicosanoic acid hydrochloride 4·HCl

Compound **24** (17 mg, 29.7 μmol) was treated with a 6 M aqueous HCl solution (1.4 mL), and the resulting mixture was stirred and heated at 100 °C for 4 h. Removal of the solvent gave a residue which was diluted with Et_2O/hexane (1:5). The solid was filtered off, washed several times with Et_2O and dried on a pump for 10 h at room temperature. This procedure yielded 11 mg (87%) of **4·HCl** as a white amorphous solid. $[\alpha]_D^{23} = -3.5$ (*c* 0.18, CH_3OH). ^1H NMR (600 MHz, CD_3OD): δ 0.88 (3H, t, J = 6.9 Hz, CH_3), 1.24–1.32 (20H, m, 10 × CH_2), 1.48–1.54 (6H, m, 3 × CH_2), 2.42 (4H, t, J = 7.3 Hz, 2 × H-13, 2 × H-15), 3.80 (1H, m, H-3), 3.86 (1H, d, $J_{H,H}$ = 11.0 Hz, CH_2OH), 4.00 (1H, d, $J_{H,H}$ = 11.0 Hz, CH_2OH). ^{13}C NMR (150 MHz, CD_3OD): δ 14.4 (C-20), 23.6 (CH_2), 24.9 (3 × CH_2), 30.0 (2 × CH_2), 30.3 (2 × CH_2), 30.6 (3 × CH_2), 30.7 (CH_2), 32.8 (CH_2), 43.5 (C-13, C-15), 64.4 (CH_2OH), 71.2 (C-2, C-3), 214.4 (C-14), not seen (COOH). Anal. Calcd for $C_{21}H_{42}ClNO_5$: C, 59.48; H, 9.98; N, 3.30. Found: C, 59.54; H, 9.92; N, 3.37.

4.17. 8-Oxotetradecyl acetate 26

To a solution of **25**[11] (5.0 g, 21.9 mmol) in dry pyridine (163 mL) were successively added Ac_2O (3.10 mL, 32.8 mmol) and DMAP (0.27 g, 2.21 mmol). After stirring at room temperature for 45 min, the resulting mixture was poured into ice water (500 mL) and extracted with Et_2O (3 × 200 mL). The combined organic layers were dried over Na_2SO_4, the solvent was removed and the residue was subjected to flash chromatography on silica gel hexane/EtOAc (9:1) to give 5.8 g (98%) of compound **26** as a colourless oil. ^1H NMR (400 MHz, $CDCl_3$): δ 0.83 (3H, t, J = 6.9 Hz, CH_3), 1.23–1.30 (12H, m, 6 × CH_2), 1.50–1.60 (6H, m, 3 × CH_2), 2.00 (3H, s, CH_3CO), 2.32–2.36 (4H, m, 2 × H-7, 2 × H-9), 4.00 (2H, t, J = 6.7 Hz, 2 × H-1). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9 (C-14), 20.9 (CH_3CO), 22.4 (CH_2), 23.6 (CH_2), 23.7 (CH_2), 25.6 (CH_2), 28.4

(CH_2), 28.8 (CH_2), 28.9 (CH_2), 29.0 (CH_2), 31.5 (CH_2), 42.6 (C-7 or C-9), 42.7 (C-7 or C-9), 64.4 (C-1), 171.1 (CH_3CO), 211.4 (C-8). Anal. Calcd for $C_{16}H_{30}O_3$: C, 71.07; H, 11.18. Found: C, 71.01; H, 11.12.

4.18. 7-(2′-Hexyl-1′,3′-dioxolan-2′-yl)heptyl acetate 27

To a solution of **26** (5.70 g, 21.1 mmol) in dry CH_2Cl_2 (135 mL) which was pre-cooled to 0 °C were successively added $(TMSOCH_2)_2$ (19.6 g, 94.9 mmol) and TMSOTf (1.02 mL, 5.28 mmol). After being stirred at 0 °C for 2 h, Et_3N (34.6 mL) was added, and the resulting mixture was poured into a saturated aqueous $NaHCO_3$ solution (100 mL) and extracted with CH_2Cl_2 (2 × 250 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated in vacuo and the residue was chromatographed on silica gel hexane/EtOAc (9:1) to afford 6.56 g (99%) of compound **27** as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86 (3H, t, J = 6.6 Hz, CH_3), 1.26–1.30 (16H, m, 8 × CH_2), 1.55–1.62 (6H, m, 3 × CH_2), 2.03 (3H, s, CH_3CO), 3.91 (4H, s, 2 × H-4′, 2 × H-5′), 4.03 (2H, t, J = 6.8 Hz, 2 × H-1). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (C-6″), 21.0 (CH_3CO), 22.6 (CH_2), 23.7 (CH_2), 23.8 (CH_2), 25.8 (CH_2), 28.5 (CH_2), 29.2 (CH_2), 29.6 (CH_2), 29.8 (CH_2), 31.8 (CH_2), 37.1 (C-7, C-1″), 64.6 (C-1), 64.8 (H-4′, H-5′), 111.8 (C-2′), 171.2 (CH_3CO). Anal. Calcd for $C_{18}H_{34}O_4$: C, 68.75; H, 10.90. Found: C, 68.71; H, 10.94.

4.19. 7-(2′-Hexyl-1′,3′-dioxolan-2′-yl)heptan-1-ol 28[6,11a]

To a solution of **27** (6.50 g, 20.7 mmol) in CH_3OH (228 mL) which was pre-cooled to 0 °C was added K_2CO_3 (1.43 g, 10.3 mmol). The mixture was stirred for 10 min at 0 °C and then for a further 3 h at room temperature. Next, Et_2O (650 mL) and solid Na_2SO_4 were added and the resulting suspension was stirred vigorously for 15 min. The insoluble parts were removed by filtration, the filtrate was concentrated and the residue was chromatographed on silica gel hexane/EtOAc (2:1) to afford 5.58 g (99%) of compound **28** as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86 (3H, t, J = 6.8 Hz, CH_3), 1.26–1.31 (16H, m, 8 × CH_2), 1.52–1.59 (6H, m, 3 × CH_2), 3.61 (2H, t, J = 6.7 Hz, 2 × H-1), 3.91 (4H, s, 2 × H-4′, 2 × H-5′). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (C-6″), 22.6 (CH_2), 23.7 (CH_2), 23.8 (CH_2), 25.6 (CH_2), 29.3 (CH_2), 29.6 (CH_2), 29.8 (CH_2), 31.8 (CH_2), 31.7 (CH_2), 37.0 (C-7 or C-1″), 37.1 (C-7 or C-1″), 62.9 (C-1), 64.8 (C-4′, C-5′), 111.8 (C-2′). Anal. Calcd for $C_{16}H_{32}O_3$: C, 70.54; H, 11.84. Found: C, 70.50; H, 11.88.

4.20. 7-(2′-Hexyl-1′,3′-dioxolan-2′-yl)heptanal 29[6,17]

To a solution of DMSO (3.2 mL, 45.0 mmol) in dry CH_2Cl_2 (39.5 mL) which was pre-cooled to −78 °C was added $(COCl)_2$ (1.94 mL, 22.6 mmol) in dry CH_2Cl_2 (39.5 mL), and the resulting mixture was stirred for 1 h at −78 °C. To this mixture was added dropwise a solution of **28** (5.55 g, 20.4 mmol) in dry CH_2Cl_2 (39.5 mL) at the same temperature. After stirring at −78 °C for 3 h, Et_3N (39.5 mL) and then a saturated $NaHCO_3$ solution (113 mL) were added. The aqueous phase was extracted with further portions of CH_2Cl_2 (2 × 250 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated in vacuo and the residue was chromatographed on silica gel hexane/EtOAc (2:1) to give 5.12 g (93%) of compound **29** as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (3H, t, J = 6.8 Hz, CH_3), 1.28–1.33 (14H, m, 7 × CH_2), 1.56–1.65 (6H, m, 3 × CH_2), 2.42 (2H, m, 2 × H-2), 3.92 (4H, s, 2 × H-4′, 2 × H-5′), 9.74 (1H, t, $J_{2,1}$ = 1.8 Hz, $J_{2,1}$ = 1.8 Hz, H-1). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (C-6″), 21.9 (CH_2), 22.5 (CH_2), 23.6 (CH_2), 23.8 (CH_2), 29.1 (CH_2), 29.6 (2 × CH_2), 31.8 (CH_2), 37.0 (C-7 or C-1″), 37.1 (C-7 or C-1″), 43.8 (C-2), 64.8 (C-4′, C-5′), 111.8 (C-2′), 202.8 (C-1). Anal. Calcd for $C_{16}H_{30}O_3$: C, 71.07; H, 11.18. Found: C, 71.01; H, 11.12.

4.21. Ethyl (2*Z*)-9-(2′-hexyl-1′,3′-dioxolan-2′-yl)non-2-enoate (*Z*)-30 and ethyl (2*E*)-9-(2′-hexyl-1′,3′-dioxolan-2′-yl)non-2-enoate (*E*)-30

To a solution of **29** (5.1 g, 18.9 mmol) in dry CH_2Cl_2 (71 mL) was added stabilized ylide ($Ph_3P{=}CHCO_2Et$, 7.87 g, 22.6 mmol). The mixture was stirred at room temperature for 30 min, and then further portions of ylide (2 × 2 g, 5.74 mmol) were added at 30 min intervals. One hour after the last addition, the solvent was evaporated in vacuo, and the residue was chromatographed on silica gel hexane/EtOAc (20:1) to afford 5.97 g (93%) of a mixture of esters **30** as a colourless oil.

A small amount of the mixture of **30** was separated by column chromatography on silica gel hexane/EtOAc (20:1) to provide each isomer in pure form.

*Ester (Z)-**30***: ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (3H, t, J = 6.8 Hz, CH_3), 1.26–1.36 (19H, m, 8 × CH_2, CH_3), 1.56–1.60 (4H, m, 2 × CH_2), 2.64 (2H, m, 2 × H-4), 3.92 (4H, s, 2 × H-4′, 2 × H-5′), 4.16 (2H, q, J = 7.2 Hz, CH_2), 5.75 (1H, td, $J_{4,2}$ = 1.7 Hz, $J_{4,2}$ = 1.7 Hz, $J_{3,2}$ = 11.5 Hz, H-2), 6.21 (1H, td, $J_{4,3}$ = 7.5 Hz, $J_{4,3}$ = 7.5 Hz, $J_{3,2}$ = 11.5 Hz, H-3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (CH_3), 14.3 (CH_3), 22.6 (CH_2), 23.8 (CH_2), 23.8 (CH_2), 29.0 (2 × CH_2), 29.3 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 31.8 (CH_2), 37.1 (C-9, C-1″), 59.7 (CH_2), 64.9 (C-4′, C-5′), 110.0 (C-2′), 111.9 (C-3), 150.6 (C-2), 166.5 (C-1). Anal. Calcd for $C_{20}H_{36}O_4$: C, 70.55; H, 10.66. Found: C, 70.50; H, 10.70.

*Ester (E)-**30***: ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86–0.90 (3H, m, CH_3), 1.27–1.31 (19H, m, 8 × CH_2, CH_3), 1.57–1.60 (4H, m, 2 × CH_2), 2.16–2.22 (2H, m, 2 × H-4), 3.92 (4H, s, 2 × H-4′, 2 × H-5′), 4.18 (2H, q, J = 7.2 Hz, CH_2), 5.81 (1H, td, $J_{4,2}$ = 1.5 Hz, $J_{4,2}$ = 1.5 Hz, $J_{3,2}$ = 15.6 Hz, H-2), 6.96 (1H, td, $J_{4,3}$ = 6.9 Hz, $J_{4,3}$ = 6.9 Hz, $J_{3,2}$ = 15.6 Hz, H-3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (CH_3), 14.2 (CH_3), 22.6 (CH_2), 23.7 (CH_2), 23.8 (CH_2), 27.9 (CH_2), 29.1 (CH_2), 29.6 (CH_2), 29.6 (CH_2), 31.8 (CH_2), 32.1 (CH_2), 37.0 (C-9 or C-1″), 37.1 (C-9 or C-1″), 60.1 (CH_2), 64.9 (C-4′, C-5′), 111.8 (C-2′), 121.2 (C-3), 149.3 (C-2), 166.7 (C-1). Anal. Calcd for $C_{20}H_{36}O_4$: C, 70.55; H, 10.66. Found: C, 70.59; H, 10.62.

4.22. Ethyl 9-(2′-hexyl-1′,3′-dioxolan-2′-yl)nonanoate 31

To a solution of **30** (5.90 g, 17.3 mmol) in dry EtOH (187 mL) was added 20% $Pd(OH)_2$/C (0.59 g). The resulting mixture was stirred under an atmosphere of hydrogen for 1 h, and then filtered through a pad of Celite. Evaporation of the solvent and chromatography of the residue on silica gel hexane/EtOAc (20:1) gave 5.64 g (95%) of compound **31** as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.84 (3H, t, J = 6.7 Hz, CH_3), 1.19–1.31 (21H, m, 9 × CH_2, CH_3), 1.52–1.59 (6H, m, 3 × CH_2), 2.24 (2H, t, J = 7.5 Hz, 2 × H-2), 3.88 (4H, s, 2 × H-4′, 2 × H-5′), 4.08 (2H, q, J = 7.1 Hz, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (CH_3), 14.2 (CH_3), 22.5 (CH_2), 23.7 (2 × CH_2), 24.9 (CH_2), 29.0 (CH_2), 29.1 (CH_2), 29.3 (CH_2), 29.5 (CH_2), 29.8 (CH_2), 31.8 (CH_2), 34.3 (CH_2), 37.0 (C-9 or C-1″), 37.1 (C-9 or C-1″), 60.0 (CH_2), 64.8 (C-4′, C-5′), 111.8 (C-2′), 173.7 (C-1). Anal. Calcd for $C_{20}H_{38}O_4$: C, 70.13; H, 11.18. Found: C, 70.18; H, 11.13.

4.23. 9-(2′-Hexyl-1′,3′-dioxolan-2′-yl)nonan-1-ol 32

Lithium aluminum hydride (1.24 g, 32.7 mmol) was added portionwise to a solution of **31** (5.60 g, 16.3 mmol) in dry Et_2O (96 mL) which was pre-cooled to 0 °C. The resulting mixture was stirred at 0 °C for 15 min and then for another 45 min at room temperature. Water (5.2 mL) was then added and the solid parts were removed by filtration. The filtrate obtained was dried over Na_2SO_4, the solvent was taken down, and residue was chromatographed on silica gel hexane/EtOAc (20:1) to provide 4.81 g (98%) of compound **32** as

a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86–0.90 (3H, m, CH_3), 1.29–1.35 (20H, m, 10 × CH_2), 1.52–1.61 (6H, m, 3 × CH_2), 3.63 (2H, t, J = 7.5 Hz, 2 × H-1), 3.92 (4H, s, 2 × H-4′, 2 × H-5′). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (C-6″), 22.5 (CH_2), 23.8 (2 × CH_2), 25.7 (CH_2), 29.4 (CH_2), 29.5 (2 × CH_2), 29.6 (CH_2), 29.9 (CH_2), 31.8 (CH_2), 32.7 (CH_2), 37.1 (C-9, C-1″), 62.9 (C-1), 64.8 (C-4′, C-5′), 111.9 (C-2′). Anal. Calcd for $C_{18}H_{36}O_3$: C, 71.95; H, 12.08. Found: C, 71.90; H, 12.03.

4.24. 2-(9′-Bromononyl)-2-hexyl-1,3-dioxolane 33

To a solution of **32** (4.80 g, 16.0 mmol) in dry DMF (27.0 mL) was added Ph_3P (6.50 g, 24.8 mmol) at room temperature. The resulting mixture was allowed to cool to 10 °C after which NBS (4.40 g, 24.8 mmol) was added in portions. After stirring at 10 °C for 30 min, the mixture was poured into ice water (170 mL) and extracted with Et_2O (3 × 300 mL). The combined organic layers were dried over Na_2SO_4, the solvent evaporated in vacuo and the residue was chromatographed on silica gel hexane/EtOAc (35:1) to afford 5.0 g (86%) of compound **33** as a colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.86–0.90 (3H, m, CH_3), 1.29–1.36 (20H, m, 10 × CH_2), 1.56–1.61 (4H, m, 2 × CH_2), 1.81–1.89 (2H, m, CH_2), 3.40 (2H, t, J = 6.9 Hz, 2 × H-9′), 3.92 (4H, s, 2 × H-4, 2 × H-5). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (C-6″), 22.6 (CH_2), 23.8 (2 × CH_2), 28.1 (CH_2), 28.7 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 29.6 (CH_2), 29.8 (CH_2), 31.8 (CH_2), 32.8 (CH_2), 34.0 (C-9′), 37.1 (C-1′, C-1″), 64.8 (C-4, C-5), 111.8 (C-2). Anal. Calcd for $C_{18}H_{35}BrO_2$: C, 59.50; H, 9.71. Found: C, 59.56; H, 9.77.

4.25. [9-(2′-Hexyl-1′,3′-dioxolan-2′-yl)nonyl]triphenylphosphonium bromide 11

To a solution of **33** (5.00 g, 13.8 mmol) in dry CH_3CN (55.3 mL) were successively added Ph_3P (4.51 g, 17.2 mmol) and anhydrous Na_2CO_3 (0.29 g, 2.75 mmol). The resulting mixture was stirred and heated at reflux for 72 h. After cooling to room temperature, the solvent was evaporated in vacuo and the mixture was washed repeatedly with Et_2O to remove Ph_3P. The phosphonium salt was precipitated after the addition of anhydrous Et_2O (200 mL) to the glassy material obtained. The precipitate was allowed to settle overnight, after which the clear solution was decanted, and the residue was dried on a pump for 3 days at room temperature. This procedure yielded 6.54 g (76%) of compound **11** as a white hygroscopic powder. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (3H, t, J = 6.7 Hz, CH_3), 1.20–1.27 (18H, m, 9 × CH_2), 1.53–1.63 (8H, m, 4 × CH_2), 3.73–3.82 (2H, m, 2 × H-1), 3.91 (4H, s, 2 × H-4′, 2 × H-5′), 7.69–7.74 (6H, m, Ph), 7.78–7.88 (9H, m, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (C-6″), 22.5 (CH_2), 23.0 (CH_2), 23.7 (2 × CH_2), 29.1 (CH_2), 29.2 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 29.8 (CH_2), 30.3 (CH_2), 30.4 (CH_2), 31.8 (CH_2), 37.0 (C-9 or C-1″), 37.1 (C-9 or C-1″), 64.8 (C-4′, C-5′), 111.8 (C-2′), 117.9 (2 × C_i), 118.8 (C_i), 130.4 (3 × CH_{Ph}), 130.5 (3 × CH_{Ph}), 133.6 (3 × CH_{Ph}), 133.7 (3 × CH_{Ph}), 134.9 (CH_{Ph}), 134.9 (CH_{Ph}), 134.9 (CH_{Ph}). Anal. Calcd for $C_{36}H_{50}BrO_2P$: C, 69.11; H, 8.06. Found: C, 69.18; H, 8.12.

4.26. (5*S*,6*S*)-8,8-Dimethyl-2-oxo-3,7,9-trioxa-1-azaspiro[4.5]-decane-6-carbaldehyde 9

Using the same procedure as described for the preparation of compound **6**, alcohol **10**[10g] 0.60 g, 2.76 mmol) and IBX (1.16 g, 4.14 mmol) gave after flash chromatography on silica gel (EtOAc) 0.56 g (94%) of crystalline aldehyde **9**. Mp 148–150 °C, $[\alpha]_D^{25} = -72.1$ (c 0.42, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.50 (3H, s, CH_3), 1.55 (3H, s, CH_3), 3.78 (1H, d, $J_{10,10}$ = 12.0 Hz, H-10), 3.89 (1H, d, $J_{10,10}$ = 12.0 Hz, H-10), 3.93 (1H, d, $J_{4,4}$ = 9.4 Hz, H-4), 4.14 (1H, s, H-6), 4.62 (1H, d, $J_{4,4}$ = 9.4 Hz, H-4), 6.63 (1H, br s, NH), 9.56 (1H, s, CHO). ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.7 (CH_3), 28.4 (CH_3), 56.0 (C-5), 66.7 (C-4), 67.6 (C-10), 76.4 (C-6), 100.0 (C-8), 157.8 (C-2), 200.7 (CHO). Anal. Calcd for $C_9H_{13}NO_5$: C, 50.23; H, 6.09; N, 6.51. Found: C, 50.29; H, 6.02; N, 6.58.

4.27. (5*S*,6*R*)-6-[10′-(2″-Hexyl-1″,3″-dioxolan-2″-yl)decyl]-8,8-dimethyl-3,7,9-trioxa-1-azaspiro[4.5]decan-2-one *ent*-21

Using the same procedure as described for the preparation of **20**, compound **9** (0.50 g, 2.32 mmol) and phosphonium salt **11** (4.07 g, 6.51 mmol) afforded, after flash chromatography on silica gel hexane/EtOAc (1:1), 0.65 g (58%) of an inseparable mixture of isomers **34** as a colourless oil.

To a solution of **34** (0.65 g, 1.35 mmol) in dry EtOH (14.3 mL) was added 20% $Pd(OH)_2$/C (46 mg) at room temperature. After being stirred for 2 h, the resulting mixture was filtered through a pad of Celite, the filtrate was concentrated in vacuo, and the residue was subjected to flash chromatography on silica gel hexane/EtOAc (1:1) to give 0.64 g (98%) of compound *ent*-**21** as a colourless oil.$[\alpha]_D^{23} = 17.6$ (c 0.76, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (3H, t, J = 6.8 Hz, CH_3), 1.27–1.33 (23H, m, 11 × CH_2, CH_2), 1.42 (3H, s, CH_3), 1.44 (3H, s, CH_3), 1.47–1.53 (3H, m, CH_2, CH_2), 1.57–1.61 (4H, m, 2 × CH_2), 3.65–3.67 (1H, m, H-6), 3.74 (1H, d, $J_{10,10}$ = 11.8 Hz, H-10), 3.82 (1H, d, $J_{4,4}$ = 9.4 Hz, H-4), 3.83 (1H, d, $J_{10,10}$ = 11.8 Hz, H-10), 3.93 (4H, s, 2 × H-4″, 2 × H-5″), 4.03 (1H, d, $J_{4,4}$ = 9.4 Hz, H-4), 6.04 (1H, br s, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (C-6‴), 18.6 (CH_3), 22.5 (CH_2), 23.8 (CH_2), 23.8 (CH_2), 25.3 (CH_2), 28.3 (CH_2), 28.9 (CH_2), 29.3 (CH_3), 29.5 (3 × CH_2), 29.5 (2 × CH_2), 29.9 (CH_2), 31.8 (CH_2), 37.1 (C-10′, C-1‴), 57.0 (C-5), 64.8 (C-4″, C-5″), 67.8 (C-10), 67.8 (C-4), 74.0 (C-6), 99.4 (C-2), 111.8 (C-2″), 158.0 (C-2). Anal. Calcd for $C_{27}H_{49}NO_6$: C, 67.05; H, 10.21; N, 2.90. Found: C, 67.10; H, 10.16; N, 2.95.

4.28. *tert*-Butyl (5*S*,6*R*)-6-[10′-(2″-hexyl-1″,3″-dioxolan-2″-yl)decyl]-8,8-dimethyl-2-oxo-3,7,9-trioxa-1-azaspiro[4.5]decan-1-carboxylate *ent*-22

According to the procedure described for the preparation of **22**, compound *ent*-**21** (0.30 g, 0.62 mmol), Boc_2O (0.27 g, 1.24 mmol) and DMAP (76 mg, 0.62 mmol) provided, after flash chromatography on silica gel hexane/EtOAc (3:1), 0.34 g (94%) of *ent*-**22** as a colourless oil. $[\alpha]_D^{20} = +8.9$ (c 0.78, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (3H, t, J = 6.8 Hz, CH_3), 1.26 (24H, m, 12 × CH_2), 1.31 (3H, s, CH_3), 1.44 (3H, s, CH_3), 1.51–1.67 (15H, m, 3 × CH_3, 3 × CH_2), 3.47–3.50 (1H, m, H-6), 3.52 (1H, d, $J_{10,10}$ = 11.1 Hz, H-10), 3.80 (1H, dd, $J_{10,4}$ = 1.8 Hz, $J_{4,4}$ = 9.2 Hz, H-4), 3.92 (4H, s, 2 × H-4″, 2 × H-5″), 4.30 (1H, dd, $J_{10,4}$ = 1.8 Hz, $J_{10,10}$ = 11.1 Hz, H-10), 4.37 (1H, d, $J_{4,4}$ = 9.2 Hz, H-4). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (C-6‴), 22.6 (CH_2), 23.0 (CH_3), 23.8 (CH_2), 23.8 (CH_2), 24.3 (CH_3), 26.3 (CH_2), 27.5 (CH_2), 28.0 (3 × CH_3), 29.3 (CH_2), 29.4 (CH_2), 29.5 (2 × CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.9 (CH_2), 31.8 (CH_2), 37.1 (C-10′, C-1‴), 62.0 (C-10), 64.8 (C-4″, C-5″), 65.4 (C-5), 69.8 (C-4), 73.0 (C-6), 84.5 (C_q), 101.7 (C-8), 111.8 (C-2″), 149.6 (C=O), 152.7 (C-2). Anal. Calcd for $C_{32}H_{57}NO_8$: C, 65.83; H, 9.84; N, 2.40. Found: C, 65.87; H, 9.88; N, 2.44.

4.29. *tert*-Butyl {(4*R*,5*R*)-4-[10′-(2″-hexyl-1″,3″-dioxolan-2″-yl) decyl]-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxan-5-yl}carba mate *ent*-23

Using the same procedure as described for the preparation of derivative **23**, *ent*-**22** (0.34 g, 0.58 mmol) and Cs_2CO_3 (57 mg, 0.17 mmol) afforded, after flash chromatography on silica gel hexane/EtOAc (5:1), 0.30 g (92%) of compound *ent*-**23** as a colourless oil. $[\alpha]_D^{20} = -21.1$ (c 0.62, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (3H, t, J = 6.8 Hz, CH_3), 1.25–1.30 (26H, m, 13 × CH_2), 1.42

(6H, br s, 2 × CH_3), 1.45 (9H, s, 3 × CH_3), 1.56–1.60 (4H, m, 2 × CH_2), 3.39–3.45 (1H, m, CH_2OH), 3.63–3.66 (1H, m, H-4), 3.76 (1H, d, $J_{6,6}$ = 12.3 Hz, H-6), 3.91–3.96 (5H, m, 2 × H-4″, 2 × H-5″, CH_2OH), 3.99 (1H, d, $J_{6,6}$ = 12.3 Hz, H-6), 4.77 (1H, dd, $J_{H,OH}$ = 2.9 Hz, $J_{H,OH}$ = 10.0 Hz, OH), 5.35 (1H, br s, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1 (C-6‴), 18.6 (CH_3), 22.6 (CH_2), 23.8 (CH_2), 23.8 (2 × CH_2), 25.5 (CH_2), 28.3 (3 × CH_3), 28.7 (CH_2), 29.3 (CH_3), 29.4 (CH_2), 29.5 (2 × CH_2), 29.6 (2 × CH_2), 29.9 (CH_2), 31.8 (CH_2), 37.1 (C-10′, C-1‴), 55.7 (C-5), 64.9 (C-4″, C-5″, CH_2OH), 65.0 (C-6), 74.7 (C-4), 80.3 (C_q), 98.9 (C-2), 111.9 (C-2″), 157.2 (C=O). Anal. Calcd for $C_{31}H_{59}NO_7$: C, 66.75; H, 10.66; N, 2.51. Found: C, 66.80; H, 10.61; N, 2.56.

4.30. (4*R*,5*R*)-5-[(*tert*-Butoxycarbonyl)amino]-4-[10′-(2″-hexyl-1″,3″-dioxolan-2″-yl)decyl]-2,2-dimethyl-1,3-dioxane-5-carboxylic acid *ent*-24

To a solution of DMSO (0.13 mL, 1.83 mmol) in dry CH_2Cl_2 (1 mL) which was pre-cooled to −78 °C, was added $(COCl)_2$ (0.76 mL, 8.84 mmol) in dry CH_2Cl_2 (1 mL), and the resulting mixture was stirred for 1 h at −78 °C. To this mixture was added dropwise a solution of *ent*-**23** (0.30 g, 0.54 mmol) in CH_2Cl_2 (2 mL) at the same temperature. After stirring at −78 °C for 3 h, Et_3N (1.55 mL) and then a saturated $NaHCO_3$ solution (13 mL) were added successively. The aqueous phase was extracted with further portions of CH_2Cl_2 (2 × 48 mL). The combined organic layers were dried over Na_2SO_4, the solvent removed and the residue was chromatographed on silica gel hexane/EtOAc (5:1) to provide 0.27 g (93%) of an aldehyde as a colourless oil which was used immediately in the next reaction.

To a solution of the aldehyde obtained (0.27 g, 0.49 mmol) in a mixture of 4:4:1 CH_3CN/*t*-BuOH/2-methylbut-2-ene (11.0 mL) was added a solution of $NaClO_2$ (0.42 g, 4.64 mmol) and $NaH_2PO_4{\cdot}2H_2O$ (0.52 g, 3.33 mmol) in water (2.5 mL) at 0 °C. After being stirred at 0 °C for 30 min, the mixture was poured into a saturated NaCl solution (6.5 mL) and extracted with EtOAc (2 × 21 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated in vacuo, and the residue was subjected to flash chromatography on silica gel hexane/EtOAc (1:1) to give 244 mg (88%) of *ent*-**24** as a colourless oil. $[\alpha]_D^{20} = +12.1$ (*c* 0.24, $CHCl_3$). ^{1}H NMR (400 MHz, CD_3OD): δ 0.89 (3H, t, *J* = 6.9 Hz, CH_3), 1.28–1.34 (24H, m, 12 × CH_2), 1.35–1.36 (2H, m, CH_2), 1.37 (3H, s, CH_3), 1.44 (9H, s, 3 × CH_3), 1.45 (3H, s, CH_3), 1.54–1.57 (4H, m, 2 × CH_2), 3.89 (4H, s, 2 × H-4″, 2 × H-5″), 4.04–4.07 (1H, m, H-4), 4.13 (1H, d, $J_{6,6}$ = 11.8 Hz, H-6), 4.24 (1H, d, $J_{6,6}$ = 11.8 Hz, H-6). ^{13}C NMR (100 MHz, CD_3OD): δ 14.5 (C-6‴), 19.2 (CH_3), 23.7 (CH_2), 24.9 (2 × CH_2), 26.8 (CH_2), 28.8 (3 × CH_3), 29.3 (CH_3), 30.4 (CH_2), 30.6 (CH_2), 30.7 (CH_2), 30.7 (2 × CH_2), 30.8 (CH_2), 31.0 (CH_2), 33.0 (CH_2), 38.1 (C-10′, C-1‴), 61.1 (C-5), 64.9 (C-6), 65.9 (C-4″, C-5″), 74.6 (C-4), 80.7 (C_q), 100.4 (C-2), 113.0 (C-2″), 157.0 (C=O), 173.3 (C-1). Anal. Calcd for $C_{31}H_{57}NO_8$: C, 65.12; H, 10.05; N, 2.45. Found: C, 65.18; H, 10.12; N, 2.51.

4.31. (2*R*,3*R*)-2-Amino-3-hydroxy-2-(hydroxymethyl)-14-oxoicosanoic acid hydrochloride *ent*-4·HCl

According to the same procedure described for the preparation of mycestericin F·HCl **4·HCl**, compound *ent*-**24** (36 mg, 63.0 μmol) was transformed into *ent*-**4·HCl** (18 mg 64%, white amorphous solid). $[\alpha]_D^{24} = +4.4$ (*c* 0.16, CH_3OH). ^{1}H NMR (600 MHz, CD_3OD): δ 0.87 (3H, t, *J* = 6.9 Hz, CH_3), 1.23–1.31 (20H, m, 10 × CH_2), 1.48–1.54 (6H, m, 3 × CH_2), 2.41 (4H, t, *J* = 7.3 Hz, 2 × H-13, 2 × H-15), 3.80 (1H, m, H-3), 3.86 (1H, d, $J_{H,H}$ = 11.2 Hz, CH_2OH), 4.00 (1H, d, $J_{H,H}$ = 11.2 Hz, CH_2OH). ^{13}C NMR (150 MHz, CD_3OD): δ 14.4 (C-20), 23.6 (CH_2), 24.9 (3 × CH_2), 30.0 (2 × CH_2), 30.3 (2 × CH_2), 30.6 (3 × CH_2), 30.7 (CH_2), 32.8 (CH_2), 43.5 (C-13, C-15), 64.4 (CH_2OH), 71.1 (C-2, C-3), 171.8 (C-1), 214.4 (C-14). Anal. Calcd for $C_{21}H_{42}ClNO_5$: C, 59.48; H, 9.98; N, 3.30. Found: C, 59.41; H, 9.91; N, 3.25.

4.32. (4*S*)-4-[(1′*R*)-1′-Hydroxy-12′-oxooctadecyl]-4-(hydroxymethyl)oxazolidin-2-one 35

A solution of **21** (0.27 g, 0.56 mmol) in a mixture of 7:3 AcOH/H_2O (55 mL) was heated for 6 h at 80 °C, and then for a further 16 h at 40 °C before evaporation of the solvent. The residue was chromatographed on silica gel hexane/EtOAc (1:1) to afford 136 mg (79%) of crystalline compound **35**. Mp 57–59 °C, $[\alpha]_D^{25} = +9.3$ (*c* 0.54, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (3H, t, *J* = 6.8 Hz, CH_3), 1.24–1.42 (20H, m, 10 × CH_2), 1.52–1.55 (6H, m, 3 × CH_2), 2.38 (4H, t, *J* = 7.5 Hz, 2 × H-11′, 2 × H-13′), 3.61–3.71 (1H, m, H-1′), 3.62 (1H, d, $J_{H,H}$ = 11.7 Hz, CH_2OH), 3.69 (1H, d, $J_{H,H}$ = 11.7 Hz, CH_2OH), 4.21 (1H, d, $J_{5,5}$ = 8.7 Hz, H-5), 4.30 (1H, d, $J_{5,5}$ = 8.7 Hz, H-5), 6.91 (1H, br s, NH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (C-18′), 22.5 (CH_2), 23.8 (3 × CH_2), 26.0 (CH_2), 28.9 (CH_2), 29.2 (CH_2), 29.4 (2 × CH_2), 29.5 (2 × CH_2), 30.7 (CH_2), 31.6 (CH_2), 42.8 (C-11′, C-13′), 64.3 (CH_2OH), 65.9 (C-4), 68.8 (C-5), 72.5 (C-1′), 161.0 (C-2), 212.1 (C-12′). Anal. Calcd for $C_{22}H_{40}NO_5$: C, 66.13; H, 10.34; N, 3.51. Found: C, 66.18; H, 10.29; N, 3.56.

4.33. (4*S*)-4-[(1′*R*)-1′-Hydroxy-12′-oxooctadecyl]-4-(trityloxymethyl)oxazolidin-2-one 36

To a solution of **35** (0.13 g, 0.42 mmol) in dry pyridine (3.4 mL) were successively added TrCl (0.45 g, 1.61 mmol) and DMAP (80 mg, 0.65 mmol). After stirring at 60 °C for 24 h, the resulting mixture was poured into ice water (15 mL) and extracted with Et_2O (3 × 30 mL). The combined organic layers were dried over Na_2SO_4, the solvent was removed, and the residue was chromatographed on silica gel hexane/EtOAc (1:1) to afford 0.24 g (88%) of compound **36** as a colourless oil. $[\alpha]_D^{23} = +20.0$ (*c* 0.12, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (3H, t, *J* = 6.8 Hz, CH_3), 1.13–1.32 (20H, m, 10 × CH_2), 1.52–1.57 (6H, m, 3 × CH_2), 2.38 (4H, t, *J* = 7.5 Hz, 2 × H-11′, 2 × H-13′), 2.62 (1H, d, $J_{1',OH}$ = 4.3 Hz, OH), 3.21 (1H, d, $J_{H,H}$ = 9.5 Hz, CH_2O), 3.38 (1H, d, $J_{H,H}$ = 9.5 Hz, CH_2O), 3.76–3.78 (1H, m, H-1′), 3.99 (1H, d, $J_{5,5}$ = 8.9 Hz, H-5), 4.28 (1H, d, $J_{5,5}$ = 8.9 Hz, H-5), 6.06 (1H, br s, NH), 7.21–7.31 (9H, m, Ph), 7.39–7.41 (6H, m, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (C-18′), 22.5 (CH_2), 23.8 (2 × CH_2), 26.1 (CH_2), 28.9 (CH_2), 29.2 (CH_2), 29.3 (2 × CH_2), 29.4 (CH_2), 29.4 (2 × CH_2), 30.2 (CH_2), 31.6 (CH_2), 42.8 (C-11′, C-13′), 64.1 (C-4), 65.5 (CH_2O), 69.1 (C-5), 72.7 (C-1′), 87.1 (C_{qTr}), 127.3 (3 × CH_{Ph}), 128.0 (6 × CH_{Ph}), 128.5 (6 × CH_{Ph}), 142.9 (3 × C_i), 159.6 (C-2), 211.9 (C-12′). Anal. Calcd For $C_{41}H_{55}NO_5$: C, 76.72; H, 8.64; N, 2.18. Found: C, 76.77; H, 8.59; N, 2.12.

4.34. (1*R*)-12-Oxo-1-[(4′*S*)-2′-oxo-4′-(trityloxymethyl)oxazolidin-4′-yl]octadecyl benzoate 37

To a solution of **36** (0.24 g, 0.37 mmol) in dry pyridine (3.6 mL) were successively added BzCl (0.26 mL, 2.24 mmol) and DMAP (4.6 mg, 37.6 μmol). After being stirred at room temperature for 4.5 h, the resulting mixture was poured into ice water (11 mL) and extracted with Et_2O (3 × 15 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated in vacuo, and the residue was chromatographed on silica gel hexane/EtOAc (3:1, then 1:1) to provide 0.22 g (80%) of compound **37** as a colourless oil. $[\alpha]_D^{20} = -1.4$ (*c* 0.72, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (3H, t, *J* = 6.9 Hz, CH_3), 1.18–1.27 (20H, m, 10 × CH_2), 1.32–1.33 (1H, m, CH_2), 1.41–1.46 (1H, m, CH_2), 1.51–1.57 (4H, m, 2 × CH_2), 2.34–2.39 (4H, m, 2 × H-11′, 2 × H-13′), 3.19 (1H, d, $J_{H,H}$ = 9.6 Hz, CH_2O), 3.42 (1H, d, $J_{H,H}$ = 9.6 Hz, CH_2O), 3.96 (1H, d, $J_{5',5'}$ = 9.0 Hz,

H-5′), 4.36 (1H, d, $J_{5',5'}$ = 9.0 Hz, H-5′), 5.55 (1H, dd, $J_{2,1}$ = 1.7 Hz, $J_{2,1}$ = 10.7 Hz, H-1), 5.71–5.75 (1H, br s, NH), 7.21–7.30 (10H, m, Ph_{Tr}), 7.40–7.42 (5H, m, Ph_{Tr}), 7.44–7.46 (2H, m, Ph_{Bz}), 7.56–7.60 (1H, m, Ph_{Bz}), 7.95–7.97 (2H, m, Ph_{Bz}). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (C-18), 22.5 (CH_2), 23.8 (2 × CH_2), 25.7 (CH_2), 28.8 (CH_2), 28.9 (CH_2), 29.2 (CH_2), 29.2 (CH_2), 29.3 (CH_2), 29.3 (2 × CH_2), 29.4 (CH_2), 31.6 (CH_2), 42.7 (C-11 or C-13), 42.8 (C-11 or C-13), 63.6 (C-4′), 65.3 (CH_2O), 68.5 (C-5′), 73.9 (C-1), 87.2 (C_{qTr}), 127.4 (4 × CH_{Tr}), 128.0 (6 × CH_{Tr}), 128.5 (7 × CH_{Tr}, 2 × CH_{Bz}) 129.3 ($C_{i\text{-}Bz}$), 129.7 (2 × CH_{Bz}), 133.3 (CH_{Bz}), 142.8 (3 × $C_{i\text{-}Tr}$), 158.3 (C-2′), 166.2 (C═O), 211.7 (C-12). Anal. Calcd for $C_{48}H_{59}NO_6$: C, 77.28; H, 7.97; N, 1.88. Found: C, 77.21; H, 7.90; N, 1.81.

4.35. (1*R*)-1-[(4′*S*)-4′-(Hydroxymethyl)-2′-oxooxazolidin-4′-yl)-12-oxooctadecyl benzoate 38

To a solution of **37** (0.20 g, 0.27 mmol) in a mixture of 2:1 CH_2Cl_2/CH_3OH (3.3 mL) was added *p*-TsOH (51 mg, 0.27 mmol). After stirring at room temperature for 1.5 h, another portion of *p*-TsOH (102 mg, 0.54 mmol) was added. Twenty two hours after the last addition, the reaction was quenched with Et_3N (0.15 mL). The solvent was removed under reduce pressure, and the residue was subjected to flash chromatography through a short column of silica gel hexane/EtOAc (1:1) to afford 122 mg (91%) of compound **38** as a colourless oil. $[\alpha]_D^{23} = +35.2$ (*c* 0.44, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.87 (3H, t, *J* = 6.8 Hz, CH_3), 1.21–1.38 (20H, m, 10 × CH_2), 1.51–1.57 (4H, m, 2 × CH_2), 1.68–1.75 (2H, m, CH_2), 2.35–2.39 (4H, m, 2 × H-11, 2 × H-13), 3.44–3.47 (1H, m, OH), 3.61–3.70 (2H, m, CH_2OH), 4.31 (1H, d, $J_{5',5'}$ = 9.1 Hz, H-5′), 4.39 (1H, d, $J_{5',5'}$ = 9.1 Hz, H-5′), 5.38 (1H, dd, $J_{2,1}$ = 3.4 Hz, $J_{2,1}$ = 9.8 Hz, H-1), 6.27–6.32 (1H, m, NH), 7.43–7.47 (2H, m, Ph), 7.57–7.61 (1H, m, Ph), 8.02–8.04 (2H, m, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0 (C-18), 22.5 (CH_2), 23.8 (2 × CH_2), 25.7 (CH_2), 28.9 (CH_2), 29.2 (2 × CH_2), 29.3 (2 × CH_2), 29.3 (CH_2), 29.7 (CH_2), 31.6 (CH_2), 42.8 (C-11, C-13), 64.4 (CH_2OH), 67.5 (C-4′), 68.9 (C-5′), 74.2 (C-1), 128.6 (2 × CH_{Ph}), 129.0 (CH_{Ph}), 129.8 (CH_{Ph}), 133.7 (C_i), 159.4 (C-2′), 166.8 (C═O), 211.9 (C-12). Anal. Calcd for $C_{29}H_{45}NO_6$: C, 69.15; H, 9.01; N, 2.78. Found: C, 69.16; H, 9.07; N, 2.72.

4.36. (4*S*)-4-[(1′*R*)-1′-(Benzoyloxy)-12′-oxooctadecyl]-2-oxooxazolidine-4-carboxylic acid 39

To a stirred solution of **38** (0.12 g, 0.24 mmol) in CH_3CN (4.6 mL) was added IBX (0.10 g, 0.36 mmol) at room temperature. After being heated at reflux for 1 h, the reaction mixture was allowed to cool to room temperature and the insoluble parts were removed by filtration. The filtrate was concentrated in vacuo, and the residue was used immediately in the next reaction.

To a solution of the crude aldehyde (0.12 g, 0.24 mmol) in a mixture of 4:4:1 CH_3CN/*t*-BuOH/2-methylbut-2-ene (5.1 mL) was added at 0 °C a solution of $NaH_2PO_4{\cdot}2H_2O$ (0.25 g, 1.60 mmol) and $NaClO_2$ (0.20 g, 2.21 mmol) in water (1.2 mL). After stirring for 30 min at the same temperature, the mixture was poured into a saturated NaCl solution (3 mL) and extracted with EtOAc (2 × 10 mL). The combined organic layers were dried over Na_2SO_4, the solvent was removed, and the residue was chromatographed on silica gel CH_2Cl_2/CH_3OH (7:1) to give 0.10 g (84%) of compound **39** as a colourless oil, $[\alpha]_D^{21} = +24.7$ (*c* 0.38, CD_3OD). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (3H, t, *J* = 6.9 Hz, CH_3), 1.22–1.36 (20H, m, 10 × CH_2), 1.49–1.53 (4H, m, 2 × CH_2), 1.70 (2H, m, CH_2), 2.38–2.43 (4H, m, 2 × H-11′ 2 × H-13′), 4.54 (1H, d, $J_{5,5}$ = 9.0 Hz, H-5), 4.73 (1H, d, $J_{5,5}$ = 8.9 Hz, H-5), 5.60–5.62 (1H, m, H-1′), 7.45–7.49 (2H, m, Ph), 7.58–7.62 (1H, m, Ph), 8.04–8.06 (2H, m, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.4 (C-18′), 23.6 (CH_2), 24.9 (2 × CH_2), 27.0 (CH_2), 30.0 (CH_2), 30.3 (CH_2), 30.4 (2 × CH_2), 30.5 (2 × CH_2), 30.5 (2 × CH_2), 32.8 (CH_2), 43.5 (C-11′, C-13′), 69.7 (C-4), 70.1 (C-5), 76.9 (C-1′), 129.7 (2 × CH_{Ph}), 130.9 (2 × CH_{Ph}), 131.2 (C_i), 134.5 (CH_{Ph}), 161.2 (C-2), 167.6 (C═O), 176.8 (C-1), 214.4 (C-12′). Anal. Calcd for $C_{29}H_{43}NO_7$: C, 67.29; H, 8.37; N, 2.71. Found: C, 67.23; H, 8.31; N, 2.76.

4.37. (2*S*,3*R*)-2-Amino-3-hydroxy-2-(hydroxymethyl)-14-oxoicosanoic acid hydrochloride 5·HCl

To a solution of **39** (25 mg, 48.3 μmol) in CH_3OH (1.7 mL) was added 10% aqueous NaOH solution (1.7 mL) at room temperature. The mixture was stirred at 80 °C for 3 h, and then a 6 M aqueous HCl was added to pH 1–2. After being stirred and heated at 80 °C for another 30 min, the solvents were removed under reduced pressure. The solid parts obtained were washed several times with water, then with a mixture hexane/Et_2O (5:1), and dried on a pump for 10 h at room temperature. This procedure yielded 12.6 mg (62%) of mycestericin G·HCl **5·HCl** as a white amorphous solid. $[\alpha]_D^{24} = +10.5$ (*c* 0.24, CH_3OH). ^{1}H NMR (600 MHz, CD_3OD): δ 0.87 (3H, t, *J* = 6.9 Hz, CH_3), 1.22–1.38 (20H, m, 10 × CH_2), 1.49–1.61 (6H, m, 3 × CH_2), 2.41 (4H, t, *J* = 7.3 Hz, 2 × H-13, 2 × H-15), 3.74 (1H, d, $J_{H,H}$ = 11.2 Hz, CH_2OH), 3.90 (1H, m, H-3), 3.98 (1H, d, $J_{H,H}$ = 11.2 Hz, CH_2OH). ^{13}C NMR (150 MHz, CD_3OD): δ 14.4 (C-20), 23.6 (CH_2), 24.9 (3 × CH_2), 30.0 (2 × CH_2), 30.3 (CH_2), 30.4 (CH_2), 30.6 (2 × CH_2), 30.7 (2 × CH_2), 32.8 (2 × CH_2), 43.5 (C-13, C-15), 62.1 (CH_2OH), 70.7 (C-2), 71.7 (C-3), 171.7 (C-1), 214.5 (C-14). Anal. Calcd for $C_{21}H_{42}ClNO_5$: C, 59.48; H, 9.98; N, 3.30. Found: C, 59.55; H, 9.94; N, 3.35.

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References

1. (a) Sasaki, S.; Hashimoto, R.; Kiuchi, M.; Inoue, K.; Ikumoto, T.; Hirose, R.; Chiba, K.; Hoshino, Y.; Okumoto, T.; Fujita, T. *J. Antibiot.* **1994**, *47*, 420–433; (b) Fujita, T.; Hamamichi, N.; Kiuchi, M.; Matsuzaki, T.; Kitao, Y.; Inoue, K.; Hirose, R.; Yoneta, M.; Sasaki, S.; Chiba, K. *J. Antibiot.* **1996**, *49*, 846–853.
2. Fujita, T.; Inoue, K.; Yamamoto, S.; Ikumoto, T.; Sasaki, S.; Toyama, R.; Chiba, K.; Hoshino, Y.; Okumoto, T. *J. Antibiot.* **1994**, *47*, 208–215.
3. For recent reviews on the synthesis of natural products possessing an α-substituted serine scaffold, see: (a) Brunner, M.; Koskinen, A. M. P. *Curr. Org. Chem.* **2004**, *8*, 1629–1645; (b) Kang, S. H.; Kang, S. Y.; Lee, H.-S.; Buglass, A. J. *Chem. Rev.* **2005**, *105*, 4537–4558; (c) Ohflune, Y.; Shinada, T. *Eur. J. Org. Chem* **2005**, 5127–5134; (d) Byun, H.-S.; Lu, X.; Bittman, R. *Synthesis* **2006**, 2447–2474.
4. (a) Sato, H.; Sato, K.; Iida, M.; Yamanaka, H.; Oishi, T.; Chida, N. *Tetrahedron Lett.* **2008**, *49*, 1943–1947; (b) Yamanaka, H.; Sato, K.; Sato, H.; Iida, M.; Oishi, T.; Chida, N. *Tetrahedron* **2009**, *65*, 9188–9201.
5. (a) Shibata, K.; Shingu, K.; Vassilev, V. P.; Nishide, K.; Fujita, T.; Node, M.; Kajimoto, T.; Wong, C.-H. *Tetrahedron Lett.* **1996**, *37*, 2791–2794; (b) Nishide, K.; Shibata, K.; Fujita, T.; Kajimoto, T.; Wong, C.-H.; Node, M. *Heterocycles* **2000**, *52*, 1191–1201.
6. Fujita, T.; Hamamichi, N.; Matsuzaki, T.; Kitao, Y.; Kiuchi, M.; Node, M.; Hirose, R. *Tetrahedron Lett.* **1995**, *36*, 8599–8602.
7. Iwabuchi, Y.; Furukawa, M.; Esumi, T.; Hatakeyama, S. *Chem. Commun.* **2001**, 2030–2031.
8. Berhal, F.; Takechi, S.; Kumagai, N.; Shibasaki, M. *Chem. Eur. J.* **2011**, *17*, 1915–1921.
9. Fairhurst, N. W. G.; Mahon, M. F.; Munday, R. H.; Carbery, D. R. *Org. Lett.* **2012**, *14*, 756–759.
10. (a) Gonda, J.; Martinková, M.; Raschmanová, J.; Balentová, E. *Tetrahedron: Asymmetry* **2006**, *17*, 1875–1882; (b) Martinková, M.; Gonda, J.; Raschmanová, J. *Molecules* **2006**, *11*, 564–573; (c) Martinková, M.; Gonda, J.; Raschmanová, J.; Vojtíčková, M. *Tetrahedron* **2007**, *63*, 10603–10607; (d) Martinková, M.; Gonda, J.; Raschmanová, J.; Uhríková, A. *Tetrahedron: Asymmetry* **2008**, *19*, 1879–1885; (e) Martinková, M.; Gonda, J.; Špaková Raschmanová, J.; Slaninková, M.; Kuchár, J. *Carbohydr. Res.* **2010**, *345*, 2427–2437; (f) Martinková, M.; Gonda, J.; Uhríková, A.; Kováčová, M. *Chem. Pap.* **2011**, *65*, 527–535; (g) Martinková, M.; Gonda, J.; Uhríková, A.; Špaková, Raschmanová, J.; Kuchár, J. *Carbohydr. Res.* **2012**, *352*, 23–36; (h) Martinková, M.; Gonda, J.; Špaková Raschmanová, J.; Kožíšek, J.; Kuchár, J. *Tetrahedron: Asymmetry* **2012**, *23*, 536–546.

11. (a) Payette, D. R.; Just, G. *Can. J. Chem.* **1981**, *59*, 269–282; (b) Sano, S.; Kobayashi, Y.; Kondo, T.; Takebayashi, M.; Maruyama, S.; Fujita, T.; Nagao, Y. *Tetrahedron Lett.* **1995**, *36*, 2097–2100.
12. (a) More, J. D.; Finney, N. S. *Org. Lett.* **2002**, *4*, 3001–3003; (b) Satam, V.; Harad, A.; Rajule, R.; Pati, H. *Tetrahedron* **2010**, *66*, 7659–7706 and references cited therein.
13. (a) Honda, M.; Ueda, Y.; Sugiyama, S.; Komori, T. *Chem. Pharm. Bull.* **1991**, *39*, 1385–1391; (b) Julina, R.; Herzig, T.; Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1986**, *69*, 368–373.
14. King, A. O.; Shinkai, I. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: Chichester, 1995; pp 3888–3889.
15. Ishizuka, T.; Kunieda, T. *Tetrahedron Lett.* **1987**, *28*, 4185–4188.
16. Oishi, T.; Ando, K.; Inomiya, K.; Sato, H.; Iida, M.; Chida, N. *Bull. Chem. Soc. Jpn.* **2002**, *75*, 1927–1947.
17. Hayes, C. J.; Bradley, D. M.; Thomson, N. M. *J. Org. Chem.* **2006**, *71*, 2661–2665.