A general and concise asymmetric synthesis of sphingosine, safingol and phytosphingosines *via* tethered aminohydroxylation†

Pradeep Kumar,*[a] Abhishek Dubey[a] and Vedavati G. Puranik[b]

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A novel, practical and efficient enantioselective synthesis of sphingoid bases, L-*threo*-[2*S*,3*S*]-sphinganine (safingol), L-*threo*-[2*S*,3*S*]-sphingosine, L-*arabino*-[2*R*,3*S*,4*R*] and L-*xylo*-[2*R*,3*S*,4*S*]-C_{18}-phytosphingosine is described. The synthetic strategy features the Sharpless kinetic resolution and tethered aminohydroxylation (TA) as the key steps.

Introduction

Sphingolipids are structurally diverse constituents of membranes in mammals, plants, fungi, yeast and in some prokaryotic organisms and viruses.[1] Sphingolipids and some of their metabolites exhibit essentially all types of cell regulation such as cell proliferation, differentiation, immune response, cell recognition, apoptosis, adhesion and signal transduction.[2] Studies have shown that defects in sphingolipid metabolism lead to several inherited and most common human diseases, including diabetes,[3] cancers,[4] infection by microorganisms,[5] Alzheimer's disease,[6] heart disease and an array of neurological syndromes.[7]

In recent times, there has been a tremendous upsurge of interest in the synthesis of structurally modified sphingosines and phytosphingosines, as some of their analogues have been shown to bring morphological changes in neuronal cells[8] and behave as enzyme inhibitors.[9] The most important sphingolipids are sphingosine and phytosphingosine (Fig. 1).

Sphingosines[10] are known inhibitors of protein kinase C[11] and they are the backbone of glycosphingolipids and phosphosphingolipids. Although a number of structurally related sphingoid base structures[12] are known, the most abundant sphingoid base in nature is D-*erythro*-C_{18}-sphingosine, *i.e.* (2*S*,3*R*,4*E*)-2-aminooctadec-4-ene-1,3-diol. Phytosphingosine exists in nature as one of the molecular species of sphingolipids in microorganisms, plants and many mammalian tissues such as brain, hair, intestine,[13] uterus,[14] liver,[15] skin,[16] kidney,[17] and in blood plasma[18] (Fig. 1). Phytosphingosine is a potential heat stress signal in yeast cells[19a,b] and some of its derivatives exhibit important physiological activity. α- and β-galactosyl and glucosylphytoceramides are highly potent against tumors.[19c] Natural sphingoid bases occur in the D-*erythro*-(2*S*,3*R*) configuration, but three additional unnatural isomers have also been reported.[20] Among the unnatural sphingoid bases, L-*threo*-(2*S*,3*S*)-dihydrosphingosine (safingol) is of particular interest due to its medicinal importance. Safingol is an antineoplastic, antipsoriatic drug[21] and an inhibitor of protein kinase C (PKC)[22] and is known to act synergistically with anticancer drugs.[23]

Structurally, sphingolipids[24] are formed from two different units: a polar head group (carbohydrates) and a ceramide. The ceramide moiety consists of a sphingoid base (amino alcohol) linked through an amide bond to a fatty acyl chain. These have long-chain bases as the backbone, *i.e.* sphingosine (**1**), phytosphingosine (**3**) and the biosynthetic precursor of both, sphinganine (**2**) (Fig. 1) which are most abundant long-chain amino alcohols with generally 18 or 20 carbon atoms.

Due to their wide variety of biological activities, and unique structure with an array of functionalities, sphingolipids have been targets of synthetic interest, and therefore a great deal of effort has been devoted towards their synthesis.[25] Most synthetic studies have been focused either starting from the chiral pool materials, particularly serine[26] and carbohydrate,[27] or by asymmetric

[a]*Division of Organic Chemistry, National Chemical Laboratory, Pune 411008, India. E-mail: pk.tripathi@ncl.res.in; Fax: +91–20–25902050; Tel: +91–20–25902629*
[b]*Center for Materials Characterization, National Chemical Laboratory, Pune 411008, India*

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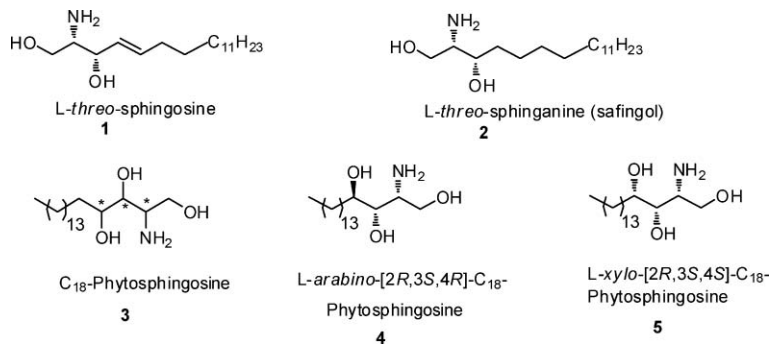


Fig. 1

synthesis.[28] Asymmetric syntheses reported mainly involve the use of chiral auxiliaries, such as sulfoxides,[29] chiral aziridines,[30] chiral sulfur[31] and nitrogen[32] ylides. The asymmetric catalytic procedures employ Sharpless asymmetric epoxidation[33] and dihydroxylation reactions.[34,35] Also, the aldol reaction[36] and organocatalytic procedures have also been described.[37] Although several procedures for the target compound have been reported,[38–41] most of these methods suffer either from a large number of steps, low yields or from low stereo- or regioselectivity. Therefore, a practical, concise expeditious and high yield synthesis of these target molecules is highly desirable. A literature search revealed that there has been no synthesis of these compounds using tethered aminohydroxylation (TA) as a source to generate both the amino and hydroxyl functionality. The tethered aminohydroxylation[42] has recently emerged as a powerful method of preparing vicinal amino alcohols in a regio- and stereoselective manner. This method overcomes the problem of low regioselectivity mainly encountered during the asymmetric aminohydroxylation (AA)[43] of unsymmetrical olefins, a recent discovery of Sharpless to introduce amine and alcohol functionality in a single step in an enantio- and stereoselective way. Donohoe *et al.* have extended the scope of the AA reaction and solved the problem of regioselectivity by tethering the nitrogen source (typically a carbamate unit) to an allylic alcohol, thus constituting a tethered aminohydroxylation (TA). A variety of TA protocols were developed to improve the yield and efficacy of the reaction. Initially, allylic carbamates were oxidised with *t*-BuOCl using the Sharpless original AA reaction conditions (**TA protocol A**, hereafter).[42a–d] However, it was observed that the chlorination of the alkene unit was a competing side reaction responsible for lowering the yield of the product. Subsequent replacement of *N*-halocarbamate salt by the *N*-mesitylsulfonyloxy derivatives (*N*–Cl → *N*–*O*–SO_2Mes) (**TA protocol B**)[42e] proved capricious and substrate specific. A recent modification of the TA protocol by Donohoe *et al.* relies on the acyl-based leaving group, in which the hydroxycarbamate derived from an allylic alcohol is treated with different acid chlorides to yield the corresponding *O*-derivatized hydroxyl carbamates which were subjected to the new TA conditions (**TA protocol C**, hereafter).[42f]

As a part of our research interest in the asymmetric synthesis of bioactive molecules such as lactones[44] and amino alcohols[45a–d] including sphingolipids,[45e–j] we became interested in developing a new and highly concise route to sphingoid bases. Herein, we report a general and efficient synthesis of L-*threo*-[2*S*,3*S*]-sphinganine, L-*threo*-[2*S*,3*S*]-sphingosine, L-*arabino*-[2*R*,3*S*,4*R*] and L-*xylo*-[2*R*,3*S*,4*S*]-C_{18}-phytosphingosine employing Sharpless kinetic resolution and tethered aminohydroxylation as the key steps.

Synthetic plan

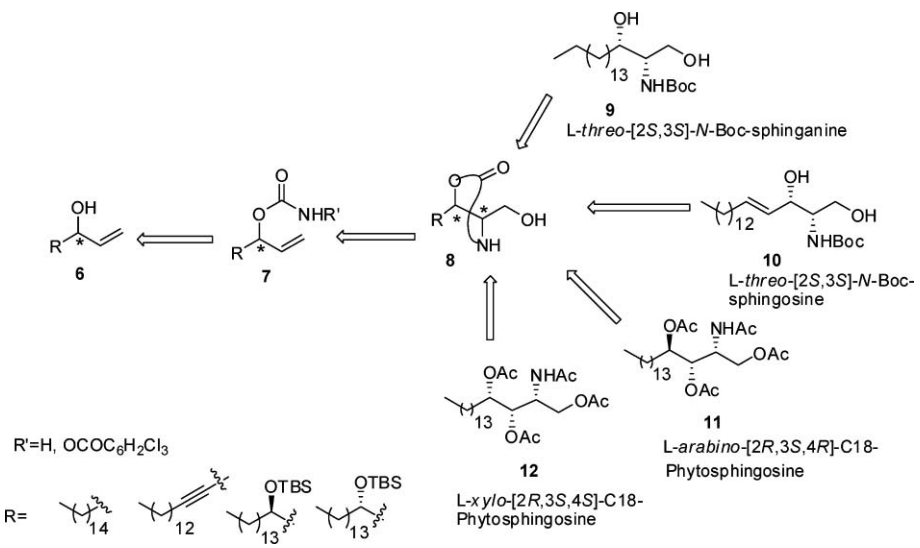
Our retrosynthetic analysis is outlined in Scheme 1.

Our synthetic approach for the synthesis of sphingoid bases was envisioned through the retrosynthetic analysis as shown in Scheme 1. We visualized compound **8** as an important precursor from which all the target sphingoid bases (**9–12**) could be constructed. The amino stereocenter in **8** could be introduced by tethered aminohydroxylation, which in turn would be obtained from carbamate **7**. The carbamate **7** could be prepared from an allylic alcohol **6** which in turn would be derived from the Sharpless kinetic resolution. In this strategy, the amino center could be installed using tethered aminohydroxylation in a highly regio- and stereoselective manner while the hydroxyl centre would be derived from Sharpless kinetic resolution.

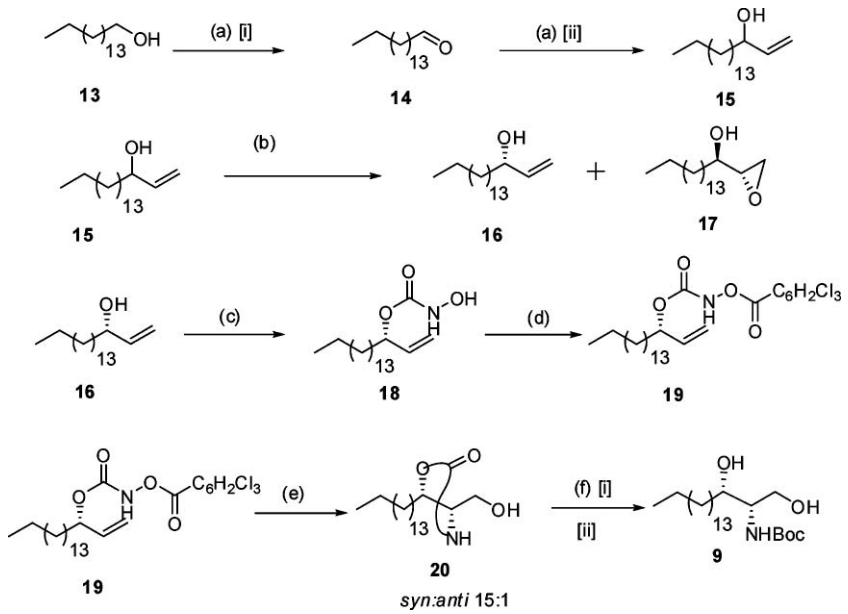
Results and discussion

Synthesis of L-*threo*-sphinganine (Scheme 2)

The synthesis of L-*threo*-[2*S*,3*S*]-sphinganine (safingol) started from commercially available hexadecanol **13**. Compound **13** was oxidized using DMSO–pivaloyl chloride[46] to give the aldehyde **14**, which on Grignard reaction with vinyl magnesium bromide furnished the allylic alcohol **15** in 82% yield. The treatment of **15** with titanium tetraisopropoxide and *tert*-butylhydroperoxide in the presence of (–)-DIPT under Sharpless asymmetric kinetic resolution conditions[47] provided the epoxy alcohol **17** and chiral allylic alcohol **16** in 47% yield and 97% ee (determined from the



Scheme 1 Retrosynthetic route to various sphingoid bases.



Scheme 2 Reagents and conditions: (a) [i] pivaloyl chloride, DMSO, Et_3N, –78 °C; [ii] vinyl bromide, Mg, 0 °C, 2 h, 82% yield of two steps; (b) (–)-DIPT, Ti(*O*-^{i}Pr)$_4$, TBHP, dry CH_2Cl_2, molecular sieves, 3 Å, –20 °C, 4 d, 47% for **16** and 48% for **17**; (c) CDI, then $NH_2OH{\cdot}HCl$, pyridine, rt, 85%; (d) 2,4,6-trichlorobenzoyl chloride, Et_3N, Et_2O, 0 °C, 85%; (e) potassium osmate *t*-BuOH : H_2O, 20 min, 75%; (f) [i] K_2CO_3, MeOH, rt, 6 h; [ii] Boc_2O, dioxane, 72%.

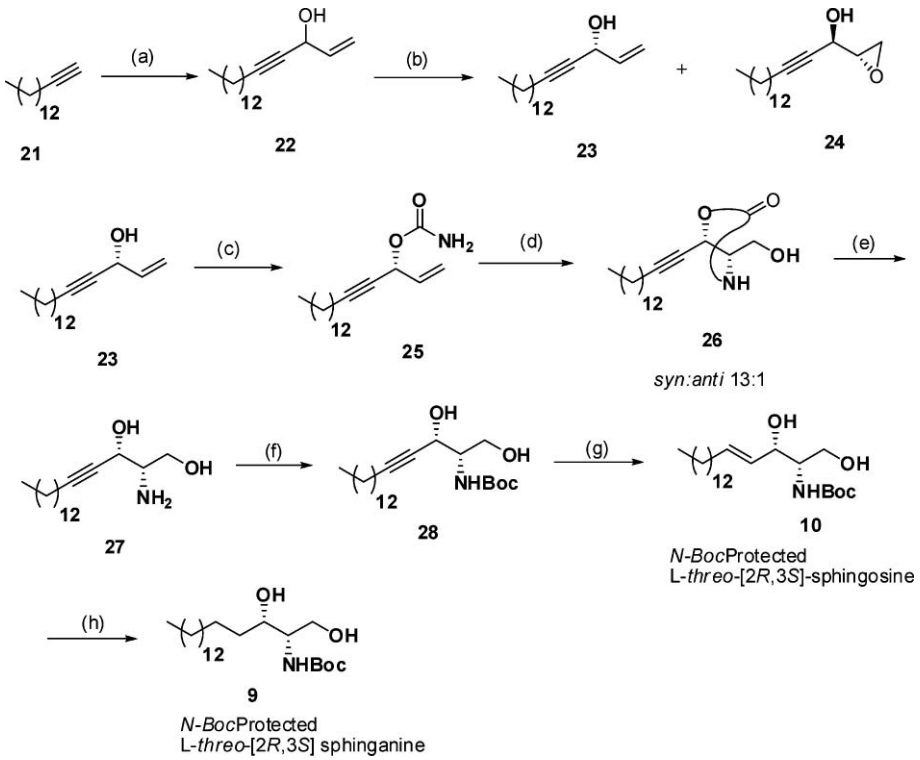
^{1}H NMR of the corresponding Mosher's ester). For introduction of the amino functionality, we then applied the new modified tethered aminohydroxylation procedure (**TA protocol C**).[42e] Thus, the alcohol **16** was reacted with CDI in pyridine, followed by the addition of hydroxylamine hydrochloride to afford the hydroxy carbamate **18** in excellent yield. The resulting hydroxycarbamate **18** was then treated with pentafluorobenzoyl chloride in ether to yield the pentafluorobenzoyl *O*-derivatized hydroxycarbamate, which was found to decompose during the reaction and purification on column chromatography. We then decided to explore yet another reagent, trichlorobenzoyl chloride, for tethering the substrate **18**. To our delight the reaction proceeded smoothly to furnish the trichlorobenzoyl *O*-derivatized hydroxycarbamates **19** in 85% yield. The trichlorobenzoyl *O*-derivatized hydroxycarbamates **19** were subjected to TA reaction to furnish the protected aminoalcohol **20** in 75% yield with complete regio- and excellent diastereoselectivity (*syn* : *anti* 15 : 1, determined from ^{1}H NMR). The diastereomeric mixture could easily be separated by column chromatography, which on hydrolysis with K_2CO_3 in methanol afforded the crude aminoalcohol. Subsequent Boc protection using Boc_2O in the presence of dioxane furnished the enantiomerically pure *N*-Boc-L-*threo*-sphinganine **9**[38b] in 72% yield. The overall yield of the target compound **9** was found to be 15% from seven steps. Our synthesis of **9** proved to be efficient in comparison with a literature report[38g] of its synthesis in 10 steps in overall ~4% yield.

Synthesis of *N*-Boc-L-*threo*-sphingosine (Scheme 3)

The synthesis of L-*threo*-sphingosine (Scheme 3) started from commercially available pentadec-1-yne **21**. Treatment of **21** with *n*-BuLi in THF at –78 °C followed by addition of freshly distilled acrolein furnished the allylic alcohol **22** in 70% yield. The treatment of **22** with titanium tetraisopropoxide and *tert*-butylhydroperoxide in the presence of (–)-DIPT under Sharpless asymmetric kinetic resolution conditions provided the epoxy alcohol **24** and chiral allylic alcohol **23** in 45% yield and 96% ee (determined from the ^{1}H NMR of the corresponding Mosher's ester). Then we used trichloroacetyl isocyanate reagent for tethered aminohydroxylation (**TA protocol A**).[42a]

Alcohol **23** was then reacted with trichloroacetyl isocyanate in CH_2Cl_2 to give the corresponding isocyanate, which on treatment with aq. K_2CO_3 and methanol furnished the carbamate **25** in 85% yield. The carbamate was converted into the oxazolidinone derivative **26** by a tethered aminohydroxylation protocol[42a] using *tert*-butylhypochlorite as the oxidant, potassium osmate, NaOH, ^{i}Pr$_2$EtN and propanol as the solvent. The reaction proceeded smoothly to furnish the protected aminoalcohol **26** in 65% yield with complete regio- and good diastereoselectivity (*syn* : *anti* 13 : 1, determined from ^{1}H NMR). The diastereomeric mixture could easily be separated by column chromatography. The desired *syn*-diastereomer was subjected to hydrolysis with K_2CO_3 in methanol to furnish the crude aminoalcohol **27**. Subsequent Boc protection using Boc_2O in the presence of dioxane gave the Boc protected **28** in 82% yield, which was finally converted to the crystalline, enantiomerically pure *N*-Boc-L-*threo*-sphingosine **10**[26a] in 65% yield by selective reduction of the C–C bond with Red-Al in Et_2O, followed by its subsequent conversion into *N*-Boc-L-*threo*-sphinganine **9** in 85% yield by reduction of the double bond under $Pd(OH)_2/H_2$ conditions. The overall yield of the target compound **10** was found to be 14% from seven steps. Our synthesis of **10** proved to be efficient in comparison with literature reports (Kitagawa *et al.*,[40l] 7 steps, 12% yield; Griengl *et al.*[40f] 14 steps, 12% yield; Hudlicky *et al.*[40h] 10 steps, 9% yield).

The relative stereochemistry of the TA product was confirmed by single crystal X-ray crystallography of compound **27** (Fig. 2),



Scheme 3 Reagents and conditions: (a) *n*-BuLi, freshly distilled acrolein, THF, −78 °C, 2 h, 70%; (b) (–)-DIPT, Ti(*O*-^{i}Pr)$_4$, TBHP, dry CH_2Cl_2, molecular sieves, 3 Å, −20 °C, 3 d, 45% for **23** and 49% for **24**; (c) $Cl_3CCONCO$, K_2CO_3, CH_2Cl_2–CH_3OH (1.5 : 1), 4 h, 85%; (d) NaOH, *t*-BuOCl, $^{i}Pr_2EtN$, potassium osmate, propanol, 2.5 h, 65%; (e) K_2CO_3, MeOH, rt, 6 h; (f) Boc_2O, dioxane, 82%; (g) Red-Al/Et_2O, 0 °C–r.t. 65%; (h) H_2/Pd, EtOAc, 85%.

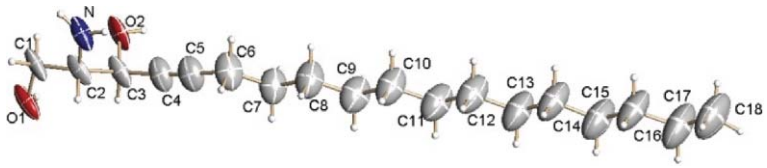


Fig. 2 ORTEP diagram of **27**.

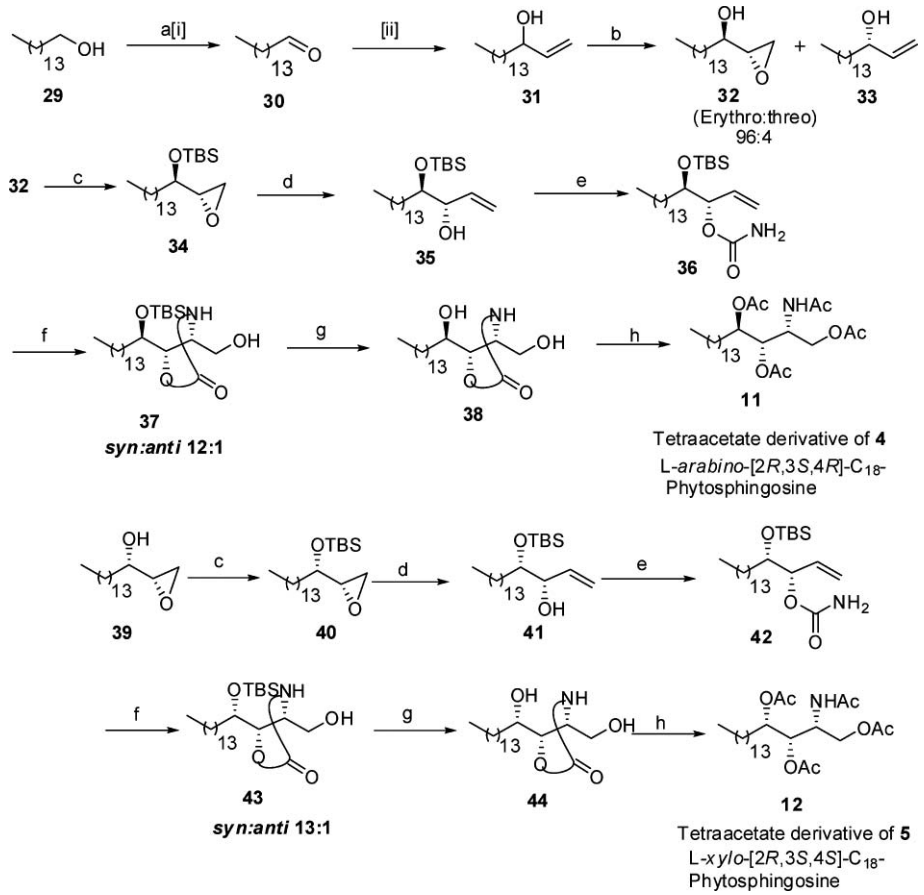
which shows that the amino and alcohol functional groups are *syn* to each other.

Synthesis of L-*arabino*-[2*R*,3*S*,4*R*]-C_{18}-phytosphingosine and L-*xylo*-[2*R*,3*S*,4*S*]-C_{18}-phytosphingosine (Scheme 4)

The tethered aminohydroxylation route was then further extended to the synthesis of a few selected isomers of phytosphingosine. As depicted in Scheme 4, the synthesis of L-*arabino*-[2*R*,3*S*,4*R*]-C_{18}-phytosphingosine started from commercially available pentadecanol **29**. Subsequent oxidation of alcohol **29** using DMSO–pivaloyl chloride followed by Grignard reaction with vinyl magnesium bromide furnished the allylic alcohol **31** in 88% yield. Compound **31** was treated with titanium tetraisopropoxide and *tert*-butylhydroperoxide in the presence of (–)-DIPT under Sharpless asymmetric kinetic resolution conditions to provide the epoxy alcohol **32** and chiral allylic alcohol **33** in 46% yield and 97% ee (determined from ^{1}H NMR of the corresponding Mosher's ester). The epoxide **32** was found to be a mixture of *erythro* and *threo* (96 : 4), which was subsequently treated with TBSOTf in the presence 2,6-lutidine to furnish the silylated derivative **34** in good yield.

The required *erythro*-isomer **34** could easily be separated by column chromatography in 90% yield. Epoxide **34** was treated with excess dimethylsulfonium methylide[48] (generated from trimethylsulfonium iodide and *n*-BuLi) to furnish the allylic alcohol **35** in 75% yield. Alcohol **35** was then reacted with trichloroacetyl isocyanate in the presence of CH_2Cl_2 to give the corresponding isocyanate, which on treatment with aq. K_2CO_3 and methanol furnished the carbamate **36** in 90% yield. The carbamate was converted into the oxazolidinone derivative **37** by a tethered aminohydroxylation protocol using *tert*-butyl hypochlorite as the oxidant, potassium osmate, NaOH, $^{i}Pr_2EtN$ and propanol as the solvent (**TA protocol A**). The reaction proceeded smoothly to furnish the protected aminoalcohol **37** in 66% yield with complete regio- and excellent diastereoselectivity (*syn* : *anti* 12 : 1, determined from ^{1}H NMR). The diastereomeric mixture could easily be separated by column chromatography.

The key step in the TA as depicted in Fig. 3 is the intramolecular addition of the RN═Os═O fragment across the alkene leading to *syn* or *anti* relative stereochemistry. Generally the 1,3-allylic interaction plays a major role in determining the stereoselective outcome of the reaction. Between the two possible conformations, **A** and **B** of tethered [3 + 2] cycloaddition, the 1,3-allylic



Scheme 4 Reagents and conditions: (a) [i] pivaloyl chloride, DMSO, Et_3N, –78 °C; [ii] vinyl bromide, Mg, –78 °C, 2 h, 88%; (b) (–)-DIPT, Ti(*O*-^{i}Pr)$_4$, TBHP, dry CH_2Cl_2, molecular sieves, 3 Å, –20 °C, 4 d, 49% for **32** and 46% for **33**; (c) TBSOTf, 2,6-lutidine, dry CH_2Cl_2, 15 min, –10 °C, 90%; (d) $(CH_3)_3S^+I^-$, *n*-BuLi, –20 °C, 75%; (e) $Cl_3CCONCO$, K_2CO_3, CH_2Cl_2–CH_3OH (1.5 : 1), 4 h, 90%; (f) NaOH, *t*-BuOCl, ^{i}Pr$_2$EtN, potassium osmate, propanol, 2.5 h, 66%; (g) TsOH (cat.), MeOH, 78%; (h) (i) K_2CO_3, MeOH, rt, 6 h; (ii) Ac_2O, pyridine, DMAP (cat), overnight, 82%.

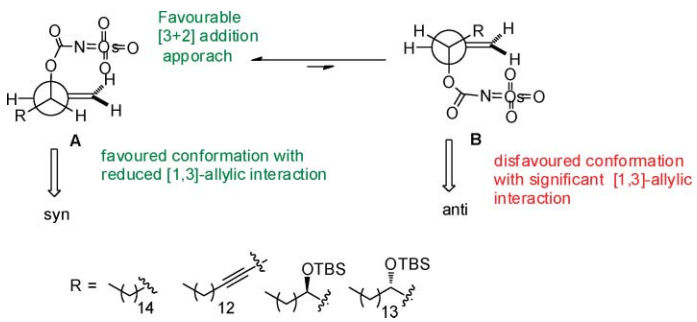


Fig. 3 Proposed transition states for the *syn*/*anti* selectivity observed during the TA reaction.

interactions are minimised in conformation **A**, while such interactions are significant in conformation **B**. One would predict conformation **A** to be lower in energy and therefore the equilibrium is shifted towards the more stable conformation **A**, thus leading to major *syn* product.

The compound **37** was desilylated using *p*-TSA and methanol to give the alcohol **38** in 78% yield, which on hydrolysis with K_2CO_3 in methanol furnished the crude aminoalcohol. Subsequent acylation using Ac_2O in the presence of pyridine and catalytic amount of DMAP produced the tetraacetate derivative of phytosphingosine[26j] **4** in 82% yield. Our synthetic approach proved to be efficient as the overall yield of the target compound **11** was found to be 11% from eight steps in comparison with a literature report[26j] of overall yield of ~7% in three steps.

For the synthesis of L-*xylo*-[2*R*,3*S*,4*S*]-C_{18}-phytosphingosine, the allylic alcohol **33** obtained by the chiral resolution of **31** was subjected to Sharpless asymmetric epoxidation to give the epoxide **39** in 75% yield as a single diastereomer, which was converted into the tetraacetate derivative of L-*xylo*-[2*R*,3*S*,4*S*]-C_{18}-phytosphingosine **5** following the same sequence of reactions as described for **4** (Scheme 4). The physical and spectroscopic data of **12** were in accordance with those described in literature.[41,45e]

Conclusions

In summary, we have developed a facile and practical enantioselective synthesis of sphingoid bases in high overall yields. The main advantage of this strategy is its versatility, leading to the synthesis of *N*-Boc-L-*threo*-sphinganine, *N*-Boc-L-*threo*-sphingosine, L-*arabino*-[2*R*,3*S*,4*R*]-C_{18}-phytosphingosine and L-*xylo*-[2*R*,3*S*,4*S*]-C_{18}-phytosphingosine. The synthetic strategy is flexible and would permit the synthesis of not only the stereoisomers of sphingoid bases but also the other lipids bearing skeleton-modified sphingoid

base backbones with different chain lengths and substitution patterns.

Experimental section

General Methods

All reactions requiring anhydrous conditions were performed under a positive pressure of argon using oven-dried glassware (110 °C), which was cooled under argon. Solvents used for chromatography were distilled at their respective boiling points using known procedures. All commercial reagents were obtained from Sigma-Aldrich Chemical Co. and Lancaster Chemical Co. (UK). The progress of the reactions was monitored by TLC using precoated aluminium plates (Merck silica gel 60 F254). Column chromatography was performed on silica gel 60–120/100–200/230–400 mesh obtained from S. D. Fine Chemical Co. India or Spectrochem India. Typical syringe and cannula techniques were used to transfer air- and moisture-sensitive reagents. IR spectra were recorded on a Perkin-Elmer infrared spectrometer model 599-B and model 1620 FTIR. ^{1}H NMR spectra were recorded on Bruker AC-200 MHz, Bruker AV-400 MHz and Bruker DRX–500 MHz instruments using deuterated solvent. Chemical shifts are reported in ppm. Proton coupling constants (J) are reported as absolute values in Hz and multiplicity (brs, broad; s, singlet; d, doublet; t, triplet; m, multiplet). ^{13}C NMR spectra were recorded on Bruker AC-200, Bruker AV-400 and Bruker DRX-500 instruments operating at 50 MHz, 100 MHz, and 125 MHz, respectively. ^{13}C NMR chemical shifts are reported in ppm relative to the central line of $CDCl_3$ (δ 77.0). Mass spectra were recorded on PE SCIEX API QSTAR pulsar (LC-MS). HRMS was taken by EI method using DIP. Microanalytical data were obtained using a Carlo–Erba CHNS-0 EA 1108 elemental analyzer. All the melting points were recorded on a Büchi B-540 electrothermal melting point apparatus. Yields refer to chromatographically and spectroscopically pure compounds. Enantiomeric excess was determined using Mosher analysis.

1-Hexadecanal (14)

To a stirred solution of pivaloyl chloride (10.14 mL, 82.4 mmol) in dry CH_2Cl_2 (100 mL) cooled to −78 °C was added dropwise dry DMSO (8.77 mL, 123.6 mmol) in dry CH_2Cl_2 (20 mL) over 20 min. The reaction mixture was stirred for 30 min. Alcohol **13** (10 g, 41 mmol) in dry CH_2Cl_2 (20 mL) was added dropwise to the above reaction mixture over 20 min. After consumption of the starting material (2 h), Et_3N (28.7 mL, 206 mmol) was added and stirred at −78 °C for further 30 min. The reaction mixture was brought to room temperature slowly and stirred for 30 min. The reaction mixture was poured into H_2O (150 mL) and the organic layer separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL) and combined organic layers were washed with H_2O (3 × 50 mL), brine (50 mL), dried (Na_2SO_4) and passed through short pad of silica gel. The filtrate was concentrated to give the aldehyde **14** (9.7 g) as pale yellow oil, which was used as such for the next step without purification.

Octadec-1-en-3-ol (15)

To a stirred solution of Mg (2.94 g, 120.9 mmol) in dry THF (30 mL), vinyl bromide (40.32 mL, 2.0 M solution in dry THF, 80.6 mmol) was added dropwise over 30 min and the Grignard reagent thus formed was cooled to 0 °C. Aldehyde **14** (9.7 g, 40.3 mmol) in dry THF (10 mL) was added dropwise to the above reaction mixture over 20 min. After 2 h stirring at 0 °C the reaction mixture was quenched with saturated NH_4Cl solution (10 mL), and the aqueous layer was extracted with EtOAc (4 × 20 mL) and the combined organic layers were washed with brine and dried over Na_2SO_4. The extracts were concentrated to near dryness and purified by silica gel column chromatography using petroleum ether–EtOAc (96 : 4) as eluent to give **15** (9.08 g, 82% yield) as a pale yellow solid: mp 46–48 °C.

3-(*S*)-Octadec-1-en-3-ol (16)

To a mixture of 3 Å molecular sieves (225 mg) and Ti(^{i}-PrO)$_4$ (1.34 mL, 4.50 mmol) in dry CH_2Cl_2 (40 mL) (−)-DIPT (1.2 mL, 5.73 mmol) was added dropwise over 10 min at −20 °C. The mixture was stirred for 20 min at −20 °C and a solution of **15** (1.1 g, 4.09 mmol) in dry CH_2Cl_2 (5 mL) was added over 10 min. The reaction mixture was stirred for an additional 30 min at −20 °C and TBHP (3.4 mL, 3 M solution in toluene, 10.24 mmol) was added dropwise over 15 min. The reaction mixture was kept at −20 °C by constant temperature bath and after 4 d the reaction was warmed to 0 °C, and quenched with H_2O (30 mL) and the mixture was stirred for 30 min, and then precooled (0 °C) freshly prepared ferrous sulfate heptahydrate (278 mg, 1 mmol) in 10 mL of water was added and the reaction mixture stirred for 30 min at rt. The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 30 mL). The combined organic layers were treated with 6 mL of a precooled (0 °C) solution of 30% NaOH w/v in saturated brine. The two phase mixture was stirred vigorously for 1 h at 0 °C, followed by dilution with 50 mL of water. The phases were separated and the aqueous layer extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated to dryness. The crude product was then purified by flash chromatography on silica gel using petroleum ether–EtOAc (96 : 4) as eluent to give chiral hydroxy olefin **16** (0.52 g, 47% yield, based on 50% conversion) as a white solid. mp 46–48 °C; $[\alpha]_D^{25}$: +8.3 (c 0.32, $CHCl_3$); Anal. Calcd for $C_{18}H_{36}O$ (268.48): C, 80.53; H, 13.52%; Found: C, 80.43; H, 13.49%; IR ($CHCl_3$, cm^{-1}): ν_{max} 3499, 1611; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.88 (3H, t, J = 6.1 Hz), 1.26 (26H, brs), 1.41–1.55 (2H, m), 1.59 (1H, brs), 4.05–4.15 (1H, m), 5.07–5.27 (2H, m), 5.79–5.96 (1H, m); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 14.1, 22.7, 25.3, 25.7, 29.3, 29.7, 31.9, 37.0, 73.2, 114.4, 141.3. MS(ESI): m/z 269.44 (M+H)$^+$, 291.48 (M+Na)$^+$.

Further elution with petroleum ether–/EtOAc (92 : 8) gave the epoxide **17** as a white solid.

1-Oxiranyl-hexadecan-1-ol (17)

(0.56 g, 48% yield, based on 50% conversion): mp 56–57 °C; $[\alpha]_D^{25}$: −6.3 (c 1.3, $CHCl_3$); Anal. Calcd for $C_{18}H_{36}O_2$ (284.48): C, 76.0; H, 12.76%; Found: C, 75.89; H, 12.64%; IR ($CHCl_3$, cm^{-1}): ν_{max} 3482, 2854, 1211; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.89 (3H, t, J = 6.1 Hz), 1.26 (26H, brs), 1.49–1.59 (2H, m), 2.71–2.84 (2H, m), 3.04–3.21 (1H, m), 3.86–3.94 (1H, m), 4.48 (1H, brs); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 13.9, 21.6, 22.5, 25.2, 29.2, 31.8, 33.4, 43.4, 54.6, 68.4, 70.1, 72.1; MS(ESI): m/z 307.48 (M+Na)$^+$.

(*S*)-Octadec-1-en-3-ylhydroxycarbamate (18)

N,*N*-Carbonyldiimidazole (1.81 g, 11.16 mmol) was added to alcohol **16** (2 g 7.44 mmol) in pyridine (30 mL) at 40 °C. After complete adduct formation between the alcohol and *N*,*N*-carbonyldiimidazole (~4 h), hydroxylamine hydrochloride (1.29 g, 18.61 mmol) was added and the reaction mixture stirred for 24 h at 40 °C. The reaction was quenched with 1 M hydrochloric acid (10 mL), partitioned, and the aqueous layer extracted with Et_2O (35 mL) and EtOAc (3 × 30 mL). The combined organic layers were then washed sequentially with H_2O (30 mL) and brine (2 × 30 mL), dried (Na_2SO_4), filtered and the solvent was azeotropically removed with toluene. The crude product was then purified by flash chromatography on silica gel using petroleum ether–EtOAc (85 : 15) as eluent to give hydroxyl carbamate **18** (2.07 g, 85% yield) as a white crystalline solid: mp 72–74 °C; $[\alpha]_D^{25}$: –4.3 (*c* 1.0, $CHCl_3$); Anal. Calcd for $C_{19}H_{37}NO_3$ (327.50): C, 69.68; H, 11.39; N, 4.28%; Found: C, 69.87; H, 11.31; N, 4.38%; IR ($CHCl_3$, cm^{-1}): ν_{max} 3482, 2854, 1716; ^1H NMR ($CDCl_3$, 200 MHz): δ 0.88 (3H, t, J = 6.1 Hz), 1.26 (26H, brs), 1.53–1.68 (2H, m), 5.16–5.31 (3H, m), 5.69–5.86 (1H, m), 7.20 (1H, brs); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 14.1, 22.7, 24.9, 29.3, 29.6, 31.9, 34.2, 77.1, 117.1, 136.1, 159.1; MS(ESI): m/z 350.43 $(M+Na)^+$, 366.3549 $(M+K)^+$.

(*S*)-Octadec-1-en-3-yl-2,4,6-trichlorobenzoyloxycarbamate (19)

To an ice-cold solution of hydroxycarbamate **18** (2.2 g, 6.71 mmol) in Et_2O (4 : 1; 5 mL $mmol^{-1}$) was added Et_3N (1.02 mL, 7.38 mmol), before the addition of the 2,4,6-trichlorobenzoyl chloride (1.03 mL, 6.71 mmol) in small portions. The reaction was quenched with HCl (1 M aq. sol., 20 mL) and the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic layers were washed sequentially with H_2O (30 mL), $NaHCO_3$ (aq. sat. sol., 30 mL) and brine (30 mL), dried (Na_2SO_4), filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel using petroleum ether–EtOAc (96 : 4) as eluent to give *O*-trichloro substituted hydroxycarbamate **19** (3.05 g, 85% yield) as a white solid compound: mp 46–47 °C; $[\alpha]_D^{25}$: –8.8 (*c* 1.0, $CHCl_3$); Anal. Calcd for $C_{26}H_{38}Cl_3NO_4$ (534.94): C, 58.38; H, 7.16; N, 2.62%; Found: C, 58.30; H, 7.02; N, 2.55%; IR ($CHCl_3$, cm^{-1}): ν_{max} 3420, 2982, 1745, 1710, 1660; ^1H NMR ($CDCl_3$, 200 MHz): δ 0.88 (3H, t, J = 5.9 Hz), 1.25 (26H, brs), 1.55–1.78 (2H, m), 5.20–5.36 (3H, m), 5.72–5.89 (1H, m), 7.41 (2H, s); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 14.1, 22.7, 24.9, 29.3, 29.7, 31.9, 34.2, 78.4, 117.7, 128.3, 128.6, 133.6, 135.5, 137.7, 155.4, 163.1; MS(ESI): m/z 556.317 $(M+Na)^+$, 558.33 $(M+2+Na)^+$.

(4*R*,5*R*)-4-(Hydroxymethyl)-5-pentadecyloxazolidine-2-one (20)

To a solution of *O*-trichlorobenzoyl-substituted hydroxycarbamate **19** (0.50 g, 0.93 mmol) in *t*-butanol and H_2O (18 mL, 3 : 1, 20 mL $mmol^{-1}$) was added dropwise a solution of potassium osmate dihydrate (13.7 mg, 4 mol%) in H_2O (0.5 mL) over 10 min. The reaction was quenched by addition of sodium sulfite (200 mg $mmol^{-1}$) and the solvent azeotropically removed with toluene. The crude product was found to be a mixture of ratio *syn* : *anti* 15 : 1 (determined from ^1H NMR of crude compound), which was purified by flash column chromatography on silica gel using petroleum ether–EtOAc (6 : 4) as eluent to give the aminoalcohol **20** (230 mg, 75% yield) as white solid: mp 87–89 °C; $[\alpha]_D^{25}$: –9.8 (*c* 1.0, $CHCl_3$); Anal. Calcd for $C_{19}H_{37}NO_3$ (327.50): C, 69.68; H, 11.39; N, 4.28%; Found: C, 69.56; H, 11.33; N, 4.38%; IR ($CHCl_3$, cm^{-1}): ν_{max} 3438, 2949, 1710; ^1H NMR ($CDCl_3$, 500 MHz): δ 0.88 (3H, t, J = 5.9 Hz), 1.26–1.91 (28H, m), 3.53–3.83 (3H, m), 4.31–4.40 (1H, m), 6.41 (1H, s); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 14.1, 22.7, 24.6, 29.3, 29.6, 29.7, 31.9, 34.8, 59.5, 63.5, 79.2, 160.4; MS(ESI): m/z 350.3427 $(M+Na)^+$.

***tert*-Butyl-(2*S*,3*S*)-1,3-dihydroxyoctadecane-2-yl)carbamate (9)**

To a stirred solution of TA product **20** (300 mg, 0.92 mmol) in MeOH (5 mL) was added K_2CO_3 (379 mg, 2.74 mmol) and the reaction mixture was stirred until completion of the starting material (6 h), and methanol was removed *in vacuo*. Water was added to the crude product and extracted with EtOAc (3 × 10 mL), dried over sodium sulfate and concentrated to near dryness. The residue was subsequently treated with Boc_2O (0.32 mL, 1.38 mmol) in dioxane and the reaction mixture stirred until consumption of the starting material (8 h), and the solvent was removed by vacuum evaporation. Purification by silica gel flash chromatography ($MeOH–CH_2Cl_2$, 5 : 95) gave **9** (265 mg, 72% yield for two steps) as a white solid: mp 80–81 °C; $[\alpha]_D^{25}$: +18.8 (*c* 1.0, $CHCl_3$); lit.[38b] $[\alpha]_D^{21}$: +19.8 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): ν_{max} 3400, 2970, 1690; ^1H NMR ($CDCl_3$, 400 MHz): δ 0.88 (3H, t, J = 6.5 Hz), 1.26 (26H, brs), 1.46 (9H, s), 1.50–1.56 (2H, m), 2.10 (2H, brs), 3.53 (1H, brs), 3.75–3.80 (2H, m), 4.01 (1H, dd, J = 3.5, 11.5 Hz), 5.32–5.48 (1H, brs); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 22.7, 25.9, 28.4, 29.4, 29.7, 31.9, 34.5, 54.6, 62.6, 74.5, 79.7, 156.0; MS(ESI): m/z 424.33 $(M+Na)^+$.

Octadec-1-en-4-yn-3-ol (22)

n-BuLi (1.6 M solution in hexane, 6.6 mL, 10.56 mmol) was added dropwise over 10 min to a solution of 1-pentadecyne **21** (2 g, 9.6 mmol) in dry THF (50 mL) at –78 °C. After stirring at –78 °C for 30 min, a solution of acrolein (2.15 g, 38.39 mol) in abs. THF (20 mL) was added. The reaction mixture was stirred at –78 °C for 30 min, and allowed to warm to –20 °C for 2 h, then quenched by the addition of sat. NH_4Cl (10 mL) and extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with brine, dried (Na_2SO_4) and concentrated. Filtration through a silica gel column using petroleum ether as the solvent to recover excess 1-pentadecyne followed by elution with petroleum ether–EtOAc (96 : 4) gave **22** (1.77 g, 70% yield) as a low melting solid.

(*R*)-Octadec-1-en-4-yn-3-ol (23)

To a mixture of 3 Å molecular sieves (1.2 g) and Ti(^{i}-PrO)$_4$ (6.19 mL, 20.79 mmol) in dry CH_2Cl_2 (40 mL), (–)-DIPT (5.23 mL, 24.96 mmol) was added dropwise over 10 min at –20 °C. The mixture was stirred for 20 min at –20 °C, and a solution of mixture of **22** (5.5 g, 20.79 mmol) in dry CH_2Cl_2 (20 mL) was added over 15 min. The reaction mixture was stirred for an additional 30 min at –20 °C and TBHP (2.27 mL, 5.5 M solution in toluene, 12.48 mmol) was added dropwise over 15 min. The reaction mixture was kept at –20 °C by constant temperature bath and after 3 days the reaction was warmed to 0 °C, quenched with H_2O (100 mL) and the mixture was stirred for 30 min, and then precooled (0 °C) freshly prepared ferrous sulfate heptahydrate

(1.44 g, 5.19 mmol) in 10 mL of water was added and reaction mixture is stirred for 30 min at rt. The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were treated with 30 mL of a precooled (0 °C) solution of 30% NaOH w/v in saturated brine. The two phase mixture was stirred vigorously for 1 h at 0 °C, followed by dilution with 50 mL of water. The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated to dryness. The crude product was then purified by flash chromatography on silica gel using petroleum ether–EtOAc (96 : 4) to give chiral hydroxy olefin **23** as a white solid compound (2.48 g, 45% yield, based on 50% conversion): mp 35–37 °C; $[\alpha]_D^{25}$: −3.76 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): ν_{max} 3440, 2210, 1611; ^1H NMR (200 MHz, $CDCl_3$): 0.88 (3H, t, *J* = 6.1 Hz), 1.26–1.52 (22H, m), 1.89 (1H, d, *J* = 6.1 Hz), 2.20–2.27 (2H, t, *J* = 6.9 Hz), 4.84–4.90 (1H, m), 5.17–5.49 (2H, m), 5.9–6.01 (1H, m); ^{13}C NMR (50 MHz, $CDCl_3$): 14.1, 18.7, 22.6, 28.5, 28.8, 29.1, 29.3, 29.6, 31.9, 63.3, 78.9, 87.3, 115.9, 137.6; MS(ESI): *m/z* 287.477 (M^++Na). HRMS, (EI/DIP) for (M^+): calc. 264.24729, Found: 264.24697.

(*R*)-1-((*S*)-Oxirane-2-yl)hexadec-2-yn-1-ol (24)

(2.85 g, 49% yield, based on 50% conversion); m.p. 48–49 °C; $[\alpha]_D^{25}$: −16.31 (*c* 1.0, $CHCl_3$); Anal. Calcd for $C_{18}H_{32}O_2$ (280.45): C, 77.09; H, 11.50%; Found: C, 77.19; H, 11.44%; IR ($CHCl_3$, cm^{-1}): ν_{max} 3482, 3100, 2900, 2200; ^1H NMR (200 MHz, $CDCl_3$): 0.88 (3H, t, *J* = 6.1 Hz), 1.26–1.58 (22H, m), 2.11 (1H, d, *J* = 5.0 Hz), 2.23 (2H, dt, *J* = 6.9, 14.0 Hz), 2.82 (1H, q, *J* = 3.9, 4.9 Hz), 2.92 (1H, q, *J* = 2.6, 5.0 Hz), 3.25 (1H, dt, *J* = 2.7, 3.9 Hz), 4.63 (1H, sextet, *J* = 2.1, 4.9, 7.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): 14.0, 18.6, 22.6, 28.4, 28.9, 29.0, 29.4, 29.6, 31.8, 44.3, 53.9, 61.1, 76.1, 87.6.

(*R*)-Octadec-1-en-4-yn-3-ylcarbamate (25)

Trichloroacetyl isocyanate (0.54 mL, 4.54 mmol) was added dropwise over 10 min to a solution of alcohol **23** (1.0 g, 3.78 mmol) in dry CH_2Cl_2 (5.67 mL, 1.5 mL $mmol^{-1}$) at 0 °C. After stirring for 2 h, or until TLC showed no starting material present, the mixture was concentrated under reduced pressure. The residue was dissolved in MeOH (7.56 mL, 2 mL $mmol^{-1}$), cooled to 0 °C and an aqueous K_2CO_3 solution (1.56 g, 11.34 mmol, 2 mL $mmol^{-1}$) was added. The cooling bath was removed and the mixture was allowed to stir for 4 h, by which time TLC showed complete conversion. The solvent was evaporated under reduced pressure and the aqueous residue was extracted with CH_2Cl_2 (3 × 25 mL). The combined organics were washed with brine (10 mL), dried over Na_2SO_4 and concentrated under reduced pressure to yield the crude carbamate, which was purified by flash column chromatography on silica gel using petroleum ether–EtOAc (8 : 2) as eluent to give carbamate **25** (0.98 g, 85% yield) as a white solid: mp 50–51 °C; $[\alpha]_D^{25}$: −3.67 (*c* 1.2, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): ν_{max} 3346, 1654; ^1H NMR (200 MHz, $CDCl_3$): 0.87 (3H, t, *J* = 6.0 Hz), 1.25–1.55 (22H, m), 2.19–2.27 (2H, m), 5.07 (2H, brs), 5.24–5.57 (2H, dd, *J* = 1.2, 18.0 Hz), 5.78–5.96 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$): 14.1, 18.7, 22.6, 28.4, 28.8, 29.0, 29.4, 29.6, 31.9, 65.6, 75.4, 88.4, 118.1, 133.8, 155.9; HRMS, (EI/DIP) for (M^+): calc. 307.25074, Found: 307.25068.

(4*R*,5*S*)-4-(Hydroxymethyl)5-(pentadec-1-ynyl)oxazolidin-2-one (26)

A fresh aqueous solution of sodium hydroxide (18 mL, 0.08M, 58 mg, 1.46 mmol) was prepared. All but a few drops of this was added in one portion to a stirred solution of the allylic carbamate **25** (0.50 g, 1.62 mmol) in propan-1-ol (19.44 mL, 12 mL $mmol^{-1}$). The solution was allowed to stir for 5 min, before freshly prepared *tert*-butyl hypochlorite (0.176 g, 1.62 mmol) was added. The mixture was again allowed to stir for 5 min, to this was added $^iPr_2EtN$ (14 mg, 5 mol%) in one portion. The mixture was allowed to stir for a further 5 min before the final addition of a solution of potassium osmate (23 mg, 4 mol%) in the remainder of the NaOH solution made earlier. The reaction was monitored by TLC and halted when no further change was detected. The reaction was quenched by the addition of sodium sulfite (100 mg $mmol^{-1}$), and allowed to stir for 30 min. The mixture was extracted with EtOAc (5 × 25 mL). The combined organics were washed with brine, dried over sodium sulfate and concentrated under reduced pressure to give the crude product which was found to be a mixture of ratio *syn* : *anti* 13 : 1 (determined from ^1H NMR of crude compound). Purification by flash column chromatography on silica gel using petroleum ether–EtOAc (1 : 1) as eluent gave the carbamate **26** (0.34 g, 65% yield) as a white solid: mp 53–55 °C; $[\alpha]_D^{25}$: −8.39 (*c* 0.9, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): ν_{max} 3400, 2922, 2100, 1653; ^1H NMR (200 MHz, $CDCl_3$): 0.88 (3H, t, *J* = 6.0 Hz), 1.24–1.52 (22H, m), 1.84 (1H, brs) 2.18–2.25 (2H, m), 4.20–4.25 (1H, m), 4.47–4.68 (2H, m), 5.45 (1H, d, *J* = 7.9 Hz), 6.73 (1H, brs); ^{13}C NMR (50 MHz, $CDCl_3$): 14.4, 18.7, 22.8, 28.1, 28.9, 29.1, 29.3, 29.5, 31.9, 58.4, 65.0, 68.6, 74.6, 90.8, 157.9; MS(ESI): *m/z* 346.561 ($M+Na)^+$; HRMS, (EI/DIP) for (M^+): calc. 323.24354, Found: 323.24346.

(2*S*,3*S*)-2-Aminooctadec-4-yne-1,3-diol (27)

To a stirred solution of TA product **26** (900 mg, 2.78 mmol) in MeOH (10 mL) was added K_2CO_3 (1.15 g, 8.35 mmol) and the reaction mixture was stirred for 6 h at room temperature until consumption of the starting material and methanol was removed *in vacuo*. H_2O was added to the crude product, which was extracted with EtOAc (3 × 30 mL) and dried over sodium sulfate, concentrated to near dryness and crystallised from DCM–petroleum ether to give **27** (703 mg, 85% yield) as white shiny crystal. mp 81–83 °C; lit.[26k] mp 82–83 °C; IR ($CHCl_3$, cm^{-1}): ν_{max} 3460, 3300, 2184; ^1H NMR (500 MHz, $CDCl_3$): 0.88 (3H, t, *J* = 6.1 Hz), 1.15–1.72 (22H, m), 1.98–2.5 (2H m), 3.4–5.5 (5H, m), 7.79 (2H, brs); ^{13}C NMR (50 MHz, $CDCl_3$): 14.1, 18.9, 22.7, 28.7, 29.3, 29.4, 29.7, 29.8, 31.9, 58.9, 60.2, 65.6, 76.5, 88.9; HRMS, (EI/DIP) for (M^+): calc. 297.2649, found 297.2643.

tert-Butyl(2*S*,3*S*)-1,3-dihydroxyoctadec-4-yn-2-ylcarbamate (28)

Compound **27** (500 mg, 1.68 mmol) was treated with Boc_2O (0.58 mL, 2.52 mmol) in dioxane and the reaction mixture stirred until consumption of the starting material (8 h) and solvent was removed by vacuum evaporation. The crude material was purified by flash column chromatography on silica gel using petroleum ether–EtOAc (6 : 1) as eluent to give **28** (547 mg, 82% yield) as a colorless oil: $[\alpha]_D^{25}$: −14.8 (*c* 0.5, $CHCl_3$); lit.[26a] $[\alpha]_D^{25}$ − 14.0 (*c* 0.5, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): ν_{max} 3485, 2187, 1675; ^1H NMR

(200 MHz, $CDCl_3$): 0.88 (3H, t, J = 5.9 Hz), 1.25–1.63 (31H, m), 2.21 (2H, t, J = 6.8 Hz), 2.57 (2H, brs), 3.79–3.92 (3H, m), 4.58–4.61 (1H, m), 5.17 (1H, brs); ^{13}C NMR (50 MHz, $CDCl_3$): 14.1, 18.7, 22.6, 28.3, 28.5, 28.9, 29.1, 29.3, 29.5, 29.6, 31.9, 55.9, 62.9, 63.4, 80.0, 87.3, 156.4; MS(ESI): m/z 420.22 $(M+Na)^+$.

tert-Butyl-(2*S*,3*S*,*E*)-1,3-dihydroxyoctadec-4-en-2-ylcarbamate (10)

A solution of **28** (0.20 g, 0.5 mmol) in abs. Et_2O (5 mL) was added dropwise over 10 min to Red-Al (3.5 M in toluene, 0.71 mL, 2.5 mmol) and abs. Et_2O (3 mL) at 0 °C. The clear solution was stirred at room temperature for 24 h, then MeOH (1 mL) was added dropwise at 0 °C. After dilution with Et_2O (5 mL) and addition of sat. potassium sodium tartrate (3 mL), the mixture was vigorously stirred at room temperature for 3 h. The aq. layer was separated and extracted with Et_2O (2 × 10 mL). The combined Et_2O extracts were washed with sat. potassium sodium tartrate and sat. NaCl, dried over Na_2SO_4 and concentrated to near dryness. The crude material was purified by flash column chromatography on silica gel using petroleum ether–EtOAc (1 : 1) as eluent to give **10** (0.13 g, 65% yield) as a white solid: mp 58–60 °C; $[\alpha]_D^{25}$: –0.56 (c 1.0, $CHCl_3$); lit.[26a] $[\alpha]_D^{25}$ – 0.4 (c 1.0, $CHCl_3$); IR ($CHCl_3$, cm^{-1}): ν_{max} 3460, 2900, 1670; ^{1}H NMR (200 MHz, $CDCl_3$): 0.89 (3H, t, J = 6.8 Hz), 1.26–1.46 (31H, m), 2.03–2.09 (2H, m), 2.65 (1H, brs) 3.58 (1H, brs), 3.70 (1H, dd, J = 3.5, 11.2 Hz), 3.94 (1H, dd, J = 3.5, 11.2 Hz), 4.31 (1H, t, J = 4.5 Hz), 5.31 (1H, d, J = 7.0 Hz), 5.53 (1H, q, J = 6.2, 15.5 Hz), 5.79 (1H, q, J = 6.5, 14.5 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): 14.1, 22.7, 28.4, 29.1, 29.2, 29.3, 29.7, 31.9, 32.3, 55.4, 62.6, 74.8, 79.8, 128.9, 134.2, 156.2.

Pentadecanal-1 (30)

Following the procedure as described for **14**, the crude aldehyde **30** was prepared and used as such in the next reaction.

Heptadec-1-en-3-ol (31)

To a stirred solution of Mg (2.57 g, 106 mmol) in dry THF (30 mL), vinyl bromide (29.4 mL, 3.0 M solution in dry THF, 88.33 mmol) was added dropwise over 30 min and the Grignard reagent thus formed was cooled to 0 °C. Aldehyde **30** (8 g, 35.3 mmol) in dry THF (30 mL) was added dropwise over 20 min to the above reaction mixture. After 2 h stirring at 0 °C the reaction mixture was quenched with saturated NH_4Cl solution (20 mL), and the aqueous layer was extracted with EtOAc (4 × 50 mL) and the combined organic layers were washed with brine and dried over Na_2SO_4. The extracts were concentrated to near dryness and purified by silica gel column chromatography using petroleum ether–EtOAc (95 : 5) as eluent to give **31** (7.84 g, 88% yield) as a pale yellow solid: mp 46–47 °C.

(*S*)-Heptadec-1-en-3-ol (33)

To a mixture of 3 Å molecular sieves (1.5 g) and $Ti(^i\text{-PrO})_4$ (9.0 mL, 30.26 mmol) in dry CH_2Cl_2 (100 mL), (–)-DIPT (8.07 mL, 38.51 mmol) was added dropwise over 10 min at –20 °C. The mixture was stirred for 20 min at –20 °C, and a solution of **31** (7.0 g, 27.5 mmol) in dry CH_2Cl_2 (25 mL) was added dropwise over 10 min. The reaction mixture was stirred for additional 30 min at –20 °C and TBHP (12.5 mL, 5.5 M solution in toluene, 68.75 mmol) was added dropwise over 10 min. The reaction mixture was kept at –20 °C by constant temperature bath and after 4 d was warmed to 0 °C, and quenched with H_2O (100 mL). The mixture was stirred for 60 min, and then precooled (0 °C) freshly prepared ferrous sulfate heptahydrate (1.52 g, 5.5 mmol) in 10 mL of water was added and the reaction mixture was stirred for 30 min at room temperature. The two phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were treated with 30 mL of a precooled (0 °C) solution of 30% NaOH w/v in saturated brine. The two phase mixture was stirred vigorously for 1 h at 0 °C, followed by dilution with 50 mL of water, the phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated to dryness. The crude product was then purified by flash chromatography on silica gel using petroleum ether–EtOAc (95 : 5) as eluent to give chiral hydroxy olefin **33** as a white solid. (3.22 g, 46% yield, based on 50% conversion). Further elution with petroleum ether–EtOAc (9 : 1) gave the epoxide **32** as a white solid (3.64 g, 49% yield, based on 50% conversion): mp 46–47 °C; $[\alpha]_D^{25}$ +2.38 (c 1.0, $CHCl_3$); Anal. Calcd. for $C_{17}H_{34}O$ (254.45): C, 80.24; H, 13.47%. Found: C, 79.95; H, 13.73%; IR ($CHCl_3$, cm^{-1}) : ν_{max} 3499, 2899, 1611; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 0.89 (3H, t, J = 6.1 Hz), 1.26–1.55 (26H, m), 4.05–4.15 (1H, m), 5.08–5.27 (2H, m), 5.79–5.96 (1H, m); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 14.1, 22.7, 25.3, 29.3, 29.7, 31.9, 37.0, 73.2, 114.4, 141.3.

tert-Butyldimethyl((*R*)-1-((*S*)-oxiran-2-yl)pentadecyl)oxy) silane (34)

To a solution of **32** (3.0 g, 11.09 mmol) in dry CH_2Cl_2 (10 mL) was added 2,6-lutidine (2.08 mL, 17.88 mmol) at 0 °C and stirred for 15 min. To this TBSOTf (2.18 mL, 13.31 mmol) was added dropwise over 10 min and stirred for 10 min. After TLC diagnosis, the ice-cooled solution was added to the reaction mixture and then the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL), dried over anhydrous Na_2SO_4 and concentrated to near dryness. The crude product was purified by silica gel column chromatography using petroleum ether–EtOAc (99 : 1) as eluent to give **34** (3.84 g, 90% yield) as a colorless liquid: $[\alpha]_D^{25}$ –4.1 (c 1.0, $CHCl_3$); Anal. Calcd for $C_{23}H_{48}O_2Si$ (384.71): C, 71.81; H, 12.58%. Found: C, 71.65; H, 12.73%; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.07 (3H, s), 0.12 (3H, s), 0.85–0.93 (12H, m), 1.26 (24H, brs), 1.48–1.56 (2H, m), 2.55 (1H, q, J = 2.7, 5.1 Hz), 2.76–2.81 (1H, m), 2.89–2.96 (1H, m), 3.21–3.30 (1H, m); ^{13}C NMR (50 MHz, $CDCl_3$): δ –4.9, –4.4, 14.1, 18.2, 22.7, 24.9, 25.7, 25.8, 29.4, 29.7, 31.9, 35.3, 44.7, 54.8, 71.3; MS(ESI): m/z 385.7 $(M+H)^+$, 407.61 $(M+Na)^+$.

(3*S*,4*R*)-4-((*tert*-Butyldimethylsilyl)oxy)octadec-1-en-3-ol (35)

To a suspension of trimethylsulfonium iodide (6.47 g, 31.71 mmol) in dry THF (20 mL) at –20 °C was added *n*-BuLi (21.07 mL, 1.6 M solution in hexane, 31.71 mmol) dropwise over 20 min and stirred for 30 min. Then the epoxide **34** (2.0 g, 5.19 mmol) in dry THF (10 mL) was added to the above reaction mixture and slowly allowed to warm to 0 °C over 1 h. The reaction mixture was then stirred at ambient temperature for 2 h. After

consumption of the starting material the reaction mixture was quenched with H_2O (20 mL) and extracted with EtOAc (4 × 30 mL). The combined extracts were washed with brine (50 mL), dried over Na_2SO_4, filtered and concentrated to near dryness. The residue was purified by flash silica gel column chromatography using petroleum ether–EtOAc (94 : 6) as eluent to give **35** (1.55 g, 75% yield) as a colorless liquid: $[\alpha]_D^{25}$ −2.5 (*c* 1.0, $CHCl_3$); Anal. Calcd for $C_{24}H_{50}O_2Si$ (398.74): C, 72.29; H, 12.64%. Found: C, 72.27; H, 12.63%; IR ($CHCl_3$, cm^{-1}): ν_{max} 3446, 1614; ^1H NMR (200 MHz, $CDCl_3$): δ 0.09 (3H, s), 0.10 (3H, s), 0.85–0.91 (12H, m), 1.26–1.43 (26H, m), 2.27 (1H, brs), 3.66–3.71 (1H, m), 4.08–4.12 (1H, m), 5.17–5.34 (2H, m), 5.77–5.94 (1H, m); ^{13}C NMR (50 MHz, $CDCl_3$): δ −4.5, −4.4, 14.1, 18.1, 22.7, 25.6, 25.7, 25.8, 29.4, 29.6, 29.7, 31.6, 31.9, 75.4, 75.9, 116.4, 136.5; MS(ESI): *m*/*z*; 421.72 $(M+Na)^+$.

(3*S*,4*R*)-4-((*tert*-Butyldimethylsilyl)oxy)octadec-1-en-3-yl carbamate (36)

Trichloroacetyl isocyanate (0.536 mL, 4.51 mmol) was added dropwise over 10 min to a solution of alcohol **35** (1.5 g, 3.76 mmol) in dry CH_2Cl_2 (1.7 mL) at 0 °C. After stirring for 2 h, or until TLC showed no starting material present, the mixture was concentrated under reduced pressure. The residue was dissolved in MeOH (2.2 mL), cooled to 0 °C and aqueous K_2CO_3 solution (1.55 g, 3.4 mL, 11.28 mmol) was added. The cooling bath was removed and the mixture was allowed to stir for 4 h, by which time TLC showed complete conversion. The solvent was evaporated under reduced pressure and the residue was extracted with CH_2Cl_2 (4 × 25 mL). The extracts were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure to yield the crude carbamate, which was purified by flash silica gel column chromatography using petroleum ether–EtOAc (8 : 2) as eluent to give **36** (1.49 g, 90% yield) as a colorless syrupy liquid: $[\alpha]_D^{25}$ −27.5 (*c* 1.0, $CHCl_3$); Anal. Calcd for $C_{25}H_{51}NO_3Si$ (441.76): C, 67.97; H, 11.64; N, 3.17%. Found: C, 67.81; H, 11.69; N, 3.25%; IR ($CHCl_3$, cm^{-1}): ν_{max} 3446, 1644; ^1H NMR (200 MHz, $CDCl_3$): δ 0.06 (3H, s), 0.08 (3H, s), 0.88–0.91 (12H, m), 1.26–1.41 (26H, m), 3.77–3.84 (1H, m), 4.79 (2H, brs), 5.01–5.06 (1H, m), 5.24–5.34 (2H, m); 5.81–5.98 (1H, m); ^{13}C NMR (50 MHz, $CDCl_3$): δ −4.6, −4.4, 14.1, 18.2, 22.7, 25.4, 25.9, 29.3, 29.5, 29.7, 31.9, 33.6, 73.7, 78.8, 118.7, 132.9, 156.3. MS(ESI): *m*/*z* 442.39 $(M+H)^+$.

(4*S*,5*R*)-5-((*R*)-1-(*tert*-Butyldimethylsilyl)pentadecyl)-4-(hydroxymethyl)oxazolidin-2-one (37)

A solution of sodium hydroxide (12.5 mL, 0.08M, 43 mg, 1.08 mmol) was prepared. A small amount of this solution was used to dissolve potassium osmate dihydrate (17 mg, 4 mol%) in a separate vial and the remaining sodium hydroxide solution was added in one portion to a stirred solution of the allylic carbamate **36** (0.53 g, 1.2 mmol) in propan-1-ol (14.5 mL, 12 mL $mmol^{-1}$). To this reaction mixture was added freshly prepared *t*-butyl hypochlorite (0.12 mL, 1.13 mmol) and the mixture was allowed to stir for 5 min. To this was added $^iPr_2EtN$ (10 mg, 5 mol%) in one portion. The mixture was allowed to stir for a further 5 min before the final addition of a solution of potassium osmate in the remainder of the NaOH solution made earlier. The reaction mixture was stirred until consumption of the starting material and was then quenched with sodium sulfite (100 mg $mmol^{-1}$), and subsequently diluted with EtOAc. The reaction mixture was extracted with EtOAc (3 × 10 mL), dried over Na_2SO_4 and concentrated to near dryness. The crude product was found to be a mixture of *syn* : *anti* 12 : 1 (determined from ^1H NMR of crude compound) and was purified by flash silica gel column chromatography using petroleum ether–EtOAc (7 : 3) as eluent to give **37** (0.36 g, 66% yield), as a thick syrupy liquid: $[\alpha]_D^{25}$ +28.47 (*c* 1.3, $CHCl_3$); Anal. Calcd for $C_{25}H_{51}NO_4Si$ (457.76): C, 65.59; H, 11.23; N, 3.06%. Found: C, 65.35; H, 11.48; N, 3.36%; ^1H NMR (400 MHz, $CDCl_3$): δ 0.09 (3H, s), 0.10 (3H, s), 0.88–0.91 (12H, m), 1.26 (24H, m), 1.39–1.53 (2H, m), 3.42–3.6 (1H, m), 3.65–3.8 (1H, m), 3.85–4.0 (2H, m), 4.32 (1H, m), 6.55 (1H, s); ^{13}C NMR (50 MHz, $CDCl_3$): δ −4.6, −4.4, 14.0, 17.9, 22.6, 24.9, 25.7, 29.3, 29.6, 31.8, 32.8, 54.3, 63.8, 71.9, 80.3, 160.3; MS(ESI): *m*/*z* Anal. 480.70 $(M+Na)^+$.

(4*S*,5*R*)-4-(Hydroxymethyl)-5-((*R*)-1-hydroxypentadecyl) oxazolidin-2-one (38)

To a solution of TA product **37** (0.2 g, 0.43 mmol) in MeOH (5 mL) was added catalytic amount of *p*-TSA. The reaction mixture was stirred for 1 h and it was filtered and concentrated to near dryness. The crude product was purified by silica gel column chromatography using petroleum ether–EtOAc (3 : 7) as eluent to afford **38** (0.117 g, 78% yield) as a white solid: mp 60–62 °C; $[\alpha]_D^{25}$ +8.70 (*c*, $CHCl_3$); Anal. Calcd for $C_{19}H_{37}NO_4$ (343.50): C, 66.43; H, 10.86; N, 4.08%. Found: C, 66.38; H, 10.85; N, 4.03%; IR ($CHCl_3$, cm^{-1}): ν_{max} 3340, 2800, 1650; ^1H NMR (200 MHz, $CDCl_3$): δ 0.88 (3H, t, *J* = 6.1 Hz), 1.26–1.73 (26H, m), 2.30–2.37 (1H, m), 3.37–3.95 (4H, m), 4.10 (1H, t, *J* = 3.7 Hz), 4.24–4.28 (1H, m), 6.99 (1H, brs); ^{13}C NMR (50 MHz, DMSO-d_6): δ 14.5, 22.6, 25.5, 29.2, 29.5 31.8, 32.3, 54.9, 63.6, 70.9, 80.6, 159.1; MS(ESI): *m*/*z* 344.48 $(M+H)^+$.

(2*R*,3*S*,4*R*)-2-Acetamidooctadecane-1,3,4-triyltriacetate (11)

To a stirred solution of **38** (90 mg, 0.26 mmol) in MeOH (3 mL) was added K_2CO_3 (72 mg, 0.39 mmol) and the reaction mixture was stirred for 6 h until consumption of the starting material and methanol was removed *in vacuo*. H_2O was added to the crude product and extracted with EtOAc (3 × 10 mL), dried over Na_2SO_4 and concentrated to near dryness. The crude material was subsequently acetylated with acetic anhydride (0.053 g, 0.52 mmol), pyridine (0.043 g, 0.54 mmol) and DMAP (cat). After overnight stirring, the solvent was evaporated and the residue was purified on a silica gel column using petroleum ether–EtOAc (5 : 1) as eluent to give tetraacetate **11** (104 mg, 82% yield) as a white solid. Spectroscopic data of tetraacetate are in full agreement with those reported in literature.[26j] mp 48–49 °C; $[\alpha]_D^{20}$ − 25.95 (*c* 1.5, $CHCl_3$); lit.[26j] $[\alpha]_D^{20}$ − 25.10 (*c* 1.5, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): 0.86 (3H, t, *J* = 6.0 Hz), 1.2–1.3 (24H, m), 1.55 (2H, m), 2.03 (3H, s), 2.04 (6H, s), 2.07 (3H, s), 3.95–4.05 (2H, m), 4.5 (1H, m), 5.02–5.18 (2H, m), 5.92 (1H, d, *J* = 10.0 Hz); ^{13}C NMR (50 MHz, $CDCl_3$): δ 14.6, 21.2, 21.4, 23.6, 25.5, 30.1, 32.4, 33.9, 47.5, 63.5, 71.4, 72.4, 170.3, 170.6, 170.7, 171.1; MS(ESI): *m*/*z* 486.645 $(M+H)^+$, 508.641 $(M+Na)^+$.

(*S*)-1-((*S*)-Oxiran-2-yl)pentadecan-1-ol (39)

To a mixture of 3 Å molecular sieves (600 mg) and Ti(^{i}-PrO)$_4$ (3.57 mL, 11.79 mmol) in dry CH_2Cl_2 (50 mL) (–)-DIPT (2.46 mL, 11.79 mmol) was added dropwise over 10 min at –20 °C. The mixture was stirred for 20 min at –20 °C, and a solution of **33** (3 g, 11.79 mmol) in dry CH_2Cl_2 (25 mL) was added slowly over 15 min. The reaction mixture was stirred for additional 30 min at –20 °C and TBHP (4.2 mL, 5.5M solution in toluene, 23.58 mmol) was added over 15 min. The reaction mixture was kept at –20 °C by constant temperature bath and after 4 d the reaction was warmed to 0 °C and quenched with H_2O (100 mL). The mixture was stirred for 40 min, and then precooled (0 °C) freshly prepared ferrous sulfate heptahydrate (819 mg, 2.94 mmol) in 10 mL of water was added and the reaction mixture was stirred for 30 min at rt. The two phases were separated and the aqueous phase extracted with CH_2Cl_2 (2 × 20 mL). The combined organic layers were treated with 20 mL of a precooled (0 °C) solution of 30% NaOH w/v in saturated brine. The two phase mixture was stirred vigorously for 1 h at 0 °C. Followed by dilution with 50 mL of water. The phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated to dryness. The crude product was then purified by flash chromatography on silica gel using petroleum ether–EtOAc (9 : 1) as eluent to give epoxide **39** (2.39 g, 75%) as a white solid: mp 46–48 °C; $[\alpha]_D^{25}$ –3.83 (*c* 1.0, $CHCl_3$); Anal. Calcd for $C_{17}H_{34}O_2$ (270.45): C, 75.50; H, 12.67%. Found: C, 75.65; H, 12.58%; ^{1}H NMR (200 MHz, $CDCl_3$): 0.88 (3H, t, J = 6.0 Hz), 1.26–1.61 (26H, m), 1.78 (1H, s), 2.72–2.78 (1H, m), 2.81–2.82 (1H, m), 3.01–3.06 (1H, m), 3.82–3.89 (1H, m); ^{13}C NMR (50 MHz, $CDCl_3$): δ 14.1, 22.7, 25.3, 29.3, 29.5, 29.6, 31.9, 33.4, 43.4, 54.5, 68.4; MS(ESI): *m*/*z* 293.41 $(M+Na)^+$.

***tert*-Butyldimethyl-((*S*)-1-((*S*)-oxiran-2-yl)pentadecyl)oxy) silane (40)**

Compound **40** was prepared following the procedure as described for **34**: Yield 85%; colorless liquid; $[\alpha]_D^{25}$ –4.16 (*c* 1.0, $CHCl_3$); Anal. Calcd for $C_{23}H_{48}O_2Si$ (384.71): C, 71.81; H, 12.58%. Found: C, 71.73; H, 12.66%; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.07 (3H, s), 0.12 (3H, s), 0.84–0.93 (12H, m), 1.26 (24H, s), 1.49–1.53 (2H, m), 2.55 (1H, q, J = 2.7, 5.1 Hz), 2.75–2.83 (1H, m), 2.87–2.97 (1H, m), 3.19–3.33 (1H, m); ^{13}C NMR (50 MHz, $CDCl_3$): δ –4.8, –4.4, 14.1, 18.1, 22.6, 24.8, 25.2, 25.6, 25.7, 25.9, 29.3, 29.5, 29.6, 29.7, 31.9, 35.2, 44.8, 54.7, 72.3; MS(ESI): *m*/*z* 385.73 $(M+H)^+$, 407.54 $(M+Na)^+$.

(3*S*,4*S*)-4-(*tert*-Butyldimethylsilyl)oxy)octadec-1-en-3-ol (41)

Compound **41** was prepared following the procedure as described for compound **35**: Yield 70%; colorless liquid; $[\alpha]_D^{25}$ –1.78 (*c* 1.0, $CHCl_3$); Anal. Calcd for $C_{23}H_{50}O_2Si$ (398.74): C, 72.29; H, 12.64%. Found: C, 72.36; H, 12.56%; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.09 (3H, s), 0.10 (3H, s), 0.89–0.91 (12H, m), 1.26–1.52 (26H, m), 3.66–3.74 (1H, m), 4.08–4.12 (1H, m), 5.16–5.35 (2H, m), 5.77–5.94 (1H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ: –4.5, –4.4, 14.1, 18.1, 22.9, 25.6, 25.7, 25.8, 29.4, 29.5, 29.6, 29.7, 31.6, 31.9, 75.4, 75.8, 116.4, 136.6.

(3*S*,4*S*)-4-(*tert*-Butyldimethylsilyl)oxy)octadec-1-en-3-yl carbamate (42)

Compound **42** was prepared following the procedure as described for compound **36**: Yield 90%; colorless syrupy liquid; $[\alpha]_D^{25}$ –27.5 (*c* 1.0, $CHCl_3$); Anal. Calcd for $C_{25}H_{51}NO_3Si$ (441.76): C, 67.97; H, 11.64; N, 3.17%. Found: C, 68.11; H, 11.67; N, 3.22%; IR ($CHCl_3$, cm^{-1}): ν_{max} 3446, 1644; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.07 (3H, s), 0.10 (3H, s), 0.85–0.90 (12H, m), 1.26–1.43 (26H, m), 3.69–3.77 (1H, m), 4.60–4.77 (2H, brs), 5.07–5.35 (3H, m), 5.78–5.95 (1H, m); ^{13}C NMR (50 MHz, $CDCl_3$): δ –4.8, –4.4, 14.1, 18.2, 22.7, 25.4, 25.8, 29.5, 29.6, 29.7, 31.9, 33.6, 73.9, 79.8, 118.7, 132.9, 159; MS(ESI): *m*/*z* 442.39 $(M+H)^+$.

(4*S*,5*R*)-5-((*S*)-1-(*tert*-Butyldimethylsilyl)oxy)pentadecyl)-4-(hydroxymethyl)oxazolidin-2-one (43)

Compound **43** was prepared following the procedure as described for compound **37**: Yield 55%, thick syrupy liquid; $[\alpha]_D^{25}$ +8.70 (*c* 1.0, $CHCl_3$); Anal. Calcd for $C_{25}H_{51}NO_4Si$ (457.76): C, 65.59; H, 11.23; N, 3.06%. Found: C, 65.64; H, 11.28; N, 3.18%; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.09 (3H, s), 0.10 (3H, s), 0.87–0.92 (12H, m), 1.26–1.55 (26H, m), 2.51 (1H, brs), 3.50–3.56 (1H, m), 3.70–3.74 (1H, m), 3.91–3.98 (2H, m), 4.27–4.32 (1H, m), 6.14 (1H, s); ^{13}C NMR (50 MHz, $CDCl_3$): δ –4.6, –4.4, 14.1, 18.0, 22.7, 25.0, 25.7, 25.8, 29.4, 29.6, 29.7, 31.9, 33.0, 54.0, 63.3, 72.0, 80.3, 159.8; MS(ESI): *m*/*z* Anal. 480.70 $(M+Na)^+$.

(4*S*,5*R*)-4-(Hydroxymethyl)-5-((*S*)-1-hydroxypentadecyl) oxazolidin-2-one (44)

Compound **44** was prepared following the procedure as described for compound **38**: Yield 75%, white solid; mp 58–59 °C; $[\alpha]_D^{25}$ +43.48 (*c* 1.0, $CHCl_3$); Anal. Calcd for $C_{19}H_{37}NO_4$ (343.50): C, 66.43; H, 10.86; N, 4.08%. Found: C, 66.35; H, 10.85; N, 4.02%; IR ($CHCl_3$, cm^{-1}): ν_{max} 3378, 1675; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.88 (3H, t, J = 6.1 Hz), 1.26–1.75 (26H, m) 2.34 (1H, brs), 3.54–3.94 (4H, m), 4.10 (1H, t, J = 3.7 Hz), 4.24–4.28 (1H, m), 6.97 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.1, 22.7, 25.0, 29.3, 29.5, 29.6, 29.7, 31.9, 32.9, 53.4, 63.7, 73.4, 79.8, 158.4; MS(ESI): *m*/*z* 344.47 $(M+H)^+$.

(2*R*,3*S*,4*S*)-2-Acetamidooctadecane-1,3,4-triyltriacetate (12)

Compound **12** was prepared following the procedure as described for compound **11**: Yield 72%, white solid; mp 51–52 °C; $[\alpha]_D^{20}$ – 7.0 (*c* 1.2, $CHCl_3$); lit.[41,45e] $[\alpha]_D^{20}$ – 7.2 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): 0.88 (3H, t, J = 6.2 Hz), 1.26 (24H, brs), 1.51–1.72 (2H, m), 2.05–2.09 (12H, m), 4.19–4.22 (1H, m), 4.40–4.47 (2H, m), 4.55–4.57 (1H, m), 5.06–5.09 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 20.6, 20.9, 22.6, 23.0, 24.9, 25.8, 29.2, 30.1, 31.8, 33.3, 46.9, 62.9, 70.4, 71.9, 169.7, 170.0, 170.1, 170.5; MS(ESI): *m*/*z* 486.645 $(M+H)^+$, 508.641 $(M+Na)^+$.

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