Syntheses of 3-*C*-Methylceramides

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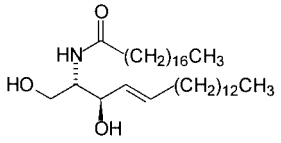
We report on the synthesis of a series of 3-*C*-methylceramide derivatives **2a**,**b**, **12a**,**b**, **13a**,**b**, and **14a**,**b**.

Introduction

Ceramide (*N*-acylsphingosine **1**, Scheme 1) is the hydrophobic membrane anchor of mammalian glycosphingolipids and a vital component of the human skin.[1] In addition, ceramide attracted attention as a signaling substance that has been implicated in a variety of biological processes.[2,3] In living cells, it usually occurs in low concentrations as an intermediate in sphingolipid- and glycosphingolipid metabolism, and, in higher concentrations, in the epidermis of human skin.[1] A variety of ceramide analogs has been prepared and investigated as potential enzyme inhibitors or as ligands of putative ceramide binding proteins.[1,4] We report on the synthesis of 3-*C*-methyl-substituted ceramide derivatives like **2a** (Scheme 3) as conceptionally novel tools for cell surface engineering.



1

Scheme 1

Compared with naturally occurring ceramide, the target compounds are structurally modified in the sphingosine backbone. *C*-Methyl-substituted sphingosine derivatives have been prepared before.[5] Interest in such derivatives resulted from the observation that the 4-methyl derivative of (*Z*)-sphingosine[5] inhibits sphingolipid biosynthesis and induces morphological changes in neuronal cells treated with this compound.[6] The structurally related sphingosine analogs (*E*)-4-methylsphingosine, (*Z*)-5-methylsphingosine, (*E*)-5-methylsphingosine, (*Z*)-sphingosine and 1-deoxysphingosine inhibited sphingolipid biosynthesis less efficiently than (*Z*)-4-methylsphingosine and had no influence on cell morphology. Some of the observed effects appear to be mediated by the 1-phosphorylated derivative of (*Z*)-4-methylsphingosine, which might act as a metabolically stable analog of sphingosine-1-phosphate.[7,8] 3-*C*-Methyl-substituted sphinganine has been prepared as a mixture of stereoisomers and its effect on the incorporation of a metabolic precursor, [3-^{14}C]L-serine, into sphingolipids of neuronal cells has been investigated.[9]

We decided to prepare 3-*C*-methyl-substituted ceramides as cell-permeable prodrugs of neoglycosphingolipids with a structurally modified membrane anchor. The stereospecific substitution of the hydrogen atom in position 3 of the sphingoid backbone by a methyl group is a small, but structurally defined modification. After addition of the target compounds to cultured cells, we expect intracellular metabolic conversion of some of the target molecules into membrane neoglycosphingolipids,[4] which, in turn, might alter the properties of membrane-resident proteins ("cell surface engineering"). It has been demonstrated that some ceramide analogs can be metabolized to neoglycolipids (review, see ref.[4]). More and more evidence is accumulating that suggests that the properties of membrane proteins can be drastically influenced by the composition of their lipid surroundings.[10] Physiologically relevant data on the interference of membrane proteins with glycosphingolipids are rare, but several examples indicate that the activity of pharmacologically relevant receptors can be modified by glycosphingolipids.[1] This has been most convincingly demonstrated for the down-regulation of the insulin receptor by ganglioside GM3 in ganglioside GM3-synthase knockout-mice.[11] Therefore, it would be interesting to know if addition of the target compounds to cultured cells leads to the formation of membrane glycosphingolipids modified in the lipid moiety, and if functional membrane properties can be influenced by this modification. In addition to this modulation of cellular plasma membranes, therapeutic applications of ceramide analogs are discussed for the treatment of several disease states.[1,4]

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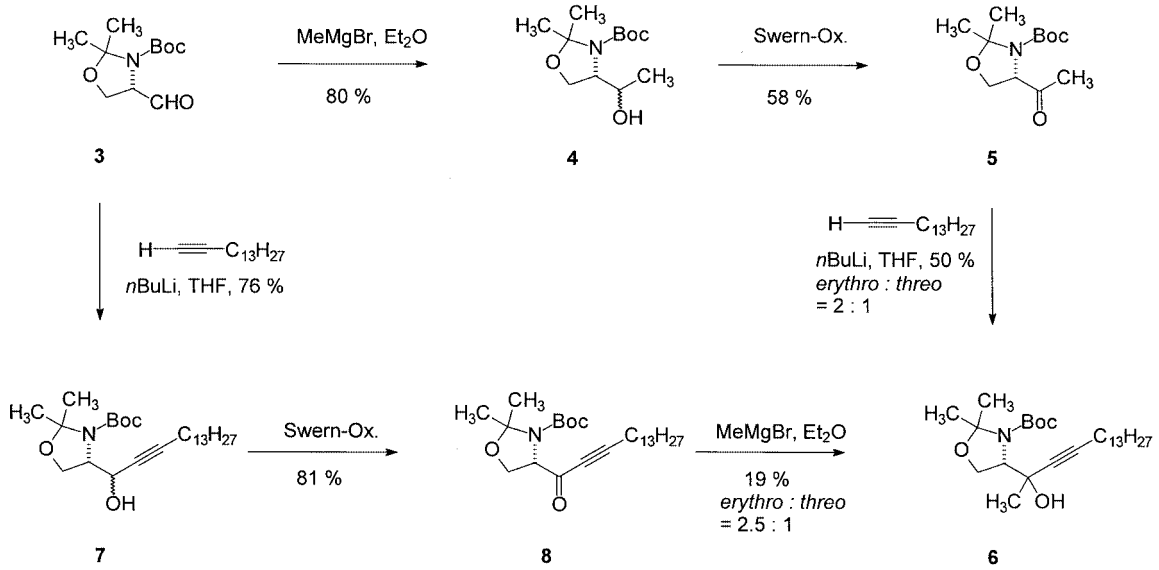
To investigate the influence of the additional methyl group in position 3 of the sphingoid backbone, we decided to synthesize stereoisomerically pure 3-*C*-methylceramide **2a** in the D-*erythro* configuration of the naturally occurring lipid. For structure-activity relationships, we prepared the target compound in the L-*threo* configuration also (**2b**, Scheme 3). An important role has been attributed to the (4*E*)-double bond of ceramide, since 4,5-dihydroceramide derivatives are much less active as signaling substances.[12] Therefore, we decided to vary the nature of the C-4−C-5 bond in addition to the replacement of the hydrogen atom at C-3 by the methyl group. Two series of ceramide analogs in L-*threo* and D-*erythro* configuration resulted from this additional modification of the C-4−C-5 bond. In addition to **2a**,**b** we prepared the target compounds also with C-4−C-5 single bonds, with (*Z*)-configured double bonds (**12a**,**b**), and with triple bonds (**13a**,**b**). For the purpose of cell culture application, the target compounds were synthesized with an acyl chain length of 12 instead of the 18 carbon atoms predominantly found in the natural product. This leads to higher solubility in water and easier application to cultured cells.[4] Compared with previously prepared sphinganine analogs,[9] we expect a lower degree of toxicity of the acylated compounds and different intracellular distribution.

Several preparative approaches to sphingolipids have been reported (reviews: refs.[13−16]), which can be modified for the synthesis of sphingolipid analogs and derivatives.[17] For the purpose of this study, we decided to start with the configuratively stable serine aldehyde **3**,[18] since the stereochemistry of the desired modification at the 3-position in the sphingosine backbone can be controlled, while the (2*S*) configuration is easily preserved during the subsequent reactions.

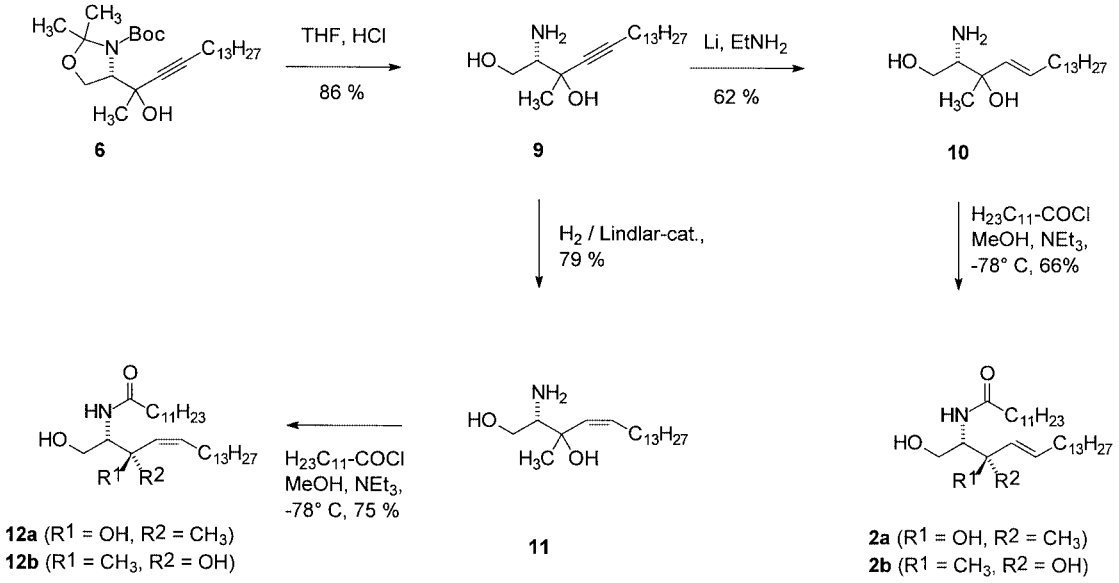
Results

A key intermediate in the synthesis of the target compounds **2a**,**b**, **12a**,**b**, **13a**,**b**, and **14a**,**b** is alkyne **6**, which resulted from the two carbon−carbon bond-formation reactions of the chosen synthetic route (Scheme 2). Aldehyde **3** was synthesized most efficiently according to a procedure reported for its (*R*) enantiomer[19] starting from L-serine. The synthesis of **6** from Garner's aldehyde **3** can alternatively be achieved by two reaction sequences, which differ by the order of the alkylation/alkynylation steps. Addition of a methyl Grignard reagent to aldehyde **3** afforded amino alcohol **4** in 80% yield as a mixture of diastereomers. Subsequent Swern oxidation led to the amino ketone **5** in 58% yield. Compound **5** has been prepared before by an independent method.[20] An X-ray structure of the racemic compound is available.[21] Alkynylation of **5** afforded key intermediate **6** in 50% yield. Compound **6** was obtained as a mixture of diastereomers, which was only separable on a preparative scale after further transformation (Schemes 3 and 4). The diastereomeric ratio of 2:1 is in agreement with the assumption of nonchelating reaction conditions and with published data on related reactions.[20]

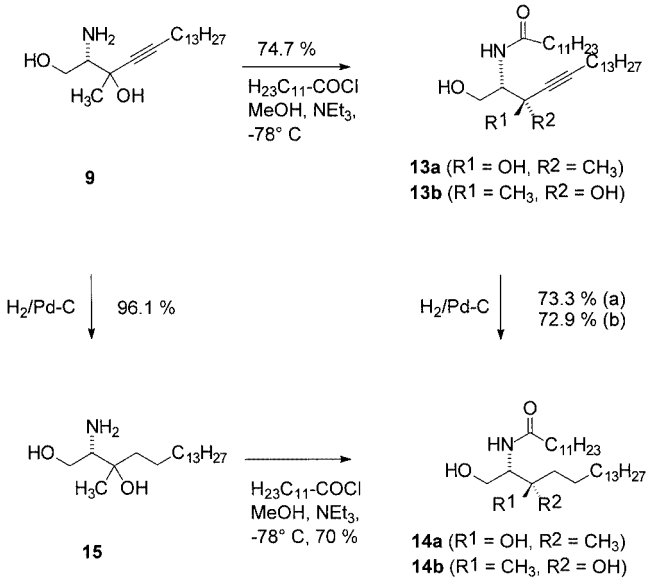
The alternative order of alkylation/alkynylation reactions turned out to be less suitable in terms of overall yield: Alkynylation of Garner's aldehyde with an alkynyllithium compound to **7**,[22−24] and the subsequent Swern oxidation to amino ketone **8** proceeded in satisfactory yield. However, the Grignard reaction leading to **6** was only achieved in low yields. The diastereoselectivity of the reaction as determined by NMR spectroscopy favors the *anti*-Felkin product in a 2.5:1 ratio and can be explained by the assumption of chelate control of the reaction.[20] The subsequent synthetic steps utilize **6**, which has been prepared via the intermediates **4** and **5**.



Scheme 2



Scheme 3

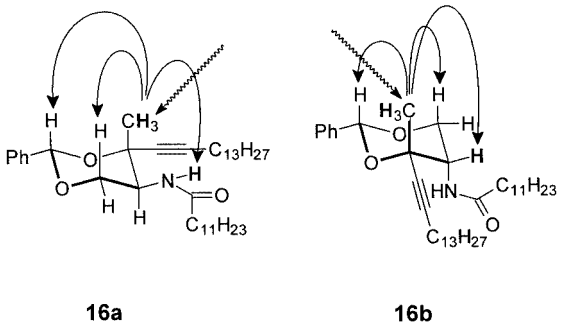


Scheme 4

For the synthesis of the target compounds **2a** and **2b** in D-*erythro* and L-*threo* configurations, respectively, alkyne **6** was deprotected to **9** with HCl in THF[20] in 86% yield (Scheme 3). Reduction of the alkyne **9** to the (*E*)-alkene with lithium in ethylamine[25] led to 3-*C*-methylsphingosine (**10**) as a mixture of diastereomers. Attempts for the separation of the diastereomers on a preparative scale were not successful. However, separation of the target compounds **2a** and **2b**, which were derived from **10** by acylation with lauroyl chloride at −78 °C in 66% yield, was easily achieved. To avoid the formation of 3-*C*-methylceramide esters as side products, we used methanol as solvent; for complete acylation, 2 equiv. of lauroyl chloride were necessary.

For the synthesis of the (*Z*)-3-*C*-methylceramides **12a** and **12b** (Scheme 3), alkyne **9** was hydrogenated in the presence of Lindlar catalyst to afford (*Z*)-3-*C*-methylsphingosine (**11**) in 79% yield as a mixture of diastereomers. Acylation led to the target compounds, which were readily separated by column chromatography, in 74% yield.

The 3-*C*-methylceramides **13a** and **13b** with a triple bond in both configurations at C-3 were prepared by acylation of the alkyne analog of 3-*C*-methylsphingosine (**9**, Scheme 4). The separated diastereomers were independently subjected to catalytic hydrogenation with palladium on charcoal in methanol to give the saturated target compounds **14a** and **14b**. An alternative route uses the reversed order of acylation and hydrogenation, and is also shown in Scheme 4. The compound 3-*C*-methylsphinganine (**15**) that is derived from **9** by hydrogenation is an intermediate in this strategy. Acylation of **15** and subsequent separation of the stereoisomers gives access to the target compounds **14a** and **14b**. The assignment of the relative configuration to the target compounds was made after transformation of **13a** and **13b** into the corresponding 1,3-benzylidene acetals **16a** and **16b**, respectively (Scheme 5).



Scheme 5

Contacts in the NOE differential spectra between the protons of the 3-methyl group and the amide proton in **16a** were used for the assignment of the relative *erythro* configuration to this compound, while **16b** showed a contact between the 3-methyl protons and 2-H, which can be expected for a substance with a *threo* configuration. The assignment of the relative configuration to the other target molecules was achieved after their respective hydrogenation and comparison of their TLC mobilities with those of the hydrogenated compounds derived from **13a** and **13b**. Compound **13a** was used to demonstrate the configurative integrity of the target compounds. Enantiomeric purity was determined by ^{1}H NMR spectroscopy using Eu(hfc)$_3$ as chiral shift reagent. The amount of the racemic by-product was less than 1%.

Discussion

We report on a preparative approach to ceramide analogs bearing an additional methyl group at the 3-position of the sphingoid backbone. The key step is the C−C bond-forming reaction with the addition of alkylmagnesium and alkynyllithium reagents to *N*-protected α-amino carbonyl compounds **3**, **5**, and **8**, without loss of optical purity.[26,28]

The synthesis afforded the target compound **2a** in an efficient and straightforward manner (Schemes 2 and 3). It also gives access to diastereomer **2b** with the L-*threo* configuration and permits investigation of the role of the stereochemistry at this position. Further modifications reported in this manuscript refer to the C-4−C-5 double bond, which has been reported to drastically alter the signaling properties of ceramide.[12] The synthesis also allows access to the 3-methyl-modified sphingosine derivatives **9**, **10**, **11**, and **15**, which were, however, only obtained as mixtures of diastereomers. Access to these compounds as pure stereoisomers would require deacylation of the corresponding separated ceramide derivatives **13a**,**b**, **2a**,**b**, **12a**,**b**, and **14a**,**b**.

This series of structural ceramide analogs enables structure-activity analyses with compounds of chemically defined structure. At room temperature, the NMR spectra of compounds **4**, **5**, **6**, and **8** are complex due to the presence of rotamers, or diastereomeric mixtures and rotamers. For compound **5**, a less complex spectrum was obtained in [D$_6$]DMSO at 120 °C due to the coalescence of signals.[20] The optical rotation determined for compound **5** is in excellent agreement with the published data; however, no literature data are available for substance **8**. Remarkably, after storage for some weeks at 4 °C, complete racemization of **5** was observed, such that X-ray data could be obtained only for the racemic compound.[21] Therefore, in agreement with reports on related derivatives,[28] the storage of the *N*-protected α-amino carbonyl compounds described here should be avoided in order to preserve their configurational integrity.

Conclusion

We present a straightforward preparative approach to a series of 3-*C*-methylceramide derivatives.

Experimental Section

General Remarks: Melting points are uncorrected. NMR shifts (δ) are given in ppm. ^{1}H NMR spectra: Bruker AM-400 (400 MHz) instrument, temperature of measurement 303 K, solvent as internal standard ($CDCl_3$: δ_H = 7.24 ppm). ^{13}C NMR spectra: Bruker AM-400 (100 MHz), temperature of measurement 303 K, solvent as internal standard ($CDCl_3$: δ_C = 77.0 ppm). For the assignment of NMR signals to individual atoms within the C_{18} alkyl chain, sphingosine numbering is used; 3-H of 2-aminooctadec-4-ene-1,3-diol is replaced by a methyl group. FAB-mass spectra (MS): Kratos Concept 1 H, matrix = *m*-nitrobenzoic acid. Optical rotations: Perkin−Elmer 343 Polarimeter. Column chromatography: silica gel 60 (E. Merck, Darmstadt, Germany), thin-layer chromatography: silica gel plates 60, thickness 0.25 mm (E. Merck, Darmstadt, Germany). Elemental analyses were performed in the microanalytical department of the Kekulé-Institut für Organische Chemie und Biochemie, Bonn.

***tert*-Butyl (4*S*)-4-[(1*R*/*S*)1-Hydroxyethyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (4):** Compound **3** [7.99 g, 34.85 mmol; preparation according to the (*R*) enantiomer as reported by Campbell et al.[19]] was dissolved in diethyl ether (100 mL) and stirred under reflux. Methylmagnesium bromide (3 M in diethyl ether, 35 mL, 0.105 mol) was added slowly, and the solution was subsequently stirred for 18 h at room temperature. The solution was diluted with water and extracted with dichloromethane. The organic layer was separated, dried with sodium sulfate, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel [R_F = 0.27 (cyclohexane/ethyl acetate, 7:3)] to give 6.80 g of **4** as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, mixture of rotamers): δ = 1.18−1.34 [m, 3 H, CH(OH)C*H*$_3$], 1.48−1.56 (m, 12 H, CH_3), 1.65 (m, br., 1 H, OH), 3.45−4.25 (m, 4 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, major rotamer): δ = 17.8 [CH(OH)*C*H$_3$], 27.0, 28.3 and 29.6 (CH_3), 47.8 (C-4), 65.0 (C-5), 67.2 [*C*H(OH)CH$_3$], 79.2 [*C*(CH$_3$)$_3$], 98.8 (C-2), 155.9 (NCO) ppm. $C_{12}H_{23}NO_4$ (245.32): calcd. C 58.75, H 9.45, N 5.71; found C 58.93, H 9.51, N 5.63. FAB-MS (70 eV): *m*/*z* calcd. for $C_{12}H_{24}NO_4$ [M + H]$^+$ 246.2; found 246.1.

***tert*-Butyl (4*S*)-4-Acetyl-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (5):** The experimental conditions[26] were the same as those described for the synthesis of compound **8**. R_F = 0.15 (cylohexane/ethyl acetate, 10:1). Preparation: **3** (6.80 g, 27.74 mmol) in dichloromethane (120 mL), oxalyl chloride (3.58 mL, 41.56 mmol) in dichloromethane (90 mL), DMSO (6.07 mL, 83.12 mmol), diisopropylethylamine (29.05 mL, 166.25 mmol in 120 mL dichloromethane), 0.5 N HCl (250 mL). Yield: 3.90 g; colorless oil. [α_D] = −53.8 (*c* = 1.66, $CHCl_3$) {ref.[19] +55.7 (*c* = 2.34, $CHCl_3$) for the (*R*) enantiomer}. ^{1}H NMR (400 MHz, $CDCl_3$, major rotamer): δ = 1.34−1.61 (m, 15 H, CH_3), 2.10 (m, 3 H, COC*H*$_3$), 3.85 (dd, *J* = 3.0, *J* = 9.4 Hz, 1 H, 5-H$_a$), 4.07 (dd, *J* = 7.6, *J* = 9.4 Hz, 1 H, 5-H$_b$), 4.23 (dd, *J* = 3.0, *J* = 7.6 Hz, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, major rotamer): δ = 23.5(CO*C*H$_3$), 25.8, 26.1, 26.2, 28.1 and 28.1 (CH_3), 64.9 (C-4), 65.4 (C-5), 80.6 [*C*(CH$_3$)$_3$], 94.8 (C-2), 151.1 (NCO), 206.1 (*C*OCH$_3$) ppm. $C_{12}H_{21}O_4N$ (243.28): calcd. C 59.24, H 8.70, N 5.76; found C 59.11, H 8.76, N 5.90. FAB-MS (70 eV): *m*/*z* calcd. for $C_{12}H_{22}O_4N$ [M + H]$^+$

244.15; found 244.1. **5** is further characterized by X-ray data of the racemic compound.[21]

***tert*-Butyl (4*S*)-4-[(1*R*/*S*)-1-Hydroxy-1-methylhexadec-2-ynyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (6):** The experimental conditions for the preparation of **6** from **5** were the same as those described for the synthesis of compound **7**. Preparation: **5** (2.53 g, 10.36 mmol) in THF (50 mL), 1-pentadecyne (2.41 mL, 14.55 mmol) in THF (100 mL), *n*-butyllithium (5.41 mL, 12.48 mmol, 2.3 M in *n*-hexane). R_F = 0.25 (petroleum ether/ethyl acetate, 10:1). Yield: 2.36 g as a mixture of diastereomers (D-*erythro*/L-*threo* = 2:1, according to the analysis of the ^{13}C NMR spectrum); colorless oil. The spectroscopic data correspond to those of the product obtained by alkylation of **8**. $C_{27}H_{49}NO_4 \times H_2O$ (469.69): calcd. C 69.05, H 10.94, N 2.98; found C 69.60, H 10.65, N 3.27. FAB-MS (70 eV): *m*/*z* calcd. for $C_{27}H_{50}NO_4$ $[M + H]^+$ 452.4; found 452.3.

***tert*-Butyl (4*S*)-4-[(1*R*/*S*)-1-Hydroxy-1-methylhexadec-2-ynyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (6) from 8:** Compound **6** was synthesized according to the procedure described for **4**. Preparation: **8** (98.1 mg, 1.60 mmol) in diethyl ether (20 mL), methylmagnesium bromide (1.6 mL, 4.80 mmol; 3 M in diethyl ether). R_F = 0.25 (petroleum ether/ethyl acetate, 10:1). Yield: 139.7 mg as colorless oil. **6** was obtained as a mixture of diastereomers (D-*erythro*/L-*threo* = 2.5:1). ^1H NMR (400 MHz, $CDCl_3$, mixture of rotamers): δ = 0.81 (t, *J* = 7 Hz, 3 H, CH_3), 1.19 (m, 22 H, CH_2), 1.30−1.66 (m, 18 H, CH_3), 2.11 (m, 2 H, CH_2), 3.57−4.18 (m, 2 H), 4.45 (m, br., 1 H, OH), 4.50−5.23 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, major rotamer): δ = 14.1 (CH_3), 18.7−31.9 (CH_2), 21.86, 27.5, 27.8, 28.3, 29.7 and 31.2 (CH_3), 51.3 (C-4), 62.5 (C-5), 67.0 (C−OH), 79.5 [*C*(CH_3)$_3$], 81.5 and 95.2 (alkyne-C), 100.0 (C-2), 155.6 (NCO) ppm. $C_{27}H_{49}NO_4$ (451.69): calcd. C 71.80, H 10.93, N 3.10; found C 71.36, H 10.44, N 3.49. FAB-MS (70 eV): *m*/*z* calcd. for $C_{27}H_{50}NO_4$ $[M + H]^+$ 452.6; found 452.3.

***tert*-Butyl (4*S*)-4-[(1*R*/*S*)-1-Hydroxyhexadec-2-ynyl]-2,2-dimethyl-1,3-oxazolidine-3-carboxylate (7):** **7** was synthesized from **3** (593.5 mg, 2.59 mmol) according to ref.[23] The analytical data are in agreement with those published. Yield: 862.2 mg of a colorless oil.

***tert*-Butyl (4S)-2,2-Dimethyl-4-(pent-2-ynoyl)-1,3-oxazolidine-3-carboxylate (8):** Procedure according to ref.[26] Dimethyl sulfoxide (260 μL, 3.94 mmol) was added to a solution of oxalyl chloride (170 μL, 1.97 mmol) in dichloromethane (3 mL) at −78 °C for 20 min. The solution was allowed to warm up to −60 °C, and **7** (863.5 mg, 1.97 mmol), dissolved in dichloromethane (10 mL), was added dropwise. After warming up to −45 °C, diisopropylethylamine (1.37 mL, 7.88 mmol), dissolved in dichloromethane (6 mL), was added. The cooling bath was removed, and the mixture was allowed to warm up to 0 °C. After quenching with cooled (0 °C) 0.5 N HCl (15 mL), the solution was diluted with water and extracted with dichloromethane. The organic layer was dried with sodium sulfate, and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography; R_F = 0.32 (petroleum ether/ethyl acetate, 10:1) to give 697.1 mg of **8** as a colorless oil. $[\alpha_D]$ = −52.0 (*c* = 2.02, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, major rotamer): δ = 0.81 (t, *J* = 7 Hz, 3 H, CH_3), 1.19 (m, 22 H, CH_2), 1.35 (s, 3 H, CH_3), 1.44 (s, 3 H, CH_3), 1.48 (s, 3 H, CH_3), 1.63 (s, 3 H, CH_3), 2.30 (m, 2 H, CH_2), 4.00 (dd, *J* = 3.7, *J* = 9.4 Hz, 1 H, H-5$_a$), 4.10 (dd, *J* = 7.4, *J* = 9.4 Hz, 1 H, H-5$_b$), 4.29 (dd, *J* = 3.7, *J* = 7.4 Hz, 1 H, H-4) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, major rotamer): δ = 14.1 (CH_3), 19.1−31.9 (CH_2), 24.3, 25.1, 25.2, 26.2 and 27.6 (CH_3), 65.8 (C-5), 66.7 (C-4), 78.7 [*C*(CH_3)$_3$], 80.7 and 95.3 (alkyne-C), 98.2 (C-2), 151.3 (NCO), 186.0 (CO) ppm. $C_{26}H_{45}NO_4$ (435.65): calcd. C 71.68, H 10.41, N 3.22; found C 71.41, H 10.47, N 4.29. FAB-MS (70 eV): *m*/*z* calcd. for $C_{26}H_{46}NO_4$ $[M + H]^+$ 436.7; found 436.7.

(2*S*,3*R*/*S*)-2-Amino-3-methyloctadec-4-yne-1,3-diol (9): **6** (2.27 g, 5.02 mmol) was dissolved in THF/1 N HCl (1:1; 50 mL) and stirred at 80 °C for 18 h. After cooling to room temperature, the reaction mixture is treated with 1 N NaOH until pH = 8−9. The organic solvent was removed under reduced pressure and the residue extracted with ethyl acetate. The organic layer was dried with sodium sulfate, concentrated under reduced pressure and the residue was purified by column chromatography on silica gel; R_F = 0.33 (D-*erythro*) and 0.38 (L-*threo*) (chloroform/methanol, 1:1) to give 1.35 g of a white solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7 Hz, 3 H, CH_3), 1.24 (m, 22 H, CH_2), 1.46 (s, 3 H, 3-CH_3), 2.17 (m, 2 H, CH_2), 2.83 (m, 1 H, 2-H), 2.97 (m, br., 4 H), 3.66 (m, 1 H, 1-H$_a$), 3.84 (m, 1 H, 1-H$_b$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, mixture of D-*erythro* and L-*threo* diastereomers, ratio 2:1): δ = 14.1 (CH_3), 18.6−31.9 (CH_2), 26.7 (3-CH_3, L-*t*), 27.3 (3-CH_3, D-*e*), 60.1 (C-2, L-*t*), 60.8 (C-2, D-*e*), 62.7 (C-1, L-*t*), 63.5 (C-1, D-*e*), 69.3 (C-3, D-*e*), 70.4 (C-3, L-*t*), 81.4 (D-*e*), 82.1 (L-*t*), 85.4 (L-*t*), 86.0 (D-*e*) (C-4 and C-5) ppm. $C_{19}H_{37}NO_2$ (311.51): calcd. C 73.26, H 11.97, N 4.50; found C 72.61, H 11.87, N 4.04. FAB-MS (70 eV): *m*/*z* calcd. for $C_{19}H_{38}NO_2$ $[M + H]^+$ 312.3; found 312.2.

(2*S*,3*R*/*S*,4*E*)-2-Amino-3-methyloctadec-4-ene-1,3-diol (10): **9** (339.8 mg, 1.09 mmol) was dissolved in THF (25 mL) and added slowly by syringe to a mixture of ethylamine (15 mL) and lithium (117.3 mg, 16.90 mmol; deep blue solution) at −20 °C. Stirring was continued overnight, and the solution was allowed to warm up to room temperature. Solid ammonium chloride (3 g) was added, and the reaction mixture was concentrated under reduced pressure. The solid residue was extracted with a mixture of water and diethyl ether, the organic phase was dried with sodium sulfate, filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, R_F = 0.58 (D-*erythro*) and 0.62 (L-*threo*) (chloroform/methanol, 1:1), to afford 213.3 mg of a white solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.85 (t, *J* = 7 Hz, 3 H, CH_3), 1.22 (m, 22 H, CH_2), 1.44 (s, 3 H, 3-CH_3), 2.01 (m, 2 H, CH_2), 3.47 (m, 1 H, 2-H), 3.77 (md, *J* = 11.5 Hz, 1 H, 1-H$_a$), 3.89 (md, *J* = 11.5 Hz, 1 H, 1-H$_b$), 5.42 (d, *J* = 15.3 Hz, 1 H, 4-H), 5.79 (td, *J* = 7, *J* = 15.3 Hz, 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, mixture of D-*erythro* and L-*threo* diastereomers; only the chemical shifts for the D-*erythro* diastereomer are given): δ = 14.1 (CH_3), 22.7−32.4 (CH_2), 26.8 (3-CH_3), 59.6 (C-2), 60.9 (C-1), 72.3 (C-3), 130.5 and 132.1 (C-4 and C-5) ppm. $C_{19}H_{39}NO_2$ (313.52): calcd. C 72.79, H 12.54 N, 4.47; found C 72.42, H 11.98, N 4.18. FAB-MS (70 eV): *m*/*z* calcd. for $C_{19}H_{40}NO_2$ $[M + H]^+$ 314.3; found 314.3.

(2*S*,3*R*/*S*,4*Z*)-2-Amino-3-methyloctadec-4-ene-1,3-diol (11): The experimental conditions corresponded to those used in the synthesis of **15**. Product formation was carefully controlled by TLC to avoid over-reduction to the saturated compound. Experimental details: **9** (217.4 mg, 697.9 μmol), catalytic amount of Lindlar catalyst (5% Pd on $CaCO_3$, poisoned with lead, Fluka), methanol (10 mL). R_F = 0.14 (chloroform/methanol, 1:1) (D-*erythro* and L-*threo* form). Yield: 173.3 mg as a white solid. ^1H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 7 Hz, 3 H, CH_3), 1.19 (m, 22 H, CH_2), 1.27 (s, 3 H, 3-CH_3), 2.22 (m, 2 H, CH_2), 2.74 (dd *J* = 3.5, *J* = 6.6 Hz, 1 H, 2-H), 2.88 (m, br., 4 H), 3.58 (dd, *J* = 6.6, *J* = 10.8 Hz, 1 H, 1-H$_a$), 3.70 (dd, *J* = 3.5, *J* = 10.8 Hz, 1 H, 1-H$_b$), 5.23 (d, *J* = 12.1 Hz, 1 H, 4-H), 5.35 (td, *J* = 7.4, *J* = 12.1 Hz, 1 H, 5-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, mixture of D-*erythro* and L-

threo diastereomers, ratio 2:1): δ = 14.1 (CH_3), 22.7−31.9 (CH_2), 25.4 (3-CH_3, L-*t*), 26.7 (3-CH_3, D-*e*), 59.5 (C-2, L-*t*), 59.9 (C-2, D-*e*), 62.7 (C-1, L-*t*), 63.5 (C-1, D-*e*), 75.4 (C-3, L-*t*), 75.8 (C-3, D-*e*), 132.5 (D-*e*), 132.7 (D-*e*), 133.2 (L-*t*), 133.9 (L-*t*) (C-4 and C-5) ppm. $C_{19}H_{39}NO_2$ (313.52): calcd. C 72.79, H 12.54 N, 4.47; found C 71.99, H 12.45, N 4.32. FAB-MS (70 eV): *m*/*z* calcd. for $C_{19}H_{40}NO_2$ [M + H]$^+$ 314.3; found 314.4.

***N*-[(1*S*,2*R*,3*Z*)-2-Hydroxy-1-(hydroxymethyl)-2-methylheptadec-3-enyl]dodecanamide (12a):** The experimental conditions were the same as those described for the synthesis of compound **13a**. Preparation: **11** (mixture of diastereomers, 159.0 mg, 507.1 μmol), triethylamine (210 μL, 1.52 mmol), lauroyl chloride (240 μL, 1.01 mmol), methanol (15 mL). R_F = 0.26 (chloroform/methanol, 30:1). The two diastereomers **12a** and **12b** were readily separated in this workup procedure to give 122.5 mg of **12a** and 65.3 mg of **12b** as white solids. [α_D] = −10.2 (*c* = 0.16, $CHCl_3$). M.p. 44−45 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 7 Hz, 6 H, CH_3), 1.20 (m, 38 H, CH_2), 1.36 (s, 3 H, 3-CH_3), 1.58 (m, 2 H, CH_2), 2.18 (m, 4 H, CH_2), 3.59 (m, br., 1 H, OH), 3.65 (dd, *J* = 2.5, *J* = 10.8 Hz, 1 H, 1-H_a), 3.70 (m, br., 1 H, OH), 3.86 (ddd, *J* = 2.5, *J* = 3.0, *J* = 9.1 Hz, 1 H, 2-H), 3.98 (dd, *J* = 3.0, *J* = 10.8 Hz, 1 H, 1-H_b), 5.35 (md, *J* = 12.1 Hz, 2 H, 4-H and 5-H), 6.54 (d, *J* = 9.1 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.7−37.0 (CH_2), 27.8 (3-CH_3), 55.8 (C-2), 63.7 (C-1), 77.4 (C-3), 132.4 (C-5), 133.4 (C-4), 174.1 (NCO) ppm. $C_{31}H_{61}NO_3$ (495.83): calcd. C 75.09, H 12.40 N, 2.83; found C 74.96, H 12.42, N 2.59. FAB-MS (70 eV): *m*/*z* calcd. for $C_{31}H_{62}NO_3$ [M + H]$^+$ 496.5; found 496.4.

***N*-[(1*S*,2*S*,3*Z*)-2-Hydroxy-1-(hydroxymethyl)-2-methylheptadec-3-enyl]dodecanamide (12b):** R_F = 0.16 (chloroform/methanol, 30:1). [α_D] = −13.8 (*c* = 0.86, $CHCl_3$). M.p. 36−38 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 7 Hz, 6 H, CH_3), 1.19 (m, 42 H, CH_2), 1.39 (s, 3 H, 3-CH_3), 2.14 (t, *J* = 8 Hz, 2 H, CH_2), 3.47 (m, br., 2 H, OH), 3.75 and 3.82 (m, 2 H, 1-H_a and 2-H), 3.94 (dd, *J* = 3.4, *J* = 11.3 Hz, 1 H, 1-H_b), 5.20 (d, *J* = 12.1 Hz, 2 H, 4-H), 5.31 (td, *J* = 7, *J* = 12.1 Hz, 1 H, 5-H), 6.33 (d, *J* = 8.1 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.7−37.0 (CH_2), 26.9 (3-CH_3), 57.3 (C-2), 62.9 (C-1), 76.8 (C-3), 132.9 (C-5), 133.1 (C-4), 174.0 (NCO) ppm. $C_{31}H_{61}NO_3$ (495.83): calcd. C 75.09, H 12.40 N, 2.83; found C 74.77, H 12.52, N 2.59. FAB-MS (70 eV): *m*/*z* calcd. for $C_{31}H_{62}NO_3$ [M + H]$^+$ 496.5; found 496.4.

***N*-[(1*S*,2*R*)-2-Hydroxy-1-(hydroxymethyl)-2-methylheptadec-3-ynyl]dodecanamide (13a): 9** (470.3 mg, 1.51 mmol) and triethylamine (630 μL, 4.53 mmol) were dissolved in methanol (15 mL) and cooled to −78 °C. To this stirred solution, lauroyl chloride (720 μL, 3.02 mmol) was added dropwise and stirring was continued for 18 h, which allowed the temperature to raise to room temperature. The solution was concentrated under reduced pressure, and the residue was purified by column chromatography on silica gel; R_F = 0.26 (chloroform/methanol, 30:1). The two diastereomers **13a** and **13b** were readily separated in this workup procedure to give 372.6 mg of **13a** and 185.3 mg of **13b** as white solids. [α_D] = +20.9 (*c* = 0.57, $CHCl_3$). M.p. 54−55 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7 Hz, 6 H, CH_3), 1.24 (m, 36 H, CH_2), 1.43 (s, 3 H, 3-CH_3), 1.47 (m, 2 H, CH_2), 1.63 (m, 2 H, CH_2), 2.18 (t, *J* = 7.5 Hz, 2 H, CH_2), 2.24 (t, *J* = 7.5 Hz, 2 H, CH_2), 3.20 (m, br., 2 H, OH), 3.78 (dd, *J* = 3.2, *J* = 11.1 Hz, 1 H, 1-H_A), 3.96 (ddd, *J* = 3.2, *J* = 3.4, *J* = 9.1 Hz, 1 H, 2-H), 4.29 (dd, *J* = 3.4, *J* = 11.1 Hz, 1 H, 1-H_B), 6.41 (d, *J* = 9.1 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3), 18.7−37.0 (CH_2), 28.6 (3-CH_3), 56.4 (C-2), 64.2 (C-1), 70.7 (C-3), 81.7 (C-5), 86.6 (C-4), 174.1 (NCO) ppm. $C_{31}H_{59}NO_3$ (493.81): calcd. C 75.40, H 12.04, N 2.84; found C 74.67, H 11.96, N 2.57. FAB-MS (70 eV): *m*/*z* calcd. for $C_{31}H_{59}NO_3$ [M$^+$] 493.45; found 494.5 [M + H$^+$].

***N*-[(1*S*,2*S*)-2-Hydroxy-1-(hydroxymethyl)-2-methylheptadec-3-ynyl]dodecanamide (13b):** R_F = 0.16 (chloroform/methanol, 30:1). [α_D] = −20.9 (*c* = 1.02, $CHCl_3$). M.p. 42 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7 Hz, 6 H, CH_3), 1.25 (m, 38 H, CH_2), 1.51 (s, 3 H, 3-CH_3), 1.63 (m, 2 H, CH_2), 2.19 (t, *J* = 7 Hz, 2 H, CH_2), 2.24 (t, *J* = 7.5 Hz, 2 H, CH_2), 3.32 (m, br., 2 H, OH), 3.89 (m, 2 H, 1-H_A and 1-H_B), 4.06 (ddd, *J* = 4.7, *J* = 5, *J* = 8.5 Hz, 1 H, 2-H), 6.00 (d, *J* = 8.5 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3), 18.6−37.0 (CH_2), 30.3 (3-CH_3), 57.3 (C-2), 63.0 (C-1), 70.8 (C-3), 81.3 (C-5), 86.1 (C-4), 173.8 (NCO) ppm. $C_{31}H_{59}NO_3$ (493.81): calcd. C 75.40, H 12.04, N 2.84; found C 75.21, H 11.91, N 2.57. FAB-MS (70 eV): *m*/*z* calcd. for $C_{31}H_{60}NO_3$ [M + H]$^+$ 494.45; found 494.4.

***N*-[(1*S*,2*R*)-2-Hydroxy-1-(hydroxymethyl)-2-methylheptadecyl]-dodecanamide (14a):** Route 1: **13a** (154.3 mg, 312.4 μmol) was dissolved in methanol (10 mL) and degassed with stirring. A catalytic amount of palladium on charcoal (10%) was added, and the solution was stirred under hydrogen for 18 h. The reaction mixture was filtered, and the solvent was evaporated under reduced pressure. The remaining residue was purified by column chromatography on silica gel, R_F = 0.16 (chloroform/methanol, 30:1), to give 114.0 mg of **14a** as a white solid. Route 2: The synthesis was analogous to the synthesis of **13a**. Experimental details: **13a** (mixture of diastereomers, 97.1 mg, 307.7 μmol), triethylamine (130 μL, 923.2 μmol), lauroyl chloride (150 μL, 615.5 μmol), and methanol (10 mL). The two diastereomers **14a** and **14b** were readily separated in this workup procedure to give 97.1 mg of **14a** and 35.4 mg of **14b** as white solids. [α_D] = +21.5 (*c* = 0.38, $CHCl_3$). M.p. 70−71 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 7 Hz, 6 H, CH_3), 1.06 (s, 3 H, 3-CH_3), 1.19 (m, 40 H, CH_2), 1.56 (m, 2 H, CH_2), 2.17 (t, *J* = 7.5 Hz, 2 H, CH_2), 3.36 (m, br., 2 H, OH), 3.68 (dd, *J* = 2, *J* = 11.1 Hz, 1 H, 1-H_A), 3.75 (td, *J* = 2, *J* = 8.9 Hz, 1 H, 2-H), 3.92 (dd, *J* = 2.5, *J* = 11.1 Hz, 1 H, 1-H_B), 6.54 (d, *J* = 8.4 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.7−40.4 (CH_2), 24.2 (3-CH_3), 55.0 (C-2), 62.9 (C-1), 75.5 (C-3), 174.0 (NCO) ppm. $C_{31}H_{63}NO_3$ (497.85): calcd. C 74.79, H 12.76 N, 2.81; found C 74.75, H 12.65, N 2.48. FAB-MS (70 eV): *m*/*z* calcd. for $C_{31}H_{64}NO_3$ [M + H]$^+$ 498.5; found 498.4.

***N*-[(1*S*,2*S*)-2-Hydroxy-1-(hydroxymethyl)-2-methylheptadecyl]-dodecanamide (14b):** The experimental conditions were the same as those described for the synthesis of **14a**. Route 1: Experimental details: **13b** (99.2 mg, 200.9 μmol), catalytic amount of palladium on charcoal (10%), and methanol (10 mL). R_F = 0.15 (chloroform/methanol, 30:1). [α_D] = +13.8 (*c* = 0.44, $CHCl_3$). M.p. 67 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 7 Hz, 6 H, CH_3), 1.24 (m, 40 H, CH_2), 1.29 (s, 3 H, 3-CH_3), 1.64 (m, 2 H, CH_2), 2.22 (t, *J* = 7.5 Hz, 2 H, CH_2), 3.32 (m, br., 2 H, OH), 3.79 (m, 2 H, 1-H_A and 1-H_B), 3.98 (md, *J* = 8.6 Hz, 1 H, 2-H), 6.49 (d, *J* = 8.1 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.7−40.0 (CH_2), 24.5 (3-CH_3), 54.7 (C-2), 63.5 (C-1), 75.3 (C-3), 173.8 (NCO) ppm. $C_{31}H_{63}NO_3$ (497.85): calcd. C 74.79, H 12.76 N, 2.81; found C 74.98, H 12.70, N 2.54. FAB-MS (70 eV): *m*/*z* calcd. for $C_{31}H_{64}NO_3$ [M + H]$^+$ 498.5; found 498.4.

(2*S*,3*R*/*S*)-2-Amino-3-methyloctadecane-1,3-diol (15): The experimental conditions were the same as those described for the synthesis of compound **14**. Experimental details: **9** (115.4 mg, 370.4 μmol), catalytic amount of palladium on charcoal (10%), and methanol (10 mL). R_F = 0.14 (chloroform/methanol, 1:1), D-*er*-

ythro and L-*threo* form. Yield: 112.3 mg of a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 7 Hz, 3 H, CH_3), 1.19 (m, 28 H, CH_2), 1.36 (s, 3 H, 3-CH_3), 2.73 (m, 1 H, 2-H), 2.95 (m, br., 4 H), 3.57 (dd, *J* = 7, *J* = 10.5 Hz, 1 H, 1-H_A), 3.70 (dd, *J* = 3, *J* = 10.5 Hz, 1 H, 1-H_B), 5.23 (d, *J* = 12.1 Hz, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$; mixture of D-*erythro* and L-*threo* diastereomers; only the chemical shifts for the D-*erythro* diastereomer are given): δ = 14.1 (CH_3), 22.5−32.0 (CH_2), 24.2 (3-CH_3), 38.7 (C-4), 59.0 (C-2), 62.6 (C-1), 73.7 (C-3) ppm. $C_{19}H_{41}NO_2$ (315.54): calcd. C 72.32, H 13.10 N, 4.44; found C 72.23, H 12.95, N 4.07. FAB-MS (70 eV): *m*/*z* calcd. for $C_{19}H_{42}NO_2$ [M + H]$^+$ 316.3; found 316.3.

***N*-[(4*R*,5*S*)-4-Methyl-2-phenyl-4-(tridec-1-ynyl)-1,3-dioxan-5-yl]-dodecanamide (16a):** The synthesis follows the procedure reported by Brockway et al.[27] **13a** (100.3 mg, 203.0 μmol), *p*-toluenesulfonic acid monohydrate (16 mg, 83 μmol), and benzaldehyde dimethyl acetal (60 μL, 368.6 μmol) were dissolved in DMF (5 mL) and stirred at room temperature for 4d. Water (4 °C) was added, and the mixture was extracted with ethyl acetate. The organic layer was dried with sodium sulfate, filtered and concentrated under reduced pressure. The remaining residue was purified by column chromatography on silica gel, R_F = 0.33 (petroleum ether/ethyl acetate, 10:1), to give 11.7 mg of a white solid. [α_D] = +36.4 (*c* = 0.86, $CHCl_3$). M.p. 52−53 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 7 Hz, 6 H, CH_3), 1.18 (m, 34 H, CH_2), 1.34 (m, 2 H, CH_2), 1.41 (s, 3 H, 3-CH_3), 1.48 (m, 2 H, CH_2), 1.58 (m, 2 H, CH_2), 2.17 (t, *J* = 7.5 Hz, 2 H, CH_2), 2.22 (t, *J* = 7 Hz, 2 H, CH_2), 3.58 (dd, *J* = 1.7, *J* = 11.6 Hz, 1 H, 1-H_A), 4.01 (td, *J* = 2, *J* = 10 Hz, 1 H, 2-H), 4.55 (dd, *J* = 1.5, *J* = 11.6 Hz, 1 H, 1-H_B), 6.04 (s, 1 H, ArC*H*O_2); 6.18 (d, *J* = 10 Hz, 1 H, NH), 7.31 (m, 3 H, Ar-H), 7.43 (m, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3), 18.7−37.0 (CH_2), 25.7 (3-CH_3), 49.7 (C-2), 69.1 (C-1), 73.3 (C-3), 78.7 and 90.4 (C-4 and C-5), 97.0 (ArC*H*O_2), 126.0, 128.3, 129.0 and 138.0 (Ar-C), 172.9 (NCO) ppm. $C_{38}H_{63}NO_3\times1/2H_2O$ (590.92): calcd. C 77.17, H 10.83 N, 2.37; found C 77.82, H 11.07, N 2.37. FAB-MS (70 eV): *m*/*z* calcd. for $C_{38}H_{63}NO_3$ [M + H]$^+$ 582.5; found 582.4.

***N*-[(4*S*,5*S*)-4-Methyl-2-phenyl-4-(tridec-1-ynyl)-1,3-dioxan-5-yl]-dodecanamide (16b):** The experimental conditions were the same as those described for the synthesis of **16a**. Procedure: **13b** (86.1 mg, 173.5 μmol), *p*-toluenesulfonic acid monohydrate (13.6 mg, 71.4 μmol), benzaldehyde dimethyl acetal (50 μL, 317.4 μmol), and DMF (5 mL). R_F = 0.27 (petroleum ether/ethyl acetate, 10:1). Yield: 52.2 mg as a white solid. [α_D] = −32.7 (*c* = 2.48, $CHCl_3$). M.p. 44 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.81 (t, *J* = 7 Hz, 6 H, CH_3), 1.19 (m, 34 H, CH_2), 1.37 (m, 2 H, CH_2), 1.49 (s, 3 H, 3-CH_3), 1.55 (m, 4 H, CH_2), 2.14 (t, *J* = 7.5 Hz, 2 H, CH_2), 2.27 (t, *J* = 7 Hz, 2 H, CH_2), 3.63 (t, *J* = 10.8 Hz, 1 H, 1-H_A), 4.00 (dd, *J* = 5.2, *J* = 10.8 Hz, 1 H, 1-H_B), 4.20 (ddd, *J* = 5.2, *J* = 10.6, *J* = 10.8 Hz, 1 H, 2-H), 5.28 (d, *J* = 10 Hz, 1 H, NH), 5.84 (s, 1 H, ArC*H*O_2), 7.28 (m, 3 H, Ar-H), 7.42 (m, 2 H, Ar-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3), 18.7−37.0 (CH_2), 27.00 (3-CH_3), 49.2 (C-2), 66.8 (C-1), 74.6 (C-3), 77.1 and 90.8 (C-4 and C-5), 96.9 (Ar*C*HO_2), 126.4, 128.3, 129.0 and 137.7 (Ar-C), 172.8 (NCO) ppm. $C_{38}H_{63}NO_3\times1/2H_2O$ (590.92): calcd. C 77.17, H 10.83 N, 2.37; found C 77.87, H 10.98, N 2.48. FAB-MS (70 eV): *m*/*z* calcd. for $C_{38}H_{64}NO_3$ [M + H]$^+$ 582.5; found 582.4.

***N*-[(1*S*,2*R*,3*E*)-2-Hydroxy-1-(hydroxymethyl)-2-methylheptadec-3-enyl]dodecanamide (2a):** The experimental conditions are the same as those described for the synthesis of compound **13a**. Experimental details: **10** (mixture of diastereomers, 213.3 mg, 680.2 μmol), triethylamine (280 μL, 2.04 mmol), lauroyl chloride (320 μL, 1.36 mmol), and methanol (5 mL). R_F: 0.26 (chloroform/methanol, 30:1). The two diastereomers **2a** and **2b** were readily separated in this workup procedure to give 122.5 mg of **2a** and 65.3 mg of **2b** as white solids. [α_D] = +5.5 (*c* = 1.13, $CHCl_3$). M.p. 75 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, *J* = 7 Hz, 6 H, CH_3), 1.25 (m, 38 H, CH_2), 1.31 (s, 3 H, 3-CH_3), 1.65 (m, 2 H, CH_2), 2.06 (m, 2 H, CH_2), 2.26 (t, *J* = 7.5 Hz, 2 H, CH_2), 2.70 (m, br., 2 H, OH), 3.68 (dd, *J* = 2.7, *J* = 11.1 Hz, 1 H, 1-H_A), 3.85 (ddd, *J* = 2.7, *J* = 3.0, *J* = 8.6 Hz, 1 H, 2-H), 3.98 (dd, *J* = 3.0, *J* = 11.1 Hz, 1 H, 1-H_B), 5.54 (d, *J* = 15.5 Hz, 1 H, 4-H), 5.77 (td, *J* = 7, *J* = 15.5 Hz, 1 H, 5-H), 6.40 (d, *J* = 8.6 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.7−37.0 (CH_2), 26.8 (3-CH_3), 55.6 (C-2), 63.7 (C-1), 76.3 (C-3), 129.8 (C-5), 134.0 (C-4), 173.8 (NCO) ppm. $C_{31}H_{61}NO_3$ (495.83): calcd. C 75.10, H 12.40 N, 2.83; found C 74.67, H 12.11, N 2.33. FAB-MS (70 eV): *m*/*z* calcd. for $C_{31}H_{62}NO_3$ [M + H]$^+$ 496.5; found 496.4.

***N*-[(1*S*,2*S*,3*E*)-2-Hydroxy-1-(hydroxymethyl)-2-methylheptadec-3-enyl]dodecanamide (2b):** R_F = 0.13 (chloroform/methanol, 30:1). [α_D] = −4.6 (*c* = 0.69, $CHCl_3$). M.p. 74−75 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7 Hz, 6 H, CH_3), 1.25 (m, 40 H, CH_2, OH), 1.38 (s, 3 H, 3-CH_3), 1.60 (m, 2 H, CH_2), 2.01 (m, 2 H, CH_2), 2.19 (td, *J* = 2, *J* = 7 Hz, 2 H, CH_2), 3.82 (m, 1 H, 2-H), 3.85 (dd, *J* = 3.0, *J* = 11.1 Hz, 1 H, 1-H_A), 3.99 (dd, *J* = 3.0, *J* = 11.1 Hz, 1 H, 1-H_B), 5.44 (d, *J* = 15.5 Hz, 1 H, 4-H), 5.67 (td, *J* = 7, *J* = 15.5 Hz, 1 H, 5-H), 6.18 (d, *J* = 7.4 Hz, 1 H, NH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1 (CH_3), 22.7−37.0 (CH_2), 26.6 (3-CH_3), 56.4 (C-2), 63.1 (C-1), 75.3 (C-3), 129.8 (C-5), 134.0 (C-4), 173.7 (NCO) ppm. $C_{31}H_{61}NO_3\times1/2H_2O$ (404.83): calcd. C 73.55, H 12.18 N, 2.78; found C 74.03, H 12.21, N 2.52. FAB-MS (70 eV): *m*/*z* calcd. $C_{31}H_{62}NO_3$ [M + H]$^+$ 496.5; found 496.4.

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