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A straightforward approach toward cytotoxic pyrrolidine alkaloids: Novel analogues of natural broussonetines

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ABSTRACT

Straightforward access to a series of the cytotoxic sphingolipid-derived alkaloids possessing a pyrrolidine unit and a long hydrophobic side chain was accomplished. Two simple carbohydrate chirons, protected D- and L-erythrofuranose, were chosen as the starting material, and [3,3]-sigmatropic rearrangements, a late stage cross metathesis and an intramolecular nucleophilic substitution were involved as the key transformations. The final analogues of natural broussonetines were evaluated for their capacity to alter the proliferation of cancer cells.

1. Introduction

Broussonetines, including their stereoisomeric broussonetinines (Fig. 1) represent a wide class of more than the 39 compounds isolated from the mulberry tree *Broussonetia kazinoki* by Kusano and coworkers. Apart from broussonetines N (**1**), U (**2**) and U_1 (**3**), with pyrrolizidine and pyrroline cores, respectively (Fig. 1), the remaining members of this special family possess a hydroxylated pyrrolidine unit with a variable 13-carbon side chain. The aforementioned common heterocyclic system is usually (2*R*,3*R*,4*R*,5*R*)-configured, with some exceptions - broussonetine V (**4**) and broussonetinines A (**5**) and B (**6**) - bearing (2*R*,3*S*,4*R*,5*R*)-stereochemistry (Fig. 1).

Biosynthetic studies using 1-[^{13}C]-glucose revealed that broussonetines would arise through routes similar to the first step of the *de novo* synthesis of sphingolipids, starting from the condensation of D-serine and palmitoyl-CoA [1b,2]. Most broussonetines were found to be potent and selective glycosidase inhibitors against various β-glycosidases obtained from various sources (β-glucosidases, β-galactosidases or β-mannosidases), with the IC_{50} values near to the nanomolar concentrations [1a-b,1e,1g,1i,1k,3]. Moreover, three recent studies on the preliminary structure-activity relationships [3] showed that several antipodes of natural broussonetines, such as *ent*-I (*ent*-**7**) [3a], *ent*-J_2 (*ent*-**8**) [3a], *ent*-W (*ent*-**9**) [3b], *ent*-M (*ent*-**10**) [3c] and further analogues [3b-c] with the modified carbon side chain, exhibit different glycosidase inhibitory properties against a range enzymes than the corresponding mother compounds. It was shown that the aforementioned antipodes of the natural products, as well as the corresponding enantio- or epimers of the prepared analogues (Fig. 2), inhibited α-glucosidases selectively [3].

In view of their impressive architecture and interesting biological properties, broussonetines, together with their related derivatives [3], have attracted much attention from the synthetic organic community [3–5]. Up to now, one formal and 17 total syntheses of these pyrrolidine alkaloids have been accomplished. The majority of developed strategies rely on the well-established Chiron approach. On the other hand, Trost and coworkers [5c-d] employed the catalytic asymmetric methods in their enantioselective construction of broussonetine G (**11**) and Carreira's group

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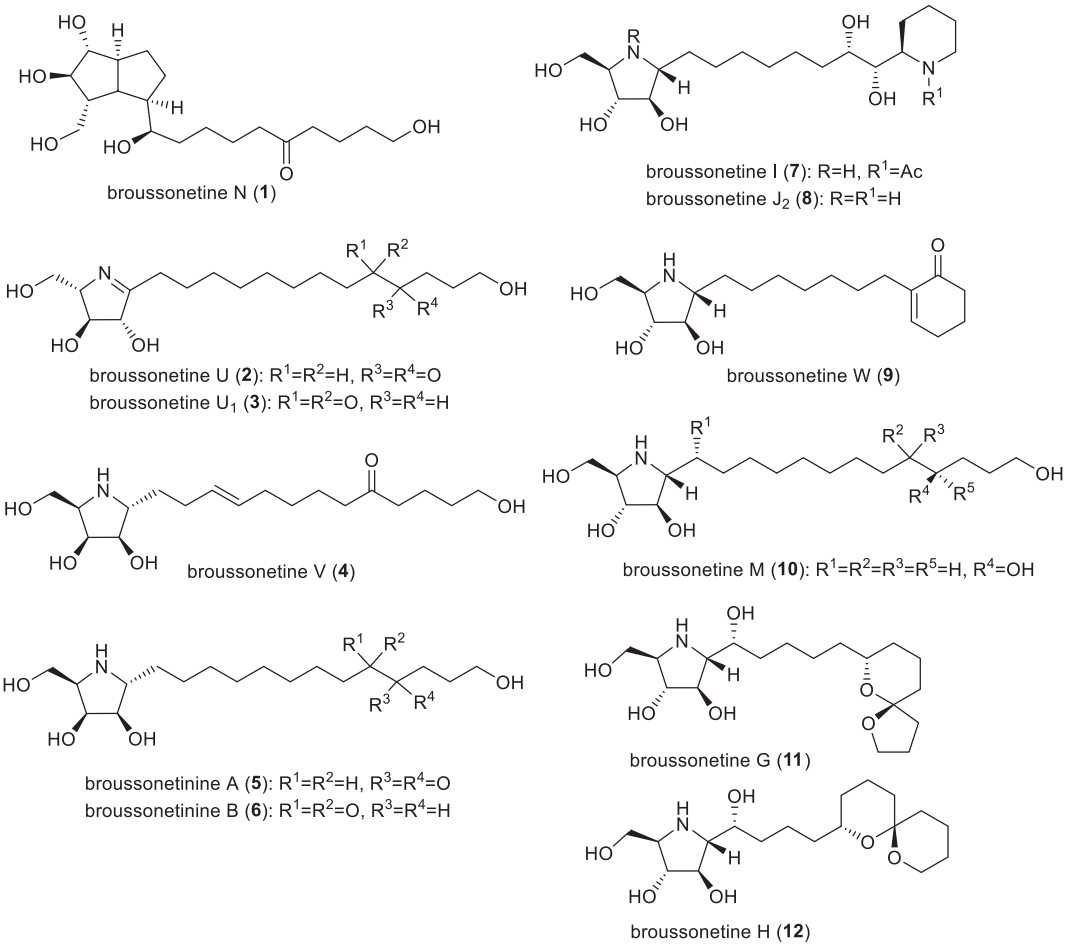


Fig. 1. Representative structures of broussonetines and broussonetinines A and B.

[5h] used the same method to build the spiroketal motif during the formal synthesis of broussonetine H (**12**) (Fig. 1). It should be noted that the same spiro-scaffold was also prepared by Brimble and coworkers in 2003 using the chiral pool methodology [6].

A recent study of Kato and coworkers [7] showed that a broussonetine derivative with a simple tridecyl chain on the polyhydroxylated pyrrolidine core has strong human β-glucocerebrosidase inhibitory activity with $IC_{50} = 0.77$ μM and represents a novel pharmacological chaperone for the treatment of Gaucher disease. Inspired by these findings, we conducted the synthesis of the four such diastereoisomeric congeners [8], including Kato's compound, and investigated the evaluation of their *in vitro* antiproliferative/cytotoxic activities on a panel of several cancer cell lines, revealing significant anticancer potency for three of them [8]. With the aim of searching for novel sphingolipid-derived structures potentially interfering with ceramide metabolism in cancer cells, we herein describe an efficient synthesis and preliminary screening of 12 novel broussonetine derivatives - **13**–**18** and *ent*-**13**-*ent*-**18** -without the hydroxymethyl group at the C-5 position and with the variable side chain lengths at C-2 on the pyrrolidine skeleton. For their construction, we were motivated by two studies of Davies's research group [9], which identified pyrrolidine-based iminosugars with the absence of the $-CH_2OH$ moiety as inhibitors of human glucosylceramide synthase (GCS) and several non-mammalian glycosidases (Fig. 3). We anticipate that our dihydroxylated pyrrolidine scaffold with the long chain unit could represent a novel structure bearing a resemblance to broussonetines and thus it could mimic their biological profile.

2. Results and discussion

2.1. Chemistry

Our retrosynthetic analysis toward the final pyrrolidine analogues **13**–**18** and *ent*-**13**-*ent*-**18** is depicted in Scheme 1.

We envisioned that **13**–**18** and *ent*-**13**-*ent*-**18** would be obtained through the intramolecular S_N2 cyclization of the activated isomeric phytosphingosines **19**–**24** and *ent*-**19**-*ent*-**24**, respectively. Compounds **19**–**24** and their antipodes *ent*-**19**-*ent*-**24** would be constructed from the common intermediates **25**–**26** and *ent*-**25**-*ent*-**26** using olefin cross metathesis with tri-, tetra- and pentadec-1-ene. The novel C–N bond in **25**–**26** and *ent*-**25**-*ent*-**26** would be introduced via [3,3]-heterosigmatropic rearrangements [10] of allylic substrates derived from the protected D-erythrofuranose **27** and its antipode *ent*-**27**. The corresponding chirons **27** and *ent*-**27** can be readily prepared from D-lyxose and D-ribose, respectively.

The synthesis started with protection of the commercially available D-lyxose and D-ribose to produce 2,3-*O*-cyclohexylidene-D-lyxofuranose **28** [11] (86 %) and 2,3-*O*-cyclohexylidene-D-ribofuranose **29** [12] (96 %). Following the literature protocol [13], the resulting derivatives **28** and **29** were converted into the corresponding lactols **27** (87 %) and *ent*-**27** (92 %), respectively (Scheme 2). Both **27** and *ent*-**27** were submitted to Wittig olefination with a stabilized ylide ($Ph_3P = CHCO_2Et$) in refluxing CH_2Cl_2 to afford

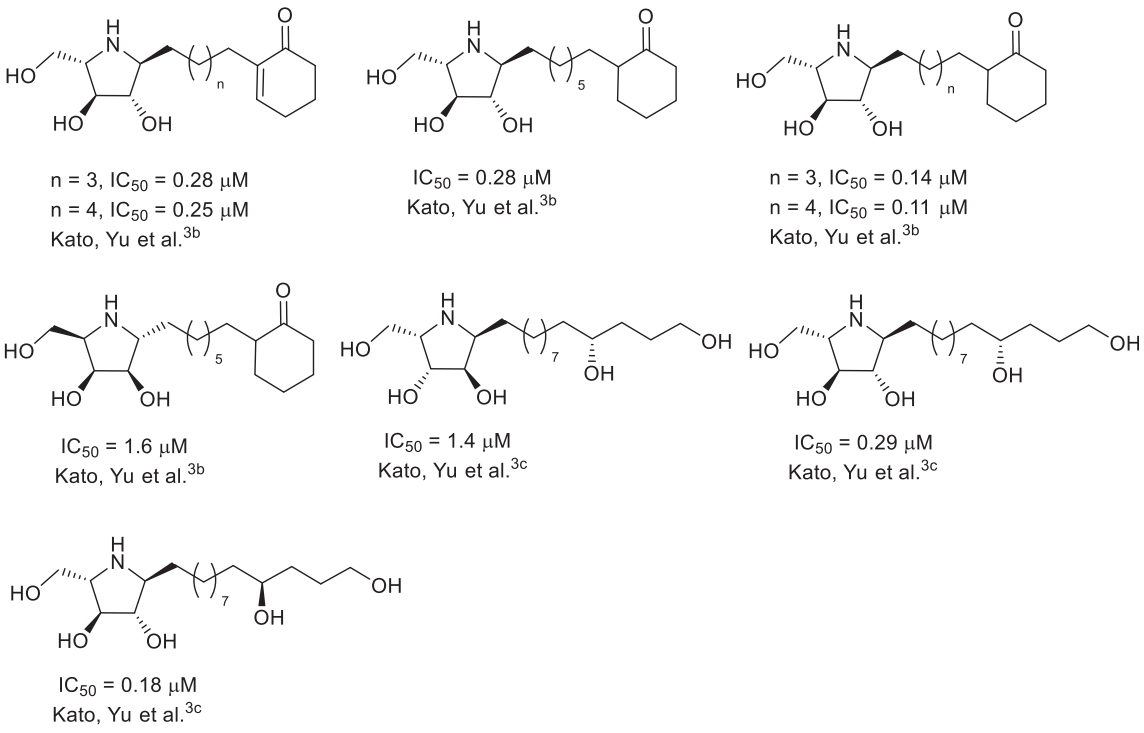


Fig. 2. Examples of analogues of broussonetines W and M, respectively, and their α-glucosidase inhibitory activity.

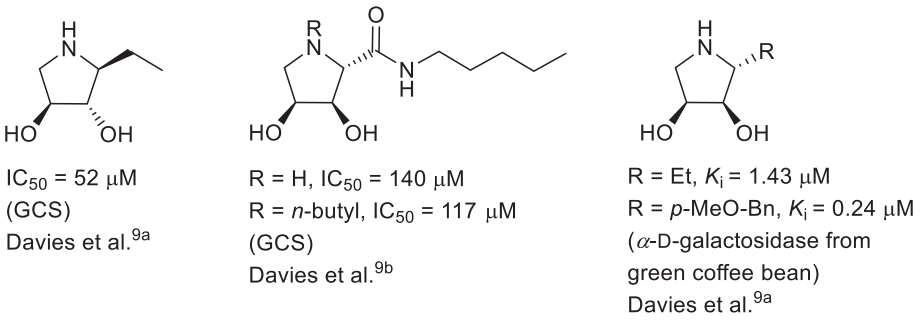


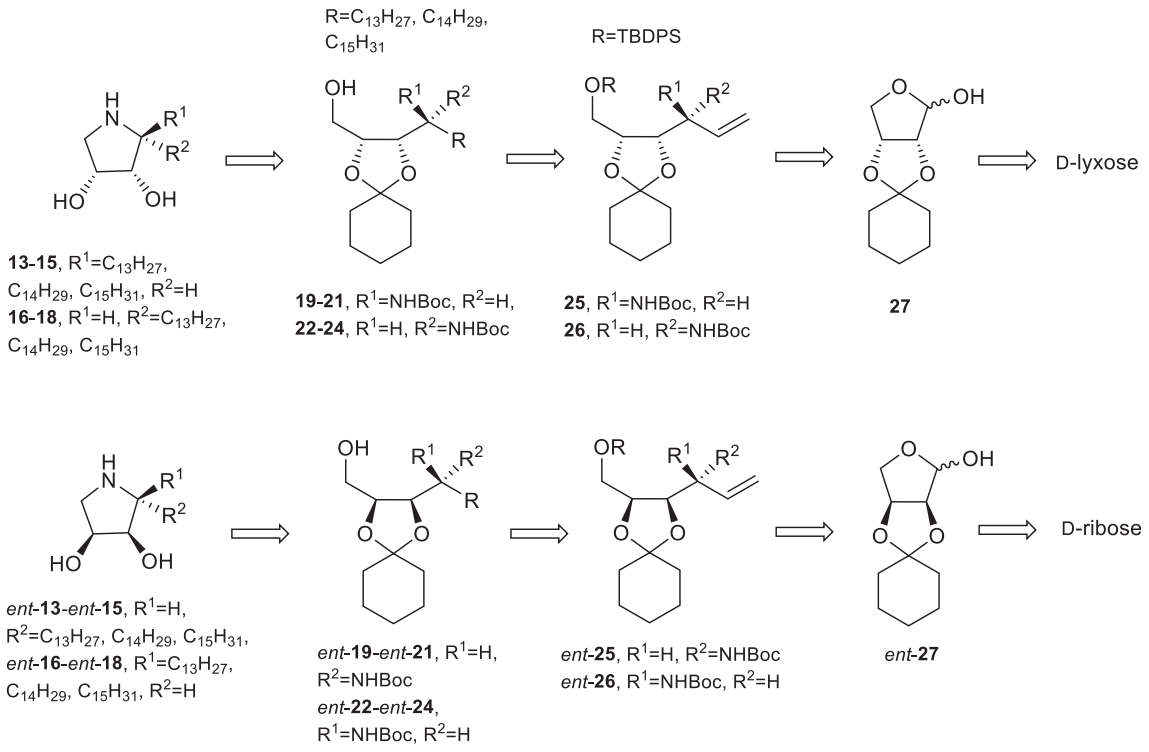
Fig. 3. Examples of pyrrolidine-based inhibitors of human GCS and non-mammalian α-D-galactosidase.

esters (*E*)-**30**, (*Z*)-**30** (*E*/*Z* = 25:75, 95 %) and *ent*-(*E*)-**30**, *ent*-(*Z*)-**30** (*E*/*Z* = 25:75, 91 %). Standard column chromatography allowed the straightforward separation of the major isomers (*Z*)-**30** and *ent*-(*Z*)-**30**, silylation of which (TBDPSCl, imidazole, CH_2Cl_2) provided products **31** and *ent*-**31** in 98 % and 96 % yields, respectively. A reduction of the ester functionality in **31** and *ent*-**31** was achieved with DIBAl-H to give allylic alcohols **32** (96 %) and *ent*-**32** (98 %).

Subsequent treatment of **32** and *ent*-**32**, first with MsCl and Et_3N in CH_2Cl_2 and then with KSCN in acetonitrile, led to the formation of thiocyanates **33** (90 %) and *ent*-**33** (85 %). On the other hand, exposure of **32** and *ent*-**32** to trichloroacetonitrile (Cl_3CCN) and a catalytic amount of DBU provided the desired imidates **34** and *ent*-**34**, which were used in the crude form (Scheme 2).

To incorporate the novel C—N bond into our expected molecules, the [3,3]-sigmatropic rearrangements of the thiocyanates **33** and *ent*-**33** as well as the trichloroacetimidates **34** and *ent*-**34** were investigated. In the case of substrates **33** and *ent*-**33**, the experiments were carried out in *n*-heptane at various temperatures using both conventional heating and sealed vessel microwave irradiation conditions and afforded the rearranged products **35**, **36** and *ent*-**35**, *ent*-**36** in moderate yields (Table 1, Scheme 3). During these reactions, the starting material as the corresponding mixture of *E*/*Z*-isomers was also recovered in amounts of 33—45 % (Table 1). Higher temperatures were found to be detrimental to the selectivity of the proceeding transformation (Table 1, entries 4—6, 10—12) and decreased the preference of the 3,4-*erythro*-product **35** or *ent*-**35**. We anticipate that the major isothiocyanates **35** and *ent*-**35** are kinetic reaction products, and the realization of the rearrangement at lower temperature (70 °C) enabled control of the selectivity (Table 1, entries 1 and 7, respectively), while still providing a satisfying yield (47 % and 46 %, respectively) of this transformation (thermodynamically controlled reactions under kinetic conditions). The obtained diastereoselectivity seems to be in accordance with those observations previously reported [14].

On the other hand, the use of microwave-assisted synthesis and higher temperatures was shown to be detrimental for the selectivity of the proceeding transformation and revealed that the equilibrium of the studied reaction was shifted to the thermodynamically more stable isothiocyanates **36** and *ent*-**36** to dramatically decrease the diastereoselectivity of the rearrangement



Scheme 1. Retrosynthetic analysis of the final pyrrolidine analogues **13**–**18** and *ent*-**13**-*ent*-**18**.

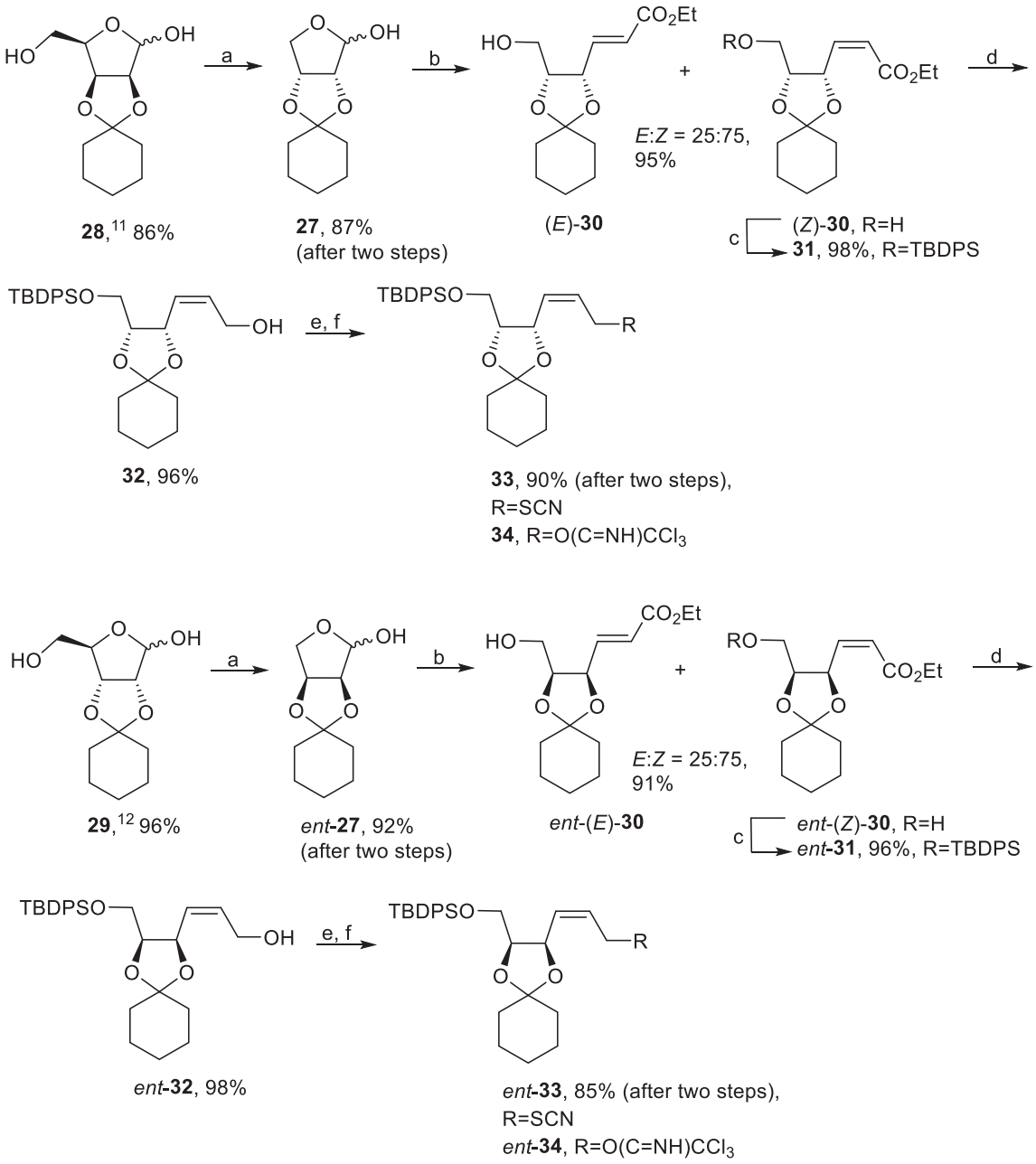
(Table 1, entries 4–6 and 10–12, respectively).

The microwave-promoted thermal Overman rearrangement of imidates **34** and *ent*-**34** was realized in *o*-xylene in the presence of K_2CO_3[15] at four different temperatures and provided the corresponding trichloroacetamides **37**, **38** and *ent*-**37**, *ent*-**38** in very good yields (Table 2, entries 2, 3, 6 and 7). As seen in Table 2, the observed diastereoselectivity in the studied *aza*-Claisen rearrangement was found to be moderate, with 3,4-*anti*-amide **37** or *ent*-**37** as the prevalent diastereoisomer. The stereochemical outcome of the rearrangement of **34** and *ent*-**34** was in good agreement with our previous observations [16] and supports the *erythro* configuration of the vicinal aminoalcohol motif in the major rearranged products **37** and *ent*-**37**. In addition, the Overman product **37** was isolated as a crystalline compound, crystallographic analysis of which revealed an (*S*)-configured stereocentre bearing a protected amino group (Fig. 4). The stereochemistry of **35** and **36**, along with their antipodes, was assigned *via* the chemical correlation methodology (*vide infra*, Scheme 4).

With the rearranged products in hand (Scheme 3), our focus then shifted to the construction of the common intermediates **25**, **26** and *ent*-**25**, *ent*-**26** (Scheme 4). Their preparation relied on two simple modifications which involved the transformation of the isothiocyanato and trichloroacetamido functionality to the amino group and its subsequent *tert*-butoxycarbonylation. Thus, the treatment of **35** and **36** with bis(*n*-tributyltin) oxide TBTO [17] in toluene gave the crude amines, which were then submitted to the reaction with Boc_2O and Et_3N to furnish the carbamates **25** and **26**, respectively. On the other hand, DIBAl-H reduction of **37** and **38** followed by the Boc protection [18] delivered the required compounds **25** and **26**. Analogously, the corresponding antipodes *ent*-**25** and *ent*-**26** were prepared in parallel fashion according to the same reaction sequence (Scheme 4). It should be noted that the synthetic route toward **25** and **26** starting from the amides **37** and **38** was more effective than their construction from the isothiocyanates **35** and **36**, respectively, and therefore was utilized for the total synthesis of our target pyrrolidines.

With the common intermediates **25**, **26** and *ent*-**25**, *ent*-**26** in hand, we focused our attention on introducing the alkyl side chain using the olefin cross-metathesis reaction [19] with commercially available alkenes such as tri-, tetra- and pentadec-1-ene (Scheme 5). The corresponding couplings were conducted in the presence of Grubbs 2nd generation catalyst in dichloromethane under reflux conditions and in all cases provided (*E*)-configured alkenes **39**–**44** and *ent*-**39**-*ent*-**44** in very good yields. Catalytic hydrogenation, followed by cleavage of the silyl ether moiety in **45**–**50** and *ent*-**45**-*ent*-**50** with TBAF in THF, afforded the isomeric phytosphingosines **19**–**24** and *ent*-**19**-*ent*-**24**, with the liberated primary alcohol group required for the subsequent activation with TsCl (Et_3N, Me_3N.HCl) [20]. The NaH-mediated [21] intramolecular nucleophilic cyclization of *in situ* generated tosylates was carried out in DMF at 0 °C and resulted in the creation of the desired pyrrolidine derivatives **51**–**56** and *ent*-**51**-*ent*-**56**. The deprotected broussonetine analogues **13**–**18** and *ent*-**13**-*ent*-**18** were finally obtained after the simultaneous removal of the *tert*-butoxycarbonyl and ketal group with 6 M HCl at 70 °C.

In the course of this work we have also accomplished the construction of the long chain 4-amino-1,2,3-triols **57** and **58** having a C_{18} aliphatic skeleton. These unusual sphingoid bases represent the isomeric analogues of natural D-*ribo*-phytosphingosine [22] with a permutation of the C-2 and C-4 substituents along the carbon backbone (Scheme 6). Génisson and co-workers [23] communicated the first synthesis of such sphingosines in 2011 together with the biological screening that revealed their potency to alert the viability of cancer cells. Recently, our group also reported the preparation of the aforementioned isophytosphingosine congeners, including *ent*-**57** [24a] and *ent*-**58** [24a], with interesting antiproliferative/cytotoxic properties [24]. Compounds **57** (82 %) and **58** (85 %) were obtained from the corresponding intermediates *ent*-**20** and *ent*-**23**, respectively, by acidic hydrolysis of the protecting groups with 6 M hydrochloric acid in MeOH at 70 °C. The



Scheme 2. *Reagents and conditions:* (a) (i) $NaBH_4$, MeOH, 0 °C; (ii) $NaIO_4$, MeOH/H_2O, rt; (b) $Ph_3P{=}CHCO_2Et$, CH_2Cl_2, reflux; (c) TBDPSCl, CH_2Cl_2, imidazole, rt; (d) DIBAl-H, CH_2Cl_2, −50 °C→−30 °C; (e) (i) MsCl, Et_3N, CH_2Cl_2, 0 °C; (ii) KSCN, MeCN, 0 °C→rt; (f) CCl_3CN, DBU, CH_2Cl_2, 0 °C.

spectroscopic data for **57** and **58** were in very good agreement with those reported in the literature for their antipodes [24a]. As expected, the optical rotation values for **57** {$[\alpha]_D^{21}$ +19.6 (*c* 0.23, MeOH)} and **58** {$[\alpha]_D^{21}$ +9.1 (*c* 0.22, MeOH)} were opposite in sign but displayed comparable magnitudes to those described for *ent*-**57** {$[\alpha]_D^{20}$ −15.0 (*c* 0.28, MeOH)} and *ent*-**58** {$[\alpha]_D^{21}$ −13.6 (*c* 0.22, MeOH)} [24a].

2.2. Antiproliferative/cytotoxic activity

The ability of the target pyrrolidine-based derivatives **13**–**18**, *ent*-**13**-*ent*-**18** and two isomeric phytosphingosines **57** and **58** to inhibit cancer cells proliferation was evaluated on a panel of five human malignant cell lines: BLM (human melanoma cells), MCF-7 (mammary gland adenocarcinoma), HCT-116 (human colon carcinoma), HeLa (cervical adenocarcinoma) and Jurkat (human acute T-lymphoblastic leukaemia). Two non-malignant cell lines - NiH 3T3 (mouse fibroblasts) and BJ-5ta hTERT (immortalised foreskin fibroblast cells) - were also included. The potency of the screened compounds was determined by MTT assay with triplicate experiments [25]. To allow comparisons, the IC_{50} values for the conventional anticancer agents cisplatin, etoposide and doxorubicin are also included. As seen in Table 3, all of evaluated pyrrolidines **13**–**18** and their corresponding antipodes *ent*-**13**-*ent*-**18** exhibit strong antiproliferative/cytotoxicity potency, especially against the Jurkat, HeLa and HCT-116 cell lines, while being less active on BLM and MCF-7 cells. Overall, all of novel analogues of the natural broussonetines display higher *in vitro* potency than cisplatin. Moreover,

Table 1
[3,3]-Sigmatropic rearrangement of thiocyanates **33** and *ent*-**33**.

Entry	Thiocyanates	Conditions[a]	Time (h)	Ratio[b]	Yield[c] (%)	Isolated thiocyanates[d] (%)
1	**33**	Δ, 70 °C	10	80:20	47	42
2	**33**	Δ, 90 °C	6	70:30	50	43
3	**33**	MW, 90 °C	6	66:34	52	41
4	**33**	MW, 110 °C	3	55:45	54	35
5	**33**	MW, 130 °C	2	55:45	55	38
6	**33**	MW, 150 °C	1	55:45	55	44
7	*ent*-**33**	Δ, 70 °C	10	79:21	46	44
8	*ent*-**33**	Δ, 90 °C	6	72:28	51	40
9	*ent*-**33**	MW, 90 °C	6	62:38	55	43
10	*ent*-**33**	MW, 110 °C	3	57:43	56	33
11	*ent*-**33**	MW, 130 °C	2	56:44	55	36
12	*ent*-**33**	MW, 150 °C	1	56:44	53	45

[a] In *n*-heptane.
[b] Ratio in the crude reaction mixtures (**35**:**36** and *ent*-**35**:*ent*-**36**, respectively). Determined by ^{1}H NMR analysis.
[c] Isolated combined yields of **35**:**36** and *ent*-**35**:*ent*-**36**, respectively.
[d] Isolated thiocyanates (*E*)-**33**:(*Z*)-**33** and *ent*-(*E*)-**33**:*ent*-(*Z*)-**33**, respectively.

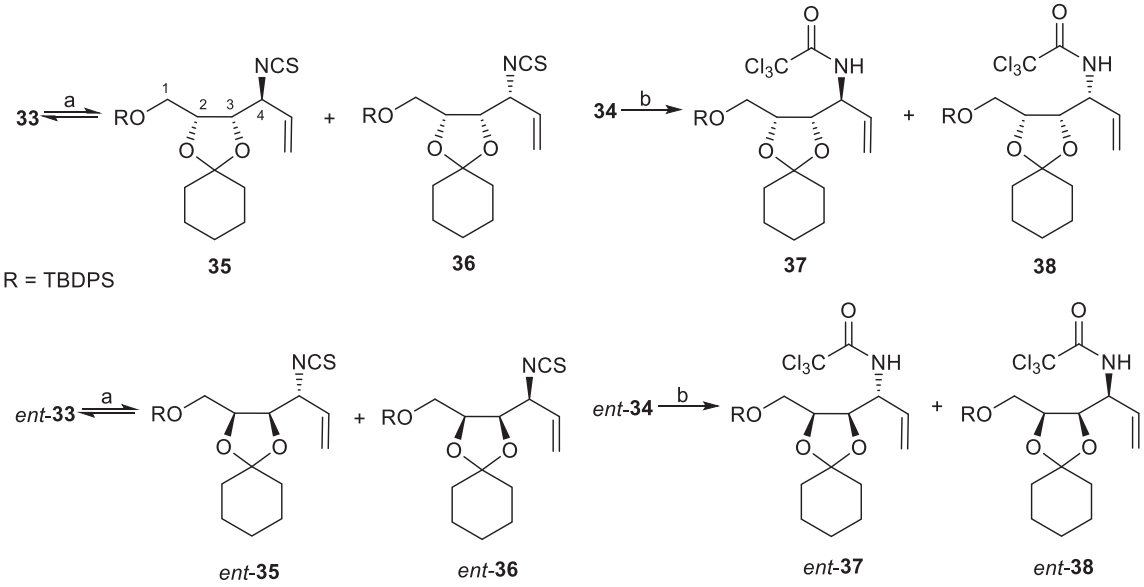
Table 2
Overman rearrangement of imidates **34** and *ent*-**34**.

Entry	Imidates	Conditions[a]	Time (h)	Ratio[b]	Yield[c] (%)
1	**34**	MW, 170 °C	11.5	64:36	76
2	**34**	MW, 190 °C	5	64:36	90
3	**34**	MW, 210 °C	1.5	64:36	90
4	**34**	MW, 230 °C	0.5	63:37	73
5	*ent*-**34**	MW, 170 °C	11.5	66:34	65
6	*ent*-**34**	MW, 190 °C	5	64:36	87
7	*ent*-**34**	MW, 210 °C	1.5	66:34	91
8	*ent*-**34**	MW, 230 °C	0.5	60:40	79

[a] In *o*-xylene, in the presence of K_2CO_3.
[b] Ratio in the crude reaction mixtures (**37**:**38** and *ent*-37:*ent*-**38**, respectively). Determined by ^{1}H NMR analysis.
[c] Isolated combined yields of **37**:**38** and *ent*-**37**:*ent*-**38**, respectively.

compounds **13**, **14** and *ent*-**13** were found be more active on HeLa cells than etoposide. Similarly, derivatives **13** and **16** are at least 3 × more potent than etoposide against the MCF-7 breast cancer cell line (Table 3). Out of 12 tested derivatives, compound **14** bearing the naturally occurring alkyl side chain was the most significant on the cell lines (Jurkat: IC_{50} 0.59 μM, HeLa: IC_{50} 0.63 μM and HCT-116: IC_{50} 0.68 μM), followed by **13** (Jurkat: IC_{50} 0.59 μM and HeLa: IC_{50} 0.78 μM), **15** (Jurkat: IC_{50} 0.69 μM) and *ent*-**16** (Jurkat: IC_{50} 0.83 μM). The viability experiments revealed that the (2*S*)-stereochemistry on the pyrrolidine core (compounds **13**–**15**, *ent*-**16**) seems to be important for obtaining better antiproliferative/cytotoxic activities. Unfortunately, the selectivity in cytotoxicity between malignant and non-malignant cell lines for the aforementioned target pyrrolidine alkaloids was fundamentally reduced, with the exception of *ent*-**13** ($IC_{50\ [BJ]}/IC_{50\ [HeLa]}$ = ~9) and *ent*-**17** ($IC_{50\ [BJ]}/IC_{50\ [HeLa]}$ = ~3.5).

Table 3 also includes IC_{50} values for the protected open-chain isophytosphingosines **20** and **23**, which displayed the lowest potency among all the tested compounds against the used cancer cell lines. On the other hand, free unusual sphingoid bases **57** and **58**, prepared from the *ent*-**20** and *ent*-**23**, respectively, are significantly more potent and exhibit higher activities than cisplatin on Jurkat and HCT-116 cells. In addition, derivative **58**, with the (2*S*,3*R*,4*S*)-configuration, demonstrated remarkable activity against HeLa cell line with an IC_{50} value comparable to that of etoposide. Further, compound **58** shows a quite promising selectivity in cytotoxicity between the cancer cell lines and non-malignant human fibroblasts



Scheme 3. *Reagents and conditions:* (a) Table 1; (b) Table 2.

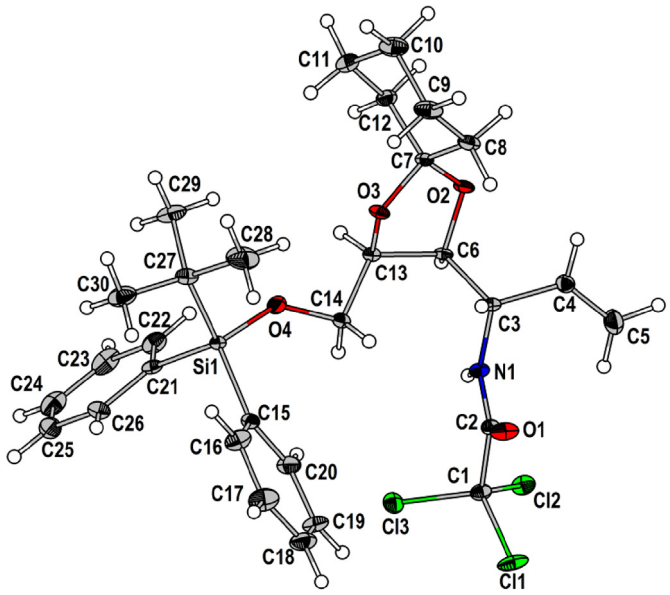


Fig. 4. ORTEP structure of **37** showing the crystallographic numbering.

BJ, with an $IC_{50\ (BJ)}/IC_{50\ (Jurkat)}$ ratio = ~10 = SI (selectivity index).

3. Conclusion

In conclusion, we described the straightforward access to novel broussonetine analogues bearing a simple alkyl side chain. The construction of these alkaloids relied on [3,3]-sigmatropic rearrangements to introduce the amino functionality, the late stage olefin cross metathesis reaction to install the hydrophobic segment, and NaH-mediated intramolecular cyclization to create the pyrrolidine unit. The synthesized derivatives were evaluated for their antiproliferative/cytotoxic activities on a panel of human malignant cell lines using a colourimetric MTT assay. All of the target pyrrolidines demonstrate promising activity against most tested human cancer cells. Based on a comparison of the cytotoxic results, we can conclude that the configuration at the C-2 position on the pyrrolidine core seems to be determinant for obtaining better antiproliferative/cytotoxic potencies. Based on this premise, compounds **13**, **14** and *ent*-**16** were selected as potential candidates for further anticancer-oriented drug discovery development. Continuing studies are underway in our laboratory and will be reported in due course.

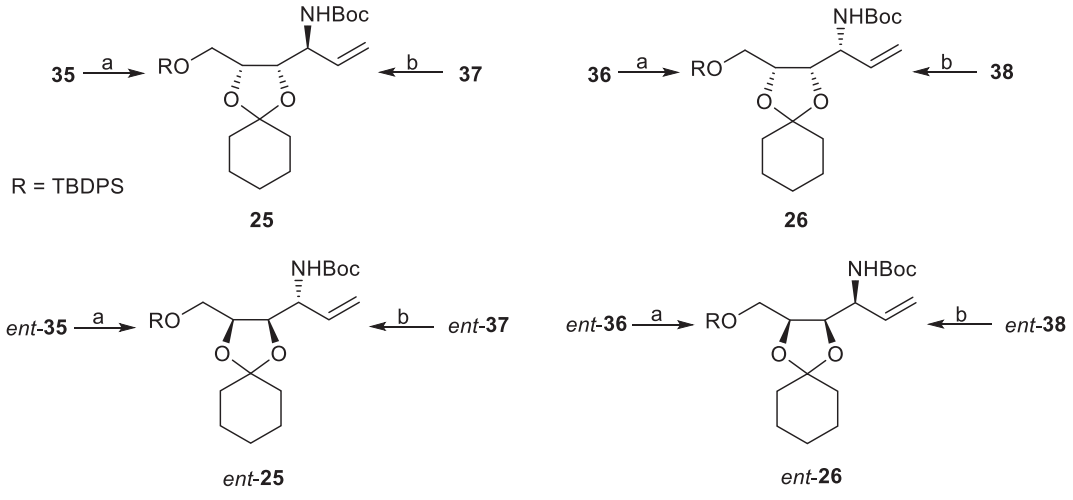
4. Experimental section

4.1. General methods

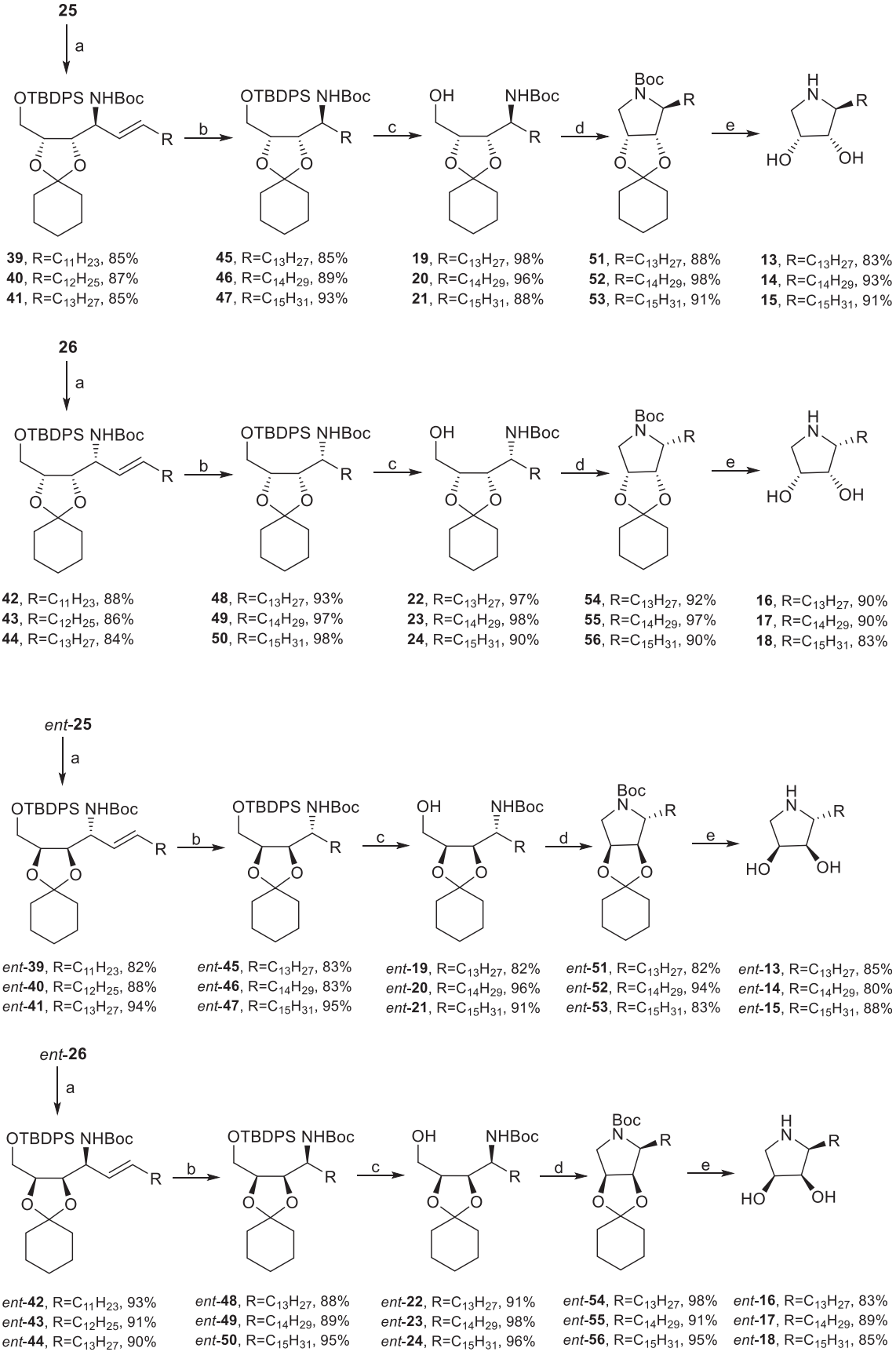
Column chromatography was run on silica gel Kieselgel 60 (0.040–0.063 mm, 230–400 mesh, Merck) under pressure, with solvents that had been distilled prior to use. Analytical thin layer chromatography was performed on Merck silica gel 60 F_{254} plates and the visualization utilized either UV light (254 nm) or spraying with a solution of phosphomolybdic acid, with subsequent heating. NMR spectra were recorded on a Varian Mercury Plus 400 FT NMR (400.13 MHz for ^1H and 100.61 MHz for ^{13}C) spectrometer. For ^1H, δ are given in parts per million (ppm) either relative to TMS ($\delta = 0.0$) as the internal standard or to the solvent signals $CDCl_3$ ($\delta = 7.26$ ppm) and CD_3OD ($\delta = 3.31$) and for ^{13}C relative to $CDCl_3$ ($\delta = 77.16$) and CD_3OD ($\delta = 49.00$). The multiplicity of the ^{13}C NMR signals concerning the $^{13}C-^1H$ coupling was determined by the HSQC method. Chemical shifts (in ppm) and coupling constants (in Hz) were obtained by first-order analysis; assignments were derived from COSY and H/C correlation spectra. Infrared (IR) spectra were measured with a Nicolet 6700 FT-IR spectrometer and reported in wavenumber (cm^{-1}). High-resolution mass spectra (HRMS) were recorded on a micrOTOF-Q II quadrupole-time of flight hybrid mass spectrometer (Bruker Daltonics). Optical rotations were determined using a P-2000 Jasco polarimeter. Melting points were recorded on a Kofler hot block and are uncorrected. Microwave reactions were carried out on a focused microwave system (Anton Paar Monowave 200). The contents of the vessel were cooled rapidly using a stream of compressed air. All commercial reagents were purchased from suppliers such as Sigma-Aldrich or Acros Organics. Solvents were dried and purified before use according to standard procedures.

4.1.1. 2,3-O-Cyclohexylidene-D-lyxofuranose **28** [11]

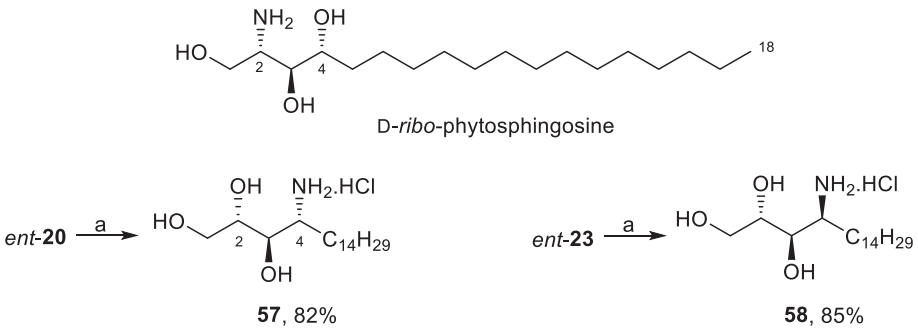
A suspension of D-lyxose (1.20 g, 8.0 mmol) in cyclohexanone (6.60 mL, 64.0 mmol) was treated with *p*-TsOH (0.304 g, 1.6 mmol).



Scheme 4. *Reagents and conditions:* (a) (i) TBTO, toluene, 90 °C; (ii) Boc_2O, Et_3N, CH_2Cl_2, rt; **25** (64 %) from **35**, **26** (44 %) from **36**, *ent*-**25** (47 %) from *ent*-**35**, *ent*-**26** (52 %) from *ent*-**36** (over two steps); (b) (i) DIBAl-H, CH_2Cl_2, –50 °C→–30 °C; (ii) Boc_2O, Et_3N, CH_2Cl_2, **25** (81 %) from **37**, **26** (73 %) from **38**, *ent*-**25** (81 %) from *ent*-**37**, *ent*-**26** (75 %) from *ent*-**38** (over two steps).



Scheme 5. *Reagents and conditions:* (a) tridec-1-ene or tetradec-1-ene or pentadec-1-ene, Grubbs II, CH_2Cl_2, reflux; (b) H_2, 10 % Pd/C/20 % $Pd(OH)_2$/C, MeOH, rt; (c) TBAF, THF, rt; (d) (i) TsCl, Et_3N, Me_3N.HCl, CH_2Cl_2, rt; (ii) NaH, DMF, 0 °C; (e) 6 M HCl, MeOH, 70 °C.



Scheme 6. *Reagents and conditions:* (a) 6 M aq HCl, MeOH, 70 °C.

Table 3
Antiproliferative/cytotoxic activities of compounds **13**–**18**, *ent*-**13**-*ent*-**18**, **57** and **58** on five human cancer cell lines (BLM, MCF-7, HCT-116, Jurkat and HeLa) and two non-malignant cell lines (BJ and NiH 3T3).

Compd no.	Cell line, IC_{50}[a] ± SD (μmol × L^{-1})						
	BLM	MCF-7	HCT-116	Jurkat	HeLa	BJ	NiH 3T3
13	4.52 ± 0.47	3.32 ± 0.38	3.97 ± 0.06	0.59 ± 0.01	0.78 ± 0.05	0.68 ± 0.07	0.73 ± 0.12
14	2.35 ± 0.03	15.11 ± 0.51	0.68 ± 0.09	0.59 ± 0.01	0.63 ± 0.02	0.67 ± 0.03	0.62 ± 0.01
15	5.12 ± 0.37	11.3 ± 2.71	2.89 ± 0.79	0.69 ± 0.04	1.78 ± 1.55	0.85 ± 0.30	1.68 ± 1.38
16	4.28 ± 0.75	3.28 ± 0.25	3.17 ± 0.56	2.62 ± 0.69	1.74 ± 1.03	4.15 ± 0.71	3.48 ± 0.30
17	3.55 ± 0.16	3.55 ± 0.24	4.96 ± 2.32	2.88 ± 0.37	3.72 ± 0.73	4.96 ± 1.66	3.74 ± 0.26
18	29.79 ± 4.82	5.68 ± 1.98	5.11 ± 1.83	2.29 ± 1.71	2.23 ± 1.06	4.16 ± 2.32	3.11 ± 1.30
ent-**13**	24.92 ± 5.22	7.27 ± 0.65	2.56 ± 0.06	0.99 ± 0.07	0.95 ± 0.04	8.74 ± 1.02	2.98 ± 1.05
ent-**14**	3.70 ± 0.16	4.32 ± 0.44	3.89 ± 1.49	5.94 ± 5.75	3.31 ± 0.25	3.65 ± 0.51	3.80 ± 0.47
ent-**15**	28.52 ± 2.45	7.29 ± 1.92	5.68 ± 0.07	4.16 ± 0.67	3.68 ± 0.39	4.44 ± 1.26	8.84 ± 1.96
ent-**16**	3.30 ± 0.61	12.26 ± 2.57	2.11 ± 0.54	0.83 ± 0.17	1.28 ± 0.52	2.41 ± 0.19	1.48 ± 0.15
ent-**17**	8.51 ± 0.19	4.36 ± 0.72	2.76 ± 0.10	2.75 ± 0.77	1.82 ± 0.87	6.32 ± 1.57	3.84 ± 0.27
ent-**18**	3.43 ± 0.17	7.19 ± 0.99	4.65 ± 1.44	4.08 ± 0.03	5.98 ± 1.58	4.52 ± 1.07	6.97 ± 1.24
57	27.81 ± 0.18	35.80 ± 5.31	6.22 ± 1.19	4.37 ± 0.33	14.38 ± 0.36	44.42 ± 14.1	14.63 ± 3.34
58	8.23 ± 1.22	13.05 ± 5.04	3.24 ± 0.81	4.09 ± 0.94	1.45 ± 0.77	8.79 ± 0.72	4.32 ± 1.00
20	38.66 ± 10.4	45.98 ± 1.14	28.82 ± 2.39	32.51 ± 1.14	30.44 ± 2.16	30.25 ± 4.78	33.56 ± 6.26
23	41.11 ± 8.75	96.26 ± 0.57	19.49 ± 5.01	24.40 ± 6.39	34.39 ± 1.63	34.86 ± 0.24	99.17 ± 0.90
cisplatin[b]	NT	15.6 ± 0.3	15.3 ± 0.5	16.2 ± 0.6	13.1 ± 0.2	NT	20.9 ± 0.3
Etoposide[b]	NT	10.9 ± 2.1	NT	NT	1.2 ± 1.5	NT	NT
Doxorubicin[b]	NT	0.5 ± 0.024	NT	NT	0.078 ± 0.02	NT	NT

NT - not tested.
[a] The potency of the compounds was determined using MTT assay after 72 h incubation of cells and given as IC_{50} (concentration of a tested compound that decreased the amount of viable cells to 50 % relative to untreated control cells, see Experimental part, section 4.2.2.
[b] Values for the clinically available anticancer drugs are reported in Refs. [8a] and [26], respectively, and were selected from the same sources.

After being stirred at room temperature for 24 h, the whole mixture was extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with water (30 mL), dried over Na_2SO_4, and then concentrated. Chromatography of the residue on silica gel (*n*-hexane/EtOAc, 1:1) afforded 1.58 g (86 %) of compound **28** (colourless oil), which was identical to reported data [11]. ESI-HRMS: *m/z* calcd for $C_{11}H_{19}O_5$ $[M + H]^+$ 231.1227, found 231.1225.

*4.1.2. 2,3-O-Cyclohexylidene-D-erythrofuranose **27***

To a solution of **28** (1.50 g, 6.50 mmol) in methanol (13 mL) that had been pre-cooled to 0 °C was added $NaBH_4$ in four portions at 15 min intervals, so that the total amount of $NaBH_4$ was 1.97 g (52.0 mmol). Thirty minutes after the last addition, the reaction mixture was diluted with water (13 mL) and neutralized with HCl (~35 %). Then $NaIO_4$ (2.80 g, 13.0 mmol) was added, the mixture was stirred for 1 h, and then poured into a saturated aq $NaHCO_3$ solution. The whole mixture was extracted with CH_2Cl_2 (3 × 40 mL), the combined organic layers were dried over Na_2SO_4 and concentrated. Chromatography of the residue on silica gel (*n*-hexane/EtOAc, 3:1) gave 1.13 g (87 %) of an inseparable mixture of lactols **27** (α:β = 2:98, determined by ^{1}H NMR spectroscopic analysis) as a white solid; IR (neat) ν 3484, 2934, 2861, 1713, 1191, 1029 cm^{-1}; ESI-HRMS: *m/z* calcd for $C_{10}H_{16}NaO_4$ $[M + Na]^+$ 223.0941, found 223.0939.

Selected NMR data for β-**27**: ^{1}H NMR (400 MHz, CD_3OD) δ 1.36–1.44 (m, 2H, CH_2), 1.52–1.66 (m, 8H, 4 × CH_2), 3.90 (d, 1H, J = 10.3 Hz, H-5), 4.00 (dd, 1H, J = 10.4, 3.6 Hz, H-5), 4.49 (d, 1H, J = 5.9 Hz, H-3), 4.82 (dd, 1H, J = 5.8, 3.7 Hz, H-4), 5.25 (s, 1H, H-2); ^{13}C NMR (101 MHz, CD_3OD) δ 24.8 (CH_2), 25.0 (CH_2), 26.2 (CH_2), 35.2 (CH_2), 37.1 (CH_2), 72.6 (C-5), 80.9 (C-4), 86.4 (C-3), 102.9 (C-2), 113.8 (OCO).

*4.1.3. Ethyl (4S,5R,2E)-6-hydroxy-4,5-(cyclohexylidenedioxy)hex-2-enoate (E)-**30** and ethyl (4S,5R,2Z)-6-hydroxy-4,5-(cyclohexylidenedioxy)hex-2-enoate (Z)-**30***

A solution of **27** (1.1 g, 5.50 mmol) in dry CH_2Cl_2 (13 mL) was treated with Ph_3P = $CHCO_2Et$ (2.60 g, 7.43 mmol). After being stirred and heated under reflux for 8 h, the solvent was evaporated, and the residue was subjected to flash chromatography on silica gel (*n*-hexane/EtOAc, 4:1) to afford 1.06 g (71 %) of (*Z*)-**30** and 0.357 g (24 %) of (*E*)-**30**.

Isomer (*Z*)-**30**: colourless oil; $[\alpha]_D^{21}$ +116.2 (*c* 0.37, $CHCl_3$). IR (neat) ν 3484, 2934, 2861, 1713, 1191, 1029 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (t, 3H, J = 7.1 Hz, CH_3), 1.38–1.47 (m, 2H, CH_2), 1.54–1.75 (m, 8H, 4 × CH_2), 2.03–2.06 (m, 1H, OH), 3.43–3.50 (m, 1H, H-6), 3.58–3.64 (m, 1H, H-6), 4.18 (q, 2H, J = 7.2 Hz, CH_2), 4.57

(ddd, 1H, J = 7.3, 5.0, 3.9 Hz, H-5), 5.57–5.61 (m, 1H, H-4), 5.93 (dd, 1H, J = 11.6, 1.8 Hz, H-2), 6.40 (dd, 1H, J = 11.6, 7.0 Hz, H-3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 23.7 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 34.2 (CH_2), 37.4 (CH_2), 60.7 (CH_2), 61.7 (C-6), 74.5 (C-4), 78.5 (C-5), 109.7 (OCO), 121.0 (C-2), 147.6 (C-3), 166.1 (C=O). ESI-HRMS: m/z calcd for $C_{14}H_{22}NaO_5$ $[M + Na]^+$ 293.1359, found 293.1363.

Isomer (*E*)-**30**: colourless oil; $[\alpha]_D^{21}$ +27.2 (c 0.25, $CHCl_3$). IR (neat) ν 3402, 2934, 2861, 1716, 1270, 1031 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (t, 3H, J = 7.1 Hz, CH_3), 1.36–1.48 (m, 2H, CH_2), 1.55–1.74 (m, 8H, 4 × CH_2), 1.92–2.01 (m, 1H, OH), 3.52–3.60 (m, 2H, 2 × H-6), 4.21 (q, 2H, J = 7.1 Hz, CH_2), 4.34–4.38 (m, 1H, H-5), 4.80 (ddd, 1H, J = 7.0, 5.5, 1.6 Hz, H-4), 6.14 (dd, 1H, J = 15.6, 1.6 Hz, H-2), 6.89 (dd, 1H, J = 15.6, 5.5 Hz, H-3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 23.8 (CH_2), 24.2 (CH_2), 25.2 (CH_2), 34.8 (CH_2), 37.7 (CH_2), 60.7 (CH_2), 62.1 (C-6), 75.7 (C-4), 77.9 (C-5), 110.3 (OCO), 123.2 (C-2), 142.4 (C-3), 166.0 (C=O). ESI-HRMS: m/z calcd for $C_{14}H_{22}NaO_5$ $[M + Na]^+$ 293.1359, found 293.1367.

4.1.4. Ethyl (4S,5R,2Z)-6-[(tert-butyldiphenylsilyl)oxy]-4,5-(cyclohexylidenedioxy)hex-2-enoate **31**

To a solution of (*Z*)-**30** (0.97 g, 3.60 mmol) in dry CH_2Cl_2 (20 mL) were successively added imidazole (0.735 g, 10.80 mmol) and *tert*-butyldiphenylsilyl chloride (1.60 mL, 6.12 mmol). After being stirred for 30 min at room temperature, the whole mixture was diluted with a saturated aq NH_4Cl solution (30 mL). The aqueous phase was then extracted with further portions of CH_2Cl_2 (2 × 20 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated in vacuo, and the residue was chromatographed on silica gel (*n*-hexane/EtOAc, 20:1) to give 1.80 g (98 %) of compound **31** as a colourless oil; $[\alpha]_D^{21}$ +102.4 (c 0.34, $CHCl_3$). IR (neat) ν 2932, 2856, 1714, 1191, 1111 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (s, 9H, 3 × CH_3), 1.27 (t, 3H, J = 7.1 Hz, CH_3), 1.37–1.44 (m, 2H, CH_2), 1.55–1.74 (m, 8H, 4 × CH_2), 3.52 (dd, 1H, J = 11.1, 4.3 Hz, H-6), 3.72 (dd, 1H, J = 11.1, 4.3 Hz, H-6), 4.14 (q, 2H, J = 7.1 Hz, CH_2), 4.51–4.55 (m, 1H, H-5), 5.69 (td, 1H, J = 7.4, 1.6 Hz, H-4), 5.83 (dd, 1H, J = 11.6, 1.6 Hz, H-2), 6.44 (dd, 1H, J = 11.6, 7.4 Hz, H-3), 7.34–7.44 (m, 6H, Ph), 7.66–7.73 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.4 (CH_3), 19.3 (C_q), 23.9 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 26.9 (3 × CH_3), 34.6 (CH_2), 37.3 (CH_2), 60.5 (CH_2), 63.1 (C-6), 74.1 (C-4), 78.7 (C-5), 109.7 (OCO), 120.7 (C-2), 127.7 (4 × CH_{Ph}), 129.7 (2 × CH_{Ph}), 133.5 (C_i), 133.6 (C_i), 135.8 (4 × CH_{Ph}), 147.5 (C-3), 165.9 (C=O). ESI-HRMS: m/z calcd for $C_{30}H_{41}O_5Si$ $[M + H]^+$ 509.2718, found 509.2721.

4.1.5. (4S,5R,2Z)-6-[(tert-Butyldiphenylsilyl)oxy]-4,5-(cyclohexylidenedioxy)hex-2-en-1-ol **32**

A solution of compound **31** (1.58 g, 3.10 mmol) in dry CH_2Cl_2 (14 mL) that had been pre-cooled to −50 °C was treated with DIBAl-H (7.70 mL, 9.30 mmol, ~1.2 M solution in toluene). After being stirred at −30 °C for 20 min, the reaction was quenched with methanol (2.5 mL), then a 30 % aq K/Na tartrate solution (68 mL) was added and stirring was continued for another hour at room temperature. The whole mixture was extracted with CH_2Cl_2 (3 × 50 mL), the combined organic layers were dried over Na_2SO_4 and concentrated. Chromatography of the residue on silica gel (*n*-hexane/EtOAc, 6:1) furnished 1.39 g (96 %) of compound **32** as a colourless oil; $[\alpha]_D^{21}$ +14.6 (c 0.26, $CHCl_3$). IR (neat) ν 3401, 2931, 2856, 1427, 1105, 1030 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04 (s, 9H, 3 × CH_3), 1.33–1.42 (m, 2H, CH_2), 1.53–1.64 (m, 8H, 4 × CH_2), 1.90 (br s, 1H, OH), 3.63–3.72 (m, 2H, 2 × H-6), 4.09–4.16 (m, 1H, H-1), 4.21–4.28 (m, 2H, H-1, H-5), 5.00–5.04 (m, 1H, H-4), 5.63–5.69 (m, 1H, H-3), 5.79–5.86 (m, 1H, H-2), 7.36–7.45 (m, 6H, Ph), 7.66–7.69 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 19.3 (C_q), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 27.0 (3 × CH_3), 34.8 (CH_2), 37.8 (CH_2), 58.9 (C-1), 63.3 (C-6), 73.2 (C-4), 78.3 (C-5), 109.4 (OCO), 127.8 (4 × CH_{Ph}) 128.2 (C-3), 129.9 (2 × CH_{Ph}), 132.6 (C-2), 133.3 (C_i), 133.5 (C_i), 135.7 (2 × CH_{Ph}), 135.8 (2 × CH_{Ph}). ESI-HRMS: m/z calcd for $C_{28}H_{38}NaO_4Si$ $[M + Na]^+$ 489.2432, found 489.2421.

4.1.6. tert-Butyl{[(2R,3S,4Z)-2,3-(cyclohexylidenedioxy)-6-thiocyanatohex-4-en-1-yl]oxy}diphenylsilane **33**

To a solution of compound **32** (0.61 g, 1.30 mmol) in dry CH_2Cl_2 (4.7 mL) that had been pre-cooled to 0 °C were successively added Et_3N (0.24 mL, 1.70 mmol) and MsCl (0.13 mL, 1.70 mmol). After stirring for 20 min at the same temperature, the solvent was evaporated and the residue was treated with Et_2O. The insoluble parts were removed by filtration and the filtrate was concentrated. The obtained product was used to the next reaction without further purification and characterization.

KSCN (0.19 g, 1.95 mmol) was added to a solution of the crude mesylate (0.71 g, 1.30 mmol) in dry MeCN (4.7 mL) at 0 °C. After being stirred for 1 h at 0 °C and then for further 3 h at room temperature, the mixture was concentrated and the residue was diluted with Et_2O. The insoluble solid material was filtered off, the filtrate was concentrated, and the residue was subjected to flash chromatography on silica gel (*n*-hexane/EtOAc, 20:1) to afford 0.59 g (90 %) of compound **33** as a colourless oil; $[\alpha]_D^{20}$ +6.0 (c 0.35, $CHCl_3$). IR (neat) ν 3071, 2930, 2855, 2154, 1427, 1110 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05 (s, 9H, 3 × CH_3), 1.35–1.42 (m, 2H, CH_2), 1.54–1.66 (m, 8H, 4 × CH_2), 3.63–3.81 (m, 4H, 2 × H-1, 2 × H-6), 4.27–4.32 (m, 1H, H-2), 4.94 (t, 1H, J = 6.9 Hz, H-3), 5.69–5.76 (m, 1H, H-5), 5.89–5.94 (m, 1H, H-4), 7.37–7.45 (m, 6H, Ph), 7.66–7.68 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 19.3 (C_q), 23.9 (CH_2), 24.2 (CH_2), 25.2 (CH_2), 27.0 (3 × CH_3), 31.1 (C-6), 34.7 (CH_2), 37.7 (CH_2), 63.2 (C-1), 73.2 (C-3), 78.4 (C-2), 109.9 (OCO), 112.0 (SCN), 125.2 (C-5), 127.8 (4 × CH_{Ph}), 129.9 (2 × CH_{Ph}), 131.9 (C-4), 133.2 (C_i), 133.3 (C_i), 135.7 (2 × CH_{Ph}), 135.8 (2 × CH_{Ph}). ESI-HRMS: m/z calcd for $C_{29}H_{37}NaNO_3SSi$ $[M + Na]^+$ 530.2156, found 530.2155.

4.1.7. tert-Butyl{[(2R,3S,4S)-4-isothiocyanato-2,3-(cyclohexylidenedioxy)hex-5-en-1-yl]oxy}diphenylsilane **35** and tert-butyl{[(2R,3S,4R)-4-isothiocyanato-2,3-(cyclohexylidenedioxy)hex-5-en-1-yl]oxy}diphenylsilane **36**

*4.1.7.1. [3,3]-Sigmatropic rearrangement of **33** under thermal conditions (general procedure).* Thiocyanate **33** (81 mg, 1.60 mmol) was dissolved in *n*-heptane (0.6 mL) and the resulting solution was stirred and heated under an atmosphere of nitrogen (for the reaction temperatures and times, see Table 1). After the solvent was evaporated, the residue was chromatographed on silica gel (*n*-hexane/EtOAc, 35:1 → 20:1) to give the corresponding rearranged products **35** and **36** as colourless oils (for their combined yields, see Table 1).

*4.1.7.2. Microwave assisted [3,3]-sigmatropic rearrangemet of **33** (general procedure).* The corresponding thiocyanate **33** (81 mg, 1.60 mmol) was weighed into a tube equipped with a magnetic stirbar. Then *n*-heptane (0.6 mL) was added and the solution was submitted to microwave irradiation conditions (for the temperatures, see Table 1). After the solvent was evaporated, the residue was purified by flash chromatography on silica gel (*n*-hexane/EtOAc, 35:1 → 20:1) to afford isothiocyanates **35** and **36** (for their combined yields, see Table 1).

Diastereoisomer **35**: $[\alpha]_D^{20}$ −9.0 (c 0.68, $CHCl_3$). IR (neat) ν 3071, 2932, 2856, 2048, 1427, 1110 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (s, 9H, 3 × CH_3), 1.30–1.68 (m, 10H, 5 × CH_2), 3.90 (dd, 1H, J = 11.5, 4.4 Hz, H-1), 3.99 (dd, 1H, J = 11.5, 4.2 Hz, H-1), 4.08 (dd, 1H, J = 8.2, 6.3 Hz, H-3), 4.26–4.30 (m, 1H, H-2), 4.54–4.60 (m, 1H, H-4), 5.31 (d, 1H, J = 10.3 Hz, H-6), 5.39 (d, 1H, J = 17.0 Hz, H-6), 5.92–6.04 (m, 1H, H-5), 7.38–7.45 (m, 6H, Ph), 7.73–7.76 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 19.4 (C_q), 23.9 (CH_2), 24.1 (CH_2), 25.2 (CH_2), 27.0 (3 × CH_3), 34.7 (CH_2), 37.3 (CH_2), 58.8 (C-4), 62.4 (C-1), 77.4 (C-2),

78.5 (C-3), 109.9 (OCO), 117.7 (C-6), 127.9 (4 × CH_{Ph}), 129.9 (2 × CH_{Ph}), 133.2 (2 × C_i), 133.4 (C-5), 134.7 (NCS), 135.8 (4 × CH_{Ph}). ESI-HRMS: *m/z* calcd for $C_{29}H_{37}NaNO_3SSi$ $[M + Na]^+$ 530.2156, found 530.2158.

Diastereoisomer **36**: $[\alpha]_D^{21}$ −10.9 (*c* 0.26, $CHCl_3$). IR (neat) *ν* 3071, 2932, 2857, 2048, 1427, 1104 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.07 (s, 9H, 3 × CH_3), 1.34−1.40 (m, 2H, CH_2), 1.48−1.72 (m, 8H, 4 × CH_2), 3.87−3.97 (m, 2H, 2 × H-1), 4.13−4.15 (m, 1H, H-3), 4.28−4.33 (m, 1H, H-2), 4.49−4.51 (m, 1H, H-4), 5.28 (d, 1H, *J* = 10.2 Hz, H-6), 5.36 (d, 1H, *J* = 16.9 Hz, H-6), 5.89−5.99 (m, 1H, H-5), 7.38−7.48 (m, 6H, Ph), 7.65−7.68 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 19.3 (C_q), 23.9 (CH_2), 24.1 (CH_2), 25.2 (CH_2), 27.0 (3 × CH_3), 34.4 (CH_2), 36.9 (CH_2), 59.2 (C-4), 62.4 (C-1), 76.3 (C-2), 78.4 (C-3), 110.2 (OCO), 118.1 (C-6), 128.0 (4 × CH_{Ph}), 130.1 (2 × CH_{Ph}), 132.9 (2 × C_i), 133.5 (C-5), 135.0 (NCS), 135.7 (4 × CH_{Ph}). ESI-HRMS: *m/z* calcd for $C_{29}H_{37}NaNO_3SSi$ $[M + Na]^+$ 530.2156, found 530.2167.

4.1.8. N-[(3′S,4′S,5′R)-6′-[(tert-Butyldiphenylsilyl)oxy]-4′,5′-(cyclohexylidenedioxy)hex-1′-en-3′-yl]-2,2,2-trichloroacetamide **37** and N-[(3′R,4′S,5′R)-6′-[(tert-Butyldiphenylsilyl)oxy]-4′,5′-(cyclohexylidenedioxy)hex-1′-en-3′-yl]-2,2,2-trichloroacetamide **38**

A solution of compound **32** (70 mg, 0.15 mmol) in dry CH_2Cl_2 (0.8 mL) that had been pro-cooled to 0 °C was successively treated with DBU (2 μL, 15 μmol) and Cl_3CCN (30 μL, 0.30 mmol). After being stirred for 15 min at the same temperature, the mixture was filtered through a small pad of Celite and concentrated. The isolated product **34** was used to the next reaction without further purification.

The crude imidate **34** (92 mg, 0.15 mmol) was dissolved in *o*-xylene (2 mL) and transferred to a tube equipped with a stirbar. The anhydrous K_2CO_3 (24 mg, 0.17 mmol) was added and the reaction mixture was subjected to microwave irradiation (for the reaction times and temperatures, see Table 2). After the solvent was evaporated, the residue was chromatographed on silica gel (*n*-hexane/EtOAc, 25:1) to give diastereoisomeric amides **37** and **38** (for their combined yields, see Table 2). To obtain a greater amount (more than 1 g) of the corresponding products **37** and **38**, we utilized the experiment carried out at 210 °C (Table 2, entry 3).

Diastereoisomer **37**: white crystals; mp 77−79 °C; $[\alpha]_D^{21}$ −43.9 (*c* 0.31, $CHCl_3$). IR (neat) *ν* 2932, 2855, 1528, 1701, 1107 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.09 (s, 9H, 3 × CH_3), 1.30−1.45 (m, 2H, CH_2), 1.50−1.65 (m, 8H, 4 × CH_2), 3.84 (dd, 1H, *J* = 11.0, 5.8 Hz, H-6′), 3.92 (dd, 1H, *J* = 11.0, 6.4 Hz, H-6′), 4.25−4.34 (m, 2H, H-4′, H-5′), 4.72−4.76 (m, 1H, H-3′), 5.18−5.25 (m, 2H, 2 × H-1′), 5.94 (ddd, 1H, *J* = 16.9, 10.4, 6.2 Hz, H-2′), 7.10 (d, 1H, *J* = 8.5 Hz, NH), 7.37−7.45 (m, 6H, Ph), 7.67−7.72 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 19.3 (C_q), 23.8 (CH_2), 24.1 (CH_2), 25.2 (CH_2), 27.1 (3 × CH_3), 34.4 (CH_2), 36.8 (CH_2), 54.0 (C-3′), 62.2 (C-6′), 76.9 (C-5′), 77.5 (C-4′), 92.8 (C_q), 109.6 (OCO), 118.7 (C-1′), 127.9 (4 × CH_{Ph}), 130.0 (2 × CH_{Ph}), 133.1 (C_i), 133.2 (C_i), 133.5 (C-2′), 135.8 (4 × CH_{Ph}), 161.1 (C=O). ESI-HRMS: *m/z* calcd for $C_{30}H_{39}Cl_3NO_4Si$ $[M + H]^+$ 610.1708, found 610.1707.

Diastereoisomer **38**: colourless oil; $[\alpha]_D^{21}$ −20.0 (*c* 0.31, $CHCl_3$). IR (neat) *ν* 3419, 2932, 2857, 1720, 1490, 1427, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.07 (s, 9H, 3 × CH_3), 1.30−1.71 (m, 10H, 5 × CH_2), 3.77−3.86 (m, 2H, 2 × H-6′), 4.33−4.42 (m, 2H, H-4′, H-5′), 4.70−4.74 (m, 1H, H-3′), 5.23−5.31 (m, 2H, 2 × H-1′), 5.86 (ddd, 1H, *J* = 16.6, 10.2, 6.1 Hz, H-2′), 7.14 (d, 1H, *J* = 7.8 Hz, NH), 7.35−7.45 (m, 6H, Ph), 7.66−7.68 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 19.3 (C_q), 23.7 (CH_2), 24.1 (CH_2), 25.2 (CH_2), 27.0 (3 × CH_3), 33.5 (CH_2), 36.8 (CH_2), 52.6 (C-3′), 62.7 (C-6′), 77.1 (C-5′), 77.4 (C-4′), 92.8 (C_q), 109.5 (OCO), 117.3 (C-1′), 127.9 (4 × CH_{Ph}), 129.9 (2 × CH_{Ph}), 133.0 (C_i), 133.3 (C_i), 134.9 (C-2′), 135.8 (4 × CH_{Ph}), 160.7 (C=O). ESI-HRMS: *m/z* calcd for $C_{30}H_{38}Cl_3NaNO_4Si$ $[M + Na]^+$ 632.1528, found 632.1530.

4.1.9. tert-Butyl [(3S,4S,5R)-6-[(tert-butyldiphenylsilyl)oxy]-4,5-(cyclohexylidenedioxy)hex-1-en-3-yl]carbamate **25**

*4.1.9.1. Synthesis of **25** from isothiocyanate **35**.* A solution of isothiocyanate **35** (81 mg, 0.16 mmol) in dry toluene (0.7 mL) was treated with TBTO (0.16 mL, 0.32 mmol). After being stirred and heated at 90 °C for 30 min, the solvent was evaporated and the obtained amine was subjected to the next reaction without purification.

To a solution of the crude amine (73 mg, 0.16 mmol) in dry CH_2Cl_2 (1.6 mL) were successively added Et_3N (22 μL, 0.16 mmol) and Boc_2O (87 mg, 0.4 mmol). After stirring for 24 h at room temperature, the solvent was removed under reduced pressure, and the residue was chromatographed on silica gel (*n*-hexane/EtOAc, 15:1) to give 58 mg (64 %) of compound **25**.

*4.1.9.2. Synthesis of **25** from trichloroacetamide **37**.* To a solution of **37** (0.41 g, 0.67 mmol) in dry CH_2Cl_2 (3.4 mL) that had been pre-cooled to −50 °C wad added DIBAl-H (1.70 mL, 2.0 mmol, ~1.2 M solution in toluene). After being stirred for 30 min at −30 °C, the reaction was quenched with MeOH (0.6 mL) and poured into a 30 % aq K/Na tartrate solution (15 mL). The resulting mixture was vigorously stirred for another hour at room temperature and then was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated. The prepared amine was used to the next reaction without purification.

A solution of the crude amine (0.312 g, 0.67 mmol) in dry CH_2Cl_2 (7 mL) was successively treated with Et_3N (94 μL, 0.67 mmol) and Boc_2O (0.37 g, 1.70 mmol). After being stirred for 24 h at room temperature, the solvent was evaporated, and the residue was chromatographed on silica gel (*n*-hexane/EtOAc, 15:1) to afford 0.307 g (81 %) of compound **25** as a colourless oil; $[\alpha]_D^{21}$ −26.5 (*c* 0.62, $CHCl_3$). IR (neat) *ν* 2932, 2857, 1702, 1500, 1365, 1111 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.08 (s, 9H, 3 × CH_3), 1.24−1.42 (m, 11H, 3 × CH_3, CH_2), 1.50−1.66 (m, 8H, 4 × CH_2), 3.82 (dd, 1H, *J* = 11.1, 5.8 Hz, H-6), 3.93 (dd, 1H, *J* = 11.1, 5.4 Hz, H-6), 4.12 (t, 1H, *J* = 5.6 Hz, H-4), 4.22−4.36 (m, 2H, H-3, H-5), 5.11−5.21 (m, 3H, 2 × H-1, NH), 5.86−5.95 (m, 1H, H-2), 7.35−7.45 (m, 6H, Ph), 7.70−7.72 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 19.4 (C_q), 23.9 (CH_2), 24.1 (CH_2), 25.3 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 34.6 (CH_2), 37.0 (CH_2), 53.1 (C-3), 62.3 (C-6), 77.4 (C-5), 78.2 (C-4), 79.5 (C_q), 109.2 (OCO), 116.4 (C-1), 127.8 (4 × CH_{Ph}), 129.8 (CH_{Ph}), 129.9 (CH_{Ph}), 133.3 (C_i), 133.4 (C_i), 135.8 (4 × CH_{Ph}), 136.0 (C-2), 155.3 (C=O). ESI-HRMS: *m/z* calcd for $C_{33}H_{48}NO_5Si$ $[M + H]^+$ 566.3296, found 566.3292.

4.1.10. tert-Butyl [(3R,4S,5R)-6-[(tert-butyldiphenylsilyl)oxy]-4,5-(cyclohexylidenedioxy)hex-1-en-3-yl]carbamate **26**

*4.1.10.1. Synthesis of **26** from isothiocyanate **36**.* Using the same procedure as described for the construction of **25**, isothiocyanate **36** (96 mg, 0.19 mmol) was converted into derivative **26** (colourless oil, 47 mg, 44 %, *n*-hexane/EtOAc, 15:1).

*4.1.10.2. Synthesis of **26** from trichloroacetamide **38**.* Using the same procedure as described for the conversion of **37** to **25**, compound **38** (0.305 g, 0.50 mmol) was transformed into derivative **26** (0.207 g, 73 %, *n*-hexane/EtOAc, 15:1); $[\alpha]_D^{21}$ +1.1 (*c* 0.35, $CHCl_3$). IR (neat) *ν* 2932, 2857, 1716, 1487, 1163, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.07 (s, 9H, 3 × CH_3), 1.32−1.37 (m, 11H, 3 × CH_3, CH_2), 1.49−1.65 (m, 8H, 4 × CH_2), 3.80 (dd, 1H, *J* = 10.5, 5.7 Hz, H-6), 3.93 (dd, 1H, *J* = 10.5, 6.9 Hz, H-6), 4.19−4.26 (m, 1H, H-4), 4.28−4.33 (m, 1H, H-5), 4.37−4.49 (m, 1H, H-3), 5.13−5.23 (m, 3H, NH, 2 × H-1), 5.86−5.96 (m, 1H, H-2), 7.36−7.44 (m, 6H, Ph), 7.68−7.70 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 19.3 (C_q), 23.7 (CH_2), 24.1 (CH_2), 25.3 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 33.8 (CH_2), 36.9 (CH_2), 52.0 (C-3), 62.9 (C-6), 77.5 (C-5), 77.8 (C-4), 79.5 (C_q), 108.9 (OCO), 115.4 (C-1), 127.8 (4 × CH_{Ph}), 129.8 (CH_{Ph}), 129.9 (CH_{Ph}), 133.4

(2 × C_i), 135.7 (2 × CH_{Ph}), 135.8 (2 × CH_{Ph}), 136.9 (C-2), 155.2 (C=O). ESI-HRMS: *m/z* calcd for $C_{33}H_{48}NO_5Si$ $[M + H]^+$ 566.3296, found 566.3292.

4.1.11. tert-Butyl [(2R,3S,4S,5E)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)heptadec-5-en-4-yl]carbamate **39**

To a solution of compound **25** (0.209 g, 0.37 mmol) in dry CH_2Cl_2 (6 mL) was successively added tridec-1-ene (0.44 mL, 1.85 mmol) and second generation Grubbs catalyst (15.7 mg, 18.5 μmol). After being stirred and heated to reflux for 6 h, the reaction mixture was allowed to cool to room temperature, and the solvent was evaporated. Chromatography of the residue on silica gel (*n*-hexane/EtOAc, 20:1) gave 0.226 mg (85 %) of compound **39** as a colourless oil. IR (neat) ν 3346, 2925, 2853, 1716, 1364, 1111 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, $J = 6.8$ Hz, CH_3), 1.08 (s, 9H, 3 × CH_3), 1.22–1.44 (m, 29H, 3 × CH_3, 10 × CH_2), 1.49–1.65 (m, 8H, 4 × CH_2), 1.89–1.94 (m, 2H, CH_2), 3.80 (dd, 1H, $J = 11.1$, 6.1 Hz, H-1), 3.91 (dd, 1H, $J = 11.1$, 5.4 Hz, H-1), 4.11–4.14 (m, 1H, H-3), 4.19–4.28 (m, 2H, H-2, H-4), 5.14 (br s, 1H, NH), 5.45 (dd, 1H, $J = 15.6$, 6.3 Hz, H-5), 5.53–5.60 (m, 1H, H-6), 7.35–7.45 (m, 6H, Ph), 7.69–7.72 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.9 (CH_2), 24.1 (CH_2), 25.3 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.1 (CH_2), 29.3 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.8 (3 × CH_2), 32.1 (CH_2), 32.5 (CH_2), 34.5 (CH_2), 37.0 (CH_2), 52.7 (C-4), 62.5 (C-1), 77.4 (C-2), 78.5 (C-3), 79.3 (C_q), 109.0 (OCO), 127.2 (C-5), 127.8 (4 × CH_{Ph}), 129.8 (2 × CH_{Ph}), 133.3 (C-6), 133.4 (2 × C_i), 135.8 (4 × CH_{Ph}), 155.3 (C=O). ESI-HRMS: *m/z* calcd for $C_{44}H_{69}NaNO_5Si$ $[M + Na]^+$ 742.4837, found 742.4849.

Due to the presence of a small amount of (*Z*)-isomer (very similar R_f values for both isomers), we were unable to obtain (*E*)-**39** in pure form. Therefore, the optical rotation of **39** is not reported.

4.1.12. tert-Butyl [(2R,3S,4S,5E)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)octadec-5-en-4-yl]carbamate **40**

Using the same procedure as described for the construction of **39**, compound **25** (0.28 g, 0.50 mmol), tetradec-1-ene (0.63 mL, 2.5 mmol) and Grubbs II (21 mg, 25 μmol) gave after reflux (7 h) the corresponding alkene **40** (colourless oil, 0.319 g, 87 %, *n*-hexane/EtOAc, 20:1). IR (neat) ν 2925, 2853, 1716, 1490, 1165 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, $J = 6.8$ Hz, CH_3), 1.08 (s, 9H, 3 × CH_3), 1.22–1.40 (m, 31H, 3 × CH_3, 11 × CH_2), 1.51–1.66 (m, 8H, 4 × CH_2), 1.89–1.93 (m, 2H, CH_2), 3.80 (dd, 1H, $J = 11.1$, 6.1 Hz, H-1), 3.91 (dd, 1H, $J = 11.1$, 5.4 Hz, H-1), 4.11–4.14 (m, 1H, H-3), 4.19–4.28 (m, 2H, H-2, H-4), 5.15 (br s, 1H, NH), 5.45 (dd, 1H, $J = 15.5$, 6.3 Hz, H-5), 5.53–5.60 (m, 1H, H-6), 7.35–7.45 (m, 6H, Ph), 7.69–7.72 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.1 (CH_2), 29.3 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.8 (4 × CH_2), 32.1 (CH_2), 32.5 (CH_2), 34.6 (CH_2), 37.0 (CH_2), 52.8 (C-4), 62.5 (C-1), 77.4 (C-2), 78.5 (C-3), 79.3 (C_q), 109.0 (OCO), 127.3 (C-5), 127.8 (4 × CH_{Ph}), 129.8 (2 × CH_{Ph}), 133.4 (2 × C_i), 133.5 (C-6), 135.8 (2 × CH_{Ph}), 135.9 (2 × CH_{Ph}), 155.3 (C=O). ESI-HRMS: *m/z* calcd for $C_{45}H_{72}NO_5Si$ $[M + H]^+$ 734.5174, found 734.5184.

Due to the presence of a small amount of (*Z*)-isomer (very similar R_f values for both isomers), we were unable to obtain (*E*)-**40** in pure form. Therefore, the optical rotation of **40** is not reported.

4.1.13. tert-Butyl [(2R,3S,4S,5E)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)nonadec-5-en-4-yl]carbamate **41**

According to the same procedure described for the conversion of **25** to **39**, compound **25** (0. 13 g, 0.23 mmol), pentadec-1-ene (0.31 mL, 1.15 mmol) and Grubbs II (9.8 mg, 11.5 μmol) afforded after reflux (5 h) olefin **41** as a colourless oil (0.146 g, 85 %, *n*-hexane/EtOAc, 20:1). IR (neat) ν 2924, 2853, 1716, 1490, 1365, 1111 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, $J = 6.8$ Hz, CH_3), 1.08 (s, 9H, 3 × CH_3), 1.22–1.45 (m, 33H, 3 × CH_3, 12 × CH_2), 1.49–1.65 (m, 8H, 4 × CH_2), 1.89–1.94 (m, 2H, CH_2), 3.80 (dd, 1H, $J = 11.1$, 6.0 Hz, H-1), 3.92 (dd, 1H, $J = 11.1$, 5.4 Hz, H-1), 4.12–4.14 (m, 1H, H-3), 4.24–4.28 (m, 2H, H-2, H-4), 5.16 (br s, 1H, NH), 5.46 (dd, 1H, $J = 15.5$, 6.3 Hz, H-5), 5.53–5.60 (m, 1H, H-6), 7.35–7.45 (m, 6H, Ph), 7.70–7.73 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.9 (CH_2), 24.1 (CH_2), 25.3 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.1 (CH_2), 29.3 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 29.8 (4 × CH_2), 32.1 (CH_2), 32.5 (CH_2), 34.5 (CH_2), 36.9 (CH_2), 52.7 (C-4), 62.5 (C-1), 77.4 (C-2), 78.5 (C-3), 79.3 (C_q), 109.0 (OCO), 127.2 (C-5), 127.8 (4 × CH_{Ph}), 129.8 (2 × CH_{Ph}), 133.3 (C_i), 2 × 133.4 (C-6, C_i), 135.8 (4 × CH_{Ph}), 155.3 (C=O). ESI-HRMS: *m/z* calcd for $C_{46}H_{73}NaNO_5Si$ $[M + Na]^+$ 770.5150, found 770.5150.

Due to the presence of a small amount of (*Z*)-isomer (very similar R_f values for both isomers), we were unable to obtain (*E*)-**41** in pure form. Therefore, the optical rotation of **41** is not reported.

4.1.14. tert-Butyl [(2R,3S,4R,5E)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)heptadec-5-en-4-yl]carbamate **42**

Using the same procedure as described for the preparation of **39**, compound **26** (0.198 g, 0.35 mmol), tridec-1-ene (0.42 mL, 1.75 mmol) and catalyst Grubbs II (14.8 mg, 17.5 μmol) afforded under reflux (4 h) alkene **42** as a colourless oil (0.222 g, 88 %, *n*-hexane/EtOAc, 20:1). IR (neat) ν 3453, 2925, 2854, 1717, 1165, 1487, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, $J = 6.8$ Hz, CH_3), 1.07 (s, 9H, 3 × CH_3), 1.25–1.41 (m, 29H, 3 × CH_3, 10 × CH_2), 1.49–1.65 (m, 8H, 4 × CH_2), 1.96–2.01 (m, 2H, CH_2), 3.78 (dd, 1H, $J = 10.7$, 6.0 Hz, H-1), 3.92 (dd, 1H, $J = 10.7$, 6.4 Hz, H-1), 4.14–4.16 (m, 1H, H-3), 4.25–4.37 (m, 2H, H-2, H-4), 5.01 (br s, 1H, NH), 5.46 (dd, 1H, $J = 15.4$, 6.4 Hz, H-5), 5.56–5.63 (m, 1H, H-6), 7.35–7.44 (m, 6H, Ph), 7.68–7.70 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.3 (2 × CH_2), 29.5 (CH_2), 29.7 (CH_2), 29.8 (3 × CH_2), 32.1 (CH_2), 32.4 (CH_2), 34.0 (CH_2), 37.0 (CH_2), 51.7 (C-4), 63.1 (C-1), 77.7 (C-2), 78.3 (C-3), 79.3 (C_q), 108.8 (OCO), 127.8 (4 × CH_{Ph}), 128.5 (C-5), 129.8 (2 × CH_{Ph}), 132.4 (C-6), 133.5 (2 × C_i), 135.8 (4 × CH_{Ph}), 155.3 (C=O). ESI-HRMS: *m/z* calcd for $C_{44}H_{69}NaNO_5Si$ $[M + Na]^+$ 742.4837, found 742.4849.

Due to the presence of a small amount of (*Z*)-isomer (very similar R_f values for both isomers), we were unable to obtain (*E*)-**42** in pure form. Therefore, the optical rotation of **42** is not reported.

4.1.15. tert-Butyl [(2R,3S,4R,5E)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)octadec-5-en-4-yl]carbamate **43**

According to the same procedure described for the conversion of **25** to **39**, compound **26** (0.192 g, 0.34 mmol), tetradec-1-ene (0.43 mL, 1.7 mmol) and second generation Grubbs catalyst (14 mg, 17 μmol) afforded after reflux (4 h) the corresponding alkene **43** as a colourless oil (0.21 g, 86 %, *n*-hexane/EtOAc, 20:1); IR (neat) ν 2925, 2853, 1716, 1490, 1165 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, $J = 6.9$ Hz, CH_3), 1.07 (s, 9H, 3 × CH_3), 1.24–1.42 (m, 31H, 3 × CH_3, 11 × CH_2), 1.52–1.61 (m, 8H, 4 × CH_2), 1.96–2.01 (m, 2H, CH_2), 3.78 (dd, 1H, $J = 10.7$, 6.0 Hz, H-1), 3.92 (dd, 1H, $J = 10.7$, 6.4 Hz, H-1), 4.14–4.16 (m, 1H, H-3), 4.25–4.37 (m, 2H, H-2, H-4), 5.01 (br s, 1H, NH), 5.45 (dd, 1H, $J = 15.4$, 6.4 Hz, H-5), 5.56–5.63 (m, 1H, H-6), 7.35–7.44 (m, 6H, Ph), 7.68–7.70 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 27.1 (3 × CH_3), 28.5 (3 × CH_3), 29.3 (2 × CH_2), 29.5 (CH_2), 29.7 (CH_2), 29.8 (4 × CH_2), 32.1 (CH_2), 32.4 (CH_2), 34.0 (CH_2), 37.0 (CH_2), 51.8 (C-4), 63.1 (C-1), 77.8 (C-2), 78.3 (C-3), 79.3 (C_q), 108.8 (OCO), 127.8 (4 × CH_{Ph}), 128.5 (C-5), 129.8 (2 × CH_{Ph}), 132.4 (C-6), 133.5 (2 × C_i), 135.8 (4 × CH_{Ph}), 155.2 (C=O). ESI-HRMS: *m/z* calcd for $C_{45}H_{72}NO_5Si$ $[M + H]^+$ 734.5174, found 734.5184.

Due to the presence of a small amount of (*Z*)-isomer (very

similar R_f values for both isomers), we were unable to obtain (*E*)-**43** in pure form. Therefore, the optical rotation of **43** is not reported.

4.1.16. tert-Butyl [(2R,3S,4R,5E)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)nonadec-5-en-4-yl]carbamate **44**

According to the same procedure employed for the construction of **39**, compound **26** (0.17 g, 0.30 mmol), pentadec-1-ene (0.41 mL, 1.50 mmol) and Grubbs II catalyst (13 mg, 15 μmol) provided under reflux (4 h) olefin **44** as a colourless oil (0.189 g, 84 %, *n*-hexane/EtOAc, 20:1). IR (neat) ν 3454, 2924, 2853, 1717, 1487, 1365, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, $J = 6.8$ Hz, CH_3), 1.07 (s, 9H, 3 × CH_3), 1.24–1.41 (m, 33H, 3 × CH_3, 12 × CH_2), 1.52–1.61 (m, 8H, 4 × CH_2), 1.96–2.01 (m, 2H, CH_2), 3.78 (dd, 1H, $J = 10.7$, 6.0 Hz, H-1), 3.92 (dd, 1H, $J = 10.7$, 6.4 Hz, H-1), 4.14–4.16 (m, 1H, H-3), 4.25–4.37 (m, 2H, H-2, H-4), 5.02 (br s, 1H, NH), 5.45 (dd, 1H, $J = 15.4$, 6.4 Hz, H-5), 5.56–5.63 (m, 1H, H-6), 7.35–7.44 (m, 6H, Ph), 7.68–7.70 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 27.1 (3 × CH_3), 28.5 (3 × CH_3), 29.3 (2 × CH_2), 29.5 (CH_2), 29.7 (CH_2), 29.8 (5 × CH_2), 32.1 (CH_2), 32.4 (CH_2), 34.0 (CH_2), 37.0 (CH_2), 51.8 (C-4), 63.1 (C-1), 77.7 (C-2), 78.3 (C-3), 79.3 (C_q), 108.8 (OCO), 127.8 (4 × CH_{Ph}), 128.5 (C-5), 129.8 (2 × CH_{Ph}), 132.5 (C-6), 133.5 (2 × C_i), 135.8 (4 × CH_{Ph}), 155.2 (C=O). ESI-HRMS: *m/z* calcd for $C_{46}H_{73}NaNO_5Si$ $[M + Na]^+$ 770.5150, found 770.5143.

Due to the presence of a small amount of (*Z*)-isomer (very similar R_f values for both isomers), we were unable to obtain (*E*)-**44** in pure form. Therefore, the optical rotation of **44** is not reported.

4.1.17. tert-Butyl [(2R,3S,4S)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)heptadecan-4-yl]carbamate **45**

A solution of compound **39** (0.209 g, 0.29 mmol) in dry MeOH (11 mL) was successively treated with two catalysts: 10 % Pd/C and 20 % $Pd(OH)_2$/C (1:1, 34 mg). After stirring for 3 h at room temperature under an atmosphere of hydrogen, the mixture was filtered through a small pad of Celite and concentrated. The final residue was subjected to flash chromatography on silica gel (*n*-hexane/EtOAc, 25:1) to afford 0.178 g (85 %) of compound **45** as a colourless oil; $[\alpha]_D^{20}$ −5.0 (*c* 0.24, $CHCl_3$). IR (neat) ν 2924, 2853, 1703, 1504, 1365, 1165, 1111 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, $J = 6.8$ Hz, CH_3), 1.07 (s, 9H, 3 × CH_3), 1.24–1.63 (m, 43H, 3 × CH_3,17 × CH_2), 3.64–3.73 (m, 2H, H-1, H-4), 3.91 (dd, 1H, $J = 11.1$, 5.7 Hz, H-1), 4.02–4.13 (m, 1H, H-3), 4.20–4.25 (m, 1H, H-2), 4.93 (d, 1H, $J = 9.0$ Hz, NH), 7.35–7.45 (m, 6H, Ph), 7.70–7.73 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 25.8 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (2 × CH_2), 29.8 (5 × CH_2), 32.1 (CH_2), 32.2 (CH_2), 34.8 (CH_2), 37.4 (CH_2), 50.7 (C-4), 62.8 (C-1), 77.5 (C-2), 78.5 (C-3), 79.0 (C_q), 108.7 (OCO), 127.8 (4 × CH_{Ph}), 129.8 (2 × CH_{Ph}), 133.3 (C_i), 133.4 (C_i), 135.7 (2 × CH_{Ph}), 135.8 (2 × CH_{Ph}), 155.7 (C=O). ESI-HRMS: *m/z* calcd for $C_{44}H_{71}NaNO_5Si$ $[M + Na]^+$ 744.4994, found 744.4997.

4.1.18. tert-Butyl [(2R,3S,4S)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)octadecan-4-yl]carbamate **46**

Using the same procedure as described for the transformation of **39** to **45**, compound **40** (0.29 g, 0.40 mmol) in dry MeOH (13 mL) was converted into derivative **46** (colourless oil, 0.26 g, 89 %, *n*-hexane/EtOAc, 25:1); $[\alpha]_D^{21}$ −3.5 (*c* 0.66, $CHCl_3$). IR (neat) ν 2924, 2853, 1702, 1502, 1165, 1112 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, $J = 6.6$ Hz, CH_3), 1.07 (s, 9H, 3 × CH_3), 1.24–1.63 (m, 45H, 3 × CH_3, 18 × CH_2), 3.59–3.73 (m, 2H, H-1, H-4), 3.91 (dd, 1H, $J = 11.1$, 5.5 Hz, H-1), 4.00–4.15 (m, 1H, H-3), 4.20–4.24 (m, 1H, H-2), 4.90 (d, 1H, $J = 8.0$ Hz, NH), 7.35–7.44 (m, 6H, Ph), 7.70–7.72 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 25.8 (CH_2), 27.1 (3 × CH_3), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (2 × CH_2), 29.8 (5 × CH_2), 29.9 (CH_2), 32.1 (CH_2), 32.2 (CH_2), 34.8 (CH_2), 37.5 (CH_2), 50.8 (C-4), 62.8 (C-1), 77.5 (C-2), 78.5 (C-3), 79.1 (C_q), 108.8 (OCO), 127.8 (4 × CH_{Ph}), 129.8 (2 × CH_{Ph}), 133.3 (C_i), 133.5 (C_i), 135.8 (2 × CH_{Ph}), 135.9 (2 × CH_{Ph}), 155.7 (C=O). ESI-HRMS: *m/z* calcd for $C_{45}H_{74}NO_5Si$ $[M + H]^+$ 736.5331, found 736.5344.

4.1.19. tert-Butyl [(2R,3S,4S)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)nonadecan-4-yl]carbamate **47**

According to the same procedure employed for the preparation of **45**, compound **41** (0.127 g, 0.17 mmol) was converted into derivative **47** (colourless oil, 0.118 g, 93 %, *n*-hexane/EtOAc, 25:1); $[\alpha]_D^{20}$ −5.5 (*c* 0.22, $CHCl_3$). IR (neat) ν 2924, 2853, 1702, 1502, 1428, 1365 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, $J = 6.9$ Hz, CH_3), 1.07 (s, 9H, 3 × CH_3), 1.23–1.65 (m, 47H, 3 × CH_3, 19 × CH_2), 3.60–3.72 (m, 2H, H-1, H-4), 3.91 (dd, 1H, $J = 11.1$, 5.7 Hz, H-1), 4.01–4.13 (m, 1H, H-3), 4.20–4.24 (m, 1H, H-2), 4.91 (d, 1H, $J = 8.9$ Hz, NH), 7.35–7.45 (m, 6H, Ph), 7.70–7.73 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 25.8 (CH_2), 27.1 (3 × CH_3), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (2 × CH_2), 29.8 (4 × CH_2), 29.9 (3 × CH_2), 32.1 (CH_2), 32.2 (CH_2), 34.8 (CH_2), 37.5 (CH_2), 50.8 (C-4), 62.8 (C-1), 77.4 (C-2), 78.5 (C-3), 79.1 (C_q), 108.8 (OCO), 127.8 (4 × CH_{Ph}), 129.8 (2 × CH_{Ph}), 133.3 (C_i), 133.5 (C_i), 135.8 (2 × CH_{Ph}), 135.9 (2 × CH_{Ph}), 155.7 (C=O). ESI-HRMS: *m/z* calcd for $C_{46}H_{75}NaNO_5Si$ $[M + Na]^+$ 772.5307, found 772.5332.

4.1.20. tert-Butyl [(2R,3S,4R)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)heptadecan-4-yl]carbamate **48**

Using the same procedure as described for the conversion of **39** to **45**, compound **42**, (0.216 g, 0.30 mmol) was modified to derivative **48** (colourless oil, 0.201 g, 93 %, *n*-hexane/EtOAc, 25:1); $[\alpha]_D^{20}$ − 4.3 (*c* 0.30, $CHCl_3$). IR (neat) ν 3453, 2926, 2854, 1716, 1492, 1365, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 50 °C) δ 0.88 (t, 3H, $J = 6.9$ Hz, CH_3), 1.07 (s, 9H, 3 × CH_3), 1.26–1.61 (m, 43H, 17 × CH_2, 3 × CH_3), 3.66–3.80 (m, 1H, H-4), 3.82–3.91 (m, 2H, 2 × H-1), 4.08–4.18 (m, 1H, H-3), 4.26–4.31 (m, 1H, H-2), 4.73 (br s, 1H, NH), 7.32–7.41 (m, 6H, Ph), 7.68–7.70 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 26.2 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (CH_2), 29.8 (6 × CH_2), 32.1 (CH_2), 33.9 (CH_2), 34.6 (CH_2), 36.9 (CH_2), 49.4 (C-4), 63.2 (C-1), 77.4 (C-3), 77.9 (C-2), 79.0 (C_q), 108.6 (OCO), 127.7 (2 × CH_{Ph}), 127.8 (3 × CH_{Ph}), 129.7 (CH_{Ph}), 133.6 (2 × C_i), 135.7 (2 × CH_{Ph}), 135.8 (2 × CH_{Ph}) 155.2 (C=O). ESI-HRMS: *m/z* calcd for $C_{44}H_{71}NaNO_5Si$ $[M + Na]^+$ 744.4994, found 744.4990.

4.1.21. tert-Butyl [(2R,3S,4R)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)octadecan-4-yl]carbamate **49**

Using the same procedure as described for the preparation of **45**, compound **43** (0.19 g, 0.26 mmol) was converted into derivative **49** (colourless oil, 0.186 g, 97 %, *n*-hexane/EtOAc, 25:1); $[\alpha]_D^{21}$ − 7.6 (*c* 0.60, $CHCl_3$). IR (neat) ν 2925, 2853, 1716, 1492, 1165, 1106 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 50 °C) δ 0.89 (t, 3H, $J = 6.6$ Hz, CH_3), 1.08 (s, 9H, 3 × CH_3), 1.27–1.57 (m, 45H, 18 × CH_2, 3 × CH_3), 3.68–3.80 (m, 1H, H-4), 3.83–3.92 (m, 2H, 2 × H-1), 4.10–4.19 (m, 1H, H-3), 4.27–4.31 (m, 1H, H-2), 4.74 (br s, 1H, NH), 7.34–7.42 (m, 6H, Ph), 7.69–7.71 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 26.2 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (CH_2), 29.8 (6 × CH_2), 29.9 (CH_2), 32.1 (CH_2), 33.9 (CH_2), 34.6 (CH_2), 37.0 (CH_2), 49.4 (C-4), 63.2 (C-1), 77.4 (C-3), 78.0 (C-2), 79.0 (C_q), 108.6 (OCO), 127.7 (2 × CH_{Ph}), 127.8 (2 × CH_{Ph}), 129.7 (2 × CH_{Ph}), 133.6 (C_i), 133.7 (C_i), 135.8 (4 × CH_{Ph}), 155.2 (C=O). ESI-HRMS: *m/z* calcd for $C_{45}H_{74}NO_5Si$ $[M + H]^+$ 736.5331, found 736.5343.

4.1.22. tert-Butyl [(2R,3S,4R)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)nonadecan-4-yl]carbamate ***50***

According to the same procedure described for the preparation of **45**, compound **44** (0.172 g, 0.23 mmol) was converted to derivative **50** (colourless oil, 0.169 g, 98 %, *n*-hexane/EtOAc, 25:1); $[\alpha]_D^{20}$ −8.1 (*c* 0.37, $CHCl_3$). IR (neat) *ν* 3453, 2924, 2853, 1716, 1491, 1165, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 50 °C) *δ* 0.88 (t, 3H, *J* = 6.8 Hz, CH_3), 1.06 (s, 9H, 3 × CH_3), 1.25−1.61 (m, 47H, 19 × CH_2, 3 × CH_3), 3.69−3.80 (m, 1H, H-4), 3.82−3.91 (m, 2H, 2 × H-1), 4.08−4.18 (m, 1H, H-3), 4.26−4.30 (m, 1H, H-2), 4.73 (br s, 1H, NH), 7.32−7.41 (m, 6H, Ph), 7.67−7.70 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 26.2 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (CH_2), 29.8 (5 × CH_2), 29.9 (3 × CH_2), 32.1 (CH_2), 33.9 (CH_2), 34.6 (CH_2), 37.0 (CH_2), 49.4 (C-4), 63.2 (C-1), 77.5 (C-3), 77.9 (C-2), 79.0 (C_q), 108.6 (OCO), 127.7 (2 × CH_{Ph}), 127.8 (3 × CH_{Ph}), 129.7 (CH_{Ph}), 133.6 (C_i), 133.7 (C_i), 135.8 (4 × CH_{Ph}) 155.2 (C=O). ESI-HRMS: *m/z* calcd for $C_{46}H_{75}NaNO_5Si$ $[M + Na]^+$ 772.5307, found 772.5310.

4.1.23. tert-Butyl [(2R,3S,4S)-2,3-(cyclohexylidenedioxy)-1-hydroxyheptadecan-4-yl]carbamate ***19***

Tetrabutylammonium fluoride (TBAF, 0.22 mL, 1 M in THF, 0.22 mmol) was added dropwise to a solution of compound **45** (0.159 g, 0.22 mmol) in THF (2.2 mL) at room temperature. After being stirred for 1 h, the whole mixture was poured into a saturated aq NH_4Cl solution (14 mL) and extracted with EtOAc (3 × 14 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated, and the residue was chromatographed on silica gel (*n*-hexane/EtOAc, 5:1). This procedure yielded 0.104 g (98 %) of compound **19** as a white amorphous solid; $[\alpha]_D^{21}$ −5.8 (*c* 0.26, $CHCl_3$). IR (neat) *ν* 3510, 3387, 2918, 2850, 1685, 1513, 1365, 1164 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.5 Hz, CH_3), 1.26−1.62 (m, 42H, 3 × CH_3,16 × CH_2, *H*−CH_2), 1.74−1.85 (m, 1H, *H*−CH_2), 2.52 (br s, 1H, OH), 3.61−3.80 (m, 3H, 2 × H-1, H-4), 3.92−4.95 (m, 1H, H-3), 4.19−4.23 (m, 1H, H-2), 4.44 (d, 1H, *J* = 10.0 Hz, NH); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.2 (CH_3), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.1 (CH_2), 25.2 (CH_2), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (3 × CH_2), 29.8 (4 × CH_2), 32.0 (CH_2), 33.6 (CH_2), 35.0 (CH_2), 37.9 (CH_2), 49.8 (C-4), 61.7 (C-1), 78.0 (C-2), 78.6 (C-3), 79.9 (C_q), 109.1 (OCO), 155.9 (C=O). ESI-HRMS: *m/z* calcd for $C_{28}H_{53}NaNO_5$ $[M + Na]^+$ 506.3816, found 506.3825.

4.1.24. tert-Butyl [(2R,3S,4S)-2,3-(cyclohexylidenedioxy)-1-hydroxyoktadecan-4-yl]carbamate ***20***

Using the same procedure as described for the construction of **19**, compound **46** (0.25 g, 0.34 mmol) in THF (3.4 mL) provided after the treatment with 1 M TBAF (0.34 ml, 0.23 mmol) derivative **20** as white amorphous solid (0.162 g, 96 %, *n*-hexane/EtOAc, 5:1); $[\alpha]_D^{21}$ −3.4 (*c* 0.35, $CHCl_3$). IR (neat) *ν* 3514, 3389, 2918, 2849, 1684, 1513, 1365, 1164 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.5 Hz, CH_3), 1.26−1.62 (m, 44H, 3 × CH_3, 17 × CH_2, *H*−CH_2), 1.74−1.85 (m, 1H, *H*−CH_2), 2.52 (br s, 1H, OH), 3.61−3.83 (m, 3H, 2 × H-1, H-4), 3.91−4.95 (m, 1H, H-3), 4.19−4.23 (m, 1H, H-2), 4.44 (d, 1H, *J* = 10.0 Hz, NH); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.2 (CH_3), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.1 (CH_2), 25.2 (CH_2), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (3 × CH_2), 29.8 (5 × CH_2), 32.0 (CH_2), 33.6 (CH_2), 35.0 (CH_2), 37.9 (CH_2), 49.8 (C-4), 61.7 (C-1), 78.0 (C-2), 78.6 (C-3), 80.0 (C_q), 109.1 (OCO), 155.9 (C=O). ESI-HRMS: *m/z* calcd for $C_{29}H_{55}NaNO_5$ $[M + Na]^+$ 520.3972, found 520.3973.

4.1.25. tert-Butyl [(2R,3S,4S)-2,3-(cyclohexylidenedioxy)-1-hydroxynonadecan-4-yl]carbamate ***21***

According to the same procedure employed for the construction of **19**, compound **47** (98 mg, 0.13 mmol) was converted into derivative **21** (white amorphous solid, 59 mg, 88 %, *n*-hexane/EtOAc, 5:1); $[\alpha]_D^{21}$ +3.7 (*c* 0.38, $CHCl_3$). IR (neat) *ν* 3513, 3389, 2917, 2849, 1684, 1512, 1365, 1163 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.9 Hz, CH_3), 1.25−1.62 (m, 46H, 3 × CH_3,18 × CH_2, *H*−CH_2), 1.73−1.86 (m, 1H, *H*−CH_2), 2.45 (br s, 1H, OH), 3.60−3.82 (m, 3H, 2 × H-1, H-4), 3.91−3.95 (m, 1H, H-3), 4.19−4.23 (m, 1H, H-2), 4.39 (d, 1H, *J* = 6.9 Hz, NH); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.3 (CH_3), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.2 (2 × CH_2), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (2 × CH_2), 29.8 (7 × CH_2), 32.1 (CH_2), 33.7 (CH_2), 35.0 (CH_2), 38.0 (CH_2), 49.8 (C-4), 61.7 (C-1), 78.1 (C-2), 78.6 (C-3), 80.0 (C_q), 109.1 (OCO), 155.9 (C=O). ESI-HRMS: *m/z* calcd for $C_{30}H_{57}NaNO_5$ $[M + Na]^+$ 534.4129, found 534.4127.

4.1.26. tert-Butyl [(2R,3S,4R)-2,3-(cyclohexylidenedioxy)-1-hydroxyheptadecan-4-yl]carbamate ***22***

Using the same procedure as described for the transformation of **45** to **19**, compound **48** (0.188 g, 0.26 mmol) was converted into derivative **22** (white amorphous solid, 0.122 g, 97 %, *n*-hexane/EtOAc, 5:1); $[\alpha]_D^{20}$ +18.6 (*c* 0.29, $CHCl_3$). IR (neat) *ν* 3449, 2923, 2853, 1694, 1499, 1365, 1164 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.9 Hz, CH_3), 1.25−1.65 (m, 43H, 3 × CH_3, 17 × CH_2), 2.68 (t, 1H, *J* = 6.0 Hz, OH), 3.63−3.72 (m, 2H, 2 × H-1), 3.84−3.89 (m, 1H, H-4), 4.13−4.15 (m, 1H, H-3), 4.23−4.28 (m, 1H, H-2), 4.79 (d, 1H, *J* = 9.8 Hz, NH); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.3 (CH_3), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 25.9 (CH_2), 28.6 (3 × CH_3), 29.5 (CH_2), 29.6 (CH_2), 29.7 (2 × CH_2), 29.8 (4 × CH_2), 32.1 (CH_2), 34.2 (CH_2), 35.4 (CH_2), 37.3 (CH_2), 48.6 (C-4), 61.8 (C-1), 77.6 (C-2, C-3), 79.8 (C_q), 108.6 (OCO), 156.2 (C=O). ESI-HRMS: *m/z* calcd for $C_{28}H_{53}NaNO_5$ $[M + Na]^+$ 506.3816, found 506.3823.

4.1.27. tert-Butyl [(2R,3S,4R)-2,3-(cyclohexylidenedioxy)-1-hydroxyoctadecan-4-yl]carbamate ***23***

According to the same procedure employed for the preparation of **19**, compound **49** (0.17 g, 0.23 mmol) was converted into derivative **23** (white amorphous solid, 0.112 g, 98 %, *n*-hexane/EtOAc, 5:1); $[\alpha]_D^{21}$ +13.1 (*c* 0.29, $CHCl_3$). IR (neat) *ν* 3453, 3401, 2920, 2852, 1692, 1522, 1171, 1059 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.6 Hz, CH_3), 1.25−1.65 (m, 45H, 3 × CH_3, 18 × CH_2), 2.73 (br s, 1H, OH), 3.62−3.75 (m, 2H, 2 × H-1), 3.84−3.90 (m, 1H, H-4), 4.13−4.15 (m, 1H, H-3), 4.23−4.28 (m, 1H, H-2), 4.79 (d, 1H, *J* = 9.7 Hz, NH); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.3 (CH_3), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 25.9 (CH_2), 28.5 (3 × CH_3), 29.5 (CH_2), 29.6 (CH_2), 29.7 (2 × CH_2), 29.8 (5 × CH_2), 32.1 (CH_2), 34.2 (CH_2), 35.7 (CH_2), 37.3 (CH_2), 48.6 (C-4), 61.8 (C-1), 77.5 (C-3), 77.6 (C-2), 79.8 (C_q), 108.6 (OCO), 156.2 (C=O). ESI-HRMS: *m/z* calcd for $C_{29}H_{55}NaNO_5$ $[M + Na]^+$ 520.3972, found 520.3978.

4.1.28. tert-Butyl [(2R,3S,4R)-2,3-(cyclohexylidenedioxy)-1-hydroxynonadecan-4-yl]carbamate ***24***

Using the same procedure as described for the construction of **19**, compound **50** (0.15 g, 0.20 mmol) was transformed to derivative **24** (white amorphous solid, 92 mg, 90 %, *n*-hexane/EtOAc, 5:1); $[\alpha]_D^{20}$ +15.0 (*c* 0.32, $CHCl_3$). IR (neat) *ν* 3457, 3401, 2920, 2852, 1692, 1522, 1366, 1171, 1058 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.9 Hz, CH_3), 1.25−1.66 (m, 47H, 3 × CH_3, 19 × CH_2), 2.64−2.67 (m, 1H, OH), 3.63−3.72 (m, 2H, 2 × H-1), 3.84−3.90 (m, 1H, H-4), 4.13−4.15 (m, 1H, H-3), 4.23−4.28 (m, 1H, H-2), 4.79 (d, 1H, *J* = 9.7 Hz, NH); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.3 (CH_3), 22.8 (CH_2), 23.8 (CH_2), 24.3 (CH_2), 25.3 (CH_2), 26.0 (CH_2), 28.6 (3 × CH_3), 29.5 (CH_2), 29.6 (CH_2), 29.7 (2 × CH_2), 29.8 (6 × CH_2), 32.1 (CH_2), 34.2 (CH_2), 35.8 (CH_2), 37.3 (CH_2), 48.6 (C-4), 61.8 (C-1), 77.6 (C-2, C-3), 79.9 (C_q), 108.6 (OCO), 156.2 (C=O). ESI-HRMS: *m/z* calcd for $C_{30}H_{58}NO_5$ $[M + H]^+$ 512.4310, found 512.4318.

*4.1.29. tert-Butyl (2S,3S,4R)-3,4-(cyclohexylidenedioxy)-2-tridecylpyrrolidine-1-carboxylate **51***

A solution of **19** (87 mg, 0.18 mmol) in dry CH_2Cl_2 (0.8 mL) was successively treated with TsCl (86 mg, 0.45 mmol), Et_3N (0.13 mL, 0.90 mmol) and $Me_3N.HCl$ (8.6 mg, 90 μmol) at room temperature. After being stirred for 15 min, the mixture was diluted with a saturated aq NH_4Cl solution (5 mL) and then extracted with CH_2Cl_2 (3 × 11 mL). The combined organic layers were dried over Na_2SO_4, and the solvent was evaporated. The obtained tosylate was submitted to the next reaction without further purification.

To a solution of the crude tosylate (0.114 g, 0.18 mmol) in dry DMF (0.6 mL) that had been pre-cooled to 0 °C was added NaH (41 mg, 1.08 mmol, ~60 % suspension in mineral oil). After being stirred for 30 min at the same temperature, the whole mixture was diluted with saturated aq NH_4Cl (6 mL) and extracted with CH_2Cl_2 (3 × 12 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated, and the residue was chromatographed on silica gel (*n*-hexane/EtOAc, 13:1). This procedure yielded 74 mg (88 %) of product **51** as a colourless oil; $[\alpha]_D^{21}$ +25.7 (*c* 0.26, $CHCl_3$). IR (neat) *ν* 2923, 2853, 1697, 1450, 1402, 1365, 1163, 1100 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.9 Hz, CH_3), 1.25–1.65 (m, 43H, 3 × CH_3, 17 × CH_2), 3.28 (dd, 1H, *J* = 13.1, 5.1 Hz, H-5), 3.77–3.91 (m, 1H, H-5), 3.98–4.10 (m, 1H, H-2), 4.38 (d, 1H, *J* = 5.8 Hz, H-3), 4.64–4.72 (m, 1H, H-4). ESI-HRMS: *m/z* calcd for $C_{28}H_{51}NaNO_4$ $[M + Na]^+$ 488.3710, found 488.3715.

Due to the presence of rotamers in the ^{13}C NMR spectra recorded at ambient temperature, as well as at 50 °C, the corresponding spectroscopic data are not reported.

*4.1.30. tert-Butyl (2S,3S,4R)-3,4-(cyclohexylidenedioxy)-2-tetradecylpyrrolidine-1-carboxylate **52***

Using the same procedure as described for the conversion of **19** to **51**, compound **20** (90 mg, 0.18 mmol) was modified into derivative **52** (colourless oil, 84 mg, 98 %, *n*-hexane/EtOAc, 13:1); $[\alpha]_D^{21}$ +22.5 (*c* 0.45, $CHCl_3$). IR (neat) *ν* 2923, 2852, 1697, 1401, 1365, 1163, 1100 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 50 °C) *δ* 0.88 (t, 3H, *J* = 6.9 Hz, CH_3), 1.26–1.48 (m, 37H, 3 × CH_3, 14 × CH_2), 1.50–1.62 (m, 8H, 4 × CH_2), 3.27 (dd, 1H, *J* = 13.0, 5.1 Hz, H-5), 3.74–3.93 (m, 1H, H-5), 3.94–4.12 (m, 1H, H-2), 4.37 (d, 1H, *J* = 5.8 Hz, H-3), 4.65–4.67 (m, 1H, H-4). ESI-HRMS: *m/z* calcd for $C_{29}H_{53}NaNO_4$ $[M + Na]^+$ 502.3867, found 502.3855.

Due to the presence of rotamers in the ^{13}C NMR spectra recorded at ambient temperature as well as at 50 °C, the corresponding spectroscopic data are not reported.

*4.1.31. tert-Butyl (2S,3S,4R)-3,4-(cyclohexylidenedioxy)-2-pentadecylpyrrolidine-1-carboxylate **53***

According to the same procedure employed for the preparation of **51**, compound **21** (46 mg, 90 μmol) was modified into derivative **53** (colourless oil, 40 mg, 91 %, *n*-hexane/EtOAc, 13:1); $[\alpha]_D^{20}$ +17.6 (*c* 0.28, $CHCl_3$). IR (neat) *ν* 2922, 2852, 1697, 1401, 1365, 1163 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.9 Hz, CH_3), 1.21–1.65 (m, 47H, 3 × CH_3, 19 × CH_2), 3.27 (dd, 1H, *J* = 13.0, 5.1 Hz, H-5), 3.74–3.94 (m, 1H, H-5), 3.95–4.13 (m, 1H, H-2), 4.37 (d, 1H, *J* = 5.8 Hz, H-3), 4.65–4.67 (m, 1H, H-4). ESI-HRMS: *m/z* calcd for $C_{30}H_{55}NaNO_4$ $[M + Na]^+$ 516.4023, found 516.4025.

Due to the presence of rotamers in the ^{13}C NMR spectra recorded at ambient temperature as well as at 50 °C, the corresponding spectroscopic data are not reported.

*4.1.32. tert-Butyl (2R,3S,4R)-3,4-(cyclohexylidenedioxy)-2-tridecylpyrrolidine-1-carboxylate **54***

Using the same procedure as described for the preparation of **51**, compound **22** (0.106 g, 0.22 mmol) was converted into derivative **54** (colourless oil, 94 mg, 92 %, *n*-hexane/EtOAc, 13:1); $[\alpha]_D^{21}$ − 31.5 (*c* 0.26, $CHCl_3$). IR (neat) *ν* 2923, 2853, 1697, 1391, 1365, 1162, 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.9 Hz, CH_3), 1.21–1.80 (m, 43H, 3 × CH_3, 17 × CH_2), 3.22–3.26 (m, 1H, H-5), 3.82–3.87 (m, 2H, H-2, H-5), 4.65–4.70 (m, 2H, H-3, H-4); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.1 (CH_3), 22.7 (CH_2), 23.7 (CH_2), 24.1 (CH_2), 25.1 (CH_2), 26.2 (CH_2), 28.4 (3 × CH_3), 29.3 (CH_2), 29.5 (CH_2), 29.6 (3 × CH_2), 29.7 (3 × CH_2), 29.8 (CH_2), 31.9 (CH_2), 34.6 (CH_2), 36.5 (CH_2), 50.3 (C-5), 59.6 (C-2), 77.2 (C-4), 79.5 (C_q), 79.6 (C-3), 113.5 (OCO), 154.4 (C=O). ESI-HRMS: *m/z* calcd for $C_{28}H_{51}NaNO_4$ $[M + Na]^+$ 488.3710, found 488.3712.

*4.1.33. tert-Butyl (2R,3S,4R)-3,4-(cyclohexylidenedioxy)-2-tetradecylpyrrolidine-1-carboxylate **55***

According to the same procedure employed for the conversion of **19** to **51**, compound **23** (60 mg, 0.12 mmol) was converted into product **55** (colourless oil, 55 mg, 97 %, *n*-hexane/EtOAc, 13:1); $[\alpha]_D^{21}$ − 26.9 (*c* 0.29, $CHCl_3$). IR (neat) *ν* 2922, 2852, 1697, 1391, 1365, 1162 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.87 (t, 3H, *J* = 6.9 Hz, CH_3), 1.20–1.49 (m, 35H, 3 × CH_3, 13 × CH_2), 1.50–1.77 (m, 10H, 5 × CH_2), 3.21–3.25 (m, 1H, H-5), 3.81–3.86 (m, 2H, H-2, H-5), 4.64–4.69 (m, 2H, H-3, H-4); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.3 (CH_3), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 26.4 (CH_2), 28.6 (3 × CH_3), 29.5 (CH_2), 29.7 (3 × CH_2), 29.8 (5 × CH_2), 29.9 (CH_2), 32.1 (CH_2), 34.8 (CH_2), 36.7 (CH_2), 50.5 (C-5), 59.7 (C-2), 77.5 (C-4), 79.7 (C-3), 79.8 (C_q), 113.5 (OCO), 154.5 (C=O). ESI-HRMS: *m/z* calcd for $C_{29}H_{53}NaNO_4$ $[M + Na]^+$ 502.3867, found 502.3855.

*4.1.34. tert-Butyl (2R,3S,4R)-3,4-(cyclohexylidenedioxy)-2-pentadecylpyrrolidine-1-carboxylate **56***

Using the same procedure as described for the preparation of **51**, compound **24** (81 mg, 0.16 mmol) was converted to derivative **56** (colourless oil, 71 mg, 90 %, *n*-hexane/EtOAc, 13:1); $[\alpha]_D^{21}$ −32.5 (*c* 0.43, $CHCl_3$). IR (neat) *ν* 2922, 2852, 1697, 1391, 1365, 1162, 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.8 Hz, CH_3), 1.21–1.47 (m, 37H, 3 × CH_3, 14 × CH_2), 1.52–1.78 (m, 10H, 5 × CH_2), 3.22–3.26 (m, 1H, H-5), 3.81–3.86 (m, 2H, H-2, H-5), 4.65–4.70 (m, 2H, H-3, H-4); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.3 (CH_3), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 26.4 (CH_2), 28.6 (3 × CH_3), 29.5 (CH_2), 29.7 (2 × CH_2), 29.8 (7 × CH_2), 29.9 (CH_2), 32.1 (CH_2), 34.8 (CH_2), 36.6 (CH_2), 50.5 (C-5), 59.7 (C-2), 77.5 (C-3 alebo C-4), 79.7 (C_q), 79.8 (C-3 alebo C-4), 113.5 (OCO), 154.5 (C=O). ESI-HRMS: *m/z* calcd for $C_{30}H_{55}NaNO_4$ $[M + Na]^+$ 516.4023, found 516.4031.

*4.1.35. (2S,3S,4R)-2-Tridecylpyrrolidine-3,4-diol hydrochloride **13***

A solution of compound **51** (51 mg, 0.11 mmol) in MeOH (0.5 mL) was treated with 6 M aq HCl (5.3 mL) at room temperature. The resulting mixture was stirred and heated at 70 °C for 5 h. After completion of the reaction, the mixture was concentrated, and the residue was suspended in dry Et_2O. Filtration of an ethereal suspension afforded 29 mg (83 %) of compound **13** as a white amorphous solid; $[\alpha]_D^{21}$ −27.6 (*c* 0.21, MeOH). IR (neat) *ν* 3396, 2953, 2918, 2848, 1462, 1110 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) *δ* 0.90 (t, 3H, *J* = 6.8 Hz, CH_3), 1.29–1.54 (m, 22H, 11 × CH_2), 1.62–1.71 (m, 1H, *H*–CH_2), 1.81–1.90 (m, 1H, *H*–CH_2), 3.22 (dd, 1H, *J* = 12.6, 1.8 Hz, H-5), 3.35–3.44 (m, 2H, H-2, H-5), 3.89 (dd, 1H, *J* = 8.6, 4.0 Hz, H-3), 4.21–4.23 (m, 1H, H-4); ^{13}C NMR (101 MHz, CD_3OD) *δ* 14.4 (CH_3), 23.7 (CH_2), 27.6 (CH_2), 30.4 (CH_2), 30.5 (2 × CH_2), 30.7 (CH_2), 30.8 (4 × CH_2), 31.6 (CH_2), 33.1 (CH_2), 50.6 (C-5), 62.3 (C-2), 70.9 (C-4), 76.9 (C-3). ESI-HRMS: *m/z* calcd for $C_{17}H_{36}NO_2$ $[M - Cl]^+$ 286.2741, found 286.2749.

*4.1.36. (2S,3S,4R)-2-Tetradecylpyrrolidine-3,4-diol hydrochloride **14***

Using the same procedure as described for the preparation of **13**, compound **52** (62 mg, 0.13 mmol) was converted into derivative **14**

(white amorphous solid, 41 mg, 93 %); $[\alpha]_D^{21}$ − 40.5 (*c* 0.23, MeOH). IR (neat) *ν* 3395, 3343, 2918, 2848, 1467, 1110 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) *δ* 0.90 (t, 3H, *J* = 6.9 Hz, CH_3), 1.29−1.54 (m, 24H, 12 × CH_2), 1.62−1.71 (m, 1H, *H*−CH_2), 1.81−1.90 (m, 1H, *H*−CH_2), 3.22 (dd, 1H, *J* = 12.6, 1.6 Hz, H-5), 3.37−3.44 (m, 2H, H-2, H-5), 3.89 (dd, 1H, *J* = 8.5, 4.0 Hz, H-3), 4.21−4.23 (m, 1H, H-4); ^{13}C NMR (101 MHz, CD_3OD) *δ*14.3 (CH_3), 23.7 (CH_2), 27.6 (CH_2), 30.4 (CH_2), 30.5 (2 × CH_2), 30.7 (2 × CH_2), 30.8 (4 × CH_2), 31.6 (CH_2), 33.1 (CH_2), 50.6 (C-5), 62.3 (C-2), 70.9 (C-4), 76.9 (C-3). ESI-HRMS: *m/z* calcd for $C_{18}H_{38}NO_2$ $[M - Cl]^+$ 300.2897, found 300.2900.

4.1.37. (2S,3S,4R)-2-Pentadecylpyrrolidine-3,4-diol hydrochloride **15**

According to the same procedure employed for the construction of **13**, compound **53** (35 mg, 70 μmol) was transformed to derivative **15** (white amorphous solid, 22 mg, 91 %); $[\alpha]_D^{21}$ −44.0 (*c* 0.20, MeOH). IR (neat) *ν* 3398, 3346, 2919, 2848, 1466, 1110 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) *δ* 0.90 (t, 3H, *J* = 6.8 Hz, CH_3), 1.29−1.53 (m, 26H, 13 × CH_2), 1.62−1.72 (m, 1H, *H*−CH_2), 1.81−1.90 (m, 1H, *H*−CH_2), 3.22 (dd, 1H, *J* = 12.6, 1.8 Hz, H-5), 3.37−3.44 (m, 2H, H-2, H-5), 3.89 (dd, 1H, *J* = 8.5, 4.0 Hz, H-3), 4.22 (td, 1H, *J* = 4.0, 1.8 Hz, H-4); ^{13}C NMR (101 MHz, CD_3OD) *δ* 14.4 (CH_3), 23.7 (CH_2), 27.6 (CH_2), 30.4 (CH_2), 30.5 (2 × CH_2), 30.7 (2 × CH_2), 30.8 (5 × CH_2), 31.5 (CH_2), 33.1 (CH_2), 50.6 (C-5), 62.3 (C-2), 70.9 (C-4), 76.9 (C-3). ESI-HRMS: *m/z* calcd for $C_{19}H_{40}NO_2$ $[M - Cl]^+$ 314.3054, found 314.3052.

4.1.38. (2R,3S,4R)-2-Tridecylpyrrolidine-3,4-diol hydrochloride **16**

Using the same procedure as described for the preparation of **13**, compound **54** (47 mg, 0.10 mmol) was modified into derivative **16** (white amorphous solid, 29 mg, 90 %); $[\alpha]_D^{21}$ −9.5 (*c* 0.32, MeOH). IR (neat) *ν* 3406, 2918, 2848, 1588, 1473, 1461, 1129 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) *δ* 0.90 (t, 3H, *J* = 6.8 Hz, CH_3), 1.29−1.47 (m, 22H, 11 × CH_2), 1.68−1.76 (m, 1H, *H*−CH_2), 1.84−1.93 (m, 1H, *H*−CH_2), 3.06 (dd, 1H, *J* = 11.6, 8.1 Hz, H-5), 3.40−3.48 (m, 2H, H-2, H-5), 4.06−4.08 (m, 1H, H-3), 4.40 (td, 1H, *J* = 8.1, 3.8 Hz, H-4); ^{13}C NMR (101 MHz, CD_3OD) *δ* 14.4 (CH_3), 23.7 (CH_2), 27.2 (CH_2), 27.8 (CH_2), 30.5 (3 × CH_2), 30.6 (CH_2), 30.8 (4 × CH_2), 33.1 (CH_2), 48.4 (C-5), 63.8 (C-2), 71.6 (C-3), 72.0 (C-4). ESI-HRMS: *m/z* calcd for $C_{17}H_{36}NO_2$ $[M - Cl]^+$ 286.2741, found 286.2750.

4.1.39. (2R,3S,4R)-2-Tetradecylpyrrolidine-3,4-diol hydrochloride **17**

According to the same procedure employed for the preparation of **13**, compound **55** (67 mg, 0.14 mmol) was converted into derivative **17** (white amorphous solid, 42 mg, 90 %); $[\alpha]_D^{21}$ − 27.6 (*c* 0.21, MeOH). IR (neat) *ν* 3382, 3194, 2917, 2849, 2720, 1467, 1132 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.90 (t, 3H, *J* = 6.8 Hz, CH_3), 1.29−1.47 (m, 24H, 12 × CH_2), 1.68−1.77 (m, 1H, *H*−CH_2), 1.84−1.93 (m, 1H, *H*−CH_2), 3.06 (dd, 1H, *J* = 11.6, 8.0 Hz, H-5), 3.39−3.48 (m, 2H, H-2, H-5), 4.06−4.08 (m, 1H, H-3), 4.40 (td, 1H, *J* = 8.0, 3.8 Hz, H-4); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.4 (CH_3), 23.7 (CH_2), 27.2 (CH_2), 27.8 (CH_2), 30.5 (3 × CH_2), 30.7 (CH_2), 30.8 (5 × CH_2), 33.1 (CH_2), 48.4 (C-5), 63.7 (C-2), 71.6 (C-3), 72.0 (C-4). ESI-HRMS: *m/z* calcd for $C_{18}H_{38}NO_2$ $[M - Cl]^+$ 300.2897, found 300.2900.

4.1.40. (2R,3S,4R)-2-Pentadecylpyrrolidine-3,4-diol hydrochloride **18**

Using the same procedure as described for the preparation of **13**, compound **56** (52 mg, 0.10 mmol) was transformed to derivative **18** (white amorphous solid, 35 mg, 83 %); $[\alpha]_D^{21}$ −2.9 (*c* 0.17, MeOH). IR (neat) *ν* 3406, 2918, 2848, 1588, 1473, 1461, 1129 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) *δ* 0.90 (t, 3H, *J* = 6.8 Hz, CH_3), 1.29−1.47 (m, 26H, 13 × CH_2), 1.68−1.77 (m, 1H, *H*−CH_2), 1.84−1.93 (m, 1H, *H*−CH_2), 3.07 (dd, 1H, *J* = 11.6, 8.0 Hz, H-5), 3.39−3.48 (m, 2H, H-2, H-5), 4.06−4.08 (m, 1H, H-3), 4.40 (td, 1H, *J* = 8.0, 3.8 Hz, H-4); ^{13}C NMR (101 MHz, CD_3OD) *δ*14.4 (CH_3), 23.7 (CH_2), 27.2 (CH_2), 27.8 (CH_2), 30.5 (3 × CH_2), 30.6 (CH_2), 30.8 (6 × CH_2), 33.1 (CH_2), 48.4 (C-5), 63.8 (C-2), 71.6 (C-3), 72.0 (C-4). ESI-HRMS: *m/z* calcd for $C_{19}H_{40}NaNO_2$ $[M - Cl + Na]^+$ 314.3054, found 314.3052.

4.1.41. 2,3-O-Cyclohexylidene-D-ribofuranose **29** [12]

To a suspension of D-ribose (1.00 g, 6.66 mmol) in cyclohexanone (6.89 mL, 66.60 mmol) was added *p*-TsOH (25 mg, 1.23 mmol). After being stirred for 8 h at room temperature, the whole mixture was poured into a saturated aq $NaHCO_3$ solution (15 mL) and extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, the filtrate was concentrated, and the residue was subjected to flash chromatography on silica gel (*n*-hexane/EtOAc, 3:1) to give 1.47 (96 %) of compound **29** (colourless oil), which was identical to reported data [12].

4.1.42. 2,3-O-Cyclohexylidene-L-erythrofuranose ent-**27**

Using the same procedure as described for the preparation of **27**, compound **29** (1.35 g, 5.87 mmol) was converted to lactols *ent*-**27** (white solid, 1.08 g, 92 %, *n*-hexane/EtOAc, 3:1, *α*:*β* = 2:98, determined by ^1H NMR spectroscopic analysis). IR (neat) *ν* 3319, 2934, 2853, 1365, 1166, 1096 cm^{-1}; ESI-HRMS: *m/z* calcd for $C_{10}H_{16}NaO_4$ $[M + Na]^+$ 223.0941, found 223.0943.

Selected NMR data for *ent*-*β*-**27**: ^1H NMR (400 MHz, CD_3OD) *δ* 1.36−1.44 (m, 2H, CH_2), 1.52−1.66 (m, 8H, 4 × CH_2), 3.90 (d, 1H, *J* = 10.3 Hz, H-4), 4.00 (dd, 1H, *J* = 10.3, 3.6 Hz, H-4), 4.49 (d, 1H, *J* = 5.8 Hz, H-2), 4.82 (dd, 1H, *J* = 5.8, 3.6 Hz, H-3), 5.25 (s, 1H, H-1); ^{13}C NMR (101 MHz, CD_3OD) *δ* 24.8 (CH_2), 25.0 (CH_2), 26.2 (CH_2), 35.2 (CH_2), 37.1 (CH_2), 72.6 (C-4), 80.9 (C-3), 86.4 (C-2), 102.9 (C-1), 113.8 (OCO).

4.1.43. Ethyl (4R,5S,2E)-6-hydroxy-4,5-(cyclohexylidenedioxy)hex-2-enoate ent-(E)-**30** and ethyl (4R,5S,2Z)-6-hydroxy-4,5-(cyclohexylidenedioxy)hex-2-enoate ent-(Z)-**30**

Using the same procedure as described for the construction of (*E*)-**30** and (*Z*)-**30**, compound *ent*-**27** (1.00 g, 4.99 mmol) was converted to the corresponding esters *ent*-(*E*)-**30** (0.364 g, 27 %, *n*-hexane/EtOAc, 4:1) and *ent*-(*Z*)-**30** (0.864 g, 64 %, *n*-hexane/EtOAc, 4:1).

Isomer *ent*-(*Z*)-**30**: colourless oil; $[\alpha]_D^{21}$ − 120.3 (*c* 0.14, $CHCl_3$). IR (neat) *ν* 3494, 2931, 2859, 1712, 1188, 1029 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.30 (t, 3H, *J* = 7.1 Hz, CH_3), 1.38−1.47 (m, 2H, CH_2), 1.54−1.75 (m, 8H, 4 × CH_2), 2.05−2.13 (m, 1H, OH), 3.43−3.49 (m, 1H, H-6), 3.58−3.64 (m, 1H, H-6), 4.18 (q, 2H, *J* = 7.1 Hz, CH_2), 4.57 (ddd, 1H, *J* = 7.4, 5.0, 3.9 Hz, H-5), 5.57−5.61 (m, 1H, H-4), 5.93 (dd, 1H, *J* = 11.6, 1.7 Hz, H-2), 6.40 (dd, 1H, *J* = 11.6, 7.0 Hz, H-3); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.3 (CH_3), 23.7 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 34.2 (CH_2), 37.4 (CH_2), 60.7 (CH_2), 61.7 (C-6), 74.5 (C-4), 78.5 (C-5), 109.7 (OCO), 121.1 (C-2), 147.6 (C-3), 166.1 (C=O). ESI-HRMS: *m/z* calcd for $C_{14}H_{22}NaO_5$ $[M + Na]^+$ 293.1359, found 293.1365.

Isomer *ent*-(*E*)-**30**: colourless oil; $[\alpha]_D^{21}$ − 31.6 (*c* 0.25, $CHCl_3$). IR (neat) *ν* 3450, 2934, 2859, 1718, 1266, 1032 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.30 (t, 3H, *J* = 7.1 Hz, CH_3), 1.36−1.48 (m, 2H, CH_2), 1.55−1.74 (m, 8H, 4 × CH_2), 1.92−1.99 (m, 1H, OH), 3.52−3.60 (m, 2H, H-6), 4.21 (q, 2H, *J* = 7.1 Hz, CH_2), 4.34−4.38 (m, 1H, H-5), 4.80 (ddd, 1H, *J* = 7.0, 5.5, 1.6 Hz, 1H, H-4), 6.14 (dd, 1H, *J* = 15.6, 1.6 Hz, H-2), 6.89 (dd, 1H, *J* = 15.6, 5.5 Hz, H-3); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.3 (CH_3), 23.8 (CH_2), 24.2 (CH_2), 25.2 (CH_2), 34.8 (CH_2), 37.7 (CH_2), 60.7 (CH_2), 62.1 (C-6), 75.7 (C-4), 77.9 (C-5), 110.3 (OCO), 123.2 (C-2), 142.4 (C-3), 166.0 (C=O). ESI-HRMS: *m/z* calcd for $C_{14}H_{22}NaO_5$ $[M + Na]^+$ 293.1359, found 293.1358.

4.1.44. Ethyl (4R,5S,2Z)-6-[(tert-butyldiphenylsilyl)oxy]-4,5-(cyclohexylidenedioxy)hex-2-enoate ent-**31**

Using the same procedure as described for the preparation of **31**,

compound *ent-(Z)*-**30** (1.00 g, 3.69 mmol) was modified to derivative *ent*-**31** (colourless oil, 1.80 g, 96 %, *n*-hexane/EtOAc, 20:1); $[\alpha]_D^{20}$ − 100.5 (*c* 0.57, $CHCl_3$). IR (neat) *ν* 2936, 2848, 1712, 1188, 1100 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.02 (s, 9H, 3 × CH_3), 1.27 (t, 3H, *J* = 7.1 Hz, CH_3), 1.37–1.44 (m, 2H, CH_2), 1.55–1.74 (m, 8H, 4 × CH_2), 3.52 (dd, 1H, *J* = 11.1, 4.3 Hz, H-6), 3.72 (dd, 1H, *J* = 11.1, 4.3 Hz, H-6), 4.14 (q, 2H, *J* = 7.1 Hz, CH_2), 4.51–4.55 (m, 1H, H-5), 5.69 (td, 1H, *J* = 7.4, 1.6 Hz, H-4), 5.83 (dd, 1H, *J* = 11.6, 1.6 Hz, H-2), 6.44 (dd, 1H, *J* = 11.6, 7.4 Hz, H-3), 7.34–7.44 (m, 6H, Ph), 7.66–7.72 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.4 (CH_3), 19.3 (C_q), 23.9 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 26.9 (3 × CH_3), 34.6 (CH_2), 37.3 (CH_2), 60.5 (CH_2), 63.1 (C-6), 74.1 (C-4), 78.8 (C-5), 109.7 (OCO), 120.7 (C-2), 127.7 (4 × CH_{Ph}), 129.7 (2 × CH_{Ph}), 133.5 (C_i), 133.6 (C_i), 135.8 (4 × CH_{Ph}), 147.5 (C-3), 165.9 (C=O). ESI-HRMS: *m/z* calcd for $C_{30}H_{40}NaO_5Si$ $[M + Na]^+$ 531.2537, found 531.2539.

4.1.45. (4R,5S,2Z)-6-[(tert-Butyldiphenylsilyl)oxy]-4,5-(cyclohexylidenedioxy)hex-2-en-1-ol ent-32

According to the same procedure employed for the construction of **32**, compound *ent*-**31** (1.75 g, 3.44 mmol) was transformed to derivative *ent*-**32** (colourless oil, 1.57 g, 98 %, *n*-hexane/EtOAc, 6:1); $[\alpha]_D^{21}$ − 14.5 (*c* 0.78, $CHCl_3$). IR (neat) *ν* 3389, 2928, 2856, 1424, 1110, 1030 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ*1.04 (s, 9H, 3 × CH_3), 1.33–1.42 (m, 2H, CH_2), 1.53–1.66 (m, 8H, 4 × CH_2), 2.00 (br s, 1H, OH), 3.63–3.72 (m, 2H, H-6), 4.08–4.16 (m, 1H, H-1), 4.21–4.28 (m, 2H, H-1, H-5), 5.00–5.04 (m, 1H, H-4), 5.62–5.68 (m, 1H, H-3), 5.78–5.85 (m, 1H, H-2), 7.36–7.45 (m, 6H, Ph), 7.66–7.69 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 19.3 (C_q), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 27.0 (3 × CH_3), 34.8 (CH_2), 37.8 (CH_2), 58.9 (C-1), 63.3 (C-6), 73.2 (C-4), 78.3 (C-5), 109.4 (OCO), 127.8 (4 × CH_{Ph}) 128.2 (C-3), 129.9 (2 × CH_{Ph}), 132.6 (C-2), 133.3 (C_i), 133.5 (C_i), 135.7 (2 × CH_{Ph}), 135.8 (2 × CH_{Ph}). ESI-HRMS: *m/z* calcd for $C_{28}H_{38}NaO_4Si$ $[M + Na]^+$ 489.2432, found 489.2444.

4.1.46. tert-Butyl{[(2S,3R,4Z)-2,3-(cyclohexylidenedioxy)-6-thiocyanatohex-4-en-1-yl]oxy}diphenylsilane ent-33

Using the same procedure as described for the preparation of **33**, compound *ent*-**32** (0.61 g, 1.31 mmol) was converted into derivative *ent*-**33** (colourless oil, 0.563 g, 85 %, *n*-hexane/EtOAc, 20:1); $[\alpha]_D^{20}$ − 9.6 (*c* 0.23, $CHCl_3$). IR (neat) *ν* 3071, 2931, 2862, 2157, 1427, 1110 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.05 (s, 9H, 3 × CH_3), 1.35–1.42 (m, 2H, CH_2), 1.54–1.64 (m, 8H, 4 × CH_2), 3.63–3.81 (m, 4H, 2 × H-1, 2 × H-6), 4.27–4.32 (m, 1H, H-2), 4.94 (t, 1H, *J* = 7.0 Hz, H-3), 5.69–5.76 (m, 1H, H-5), 5.89–5.94 (m, 1H, H-4), 7.34–7.45 (m, 6H, Ph), 7.66–7.68 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 19.3 (C_q), 23.9 (CH_2), 24.2 (CH_2), 25.2 (CH_2), 27.0 (3 × CH_3), 31.1 (C-6), 34.7 (CH_2), 37.7 (CH_2), 63.2 (C-1), 73.2 (C-3), 78.4 (C-2), 109.9 (OCO), 112.0 (SCN), 125.2 (C-5), 127.8 (4 × CH_{Ph}), 129.9 (2 × CH_{Ph}), 131.9 (C-4), 133.3 (C_i), 133.4 (C_i), 135.7 (2 × CH_{Ph}), 135.8 (2 × CH_{Ph}). ESI-HRMS: *m/z* calcd for $C_{29}H_{37}NaNO_3SSi$ $[M + Na]^+$ 530.2156, found 530.2168.

4.1.47. tert-Butyl{[(2S,3R,4R)-4-isothiocyanato-2,3-(cyclohexylidenedioxy)hex-5-en-1-yl]oxy}diphenylsilane ent-35 and tert-butyl{[(2S,3R,4S)-4-isothiocyanato-2,3-(cyclohexylidenedioxy)hex-5-en-1-yl]oxy}diphenylsilane ent-36

*4.1.47.1. [3,3]-Sigmatropic rearrangement of ent-**33** under thermal conditions (general procedure).* According to the same procedure employed for the preparation of **35** and **36**, compound *ent*-**33** (80 mg, 1.57 mmol) was converted under thermal conditions into the corresponding isothiocyanates *ent*-**35** and *ent*-**36** (*n*-hexane/EtOAc, 35:1 → 20:1, for the combined yields, temperatures and reaction times, see Table 1).

*4.1.47.2. Microwave assisted [3,3]-sigmatropic rearrangemet of ent-**33** (general procedure).* Using the same procedure as described for the construction of **35** and **36**, compound *ent*-**33** (80 mg, 1.57 mmol) was converted under microwave induced thermal conditions to derivatives *ent*-**35** and *ent*-**36** (*n*-hexane/EtOAc, 35:1 → 20:1, for the combined yields, temperatures and reaction times, see Table 1).

Diastereoisomer *ent*-**35**: colourless oil; $[\alpha]_D^{20}$ +8.8 (*c* 0.77, $CHCl_3$). IR (neat) *ν* 3070, 2929, 2851, 2051, 1424, 1110 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.07 (s, 9H, 3 × CH_3), 1.29–1.68 (m, 10H, 5 × CH_2), 3.90 (dd, 1H, *J* = 11.5, 4.4 Hz, H-1), 3.99 (dd, 1H, *J* = 11.5, 4.4 Hz, H-1), 4.08 (dd, 1H, *J* = 8.5, 6.0 Hz, H-3), 4.26–4.30 (m, 1H, H-2), 4.55–4.60 (m, 1H, H-4), 5.31 (d, 1H, *J* = 10.3 Hz, H-6), 5.39 (d, 1H, *J* = 17.0 Hz, H-6), 5.94–6.02 (m, 1H, H-5), 7.37–7.46 (m, 6H, Ph), 7.72–7.76 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 19.4 (C_q), 23.9 (CH_2), 24.1 (CH_2), 25.2 (CH_2), 27.0 (3 × CH_3), 34.7 (CH_2), 37.3 (CH_2), 58.8 (C-4), 62.4 (C-1), 77.4 (C-2), 78.5 (C-3), 109.9 (OCO), 117.7 (C-6), 127.9 (4 × CH_{Ph}), 129.9 (2 × CH_{Ph}), 133.2 (2 × C_i), 133.4 (C-5), 134.7 (NCS), 135.8 (4 × CH_{Ph}). ESI-HRMS: *m/z* calcd for $C_{29}H_{37}NaNO_3SSi$ $[M + Na]^+$ 530.2156, found 530.2155.

Diastereoisomer *ent*-**36**: colourless oil; $[\alpha]_D^{21}$ +11.2 (*c* 0.26, $CHCl_3$). IR (neat) *ν* 3069, 2928, 2856, 2045, 1424, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.07 (s, 9H, 3 × CH_3), 1.34–1.40 (m, 2H, CH_2), 1.49–1.73 (m, 8H, 4 × CH_2), 3.87–3.97 (m, 2H, 2 × H-1), 4.13–4.15 (m, 1H, H-3), 4.28–4.33 (m, 1H, H-2), 4.49–4.51 (m, 1H, H-4), 5.28 (d, 1H, *J* = 10.2 Hz, H-6), 5.36 (d, 1H, *J* = 16.9 Hz, H-6), 5.90–5.98 (m, 1H, H-5), 7.37–7.48 (m, 6H, Ph), 7.64–7.68 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 19.3 (C_q), 23.9 (CH_2), 24.1 (CH_2), 25.2 (CH_2), 27.0 (3 × CH_3), 34.4 (CH_2), 36.9 (CH_2), 59.2 (C-4), 62.4 (C-1), 76.3 (C-2), 78.4 (C-3), 110.2 (C_q), 118.1 (C-6), 128.0 (4 × CH_{Ph}), 130.1 (2 × CH_{Ph}), 132.9 (2 × C_i), 133.5 (C-5), 135.0 (NCS), 135.7 (4 × CH_{Ph}). ESI-HRMS: *m/z* calcd for $C_{29}H_{37}NaNO_3SSi$ $[M + Na]^+$ 530.2156, found 530.2161.

4.1.48. N-[(3R,4R,5S)-6-[(tert-Butyldiphenylsilyl)oxy]-4,5-(cyclohexylidenedioxy)hex-1-en-3-yl]-2,2,2-trichloroacetamide ent-37 and N-[(3S,4R,5S)-6-[(tert-butyldiphenylsilyl)oxy]-4,5-(cyclohexylidenedioxy)hex-1-en-3-yl]-2,2,2-trichloroacetamide ent-38

Using the same procedure as described for the preparation of **37** and **38**, compound *ent*-**33** (70 mg, 0.15 mmol) was converted to imidate *ent*-**34** (92 mg, 0.15 mmol) whose Overman rearrangement provided the corresponding amides *ent*-**37** and *ent*-**38** (*n*-hexane/EtOAc, 25:1, for the combined yields, temperatures and reaction times, see Table 2).

To obtain a greater amount (more than 1 g) of the corresponding amides *ent*-**37** and *ent*-**38**, we utilized the experiment carried out at 210 °C (Table 2, entry 7).

Diastereoisomer *ent*-**37**: white crystals; mp 77–79 °C; $[\alpha]_D^{20}$ +40.7 (*c* 0.29, $CHCl_3$). IR (neat) *ν* 2928, 2853, 1701, 1532, 1105 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.09 (s, 9H, 3 × CH_3), 1.30–1.45 (m, 2H, CH_2), 1.50–1.65 (m, 8H, 4 × CH_2), 3.84 (dd, 1H, *J* = 11.1, 5.8 Hz, H-6), 3.92 (dd, 1H, *J* = 11.1, 6.3 Hz, H-6), 4.25–4.34 (m, 2H, H-4, H-5), 4.72–4.76 (m, 1H, H-3), 5.18–5.25 (m, 2H, 2 × H-1), 5.94 (ddd, 1H, *J* = 17.0, 10.5, 6.2 Hz, H-2), 7.09 (d, 1H, *J* = 8.7 Hz, NH), 7.37–7.45 (m, 6H, Ph), 7.66–7.72 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 19.3 (C_q), 23.8 (CH_2), 24.1 (CH_2), 25.2 (CH_2), 27.1 (3 × CH_3), 34.4 (CH_2), 36.8 (CH_2), 54.0 (C-3), 62.2 (C-6), 76.9 (C-5), 77.5 (C-4), 92.8 (C_q), 109.6 (OCO), 118.7 (C-1), 127.9 (4 × CH_{Ph}), 130.0 (2 × CH_{Ph}), 133.1 (C_i), 133.2 (C_i), 133.5 (C-2), 135.8 (4 × CH_{Ph}), 161.1 (C=O). ESI-HRMS: *m/z* calcd for $C_{30}H_{39}Cl_3NO_4Si$ $[M + H]^+$ 610.1708, found 610.1707.

Diastereoisomer *ent*-**38**: colourless oil; $[\alpha]_D^{21}$ +22.2 (*c* 0.21, $CHCl_3$). IR (neat) *ν* 3406, 2925, 2850, 1720, 1499, 1427, 1100 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.07 (s, 9H, 3 × CH_3), 1.30–1.71 (m, 10H,

5 × CH_2), 3.77–3.86 (m, 2H, 2 × H-6), 4.33–4.42 (m, 2H, H-4, H-5), 4.70–4.74 (m, 1H, H-3), 5.23–5.31 (m, 2H, 2 × H-1), 5.86 (ddd, 1H, J = 17.1, 10.3, 6.1 Hz, H-2), 7.14 (d, 1H, J = 7.9 Hz, NH), 7.35–7.45 (m, 6H, Ph), 7.66–7.68 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 19.3 (C_q), 23.7 (CH_2), 24.1 (CH_2), 25.2 (CH_2), 27.0 (3 × CH_3), 33.5 (CH_2), 36.8 (CH_2), 52.6 (C-3), 62.7 (C-6), 77.1 (C-5), 77.4 (C-4), 92.8 (C_q), 109.5 (OCO), 117.3 (C-1), 127.9 (4 × CH_{Ph}), 129.9 (2 × CH_{Ph}), 133.0 (C_i), 133.3 (C_i), 134.9 (C-2), 135.8 (4 × CH_{Ph}), 160.7 (C=O). ESI-HRMS: m/z calcd for $C_{30}H_{38}Cl_3NaNO_4Si$ [M + Na]$^+$ 632.1528, found 632.1531.

4.1.49. tert-Butyl [(3R,4R,5S)-6-[(tert-butyldiphenylsilyl)oxy]-4,5-(cyclohexylidenedioxy)hex-1-en-3-yl]carbamate ent-25

4.1.49.1. Synthesis of ent-25 from isothiocyanate ent-35. According to the same procedure employed for the transformation of **35** to **25**, compound *ent*-**35** (50 mg, 98 μmol) was converted into derivative *ent*-**25** (colourless oil, 26 mg, 47 %, *n*-hexane/EtOAc, 15:1).

4.1.49.2. Synthesis of ent-25 from trichloroacetamide ent-37. Using the same procedure as described for the modification of **37** to **25**, compound *ent*-**37** (0.16 g, 0.26 mmol) was converted into derivative *ent*-**25** (0.12 g, 81 %, *n*-hexane/EtOAc, 15:1); $[\alpha]_D^{21}$ +21.4 (*c* 0.90, $CHCl_3$). IR (neat) ν 2928, 2850, 1701, 1363, 1110 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (s, 9H, 3 × CH_3), 1.24–1.42 (m, 11H, 3 × CH_3, CH_2), 1.50–1.60 (m, 8H, 4 × CH_2), 3.82 (dd, 1H, J = 11.2, 5.8 Hz, H-6), 3.93 (dd, 1H, J = 11.2, 5.5 Hz, H-6), 4.12 (t, 1H, J = 6.0 Hz, H-4), 4.22–4.36 (m, 2H, H-3, H-5), 5.11–5.21 (m, 3H, 2 × H-1, NH), 5.86–5.95 (m, 1H, H-2), 7.35–7.45 (m, 6H, Ph), 7.70–7.72 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 19.4 (C_q), 23.9 (CH_2), 24.1 (CH_2), 25.3 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 34.6 (CH_2), 37.0 (CH_2), 53.1 (C-3), 62.3 (C-6), 77.4 (C-5), 78.2 (C-4), 79.5 (C_q), 109.2 (OCO), 116.4 (C-1), 127.8 (4 × CH_{Ph}), 129.8 (CH_{Ph}) 129.9 (CH_{Ph}), 133.3 (C_i), 133.4 (C_i) 135.8 (4 × CH_{Ph}), 136.0 (C-2), 155.3 (C=O). ESI-HRMS: m/z calcd for $C_{33}H_{48}NO_5Si$ [M + H]$^+$ 566.3296, found 566.3292.

4.1.50. tert-Butyl [(3S,4R,5S)-6-[(tert-butyldiphenylsilyl)oxy]-4,5-(cyclohexylidenedioxy)hex-1-en-3-yl]carbamate ent-26

4.1.50.1. Synthesis of ent-26 from isothiocyanate ent-36. Using the same procedure as described for the modification of **36** to **26**, compound *ent*-**36** (48 mg, 94 μmol) was converted into derivative *ent*-**26** (colourless oil, 28 mg, 52 %, *n*-hexane/EtOAc, 15:1).

4.1.50.2. Synthesis of ent-26 from trichloroacetamide ent-38. According to the same procedure employed for the transformation of **38** to **26**, compound *ent*-**38** (0.50 g, 0.82 mmol) was converted to derivative *ent*-**26** (0.348 g, 75 %, *n*-hexane/EtOAc, 15:1); $[\alpha]_D^{21}$ − 1.5 (*c* 1.12, $CHCl_3$). IR (neat) ν 2932, 2857, 1716, 1487, 1163, 1105 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (s, 9H, 3 × CH_3), 1.32–1.37 (m, 11H, 3 × CH_3, CH_2), 1.49–1.65 (m, 8H, 4 × CH_2), 3.80 (dd, 1H, J = 10.3, 5.7 Hz, H-6), 3.93 (dd, 1H, J = 10.3, 7.0 Hz, H-6), 4.19–4.26 (m, 1H, H-4), 4.28–4.33 (m, 1H, H-5), 4.37–4.49 (m, 1H, H-3), 5.13–5.23 (m, 3H, NH, 2 × H-1), 5.86–5.96 (m, 1H, H-2), 7.36–7.44 (m, 6H, Ph), 7.68–7.70 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 19.3 (C_q), 23.7 (CH_2), 24.1 (CH_2), 25.3 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 33.8 (CH_2), 36.9 (CH_2), 52.1 (C-3), 62.9 (C-6), 77.5 (C-5), 77.8 (C-4), 79.5 (C_q), 108.9 (OCO), 115.4 (C-1), 127.8 (4 × CH_{Ph}), 129.8 (CH_{Ph}), 129.9 (CH_{Ph}), 133.4 (2 × C_i), 135.7 (2 × CH_{Ph}), 135.8 (2 × CH_{Ph}), 136.9 (C-2), 155.2 (C=O). ESI-HRMS: m/z calcd for $C_{33}H_{48}NO_5Si$ [M + H]$^+$ 566.3296, found 566.3292.

4.1.51. tert-Butyl [(2S,3R,4R,5E)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)heptadec-5-en-4-yl]carbamate ent-39

Using the same procedure as described for the preparation of **39**, compound *ent*-**25** (0.185 g, 0.32 mmol) was converted into derivative *ent*-**39** (colourless, oil, 0.139 g, 82 %, *n*-hexane/EtOAc, 20:1). IR (neat) ν 3348, 2925, 2853, 1715, 1364, 1110 cm^{-1}; 1H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 6.8 Hz, CH_3), 1.08 (s, 9H, 3 × CH_3), 1.22–1.44 (m, 29H, 3 × CH_3, 10 × CH_2), 1.49–1.65 (m, 8H, 4 × CH_2), 1.89–1.94 (m, 2H, CH_2), 3.80 (dd, 1H, J = 11.1, 6.1 Hz, H-1), 3.92 (dd, 1H, J = 11.1, 5.4 Hz, H-1), 4.11–4.14 (m, 1H, H-3), 4.19–4.28 (m, 2H, H-2, H-4), 5.13 (br s, 1H, NH), 5.46 (dd, 1H, J = 15.6, 6.3 Hz, H-5), 5.53–5.60 (m, 1H, H-6), 7.34–7.45 (m, 6H, Ph), 7.69–7.72 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.1 (CH_2), 29.3 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.8 (3 × CH_2), 32.1 (CH_2), 32.5 (CH_2), 34.5 (CH_2), 37.0 (CH_2), 52.7 (C-4), 62.5 (C-1), 77.4 (C-2), 78.5 (C-3), 79.3 (C_q), 109.0 (OCO), 127.3 (C-5), 127.8 (4 × CH_{Ph}), 129.8 (2 × CH_{Ph}), 133.3 (C-6), 133.4 (2 × C_i), 135.8 (4 × CH_{Ph}), 155.3 (C=O). ESI-HRMS: m/z calcd for $C_{44}H_{70}NO_5Si$ [M + H]$^+$ 720.5018, found 720.5018.

Due to the presence of a small amount of (*Z*)-isomer (very similar R_f values for both isomers), we were unable to obtain *ent*-(*E*)-**39** in pure form. Therefore, the optical rotation of *ent*-**39** is not reported.

4.1.52. tert-Butyl [(2S,3R,4R,5E)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)octadec-5-en-4-yl]carbamate ent-40

According to the same procedure applied for the construction of **39**, compound *ent*-**25** (0.182 g, 0.32 mmol) was converted into derivative *ent*-**40** (colourless oil, 0.207 g, 88 %, *n*-hexane/EtOAc, 20:1). IR (neat) ν 2931, 2850, 1715, 1490, 1171 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 6.9 Hz, CH_3), 1.07 (s, 9H, 3 × CH_3), 1.22–1.40 (m, 31H, 10 × CH_2), 1.51–1.66 (m, 8H, 4 × CH_2), 1.88–1.93 (m, 2H, CH_2), 3.79 (dd, 1H, J = 11.1, 6.1 Hz, H-1), 3.91 (dd, 1H, J = 11.1, 5.4 Hz, H-1), 4.11–4.14 (m, 1H, H-3), 4.19–4.28 (m, 2H, H-2, H-4), 5.14 (br s, 1H, NH), 5.45 (dd, 1H, J = 15.6, 6.4 Hz, H-5), 5.52–5.60 (m, 1H, H-6), 7.35–7.45 (m, 6H, Ph), 7.69–7.72 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.1 (CH_2), 29.3 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.8 (4 × CH_2), 32.1 (CH_2), 32.5 (CH_2), 34.6 (CH_2), 37.0 (CH_2), 52.8 (C-4), 62.5 (C-1), 77.4 (C-2), 78.5 (C-3), 79.3 (C_q), 109.0 (OCO), 127.3 (C-5), 127.8 (4 × CH_{Ph}), 129.8 (2 × CH_{Ph}), 133.4 (2 × C_i), 133.5 (C-6), 135.8 (2 × CH_{Ph}), 135.9 (2 × CH_{Ph}), 155.3 (C=O). ESI-HRMS: m/z calcd for $C_{45}H_{72}NO_5Si$ [M + H]$^+$ 734.5174, found 734.5176.

Due to the presence of a small amount of (*Z*)-isomer (very similar R_f values for both isomers), we were unable to obtain *ent*-(*E*)-**40** in pure form. Therefore, the optical rotation of *ent*-**40** is not reported.

4.1.53. tert-Butyl [(2S,3R,4R,5E)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)nonadec-5-en-4-yl]carbamate ent-41

According to the same procedure described for the preparation of **39**, compound *ent*-**25** (0.136 g, 0.24 mmol) was converted into derivative *ent*-**41** (colourless oil, 0.17 g, 94 %, *n*-hexane/EtOAc, 20:1). IR (neat) ν 2924, 2853, 1715, 1489, 1364, 1110 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 6.8 Hz, CH_3), 1.07 (s, 9H, 3 × CH_3), 1.22–1.45 (m, 33H, 3 × CH_3, 12 × CH_2), 1.49–1.65 (m, 8H, 4 × CH_2), 1.89–1.93 (m, 2H, CH_2), 3.80 (dd, 1H, J = 11.1, 6.0 Hz, H-1), 3.92 (dd, 1H, J = 11.1, 5.4 Hz, H-1), 4.11–4.14 (m, 1H, H-3), 4.23–4.28 (m, 2H, H-2, H-4), 5.13 (br s, 1H, NH), 5.45 (dd, 1H, J = 15.5, 6.3 Hz, H-5), 5.52–5.59 (m, 1H, H-6), 7.34–7.44 (m, 6H, Ph), 7.69–7.72 (m, 4H, 4 Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.1 (CH_2), 29.3 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.8 (5 × CH_2), 32.1 (CH_2), 32.5 (CH_2), 34.6 (CH_2), 37.0 (CH_2), 52.7 (C-4), 62.5 (C-1), 77.4 (C-2), 78.5 (C-3), 79.3 (C_q), 109.0 (OCO), 127.3 (C-5), 127.8 (4 × CH_{Ph}), 129.8 (2 × CH_{Ph}), 133.4 (C_i, C-6), 133.5 (C_i), 135.8 (4 × CH_{Ph}), 155.3 (C=O). ESI-HRMS: m/z calcd for $C_{46}H_{74}NO_5Si$ [M +

H]$^+$ 748.5331, found 748.5336.

Due to the presence of a small amount of (*Z*)-isomer (very similar R_f values for both isomers), we were unable to obtain *ent*-(*E*)-**41** in pure form. Therefore, the optical rotation of *ent*-**41** is not reported.

4.1.54. tert-Butyl [(2S,3R,4S,5E)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)heptadec-5-en-4-yl]carbamate ent-42

Using the same procedure as described for the construction of **39**, compound *ent*-**26** (84 mg, 0.15 mmol) was converted into derivative *ent*-**42** (colourless oil, 0.10 g, 93 %, *n*-hexane/EtOAc, 20:1). IR (neat) ν 3454, 2925, 2853, 1716, 1486, 1164, 1105 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 6.8 Hz, CH_3), 1.07 (s, 9H, 3 × CH_3), 1.24–1.41 (m, 29H, 3 × CH_3, 10 × CH_2), 1.49–1.65 (m, 8H, 4 × CH_2), 1.96–2.01 (m, 2H, CH_2), 3.78 (dd, 1H, J = 10.7, 6.0 Hz, H-1), 3.92 (dd, 1H, J = 10.7, 6.4 Hz, H-1), 4.14–4.16 (m, 1H, H-3), 4.25–4.38 (m, 2H, H-2, H-4), 5.01 (br s, 1H, NH), 5.46 (dd, 1H, J = 15.4, 6.4 Hz, H-5), 5.56–5.63 (m, 1H, H-6), 7.35–7.44 (m, 6H, Ph), 7.68–7.70 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.3 (2 × CH_2), 29.5 (CH_2), 29.7 (CH_2), 29.8 (3 × CH_2), 32.1 (CH_2), 32.4 (CH_2), 34.0 (CH_2), 37.0 (CH_2), 51.7 (C-4), 63.1 (C-1), 77.7 (C-2), 78.3 (C-3), 79.3 (C_q), 108.8 (OCO), 127.8 (4 × CH_{Ph}), 128.5 (C-5), 129.8 (2 × CH_{Ph}), 132.4 (C-6), 133.5 (2 × C_i), 135.8 (4 × CH_{Ph}), 155.2 (C=O). ESI-HRMS: *m/z* calcd for $C_{44}H_{70}NaNO_5Si$ [M + H]$^+$ 720.5018, found 720.5018.

Due to the presence of a small amount of (*Z*)-isomer (very similar R_f values for both isomers), we were unable to obtain *ent*-(*E*)-**42** in pure form. Therefore, the optical rotation of *ent*-**42** is not reported.

4.1.55. tert-Butyl [(2S,3R,4S,5E)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)octadec-5-en-4-yl]carbamate ent-43

According to the same procedure described for the construction of **39**, compound *ent*-**26** (0.20 g, 0.35 mmol) was converted into derivative *ent*-**43** (colourless oil, 0.235 g, 91 %, *n*-hexane/EtOAc, 20:1). IR (neat) ν 2924, 2853, 1716, 1490, 1164 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 6.8 Hz, CH_3), 1.07 (s, 9H, 3 × CH_3), 1.24–1.42 (m, 31H, 3 × CH_3, 11 × CH_2), 1.52–1.61 (m, 8H, 4 × CH_2), 1.96–2.01 (m, 2H, CH_2), 3.78 (dd, 1H, J = 10.7, 6.0 Hz, H-1), 3.92 (dd, 1H, J = 10.7, 6.3 Hz, H-1), 4.13–4.16 (m, 1H, H-3), 4.25–4.37 (m, 2H, H-2, H-4), 5.01 (br s 1H, NH), 5.45 (dd, 1H, J = 15.4, 6.4 Hz, H-5), 5.56–5.63 (m, 1H, H-6), 7.35–7.44 (m, 6H, Ph), 7.68–7.70 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.3 (2 × CH_2), 29.5 (CH_2), 29.7 (CH_2), 29.8 (4 × CH_2), 32.1 (CH_2), 32.4 (CH_2), 34.0 (CH_2), 37.0 (CH_2), 51.8 (C-4), 63.0 (C-1), 77.7 (C-2), 78.3 (C-3), 79.3 (C_q), 108.8 (OCO), 127.8 (4 × CH_{Ph}), 128.5 (C-5), 129.8 (2 × CH_{Ph}), 132.4 (C-6), 133.5 (2 × C_i), 135.8 (4 × CH_{Ph}), 155.2 (C=O). ESI-HRMS: *m/z* calcd for $C_{45}H_{71}NaNO_5Si$ [M + Na]$^+$ 756.4994, found 756.5000.

Due to the presence of a small amount of (*Z*)-isomer (very similar R_f values for both isomers), we were unable to obtain *ent*-(*E*)-**43** in pure form. Therefore, the optical rotation of *ent*-**43** is not reported.

4.1.56. tert-Butyl [(2S,3R,4S,5E)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)nonadec-5-en-4-yl]carbamate ent-44

Using the same procedure as described for the construction of **39**, compound *ent*-**26** (86 mg, 0.15 mmol) was converted into derivative *ent*-**44** (colourless oil, 0.103 g, 90 %, *n*-hexane/EtOAc, 20:1). IR (neat) ν 3454, 2924, 2853, 1717, 1486, 1364, 1105 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 6.9 Hz, CH_3), 1.07 (s, 9H, 3 × CH_3), 1.24–1.41 (m, 33H, 3 × CH_3, 12 × CH_2), 1.52–1.61 (m, 8H, 4 × CH_2), 1.96–2.01 (m, 2H, CH_2), 3.78 (dd, 1H, J = 10.7, 6.0 Hz, H-1), 3.92 (dd, 1H, J = 10.7, 6.4 Hz, H-1), 4.14–4.16 (m, 1H, H-3), 4.25–4.37 (m, 2H, H-2, H-4), 5.02 (br s, 1H, NH), 5.46 (dd, 1H, J = 15.4, 6.4 Hz, H-5), 5.56–5.63 (m, 1H, H-6), 7.35–7.44 (m, 6H, Ph), 7.68–7.70 (m, 4H, 4 Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.3 (2 × CH_2), 29.5 (CH_2), 29.7 (CH_2), 29.8 (5 × CH_2), 32.1 (CH_2), 32.4 (CH_2), 34.0 (CH_2), 37.0 (CH_2), 51.8 (C-4), 63.1 (C-1), 77.7 (C-2), 78.3 (C-3), 79.3 (C_q), 108.8 (OCO), 127.8 (4 × CH_{Ph}), 128.5 (C-5), 129.8 (2 × CH_{Ph}), 132.4 (C-6), 133.5 (2 × C_i), 135.8 (4 × CH_{Ph}), 155.2 (C=O). ESI-HRMS: *m/z* calcd for $C_{46}H_{74}NO_5Si$ [M + H]$^+$ 748.5331, found 748.5330.

Due to the presence of a small amount of (*Z*)-isomer (very similar R_f values for both isomers), we were unable to obtain *ent*-(*E*)-**44** in pure form. Therefore, the optical rotation of *ent*-**44** is not reported.

4.1.57. tert-Butyl [(2S,3R,4R)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)heptadecan-4-yl]carbamate ent-45

Using the same procedure as described for the modification of **39** to **45**, compound *ent*-**39** (0.181 g, 0.25 mmol) was converted into derivative *ent*-**45** (colourless oil, 0.15 g, 83 %, *n*-hexane/EtOAc, 25:1); $[\alpha]_D^{20}$ +3.7 (*c* 0.19, $CHCl_3$). IR (neat) ν 2924, 2853, 1701, 1505, 1365, 1165, 1111 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 6.8 Hz, CH_3), 1.07 (s, 9H, 3 × CH_3), 1.23–1.63 (m, 43H, 3 × CH_3,17 × CH_2), 3.64–3.73 (m, 2H, H-1, H-4), 3.91 (dd, 1H, J = 11.0, 5.6 Hz, H-1), 4.02–4.12 (m, 1H, H-3), 4.20–4.24 (m, 1H, H-2), 4.89 (d, 1H, J = 8.5 Hz, NH), 7.35–7.45 (m, 6H, Ph), 7.69–7.73 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 25.8 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (2 × CH_2), 29.8 (5 × CH_2), 32.1 (CH_2), 32.2 (CH_2), 34.8 (CH_2), 37.4 (CH_2), 50.7 (C-4), 62.8 (C-1), 77.5 (C-2), 78.5 (C-3), 79.0 (C_q), 108.8 (OCO), 127.8 (4 × CH_{Ph}), 129.8 (2 × CH_{Ph}), 133.3 (C_i), 133.5 (C_i), 135.8 (2 × CH_{Ph}), 135.9 (2 × CH_{Ph}), 155.7 (C=O). ESI-HRMS: *m/z* calcd for $C_{44}H_{71}NaNO_5Si$ [M + Na]$^+$ 744.4994, found 744.5002.

4.1.58. tert-Butyl [(2S,3R,4R)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)octadecan-4-yl]carbamate ent-46

According to the same procedure applied for the construction of **45**, compound *ent*-**40** (0.183 g, 0.25 mmol) was modified to derivative *ent*-**46** (colourless oil, 0.153 g, 83 %, *n*-hexane/EtOAc, 25:1); $[\alpha]_D^{21}$ +2.1 (*c* 0.66, $CHCl_3$). IR (neat) ν 2923, 2853, 1702, 1502, 1165, 1111 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 6.6 Hz, CH_3), 1.07 (s, 9H, 3 × CH_3), 1.24–1.63 (m, 45H, 3 × CH_3, 18 × CH_2), 3.59–3.73 (m, 2H, H-1, H-4), 3.91 (dd, 1H, J = 11.0, 5.6 Hz, H-1), 4.00–4.15 (m, 1H, H-3), 4.20–4.24 (m, 1H, H-2), 4.90 (br d, 1H, J = 8.4 Hz, NH), 7.35–7.44 (m, 6H, Ph), 7.70–7.72 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 25.8 (CH_2), 27.1 (3 × CH_3), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (2 × CH_2), 29.8 (5 × CH_2), 29.9 (CH_2), 32.1 (CH_2), 32.2 (CH_2), 34.8 (CH_2), 37.5 (CH_2), 50.8 (C-4), 62.8 (C-1), 77.5 (C-2), 78.5 (C-3), 79.1 (C_q), 108.8 (OCO), 127.8 (4 × CH_{Ph}), 129.8 (2 × CH_{Ph}), 133.3 (C_i), 133.5 (C_i), 135.8 (2 × CH_{Ph}), 135.9 (2 × CH_{Ph}), 155.7 (C=O). ESI-HRMS: *m/z* calcd for $C_{45}H_{73}NNaO_5Si$ [M + Na]$^+$ 758.5150, found 758.5161.

4.1.59. tert-Butyl [(2S,3R,4R)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)nonadecan-4-yl]carbamate ent-47

Using the same procedure as described for the preparation of **45**, compound *ent*-**41** (0.15 g, 0.20 mmol) was transformed to derivative *ent*-**47** (colourless oil, 0.143 g, 95 %, *n*-hexane/EtOAc, 25:1); $[\alpha]_D^{20}$ +5.7 (*c* 0.26, $CHCl_3$). IR (neat) ν 2923, 2853, 1703, 1504, 1427, 1364 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 6.9 Hz, CH_3), 1.07 (s, 9H, 3 × CH_3), 1.23–1.66 (m, 47H, 3 × CH_3, 19 × CH_2), 3.60–3.72 (m, 2H, H-1, H-4), 3.91 (dd, 1H, J = 11.0, 5.7 Hz, H-1),

4.01–4.13 (m, 1H, H-3), 4.20–4.24 (m, 1H, H-2), 4.94 (d, 1H, J = 8.9 Hz, NH), 7.35–7.45 (m, 6H, Ph), 7.70–7.73 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 25.8 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (2 × CH_2), 29.8 (4 × CH_2), 29.9 (3 × CH_2), 32.1 (CH_2), 32.2 (CH_2), 34.8 (CH_2), 37.4 (CH_2), 50.7 (C-4), 62.8 (C-1), 77.5 (C-2), 78.5 (C-3), 79.0 (C_q), 108.8 (OCO), 127.8 (4 × CH_{Ph}), 129.8 (2 × CH_{Ph}), 133.3 (C_i), 133.5 (C_i), 135.8 (2 × CH_{Ph}), 135.9 (2 × CH_{Ph}), 155.7 (C=O). ESI-HRMS: m/z calcd for $C_{46}H_{75}NaNO_5Si$ $[M + Na]^+$ 772.5307, found 772.5314.

4.1.60. tert-Butyl [(2S,3R,4S)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)heptadecan-4-yl]carbamate ent-48

According to the same procedure employed for the construction of **45**, compound *ent*-**42** (89 mg, 0.12 mmol) was converted into derivative *ent*-**48** (colourless oil, 78 mg, 88 %, *n*-hexane/EtOAc, 25:1); $[\alpha]_D^{20}$ +4.0 (*c* 0.29, $CHCl_3$). IR (neat) ν 3453, 2924, 2853, 1716, 1491, 1364, 1105 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ 0.88 (t, 3H, J = 6.9 Hz, CH_3), 1.06 (s, 9H, 3 × CH_3), 1.25–1.61 (m, 43H, 17 × CH_2, 3 × CH_3), 3.66–3.80 (m, 1H, H-4), 3.82–3.91 (m, 2H, 2 × H-1), 4.08–4.18 (m, 1H, H-3), 4.26–4.31 (m, 1H, H-2), 4.73 (br s, 1H, NH), 7.32–7.41 (m, 6H, Ph), 7.67–7.70 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 26.2 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (CH_2), 29.8 (6 × CH_2), 32.1 (CH_2), 33.9 (CH_2), 34.6 (CH_2), 36.9 (CH_2), 49.4 (C-4), 63.2 (C-1), 77.4 (C-3), 77.9 (C-2), 78.9 (C_q), 108.6 (OCO), 127.7 (2 × CH_{Ph}), 127.8 (3 × CH_{Ph}), 129.7 (CH_{Ph}), 133.6 (2 × C_i), 135.7 (2 × CH_{Ph}), 135.8 (2 × CH_{Ph}) 155.2 (C=O). ESI-HRMS: m/z calcd for $C_{44}H_{72}NO_5Si$ $[M + H]^+$ 722.5174, found 722.5182.

4.1.61. tert-Butyl [(2S,3R,4S)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)octadecan-4-yl]carbamate ent-49

Using the same procedure as described for the preparation of **45**, compound *ent*-**43** (0.235 g, 0.32 mmol) was converted into derivative *ent*-**49** (colourless oil, 0.211 g, 89 %, *n*-hexane/EtOAc, 25:1); $[\alpha]_D^{22}$ +4.2 (*c* 0.61, $CHCl_3$). IR (neat) ν 2924, 2853, 1716, 1490, 1165, 1111 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ 0.89 (t, 3H, J = 6.8 Hz, CH_3), 1.08 (s, 9H, 3 × CH_3), 1.27–1.62 (m, 45H, 18 × CH_2, 3 × CH_3), 3.68–3.80 (m, 1H, H-4), 3.83–3.92 (m, 2H, 2 × H-1), 4.10–4.19 (m, 1H, H-3), 4.27–4.31 (m, 1H, H-2), 4.74 (br s, 1H, NH), 7.33–7.42 (m, 6H, Ph), 7.69–7.71 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 26.2 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (CH_2), 29.8 (6 × CH_2), 29.9 (CH_2), 32.1 (CH_2), 33.9 (CH_2), 34.6 (CH_2), 37.0 (CH_2), 49.4 (C-4), 63.2 (C-1), 77.4 (C-3), 78.0 (C-2), 79.0 (C_q), 108.6 (OCO), 127.7 (2 × CH_{Ph}), 127.8 (2 × CH_{Ph}), 129.7 (2 × CH_{Ph}), 133.6 (C_i), 133.7 (C_i), 135.8 (4 × CH_{Ph}), 155.2 (C=O). ESI-HRMS: m/z calcd for $C_{45}H_{73}NNaO_5Si$ $[M + Na]^+$ 758.5150, found 758.5161.

4.1.62. tert-Butyl [(2S,3R,4S)-1-[(tert-butyldiphenylsilyl)oxy]-2,3-(cyclohexylidenedioxy)pentadecan-4-yl]carbamate ent-50

Using the same procedure as described for the preparation of **45**, compound *ent*-**44** (81 mg, 0.11 mmol) was modified to derivative *ent*-**50** (colourless oil, 81 mg, 95 %, *n*-hexane/EtOAc, 25:1); $[\alpha]_D^{21}$ +6.1 (*c* 0.34, $CHCl_3$). IR (neat) ν 3454, 2923, 2853, 1716, 1491, 1164, 1105 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, 50 °C) δ 0.88 (t, 3H, J = 6.9 Hz, CH_3), 1.06 (s, 9H, 3 × CH_3), 1.25–1.61 (m, 47H, 19 × CH_2, 3 × CH_3), 3.69–3.80 (m, 1H, H-4), 3.82–3.91 (m, 2H, 2 × H-1), 4.08–4.16 (m, 1H, H-3), 4.26–4.30 (m, 1H, H-2), 4.73 (br s, 1H, NH), 7.32–7.41 (m, 6H, Ph), 7.67–7.70 (m, 4H, Ph); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 19.4 (C_q), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.4 (CH_2), 26.2 (CH_2), 27.0 (3 × CH_3), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (CH_2), 29.8 (5 × CH_2), 29.9 (3 × CH_2), 32.1 (CH_2), 33.9 (CH_2), 34.6 (CH_2), 37.0 (CH_2), 49.4 (C-4), 63.2 (C-1), 77.5 (C-3), 78.0 (C-2), 79.0 (C_q), 108.6 (OCO), 127.7 (2 × CH_{Ph}), 127.8 (3 × CH_{Ph}), 129.7 (CH_{Ph}), 133.6 (C_i), 133.7 (C_i), 135.8 (4 × CH_{Ph}) 155.2 (C=O). ESI-HRMS: m/z calcd for $C_{46}H_{75}NaNO_5Si$ $[M + Na]^+$ 772.5307, found 772.5310.

4.1.63. tert-Butyl [(2S,3R,4R)-2,3-(cyclohexylidenedioxy)-1-hydroxyheptadecan-4-yl]carbamate ent-19

Using the same procedure as described for the preparation of **19**, compound *ent*-**45** (90 mg, 0.12 mmol) was converted into derivative *ent*-**19** (colourless oil, 52 mg, 82 %, *n*-hexane/EtOAc, 5:1); $[\alpha]_D^{21}$ +4.5 (*c* 0.40, $CHCl_3$). IR (neat) ν 3505, 3385, 2919, 2851, 1684, 1513, 1365, 1164 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 6.5 Hz, CH_3), 1.26–1.62 (m, 42H, 3 × CH_3,16 × CH_2, H–CH_2), 1.74–1.85 (m, 1H, H–CH_2), 2.43 (br s, 1H, OH), 3.60–3.80 (m, 3H, 2 × H-1, H-4), 3.91–3.95 (m, 1H, H-3), 4.19–4.23 (m, 1H, H-2), 4.37 (d, 1H, J = 9.3 Hz, NH); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.2 (CH_3), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.1 (CH_2), 25.2 (CH_2), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (3 × CH_2), 29.8 (4 × CH_2), 32.0 (CH_2), 33.6 (CH_2), 35.0 (CH_2), 37.9 (CH_2), 49.8 (C-4), 61.7 (C-1), 78.0 (C-2), 78.6 (C-3), 80.0 (C_q), 109.1 (OCO), 155.9 (C=O). ESI-HRMS: m/z calcd for $C_{28}H_{53}NaNO_5$ $[M + Na]^+$ 506.3816, found 506.3820.

4.1.64. tert-Butyl [(2S,3R,4R)-2,3-(cyclohexylidenedioxy)-1-hydroxyoctadecan-4-yl]carbamate ent-20

According to the same procedure employed for the construction of **19**, compound *ent*-**46** (0.151 g, 0.21 mmol) was converted to derivative *ent*-**20** (colourless oil, 98 mg, 96 %, *n*-hexane/EtOAc, 5:1); $[\alpha]_D^{22}$ +3.3 (*c* 0.24, $CHCl_3$). IR (neat) ν 3513, 3389, 2918, 2850, 1684, 1513, 1365, 1164 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 6.8 Hz, CH_3), 1.25–1.62 (m, 44H, 3 × CH_3, 17 × CH_2, H–CH_2), 1.74–1.85 (m, 1H, H–CH_2), 2.49 (br s, 1H, OH), 3.61–3.82 (m, 3H, 2 × H-1, H-4), 3.91–3.95 (m, 1H, H-3), 4.19–4.23 (m, 1H, H-2), 4.40 (d, 1H, J = 10.0 Hz, NH); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.2 (CH_3), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.1 (CH_2), 25.2 (CH_2), 28.4 (3 × CH_3), 29.5 (CH_2), 29.6 (CH_2), 29.7 (2 × CH_2), 29.8 (5 × CH_2), 32.0 (CH_2), 33.6 (CH_2), 34.9 (CH_2), 37.9 (CH_2), 49.8 (C-4), 61.7 (C-1), 78.0 (C-2), 78.6 (C-3), 80.0 (C_q), 109.1 (OCO), 155.9 (C=O). ESI-HRMS: m/z calcd for $C_{29}H_{55}NaNO_5$ $[M + Na]^+$ 520.3972, found 520.3985.

4.1.65. tert-Butyl [(2S,3R,4R)-2,3-(cyclohexylidenedioxy)-1-hydroxynonadecan-4-yl]carbamate ent-21

Using the same procedure as described for the preparation of **19**, compound *ent*-**47** (0.115 g, 0.15 mmol) was converted into derivative *ent*-**21** (colourless oil, 71 mg, 91 %, *n*-hexane/EtOAc, 5:1); $[\alpha]_D^{21}$ –3.2 (*c* 0.37, $CHCl_3$). IR (neat) ν 3513, 3389, 2917, 2849, 1684, 1512, 1365, 1163 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 6.8 Hz, CH_3), 1.25–1.62 (m, 46H, 3 × CH_3,18 × CH_2, H–CH_2), 1.73–1.86 (m, 1H, H–CH_2), 2.44 (br s, 1H, OH), 3.60–3.82 (m, 3H, 2 × H-1, H-4), 3.91–3.95 (m, 1H, H-3), 4.19–4.23 (m, 1H, H-2), 4.38 (d, 1H, J = 9.4 Hz, NH); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.2 (2 × CH_2), 28.5 (3 × CH_3), 29.5 (CH_2), 29.7 (2 × CH_2), 29.8 (7 × CH_2), 32.1 (CH_2), 33.7 (CH_2), 35.0 (CH_2), 38.0 (CH_2), 49.8 (C-4), 61.7 (C-1), 78.1 (C-2), 78.6 (C-3), 80.0 (C_q), 109.1 (OCO), 155.9 (C=O). ESI-HRMS: m/z calcd for $C_{30}H_{57}NaNO_5$ $[M + Na]^+$ 534.4129, found 534.4129.

4.1.66. tert-Butyl [(2S,3R,4S)-2,3-(cyclohexylidenedioxy)-1-hydroxyheptadecan-4-yl]carbamate ent-22

According to the same procedure employed for the preparation of **19**, compound *ent*-**48** (86 mg, 0.12 mmol) was converted into derivative *ent*-**22** (colourless oil, 53 mg, 91 %, *n*-hexane/EtOAc, 5:1); $[\alpha]_D^{20}$ –18.4 (*c* 0.24, $CHCl_3$). IR (neat) ν 3448, 2922, 2852, 1693, 1498, 1365, 1164 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, 3H, J = 6.9 Hz, CH_3), 1.25–1.66 (m, 43H, 3 × CH_3, 17 × CH_2), 2.71 (br s, 1H, OH), 3.63–3.72 (m, 2H, 2 × H-1), 3.83–3.90 (m, 1H, H-4), 4.13–4.15 (m, 1H, H-3), 4.23–4.28 (m, 1H, H-2), 4.79 (d, 1H, J = 9.9 Hz, NH); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.3 (CH_3), 22.8 (CH_2), 23.8 (CH_2), 24.2

(CH_2), 25.3 (CH_2), 25.9 (CH_2), 28.5 (3 × CH_3), 29.5 (CH_2), 29.6 (CH_2), 29.7 (2 × CH_2), 29.8 (4 × CH_2), 32.1 (CH_2), 34.2 (CH_2), 35.7 (CH_2), 37.3 (CH_2), 48.6 (C-4), 61.8 (C-1), 77.6 (C-2, C-3), 79.8 (C_q), 108.6 (OCO), 156.1 (C=O). ESI-HRMS: *m/z* calcd for $C_{28}H_{53}NaNO_5$ $[M + Na]^+$ 506.3816, found 506.3814.

4.1.67. tert-Butyl [(2S,3R,4S)-2,3-(cyclohexylidenedioxy)-1-hydroxyoctadecan-4-yl]carbamate ent-**23**

Using the same procedure as described for the construction of **19**, compound *ent*-**49** (0.20 g, 0.27 mmol) was converted into derivative *ent*-**23** (colourless oil, 0.133 g, 98 %, *n*-hexane/EtOAc, 5:1); $[\alpha]_D^{22}$ −16.0 (*c* 0.28, $CHCl_3$). IR (neat) *ν* 3453, 3400, 2920, 2852, 1692, 1522, 1171, 1059 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.8 Hz, CH_3), 1.25−1.65 (m, 45H, 3 × CH_3, 18 × CH_2), 2.69 (br s, 1H, OH), 3.62−3.75 (m, 2H, 2 × H-1), 3.84−3.90 (m, 1H, H-4), 4.13−4.15 (m, 1H, H-3), 4.23−4.28 (m, 1H, H-2), 4.79 (br d, 1H, *J* = 9.8 Hz, NH); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.3 (CH_3), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 25.9 (CH_2), 28.5 (3 × CH_3), 29.5 (CH_2), 29.6 (CH_2), 29.7 (2 × CH_2), 29.8 (5 × CH_2), 32.1 (CH_2), 34.2 (CH_2), 35.7 (CH_2), 37.3 (CH_2), 48.6 (C-4), 61.8 (C-1), 77.5 (C-3), 77.6 (C-2), 79.8 (C_q), 108.6 (OCO), 156.2 (C=O). ESI-HRMS: *m/z* calcd for $C_{29}H_{55}NaNO_5$ $[M + Na]^+$ 520.3972, found 520.3985.

4.1.68. tert-Butyl [(2S,3R,4S)-2,3-(cyclohexylidenedioxy)-1-hydroxynonadecan-4-yl]carbamate ent-**24**

According to the same procedure employed for the preparation of **19**, compound *ent*-**50** (72 mg, 0.09 mmol) was converted into derivative *ent*-**24** (colourless oil, 47 mg, 96 %, *n*-hexane/EtOAc, 5:1); $[\alpha]_D^{20}$ −16.7 (*c* 0.37, $CHCl_3$). IR (neat) *ν* 3456, 3401, 2920, 2851, 1692, 1522, 1366, 1171, 1058 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.8 Hz, CH_3), 1.25−1.65 (m, 47H, 3 × CH_3, 19 × CH_2), 2.57−2.64 (m, 1H, OH), 3.63−3.72 (m, 2H, 2 × H-1), 3.84−3.90 (m, 1H, H-4), 4.13−4.15 (m, 1H, H-3), 4.22−4.27 (m, 1H, H-2), 4.78 (d, 1H, *J* = 9.6 Hz, NH); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.3 (CH_3), 22.8 (CH_2), 23.8 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 25.9 (CH_2), 28.6 (3 × CH_3), 29.5 (CH_2), 29.6 (CH_2), 29.7 (2 × CH_2), 29.8 (6 × CH_2), 32.1 (CH_2), 34.2 (CH_2), 35.7 (CH_2), 37.3 (CH_2), 48.6 (C-4), 61.8 (C-1), 77.6 (C-2, C-3), 79.8 (C_q), 108.6 (OCO), 156.2 (C=O). ESI-HRMS: *m/z* calcd for ESI-HRMS: *m/z* calcd for $C_{30}H_{57}NaNO_5$ $[M + Na]^+$ 534.4129, found 534.4123.

4.1.69. tert-Butyl (2R,3R,4S)-3,4-(cyclohexylidenedioxy)-2-tridecylpyrrolidine-1-carboxylate ent-**51**

Using the same procedure as described for the construction of **51**, compound *ent*-**19** (52 mg, 0.11 mmol) was modified to derivative *ent*-**51** (colourless oil, 41 mg, 82 %, *n*-hexane/EtOAc, 13:1); $[\alpha]_D^{21}$ −21.6 (*c* 0.18, $CHCl_3$). IR (neat) *ν* 2922, 2852, 1696, 1450, 1401, 1364, 1162, 1100 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.9 Hz, CH_3), 1.25−1.65 (m, 43H, 3 × CH_3, 17 × CH_2), 3.29 (dd, 1H, *J* = 13.1 Hz, *J* = 5.0 Hz, H-5), 3.78−3.91 (m, 1H, H-5), 3.98−4.10 (m, 1H, H-2), 4.38 (d, 1H, *J* = 5.8 Hz, H-3), 4.64−4.72 (m, 1H, H-4). ESI-HRMS: *m/z* calcd for $C_{28}H_{51}NaNO_4$ $[M + Na]^+$ 488.3710, found 488.3712.

Due to the presence of rotamers in the ^{13}C NMR spectra recorded at ambient temperature, as well as at 50 °C, the corresponding spectroscopic data are not reported.

4.1.70. tert-Butyl (2R,3R,4S)-3,4-(cyclohexylidenedioxy)-2-tetradecylpyrrolidine-1-carboxylate ent-**52**

According to the same procedure described for the preparation of **51**, compound *ent*-**20** (55 mg, 0.11 mmol) was converted into derivative *ent*-**52** (colourless, oil, 45 mg, 94 %, *n*-hexane/EtOAc, 13:1); $[\alpha]_D^{21}$ −19.3 (*c* 0.67, $CHCl_3$). IR (neat) *ν* 2922, 2852, 1697, 1365,1162 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$, 50 °C) *δ* 0.88 (t, 3H, *J* = 6.0 Hz, CH_3), 1.26−1.48 (m, 37H, 3 × CH_3, 14 × CH_2), 1.50−1.62 (m, 8H, 4 × CH_2), 3.27 (dd, 1H, *J* = 12.8, 4.7 Hz, H-5), 3.74−3.93 (m, 1H, H-5), 3.94−4.12 (m, 1H, H-2), 4.37 (d, 1H, *J* = 5.6 Hz, H-3), 4.65−4.67 (m, 1H, H-4). ESI-HRMS: *m/z* calcd for $C_{29}H_{53}NNaO_4$ $[M + Na]^+$ 502.3867, found 502.3875.

Due to the presence of rotamers in the ^{13}C NMR spectra recorded at ambient temperature, as well as at 50 °C, the corresponding spectroscopic data are not reported.

4.1.71. tert-Butyl (2R,3R,4S)-3,4-(cyclohexylidenedioxy)-2-pentadecylpyrrolidine-1-carboxylate ent-**53**

Using the same procedure as described for the preparation of **51**, compound *ent*-**21** (70 mg, 0.14 mmol) was converted into derivative *ent*-**53** (colourless oil, 57 mg, 83 % *n*-hexane/EtOAc, 13:1); $[\alpha]_D^{20}$ −18.8 (*c* 0.26, $CHCl_3$). IR (neat) *ν* 2922, 2852, 1697, 1401, 1364, 1163 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.8 Hz, CH_3), 1.21−1.65 (m, 47H, 3 × CH_3, 19 × CH_2), 3.28 (dd, 1H, *J* = 13.1, 5.1 Hz, H-5), 3.74−3.94 (m, 1H, H-5), 3.95−4.13 (m, 1H, H-2), 4.38 (d, 1H, *J* = 5.8 Hz, H-3), 4.66−4.68 (m, 1H, H-4). ESI-HRMS: *m/z* calcd for $C_{30}H_{55}NaNO_4$ $[M + Na]^+$ 516.4023, found 516.4028.

Due to the presence of rotamers in the ^{13}C NMR spectra recorded at ambient temperature, as well as at 50 °C, the corresponding spectroscopic data are not reported.

4.1.72. tert-Butyl (2S,3R,4S)-3,4-(cyclohexylidenedioxy)-2-tridecylpyrrolidine-1-carboxylate ent-**54**

According to the same procedure described for the preparation of **51**, compound *ent*-**22** (49 mg, 0.10 mmol) was transformed to derivative *ent*-**54** (colourless oil, 46 mg, 98 %, *n*-hexane/EtOAc, 13:1); $[\alpha]_D^{22}$ +34.9 (*c* 0.42, $CHCl_3$). IR (neat) *ν* 2922, 2852, 1696, 1391, 1365, 1162, 1092 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.8 Hz, CH_3), 1.21−1.80 (m, 43H, 3 × CH_3, 17 × CH_2), 3.22−3.25 (m, 1H, H-5), 3.82−3.87 (m, 2H, H-2, H-5), 4.65−4.70 (m, 2H, H-3, H-4); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.3 (CH_3), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 26.4 (CH_2), 28.6 (3 × CH_3), 29.5 (CH_2), 29.7 (CH_2), 29.8 (3 × CH_2), 29.9 (3 × CH_2), 29.9 (CH_2), 32.1 (CH_2), 34.8 (CH_2), 36.6 (CH_2), 50.4 (C-5), 59.7 (C-2), 77.4 (C-4), 79.7 (C_q), 79.8 (C-3), 113.5 (OCO), 154.5 (C=O). ESI-HRMS: *m/z* calcd for $C_{28}H_{51}NaNO_4$ $[M + Na]^+$ 488.3710, found 488.3709.

4.1.73. tert-Butyl (2S,3R,4S)-3,4-(cyclohexylidenedioxy)-2-tetradecylpyrrolidine-1-carboxylate ent-**55**

Using the same procedure as described for the preparation of **51**, compound *ent*-**23** (57 mg, 0.11 mmol) was converted into derivative *ent*-**55** (colourless oil, 50 mg, 91 %, *n*-hexane/EtOAc, 13:1); $[\alpha]_D^{21}$ +32.3 (*c* 0.27, $CHCl_3$). IR (neat) *ν* 2922, 2852, 1697, 1391, 1365, 1163, 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.87 (t, 3H, *J* = 6.9 Hz, CH_3), 1.20−1.49 (m, 35H, 3 × CH_3, 13 × CH_2), 1.50−1.77 (m, 10H, 5 × CH_2), 3.21−3.25 (m, 1H, H-5), 3.81−3.86 (m, 2H, H-5, H-2), 4.64−4.69 (m, 2H, H-3, H-4); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.3 (CH_3), 22.8 (CH_3), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 26.4 (CH_2), 28.6 (3 × CH_3), 29.5 (CH_2), 29.7 (3 × CH_2), 29.8 (5 × CH_2), 29.9 (CH_2), 32.1 (CH_2), 34.8 (CH_2), 36.7 (CH_2), 50.5 (C-5), 59.7 (C-2), 77.5 (C-4), 79.7 (C-3), 79.8 (C_q), 113.5 (OCO), 154.5 (C=O). ESI-HRMS: *m/z* calcd for $C_{29}H_{53}NNaO_4$ $[M + Na]^+$ 502.3867, found 502.3883.

4.1.74. tert-Butyl (2S,3R,4S)-3,4-(cyclohexylidenedioxy)-2-pentadecylpyrrolidine-1-carboxylate ent-**56**

According to the same procedure described for the preparation of **51**, compound *ent*-**24** (39 mg, 76 μmol) was converted into derivative *ent*-**56** (colourless oil, 36 mg, 95 %, *n*-hexane/EtOAc, 13:1); $[\alpha]_D^{21}$ +29.8 (*c* 0.42, $CHCl_3$). IR (neat) *ν* 2921, 2852, 1697, 1391, 1364, 1162, 1093 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) *δ* 0.88 (t, 3H, *J* = 6.9 Hz, CH_3), 1.21−1.47 (m, 37H, 3 × CH_3, 14 × CH_2), 1.52−1.78 (m, 10H, 5 × CH_2), 3.22−3.25 (m, 1H, H-5), 3.81−3.87 (m, 2H, H-2, H-5), 4.65−4.70 (m, 2H, H-3, H-4); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 14.3

(CH_3), 22.8 (CH_2), 23.9 (CH_2), 24.2 (CH_2), 25.3 (CH_2), 26.4 (CH_2), 28.6 (3 × CH_3), 29.5 (CH_2), 29.7 (2 × CH_2), 29.8 (7 × CH_2), 29.9 (CH_2), 32.1 (CH_2), 34.8 (CH_2), 36.6 (CH_2), 50.5 (C-5), 59.7 (C-2), 77.5 (C-3 or C-4), 79.7 (C_q), 79.8 (C-3 or C-4), 113.5 (OCO), 154.5 (C=O). ESI-HRMS: *m/z* calcd for ESI-HRMS: *m/z* calcd for $C_{30}H_{55}NaNO_4$ $[M + Na]^+$ 516.4023, found 516.4020.

4.1.75. (2R,3R,4S)-2-Tridecylpyrrolidine-3,4-diol hydrochloride ent-13

Using the same procedure as described for the construction of **13**, compound *ent*-**51** (41 mg, 88 μmol) was modified to derivative *ent*-**13** (white amorphous solid, 30 mg, 85 %); $[\alpha]_D^{21}$ +30.7 (*c* 0.24, MeOH). IR (neat) *ν* 3395, 2953, 2918, 2848, 1462, 1110 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) *δ* 0.90 (t, 3H, *J* = 6.8 Hz, CH_3), 1.29–1.54 (m, 22H, 11 × CH_2), 1.63–1.74 (m, 1H, *H*–CH_2), 1.81–1.90 (m, 1H, *H*–CH_2), 3.22 (dd, 1H, *J* = 12.6, 1.8 Hz, H-5), 3.35–3.46 (m, 2H, H-2, H-5), 3.90 (dd, 1H, *J* = 8.6, 4.0 Hz, H-3), 4.21–4.24 (m, 1H, H-4); ^{13}C NMR (101 MHz, CD_3OD) *δ* 14.4 (CH_3), 23.7 (CH_2), 27.6 (CH_2), 30.4 (CH_2), 30.5 (2 × CH_2), 30.7 (CH_2), 30.8 (4 × CH_2), 31.5 (CH_2), 33.1 (CH_2), 50.6 (C-5), 62.2 (C-2), 70.9 (C-4), 76.9 (C-3). ESI-HRMS: *m/z* calcd for $C_{17}H_{36}NO_2$ $[M - Cl]^+$ 286.2741, found 286.2749.

4.1.76. (2R,3R,4S)-2-Tetradecylpyrrolidine-3,4-diol hydrochloride ent-14

Using the same procedure as described for the preparation of **13**, compound *ent*-**52** (43 mg, 90 mmol) was transformed to derivative *ent*-**14** (white amorphous solid, 24 mg, 80 %); $[\alpha]_D^{21}$ +42.2 (*c* 0.21, $CHCl_3$). IR (neat) *ν* 3396, 3344, 2918, 2848, 1109 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) *δ* 0.90 (t, 3H, *J* = 6.8 Hz, CH_3), 1.29–1.54 (m, 24H, 12 × CH_2), 1.62–1.71 (m, 1H, *H*–CH_2), 1.81–1.90 (m, 1H, *H*–CH_2), 3.22 (dd, 1H, *J* = 12.6, 1.7 Hz, H-5), 3.37–3.45 (m, 2H, H-2, H-5), 3.90 (dd, 1H, *J* = 8.5, 4.0 Hz, H-3), 4.21–4.23 (m, 1H, H-4); ^{13}C NMR (101 MHz, CD_3OD) *δ*14.4 (CH_3), 23.7 (CH_2), 27.6 (CH_2), 30.4 (CH_2), 30.5 (2 × CH_2), 30.7 (2 × CH_2), 30.8 (4 × CH_2), 31.6 (CH_2), 33.1 (CH_2), 50.6 (C-5), 62.3 (C-2), 70.9 (C-4), 76.9 (C-3). ESI-HRMS: *m/z* calcd for $C_{18}H_{38}NO_2$ $[M - Cl]^+$ 300.2897, found 300.2900.

4.1.77. (2R,3R,4S)-2-Pentadecylpyrrolidine-3,4-diol hydrochloride ent-15

According to the same procedure employed for the construction of **13**, compound *ent*-**53** (57 mg, 0.11 mmol) was converted into derivative *ent*-**15** (white amorphous solid, 37 mg, 88 %); $[\alpha]_D^{21}$ +45.5 (*c* 0.29, MeOH). IR (neat) *ν* 3396, 3344, 2919, 2848, 1466, 1110 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) *δ* 0.89 (t, 3H, *J* = 6.8 Hz, CH_3), 1.28–1.53 (m, 26H, 13 × CH_2), 1.61–1.71 (m, 1H, *H*–CH_2), 1.80–1.89 (m, 1H, *H*–CH_2), 3.21 (dd, 1H, *J* = 12.6, 1.8 Hz, H-5), 3.36–3.44 (m, 2H, H-2, H-5), 3.89 (dd, 1H, *J* = 8.6, 4.0 Hz, H-3), 4.21 (td, 1H, *J* = 4.0, 1.8 Hz, H-4); ^{13}C NMR (101 MHz, CD_3OD) *δ* 14.4 (CH_3), 23.7 (CH_2), 27.6 (CH_2), 30.4 (CH_2), 30.5 (2 × CH_2), 30.7 (2 × CH_2), 30.8 (5 × CH_2), 31.6 (CH_2), 33.1 (CH_2), 50.6 (C-5), 62.3 (C-2), 70.9 (C-4), 76.9 (C-3). ESI-HRMS: *m/z* calcd for $C_{19}H_{40}NO_2$ $[M - Cl]^+$ 314.3054, found 314.3059.

4.1.78. (2S,3R,4S)-2-Tridecylpyrrolidine-3,4-diol hydrochloride ent-16

Using the same procedure as described for the preparation of **13**, compound *ent*-**54** (43 mg, 92 μmol) was modified to derivative *ent*-**16** (white amorphous solid, 30 mg, 83 %); $[\alpha]_D^{21}$ +11.2 (*c* 0.28, MeOH). IR (neat) *ν* 3406, 2917, 2848, 1588, 1472, 1461, 1128 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) *δ* 0.90 (t, 3H, *J* = 6.8 Hz, CH_3), 1.29–1.47 (m, 22H, 11 × CH_2), 1.68–1.76 (m, 1H, *H*–CH_2), 1.83–1.93 (m, 1H, *H*–CH_2), 3.06 (dd, 1H, *J* = 11.6, 8.0 Hz, H-5), 3.40–3.48 (m, 2H, H-2, H-5), 4.06–4.08 (m, 1H, H-3), 4.40 (td, 1H, *J* = 8.0, 3.8 Hz, H-4); ^{13}C NMR (101 MHz, CD_3OD) *δ* 14.4 (CH_3), 23.7 (CH_2), 27.2 (CH_2), 27.8 (CH_2), 30.5 (3 × CH_2), 30.6 (CH_2), 30.8 (4 × CH_2), 33.1 (CH_2), 48.4 (C-5), 63.8 (C-2), 71.6 (C-3), 72.0 (C-4). ESI-HRMS: *m/z* calcd for $C_{17}H_{36}NO_2$ $[M - Cl]^+$ 286.2741, found 286.2745.

4.1.79. (2S,3R,4S)-2-Tetradecylpyrrolidine-3,4-diol hydrochloride ent-17

According to the same procedure described for the construction of **13**, compound *ent*-**55** (48 mg, 0.10 mmol) was converted into derivative *ent*-**17** (white amorphous solid, 30 mg, 89 %); $[\alpha]_D^{21}$ +28.6 (*c* 0.23, MeOH). IR (neat) *ν* 3383, 3192, 2917, 2848, 2720, 1466, 1132 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) *δ* 0.90 (t, 3H, *J* = 6.8 Hz, CH_3), 1.29–1.47 (m, 24H, 12 × CH_2), 1.68–1.77 (m, 1H, *H*–CH_2), 1.84–1.93 (m, 1H, *H*–CH_2), 3.06 (dd, 1H, *J* = 11.6, 8.0 Hz, H-5), 3.39–3.48 (m, 2H, H-5, H-2), 4.06–4.08 (m, 1H, H-3), 4.40 (td, 1H, *J* = 8.0, 3.8 Hz, H-4); ^{13}C NMR (101 MHz, CD_3OD) *δ* 14.4 (CH_3), 23.7 (CH_2), 27.2 (CH_2), 27.8 (CH_2), 30.5 (3 × CH_2), 30.7 (CH_2), 30.8 (5 × CH_3), 33.1 (CH_2), 48.4 (C-5), 63.7 (C-2), 71.6 (C-3), 72.0 (C-4). ESI-HRMS: *m/z* calcd for $C_{18}H_{38}NO_2$ $[M - Cl]^+$ 300.2897, found 300.2900.

4.1.80. (2S,3R,4S)-2-Pentadecylpyrrolidine-3,4-diol hydrochloride ent-18

Using the same procedure as described for the construction of **13**, compound *ent*-**56** (35 mg, 70 μmol) was converted into derivative *ent*-**18** (white amorphous solid, 26 mg, 85 %); $[\alpha]_D^{21}$ +4.0 (*c* 0.17, MeOH). IR (neat) *ν* 3383, 2918, 2849, 1588, 1466, 1461, 1133 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) *δ* 0.90 (t, 3H, *J* = 6.8 Hz, CH_3), 1.29–1.47 (m, 26H, 13 × CH_2), 1.67–1.77 (m, 1H, *H*–CH_2), 1.84–1.93 (m, 1H, *H*–CH_2), 3.06 (dd, 1H, *J* = 11.6, 8.0 Hz, H-5), 3.39–3.48 (m, 2H, H-2, H-5), 4.06–4.08 (m, 1H, H-3), 4.40 (td, 1H, *J* = 8.0, 3.8 Hz, H-4); ^{13}C NMR (101 MHz, CD_3OD) *δ* 14.4 (CH_3), 23.7 (CH_2), 27.2 (CH_2), 27.8 (CH_2), 30.5 (3 × CH_2), 30.7 (CH_2), 30.8 (6 × CH_2), 33.1 (CH_2), 48.4 (C-5), 63.8 (C-2), 71.6 (C-3), 72.0 (C-4). ESI-HRMS: *m/z* calcd for ESI-HRMS: *m/z* calcd for $C_{19}H_{40}NO_2$ $[M - Cl]^+$ 314.3054, found 314.3050.

4.1.81. (2S,3R,4R)-4-Aminooctadecane-1,2,3-triol hydrochloride 57

A solution of *ent*-**20** (43 mg, 76 μmol) in MeOH (0.3 mL) was treated with a 6 M aq HCl solution (4.5 mL) at room temperature. After being stirred and heated at 70 °C for 5 h, the whole mixture was concentrated in vacuo, and the residue was washed three times with dry E_2O. The ethereal solution was removed by decantation and the solid product was dried to give 30 mg (82 %) of compound **57** as an amorphous solid; $[\alpha]_D^{21}$ +19.6 (*c* 0.23, MeOH), lit [24a]. $[\alpha]_D^{20}$ –15.0 (*c* 0.28, MeOH). IR (neat) *ν* 3295, 2915, 1592, 1528, 1465 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) *δ* 0.90 (t, 3H, *J* = 6.9 Hz, CH_3), 1.24–1.55 (m, 24H, 12 × CH_2), 1.59–1.68 (m, 1H, *H*–CH_2), 1.75–1.83 (m, 1H, *H*–CH_2), 3.41 (dt, 1H, *J* = 9.5, 3.7 Hz, H-4), 3.56 (ddd, 1H, *J* = 8.6, 5.1, 3.5 Hz, H-2), 3.63 (dd, 1H, *J* = 11.3, 5.1 Hz, H-1), 3.71 (dd, 1H, *J* = 8.8, 3.7 Hz, H-3), 3.77 (dd, 1H, *J* = 11.3, 3.5 Hz, H-1); ^{13}C NMR (101 MHz, CD_3OD) *δ* 14.4 (CH_3), 23.7 (CH_2), 26.7 (CH_2), 27.8 (CH_2), 30.5 (2 × CH_2), 30.7 (CH_2), 30.8 (6 × CH_2), 33.1 (CH_2), 55.2 (C-4), 64.6 (C-1), 71.7 (C-3), 73.4 (C-2). ESI-HRMS: *m/z* calcd for $C_{18}H_{40}NO_3$ $[M - Cl]^+$ 318.3003, found 318.3008.

4.1.82. (2S,3R,4S)-4-Aminooctadecane-1,2,3-triol hydrochloride 58

Using the same procedure as described for the conversion of *ent*-**20** to **57**, compound *ent*-**23** (88 mg, 0.15 mmol) was converted into derivative **58** (white amorphous solid, 53 mg, 85 %); $[\alpha]_D^{21}$ +9.1 (*c* 0.22, MeOH); lit [24a]. $[\alpha]_D^{21}$ –13.6 (*c* 0.22, MeOH). IR (neat) *ν* 3225, 2914, 2848, 1492, 1094 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) *δ* 0.90 (t, 3H, *J* = 6.7 Hz, CH_3), 1.29–1.46 (m, 24H, 12 × CH_2), 1.60–1.69 (m, 2H, CH_2), 1.73–1.82 (m, 1H, *H*–CH_2), 3.42–3.46 (m, 1H, H-4), 3.59–3.64 (m, 1H, H-1); 3.67–3.73 (m, 3H, H-1, H-2, H-3); ^{13}C NMR (101 MHz, CD_3OD) *δ* 14.5 (CH_3), 23.8 (CH_2), 26.6 (CH_2), 30.5 (3 × CH_2), 30.7 (CH_2), 30.8 (5 × CH_2), 31.5 (CH_2), 33.1 (CH_2), 53.6 (C-4), 64.2 (C-1), 69.6 (C-3), 74.3 (C-2). ESI-HRMS: *m/z* calcd for $C_{18}H_{40}NO_3$ $[M - Cl]^+$ 318.3003, found 318.2996.

4.2. Antiproliferative/cytotoxic activity

4.2.1. Cell culture

Cell lines Jurkat (human acute T-lymphoblastic leukaemia), HeLa (human cervical carcinoma), HCT-116 (human colon carcinoma) maintained in RPMI 1640 medium, MCF-7 (human mammary gland adenocarcinoma), BLM (human melanoma cells) maintained in DMEM medium and BJ-5ta hTERT (immortalised foreskin fibroblast cells) maintained in DMEM: M199 medium (4:1) (Biosera, Kansas City, MO, USA), were supplemented with 10 % fetal bovine serum and 1 × HyClone™ antibiotic/antimycotic solution (PNC/STR/AMB) (GE Healthcare, Little Chalfont, UK) in humidified air atmosphere at 37 °C containing 5 % CO_2. Cell viability was estimated using the dye exclusion test with trypan blue and was greater than 95 % before each experiment.

4.2.2. Cytotoxicity assay

The antiproliferative effect of the tested compounds (Table 3) was studied by colorimetric microculture assay with the MTT endpoint. The amount of tetrazolium dye MTT 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide reduced to formazan was proportional to the number of viable cells [25]. The cells were seeded at density 5 × 10^3 cells/well in 96-well polystyrene microplates (SARSTEDT, Nümbrecht, Germany). Tested compounds were added at concentrations 0.1–100 μM 24 h after cell seeding. After 72 h of incubation 10 μL of MTT (5 mg/mL) to each well was added and incubated for an additional 4 h at 37 °C in 5 % CO_2 during which insoluble formazan was produced. To dissolve formazan, 100 μL of 10 % sodium dodecyl sulfate was added to each well for another 12 h. The absorbance was measured at 540 nm using Cytation™ 3 Cell Imaging Multi-Mode Reader (Biotek, Winooski, VT, USA). The measured values were shown as a percentage of metabolic activity of the cells relative to unaffected control, which amounted to 100 %.

Declaration of competing interest

The authors declare no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.tet.2021.132380.

References

[1] (For isolation, biological activity and biosynthesis of broussonetines and broussonetinines, see:). (a) D. Tsukamoto, M. Shibano, G. Kusano, Nat. Med. 37 (2003) 68–72;
(b) M. Shibano, D. Tsukamoto, G. Kusano, Heterocycles 57 (2002) 1539–1553;
(c) D. Tsukamoto, M. Shibano, G. Kusano, Chem. Pharm. Bull. 49 (2001) 1487–1491;
(d) D. Tsukamoto, M. Shibano, R. Okamoto, G. Kusano, Chem. Pharm. Bull. 49 (2001) 492–496;
(e) M. Shibano, D. Tsukamoto, R. Fujimoto, Y. Masui, H. Sugimoto, G. Kusano, Chem. Pharm. Bull. 48 (2000) 1281–1285;
(f) M. Shibano, D. Tsukamoto, G. Kusano, Chem. Pharm. Bull. 47 (1999) 907–908;
(g) M. Shibano, S. Nakamura, N. Moyoa, G. Kusano, Chem. Pharm. Bull. 47 (1999) 472–476;
(h) M. Shibano, S. Nakamura, M. Kubori, K. Minoura, G. Kusano, Chem. Pharm. Bull. 46 (1998) 1416–1420;
(i) M. Shibano, S. Nakamura, N. Akazawa, G. Kusano, Chem. Pharm. Bull. 46 (1998) 1048–1050;
(j) M. Shibano, S. Kitagawa, S. Nakamura, N. Akazawa, G. Kusano, Chem. Pharm. Bull. 45 (1997) 700–705;
(k) M. Shibano, S. Kitagawa, G. Kusano, Chem. Pharm. Bull. 45 (1997) 505–508.
[2] M. Shibano, D. Tsukamoto, T. Inoue, Y. Takase, G. Kusano, Chem. Pharm. Bull. 49 (2001) 504–506.
[3] (a) H. Zhao, A. Kato, K. Sato, Y.-M. Jia, C.-Y. Yu, J. Org. Chem. 78 (2013) 7896–7902;
(b) Y.-Y. Song, K. Kinami, A. Kato, Y.-M. Jia, Y.-X. Li, G.W.J. Fleet, C.-Y. Yu, Org. Biomol. Chem. 14 (2016) 5157–5174;
(c) Q.-K. Wu, K. Kinami, A. Kato, Y.-X. Li, Y.-M. Jia, G.W.J. Fleet, C.-Y. Yu, Molecules 24 (2019) 3712, 1–19.
[4] (For review on the syntheses of broussonetines, see:) S. Ballereau, M. Baltas, Y. Génisson, Curr. Org. Chem. 15 (2011) 953–986.
[5] (a) H. Yoda, T. Shimojo, K. Takabe, Tetrahedron Lett. 40 (1999) 1335–1336;
(b) P. Perlmutter, F. Vounatsos, J. Carbohydr. Chem. 22 (2003) 719–732;
(c) B.M. Trost, D.B. Horne, M.J. Woltering, Angew. Chem. Int. Ed. 42 (2003) 5987–5990;
(d) B.M. Trost, D.B. Horne, M.J. Woltering, Chem. Eur J. 12 (2006) 6607–6620;
(e) C. Ribes, E. Falomir, J. Murga, M. Carda, J.A. Marco, Org. Biomol. Chem. 7 (2009) 1355–1360;
(f) C. Ribes, E. Falomir, J. Murga, M. Carda, J.A. Marco, Tetrahedron 65 (2009) 10612–10616;
(g) N. Hama, T. Aoki, S. Miwa, M. Yamazaki, T. Sato, N. Chida, Org. Lett. 13 (2011) 616–619;
(h) S.L. Rössler, B.S. Schreib, M. Ginterseder, J.Y. Hamilton, E.M. Carreira, Org. Lett. 19 (2017) 5533–5536;
(i) I.-S. Myeong, W.-H. Ham, Eur. J. Org Chem. (2019) 1077–1082;
(j) L. Zhou, S.-Y. Yu, Y. Tang, L. Wang, Angew. Chem. Int. Ed. 58 (2019) 15016–15020.
[6] M.A. Brimble, J.H. Park, C.M. Taylor, Tetrahedron 59 (2003) 5861–5868.
[7] A. Kato, I. Nakagome, K. Sato, A. Yamamoto, I. Adachi, R.J. Nash, G.W.J. Fleet, Y. Natori, Y. Watanabe, T. Imahori, Y. Yoshimura, H. Takahata, S. Hirono, Org. Biomol. Chem. 14 (2016) 1039–1048.
[8] (a) D. Jacková, M. Martinková, J. Gonda, M. Vilková, M. Bago Pilátová, P. Takáč, Tetrahedron: Asymmetry 28 (2017) 1175–1182;
(b) D. Jacková, M. Martinková, J. Gonda, K. Stanková, M. Bago Pilátová, P. Herich, J. Kožíšek, Carbohydr. Res. 451 (2017) 59–71.
[9] (a) T.M. Chapman, S. Courtney, P. Hay, B.G. Davis, Chem. Eur J. 9 (2003) 3397–3414;
(b) T.M. Chapman, I.G. Davies, B. Gu, T.M. Block, D.I.C. Scopes, P.A. Hay, S.M. Courtney, L.A. McNeill, C.J. Schofield, B.G. Davis, J. Am. Chem. Soc. 127 (2005) 506–507.
[10] (For thio and aza-Claisen rearrangements, see:)M. Hiersemann, U. Nubbemeyer (Eds.), The Claisen Rearrangement, Wiley-VCH, Weinheim, Germany, 2007 (For the Overman rearrangement, see:). L.E. Overman, N.E. Carpenter, In Organic Reactions; L.E. Overman, ed.; Wiley: New York, NY, Vol. 66 (2005) pp. 1–107 (and references cited therein). (For a review on utilization of the Overman rearrangement in synthesis of natural products, see:). R.A. Fernandes, P. Kattanguru, S.P. Gholap, D.A. Chaudhari, Org. Biomol. Chem. 15 (2017) 2672–2710.
[11] A.S. Miller, A.R. Chamberlin, J. Am. Chem. Soc. 112 (1990) 8100–8112.
[12] K. Mori, H. Kikuchi, Liebigs Ann. Chem. 12 (1989) 1267–1269.
[13] S. Tsuzaki, S. Usui, H. Oishi, D. Yasushima, T. Fukuyasu, T. Oishi, T. Sato, N. Chida, Org. Lett. 17 (2015) 1704–1707.
[14] M. Čonková, M. Martinková, J. Gonda, D. Jacková, M. Bago Pilátová, D. Kupka, D. Jáger, Carbohydr. Res. 472 (2019) 76–85.
[15] T. Nishikawa, M. Asai, N. Ohyabu, M. Isobe, J. Org. Chem. 63 (1998) 188–192.
[16] M. Martinková, J. Gonda, K. Pomikalová, J. Kožíšek, J. Kuchár, Carbohydr. Res. 346 (2011) 1728–1738.
[17] J. Isac-García, F.G. Calvo-Flores, F. Hernández-Mateo, F. Santoyo-Gonzáles, Eur. J. Org Chem. (2001) 383–390.
[18] B. Cai, J.S. Panek, S. Amar, J. Med. Chem. 59 (2016) 6878–6890.
[19] (a) Y. Cai, C.-C. Ling, D.R. Bundle, Carbohydr. Res. 344 (2009) 2120–2126;
(b) M. Passinieni, A.M.P. Koskinen, Org. Biomol. Chem. 9 (2011) 1774–1783;
(c) T. Fujiwara, B. Liu, W. Niu, K. Hashimoto, H. Nambu, T. Yakura, Chem. Pharm. Bull. 64 (2016) 179–188;
(d) P. Das, S. Kundooru, A.K. Shaw, RSC Adv. 6 (2016) 14505–14511;
(e) T. Miyagawa, S. Inuki, M. Honda, S. Nakamura, I. Nakanishi, N. Fujii, S. Oishi, H. Ohno, Tetrahedron 74 (2018) 1802–1809.
[20] T. Yoshimoto, S. Unuki, S. Oishi, N. Fujii, H. Ohno, J. Org. Chem. 75 (2010) 3843–3846.
[21] T. Fujiwara, K. Hashimoto, M. Umeda, S. Murayama, Y. Ohno, B. Liu, H. Nambu, T. Yakura, Tetrahedron 74 (2018) 4578–4591.
[22] (For reviews on isolation, biological properties and syntheses of d-*ribo*-phytosphingosine, see:). (a) A.R. Howell, A.J. Ndakala, Curr. Org. Chem. 6 (2002) 365–391;

(b) J.A. Morales-Serna, J. Llaveria, Y. Díaz, M.I. Matheu, S. Castillón, Curr. Org. Chem. 14 (2010) 2483–2521;
(c) Y. Gao, X. He, F. Ding, Y. Zhang, Synthesis 48 (2016) 4017–4037.
[23] A. Rives, C. Baudoin-Deboux, N. Saffon, N. Andrieu-Abadie, Y. Génisson, Org. Biomol. Chem. 9 (2011) 8163–8170.
[24] (a) M. Fabišíková, M. Martinková, J. Gonda, D. Jacková, M. Bago Pilátová, J. Kuchár, Carbohydr. Res. 468 (2018) 51–63;
(b) J. Špaková Raschmanová, M. Martinková, J. Gonda, M. Bago Pilátová, D. Kupka, D. Jáger, Carbohydr. Res. 468 (2018) 1–12.
[25] T. Mosmann, T.J. Immunol, Methods 65 (1983) 55–63.
[26] M. Budovská, M. Pilátová, L. Varinská, J. Mojžiš, R. Mezencev, Bioorg. Med. Chem. 21 (2013) 6623–6633.