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Total synthesis of a protected form of sphingofungin E using the [3,3]-sigmatropic rearrangement of an allylic thiocyanate as the key reaction

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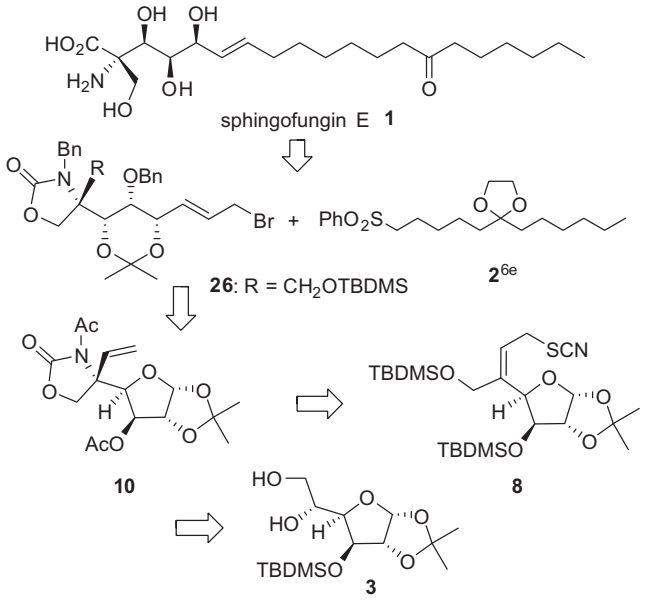
ABSTRACT

An approach to the stereocontrolled synthesis of the protected form of sphingofungin E (**32**) starting from the known protected D-glucose derivative **3** is described herein. For the construction of a tetrasubstituted carbon atom that is substituted with nitrogen, the [3,3]-sigmatropic rearrangement of thiocyanate **8** was employed. Subsequent functional group interconversions afforded the highly functionalized fragment, allylic bromide **26**. Its coupling reaction with the known C_{12} hydrophobic segment **2**, followed by further manipulation, completed the total synthesis.

1. Introduction

Sphingofungin E (**1**) is a complex amino acid natural product that was reported in 1992 by a group at Merck. The compound was isolated from the fermentation broth of *Paecilomyces variotii* together with sphingofungin F.[1] Both compounds are reported to be inhibitors[2] of serine palmitoyltransferase (SPT),[3,4] an essential enzyme involved in the first step of sphingolipid biosynthesis, with antifungal activity against several human pathogenic fungi.[1] From a structural standpoint, sphingofungin E (**1**) (Scheme 1) possesses an intriguing α-substituted α-amino acid motif[5] connected with trihydroxylated alkyl chain. Its significant biological properties, as well as the above-mentioned structural features, had made sphingofungin E an attractive target for synthetic chemists and four total syntheses of **1** have been developed.[6] Generally, the strategies used in these works[6] are organised into three parts: the construction of the side chain segment with a keto group at C-14, the preparation of the polar head group bearing four stereogenic centres and the cross-coupling reaction of these two fragments. For the stereoselective introduction of a quaternary stereocentre, Chida's group employed the Overman rearrangement of allylic trichloroacetimidates derived from D-glucose,[6e,f] while Nakamura and Shiozaki[6c,d] used the condensation of a 2-ulose prepared from a protected D-glucose derivative with dichloromethyllithium followed by treatment with NaN_3. Trost and Lee[6b] installed the tetrasubstituted carbon by Pd-catalysed asymmetric alkylation of an azlactone prepared from methyl *N*-benzoylglycine, and Lin and co-workers[6a,g] reported the total synthesis of **1** from L-tartaric acid, in which the Baylis–Hillman reaction and Hatakeyama's methodology were involved as the key steps for a preparation of an oxazoline derivative possessing the tetrasubstituted carbon.



Scheme 1. Retrosynthetic route to sphingofungin E (**1**).

In this paper, we would like to describe the total synthesis of the protected form of sphingofungin E (**32**) starting from D-glucose, which utilised a [3,3]-sigmatropic aza-Claisen rearrangement[6e,f,7]

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of the allylic thiocyanates as one of the fascinating methodologies for the installment of the tetrasubstituted carbon with nitrogen, which was developed in our laboratory.[8]

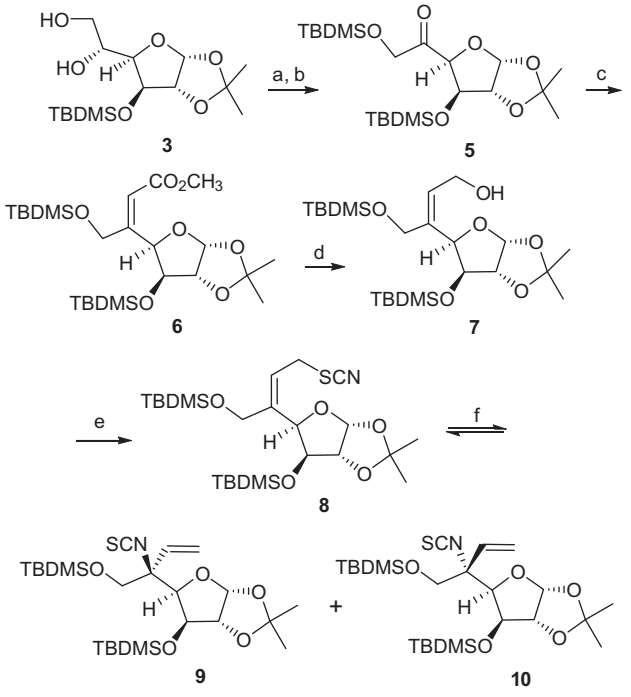
2. Results and discussion

Based on the retrosynthetic analysis illustrated in Scheme 1, our stereocontrolled approach towards **1** divided this molecule into two major segments. For the construction of the non-polar side chain **2**[6e] as well as the coupling of this lipophilic part and the hydrophilic segment **26**, we adopted the sulfone-mediated protocol reported by Chida and co-workers.[6e] The C-1–C-8 fragment **26** possessing an (*E*)-allylic bromide function was prepared from the highly functionalized cyclic carbamate **13** that contained the necessary α-substituted serine moiety and the remaining contiguous stereogenic centres. The aza-Claisen rearrangement of thiocyanate **8**, derived from the known[9] protected α-D-glucofuranose **3**, generated a quaternary carbon with the amino function in **13**.

2.1. Preparation of the functionalized cyclic carbamate 13

Synthesis of the functionalized part **13** commenced with 3-*O*-(*tert*-butyldimethylsilyl)-1,2-*O*-isopropylidene-α-D-glucofuranose **3**[9] prepared from 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose in two steps: (i) the 3-O-silylation with TBDMSCl/imidazole in DMF at 70 °C (85.5%); (ii) the selective removal of the 5,6-*O*-isopropylidene group with 4:1 CH_3CO_2H–H_2O (40 °C, 80%). The primary alcohol function in the resulting diol **3** was selectively silylated (TBDMSCl, Et_3N, DMAP and CH_2Cl_2) to afford **4** in 92% yield (Scheme 2). Its oxidation with IBX[10] in acetonitrile gave 5-ulose **5** (97%), which was subsequently treated with the stabilized ylide ($Ph_3P{=}CHCO_2CH_3$, toluene, reflux) to afford (*Z*)-α,β-unsaturated ester **6** exclusively in 97% yield (Scheme 2).

Its structure was determined by ^1H and ^{13}C NMR spectroscopy, including NOE experiments. Reduction of **6** using the standard procedure with $LiAlH_4$ resulted in allylic alcohol **7** (81%, Scheme 2), which was converted into thiocyanate **8** in two reaction steps. It was shown that O-mesylation of the corresponding alcohol **7**, followed by treatment with KSCN[8b] in acetonitrile, confirmed satisfactory results, and the desired **8** was obtained in 67% yield after flash chromatography (Scheme 2).



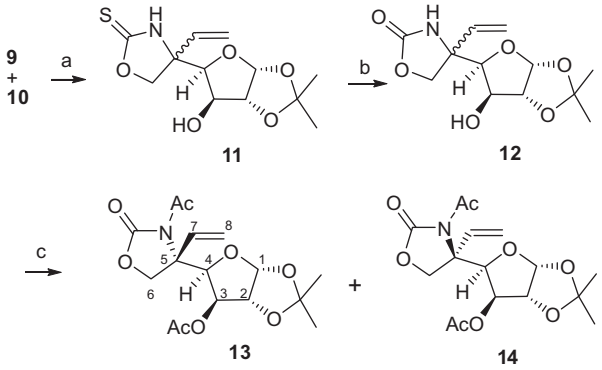
Scheme 2. Reagents and conditions: (a) TBDMSCl, Et_3N, DMAP, CH_2Cl_2, rt, **4**, 92%; (b) IBX, CH_3CN, reflux, 97%; (c) $Ph_3P{=}CHCO_2CH_3$, toluene, reflux, 97%; (d) $LiAlH_4$, Et_2O, 0 °C→rt, 81%; (e) (i) MsCl, Et_3N, CH_2Cl_2, 0 °C→rt; (ii) KSCN, CH_3CN, rt, 67%; (f) (i) *n*-heptane, 90 °C, 24 h, 72% or (ii) MW, *n*-heptane, 90 °C, 3 h, 69%.

With allylic thiocyanate **8** in hand, we then performed the thermal aza-Claisen rearrangement of **8**, which was carried out at 90 °C in *n*-heptane under a nitrogen atmosphere and to give the rearranged products **9** and **10** in 72% overall yield, as a barely separable mixture of diastereoisomers (**9**:**10** = 65:35 ratio, determined by ^1H NMR spectroscopy). On the other hand, the remarkable acceleration of the thermal [3,3]-sigmatropic rearrangement of **8** (from 24 h to 3 h) with satisfactory yield (69%) was observed using sealed vessel microwave irradiation conditions[11] in *n*-heptane at 90 °C; however, it had practically no influence on the diastereoselectivity (**9**:**10** = 70:30, determined by ^1H NMR spectroscopy). The stereochemistry of the newly constructed tetrasubstituted carbon was assigned by transformation of a mixture of isothiocyanates **9** and **10** into cyclic carbamates **13** and **14** by the following sequence of reaction steps (Scheme 3).

Thus, desilylation of the rearranged products **9** and **10** (ca. 2:1, prepared from **8**) using tetrabutylammonium fluoride in THF gave the corresponding thiocarbamates **11** in 75% yield. The replacement of the sulfur atom by oxygen was accomplished under very mild conditions by the action of mesitylnitrile oxide[12] (MNO) in CH_3CN to afford carbamates **12** (95%, Scheme 3). Acetylation of a mixture of the cyclic urethanes **12** with acetic anhydride in pyridine in the presence of DMAP as a catalyst provided crystalline diacetates **13** and **14** in 85% yield as a separable mixture of diastereoisomers. Although both compounds **13** and **14** crystallized well from a mixture of ether and hexane, only acetate **13** afforded single crystals that upon X-ray diffraction analysis (Fig. 1) clearly showed that the newly incorporated quaternary centre in **13** possesses the 5*S* configuration. These results show that the minor stereoisomer of the rearrangement **10** has the same configuration at C-5 position.

2.2. Synthesis of the key alcohol 25

Having revealed the structure of the highly functionalized fragment **13**, our strategy employed in the synthesis of C-1–C-8 fragment **26** was achieved by a series of functional group manipulations. In order to obtain the key allylic alcohol **25**, deprotection of the acetyl groups in **13** was realised under basic conditions (K_2CO_3, CH_3OH) and afforded product **12*S*** in 95% yield (Scheme 4). Exposure of **12*S*** to benzyl bromide in dry DMF using sodium hydride and catalytic amounts of tetrabutylammonium iodide produced the completely protected derivative **15** (96%, Scheme 4).



Scheme 3. Reagents and conditions: (a) TBAF, THF, 0 °C→rt, 75%; (b) MNO, CH_3CN, rt, 95%; (c) Ac_2O, Py, DMAP, rt, 85%.

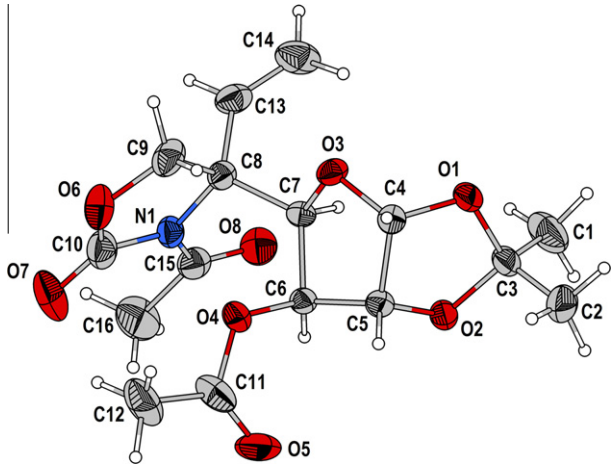
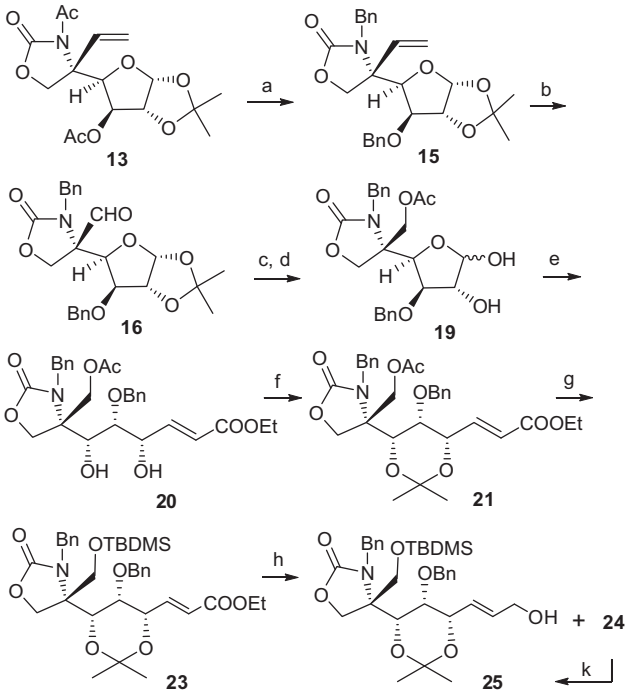


Figure 1. ORTEP structure of **13** showing the crystallographic numbering.



Scheme 4. Reagents and conditions: (a) (i) K_2CO_3, CH_3OH, rt, **12*S***, 95%; (ii) NaH, BnBr, TBAI, DMF, rt, 96%, (b) O_3, CH_3OH, −78 °C, Ph_3P, CH_2Cl_2, rt, 89%; (c) (i) $NaBH_4$, CH_3OH, 0 °C→rt, **17**, 95%; (ii) Ac_2O, DMAP, py, rt, **18**, 94%; (d) 8:2 TFA–H_2O, rt, 94%; (e) $Ph_3P{=}CHCO_2Et$, $PhCO_2H$, CH_2Cl_2, rt, 91%; (f) 2,2-DMP, CSA, rt, 81%; (g) (i) EtONa, EtOH, 0 °C, **22**, 92%; (ii) TBDMSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C→rt, 94%; (h) (i) DIBAl-H, CH_2Cl_2, −78 °C, **24**, 35%, **25**, 51%; (k) $NaBH_4$, CH_3OH, 0 °C→rt, 94%.

Ozonolysis of **15**, followed by PPh_3 treatment, successfully provided corresponding aldehyde **16** (89%), which was immediately reduced with $NaBH_4$ in methanol to give alcohol **17** in 95% yield (Scheme 4). The primary hydroxyl group present in **17** was protected as the acetate using acetic anhydride, dry pyridine and DMAP as a catalyst to produce **18** in 94% isolated yield. Exposure of compound **18** to trifluoroacetic acid resulted in the cleavage of the 1,2-*O*-isopropylidene group, and the corresponding lactol **19** was isolated as an inseparable mixture of anomers. Homologation of the resulting furanose **19** via a Wittig reaction ($Ph_3P{=}CHCO_2Et$, CH_2Cl_2) afforded (*E*)-α,β-unsaturated ester **20** as the sole product in 91% yield (Scheme 4). This product after flash chromatography and a rapid ^1H NMR analysis was immediately used in the next reaction.

The observed coupling constant in **20** (J = 15.7 Hz) proved the trans-configuration of the double bond. The treatment of **20** with 2,2-dimethoxypropane[13] and catalytic amounts of CSA resulted in the formation of the corresponding isopropylidene derivative **21** in 81% yield (Scheme 4). Cleavage of the acetate in **21** was achieved by employing sodium ethoxide in ethanol to give alcohol **22** (92%, Scheme 4). The recovered hydroxyl group in **22** was protected as its *tert*-butyldimethylsilyl ether **23** (94%, Scheme 4) using TBDMSOTf and 2,6-lutidine in dichloromethane. Reduction of the unsaturated ester **23** with DIBAL-H in CH_2Cl_2 at −78 °C afforded the allylic alcohol **25** (51%), together with the α,β-unsaturated aldehyde **24** (35%), which was immediately reduced with $NaBH_4$ to furnish **25** in 94% yield.

2.3. Coupling reaction and completion of the synthesis of 32

Alcohol **25** was subsequently transformed into the fully protected bromide **26** in 85.5% yield by a two-step sequence of functional group manipulations: (i) the mesylation of the resulting allylic alcohol **25** with $MsCl/Et_3N$ in CH_2Cl_2; and (ii) the displacement of the *O*-mesyl group by treatment with LiBr[6e] (Scheme 5). As was mentioned above, based on the retrosynthetic analysis (Scheme 1), we adopted the reported sulfone-mediated coupling reaction, which has been used for the total synthesis of both myriocin and sphingofungin E by Chida and co-workers.[6e,f]

Sulfone **2**,[6e] after reaction with *n*-BuLi at −78 °C in THF, was then treated with the bromide **26** to generate the product **27** as a mixture of inseparable diastereoisomers on silica gel (~1:0.7 ratio, determined by ^1H NMR spectroscopy) in 95% yield (Scheme 5). Since the attempted desulfonation of **27** by either aluminum amalgam[14] or Li-naphthalene[6e,15] afforded unidentified products, we decided to search for more effective reaction conditions. In the end, desulfonation of **27** was achieved using 6% sodium amalgam[16] in dry methanol and resulted in the formation of the fully protected aminopolyol **28** (64%). After routine deprotection of **28** with TBAF, the resulting alcohol **29** (88%) was subsequently treated with PDC in DMF to furnish the desired α-substituted α-amino acid **30** (65%) that possessed the correct stereochemistry at all stereogenic centres (Scheme 5). Finally, deprotection of both the ethylene ketal and the 1,3-*O*-isopropylidene groups in **30** by acid hydrolysis (2 M aq HCl) provided δ-lactone **31** in 72% yield. Treatment of **31** with 10% aq sodium hydroxide in methanol and subsequent neutralisation with Amberlite IR 120 H^+ furnished **32** (81%, Scheme 5) as the protected form of sphingofungin E (**1**).

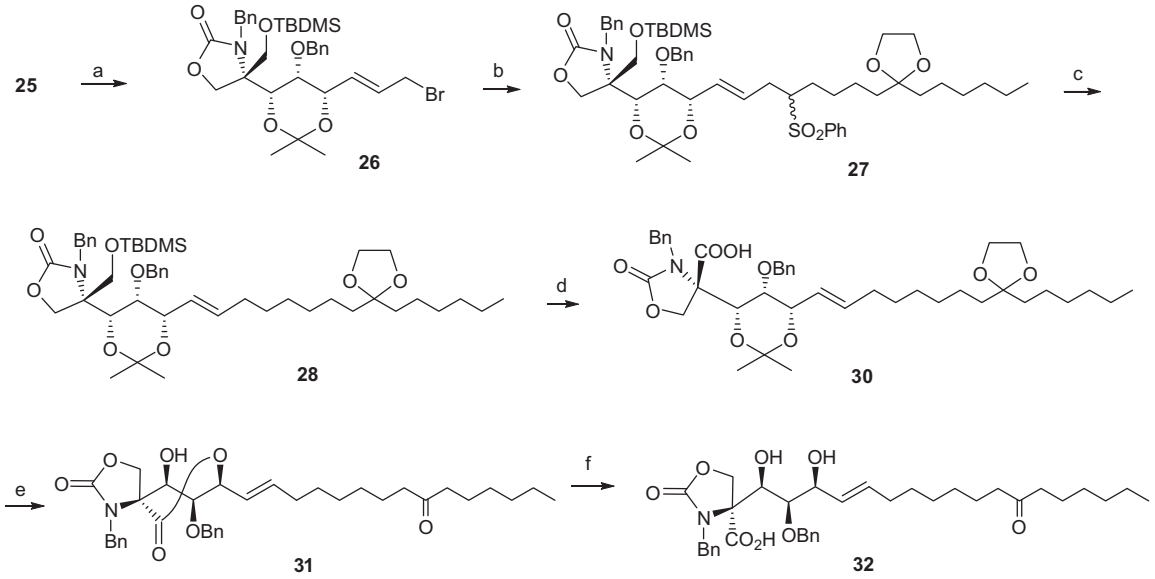
3. Conclusions

In conclusion, the total synthesis of the protected form of sphingofungin E (**32**) has been accomplished starting from the known α-D-glucofuranose **3**. This work demonstrates that our described methodology using an aza-Claisen rearrangement of the allylic thiocyanates derived from various sugar molecules has more general utility, and from this viewpoint it appeared particularly interesting to apply this above-mentioned strategy for the construction of other natural products containing the α-substituted α-amino acid motif. Further studies towards the total synthesis of such compounds are in progress in our laboratory.

4. Experimental

4.1. General methods

All commercial reagents were used in the highest available purity from Aldrich, Fluka, E. Merck or Acros Organics without further purification. Solvents were dried and purified before use according



Scheme 5. Reagent and conditions: (a) (i) MsCl, Et_3N, CH_2Cl_2, 0 °C→rt; (ii) LiBr, THF, rt, 85.5%; (b) **2**,[6e] BuLi, −78 °C, 95%; (c) 6% Na/Hg, CH_3OH, Na_2HPO_4, 0 °C→rt, 64%; (d) (i) TBAF, THF, 0 °C→rt, **29**, 88%; (ii) PDC, DMF, rt, 65%; (e) 2 M aq HCl, THF, reflux, 72%; (f) 10% aq NaOH, CH_3OH, 80 °C, 81%.

to standard procedures. For flash column chromatography on silica gel, Kieselgel 60 (0.040–0.063 mm, 230–400 mesh, E. Merck) was used. Solvents for flash chromatography (hexane, ethyl acetate, MeOH, dichloromethane) were distilled before using. Thin-layer chromatography was run on E. Merck Silica Gel 60 F_{254} analytical plates; detection was carried out with either ultraviolet light (254 nm), or by spraying with a solution of phosphomolybdic acid, potassium permanganate basic solution, a solution of concentrated H_2SO_4 with subsequent heating. ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ and CD_3OD (the deuterium content of used solvents lay between 98% and 99%) at ambient temperature on a Varian Mercury Plus 400 FT NMR (400.13 MHz for ^1H and 100.6 MHz for ^{13}C) or on a Varian Premium COMPACT 600 (599.87 MHz for ^1H and 150.84 MHz for ^{13}C) spectrometers using TMS as internal reference. For ^1H δ are given in parts per million (ppm) relative to TMS ($\delta = 0.0$) and for ^{13}C relative to $CDCl_3$ ($\delta = 77.0$) or CD_3OD ($\delta = 49.05$). The multiplicity of the ^{13}C NMR signals concerning the ^{13}C–^1H coupling was determined by the DEPT method. Chemical shifts (in ppm) and coupling constants (in Hz) were obtained by first-order analysis; assignments were derived from COSY and H/C correlation spectra. Infrared (IR) spectra were measured with a Nicolet Avatar 330 FTIR spectrometer as KBr pellets and expressed in ν values (cm^{-1}). Optical rotations were measured on a P3002 Krüss polarimeter and reported as follows: $[\alpha]_D$ (c in grams per 100 mL, solvent). Melting points were recorded on a Kofler hot block, and are uncorrected. Microwave reactions were carried out in a focused microwave system (CEM Discover). The temperature content of the vessel was monitored using a calibrated infrared sensor mounted under the vessel. At the end of all reactions, the contents of vessel were cooled rapidly using a stream of compressed air. Small quantities of reagents (μL) were measured with appropriate syringes (Hamilton). All reactions were performed under an atmosphere of nitrogen unless otherwise noted.

4.2. 3,6-Bis(*O*-*tert*-butyldimethylsilyl)-1,2-*O*-isopropylidene-α-D-glucofuranose (4)

To a solution of known **3**[9] (17.58 g, 52.56 mmol) in dry CH_2Cl_2 (272 mL) Et_3N (8.89 mL, 63.26 mmol), DMAP (0.91 g, 7.45 mmol) and *tert*-butyldimethylsilyl chloride (9.06 g, 60.11 mmol) were added at room temperature. The resulting mixture was stirred for 20 h at the same temperature and then poured into 1 M aq $KHSO_4$ solution (183 mL). The organic layer was washed with brine (90 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (15:1 hexane–EtOAc) to afford 21.7 g (92%) of crystalline product **4**: mp 56–57 °C; $[\alpha]_D^{20}$ −104.1 (c 0.27, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): δ 0.08 (s, 6H, 2 × CH_3), 0.14 (s, 3H, CH_3), 0.15 (s, 3H, CH_3), 0.90 (s, 9H, 3 × CH_3), 0.91 (s, 9H, 3 × CH_3), 1.31 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 2.52 (d, $J_{5,OH} = 6.2$ Hz, 1H, OH), 3.74 (dd, $J_{6,6} = 10.7$ Hz, $J_{6,5} = 5.7$ Hz, 1H, H-6), 3.81–3.86 (m, 2H, H-6, H-5), 4.02 (dd, $J_{5,4} = 8.5$ Hz, $J_{4,3} = 2.6$ Hz, 1H, H-4), 4.30 (d, $J_{4,3} = 2.6$ Hz, 1H, H-3), 4.35 (d, $J_{2,1} = 3.6$ Hz, 1H, H-2), 5.87 (d, $J_{2,1} = 3.6$ Hz, 1H, H-1). ^{13}C NMR ($CDCl_3$, 100 MHz): δ −5.4 (CH_3), −5.4 (CH_3), −5.2 (CH_3), −4.9 (CH_3), 18.1 (C), 18.3 (C), 25.7 (3 × CH_3), 25.9 (3 × CH_3), 26.4 (CH_3), 26.8 (CH_3), 64.4 (CH_2), 68.0 (CH), 75.5 (CH), 80.2 (CH), 85.4 (CH), 105.1 (CH), 111.7 (C). Anal. Calcd for $C_{21}H_{44}O_6Si_2$: C, 56.21; H, 9.88. Found: C, 56.15; H, 9.95.

4.3. 3,6-Bis(*O*-*tert*-butyldimethylsilyl)-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (5)

To a solution of alcohol **4** (21.7 g, 48.36 mmol) in CH_3CN (422 mL) was added *o*-iodoxybenzoic acid (27.08 g, 96.7 mmol), and the resulting mixture was stirred for 2 h at reflux. After the starting material was completely consumed (judged by TLC), the reaction was stopped and allowed to cool to room temperature. The insoluble materials were removed by filtration, the solvent was evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel (17:1 hexane–EtOAc) to give 20.95 g (97%) of crystalline ketone **5**: mp 65–67 °C; $[\alpha]_D^{20}$ −123.3 (c 0.30, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz): δ 0.04 (s, 3H, CH_3), 0.05 (s, 3H, CH_3), 0.07 (s, 3H, CH_3), 0.09 (s, 3H, CH_3), 0.84 (s, 9H, 3 × CH_3), 0.90 (s, 9H, 3 × CH_3), 1.32 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 4.35 (d, $J_{2,1} = 3.5$ Hz, 1H, H-2), 4.48 (m, 2H, 2 × H-6), 4.55 (d, $J_{4,3} = 3.1$ Hz, 1H, H-3), 4.78 (d, $J_{4,3} = 3.1$ Hz, 1H, H-4), 6.02 (d, $J_{2,1} = 3.5$ Hz, 1H, H-1). ^{13}C NMR ($CDCl_3$, 100 MHz): δ −5.5 (CH_3), −5.4 (CH_3), −5.3 (CH_3), −4.9 (CH_3), 17.9 (C), 18.3 (C), 25.6 (3 × CH_3), 25.8 (3 × CH_3), 26.4 (CH_3), 27.0 (CH_3), 68.7 (CH_2), 77.5 (CH), 84.9 (CH), 85.7 (CH), 105.7 (CH), 112.4 (C), 205.3 (C). Anal. Calcd for $C_{21}H_{42}O_6Si_2$: C, 56.46; H, 9.48. Found: C, 56.55; H, 9.41.

4.4. 3,6-Bis(*O*-*tert*-butyldimethylsilyl)-5-*C*-(*Z*)-carbomethoxymethylene-5-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (6)

To a solution of ketone **5** (20.95 g, 46.89 mmol) in dry toluene (490 mL) was added the stabilized ylide $Ph_3P{=}CHCO_2CH_3$ (39.18 g, 117.2 mmol) and the resulting mixture was stirred at reflux. After 17 h, the reaction mixture did not contain any ketone **5**, the solvent was evaporated under reduced pressure and the residue was purified by column chromatography on silica gel (20:1 hexane–EtOAc) to afford 22.87 g (97%) of α,β-unsaturated ester **6** as a colourless oil: $[\alpha]_D^{20}$ +125.8 (*c* 0.24, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ −0.06 (s, 3H, CH_3), 0.04 (s, 3H, CH_3), 0.06 (s, 6H, 2 × CH_3), 0.84 (s, 9H, 3 × CH_3), 0.91 (s, 9H, 3 × CH_3), 1.33 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 3.70 (s, 3H, OCH_3), 4.35 (d, $J_{2,1}$ = 3.7 Hz, 1H, H-2), 4.40–4.48 (m, 2H, 2 × H-6), 4.67 (d, $J_{4,3}$ = 3.0 Hz, 1H, H-3), 5.82 (m, 1H, H-4), 5.93 (d, $J_{2,1}$ = 3.7 Hz, 1H, H-1), 6.14 (dd, $J_{7,6}$ = 3.9 Hz, $J_{7,6}$ = 2.2 Hz, 1H, H-7). ^{13}C NMR ($CDCl_3$, 100 MHz): δ −5.5 (CH_3), −5.5 (CH_3), −5.3 (CH_3), −5.1 (CH_3), 17.9 (C), 18.2 (C), 25.7 (3 × CH_3), 25.8 (3 × CH_3), 26.6 (CH_3), 27.1 (CH_3), 51.1 (CH_3), 63.2 (CH_2), 77.7 (CH), 80.9 (CH), 85.6 (CH), 104.9 (CH), 111.9 (C), 112.5 (CH), 159.2 (C), 166.7 (C). Anal. Calcd for $C_{24}H_{46}O_7Si_2$: C, 57.33; H, 9.22. Found: C, 57.25; H, 9.31.

4.5. 3,6-Bis(*O*-*tert*-butyldimethylsilyl)-5-deoxy-5-*C*-(*Z*)-(2-hydroxyethylidene)-1,2-*O*-isopropylidene-α-D-glucofuranose (7)

Lithium aluminum hydride (4.31 g, 113.6 mmol) was added portionwise to a solution of ester **6** (22.87 g, 45.48 mmol) in dry Et_2O (280 mL) pre-cooled to 0 °C. The reaction mixture was stirred for a further 15 min at 0 °C and then for 2 h at room temperature. The stirring solution was then quenched by dropwise addition of water (45 mL), and the salts were removed by filtration and washed with Et_2O. The resulting filtrate was dried over Na_2SO_4, the solvent was evaporated in vacuo and the residue was purified on silica gel (7:1 hexane–EtOAc) to give 17.49 g (81%) of alcohol **7** as a colourless oil: $[\alpha]_D^{20}$ +107.8 (*c* 0.25, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.02 (s, 3H, CH_3), 0.06 (s, 6H, 2 × CH_3), 0.08 (s, 3H, CH_3), 0.87 (s, 9H, 3 × CH_3), 0.91 (s, 9H, 3 × CH_3), 1.33 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 4.13–4.29 (m, 5H, H-3, 2 × H-6, 2 × H-8), 4.38 (d, $J_{2,1}$ = 3.7 Hz, 1H, H-2), 4.92 (d, $J_{4,3}$ = 2.5 Hz, 1H, H-4), 5.96 (m, 2H, H-1, H-7). ^{13}C NMR ($CDCl_3$, 100 MHz): δ −5.4 (CH_3), −5.4 (CH_3), −5.0 (CH_3), −4.8 (CH_3), 18.1 (C), 18.3 (C), 25.7 (3 × CH_3), 25.9 (3 × CH_3), 26.3 (CH_3), 26.8 (CH_3), 58.6 (CH_2), 64.7 (CH_2), 77.9 (CH), 80.3 (CH), 85.4 (CH), 104.2 (CH), 111.7 (C), 126.3 (CH), 136.4 (C). Anal. Calcd for $C_{23}H_{46}O_6Si_2$: C, 58.18; H, 9.77. Found: C, 58.09; H, 9.81.

4.6. 3,6-Bis(*O*-*tert*-butyldimethylsilyl)-5-deoxy-1,2-*O*-isopropylidene-5-*C*-(*Z*)-(2-thiocyanatoethylidene)-α-D-glucofuranose (8)

Et_3N (10.4 mL, 74.0 mmol) was added to a solution of alcohol **7** (17.49 g, 36.84 mmol) in dry CH_2Cl_2 (273 mL) pre-cooled to 0 °C and methanesulfonyl chloride (3.42 mL, 44.21 mmol) was then added dropwise. After stirring at 0 °C for 15 min and then at room temperature for 45 min, the solvent was removed under reduced pressure. The residue was diluted with Et_2O (100 mL) and the salts were removed by filtration and washed with Et_2O. Evaporation of the solvent at reduced pressure afforded a crude mesylate that was used in the subsequent reaction directly without further purification. To a solution of crude mesylate (20.37 g, 36.84 mmol) in dry CH_3CN (250 mL) was added KSCN (5.37 g, 55.26 mmol). After stirring for 3 h at room temperature, the solvent was evaporated under reduced pressure. The residue was diluted with Et_2O (100 mL), the salts were filtered off, the solvent was removed and the residue was chromatographed on silica gel (17:1 hexane–EtOAc) to yield 12.73 g (67%) of thiocyanate **8** as a colourless oil: $[\alpha]_D^{20}$ +110.9 (*c* 0.24, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.03 (s, 3H, CH_3), 0.07 (s, 3H, CH_3), 0.07 (s, 3H, CH_3), 0.09 (s, 3H, CH_3), 0.87 (s, 9H, 3 × CH_3), 0.91 (s, 9H, 3 × CH_3), 1.33 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 3.67 (dd, $J_{8,8}$ = 12.6 Hz, $J_{8,7}$ = 7.8 Hz, 1H, H-8), 4.06 (dd, $J_{8,8}$ = 12.6 Hz, $J_{8,7}$ = 8.8 Hz, 1H, H-8), 4.17 (m, 2H, 2 × H-6), 4.19 (d, $J_{4,3}$ = 2.7 Hz, 1H, H-3), 4.38 (d, $J_{2,1}$ = 3.7 Hz, 1H, H-2), 4.85 (d, $J_{4,3}$ = 2.7 Hz, 1H, H-4), 5.86 (m, 1H, H-7), 5.93 (d, $J_{2,1}$ = 3.7 Hz, 1H, H-1). ^{13}C NMR ($CDCl_3$, 100 MHz): δ −5.4 (CH_3), −5.4 (CH_3), −4.9 (CH_3), −4.7 (CH_3), 18.1 (C), 18.3 (C), 25.8 (3 × CH_3), 25.9 (3 × CH_3), 26.3 (CH_3), 26.8 (CH_3), 31.9 (CH_2), 64.8 (CH_2), 77.9 (CH), 80.1 (CH), 85.2 (CH), 104.1 (CH), 111.8 (C), 112.9 (SCN), 120.0 (CH), 139.9 (C). Anal. Calcd for $C_{24}H_{45}NO_5SSi_2$: C, 55.88; H, 8.79; N, 2.72. Found: C, 55.85; H, 8.71; N, 2.75.

4.7. A mixture of 3,6-bis(*O*-*tert*-butyldimethylsilyl)-5-deoxy-1,2-*O*-isopropylidene-5-isothiocyanato-5-*C*-vinyl-α-D-glucofuranose (9) and 3,6-bis(*O*-*tert*-butyldimethylsilyl)-5-deoxy-1,2-*O*-isopropylidene-5-isothiocyanato-5-*C*-vinyl-β-L-idofuranose (10)

4.7.1. Microwave-assisted synthesis

Thiocyanate **8** (0.10 g, 0.194 mmol) was weighed in a 10-mL glass pressure microwave tube equipped with a magnetic stirbar. Heptane (3.6 mL) was added, the tube was closed with a silicone septum and the reaction mixture was subjected to microwave irradiation for 3 h at 90 °C. Evaporation of the solvent and chromatography on silica gel (35:1 hexane–EtOAc) gave 69 mg (69%) of a mixture of diastereoisomeric isothiocyanates **9** and **10** as colourless oils.

4.7.2. Conventional method

A solution of thiocyanate **8** (12.73 g, 24.68 mmol) in heptane (60 mL) was heated at 90 °C for 24 h. Evaporation of the solvent and chromatography on silica gel (35:1 hexane–EtOAc) afforded 9.17 g (72%) of a mixture of isothiocyanates **9** and **10** as colourless oils.

A small amount of the mixture of isothiocyanates was separated by column chromatography on silica gel (35:1 hexane–EtOAc) to afford each diastereoisomer in pure form and for use as analytical samples.

Diastereoisomer **9**: R_f 0.37 (35:1 hexane–EtOAc); $[\alpha]_D^{20}$ −118.6 (*c* 0.29, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.09 (s, 3H, CH_3), 0.11 (s, 3H, CH_3), 0.11 (s, 3H, CH_3), 0.16 (s, 3H, CH_3), 0.89 (s, 9H, 3 × CH_3), 0.92 (s, 9H, 3 × CH_3), 1.32 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 3.46 (d, $J_{6,6}$ = 10.0 Hz, 1H, H-6), 3.79 (d, $J_{6,6}$ = 10.0 Hz, 1H, H-6), 4.31 (d, $J_{2,1}$ = 3.5 Hz, 1H, H-2), 4.35 (d, $J_{4,3}$ = 2.7 Hz, 1H, H-3), 4.52 (d, $J_{4,3}$ = 2.7 Hz, 1H, H-4), 5.17 (d, $J_{8cis,7}$ = 10.7 Hz, 1H, H-8$_{cis}$), 5.35 (d, $J_{8trans,7}$ = 17.2 Hz, 1H, H-8$_{trans}$), 5.91 (d, $J_{2,1}$ = 3.5 Hz, 1H, H-1), 6.03 (dd, $J_{8trans,7}$ = 17.2 Hz, $J_{8cis,7}$ = 10.7 Hz, 1H, H-7). ^{13}C NMR ($CDCl_3$, 100 MHz): δ −5.5 (CH_3), −5.4 (CH_3), −5.0 (CH_3), −4.6 (CH_3), 18.0 (C), 18.2 (C), 25.8 (3 × CH_3), 25.9 (3 × CH_3), 26.5 (CH_3), 27.0 (CH_3), 68.4 (C), 68.4 (CH_2), 76.1 (CH), 79.5 (CH), 85.6 (CH), 105.0 (CH), 112.1 (C), 115.3 (CH_2), 134.0 (CH), 136.4 (C). Anal. Calcd for $C_{24}H_{45}NO_5SSi_2$: C, 55.88; H, 8.79; N, 2.72. Found: C, 55.93; H, 8.83; N, 2.68.

Diastereoisomer **10**: R_f 0.33 (hexane–EtOAc 35:1); $[\alpha]_D^{20}$ +59.5 (*c* 0.60, $CHCl_3$). ^{1}H NMR (C_6D_6, 400 MHz): δ −0.02 (s, 3H, CH_3), 0.01 (s, 3H, CH_3), 0.05 (s, 3H, CH_3), 0.06 (s, 3H, CH_3), 0.92 (s, 9H, 3 × CH_3), 1.00 (s, 9H, 3 × CH_3), 1.09 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 3.73 (d, $J_{6,6}$ = 8.9 Hz, 1H, H-6), 4.05 (d, $J_{6,6}$ = 8.9 Hz, 1H, H-6), 4.25 (d, $J_{4,3}$ = 3.0 Hz, 1H, H-3), 4.37 (d, $J_{2,1}$ = 3.6 Hz, 1H, H-2), 4.50 (d, $J_{4,3}$ = 3.0 Hz, 1H, H-4), 5.02 (dd, $J_{8cis,7}$ = 10.6 Hz, $J_{8trans,8cis}$ = 0.9 Hz, 1H, H-8$_{cis}$), 5.51 (dd, $J_{8trans,7}$ = 17.1 Hz, $J_{8trans,8cis}$ = 0.9 Hz, 1H, H-8$_{trans}$), 5.76 (dd, $J_{8trans,7}$ = 17.1 Hz, $J_{8cis,7}$ = 10.6 Hz, 1H, H-7), 5.97 (d, $J_{2,1}$ = 3.6 Hz, 1H, H-1). ^{13}C NMR ($CDCl_3$, 100 MHz): δ −5.5

(CH_3), −5.5 (CH_3), −4.6 (CH_3), −4.5 (CH_3), 17.9 (C), 18.1 (C), 25.8 (3 × CH_3), 25.8 (3 × CH_3), 26.5 (CH_3), 27.0 (CH_3), 68.4 (CH_2), 68.6 (C), 76.2 (CH), 79.7 (CH), 85.5 (CH), 104.5 (CH), 111.9 (C), 117.1 (CH_2), 133.6 (CH), 136.7 (C). Anal. Calcd for $C_{24}H_{45}NO_5SSi_2$: C, 55.88; H, 8.79; N, 2.72. Found: C, 55.83; H, 8.73; N, 2.78.

4.8. A mixture of (4*S*)-4-[(3a*R*,6*S*,6a*R*)-6-hydroxy-2,2-dimethyltetrahydrofuro[2.3-*d*][1.3]dioxol-5-yl]-4-vinyloxazolidine-2-thione (4*S*-11) and (4*R*)-4-[(3a*R*,6*S*,6a*R*)-6-hydroxy-2,2-dimethyltetrahydrofuro[2.3-*d*][1.3]dioxol-5-yl]-4-vinyloxazolidine-2-thione (4*R*-11)

To a solution of the mixture of isothiocyanates **9** and **10** (8.07 g, 15.6 mmol) in dry THF (156 mL) were added activated 4 Å powdered molecular sieves (2.88 g). The suspension was treated with a 1 M solution of Bu_4NF (15.6 mL, 15.6 mmol) in THF at 0 °C. The resulting reaction mixture was stirred for a further 10 min at 0 °C and then at room temperature for 1 h 20 min. The solid material was removed by filtration, and washed with tetrahydrofuran, and the solvent was evaporated. The residue was partitioned between EtOAc (45 mL) and brine (55 mL), and the water phase was extracted with further portions of EtOAc (2 × 40 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated and the residue was chromatographed on silica gel (1:1 hexane–EtOAc) to afford 3.37 g (75%) of a mixture of thiocarbamates **11** as a colourless oil.

A small amount of the mixture of thiocarbamates was separated by column chromatography on silica gel (1:1 hexane–EtOAc) to give each diastereoisomer in pure form and for use as analytical samples.

Diastereoisomer (4*S*-**11**): R_f 0.29 (1:1 hexane–EtOAc); $[\alpha]_D^{20}$ +107.4 (*c* 0.25, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.32 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 4.14 (d, $J_{4,3}$ 2.8 Hz, 1H, H-4), 4.36 (d, $J_{4,3}$ 2.8 Hz, 1H, H-3), 4.46 (d, $J_{6,6}$ 8.6 Hz, 1H, H-6), 4.61 (d, $J_{2,1}$ 3.4 Hz, 1H, H-2), 4.85 (d, $J_{6,6}$ 8.6 Hz, 1H, H-6), 5.43 (d, $J_{8cis,7}$ 10.7 Hz, 1H, H-8$_{cis}$), 5.44 (d, $J_{8trans,7}$ 17.3 Hz, 1H, H-8$_{trans}$), 5.95 (dd, $J_{8trans,7}$ 17.3 Hz, $J_{8cis,7}$ 10.7 Hz, 1H, H-7), 6.01 (d, $J_{2,1}$ 3.7 Hz, 1H, H-1), 8.00 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 26.1 (CH_3), 26.8 (CH_3), 67.3 (C), 75.2 (CH), 78.4 (CH_2), 80.2 (CH), 85.2 (CH), 104.9 (CH), 112.1 (C), 117.7 (CH_2), 134.9 (CH), 189.9 (C). Anal. Calcd for $C_{12}H_{17}NO_5S$: C, 50.16; H, 5.96; N, 4.87. Found: C, 50.13; H, 5.98; N, 4.92.

Diastereoisomer (4*R*-**11**): R_f 0.25 (hexane–EtOAc, 1:1); $[\alpha]_D^{20}$ −47.3 (*c* 0.37, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.31 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 4.32 (d, $J_{4,3}$ 3.1 Hz, 1H, H-3), 4.34 (d, $J_{4,3}$ 3.1 Hz, 1H, H-4), 4.41 (d, $J_{6,6}$ 9.4 Hz, 1H, H-6), 4.53 (d, $J_{2,1}$ 3.7 Hz, 1H, H-2), 4.94 (d, $J_{6,6}$ 9.4 Hz, 1H, H-6), 5.40 (d, $J_{8cis,7}$ 10.7 Hz, 1H, H-8$_{cis}$), 5.48 (d, $J_{8trans,7}$ 17.3 Hz, 1H, H-8$_{trans}$), 6.02 (d, $J_{2,1}$ 3.7 Hz, 1H, H-1), 6.05 (dd, $J_{8trans,7}$ 17.3 Hz, $J_{8cis,7}$ 10.7 Hz, 1H, H-7), 8.46 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 26.2 (CH_3), 26.8 (CH_3), 67.3 (C), 74.5 (CH), 77.6 (CH_2), 82.0 (CH), 85.5 (CH), 105.0 (CH), 112.0 (C), 117.6 (CH_2), 135.7 (CH), 188.9 (C). Anal. Calcd for $C_{12}H_{17}NO_5S$: C, 50.16; H, 5.96; N, 4.87. Found: C, 50.23; H, 5.93; N, 4.82.

4.9. A mixture of (4*S*)-4-[(3a*R*,6*S*,6a*R*)-6-hydroxy-2,2-dimethyltetrahydrofuro[2.3-*d*][1.3]dioxol-5-yl]-4-vinyloxazolidine-2-one (4*S*-12) and (4*R*)-4-[(3a*R*,6*S*,6a*R*)-6-hydroxy-2,2-dimethyltetrahydrofuro[2.3-*d*][1.3]dioxol-5-yl]-4-vinyloxazolidine-2-one (4*R*-12)

To a solution of the mixture of thiocarbamates **11** (3.37 g, 11.73 mmol) in dry CH_3CN (114 mL) was added mesitylnitrile oxide (2.27 g, 14.1 mmol). The reaction mixture was stirred at room temperature for 30 min. Evaporation of the solvent left a residue that was purified by column chromatography on silica gel (1:2 hexane–EtOAc) to give 3.02 g (95%) of a mixture of carbamates **12** as a colourless oil.

A small amount of the mixture of carbamates was separated by column chromatography on silica gel (1:2 hexane–EtOAc) to provide each diastereoisomer in pure form for use as analytical samples.

Diastereoisomer (4*S*-**12**): R_f 0.21 (1:2 hexane–EtOAc); mp 142–143 °C; $[\alpha]_D^{20}$ +132.1 (*c* 0.27, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.31 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 4.06 (d, $J_{4,3}$ 2.8 Hz, 1H, H-4), 4.17 (d, $J_{6,6}$ 8.2 Hz, 1H, H-6), 4.26 (m, 1H, H-3), 4.47 ($J_{3,OH}$ 2.4 Hz, 1H, OH), 4.53 (d, $J_{2,1}$ 3.5 Hz, 1H, H-2), 4.59 (d, $J_{6,6}$ 8.2 Hz, 1H, H-6), 5.36 (d, $J_{8cis,7}$ 10.7 Hz, 1H, H-8$_{cis}$), 5.46 (d, $J_{8trans,7}$ 17.3 Hz, 1H, H-8$_{trans}$), 5.95 (dd, $J_{8trans,7}$ 17.3 Hz, $J_{8cis,7}$ 10.7 Hz, 1H, H-7), 6.00 (d, $J_{2,1}$ 3.5 Hz, 1H, H-1), 6.40 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 26.1 (CH_3), 26.8 (CH_3), 62.8 (C), 73.9 (CH_2), 75.3 (CH), 81.4 (CH), 85.1 (CH), 104.9 (CH), 111.8 (C), 116.6 (CH_2), 136.2 (CH), 160.4 (C). Anal. Calcd for $C_{12}H_{17}NO_6$: C, 53.13; H, 4.32; N, 5.16. Found: C, 53.15; H, 4.38; N, 5.12.

Diastereoisomer (4*R*-**12**): R_f 0.16 (hexane–EtOAc, 1:2); $[\alpha]_D^{20}$ −44.3 (*c* 0.26, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.31 (s, 3H, CH_3), 1.49 (s, 3H, CH_3), 3.29 (br d, $J_{3,OH}$ 2.5 Hz, 1H, OH), 4.14 (d, $J_{6,6}$ 9.0 Hz, 1H, H-6), 4.15 (d, $J_{4,3}$ 3.3 Hz, 1H, H-4), 4.31 (m, 1H, H-3), 4.50 (d, $J_{2,1}$ 3.6 Hz, 1H, H-2), 4.68 (d, $J_{6,6}$ 9.0 Hz, 1H, H-6), 5.34 (d, $J_{8cis,7}$ 10.7 Hz, 1H, H-8$_{cis}$), 5.45 (d, $J_{8trans,7}$ 17.3 Hz, 1H, H-8$_{trans}$), 6.01 (d, $J_{2,1}$ 3.6 Hz, 1H, H-1), 6.10 (dd, $J_{8trans,7}$ 17.3 Hz, $J_{8cis,7}$ 10.7 Hz, 1H, H-7), 6.35 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 26.2 (CH_3), 26.8 (CH_3), 62.8 (C), 73.0 (CH_2), 74.7 (CH), 82.9 (CH), 85.5 (CH), 105.0 (CH), 112.0 (C), 116.2 (CH_2), 137.1 (CH), 159.8 (C). Anal. Calcd for $C_{12}H_{17}NO_6$: C, 53.13; H, 4.32; N, 5.16. Found: C, 53.03; H, 4.28; N, 5.20.

4.10. (4*S*)-3-Acetyl-4-[(3a*R*,6*S*,6a*R*)-6-acetoxy-2,2-dimethyltetrahydrofuro[2.3-*d*][1.3]dioxol-5-yl]-4-vinyloxazolidine-2-one (13) and (4*R*)-3-acetyl-4-[(3a*R*,6*S*,6a*R*)-6-acetoxy-2,2-dimethyltetrahydrofuro[2.3-*d*][1.3]dioxol-5-yl]-4-vinyloxazolidine-2-one (14)

To a solution of the mixture of carbamates **12** (3.02 g, 11.1 mmol) in pyridine (85 mL) were added DMAP (0.27 g, 2.21 mmol) and Ac_2O (3.16 mL, 33.43 mmol) at room temperature. The resulting reaction mixture was stirred overnight at the same temperature, then poured into ice water (160 mL) and extracted with Et_2O (3 × 45 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated and the residue was chromatographed on silica gel (5:1 hexane–EtOAc) to afford 2.24 g (57%) of **13** and 1.12 g (28%) of **14** as white crystals.

Diastereoisomer **13**: R_f 0.35 (3:1 hexane–EtOAc); mp 128 °C; $[\alpha]_D^{20}$ +120.0 (*c* 0.25, $CHCl_3$); IR (KBr) ν_{max} (cm^{-1}) 2991, 1780, 1756, 1707, 1644, 1483, 1374, 1292, 1215. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.31 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 2.10 (s, 3H, CH_3CO), 2.48 (s, 3H, CH_3CO), 4.06 (d, $J_{6,6}$ 9.3 Hz, 1H, H-6), 4.45 (d, $J_{2,1}$ 3.8 Hz, 1H, H-2), 4.85 (d, $J_{6,6}$ 9.3 Hz, 1H, H-6), 5.13 (d, $J_{4,3}$ 3.2 Hz, 1H, H-4), 5.25 (d, $J_{4,3}$ 3.2 Hz, 1H, H-3), 5.30 (d, $J_{8trans,7}$ 17.4 Hz, 1H, H-8$_{trans}$), 5.32 (d, $J_{8cis,7}$ 10.8 Hz, 1H, H-8$_{cis}$), 6.00 (d, $J_{2,1}$ 3.8 Hz, 1H, H-1), 6.14 (dd, $J_{8trans,7}$ 17.4 Hz, $J_{8cis,7}$ 10.8 Hz, 1H, H-7). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.5 (CH_3), 24.6 (CH_3), 26.3 (CH_3), 26.8 (CH_3), 63.4 (C), 69.5 (CH_2), 76.6 (CH), 79.1 (CH), 83.5 (CH), 105.1 (CH), 112.7 (C), 115.4 (CH_2), 138.2 (CH), 153.7 (C), 169.2 (C), 170.7 (C). Anal. Calcd for $C_{16}H_{21}NO_8$: C, 54.08; H, 5.96; N, 3.94. Found: C, 54.11; H, 5.90; N, 4.00.

Diastereoisomer **14**: R_f 0.20 (3:1 hexane–EtOAc); mp 207–211 °C; $[\alpha]_D^{20}$ −51.2 (*c* 0.26, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.31 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 2.08 (s, 3H, CH_3CO), 2.54 (s, 3H, CH_3CO), 4.21 (d, $J_{6,6}$ 9.2 Hz, 1H, H-6), 4.47 (d, $J_{2,1}$ 3.7 Hz, 1H, H-2), 4.75 (d, $J_{6,6}$ 9.2 Hz, 1H, H-6), 5.23 (d, $J_{4,3}$ 3.4 Hz, 1H, H-3), 5.34 (d, $J_{8trans,7}$ 17.5 Hz, 1H, H-8$_{trans}$), 5.39 (d, $J_{8cis,7}$ 10.9 Hz, 1H,

H-8$_{cis}$), 5.56 (d, $J_{4,3}$ 3.4 Hz, 1H, H-4), 5.95 (d, $J_{2,1}$ 3.7 Hz, 1H, H-1), 6.14 (dd, $J_{8trans,7}$ 17.5 Hz, $J_{8cis,7}$ 10.9 Hz, 1H, H-7). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.0 (CH_3), 25.6 (CH_3), 26.5 (CH_3), 26.9 (CH_3), 66.3 (C), 67.5 (CH_2), 76.1 (CH), 76.7 (CH), 83.5 (CH), 104.7 (CH), 113.0 (C), 117.9 (CH_2), 133.6 (CH), 153.5 (C), 168.7 (C), 171.3 (C). Anal. Calcd for $C_{16}H_{21}NO_8$: C, 54.08; H, 5.96; N, 3.94. Found: C, 54.03; H, 6.01; N, 3.90.

4.11. (4*S*)-3-Benzyl-4-[(3a*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2.3-*d*][1.3]dioxol-5-yl]-4-vinyloxazolidin-2-one (15)

To a solution of acetate **13** (1.62 g, 4.56 mmol) in MeOH (51 mL) was added K_2CO_3 (0.126 g, 0.91 mmol) at room temperature. After 25 min, at which point no starting material was detected (TLC), the reaction mixture was then neutralised with Amberlite IR-120 (H^+) and filtered. Evaporation of the solvent and chromatography on silica gel (1:2 hexane–EtOAc) afforded 1.17 g (95%) of **12*S***. Compound **12*S*** (1.17 g, 4.31 mmol) was dissolved in dry DMF (17.4 mL) and to this solution pre-cooled to 0 °C was added NaH (0.45 g, 8.53 mmol, 60% dispersion in mineral oil, freed of oil with anhyd THF). The reaction was stirred for 10 min at 0 °C, then benzyl bromide (1.51 mL, 12.62 mmol) and tetrabutylammonium iodide (33 mg, 0.09 mmol) were added at the same temperature. The mixture was allowed to warm to room temperature and the stirring was continual for another 30 min. The excess hydride was decomposed with MeOH (1.3 mL) and the mixture was partitioned between ice water (45 mL) and Et_2O (50 mL). The aqueous phase was extracted with an additional portion of Et_2O (50 mL), the combined organic layers were dried over Na_2SO_4, the solvent was evaporated and the residue was chromatographed on silica gel (3:1 hexane–EtOAc) to give 1.87 g (96%) of compound **15** as a colourless oil: $[\alpha]_D^{20}$ −58.3 (*c* 0.23, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.22 (s, 3H, CH_3), 1.24 (s, 3H, CH_3), 3.47 (d, $J_{4,3}$ 3.6 Hz, 1H, H-3), 3.97 (d, $J_{6,6}$ 8.7 Hz, 1H, H-6), 4.10 (d, $J_{H,H}$ 15.1 Hz, 1H, NCH_2Ph), 4.17 (d, $J_{4,3}$ 3.6 Hz, 1H, H-4), 4.28 (d, $J_{6,6}$ 8.7 Hz, 1H, H-6), 4.36 (d, $J_{H,H}$ 11.4 Hz, 1H, OCH_2Ph), 4.43 (d, $J_{2,1}$ 3.9 Hz, 1H, H-2), 4.47 (d, $J_{H,H}$ 11.4 Hz, 1H, OCH_2Ph), 4.76 (d, $J_{H,H}$ 15.1 Hz, 1H, NCH_2Ph), 5.25 (d, $J_{8trans,7}$ 17.6 Hz, 1H, H-8$_{trans}$), 5.37 (d, $J_{8cis,7}$ 10.8 Hz, 1H, H-8$_{cis}$), 5.91 (d, $J_{2,1}$ 3.9 Hz, 1H, H-1), 6.09 (dd, $J_{8trans,7}$ 17.6 Hz, $J_{8cis,7}$ 10.8 Hz, 1H, H-7), 7.25–7.45 (m, 10H, Ph). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 26.1 (CH_3), 26.6 (CH_3), 45.8 (CH_2), 65.7 (C), 69.7 (CH_2), 72.1 (CH_2), 81.0 (CH), 81.2 (CH), 82.6 (CH), 105.2 (CH), 111.6 (C), 116.7 (CH_2), 127.7 (CH_{Ph}), 128.2 (2 × CH_{Ph}), 128.3 (CH_{Ph}), 128.5 (2 × CH_{Ph}), 128.6 (2 × CH_{Ph}), 128.8 (2 × CH_{Ph}), 136.3 (CH), 137.6 (C_i), 138.2 (C_i), 158.7 (C). Anal. Calcd for $C_{26}H_{29}NO_6$: C, 69.16; H, 6.47; N, 3.10. Found: C, 69.21; H, 6.42; N, 3.12.

4.12. (4*S*)-3-Benzyl-4-[(3a*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2.3-*d*][1.3]dioxol-5-yl]-2-oxooxazolidine-4-carbaldehyde (16)

Ozone was introduced into a solution of **15** (1.87 g, 4.14 mmol) in dry MeOH (118 mL) at −78 °C for 1 h. This resulted in the formation of a slightly blue solution. Dry N_2 was passed through the cold solution in order to remove excess of ozone. Then, Ph_3P (1.09 g, 4.14 mmol) in CH_2Cl_2 (60 mL) was added and the stirred mixture was allowed to warm to room temperature. After 1.5 h, the solvent was evaporated, and the residue was purified by column chromatography on silica gel (1:1 hexane–EtOAc) to afford 1.67 g (89%) of aldehyde **16** as a colourless oil that was used immediately in the next step. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.25 (s, 3H, CH_3), 1.30 (s, 3H, CH_3), 3.77 (d, $J_{6,6}$ 9.6 Hz, 1H, H-6), 3.94 (d, $J_{4,3}$ 3.6 Hz, 1H, H-3 or H-4), 4.30 (d, $J_{6,6}$ 9.6 Hz, 1H, H-6), 4.37 (d, $J_{H,H}$ 15.4 Hz, 1H, NCH_2Ph), 4.39 (d, $J_{H,H}$ 11.5 Hz, 1H, OCH_2Ph), 4.46 (d, $J_{4,3}$ 3.6 Hz, 1H, H-3 or H-4), 4.61 (d, $J_{2,1}$ 3.8 Hz, 1H, H-2), 4.63 (d, $J_{H,H}$ 11.5 Hz, 1H, OCH_2Ph), 4.79 (d, $J_{H,H}$ 15.4 Hz, 1H, NCH_2Ph), 6.00 (d, $J_{2,1}$ 3.8 Hz, 1H, H-1), 7.22–7.30 (m, 4H, Ph), 7.35–7.41 (m, 6H, Ph), 9.60 (s, 1H, CHO). Anal. Calcd for $C_{25}H_{27}NO_7$: C, 66.21; H, 6.00; N, 3.09. Found: C, 66.16; H, 6.06; N, 3.12.

4.13. (4*S*)-3-Benzyl-4-[(3a*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2.3-*d*][1.3]dioxol-5-yl]-4-(hydroxymethyl)-oxazolidin-2-one (17)

To a solution of **16** (1.67 g, 3.68 mmol) in MeOH (30 mL) that was pre-cooled to 0 °C was added $NaBH_4$ (0.154 g, 4.07 mmol). The resulting mixture was stirred for 10 min at 0 °C and for an additional 20 min at room temperature. The mixture was neutralized with Amberlite IR-120 (H^+). The insoluble materials were removed by filtration, the solvent was evaporated and the residue was chromatographed on silica gel (1:1 hexane–EtOAc) to afford 1.59 g (95%) of alcohol **17** as a colourless oil: $[\alpha]_D^{20}$ −65.9 (*c* 0.19, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.28 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 3.58 (d, $J_{4,3}$ 3.5 Hz, 1H, H-3), 3.69 (d, $J_{H,H}$ 12.2 Hz, 1H, CH_2O), 3.74 (d, $J_{H,H}$ 12.2 Hz, 1H, CH_2O), 4.11 (d, $J_{6,6}$ 8.8 Hz, 1H, H-6), 4.21 (d, $J_{4,3}$ 3.5 Hz, 1H, H-4), 4.28 (d, $J_{6,6}$ 8.8 Hz, 1H, H-6), 4.41 (d, $J_{H,H}$ 11.4 Hz, 1H, OCH_2Ph), 4.46 (d, $J_{2,1}$ 3.9 Hz, 1H, H-2), 4.47 (d, $J_{H,H}$ 15.1 Hz, 1H, NCH_2Ph), 4.50 (d, $J_{H,H}$ 11.4 Hz, 1H, OCH_2Ph), 4.55 (d, $J_{H,H}$ 15.1 Hz, 1H, NCH_2Ph), 5.89 (d, $J_{2,1}$ 3.9 Hz, 1H, H-1), 7.30–7.40 (m, 8H, Ph), 7.42–7.46 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 26.1 (CH_3), 26.6 (CH_3), 45.3 (CH_2), 63.5 (CH_2), 64.9 (C), 66.5 (CH_2), 72.1 (CH_2), 81.0 (CH), 81.1 (CH), 82.1 (CH), 105.0 (CH), 111.8 (C), 128.0 (CH_{Ph}), 128.4 (CH_{Ph}), 128.5 (2 × CH_{Ph}), 128.5 (2 × CH_{Ph}), 128.6 (2 × CH_{Ph}), 128.9 (2 × CH_{Ph}), 136.1 (C_i), 138.3 (C_i), 158.9 (C). Anal. Calcd for $C_{25}H_{29}NO_7$: C, 65.92; H, 6.42; N, 3.08. Found: C, 65.86; H, 6.48; N, 3.12.

4.14. (4*S*)-4-(Acetoxymethyl)-3-benzyl-4-[(3a*R*,6*S*,6a*R*)-6-(benzyloxy)-2,2-dimethyltetrahydrofuro[2.3-*d*][1.3]dioxol-5-yl]-oxazolidin-2-one (18)

To a solution of **17** (1.59 g, 3.49 mmol) in pyridine (26.4 mL) were added DMAP (43 mg, 0.35 mmol) and Ac_2O (0.50 mL, 5.29 mmol) at room temperature. After 30 min, no starting compound was detected (TLC) in the reaction mixture, which was then poured into ice water (50 mL) and extracted with Et_2O (3 × 35 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated in vacuo, and the residue was subjected to flash chromatography on silica gel (3:1 hexane–EtOAc) to afford 1.63 g (94%) of crystalline derivative **18**: mp 158–160 °C; $[\alpha]_D^{20}$ −80.8 (*c* 0.23, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.27 (s, 3H, CH_3), 1.28 (s, 3H, CH_3), 1.98 (s, 3H, CH_3CO), 3.69 (d, $J_{4,3}$ 3.6 Hz, 1H, H-3), 4.11 (s, 2H, 2 × H-6), 4.19 (d, $J_{4,3}$ 3.6 Hz, 1H, H-4), 4.27 (d, $J_{H,H}$ 12.4 Hz, 1H, CH_2O), 4.36 (d, $J_{H,H}$ 15.3 Hz, 1H, NCH_2Ph), 4.39 (d, $J_{H,H}$ 11.6 Hz, 1H, OCH_2Ph), 4.44 (d, $J_{H,H}$ 12.4 Hz, 1H, CH_2O), 4.47 (d, $J_{2,1}$ 3.8 Hz, 1H, H-2), 4.53 (d, $J_{H,H}$ 15.3 Hz, 1H, NCH_2Ph), 4.55 (d, $J_{H,H}$ 11.6 Hz, 1H, OCH_2Ph), 5.91 (d, $J_{2,1}$ 3.8 Hz, 1H, H-1), 7.24–7.44 (m, 10H, Ph). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.6 (CH_3), 26.1 (CH_3), 26.6 (CH_3), 45.1 (CH_2), 63.8 (CH_2), 63.8 (C), 66.8 (CH_2), 72.0 (CH_2), 80.8 (CH), 81.9 (CH), 82.0 (CH), 105.1 (CH), 111.9 (C), 127.7 (CH_{Ph}), 128.4 (2 × CH_{Ph}), 128.5 (2 × CH_{Ph}), 128.5 (CH_{Ph}), 128.6 (2 × CH_{Ph}), 128.7 (2 × CH_{Ph}), 135.9 (C_i), 137.8 (C_i), 158.4 (C), 170.4 (C). Anal. Calcd for $C_{27}H_{31}NO_8$: C, 65.18; H, 6.28; N, 2.82. Found: C, 65.25; H, 6.23; N, 2.92.

4.15. Ethyl (4*S*,5*R*,6*R*,2*E*)-6-[(*S*)-4′-(acetoxymethyl)-3′-benzyl-2′-oxooxazolidin-4′-yl]-5-(benzyloxy)-4,6-dihydroxyhex-2-enoate (20)

Compound **18** (1.63 g, 3.28 mmol) was treated with a mixture of 4:1 TFA–H_2O (27 mL) for 1.5 h at room temperature. The solvent

was removed under reduced pressure, and the residue was subjected to flash chromatography through a short column of silica gel (1:2 hexane–EtOAc) to afford 1.41 g (94%) of furanose **19** as a colourless oil. The obtained lactol **19** (1.41 g, 3.08 mmol) was dissolved in dry dichloromethane (18 mL), and to this solution were successively added benzoic acid (38 mg, 0.31 mmol) and the stabilized ylide, $Ph_3P{=}CHCO_2Et$, (3.20 g, 9.19 mmol) at room temperature. After 19 h, the mixture did not contain (TLC) any starting compound **19**. Evaporation of the solvent and chromatography of the residue on silica gel (1:1 hexane/EtOAc) gave 1.48 g (91%) of unsaturated ester **20** as a colourless oil which was used immediately in the next step to avoid problems connected with its possible instability. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.31 (t, J 7.1 Hz, 3H, CH_3), 1.97 (s, 3H, CH_3CO), 3.45 (m, 1H, H-5), 3.84 (m, 1H, H-6), 3.93 (m, 1H, H-4), 3.97 (d, $J_{5',5'}$ 9.1 Hz, 1H, H-5′), 4.20 (d, $J_{H,H}$ 12.5 Hz, 1H, CH_2O), 4.21 (q, J = 7.1 Hz, 2H, CH_2), 4.29 (d, $J_{H,H}$ 12.5 Hz, 1H, CH_2O), 4.36 (d, $J_{H,H}$ 15.6 Hz, 1H, NCH_2Ph), 4.55–4.59 (m, 3H, NCH_2Ph, OCH_2Ph), 4.96 (d, $J_{5',5'}$ 9.1 Hz, 1H, H-5′), 6.01 (dd, $J_{3,2}$ 15.7 Hz, $J_{4,2}$ 2.0 Hz, 1H, H-2), 6.78 (dd, $J_{3,2}$ 15.7 Hz, $J_{4,3}$ 4.2 Hz, 1H, H-3), 7.28–7.43 (m, 10H, Ph). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.2 (CH_3), 20.6 (CH_3), 45.3 (CH_2), 60.6 (CH_2), 63.6 (CH_2), 65.3 (C), 65.4 (CH_2), 70.0 (CH), 71.6 (CH), 74.2 (CH_2), 76.5 (CH), 121.6 (CH), 128.1 (CH_{Ph}), 128.5 ($4 \times CH_{Ph}$), 128.6 (CH_{Ph}), 128.7 ($2 \times CH_{Ph}$), 128.8 ($2 \times CH_{Ph}$), 136.4 (C_i), 137.5 (C_i), 145.9 (CH), 159.0 (C), 166.0 (C), 170.2 (C). Anal. Calcd for $C_{28}H_{33}NO_9$: C, 63.75; H, 6.30; N, 2.65. Found: C, 63.71; H, 6.33; N, 2.69.

4.16. Ethyl (4*S*,5*R*,6*R*,2*E*)-6-[(*S*)-4′-(acetoxymethyl)-3′-benzyl-2′-oxooxazolidin-4′-yl]-5-(benzyloxy)-4,6-(isopropylidenedioxy)-hex-2-enoate (21)

To a solution of ester **20** (1.41 g, 2.67 mmol) in 2,2-dimethoxypropane (22.8 mL) was added CSA (0.123 g, 0.53 mmol) at room temperature. After being stirred for 3 h, the solvent was evaporated in vacuo and the residue was partitioned between CH_2Cl_2 (50 mL) and satd aq $NaHCO_3$ (15 mL). The organic layer was dried over Na_2SO_4, and concentrated, and the residue was purified by flash chromatography on silica gel (2:1 hexane–EtOAc) to afford 1.23 g (81%) of **21** as a colourless oil: $[\alpha]_D^{20}$ −44.2 (*c* 0.27, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.20 (s, 3H, CH_3), 1.26 (t, J 7.1 Hz, 3H, CH_3), 1.37 (s, 3H, CH_3), 2.05 (s, 3H, CH_3CO), 2.77 (t, $J_{6,5}$ = 1.4 Hz, $J_{5,4}$ 1.4 Hz, 1H, H-5), 3.80 (d, $J_{6,5}$ 1.4 Hz, 1H, H-6), 3.84 (d, $J_{5',5'}$ 8.8 Hz, 1H, H-5′), 3.96 (ddd, $J_{4,3}$ 4.7 Hz, $J_{4,2}$ 1.8 Hz, $J_{5,4}$ 1.4 Hz, 1H, H-4), 4.17 (q, J = 7.1 Hz, 2H, CH_2), 4.18 (d, $J_{H,H}$ 12.4 Hz, 1H, CH_2O), 4.20 (d, $J_{H,H}$ 10.4 Hz, 1H, OCH_2Ph), 4.24 (d, $J_{H,H}$ 15.4 Hz, 1H, NCH_2Ph), 4.34 (d, $J_{H,H}$ 10.4 Hz, 1H, OCH_2Ph), 4.37 (d, $J_{H,H}$ 12.4 Hz, 1H, CH_2O), 4.78 (d, $J_{H,H}$ 15.4 Hz, 1H, NCH_2Ph), 4.96 (d, $J_{5',5'}$ 8.8 Hz, 1H, H-5′), 6.01 (dd, $J_{3,2}$ 15.6 Hz, $J_{4,2}$ 1.8 Hz, 1H, H-2), 6.72 (dd, $J_{3,2}$ 15.6 Hz, $J_{4,3}$ 4.7 Hz, 1H, H-3), 7.27–7.33 (m, 5H, Ph), 7.36–7.43 (m, 3H, Ph), 7.44–7.48 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.2 (CH_3), 18.5 (CH_3), 20.7 (CH_3), 29.1 (CH_3), 45.7 (CH_2), 60.5 (CH_2), 64.0 (CH_2), 64.3 (C), 66.1 (CH_2), 71.7 (CH), 72.1 (CH), 72.6 (CH), 74.4 (CH_2), 99.5 (C), 122.4 (CH), 127.8 (CH_{Ph}), 128.2 ($2 \times CH_{Ph}$), 128.3 (CH_{Ph}), 128.4 ($2 \times CH_{Ph}$), 128.8 ($2 \times CH_{Ph}$), 128.9 ($2 \times CH_{Ph}$), 136.9 (C_i), 138.1 (C_i), 142.9 (CH), 159.0 (C), 165.9 (C), 170.3 (C). Anal. Calcd for $C_{31}H_{37}NO_9$: C, 65.59; H, 6.57; N, 2.47. Found: C, 65.55; H, 6.63; N, 2.53.

4.17. Ethyl (4*S*,5*R*,6*R*,2*E*)-6-[(*S*)-3′-benzyl-4′-(hydroxymethyl)-2′-oxooxazolidin-4′-yl]-5-(benzyloxy)-4,6-(isopropylidenedioxy)-hex-2-enoate (22)

NaOEt (29.4 mg, 0.43 mmol) was added to a solution of **21** (1.23 g, 2.17 mmol) in EtOH (13.7 mL) that was pre-cooled to 0 °C. The reaction mixture was stirred at 0 °C for 1 h, then neutralized with Amberlite IR-120 (H^+) at the same temperature. The insoluble materials were removed by filtration, the solvent was evaporated and the residue was chromatographed on silica gel (1:1 hexane–EtOAc). This procedure yielded 1.05 g (92%) of **22** as a colourless oil: $[\alpha]_D^{20}$ −45.3 (*c* 0.40, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.25 (t, J 7.1 Hz, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 2.84 (m, 1H, H-5), 3.70 (d, $J_{H,H}$ 11.9 Hz, 1H, CH_2O), 3.74 (d, $J_{H,H}$ 11.9 Hz, 1H, CH_2O), 3.84 (d, $J_{5',5'}$ 8.6 Hz, 1H, H-5′), 3.96 (d, $J_{6,5}$ 1.4 Hz, 1H, H-6), 4.04 (ddd, $J_{4,3}$ 4.7 Hz, $J_{4,2}$ 1.8 Hz, $J_{5,4}$ 1.4 Hz, 1H, H-4), 4.17 (q, J 7.1 Hz, 2H, CH_2), 4.24 (d, $J_{H,H}$ 10.2 Hz, 1H, OCH_2Ph), 4.39 (d, $J_{H,H}$ 10.2 Hz, 1H, OCH_2Ph), 4.55 (d, $J_{H,H}$ 15.2 Hz, 1H, NCH_2Ph), 4.64 (d, $J_{H,H}$ 15.2 Hz, 1H, NCH_2Ph), 4.91 (d, $J_{5',5'}$ 8.6 Hz, 1H, H-5′), 6.04 (dd, $J_{3,2}$ 15.6 Hz, $J_{4,2}$ 1.8 Hz, 1H, H-2), 6.78 (dd, $J_{3,2}$ 15.6 Hz, $J_{4,3}$ 4.7 Hz, 1H, H-3), 7.29–7.31 (m, 5H, Ph), 7.39–7.42 (m, 3H, Ph), 7.50–7.52 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.2 (CH_3), 18.8 (CH_3), 29.2 (CH_3), 45.7 (CH_2), 60.5 (CH_2), 64.1 (CH_2), 65.6 (C), 66.1 (CH_2), 71.6 (CH), 72.0 (CH), 72.8 (CH), 74.3 (CH_2), 99.4 (C), 122.3 (CH), 127.7 (CH_{Ph}), 128.1 ($2 \times CH_{Ph}$), 128.3 ($2 \times CH_{Ph}$), 128.4 (CH_{Ph}), 128.9 ($2 \times CH_{Ph}$), 129.0 ($2 \times CH_{Ph}$), 137.1 (C_i), 138.5 (C_i), 143.2 (CH), 159.3 (C), 166.0 (C). Anal. Calcd for $C_{29}H_{35}NO_8$: C, 66.27; H, 6.71; N, 2.66. Found: C, 66.35; H, 6.65; N, 2.73.

4.18. Ethyl (4*S*,5*R*,6*R*,2*E*)-6-[(*R*)-3′-benzyl-4′-[(*tert*-butyldimethylsilyloxy)methyl]-2′-oxooxazolidin-4′-yl]-5-(benzyloxy)-4,6-(isopropylidenedioxy)hex-2-enoate (23)

To a solution of **22** (1.05 g, 2.00 mmol) and 2,6-lutidine (0.70 mL, 6.01 mmol) in dry CH_2Cl_2 (12.3 mL), pre-cooled to 0 °C, was added *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.69 mL, 3.00 mmol). The reaction mixture was stirred at room temperature for 30 min and then poured into satd aq $NaHCO_3$ (30 mL). The aq phase was extracted with additional portions of CH_2Cl_2 (2×25 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated, and the residue was purified by flash chromatography on silica gel (5:1 hexane–EtOAc) to give 1.20 g (94%) of crystalline compound **23**; mp 147–149 °C; $[\alpha]_D^{20}$ +46.3 (*c* 0.30, $CHCl_3$); IR (KBr) ν_{max} (cm^{-1}) 2956, 2931, 1724, 1656, 1472, 1414, 1261, 1185. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.09 (s, 3H, CH_3), 0.12 (s, 3H, CH_3), 0.93 (s, 9H, $3 \times CH_3$), 1.23 (s, 3H, CH_3), 1.25 (t, J 7.1 Hz, 3H, CH_3), 1.35 (s, 3H, CH_3), 2.50 (dd, $J_{5,4}$ 1.4 Hz, $J_{6,5}$ 1.3 Hz, 1H, H-5), 3.69 (d, $J_{5',5'}$ 8.4 Hz, 1H, H-5′), 3.70 (d, $J_{H,H}$ 10.8 Hz, 1H, CH_2O), 3.81–3.86 (m, 3H, H-4, H-6, CH_2O), 4.07 (d, $J_{H,H}$ 10.1 Hz, 1H, OCH_2Ph), 4.17 (q, J 7.1 Hz, 2H, CH_2), 4.22 (d, $J_{H,H}$ 15.0 Hz, 1H, NCH_2Ph), 4.29 (d, $J_{H,H}$ 10.1 Hz, 1H, OCH_2Ph), 4.98 (d, $J_{5',5'}$ 8.4 Hz, 1H, H-5′), 4.98 (d, $J_{H,H}$ 15.0 Hz, 1H, NCH_2Ph), 5.95 (dd, $J_{3,2}$ 15.6 Hz, $J_{4,2}$ 1.7 Hz, 1H, H-2), 6.63 (dd, $J_{3,2}$ 15.6 Hz, $J_{4,3}$ 4.8 Hz, 1H, H-3), 7.25–7.30 (m, 5H, Ph), 7.37–7.43 (m, 3H, Ph), 7.49–7.53 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$, 100 MHz): δ −5.7 (CH_3), −5.5 (CH_3), 14.1 (CH_3), 18.1 (C), 18.8 (CH_3), 25.7 ($3 \times CH_3$), 29.1 (CH_3), 45.9 (CH_2), 60.3 (CH_2), 64.6 (CH_2), 65.7 (C), 66.4 (CH_2), 71.0 (CH), 72.0 (CH), 72.7 (CH), 74.3 (CH_2), 99.1 (C), 122.0 (CH), 127.6 (CH_{Ph}), 128.1 ($2 \times CH_{Ph}$), 128.1 (CH_{Ph}), 128.4 ($2 \times CH_{Ph}$), 128.8 ($2 \times CH_{Ph}$), 129.2 ($2 \times CH_{Ph}$), 137.1 (C_i), 138.8 (C_i), 143.3 (CH), 159.5 (C), 165.9 (C). Anal. Calcd for $C_{35}H_{49}NO_8Si$: C, 65.70; H, 7.72; N, 2.19. Found: C, 65.63; H, 7.75; N, 2.13.

4.19. (4*R*)-3-Benzyl-4-[(1′*R*,2′*R*,3′*S*,4′*E*)-2′-(benzyloxy)-6′-hydroxy-1′,3′-(isopropylidenedioxy)hex-4′-enyl]-4-[(*tert*-butyldimethylsilyloxy)methyl]oxazolidin-2-one (25)

Diisobutylaluminum hydride (2.5 mL of a 1.2 M toluene solution) was added dropwise to a solution of ester **23** (1.07 g, 1.67 mmol) in dry CH_2Cl_2 (21 mL) that was pre-cooled to −78 °C. The resulting mixture was stirred at the same temperature for 30 min and then quenched with MeOH (1.0 mL). The mixture was warmed to room temperature and poured into 30% aq K/Na

tartrate (12.3 mL). After being stirred for 30 min, the mixture was then extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated in vacuo, and the crude product was chromatographed on silica gel (1:1 hexane–EtOAc) to afford 0.35 g (35%) of α,β-unsaturated aldehyde **24** (compound **24** was subsequently converted into corresponding alcohol **25** using the same procedure as described for the preparation of compound **17**) and 0.51 g (51%) of crystalline allylic alcohol **25**: mp 205–207 °C; $[\alpha]_D^{20}$ +58.8 (*c* 0.21, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.08 (s, 3H, CH_3), 0.11 (s, 3H, CH_3), 0.93 (s, 9H, 3 × CH_3), 1.23 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 2.50 (t, $J_{2',1'}$ 1.4 Hz, $J_{3',2'}$ 1.4 Hz, 1H, H-2′), 3.69–3.75 (m, 3H, H-3′, H-5, CH_2O), 3.83 (d, $J_{2',1'}$ 1.4 Hz, 1H, H-1′), 3.84 (d, $J_{H,H}$ 10.6 Hz, 1H, CH_2O), 4.00 (m, 2H, 2 × H-6′), 4.18 (d, $J_{H,H}$ 10.8 Hz, 1H, OCH_2Ph), 4.23 (d, $J_{H,H}$ 15.1 Hz, 1H, NCH_2Ph), 4.44 (d, $J_{H,H}$ 10.8 Hz, 1H, OCH_2Ph), 4.95 (d, $J_{H,H}$ 15.1 Hz, 1H, NCH_2Ph), 4.99 (d, $J_{5,5}$ 8.4 Hz, 1H, H-5), 5.49 (tdd, $J_{5',4'}$ 15.6 Hz, $J_{4',3'}$ 6.2 Hz, $J_{6',4'}$ 1.4 Hz, $J_{6',4'}$ 1.4 Hz, 1H, H-4′), 5.70 (dtd, $J_{5',4'}$ 15.6 Hz, $J_{6',5'}$ 5.2 Hz, $J_{6',5'}$ 5.2 Hz, $J_{5',3'}$ 0.9 Hz, 1H, H-5′), 7.27–7.41 (m, 8H, Ph), 7.48–7.52 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$, 100 MHz): δ −5.7 (CH_3), −5.5 (CH_3), 18.2 (C), 18.9 (CH_3), 25.8 (3 × CH_3), 29.4 (CH_3), 45.9 (CH_2), 62.8 (CH_2), 64.6 (CH_2), 65.8 (C), 65.5 (CH_2), 71.1 (CH), 73.0 (CH), 73.8 (CH), 74.5 (CH_2), 99.0 (C), 127.6 (CH_{Ph}), 127.9 (CH), 128.0 (2 × CH_{Ph}), 128.1 (CH_{Ph}), 128.2 (2 × CH_{Ph}), 128.7 (2 × CH_{Ph}), 129.2 (2 × CH_{Ph}), 131.4 (CH), 137.9 (C_i), 138.8 (C_i), 159.6 (C). Anal. Calcd for $C_{33}H_{47}NO_7Si$: C, 66.30; H, 7.92; N, 2.34. Found: C, 66.36; H, 7.95; N, 2.30.

Aldehyde **24**: a colourless syrup; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.11 (s, 3H, CH_3), 0.14 (s, 3H, CH_3), 0.95 (s, 9H, 3 × CH_3), 1.27 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 2.55 (m, 1H, H-5), 3.70–3.73 (m, 2H, H-5′, CH_2O), 3.84–3.88 (m, 3H, H-4, H-6, CH_2O), 4.01 (d, $J_{H,H}$ 10.8 Hz, 1H, OCH_2Ph), 4.24 (d, $J_{H,H}$ 15.1 Hz, 1H, NCH_2Ph), 4.42 (d, $J_{H,H}$ 10.8 Hz, 1H, OCH_2Ph), 4.99–5.02 (m, 2H, H-5′, NCH_2Ph), 6.09 (ddd, $J_{3,2}$ 15.7 Hz, $J_{2,CHO}$ 7.7 Hz, $J_{4,2}$ 1.3 Hz, 1H, H-2), 6.29 (dd, $J_{3,2}$ 15.7 Hz, $J_{4,3}$ 4.9 Hz, 1H, H-3), 7.19–7.30 (m, 5H, Ph), 7.39–7.44 (m, 3H, Ph), 7.54–7.56 (m, 2H, Ph), 9.31 (d, $J_{2,CHO}$ 7.7 Hz, 1H, CHO). Anal. Calcd for $C_{33}H_{45}NO_7Si$: C, 66.52; H, 7.61; N, 2.35. Found: C, 66.48; H, 7.65; N, 2.32.

4.20. (4*R*)-3-Benzyl-4-[(1′*R*,2′*R*,3′*S*,4′*E*)-2′-(benzyloxy)-6′-bromo-1′,3′-(isopropylidenedioxy)hex-4′-enyl]-4-[(*tert*-butyldimethylsilyloxy)methyl]oxazolidin-2-one (26)

To a solution of allylic alcohol **25** (0.33 g, 0.55 mmol) in dry CH_2Cl_2 (8.7 mL) was added Et_3N (0.193 mL, 1.38 mmol), followed by dropwise addition of methanesulfonyl chloride (0.106 mL, 1.38 mmol) at 0 °C. After stirring at room temperature for 30 min, the solvent was evaporated in vacuo and the residue was diluted with Et_2O (5 mL). The insoluble materials were removed by filtration, the solvent was evaporated and the crude product was used directly in the next step without further purification. To a solution of crude mesylate (0.37 g, 0.547 mmol) in dry THF (8.7 mL) was added LiBr (0.475 g, 5.47 mmol). After stirring at room temperature for 40 min, the solvent was evaporated under reduced pressure. The residue was diluted with Et_2O (7 mL), the salts were removed by filtration, and washed with Et_2O, and the solvent was removed in vacuo. The residue was subjected to flash chromatography through a short column of silica gel (7:1 hexane–EtOAc) to afford 0.312 g (85.5%) of crystalline bromide **26**: mp 153–155 °C; $[\alpha]_D^{20}$ +60.9 (*c* 0.26, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.09 (s, 3H, CH_3), 0.12 (s, 3H, CH_3), 0.93 (s, 9H, 3 × CH_3), 1.23 (s, 3H, CH_3), 1.34 (s, 3H, CH_3), 2.41 (t, $J_{3',2'}$ 1.4 Hz, $J_{2',1'}$ 1.4 Hz, 1H, H-2′), 3.65–3.74 (m, 3H, H-1′, H-5, CH_2O), 3.74–3.87 (m, 4H, H-3′, 2 × H-6′, CH_2O), 4.18 (d, $J_{H,H}$ 10.7 Hz, 1H, OCH_2Ph), 4.21 (d, $J_{H,H}$ 15.3 Hz, 1H, NCH_2Ph), 4.39 (d, $J_{H,H}$ 10.7 Hz, 1H, OCH_2Ph), 4.98 (d, $J_{H,H}$ 15.1 Hz, 1H, NCH_2Ph), 4.99 (d, $J_{5,5}$ 8.4 Hz, 1H, H-5), 5.52 (m, 1H, H-4′), 5.72 (m, 1H, H-5′), 7.27–7.43 (m, 8H, Ph), 7.49–7.54 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$, 100 MHz): δ −5.7 (CH_3), −5.5 (CH_3), 18.1 (C), 18.9 (CH_3), 25.8 (3 × CH_3), 29.3 (CH_3), 31.7 (CH_2), 45.9 (CH_2), 64.6 (CH_2), 65.8 (C), 66.4 (CH_2), 70.9 (CH), 72.9 (CH), 73.7 (CH), 74.5 (CH_2), 99.1 (C), 127.6 (CH_{Ph}), 128.0 (CH_{Ph}), 128.1 (2 × CH_{Ph}), 128.2 (2 × CH_{Ph}), 128.3 (CH), 128.8 (2 × CH_{Ph}), 129.2 (2 × CH_{Ph}), 132.1 (CH), 137.7 (C_i), 138.9 (C_i), 159.5 (C). Anal. Calcd for $C_{33}H_{46}BrNO_6Si$: C, 59.99; H, 7.02; N, 2.12. Found: C, 60.03; H, 6.98; N, 2.15.

4.21. (4*R*)-3-Benzyl-4-[(1′*R*,2′*R*,3′*S*,7′*S*&*R*,4′*E*)-2′-(benzyloxy)-12′,12′-ethylenedioxy-1′,3′-(isopropylidenedioxy)-7′-(phenylsulfonyl)octadec-4′-enyl]-4-[(*tert*-butyldimethylsilyloxy)methyl]oxazolidin-2-one (27)

n-BuLi (0.94 mL, 1.6 M solution in hexane) was added dropwise to a solution of sulfone **2**[6a] (0.368 g, 0.999 mmol) in dry THF (8.1 mL) that was pre-cooled to −78 °C. The resulting yellow solution was stirred for 30 min at the same temperature. Then, the solution of bromide **26** (0.22 g, 0.333 mmol) in dry THF (9.8 mL) was added dropwise at −78 °C. The reaction mixture was stirred for 10 min at −78 °C, then poured into satd aq NH_4Cl (16 mL) and extracted with EtOAc (2 × 20 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated, and the residue was chromatographed on silica gel (5:1 hexane–EtOAc) to give 0.30 g (95%) of a mixture of diastereoisomeric coupling products **27** as a colourless oil: IR (KBr) ν_{max} (cm^{-1}) 2951, 2859, 1746, 1471, 1447, 1408, 1304, 1260, 1203, 1146, 1070, 978, 839, 731. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.07 (s, 2.1H, CH_3min.), 0.07 (s, 3H, CH_3maj.), 0.10 (s, 2.1H, CH_3min.), 0.10 (s, 3H, CH_3maj.), 0.86–0.90 (m, 5.1H, CH_3maj., CH_3min.), 0.92 (s, 6.3H, 3 × CH_3min.), 0.92 (s, 9H, 3 × CH_3maj.), 1.20–1.82 (m, 40.8H, 2 × CH_3maj., 2 × CH_3min., 9 × CH_2maj., 9 × CH_2min.), 2.25–2.33 (m, 1.7H, H-6′maj., H-6′min.), 2.39–2.44 (m, 1.7H, H-6′maj., H-6′min.), 2.45 (m, 1H, H-2′maj.), 2.48 (m, 0.7H, H-2′min.), 2.83–2.93 (m, 1.7H, H-7′min., H-7′maj.), 3.64–3.75 (m, 5.1H, H-3′maj., H-3′min., CH_2O-maj., CH_2Omin., H-5maj., H-5 min.), 3.81–3.93 (m, 10.2H, 2 × CH_2maj., 2 × CH_2min., CH_2Omaj., CH_2Omin., H-1′maj., H-1′min.), 4.18 (m, 1.7H, OCH_2Phmaj., OCH_2Phmin.), 4.22 (d, 1H, $J_{H,H}$ 15.2 Hz, NCH_2Phmaj.), 4.22 (d, 0.7H, $J_{H,H}$ 15.1 Hz, NCH_2Phmin.), 4.37 (d, 1H, $J_{H,H}$ 10.7 Hz, OCH_2Phmaj.), 4.38 (d, 0.7H, $J_{H,H}$ 10.8 Hz, OCH_2Phmin.), 4.91–4.97 (m, 3.4H, H-5maj., H-5 min., NCH_2Phmaj., NCH_2Phmin.), 5.35–5.43 (m, 1.7H, H-4′maj., H-4′min.), 5.51–5.59 (m, 0.7H, H-5′min.), 5.60–5.66 (m, 1H, H-5′maj.), 7.25–7.30 (m, 8.5H, Phmaj., Phmin.), 7.37–7.42 (m, 5.1H, Phmaj., Phmin.), 7.48–7.51 (m, 3H, Phmaj., Phmin.), 7.52–7.57 (m, 3H, Phmaj.), 7.62–7.67 (m, 2.1 H, Phmin.), 7.80–7.83 (m, 1.4H, Phmin.), 7.84–7.87 (m, 2H, Phmaj.). Anal. Calcd for $C_{53}H_{77}NO_{10}SSi$: C, 67.13; H, 8.18; N, 1.48. Found: C, 67.10; H, 8.13; N, 1.45.

4.22. (4*R*)-3-Benzyl-4-[(1′*R*,2′*R*,3′*S*,4′*E*)-2′-(benzyloxy)-12′,12′-ethylenedioxy-1′,3′-(isopropylidenedioxy)octadec-4′-enyl]-4-[(*tert*-butyldimethylsilyloxy)methyl]oxazolidin-2-one (28)

Na_2HPO_4 (0.66 g, 4.6 mmol) and sodium amalgam (1.6 g, 4.2 mmol, 6%) were added to a solution of **27** (0.20 g, 0.21 mmol) in dry MeOH (4.1 mL) that was pre-cooled to 0 °C. The reaction mixture was stirred for 1 h at room temperature and then another portion of Na_2HPO_4 (0.66 g, 4.6 mmol) and sodium amalgam (1.6 g, 4.2 mmol, 6%) was added at 0 °C. This procedure was repeated twice at 1-h intervals, so that the total amount of Na_2HPO_4 was 2.64 g (18.48 mmol) and the total amount of sodium amalgam was 6.56 g (16.8 mmol). The mixture was then diluted with CH_2Cl_2 (25 mL) and filtered through a pad of Celite. The filtrate was washed with ice water (8 mL), and dried over Na_2SO_4, and the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (7:1 hexane–EtOAc)

to give 0.11 g (64%) of product **28** as a colourless oil: $[\alpha]_D^{20}$ +21.3 (*c* 0.25, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz): δ 0.07 (s, 3H, CH_3), 0.10 (s, 3H, CH_3), 0.88 (t, 3H, J = 6.9 Hz, CH_3), 0.92 (s, 9H, 3 × CH_3), 1.21 (s, 3H, CH_3), 1.24–1.33 (m, 16H, 8 × CH_2), 1.34 (s, 3H, CH_3), 1.56–1.60 (m, 4H, 2 × CH_2), 1.88–2.02 (m, 2H, 2 × H-6′), 2.45 (t, $J_{2',1'}$ = 1.4 Hz, $J_{3',2'}$ = 1.4 Hz, 1H, H-2′), 3.65 (m, 1H, H-3′), 3.70 (d, $J_{H,H}$ = 10.7 Hz, 1H, CH_2O), 3.71 (d, $J_{5,5}$ = 8.4 Hz, 1H, H-5), 3.81 (d, $J_{2',1'}$ = 1.4 Hz, 1H, H-1′), 3.83 (d, $J_{H,H}$ = 10.7 Hz, 1H, CH_2O), 3.89–3.93 (m, 4H, 2 × CH_2), 4.22 (d, $J_{H,H}$ = 15.1 Hz, 1H, NCH_2Ph), 4.27 (d, $J_{H,H}$ = 10.5 Hz, 1H, OCH_2Ph), 4.36 (d, $J_{H,H}$ = 10.5 Hz, 1H, OCH_2Ph), 4.94 (d, $J_{H,H}$ = 15.1 Hz, 1H, NCH_2Ph), 4.97 (d, $J_{5,5}$ = 8.4 Hz, 1H, H-5), 5.38 (tdd, $J_{5',4'}$ = 15.4 Hz, $J_{4',3'}$ = 7.3 Hz, $J_{6',4'}$ = 1.2 Hz, $J_{6',4'}$ = 1.2 Hz, 1H, H-4′), 5.50 (td, $J_{5',4'}$ = 15.4 Hz, $J_{6',5'}$ = 6.6 Hz, $J_{6',5'}$ = 6.6 Hz, 1H, H-5′), 7.25–7.27 (m, 1H, Ph), 7.29–7.39 (m, 7H, Ph), 7.48–7.51 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$, 100 MHz): δ −5.7 (CH_3), −5.5 (CH_3), 14.1 (CH_3), 18.1 (C), 18.9 (CH_3), 22.6 (CH_2), 23.8 (CH_2), 23.8 (CH_2), 25.8 (3 × CH_3), 28.8 (CH_2), 29.3 (CH_3), 29.4 (CH_2), 29.6 (CH_2), 29.8 (CH_2), 31.8 (CH_2), 32.3 (CH_2), 37.1 (2 × CH_2), 45.9 (CH_2), 64.5 (CH_2), 64.9 (2 × CH_2), 65.8 (C), 66.5 (CH_2), 71.1 (CH), 73.3 (CH), 74.5 (CH_2), 74.9 (CH), 98.9 (C), 111.8 (C), 127.0 (CH), 127.5 (CH_{Ph}), 128.0 (CH_{Ph}), 128.1 (2 × CH_{Ph}), 128.1 (2 × CH_{Ph}), 128.7 (2 × CH_{Ph}), 129.1 (2 × CH_{Ph}), 133.8 (CH), 137.8 (C_i), 138.9 (C_i), 159.6 (C). Anal. Calcd for $C_{47}H_{73}NO_8Si$: C, 69.85; H, 9.10; N, 1.73. Found: C, 69.82; H, 9.13; N, 1.75.

4.23. (4*S*)-3-Benzyl-4-[(1′*R*,2′*R*,3′*S*,4′*E*)-2′-(benzyloxy)-12′,12′-ethylenedioxy-1′,3′-(isopropylidenedioxy)octadec-4′-enyl]-4-(hydroxymethyl)oxazolidin-2-one (29)

A solution of Bu_4NF in THF (1 M, 0.14 mL, 0.14 mmol) was added dropwise to a solution of **28** (0.11 g, 0.14 mmol) in dry tetrahydrofuran (1.4 mL) that was pre-cooled to 0 °C. The reaction mixture was stirred for 10 min at 0 °C and then for 20 min at room temperature. The solvent was evaporated in vacuo and the residue was partitioned between EtOAc (5 mL) and water (2 mL). The aqueous phase was extracted with further portions of EtOAc (2 × 5 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was evaporated. Chromatography of the residue on silica gel (2:1 hexane–EtOAc) afforded 83 mg (88%) of alcohol **29** as a colourless oil: $[\alpha]_D^{20}$ +73.5 (*c* 0.20, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz): δ 0.88 (t, 3H, J = 6.9 Hz, CH_3), 1.23–1.35 (m, 19H, 8 × CH_2, CH_3), 1.40 (s, 3H, CH_3), 1.55–1.60 (m, 4H, 2 × CH_2), 1.91–2.05 (m, 2H, 2 × H-6′), 2.85 (m, 1H, H-2′), 3.69 (m, 2H, 2 × CH_2O), 3.86 (d, $J_{5,5}$ = 8.6 Hz, 1H, H-5), 3.88–3.93 (m, 5H, 2 × CH_2, H-3′), 3.95 (m, 1H, H-1′), 4.46 (s, 2H, 2 × OCH_2Ph), 4.55 (d, $J_{H,H}$ = 15.2 Hz, 1H, NCH_2Ph), 4.61 (d, $J_{H,H}$ = 15.2 Hz, 1H, NCH_2Ph), 4.88 (d, $J_{5,5}$ = 8.6 Hz, 1H, H-5), 5.49 (dd, $J_{5',4'}$ = 15.4 Hz, $J_{4',3'}$ = 7.2 Hz, 1H, H-4′), 5.66 (td, $J_{5',4'}$ = 15.4 Hz, $J_{6',5'}$ = 6.7 Hz, $J_{6',5'}$ = 6.7 Hz, 1H, H-5′), 7.27–7.42 (m, 8H, Ph), 7.49–7.53 (m, 2H, Ph). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 14.1 (CH_3), 19.0 (CH_3), 22.6 (CH_2), 23.8 (CH_2), 23.8 (CH_2), 28.8 (CH_2), 29.3 (CH_2), 29.5 (CH_3), 29.6 (CH_2), 29.8 (CH_2), 31.8 (CH_2), 32.3 (CH_2), 37.1 (CH_2), 37.2 (CH_2), 45.7 (CH_2), 64.4 (CH_2), 64.9 (2 × CH_2), 65.5 (C), 66.1 (CH_2), 71.9 (CH), 73.3 (CH), 74.5 (CH_2), 75.1 (CH), 99.1 (C), 111.8 (C), 126.9 (CH), 127.6 (CH_{Ph}), 127.9 (2 × CH_{Ph}), 128.2 (2 × CH_{Ph}), 128.3 (CH_{Ph}), 128.6 (2 × CH_{Ph}), 129.0 (2 × CH_{Ph}), 134.2 (CH), 137.7 (C_i), 138.5 (C_i), 159.2 (C). Anal. Calcd for $C_{41}H_{59}NO_8$: C, 70.97; H, 8.57; N, 2.02. Found: C, 70.92; H, 8.60; N, 2.05.

4.24. (4*S*)-3-Benzyl-4-[(1′*R*,2′*R*,3′*S*,4′*E*)-2′-(benzyloxy)-12′,12′-ethylenedioxy-1′,3′-(isopropylidenedioxy)octadec-4′-enyl]-2-oxooxazolidine-4-carboxylic acid (30)

Pyridinium dichromate (0.640 g, 1.70 mmol) was added to a solution of alcohol **29** (76 mg, 0.11 mmol) in dry DMF (0.63 mL). After stirring at room temperature for 24 h, the reaction mixture was poured into ice water (6.5 mL) and extracted with Et_2O (5 × 10 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated in vacuo and the residue was subjected to flash chromatography through a short column of silica gel (9:1 CH_2Cl_2–MeOH). This afforded 50 mg (65%) of carboxylic acid **30** as a colourless oil: $[\alpha]_D^{20}$ +20.1 (*c* 0.20, CH_3OH). ^1H NMR (CD_3OD, 600 MHz): δ 0.90 (t, J = 6.8 Hz, 3H, CH_3), 1.25–1.38 (m, 19H, CH_3, 8 × CH_2), 1.39 (s, 3H, CH_3), 1.53–1.58 (m, 4H, 2 × CH_2), 1.92–2.06 (m, 2H, 2 × H-6′), 2.40 (m, 1H, H-2′), 3.84–3.91 (m, 5H, 2 × CH_2, H-3′), 4.23 (d, $J_{H,H}$ = 10.2 Hz, 1H, OCH_2Ph), 4.30 (m, 2H, OCH_2Ph, NCH_2Ph), 4.67 (m, 2H, H-5, H-1′), 4.85 (m, 1H, NCH_2Ph), 5.06 (d, $J_{5,5}$ = 7.6 Hz, 1H, H-5), 5.35 (dd, $J_{5',4'}$ = 15.5 Hz, $J_{4',3'}$ = 7.0 Hz, 1H, H-4′), 5.54 (m, 1H, H-5′), 7.25–7.35 (m, 5H, Ph), 7.35–7.44 (m, 3H, Ph), 7.54–7.59 (m, 2H, Ph). ^{13}C NMR (CD_3OD, 150 MHz): δ 14.5 (CH_3), 19.3 (CH_3), 23.7 (CH_2), 24.9 (2 × CH_2), 29.6 (CH_3), 30.0 (CH_2), 30.3 (CH_2), 30.7 (CH_2), 30.8 (CH_2), 33.0 (CH_2), 33.3 (CH_2), 38.1 (CH_2), 38.1 (CH_2), 47.9 (CH_2), 65.9 (2 × CH_2), 68.9 (CH_2), 70.6 (C), 72.5 (CH), 75.3 (CH), 75.9 (CH_2), 76.2 (CH), 100.7 (C), 113.0 (C), 128.7 (CH), 128.8 (CH_{Ph}), 129.3 (2 × CH_{Ph}), 129.4 (2 × CH_{Ph}), 129.5 (CH_{Ph}), 129.9 (2 × CH_{Ph}), 130.8 (2 × CH_{Ph}), 134.6 (CH), 139.2 (C_i), 139.7 (C_i), 161.5 (C), 174.2 (C). Anal. Calcd for $C_{41}H_{57}NO_9$: C, 69.56; H, 8.12; N, 1.98. Found: C, 69.60; H, 8.13; N, 1.95.

4.25. (5*S*,8*S*,9*S*,10*R*)-1-Benzyl-9-(benzyloxy)-10-hydroxy-8-[(1′*E*)-9-oxopentadec-1-enyl)]-3,7-dioxa-1-azaspiro[4.5]-decane-2,6-dione (31)

Aq HCl (2 M, 1.56 mL) was added dropwise to a solution of acid **30** (50 mg, 0.07 mmol) in tetrahydrofuran (4.5 mL) and the mixture was refluxed for 7 h. Then, the mixture was cooled to room temperature and neutralized by cautious addition of satd aq $NaHCO_3$ and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried over Na_2SO_4, the solvent was evaporated, and the residue was subjected to flash chromatography through a short silica gel column (2:1 hexane–EtOAc) to afford 31 mg (72%) of lactone **31** as a colourless oil: $[\alpha]_D^{20}$ +79.1 (*c* 0.26, $CHCl_3$). ^1H NMR ($CDCl_3$, 600 MHz): δ 0.88 (t, J = 6.9 Hz, 3H, CH_3), 1.23–1.33 (m, 10H, 5 × CH_2), 1.34–1.41 (m, 2H, CH_2), 1.51–1.58 (m, 4H, 2 × CH_2), 2.01–2.11 (m, 2H, 2 × H-3′), 2.26–2.31 (m, 1H, OH), 2.37 (t, J = 7.2 Hz, 4H, 2 × CH_2), 3.61 (dd, $J_{10,9}$ = 4.3 Hz, $J_{9,8}$ = 2.2 Hz, 1H, H-9), 4.01 (d, $J_{H,H}$ = 16.5 Hz, 1H, NCH_2Ph), 4.14 (t, $J_{10,9}$ = 4.4 Hz, $J_{10,OH}$ = 4.4 Hz, 1H, H-10), 4.21 (d, $J_{H,H}$ = 10.2 Hz, 1H, OCH_2Ph), 4.47 (d, $J_{H,H}$ = 10.2 Hz, 1H, OCH_2Ph), 4.56 (d, $J_{4,4}$ = 11.5 Hz, 1H, H-4), 4.59 (d, $J_{4,4}$ = 11.5 Hz, 1H, H-4), 5.04 (d, $J_{H,H}$ = 16.5 Hz, 1H, NCH_2Ph), 5.16 (m, 1H, H-8), 5.63 (tdd, $J_{2',1'}$ = 15.3 Hz, $J_{8,1'}$ = 7.9 Hz, $J_{3',1'}$ = 1.4 Hz, $J_{3',1'}$ = 1.4 Hz, 1H, H-1′), 5.85 (td, $J_{2',1'}$ = 15.3 Hz, $J_{3',2'}$ = 6.7 Hz, $J_{3',2'}$ = 6.7 Hz, 1H, H-2′), 7.24–7.39 (m, 10H, Ph). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 14.0 (CH_3), 22.5 (CH_2), 23.7 (CH_2), 23.8 (CH_2), 28.4 (CH_2), 28.9 (CH_2), 28.9 (CH_2), 29.0 (CH_2), 31.6 (CH_2), 32.2 (CH_2), 42.7 (CH_2), 42.8 (CH_2), 49.1 (CH_2), 67.2 (C), 69.6 (CH_2), 72.4 (CH), 74.3 (CH_2), 77.6 (CH), 80.4 (CH), 123.2 (CH), 126.7 (2 × CH_{Ph}), 127.8 (CH_{Ph}), 128.0 (2 × CH_{Ph}), 128.6 (CH_{Ph}), 128.7 (2 × CH_{Ph}), 129.2 (2 × CH_{Ph}), 136.2 (C_i), 137.4 (CH), 138.4 (C_i), 159.8 (C), 169.9 (C), 211.6 (C). Anal. Calcd for $C_{36}H_{47}NO_7$: C, 71.38; H, 7.82; N, 2.31. Found: C, 71.42; H, 7.85; N, 2.27.

4.26. (4*S*)-3-Benzyl-4-[(1′*R*,2′*R*,3′*S*,4′*E*)-2′-(benzyloxy)-1′,3′-dihydroxy-12′-oxooctadec-4′-enyl]-2-oxooxazolidine-4-carboxylic acid (32)

Aq NaOH (10%, 1.2 mL) was added dropwise to a solution of lactone **31** (24 mg, 0.04 mmol) in MeOH (1.2 mL) and the reaction mixture was stirred at 80 °C for 30 min. Then, the mixture was cooled to room temperature and neutralized with Amberlite IR-120 (H^+). Insoluble materials were removed by filtration, and

Table 1
Crystal data and structure refinement parameters for compound **13**

	13
Empirical formula	$C_{16}H_{21}NO_8$
Formula weight	355.34
Temperature, T (K)	293(2)
Wavelength, λ (Å)	0.71073
Crystal system	Monoclinic
Space group	$P2_1$
Unit cell dimensions	
a (Å)	6.5654 (4)
b (Å)	14.7939 (10) $\beta = 90.701(6)^\circ$
c (Å)	9.2768 (6)
V (Å^3)	900.97 (10)
Formula per unit cell, Z	2
D_{calcd} (g/cm^3)	1.310
Absorption coefficient, μ (mm^{-1})	0.106
F(0 0 0)	376
Crystal size (mm)	0.5 × 0.414 × 0.037
θ Range for data collection (°)	3.10–26.50
Index ranges	$-7 \leqslant h \leqslant 8$ $-18 \leqslant k \leqslant 18$ $-11 \leqslant l \leqslant 11$
Independent reflections (*R*int)	3647 (0.0374)
Absorption correction	Analytical
Max. and min. transmission	0.998 and 0.974
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	364/1/243
Goodness-of-fit on F^2	0.805
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0359$, $wR_2 = 0.0571$
R indices (all data)	$R_1 = 0.0976$, $wR_2 = 0.0655$
Largest diff. peak and hole (e/Å^{-3})	0.103 and −0.116

washed with MeOH, and the solvent was evaporated under reduced pressure. The residue was chromatographed through a short column of silica gel (7:1 CH_2Cl_2–MeOH) to afford 20 mg (81%) of compound **32** as a colourless oil: $[\alpha]_D^{20}$ +49.3 (*c* 0.27, CH_3OH). ^{1}H NMR (CD_3OD, 600 MHz): δ 0.88 (t, J = 6.8 Hz, 3H, CH_3), 1.24–1.37 (m, 12H, 6 × CH_2), 1.48–1.55 (m, 4H, 2 × CH_2), 1.93–1.99 (m, 2H, 2 × H-6′), 2.41 (t, J = 7.3 Hz, 4H, 2 × CH_2), 3.09 (m, 1H, H-2′), 3.91 (m, 1H, H-3′), 4.13 (d, $J_{H,H}$ = 15.4 Hz, 1H, NCH_2Ph), 4.18 (m, 1H, H-1′), 4.39–4.43 (m, 2H, H_5, OCH_2Ph), 4.68–4.72 (m, 1H, OCH_2Ph), 4.80 (d, $J_{H,H}$ = 15.4 Hz, 1H, NCH_2Ph), 5.02 (dd, $J_{5',4'}$ = 15.4 Hz, $J_{4',3'}$ = 7.1 Hz, 1H, H-4′), 5.05 (d, $J_{5,5}$ = 8.3 Hz, 1H, H-5), 5.49–5.56 (m, 1H, H-5′), 7.22–7.25 (m, 1H, Ph), 7.26–7.32 (m, 3H, Ph), 7.32–7.36 (m, 4H, Ph), 7.40–7.43 (m, 2H, Ph). ^{13}C NMR (CD_3OD, 150 MHz): δ 14.4 (CH_3), 23.6 (CH_2), 24.9 (CH_2), 24.9 (CH_2), 30.0 (CH_2), 30.1 (CH_2), 30.2 (CH_2), 30.2 (CH_2), 32.8 (CH_2), 33.3 (CH_2), 43.5 (CH_2), 43.5 (CH_2), 48.7 (CH_2), 69.6 (CH_2), 71.6 (C), 72.7 (CH), 75.9 (CH_2), 76.4 (CH), 81.0 (CH), 128.7 (CH_{Ph}), 129.0 (CH_{Ph}), 129.3 (2 × CH_{Ph}), 129.4 (2 × CH_{Ph}), 129.9 (2 × CH_{Ph}), 130.2 (2 × CH_{Ph}), 131.2 (CH), 133.8 (CH), 139.5 (C_i), 139.6 (C_i), 162.3 (C), 177.5 (C), 214.3 (C). Anal. Calcd for $C_{36}H_{49}NO_8$: C, 69.32; H, 7.92; N, 2.25. Found: C, 69.30; H, 7.95; N, 2.20.

4.27. X-ray techniques

Single crystals of **13** suitable for X-ray diffraction were obtained from a mixture of Et_2O and hexane by slow evaporation at room temperature. The intensities were collected at 293(2) K on a Oxford Diffraction XCalibur2 CCD diffractometer using Mo Kα radiation (λ = 0.71073 Å). Selected crystallographic and other relevant data for the compound **13** are listed in Table 1. The structure was solved by direct methods.[17] All non-hydrogen atoms were refined anisotropically by full-matrix least-squares calculations based on F^2.[17] All hydrogen atoms were included in calculated positions as riding atoms, with SHELXL97[17] defaults. PLATON[18] programme was used for structure analysis and molecular and crystal structure drawings preparation.

Supplementary data

Complete crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 738648. These data can be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: + 44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or via: www.ccdc.cam.ac.uk).

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