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Total Synthesis of 3-*O*-Benzyl-1,3,5-tri-*epi*-calystegine B_2 from L-Sorbose

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Dedicated to Professor Isidoro Izquierdo Cubero on the occasion of his retirement

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The well known 2,3:4,6-di-*O*-isopropylidene-α-L-sorbofuranose (**12**) was chosen as starting material for the synthesis of (1*S*,4*R*,5*S*,6*S*,7*S*)-4-amino-6-benzyloxy-1,7-isopropylidenedioxy-8-oxabicyclo[3.2.1]octane (**33**) and (1*S*,4*S*,5*S*,6*S*,7*S*)-4-amino-6-benzyloxy-1,7-isopropylidenedioxy-8-oxabicyclo-[3.2.1]octane (**34**) through carbon chain-lengthening at C-1 and C-6 by Wittig and magnesium-mediated alkylation methodology, respectively, followed by ring-closing olefin metathesis (RCM). These promising oxabicyclic compounds were key intermediates for the preparation of the polyhydroxylated *nor*-tropane alkaloid 1,3,5-tri-*epi*-calystegine B_2 (**10**) as its 3-*O*-benzyl derivative **35**.

Introduction

The *nor*-tropane alkaloids are bicyclic amines each combining a piperidine (six carbons) and a pyrrolidine (five carbons) ring. They were first isolated from the roots of *Calystegia sepium* (Convolvulaceae)[1] and since then many others have been found from a variety of vascular plants, their only natural source.[2] Structurally, these naturally occurring iminosugars have been traditionally classified (Figure 1) into three groups on the basis of their hydroxylation patterns: the A series (with three OH groups), the B series (with four OH groups), and the C series (with five OH groups). A fourth group of calystegines, the N series, presenting an amino group instead of a hydroxy moiety in the aminoketal functionality at the bicyclic ring bridgehead, has also been isolated,[3] from *Hyoscyamus niger* (Solanaceae).

A number of calystegines have been discovered to date,[3,4] but the most abundant among them is calystegine B_2, found in all the plants so far tested for the presence of these types of alkaloids. Despite their natural occurrence, the biological activities of *nor*-tropane alkaloids have not been extensively studied as is the case with other related sugar mimics.[5] Calystegines do, however, show remarkable inhibitory activities against several glycosidase enzymes, in comparison with other alkaloidal glycosidase inhibitors.[4a] Calystegine B_2 inhibits almond β-glucosidase and green coffee α-galactosidase with K_i values of 1.2 and 0.86 μM, respectively,[6] and human lysosomal α-galactosidase with an IC_{50} value of 30 μM.[2b]

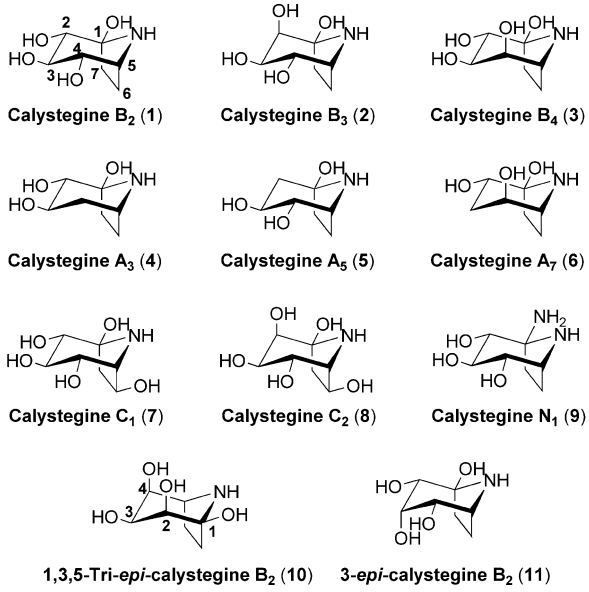

Figure 1. Examples of some naturally occurring calystegines and the unnatural analogues **10** and **11**.

Their inhibitory mechanism is not yet well understood. It has been proposed[6,7] that their mode of action resembles those of other glycosidase inhibitors that have been studied. However, despite their close structural similarities with well known α-glucosidase inhibitors such as 1-deoxynojirimycin and castanospermine, calystegines in general show signifi-

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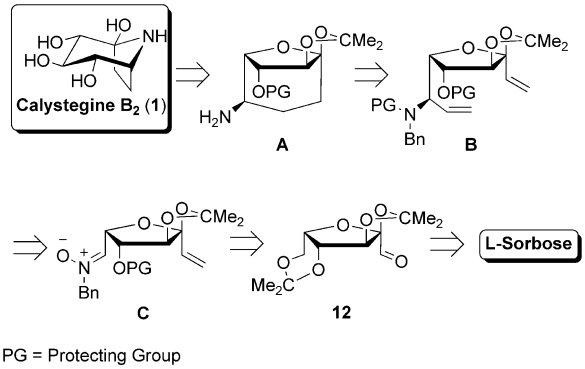
cant inhibitory activity against β-glucosidases but little or no inhibition of α-glucosidases. This notwithstanding, calystegine B_2 has also demonstrated a potent inhibition against α-galactosidases,[2b] a fact that suggest a different recognition pattern depending on the type of enzyme been inhibited.[7]

For these reasons, methods for the enantioselective synthesis of new calystegines are strongly desired. In the literature,[8] all the procedures described involve the obtention of an amino polyhydroxycycloheptane derivative that undergoes cyclization – either spontaneous or base-catalysed – to the corresponding calystegine, depending on the instability of the aminoketal function. It is in the creation of these polyhydroxycycloheptane derivatives that these syntheses differ. Routes that involve the use of enantiopure carbohydrates as starting materials[8a–8j,8l,8o–8s] predominate in the literature, with methodologies that vary from intramolecular nitrone–alkene cycloaddition (INAC)[8c] to ring-closing metathesis (RCM)[8g] or anionic cyclization of epoxide dithioacetal derivatives.[8a] Other routes not based on sugars but taking advantages of nitroso–alkene cycloaddition[8d,8k,8n] as the way to obtain the amino polyhydroxycycloheptane derivative have also been employed.

In continuation of our efforts[9] in the use of common hexuloses (D-fructose and L-sorbose) as sources of functionalization and chirality in the asymmetric synthesis of biologically active azasugars, in the course of our studies toward the synthesis of calystegine B_2 we describe here for the first time the total synthesis of unnatural 1,3,5-tri-*epi*-calystegine B_2 (**10**) as its 3-*O*-benzyl derivative **35** from L-sorbose.

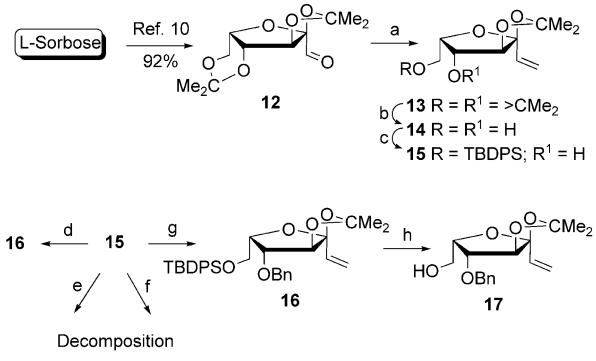
According to our retrosynthetic analysis for calystegine B_2 (**1**, Scheme 1), the already described L-sorbose derivative **12** should be an appropriate substrate for the preparation of intermediate **C** through chain-lengthening at C-1 and nitrone formation at C-6. Nitrone **C** could then be alkylated to provide 1,8-nonadiene **B**, a suitable substrate for a RCM reaction to achieve the tricyclic key intermediate **A**, which should then be easily transformable into the desired calystegine B_2.



Scheme 1. Retrosynthetic analysis of calystegine B_2 (**1**).

Results and Discussion

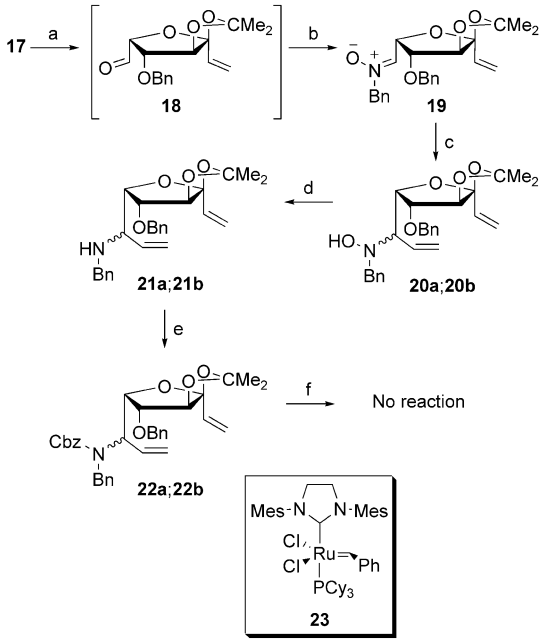
Our synthetic route starts with 2,3:4,6-di-*O*-isopropylidene-α-L-*xylo*-hexos-2-ulofuranose (**12**), a previously described[10] L-sorbose derivative. Firstly, we carried out the chain-lengthening at C-1 of **12**; this step was achieved through a methylenation reaction by Wittig's methodology (Scheme 2) and afforded 1,2-dideoxy-3,4:5,7-di-*O*-isopropylidene-α-L-*xylo*-hept-1-en-3-ulofuranose (**13**). We next approached the nitrone insertion at C-6; consequently, compound **13** was subjected to acid-catalysed deacetonation of its 5,7-*O*-isopropylidene protecting group to provide diol **14** exclusively. Accordingly, we proceeded to protect both OH groups in **14** orthogonally. We first regioselectively protected the primary OH in **14** by treatment with *tert*-butylchlorodiphenylsilane as the silylating agent to provide alcohol **15**. Next came the protection of the secondary OH at C-5 in **15**. A benzyl ether was the protecting group of choice here because of its stability and the simplicity of its removal. Alcohol **15** was thus treated with NaH and BnBr in anhydrous DMF, the classical Williamson reaction, but an unexpected low yield (20%) of the desired benzyl ether **16** was obtained. Changing the solvent to DMSO afforded a complex mixture of products not further analysed. In view of these results, we decided to modify the benzylation conditions and instead employed an acidic medium. Alcohol **15** was thus treated with benzyl trichloroacetimidate in the presence of triflic acid, but a complex mixture of products was again obtained. These negative results, both in basic and in acidic media, moved us to try the reaction under neutral conditions. Dudley et al. recently published[11] a paper describing the conversion of alcohols into benzyl ethers in neutral media,[12] and under these conditions alcohol **15** was easily converted into benzyl ether **16** in good yield (72%, Scheme 2). Compound **16** was subsequently subjected to desilylation, affording 5-*O*-benzyl-1,2-dideoxy-3,4-*O*-isopropylidene-α-L-*xylo*-hept-1-en-3-ulofuranose (**17**), a suitable substrate for introduction of the nitrone functional group at the C-6 position.



Scheme 2. Synthesis of benzyl ether **17** from "diacetone hexulose aldehyde" **12**: a) Ph_3PMeBr, THF, *t*BuOK, 5 h, room temp. (59%); b) aqueous AcOH (50%), 30 min, 50 °C (93%); c) TBDPSCl, DCM, TEA, DMAP (cat.), 2 h, room temp. (84%); d) BnBr, NaH, anh. DMF, 25 h, 0 °C (20%); e) BnBr, NaH, anh. DMSO, 25 h, room temp.; f) benzyl 2,2,2-trichloroacetimidate, TfOH, Et_2O, 2 h, 0 °C; g) 2-benzyloxy-1-methylpyridinium triflate, MgO, CF_3Ph, 24 h, 90 °C (72%); h) TBAF·3 H_2O, THF, 7 h, room temp. (73%).

To achieve our next step, nitrone formation at C-6, alcohol **17** was subjected to Dess–Martin oxidation to afford aldehyde **18** (Scheme 3), which was not fully charac-

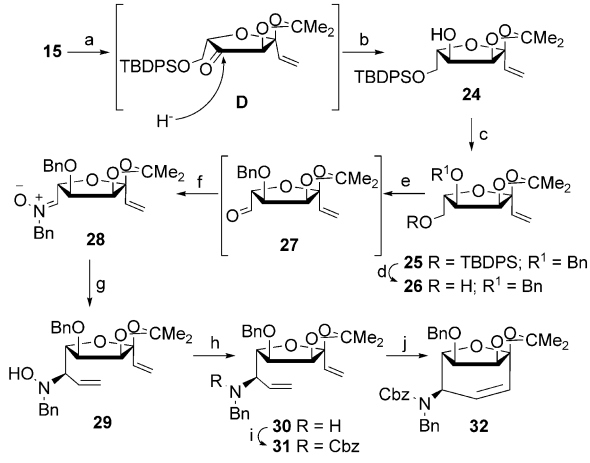
terized but immediately treated with benzylhydroxylamine hydrochloride to give nitrone **19** in excellent yield (90%). The configuration of the new C–N double bond was established as *Z* from the chemical shift of its azomethinic proton, which appeared at δ = 6.95 ppm, outside the expected resonance range (8.0–8.5 ppm) for the *E* configuration.[13] Because of the highly polarised state of the nitrone functionality, addition of several nucleophiles has been extensively studied.[14] With this in mind, treatment of nitrone **19** with vinylmagnesium bromide yielded a 2:1 mixture (^{1}H NMR evidence) of hydroxylamines **20a** and **20b**, which could be separated by column chromatography; their configurations at C-7 were not established at this point. Reduction of **20a** and **20b** to the corresponding amines **21a** and **21b** was carried out under mild conditions because of the presence of two reactive vinyl groups in the molecule. We thus took advantages of the methodology described by Goti et al.,[15] which employs In^0 as reducing agent in a mildly acidic medium. Cbz protection of amines **21a** and **21b** with benzyl chloroformate finally afforded dienes **22a** and **22b** in excellent yield (92%).



Scheme 3. Synthesis of amine **22** from alcohol **17** and initial approach to RCM. a) Dess–Martin, DCM, 24 h, room temp. (98%); b) BnNHOH·HCl, AcONa, MS (3 Å), MeOH, 18 h, room temp. (71%); c) CH_2=CHMgBr, THF, 3 h, –78 °C, **20a** (60%) and **20b** (30%); d) In, EtOH, NH_4Cl, 48 h, 120 °C, **21a** (96%) and **21b** (94%); e) CbzCl, K_2CO_3, acetone, 3 h, room temp., **22a** (92%) and **22b** (94%); f) **23**, microwave irradiation, DCM, 60 min, 100 °C.

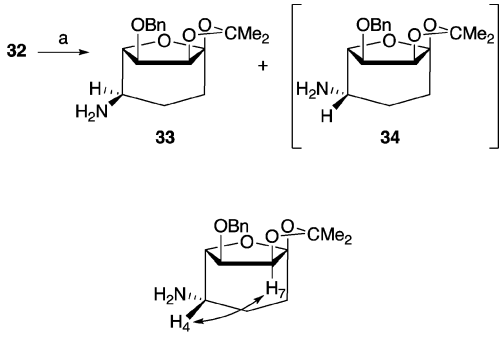
Next in the reaction sequence was the olefin RCM of **22a** and **22b**. The second-generation Grubbs catalyst[16] (**23**, Scheme 3) was employed but did not provide the RCM adducts, even not under microwave conditions. Other authors have described similar difficulties in the preparation of similar or even less sterically demanding polycyclic compounds.[17]

This unsuccessful result made us think that the configuration at C-5 was playing an important role in the failure of the RCM, so a different approach, in which the same reaction sequence was attempted on the C-5 epimer of **17**, was designed. This change in the configuration of C-5 would led us to the synthesis not of calystegine B_2 (**1**) as initially planned, but of 1,3,5-tri*epi*-calystegine B_2 (**10**) and 3-*epi*-calystegine B_2 (**11**). Alcohol **15** was therefore oxidized to diulose **D** (not isolated) and then immediately reduced with $NaBH_4$ to afford 7-*O*-*tert*-butyldiphenylsilyl-1,2-dideoxy-3,4-*O*-isopropylidene-α-L-*ribo*-hept-1-en-3-ulofuranose (**24**, Scheme 4), obtained as a single diastereoisomer. It is worth mentioning that the high stereoselectivity of the reduction reaction was due to the steric hindrance resulting from the isopropylidene group in **D** directing the hydride approach through the *re* face. Benzyl protection of **24** was this time accomplished with BnBr/NaH in a good yield (70%), affording benzyl derivative **25**. Silyl deprotection of **25** yielded alcohol **26**, which was straightforwardly transformed into nitrone **28** through condensation of aldehyde **27** (not isolated) with benzylhydroxylamine hydrochloride. Nitrone **28** was subjected to alkylation with vinylmagnesium bromide as described earlier. We were only able to isolate hydroxylamine **29**, which was reduced to amine **30** as before. The absolute configuration of the new stereogenic centre at C-7 in **29** could not be determined at this point because of the free rotation of the C(6)–C(7) bond, although after completion of the cyclization it was shown to be the *R* diastereoisomer. *N*-Protection of **30** as carbamate **31**, followed by RCM with the second-generation Grubbs catalyst (**23**), to our delight afforded (1*S*,4*R*,5*S*,6*S*,7*S*)-6-benzyloxy-4-[(benzyl)(benzyloxy-carbonyl)amino]-1,7-isopropylidenedioxy-8-oxabicyclo[3.2.1]oct-2-ene (**32**, Scheme 4) in good yield (79%).



Scheme 4. a) TPAP, NMO, MS (4 Å), DCM, 2 h, room temp.; b) $NaBH_4$, MeOH, 30 min, room temp. (76%); c) NaH, BnBr, DMF, 24 h, room temp. (70%); d) TBAF·3H_2O, THF, 5 h, room temp. (95%); e) Dess–Martin, DCM, 18 h, room temp. (97%); f) BnNHOH·HCl, AcONa, MS (3 Å), MeOH, 18 h, room temp. (79%); g) CH_2=CHMgBr, THF, 2 h, –78 °C (90%); h) In, EtOH, NH_4Cl, 24 h, 120 °C (92%); i) CbzCl, K_2CO_3, acetone, 2.5 h, room temp. (97%); j) **23**, microwave irradiation, DCM, 60 min, 100 °C (79%).

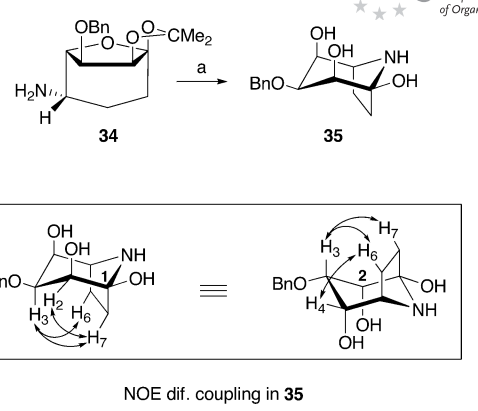
Full characterisation of tricycle **32** probed difficult, though, because of the occurrence of two rotamers in its NMR spectra due to the presence of the carbamate protecting group in the molecule.[18] However, when **32** was subjected to catalytic hydrogenation, removal of the *N*-protecting groups and reduction of the C=C bond took place to yield amine **33**, which could be fully characterized (Scheme 5). ^{1}H NMR studies on **33** confirmed the *R* configuration at C-4 by the coupling constant of H-4,5 ($J_{4,5}$ = 5.5 Hz). Previous studies done by us[19] have shown that in similar tricyclic rings, values of $J_{4,5}$ = 3.2–6.9 Hz are associated with 4*R* configurations whereas values of $J_{4,5}$ = 0–1.6 Hz correspond with the 4*S* stereochemistry. Moreover, when catalytic hydrogenation of **32** was repeated on a 3 g scale, compound **34**, the C-4 epimer of **33**, could also be isolated. This compound, as predicted by our studies, has a $J_{4,5}$ coupling constant of 0 Hz, and NOE experiments show a positive H(4)–H(7) coupling, thus confirming a 4*S* stereochemistry (Scheme 5).



Scheme 5. Synthesis of tricycles **33** and **34** and NOE dif. couplings of **34**. a) H_2, Pd–C (10%), MeOH, 7 h, room temp., **33** (85%) and **34** (14%).

Once the absolute configurations of both amines **33** and **34** had been correctly established, we proceeded to accomplish the synthesis of 1,3,5-tri-*epi*-calystegine B_2 (**10**) and 3-*epi*-calystegine B_2 (**11**) by removing the remaining protecting groups in **33** and **34**, respectively. Treatment of amine **34** with HCl (1 N) for 10 h thus yielded compound **35** as a single compound (Scheme 6). Its analytical and spectroscopic data confirmed the *nor*-tropanic ring structure with a *cis* disposition for H(2), H(3) and H(4), and NOE dif. couplings between H(3)–H(6)*endo*, H(3)–H(7)*endo*, and H(4)–H(6)*endo*, corroborating once again the configurations assigned to C-4 in **33** and **34** (see Scheme 6).

To the best of our knowledge, this is the first synthesis of a *nor*-tropanic ring with two of its piperidinic OH groups in an axial disposition. Unfortunately, final debenzylation of **35** afforded a mixture of compounds that appeared as single spot by TLC. NMR studies showed a complex mixture of compounds, presumably the bicyclic and monocyclic rings of the 1,3,5-tri-*epi*-calystegine B_2 (**10**). Other deprotection methods were also tried with the same results. We suppose that final product **10** could not be properly isolated because of the instability of the *nor*-tropanic bicyclic ring,



Scheme 6. Synthesis of 3-*O*-benzyl-1,3,5-tri-*epi*-calystegine B_2 (**35**). NOE dif. couplings of **35**. a) HCl (1 N), 10 h, room temp., **35** (53%).

presumably due to the axial dispositions of its OH groups at C-2 and C-4. In addition, no natural *nor*-tropanic alkaloid presenting such a hydroxylation pattern has to date been described, possibly because of low stability. In the same way, attempts to obtain 3-*epi*-calystegine B_2 (**11**) yielded a complex mixture of compounds, presumably those corresponding to the bicyclic and monocyclic rings of 3-*epi*-calystegine B_2 (**11**, Figure 2). Similar results have been described by Madsen[8f] in the synthesis of three different isomers of **11** presenting the same axial disposition of the OH group at C-3 and are probably due to a destabilizing 1,3-diaxial interaction between the OH group at C-3 and the methylene groups.

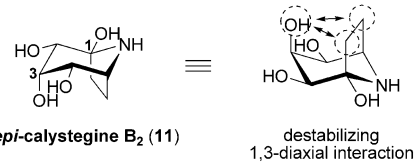


Figure 2. Proposed destabilizing interaction in 3-*epi*-calystegine (**11**).

Conclusions

We describe a total synthesis of 1,3,5-tri-*epi*-calystegine B_2 (**10**) as its 3-*O*-benzyl derivative **35**, starting from the common sugar L-sorbose. The synthetic route includes a stereoselective nitrone alkylation combined with RCM to afford a tricyclic intermediate easily transformed into the desired calystegine. This is a rare example of a polyhydroxylated *nor*-tropanic ring with two of its piperidic OH groups in an axial disposition.

Experimental Section

General: Solutions were dried with $MgSO_4$ before concentration under reduced pressure. The ^{1}H and ^{13}C NMR spectra were recorded with Variant INOVA UNITY 300 MHz, Variant DIRECT DRIVE 400 MHz and 500 MHz spectrometers. Chemical shifts are

quoted in ppm and are referenced to residual H in the deuterated solvent as the internal standard. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; m, multiplet and br, broad. IR spectra were recorded with a Perkin–Elmer FT-IR Spectrum One instrument and mass spectra were recorded with Hewlett–Packard HP-5988-A and Fisons mod. Platform II and VG Autospec-Q mass spectrometers. Optical rotations were measured, unless otherwise stated, for solutions in $CHCl_3$ (1 dm tube) with a Jasco DIP-370 polarimeter. TLC was performed on precoated silica gel (60 F_{254}) aluminium sheets and compounds were detected with a mixture of ammonium molybdate (10% w/v) in aqueous sulfuric acid (10%) containing cerium sulfate (0.8% w/v) and heating. R_f values refer to these TLC plates developed in the solvents indicated. Column chromatography was performed on silica gel (Merck, 7734). Non-crystalline compounds were shown to be homogeneous by chromatographic methods and characterized by NMR and HRMS (LSIMS).

1,2-Dideoxy-3,4:5,7-di-*O*-isopropylidene-α-L-*xylo*-hept-1-en-3-ulofuranose (13): A solution of *t*BuOK (5.5 g, 46 mmol) in anhydrous THF (30 mL) was added under Ar to a stirred suspension of methyltriphenylphosphonium bromide (16.8 g, 46 mmol) in a solution of **12**[10] (7.9 g, 30 mmol) in anhydrous THF (30 mL). After 5 h the reaction mixture was diluted with diethyl ether, washed with aqueous $KHSO_4$ (10%) and brine and then concentrated to a residue. Column chromatography (diethyl ether/hexane, 1:2) gave **13** (4.14 g, 60%) as a colourless syrup. R_f = 0.7 (diethyl ether). $[\alpha]_D^{25}$ = +20 (*c* = 1.6, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.05 (dd, $J_{1trans,2}$ = 17.1, $J_{1cis,2}$ = 10.4 Hz, 1 H, 2-H), 5.70 (dd, J_{gem} = 1.7 Hz, 1 H, 1*trans*-H), 5.29 (dd, 1 H, 1*cis*-H), 4.30 (d, $J_{5,6}$ = 2.1 Hz, 1 H, 5-H), 4.28 (s, 1 H, 4-H), 4.09–4.07 (m, 3 H, 6,7,7′-H), 1.52, 1.43, 1.36 and 1.35 (4×s, 12 H, 2×CMe_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.1 (C-2), 117.2 (C-1), 112.9 (C-3), 111.5 (1,3-dioxolane, *C*Me_2), 97.2 (*C*Me_2, 1,3-dioxane), 87.7 (C-4), 73.6 (C-6), 72.4 (C-5), 60.2 (C-7), 28.8 and 18.6 (C*Me*$_2$, 1,3-dioxane), 27.0 and 26.0 (C*Me*$_2$, 1,3-dioxolane) ppm. IR: $\tilde{\nu}_{max}$ = 1383 and 1375 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{13}H_{20}NaO_5$ [M + Na]$^+$ 279.1208; found 279.1208 (deviation +0.2 ppm).

1,2-Dideoxy-3,4-*O*-isopropylidene-α-L-*xylo*-hept-1-en-3-ulofuranose (14): A solution of **13** (16.34 g, 63.37 mmol) in aqueous AcOH (50%, 100 mL) was heated at 50 °C for 2 h. TLC (diethyl ether) showed the absence of **13** and the presence of a new compound of lower R_f. The solvent was removed, the obtained residue was dissolved in EtOAc and neutralized with K_2CO_3, and the solvent was removed again. Column chromatography of the residue (diethyl ether/hexane, 3:2 → diethyl ether/MeOH, 20:1) yielded **14** (12.24 g, 93%) as a colourless syrup. R_f = 0.3 (diethyl ether). $[\alpha]_D^{26}$ = +30 (*c* = 1.2, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.04 (dd, $J_{1trans,2}$ = 17.1, $J_{1cis,2}$ = 10.6 Hz, 1 H, 2-H), 5.64 (dd, J_{gem} = 1.4 Hz, 1 H, 1*trans*-H), 5.28 (dd, 1 H, 1*cis*-H), 4.31 (d, $J_{5,6}$ = 3.0 Hz, 1 H, 5-H), 4.30 (s, 1 H, 4-H), 4.22 (q, $J_{6,7}$ = $J_{6,7'}$ = 3.0 Hz, 1 H, 6-H), 4.11 (dd, $J_{7,7'}$ = 12.5 Hz, 1 H, 7-H), 4.03 (dd, 1 H, 7′-H), 1.50 and 1.32 (2×s, 6 H, CMe_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.2 (C-2), 117.1 (C-1), 112.6 (C-3), 111.7 (*C*Me_2), 88.6 (C-4), 79.5 and 77.6 (C-5,6), 61.4 (C-7), 27.1 and 26.1 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3444 (OH), 1381 and 1373 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{10}H_{16}NaO_5$ [M + Na]$^+$ 239.0898; found 239.0895 (deviation –1.1 ppm).

7-*O*-*tert*-Butyldiphenylsilyl-1,2-dideoxy-3,4-*O*-isopropylidene-α-L-*xylo*-hept-1-en-3-ulofuranose (15): Et_3N (0.9 mL, 6.3 mmol), DMAP (6 mg) and *tert*-butylchlorodiphenylsilane (1.2 mL, 4.7 mmol) were added under Ar to a stirred solution of **14** (680 mg, 3.15 mmol) in anhydrous DCM (15 mL). The mixture was stirred at room temp. for 2 h, and TLC (diethyl ether) revealed the presence of a new compound of higher mobility. MeOH (1 mL) was added and the reaction mixture was stirred for 20 min, DCM (15 mL) was then added, and the mixture was washed successively with aqueous HCl (10%), H_2O, aqueous $NaHCO_3$ (10%) and H_2O. The organic phase was concentrated to a residue and column chromatographed (diethyl ether/hexane, 1:5 → diethyl ether) to yield **15** (1.2 g, 84%) as a colourless syrup. R_f = 0.6 (diethyl ether/hexane, 1:1). $[\alpha]_D^{25}$ = –10 (*c* = 1.6, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75–7.36 (m, 10 H, 2×Ph), 6.09 (dd, $J_{1trans,2}$ = 17.1, $J_{1cis,2}$ = 10.5 Hz, 1 H, 2-H), 5.70 (dd, J_{gem} = 1.6 Hz, 1 H, 1*trans*-H), 5.18 (dd, 1 H, 1*cis*-H), 4.38 (brt, $J_{5,6}$ = $J_{5,HO}$ = 2.4 Hz, 1 H, 5-H), 4.35 (s, 1 H, 4-H), 4.25 (d, 1 H, HO), 4.23–4.08 (m, 3 H, 6,7,7′-H), 1.49 and 1.46 (2×s, 6 H, CMe_2) and 1.04 (s, 9 H, CMe_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.5 (C-2), 135.8, 135.6, 132.4, 132.0, 130.2 and 128.0 (Ph), 116.9 (C-1), 112.7 and 111.4 (C-3,*C*Me_2), 88.5 (C-4), 79.1 and 77.7 (C-5,6), 63.1 (C-7), 27.2 and 26.2 (C*Me*$_2$), 26.8 (C*Me*$_3$) and 19.1 (*C*Me_3) ppm. IR: $\tilde{\nu}_{max}$ = 3460 (OH) and 1373 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{26}H_{34}NaO_5Si$ [M + Na]$^+$ 477.2074; found 477.2073 (deviation –0.1 ppm).

5-*O*-Benzyl-7-*O*-*tert*-butyldiphenylsilyl-1,2-dideoxy-3,4-*O*-isopropylidene-α-L-*xylo*-hept-1-en-3-ulofuranose (16): 2-Benzyloxy-1-methylpyridinium triflate (1.6 g, 4.6 mmol) and magnesium oxide (180 mg, 4.46 mmol) were added to a solution of **15** (421 mg, 0.93 mmol) in α,α,α-trifluorotoluene (7 mL) and the mixture was heated at 90 °C for 24 h. TLC (diethyl ether/hexane, 1:3) revealed the presence of **16** and a new product with higher R_f. The reaction mixture was filtered and washed with DCM. The filtrate was concentrated to a residue that was dissolved in DCM and washed with brine, and the solvents were evaporated. Chromatography (diethyl ether/hexane, 1:20) of the residue yielded **16** (364 mg, 72%) as a colourless syrup together with **15** (570 mg). R_f 0.7 (diethyl ether/hexane, 1:1). $[\alpha]_D^{25}$ = +20 (*c* = 1.9, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71–7.30 (m, 15 H, 3×Ph), 6.01 (dd, $J_{1cis,2}$ = 10.5, $J_{1trans,2}$ = 17.1 Hz, 1 H, 2-H), 5.61 (dd, J_{gem} = 1.5 Hz, 1 H, 1*trans*-H), 5.26 (dd, 1 H, 1*cis*-H), 4.72 and 4.63 (2×d, *J* = 11.9 Hz, 2 H, CH_2Ph), 4.47 (m, 1 H, 6-H), 4.43 (s, 1 H, 4-H), 4.13 (d, $J_{5,6}$ = 3.1 Hz, 1 H, 5-H), 4.10 (dd, $J_{6,7}$ = 8.4 Hz, 1 H, 7-H), 3.97 (dd, $J_{6,7'}$ = 5.2, $J_{7,7'}$ = 9.8 Hz, 1 H, 7′-H), 1.58 and 1.39 (2×s, 6 H, CMe_2) and 1.10 (s, 9 H, CMe_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.0, 133.5 and 133.4 (3×Ph *ipso*), 136.3 (C-2), 135.7, 129.8, 129.7, 128.4, 121.7 and 121.3 (Ph), 117.0 (C-1), 112.8 and 111.7 (C-3,*C*Me_2), 85.5, 81.9 and 81.4 (C-4,5,6), 72.1 (*C*H_2Ph), 60.5 (C-7), 27.2 and 26.3 (C*Me*$_2$), 26.9 (C*Me*$_3$) and 19.3 (*C*Me_3) ppm. IR: $\tilde{\nu}_{max}$ = 3071 (arom.) and 1373 (CMe_2) cm^{-1}. $C_{33}H_{40}O_5Si$ (544.75): calcd. C 72.76, H 7.40; found C 71.37, H 6.92.

5-*O*-Benzyl-1,2-dideoxy-3,4-*O*-isopropylidene-α-L-*xylo*-hept-1-en-3-ulofuranose (17): TBAF·3H_2O (694 mg, 2.20 mmol) was added to a stirred solution of **16** (1.04 g, 1.84 mmol) in THF (8 mL). The mixture was stirred at room temp., and after 18 h the TLC (diethyl ether/hexane, 3:1) revealed the absence of the starting material and the presence of a new compound of lower R_f. The mixture was concentrated to a residue that was dissolved in DCM and washed with H_2O, and the organic layer was then concentrated to a new residue that was chromatographed (diethyl ether/hexane, 1:1) to give **17** (412 mg, 73%) as a colourless syrup. R_f = 0.2 (diethyl ether/hexane, 3:2). $[\alpha]_D^{25}$ = +58 (*c* = 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.32 (m, 5 H, Ph), 6.06 (dd, $J_{1cis,2}$ = 10.5, $J_{1trans,2}$ = 17.1 Hz, 1 H, 2-H), 5.69 (dd, J_{gem} = 1.6 Hz, 1 H, 1*trans*-H), 5.32 (dd, 1 H, 1*cis*-H), 4.74 and 4.51 (2×d, *J* = 12.0 Hz, 2 H, CH_2Ph), 4.47 (s, 1 H, 4-H), 4.41 (m, 1 H, 6-H), 4.05 (d, $J_{5,6}$ = 3.3 Hz, 1 H, 5-H), 4.00 (dd, $J_{7,7'}$ = 11.9, $J_{6,7}$ = 5.7 Hz, 1 H, 7-H), 3.90 (dd, $J_{6,7'}$

= 4.9 Hz, 1 H, 7′-H), 1.56 and 1.40 (2×s, 6 H, CMe_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.5 (Ph *ipso*), 136.4 (C-2), 128.9, 128.4 and 127.9 (Ph), 117.5 (C-1), 113.0 and 112.1 (C-3, *C*Me_2), 85.7, 83.2 and 81.2 (C-4,5,6), 72.0 (*C*H_2Ph), 61.4 (C-7), 27.4 and 26.6 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3469 (OH), 3031 (arom.) and 1374 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{17}H_{22}NaO_5$ [M + Na]$^+$ 329.1367; found 329.1365 (deviation –0.7 ppm).

Synthesis of Nitrone 19: A solution of Dess–Martin periodinane in DCM (15%, 4.4 mL, 2.1 mmol) was added under Ar at 0 °C to a solution of **17** (536 mg, 1.75 mmol) in anhydrous DCM (7 mL) and the mixture was stirred at room temp. for 18 h. The solvent was evaporated to afford a residue that was dissolved in ether, cooled to 5 °C and filtered. The filtrate was washed with aqueous $NaHCO_3$ (10%) and the organic layer was concentrated to afford a residue. This residue was percolated with ether to yield presumably aldehyde **18** (522 mg, 98%), which was immediately used in the next step. R_f = 0.7 (diethyl ether). IR: $\tilde{\nu}_{max}$ = 3031 (arom.), 1740 (CO) and 1374 (CMe_2) cm^{-1}.

MS (3 Å, 1.3 g) and a solution of **18** (1.95 g, 6.40 mmol) in MeOH (10 mL) were added under Ar to a solution of BnNHOH·HCl (1.22 g, 7.68 mmol) and AcONa (637 mg, 7.68 mmol) in anhydrous MeOH (35 mL). The mixture was stirred at room temp. for 18 h, and TLC (diethyl ether) revealed the absence of the starting material and the presence of a new compound of lower R_f. The solvent was evaporated and the obtained residue was chromatographed (diethyl ether/hexane, 3:1) to give **19** (1.87 g, 71%). R_f = 0.4 (diethyl ether). $[\alpha]_D^{26}$ = +137 (*c* = 1.4, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.32 (m, 10 H, 2×Ph), 6.94 (d, $J_{6,7}$ = 4.5 Hz, 1 H, 7-H), 6.05 (dd, $J_{1cis,2}$ = 10.5, $J_{1trans,2}$ = 17.1 Hz, 1 H, 2-H), 5.65 (dd, J_{gem} = 1.5 Hz, 1 H, 1*trans*-H), 5.39 (br dd, 1 H, 6-H), 5.31 (dd, 1 H, 1*cis*-H), 4.92 and 4.85 (2×d, *J* = 13.6 Hz, 2 H, OC*H*$_2$Ph), 4.59 (d, $J_{5,6}$ = 3.1 Hz, 1 H, 5-H), 4.54 and 4.44 (2×d, *J* = 11.8 Hz, 2 H, NC*H*$_2$Ph), 4.43 (s, 1 H, 4-H), 1.56 and 1.37 (2×s, 6 H, CMe_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.0 and 132.5 (2×Ph *ipso*), 136.4 (C-2), 136.0 (C-7), 129.7, 129.3, 129.2, 128.1, 127.9 and 127.3 (CH_2*Ph*), 117.4 (C-1), 112.9 and 112.3 (C-3, *C*Me_2), 86.0, 82.9 and 78.9 (C-4,5,6), 72.6 (O*C*H_2Ph), 69.5 (N*C*H_2Ph), 27.4 and 26.4 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3031 (arom.) and 1374 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{24}H_{27}NNaO_5$ [M + Na]$^+$ 432.1780; found 432.1784 (deviation +0.9 ppm).

5-*O*-Benzyl-7-[(benzyl)(hydroxy)amino]-1,2,7,8,9-pentadeoxy-3,4-*O*-isopropylidene-β-D-*ido*- and -α-L-*gluco*-nona-1,8-dien-3-ulofuranose (20a and 20b): Vinylmagnesium bromide (4.7 mL, 3.3 mmol) was added at –78 °C under Ar to a stirred solution of **19** (935 mg, 2.3 mmol) in anhydrous THF (11 mL). After 2 h, TLC (diethyl ether) revealed the absence of the starting material, whereas TLC (diethyl ether/hexane, 2:1) showed the presence of two new compounds of lower R_f. MeOH (3 mL) was added, and the reaction mixture was stirred for a further 1 h. Solvent evaporation gave a residue that was column chromatographed (diethyl ether/hexane, 1:2) to give a mixture of compounds **20a** and **20b** (900 mg, 90%) in a 2:1 ratio (by ^1H NMR). Fresh column chromatography (diethyl ether/hexane, 1:4) of this mixture allowed us first to obtain compound **20a** (603 mg, 60%). R_f = 0.6 (diethyl ether/hexane, 2:1). $[\alpha]_D^{26}$ = +15 (*c* = 0.1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.24 (m, 10 H, 2×Ph), 6.16 (ddd, $J_{7,8}$ = 9.2, $J_{8,9cis}$ = 10.2, $J_{8,9trans}$ = 17.4 Hz, 1 H, 8-H), 6.00 (dd, $J_{1cis,2}$ = 10.4, $J_{1trans,2}$ = 17.0 Hz, 1 H, 2-H), 5.61 (dd, J_{gem} = 1.6 Hz, 1 H, 1*trans*-H), 5.47 (dd, J_{gem} = 1.6 Hz, 1 H, 9*cis*-H), 5.35 (dd, 1 H, 9*trans*-H), 5.24 (dd, 1 H, 1*cis*-H), 4.70 and 4.62 (2×d, *J* = 11.9 Hz, 2 H, OC*H*$_2$Ph), 4.59 (dd, $J_{5,6}$ = 2.7, $J_{6,7}$ = 9.4 Hz, 1 H, 6-H), 4.43 (br s, 1 H, OH), 4.39 (s, 1 H, 4-H), 3.95 and 3.70 (2×d, *J* = 13.5 Hz, 2 H, NC*H*$_2$Ph), 4.14 (d, 1 H, 5-H), 3.78 (t, 1 H, 7-H), 1.50 and 1.34 (2×s, 6 H, CMe_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.3 and 138.2 (2×Ph *ipso*), 138.2 (C-2), 132.5 (C-8), 129.6, 128.6, 128.5, 127.9, 127.5 and 127.4 (CH_2*Ph*), 121.4 (C-9), 117.1 (C-1), 112.7 and 111.7 (C-3, *C*Me_2), 85.4 (C-4), 82.7 (C-5), 81.3 (C-6), 72.5 (O*C*H_2Ph), 67.3 (C-7), 62.1 (N*C*H_2Ph), 27.4 and 26.5 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3467 (OH), 3030 (arom.) and 1374 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{26}H_{31}NNaO_5$ [M + Na]$^+$ 460.5181; found 460.5178 (deviation –0.6 ppm).

This was followed by **20b** (297 mg, 30%). R_f = 0.5 (diethyl ether/hexane, 2:1). $[\alpha]_D^{24}$ = +48 (*c* = 1.2, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.23 (m, 10 H, 2×Ph), 6.03 (dd, $J_{1cis,2}$ = 10.6, $J_{1trans,2}$ = 17.0 Hz, 1 H, 2-H), 5.97 (dt, 1 H, 8-H), 5.63 (dd, J_{gem} = 1.5 Hz, 1 H, 1*trans*-H), 5.35 (dd, J_{gem} = 1.9, $J_{8,9cis}$ = 10.6 Hz, 1 H, 9*cis*-H), 5.27 (dd, 1 H, 1*cis*-H), 5.23 (dd, $J_{8,9trans}$ = 17.4 Hz, 1 H, 9*trans*-H), 5.04 (br s, 1 H, OH), 4.63 (dd, $J_{5,6}$ = 2.7, $J_{6,7}$ = 9.6 Hz, 1 H, 6-H), 4.58 and 4.39 (2×d, *J* = 11.4 Hz, 2 H, OC*H*$_2$Ph), 4.37 (s, 1 H, 4-H), 3.98 and 3.82 (2×d, *J* = 13.5 Hz, 2 H, NC*H*$_2$Ph), 3.83 (d, 1 H, 5-H), 3.80 (t, $J_{7,8}$ = 10.0 Hz, 7-H), 1.55 and 1.36 (2×s, 6 H, CMe_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.4 and 137.9 (2×Ph *ipso*), 138.3 (C-2), 132.1 (C-8), 129.5, 128.6, 128.3, 127.9, 127.6 and 127.5 (CH_2*Ph*), 121.1 (C-9), 117.2 (C-1), 113.2 and 111.9 (C-3, *C*Me_2), 84.6 (C-4), 83.1 (C-5), 80.7 (C-6), 72.0 (O*C*H_2Ph), 68.0 (C-7), 61.5 (N*C*H_2Ph), 27.4 and 26.6 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3436 (OH), 3030 (arom.) and 1374 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for *m*/*z* 460.5183 [M + Na]$^+$; found $C_{26}H_{31}NNaO_5$ 460.5178 (deviation –1.0 ppm).

5-*O*-Benzyl-7-benzylamino-1,2,7,8,9-pentadeoxy-3,4-*O*-isopropylidene-β-D-*ido*- and α-L-*gluco*-nona-1,8-dien-3-ulofuranose (21a and 21b): In (488 mg, 4.25 mmol) was added to a stirred solution of **20a** (747 mg, 1.7 mmol) in EtOH/NH_4Cl (2:1, 30 mL) and the mixture was heated to 120 °C for 48 h. TLC (diethyl ether/hexane, 3:1) revealed the presence of a new compound of lower R_f. The reaction mixture was filtered under celite, diluted with AcOEt and washed with a sat. solution of Na_2CO_3. The organic layer was concentrated to give a residue that was column chromatographed (diethyl ether) to yield **21a** (690 mg, 96%). R_f = 0.4 (diethyl ether/hexane, 2:1). $[\alpha]_D^{26}$ = +30 (*c* = 1.8, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.24 (m, 10 H, 2×Ph), 6.05 (dd, $J_{1cis,2}$ = 10.5, $J_{1trans,2}$ = 17.1 Hz, 1 H, 2-H), 5.85 (ddd, $J_{7,8}$ = 7.9, $J_{8,9cis}$ = 9.6, $J_{8,9trans}$ = 17.6 Hz, 1 H, 8-H), 5.66 (dd, J_{gem} = 1.4 Hz, 1 H, 1*trans*-H), 5.34–5.27 (m, 3 H, 1*cis*,9*cis*,9*trans*-H), 4.73 and 4.55 (2×d, *J* = 11.8 Hz, 2 H, OC*H*$_2$Ph), 4.45 (s, 1 H, 4-H), 4.16 (dd, $J_{5,6}$ = 2.9, $J_{6,7}$ = 8.1 Hz, 1 H, 6-H), 4.14 (d, 1 H, 5-H), 3.88 and 3.65 (2×d, *J* = 13.0 Hz, 2 H, NC*H*$_2$Ph), 3.64 (t, 1 H, 7-H), 1.55 and 1.38 (2×s, 6 H, CMe_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.8 and 137.9 (2×Ph *ipso*), 138.1 and 136.7 (C-2,8), 128.7, 128.5, 128.4, 128.0, 127.8 and 127.0 (CH_2*Ph*), 117.7 and 117.2 (C-1,9), 112.8 and 111.7 (C-3, *C*Me_2), 85.2, 83.9 and 82.2 (C-4,5,6), 72.1 (O*C*H_2Ph), 59.3 (C-7), 51.4 (N*C*H_2Ph), 27.4 and 26.6 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3028 (arom.) and 1373 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{26}H_{31}NNaO_4$ [M + Na]$^+$ 444.5186; found 444.5184 (deviation –0.4 ppm).

Compound **20b** (1.33 g, 3.03 mmol) was treated with EtOH/NH_4Cl (3:1, 50 mL) and In (596 mg, 5.29 mmol) as in the case of **20a** to give **21b** (1.2 g, 94%). R_f = 0.3 (diethyl ether/hexane, 2:1) $[\alpha]_D^{26}$ = +3 (*c* = 1.1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.25 (m, 10 H, 2×Ph), 6.03 (dd, $J_{1cis,2}$ = 10.5, $J_{1trans,2}$ = 17.1 Hz, 1 H, 2-H), 5.72 (ddd, $J_{7,8}$ = 8.1, $J_{8,9cis}$ = 10.1, $J_{8,9trans}$ = 17.9 Hz, 1 H, 8-H), 5.62 (dd, J_{gem} = 1.5 Hz, 1 H, 1*trans*-H), 5.35 (dd, J_{gem} = 1.8 Hz, 1 H, 9*trans*-H), 5.29 (dd, 1 H, 1*cis*-H), 5.26 (dd, 1 H, 9*cis*-H), 4.62 and 4.44 (2×d, *J* = 11.5 Hz, 2 H, OC*H*$_2$Ph), 4.40 (s, 1 H,

4-H), 4.26 (dd, $J_{5,6}$ = 2.9, $J_{6,7}$ = 9.4 Hz, 1 H, 6-H), 3.89 (d, 1 H, 5-H), 3.86 and 3.68 (2 × d, J = 13.2 Hz, 2 H, NCH_2Ph), 3.73 (t, 1 H, 7-H), 1.56 and 1.37 (2 × s, 6 H, CMe_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.7 and 137.9 (2 × Ph *ipso*), 136.7 and 136.6 (C-2,8), 128.6, 128.5, 128.5, 128.0, 127.7 and 127.0 (CH_2*Ph*), 119.4 and 117.2 (C-1,9), 113.0 and 112.0 (C-3, *C*Me$_2$), 85.1, 83.7 and 82.6 (C-4,5,6), 72.0 (O*C*H$_2$Ph), 60.4 (C-7), 52.0 (N*C*H$_2$Ph), 27.3 and 26.6 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3028 (arom.) and 1373 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{26}H_{31}NNaO_4$ [M + Na]$^+$ 444.5188; found 444.5184 (deviation –0.8 ppm).

5-*O*-Benzyl-7-[(benzyl)(benzyloxycarbonyl)amino]-1,2,7,8,9-pentadeoxy-3,4-*O*-isopropylidene-β-D-*ido*- and -α-L-*gluco*-nona-1,8-dien-3-ulofuranose (22a and 22b): CbzCl (0.87 mL, 6.06 mmol) was added to a stirred suspension of **21a** (2.13 g, 5.05 mmol) and K_2CO_3 (4.88 g, 35.35 mmol) in anhydrous acetone (25 mL) and the mixture was stirred at room temp. for 4.5 h. TLC (diethyl ether/hexane, 3:1) showed a new product of lower R_f. MeOH (3 mL) was added to the reaction mixture, which was stirred for 15 min and then filtered and concentrated to afford a residue that was column chromatographed (AcOEt/hexane, 1:6) to give **22a** (2.6 g, 92%). R_f = 0.6 (diethyl ether/hexane, 2:1). $[\alpha]_D^{26}$ = +32 (c = 1.8, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.21 (m, 15 H, 3 × Ph), 6.01–5.94, 5.61–5.57, 5.26–4.56 and 4.39–3.57 (4 × m, 16 H, O*C*H$_2$Ph,N*C*H$_2$Ph, Cbz, 1*cis*,1*trans*,2,4,5,6,7,8,9*cis*,9*trans*-H), 1.29 and 1.26 (2 × s, 6 H, CMe_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.7 (Cbz), 138.8, 138.1 and 133.1 (Ph *ipso*), 137.8 and 136.6 (C-2,8), 128.7, 128.6, 128.3, 128.2 and 128.1 (Ph), 117.3 (C-1,9), 112.9 and 111.8 (C-3,*C*Me$_2$), 84.8, 82.6 and 80.9 (C-4,5,6), 71.8 (O*C*H$_2$Ph), 67.8 (Cbz), 54.1 (C-7), 51.4 (N*C*H$_2$Ph), 27.3 and 26.5 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3031 (arom.), 1699 (Cbz) and 1373 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{34}H_{37}NNaO_6$ [M + Na]$^+$ 578.2520; found 578.2519 (deviation –0.1 ppm).

Compound **21b** (1.23 g, 2.9 mmol) was treated as in the case of **21a** with K_2CO_3 (2.8 g, 20.3 mmol) in anhydrous acetone (22 mL) and CbzCl (0.5 mL, 3.5 mmol) to give **22b** (2.72 g, 94%). R_f = 0.4 (diethyl ether/hexane, 2:1). $[\alpha]_D^{27}$ = +31 (c = 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.23 (m, 15 H, 3 × Ph), 6.01–5.99, 5.66–5.53, 5.29–4.87 and 4.73–3.74 (4 × m, 16 H, O*C*H$_2$Ph,N*C*H$_2$Ph, Cbz, 1*cis*,1*trans*,2,4,5,6,7,8,9*cis*,9*trans*-H, 2 rotamers), 1.66, 1.53, 1.37 and 1.33 (4 × s, 6 H, CMe_2, 2 rotamers) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.8 (Cbz), 138.7, 138.5 and 133.5 (Ph *ipso*), 136.7 and 136.4 (C-2,8), 128.3, 128.2, 127.7, 127.3, 127.2, 127.0 and 126.9 (Ph), 118.9 and 117.0 (C-1,9), 112.7 and 111.8 (C-3, *C*Me$_2$), 85.0, 82.2 and 79.6 (C-4,5,6), 71.7 (O*C*H$_2$Ph), 66.8 (Cbz), 60.3 (C-7), 51.6 (N*C*H$_2$Ph), 27.2 and 26.5 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3030 (arom.), 1699 (Cbz) and 1373 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{34}H_{37}NNaO_6$ [M + Na]$^+$ 578.2515; found 578.2519 (deviation +0.6 ppm).

7-*O*-*tert*-Butyldiphenylsilyl-1,2-dideoxy-3,4-*O*-isopropylidene-α-L-*ribo*-hept-1-en-3-ulofuranose (24): MS (4 Å, 2 g), *N*-methylmorpholine *N*-oxide (1.85 g, 15.8 mmol) and tetrapropylammonium perruthenate (70 mg) were added to a stirred solution of **15** (4.79 g, 10.55 mmol) in anhydrous DCM (30 mL) and the mixture was stirred for 2 h at room temp. TLC (diethyl ether/hexane, 2:3) revealed the presence of a new compound of lower R_f. The mixture was diluted with diethyl ether and filtered through silica gel. The filtrate was concentrated to a residue that was dissolved in anhydrous MeOH (35 mL) and cooled to 0 °C, and $NaBH_4$ (800 mg, 21.03 mmol) was added. The reaction was complete after 30 min. TLC (diethyl ether/hexane, 1:2) showed the presence of a new compound of lower R_f. The crude product was neutralized with glacial AcOH and concentrated to give a residue that was chromatographed under column (diethyl ether/hexane, 1:4) to yield **24** (3.64 g, 76%). R_f = 0.2 (diethyl ether/hexane, 1:2). $[\alpha]_D^{25}$ = –33 (c = 1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.72–7.34 (m, 10 H, 2 × Ph), 5.96 (dd, $J_{1trans,2}$ = 17.0, $J_{1cis,2}$ = 11.4 Hz, 1 H, 2-H), 5.69 (dd, J_{gem} = 1.6 Hz, 1 H, 1*trans*-H), 5.29 (dd, 1 H, 1*cis*-H), 4.39 (d, $J_{4,5}$ = 4.7 Hz, 1 H, 4-H), 4.23 (br dt, $J_{5,6}$ = $J_{5,OH}$ = 9.0 Hz, 1 H, 5-H), 4.02 (dd, $J_{7,7'}$ = 11.3, $J_{6,7}$ = 2.4 Hz, 7-H), 3.94–3.89 (m, 1 H, 6-H), 3.86 (dd, $J_{6,7'}$ = 3.0 Hz, 7′-H), 2.19 (br d, 1 H, OH), 1.58 and 1.42 (2 × s, 6 H, CMe_2) and 1.04 (s, 9 H, CMe_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.8 (C-2), 133.3, 133.2, 129.8, 129.7 and 127.8 (Ph), 117.9 (C-1), 112.8 (*C*Me$_2$), 111.1 (C-3), 82.6 (C-4), 81.6 (C-6), 71.0 (C-5), 62.0 (C-7), 27.1 and 26.8 (C*Me*$_2$), 26.9 (C*Me*$_3$) and 19.3 (*C*Me$_3$) ppm. IR: $\tilde{\nu}_{max}$ = 3470 (OH) and 1373 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{26}H_{34}NaO_5Si$ [M + Na]$^+$ 477.2071; found 477.2073 (deviation +0.4 ppm).

5-*O*-Benzyl-7-*O*-*tert*-butyldiphenylsilyl-1,2-dideoxy-3,4-*O*-isopropylidene-α-L-*ribo*-hept-1-en-3-ulofuranose (25): Alcohol **24** (2.95 g, 6.50 mmol) was added to a stirred suspension of NaH (60% oil dispersion, 310 mg, 7.79 mmol) in anhydrous DMF (20 mL), and the reaction was allowed to proceed at room temp. for 15 min. The mixture was then cooled to 0 °C and BrBn (0.85 mL, 7.14 mmol) was added dropwise. The reaction mixture was allowed to reach room temp. and stirred for 24 h. TLC (diethyl ether/hexane, 1:2) revealed the presence of a new compound of lower R_f. MeOH (10 mL) was added, and the mixture was stirred for 15 min. Concentration of the mixture gave a residue that was dissolved in ether and washed with brine. The organic layer was evaporated and the obtained residue was chromatographed on a column (diethyl ether/hexane, 1:4) to yield **25** (2.47 g, 70%). R_f = 0.5 (diethyl ether/hexane, 1:2). $[\alpha]_D^{25}$ = –37 (c = 1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73–7.28 (m, 15 H, 3 × Ph), 5.92 (dd, $J_{1cis,2}$ = 10.4, $J_{1trans,2}$ = 17.1 Hz, 1 H, 2-H), 5.71 (dd, J_{gem} = 1.7 Hz, 1 H, 1*trans*-H), 5.25 (dd, 1 H, 1*cis*-H), 4.74 and 4.59 (2 × d, J = 11.9 Hz, 2 H, CH_2Ph), 4.40 (d, $J_{4,5}$ = 3.8 Hz, 1 H, 4-H), 4.23 (dt, $J_{6,7}$ = $J_{6,7'}$ = 1.9, $J_{5,6}$ = 9.1 Hz, 1 H, 1 H, 6-H), 4.15 (dd, 1 H, 5-H), 4.06 (dd, $J_{7,7'}$ = 11.9 Hz, 1 H, 7-H), 3.82 (dd, 1 H, 7′-H), 1.60 and 1.42 (2 × s, 6 H, CMe_2) and 1.01 (s, 9 H, CMe_3) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.8, 133.4 and 133.2 (Ph *ipso*), 136.1, 134.9, 129.7, 128.5, 127.9 and 127.8 (Ph), 135.7 (C-2), 117.9 (C-1), 112.9 and 111.0 (C-3, *C*Me$_2$), 81.1, 80.0 and 76.5 (C-4,5,6), 72.5 (*C*H$_2$Ph), 61.5 (C-7), 27.3 and 26.6 (C*Me*$_2$), 26.9 (C*Me*$_3$) and 19.3 (*C*Me$_3$) ppm. IR: $\tilde{\nu}_{max}$ = 1373 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{33}H_{40}NaO_5Si$ [M + Na]$^+$ 567.2543; found 567.2548 (deviation +0.8 ppm).

5-*O*-Benzyl-1,2-dideoxy-3,4-*O*-isopropylidene-α-L-*ribo*-hept-1-en-3-ulofuranose (26): TBAF·3 H_2O (2 g, 6.3 mmol) was added to a stirred solution of **25** (2.47 g, 4.54 mmol) in THF (30 mL) and the mixture was stirred for 5 h at room temp. TLC (diethyl ether/hexane, 3:2) revealed the presence of a new compound of lower R_f. The mixture was concentrated, the obtained residue was dissolved in DCM and washed with H_2O, and the organic layer was concentrated again. Column chromatography (diethyl ether/hexane, 1:1) of the residue gave **26** (1.3 g, 94%). R_f = 0.2 (diethyl ether/hexane, 3:2). $[\alpha]_D^{25}$ = –102 (c = 1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38–7.29 (m, 5 H, Ph), 5.88 (dd, $J_{1trans,2}$ = 17.1, $J_{1cis,2}$ = 10.5 Hz, 1 H, 2-H), 5.50 (dd, J_{gem} = 1.4 Hz, 1 H, 1*trans*-H), 5.25 (dd, 1 H, 1*cis*-H), 4.74 and 4.57 (2 × d, J = 11.9 Hz, 2 H, CH_2Ph), 4.37 (d, $J_{4,5}$ = 4.1 Hz, 1 H, 4-H), 4.21 (dt, $J_{5,6}$ = 9.2, $J_{6,7}$ = $J_{6,7'}$ = 2.9 Hz, 1 H, 6-H), 3.93 (dd, $J_{7,7'}$ = 12.5 Hz, 1 H, 7-H), 3.84 (dd, 1 H, 5-H), 3.65 (dd, 1 H, 7′-H), 1.61 and 1.39 (2 × s, 6 H, CMe_2) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.6 (Ph *ipso*), 135.8 (C-2), 128.6, 128.1, 128.0 (Ph), 117.5 (C-1), 113.1 and 111.1 (C-3, *C*Me$_2$), 81.1, 79.5 and 76.7 (C-4,5,6), 72.5 (*C*H$_2$Ph), 61.0 (C-7), 27.1 and 26.5 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3487 (OH) and 1373 (CMe_2) cm^{-1}.

HRMS (LSIMS): calcd. for $C_{17}H_{22}NaO_5$ [M + Na]$^+$ 329.1365; found 329.1363 (deviation –0.6 ppm).

Synthesis of Nitrone 28: A solution of the Dess–Martin periodinane in DCM (15%, 10 mL, 4.8 mmol) was added at 0 °C under Ar to a stirred solution of **26** (1.23 g, 4.02 mmol) in anhydrous DCM (15 mL) and the mixture was stirred at room temp. for 18 h. The reaction mixture was processed as described for compound **18**, to give **27** (1.18 g, 97%). R_f = 0.7 (diethyl ether). IR: $\tilde{\nu}_{max}$ = 1738 (CO) cm^{-1}.

Molecular sieves (3 Å, 700 mg) and a solution of **27** (600 mg, 1.98 mmol) in anhydrous MeOH (5 mL) were added under Ar to a solution of BnNHOH·HCl (410 mg, 2.57 mmol) and AcONa (210 mg, 2.57 mmol) in anhydrous MeOH (5 mL). The reaction mixture was stirred for 18 h, and TLC (diethyl ether) revealed the presence of a new compound of lower R_f. The solvent was removed, and the obtained residue was chromatographed on a column (diethyl ether/hexane, 3:1) to give **28** (640 mg, 79%). R_f = 0.4 (diethyl ether). $[\alpha]_D^{26}$ = –21 (c = 0.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46–7.38 (m, 10 H, 2 × Ph), 6.61 (d, $J_{6,7}$ = 6.6 Hz, 1 H, 7-H), 5.86 (dd, $J_{1trans,2}$ = 17.0, $J_{1cis,2}$ = 10.8 Hz, 1 H, 2-H), 5.52 (dd, J_{gem} = 1.5 Hz, 1 H, 1*trans*-H), 5.39 (dd, $J_{5,6}$ = 8.9 Hz, 1 H, 6-H), 5.24 (dd, 1 H, 1*cis*-H), 4.92 (s, 2 H, OCH_2Ph), 4.59 and 4.47 (2 × d, J = 12.5 Hz, 2 H, NCH_2Ph), 4.38 (d, $J_{4,5}$ = 4.1 Hz, 1 H, 4-H), 3.78 (dd, 1 H, 5-H), 1.64 and 1.39 (2 × s, 6 H, CMe_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.7 and 132.6 (Ph *ipso*), 135.6 (C-2), 134.6 (C-7), 129.6, 129.4, 129.2, 128.7, 128.1 and 128.0 (Ph), 118.1 (C-1), 113.8 and 111.1 (C-3, *C*Me$_2$), 82.0, 79.8 and 73.6 (C-4,5,6), 72.3 (O*C*H$_2$Ph), 70.8 (N*C*H$_2$Ph), 27.3 and 26.7 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3031 (arom.) and 1374 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{24}H_{27}NNaO_5$ [M + Na]$^+$ 432.1774; found 432.1784 (deviation +0.2 ppm).

5-*O*-Benzyl-7-[(benzyl)(hydroxy)amino]-1,2,7,8,9-pentadeoxy-3,4-*O*-isopropylidene-β-D-*talo*-nona-1,8-dien-3-ulofuranose (29): A solution of vinylmagnesium bromide in anhydrous THF (0.7 M, 12 mL, 8.4 mmol) was added at –78 °C under Ar to a solution of **28** (1.9 g, 4.6 mmol) in anhydrous THF (22 mL). After 2 h, TLC (diethyl ether) showed the absence of the starting material, whereas TLC (diethyl ether/hexane, 2:1) showed a new compound of higher R_f. MeOH (5 mL) was added, and the mixture was stirred for a further 1 h. The crude mixture was concentrated, and the residue was chromatographed on a column (diethyl ether/hexane, 1:1) to give **29** (1.8 g, 90%). R_f = 0.8 (diethyl ether). $[\alpha]_D^{26}$ = –62 (c = 2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (m, 10 H, 2 × Ph), 6.17 (ddd, $J_{7,8}$ = 8.6, $J_{8,9cis}$ = 10.6, $J_{8,9trans}$ = 17.6 Hz, 1 H, 8-H), 5.88 (dd, $J_{1cis,2}$ = 10.6, $J_{1trans,2}$ = 17.0 Hz, 1 H, 2-H), 5.57 (dd, J_{gem} = 1.6 Hz, 1 H, 1*trans*-H), 5.42 (dd, J_{gem} = 1.9 Hz, 1 H, 9*cis*-H), 5.29 (dd, 1 H, 9*trans*-H), 5.23 (dd, 1 H, 1*cis*-H), 4.67 and 4.48 (2 × d, J = 11.5 Hz, 2 H, OCH_2Ph), 4.48 (dd, $J_{5,6}$ = 9.0, $J_{6,7}$ = 3.9 Hz, 1 H, 6-H), 4.36 (d, $J_{4,5}$ = 4.3 Hz, 1 H, 4-H), 4.06 and 3.70 (2 × d, J = 13.2 Hz, 2 H, NCH_2Ph), 3.95 (dd, 1 H, 5-H), 3.50 (dd, 1 H, 7-H), 1.61 and 1.40 (2 × s, 6 H, CMe_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.3 and 137.5 (Ph, *ipso*), 136.1 (C-2), 132.5 (C-8), 129.5, 129.4, 128.7, 128.6, 128.5, 128.4 (Ph), 121.0 (C-9), 117.8 (C-1), 113.3 and 111.3 (C-3,*C*Me$_2$), 81.1, 80.9, 78.1 and 68.6 (C-4,5,6,7), 72.6 (O*C*H$_2$Ph), 61.3 (N*C*H$_2$Ph), 27.4 and 26.9 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3030 (arom.) and 1372 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{26}H_{31}NO_5$ 437.2202 [M]$^+$; found 437.2192 (deviation –2.3 ppm).

5-*O*-Benzyl-7-benzylamino-1,2,7,8,9-pentadeoxy-3,4-*O*-isopropylidene-β-D-*talo*-nona-1,8-dien-3-ulofuranose (30): In (608 mg, 5.3 mmol) was added to a stirred solution of **29** (620 mg, 1.42 mmol) in EtOH/NH_4Cl (2:1, 24 mL), and the mixture was heated at 120 °C for 24 h. TLC (diethyl ether/hexane, 3:1) revealed the presence of a new compound of lower R_f. The reaction mixture was filtered through celite and diluted with AcOEt, and was then washed with a saturated solution of Na_2CO_3 and concentrated. The residue was column chromatographed (diethyl ether) to yield **30** (550 mg, 92%). R_f = 0.5 (diethyl ether/hexane, 2:1). $[\alpha]_D^{26}$ = –67 (c = 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.29 (m, 10 H, 2 × Ph), 5.86 (dd, $J_{1cis,2}$ = 10.4, $J_{1trans,2}$ = 17.0 Hz, 1 H, 2-H), 5.80 (ddd, $J_{7,8}$ = 8.4, $J_{8,9cis}$ = 10.2, $J_{8,9trans}$ = 17.2 Hz, 1 H, 8-H), 5.49 (dd, J_{gem} = 1.4 Hz, 1 H, 1*trans*-H), 5.23 (dd, J_{gem} = 1.6 Hz, 1 H, 9*cis*-H), 5.21 (dd, 1 H, 1*cis*-H), 5.15 (dd, 1 H, 9*trans*-H), 4.63 and 4.48 (2 × d, J = 11.9 Hz, 2 H, OCH_2Ph), 4.31 (d, $J_{4,5}$ = 4.1 Hz, 2 H, 4-H), 4.19 (dd, $J_{5,6}$ = 8.8, $J_{6,7}$ = 3.7 Hz, 1 H, 6-H), 4.04 (dd, 1 H, 5-H), 3.87 and 3.56 (2 × d, J = 13.3 Hz, 2 H, NCH_2Ph), 3.15 (dd, 1 H, 7-H), 1.60 and 1.39 (2 × s, 6 H, CMe_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.9 and 138.1 (Ph, *ipso*), 137.7 and 136.2 (C-2,8), 128.6, 128.5, 128.4, 128.4, 128.2 and 127.0 (Ph), 117.4 and 117.4 (C1,9), 113.1 and 111.2 (C-3, *C*Me$_2$), 82.2, 81.4, 78.3 and 61.0 (C-4,5,6,7), 72.5 (O*C*H$_2$Ph), 50.7 (N*C*H$_2$Ph), 27.4 and 26.8 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3030 (arom.) and 1372 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{26}H_{31}NO_4$ [M]$^+$ 421.2253; found 421.2243 (deviation –2.4 ppm).

5-*O*-Benzyl-7-[(benzyl)(benzyloxycarbonyl)amino]-1,2,7,8,9-pentadeoxy-3,4-*O*-isopropylidene-β-D-*talo*-nona-1,8-dien-3-ulofuranose (31): CbzCl (0.38 mL, 2.7 mmol) was added to a stirred suspension of **30** (810 mg, 1.9 mmol) and K_2CO_3 (1.8 g, 13.6 mmol) in anhydrous acetone (15 mL) and the mixture was stirred at room temp. for 2.5 h. TLC (diethyl ether/hexane, 3:1) revealed the presence of a new compound of lower R_f. MeOH (1 mL) was added to the reaction mixture, which was then filtered, and the filtrate was concentrated to afford a residue that was chromatographed on a column (AcOEt/hexane, 1:6) to give **31** (1.04 g, 97%). R_f = 0.6 (diethyl ether/hexane, 2:1). $[\alpha]_D^{26}$ = –32 (c = 2.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.19 (m, 15 H, 3 × Ph), 6.03–5.94 (m, 1 H), 5.70–5.63 (m, 1 H), 5.25–5.12 (m, 5 H), 4.65–4.52 (m, 5 H), 4.42 (dd, 1 H), 4.21 (d, 1 H), 3.53 (dd, 1 H), 1.56 and 1.37 (2 × s, 6 H, CMe_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, inter alia): δ = 157.0 (Cbz), 136.8 and 136.0 (C-2,8), 119.5 and 117.6 (C-1,9), 113.1 and 111.3 (C-3, *C*Me$_2$), 80.9, 79.9 and 72.7 (C-4,5,6,O*C*H$_2$Ph), 67.5 (Cbz), 60.6 (C-7), 49.2 (N*C*H$_2$Ph), 27.3 and 26.9 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3031 (arom.), 1699 (CO) and 1372 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{34}H_{37}NNaO_6$ [M + Na]$^+$ 578.2523; found 578.2519 (deviation –0.6 ppm).

(1*S*,4*R*,5*S*,6*S*,7*S*)-6-Benzyloxy-4-[(benzyl)(benzyloxycarbonyl)-amino]-1,7-isopropylidenedioxy-8-oxabicyclo[3.2.1]oct-2-ene (32): A mixture of **31** (618 mg, 1.11 mmol) and the Grubbs catalyst **23** (94 mg, 110 μmol) in anhydrous DCM (5 mL) was heated in a microwave under Ar in a sealed tube at 100 °C. After 2 h, TLC (diethyl ether/hexane, 2:1) revealed the presence of a new compound of lower R_f. The reaction mixture was supported on silica gel and chromatographed on a column (diethyl ether/hexane, 1:2) to give **32** (386 mg, 79%). R_f = 0.5 (diethyl ether/hexane, 2:1). $[\alpha]_D^{26}$ = –56 (c = 0.8, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30–7.09 (m, 15 H, 3 × Ph), 6.10 (brs, 1 H), 5.55 (brs, 1 H), 4.82–3.98 (brm, 10 H), 1.66 and 1.44 (2 × s, 6 H, CMe_2) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.9, 139.7, 136.3, 138.4, 133.4, 129.8, 129.0, 128.7, 128.6, 128.5, 127.9, 127.6, 126.8, 118.2, 110.2, 109.7, 85.4, 83.9, 78.3, 72.1, 67.7, 56.6, 55.9, 50.9, 28.3 and 27.5 ppm. IR: $\tilde{\nu}_{max}$ = 3032 (arom.), 1699 (CO) and 1372 (CMe_2) cm^{-1}. HRMS (LSIMS): calcd. for $C_{32}H_{33}NNaO_6$ [M + Na]$^+$ 550.5970; found 550.5973 (deviation +0.5 ppm).

(1*S*,4*R*,5*S*,6*S*,7*S*)-4-Amino-6-benzyloxy-1,7-isopropylidenedioxy-8-oxabicyclo[3.2.1]octane (33) and (1*S*,4*S*,5*S*,6*S*,7*S*)-4-Amino-6-ben-

zyloxy-1,7-isopropylidenedioxy-8-oxabicyclo[3.2.1]octane (34): A solution of **32** (1.06 g, 2.01 mmol) in MeOH (55 mL) was hydrogenated at atmospheric pressure over Pd-C (10%, 200 mg) at room temp. After 7 h, TLC (diethyl ether/hexane, 2:1) revealed the presence of a new compound of lower R_f. The reaction mixture was filtered, the catalyst was washed with MeOH, and the filtrate was concentrated and chromatographed on a column (DCM/MeOH 20:1) to give **33** (550 mg, 85%) as a colourless syrup. R_f = 0.5 (AcOEt/MeOH, 1:1). $[\alpha]_D^{26}$ = –56 (c = 0.4, in MeOH). ^{1}H NMR (400 MHz, [D$_4$]MeOH): δ = 7.41–7.26 (m, 5 H, Ph), 4.82 and 4.52 (2 × d, J = 11.7 Hz, 2 H, CH_2Ph), 4.37 (dd, $J_{5,6}$ = 0.7, $J_{6,7}$ = 5.5 Hz, 1 H, 6-H), 4.16 (br d, 1 H, 5-H), 4.09 (d, 1 H, 7-H), 3.02 (dt, $J_{3,4}$ = $J_{4,5}$ = 5.5, $J_{3',4}$ = 11.3 Hz, 1 H, 4-H), 2.09 (dt, J = 5.5, J = 12.9 Hz, 1 H, 2-H), 1.96 (m, 1 H, 3-H), 1.71 (m, 1 H, 2′-H), 1.67 and 1.45 (2 × s, 6 H, CMe$_2$) and 1.05 (dq, J = 5.5, J = 12.9 Hz, 3′-H) ppm. ^{13}C NMR (100 MHz, [D$_4$]MeOH): δ = 139.5, 129.3, 129.0 and 128.7 (CH$_2$*Ph*), 118.5 and 115.2 (C-1, *C*Me$_2$), 84.5 (C-5), 84.0 (C-6), 78.6 (C-7), 73.6 (*C*H$_2$Ph), 48.5 (C-4), 30.0 (C-3), 25.7 (C-2), 28.3 and 28.0 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3030 (arom.) and 1372 (CMe$_2$) cm^{-1}. HRMS (LSIMS): calcd. for $C_{17}H_{23}NNaO_4$ [M + Na]$^+$ 328.3580; found 328.3586 (deviation +1.8 ppm).

When the reaction was scaled up (3.04 g, 5.76 mmol of **32**), **33** (1.41 g, 80%) was isolated first, followed by (1*S*,4*S*,5*S*,6*S*,7*S*)-4-amino-6-benzyloxy-1,7-isopropylidenedioxy-8-oxabicyclo[3.2.1]octane (**34**, 246 mg, 14%). R_f = 0.2 (AcOEt/MeOH, 1:1). $[\alpha]_D^{26}$ = –59 (c = 0.5, CHCl$_3$). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.30–7.27 (m, 5 H, Ph), 4.77 and 4.47 (2 × d, J = 11.6 Hz, 2 H, CH_2Ph), 4.41 (d, $J_{6,7}$ = 5.2 Hz, 1 H, 6-H), 4.25 (s, 1 H, 5-H), 3.83 (d, 1 H, 7-H), 2.70 (br s, 1 H, 4-H), 2.26–2.19 (m, 1 H, 2-H), 1.75–1.72 (m, 1 H, 3-H), 1.65–1.58 (m, 2 H, 2′,3′-H), 1.66 and 1.45 (2 × s, 6 H, CMe$_2$) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 138.2, 128.6, 128.2 and 128.1 (CH$_2$*Ph*), 117.0 and 114.0 (C-1, *C*Me$_2$), 88.2 (C-5), 82.1 (C-6), 79.7 (C-7), 72.3 (*C*H$_2$Ph), 46.9 (C-4), 28.4 (C-3), 27.1 (C-2), 28.1 and 28.0 (C*Me*$_2$) ppm. IR: $\tilde{\nu}_{max}$ = 3030 (arom.) and 1371 (CMe$_2$) cm^{-1}. HRMS (LSIMS): calcd. for $C_{17}H_{23}NNaO_4$ [M + Na]$^+$ 328.3582; found 328.3586 (deviation +1.2 ppm).

(1*S*,2*S*,3*S*,4*S*,5*S*)-3-*O*-Benzyl-8-azabicyclo[3.2.1]octane-1,2,3,4-tetraol (3-*O*-Benzyl-1,3,5-tri-*epi*-calystegine B$_2$, 35): A solution of **34** (99 mg, 0.31 mmol) in HCl (1 N, 6.25 mL) was stirred at room temp. for 10 h. TLC (AcOEt/MeOH, 1:1) revealed the presence of a new compound of lower R_f. The mixture was neutralized with AMBERLITA® IRA 400 (OH$^-$ form) and then concentrated to a residue that was column chromatographed with DOWEX 50 WX8 resin as the stationary phase and MeOH (15 mL), H$_2$O (20 mL) and NH$_4$OH in MeOH (7%, 40 mL) as the mobile phase. Compound **35** (44 mg, 53%) was obtained as an amorphous white solid. R_f = 0.8 (AcOEt/MeOH, 2:1). $[\alpha]_D^{28}$ = –13 (c = 2.2, in MeOH). ^{1}H NMR (400 MHz, [D$_4$]MeOH): δ = 7.44–7.33 (m, 5 H, Ph), 4.71 (s, 2 H, CH_2Ph), 3.89 (d, $J_{2,3}$ = 3.4 Hz, 1 H, 2-H), 3.72 (br s, 1 H, 4-H), 3.51 (t, $J_{3,4}$ = 3.7 Hz, 1 H, 3-H), 3.38 (m, 1 H, 5-H), 1.99 (m, 1 H, 6*exo*-H), 1.70 (dt, J = 4.3, J = 13.1 Hz, 1 H, 7*exo*-H), 1.61 (m, 1 H, 7*endo*-H) and 1.32 (m, 1 H, 6*endo*-H) ppm. ^{13}C NMR (100 MHz, [D$_4$]MeOH): δ = 138.2, 128.3, 128.1 and 127.8 (CH$_2$*Ph*), 89.6 (C-1), 73.7 (C-2), 72.8 (C-3), 70.0 (*C*H$_2$Ph), 69.0 (C-4), 57.2 (C-5), 30.8 (C-7) and 22.3 (C-6) ppm. HRMS (LSIMS): calcd. for $C_{14}H_{19}NNaO_4$ [M + Na]$^+$ 288.1219; found 288.1212 (deviation –2.4 ppm).

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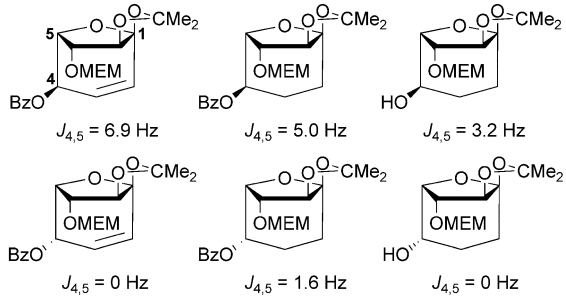

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