Synthesis of tetrahydroxy perhydroaza-azulenes: tandem Johnson–Claisen rearrangement of D-glucose-derived allylic alcohols†

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The Johnson–Claisen rearrangement of D-glucose-derived allylic alcohols **5a**,**b** afforded sugar-substituted γ,δ-unsaturated ester **6** in high yield. Conversion of the ester group to an azidomethyl group, epoxidation of the double bond and hydrogenation gave pyrrolidine ring skeletons **13a** and **13b**, which were transformed to tetrahydroxy perhydroaza-azulenes **1a** and **1b**, respectively. Glycosidase inhibitory activity was also evaluated.

Introduction

The Johnson–Claisen rearrangement of allyl alcohols using trimethyl orthoacetate and propionic acid (under reflux in xylene) occupies a unique position in the formation of γ,δ-unsaturated esters with exclusive *E* geometry of the olefin functionality.[1] In general, aliphatic or aromatic allyl alcohols are utilized in this reaction and the products thus obtained have been exploited in the synthesis of natural products.[2] However, only limited attention has been focused on sugar-derived allyl alcohols, probably due to the belief that the protected sugars are not compatible with the reaction conditions.[3] While working in the area of polyhydroxylated azepanes[4] and bicyclic azasugars,[5] we studied the [3,3]-sigmatropic rearrangement of D-glucose-derived allylic alcohols and have exploited it in the synthesis of bicyclic azasugars, namely tetrahydroxylated perhydroaza-azulenes **1a** and **1b** (Fig. 1).

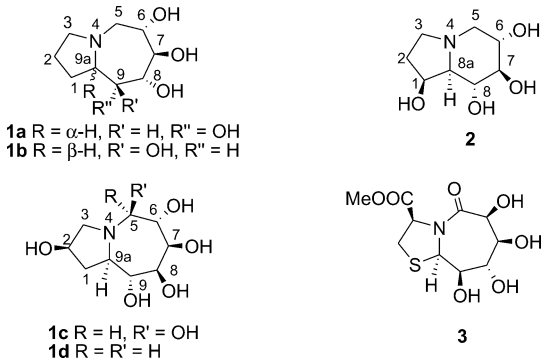

Fig. 1 Polyhydroxylated indolizidine and perhydroaza-azulenes.

This class of compounds, in which the five-membered ring is fused with the hydroxylated seven-membered ring, with a nitrogen atom at the ring junction, can be considered as higher ring homologue of polyhydroxylated indolizidine alkaloids. The diverse bioactivities of indolizidine azasugars (for example, the naturally occurring castanospermine **2** and its analogues, as promising glycosidase inhibitors in the treatment of various diseases such as diabetes, cancer, immunosuppressive and viral infections, including AIDS) have attracted increasing interest in recent years.[6] In addition, the presence of the polyhydroxylated seven-membered ring in **1a**/**1b** could also result in a change in the conformation of the bicyclic system due to the hydrogen bonding of the hydroxyl groups with the ring nitrogen. Therefore **1a**/**1b** may act as DNA minor groove binding ligands (MGBL), analogous to pohydroxylated azepanes.[7] In this respect, Lindsay and Pyne first reported trihydroxy perhydroaza-azulenes,[8a] while M. Gomez-Guillen and co-workers reported the syntheses and glycosidase inhibitory activities of hexahydroxy- and pentahydroxy perhydroaza-azulenes **1c** and **1d**, using 1,3-dipolar cycloaddition of a D-galactose-derived nitrone and methyl acrylate as a key step.[8b] Another report, from Geyer's group, described the synthesis of a tetrahydroxy octahydro-5-oxothiazolo[3,2-*a*]azepine **3** from D-γ-glucuronolactone, its conversion into a hexapeptide mimetic, and studies of polyproline II helix conformation.[9] Our approach to the new polyhydroxylated perhydroaza-azulenes **1a** and **1b** is based on the [3,3]-sigmatropic rearrangement of allylic alcohols **5a**,**b**, derived from α-D-*xylo*-pentodialdose **4**. This provides a γ,δ-unsaturated ester that gives the five-membered pyrrolidine ring skeleton by conversion of the ester to an azidomethyl group, and epoxidation of the double bond followed by 5-*exo*-*tet* reductive cyclization. Ring fusion by formation of a bond between the nitrogen of the pyrrolidine ring with C-1 leads to the target molecules. Our efforts in the successful implementation of this strategy are reported herein.

Results and discussion

The Grignard reaction of 1,2-*O*-isopropylidene 3-*O*-benzyl-α-D-*xylo*-pentodialdose **4**, easily available from D-glucose,[10] with vinyl magnesium bromide (1 M) at −78 °C (with warming to 0 °C) afforded the required allylic alcohols **5a** and **5b** (with D-*gluco*- and

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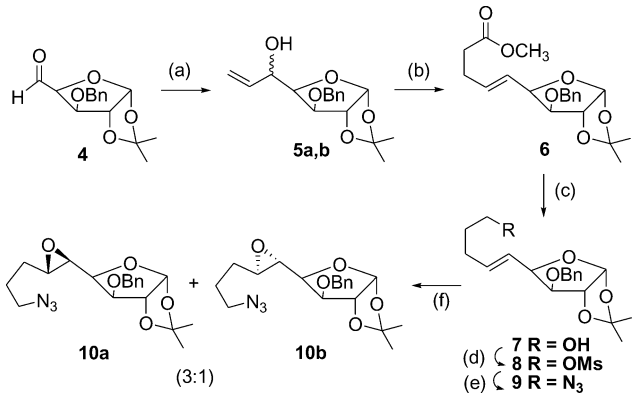
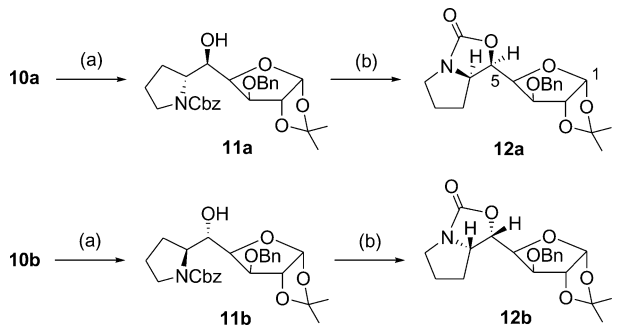
† Electronic supplementary information (ESI) available: General experimental methods, copies of ^{1}H and ^{13}C NMR spectra of compounds **1a**, **1b**, **1e**, **1f**, **6**, **7**, **8**, **9**, **10a**, **10b**, **11a**, **11b**, **12a**, **12b**, **13a** and **13b**, and crystallographic data for **12a**. See DOI: 10.1039/b603545k

L-*ido*-configurations, respectively) in a 2 : 3 ratio, as reported earlier[11] (Scheme 1). The individual treatment of **5a** and **5b** with trimethyl orthoacetate and catalytic propionic acid at reflux in xylene for 6 h afforded the same γ,δ-unsaturated methyl ester **6** as a syrup in 90% yield.[12]



Scheme 1 *Reagents and conditions*: (a) CH_2=CHMgBr, THF, −78 °C to 0 °C, 2 h; (b) $CH_3C(OCH_3)_3$, EtCOOH, xylene, 145 °C, 6 h; (c) LAH, THF, 0 °C, 1 h; (d) MsCl, Et_3N, CH_2Cl_2, 0 °C, 2 h; (e), NaN_3, DMF, 70 °C, 1 h; (f) *m*-CPBA, CH_2Cl_2, 0 °C to 25 °C, 15 h.

Reduction of the ester group in **6** with LAH in THF afforded alcohol **7**, which on mesylation and nucleophilic azide displacement furnished azidomethyl compound **9** in good yield. In the next step, epoxidation of **9** with *m*-chloroperbenzoic acid afforded a diastereomeric mixture of β- and α-azido-epoxides **10a** and **10b** in a 3 : 1 ratio. The appreciable difference in the R_f value allowed us to separate the two diastereomeric epoxides by column chromatography. The relative configuration at the newly generated stereocenters C5 and C6 was assigned in the subsequent steps. Thus, treatment of **10a** with triphenylphosphine in THF–H_2O followed by selective protection of the secondary amine with benzyloxycarbonyl chloride afforded *N*-Cbz-protected pyrrolidine **11a** as a thick liquid (Scheme 2). This reaction sequence probably involves reduction of the azide functionality under the Staudinger reaction conditions to give a primary amine that concomitantly undergoes 5-*exo-tet* cyclization and opening of the oxirane ring to give a pyrrolidine ring, which then undergoes protection.



Scheme 2 *Reagents and conditions*: (a) (i) PPh_3, THF, H_2O, 25 °C, 48 h; (ii) CbzCl, $NaHCO_3$, MeOH–H_2O (5 : 1), 0 °C to 25 °C, 3.5 h; (b) K_2CO_3, MeOH, 0 °C to 25 °C, 36 h.

Similarly, **10b** was converted to *N*-Cbz-protected pyrrolidine **11b**. The ^{1}H NMR of **11a** and **11b** showed doubling of signals, probably due to the presence of *N*-Cbz group.[13] In order to study 5-*exo-tet versus* 6-*endo-tet* cyclization, compounds **11a** and **11b** were individually treated with potassium carbonate in methanol at 0 °C (with warming to room temperature), to afford the 5,5-fused bis-carbamates **12a** and **12b**, respectively, in good yields. The H-5 signals in the ^{1}H NMR spectra of **12a** and **12b** are informative. Thus, in **12a** the H-5 appeared at δ 4.95 as a doublet of doublets with coupling constants of 9.9 and 7.5 Hz, while in **12b** the H-5 appeared at δ 4.80 as a doublet of doublets with coupling constants of 8.1 and 7.5 Hz, indicating the formation of the 5-*exo-tet* product in the Staudinger reaction.[14] Fortunately, **12a** was obtained as a colorless solid, and the single-crystal X-ray analysis (Fig. 2) established the relative stereochemistry of the six chiral centres at C1, C2, C3, C4, C5 and C6. Knowing the absolute configurations of the C1–C4 centres (as *R*,*R*,*S*,*S*) from the synthesis then allowed us to deduce the absolute configurations at the newly generated stereocentres as 5*R* and 6*R*. The formation of the β-epoxide **10a** as a major product can be explained by the preferred hydrogen bonding of *m*-CPBA with the oxygen of the β-oriented C3–OBn group, while the hydrogen bonding of *m*-CPBA with the furanose ring oxygen, which is sterically compressed, afforded α-epoxide **10b** as the minor product with 5*S* and 6*S* absolute configurations.

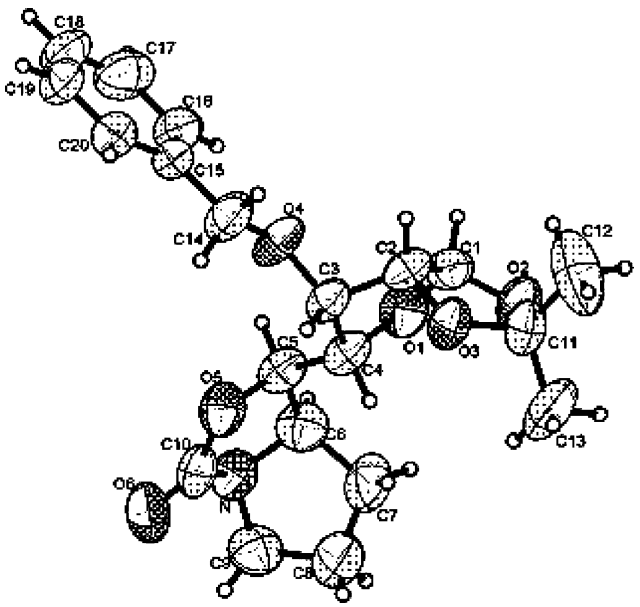
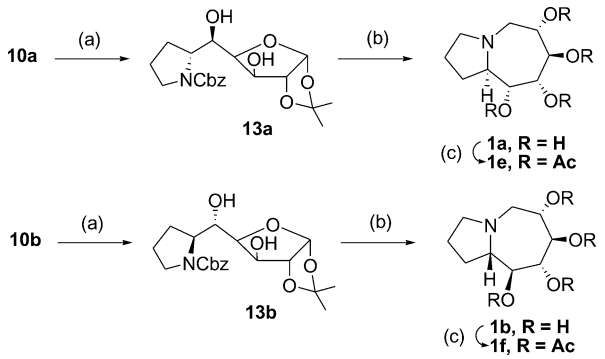


Fig. 2 ORTEP drawing of compound **12a**. The ellipsoids are drawn at 50% probability.

The utility of epoxides **10a** and **10b** was demonstrated by the formation of the corresponding new polyhydroxylated perhydroaza-azulenes **1a** and **1b** (Scheme 3). Thus, β-epoxide **10a** was treated with ammonium formate in the presence of 10% Pd/C in dry methanol at 80 °C for 1 h, resulting in reduction of the azido group, 5-*exo-tet* cyclization with epoxide ring opening, and hydrogenolysis in one step. The crude amino alcohol was directly treated with benzyloxycarbonyl chloride to afford **13a** as a thick liquid. Finally, **13a** was treated with TFA–H_2O (2 : 1), and the hemiacetal thus obtained was subjected to hydrogenation (with ammonium formate and 10% Pd/C in methanol at reflux for 1 h) to afford tetrahydroxy perhydroaza-azulene **1a** as a sticky liquid, which was then converted to the per-acetylated derivative **1e**.



Scheme 3 *Reagents and conditions*: (a) (i) $HCOONH_4$, Pd/C, MeOH, 80 °C, 1 h; (ii) CbzCl, $NaHCO_3$, MeOH–H_2O (5 : 1), 0 °C to 25 °C, 3.5 h; (b) (i) TFA–H_2O (2 : 1), rt, 2.5 h; (ii) $HCOONH_4$, 10% Pd/C, MeOH, 80 °C, 1 h; (c) pyridine, Ac_2O, 0 °C to rt, 12 h.

The same reaction sequence was repeated for the α-epoxide **10b**. The corresponding diastereomer **13b** was isolated and subjected to 1,2-acetonide cleavage and hydrogenation to give **1b** and its per-acetylated derivative **1f**.

Biological activity

Compounds **1a** and **1b** were assayed for inhibitory activity against α-mannosidase (E.C. 3.2.1.24), β-glucosidase (E.C. 3.2.1.20), α-glucosidase (E.C. 3.2.1.21), amyloglucosidase (E.C. 3.2.1.3), α-amylase (E.C. 3.2.1.1) and human salivary amylase. However, neither **1a** nor **1b** showed any inhibitory activity, even at 10 mM concentration, for any of the enzymes tested under our assay conditions.

Conclusions

In conclusion, we have demonstrated the utility of D-glucose-derived allylic alcohols **5a**,**b** in the synthesis of new tetrahydroxy perhydroaza-azulenes **1a** and **1b**, employing a tandem orthoester Johnson–Claisen rearrangement as a key step. The regioselective 5-*exo*-*tet*-cyclization of azido-epoxide was elegantly used to build the pyrrolidine ring of a bicyclic system. The easy availability of reagents, high-yielding steps and good regio- and stereoselectivity in this process gives easy access to tetrahydroxy perhydoaza-azulenes.

Experimental

General methods

Melting points were recorded with melting point apparatus and are uncorrected. IR spectra were recorded with an FTIR instrument as a thin film, a Nujol mull or using KBr pellets, and are expressed in cm^{-1}. ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded using $CDCl_3$ and/or D_2O as the solvent(s). Chemical shifts were reported in δ units (ppm) with reference to TMS as an internal standard, and J values are given in Hz. Decoupling and DEPT experiments confirmed the assignments of the signals. Elemental analyses were carried out with a C,H analyzer. Optical rotations were measured using a polarimeter at 25 °C. Thin layer chromatography was performed on pre-coated plates (0.25 mm, silica gel 60 F_{254}). Column chromatography was carried out with silica gel (100–200 mesh). The reactions were carried out in oven-dried glassware under dry N_2. Methanol, pyridine and THF were purified and dried before use. Distilled *n*-hexane and ethyl acetate were used for column chromatography. Sodium azide, mesyl chloride, benzyl chloroformate and *m*-chloroperbenzoic acid were purchased from Merck. 10% Pd/C was purchased from Aldrich and/or Fluka. After decomposition of the reaction with water, the work-up involved washing of combined organic layers with water followed by brine, drying over anhydrous sodium sulfate and evaporation of solvent under reduced pressure.

Methyl 3-*O*-benzyl-5,6,7,8-tetradeoxy-1,2-*O*-isopropylidene-α-D-*xylo*-5(*E*)-enononahepto-furanuronate 6. To a solution of allylic alcohols **5a**,**b** (3.0 g, 9.80 mmol) in dry xylene (20 cm^3) were added trimethyl orthoacetate (3.74 cm^3, 29.41 mmol) and propanoic acid (0.3 cm^3) at room temperature. Resulting reaction mixture was heated at 145 °C for 6 h. Xylene was removed under high vacuum and the reaction mixture was extracted with ethyl acetate (3 × 20 cm^3). The combined organic layer was washed with saturated sodium bicarbonate. Usual workup and column purification on silica (*n*-hexane–ethyl acetate, 9 : 1) afforded methyl ester **6** (3.2 g, 90%) as an oil. Found: C, 66.35; H, 7.25; calcd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23; R_f 0.54 (20% ethyl acetate–*n*-hexane); $[\alpha]_D^{25}$ −47.0 (*c* 1.15 in $CHCl_3$); $\nu_{max.}$(neat)/cm^{-1} 1736, 1628, 1445 and 1373; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.32 (3H, s, -CH_3), 1.49 (3H, s, -CH_3), 2.43 (4H, broad d, *J* 3.0 Hz, *H*-7a,b and *H*-8a,b), 3.66 (3H, s, -OCH_3), 3.82 (1H, d, *J* 3.0 Hz, *H*-3), 4.53 (1H, d, *J* 12.3 Hz, -OCH_2Ph), 4.58 (1H, dd, *J* 7.5, 3.0 Hz, *H*-4), 4.62 (1H, d, *J* 3.6 Hz, *H*-2), 4.65 (1H, d, *J* 12.3 Hz, -OCH_2Ph), 5.72 (1H, dd, *J* 15.6, 7.5 Hz, *H*-5), 5.85 (1H, dt, *J* 15.6, 3.0 Hz, *H*-6), 5.94 (1H, d, *J* 3.6 Hz, *H*-1), 7.25–7.38 (5H, m, Ar-*H*'s); δ_C(75 MHz; $CDCl_3$; Me_4Si) 26.1 (-CH_3), 26.6 (-CH_3), 27.5, 33.2 (*C*-7/*C*-8), 51.5 (-OCH_3), 71.9 (-OCH_2Ph), 81.0, 82.8, 83.2 (*C*-2/*C*-3/*C*-4), 104.6 (*C*-1), 111.3 (O–*C*–O), 124.9 (*C*-5/*C*-6), 127.4 (strong), 127.7, 128.3 (strong) (Ar-*C*'s), 133.9 (*C*-5/*C*-6), 137.5 (Ar-*C*), 173.2 (*C*=O).

3-*O*-Benzyl-5,6,7,8-tetradeoxy-1,2-*O*-isopropylidene-α-D-*xylo*-non-5-en-1,4-furanose 7. To an ice-cooled suspension of LAH (0.89 g, 24.62 mmol) in dry THF (6 cm^3) was added methyl ester **6** (3.0 g, 8.29 mmol) in dry THF (30 cm^3) at 0 °C. The mixture was stirred for 60 min, and the reaction quenched by adding ethyl acetate (20 cm^3), followed by aqueous solution of ammonium chloride (2 cm^3). The reaction mixture was filtered through a pad of Celite, and the filtrate was concentrated under vacuum. The filtrate purified by column chromatography (*n*-hexane–ethyl acetate, 4 : 1) gave **7** (2.77 g, 87%) as a thick liquid. Found: C, 68.19; H, 7.89; calcd for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84; R_f 0.56 (40% ethyl acetate–*n*-hexane); $[\alpha]_D^{25}$ −48.3 (*c* 1.20 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3200–3600 (broad) and 1625; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.35 (3H, s, -CH_3), 1.53 (3H, s, -CH_3), 1.60–1.67 (1H, broad s, D_2O-exchangeable, -O*H*), 1.71 (2H, quintet, *J* 6.6 Hz, *H*-8a,b), 2.22 (2H, q, *J* 7.5 Hz, *H*-7a,b), 3.67 (2H, t, *J* 6.6 Hz, *H*-9a,b), 3.86 (1H, d, *J* 3.0 Hz, *H*-3), 4.57 (1H, d, *J* 12.0 Hz, -OCH_2Ph), 4.63 (1H, dd, *J* 9.0, 3.0 Hz, *H*-4), 4.65 (1H, d, *J* 3.9 Hz, *H*-2), 4.69 (1H, d, *J* 12.0 Hz, -OCH_2Ph), 5.73 (1H, dd, *J* 15.6, 7.5 Hz, *H*-5), 5.89 (1H, dt, *J* 15.6, 9.0 Hz, *H*-6), 5.97 (1H, d, *J* 3.9 Hz, *H*-1), 7.30–7.50 (5H, m, Ar-*H*'s); δ_C(75 MHz; $CDCl_3$; Me_4Si) 26.0 (-CH_3), 26.5 (-CH_3), 28.6, 31.5 (*C*-7/*C*-8), 61.6 (*C*-9), 71.8 (-OCH_2Ph), 81.1, 82.7, 83.2

(*C*-2/*C*-3/*C*-4), 104.4 (*C*-1), 111.2 (O–*C*–O), 124.0 (*C*-6), 127.3 (strong), 127.6, 128.2 (strong) (Ar-*C*'s), 135.5 (*C*-5), 137.4 (Ar-*C*).

3-*O*-Benzyl-1,2-*O*-isopropylidene-9-*O*-methanesulfonyl-5,6,7,8-tetradeoxy-α-D-*xylo*-non-5-en-1,4-furanose 8. To a solution of alcohol **7** (2.0 g, 5.99 mmol) in CH_2Cl_2 (40 cm^3) at 0 °C were added Et_3N (1.81 g 17.97 mmol), followed by methanesulfonyl chloride (1.02 g, 8.98 mmol) over a period of 10 min. The resultant reaction mixture was stirred at the same temperature for 2 h and aqueous phase was extracted with CH_2Cl_2 (3 × 30 cm^3). Usual workup and purification by column chromatography on silica (*n*-hexane–ethyl acetate, 4 : 1) gave **8** (2.4 g, 94%) as a thick liquid. Found: C, 58.20; H, 6.85; calcd for $C_{20}H_{28}O_7S$: C, 58.23; H, 6.84; R_f 0.63 (40% ethyl acetate–*n*-hexane); $[\alpha]_D^{25}$ −43.0 (*c* 2.0 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1628, 1452, 1350, 1170 and 1074; δ_H (300 MHz; $CDCl_3$; Me_4Si) 1.38 (3H, s, -CH_3), 1.56 (3H, s, -CH_3), 1.92 (2H, quintet, *J* 6.9 Hz, *H*-8a,b), 2.29 (2H, q, *J* 6.9 Hz, *H*-7a,b), 3.04 (3H, s, -SO_2CH_3), 3.90 (1H, d, *J* 3.3 Hz, *H*-3), 4.28 (2H, t, *J* 6.9 Hz, *H*-9a,b), 4.59 (1H, d, *J* 12.0 Hz, -OCH_2Ph), 4.66 (1H, dd, *J* 7.2, 3.3 Hz, *H*-4), 4.69 (1H, d, *J* 3.9 Hz, *H*-2), 4.72 (1H, d, *J* 12.0 Hz, -OCH_2Ph), 5.77 (1H, dd, *J* 15.6, 7.5 Hz, *H*-5), 5.89 (1H, dt, *J* 15.6, 6.9 Hz, *H*-6), 6.00 (1H, d, *J* 3.9 Hz, *H*-1), 7.33–7.44 (5H, m, Ar-*H*'s); δ_C(75 MHz; $CDCl_3$; Me_4Si) 26.1 (-*C*H_3), 26.7 (-*C*H_3), 28.2, 31.5 (*C*-7/*C*-8), 37.2 (-SO_2*C*H_3), 69.2 (*C*-9), 72.0 (-O*C*H_2Ph), 81.0, 82.7, 83.3 (*C*-2/*C*-3/*C*-4), 104.6 (*C*-1), 111.4 (O–*C*–O), 125.4 (*C*-5), 127.5 (strong), 127.8, 128.4 (strong) (Ar-*C*'s), 133.8 (*C*-6), 137.5 (Ar-*C*).

9-Azido-3-*O*-benzyl-1,2-*O*-isopropylidene-5,6,7,8,9-pentadeoxy-α-D-*xylo*-non-5-en-1,4-furanose 9. To a solution of mesylate **8** (2.4 g, 5.61 mmol) in DMF (20 cm^3) was added sodium azide (2.19 g, 33.64 mmol), and the reaction mixture was stirred at 60 °C for 1 h. The solution was cooled to room temperature and then poured into EtOAc–H_2O (50 cm^3, 1 : 1). The aqueous phase was extracted with ethyl acetate (3 × 30 cm^3). Usual workup and column purification on silica (*n*-hexane–ethyl acetate, 9 : 1) afforded **9** (1.8 g, 82%) as a thick liquid. Found: C, 63.55; H, 7.05; calcd for $C_{19}H_{25}N_3O_4$: C, 63.49; H, 7.01; R_f 0.52 (20% ethyl acetate–*n*-hexane); $[\alpha]_D^{25}$ −6.4 (*c* 2.5 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 2097, 1647, 1452, 1377, 1217, 1078 and 1026; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.36 (3H, s, -CH_3), 1.54 (3H, s, -CH_3), 1.74 (2H, quintet, *J* 6.9 Hz, *H*-8a,b), 2.23 (2H, q, *J* 6.9 Hz, *H*-7a,b), 3.32 (2H, t, *J* 6.9 Hz, *H*-9a,b), 3.87 (1H, d, *J* 3.0 Hz, *H*-3), 4.57 (1H, d, *J* 12.3 Hz, -OCH_2Ph), 4.63 (1H, dd, *J* 7.5, 3.0 Hz, *H*-4), 4.67 (1H, d, *J* 3.9 Hz, *H*-2), 4.70 (1H, d, *J* 12.3 Hz, -OCH_2Ph), 5.74 (1H, dd, *J* 15.6, 7.5 Hz, *H*-5), 5.87 (1H, dt, *J* 15.6, 6.9 Hz, *H*-6), 5.98 (1H, d, *J* 3.9 Hz, *H*-1), 7.33–7.44 (5H, m, Ar-*H*'s); δ_C(75 MHz; $CDCl_3$; Me_4Si) 26.1 (-*C*H_3), 26.7 (-*C*H_3), 28.0, 29.4 (*C*-7/*C*-8), 50.6 (*C*-9), 71.9 (-O*C*H_2Ph), 81.1, 82.7, 83.2 (*C*-2/*C*-3/*C*-4), 104.6 (*C*-1), 111.4 (O–*C*–O), 125.0 (*C*-5), 127.5 (strong), 127.8, 128.4 (strong) (Ar-*C*'s), 134.3 (*C*-6), 137.5 (Ar-*C*).

3-*O*-Benzyl-1,2-*O*-isopropylidene-7,8,9-trideoxy-9-azido-5,6-oxirano-β-L-*glycero*-D-*gluco*-nona-1,4-furanose 10a and 3-*O*-benzyl-1,2-*O*-isopropylidene-7,8,9-trideoxy-9-azido-5,6-oxirano-α-D-*glycero*-L-*ido*-nona-1,4-furanose 10b. To a solution of **9** (1.80 g, 4.60 mmol) in CH_2Cl_2 (40 cm^3) was added *m*-chloroperbenzoic acid (1.19 g, 6.90 mmol) at 0 °C. The resulting reaction mixture was stirred at room temperature for 15 h. The aqueous phase was extracted with CH_2Cl_2 (3 × 30 cm^3). The combined organic phase was washed with 2 N NaOH and worked up to afford a diastereomeric mixture of epoxides **10a** and **10b**. Purification by column chromatography on silica and elution with *n*-hexane–ethyl acetate (9.5 : 0.5) gave **10a** (1.0 g, 53%) as a thick liquid. Found: C, 60.80; H, 6.69; calcd for $C_{19}H_{25}N_3O_5$: C, 60.79; H, 6.71; R_f 0.45 (20% ethyl acetate–*n*-hexane); $[\alpha]_D^{25}$ −50.53 (*c* 1.9 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 2098, 1456, 1377, 1217, 1080 and 1022; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.34 (3H, s, -CH_3), 1.49 (3H, s, -CH_3), 1.60–1.72 (1H, m, *H*-8a), 1.73–1.86 (3H, m, *H*-8b, *H*-7a,b), 3.03 (1H, ddd, *J* 6.6, 4.5, 2.1 Hz, *H*-6), 3.08 (1H, dd, *J* 6.9, 2.1 Hz, *H*-5), 3.38 (2H, t, *J* 6.6 Hz, *H*-9a,b), 3.85 (1H, dd, *J* 6.9, 3.3 Hz, *H*-4), 4.09 (1H, d, *J* 3.3 Hz, *H*-3), 4.67 (1H, d, *J* 3.6 Hz, *H*-2), 4.72 (2H, ABq, *J* 11.7 Hz, -OCH_2Ph), 5.98 (1H, d, *J* 3.6 Hz, *H*-1), 7.31–7.44 (5H, m, Ar-*H*'s); δ_C(75 MHz; $CDCl_3$; Me_4Si) 25.4 (-*C*H_3), 26.2 (-*C*H_3), 26.7, 28.7 (*C*-7/*C*-8), 50.8, 54.1 (*C*-5/*C*-6), 57.7 (*C*-9), 72.3 (-O*C*H_2Ph), 81.1, 81.9, 82.6 (*C*-2/*C*-3/*C*-4), 105.3 (*C*-1), 111.9 (O–*C*–O), 127.6 (strong), 128.0, 128.5 (strong), 137.5 (Ar-*C*'s). Further elution with *n*-hexane–ethyl acetate (9.4 : 0.6) afforded **10b** (0.34 g, 18%) as a thick liquid. Found: C, 60.85; H, 6.74; calcd for $C_{19}H_{25}N_3O_5$: C, 60.79; H, 6.71; R_f 0.35 (20% ethyl acetate–*n*-hexane); $[\alpha]_D^{25}$ −30.0 (*c* 2.4 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 2100, 1450, 1378, 1215, 1060 and 1020; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.38 (3H, s, -CH_3), 1.48 (3H, s, -CH_3), 1.55–1.62 (1H, m, *H*-8a), 1.63–1.82 (3H, m, *H*-8b, *H*-7a,b), 2.87 (1H, ddd, *J* 6.3, 3.9, 2.4 Hz, *H*-6), 3.09 (1H, dd, *J* 5.7, 2.4 Hz, *H*-5), 3.26–3.42 (2H, m, *H*-9a,b), 3.92 (1H, dd, *J* 5.7, 3.6 Hz, *H*-4), 4.02 (1H, d, *J* 3.6 Hz, *H*-3), 4.54 (1H, d, *J* 12.0 Hz, -OCH_2Ph), 4.68 (1H, d, *J* 3.9 Hz, *H*-2), 4.77 (1H, d, *J* 12.0 Hz, -OCH_2Ph), 6.02 (1H, d, *J* 3.9 Hz, *H*-1), 7.32–7.44 (5H, m, Ar-*H*'s); δ_C(75 MHz; $CDCl_3$; Me_4Si) 25.3 (-*C*H_3), 26.2 (-*C*H_3), 26.8, 28.6 (*C*-7/*C*-8), 50.9, 54.0 (*C*-5/*C*-6), 55.8 (*C*-9), 71.8 (-O*C*H_2Ph), 81.1, 82.1, 82.7 (*C*-2/*C*-3/*C*-4), 105.3 (*C*-1), 111.9 (O–*C*–O), 127.7 (strong), 128.1, 128.5 (strong), 137.1 (Ar-*C*'s).

3-*O*-Benzyl-6-(*N*-benzyloxycarbonylamino)-6,7,8,9-tetradeoxy-1,2-*O*-isopropylidene-α-D-*glycero*-D-*gluco*-nonofuranose 11a. To a solution of azido epoxide **10a** (0.98 g, 2.61 mmol) in THF (13 cm^3) and H_2O (1.5 cm^3) was added triphenylphosphine (1.04 g, 3.97 mmol). The reaction mixture was stirred at room temperature for 48 h. The THF and H_2O were removed under reduced pressure, and the thick mass dissolved in 10 cm^3 of MeOH–H_2O (5 : 1) at 0 °C. Sodium bicarbonate (0.66 g, 7.83 mmol) and benzyl chloroformate (0.55 cm^3, 3.92 mmol) were added and the resulting reaction mixture was stirred at 0 °C for 3.5 h. The methanol was removed under reduced pressure and the residue extracted with chloroform (3 × 20 cm^3). Usual workup and purification by column chromatography on silica (*n*-hexane–ethyl acetate, 4 : 1) gave **11a** (1.1 g, 87%) as a thick liquid. Found: C, 67.10; H, 6.90; calcd for $C_{27}H_{33}NO_7$: C, 67.06; H, 6.88; R_f 0.53 (30% ethyl acetate–*n*-hexane); $[\alpha]_D^{25}$ +20.0 (*c* 0.5 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3200–3600 (broad) and 1667; δ_H(300 MHz; $CDCl_3$ + D_2O; Me_4Si) 1.34 (3H, s, -CH_3), 1.43 (3H, s, -CH_3), 1.62–1.82 (1H, m, *H*-8a), 1.92–2.08 (2H, m, *H*-8b, H-7a), 2.12–2.24 (1H, m, *H*-7b), 3.40 (1H, ddd, *J* 10.5, 7.5, 3.6 Hz, *H*-9a), 3.67 (1H, ddd, *J* 10.5, 7.5, 4.0 Hz, *H*-9a), 4.04–4.28 (4H, m, *H*-6/*H*-5/*H*-4/*H*-3), 4.57 (1H, d, *J* 3.6 Hz, *H*-2), 4.73 (2H, broad s, -OCH_2Ph), 5.18 (2H, ABq, *J* 12.3 Hz, -OCH_2Ph), 5.94 (1H, d, *J* 3.6 Hz, *H*-1), 7.32–7.39 (10H, m, Ar-*H*'s); δ_C(75 MHz; $CDCl_3$; Me_4Si) 24.1, 26.4 (*C*-7/*C*-8), 26.8 (-*C*H_3), 27.6 (-*C*H_3), 47.7 (*C*-9), 62.9, 67.1 (*C*-5/*C*-6), 69.8,

72.5 (2 × -OCH_2Ph), 79.9, 82.0, 82.7 (*C*-2/*C*-3/*C*-4), 105.3 (*C*-1), 111.6 (O–*C*–O), 127.8 (strong), 127.9, 128.0, 128.4 (strong), 136.5, 137.6 (Ar-*C*'s), 156.9 (*C*=O).

3-*O*-Benzyl-6-(*N*-benzyloxycarbonylamino)-6,7,8,9-tetradeoxy-1,2-*O*-isopropylidene-β-L-*glycero*-L-*ido*-nonofuranose 11b. The azido epoxide **10b** (0.35 g, 0.93 mmol) was treated with triphenylphosphine (0.37 g, 1.42 mmol) in THF (5 cm^3) and H_2O (0.5 cm^3) and the crude mixture was then treated with $NaHCO_3$ (0.23 g, 2.76 mmol) and benzyl chloroformate (0.2 cm^3, 1.38 mmol), as described in the synthesis of **11a**, to afford **11b** (0.34 g, 76%) as a thick liquid. Found: C, 67.01; H, 6.92; calcd for $C_{27}H_{33}NO_7$: C, 67.06; H, 6.88; R_f 0.47 (30% ethyl acetate–*n*-hexane); $[\alpha]_D^{25}$ −53.30 (*c* 0.75 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3200–3600 (broad) and 1669; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.32 (3H, s, -CH_3), 1.48 (3H, s, -CH_3), 1.68–1.88 (2H, m, *H*-8a,b), 1.90–2.18 (1H, m, *H*-7a), 2.22–2.38 (1H, m, *H*-7b), 3.28–3.68 (2H, m, *H*-9a,b), 3.94 (2H, broad s, *H*-5/*H*-6), 4.05 (1H, broad s, *H*-4), 4.21 (1H, broad s, *H*-3), 4.42–4.56 (2H, broad s, D_2O-exchangeable, -O*H*, -OCH_2Ph), 4.52 (1H, d, *J* 11.7 Hz, -OCH_2Ph), 4.60 (1H, d, *J* 3.9 Hz, *H*-2), 5.14 (2H, ABq, *J* 12.3 Hz, -OCH_2Ph), 6.01 (1H, d, *J* 3.9 Hz, *H*-1), 7.29–7.42 (10H, m, Ar-*H*'s); δ_C(75 MHz; $CDCl_3$; Me_4Si) 24.4, 25.5 (*C*-7/*C*-8), 26.1 (-*C*H_3), 26.5 (-*C*H_3), 46.7 (*C*-9), 60.9, 66.3 (*C*-5/*C*-6), 69.1, 71.8 (2 × -O*C*H_2Ph), 79.7, 81.5, 84.1 (*C*-2/*C*-3/*C*-4), 104.6 (*C*-1), 111.4 (O–*C*–O), 127.6 (strong), 127.7 (strong), 127.9 (strong), 128.1 (strong), 128.3 (strong), 136.4 (Ar-*C*'s), 155.0 (*C*=O).

3-*O*-Benzyl-(6-*N*,5-*O*-carbonyl)-6,7,8,9-tetradeoxy-1,2-*O*-isopropylidene-α-D-*glycero*-D-*gluco*-nonofuranose 12a. To a solution of α-hydroxy Cbz compound **11a** (0.25 g, 0.52 mmol) in dry methanol (5 cm^3) was added K_2CO_3 (0.43 g, 0.31 mmol) at 0 °C. The resulting reaction mixture was warmed to room temperature and stirred for 36 h. The reaction was quenched by adding saturated NH_4Cl (2 cm^3), and extracted with dichloromethane (3 × 10 cm^3). Usual workup and purification by column chromatography on silica (*n*-hexane–ethyl acetate, 4 : 1) gave **12a** (0.16 g, 82%) as a white solid, mp 135–136 °C (*n*-hexane–ethyl acetate, 4 : 1). Found: C, 64.04; H, 6.74; calcd for $C_{20}H_{25}NO_6$: C, 63.99; H, 6.71; R_f 0.58 (30% ethyl acetate–*n*-hexane); $[\alpha]_D^{25}$ −28.00 (*c* 1.0 in $CHCl_3$); ν_{max}(KBr)/cm^{-1} 1751, 1456, 1383, 1225 and 1024; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.31 (3H, s, -CH_3), 1.46 (3H, s, -CH_3), 1.54–1.70 (2H, m, *H*-7a,b), 1.84–2.14 (2H, m, *H*-8a,b), 3.21 (1H, ddd, *J* 11.4, 9.6, 3.3 Hz, *H*-9a), 3.62 (1H, ddd, *J* 11.4, 8.4, 4.5 Hz, *H*-9b), 3.93 (1H, ddd, *J* 10.5, 5.4, 3.0 Hz, *H*-6), 4.11 (1H, d, *J* 3.0 Hz, *H*-3), 4.23 (1H, dd, *J* 9.9, 3.0 Hz, *H*-4), 4.59 (1H, d, *J* 3.6 Hz, *H*-2), 4.65 (2H, s, -OCH_2Ph), 4.95 (1H, dd, *J* 9.9, 7.5 Hz, *H*-5), 5.88 (1H, d, *J* 3.6 Hz, *H*-1), 7.23–7.37 (5H, m, Ar-*H*'s); δ_C(75 MHz; $CDCl_3$; Me_4Si) 25.3, 25.8 (*C*-7/*C*-8), 26.3 (-*C*H_3), 27.0 (-*C*H_3), 45.6 (*C*-9), 62.1 (*C*-6), 71.0 (-O*C*H_2Ph), 72.9 (*C*-5), 78.0, 81.4, 82.4 (*C*-2/*C*-3/*C*-4), 105.2 (*C*-1), 112.1 (O–*C*–O), 127.6 (strong), 127.9, 128.3 (strong), 137.0 (Ar-*C*'s), 160.7 (*C*=O).

Crystal data. Single crystals of compound **12a** suitable for X-ray diffraction were selected directly from the analytical samples. $C_{20}H_{25}NO_6$, M = 375.41, orthorhombic, a = 5.5259(4) Å, b = 10.0212(7) Å, c = 34.600(2) Å, U = 1916.0(2) $Å^3$, T = 293(2) K, space group $P2_12_12_1$. Reflections collected/unique 9697/3372 [R(int) = 0.0270], final R indices [$I > 2\sigma(I)$], $R1$ = 0.0622, $wR2$ = 0.1473, R indices (all data): $R1$ = 0.0694, $wR2$ = 0.1516. CCDC reference number 600972. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b603545k

3-*O*-Benzyl-(6-*N*,5-*O*-carbonyl)-6,7,8,9-tetradeoxy-1,2-*O*-isopropylidene-β-L-*glycero*-L-*ido*-nonofuranose 12b. Compound **11b** (0.15 g, 0.31 mmol) was treated with K_2CO_3 (0.26 g, 1.88 mmol) in methanol (4 cm^3), as described in the synthesis of **12a**, to afford **12b** (0.086 g, 74%) as a thick liquid. Found: C, 63.95; H, 6.77; calcd for $C_{20}H_{25}NO_6$: C, 63.99; H, 6.71; R_f 0.51 (40% ethyl acetate–*n*-hexane); $[\alpha]_D^{25}$ −88.6 (*c* 0.7 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1749, 1456, 1383 and 1225; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.34 (3H, s, -CH_3), 1.48 (3H, s, -CH_3), 1.54–1.68 (1H, m, *H*-7a), 1.88–2.26 (3H, m, *H*-7b, *H*-8a,b), 3.00–3.13 (1H, m, *H*-9a), 3.49–3.61 (2H, m, *H*-9a/*H*-6), 3.96 (1H, d, *J* 3.9 Hz, *H*-3), 4.27 (1H, dd, *J* 8.1, 3.9 Hz, *H*-4), 4.36 (1H, d, *J* 12.0 Hz, -OCH_2Ph), 4.68 (1H, d, *J* 3.9 Hz, *H*-2), 4.74 (1H, d, *J* 12.0 Hz, -OCH_2Ph), 4.80 (1H, dd, *J* 8.1, 7.5 Hz, *H*-5), 6.01 (1H, d, *J* 3.6 Hz, *H*-1), 7.25–7.41 (5H, m, Ar-*H*'s); δ_C(75 MHz; $CDCl_3$; Me_4Si) 25.2, 25.3 (C-7/C-8), 26.2 (-*C*H_3), 26.7 (-*C*H_3), 45.0 (*C*-9), 60.8 (*C*-6), 71.1 (-O*C*H_2Ph), 75.1 (*C*-5), 79.7, 80.9, 81.4 (*C*-2/*C*-3/*C*-4), 105.1 (*C*-1), 111.7 (O–*C*–O), 128.2, 128.3 (strong), 128.4 (strong), 135.9 (Ar-*C*'s), 160.7 (*C*=O).

6-(*N*-Benzyloxycarbonylamino)-6,7,8,9-tetradeoxy-1,2-*O*-isopropylidene-α-D-*glycero*-D-*gluco*-nonofuranose 13a. A solution of azido-epoxide **10a** (1.0 g, 2.67 mmol), 10% Pd/C (0.20 g) and ammonium formate (1.01 g, 16.00 mmol) in methanol (10 cm^3) was refluxed for 1 h. The reaction mixture was filtered through a pad of Celite and the filtrate evaporated to give a thick oil. To a cooled solution of the amino alcohol (0.69 g, 2.66 mmol) in methanol–water (10 cm^3, 9 : 1) was added sodium bicarbonate (0.67 g, 7.98 mmol) and benzyl chloroformate (0.68 g, 3.99 mmol) at 0 °C, and the mixture stirred for 3.5 h. The methanol was evaporated under reduced pressure and the residue was extracted with chloroform (3 × 20 cm^3). Usual workup and purification by column chromatography on silica (*n*-hexane–ethyl acetate, 7 : 3) gave **13a** (0.79 g, 75%) as a thick liquid. Found: C, 61.08; H, 6.95; calcd for $C_{20}H_{27}NO_7$: C, 61.06; H, 6.92; R_f 0.40 (40% ethyl acetate–*n*-hexane); $[\alpha]_D^{25}$ +37.33 (*c* 0.75 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3200–3600 (broad), 1670, 1377, 1244, 1099 and 1024; δ_H(300 MHz; $CDCl_3 + D_2O$; Me_4Si) 1.34 (3H, s, -CH_3), 1.46 (3H, s, -CH_3), 1.51–1.83 (1H, m, *H*-8a), 1.98–2.20 (3H, m, *H*-8b, *H*-7a,b), 3.42 (1H, ddd, *J* 10.8, 7.2, 3.0 Hz, *H*-9b), 3.66 (1H, ddd, *J* 10.8, 7.5, 5.7 Hz, *H*-9b), 4.09 (2H, broad s, *H*-4/*H*-5), 4.22 (1H, t, *J* 7.2 Hz, *H*-6), 4.39 (1H, broad s, *H*-3), 4.53 (1H, d, *J* 3.6 Hz, *H*-2), 5.17 (2H, s, -OCH_2Ph), 5.98 (1H, d, *J* 3.6 Hz, *H*-1), 7.28–7.39 (5H, m, Ar-*H*'s); δ_C(75 MHz; $CDCl_3$; Me_4Si) 24.1, 26.3 (*C*-7/*C*-8), 26.7 (-*C*H_3), 26.8 (-*C*H_3), 47.8 (*C*-9), 61.7 (*C*-6), 67.3 (*C*-5), 70.4 (-O*C*H_2Ph), 77.2, 80.1, 84.4 (*C*-2/*C*-3/*C*-4), 105.2 (*C*-1), 111.5 (O–*C*–O), 127.7 (strong), 128.0, 128.5 (strong), 136.2 (Ar-*C*'s), 156.8 (*C*=O).

6-(*N*-Benzyloxycarbonylamino)-6,7,8,9-tetradeoxy-1,2-*O*-isopropylidene-β-L-*glycero*-L-*ido*-nonofuranose 13b. Azido epoxide **10b** (0.34 g, 0.91 mmol) was treated with ammonium formate (0.34 g, 5.44 mmol) and 10% Pd/C (0.07 g) in methanol (5 cm^3), followed by $NaHCO_3$ (0.22 g, 2.66 mmol) and benzyl chloroformate (0.18 g, 1.068 mmol), as described in the synthesis of **13a**. This afforded **13b** (0.28 g, 79%) as a thick liquid. Found: C, 61.10; H, 6.98; calcd for $C_{20}H_{27}NO_7$: C, 61.06; H, 6.92; R_f 0.40 (40% ethyl acetate–*n*-hexane); $[\alpha]_D^{25}$ −24.00 (*c* 0.5 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 3200–3600 (broad), 1664, 1383 and 1244;

δ_H(300 MHz; $CDCl_3 + D_2O$; Me_4Si) 1.35 (3H, s, -CH_3), 1.52 (3H, s, -CH_3), 1.81–2.01 (2H, m, *H*-7a,b), 2.03–2.18 (2H, m, *H*-8a,b), 3.40–3.58 (2H, m, *H*-9a,b), 3.95–4.03 (1H, m, *H*-6), 4.04 (1H, dd, *J* 6.6, 2.4 Hz, *H*-4), 4.25 (1H, dd, *J* 6.6, 1.5 Hz, *H*-5), 4.29 (1H, d, *J* 2.4 Hz, *H*-3), 4.58 (1H, d, *J* 3.6 Hz, *H*-2), 5.18 (2H, ABq, *J* 12.3 Hz, -OCH_2Ph), 5.98 (1H, d, *J* 3.6 Hz, *H*-1), 7.32–7.43 (5H, m Ar-*H*'s); δ_C(75 MHz; $CDCl_3$; Me_4Si) 24.8, 25.6 (*C*-7/*C*-8), 26.6 (-*C*H_3), 26.7 (-*C*H_3), 46.7 (*C*-9), 59.7 (*C*-6), 67.1 (*C*-5), 71.8 (-O*C*H_2Ph), 75.8, 80.2, 85.0 (*C*-2/*C*-3/*C*-4), 104.9 (*C*-1), 111.4 (O–*C*–O), 127.7 (strong), 127.9, 128.4 (strong), 136.3 (Ar-*C*'s), 156.2 (*C*=O).

4-Azabicyclo-[5.3.0]-6(*S*),7(*R*),8(*R*),9(*S*),9a(*S*)-tetrahydroxydecane 1a. Compound **13a** (0.10 g, 0.25 mmol) was treated with TFA–H_2O (3 cm^3, 2 : 1) at room temperature for 2.5 h. The trifluroacetic acid was co-evaporated with benzene to furnish a thick liquid. To a solution of the hemiacetal (0.09 g, 0.25 mmol) in methanol (5 cm^3) were added ammonium formate (0.09 g, 1.5 mmol) and 10% Pd/C (0.02 g). The resulting mixture was heated to 80 °C for 1 h. The catalyst was filtered through a pad of Celite and washed with methanol. The solvent was evaporated under reduced pressure and the crude mixture was loaded on Dowex 50 W × 8 (100–200 mesh) resin. Elution with chloroform–methanol–25% aq. ammonia (90 : 9 : 1) afforded **1a** (0.035 g, 68%) as a sticky liquid. Found: C, 53.22; H, 8.41; calcd. for $C_9H_{17}NO_4$: C, 53.19; H, 8.43; R_f 0.40 (methanol); $[\alpha]_D^{25}$ +20.0 (*c* 0.5 in MeOH); ν_{max}(neat)/cm^{-1} 3200–3600 (broad); δ_H(300 MHz; D_2O) 1.82–2.16 (3H, m, *H*-1a,b/*H*-2a), 2.24–2.38 (1H, m, *H*-2b), 3.14 (1H, dd, *J* 14.1, 7.2 Hz, *H*-5a), 3.16–3.26 (1H, m, *H*-3a), 3.43 (1H, dd, *J* 14.1, 1.5 Hz, *H*-5b), 3.42–3.52 (1H, m, *H*-3b), 3.66 (1H, broad q, *J* 9.3 Hz, *H*-9a), 3.80 (1H, dd, *J* 9.9, 4.8 Hz, *H*-7), 3.83–3.89 (2H, m, *H*-8/*H*-9), 3.98 (1H, dd, *J* 7.6, 1.2 Hz, *H*-6); δ_C(75 MHz; D_2O) 22.2, 29.1 (*C*-1/*C*-2), 52.1, 58.2, 63.5 (*C*-3/*C*-5/*C*-9a), 68.2, 68.5, 70.8, 75.6 (*C*-6/*C*-7/*C*-8/*C*-9).

4-Azabicyclo-[5.3.0]-6(*S*),7(*R*),8(*R*),9(*R*),9a(*R*)-tetrahydroxydecane 1b. Compound **13b** (0.10 g, 0.25 mmol) was treated with TFA–H_2O (3 cm^3, 2 : 1), ammonium formate (0.09 g, 1.5 mmol) and 10% Pd/C (0.02 g), as described in the synthesis of **1a**. This afforded **1b** (0.045 g, 87%) as a thick liquid. Found: C, 53.24; H, 8.47; calcd for $C_9H_{17}NO_4$: C, 53.19; H, 8.43; R_f 0.35 (methanol); $[\alpha]_D^{25}$ +40.0 (*c* 0.45 in MeOH); ν_{max}(neat)/cm^{-1} 3200–3600 (broad); δ_H(300 MHz; D_2O) 1.62–1.78 (3H, m, *H*-1a,b/*H*-2a), 2.06–2.18 (1H, m, *H*-2a), 2.58–2.78 (2H, m, *H*-3a/*H*-9a), 2.89 (1H, dd, *J* 14.1, 3.6 Hz, *H*-5a), 2.99 (1H, dd, *J* 14.1, 4.8 Hz, *H*-5b), 3.08 (1H, ddd, *J* 15.3, 10.5, 6.0 Hz, *H*-3b), 3.31 (1H, t, *J* 7.8 Hz, *H*-8), 3.33 (1H, dd, *J* 7.8, 3.0 Hz, *H*-9), 3.52 (1H, t, *J* 7.8 Hz, *H*-7), 3.70 (1H, ddd, *J* 7.8, 4.8, 3.9 Hz, *H*-6); δ_C(75 MHz; D_2O) 23.4, 32.4 (*C*-1/*C*-2), 58.8, 60.2, 69.8 (*C*-3/*C*-5/*C*-9a), 72.9, 76.9, 77.3, 77.9 (*C*-6/*C*-7/*C*-8/*C*-9).

4-Azabicyclo-[5.3.0]-6(*S*),7(*R*),8(*R*),9(*S*),9a(*S*)-tetraacetoxydecane 1e. To an ice-cooled solution of **1a** (0.03 g, 0.15 mmol) in dry pyridine (0.4 g, 4.4 mmol) were added acetic anhydride (1.0 g, 10.0 mmol) and DMAP (0.002 g, 0.015 mmol), and the mixture was stirred for 12 h at room temperature. The reaction mixture was decomposed with cold water (2 cm^3) and extracted with chloroform (3 × 5 cm^3). The usual work-up followed by column purification on silica (*n*-hexane–ethyl acetate, 4 : 1) afforded **1e** (0.04 g, 73%) as a thick gum. Found: C, 55.04; H, 6.76; calcd for $C_{17}H_{25}NO_8$: C, 54.98; H, 6.79; R_f 0.47 (50% ethyl acetate–*n*-hexane); $[\alpha]_D^{25}$ +25.6 (*c* 0.62 in $CHCl_3$); ν_{max}(neat)/cm^{-1} 1733 (broad); δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.99 (1H, broad s, *H*-2a), 2.00–2.08 (3H, m, *H*-2b,*H*-1a,b), 2.03 (3H, s, -COCH_3), 2.04 (3H, s, -COCH_3), 2.05 (3H, s, -COCH_3), 2.13 (3H, s, -COCH_3), 2.54–2.64 (1H, m, *H*-3a), 2.66–2.78 (2H, m, *H*-3b,*H*-9a), 3.11 (1H, dd, *J* 12.0, 5.1 Hz, *H*-5a), 3.16 (1H, dd, *J* 12.0, 3.3 Hz, *H*-5b), 5.07 (1H, ddd, *J* 7.8, 5.1, 3.3 Hz, *H*-6), 5.17 (1H, dd, *J* 4.5, 1.8 Hz, *H*-9), 5.34 (1H, dd, *J* 8.4, 1.8 Hz, *H*-8), 5.46 (1H, dd, *J* 8.4, 7.8 Hz, *H*-7); δ_C(75 MHz; $CDCl_3$; Me_4Si) 20.6 (-CO*C*H_3), 20.7 (-CO*C*H_3), 20.8 (-CO*C*H_3), 21.0 (-CO*C*H_3), 21.9, 30.3 (*C*-1/*C*-2), 51.7, 55.4, 65.6 (*C*-3/*C*-5/*C*-9a), 69.8, 71.4, 72.8, 74.1 (*C*-6/*C*-7/*C*-8/*C*-9), 169.4 (-*C*OCH_3), 169.6 (-*C*OCH_3), 169.8 (-*C*OCH_3), 170.0 (-*C*OCH_3).

4-Azabicyclo-[5.3.0]-6(*S*),7(*R*),8(*R*),9(*R*),9a(*R*)-tetraacetoxydecane 1f. Compound **1b** (0.028 g, 0.14 mmol) was treated with pyridine (0.32 g, 4.11 mmol) and acetic anhydride (0.95 g, 9.33 mmol), as described in the synthesis of **1e**, to afford **1f** (0.042 g, 82%) as a white solid, mp 123–125 °C (50% ethyl acetate–*n*-hexane). Found: C, 55.02; H, 6.84; calcd for $C_{17}H_{25}NO_8$: C, 54.98; H, 6.79; R_f 0.40 (50% ethyl acetate–*n*-hexane); $[\alpha]_D^{25}$ +35.56 (*c* 0.45, $CHCl_3$); ν_{max}(KBr)/cm^{-1} 1738 (broad); δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.66–1.94 (4H, m, *H*-1a,b,*H*-2a,b), 2.02 (3H, s, -COCH_3), 2.029 (3H, s, -COCH_3), 2.033 (3H, s, -COCH_3), 2.07 (3H, s, -COCH_3), 2.49 (1H, ddd, *J* 15.0, 9.6, 6.9 Hz, *H*-3a), 2.92 (1H, ddd, *J* 15.0, 8.7, 5.4 Hz, *H*-3b), 2.96 (1H, dd, *J* 13.8, 5.4 Hz, *H*-5a), 3.04 (1H, dd, *J* 13.8, 4.2 Hz, *H*-5b), 3.11 (1H, broad t, *J* 8.4, 5.1 Hz, *H*-9a), 5.00 (1H, t, *J* 9.3 Hz, *H*-9), 5.08 (1H, dt, *J* 8.4, 5.1 Hz, *H*-6), 5.16 (1H, t, *J* 9.3 Hz, *H*-8), 5.53 (1H, dd, *J* 9.3, 8.4 Hz, *H*-7); δ_C(75 MHz; $CDCl_3$; Me_4Si) 20.5 (-CO*C*H_3), 20.6 (-CO*C*H_3), 20.7 (-CO*C*H_3), 20.9 (-CO*C*H_3), 22.6, 29.9 (*C*-1/*C*-2), 55.8, 57.4, 64.9 (*C*-3/*C*-5/*C*-9a), 70.8, 72.0, 72.6, 75.9 (*C*-6/*C*-7/*C*-8/*C*-9), 169.2 (-*C*OCH_3), 169.5 (-*C*OCH_3), 169.7 (-*C*OCH_3), 170.0 (-*C*OCH_3).

Procedure for inhibition assay

Inhibition potencies of **1a** and **1b** were determined by measuring the residual hydrolytic activities of the glycosidases. Glycosidases, namely α-mannosidase (Jack Bean), α-glucosidase (Baker's yeast), β-glucosidase (almonds), α-amylase (*Aspergillus oryzae*), amyloglycosidase (*Rhizopus* mold) and human salivary amylase were purchased from Sigma Chemicals Co., USA. The substrates (all purchased from Sigma Chemicals Co., USA), *p*-nitrophenyl-β-D-glucopyranoside, and *p*-nitrophenyl-α-D-glucopyranoside, of 2 mM concentration, were prepared in 0.025 M citrate buffer with pH 6.0, and *p*-nitrophenyl-α-D-mannopyranoside, of 2 mM concentration, was prepared in 0.025 M citrate buffer with pH 4.5. The test compound (of various concentrations between 0.5 μM and 10 mM) was preincubated with the enzyme, buffered at its optimal pH, for 30 min at 25 °C. The enzyme reaction was initiated by the addition of 100 μL of substrate. Controls were run simultaneously in the absence of test compound. The reaction was terminated at the end of 10 min by the addition of 0.05 M borate buffer (pH 9.8), and absorbance of the liberated *p*-nitrophenol was measured at 405 nm with a Shimadzu Spectrophotometer UV-1601.[15] For amyloglucosidase (pH 4.5, 55 °C) and amylase (pH 6.9, 37 °C) starch was used as substrate, and DNSA reagent for evaluation of reducing sugar released as described by Miller *et al.*[16]

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