Total synthesis of (5*S*,6*S*)-6-amino-2,8-dimethylnonan-5-ol and (5*S*,6*S*)-6-amino-7-cyclohexyl-2-methylheptan-5-ol

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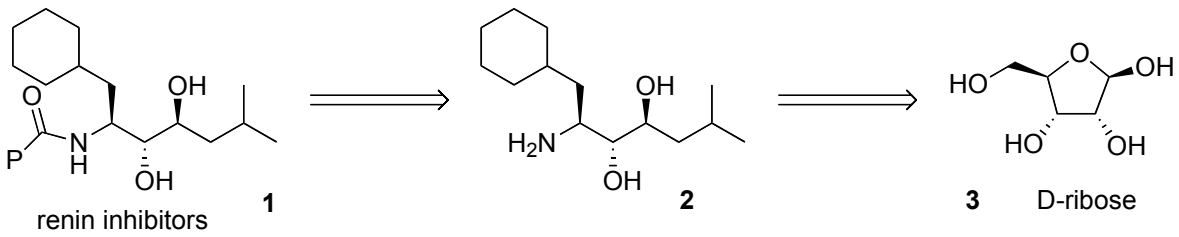
Abstract
A stereoselective synthesis of two complex 1,2-dialkyl-2-amino-1-ethanols [(5*S*,6*S*)-6-amino-2,8-dimethylnonan-5-ol and (5*S*,6*S*)-6-amino-7-cyclohexyl-2-methylheptan-5-ol] is described from 5-azido-3,5,6-trideoxy-6-isopropyl-L-idose and 5-azido-3,5,6-trideoxy-6-cyclohexyl-L-idose respectively.

Keywords: Carbohydrates, azides, Wittig reaction, aminoalcohols

Introduction

The Chiron Approach[1] to the synthesis of chiral target molecules from carbohydrates is now a well established tool in organic chemistry and this approach recently allowed us to make new contributions to the field of carbasugars consisting of new syntheses of cyclohexane α-amino acids[2], dehydrohydroxymethylinositols[3] and cyclopentane β-amino acids[4], among others. The large number of additional synthetic applications for this strategy include the transformation of D-ribose into compound **2**[5], an isostere incorporated in several type 1 renin inhibitors[5,6] currently used as agents to lower blood pressure. However, other type **2** compounds have yet to be prepared from carbohydrates.



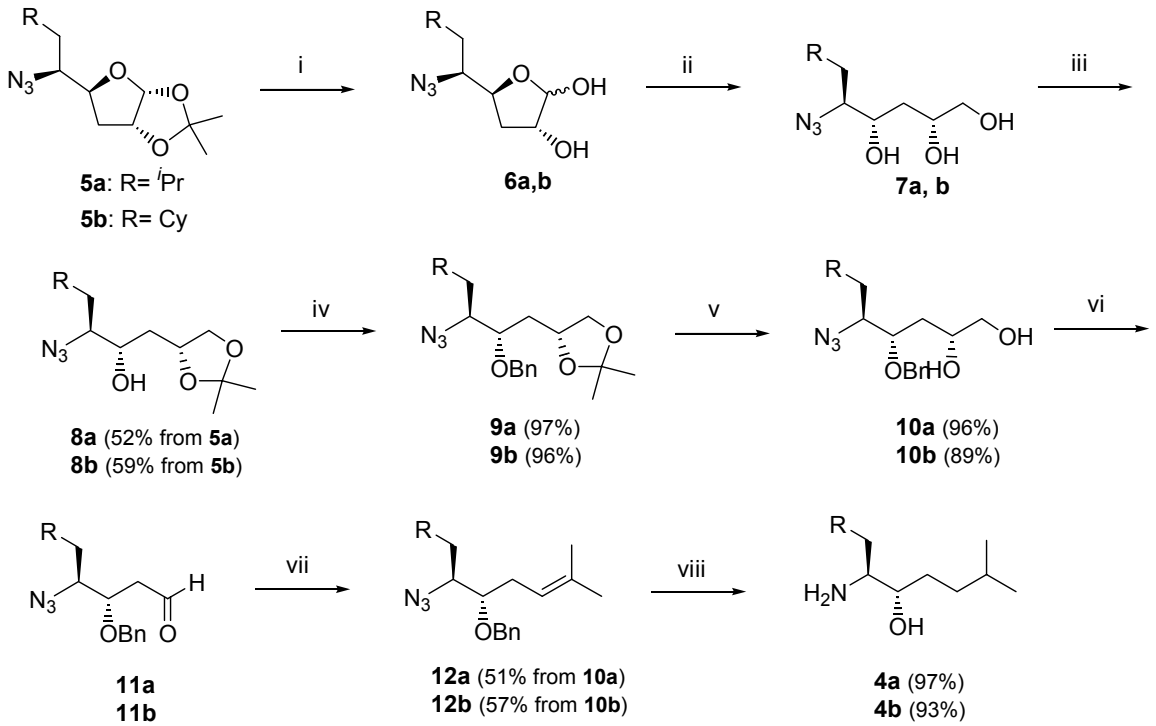
Scheme 1

In connection with this work and as a part of our ongoing programme aimed at the design, synthesis and pharmacological evaluation of new β-secretase inhibitors for the treatment of Alzheimer's disease, we became interested in the preparation of aminoalcohols **4a** and **4b**[7], which were efficiently prepared from D-glucose.

Figure 1

Results and Discussion

We first studied the preparation of amino alcohol **4a** starting from the known azidofuranose **5a**[8], which is easily prepared from D-glucose. Removal of the acetonide protecting group of **5a** using a standard procedure[9] provided lactol **6a** as an unstable gum, which was directly reduced[10] with $NaBH_4$ to the corresponding azidotriol **7a**.



Scheme 2. Conditions:i) $AcOH/H_2O$ (4:1). ii) $NaBH_4$/EtOH. iii) $Me_2C(OMe)_2$/acetone/PTSA. iv) NaH/$^nBu_4NI$/THF, then BnBr. v) $MeOH/H_2O$/AcOH (1:1:1). vi) $NaIO_4$/$EtOH/H_2O$. vii) $Ph_3P = CMe_2$/THF. viii) H_2/Pd-C/MeOH.

In accordance with our synthetic plan, we proceeded to carry out an indirect selective protection of the hydroxyl group at position C_4 of compound **7a** in a three-step sequence. Once the terminal 1,2-diol system of this compound was selectively protected as the acetonide by treatment with 2,2-dimethoxypropane and *p*-toluensulfonic acid[10], the free OH group of the resulting compound **8a** was protected[11] as the benzyloxy derivative and, finally, the fully protected compound **9a** readily provided the desired 1,2-diol-5-azido derivative **10a** by removal[11] of the acetonide protecting group. The mass spectrum of **8a** confirmed the molecular formula $C_{12}H_{23}N_3O_3$ and the selective protection of its 1,2-diol system was easily established from the ^{1}H NMR spectrum, which showed two singlets at 1.37 and 1.44 ppm corresponding to the two methyl groups of the acetonide subunit. The presence of the free OH group at C_4 was easily deduced from the presence of a band at 3475 cm^{-1} in the IR spectrum. In addition, protection of this free OH group as the benzyloxy derivative was confirmed by the expected signals for the benzyl group in the ^{1}H NMR spectrum of **9a**: two doublets at 4.55 and 4.60 ppm corresponding to the two protons of the methylene subunit together with a multiplet at 7.34–7.36 ppm due to the five protons of the benzene ring. Finally, the molecular formula $C_{16}H_{25}N_3O_3$ established for compound **10a** from its mass spectrum confirmed the desired selective deprotection of the 1,2-diol system, a situation further confirmed by the spectroscopic data, mainly from the ^{1}H NMR spectrum, which showed the expected signals for all twenty five protons, including two doublets at 4.58 and 4.64 ppm corresponding to two protons and a multiplet at 7.29–7.36 ppm due to five protons. Both of these signals are due to the benzyloxy substituent. A broad singlet was also observed at 2.90 ppm due to a free OH group and a multiplet at 3.38–3.87 ppm corresponding to the second free OH group and the five protons at positions C_1, C_2, C_4 and C_5.

We next reacted diol **10a** with $NaIO_4$ to produce the key aldehyde **11a**,[11] which was subjected to a Wittig olefination[12] by treatment with $Ph_3P{=}C(CH_3)_2$ in THF. The molecular formula ($C_{18}H_{27}N_3O$) of the resulting olefin **12a** was confirmed by the mass spectrum (*m*/*z* = 302, MH^+) and the presence of a double bond was easily established from the ^{1}H NMR spectrum: a singlet due to three protons was observed at 1.64 ppm along with a second singlet (three protons) at 1.71 ppm – these two signals correspond to the two methyl groups at position C_2. A multiplet corresponding to one proton was seen at 5.09–5.17 ppm and this is due to proton H_3. The presence of a strong band at 2105 cm^{-1} in the IR spectrum confirmed that the azide substituent at position C_6 remained unaltered during the synthetic sequence leading to olefin **12a**.

Finally, exhaustive catalytic hydrogenation[13] of **12a** allowed the simultaneous reduction of the double bond and the azido group together with the hydrogenolysis of the benzyl substituent, to give our first target compound [(5*S*,6*S*)-6-amino-2,8-dimethylnonan-5-ol **4a**].

Our second target compound [(5*S*,6*S*)-6-amino-7-cyclohexyl-2-methylheptan-5-ol **4b**] was obtained in a similar way from azidofuranose **5b**[10], via compounds **6b**, **7b**, **8b**, **9b**, **10b**, **11b** and **12b**.

In summary, we have demonstrated that the Chiron Approach is a useful strategy for the efficient stereospecific synthesis of complex 1,2-disusbtituted-1,2-aminoalcohols of interest for

chemical and biological purposes. Work is currently in progress aimed at the incorporation of compounds **4a** and **4b** as isosteres in a panel of peptides for subsequent evaluation as anti-Alzheimer agents.

Experimental Section

General Procedures. Melting points were determined on a Kofler Thermogerate apparatus and are uncorrected. Infrared spectra were recorded on a MIDAC FTIR spectrophotometer. Nuclear magnetic resonance spectra, unless otherwise specified, were recorded on a Bruker DPX-250 apparatus using deuterochloroform solutions containing tetramethylsilane as internal standard. Mass spectra were obtained on a HP 5988A mass spectrometer. Thin layer chromatography (tlc) was performed using Merck GF-254 type 60 silica gel and hexane/ethyl acetate mixtures as eluant; tlc spots were visualized with ultraviolet light or Hanessian mixture. Column chromatography was carried out using Merck type 60 230-400 mesh silica gel. Solvents were purified as per ref. 14. Solutions of extracts in organic solvents were dried with anhydrous sodium sulfate.

5-Azido-3,5,6-trideoxy-6-isopropyl-L-idofuranose (6a). A solution of 5-azido-3,5,6-trideoxy-6-isopropyl-1,2-*O*-isopropylidene-□-L-idofuranose (0.28 g, 1.11 mmol) in aqueous acetic acid (80%, 20 mL) was heated at 60 ºC for 20 h. The solvent was evaporated *in vacuo* and coevaporated with toluene (10 mL) to remove traces of acetic acid. The solid residue was dried under high vacuum to give 0.24 g of 5-azido-3,5,6-trideoxy-6-isopropyl-L-idofuranose (**6a**) as an unstable gum. This material was used without purification.

5-Azido-3,5,6-trideoxy-6-isopropyl-L-iditol (7a). Five portions of $NaBH_4$ (0.34 g, 9 mmol) were sequentially added to a solution of compound **6a** (0.49 g, 2.26 mmol) in absolute ethanol (35 mL) at 0 ºC and the mixture was stirred at room temperature for 8 h. The solution was neutralized with HCl (1 M) and evaporated *in vacuo* to give a residue, which was dissolved in saturated sodium chloride solution (30 mL) and extracted with ethyl acetate (3 x 30 mL). The organic layers were dried over anhydrous sodium sulfate, filtered and evaporated *in vacuo* to give 0.49 g of 5-azido-3,5,6-trideoxy-6-isopropyl-L-iditol (**7a**) as a clear gum. This material was used in the next step without further purification.

5-Azido-3,5,6-trideoxy-6-isopropyl-1,2-*O*-isopropylidene-L-iditol (**8a**). 2,2-Dimethoxypropane (45 mL), copper sulfate (1 g) and *p*-toluensulfonic acid monohydrate (0.04 g, 0.23 mmol) were added to a solution of triol **7a** (0.49 g, 2.26 mmol) in dry acetone (30 mL) and the suspension was stirred at room temperature for 24 h. The reaction mixture was neutralized with saturated aqueous sodium bicarbonate solution, filtered through Celite and the solids washed with dichloromethane. The solvent was evaporated and the residue was dissolved in water (30 mL) and extracted with dichloromethane (3 x 30 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, evaporated *in vacuo* and the resulting residue

submitted to flash column chromatography (ethyl acetate/hexane 1:6) to give 5-azido-3,5,6-trideoxy-6-isopropyl-1,2-*O*-isopropylidene-L-iditol (**8a**) as a clear oil (0.31 g, 52% yield over the three last steps). $[\alpha]_D^{20}$: –8.2º (c = 0.8, $CHCl_3$). IR ($\bar{\upsilon}$, cm^{-1}): 3475 (OH); 2108 (N_3). ^1H NMR (δ, ppm): 0.94-0.98 (m, 6 H, 2 x CH_3-^{i}Pr); 1.37 (s, 3 H, CH_3); 1.39–1.48 (m, 1 H, CH-^{i}Pr); 1.44 (s, 3 H, CH_3); 1.57–1.90 (m, 4 H, H-3, H-3´, H-6 and H-6´); 3.17–3.25 (m, 1 H, H-5); 3.32 (d, 1 H, *J* = 2.1 Hz, OH); 3.60 (dd, 1 H, $J_{1,2}$ = 7.3 Hz, $J_{1,1'}$ = 8.2 Hz, H-1); 3.82–3.89 (m, 1 H, H-4); 4.12 (dd, 1 H, $J_{1',2}$ = 6.1 Hz, $J_{1,1'}$ = 8.2 Hz, H-1´); 4.25–4.35 (m, 1 H, H-2). ^{13}C NMR (δ, ppm): 21.7 (CH_3); 23.2 (CH_3); 24.9 (CH); 25.7 (CH_3); 26.8 (CH_3); 37.0 (CH_2); 38.8 (CH_2); 64.0 (CH); 69.6 (CH_2); 73.4 (CH); 75.3 (CH); 109.6 (C). MS (*m/z*, %): 258 (4, MH^+); 157 (1, MH^+ – $C_5H_9O_2$); 101 (27, $[C_5H_9O_2]^+$); 59 (81, $[C_3H_7O]^+$); 41 (100, $[C_3H_5]^+$). Anal. Calcd. for $C_{12}H_{23}N_3O_3$: C, 56.01; H, 9.01; N, 16.33. Found C, 56.13; H, 8.87; N, 16.58.

5-Azido-4-*O*-benzyl-3,5,6-trideoxy-6-isopropyl-1,2-*O*-isopropylidene-L-iditol (**9a**). Sodium hydride (60% mineral oil dispersion, 0.04 g, 1.00 mmol) was placed in to a dry 10 mL round-bottom flask under argon, washed with dry hexane (3 x 1 mL), suspended in dry THF (2 mL), and tetrabutylammonium iodide (0.003 g, 0.008 mmol) was added. A solution of compound **8a** (0.21 g, 0.80 mmol) in dry THF (2 mL) was added to the above suspension at 0 ºC and the mixture was stirred for 10 min and then allowed to warm up to room temperature. Benzyl bromide (0.11 mL, 0.88 mmol) was added and the resulting reaction mixture was heated at 50 ºC for 3 h. Methanol (1 mL) was added and the heating was maintained for a further 2 h. The reaction mixture was filtered through Celite, the solids washed with dichloromethane, and the filtrate evaporated to dryness. The residue was dissolved in dichloromethane (10 mL) and washed with water (2 x 10 mL). The combined organic layers were dried with anhydrous sodium sulfate, filtered and evaporated *in vacuo* to give 5-azido-4-*O*-benzyl-3,5,6-trideoxy-6-isopropyl-1,2-*O*-isopropylidene-L-iditol (**9a**) as a yellow oil (0.27g, 97% yield). $[\alpha]_D^{20}$: –20.9º (c = 2.1, $CHCl_3$). IR ($\bar{\upsilon}$, cm^{-1}): 2107 (N_3). ^1H NMR (δ, ppm): 0.90–0.95 (m, 6 H, 2 x CH_3-^{i}Pr); 1.33 (s, 3 H, CH_3); 1.35–1.58 (m, 2 H, CH-^{i}Pr and H-6); 1.40 (s, 3 H, CH_3); 1.68–1.91 (m, 3 H, H-6´, H-3 and H-3´); 3.39–3.56 (m, 3 H, H-1, H-4 and H-5); 3.96 (dd, 1 H, $J_{1',2}$ = 6.1 Hz, $J_{1,1'}$ = 7.9 Hz, H-1´); 4.12–4.23 (m, 1 H, H-2); 4.55 (d, 1 H, *J* = 11.7 Hz, CH_2-Ph); 4.60 (d, 1 H, *J* = 11.7 Hz, CH_2-Ph); 7.34–7.36 (m, 5 H, 5 x Ar-H). ^{13}C NMR (δ, ppm): 21.5 (CH_3); 23.2 (CH_3); 25.0 (CH); 25.6 (CH_3); 26.9 (CH_3); 34.2 (CH_2); 38.6 (CH_2); 61.8 (CH); 69.4 (CH_2); 72.0 (CH_2); 72.4 (CH); 78.7 (CH); 108.8 (C); 127.7 (Ar-CH); 127.8 (2 x Ar-CH); 128.3 (2 x Ar-CH); 137.9 (Ar-C). MS (*m/z*, %): 348 (10, MH^+); 320 (100, $MH^+ - N_2$). Anal. Calcd. for $C_{19}H_{29}N_3O_3$: C, 65.68; H, 8.41; N, 12.09. Found C, 65.61; H, 8.50; N, 12.25.

5-Azido-4-*O*-benzyl-3,5,6-trideoxy-6-isopropyl-L-iditol (**10a**). A solution of azide derivative **9a** (0.27 g, 0.77 mmol) in a mixture of methanol/acetic acid/water 1:1:1 (4 mL) was stirred at 50 ºC for 12 h. The solvent was evaporated to dryness, coevaporated twice with toluene (1 mL) and the residue submitted to flash column chromatography (ethyl acetate/hexane 1:1.2) to give 0.23 g (96% yield) of 5-azido-4-*O*-benzyl-3,5,6-trideoxy-6-isopropyl-L-iditol (**10a**) as an orange oil. $[\alpha]_D^{20}$: –31.7º (c = 0.8, $CHCl_3$). IR ($\bar{\upsilon}$, cm^{-1}): 3407 (OH); 2106 (N_3). ^1H NMR (δ, ppm): 0.90–0.96 (m, 6 H, 2 x CH_3-^{i}Pr); 1.33–1.60 (m, 2 H, H-6 and H-6´); 1.69–1.74 (m, 3 H, CH-^{i}Pr, H-3

and H-3′); 2.90 (bs, OH); 3.38–3.87 (m, 6 H; OH, H-1, H-1′, H-2, H-4 and H-5); 4.58 (d, 1 H, *J* = 11.3 Hz, CH_2-Ph); 4.64 (d, 1 H, *J* = 11.3 Hz, CH_2-Ph); 7.29–7.36 (m, 5 H, 5 x Ar-H). ^{13}C NMR (δ, ppm): 21.5 (CH_3); 23.2 (CH_3); 25.0 (CH); 33.3 (CH_2); 38.3 (CH_2); 61.5 (CH); 66.5 (CH_2); 70.1 (CH); 72.4 (CH_2); 79.8 (CH); 127.8 (2 x Ar-CH); 127.9 (Ar-CH); 128.4 (2 x Ar-CH); 137.4 (Ar-C). MS (*m/z*, %): 308 (11, MH^+); 280 (100, $MH^+ - N_2$); 91 (41, $PhCH_2^+$). Anal. Calcd. for $C_{16}H_{25}N_3O_3$: C, 62.52; H, 8.20; N, 13.67. Found C, 62.49; H, 8.14; N, 13.37.

4-Azido-3-*O*-benzyl-2,4,5-trideoxy-5-isopropyl-L-xylose (**11a**). Sodium metaperiodate (0.25 g, 1.15 mmol) was added in three portions to a solution of diol **10a** (0.24 g, 0.77 mmol) in 90% ethanol (6 mL) and the resulting suspension was stirred at room temperature for 3 h. Dichloromethane (5 mL) was added, the suspension was filtered through Celite and the solids washed with dichloromethane. The filtrate was dried over anhydrous sodium sulfate, filtered and evaporated *in vacuo* to give 4-azido-3-*O*-benzyl-2,4,5-trideoxy-5-isopropyl-L-xylose (**11a**), which was used in the next step without further purification.

(5*S*,6*S*)-6-Azido-5-*O*-benzyl-2,8-dimethylnon-2-en-5-ol (**12a**). A 1.05 M solution of *n*-butyllithium (0.29 mL, 0.31 mmol) was added dropwise under argon to a solution of isopropyltriphenylphosphonium iodide (0.09 g, 0.22 mmol) in dry THF (0.5 mL) and the resulting red solution was stirred at room temperature for 3 h. The resulting solution was added dropwise to a solution of aldehyde **11a** (0.05 g, 0.18 mmol) in dry THF (2 mL) at 0 ºC and the resulting mixture was stirred at 0 ºC for 22 h. Water (3 mL) was added, the THF was evaporated *in vacuo* and the resulting aqueous solution was extracted with diethyl ether (4 x 3 mL) and washed with water (2 x 10 mL). The organic layers were dried over anhydrous sodium sulfate, filtered and evaporated to dryness under reduced pressure. The resulting pale yellow oil was submitted to flash column chromatography (ethyl acetate/hexane 1:50) to give 0.02 g of (5*S*,6*S*)-6-azido-5-*O*-benzyl-2,8-dimethylnon-2-en-5-ol (**12a**) (51% over the two last steps). $[\alpha]_D^{20}$: +2.7º (c = 1.4, $CHCl_3$). IR ($\bar{\upsilon}$, cm^{-1}): 2105 (N_3). ^{1}H NMR (δ, ppm): 0.87–0.93 (m, 6 H, 2 x CH_3-8); 1.21–1.61 (m, 3 H, H-7, H-7′ and H-8); 1.64 (s, 3 H, CH_3-2); 1.71 (s, 3 H, CH_3-2); 2.30–2.40 (m, 2 H, H-4 and H-4′); 3.24–3.40 (m, 2 H, H-5 and H-6); 4.54 (d, 1 H, *J* = 11.6 Hz, CH_2-Ph); 4.68 (d, 1 H, *J* = 11.6 Hz, CH_2-Ph); 5.09–5.17 (m, 1 H, H-3); 7.26–7.36 (m, 5 H, 5 x Ar-H). ^{13}C NMR (δ, ppm): 17.9 (CH_3); 21.7 (CH_3); 23.2 (CH_3); 25.0 (CH); 25.5 (CH_3); 29.6 (CH_2); 39.1 (CH_2); 62.1 (CH); 72.2 (CH_2); 81.3 (CH); 119.2 (CH); 127.6 (Ar-CH); 127.8 (2 x Ar-CH); 128.3 (2 x Ar-CH); 134.3 (C); 138.3 (Ar-C). MS (*m/z*, %): 302 (10, MH^+); 274 (62, $MH^+ - N_2$); 91 (100, $PhCH_2^+$). Anal. Calcd. for $C_{18}H_{27}N_3O$: C, 71.72; H, 9.03; N, 13.94. Found C, 71.97; H, 9.28; N, 13.70.

(5*S*,6*S*)-6-Amino-2,8-dimethylnonan-5-ol (**4a**). 10% palladium on activated carbon (0.06 g) was added to a deoxygenated solution of compound **12a** (0.03 g, 0.10 mmol) in methanol (1 mL). The resulting suspension was deoxygenated and stirred under a hydrogen atmosphere (1 atm) for 30 h. The mixture was filtered through Celite, the solids washed with methanol and the resulting filtrate evaporated to dryness to give (5*S*,6*S*)-6-amino-2,8-dimethylnonan-5-ol (**4a**) (0.017 g, 97%) as a clear gum. $[\alpha]_D^{20}$: –21.0º (c = 0.4, $CHCl_3$). IR ($\bar{\upsilon}$, cm^{-1}): 3326 (bs, OH and NH_2). ^{1}H NMR (δ, ppm): 0.86–0.97 (m, 12 H, 4 x CH_3); 1.07–1.80 (m, 8 H, H-2, H-3, H-3′, H-4,

H-4′, H-7, H-7′ and H-8); 2.80–2.87 (m, 1 H, H-6); 3.05–3.33 (m, 2 H, NH and H-5). ^{13}C NMR (δ, ppm): 21.7 (CH_3); 22.2 (CH); 22.6 (CH_3); 22.9 (CH_3); 23.5 (CH); 23.9 (CH_3); 29.8 (CH_2); 35.1 (CH_2); 42.7 (CH_2); 52.1 (CH); 82.3 (CH). MS (*m/z*, %): 188 (1, MH^+); 171 (3, $M^+ - OH$); 47 (100). Anal. Calcd. for $C_{11}H_{25}NO$: C, 70.53; H, 13.45; N, 7.48. Found C, 70.08; H, 13.78; N, 7.41.

5-Azido-3,5,6-trideoxy-6-cyclohexyl-L-idofuranose (**6b**). 5-Azido-3,5,6-trideoxy-6-cyclohexyl-L-idofuranose (**6b**) was prepared as an unstable gum from 5-azido-3,5,6-trideoxy-6-cyclohexyl-1,2-*O*-isopropylidene-β-L-idofuranose (**5b**) (0.28 g, 1.10 mmol) following the same procedure as for compound **6a**.

5-Azido-3,5,6-trideoxy-6-cyclohexyl-L-iditol (**7b**): Compound **7b** (0.37 g) was obtained from 5-azido-3,5,6-trideoxy-6-cyclohexyl-L-idofuranose (**6b**) (0.37 g, 1.45 mmol) following the same procedure as for **7a**.

5-Azido-3,5,6-trideoxy-6-cyclohexyl-1,2-*O*-isopropylidene-L-iditol (**8b**). Starting from compound **7b** (0.40 g, 1.45 mmol) and following the same procedure as for the preparation of **8a**, 5-azido-3,5,6-trideoxy-6-cyclohexyl-1,2-*O*-isopropylidene-L-iditol (**8b**) was obtained in 59% yield over the three last steps. $[\alpha]_D^{20}$: –11.2º (c = 0.5, $CHCl_3$). IR ($\bar{\upsilon}$, cm^{-1}): 3478 (OH); 2107 (N_3). ^{1}H NMR (δ, ppm): 0.83–1.03 (m, 2 H, 2 x H-Cy); 1.11–1.30 (m, 3 H, 3 x H-Cy); 1.36 (s, 3 H, CH_3); 1.43 (s, 3 H, CH_3); 1.46–1.90 (m, 10 H, 6 x H-Cy, H-3, H-3′, H-6 and H-6′); 3.21–3.27 (m, 1 H, H-5); 3.36 (d, 1 H, J = 1.8 Hz, OH); 3.56–3.62 (m, 1 H, H-1); 3.78–3.88 (m, 1 H, H-4); 4.11 (dd, 1 H, $J_{1',2}$ = 6.1 Hz, $J_{1,1'}$ = 7.9 Hz, H-1′); 4.24–4.34 (m, 1 H, H-2). ^{13}C NMR (δ, ppm): 25.5 (CH_3); 25.9 (CH_2); 26.1 (CH_2); 26.3 (CH_2); 26.7 (CH_3); 32.4 (CH_2); 33.8 (CH_2); 34.2 (CH); 37.0 (CH_2); 37.3 (CH_2); 63.2 (CH); 69.4 (CH_2); 73.2 (CH); 75.1 (CH); 109.4 (C). MS (*m/z*, %): 290 (1, MH^+); 262 (2, $MH^+ - N_2$); 59 (100, $[C_3H_7O]^+$). Anal. Calcd. for $C_{15}H_{27}N_3O_3$: C, 60.58; H, 9.15; N, 14.13. Found C, 60.21; H, 8.73; N, 14.25.

5-Azido-4-*O*-benzyl-3,5,6-trideoxy-6-cyclohexyl-1,2-*O*-isopropylidene-L-iditol (**9b**). Compound **9b** was prepared in 96% yield from compound **8b** (0.17 g, 0.58 mmol) following the same procedure as for compound **9a**. $[\alpha]_D^{20}$: – 21.7º (c = 1.4, $CHCl_3$). IR ($\bar{\upsilon}$, cm^{-1}): 2126 (N_3). ^{1}H NMR (δ, ppm): 0.76–1.01 (m, 3 H, 3 x H-Cy); 1.09–1.53 (m, 3 H, 3 x H-Cy); 1.32 (s, 3 H, CH_3); 1.40 (s, 3 H, CH_3); 1.60–1.96 (m, 9 H, 5 x H-Cy, H-3, H-3′, H-6 and H-6′); 3.42–3.54 (m, 3 H, H-1, H-4 and H-5); 3.95 (dd, 1 H, $J_{1',2}$ = 5.8 Hz, $J_{1,1'}$ = 7.9 Hz, H-1′); 4.11–4.21 (m, 1H, H-2); 4.54 (d, 1 H, J = 11.7 Hz, CH_2-Ph); 4.60 (d, 1 H, J = 11.7 Hz, CH_2-Ph); 7.23–7.35 (m, 5 H, 5 x Ar-H). ^{13}C NMR (δ, ppm): 25.5 (CH_3); 25.9 (CH_2); 26.1 (CH_2); 26.4 (CH_2); 26.8 (CH_3); 32.2 (CH_2); 33.8 (CH_2); 34.1 (CH_2); 34.3 (CH); 37.2 (CH_2); 61.0 (CH); 69.4 (CH_2); 71.9 (CH_2); 72.4 (CH); 78.6 (CH); 108.7 (C); 127.6 (Ar-CH); 127.7 (2 x Ar-CH); 128.2 (2 x Ar-CH); 137.8 (Ar-C). MS (*m/z*, %): 388 (7, MH^+); 360 (54, $MH^+ - N_2$); 42 (100, $[C_3H_6]^+$). Anal. Calcd. for $C_{22}H_{33}N_3O_3$: C, 68.19; H, 8.58; N, 10.84. Found C, 68.49; H, 8.50; N, 10.78.

5-Azido-4-*O*-benzyl-3,5,6-trideoxy-6-cyclohexyl-L-iditol (**10b**). 5-Azido-4-*O*-benzyl-3,5,6-trideoxy-6-cyclohexyl-L-iditol (**10b**) was prepared in 89% yield as a dark gum when 5-azido-4-*O*-benzyl-3,5,6-trideoxy-6-cyclohexyl-1,2-*O*-isopropylidene-L-iditol (**9b**) (0.21 g, 0.53 mmol) was subjected to the same procedure as for compound **10a**. $[\alpha]_D^{20}$: –37.0º (c = 0.8, $CHCl_3$). IR

($\bar{\upsilon}$, cm^{-1}): 3392 (OH); 2105 (N_3). ^1H NMR (δ, ppm): 0.73–1.00 (m, 2 H, 2 x H-Cy); 1.09–1.54 (m, 6 H, 6 x H-Cy), 1.60–1.80 (m, 7 H, 3 x H-Cy, H-3, H-3´, H-6 and H-6´); 3.19–3.82 (m, 7 H, 2 x OH, H-1, H-1´, H-2, H-4 and H-5); 4.58 (s, 2 H, CH_2-Ph); 7.27–7.36 (m, 5 H, 5 x Ar-H). ^{13}C NMR (δ, ppm): 25.8 (CH_2); 26.1 (CH_2); 26.3 (CH_2); 32.2 (CH_2); 33.3 (CH_2); 33.8 (CH_2); 34.3 (CH); 36.8 (CH_2); 60.7 (CH); 66.5 (CH_2); 70.0 (CH); 72.3 (CH_2); 79.7 (CH); 127.8 (2 x Ar-CH); 127.9 (Ar-CH); 128.4 (2 x Ar-CH); 137.3 (Ar-C). MS (*m/z*, %): 348 (6, MH^+); 320 (51, $MH^+ - N_2$); 91 (100, $PhCH_2^+$). Anal. Calcd. for $C_{19}H_{29}N_3O_3$: C, 65.68; H, 8.41; N, 12.09. Found C, 66.06; H, 8.54; N, 12.13.

4-Azido-3-*O*-benzyl-2,4,5-trideoxy-5-cyclohexyl-L-xylose (**11b**). Compound **11b** was obtained following the same procedure as for compound **11a**.

(5*S*,6*S*)-6-Azido-5-*O*-benzyl-7-cyclohexyl-2-methylhept-2-en-5-ol (**12b**). Compound **12b** was prepared in 57% over the two last steps starting from compound **11b** (0.07 g, 0.21 mmol) following the same procedure as for the transformation of **11a**. $[\alpha]_D^{20}$: –5.5º (c = 0.4, $CHCl_3$). IR ($\bar{\upsilon}$, cm^{-1}): 2104 (N_3). ^1H NMR (δ, ppm): 0.72–1.67 (m, 13 H, 11 x H-Cy, H-7 and H-7´); 1.63 (s, 3 H, CH_3); 1.71 (s, 3 H, CH_3); 2.29–2.39 (m, 2 H, H-4 and H-4´); 3.28–3.39 (m, 2 H, H-5 and H-6); 4.53 (d, 1 H, *J* = 11.7 Hz, CH_2-Ph); 4.67 (d, 1 H, *J* = 11.7 Hz, CH_2-Ph); 5.07–5.16 (m, 1 H, H-3); 7.25–7.36 (m, 5 H, 5 x Ar-H). ^{13}C NMR (δ, ppm): 17.9 (CH_3); 25.8 (CH_3); 26.0 (CH_2); 26.2 (CH_2); 26.5 (CH_2); 29.6 (CH_2); 32.4 (CH_2); 33.8 (CH_2); 34.3 (CH); 37.7 (CH_2); 61.3 (CH); 72.1 (CH_2); 81.3 (CH); 119.2 (CH); 127.6 (Ar-CH); 127.8 (2 x Ar-CH); 128.3 (2 x Ar-CH); 134.3 (C); 138.3 (Ar-C). MS (*m/z*, %): 342 (3, MH^+); 314 (16, $MH^+ - N_2$); 107 (100, $PhCH_2O^+$). Anal. Calcd. for $C_{21}H_{31}N_3O$: C, 73.86; H, 9.15; N, 12.30. Found C, 74.28; H, 8.90; N, 12.64.

(5*S*,6*S*)-6-Amino-7-cyclohexyl-2-methylheptan-5-ol (**4b**). Compound **4b** was obtained in 93% yield from compound **12b** (0.03 g, 0.10 mmol) following the same procedure as for the preparation of **4a**. $[\alpha]_D^{20}$: –30.7º (c = 0.8, $CHCl_3$). IR ($\bar{\upsilon}$, cm^{-1}): 3358 (OH and NH_2). ^1H NMR (δ, ppm): 0.78–1.03 (m, 6 H, 2 x CH_3); 1.07–1.84 (m, 18 H, 11 x H-Cy, H-2, H-3, H-3´, H-4, H-4´, H-7 and H-7´); 2.60 (m, 1H, H-6); 3.20 (m, 2H, NH and H-5). ^{13}C NMR (δ, ppm): 22.6 (CH_3); 22.9 (CH_3); 26.3 (CH_2); 26.5 (CH_2); 26.6 (CH_2); 28.3 (CH); 29.8 (CH_2); 32.6 (CH_2); 34.4 (CH); 34.6 (CH_2); 35.0 (CH_2); 43.7 (CH_2); 52.4 (CH); 80.6 (CH). MS (*m/z*, %): 228 (5, MH^+); 210 (7, $M^+ - OH$); 41 (100). Anal. Calcd. for $C_{14}H_{29}N_3O$: C, 73.95; H, 12.85; N, 6.16. Found C, 73.84; H, 12.55; N, 6.31.

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