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SYNTHESIS AND HYDROGENATION STUDIES OF 3-AZIDOHEX-2-ENOPYRANOSIDES, PRECURSORS OF THE SUGAR CONSTITUENTS OF ANTHRACYCLINE GLYCOSIDES

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ABSTRACT

Application of the allylic azide rearrangement/*N*-iodosuccinimide glycosylation procedure to 3,4-di-*O*-acetyl-L-fucal gave exclusively benzyl 4-*O*-acetyl-3-azido-2,3,6-trideoxy-2-iodo-α-L-idopyranoside. A similar reaction of 3,4-di-*O*-acetyl-L-rhamnal gave both the corresponding L-*altro* (**12**) and L-*manno* glycosides (**14**) in the ratio 4:1. Deacetylation of **12** and **14** and oxidation of the products with pyridinium dichromate also caused the elimination of hydrogen iodide and gave crystalline benzyl 3-azido-2,3,6-trideoxy-α-L-*glycero*-hex-2-enopyranosid-4-ulose (**18**). Reduction of **18** with sodium borohydride at low temperature gave benzyl 3-azido-2,3,6-trideoxy-α-L-*erythro*-hex-2-enopyranoside (**19**). The crystalline mesylate of **19** was treated with caesium propionate, and the product **22** was saponified to give benzyl 3-azido-2,3,6-trideoxy-α-L-*threo*-hex-2-enopyranoside, a suitable A unit precursor for the sequential synthesis of class II anthracycline oligosaccharides. The stereospecific formation of the 3-acetamido-2,3,6-trideoxy-α-L-glycosides with the *ribo* or *xylo* configurations could be achieved by reduction of **19** and **22**, respectively, with sodium borohydride.

INTRODUCTION

Anthracycline antibiotics, such as daunorubicin and the less toxic adriamycin (class I anthracycline glycosides), are widely used in the treatment of a variety of human tumours[1,2]. A severe side-effect of adriamycin is cumulative dose-dependent cardiotoxicity[3]. Recently, clinical interest was developed in the oligosaccharide analogues (class II anthracyclines), *e.g.*, the aclacinomycins[3–6] or marcellomycin[7,8]. Structure–activity correlations for various class I and class II species gave evidence

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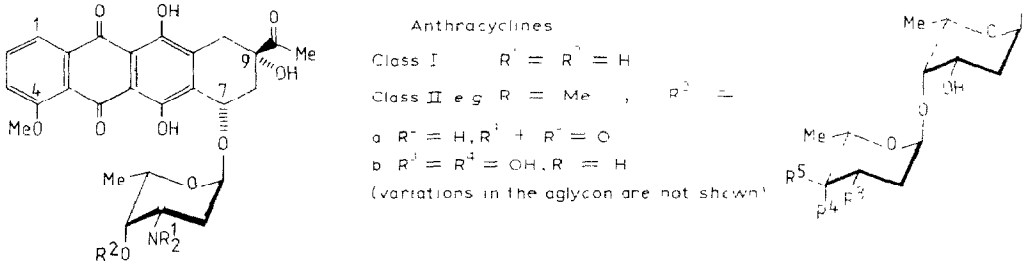
of the enhanced activities and potencies of the latter[9], as well as reduced cardiotoxicity[3].



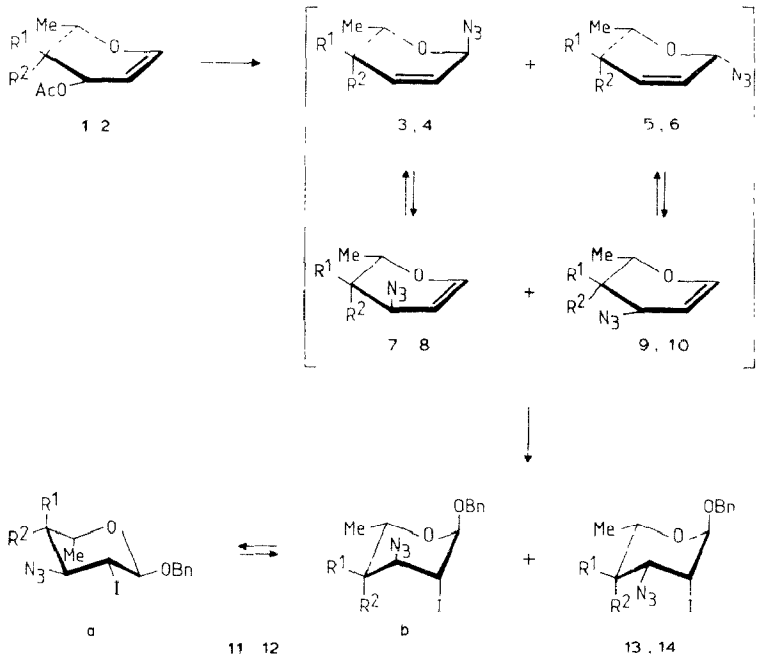
We have described[10,11] different approaches to the synthesis of the terminal C–B disaccharides and modified derivatives of class II anthracycline trisaccharides of the cinerubin and aclacinomycin type. Other groups have also developed pathways to the preparation of disaccharide compounds[12–14], and Monneret *et al*.[15] and we[16] have recently reported the first synthetic approaches towards the trisaccharide units.

The problem in the sequential construction of a C–B–A trisaccharide unit by any glycosylation procedure involves the low reactivity of the axial HO-4 in the essential *lyxo* derivatives. Accordingly, it was necessary to have an appropriate precursor for the 3-amino-2,3,6-trideoxy unit A. Ideally suited to fulfil these requirements would be a dihydropyran derivative containing an allylic alcohol function with enhanced nucleophilicity and reduced steric congestion, and we now report on the synthesis of such compounds.

RESULTS AND DISCUSSION

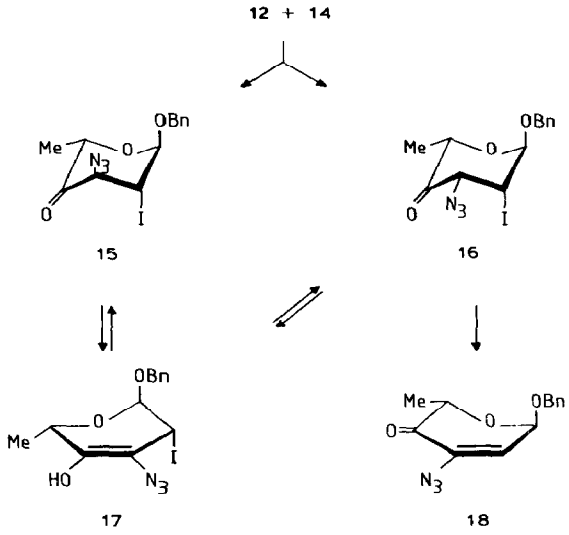
Previously, we have applied the combined azide/*N*-iodosuccinimide procedure for the synthesis of 3-amino-2,3,6-trideoxy-α-glycosides, which represent the type of sugar unit attached to the tetracyclic aglycon[17]. Because these sugars (*e.g.*, daunosamine and rhodosamine) have the L-*lyxo* configuration, the synthesis was started from 3,4-di-*O*-acetyl-L-fucal (**1**). Reaction of **1** with sodium azide in the presence of boron trifluoride etherate was expected[17,18] to give the intermediate 4-*O*-acetyl-α- (**3**) and -β-L-*threo*-hex-2-enopyranosyl azides (**5**), which should equilibrate with **7** and **9**, respectively, involving a [3,3]sigmatropic rearrangement. On treatment of this mixture with *N*-iodosuccinimide and benzyl alcohol, the enol ether derivatives **7** and **9** should be markedly more reactive than the olefinic derivatives **3** and **5**, resulting in displacement of the equilibria and the formation of the glycosides **11** and **13**. However, reaction at low temperature gave exclusively benzyl 4-*O*-acetyl-3-azido-2,3,6-trideoxy-2-iodo-α-L-idopyranoside (**11**) in 35% yield. Whereas the coupling constant $J_{2,3}$ 9.1 indicates that **11** preferentially adopts the $^4C_1$(L) chair conformation, $J_{1,2}$ 5.7 as well as $J_{3,4}$ 7.0 point to some distortion. The

α-L-*talo* 3-epimer **13** could not be detected and the stereospecific formation of **11** suggested the exclusive preliminary formation of **3**. The outcome of this reaction implies that the projected approach to 3-amino-2,3,6-trideoxy-L-*lyxo* derivatives cannot be followed (*cf.* ref. 19).



Attention was then turned to 3,4-di-*O*-acetyl-L-rhamnal (**2**), since inversion of configuration at C-4 leads to the desired L-*lyxo* series. Treatment of **2** as described above for **1** gave the α- (**4**) and β-L-*erythro* (**6**) azides which equilibrated with the 3-azido-L-*ribo*- (**8**) and -L-*arabino*-glycals (**10**)[17,20], respectively. Treatment of the equilibrium mixture of **4**, **6**, **8**, and **10** with *N*-iodosuccinimide and benzyl alcohol gave the α-L-*altro* (**12**) and α-L-*manno* (**14**) glycosides in the ratio 4:1 (70% combined yield). The syrupy minor L-*manno* compound **14** showed coupling constants which indicated the expected $^1C_4$(L) conformation. However, the crystalline L-*altro* derivative **12**, in solution in chloroform at room temperature, showed a conformational equilibrium of the $^4C_1$(L) (**12a**) and $^1C_4$(L) (**12b**) conformations in the ratio ~2:3, as deduced from the coupling constants ($J_{1,2}$ 3.1, $J_{2,3}$ 5.6, $J_{3,4}$ 3.6, and $J_{4,5}$ 7.5 Hz).

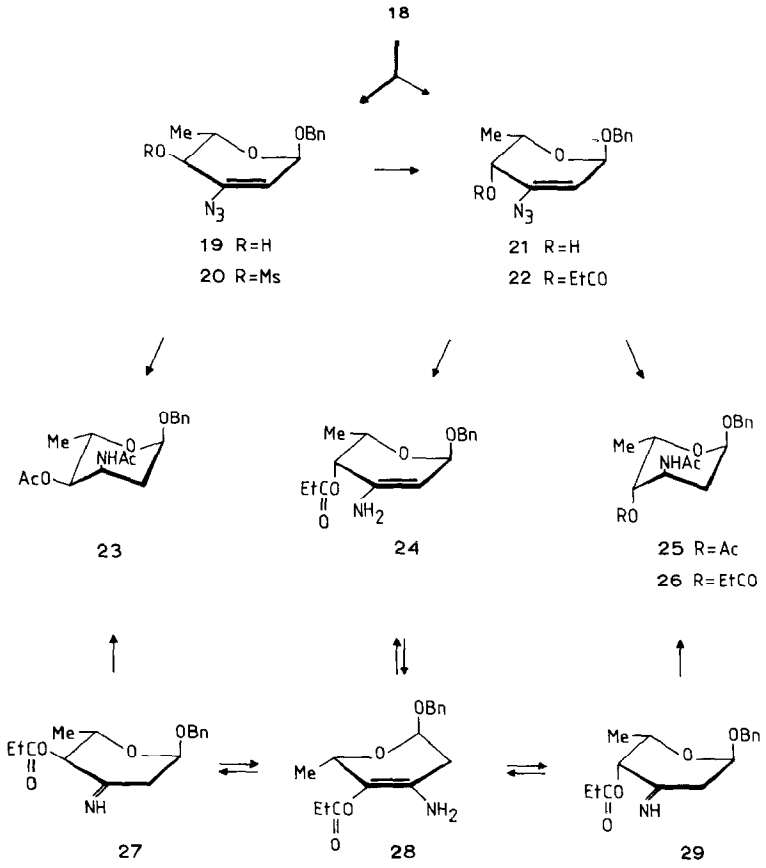
Unfortunately, only the minor isomer **14** was suitable for the planned synthesis. Zemplén transesterification of **14** and oxidation of the product with pyridinium dichromate[21] surprisingly gave crystalline benzyl 3-azido-2,3,6-trideoxy-α-L-*glycero*-hex-2-enopyranosid-4-ulose (**18**) in good yield. The structure of this quite unusual α-carbonyl-stabilised vinyl azide (azido-enosidulose) became evident from the ^{1}H-n.m.r. spectrum which contained resonances for only three ring protons, that for H-2 being at low field indicating an olefinic sugar. The ^{13}C-n.m.r. spectrum contained signals for α-alkoxy (C-1,5), olefinic (C-2,3), and carbonyl (C-4) carbon atoms. The presence of the azide group was indicated by the i.r. absorption at 2100 cm^{-1}.



Thus, after oxidation at C-4 to give **16**, H-3 could be abstracted easily by the base in the oxidation reagent to give, after *trans*-elimination of hydrogen iodide, **18**. Similar treatment of the α-L-*altro* 3-epimer **12** also gave **18**. This result can be understood by a primary oxidation at C-4 to give **15**, which enolised with base to yield the enol (**17**) of **16** which then lost hydrogen iodide to give **18**. Thus, there was no need to isolate **12** and **14**, and the mixture could be converted directly into **18**.

Borohydride reduction of the carbonyl group in **18** at room temperature in ethanol was stereoselective, the labile, syrupy α-L-*erythro* derivative **19** and its α-L-*threo* epimer **21** being obtained in the ratio ~7:2 (70%) and isolated by chromatography. The structures were assigned on the basis of the ^{1}H-n.m.r. data. Thus, **19** showed an allylic coupling ($J_{2,4}$ 1.4 Hz) and a large $J_{4,5}$ value (8.8 Hz), whereas **21** showed a small $J_{4,5}$ value (2.2 Hz). Borohydride reduction of **18** at −20° yielded **19** exclusively.

The inversion of configuration at C-4 in the α-L-*erythro* compound **19** could be effected by treatment[22] of the crystalline mesylate **20** with caesium propionate in *N,N*-dimethylformamide at 60°, which gave an almost quantitative yield of the crystalline α-L-*threo* 4-propionate **22**. The α-L-*threo* derivatives **21** and **22** are precursors for unit A of anthracycline oligosaccharides and, in contrast to the α-L-*lyxo* compounds, contain a sufficiently reactive secondary allylic alcohol group for glycosylation reactions. Their synthesis involved seven steps and an overall yield of 23% from **2**.



Although glycosylation reactions with **21** gave trisaccharides[16], it was necessary to demonstrate the conversion of the vinyl azides into the saturated 3-amino derivatives. Hydrogenation of **22** using various heterogeneous catalysts was unsuccessful. Pressure hydrogenolysis of a solution in 1,4-dioxane over Pt/C at room temperature for 24 h gave, after acetylation and a tedious work-up procedure, only 22% of benzyl 3-acetamido-2,3,6-trideoxy-4-*O*-propionyl-α-L-*xylo*-

hexopyranoside (**26**) together with 6% of the epimer **23**. Hydrogenolysis of **22** should lead to the intermediate enamine **24** which can rearrange into the, presumably, more-stable acyloin-type enamine **28**. This intermediate should be in equilibrium with the imines **29** and **27**, which will add hydrogen exclusively from the less-hindered side ("below"), and *N*-acetylation would then give **26** and **23**. The low yields may be due partly to hydrolysis of the intermediate enamines as detected by t.l.c.

An effective and much simpler reduction of **19** could be achieved with sodium borohydride in boiling ethanol. Acetylation of the product gave only the 3-acetamido-α-L-*ribo* derivative **23** (benzyl *N*-acetyl-*O*-acetyl-α-L-ristosaminide) in acceptable yield. Similarly, reduction of the α-L-*threo* compound **21** gave the 3-acetamido-α-L-*xylo* derivative **25** exclusively, which is a 3-epi-daunosaminide.

Applications of the above procedures in the synthesis of trisaccharide derivatives[16] are presently being investigated.

EXPERIMENTAL

General. — Reactions were monitored by t.l.c. on silica gel 60 GF_{254} (Merck) with detection by u.v. light or charring with sulfuric acid. Preparative t.l.c. (0.25-mm and 0.5-mm layers with and without a concentrating zone) was also done on silica gel 60 GF_{254}. Silica gel 60 (Merck) was used for column chromatography. Melting points were determined with a Leitz melting-point microscope or a Mettler FP-61 apparatus, and are uncorrected. Optical rotations (1-dm path length) were recorded at 589 nm with a Perkin–Elmer 241 polarimeter. ^{1}H-N.m.r. spectra (internal Me_4Si) were recorded at 270 (Bruker WH 270) or 400 MHz (Bruker WM 400), and ^{13}C-n.m.r. spectra were recorded at 20.15 MHz (Bruker WP 80). Microanalyses were performed by Analysenabteilung, Institut für Organische Chemie, Universität Hamburg.

Benzyl 4-O-acetyl-3-azido-2,3,6-trideoxy-2-iodo-α-L-idopyranoside (**11**). — A solution of 3,4-di-*O*-acetyl-L-fucal (**1**; 100 mg, 0.47 mmol) and sodium azide (94 mg, 1.45 mmol) in dry acetonitrile (2 mL) was stirred with boron trifluoride etherate (200 μL, 198 mg) at −25°. The temperature was allowed to rise to −5° during 1 h, until t.l.c. (ethyl acetate–toluene, 1:3) showed no remaining **1**. After the addition of sodium hydrogencarbonate (400 mg), the mixture was stirred at room temperature for 30 min, filtered, and concentrated, and a solution of the residue in dichloromethane was washed with water, dried ($MgSO_4$), and concentrated. A solution of the residue in dry acetonitrile (4 mL) was stirred with an excess of molecular sieves (4 Å), benzyl alcohol (130 mg, 1.2 mmol), and *N*-iodosuccinimide (100 mg, 0.44 mmol) for 2 h at room temperature. A single product was formed (t.l.c.). The mixture was concentrated *in vacuo*, and a solution of the residue in dichloromethane was washed successively with aqueous sodium thiosulfate and water, dried ($MgSO_4$), and concentrated. Column chromatography (ethyl acetate–light petroleum, 1:10) of the residue gave **11** (70 mg, 35%) as a

colourless syrup, $[\alpha]_D^{20}$ −24° (*c* 1.9, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.09 (d, H-1), 3.91 (dd, H-2), 3.95 (dd, H-3), 4.83 (dd, H-4), 4.35 (dq, H-5), 1.18 (d, 3 H, CH*Me*), 4.55 and 4.73 (ABq, 2 H, J_{AB} 11.8 Hz, PhCH_2), 2.15 (s, 3 H, OAc), 7.25–7.38 (m, 5 H, Ph); $J_{1,2}$ 5.7, $J_{2,3}$ 9.1, $J_{3,4}$ 7.0, $J_{4,5}$ 4.5, $J_{5,6}$ 6.8 Hz.

Anal. Calc. for $C_{15}H_{18}IN_3O_4$ (431.2): C, 41.78; H, 4.21; I, 29.43; N, 9.74. Found: C, 41.59; H, 4.16; I, 30.19; N, 9.71.

*Benzyl 4-O-acetyl-3-azido-2,3,6-trideoxy-2-iodo-α-*L*-altro-* (**12**) *and -α-*L*-mannopyranoside* (**14**). — Compound **2** (257 mg, 1.20 mmol) was transformed[17] into a mixture of **4**, **6**, **8**, and **10**. A solution of this mixture (196 mg) in dry acetonitrile (4 mL) was stirred with benzyl alcohol (200 mg, 1.85 mmol) and *N*-iodosuccinimide (293 mg, 1.3 mmol) at room temperature for 12 h. After work-up as described for **11**, the residue was subjected to column chromatography (ethyl acetate–toluene, 1:20→1:30). Eluted first was **14** (70 mg, 14%), isolated as a colourless syrup, $[\alpha]_D^{20}$ −53° (*c* 1.3, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.15 (d, H-1), 4.31 (dd, H-2), 3.56 (dd, H-3), 5.06 (dd~t, H-4), 3.89 (dq, H-5), 1.19 (d, 3 H, CH*Me*), 2.10 (s, 3 H, OAc), 4.49 and 4.65 (ABq, 2 H, J_{AB} 11.8 Hz, PHCH_2), 7.26–7.37 (m, 5 H, Ph); $J_{1,2}$ 1.2, $J_{2,3}$ 4.1, $J_{3,4}$ 9.5, $J_{4,5}$ 9.5, $J_{5,6}$ 6.3 Hz.

Eluted second was **12** (272 mg, 53%), m.p. 67° (from ether–hexane), $[\alpha]_D^{20}$ −47° (*c* 1.4, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.05 (d, H-1), 4.32 (dd, H-2), 4.12 (dd, H-3), 5.18 (dd, H-4), 4.23 (dq, H-5), 1.22 (d, 3 H, CH*Me*), 2.13 (s, 3 H, OAc), 4.53 and 4.74 (ABq, 2 H, J_{AB} 11.8 Hz, PhCH_2), 7.26–7.38 (m, 5 H, Ph); $J_{1,2}$ 3.1, $J_{2,3}$ 5.6, $J_{3,4}$ 3.6, $J_{4,5}$ 7.5, $J_{5,6}$ 6.6 Hz.

Anal. Calc. for $C_{15}H_{18}IN_3O_4$ (431.2): C, 41.78; H, 4.21; I, 29.43; N, 9.74. Found for **12**: C, 41.76; H, 4.22; I, 27.70; N, 9.73. Found for **14**: C, 41.68; H, 4.20; I, 29.55; N, 9.75.

*Benzyl 3-azido-2,3,6-trideoxy-α-*L*-glycero-hex-2-enopyranosid-4-ulose* (**18**). — A mixture of **12** and **14** (1.10 g, 2.55 mmol) was deacetylated conventionally using methanolic sodium methoxide. A solution of the syrupy product in dichloromethane (10 mL) was stirred with pulverised molecular sieves (4 Å; 1.0 g) and pyridinium dichromate (1.5 g, 4.00 mmol) for 12 h at room temperature, filtered, concentrated to 5 mL, diluted with ether (100 mL), filtered, washed successively with aqueous sodium thiosulfate and water, dried ($MgSO_4$), filtered through silica gel, and concentrated *in vacuo*. The residue was recrystallised from aqueous ethanol to give **18** (433 mg, 65%) as pale-yellow crystals, m.p. 64°, $[\alpha]_D^{20}$ +56.5° (*c* 1.1, chloroform); ν_{max} 2100 cm^{-1} (N_3). N.m.r. data ($CDCl_3$): ^{1}H, δ 5.34 (d, H-1), 6.15 (d, H-2), 4.62 (q, H-5), 1.41 (d, 3 H, CH*Me*), 4.64 and 4.79 (ABq, 2 H, J_{AB} 11.8 Hz, PhCH_2), 7.28–7.40 (m, 5 H, Ph); $J_{1,2}$ 4.0, $J_{5,6}$ 6.7 Hz; ^{13}C, δ 15.3 (C-6), 70.5 and 70.9 (C-5 and PhCH_2), 93.2 (C-1), 124.9, 128.1 and 128.5 (C-2 and aryl-C), 134.2 (aryl-C), 137.0 (C-3), 192.7 (C-4).

Anal. Calc. for $C_{13}H_{13}N_3O_3$ (259.3): C, 60.23; H, 5.05; N, 16.21. Found: C, 60.19; H, 5.02; N, 15.99.

*Benzyl 3-azido-2,3,6-trideoxy-α-*L*-erythro-* (**19**) *and -α-*L*-threo-hex-2-enopyranoside* (**21**). — (*a*) A solution of **18** (450 mg, 1.74 mmol) in dry ethanol (5 mL)

was stirred with sodium borohydride (200 mg, 5.29 mmol) at room temperature. After a few minutes, t.l.c. (ethyl acetate–hexane, 1:5) showed reaction to be complete, and water was added dropwise. The mixture was concentrated, and a solution of the residue in dichloromethane was washed with water, dried ($MgSO_4$), and concentrated *in vacuo*. Column chromatography (ethyl acetate–light petroleum, 1:20) of the residue gave **19** (247 mg, 54%) and **21** (68 mg, 15%).

(*b*) When the reaction was performed at −20° for 30 min, work-up as above gave **19** (450 mg, 100%), and column chromatography was unnecessary.

Compound **19** was obtained as a colourless syrup, $[\alpha]_D^{20}$ −87° (*c* 2.5, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.15 (d, H-1), 5.37 (dd, H-2), 3.79 (m, H-4), 3.89 (dq, H-5), 1.26 (d, 3 H, CH*Me*), 2.47 (d, HO-4), 4.61 and 4.77 (ABq, 2 H, J_{AB} 11.9 Hz, PhCH_2), 7.26–7.40 (m, 5 H, Ph); $J_{1,2}$ 3.4, $J_{2,4}$ 1.4, $J_{4,5}$ 8.8, $J_{4,HO-4}$ 6.2, $J_{5,6}$ 6.2 Hz.

Compound **21** was obtained as a colourless syrup, $[\alpha]_D^{20}$ +32° (*c* 0.68, ethyl acetate). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.13 (d, H-1), 5.36 (d, H-2), 3.47 (dd, H-4), 4.14 (dq, 5-H), 1.20 (d, 3 H, CH*Me*), 1.83 (d, HO-4), 4.52 and 4.68 (ABq, 2 H, J_{AB} 11.7 Hz, PhCH_2), 7.18–7.31 (m, 5 H, Ph); $J_{1,2}$ 3.6, $J_{4,5}$ 2.2, $J_{4,HO-4}$ 10.1, $J_{5,6}$ 6.5 Hz.

Compounds **19** and **21** were rather labile; satisfactory combustion analyses could not be obtained.

Benzyl 3-azido-2,3,6-trideoxy-4-O-methanesulfonyl-α-L-erythro-*hex-2-enopyranoside* (**20**). — A solution of **19** (227 mg, 0.87 mmol) in dry pyridine (5 mL) was stirred at 0° with methanesulfonyl chloride (1.5 mL) and then overnight at 5°. T.l.c. (ethyl acetate–hexane, 1:5) then showed reaction to be complete and the mixture was poured onto crushed ice (50 g). The precipitate was collected, dried, and recrystallised from ether–hexane to give **20** (247 mg, 84%) as colourless crystals, m.p. 84–85°, $[\alpha]_D^{20}$ −150° (*c* 1.5, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.25 (d, H-1), 5.58 (dd, H-2), 4.78 (dd, H-4), 4.20 (dq, H-5), 1.38 (d, 3 H, CH*Me*), 3.20 (s, 3 H, OMs), 4.63 and 4.77 (ABq, 2 H, J_{AB} 11.7 Hz, PhCH_2), 7.31–7.40 (m, 5 H, Ph); $J_{1,2}$ 3.5, $J_{2,4}$ 1.4, $J_{4,5}$ 8.7, $J_{5,6}$ 6.3 Hz.

Anal. Calc. for $C_{14}H_{17}N_3O_5S$ (339.4): C, 49.55; H, 5.05; N, 12.38; S, 9.45. Found: C, 49.57; H, 5.07; N, 12.35; S, 9.26.

Benzyl 3-azido-2,3,6-trideoxy-4-O-propionyl-α-L-threo-*hex-2-enopyranoside* (**22**). — To a solution of **20** (63 mg, 0.19 mmol) in dry *N,N*-dimethylformamide (3 mL) was added caesium propionate (150 mg, 0.73 mmol), and the mixture was stirred at 60°. The reaction was complete after 4 h (t.l.c.; ethyl acetate–hexane, 1:3); the mixture was then filtered and concentrated *in vacuo*, a solution of the residue in dichloromethane was filtered through silica gel and concentrated, and the residue was crystallised from hexane to give **22** (56 mg, 92%) as colourless crystals, m.p. 65–67°, $[\alpha]_D^{20}$ +50° (*c* 1, ethyl acetate). ^{1}H-N.m.r. data (C_6D_6): δ 5.00 (d, H-1), 5.27 (d, H-2), 5.06 (d, H-4), 4.05 (dq, H-5), 1.08 (d, 3 H, CH*Me*), 2.08 (cm, 2 H, CH_3CH_2CO), 0.93 (t, 3 H, CH_3CH_2CO), 4.34 and 4.59 (ABq, 2 H, J_{AB} 12.0 Hz, PhCH_2), 7.10–7.31 (m, 5 H, Ph); $J_{1,2}$ 3.5, $J_{4,5}$ 2.5, $J_{5,6}$ 6.5, J_{CH_3,CH_2} 7.2 Hz.

Anal. Calc. for $C_{16}H_{19}N_3O_4$ (317.3): C, 60.56; H, 6.03; N, 13.24. Found: C, 59.57; H, 6.08; N, 13.20.

*Benzyl 3-acetamido-4-*O*-acetyl-2,3,6-trideoxy-α-*L*-xylo-hexopyranoside* (**25**). — A solution of **21** (20 mg, 0.06 mmol) in ethanol (2 mL) containing sodium borohydride (20 mg, 0.53 mmol) was boiled under reflux for 4 h, diluted with water (10 mL), and extracted with dichloromethane. The extract was washed several times with water, dried ($MgSO_4$), and concentrated, and the residue was conventionally acetylated (acetic anhydride–pyridine). The product was subjected to preparative t.l.c. (ethyl acetate–toluene, 2:1; 2 developments) to give **25** (10 mg, 52%) as a colourless syrup, $[\alpha]_D^{20}$ −99° (*c* 0.17, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.06 (dd~d, H-1), 2.21 (ddd, H-2*a*), 1.68 (ddd, H-2*e*), 4.17 (cm, H-3), 4.82 (dd, H-4), 4.13 (dq, H-5), 1.13 (d, 3 H, CH*Me*), 6.98 (d, N*H*Ac), 1.89 and 2.13 (2 s, each 3 H, NAc and OAc), 4.53 and 4.75 (ABq, 2 H, J_{AB} 11.5 Hz, PhCH_2), 7.31–7.43 (m, 5 H, Ph); $J_{1,2a}$ 3.2, $J_{1,2e}$ 1.2, $J_{2a,2e}$ 14.5, $J_{2a,3}$ 4.5, $J_{2e,3}$ 2.3, $J_{3,4}$ 3.0, $J_{3,NH}$ 7.5, $J_{4,5}$ 1.1, $J_{5,6}$ 6.4 Hz.

Anal. Calc. for $C_{17}H_{23}NO_5$ (321.4): C, 63.54; H, 7.21; N, 4.36. Found: C, 62.20; H, 7.39; N, 4.20.

*Benzyl 3-acetamido-4-*O*-acetyl-2,3,6-trideoxy-α-*L*-ribo-hexopyranoside (benzyl N-acetyl-*O*-acetyl-α-*L*-ristosaminide)* (**23**). — A solution of **19** (75 mg, 0.29 mmol) in ethanol (3 mL) containing sodium borohydride (100 mg, 2.65 mmol) was boiled under reflux for 4 h, diluted with water (10 mL), and extracted with dichloromethane. The extract was washed with water, dried ($MgSO_4$), and concentrated, and the syrupy residue was conventionally acetylated (acetic anhydride–pyridine). The product was subjected to preparative t.l.c. (ethyl acetate–toluene, 2:1; 2 developments) to give **23** (43 mg, 46%) as a colourless syrup, $[\alpha]_D^{20}$ −92° (*c* 1.6, chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.01 (dd~d, H-1), 2.10 (ddd, H-2*a*), 1.94 (ddd, H-2*e*), 4.62 (cm, H-3), 4.59 (dd, H-4), 4.02 (dq, H-5), 1.23 (d, 3 H, CH*Me*), 7.00 (d, N*H*Ac), 1.89 and 2.03 (2 s, each 3 H, NAc and OAc), 4.55 and 4.80 (ABq, 2 H, J_{AB} 11.4 Hz, PhCH_2), 7.35–7.46 (m, 5 H, Ph); $J_{1,2a}$ 4.0, $J_{1,2e}$ 1.2, $J_{2a,2e}$ 14.5, $J_{2a,3}$ 3.5, $J_{2e,3}$ 2.8, $J_{3,4}$ 3.9, $J_{3,NH}$ 8.5, $J_{4,5}$ 9.8, $J_{5,6}$ 6.3 Hz.

Anal. Calc. for $C_{17}H_{23}NO_5$ (321.4): C, 63.54; H, 7.21; N, 4.36. Found: C, 62.48; H, 7.34; N, 4.26.

Compounds **23** and **25** were hygroscopic, which is reflected in the C,H,N values.

Hydrogenation of **22**. — A solution of **22** (10.4 mg, 0.03 mmol) in 1,4-dioxane (1 mL), acetic anhydride (0.1 mL), and ethanol (0.5 mL), together with 10% Pt/C (10 mg), was stirred for 24 h at room temperature under 10 bar of hydrogen. The mixture was then filtered through Celite, the filter pad was washed with 1,4-dioxane, and the combined filtrate and washings were concentrated with toluene. The residue was subjected to preparative t.l.c. (ethyl acetate–toluene, 2:1; 2 developments), to give, as the main product, **26** (2.2 mg, 22%), isolated as a colourless syrup, $[\alpha]_D^{20}$ −51° (*c* 0.26 chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 5.06 (dd~d, H-1), 2.21 (dddd, H-2*a*), 1.67 (ddd, H-2*e*), 4.16 (cm, H-3), 4.83 (ddd, H-4), 4.14

(dq, H-5), 1.11 (d, 3 H, CH*Me*), 6.98 (d, N*H*Ac), 1.88 (s, 3 H, NAc), 2.42 (q, 2 H, CH_3CH_2CO), 1.17 (t, 3 H, CH_3CH_2CO), 4.53 and 4.76 (ABq, 2 H, J_{AB} 11.6 Hz, $PhCH_2$), 7.31–7.44 (m, 5 H, Ph); $J_{1,2a}$ 4.0, $J_{1,2e}$ 1.2, $J_{2a,2e}$ 14.5, $J_{2a,3}$ 4.7, $J_{2e,3}$ 2.5, $J_{2e,4}$ 1.0, $J_{3,4}$ 3.2, $J_{3,NH}$ 8.0, $J_{4,5}$ 1.0, $J_{5,6}$ 6.5, J_{CH_3,CH_2} 7.5 Hz.

Compound **23** (0.6 mg, 6%) was also isolated.

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