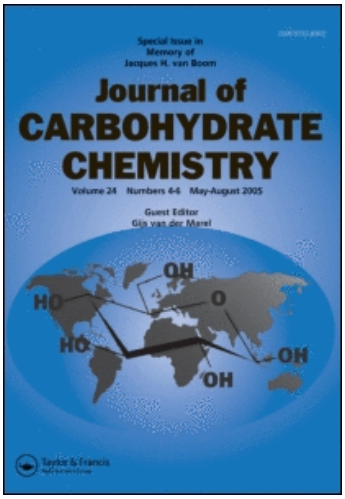

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NON-GLYCOSIDIC AZIDES OF D-ALTRO- AND D-GULOPYRANOSE

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ABSTRACT

Starting with methyl 2-*O*-cyclohexylcarbamoyl-3,4-*O*-(2,2,2-trichloroethylidene)-α-D-altropyranoside (**1**), methyl 4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranoside (**12**), and methyl 6-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranoside (**21**), the 6-azido-6-deoxyaltroses **4**, **6**, **11**, the 6-azido-6-deoxy-D-gulose **14**, the 4-azido-4,6-dideoxy-D-gulose **20**, and the 4-azido-4-deoxy-D-gulose **26** were synthesised via iodinated or tosylated precursors. Additionally, two *gluco*-configured azides, the 3-azido-3,6-dideoxy-D-glucose (**19**) and the 3-azido-3-deoxy-D-glucose (**25**), were obtained besides the desired 4-azido-4-deoxy-D-gulosides **20** and **26**, when methyl 6-deoxy-4-*O*-tosyl-β-D-gulopyranoside (**18**) and methyl 6-*O*-cyclohexylcarbamoyl-4-*O*-tosyl-β-D-gulopyranoside, respectively, were reacted with sodium azide. An X-ray analysis is presented for methyl 2,4-di-*O*-acetyl-3-azido-3,6-dideoxy-ß-D-glucose (**19**).

INTRODUCTION

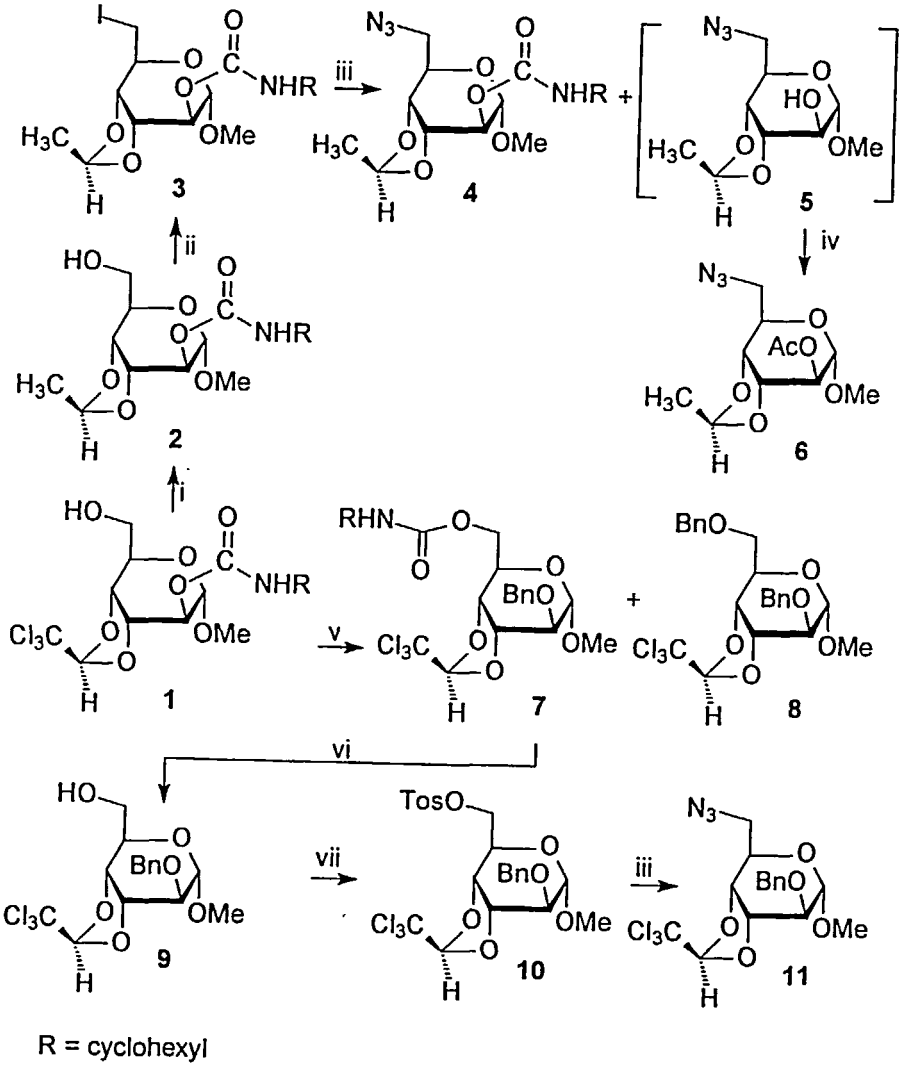
Azidosugars [1-9] serve as valuable carbohydrate building blocks, e.g. as precursors to amines,[10, 11] acylated amines,[12-15] carbamates,[16] 1,2,3-triazole derivatives,[7-9, 17, 18] and glycosyl fluorides.[7, 8] Various natural antibiotics contain carbohydrate moieties with aminodeoxy or deoxy structures. For example, 2-amino-2-deoxy-D-gulose is part of the streptothricine molecule [19, 20] and 3-amino-3,6-dideoxy-D-mannose is a component of the macrolide-antibiotic natamycine (pimaricine).[19, 21, 22] It is well-known that also numerous 1,2,3-triazoles are biologically active.[23, 24] Consequently, linking them to a hydrophilic moiety could give interesting mimetic products, e.g., nucleoside analogues and reversed nucleoside analogues accessible from azidosugars.

In this paper we describe syntheses of azides of rare monosaccharides as precursors for products mentioned above. The three starting materials **1**, **12**, and **21** are easily accessible by nonconventional one-pot epimerisation of methyl α-D-mannopyranoside and methyl ß-D-galactopyranoside, respectively.[25, 26] Some of the azides have been converted to fluorinated nucleosides and reversed nucleoside analogues by 1,3-dipolar cycloaddition with fluorinated dipolarophiles. The latter results are reported in separate papers.[27, 28]

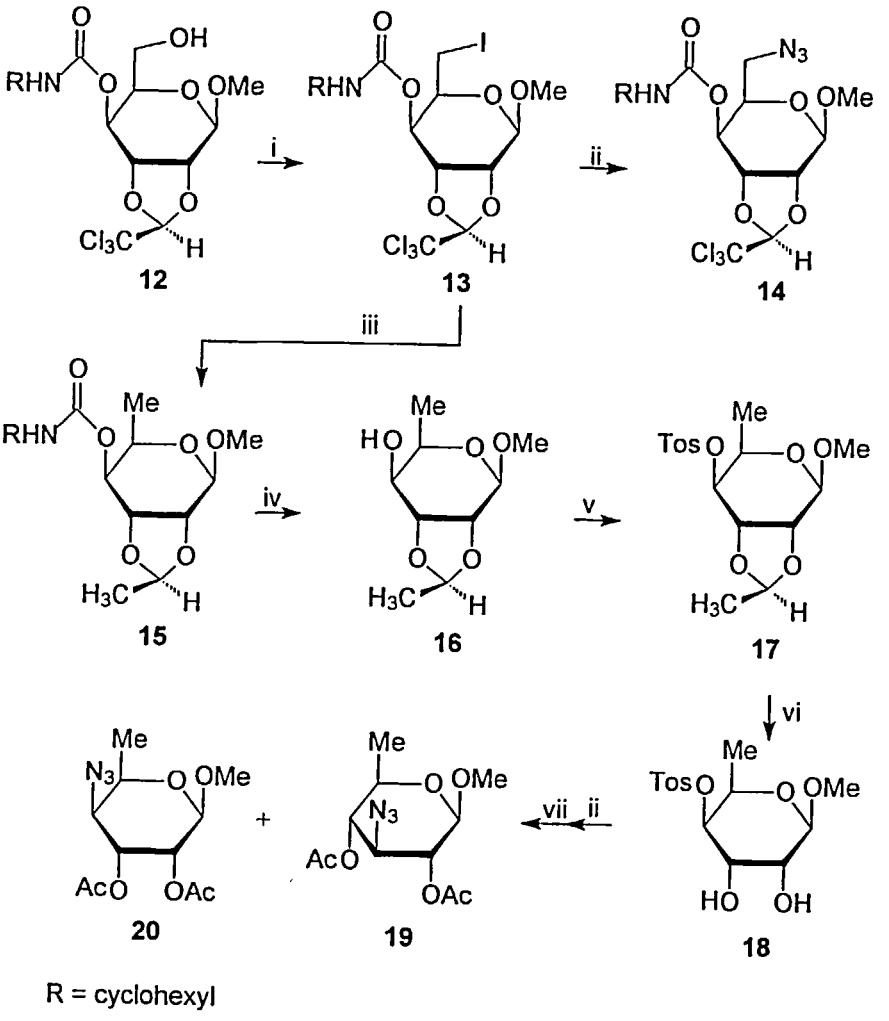
RESULTS AND DISCUSSION

The strategy of the following syntheses is largely founded on conventional methods of carbohydrate chemistry (Schemes 1-3). Starting with methyl 2-*O*-cyclohexylcarbamoyl-3,4-*O*-(2,2,2-trichloroethylidene)-α-D-altropyranoside (**1**),[25] methyl 4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranoside (**12**)[26] (see also ref. 29), and methyl 6-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranoside (**21**),[26] the 6-azido-6-deoxy-D-altroses **4**, **6**, **11** (Scheme 1), the 6-azido-6-deoxy-D-gulose **14**, the 4-azido-4,6-dideoxy-D-gulose **20**, and the 4-azido-4-deoxy-D-gulose **26** were prepared (Schemes 2 and 3).

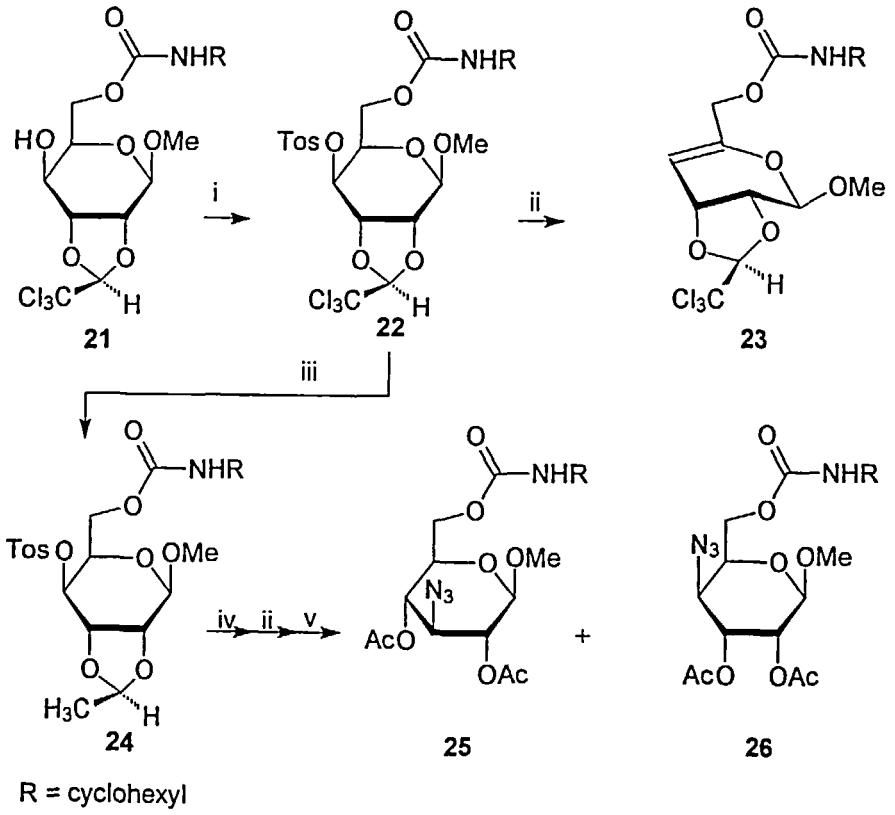
To introduce the azido group by nucleophilic substitution, either iodinated or tosylated precursors were used. The iodinated precursors, 6-deoxy-6-iodo-D-altrose **3**



Scheme 1: i = Bu_3SnH, AIBN, toluene, reflux;[31] ii = Ph_3P, imidazole, I_2, toluene, reflux; iii = NaN_3, DMF, 120 °C; iv = Ac_2O, pyr, rt; v = BnBr, NaH, THF, rt; vi = MeOH, MeONa, reflux; vii = TosCl, pyr, rt.



Scheme 2: i = Ph_3P, imidazole, I_2, toluene, reflux; ii = NaN_3, DMF, 120 °C; iii = Bu_3SnH, AIBN, toluene, 75 °C; iv = MeOH, MeONa, reflux; v = TosCl, pyr, rt; vi = CF_3COOH, H_2O, 50 °C; vii = Ac_2O, pyr, rt.



Scheme 3: i = TosCl, pyr, rt; ii = NaN_3, DMF, 120 °C; iii = Bu_3SnH, AIBN, toluene, 75 °C; iv = CF_3COOH, H_2O, 50 °C; v = Ac_2O, pyr, rt.

(Scheme 1) and 6-deoxy-6-iodo-D-gulose **13** (Scheme 2), were synthesised from the corresponding monohydroxy derivatives **2** and **12**, respectively, with the reagent system iodine/triphenyl phosphine/imidazole (procedure analogous to ref. 30). Replacement of iodide by azide was carried out with sodium azide in DMF at 120 °C. Under these reaction conditions, methyl 2-*O*-cyclohexylcarbamoyl-6-deoxy-6-iodo-3,4-*O*-ethylidene-α-D-altropyranoside (**3**) yielded two products, the methyl 6-azido-2-*O*-cyclohexylcarbamoyl-6-deoxy-3,4-*O*-ethylidene-α-D-altropyranoside (**4**) (76% yield) and the by-product **5** (20%); Scheme 1. The latter, a decarbamoylated derivative of **4**, was acetylated to **6** before analytical characterisation. Unlike iodo derivative **3**, the methyl 4-*O*-cyclohexylcarbamoyl-6-deoxy-6-iodo-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranoside (**13**) reacted more se-

lectively with sodium azide at 120 °C, i.e., the expected methyl 6-azido-4-*O*-cyclohexylcarbamoyl-6-deoxy-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranoside (**14**) was isolated in 90% yield (Scheme 2). Additionally, the guloside **13** was hydrodehalogenated to methyl 4-*O*-cyclohexylcarbamoyl-6-deoxy-2,3-*O*-ethylidene-β-D-gulopyranoside (**15**). On heating **13** with tributylstannane/AIBN in toluene the trichloroethylidene as well as the iodomethyl group were reduced (Scheme 2) giving **15** in quantitative yield.

Various intermediates presented in the Schemes 1-3 contain, besides usual protecting groups, the acid-stable trichloroethylidene acetal and a cyclohexylcarbamoyl group. The best strategy to remove a trichloroethylidene group was a two step procedure, i.e., hydrodechlorination with Bu_3SnH/AIBN[31, 32] followed by cleavage of the acid-labile ethylidene acetal by aqueous trifluoroacetic acid (TFA). Reduction of a trichloroethylidene group with Bu_3SnH/AIBN could not be carried out in the presence of an azido group, because the reagent attacks azido groups.[33] Therefore, we converted the trichloroethylidene moiety of D-altrose **1**, D-gulose **13**, and D-gulose **22** in an early synthetic step (Schemes 1-3).

Removing of carbamoyl groups was achieved by refluxing the corresponding sugar derivative with methanolic sodium methoxide.[26, 29] Some monohydroxy sugars used as starting materials for the synthesis of deoxyiodides or tosylates were generated by selective decarbamoylation or by intramolecular rearrangements of a carbamoyl group. As shown in previous papers,[26, 29] treatment of 4-*O*-carbamoyl-gulopyranosides with methanolic sodium methoxide at room temperature causes carbamoyl migration forming the corresponding 6-*O*-carbamoyl gulosides, whereas refluxing of the mixtures gave decarbamoylation. Recently, it was observed that sodium hydride likewise causes carbamoyl migrations in THF solution.[33] The following example shows that carbamoyl migration and benzylation may be combined under conventional benzylation conditions. Thus, methyl 2-*O*-cyclohexylcarbamoyl-3,4-*O*-(2,2,2-trichloroethylidene)-α-D-altropyranoside (**1**) treated with sodium hydride and benzyl bromide in THF for 24 h at room temperature, gave two products, the 2-*O*-benzyl-6-*O*-cyclohexylcarbamoyl-D-altropyranoside **7** (49%) and the 2,6-di-*O*-benzyl-D-altropyranoside **8** (10%) (Scheme 1). A longer reaction time than 24 hours or a higher excess of benzyl bromide than given in the experimental part favoured the

formation of the decarbamoylated by-product **8**. The major product **7** was subsequently decarbamoylated to **9** by refluxing with methanolic sodium methoxide. Compound **9** was the precursor for the preparation of tosylate **10** (Scheme 1).

The tosylates **10**, **17**, and **22** were synthesised by treatment of the 6-hydroxy-D-altrose derivative **9** (prepared by decarbamoylation of **7**; Scheme 1), the 4-hydroxy-6-deoxy-D-gulose derivative **16** (prepared by decarbamoylation of **15**; Scheme 2), and the 4-hydroxy-D-gulose **21** (Scheme 3), respectively, with *p*-tosyl chloride/pyridine at room temperature. These three tosylates were heated (120 °C) with sodium azide in DMF to generate the corresponding azides by nucleophilic substitution. The results were different. As expected, 6-azido-6-deoxy-D-altroside **11** was obtained from **10** in a high yield (88%) after heating the reaction mixture for 1 h (Scheme 1). Under similar reaction conditions the 4-*O*-tosylated starting material **18**, prepared by deacetalation of the ethylidene derivative **17** with aqueous TFA, produced two regioisomeric azides, methyl 3-azido-3,6-dideoxy-β-D-glucopyranoside and methyl 4-azido-4,6-dideoxy-β-D-gulopyranoside. It would appear that a 3,4-epoxide is formed as intermediate. The mixture of isomeric azides was acetylated and the two di-*O*-acetyl derivatives **19** and **20** obtained were separated by column chromatography (Scheme 2). The *gluco*-configured isomer **19** crystallised from an diethyl ether-acetone mixture, so that an X-ray analysis could be carried out (Figure 1).

Only elimination to methyl 6-*O*-cyclohexylcarbamoyl-4-deoxy-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-*erythro*-hex-4-enopyranoside (**23**) was observed when the tosylated D-guloside **22** was treated with sodium azide as described above (Scheme 3). The easy elimination of *p*-toluenesulphonic acid resulted from the *trans*-diaxial arrangement of 5-H and the tosylate group.[34] However, after the 3-position of the 4-*O*-tosylate was deprotected, introduction of an azide moiety was favoured.

As shown in Scheme 3, the azides **25** and **26** were prepared from **22** in four steps via reduction of **22** and 2,3-deacetalation of the methyl 6-*O*-cyclohexylcarbamoyl-4-*O*-tosyl-2,3-*O*-ethylidene-β-D-gulopyranoside (**24**) with aqueous TFA giving methyl 6-*O*-cyclohexylcarbamoyl-4-*O*-tosyl-β-D-gulopyranoside. The latter was heated (120 °C) for 5 h with sodium azide in DMF yielding a mixture of two isomeric azides. The two azides resulted again by opening of the 3,4-epoxide intermediate primarily formed from methyl 6-*O*-

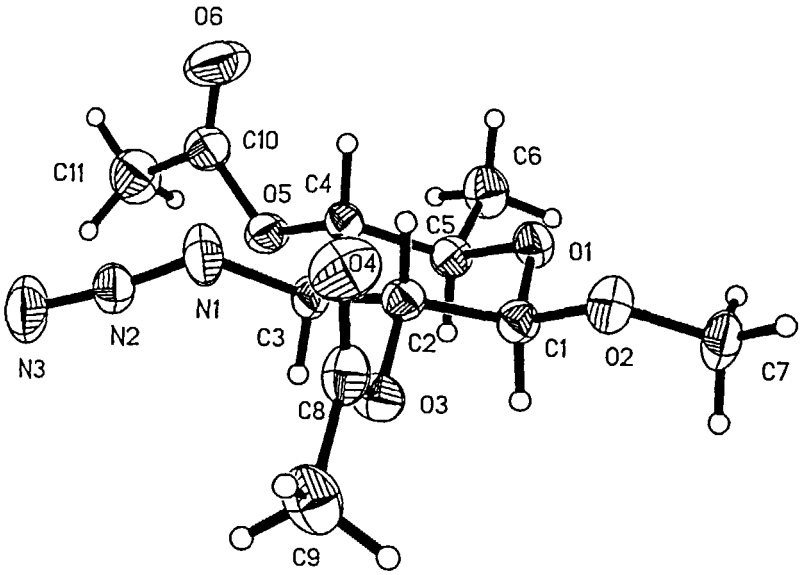


Figure 1: X-ray structure of methyl 2,4-di-*O*-acetyl-3-azido-3,6-dideoxy-β-D-glucopyranoside (**19**); 30% probability of the terminal ellipsoids.

cyclohexylcarbamoyl-4-*O*-tosyl-β-D-gulopyranoside. After acetylation of the mixture with acetic anhydride/pyridine, methyl 2,4-di-*O*-acetyl-3-azido-6-*O*-cyclohexylcarbamoyl-3-deoxy-β-D-glucopyranoside (**25**) and methyl 2,3-di-*O*-acetyl-4-azido-6-*O*-cyclohexylcarbamoyl-4-deoxy-β-D-gulopyranoside (**26**) were isolated by column chromatography in yields of 39 and 42%, respectively, related to **24**.

The structures of the compounds **3**, **4**, **6-11**, **13-20**, and **22-26** are supported by their ^{1}H and ^{13}C NMR spectra. In the case of 2-*O*-benzyl-6-*O*-carbamoyl-α-D-altropyranoside **7** ^{1}H NOE measurements were carried out. The obvious assignments of the isomers **19/20** and **25/26** to the D-*gluco*- and D-*gulo*-series, respectively, were carried out on the basis of the proton couplings. Thus, D-glucopyranose derivative **25** shows only large coupling constants ($^{3}J_{1,2} \approx 7.9$ Hz, $^{3}J_{2,3} \approx 10.4$ Hz, $^{3}J_{3,4} \approx 10.0$ Hz, $^{3}J_{4,5} \approx 9.9$ Hz) as a result of the *trans*-diaxal arrangement of all pyranose ring protons. The corresponding couplings of the D-gulopyranoside **26** are $^{3}J_{1,2} \approx 7.6$ Hz, $^{3}J_{2,3} \approx 3.3$ Hz, $^{3}J_{3,4} \approx 4.5$ Hz, and $^{3}J_{4,5} \approx 2.3$ Hz. Similar data were found for the pair of isomers **19/20** (see experimental part). The structure of *gluco*-configured azide **19** was additionally confirmed by an X-ray analysis (Figure 1). The puckering parameters[35, 36] of compound **19** indicate a slightly distorted $^{4}C_{1}$ chair conformation of the pyranose ring. With

reference to literature data of a pyranoid ring (Q = 0.56 Å, θ = 5°)[35], the total puckering amplitude (Q = 0.589 Å) and the magnitude of the distortion (θ = 7.9°) were determined; its φ–value was 310.2°.

For the X-ray structure determination a suitable crystal of **19** was fixed onto a glass fibre and a data collection started on a STOE-IPDS. The structure was solved by direct methods (SHELXS-86, G. M. Sheldrick, Universität Göttingen, 1986) and refined by the full matrix least-squares method of Bruker SHELXTL, Vers.5.10, Copyright 1997, Bruker Analytical X-ray Systems. All nonhydrogen atoms were refined anisotropically. The hydrogens were put into theoretical positions and refined using the riding model.

Further details of the data collection: Diffractometer: STOE IPDS; Radiation: λ = 0.71069 Å (Mo-K_α) with graphite monochromator; crystal size: 0.50 x 0.40 x 0.30 mm^3; formula: $C_{11}H_{17}N_3O_6$; formula weight: 287.28; temperature 200(2) K; crystal system: orthorhombic; space group: $P2_12_12_1$; unit cell dimensions: a = 8.123(1) Å, b = 9.362(1) Å, c = 19.009(2) Å; volume: 1445.6(3) $Å^3$; Z = 4; density (calcd): 1.320 Mg/m^3; absorption coefficient: 0.108 mm-1; F(000): 608; Θ range for data collection: 2.42 to 24.16° ; index ranges: -9 < = h < = 9, -10 < = k < = 10, -21 < = l < = 21; reflections collected: 5547; independent reflections: 2104; R(int) = 0.0391, completeness to Θ = 24.16° , 94.1 %; data / restraints / parameters: 2104 / 0 / 181; goodness-of-fit on F2: 0.890; final R indices [$I > 2\sigma(I)$]: R1 = 0.0315, wR2 = 0.0611; R indices (all data): R1 = 0.0495, wR2 = 0.0652; absolute structure parameter: 1.3(12); largest diff. peak and hole: 0.088 and -0.115 e/$Å^3$. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-137235. Copies of the data can be obtained free of charge an application to The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: Int.code +(1223) 336-033; e-mail:deposit@ccdc.cam.ac.uk).

EXPERIMENTAL

^1H and ^{13}C NMR: Bruker AC 250; internal standard TMS, J values in Hz. TLC: Silica gel foils 60 F_{254} (Merck). Column chromatography: Silica gel 60 (63-200 μm)

(Merck). Melting points: Polarising microscope Leitz Laborlux 12 Pol equipped with a hot stage Mettler FP 90. Optical rotation: Polar LμP (IBZ Meßtechnik). Chemicals: 60% suspension of NaH in paraffin oil (Fluka); AIBN (Fluka), Bu_3SnH (Aldrich), Amberlite IR 120 (Fluka).

Methyl 2-*O*-cyclohexylcarbamoyl-6-deoxy-3,4-*O*-ethylidene-6-iodo-α-D-altropyranoside (3). To a soln of methyl 2-*O*-cyclohexylcarbamoyl-3,4-*O*-ethylidene-α-D-altropyranoside (**2**)[31] (1.73 g, 5.0 mmol) and Ph_3P (1.97 g, 7.50 mmol) in 15 mL dried toluene, imidazole (1.02 g, 15.0 mmol) and iodine (1.90 g, 7.50 mmol) were added and the mixture was refluxed with vigorous stirring for about 20 min (TLC control). After decanting and treatment of the solid with EtOAc (twice 10 mL), the combined organic phases were subsequently washed with 10 mL of 3% aq $Na_2S_2O_4$ soln and water (twice 10 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (R_f = 0.28; heptane/EtOAc, 6:1). Yield: 2.23 g (98%), mp 121-123 °C (i-PrOH); $[\alpha]_D^{23}$ +66.7 (*c* 1.06, chloroform). ^{1}H NMR (250.1 MHz, $CDCl_3$): δ 5.38 (q, 1H, $^3J_{\text{acetal-H/ethylidene-CH3}} \approx 5.0$, acetal-H), 5.05 (dd, 1H, $^3J_{1/2} \approx 2.5$, $^3J_{2/3} \approx 4.3$, 2-H), 4.64 (d, 1H, 1-H), 4.62-4.73 (m, 1H, carbamoyl-NH), 4.16 (dd, 1H, $^3J_{3/4} \approx 5.9$, 3-H), 3.98 (dd, $^3J_{4/5} \approx 9.2$, 4-H), 3.69 (ddd, 1H, $^3J_{5/6} \approx 2.3$, $^3J_{5/6'} \approx 8.8$, 5-H), 3.54 (dd, 1H, $^2J_{6/6'} \approx 10.7$, 6-H), 3.48 (s, 3H, MeO), 3.36-3.55 (m, 1H, cyclohexyl CH), 3.21 (dd, 1H, 6'-H), 1.85-2.01 (m, 2H, cyclohexyl CH_2), 1.53-1.78 (m, 3H, cyclohexyl CH_2), 1.31 (d, 3H, ethylidene CH_3), 1.01-1.41 (m, 5H, cyclohexyl CH_2); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 155.3 (carbamoyl CO), 103.1 (acetal C), 101.0 (C-1), 75.0, 74.5, 69.1, 67.0 (C-2,3,4,5), 56.0 (MeO), 50.2 (cyclohexyl CH), 33.3, 25.4, 24.7 (cyclohexyl CH_2), 20.7 (ethylidene CH_3), 6.2 (C-6).

Anal. Calcd for $C_{16}H_{26}INO_6$ (455.3): C, 42.21; H, 5.76; N, 3.08. Found: C, 42.44; H, 5.83; N, 3.17.

Methyl 6-azido-2-*O*-cyclohexylcarbamoyl-6-deoxy-3,4-*O*-ethylidene-α-D-altropyranoside (4) and **methyl 6-azido-6-deoxy-3,4-*O*-ethylidene-α-D-altropyranoside (5).** A soln of **3** (2.28 g, 5.0 mmol) and NaN_3 (0.36 g, 5.50 mmol) in dried DMF (10 mL) was stirred for 1.5 h at 120 °C. Subsequently, the mixture was cooled down, poured on 10 g of ice and extracted with diethyl ether (3 x 10 mL). The combined organic phases were dried ($MgSO_4$), concentrated under reduced pressure and the residue was purified by column

chromatography yielding 1.41 g (76%) of the major product **4** (heptane/EtOAc 10:1; R_f = 0.15) and 0.25 g (20%) of the by-product **5** (eluent exchange to toluene/EtOAc 5:1 after separation of the main spot; R_f = 0.18). The by-product **5** was acetylated generating **6**.

4: mp 112-114 °C (i-PrOH); $[\alpha]_D^{22}$ +46.8 (*c* 1.05, chloroform); ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 5.38 (q, 1H, $^3J_{\text{acetal-H/ethylidene-CH3}} \approx 4.9$, acetal-H), 5.07 (dd, 1H, $^3J_{1/2} \approx 3.0$, $^3J_{2/3} \approx 4.7$, 2-H), 4.67 (d, 1H, $^3J_{\text{NH/CH}} \approx 7.4$, carbamoyl-NH), 4.63 (d, 1H, 1-H), 4.18 (dd, 1H, $^3J_{3/4} \approx 5.9$, 3-H), 4.09 (dd, $^3J_{4/5} \approx 9.4$, 4-H), 3.88 (ddd, 1H, $^3J_{5/6} \approx 2.9$, $^3J_{5/6'} \approx 6.6$, 5-H), 3.50 (dd, 1H, $^2J_{6/6'} \approx 13.1$, 6-H), 3.43 (s, 3H, MeO), 3.41 (dd, 1H, 6'-H), 1.85-2.00 (m, 2H, cyclohexyl CH_2), 1.52-1.77 (m, 3H, cyclohexyl CH_2), 1.30 (d, 3H, ethylidene CH_3), 1.03-1.43 (m, 5H, cyclohexyl CH_2); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 154.0 (carbamoyl CO), 101.7, 99.4 (C-1, acetal C), 74.3, 71.7, 69.0, 66.8 (C-2,3,4,5), 55.8 (MeO), 52.4 (C-6), 50.2 (cyclohexyl CH), 33.3, 25.4, 24.7 (cyclohexyl CH_2), 20.6 (ethylidene CH_3).

Anal. Calcd for $C_{16}H_{26}N_4O_6$ (370.4): C, 51.88; H, 7.08; N, 15.13. Found: C, 51.90; H, 7.01; N, 14.87.

5: ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 5.23 (q, 1H, $^3J_{\text{acetal-H/ethylidene-CH3}} \approx 4.9$, acetal-H), 4.48 (d, 1H, $^3J_{1/2} \approx 5.2$, 1-H), 4.20 (dd, 1H, $^3J_{2/3} \approx 7.7$, $^3J_{3/4} \approx 7.1$, 3-H), 4.09 (dd, $^3J_{4/5} \approx 9.4$, 4-H), 3.83 (dd, 1H, 2-H), 3.80 (ddd, 1H, $^3J_{5/6} \approx 3.0$, $^3J_{5/6'} \approx 6.7$, 5-H), 3.42 (s, 3H, MeO), 3.40 (dd, 1H, $^2J_{6/6'} \approx 13.1$, 6-H), 3.33 (dd, 1H, 6'-H), 1.29 (d, 3H, ethylidene CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 101.7, 101.2 (C-1, acetal C), 77.1, 72.9, 69.5, 68.7 (C-2,3,4,5), 55.7 (MeO), 52.6 (C-6), 19.8 (ethylidene CH_3).

Methyl 2-*O*-acetyl-6-azido-6-deoxy-3,4-*O*-ethylidene-α-D-altropyranoside (6). A soln of **5** (0.25 g, 1.0 mmol) in pyr/acetic anhydride (10 mL, 1:1 v/v) was stirred at rt for 10 h (TLC control). After evaporation of the solvents under reduced pressure, the oily residue was dissolved in diethyl ether (20 mL), washed with 3% aq $NaHSO_4$ (twice 5 mL) and water (twice 5 mL), dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (eluent: heptane/EtOAc 6:1, R_f = 0.36) giving 0.27 g (94%) of the syrupy product **6**, $[\alpha]_D^{23}$ +43.3 (*c* 1.03, chloroform); ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 5.36 (q, 1H, $^3J_{\text{acetal-H/ethylidene-CH3}} \approx 4.9$, acetal-H), 5.19 (dd, 1H, $^3J_{1/2} \approx 3.7$, $^3J_{2/3} \approx 5.7$, 2-H), 4.60 (d, 1H, 1-H), 4.20 (dd, 1H, $^3J_{3/4} \approx 6.3$, 3-H), 4.12 (dd, $^3J_{4/5} \approx 9.4$, 4-H), 3.90 (ddd, 1H, $^3J_{5/6} \approx 2.9$, $^3J_{5/6'} \approx 6.9$, 5-H), 3.49 (dd, 1H, $^2J_{6/6'} \approx 13.2$, 6-H), 3.43 (s, 3H, MeO), 3.41

(dd, 1H, 6'-H), 2.11 (s, 3H, acetyl CH_3), 1.31 (d, 3H, ethylidene CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 169.5 (acetyl CO), 101.7, 99.2 (C-1, acetal C), 74.6, 72.2, 69.0, 67.6 (C-2,3,4,5), 55.8 (MeO), 52.5 (C-6), 20.9, 20.4 (acetyl CH_3, ethylidene CH_3).

Anal. Calcd for $C_{11}H_{17}N_3O_6$ (287.3): C, 45.99; H, 5.96; N, 14.63. Found: C, 46.08; H, 6.01; N, 14.35.

Methyl 2-*O*-benzyl-6-*O*-cyclohexylcarbamoyl-3,4-*O*-(2,2,2-trichloroethylidene)-α-D-altropyranoside (7) and **methyl 2,6-di-*O*-benzyl-3,4-*O*-(2,2,2-trichloroethylidene)-α-D-altropyranoside (8)**. To a soln of methyl 2-*O*-cyclohexylcarbamoyl-3,4-*O*-(2,2,2-trichloroethylidene)-α-D-altropyranoside (1)[25] (1.0 g, 2.23 mmol) in anhyd THF (10 mL) a 60% suspension of NaH in paraffin oil (0.11 g, 2.79 mmol) was added with stirring at rt in portions. Then benzyl bromide (0.33 mL, 2.79 mmol) was added and stirring was continued. After 24 h the reaction was finished (TLC control) and nonreacted sodium hydride was carefully decomposed by adding of an ether/water mixture (10 mL, 1:1, v/v) in portions. The organic phase was separated and the aqueous phase was extracted with ether (twice 10 mL). The combined organic phases were washed with 3% aq $NaHSO_4$ soln (10 mL) and water (twice 10 mL), dried ($MgSO_4$) and the solvents were evaporated under reduced pressure. The residue was purified by column chromatography (heptane/EtOAc 5:1) yielding 0.59 g (49%) of the syrupy major product **7** (R_f = 0.23), $([\alpha]_D^{23}$ +33.8 ; *c* 1.10, chloroform), 0.11 g (10%), of the syrupy by-product **8** (R_f = 0.45), $([\alpha]_D^{25}$ +32.0; *c* 1.42, chloroform), and 0.15 g (15%) of non-reacted starting material **1** (R_f = 0.08).

7: ^1H NMR (250.1 MHz, $CDCl_3$): δ 7.26-7.41 (m, 5H, phenyl CH), 5.36 (s, 1H, acetal-H), 4.72 (s, 2H, benzyl CH_2), 4.52-4.71 (m, 4H, 1-H, 3-H, 4-H, carbamoyl-NH), 4.36 (dd, 1H, $^3J_{5/6} \approx 3.1$, $^2J_{6/6'} \approx 11.9$, 6-H), 4.21 (dd, $^3J_{5/6'} \approx 6.2$, 6'-H), 3.78-3.98 (m, 1H, 5-H), 3.62 (dd, 1H, $^3J_{1/2} \approx 3.8$, $^3J_{2/3} \approx 6.1$, 2-H), 3.39 (s, 3H, MeO), 3.32-3.59 (m, 1H, cyclohexyl CH), 1.84-2.00 (m, 2H, cyclohexyl CH_2), 1.51-1.77 (m, 3H, cyclohexyl CH_2), 1.01-1.45 (m, 5H, cyclohexyl CH_2); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 155.0 (carbamoyl CO), 137.4 (phenyl C), 128.4, 128.0, 127.9 (phenyl CH) 107.6 (acetal C), 100.7 (C-1), 99.6 (CCl_3), 78.6, 76.6, 74.0, 67.1 (C-2,3,4,5), 73.0 (benzyl CH_2), 64.0 (C-6), 55.4 (MeO), 49.9 (cyclohexyl CH), 33.3, 25.4, 24.7 (cyclohexyl CH_2).

Anal. Calcd for $C_{23}H_{30}Cl_3NO_7$ (538.9): C, 51.27; H, 5.61; N, 2.60. Found: C, 51.77; H, 5.73; N, 2.58.

8: ^{1}H NMR (250.1 MHz, $CDCl_3$): δ 7.27-7.43 (m, 10H, phenyl CH), 5.35 (s, 1H, acetal-H), 4.76 (s, 2H, benzyl CH_2), 4.71 (dd, 1H, $^3J_{2/3} \approx 1.9$, $^3J_{3/4} \approx 4.5$, 3-H), 4.70 (dd, 1H, $^3J_{4/5} \approx 8.8$, 4-H), 4.68 (d, 1H, $^3J_{1/2} \approx 4.6$, 1-H), 4.65 (d, 1H, benzyl CH_2), 4.60 (d, 1H, benzyl CH_2), 3.89 (ddd, 1H, $^3J_{5/6} \approx 2.7$, $^3J_{5/6'} \approx 5.6$, 5-H), 3.78 (dd, $^2J_{6/6'} \approx 10.9$, 6-H), 3.67 (d, 1H, 6'-H), 3.63 (dd, 1H, 2-H), 3.43 (s, 3H, MeO); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 137.9, 137.6 (phenyl C), 128.4, 127.9, 127.8, 127.6, 127.5 (phenyl CH) 107.8 (acetal C), 101.1 (C-1), 99.8 (CCl_3), 79.2 (C-3), 77.3 (C-4), 74.5 (C-2), 73.4, 72.9 (benzyl CH_2), 70.0 (C-6), 68.9 (C-5), 55.4 (MeO).

Anal. Calcd for $C_{23}H_{25}Cl_3O_6$ (503.8): C, 54.83; H, 5.00. Found: C, 54.58; H, 5.17.

Methyl 2-*O*-benzyl-3,4-*O*-(2,2,2-trichloroethylidene)-α-D-altropyranoside (9). Compd 7 (1.08 g, 2.0 mmol) dissolved in 1% methanolic NaOMe (15 mL) was decarbamoylated by heating the soln under reflux for 30 h. Subsequently, the reaction mixture was cooled and neutralised with an acidic ion exchanger resin (Amberlite IR-120). After evaporation of the solvent under reduced pressure and column chromatographic purification (toluene/EtOAc 7:1, $R_f = 0.27$) compd **9** was obtained in a yield of 0.53 g (60%), mp 86-88 °C (i-PrOH); $[\alpha]_D^{25}$ +52.8 (*c* 1.12, chloroform); ^{1}H NMR (250.1 MHz, $CDCl_3$): δ 7.26-7.42 (m, 5H, phenyl CH), 5.37 (s, 1H, acetal-H), 4.74 (s, 2H, benzyl CH_2), 4.64-4.71 (m, 3H, 1-H, 3-H, 4-H), 3.85-3.98 (m, 1H, 6-H), 3.63-3.82 (m, 3H, 2-H, 5-H, 6'-H), 3.40 (s, 3H, MeO); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 137.5 (phenyl C), 128.5, 128.0 (phenyl CH), 107.8 (acetal C), 100.8 (C-1), 99.7 (CCl_3), 78.5, 76.7, 73.0, 69.2 (C-2,3,4,5), 73.6 (benzyl CH_2), 62.9 (C-6), 55.5 (MeO).

Anal. Calcd for $C_{16}H_{19}Cl_3O_6$ (413.7): C, 46.46; H, 4.63. Found: C, 46.32; H, 4.59.

Methyl 2-*O*-benzyl-6-*O*-tosyl-3,4-*O*-(2,2,2-trichloroethylidene)-α-D-altropyranoside (10). A soln of **9** (0.41 g, 1.0 mmol) and *p*-tosyl chloride (0.24 g, 1.25 mmol) in anhyd pyridine (10 mL) was stirred for 17 h at rt (TLC control). The mixture was concentrated under reduced pressure and the residue was dissolved in diethyl ether (10 mL). Subsequently, the ethereal phase was washed with 3% aq $NaHSO_4$ soln (5 mL) and water (twice 5 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (heptane/EtOAc 6:1): $R_f = 0.22$. Yield of **10**: 0.53 g (94%), mp 85-87 °C (i-PrOH/ether v/v = 3/1); $[\alpha]_D^{22}$ +43.5 (*c* 1.15, chloroform); ^{1}H NMR (250.1 MHz, $CDCl_3$): δ 7.76-7.84 (m, 2H, tosyl CH), 7.24-7.39 (m, 7H, 2x tosyl CH, 5x

phenyl CH), 5.29 (s, 1H, acetal-H), 4.69 (s, 2H, benzyl CH_2), 4.62 (dd, 1H, $^3J_{2/3} \approx 6.0$, $^3J_{3/4} \approx 6.8$, 3-H), 4.60 (d, 1H, $^3J_{1/2} \approx 3.7$, 1-H), 4.42 (dd, 1H, $^3J_{4/5} \approx 9.3$, 4-H), 4.32 (dd, 1H, $^3J_{5/6} \approx 2.6$, $^2J_{6/6'} \approx 11.0$, 6-H), 4.14 (dd, $^3J_{5/6'} \approx 6.6$, 6'-H), 3.84 (ddd, 1H, 5-H), 3.62 (dd, 1H, 2-H), 3.34 (s, 3H, MeO), 2.43 (s, 3H, tosyl CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 145.0 (tosyl C-SO_3), 137.3 (phenyl C), 132.3 (tosyl C-CH_3), 129.9, 128.5, 128.0, 127.9 (tosyl CH, phenyl CH), 107.7 (acetal C), 100.6 (C-1), 99.5 (CCl_3), 78.5, 76.6, 73.4, 66.8 (C-2,3,4,5), 73.0 (benzyl CH_2), 69.1 (C-6), 55.4 (MeO), 21.7 (tosyl CH_3).

Anal. Calcd for $C_{23}H_{25}Cl_3O_8S$ (567.9): C, 48.65; H, 4.44; S, 5.65. Found: C, 48.61; H, 4.37; S, 5.73.

Methyl 6-azido-2-*O*-benzyl-6-deoxy-3,4-*O*-(2,2,2-trichloroethylidene)-α-D-altropyranoside (11). A soln of **10** (2.84 g, 5.0 mmol) and NaN_3 (0.36 g, 5.50 mmol) in dried DMF (10 mL) was stirred for 1 h at 120 °C. The mixture was worked-up as describe for the azide **4** yielding 1.93 g (88%) of the syrupy product **11** (heptane/EtOAc 9:1; R_f = 0.29), $[\alpha]_D^{22}$ +10.6 (*c* 1.33, chloroform); ^1H NMR (250.1 MHz, $CDCl_3$): δ 7.25-7.41 (m, 5H, phenyl CH), 5.36 (s, 1H, acetal-H), 4.74 (s, 2H, benzyl CH_2), 4.68 (d, 1H, $^3J_{1/2} \approx 3.7$, 1-H), 4.68 (dd, 1H, $^3J_{2/3} \approx 6.1$, $^3J_{3/4} \approx 6.9$, 3-H), 4.51 (dd, 1H, $^3J_{4/5} \approx 9.2$, 4-H), 3.83 (ddd, 1H, $^3J_{5/6} \approx 3.2$, $^3J_{5/6} \approx 6.9$, 5-H), 3.68 (dd, 1H, 2-H), 3.53 (dd, 1H, $^2J_{6/6'} \approx 13.3$, 6-H), 3.45 (dd, 6'-H), 3.45 (s, 3H, MeO); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 137.4 (phenyl C), 128.5, 128.0 (phenyl CH), 107.8 (acetal C), 100.9 (C-1), 99.6 (CCl_3), 78.6, 76.7, 74.8, 68.6 (C-2,3,4,5), 73.1 (benzyl CH_2), 55.7 (MeO), 52.4 (C-6).

Anal. Calcd for $C_{16}H_{18}Cl_3N_3O_5$ (438.7): C, 43.81; H, 4.14; N, 9.58. Found: C, 44.21; H, 4.15; N, 9.48.

Methyl 4-*O*-cyclohexylcarbamoyl-6-deoxy-6-iodo-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranoside (13). To a soln of methyl 4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranoside (**12**)[26] (2.24 g, 5.0 mmol) and Ph_3P (1.97 g, 7.50 mmol) in 15 mL dried toluene, imidazole (1.02 g, 15.0 mmol) and iodine (1.90 g, 7.50 mmol) were added and the mixture was refluxed with vigorous stirring for about 25 min. (TLC control). The mixture was worked-up as described for compd **3** (R_f = 0.46; heptane-EtOAc, 6:1). Yield: 2.54 g (91%), mp 189-190 °C (MeOH), $[\alpha]_D^{23}$ -22.5 (*c* 1.08, chloroform); ^1H NMR (250.1 MHz, $CDCl_3$): δ 5.46 (s, 1H, acetal-H), 5.26 (dd, 1H, $^3J_{3/4} \approx 2.6$, $^3J_{4/5} \approx 1.7$, 4-H), 4.77 (d, 1H, $^3J_{NH,CH} \approx 8.1$, carbamoyl-NH), 4.66 (dd, 1H, $^3J_{2/3} \approx 4.8$, 3-H),

4.38 (d, 1H, $^3J_{1/2} \approx 6.8$ 1-H), 4.34 (dd, 1H, 2-H) 3.95 (ddd, 1H, $^3J_{5/6} \approx 5.1$, $^3J_{5/6'} \approx 8.8$, 5-H), 3.62 (s, 3H, MeO), 3.37-3.55 (m, 1H, cyclohexyl CH), 3.26 (dd, 1H, $^2J_{6/6'} \approx 10.6$, 6-H), 3.20 (dd, 1H, 6'-H), 1.82-1.98 (m, 2H, cyclohexyl CH_2), 1.50-1.76 (m, 3H, cyclohexyl CH_2), 1.02-1.44 (m, 2H, cyclohexyl CH_2); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 153.8 (carbamoyl CO), 106.7 (acetal C), 101.8 (C-1), 98.9 (CCl_3), 77.1, 76.6, 73.5, 67.1 (C-2,3,4,5), 57.2 (MeO), 50.2 (cyclohexyl CH), 33.1, 25.4, 24.6 (cyclohexyl CH_2), 0.8 (C-6).

Anal. Calcd for $C_{16}H_{23}Cl_3INO_6$ (558.6): C, 34.40; H, 4.15; N, 2.51. Found: C, 34.57; H, 4.34; N, 2.54.

Methyl 6-azido-4-*O*-cyclohexylcarbamoyl-6-deoxy-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranoside (14). A soln of **13** (2.79 g, 5.0 mmol) and NaN_3 (0.36 g, 5.50 mmol) in dried DMF (10 mL) was stirred for 3 h at 120 °C. Subsequently, the mixture was cooled down, poured on 10 g of ice and extracted with diethyl ether (3 x 10 mL). The combined organic phases were dried ($MgSO_4$), concentrated under reduced pressure and the residue was purified by column chromatography (heptane/EtOAc 10:1, R_f = 0.30) yielding 2.13 g (90%) of the azide **14**, mp 199-201 °C (i-PrOH); $[\alpha]_D^{22}$ -74.2 (*c* 1.02, chloroform); ^1H NMR (250.1 MHz, $CDCl_3$): δ 5.47 (s, 1H, acetal-H), 5.14 (dd, 1H, $^3J_{3/4} \approx 2.5$, $^3J_{4/5} \approx 1.5$, 4-H), 4.77 (d, 1H, $^3J_{NH/CH} \approx 7.7$, carbamoyl-NH), 4.66 (dd, 1H, $^3J_{2/3} \approx 4.7$, 3-H), 4.41 (d, 1H, $^3J_{1/2} \approx 6.7$, 1-H), 4.36 (dd, 1H, 2-H), 3.97 (ddd, 1H, $^3J_{5/6} \approx 8.9$, $^3J_{5/6'} \approx 3.4$, 5-H), 3.61 (s, 3H, MeO), 3.56-3.37 (m, 1H, cyclohexyl CH), 3.53 (dd, 1H, $^2J_{6/6'} \approx 13.0$, 6-H), 3.20 (dd, 1H, 6'-H), 1.84-2.00 (m, 2H, cyclohexyl CH_2), 1.52-1.78 (m, 3H, cyclohexyl CH_2), 1.04-1.44 (m, 5H, cyclohexyl CH_2); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 153.7 (carbamoyl CO), 106.8 (acetal C), 101.7 (C-1), 98.9 (CCl_3), 76.8, 76.7, 72.7, 66.7 (C-2,3,4,5), 57.5 (MeO), 50.7 (C-6), 50.3 (cyclohexyl CH), 33.1, 25.4, 24.6 (cyclohexyl CH_2).

Anal. Calcd for $C_{16}H_{23}Cl_3N_4O_6$ (473.7): C, 40.57; H, 4.89; N, 11.83. Found: C, 40.62; H, 4.93; N, 11.68.

Methyl 4-*O*-cyclohexylcarbamoyl-6-deoxy-2,3-*O*-ethylidene-β-D-gulopyranoside (15). To a soln of **13** (0.56 g, 1.0 mmol) in toluene (10 mL) Bu_3SnH (1.4 g, 1.25 mL, 4.75 mmol) and AIBN (10 mg, 0.6 mmol) was added at 75 °C with stirring (argon atmosphere). After about 3.5 h the reaction was finished (TLC control), the mixture was shaken with 10% aq KF soln (10 mL) for 45 min and the Bu_3SnF precipitate was removed by filtration. The organic phase was washed with 3% aq $NaHSO_4$ soln (5 mL) and water (twice

5 mL), then dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (toluene/EtOAc 15:1, $R_f = 0.17$) yielding 0.33 g (100%) of **15**, mp 167-168 °C (i-PrOH); $[\alpha]_D^{23}$ -86.9 (*c* 1.12, chloroform); ^{1}H NMR (250.1 MHz, $CDCl_3$): δ 5.45 (q, 1H, $^3J_{\text{acetal-H/ethylidene-CH3}} \approx 4.9$, acetal-H), 4.95 (dd, 1H, $^3J_{3/4} \approx 2.5$, $^3J_{4/5} \approx 1.4$, 4-H), 4.79 (d, 1H, $^3J_{NH/CH} \approx 8.0$, carbamoyl-NH), 4.32 (d, 1H, $^3J_{1/2} \approx 7.2$, 1-H), 4.13 (dd, 1H, $^3J_{2/3} \approx 5.0$, 3-H), 3.99 (dd, 1H, 2-H), 3.89 (dq, 1H, $^3J_{5/6'C} \approx 6.6$, 5-H), 3.52 (s, 3H, MeO), 3.37-3.58 (m, 1H, cyclohexyl CH), 1.82-1.99 (m, 2H, cyclohexyl CH_2), 1.49-1.76 (m, 3H, cyclohexyl CH_2), 1.31 (d, 3H, ethylidene CH_3), 1.24 (d, 3H, 6-H), 1.01-1.44 (m, 5H, cyclohexyl CH_2); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 154.7 (carbamoyl CO), 102.2 (acetal C), 101.2 (C-1), 75.0, 74.5, 69.6, 68.4 (C-2,3,4,5), 56.9 (MeO), 50.0 (cyclohexyl CH), 33.2, 25.4, 24.6 (cyclohexyl CH_2), 21.5 (ethylidene CH_3), 15.6 (C-6).

Anal. Calcd for $C_{16}H_{27}NO_6$ (329.4): C, 58.53; H, 8.26; N, 4.25. Found: C, 58.42; H, 8.11; N, 4.21.

Methyl 6-deoxy-2,3-*O*-ethylidene-β-D-gulopyranoside (16). Compd **15** (0.66 g, 2.0 mmol) dissolved in 1% methanolic NaOMe (15 mL) was decarbamoylated by heating the soln under reflux for 35 h. Subsequently, the reaction mixture was cooled and neutralised with an acidic ion exchanger resin (Amberlite IR-120). After evaporation of the solvent under reduced pressure and column chromatographic purification (toluene/EtOAc 5:1, $R_f = 0.20$) the compd **16** was obtained in a yield of 0.29 g (71%), mp 86-88 °C (i-PrOH); $[\alpha]_D^{24}$ -100.9 (*c* 1.11, chloroform); ^{1}H NMR (250.1 MHz, $CDCl_3$): δ 5.46 (q, 1H, $^3J_{\text{acetal-H/ethylidene-CH3}} \approx 5.0$, acetal-H), 4.47 (d, 1H, $^3J_{1/2} \approx 5.0$, 1-H), 4.32 (dd, 1H, $^3J_{2/3} \approx 5.9$, $^3J_{3/4} \approx 2.7$, 3-H), 4.13 (dd, 1H, 2-H), 3.89 (dq, 1H, $^3J_{4/5} \approx 1.8$, $^3J_{5/6'C} \approx 6.6$, 5-H), 3.62-3.74 (m, 1H, 4-H), 3.50 (s, 3H, MeO), 2.60-2.86 (m, 1H, 4-OH), 1.31 (d, 3H, ethylidene CH_3), 1.29 (d, 3H, 6-H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 102.5 (acetal C), 100.8 (C-1), 75.6, 74.0, 69.1, 69.0 (C-2,3,4,5), 56.5 (MeO), 21.2 (ethylidene CH_3), 16.6 (C-6).

Anal. Calcd for $C_9H_{16}O_5$ (204.2): C, 52.93; H, 7.90. Found: C, 53.00; H, 7.86.

Methyl 6-deoxy-2,3-*O*-ethylidene-4-*O*-tosyl-β-D-gulopyranoside (17). A soln of **16** (0.20 g, 1.0 mmol) and *p*-tosyl chloride (0.24 g, 1.25 mmol) in anhyd pyridine (10 mL) was stirred for 18 h at rt (TLC control). The mixture was worked-up as described for tosyl derivative **10** (toluene/EtOAc 15:1, $R_f = 0.34$). Yield of tosylate **17**: 0.32 g (89%), mp 117-119 °C (i-PrOH); $[\alpha]_D^{23}$ -78.5 (*c* 1.01, chloroform); ^{1}H NMR (250.1 MHz, $CDCl_3$): δ

7.75-7.84 (m, 2H, tosyl CH), 7.29-7.38 (m, 2H, tosyl CH), 5.39 (q, 1H, $^3J_{acetal\text{-}H/ethylidene\text{-}CH3} \approx 5.0$, acetal-H), 4.64 (dd, 1H, $^3J_{3/4} \approx 2.6$, $^3J_{4/5} \approx 1.6$, 4-H), 4.28 (d, 1H, $^3J_{1/2} \approx 7.1$, 1-H), 4.20 (dd, 1H, $^3J_{2/3} \approx 5.1$, 3-H), 4.00 (dd, 1H, 2-H), 3.85 (dq, 1H, $^3J_{5/6'C} \approx 6.6$, 5-H), 3.48 (s, 3H, MeO), 2.44 (s, 3H, tosyl CH_3), 1.28 (d, 3H, ethylidene CH_3), 1.10 (d, 3H, 6-H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 145.2 (tosyl C-SO_3), 133.3 (tosyl C-CH_3), 129.9, 128.0 (tosyl CH), 102.3 (acetal C), 100.8 (C-1), 76.4, 74.6, 74.2, 68.0 (C-2,3,4,5), 56.7 (MeO), 21.4 (ethylidene CH_3), 15.8 (C-6).

Anal. Calcd for $C_{16}H_{22}O_7S$ (358.4): C, 53.62; H, 6.19; S, 8.95. Found: C, 53.62; H, 6.24; S, 9.00.

Methyl 6-deoxy-4-*O*-tosyl-β-D-gulopyranoside (18). A soln of **17** (0.36 g, 1.00 mmol) in 60% aq trifluoroacetic acid (10 mL) was stirred for about 5 h at 50 °C (TLC control). After addition of water (10 mL) the mixture was concentrated under reduced pressure. To remove water and TFA completely the residue was dissolved in 5 mL of toluene and the soln was concentrated under reduced pressure. This procedure was twice repeated followed by a column chromatographic purification of the crude product (toluene/EtOAc 1:1, $R_f = 0.27$) yielding 0.31 g (92%) of the syrupy compd **18**; $[\alpha]_D^{22}$ -65.4 (*c* 1.68, chloroform); ^1H NMR (250.1 MHz, $CDCl_3$): δ 7.75-7.84 (m, 2H, tosyl CH), 7.29-7.38 (m, 2H, tosyl CH), 4.46 (d, 1H, $^3J_{1/2} \approx 8.1$, 1-H), 4.44 (dd, 1H, $^3J_{3/4} \approx 3.6$, $^3J_{4/5} \approx 1.2$, 4-H), 4.18 (dd, 1H, $^3J_{2/3} \approx 3.3$, 3-H), 4.08 (dq, 1H, $^3J_{5/6'C} \approx 6.6$, 5-H), 3.61 (dd, 1H, 2-H), 3.49 (s, 3H, MeO), 2.43 (s, 3H, tosyl CH_3), 2.33-2.68 (m, 2H, 2-OH, 3-OH), 1.05 (d, 3H, 6-H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 145.3 (tosyl C-SO_3), 133.2 (tosyl C-CH_3), 130.0, 128.0 (tosyl CH), 101.2 (C-1), 79.3, 69.4, 68.4, 67.7 (C-2,3,4,5), 56.9 (MeO), 21.7 (tosyl CH_3), 15.8 (C-6).

Anal. Calcd for $C_{14}H_{20}O_7S$ (332.3): C, 50.59; H, 6.07; S, 9.65. Found: C, 50.13; H, 6.08; S, 9.31.

Methyl 2,4-di-*O*-acetyl-3-azido-3,6-dideoxy-β-D-glucopyranoside (19) and **methyl 2,3-di-*O*-acetyl-4-azido-4,6-dideoxy-β-D-gulopyranoside (20)**. A soln of **18** (1.66 g, 5.0 mmol) and NaN_3 (0.36 g, 5.50 mmol) in dried DMF (10 mL) was stirred for 5 h at 120 °C. The mixture was worked-up as described for the azide **4**. The crude product obtained after concentration of the organic phase was acetylated without further purification by treatment with acetic anhydride/pyr (10 mL, 1/1 v/v) for about 2 h at rt (TLC con-

trol). After evaporation of the solvents under reduced pressure, the oily residue was dissolved in diethyl ether (20 mL), washed with 3% aq $NaHSO_4$ soln (twice 5 mL) and water (twice 5 mL), and dried (Na_2SO_4). Ether was evaporated and the azides **19** and the **20** were isolated by chromatographic fractionation of the residue (toluene/EtOAc 9:1) yielding 0.63 g (44%) of the product **19** ($R_f = 0.37$); (mp 118-119 °C (ether/acetone); $[\alpha]_D^{23}$ –20.4 (*c* 1.18, chloroform) and 0.65 g (45%) of the syrupy product **20** ($R_f = 0.33$); $[\alpha]_D^{24}$ –43.00 (*c* 1.06, chloroform).

19: ^{1}H NMR (250.1 MHz, $CDCl_3$): δ 4.85 (dd, 1H, $^3J_{1/2} \approx 7.9$, $^3J_{2/3} \approx 10.2$, 2-H), 4.71 (dd, 1H, $^3J_{3/4} \approx 10.2$, $^3J_{4/5} \approx 9.6$, 4-H), 4.33 (d, 1H, 1-H), 3.55 (dd, 1H, 3-H), 3.51 (dq, 1H, $^3J_{5/6} \approx 6.2$, 5-H), 3.46 (s, 3H, MeO), 2.11 (s, 3H, acetyl CH_3), 2.11 (s, 3H, acetyl CH_3), 1.21 (d, 3H, 6-H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 169.1, 168.4 (acetyl CO), 101.5 (C-1), 73.4, 71.4, 70.9, 64.4 (C-2,3,4,5), 56.6 (MeO), 20.7, 20.7 (acetyl CH_3), 17.2 (C-6).

Anal. Calcd for $C_{11}H_{17}N_3O_6$ (287.3): C, 45.99; H, 5.96; N, 14.63. Found: C, 45.87; H, 6.09; N, 14.38.

20: ^{1}H NMR (250.1 MHz, $CDCl_3$): δ 5.43 (dd, 1H, $^3J_{2/3} \approx 3.4$, $^3J_{3/4} \approx 4.6$, 3-H), 4.97 (dd, 1H, $^3J_{1/2} \approx 7.5$, 2-H), 4.61 (d, 1H, 1-H), 4.11 (dq, 1H, $^3J_{4/5} \approx 2.3$, $^3J_{5/6'} \approx 6.6$, 5-H), 3.54 (dd, 1H, 4-H), 3.46 (s, 3H, MeO), 2.11 (s, 3H, acetyl CH_3), 2.03 (s, 3H, acetyl CH_3), 1.34 (d, 3H, 6-H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 169.5, 169.4 (acetyl CO), 99.3 (C-1), 69.1, 69.0, 67.9, 62.3 (C-2,3,4,5), 56.3 (MeO), 20.8, 20.7 (acetyl CH_3), 16.7 (C-6).

Anal. Calcd for $C_{11}H_{17}N_3O_6$ (287.3): C, 45.99; H, 5.96; N, 14.63. Found: C, 46.20, H, 5.95, N, 14.55.

Methyl 6-*O*-cyclohexylcarbamoyl-4-*O*-tosyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranoside (22). A soln of **21** (0.45 g, 1.0 mmol) and *p*-tosyl chloride (0.24 g, 1.25 mmol) in anhyd pyridine (10 mL) was stirred for 24 h at rt (TLC control). The mixture was worked-up as described for tosyl derivative **10** (heptane/EtOAc 6:1, $R_f = 0.21$) yielding 0.55 g (92%) of tosylate **22**, mp 121-123 °C (i-PrOH), $[\alpha]_D^{25}$ -56.0 (*c* 0.91, chloroform); ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 7.78-7.85 (m, 2H, tosyl CH), 7.31-7.39 (m, 2H, tosyl CH), 5.38 (s, 1H, acetal-H), 4.91 (dd, 1H, $^3J_{3/4} \approx 2.6$, $^3J_{4/5} \approx 1.8$, 4-H), 4.67 (s, 3-H), 4.55 (d, 1H, $^3J_{NH/CH} \approx 7.6$, carbamoyl-NH), 4.30-4.36 (m, 2H, 1-H,2), 4.24 (dd, $^3J_{5/6} \approx 6.0$, $^2J_{6/6'} \approx 10.5$, 6-H), 4.01 (ddd, 1H, $^3J_{5/6} \approx 7.0$, 5-H), 3.93 (dd, 1H, 6'-H), 3.50 (s, 3H, MeO), 3.36-3.50 (m, 1H, cyclohexyl CH) , 2.44 (s, 3H, tosyl CH_3), 1.85-1.99 (m, 2H,

cyclohexyl CH_2), 1.53-1.78 (m, 3H, cyclohexyl CH_2), 1.02-1.44 (m, 5H, cyclohexyl CH_2); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 154.7 (carbamoyl CO), 145.6 (tosyl C-SO_3), 133.1 (tosyl C-CH_3), 130.1, 127.9 (tosyl CH), 106.7 (acetal C), 101.0 (C-1), 98.7 (CCl_3), 76.5, 76.0, 72.4, 70.0 (C-2,3,4,5), 61.4 (C-6), 56.9 (MeO), 50.0 (cyclohexyl CH), 33.3, 25.4, 24.7 (cyclohexyl CH_2), 21.7 (tosyl CH_3).

Anal. Calcd for $C_{23}H_{30}Cl_3NO_9S$ (602.9): C, 45.82; H, 5.01; N, 2.32; S 5.32. Found: C, 45.75; H, 4.97; N, 2.39; S, 5.36.

Methyl 6-*O*-cyclohexylcarbamoyl-4-deoxy-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-*erythro*-hex-4-enopyranoside (23). A soln of **22** (3.0 g, 5.0 mmol) and NaN_3 (0.36 g, 5.50 mmol) in dried DMF (10 mL) was stirred for 18 h at 120 °C. Then, the mixture was worked-up as described for compd **4** (heptane/EtOAc 6:1, R_f = 0.35) yielding 2.11 g (98%) of the syrupy product **23**, $[\alpha]_D^{24}$ +48.2 (*c* 1.36, chloroform); ^1H NMR (250.1 MHz, C_6D_6): δ 5.45 (s, 1H, acetal-H), 4.88 (dd, 1H, $^4J_{2/4} \approx 1.0$, $^3J_{3/4} \approx 3.4$, 4-H), 4.76 (dd, 1H, $^3J_{2/3} \approx 6.1$, 3-H), 4.60 (d, 1H, $^3J_{1/2} \approx 3.3$, 1-H), 4.48-4.57 (m, 2H, 6-H), 4.27 (ddd, 1H, 2-H), 4.24 (d, 1H, $^3J_{NH/CH} \approx 7.7$ carbamoyl-NH), 3.37-3.65 (m, 1H, cyclohexyl CH), 3.06 (s, 3H, MeO), 1.60-1.84 (m, 2H, cyclohexyl CH_2), 1.20-1.52 (m, 3H, cyclohexyl CH_2), 0.66-1.17 (m, 5H, cyclohexyl CH_2); ^{13}C NMR (75.5 MHz, C_6D_6): δ 154.8 (carbamoyl CO), 150.2 (C-5), 107.1 (acetal C), 100.4 (CCl_3), 98.5 (C-1), 97.6 (C-4), 74.7, 71.4 (C-2,3), 62.9 (C-6), 56.1 (MeO), 50.1 (cyclohexyl CH), 33.3, 25.6, 24.9 (cyclohexyl CH_2).

Anal. Calcd for $C_{16}H_{22}Cl_3NO_6$ (430.7): C, 44.62; H, 5.15; N, 3.25. Found: C, 45.28; H, 5.08; N, 3.52.

Methyl 6-*O*-cyclohexylcarbamoyl-2,3-*O*-ethylidene-4-*O*-tosyl-β-D-gulopyranoside (24). Compd **22** (0.60 g, 1.0 mmol), was reduced to **24** by treatment with Bu_3SnH (1.40 mL, 5.25 mmol) and AIBN (10 mg, 0.6 mmol) in toluene (10 mL) for 2.5 h as described for **15** (eluent: toluene/EtOAc 7:1, R_f = 0.22). Yield of the product **24**, 0.46 g (92%), mp 161-162 °C (i-PrOH); $[\alpha]_D^{22}$ -77.3 (*c* 1.06, chloroform); ^1H NMR (250.1 MHz, $CDCl_3$): δ 7.76-7.84 (m, 2H, tosyl CH), 7.29-7.39 (m, 2H, tosyl CH), 5.39 (q, 1H, $^3J_{acetal\text{-}H/ethylidene\text{-}CH3} \approx 4.9$, acetal-H), 4.85 (dd, 1H, $^3J_{3/4} \approx 2.5$, $^3J_{4/5} \approx 1.8$, 4-H), 4.51 (d, 1H, $^3J_{NH/CH} \approx 8.1$, carbamoyl-NH), 4.31 (d, 1H, $^3J_{1/2} \approx 7.0$, 1-H), 4.30 (dd, 1H, $^3J_{2/3} \approx 5.1$, 3-H), 4.19 (dd, 1H, $^3J_{5/6} \approx 6.2$, $^2J_{6/6'} \approx 10.9$, 6-H), 4.04 (dd, 1H, 2-H), 3.95 (ddd, 1H, $^3J_{5/6'} \approx 6.7$,

5-H), 3.82 (dd, 1H, 6'-H), 3.48 (s, 3H, MeO), 3.31-3.52 (m, 1H, cyclohexyl CH), 2.44 (s, 3H, tosyl CH_3), 1.82-1.97 (m, 2H, cyclohexyl CH_2), 1.51-1.76 (m, 3H, cyclohexyl CH_2), 1.29 (d, 3H, ethylidene CH_3), 1.00-1.42 (m, 5H, cyclohexyl CH_2); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 154.7 (carbamoyl CO), 145.4 (tosyl C-SO_3), 133.1 (tosyl C-CH_3), 130.0, 128.0 (tosyl CH), 102.5 (acetal C), 100.9 (C-1), 74.8, 73.9, 73.2, 70.0 (C-2,3,4,5), 61.5 (C-6), 57.0 (MeO), 49.9 (cyclohexyl CH), 33.4, 25.4, 24.8 (cyclohexyl CH_2), 21.7, 21.4 (tosyl CH_3, ethylidene CH_3).

Anal. Calcd for $C_{23}H_{33}NO_9S$ (499.6): C, 55.30; H, 6.66; N, 2.80; S 6.42. Found: C, 55.32; H, 6.78; N, 2.91; S, 6.31.

Methyl 2,4-di-*O*-acetyl-3-azido-6-*O*-cyclohexylcarbamoyl-3-deoxy-β-D-gluco-pyranoside (25) and **methyl 2,3-di-*O*-acetyl-4-azido-6-*O*-cyclohexylcarbamoyl-4-deoxy-β-D-gulopyranoside (26)**. Starting with methyl 6-*O*-cyclohexylcarbamoyl-2,3-*O*-ethylidene-4-*O*-tosyl-β-D-gulopyranoside (**24**), compounds **25** and **26** were synthesised in 3 steps without chromatographic purification of the intermediates. First of all, compd **24** (2.50 g, 5.0 mmol) dissolved in 60% aq TFA (30 mL) was deacetalated as described for **18** (heating at 50 °C for 5 h). Secondly, the syrupy crude product obtained was dissolved in anhyd DMF (10 mL), sodium azide (0.36 g, 5.50 mmol) was added and the mixture was heated at 120 °C for about 5 h (TLC control). The work-up procedure was analogous as described for **4** with solvent evaporation under medium vacuum. Thirdly, the mixture of azides obtained above was dissolved in acetic anhydride/pyr (10 mL, 1/1 v/v) and the soln was stirred at rt for about 2 h (TLC control). After evaporation of the solvents under reduced pressure the oily residue was dissolved in diethyl ether (20 mL), washed with 3% aq $NaHSO_4$ soln (twice 5 mL) and water (twice 5 mL), and dried (Na_2SO_4). Ether was evaporated and the azides **25** and **26** were isolated by chromatographic fractionation of the residue (toluene/EtOAc 9 : 1, **25**: R_f = 0.13; **26**: R_f = 0.16). The *gluco*-configured azide **25** was obtained in a yield of 0.67 g (39%) related to **24**, mp 125-127 °C (ether); $[\alpha]_D^{22}$ –10.1 (*c* 0.68, chloroform); the syrupy *gulo*-derivative **26** was isolated in a yield of 0.72 g (42%), $[\alpha]_D^{22}$ –55.3 (*c* 1.14, chloroform).

25: ^1H NMR (250.1 MHz, benzene-d_6): δ 5.25 (dd, 1H, $^3J_{1/2} \approx 7.9$, $^3J_{2/3} \approx 10.4$, 2-H), 5.20 (dd, 1H, $^3J_{3/4} \approx 10.0$, $^3J_{4/5} \approx 9.9$, 4-H), 4.44 (d, 1H, $^3J_{NH/CH} \approx 7.8$, carbamoyl-NH), 4.34 (dd, 1H, $^3J_{5/6} \approx 4.3$, $^2J_{6/6'} \approx 12.1$, 6-H), 4.22 (dd, 1H, $^3J_{5/6'} \approx 2.4$, 6'-H), 4.10 (d, 1H, 1-H), 3.43-

3.63 (m, 1H, cyclohexyl CH), 3.28 (dd, 1H, 3-H), 2.28 (ddd, 1H, 5-H), 3.24 (s, 3H, MeO), 1.77 (s, 3H, acetyl CH_3), 1.73 (s, 3H, acetyl CH_3), 1.64-1.93 (m, 2H, cyclohexyl CH_2), 1.15-1.55 (m, 3H, cyclohexyl CH_2), 0.66-1.15 (m, 5H, cyclohexyl CH_2); ^{13}C NMR (62.9 MHz, benzene-d_6): δ 168.8, 168.5 (acetyl CO), 155.2 (carbamoyl CO), 101.9 (C-1), 73.6, 64.9 (C-3,5), 71.0 (C-2), 68.3 (C-4), 62.1 (C-6), 55.9 (MeO), 50.1 (cyclohexyl CH), 33.2, 25.7, 25.0 (cyclohexyl CH_2), 20.3, 20.2 (acetyl CH_3).

Anal. Calcd for $C_{18}H_{28}N_4O_8$ (428.44): C, 50.46; H, 6.59; N, 13.08. Found: C, 50.63; H, 6.33; N, 12.81.

26: ^1H NMR (250.1 MHz, benzene-d_6): δ 5.72 (dd, 1H, $^3J_{2/3} \approx 3.3$, $^3J_{3/4} \approx 4.5$, 3-H), 5.49 (dd, 1H, $^3J_{1/2} \approx 7.6$, 2-H), 4.70 (d, 1H, 1-H), 4.47 (dd, 1H, $^3J_{5/6} \approx 6.8$, $^2J_{6/6'} \approx 11.4$, 6-H), 4.33 (dd, 1H, $^3J_{5/6'} \approx 5.9$, 6'-H), 4.16-4.28 (m, 2H, 5-H, carbamoyl-NH), 3.44-3.63 (m, 1H, cyclohexyl CH), 3.41 (dd, 1H, $^3J_{4/5} \approx 2.3$, 4-H), 3.27 (s, 3H, MeO), 1.67 (s, 3H, acetyl CH_3), 1.64 (s, 3H, acetyl CH_3), 1.60-1.84 (m, 2H, cyclohexyl CH_2), 1.20-1.49 (m, 3H, cyclohexyl CH_2), 0.65-1.14 (m, 5H, cyclohexyl CH_2); ^{13}C NMR (75.5 MHz, benzene-d_6): δ 169.0, 168.8 (acetyl CO), 155.0 (carbamoyl CO), 99.8 (C-1), 71.5, 69.2, 68.5, 60.0 (C-2,3,4,5), 63.3 (C-6), 55.8 (MeO), 50.1 (cyclohexyl CH), 33.3, 25.6, 25.0 (cyclohexyl CH_2), 20.2, 20.2 (acetyl CH_3).

Anal. Calcd for $C_{18}H_{28}N_4O_8$ (428.44): C, 50.46; H, 6.59; N, 13.08. Found: C, 50.66, H, 6.45, N, 12.74.

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