Epimerisation of Carbohydrates and Cyclitols, 17.[1] Synthesis of Glycosyl Azides and *N*-Acetyl Glycosyl Amines of Rare Monosaccharides

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Dedicated to Prof. Dr. Klaus Peseke on the occasion of his 60th birthday.

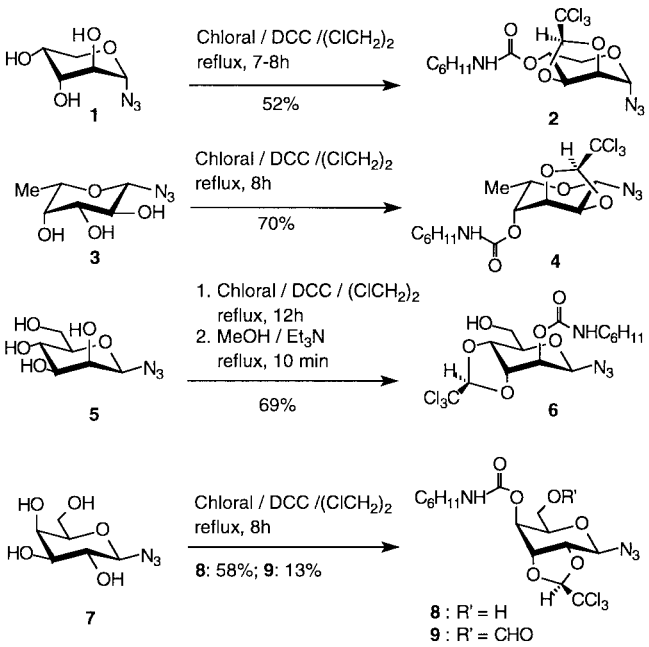
Abstract: The glycosyl azides **1** (D-*arabino*), **3** (L-*fuco*), **5** (D-*manno*), and **7** (D-*galacto*) were epimerised in a one-pot procedure by heating with chloral/DCC/1,2-dichloroethane in good yields. The respective products, epimerised at the C-3 atom , have D-*lyxo* (**2**), L-*gulo* (**4**), D-*altro* (**6**), and D-*gulo* (**8**, **9**) configuration. Compound **8**, directly generated or obtained by deformylation of its 6-*O*-formyl derivative **9**, was used as the key intermediate for further syntheses. Besides the acetylation of **8** to **10,** and decarbamoylation to the 4,6-dihydroxy derivative **11**, the latter **11** was acetylated to **12** and benzylated to **13**. Moreover, the azide function of **8** was converted into an amino group using tributyltin hydride/ AIBN or Staudinger conditions. The amino derivatives were isolated in the form of their *N*-acetyl derivatives **14** and **15**, respectively. Finally, the dichloroethylidene (**14**) and the trichloroethylidene (**15**) groups were hydrodechlorinated forming the same ethylidene derivative **16**. Crystal structures are given for the gulopyranoses **4** and **12**.

Key words: carbohydrates, azides, acetals, amides, stereoselectivity

Glycosyl azides are useful precursors and building blocks in carbohydrate chemistry. Thus, glycosylamines, valuable intermediates for the synthesis of glycoconjugates, are accessible by catalytic hydrogenation of glycosyl azides[2] or by reductive conversion with phosphines (Staudinger reaction),[3,4] thiols[4] or trimethyl chlorosilane[5] in the presence of acylation reagents. A disadvantage of the latter reactions is the 1-*N*-acylation, i.e., deactivated glycosyl amines are obtained.[4,6,7] However, glycosylated phosphinimines, the key intermediates of the Staudinger reaction with glycosyl azides, were also used to synthesise other interesting products.[8] 1,3-Dipolar cycloadditions, generating nucleoside analogs or derivatives in which the heterocyclic group is placed at positions other than the anomeric position of the sugar moiety (e.g. ref.[9]), are a further possibility for using azido sugars.

In this paper we report about syntheses of glycosyl azides of rare monosaccharides using a non-conventional one-pot acetalation/epimerisation procedure which is applicable to cyclic polyols with three contiguous hydroxyl groups in a *cis-trans* sequence,[1,10-13] for the mechanism see ref.[12, 13] This method requires a carbodiimide as co-reagent. However, carbodiimides tend to undergo cycloadditions with azides at reaction conditions similar to the above-mentioned one-pot procedure.[14,15] Thus, we have to clear up whether glycosyl azides allow an epimerisation.

α-D-Arabinopyranosyl azide (**1**), β-L-fucopyranosyl azide (**3**), β-D-mannopyranosyl azide (**5**), and β-D-galactopyranosyl azide (**7**) were selected as starting materials. On refluxing the solutions of these compounds with anhydrous chloral and DCC in 1,2-dichloroethane for 7–12 hours the D-*lyxo*-, L-*gulo*-, D-*altro*-, and D-*gulo*-configurated azides **2**, **4**, **6** and **8**/**9**, respectively, were obtained in yields of 52-70% (Scheme 1). The azide function of the sugars was not attacked by DCC.[16] It is noticeable that the primary OH-group of hexoses is also formylated, caused by a haloform reaction.[12] Thus, the mannosyl azide **5** and the galactosyl azide **7** yielded mixtures of **6** and **8**, respectively, with the corresponding 6-*O*-formyl derivatives on treatment with chloral/DCC. Because a formyl group can be selectively cleaved by heating the corresponding sugar with methanolic triethylamine,[12] the crude product mixture obtained from **5** was treated with this reagent (20:1, v/v) generating the uniform product **6** (yield: 69%). In the case of **8**/**9** the two products were separated by column chromatography and then characterised.



Scheme 1

As expected, the products **2**, **4**, **6**, **8**, and **9** are mixtures of two diastereomers, because a new stereogenic centre was formed by the chloral acetalation. The ratio of *endo*-H (major) to *exo*-H form was determined by integration of the acetal-H signals in the ^{1}H NMR spectra of the mixtures, always after the column chromatographic separation: the ratio of *endo*-H/*exo*-H for compounds **2** (9:1), **6** (12:1), **8** (6:1) and **9** (6:1). In the case of the L-*gulo*-derivative **4** and of the D-*gulo*-derivatives **8** and **9** the pure *endo*-H diastereomers were obtained from the mixtures by fractionated crystallisation from diethyl ether-heptane mixtures. The compounds **2** and **6** could only be isolated as amorphous solids; attempts of recrystallisation from methanol, isopropanol, nitromethane or from diethyl ether-heptane mixtures were not successful.

The structures of the acetalated glycosyl azides **2**, **4**, **6**, **8** and **9** are supported by their ^{1}H- and ^{13}C NMR spectral data in comparison with literature data of similar compounds, e.g. ref.[10,12] Complete spectral data, only for the major diastereomers, are given in Table 3. The spectra of the five compounds show the characteristic signals of a carbamoyl and a chloral acetal function. The location of these groups is detectable by the downfield shifts of the nearest ring protons (comparison with the spectra of the starting materials **1**, **3**, **5**, and **7**, respectively). The formyl proton (**9**: δ = 7.47 ppm) and the cyclic acetal functions ($\delta \approx$ 5.1–5.5 ppm) are represented by characteristic singlets. It is noticeable that the signal of the *endo*-H form is always shifted downfield compared to the corresponding *exo*-H singlet, see also ref.[1,10-13,20]

Additionally, the structure of 4-*O*-cyclohexylcarbamoyl-6-deoxy-2,3-*O*-(2,2,2-trichloroethylidene)-β-L-gulopyranosyl azide (**4**) was confirmed by X-ray analysis Figure 1, Table 1. The Puckering parameters[17,18] (Q = 0.541 Å, θ = 159.0°, φ = 172.0°) of **4** indicate that the pyranose ring adopts a distorted ^{1}C$_4$-chair conformation. The value θ = 159.0°, reflecting the extent of torsion of a chair conformation, is only slightly nearer to an ideal ^{1}C$_4$-chair conformation (θ = 180.0°, φ = 0°) than to an E$_O$-half-boat (θ = 125.3°, φ = 180.0°) or a ^{3}H$_2$-half-chair (θ = 129.2°, φ = 150.0°) conformation. The value φ = 172° reflecting the manner of torsion, indicates that the deformation of the ^{1}C$_4$-chair tends more to an E$_O$-half-boat than to a ^{3}H$_2$-half-chair conformation.

Scheme 2 shows some selected examples of protecting group chemistry with 4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranosyl azide (**8**) using standard methods like acetylation, benzylation, and decarbamoylation.[1,12,13] Besides the direct preparation of **8** from **7** (Scheme 1), deformylation of **9** by heating with a 5% methanolic triethylamine solution also yielded this compound (Scheme 2). In the search for a crystalline D-*gulo* derivative, which allows for an X-ray analysis, compound **8** was modified. Thus, the 6-*O*-acetyl derivative **10**, the 4,6-di-*O*-acetyl derivative **12** (via **11**), and the 4,6-di-*O*-benzyl derivative **13** (via **11**) were prepared from **8**. The crystals of 4,6-di-*O*-acetyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranosyl azide (**12**) were suitable for an X-ray measurement (Figure 2).

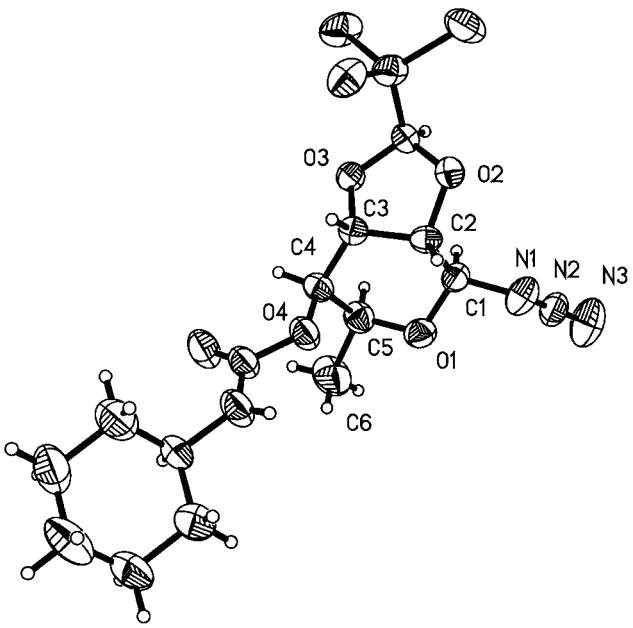


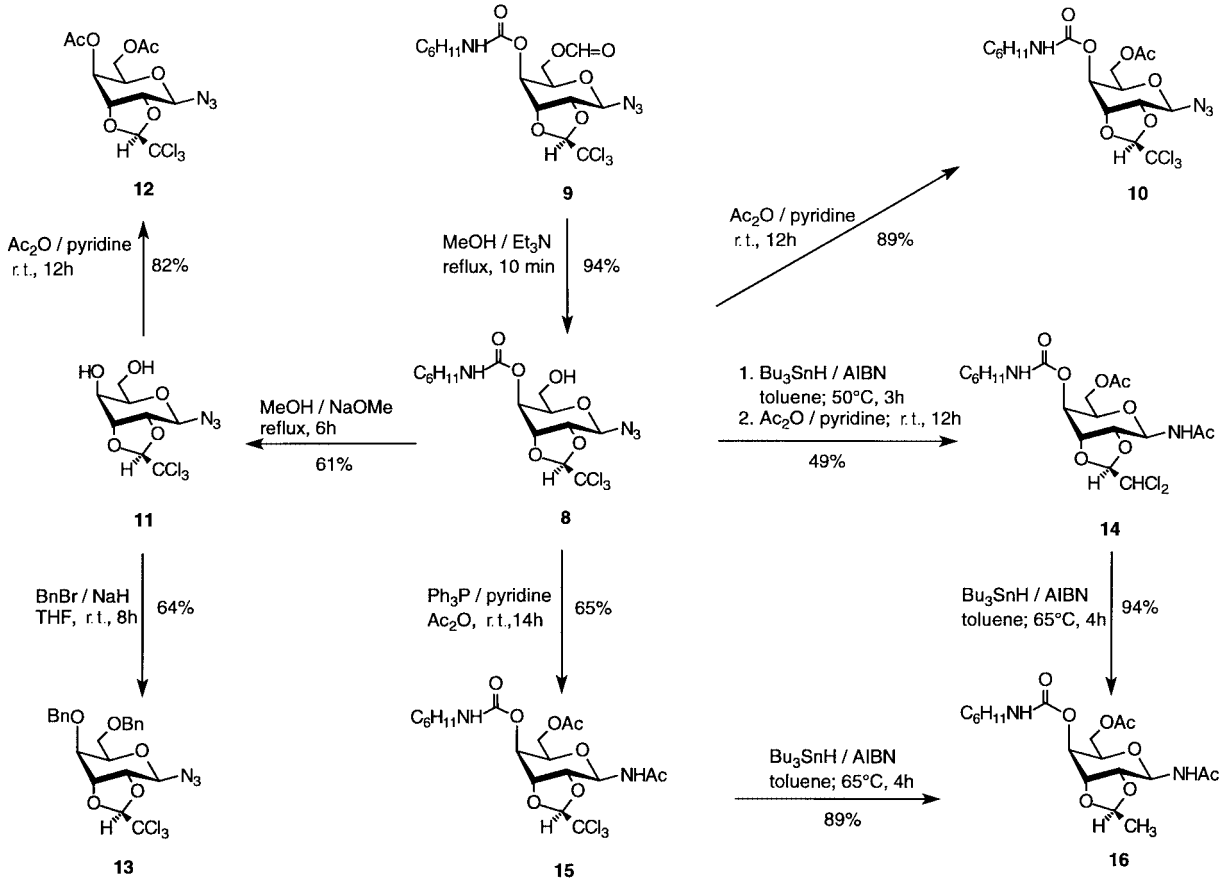
Figure 1 X-ray structure of 4-O-cyclohexylcarbamoyl-6-deoxy-2,3-O-(2,2,2-trichloroethylidene)-β-L-gulopyranosyl azide (**4**)

Like the L-*gulo* derivative **4** compound **12** does not adopt an ideal chair conformation. Based on its Puckering parameters (Q = 0.512 Å, θ = 18.1°, φ = 344°) the ring conformation fits in between a ^{4}C$_1$-chair, ^{O}*E*-half-boat, and ^{O}H$_5$-half-chair conformation. The extent of torsion reflected by θ = 18.1° indicates the structure to be nearer to a ^{4}C$_1$-chair (θ = 0.0°, φ = 0°) than to an ^{O}*E*-half-boat (θ = 54.7°, φ = 360°) or to an ^{O}H$_5$-half-chair (θ = 50.8°, φ = 330°). The kind of torsion reflected by the value for φ = 344° is unspecific, because this value is exactly between the corresponding values of the ^{O}*E*-half-boat and the ^{O}H$_5$-half-chair conformations. For selected X-ray-data see Table 1.

A comparison of the structural data of the D-*gulo* derivative **12** and the L-*gulo* derivative **4** shows that in spite of different protecting groups the two compounds adopt virtually the same conformation probably caused by the relatively stiff bicyclic segment of a trioxabicyclo[4.3.0]nonane.

Table 1 Selected X-ray Data for Compounds **4** and **12**

4 ($C_{15}H_{21}Cl_3N_4O_5$)	**12** ($C_{12}H_{14}Cl_3N_3O_7$)
Monoclinic, C2	Monoclinic, P2$_1$
a = 26.795(5) Å	a = 10.618(3) Å
b = 5.5190(11) Å	b = 6.925(2) Å
c = 15.699(3) Å	c = 13.011(4) Å
β = 116.85(3)	β = 106.770(10)
V = 2071.4(7) Å^3	V = 916.0(5) Å^3
Z = 4	Z = 2



Scheme 2

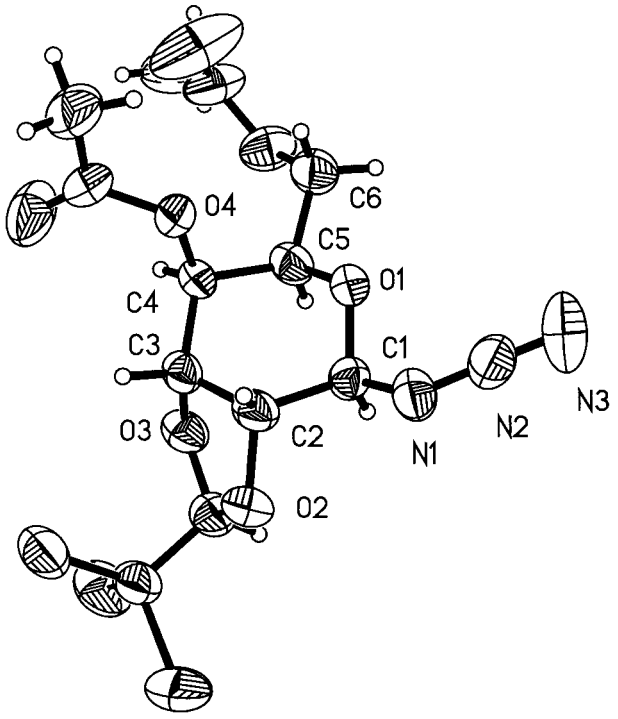


Figure 2 X-ray structure of 4,6-di-*O*-acetyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranosyl azide (**12**)

Selective conversion of the trichloroethylidene function of **8** into an ethylidene group by treatment with Bu_3SnH/AIBN, as reported in ref.,[1,13,19,20] can only be carried out after the conversion of the azido group. That is, in a later synthetic step because the reagent preferentially attacks the glycosidic azide function.[21] The resulting glycosyl amine is not stable under the reaction conditions. Only after modification of the reaction conditions, i.e., decreasing the reaction temperature to 50 °C, and reducing the reaction time to 3 hours, was a major product detectable by TLC. Because glycosyl amines are stabilised by acylation the product mixture was acetylated using acetic anhydride/pyridine. In this way the major product could be isolated as *N*-(6-*O*-acetyl-4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2-dichloroethylidene)-β-D-gulopyranosyl)acetamide (**14**) by column chromatography (yield: 49%), Scheme 2. However, *N*-acylated glycosyl amines are not very valuable *N*-nucleophiles in carbohydrate chemistry. The structure of **14** is supported by various NMR data (Table 3). Thus, the acetal-H couples with the proton of the vicinal dichloromethyl group giving doublets ($^3J \approx 3.2$). Because of the relatively small difference in their chemical shifts ($\delta_{CHCl_2} = 5.45$ ppm, $\delta_{H\text{-acetal}} = 5.57$ ppm) a significant roof-shaped effect is observed for both coupling participants. The H-1 signal of **14** ($\delta = 5.12$ ppm, $^3J_{1,2} \approx 8.7$, $^3J_{1,HAc} \approx 9.4$) is a double doublet that is signif-

Table 2 Data of the Glycosyl Azides **2**, **4**, **6**, **8**–**13** and the Glycosyl Amides **14**–**16**[a]

Product	Precursor	Yield %	Mp / °C (solvent)	Formula (molar mass)	$[\alpha]_D^{22}CHCl_3$ (c)	R_f (heptane:EtOAc, 5:1, v/v)
2	**1**	52	amorphous solid	$C_{14}H_{19}Cl_3N_4O_5$ (429.68)	[b]	0.32
4	**3**	70	128–130 (^{i}PrOH);	$C_{15}H_{21}Cl_3N_4O_5$ (443.71)	–77.3 (1.25)	0.33
6	**5**	69	68–70, amorphous solid	$C_{15}H_{21}Cl_3N_4O_6$ (459.69)	[b]	0.10
8	**7**	58	138–140 (heptane:Et_2O)	$C_{15}H_{21}Cl_3N_4O_6$ (459.69)	–60.3 (1.19)	0.11
9	**7**	13	76–78 (heptane:Et_2O)	$C_{16}H_{21}Cl_3N_4O_7$ (487.70)	–99.0 (1.07)	0.24
10	**8**	89	122–124 (heptane)	$C_{17}H_{23}Cl_3N_4O_7$ (501.75)	–75.8 (1.15)	0.15
11	**8**	61	75 (^{i}PrOH)	$C_8H_{10}Cl_3N_3O_5$ (334.54)	–85.0 (1.04)[c]	0.20[d]
12	**11**	82	103–104 (^{i}PrOH)	$C_{12}H_{14}Cl_3N_3O_7$ (418.61)	–82.4 (1.02)[e]	0.16
13	**11**	64	colourless syrup	$C_{22}H_{22}Cl_3N_3O_5$ (514.79)	–81.1 (1.03)[c]	0.32[f]
14	**8**	49	107–110 (^{i}PrOH)	$C_{19}H_{28}Cl_2N_2O_8$ (483.34)	–43.9 (1.04)[c]	0.24[g]
15	**8**	65	amorphous solid 116–121	$C_{19}H_{27}Cl_3N_2O_8$ (517.79)	–40.1 (1.01)[c]	0.10[h]
16	**14**	94	97–99	$C_{19}H_{30}N_2O_8$ (414.46)	–53.9 (1.00)	0.12[g]

[a] Satisfactory C, H, N microanalyses: C ± 0.37, H ± 0.18, N ± 0.41
[b] $[\alpha]_D$-value was not determined because the compound is an *endo*-H / *exo*-H diastereomeric mixture.
[c] $[\alpha]_D^{23}$
[d] Toluene:EtOAc, 3:1, v/v.
[e] $[\alpha]_D^{24}$
[f] Heptane:EtOAc, 10:1, v/v.
[g] Toluene:EtOAc, 1:1, v/v.
[h] Toluene:EtOAc, 2:1, v/v.

icantly shifted down field compared to the H-1 doublet of the starting material **8** ($\delta = 4.78$, $^3J_{1,2} \approx 7.3$). The acetamino group shows a broad doublet for NH at $\delta = 6.34$ ppm (Table 3).

Now, the conversion of the dichloroethylidene acetal of **14** into an ethylidene function is possible without any problems. On heating **14** with Bu_3SnH/AIBN in toluene for 4 hours at 65 °C, *N*-(6-*O*-acetyl-4-*O*-cyclohexylcarbamoyl-2,3-*O*-ethylidene-β-D-gulopyranosyl)acetamide (**16**) was generated and isolated in a yield of 94%. A second pathway to synthesise compound **16** from **8**, as shown in Scheme 2, gives some better overall yields than the former (**8** via **14**). At first the azide **8** was converted into the amide **15** (yield 65%) using Ph_3P / Ac_2O / pyridine[22] followed by reduction of the trichloroethylidene group with Bu_3SnH/AIBN. The ethylidene acetal **16** was isolated in a yield of 89%.

Mps were obtained using a Leitz Laborlux 12 Pol equipped with a hot stage Mettler FP 90. ^1H and $^{13}C\{H\}$ NMR spectra were recorded on Bruker instruments: AC 250, ARX 300, and ARX 400, internal standard TMS. Optical rotations were measured on a Polar LμP (IBZ Meßtechnik) instrument. Column chromatography: E. Merck Silica Gel 60 (63–200 μm); TLC: E. Merck Silica Gel 60 F_{254} foils. Chemicals: Chloral (Fluka), DCC (Aldrich), 60% suspension NaH in oil (Fluka), AIBN (Fluka), Bu_3SnH (Aldrich), Amberlite IR 120 (Fluka).

X-ray analysis: The data were collected in routine ω-scan on a Siemens P4 four circle diffractometer equipped with a graphite monochromator using Mo-K_α radiation. The structures were solved by direct methods and the refinement calculations were done using the full-matrix least-squares method of SHELXL-93. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-133 113 (**4**) and 133 114 (**12**). Copies of the data can be obtained free of charge on application to The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax +(1223)336033; E-mail: deposit@ccdc.cam.ac.uk).

4-*O*-Cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-α-D-lyxopyranosyl Azide (2); Typical Procedure

To a suspension of α-D-arabinopyranosyl azide (**1**)[23] (0.88 g, 5 mmol) in dry $(ClCH_2)_2$ (10 mL), chloral (2.58 g, 17.5 mmol) and DCC (2.58 g, 12.5 mmol) were sequentially added. The mixture was then refluxed with stirring for 7–8 h (TLC control); meanwhile the azide dissolved gradually. After cooling to r.t. and addition of 10% aq HOAc (15 mL), the mixture was shaken for 45 min to destroy excess DCC. The precipitated *N*,*N*′-dicyclohexylurea was removed by filtration, the organic phase was separated, and the aqueous phase was washed with CH_2Cl_2 (2 × 15 mL). The combined extracts were washed with sat. aq $NaHCO_3$ (15 mL), H_2O (2 x 15 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by column chromatography giving a mixture of the *endo*-H / *exo*-H diastereomers (9:1) of **2**, Tables 2 and 3.

Table 3 ^{1}H and ^{13}C NMR Data [$CDCl_3$/TMS, δ, *J* (Hz)] of the Azides **2**, **4**, **6**, **8**–**13** and the Glycosyl Amides **14**–**16**[a]

Product	H-1 (d)	H-2 (dd)	H-3 (dd)	H-4 (ddd)	H-5	H-5′	H-6	H-6′		NH	H-A[b] (s)	C-1, C-2, C-3 ,C-4 ,C-5, C-6, acetyl, benzyl, carbamoyl, formyl	CCl_3	C-A[c]
	$^{3}J_{1,2}$	$^{3}J_{2,3}$	$^{3}J_{3,4}$	$^{3}J_{4,5}$	$^{3}J_{4,5'}$	$^{2}J_{5,5'}$	$^{3}J_{5,6}$	$^{3}J_{5,6'}$	$^{2}J_{6,6'}$	$^{3}J_{NH/CH}$				
2	5.16 4.2	4.33 5.3	4.62 5.3	4.94 4.0	3.90 6.2	3.81 12.3				4.68 7.9	5.48 (5.30)	87.1 (C-1), 76.6, 76.2, 67.0 (C-2, 3, 4), 62.3 (C-2, 3, 4, 5), 153.9 (carbamoyl-*C*=O)	98.8	106.9
4	4.74 7.5	4.25 5.2	4.67 2.3	5.09 1.5	3.99		1.27[d] 6.3			4.78 8.0	5.47	87.8 (C-1), 76.7, 75.9, 70.3, 68.1 (C-2, 3, 4, 5), 15.5 (C-6), 154.1 (carbamoyl-*C*=O)	98.8	106.8
6	5.10 2.1	5.20 3.9	4.75 5.7	4.68 8.9	3.65		3.99 2.7	3.81 4.7	12.3	4.83 8.1	5.44 (5.30)	85.1 (C-1), 76.7, 75.9, 70.3, 68.1 (C-2, 3, 4, 5), 62.2 (C-6), 153.5 (carbamoyl-*C*=O)	99.0	107.0
8[e]	4.78 7.3	4.29 5.6	4.72 2.7	5.24 1.6	3.93		3.73 5.7	3.53 8.2	11.8	4.90 8.2	5.49 (5.31)	87.8 (C-1), 76.4 (C-3), 76.0 (C-2), 74.1 (C-5), 65.8 (C-4), 59.7 (C-6), 155.4 (carbamoyl-*C*=O)	98.7	106.7
9[f]	4.15 7.4	4.09 4.9	4.63 2.5	5.21 1.7	3.64		4.29 7.5	4.07 5.2	11.6		5.12 (4.83)	87.5 (C-1), 76.1 (C-3), 75.7 (C-2), 71.7 (C-5), 65.5 (C-4), 61.3 (C-6), 160.2 (formyl-*C*=O), 153.4 (carbamoyl-*C*=O)	98.5	106.7
10	4.79 7.4	4.30 5.4	4.76 2.5	4.22 1.1	m[g]		m[h]	m[h]		4.75 8.0	5.47	87.5 (C-1), 76.1, 75.8 (C-2, C-3), 71.8 (C-5), 65.8 (C-4), 61.8 (C-6), 170.4 (acetyl-*C*=O), 153.5 (carbamoyl-*C*=O), 20.7 (*C*H_3)	98.7	106.8
	2.07 (C*H*$_3$)													
11[i]	4.89 6.9	4.43 5.6	4.76 2.6	4.22 1.6	3.83		m[k] 4.2	m[k] 4.2			5.48	88.2 (C-1), 78.1, 75.7, 73.5, 67.2 (C-2, 3, 4, 5), 63.2 (C-6)	99.0	107.1
12	4.84 7.2	4.32 5.5	4.64 2.5	5.31 1.5	m[l]		m[l]	m[l]			5.49	87.3 (C-1), 75.7, 75.7, 71.2, 65.5 (C-2, 3, 4 ,5), 61.5 (C-6), 170.5, 169.5 (CH_3*C*O), 20.7, 20.7 (*C*H_3CO)	98.6	106.8
	2.14, 2.07 (C*H*$_3$CO)													
13[n]	4.67 7.4	4.25 5.5	4.64 2.4	3.82 2.0	3.91		3.65 6.0	3.58 6.5	9.7		5.36	87.4 (C-1), 76.3, 75.7, 73.8, 73.6, 73.5, 71.9 (C-2, 3, 4, 5, benzyl-*C*H_2), 68.1 (C-6)[m]	99.0	106.8
14	5.12 8.7	4.22 4.9	4.47 2.4	5.19 1.1	m[o]		m[o]	m[o]		4.79 8.1	5.57 3.2[p]	76.4, 76.1, 75.0, 72.3, 71.1, 66.4 (C-1, 2, 3, 4, 5, $CHCl_2$), 61.7 (C-6) 170.6, 170.6 (*C*=O), 153.7 (carbamoyl-*C*=O), 23.4, 20.7 (*C*H_3)		103.7
	5.45 (d, $CHCl_2$), 6.34 (d, $^{3}J_{1/NH} \approx 9.4$, amide), 2.04 (s, 6H, acetyl-C*H*$_3$, amide-C*H*$_3$)													
15	5.09 8.8	4.37 5.1	4.66 2.4	5.17	m[r]		m[r]	m[r]		4.97 8.2	5.46	76.7 (C-1), 76.7 (C-3), 75.5 (C-2), 72.2 (C-5), 66.2 (C-4), 61.6 (C-6), 171.1, 170.7 (*C*=O), 153.8 (carbamoyl-*C*=O), 23.7, 20.8 (*C*H_3)	98.6	106.4
	6.88 (d, $^{3}J_{1,NH} \approx 9.1$, amide-NH), 2.01, 1.99 (C*H*$_3$)													

Table 3 (continued)

Product	H-1 (d)	H-2 (dd)	H-3 (dd)	H-4 (ddd)	H-5	H-5′	H-6	H-6′		NH	H-A[b] (s)	C-1, C-2, C-3 ,C-4 ,C-5, C-6, acetyl, benzyl, carbamoyl, formyl	CCl_3	C-A[c]
	$^3J_{1,2}$	$^3J_{2,3}$	$^3J_{3,4}$	$^3J_{4,5}$	$^3J_{4,5'}$	$^2J_{5,5'}$	$^3J_{5,6}$	$^3J_{5,6'}$	$^2J_{6,6'}$	$^3J_{NH/CH}$				
16	5.19 8.8	m[s]	m[s] 2.4	5.17 1.1	m[s]		m[s]	m[s]		4.88 7.7	5.50 5.0[t]	76.1, 74.2, 74.1, 72.4, 67.1 (C-1, 2, 3, 4, 5), 62.0 (C-6), 170.6, 170.6 (*C*=O), 153.8 (carbamoyl-*C*=O), 23.2, 21.5, 20.7 (*C*H_3)		102.4
	6.44 (d, $^3J_{1/NH} \approx 9.4$, amide-NH), 2.03, 2.00 (C*H*$_3$), 1.32 (d, 3H, ethylidene-CH_3)													

[a] The cyclohexyl ring of **2**, **4**, **6**, **8**, **10**, **14**-**16** gives 4 proton multiplets: 3.35–3.60 (C*H*), 1.85–2.00 (C*H*$_2$), 1.52–1.80 (C*H*$_2$), 1.00–1.46 (C*H*$_2$), 4 carbon signals: *C*H/*C*H_2 50.2, 33.2, 25.4, 24.7.
[b] Acetal-H, (acetal-H of the *exo*-H form in brackets).
[c] Acetal-C.
[d] Doublet CH_3.
[e] 3.17 (dd, 6-OH), $^3J_{6,OH} \approx 8.5$ Hz, $^3J_{6'/OH} \approx 6.3$ Hz.
[f] Benzene-d_6, ^{1}H NMR: cyclohexyl CH 3.31–3.50 (m), CH_2 1.59–1.79 (m), 1.18–1.48 (m), 0.62–1.12 (m), 7.47 (s, formyl-H). ^{13}C NMR: cyclohexyl 50.3, 33.1, 25.3, 24.7.
[g] 4.07–4.16 (m, H-2).
[h] Multiplet 4.18–4.26 (H-6, 6′).
[i] 3.66 (d, $^3J_{4,4\text{-}OH} \approx 5.1$ Hz, 4-OH), 2.51 (t, $^3J_{6,6\text{-}OH} \approx {}^3J_{6',6\text{-}OH} \approx 6.1$ Hz, 6-OH).
[k] Multiplet 3.93–4.09 (H-6, 6′).
[l] Multiplet 4.10–4.24 (H-5, 6, 6′).
[m] 137.7, 137.1, 3 x 128.6, 2 x 128.4, 128.2, 128.0, 2 x 127.8, 127.7 (phenyl).
[n] 7.06-7.35 (phenyl), 4.58, 4.49 (d, $^2J \approx 11.8$ Hz, benzyl-CH_2), 4.48, 4.40 (d, $^2J \approx 12.0$ Hz, benzyl-CH_2).
[o] Multiplet 4.05–4.19 (H-5, 6, 6′).
[p] d, $^3J_{acetal\text{-}H/CHCl_2}$.
[r] 3.97–4.20 (m, H-5, 6, 6′).
[s] 4.04–4.22 (H-2, 3, 5, 6, 6′).
[t] q, $^3J_{acetal\text{-}H/CH_3}$.

4-*O*-Cyclohexylcarbamoyl-6-deoxy-2,3-*O*-(2,2,2-trichloroethylidene)-β-L-gulopyranosyl Azide (4)
β-L-Fucopyranosyl azide (**3**)[24] (0.95 g, 5 mmol), chloral (2.58 g, 17.5 mmol), DCC (2.58 g, 12.5 mmol) and $(ClCH_2)_2$ (15 mL) were refluxed for about 8 h (TLC control). Then the mixture was worked up as described for compound **2**. After column chromatography, afforded the pure *endo*-H diastereomer of **4**, Tables 2 and 3.

2-*O*-Cyclohexylcarbamoyl-3,4-*O*-(2,2,2-trichloroethylidene)-β-D-altropyranosyl Azide (6)
β-D-Mannopyranosyl azide (**5**)[25] (1.0 g, 5 mmol), chloral (2.58 g, 17.5 mmol), DCC (2.58 g, 12.5 mmol) and $(ClCH_2)_2$ (15 mL) were refluxed for about 12 h (TLC control). Then the mixture was worked up as described for compound **2**. The crude product, a mixture of compound **6** ($R_f \approx 0.28$, toluene: EtOAc, 8:1) and its 6-*O*-formyl derivative ($R_f \approx 0.61$), was refluxed in 5% methanolic Et_3N solution (25 mL) for about 10 min (TLC control) to deformylate the by-product. After evaporation of the solvents and column chromatographic purification compound **6** was isolated as an amorphous solid (diastereomeric mixture of the *endo*-H / *exo*-H form, 12:1), Tables 2 and 3.

4-*O*-Cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranosyl Azide (8) and 4-*O*-Cyclohexylcarbamoyl-6-*O*-formyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulo pyranosyl Azide (9)
β-D-Galactopyranosyl azide (**7**)[26] (1.0 g, 5 mmol), chloral (2.58 g, 17.5 mmol), DCC (2.58 g, 12.5 mmol) and $(ClCH_2)_2$ (15 mL) were refluxed for about 8 h (TLC control). Then the mixture was worked up as described for compound **2**. After column chromatographic separation (heptane: EtOAc, 5:1) two products were isolated; major product **8** and by-product **9**, Tables 2 and 3.

4-*O*-Cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranosyl Azide (8)
A solution of the formyl derivative **9** (0.20 g, 0.41 mmol) in 5% methanolic Et_3N (5 mL) was refluxed for about 10 min (TLC control, $R_f \approx 0.25$, toluene: EtOAc, 8:1, v/v) and then concentrated under reduced pressure. The syrupy residue was crystallised from a heptane/Et_2O mixture, mp: 138–140 °C, yield: 0.18 g (94%), Tables 2 and 3.

6-*O*-Acetyl-4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranosyl Azide (10)
A solution of D-gulosyl azide **8** (1.0 g, 2.18 mmol) in pyridine/Ac_2O (10 mL, 1:1 v/v) was stirred at r.t. for 12 h. After concentration of the mixture under reduced pressure, the syrupy residue was dissolved in Et_2O (15 mL). This solution was washed with 3% aq $NaHSO_4$ (2 x 5 mL), H_2O (2 × 5 mL) and dried ($MgSO_4$). After evaporation of the solvent and column chromatographic purification of the residue the crystalline compound **10** was isolated, Tables 2 and 3.

2,3-*O*-(2,2,2-Trichloroethylidene)-β-D-gulopyranosyl Azide (11)
Compound **8** (2.55 g, 5.55 mmol) dissolved in 1% methanolic NaOMe (60 mL) was decarbamoylated by heating the solution under reflux for 6h. Subsequently, the 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, the crystalline compound **11** was obtained, Tables 2 and 3.

4,6-Di-*O*-acetyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranosyl Azide (12)
Compound **11** (0.50 g, 1.49 mmol) was acetylated in pyridine/Ac_2O (10 mL, 1:1, v/v) as described for **10**. After column chromatography the crystalline product **12** was isolated, Tables 2 and 3.

4,6-Di-*O*-benzyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranosyl Azide (13)
To a stirred solution of the *endo*-H diastereomer **11** (0.50 g, 1.49 mmol) in dry THF (10 mL), a 60% suspension of NaH (0.19 g, 4.66 mmol) in oil was added in small doses at r.t. followed by benzyl bromide (0.44 g, 0.31 mL, 3.73 mmol). After stirring of the suspension for about 8 h and addition of Et_2O (15 mL), the mixture was carefully hydrolysed by the dropwise addition of dist. H_2O (15 mL). Then the organic phase was separated, washed with 3% aq $NaHSO_4$ (2 x 5 mL) and water (2 x 5 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Column chromatographic purification of the residue yielded a colourless syrupy product **13**, Tables 2 and 3.

***N*-[6-*O*-Acetyl-4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2-dichloroethylidene)-β-D-gulopyranosyl]acetamide (14)**
To a stirred solution of 4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranosyl azide (**8**) (3.0 g, 6.53 mmol) in toluene (100 mL), Bu_3SnH (5.70 g, 5.18 ml, 19.59 mmol) and AIBN (0.10 g, 0.61 mmol) were added at 50 °C (Ar atm) and stirring was continued for 3 h at this temperature (TLC control). After evaporation of the solvent under reduced pressure, the oily residue was dissolved in heptane (20 mL). The precipitate that formed after a short time was separated by filtration and dissolved in Ac_2O/pyridine (30 mL, 1:1, v/v). After stirring of this mixture for 12 h at r.t., the solvents were evaporated under reduced pressure. The oily residue was dissolved in Et_2O (30 mL), the solution was washed with 3% aq $NaHSO_4$ (2 × 10 mL) and H_2O (2 × 10 mL), and dried ($MgSO_4$). The crude product obtained after evaporation of the solvent was purified by column chromatography giving the crystalline product **14**, Tables 2 and 3.

***N*-[6-*O*-Acetyl-4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranosyl]acetamide (15)**
To a solution of 4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranosyl azide (**8**) (1.0 g, 2.18 mmol) in dry pyridine (10 mL), PPh_3 (1.14 g, 4.36 mmol) was added and the mixture stirred for 2 h at r.t. (TLC control). Then Ac_2O (10 mL) was added and stirring was continued for 12 h. The solvents were evaporated under reduced pressure and the residue was dissolved in Et_2O (25 mL). After washing with 3% aq $NaHSO_4$ (2 × 5 mL) and H_2O (2 × 5 mL) the ethereal solution was dried ($MgSO_4$) and concentrated under reduced pressure. Column chromatographic purification of the residue ($R_f \approx 0.38$, heptane:EtOAc, 1:2, v/v), followed by HPLC separation to remove Ph_3PO completely, yielded the amorphous product **15**, Tables 2 and 3.

***N*-(6-*O*-Acetyl-4-*O*-cyclohexylcarbamoyl-2,3-*O*-ethylidene-β-D-gulopyranosyl)acetamide (16)**
Procedure A: To a solution of *N*-(6-*O*-acetyl-4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2-dichloroethylidene)-β-D-gulopyranosyl)acetamide (**14**) (0.50 g, 1.03 mmol) in toluene (20 mL), Bu_3SnH (0.90 g, 0.82 ml, 3.09 mmol) and AIBN (0.02 g, 0.13 mmol) was added at 65 °C with stirring. After about 4 h the reaction is finished (TLC control) and the mixture was shaken with 10% aq KF (10 mL) for 45 min. Thus, Bu_3SnF formed from the soluble chloride precipitated and was removed by filtration. The organic phase was washed with 3% aq $NaHSO_4$ (5 mL) and H_2O (2 × 5 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography yielding the crystalline product **16**, Tables 2 and 3.

Procedure B: *N*-(6-*O*-acetyl-4-*O*-cyclohexylcarbamoyl-2,3-*O*-(2,2,2-trichloroethylidene)-β-D-gulopyranosyl)acetamide (**15**) (0.23 g, 0.44 mmol) dissolved in toluene (20 mL) was treated with Bu_3SnH (0.51 g, 0.47 mL, 1.76 mmol) and AIBN (0.01 g, 0.06 mmol) as described in procedure A; yield of **16**: 0.16 g (89%), Tables 2 and 3.

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