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SYNTHESIS AND STRUCTURE OF BROMO GLYCOSYL IMINES READILY OBTAINED FROM PROTECTED GLYCOSYL AZIDES

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Abstract: Treatment of various furanosyl and pyranosyl azides in the presence of *N*-bromosuccinimide in excess led to the corresponding moderately stable glycosyl bromoimines in almost quantitative yields, except for the less reactive peracetylated α-D-glucopyranosyl azide and a benzyl-protected derivative. NMR analysis and crystal structure determination showed that the C=N double bond adopted a (Z) configuration in the products which resulted primarily from homolysis of a C—H bond attached to the anomeric carbon.

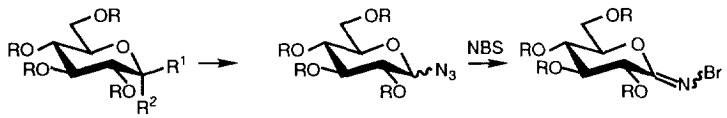
Although glycosyl azides have been known for a long time, they still receive a considerable attention[1], in connection with the versatile reactivity of the azido group. Improved synthetic procedures have made their access very easy[2]. A recent study describing the conversion of glycosyl azides into glycosyl fluorides[3] pointed out the possibility of using the azido group as a temporary protection of the anomeric carbon prior to its activation. In addition, recent findings showed that the synthetic potential of the azido group is not fully explored[4,5] as also shown by our recent studies dealing with either the photolysis of anomeric mono[6] and diazides[7] or free-radical brominations. We recently reported the efficient and unprecedented conversions of 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl azide and 2,3;5,6-di-O-(methylethylidene)-β-D-mannofuranosyl azide into the corresponding glycosyl bromoimines[8], the first members of an unknown series of compounds. This approach has been extended to α-D and β-D-configurated azido sugars of both the furanose and pyranose series, displaying a variety of protecting groups as reported here.

The azido sugars used in the present study have been prepared by repetition or adaptation of known procedures[1]. One of them involves the Lewis acid-catalyzed replacement of an anomeric acetoxy group by an azido group, in the presence of trimethylsilyl azide in excess[9,10]. The stereoselectivity of this process was found to be highly dependent on the substrate. The anchimeric assistance provided by the acetoxy group at C-2 in **1** and **7** explained the high 1,2-*trans* stereoselectivity observed for their transformation into **14** (77%)[9] and **19** (98%)[9]. In the case of **10**[10] and **13**, the absence of such a participating group accounted for the formation of mixtures of both the α-D and β-D anomers **22**[10] (29%) and **23**[10] (45%) or **26** (20%) and **27** (26%). The nucleophilic displacement of glycosyl halides by azide anions, using either polar aprotic solvents, such as dimethyl sulfoxide or phase-transfer catalysis[2a], represents another efficient method for the synthesis of glycosyl azides. The substitution of glycosyl halides by nucleophiles in polar aprotic solvents corresponds to a stereospecific S_N2 process[11,12]. This is also valid in water as shown recently[13] by the conversion of α-D-

glucopyranosyl fluoride into β-D-glucopyranosyl azide. Glycosyl halides of known anomeric configuration can be prepared easily by literature procedures: **2**[14a, 15], **3**[14b], **4**[14c], **6**[16], **8**[15], **9**[17]. Examination of ^{1}H NMR spectra and literature data allowed the determination of the anomeric configuration of the azido sugars prepared from the latter. It was found, in every case, opposite to that of the starting halides, thus confirming the possibility to control closely the anomeric configuration of the products by means of this stereospecific S_N2 displacement. The obtained azido sugars exhibited physical data in agreement with those already reported for **14**[2, 9], **15**[12], **16**[16], **18**[16], **19**[2b, 9], **20**[2b], **21**[18], **22**[10], **23**[10] and **25**[10]. Compounds **5**[19] and **12**[10,20] obtained in high yield on deacetylation of **14** or **23** also corresponded to the described structures. Permethylation of **5** afforded the unknown β-azide **17** in a 73% yield whereas tritylation of **12** gave **25**, as descrided[10].

At the outset of this work, two glycosyl azides were converted in high yield into the corresponding glycosyl bromoimines[8] on treatment with *N*-bromosuccinimide under free-radical conditions (benzoyl peroxide or light), in refluxing carbon tetrachloride. Under these conditions, the conversion of the substrate into the corresponding acid-labile product was achieved within a few minutes, making difficult the necessary monitoring (TLC) of the reaction. As soon as its completion was achieved, degradation of the product occurred rapidly at 77°C. However, we found that the reaction took place by stirring the mixture at about ~30-40°C when the reaction vessel was exposed to bright sunlight or to a tungsten lamp (60W) placed within a short distance (~4-10 cm). At these lower temperatures, completion of the reaction was observed after ~30 min to ~1.5 h. Generally, no changes could be observed by TLC monitoring during the first stages of the treatment (~20-60 min), after which the reaction occurred rapidly. Its completion which was indicated by the disappearance of the starting material on the TLC plates and the presence of a slightly more polar spot, visible under UV light, coincided with the development of a brownish colour in the reaction medium. Simple work-up allowed in most cases high-yielding preparations of the desired glycosyl bromoimines, generally as almost pure syrups. Attempted purifications by column chromatography on silica gel resulted invariably in the loss of the products probably as a result of hydrolysis, as indicated by the partial recovery of the corresponding sugar lactones. As a consequence, the prepared glycosyl bromoimines which have been identified on the basis of their spectroscopic data (Tables 4 and 5) have not been fully characterized[21] except for the more stable compound **34**.

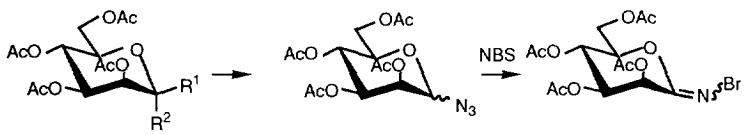
It is noteworthy that the α azide **15** was found much less reactive as compared to its β counterpart (complete conversion after 2.5 h or ~5 min, respectively at 77°C) showing once again the higher susceptibility towards homolysis of anomeric axial C—H bonds ($^4C_1$-D chair conformation of the D-pyranosyl ring) as compared to equatorial ones[22]. The reactivity difference observed for peracetylated α and β-D-mannopyranosyl azides was less pronounced and competitive experiments established the following sequence of reactivity: **20** > **14** > **19** > **15**. Interestingly, the yields corresponding to the preparations of **32** and **28** decreased following the same sequence (see scheme). For furanosyl azides, similar reactivities could be observed for both α and β anomers, probably because the orientation of the C—H bonds at the anomeric center in each anomer are more similar, as compared to pyranosyl rings. Similar observations have been made during the photobromination of D-*gluco* and D-*galacto* furanose derivatives[23] which involved homolysis of axial C—H bond at epimeric C-4 carbon atoms. A large array of protecting groups which are used commonly in carbohydrate chemistry (acetate, benzoate, methylethylidene, cyclohexylidene, methyl and trityl ether), are compatible with the reaction



	R	R^1	R^2
1	Ac	OAc	H
2	Ac	H	Br
3	Ac	Cl	H
4	Bz	H	Br
5	H	N_3	H
6	Bn	H	Cl

	R	conf.
14	Ac	β
14	Ac	β
15	Ac	α
16	Bz	β
17	CH_3	β
18	Bn	β

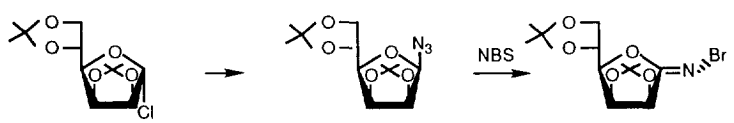
	R	%
28	Ac	92
28	Ac	0
29	Bz	~100
30	CH_3	~100
31	Bn	0



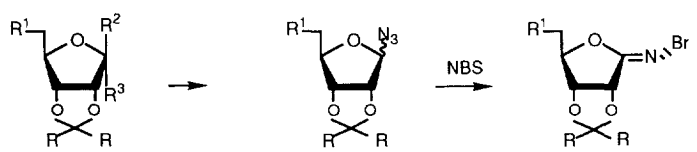
	R^1	R^2
7	OAc	H
8	H	Br

	conf.
19	α
20	β

	%
32	81
32	~100



9 **21** **33** ~100 %



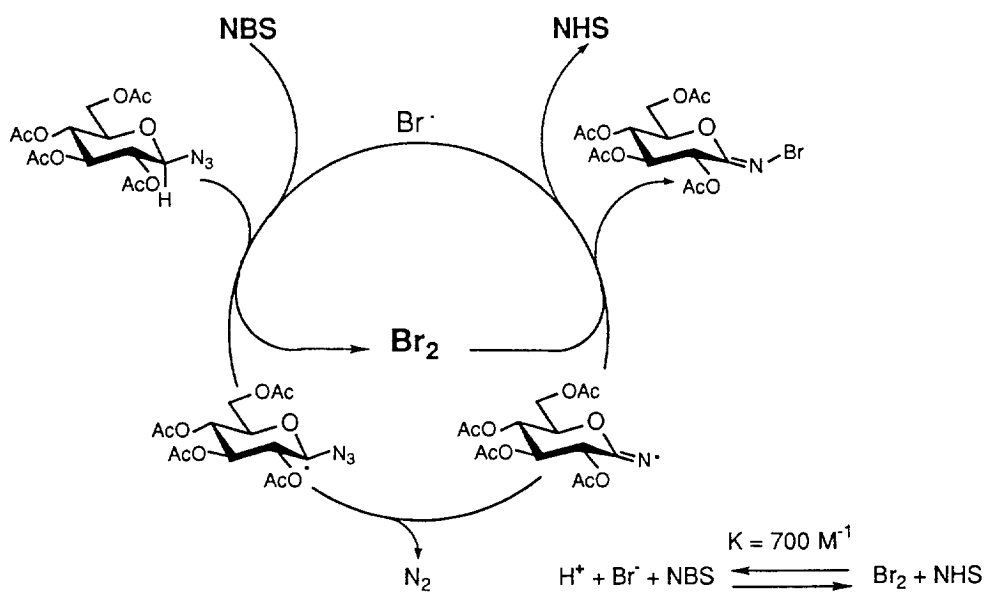
	R	R	R^1	R^2	R^3
10	CH_3	CH_3	OAc	OAc	H
11	CH_3	CH_3	OMs	Cl	H
12	CH_3	CH_3	OH	N_3	H
13	C_5H_{10}		OAc	OAc	H

	R	R	R^1	conf.
22	CH_3	CH_3	OAc	α
23	CH_3	CH_3	OAc	β
24	CH_3	CH_3	N_3	α
25	CH_3	CH_3	OTr	β
26	C_5H_{10}		OAc	α
27	C_5H_{10}		OAc	β

	R	R	R^1	%
34	CH_3	CH_3	OAc	90
34	CH_3	CH_3	OAc	80
35	CH_3	CH_3	N_3	91
36	CH_3	CH_3	OTr	~100
37	C_5H_{10}		OAc	~100

conditions. However, the unselective transformation of **18** to give several unidentified polar products showed that benzyl ethers are not suitable protective groups, probably as a result of their rapid cleavage by *N*-bromosuccinimide, under free-radical conditions[24]. Finally, conversion of the α-diazide **24** into **35** which still presented an azido group at the C-5 position showed that this transformation is restricted to azido groups at the anomeric position[25], showing the favourable influence of the endocyclic oxygen atom.

As already discussed in a note devoted to radical-mediated halogenations of anomerically *N*-substituted sugars[26], it is clear that the proposed synthesis of glycosyl bromoimines involve homolysis of an activated anomeric C—H bond as the crucial step. This is supported by the acceleration of the reaction rate in the presence of radical initiator[8, 26] or/and light[27], by the observed reactivity of the substrates and the stability of azido sugars devoid of anomeric hydrogen atom[25, 26]. On the basis of ESR experiments showing the conversion of short-lived carbon-centered radicals linked to an azido group into the corresponding imino radical[28], it is highly probable that the initial anomeric radical is converted to a nitrogen-centered radical with simultaneous release of molecular nitrogen. As already noted in the literature[28], the conjugative stabilization of the α-azido radical or the concerted loss of nitrogen to form the iminyl radical could explain the high rate of the C—H bond homolysis in alkyl or glycosyl azides. In such NBS-mediated transformations, it has been known for long time that either bromine atoms or succinimidyl radicals can act as the chain reaction carriers[29], as discussed in recent and



detailed studies[30,31]. Due to the sensitive nature of the glycosyl bromoimines, molecular bromine was not used for synthetic purposes although it brought about a fast transformation of glycosyl azides. With NBS, the transformation started after an induction period (this was also observed when **16** was reacted with *N*-bromophtalimide to give **29** as the only product) or after addition of a catalytic amount of molecular bromine. Its beneficial role was observed in the case of either heterogeneous or homogeneous reaction mixtures, when using either carbon tetrachloride or dichloromethane as the solvent, respectively. These data support the conclusion that bromine atoms produced from molecular bromine are the chain reaction carriers, as illustrated in the scheme[32]. The tested glycosyl azides were not, or only slowly transformed in the presence of NCS (**21**, **23**) or NIS (**21**), respectively. Treatment of **14** in the presence of sulfuryl chloride SO_2Cl_2 resulted in the formation of the C-5 chloride[26] as the major product (55 %). Attempts to observed minor amounts of the corresponding glycosyl chloroimine failed.

Crystal analysis of **34** demonstrated unambiguously the proposed structures (Tables 1, 2 and 3) and the (*Z*)-configuration of the C=N double bond in both independent molecule of the asymmetric unit. The C=N double bond and its three substituents are lying in the same plane. The C-4 carbon atom is ~+0.2 Å out of this plane (β side) whereas the C-3 carbon atom is ~-0.2 Å, showing a skew conformation for the furanosylidene ring. The similarities observed in the ^1H and ^{13}C NMR spectra of **34**, **35** and **37** for δH-2, $J_{2,3}$ and δC-2 in particular also support the same (*Z*) configuration which has been already mentioned for **33**[8]. The δH-2 value (5.19 ppm) of this compound fitted well that of the corresponding (*Z*)-hydroximo lactones (OH group linked to the nitrogen atom) in comparison to that of the (*E*) isomer (δH-2: 5.15[33], 5.19[34] and 5.49[34], respectively). The preference for such a (*Z*) configuration is quite common[7, 8, 34] although confusion persists in this field. For instance, comparison of the δH-2 values of the tritylated hydroximo lactone (δH-2: 5.29 ppm, $J_{2,3}$ 6 Hz[33] and 5.12 ppm, $J_{2,3}$ 6 Hz[35]) corresponding to **36** (δH-2: 5.37 ppm, $J_{2,3}$ 6 Hz), shows that the recently proposed (*E*) configuration[35] of the lactone oxime is erroneous, in accordance with the revision[34] of the tentative (*E*) configuration initialy proposed[33]. Assignment of the C=N double bond configuration in pyranosyl bromoimines rested on comparison of the chemical shifts of the H-2 proton with that of the corresponding glycono-1,5-lactones. Literature data show a deshielding of about 0.5 ppm for this proton in a (*Z*)-configurated, benzyl protected hydroximo lactone derivative[34] taking the tetrabenzyl gluconolactone **38** as a reference (δH-2: 4.12 ppm). In **28** and **32**, comparable deshieldings (0.51 and 0.19 ppm, respectively) are observed for the H-2 resonances, as compared to the corresponding tetraacetyl glyconolactones **39** (*gluco*, δH-2: 5.12 ppm) and **40** (*manno*, δH-2: 5.75 ppm). This indicates a (*Z*) configurated C=N double bond in compounds **28** and **32**, since a (*E*) configuration should increase the deshielding effect by 0.4 to 0.6 ppm, as observed in related stereoisomers [6,34] or in bromosugars[36]. Thus, in each instance, the reaction led exclusively to the more stable (*Z*) stereoisomers[37].

In conclusion, treatment of a variety of sugar azides of both the furanose and pyranose series in the presence of *N*-bromosuccinimide in excess led to the corresponding glycosyl bromoimines in almost quantitative yields, except for the less reactive peracetylated α-D-glucopyranosyl azide and a benzyl-protected derivative. The transformation involved primarily the homolysis of activated C—H bonds attached to the anomeric centre, so that azido groups located at other positions were not affected under these very mild conditions. NMR analysis

Table 1: Positional parameters and their estimated standard deviations for compound **34**

Atom	x	y	z	B_{eq} (Å^2)
Br1A	0.7010(3)	0.1818(2)	0.15603(6)	7.80(5)
O1A	0.817(1)	-0.304(1)	0.2523(3)	5.8(2)
O2A	0.696(1)	-0.094(1)	0.2770(3)	5.9(2)
O3A	0.417(1)	-0.276(1)	0.1840(3)	5.3(2)
O4A	0.266(1)	-0.394(1)	0.1414(3)	6.5(3)
O5A	0.710(1)	-0.145(1)	0.1792(3)	5.2(2)
N1A	0.633(2)	0.092(1)	0.2050(4)	6.1(3)
C1A	0.653(1)	-0.056(2)	0.2070(4)	4.4(3)
C2A	0.609(1)	-0.134(1)	0.2434(4)	4.0(3)
C3A	0.670(2)	-0.293(2)	0.2337(4)	5.2(3)
C4A	0.687(2)	-0.302(2)	0.1909(4)	4.7(3)
C5A	0.544(2)	-0.361(2)	0.1689(4)	5.1(3)
C6A	0.815(2)	-0.201(2)	0.2856(5)	6.7(4)
C7A	0.270(2)	-0.299(2)	0.1671(4)	5.2(3)
C8A	0.168(2)	-0.218(2)	0.1890(6)	8.9(5)
C9A	0.977(2)	-0.115(2)	0.2856(7)	9.6(6)
C10A	0.772(3)	-0.286(2)	0.3235(5)	8.2(5)
Br1B	0.4469(2)	0.9563(2)	0.09083(6)	7.24(4)
O1B	-0.047(1)	1.070(1)	0.0015(3)	7.1(2)
O2B	0.152(1)	0.937(1)	-0.0262(3)	5.8(2)
O3B	-0.027(1)	0.672(1)	0.0724(3)	6.0(2)
O4B	-0.143(1)	0.522(1)	0.1143(3)	7.2(3)
O5B	0.117(1)	0.949(1)	0.0734(3)	5.3(2)
N1B	0.350(1)	0.886(2)	0.0449(4)	6.2(3)
C1B	0.201(2)	0.898(1)	0.0444(4)	5.0(3)
C2B	0.113(2)	0.858(2)	0.0092(4)	5.3(3)
C3B	-0.052(2)	0.921(2)	0.0195(4)	5.6(3)
C4B	-0.052(2)	0.935(2)	0.0641(4)	6.1(4)
C5B	-0.106(2)	0.802(2)	0.0876(4)	6.0(3)
C6B	0.053(2)	1.078(1)	-0.0302(4)	4.6(3)
C7B	-0.060(2)	0.530(2)	0.0891(4)	5.6(3)
C8B	0.033(2)	0.410(2)	0.0726(5)	6.6(4)
C9B	0.147(3)	1.214(2)	-0.0228(7)	10.5(6)
C10B	-0.025(2)	1.055(2)	-0.0682(4)	6.5(4)

Anisotropically refined atoms are given in the form of the isotropic equivalent displacement parameter defined as: $B_{eq} = 4/3\ \Sigma_i\Sigma_j\beta_{ij}\ a_i a_j$

Table 2: Bond distances in Angstroms in compound **34**

Bond	Distance	Bond	Distance	Bond	Distance
Br1A - N1A	1.92(1)	C2A - C3A	1.52(2)	O3B - C7B	1.40(2)
O1A - C3A	1.43(2)	C3A - C4A	1.44(2)	O4B - C7B	1.12(2)
O1A - C6A	1.44(2)	C4A - C5A	1.54(2)	O5B - C1B	1.30(2)
O2A - C2A	1.40(2)	C6A - C9A	1.60(3)	O5B - C4B	1.51(2)
O2A - C6A	1.43(2)	C6A - C10A	1.52(2)	N1B - C1B	1.30(2)
O3A - C5A	1.43(2)	C7A - C8A	1.35(2)	C1B - C2B	1.46(2)
O3A - C7A	1.42(2)	Br1B - N1B	1.86(1)	C2B - C3B	1.58(2)
O4A - C7A	1.20(2)	O1B - C3B	1.44(2)	C3B - C4B	1.50(2)
O5A - C1A	1.31(2)	O1B - C6B	1.38(2)	C4B - C5B	1.49(2)
O5A - C4A	1.44(2)	O2B - C2B	1.42(2)	C6B - C9B	1.47(2)
N1A - C1A	1.31(2)	O2B - C6B	1.51(2)	C6B - C10B	1.46(2)
C1A - C2A	1.45(2)	O3B - C5B	1.43(2)	C7B - C8B	1.44(2)

Table 3: Bond angles in Degrees in compound **34**

Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle
C3A	O1A	C6A	107(1)	O5A	C4A	C3A	104(1)	C2B	O2B	C6B	110(1)
C2A	O2A	C6A	113(1)	O5A	C4A	C5A	108(1)	C5B	O3B	C7B	118(1)
C5A	O3A	C7A	119(1)	C3A	C4A	C5A	114(1)	C1B	O5B	C4B	112(1)
C1A	O5A	C4A	109(1)	O3A	C5A	C4A	106(1)	Br1B	N1B	C1B	116(1)
Br1A	N1A	C1A	114(1)	O1A	C6A	O2A	105(1)	O5B	C1B	N1B	126(1)
O5A	C1A	N1A	127(1)	O1A	C6A	C9A	107(1)	O5B	C1B	C2B	113(1)
O5A	C1A	C2A	114(1)	O1A	C6A	C10A	110(1)	N1B	C1B	C2B	121(1)
N1A	C1A	C2A	118(1)	O2A	C6A	C9A	110(1)	O2B	C2B	C1B	116(1)
O2A	C2A	C1A	114(1)	O2A	C6A	C10A	108(1)	O2B	C2B	C3B	103(1)
O2A	C2A	C3A	102(1)	C9A	C6A	C10A	117(2)	C1B	C2B	C3B	103(1)
C1A	C2A	C3A	99(1)	O3A	C7A	O4A	114(1)	O1B	C3B	C2B	101(1)
O1A	C3A	C2A	106(1)	O3A	C7A	C8A	108(1)	O1B	C3B	C4B	110(1)
O1A	C3A	C4A	110(1)	O4A	C7A	C8A	137(2)	C2B	C3B	C4B	104(1)
C2A	C3A	C4A	107(1)	C3B	O1B	C6B	113(1)	O5B	C4B	C3B	103(1)
O5B	C4B	C5B	105(1)	O1B	C6B	C9B	105(1)	C9B	C6B	C10B	121(1)
C3B	C4B	C5B	118(1)	O1B	C6B	C10B	111(1)	O3B	C7B	O4B	120(1)
O3B	C5B	C4B	107(1)	O2B	C6B	C9B	109(1)	O3B	C7B	C8B	112(1)
O1B	C6B	O2B	105(1)	O2B	C6B	C10B	104(1)	O4B	C7B	C8B	128(2)

Numbers in parentheses are estimated standard deviations in the least significant digits.

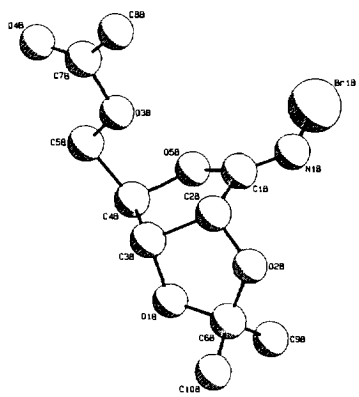


Fig. 1: PLUTO[38] drawing of **34** showing the atom numbering scheme for one molecule of the asymmetric unit

and crystal structure determination showed that the C=N double bond adopted a (Z) configuration. In spite of the moderate stability of these new compounds, their transformation into diversely functionalised opened glycono nitriles has been achieved in high yields[27]. Further investigations are in progress in order to explore the synthetic potential[39] of this new class of sugar derivatives.

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EXPERIMENTAL

β-D-Glucopyranosyl azide **5**. Deacetylation of **14** (Zemplen conditions) was achieved following a known protocol[19] to yield β-D-glucopyranosyl azide **5** as a crystalline material (three crops, 98% yield).

5-O-Mesyl-2,3-O-(methylethylidene)-β-D-ribofuranosyl chloride **11**. Methanesulfonyl chloride (0.31 mL, 4 mmol) was added to a solution of 2,3-O-(methylethylidene)-D-ribofuranose (380 mg, 2mmol) and *s*-collidine (1 mL, 8 mmol) in dichloromethane (10 mL) following a literature protocol[17] used for the preparation of **9**. After 24 h at room temperature, when TLC showed that all of the starting material had reacted to give a mixture of products, chloroform was added and the solution was washed successively with M hydrochloric acid, M sodium hydrogencarbonate, and water. The reaction mixture which was not purified further, was shown by ^{1}H NMR spectroscopy to contain mainly the chloride **11**.

2,3,4,6-Tetra-O-methyl-β-D-glucopyranosyl azide **17**. Mineral oil free sodium hydride (80 % dispersion in mineral oil) (499 mg, 30 % excess) was added under stirring to a cooled (0°C) solution of β-D-glucopyranosyl azide **5**[19] (820 mg, 4mmol) in dry dimethylformamide (25 mL). After stirring for 45 min at room temperature (~20°C), the solution was cooled down to 0°C before dropwise addition of methyl iodide (1.4 mL, ~3.18 g, 22.4 mmol, ~40 % excess) at this temperature. Stirring was continued overnight, at ~20°C. After addition of another portion of methyl iodide (0.4 mL) and stirring for 3h, reaction was over and MeOH (1 mL) was added under stirring. The residue obtained after solvent removal in vacuo (bath temperature: ~35°C) was taken up in dichloromethane (50 mL). After washings (brine, water), the organic phase was concentrated and the residue applied to a column of silica gel (Kieselgel 60 Merk, height: 19 cm, external diameter: 20 mm) irrigated with a mixture of ethyl acetate-*n*-hexane 3:6 (v/v) to yield 2,3,4,6-tetra-O-methyl-β-D-glucopyranosyl azide as a colourless oil (763 mg, 73%). Rf ~0.65 (ethyl acetate-*n*-hexane 4:6 v/v); $[\alpha]_D$ -22° (c = 2, chloroform, 20°C); IR: ν N3: 2110 cm^{-1}; ^{1}H NMR (200.13 MHz, C_6D_6, δ ppm / TMS, J Hz): 2.91 (t, 1H, $J_{2,3}$ 8.5, H-2), 3.06 (t, 1H, J $_{3,4}$ 8.8, H-3), 3.06 (m, 1H, $J_{5,6}$ 1.5, $J_{5,6'}$ 3.8, H-5), 3.14 (s, 3H, OMe), 3.22 (t, 1H, $J_{4,5}$ 9.5, H-4), 3.38, 3.40 (2s, 6H, 2 OMe), 3.41 (m, 2H, $J_{6,6'}$ not determined, H-6, H-6'), 3.50 (s, 3H, OMe), 4.12 (d, 1H, $J_{1,2}$ 8.4, H-1); ^{13}C NMR (50.32 MHz, C_6D_6): δ: 59.17, 60.25, 60.37, 60.75 (O<u>C</u>H3), 71.27 (C6), 90.13, 83.90, 79.29, 77.49, 87.30 (C1 to C5, tentative assignments, may be reversed).
Anal.: Calcd. for $C_{10}H_{19}O_5N_3$: C, 45.97; H, 7.33; N, 16.08; found: C, 46.08; H, 7.55; N, 15.79.

5-Azido-5-deoxy-2,3-O-(methylethylidene)-α-D-ribofuranosyl azide **24**. 5-O-Mesyl-2,3-O-(methylethylidene)-β-D-ribofuranosyl chloride **11** (0.573 mg, 2mmol) was added to a solution of sodium azide (0.65 g, 10 mmol) in dimethyl sulphoxide (8 mL) under stirring. After 24 h at room temperature, all the starting material had reacted to give two new compounds as shown by TLC (ethyl acetate-*n*-hexane 1:1 v/v). After addition of water, the reaction mixture was taken up in diethyl ether. Work-up and resolution of the products on a column of silica gel (ethyl acetate-*n*-hexane 1:1 v/v) yielded the diazide **24** (117 mg, 25% yield from 2,3-O-(methylethylidene)-D-ribofuranose) and 76 mg of uncompletely characterized 5-O-methanesulfonyl-2,3-O-(methylethylidene)-β-D-ribofuranosyl azide (13 % yield).
24: $[\alpha]_D$ +54° (c = 0.35, chloroform), IR: ν N3: 2110 cm^{-1}; ^{1}H NMR (200.13 MHz, $CDCl_3$, δ ppm / TMS, J Hz): 5.19 (d, 1H, $J_{1,2}$ 4.4, H-1); 4.78 (dd, 1H, $J_{2,3}$ 6.5, H-2); 4.65 (dd, 1H, $J_{3,4}$ 2.2, H-3); 4.37 (m, 1H, $J_{4,5}$ 3.8, H-4); 3.58 (dd, 1H, $J_{4,5'}$ 3.9, H-5); 3.44 (dd, 1H, $J_{5,5'}$ 13.1, H-5'); 1.60 and 1.36 (2s, 3H each, 2 Me); ^{13}C NMR (50 MHz, $CDCl_3$): 91.02 (C-1); 81.61, 81.61, 81.41 (C-2 to C-4); 52.84 (C-5); 115.18, 25.72, 24.98 (methylethylidene).
Anal.: Calcd. for $C_8H_{12}O_3N_6$: C, 39.98; H, 5.04; O, 19.99; N, 34.99; found: C, 40.21; H, 5.12; O, 19.97; N, 34.65.

2,3-O-Cyclohexylidene-5-O-acetyl-α-D and β-D-ribofuranosyl azides **26** and **27**. To 2,3-O-cyclohexylidene-1,5-di-O-acetyl-β-D-ribofuranose **13** (628 mg, 2 mmol) in dry acetonitrile (12 mL) were added trimethylsilyl azide (1.15 g, 5 eq.) and aluminium trichloride (266 mg, 1 eq.). The mixture was heated to 55°C with stirring, and the reaction was monitored by TLC (ethyl acetate-*n*-hexane 1:4 v/v). After completion of the reaction (6h), the residue was treated with cold water (40 mL) and extracted with chloroform (3 x 50 mL). The extracts were combined and evaporated, and the residue was chromatographed on a column of silica gel (ethyl acetate-*n*-hexane 1:4 v/v) to give 151 mg (26%) of the β-azide **27** as a syrup ($[\alpha]^{20}$ -149° c = 0.5, chloroform; IR: ν N3: 2110 cm^{-1}; ν C=O: 1740 cm^{-1}) and 113 mg (20 %) of the α-anomer **26** ($[\alpha]^{20}$ +13° c = 1, chloroform; IR: ν N3: 2105 cm^{-1}; ν C=O: 1740 cm^{-1}).
26: ^{1}H NMR (200.13 MHz, $CDCl_3$, δ ppm / TMS, J Hz): 5.02 (d, 1H, $J_{1,2}$ 4.1, H-1); 4.74 (dd, 1H, $J_{2,3}$ 6.3, H-2); 4.66 (dd, 1H, $J_{3,4}$ 1.8, H-3); 4.43 (dt, 1H, $J_{4,5}$ 4.1, $J_{4,5'}$ 4.1, H-4); 4.17 and 4.20 (2s, 2H, H-5, H-5');

2.09 (s, 3H, COCH3); 1.40 - 1.80 (m, 10H, cyclohexyl); ^{13}C NMR (50 MHz, $CDCl_3$): 99.85 (C-1); 79.17, 76.34, 69.70 (C-2 to C-4); 64.31 (C-5); 170.41, 20.75 (acetyl); 114.54, 34.21, 34.16, 24.77, 22.71, 22.62 (cyclohexyl).
27: ^1H NMR (200.13 MHz, $CDCl_3$, δ ppm / TMS, J Hz): 5.54 (s, 1H, $J_{1,2}$ ~0, H-1); 4.67 (d, 1H, $J_{2,3}$ 5.9, H-2); 4.47 (t, 2H, H-3, H-4); 4.19 (t, 2H, $J_{4,5}$ ~6.5,$J_{4,5'}$ ~6.2, H-5, H-5'); 2.13 (s, 3H, COCH3); 1.39 - 1.67 (m, 10H, cyclohexyl); ^{13}C NMR (50 MHz, $CDCl_3$): 97.06 (C-1); 85.20, 85.06, 81.58 (C-2 to C-4); 63.89 (C-5); 170.52, 20.74 (acetyl); 114.11, 36.27, 34.58, 24.90, 23.95, 23.72 (cyclohexyl).
Anal.: Calcd. for $C_{13}H_{19}O_5N_3$: C, 52.52; H, 6.44; N, 14.13; found: C, 52.81; H, 6.45; N, 14.05.

Typical procedure for the preparation of sugar bromoimines from glycosyl azides. a) in boiling carbon tetrachloride: A mixture of protected glycosyl azide (1mmol) and *N*-bromosuccinimide (2.5 to 4 mmol) in carbon tetrachloride (40 mL) was refluxed with a tungsten lamp (250 W) for a few minutes, whereupon TLC monitoring showed the disappearance of the substrate and the formation of a new spot, sligtly more polar and visible under UV light on TLC plates. Completion of the reaction also coincided with the development of a faint-brown colour. After immediate cooling, the insoluble residues were filtered off, rinced with carbon tetrachloride (10 mL). After washing twice the organic phase with water and drying (Na_2SO_4), the solvent was removed in vacuo at <20°C or lower to yield the corresponding bromoimino lactone derivative as an almost pure oil. *b) at ~30 - 40°*: A stirred reaction mixture, prepared as before, was exposed to bright sunlight or irradiated with a 60W tungsten lamp placed within a short distance (~10 cm). After a variable delay (~30 to 60 min), complete transformation of the substrate occurred rapidly, as shown by TLC monitoring to give a brownish solution which was treated as indicated before. Except for **34**, the oily glycosyl bromoimines thus obtained were not completely characterized due to the presence of traces of impurities which could not be removed by column chromatography. Such attempted purifications resulted in the decomposition of the products, from which small amounts of the corresponding lactones could be recovered. Compound **34** gave colourless prisms from diethyl ether-petroleum ether; mp: 105-106°C; $[\alpha]_D$ -95° c = 0.6 chloroform; IR: ν C=N: 1643 cm^{-1}, ν C=O: 1740 cm^{-1}; MS ei : m/z: 309 (5%), 307 (4%), $[M]^+$; 294 (8%), 292 (8%), $[M\text{-}CH_3]^+$; 214 (12%), $[M\text{-}CH_3\text{-}Br]^+$.
Anal.: Calc. for $C_{10}H_{14}BrNO_5$: C, 38.98, H, 4.58, Br, 25.93, N, 4.55, O, 25.96; found: C, 38.94, H, 4.64, Br, 25.24, N, 4.60, O, 26.06.
In the IR spectra, the ν C=N absorptions were found at: 1638 (**28**, **29**), 1625 (**30**), 1634 (**32**), 1648 (**33**), 1644 (**35**, **36**) and 1650 (**37**) cm^{-1}. Compound **29** crystallized from diethyl ether-petroleum ether (mp: 108-109°C) and showed the following optical rotation: $[\alpha]_D$ +37° (c = 0.5 chloroform). A solution of compound **30** in absolute ethanol showed the following UV absorptions (λ_{max}, ε): 205.6 nm, 4200; 266.0 nm, 1300. The ei mass spectrum of **35** showed the following peaks: m/z: 292, 290 (0.2%), $[M]^+$; 277, 275 (3%), $[M\text{-}CH_3]^+$.

Competitive free-radical bromination of azides **14**, **15**, **19** and **20**. 1/1 Mixtures (24 mg, 0.064 mmol) of tested azides (**14/15**, **14/19**, **14/20** and **19/20**) were stirred in dry CCl_4 (2.5 mL) in the presence of NBS (46 mg, 0.257 mmol) in a vessel maintained at ~4 cm of a 60 W tungsten lamp. Progress of the reactions was monitored by TLC (solvent: diethyl ether-petroleum ether 2:1 v/v). Complete conversion of compounds **20**, **14** and **19** occurred within ~20, ~30 and~60 min, respectively whereas **15** was still present after 2.5 h.

2,3,4,6-Tetra-O-benzyl-D-glucono-1,5-lactone **38**. This compound was prepared according to reference 40. ^1H NMR ($CDCl_3$, 300 MHz): 7.16 to 7.38 (m, 20H, phenyl); 4.98 (d, 1H, J 11.4); 4.73 (d, 1H, J 11.3); 4.70 (d, 1H, J 11.2); 4.63 (d, 1H, J 11.4); 4.59 (d, 1H, J 11.9); 4.56 (d, 1H, J 12.0); 4.51 (d, 2H, J 10.7): 8 benzylic protons; 4.45 (m, 1H, $J_{5,6}$ 2.4, H-5); 4.12 (d, 1H, $J_{2,3}$ 6.6, H-2); 3.95 (t, 1H, $J_{4,5}$ 7.0, H-4); 3.91 (t, 1H, $J_{3,4}$ 6.5 H-3); 3.73 (dd, 1H, $J_{5,6'}$3.3, H-6); 3.66 (dd, 1H, $J_{6,6'}$ 11.0, H-6'); ^{13}C NMR ($CDCl_3$, 75 MHz): δ: 169.31 (C-1); 137.56, 137.50, 137.47, 136.91 (4 aromatic C, *ipso*); 128.45, 128.41, 128.37, 128.08, 127.98, 127.95, 127.91, 127.80 (20 aromatic C-H); 80.89, 78.13, 76.03, 77.36 (C-2 to C-5); 68.22 (C-6).

Crystal data: $C_{10}H_{14}BrNO_5$, M=308.1, orthorhombic, space group $P2_12_12_1$, a=8.722(2), b=8.754(2), c=33.519(8) Å, V=2559(2) $Å^3$, Z=8, D_c=1.600 $g.cm^{-3}$. The asymmetric unit includes two molecules. Data were collected on a Nonius CAD4 diffractometer. Of 2540 unique reflections measured (2θ max=146°, μ(CuKα)=49.5 cm^{-1}, T=295 K), 2170 had $I > 3\sigma(I)$ and were used for all calculations with the Structure Diffraction Package[41]. During the data collection, the intensity of the three standard reflections decreased gradually by 28 %. The decay procedure was used to correct this problem. The hydrogen atoms were not located. The final refinement gave R=0.080. The two molecules of the asymmetric unit show the same conformation. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

Table 4: ^{1}H NMR data[a] for compounds **28** - **30** and **32** - **37**.

Compounds	H-2 *J2,3*	H-3 *J3,4*	H-4 *J4,5*	H-5 *J5,6*	H-6 *J5,6'*	H-6' *J6,6'*	$CH_3C{=}O$	CH_3	Other protons
28	5.63 *4.3*	5.24 *~5*	5.18 *9.5*	4.67 *~3.5*	4.40 *~3.5*	4.40 *b*	2.17, 2.15 2.10, 2.10		
29	6.18, d 5.0	5.89, m *b*	5.89, m *9.0*	5.13, m *2.9*	4.91, dd *4.9*	4.70, dd *12.64*			7.23 - 8.06, m, 20H aromatic
30 C_6D_6	4.15, d *1.3*	~3.5, m *b*	~3.5, m *9.5*	4.60, dt *~2.5*	~3.5, m *~3.5*	~3.5, m *b*		3.24, 3.14, 3.02, 2.92 4s, 12H	
30	4.20, d *2.3*	3.75, m *b*	3.75, m *10.0*	4.55, dq *4.0*	~3.55 *2.6*	~3.55 *b*		3.52, 3.47, 3.44, 3.41 4s, 12H	
32	5.94, d *3.6*	5.34, t *4.1*	5.16, dd *7.4*	4.52, m *b*	4.39, m *b*	4.39, m *b*	2.16, 2.15 2.14, 2.12		
33	5.19, d *5.4*	4.98, dd *3.0*	4.50, m *b*	4.50, m *b*	4.16, m *b*	4.16, m *b*		1.48, 1.47, 1.42, 1.41 4s, 12H	
	H-2 *J2,3*	H-3 *J3,4*	H-4 *J4,5*	H-5 *J4,5'*	H-5' *J5,5'*				
34 C_6D_6	4.89, d *5.7*	4.14, d *~0*	4.30, m *2.7*	3.49, dd *3.1*	3.88, dd *12.5*		1.48, s	1.15, s; 1.32, s	
34	5.14, d *5.7*	4.83, d *~0*	4.90, m *2.5*	4.23, dd *3.0*	4.44, dd *12.5*		2.09, s	1.40, s; 1.49, s	
35	5.18, d *5.8*	4.77, d *~0*	4.82, m *2.8*	3.81, m *3.1*	3.60, m *13.5*			1.39, s; 1.48, s	
36	5.37, d *5.7*	4.69, d *~0*	4.75, br. s *2.4*	3.72, dd *1.7*	3.0, dd *10.8*			1.47, s; 1.36, s	7.20 - 7.39, m, 15H, aromatic
37	5.13, d *5.7*	4.81, d *~0*	4.90, m *2.6*	4.23, dd *3.0*	4.43, dd *12.4*		2.08, s		1.40 - 1.66, m, 10H cyclohexyl

[a] - The spectra were recorded at 200 MHz for $CDCl_3$ solutions, unless otherwise indicated, using TMS as the internal reference. [b] - not determined.

Table 5: ^{13}C NMR data[a] for compounds **28** - **30** and **32** - **37**.

Compounds	C-1	C-2	to		C-5	C-6	C=O	CH_3	Other carbons
28	161.58	75.84	71.38	68.38	68.27	61.17	170.35, 169.06 169.06, 168.15	20.66, 20.60 20.54	
29	161.74	77.00	70.64	68.34	68.30	62.54	165.88, 164.71 164.52, 164.06		b
30 C_6D_6	164.59	79.00	78.18	77.26	82.82	70.58		59.69, 57.99 56.90, 56.77	
32	160.72	77.03	69.40	67.80	66.15	61.88	170.01, 168.93 168.82, 168.77	20.52, 20.49 20.47, 20.38	
33	170.84	82.27	78.71	78.22	72.62	66.16		26.88, 26.80 25.94, 25.28	114.81, 109.86
34 C_6D_6	169.19	84.16	80.99	78.06	63.26		171.65	26.85, 25.83 19.86	113.86
35	171.10	85.08	81.05	77.69	52.52			26.69, 25.62	114.20
36[c]	172.31	81.51	78.43	86.35	63.50			26.84, 25.79	113.74
37	169.83	84.38	80.35	77.41	63.49		171.41	20.62	115.10, 36.38, 35.14 24.74, 23.80, 23.71

[a] - The spectra were recorded at 50 MHz for $CDCl_3$ solutions, unless otherwise indicated, using TMS as the internal reference.

[b]- Other resonances: 129.22, 128.49, 128.31, 128.18 (4C ipso); 134.01, 133.84, 133.84, 133.36, 130.12, 129.98, 129.85, 129.78 (16C, ortho, meta); 128.69, 128.57, 128.50, 128.44 (4C, para). [c]- Other resonances: 87.82 ($C\Phi_3$); 127.41 (3C, para); 128.20 (6C); 128.51 (6C); 142.96 (3C, ipso).

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