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## Preparation and Photolysis of 1-Cyano-glycopyranosyl Azides

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Abstract: Treatment of 1-bromo-glycopyranosyl cyanides 1 and 4 with sodium azide in dimethyl sulfoxide gave 1-cyano-glycopyranosyl azides 2 and 5 in high yield, which on photolysis resulted in new oxazepine derivatives 3 and 6.

In the course of our ongoing interest in the preparation of novel structures based on anomerically bifunctional monosaccharide derivatives, we described the synthesis of 1-bromo-glycopyranosyl cyanides<sup>1</sup> and chlorides<sup>2</sup> by radical-mediated brominations.<sup>3</sup> Transformations of the first of these compounds with several nucleophiles such as acetate<sup>4</sup>, thiolates<sup>5</sup>, cyanide<sup>6</sup>, bromide<sup>7</sup> and alcohols<sup>8</sup> have been reported, while the latter ones gave access to anomeric diazides<sup>9</sup>, dihalides<sup>2</sup> and ortholactones.<sup>10</sup> On the other hand, we also prepared unprecedented derivatives by radical-mediated bromination<sup>3</sup> of glycosyl azides<sup>11</sup> to give bromoglycosylimines.<sup>12</sup> Photolytic transformations of anomeric diazides gave glycosylidene-spirocyclopropanes<sup>13</sup> and tetrazolo-oxazepine derivatives<sup>14</sup> while ring-expanded heterocycles were obtained from methyl 1-azido-D-glucopyranosides<sup>15</sup> by stereocontrolled rearrangements.

In this letter, we wish to report on the facile synthesis of 1-cyano-glycopyranosyl azides as well as their photolysis resulting in new oxazepine derivatives.

The reaction<sup>16</sup> of the 1-bromo-glycopyranosyl cyanides 1 and 4 with two equivalents of sodium azide in dimethyl sulfoxide at room temperature proved to be an unexpectedly fast (~5 min) and clean transformation to give 2 and 5, respectively. The raw products, obtained in more than 90 % yields, contained no by-products as shown by <sup>1</sup>H NMR. This reveals that the known 1,3-dipolar cycloaddition of azide ions to the cyano group<sup>17</sup> must be subordinate under the applied conditions and short reaction time.

Infrared spectra showed bands for an azido group (v N<sub>3</sub>: 2134 cm<sup>-1</sup> for 2, 2130 cm<sup>-1</sup> for 5), but not for a cyano group in keeping with the absence of such bands in the IR spectra of glycopyranosyl cyanides.<sup>18</sup> The compounds existed in the conformations depicted ( ${}^{4}C_{1}$  for 2,  ${}^{1}C_{4}$  for 5) as judged from the  ${}^{3}J_{H,H}$  couplings in the proton spectra. The anomeric configuration was deduced from the  ${}^{3}J_{H-2,CN}$ couplings (6.6 Hz for 2, 7.0 Hz for 5) which unambiguously indicated the *trans*-diaxial arrangement for the nuclei involved.<sup>1,7</sup>



i: NaN<sub>3</sub> (2 eq.), DMSO, r.t., 5 min. ii: hv, C<sub>6</sub>H<sub>6</sub>, ~3 h.

Photolysis<sup>19</sup> of the 1-cyano-glycopyranosyl azides 2 and 5 was carried out in benzene at room temperature. In both cases, the formation of two products was indicated by TLC. Proton spectra for the raw mixtures showed the presence of one major product in ~60 % ratio. This was easily isolated by column chromatography, but the other component of the reaction mixture could not be recovered from the column.

The structure of compound 6 obtained from 5 was established by X-ray crystallography.<sup>20</sup> An analogous structure for 3 was suggested by the similarities in chemical shifts and coupling constants in both <sup>1</sup>H and <sup>13</sup>C NMR spectra of 3 and 6. In addition, a 2D heteronuclear multi-bond correlation (HMBC, HMQC) recorded for 3 showed couplings between H-2 and H-5 (according to parent sugar numbering) and the  $sp^2$  hybridized carbon atom, as also observed for a structurally analogous sugar-tetrazole derivative.<sup>14</sup> From heteronuclear O.e. measurements, it was deduced that the  $sp^2$  carbon was at about the same distance from both H-2 and H-5 (~13 % and ~20 % enhancements, respectively).

The isolated yields (50 % for 3, 58 % for 6) suggested that in these reactions, migration of C-2 (b) in the intermediate nitrene is preponderant over the two other possibilities (a, c). This selectivity resemble closely that observed for the photolysis of anomeric diazides<sup>14</sup> whereas, for analogous methyl 1-azidoglucopyranosides,<sup>15</sup> the migration of the other anomeric linkages (a and c, MeO instead of CN) were more effective or comparable, respectively, to that of C-2. In keeping with our previous observations,<sup>14,15</sup> migration of C-2 occurred with retention of configuration as it could be judged from the crystallographic data as well as the  ${}^{3}J_{\rm H,H}$  couplings.



In conclusion, the easily accessible 1-cyano-glycopyranosyl azides represent a new class of anomerically disubstituted sugar derivatives. Our preliminary results show that they are suitable models for studying stereoselective rearrangements of nitrenes<sup>21</sup> attached to the anomeric centre. The observed possibility<sup>22</sup> for the transformation of either of the anomeric substituents by 1,3-dipolar cycloadditions make these compounds good precursors for novel C- and N-glycopyranosyl derivatives having a disubstituted anomeric centre, possibly with interesting biological effects. Studies in this direction as well as to clear more details of the photolytic rearrangements are in progress.

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- 16. Procedure for the preparation of 1-cyano-glycopyranosyl azides: Sodium azide (2 mmol) was dissolved in dimethyl sulfoxide (10 mL) and a solution of either 1-bromo-glycopyranosyl cyanide 1 or 4 (1 mmol) in dimethyl sulfoxide (5 mL) was added in one portion. After 5 min, the mixture was diluted with water, and extracted four times with diethyl ether. The ethereal phase was washed with water, then dried and concentrated to a syrup, which crystallized on addition of absolute ethanol to give 2 [75 %; mp: 77-79 °C;  $[\alpha]_D + 97$  (c = 1.6, CHCl3)], or 5 [80 %; mp: 82-83 °C;  $[\alpha]_D - 153$  (c = 1.6, CHCl3)], respectively.
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- Photolysis of 1-cyano-glycopyranosyl azides: A solution of 2 or 5 (0.274 mmol) in benzene (7 mL) 19. in a quartz tube was placed at a 1 cm distance from a 450 W Hanovia medium pressure mercury arc lamp. Irradiation (no filter) resulted in gas evolution and TLC monitoring showed the replacement of the starting material by two new spots during 3-4 hours. Separation by silica gel column chromatography gave as the less polar fraction 3 [50 %; mp: 96-98 °C;  $[\alpha]_D$  +96 (c = 1.3, CHCl3)]

or 6 [58 %; mp: 98-99 °C;  $[\alpha]_D$  -150 (c = 0.35, CHCl<sub>3</sub>)], respectively. The more polar fraction observed on the TLC plates could not be eluted from the column.

Crystal data: C12H14N2O7, M=298.2, monoclinic, space group P21, a=12.099(3), b=8.368(5), 20. c=20.780(3) Å,  $\beta$ =134.62(1)°, V=1497(1) Å<sup>3</sup>, Z=4, D<sub>c</sub>=1.324 g.cm<sup>-3</sup>. Data were collected on a Nonius CAD4 diffractometer. Of 3123 unique reflections measured ( $2\theta \max = 146^\circ$ ,  $\mu(CuK\alpha) = 9.6 \text{ cm}^{-1}$ ), 2753 had I >  $3\sigma(I)$  and were used for all calculations with the Structure Diffraction Package<sup>23</sup>. The hydrogen atoms of the heterocycle were set at the theoretical positions and their coordinates were not refined. The hydrogen atoms of the methyl groups were not considered for the calculations. The final refinement gave R=0.059 and Rw=0.063. The asymmetric unit included two molecules which showed the same configuration and quite similar conformations. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. Following the numbering shown on the PLUTO<sup>24</sup> drawing below, the bond distances in Å (e.s.d.) of the two independent molecules are respectively: 01-C1: 1.339(7), 1.327(7), 01-C5: 1.454(9), 1.470(9), 02-C2: 1.451(6), 1.457(5), 02-C7: 1.349(8), 1.343(8), O3-C7: 1.18(1), 1.20(1), O4-C3: 1.428(6), 1.439(6), O4-C9: 1.38(1), 1.350(9), O5-C9: 1208(8), 1248(8), O6-C4: 1441(9), 1423(8), O6-C11: 1361(8), 1362(8), O7-C11: 1200(9), 1.188(9), N1-C1: 1.258(4), 1.266(4), N1-C2: 1.446(7), 1.437(7), N2-C6: 1.13(1), 1.12(1), C1-C6: 1.45(1), 1.45(1), C2-C3: 1.52(1), 1.507(9), C3-C4: 1.509(7), 1.532(6), C4-C5: 1.520(6), 1.497(6), C7-C8: 1.507(9), 1.500(8), C9-C10: 1.540(8), 1.524(9), C11-C12: 1.52(1), 1.55(1). The bond angles in degrees (e.s.d.) are: C1-O1-C5: 122.4(4), 118.9(5), C2-O2-C7: 115.1(5), 114.7(5), C3-O4-C9: 116.0(4), 118.0(4), C4-O6-C11: 117.0(5), 117.5(5), C1-N1-C2: 126.3(6), 123.8(6), O1-C1-N1: 135.6(7), 132.5(6), O1-C1-C6: 107.9(4), 111.6(4), N1-C1-C6: 116.5(6), 115.8(6), O2-C2-N1: 104.4(5), 104.5(5), O2-C2-C3: 106.8(5), 106.2(5), N1-C2-C3: 117.2(4), 115.4(4), O4-C3-C2: 103.7(4), 105.1(4), O4-C3-C4: 109.0(5), 108.3(5), C2-C3-C4: 111.4(5), 111.8(5), O6-C4-C3: 110.7(4), 110.9(4), O6-C4-C5: 108.0(5), 109.0(5), C3-C4-C5: 113.9(6), 114.2(5), O1-C5-C4: 114.8(5), 115.1(4), N2-C6-C1: 176.9(9), 176.4(9), O2-C7-O3: 124.0(5), 122.2(4), O2-C7-C8: 110.6(6), 112.1(6), O3-C7-C8: 125.4(6), 125.3(7), O4-C9-O5: 121.4(5), 120.9(5), O4-C9-C10: 109.7(6), 111.5(6), O5-C9-C10: 128.6(8), 127.3(8), O6-C11-O7: 122.7(7), 123.5(7), O6-C11-C12: 110.5(6), 109.9(6), O7-C11-C12: 126.8(7), 126.5(7).



PLUTO<sup>24</sup> drawing of compound 6 showing the numbering scheme.

- 21. Investigations aiming at a more precise knowledge of the transient species (see ref. 14 and 15) are in progress.
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