Tetrahedron Letters, Vol. 35, No. 1, pp. 89-92, 1994
Printed in Great Britain

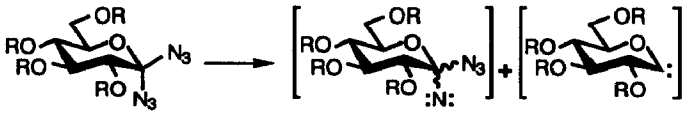
0040-4039/94 $6.00 + .00
Pergamon Press Ltd

Photolysis of Sugar Anomeric Diazides: Sugar-derived Tetrazoles as Evidences for a major Nitrene Decomposition Pathway

Jean-Pierre Praly[a]*, Carméla Di Stéfano[a], Gérard Descotes[a] and René Faure[b]
[a] *Laboratoire de Chimie Organique II associé au CNRS, ESCIL*
[b] *Laboratoire de Chimie Analytique II*
Université Claude-Bernard Lyon I, 43 Boulevard du 11 Novembre 1918
69622 Villeurbanne France

Abstract: The preponderance of regioisomeric sugar-derived tetrazoles (up to 75% total yield) obtained upon photolysis of protected (benzyl, acetyl) glucopyranosylidene diazides, even in the presence of added acrylonitrile, proved that azidonitrene intermediates predominate over anomeric carbenes, in the reaction. Revisions are presented for its mechanism and one structure.

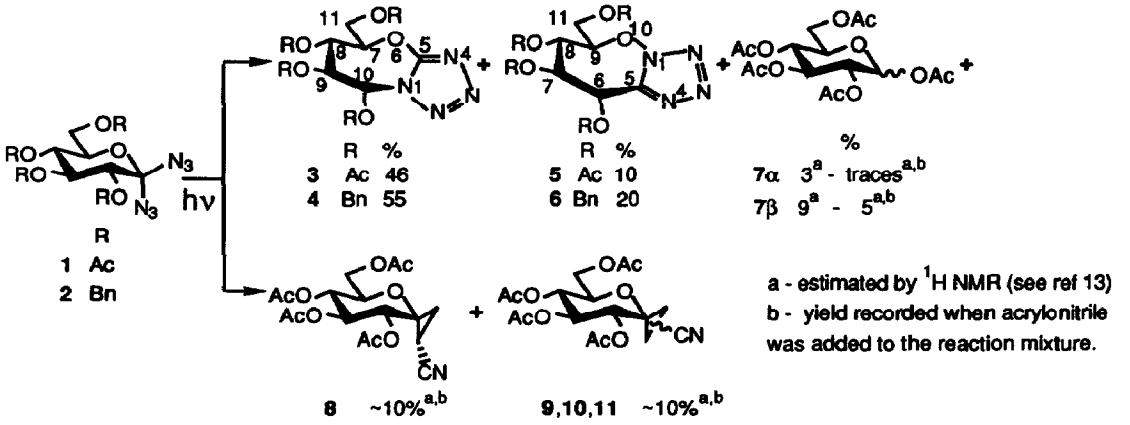
Since the synthesis of sugar anomeric diazides recently proposed by us[1], we have investigated the reactivity[2] of azido sugar derivatives and in particular their photolysis[3], under various conditions. The photolysis of azido derivatives devoid of anomeric hydrogen atom raised questions regarding the intimate decomposition pathway of the substrates, the structures of the products and their possible uses[4,5,6]. A preliminary study[7] showed that the photolytic decomposition of sugar anomeric diazides might occur via anomeric carbenes and via azidonitrenes since both spiro cyclopropanic sugars[8,9] and sugar-derived tetrazoles[9] have been observed among the products. Uncertainties pertaining to structural and mechanistic aspects have delayed the extensive publication of our work, so that the occurrence of the tetrazoles has been only briefly mentioned[9,10]. Now, these questions have been unambiguously answered and since a note on the same approach appeared recently[11], we herein describe our observations on the photolysis of acetylated or benzylated sugar anomeric diazides, in order to clarify the importance of the identified decomposition pathways (scheme below) and the structures of the nitrogen-containing products.



Solutions of the diazides **1** or **2**[12] (103 mg, 0.25 mmol) in benzene (10 mL) were irradiated with a medium pressure mercury lamp (Hanovia, 450 W) using quartz tubes (1 cm external diameter) close to the lamp device (~1 cm). Solutions containing acrylonitrile (11 eq) were also submitted to photolysis. Irradiation was continued until TLC monitoring showed the disappearance of the starting material (5-6 h). After solvent removal under reduced pressure, the crude reaction mixture was examined by ^{1}H NMR to estimate the product distribution[13]. Afterwards, the mixture was resolved by column chromatography (Silica gel 60, Merck) using ethyl acetate-*n*-hexane 4:6 v/v (acetylated series) or 3:7 v/v (benzylated series).

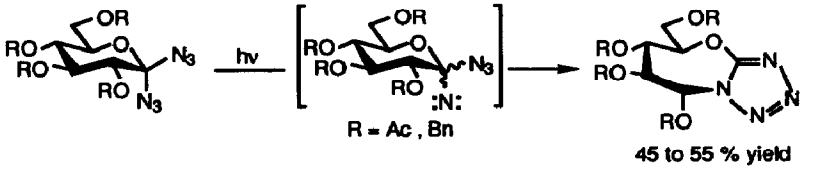
TLC and ^{1}H NMR examination of the reaction mixture resulting from the photolysis of the acetylated diazide **1** indicated the formation of five products of which four could be identified. The major ones were characterized as the sugar-derived tetrazoles **3** and **5**[12] (isolated yield: 46, 10% respectively) whereas the minor ones turned out to be the α and β anomers of peracetylated D-glucopyranose (~10 %)[13,14] plus an unidentified trace compound. Addition of acrylonitrile to the solution led to a complex mixture made of the aforementioned

tetrazoles and the spiro cyclopropanic sugars already characterized[8,9]. Under these conditions, the tetrazole content remained unchanged while the penta-O-acetyl-D-glucopyranoses are somewhat less abundant (7α: traces, 7β: ~5%). The spiro cyclopropanic sugars *which only amount to ~20 %* of the mixture were not equally distributed since only the H-5 proton of **8** (~10 %) appeared as a well-resolved, characteristic signal at 4.02 ppm in the ^{1}H NMR spectrum[13]. Addition of acetophenone (5×10^{-3} M) as a triplet sensitizer[15] or use of a Pyrex filter has no significant effect on the product distribution. When using the perbenzylated diazide **2**, the reaction mixtures were essentially made of two products as shown by ^{1}H NMR, which were characterized as the tetrazoles **4** and **6**[12] (55 and 20 % isolated yield[7]). Performing the photolysis in the presence of acrylonitrile did not lead to the formation of the expected spiro adducts in observable amounts (^{1}H NMR), as noted earlier[9].



Although the presence of a tetrazole ring in products **3-6** was easily detected (combustion analysis, MS), unambiguous assignment of the structures was not straightforward, in the absence of known related compounds. Fortunately, the minor acetylated tetrazole crystallized as colourless prisms suitable for X-ray crystal analysis. The PLUTO[16] drawing obtained for **5** clearly showed the N-1—O-10 linkage and the expected antiperiplanar orientation of protons H-(C-6) and H-(C-7) which correspond to a ^{3}J coupling equal to 7.4 Hz in the ^{1}H NMR spectrum. The ^{3}J coupling (5.0 Hz) measured for the same segment in **3** is compatible with a *trans* relationship of the corresponding protons, as a result of the retention of configuration of the migrating carbon[3]. Interruption of the carbon chain in **3** is confirmed by the observed long-range heteronuclear couplings. As compared to **3** and **5**, the benzylated analogs **4** and **6** obtained from **2** showed similar homonuclear couplings [**4**: $^3J_{9,10}$ 3.9 (4.58[11]) Hz; **6**: $^3J_{6,7}$ 6.6 Hz] and comparable NMR spectra. In particular, the large shielding of the sp^2 C-5 carbon atom in **5** and **6**, as compared to their counterparts in **3** and **4** can be better reconciled with regioisomeric structures rather than stereoisomers as proposed by Yokoyama *et al.*[11,17]. Comparison of our NMR data with those reported[11] clearly shows that the same compounds have been isolated, in comparable yield. Our spectroscopic data show, however, that they correspond to *D-gluco* configurated derivatives of tetrahydroxy-6-oxa- (major, somewhat less stable, more polar) and 10-oxa- (minor) 1,5-pentamethylenetetrazole. Accordingly, deacetylation (Zemplen conditions) of **3** and **5** gave polar compounds which, only in the case of **5**, could be assigned by NMR as the corresponding deacetylated bicyclic tetrazole. Hence, both spectroscopic data and deacetylation reactions proved that Yokoyama *et al.* erroneously assigned the structure of the minor benzylated tetrazole[17].

Although uncertainties remain as regard to the precise decomposition pathways of the studied diazides, it is probable that the tetrazoles originated from favoured azidonitrene intermediates, whatever the protecting groups in the substrates. These transcients triggered 1,2-shifts (migration of either the C-2 carbon or the O-5 oxygen[3], mainly) yielding imidoylazide intermediates prone to spontaneous heterocyclization[4]. This azidonitrene pathway appeared somewhat enhanced in the case of the benzylated compound **2**. At variance with preliminary reports[7,8,9], spirocyclopropanic sugars formed in low yield from **1** only (acetylated series) when photolysed in the presence of acrylonitrile. Hence, photolysis of glucopyranosylidene diazides, in our conditions, *is not efficient as regard to anomeric carbenes generation.* However, this approach constitutes an unprecedented access to new, fully characterized, regioisomeric sugar-derived tetrazoles via stereocontrolled rearrangements, as disclosed in the next paper.



References and notes:

1. Praly, J.-P.; El Kharraf, Z.; Descotes, G. *J. Chem. Soc., Chem. Commun.*, **1990**, 431-432.
2. Praly, J.-P.; Di Stéfano, C.; Somsàk. L.; Descotes, G. *J. Chem. Soc., Chem. Commun.*, **1992**, 200-201.
3. Di Stéfano, C.; Descotes, G.; Praly, J.-P. *following paper.*
4. Butler, R. N. *"Comprehensive Heterocyclic Chemistry"* Katritzky, A. R.; Rees, C. W., Eds, Vol 5, Pergamon Press, Oxford, 1984, pp. 791-838.
5. Buchanan, J. G.; Clelland, A. P. W.; Johnson, T.; Rennie, R. A. C.; Wightman, R. H. *J. Chem. Soc., Perkin Trans. 1*, **1992**, 2593-2601.
6. Ermert, P.; Vasella, A. *Helv. Chem. Acta*, **1991**, *74*, 2043-2053.
7. El Kharraf, Z. *PhD Thesis*, Lyon, **1990**, n° 137-90.
8. Praly, J.-P.; El Kharraf, Z.; Descotes, G. *Tetrahedron Lett*, **1990**, *31*, 4441-4442.
9. Descotes, G.; El Kharraf, Z.; Faure, R.; Fenet, B.; Praly, J.-P. *J. Carbohydr. Chem.*, **1991**, *10*, 959-968.
10. Descotes, G. *"Carbohydrates: Synthetic Methods and Applications in Medical Chemistry"*, Ogura H.; Hasegawa, A.; Suami, T.; Eds, Kodansha, VCH, Tokyo, New-York, **1992**, pp. 89-96.
11. Yokoyama, M.; Matsushita, M.; Hirano, S.; Togo, H. *Tetrahedron Lett.*, **1993**, *34*, 5097-5100.
12. ^{1}H NMR data [300 MHz (**1**, **2**, **4**, **5**, **6**), 200 MHz (**3**), $CDCl_3$, δ (ppm/TMS), J (Hz)]: **1**: 2.00, 2.04, 2.11, 2.12 (4s, 12H, acetyl), 4.17 (m, 1H, $J_{5,6}$ 4.6, H-5), 4.18 (dd, 1H, $J_{6,6'}$ 12.7, H-6'), 4.28 (dd, 1H, $J_{5,6'}$ 2.1, H-6), 5.16 (t, 1H, $J_{4,5}$ 9.6, H-4), 5.23 (d, 1H, $J_{2,3}$ 9.9, H-2), 5.37 (t, 1H, $J_{3,4}$ 9.6, H-3); **2**: 3.65 (d, 1H, $J_{2,3}$ 9.1, H-2), 3.72 (dd, 1H, $J_{6,6'}$ ~11, H-6'), 3.73 (t, 1H, $J_{4,5}$ ~9.5, H-4), 3.75 (dd, 1H, $J_{5,6'}$ ~1.5, H-6), 3.83 (t, 1H, $J_{3,4}$ ~9.5, H-3), 3.87 (m, 1H, $J_{5,6}$ ~3, H-5), 4.52, 4.55, 4.61, 4.76, 4.79, 4.81, 4.87, 4.95 (8d, $CH_2C_6H_5$), 7.2 to 7.4 (m, 20H, aromatic); **3**: 2.04, 2.14, 2.15, 2.23 (4s, 12H, acetyl), 4.34 (dd, 1H, $J_{11,11'}$ 13.2, H-11'), 4.42 (dd,1H, $J_{7,11'}$ 2.8, H-11), 5.03 (ddd,1H, $J_{7,11}$ 5.0, H-7), 5.39 (dt, 1H, $J_{7,8}$ 10.5, $J_{8,10}$ 0.8, H-8), 5.49 (dd, 1H, $J_{8,9}$ 1.25, H-9), 7.24 (dd, 1H, $J_{9,10}$ 5.0, H-10); **4**: 3.87 (m, 2H, $J_{7,11}$=$J_{7,11'}$ 2.9, H-11, H-11'), 3.99 (dd, 1H, $J_{8,9}$ 0.9, H-9), 4.16 (dd, 1H, $J_{7,8}$ 10.2, H-8), 4.24, 4.31, 4.41, 4.47, 4.58, 4.67, 4.68, 4.84 (8d, 8H, Jgem 11.6 to 12.4, $CH_2C_6H_5$), 4.87 (m, 1H, H-7), 5.84 (d, 1H, $J_{9,10}$ 3.9, H-10), 7.0 to 7.36 (m, 20H, aromatic); **5**: 2.08, 2.09, 2.15, 2.22 (4s, 12H, acetyl), 4.34 (dd, 1H, $J_{9,11'}$ 2.0, H-11), 4.40 (dd, 1H, $J_{11,11'}$ 12.9, H-11'), 4.68 (m, 1H, $J_{9,11}$ 5.3, H-9), 5.44 (t, 1H, $J_{8,9}$ 6.9, H-8), 5.54 (t, 1H, $J_{7,8}$ 7.1, H-7), 6.39 (d, 1H, $J_{6,7}$ 7.4, H-6); **6**: 3.68 (dd, 1H, $J_{11,11'}$ 11.6, H-11'), 3.79 (dd, 1H, $J_{9,11}$ 5.3, H-11), 3.92 (dd, 1H, $J_{8,9}$ 7.6, H-8), 4.42, 4.49 (2H), 4.57, 4.66 (3H), 4.86 (d, 8H, Jgem ~11.5, $CH_2C_6H_5$), 4.11 (t, 1H, $J_{7,8}$ 6.0, H-7), 4.61 (m, 1H, $J_{9,11}$ 2.6, H-9), 5.04 (d, 1H, $J_{6,7}$ 6.6, H-6), 7.12 to 7.36 (m, 20H, aromatic); ^{13}C NMR data [75 MHz (**1**, **2**, **4**, **6**), 50 MHz (**3**, **5**)]: **1**: 20.29, 20.50, 20.50, 20.63 (C=OCH$_3$), 61.11 (C-6), 67.55, 70.77, 72.10, 72.13 (C-2 to C-5), 99.9 (C-1), 169.04, 169.32, 169.81, 170.49 (C=OCH$_3$); **2**: 67.80 (C-6), 73.49, 75.17, 75.67, 75.96 (CH$_2$C$_6$H$_5$), 75.28, 76.85, 82.77, 84.14 (C-2 to C-5), 101.59 (C-1), 127.76, 127.84, 127.89, 127.91, 128.03, 128.23, 128.48 (aromatic C-H), 137.41, 138.00, 138.02, 138.32 (aromatic); **3**: 20.33, 20.45, 20.55, 20.63 (C=OCH$_3$), 62.08 (C-11), 69.20 (C-9), 69.86 (C-8), 76.00 (C-10), 80.84 (C-7), 161.95 (C-5), 167.39, 168.25, 168.38, 170.39 (C=OCH$_3$). The following heteronuclear couplings (Hz) have been measured: 152, 153, 154, 171, 150 (^{1}J for C-7 to C-11), 3.0, 3.8 ($^3J_{C5,H7}$, $^3J_{C5,H10}$)

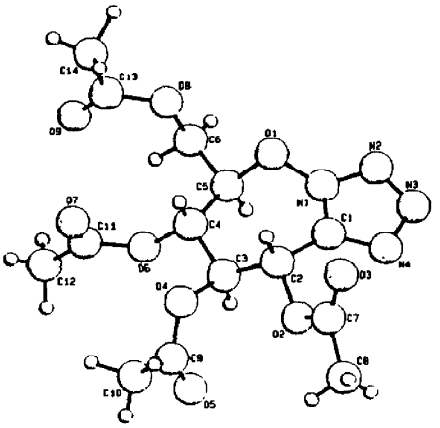
respectively; **4**: 68.6 (C-11), 76.90, 77.35, 83.54, 84.31 (C-7 to C-10), 71.5, 72.1, 72.8, 73.7 ($\underline{C}H_2C_6H_5$), 127.85, 127.90, 127.94, 128.15, 128.20, 128.35, 128.37, 128.45, 128.54, 128.63, 128.64, 131.42, 135.48, 136.15, 137.03, 137.62 (aromatic), 162.34 (C-5); **5**: 20.29, 20.34, 20.37, 20.53 ($C=O\underline{C}H_3$), 60.23 (C-11), 63.73, 68.78, 68.82, 86.86 (C-6 to C-9), 145.24 (C-5), 168.41, 168.50, 168.61, 170.13 ($\underline{C}=OCH_3$); **6**: 67.33 (C-11), 71.46, 76.45, 78.85, 89.34 (C-6 to C-9), 72.57, 73.59, 74.12, 74.46 ($\underline{C}H_2C_6H_5$), 127.92, 127.97, 128.01, 128.14, 128.19, 128.27, 128.53, 136.49, 137.00, 137.04, 137.14 (aromatic), 146.3 (C-5). Other data: **1**: syrup, $[\alpha]_D$ +141° (c = 0.6, chloroform); **2**: syrup, $[\alpha]_D$ +147° (c = 0.7, chloroform); **3**: syrup, $[\alpha]_D$ + 64° (c = 0.5 chloroform); MS FAB: *m/z* 387 $[M+1]^+$ 17 %; **4**: mp 113-114° (diethyl ether), $[\alpha]_D$ +71° (c = 0.5, chloroform); MS c.i. (isobutane) *m/z* 579 $[M+1]^+$ 3%; **5**: mp 137° (diethyl ether-petroleum ether), $[\alpha]_D$ +46° (c = 0.4, chloroform), MS c.i. (NH_3): *m/z* 387 $[M+1]^+$ 100%, 404 $[M+18]^+$ 13%; **6**: syrup, $[\alpha]_D$ +54° (c = 0.4, chloroform), MS c.i. (isobutane): *m/z* 579 $[M+1]^+$ 1%.

13. The product distribution was calculated by comparing the area of the doublets corresponding to the H-10 (**3**, **4**), H-6 (**5**, **6**), H-1 (**7**α: δ = 6.33, $J_{1,2}$ 3.7; **7**β: δ = 5.72 $J_{1,2}$ 7.9) and H-5 (**8**-**11**[9]) protons. For the acetylated series, the obtained figures were corrected by comparing the area of the deshielded acetyl resonances (**3**: δ = 2.23, **5**: δ = 2.22) with the total area of the acetyl resonances.

14. This is reminiscent of the formation of benzylated methyl D-glucopyranosides (~10%) in the glycosidation of methyl 4,6-O-benzylidene-α-D-altropyranoside with a benzylated diazirine (Bozo, E.; Vasella, A. *Helv. Chem. Acta*, **1992**, *75*, 2613-2633).

15. Albini, A.; Bettinetti, G.; Minoli, G. *J. Am. Chem. Soc.*, **1991**, *113*, 6928-6934.

16. Crystal data: $C_{14}H_{18}N_4O_9$, M = 386.3, orthorhombic, space group $P2_12_12_1$, a = 6.690(1), b = 12.199(2), c = 22.326(2) Å, V = 1822.2(7) $Å^3$, Z = 4, D_c = 1.409 $g.cm^{-3}$. Of 2110 unique reflections measured on a Nonius CAD4 diffractometer, 1894 had $I > 3\sigma(I)$ and were used for all calculations with the Structure Determination Package. The hydrogen atoms were found from ΔF syntheses and their coordinates were refined (R_{final} = 0.038 and R_w = 0.034). The dihedral angle between the two mean planes of the seven- and five-membered heterocycles is of 24.8(2)°. Following the atom numbering shown on the PLUTO drawing, torsion angles around the C-N ring junction are: N4-C1-N1-O1: -176.9°, C2-C1-N1-N2: 176.2°, N4-C1-N1-N2: -1.3°, C2-C1-N1-O1: 0.6°. Selected bond distances in Å (e.s.d.): O1-N1: 1.361(3), O1-C5: 1.467(3), N1-N2: 1.353(3), N1-C1: 1.326(4), N2-N3: 1.293(4), N3-N4: 1.369(4), N4-C1: 1.322(4), C1-C2: 1.497(4), C2-C3: 1.526(4), C3-C4: 1.520(4), C4-C5: 1.536(4), C5-C6: 1.511(4). Selected bond angles in degrees (e.s.d.): N1-O1-C5: 111.2(2), O1-N1-N2: 120.3(2), O1-N1-C1: 128.2(2), N2-N1-C1: 111.4(2), N1-N2-N3: 103.5(2), N2-N3-N4: 112.5(2), N3-N4-C1: 105.2(2), N1-C1-N4: 107.3(3), N1-C1-C2: 123.6(3), N4-C1-C2: 129.0(3), C1-C2-C3: 113.7(2), C2-C3-C4: 116.5(2), C3-C4-C5: 115.6(2), O1-C5-C4: 108.9(2). The structure parameters have been deposited at the "Cambridge Crystallographic Data Centre", U.K..



17. Besides the misleading interpretation of the NMR data (^3J couplings and δC-1) recorded for **4** and **6**, Yokoyama *et al.* proposed a mechanism for the ring expansions without supporting evidences and in contradiction with recent literature data (see discussion in ref. 3). The Beckmann rearrangement of (*Z*)-hydroximo sugar lactones[18] and the scope of the sugar diazide synthesis[1] are erroneously presented. Doubts exist on the structure of the product they obtained from **4** on debenzylation since assignment of the absolute configuration of the "hemiacetalic" C-10 carbon atom is not straightforward, as we observed in attempted deacetylations of **3**.

18. Beer, D.; Vasella, A. *Helv. Chim. Acta*, **1985**, *68*, 2254-2274.

(*Received in France* 21 *September* 1993; *accepted* 28 *October* 1993)