

Thermolysis and Photolysis of Sugar Diazides

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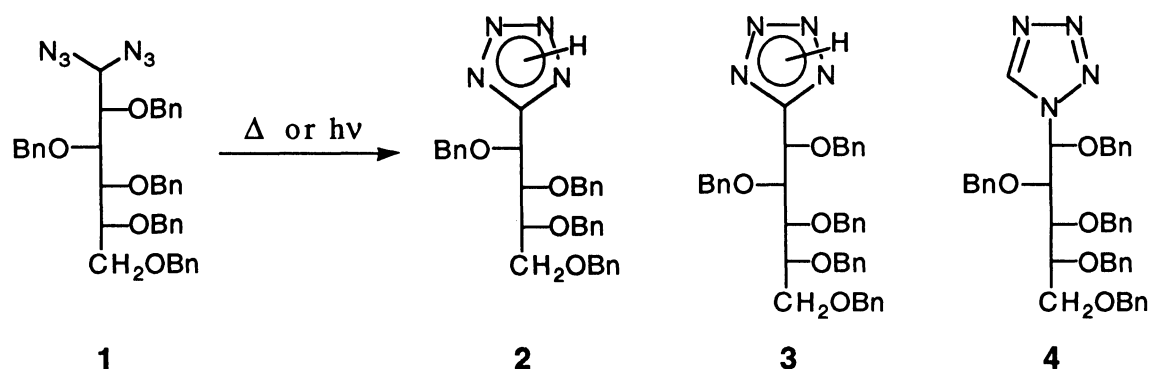
1,1-Diazido-2,3,4,5,6-penta-*O*-benzyl-D-glucose was refluxed in *o*-xylene under argon atmosphere to give 5-[(1'*R*,2'*S*,3'*R*-1',2',3',4'-tetrabenzoyloxy)butyl]tetrazole in a high yield *via* an unprecedented rearrangement with one carbon shortening of sugar skeleton. In contrast its photolysis afforded two tetrazoles caused by the rearrangements without one carbon degradation; 5-[(1'*S*,2'*R*,3'*R*,4'*R*-1',2',3',4',5'-pentabenzoyloxy)-pentyl]tetrazole and 1-[(1'*R*,2'*S*,3'*R*,4'*R*-1',2',3',4',5'-pentabenzoyloxy)pentyl]tetrazole.

Our investigation on sugar tetrazoles has shown that 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosylidene diazide is allowed to react in refluxing *o*-xylene to give the corresponding 7*R*,8*S*,9*S*,10*R*-8,9,10-tribenzoyloxy-7-benzoyloxymethyl-6-oxa-1,5-pentamethylenetetrazole *via* a ring-expansion in 82% yield.¹⁾ As the extension of our study toward the synthesis of biologically active tetrazoles, we applied this reaction to the synthesis of tetrazoles bearing acyclic sugar moiety. In this study we found a new type of rearrangement reaction and wish to present herein the structure determination of rearranged products and a plausible reaction mechanism.

1,1-Diazido-2,3,4,5,6-penta-*O*-benzyl-D-glucose **1**²⁾ of a starting compound was prepared by the following four steps: Dithioketal formation, benzylation, dithioketal cleavage,³⁾ and diazide formation of D-glucose.⁴⁾ 1,1-Diazido-2,3,4,5,6-penta-*O*-benzyl-D-mannose **5** and 1,1-diazido-2,3,4,5-tetra-*O*-benzyl-D-arabinose **6** were also prepared by the same method as mentioned above. The thermal reaction of **1** was carried out as follows: A mixture of **1** (60 mg, 0.085 mmol) and *o*-xylene (3 ml) was refluxed for 6 h under argon atmosphere. After the solvent was evaporated under reduced pressure, the resulting residue was purified by the preparative TLC on silica gel (eluent: hexane / ethyl acetate = 2 / 1) to give 5-[(1'*R*,2'*S*,3'*R*-1',2',3',4'-tetrabenzoyloxy)butyl]tetrazole **2**⁵⁾ as colorless needles (mp 155.0-155.5 °C) in 85% yield. The photochemical reaction of **1** was also performed as follows: A solution of **1** (130 mg, 0.186 mmol) in dichloromethane (10 ml) was irradiated with a high pressure mercury lamp (400 W) for 9 h at 30 °C. The resulting mixture was evaporated to give a yellow oil, which was then purified by the preparative TLC on silica gel (eluent: hexane / ethyl acetate = 2 / 1). 5-[(1'*S*,2'*R*,3'*R*,4'*R*-1',2',3',4',5'-Pentabenzoyloxy)pentyl]tetrazole **3**⁶⁾ and 1-[(1'*R*,2'*S*,3'*R*,4'*R*-1',2',3',4',5'-pentabenzoyloxy)pentyl]tetrazole **4**⁷⁾ were obtained as syrups in respective 29% and 22% yields together with the recovery **1** (6%).

Similarly, **5** was treated with the refluxing *o*-xylene to give **2** and 5-[(1'*R*,2'*S*,3'*R*,4'*R*-1',2',3',4',5'-pentabenzoyloxy)pentyl]tetrazole **7**⁸⁾ in 15% and 29% yields, respectively. As an extension to the pentoses, **6**

was refluxed in *o*-xylene for 11 h to afford 5-[(1'*S*,2'*R*-1',2',3'-tribenzyloxy)propyl]tetrazole **8**⁹⁾ in 54% yield.

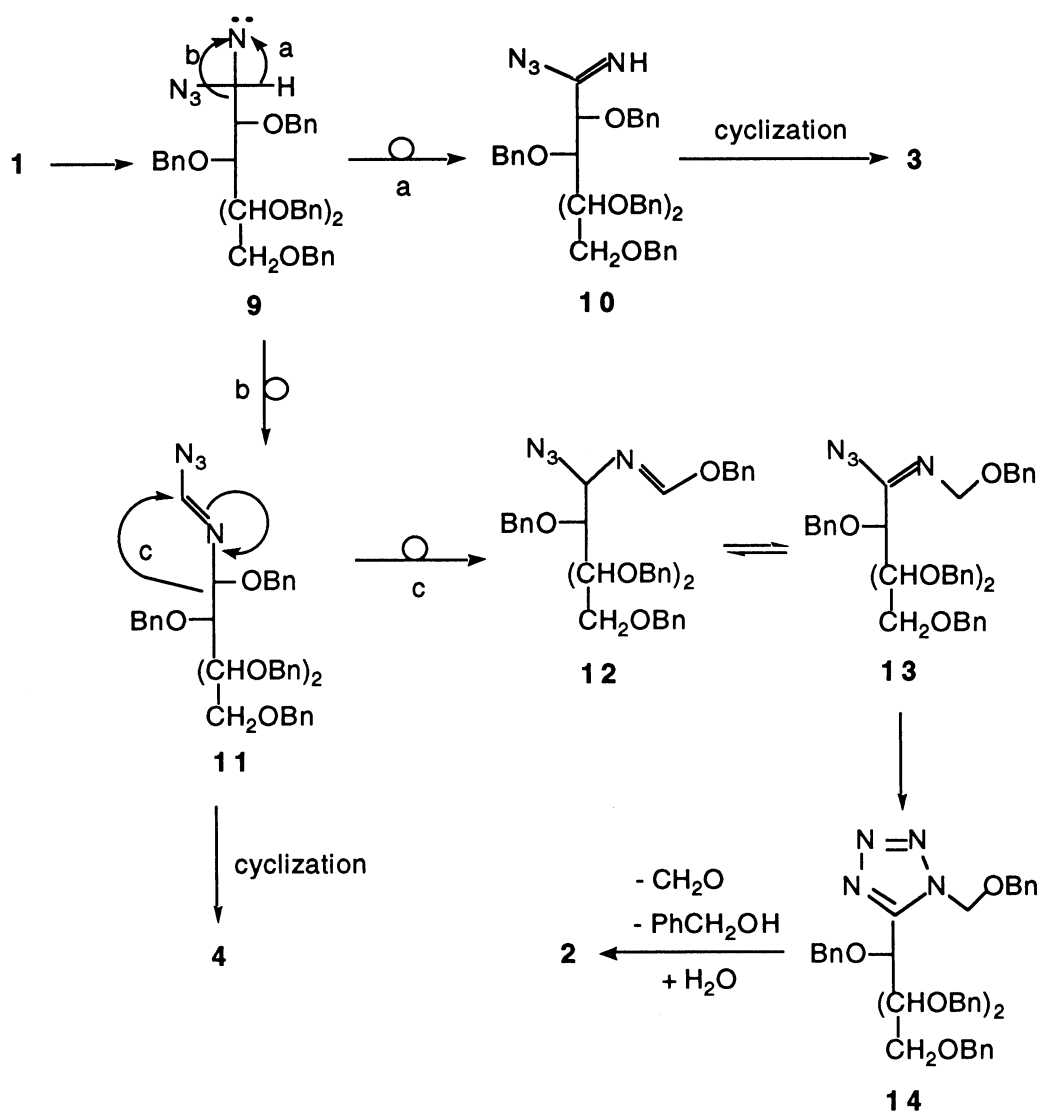


The structures of **2**, **3**, **4**, **7**, and **8** were determined by NMR and MS measurements together with elemental analysis: **2**: ¹³C-NMR (COSY), 155.3 ppm (Cq, 5-C); ¹H-NMR, 1.65 ppm (NH disappeared with D₂O); MS *m/z* (FAB), 551 (*M* + 1)⁺. **3**: ¹³C-NMR (COSY), 153.8 ppm (Cq, 5-C); ¹H-NMR, 1.60 ppm (NH disappeared with D₂O); MS *m/z* (FAB), 671 (*M* + 1)⁺. **4**: ¹³C-NMR (COSY), 142.4 ppm (Ct, 5-C); MS *m/z* (FAB), 671 (*M* + 1)⁺. **7**: ¹³C-NMR (COSY), 154.0 ppm (Cq, 5-C); ¹H-NMR, 1.67 ppm (NH disappeared with D₂O); MS *m/z* (FAB), 671 (*M* + 1)⁺. **8**: ¹³C-NMR (COSY), 138.0 ppm (Cq, 5-C); ¹H-NMR, 12.74 ppm (NH disappeared with D₂O); MS *m/z* (FAB), 431 (*M* + 1)⁺. In addition, the formation of **2** in the photolysis of **5** supported strongly the structure of sugar chain in **2** as 1'*R*, 2'*S*, 3'*R*-configuration which was the same as that of D-arabinose.

A plausible mechanism of this reaction is proposed as follows: **1** is heated in *o*-xylene to give an azidonitrene **9** with the evolution of nitrogen gas. Next, its C-2 carbon rearranges onto nitrogen atom *via* a path-b to afford **11**, which then undergoes the [1,3] sigmatropic shift *via* a path-c. The iminoazide derivative **13** thus formed is converted into the corresponding tetrazole **14**, which is quenched with water to give **2** accompanying with elimination of formaldehyde and benzylalcohol.¹⁰⁾ In the case of photolysis, the anomeric-H of **9** shifts onto its nitrene as the hydride *via* a path-a. Thus obtained **10** undergoes an intramolecular 1,3-dipolar cycloaddition with azide group to give **3**. On the other hand, **11** derived from **9** undergoes this cyclization to afford **4**. The proposed intermediate **14** was also synthesized by the reaction of **2** with benzyl chloromethyl ether and then was converted into **2** again by refluxing in *o*-xylene. The reaction temperature was an important factor to cause the path-b rearrangement: **2** (58%) under refluxing *o*-xylene; **2** (16%) and **3** (38%) under heating *o*-xylene (130 °C); **3** (57%) under refluxing toluene.

In conclusion, we found a new kind of rearrangement in the thermolysis and photolysis of sugar diazides. Although the formation of **3** and **4** can be explained easily from the nitrene intermediate, it is not clear why **2** is formed *via* a [1,3] shift such as the path-c. The elucidation of the reaction mechanism may disclose a new chemistry. We have already found that 2,3,4,6-tetra-*O*-benzyl-D-glucopyranosylidene diazide is irradiated with the high pressure mercury lamp to give the corresponding azidonitrene.¹⁾ However, Descotes *et al.* have recently reported that its acetyl derivative gives the corresponding anomeric carbene under the same conditions as above.¹¹⁾ Therefore the protective group

may play an important role in the present reaction. Further investigation is undergoing in this laboratory to elucidate the reaction mechanism.



References

- 1) M. Yokoyama, M. Matsushita, S. Hirano, and H. Togo, *Tetrahedron Lett.*, **34**, 5097 (1993).
- 2) ^1H -NMR (500 MHz, CDCl_3): δ 3.66-3.70 (m, 2H, 6-H), 3.73-3.90 (m, 4H, 2, 3', 4, 5-H), 4.42-4.76 (m, 10H, $-\text{OCH}_2\text{Ph}$), 4.79 (d, 1H, 1-H, $J_{1,2} = 5.77$ Hz), 7.12-7.34 (m, 25H, Ph). ^{13}C -NMR (100 MHz, CDCl_3): δ 69.7 (6-C), 72.5, 73.2, 73.4, 75.2, 75.5 ($\text{PhCH}_2 \times 5$), 76.8, 77.4, 79.3, 79.4, 81.6 (1,2,3,4,5-C), 127.6-128.4 (Ph), 137.8, 137.9, 138.1, 138.1, 138.3 (ipso C of $\text{Ph} \times 5$). IR (neat) 3010 (Ph), 2850 (CH), 2100 (N_3) cm^{-1} . MS m/z (FAB), 699 ($\text{M}+1$) $^+$.
- 3) V. Pozsgay and H. J. Jennings, *J. Org. Chem.*, **53**, 4042, (1988).
- 4) J. -P. Praly, Z. El Kharraf, and G. Descotes, *J. Chem. Soc., Chem. Commun.*, **1990**, 431.

- 5) ^1H -NMR (400 MHz, CDCl_3): δ 1.65 (br, 1H, NH), 3.71 (dd, 1H, 4'-H, $J_{3',4'} = 3.66$ Hz, $J_{\text{gem}} = 10.81$ Hz), 3.85 (dd, 1H, 4'-H, $J_{3',4'} = 2.75$ Hz, $J_{\text{gem}} = 10.81$ Hz), 3.91-3.95 (m, 2H, 3'-H, 2'-OCH $_2$ Ph), 4.04 (dd, 1H, 2'-H, $J_{1',2'} = 3.12$ Hz, $J_{2',3'} = 7.51$ Hz), 4.31 (d, 1H, 4'-OCH $_2$ Ph, $J_{\text{gem}} = 11.64$ Hz), 4.35 (d, 1H, 4'-OCH $_2$ Ph, $J_{\text{gem}} = 11.64$ Hz), 4.38 (d, 1H, 2'-OCH $_2$ Ph, $J_{\text{gem}} = 11.36$ Hz), 4.46 (d, 1H, 1'-OCH $_2$ Ph, $J_{\text{gem}} = 11.26$ Hz), 4.53 (s, 2H, 3'-OCH $_2$ Ph), 4.66 (d, 1H, 1'-OCH $_2$ Ph, $J_{\text{gem}} = 11.26$ Hz), 5.36 (d, 1H, 1'-H, $J_{1',2'} = 3.11$ Hz), 7.00-7.34 (m, 20H, Ph). ^{13}C -NMR (100 MHz, CDCl_3): δ 67.8 (4'-C), 72.0, 72.9, 73.5, 74.8 (PhCH $_2$ ×4), 72.4, 77.4, 79.7 (1', 2', 3'-C), 127.7-128.6 (Ph), 136.3, 136.7, 137.7, 137.8 (ipso C of Ph×4), 155.3 (5-C). IR (neat) 3000 (Ph), 2850 cm^{-1} (CH). **2** was also synthesized by the reaction of tetra-*O*-benzyl-D-arabinononitrile with ammonium azide.
- 6) ^1H -NMR (500 MHz, CDCl_3): δ 1.60 (br, 1H, NH), 3.73 (dd, 1H, 5'-H, $J_{4',5'} = 3.85$ Hz, $J_{\text{gem}} = 10.45$ Hz), 3.87-3.90 (m, 2H, 4'-H, 5'-H), 4.17-4.27 (m, 3H, 2'-H, 3'-H, -OCH $_2$ Ph), 4.40-4.58 (m, 6H, -CH $_2$ Ph), 4.62 (d, 1H, -OCH $_2$ Ph, $J_{\text{gem}} = 11.83$ Hz), 4.68 (d, 1H, -OCH $_2$ Ph, $J_{\text{gem}} = 6.87$ Hz), 4.70 (d, 1H, -OCH $_2$ Ph, $J_{\text{gem}} = 7.97$ Hz), 5.28 (d, 1H, 1'-H, $J_{1',2'} = 6.05$ Hz), 6.87-7.36 (m, 25H, Ph). ^{13}C -NMR (100 MHz, CDCl_3): δ 68.3 (5'-C), 70.9 (4'-C), 72.0, 72.6, 73.4, 74.3 (PhCH $_2$ ×4), 77.9, 78.4, 78.6 (1', 2', 3'-C), 127.8-128.6 (Ph), 136.5, 136.7, 137.2, 137.9, 138.1 (ipso C of Ph×5), 153.8 (5-C). IR (neat) 3000 (Ph), 2850 cm^{-1} (CH).
- 7) ^1H -NMR (270 MHz, CDCl_3): δ 3.59 (dd, 1H, 5'-H, $J_{4',5'} = 4.1$ Hz, $J_{\text{gem}} = 9.9$ Hz), 3.68 (dd, 1H, 5'-H, $J_{4',5'} = 4.3$ Hz, $J_{\text{gem}} = 9.9$ Hz), 3.80-3.88 (m, 2H, 3'-H, 4'-H), 3.97 (dd, 1H, 2'-H, $J_{1',2'} = 4.3$ Hz, $J_{2',3'} = 6.5$ Hz), 4.18 (d, 1H, -OCH $_2$ Ph, $J_{\text{gem}} = 11.0$ Hz), 4.30-4.61 (m, 6H, -OCH $_2$ Ph, $J_{\text{gem}} = 11.6$ Hz), 4.64-4.67 (m, 3H, OCH $_2$ Ph), 6.20 (d, 1H, 1'-H, $J_{1',2'} = 4.3$ Hz), 7.03-7.34 (m, 25H, Ph), 8.56 (s, 1H, 5-H). ^{13}C -NMR (126 MHz, CDCl_3): δ 68.1 (CH $_2$ OBn), 72.0, 72.3, 73.4, 74.5, 75.7 (PhCH $_2$ ×5), 77.7, 78.6, 80.1, 87.9 (1', 2', 3', 4'-C), 127.7-128.7 (Ph), 135.0, 136.9, 137.8, 137.8, 138.1 (ipso C of Ph×5), 142.4 (5-C). IR (neat) 3010 (Ph), 2850 cm^{-1} (CH).
- 8) ^1H -NMR (400 MHz, CDCl_3): δ 1.67 (br, 1H, NH), 3.73 (dd, 1H, 5'-H, $J_{4',5'} = 3.67$ Hz, $J_{\text{gem}} = 10.08$ Hz), 3.85-3.91 (m, 2H, 5'-H, -OCH $_2$ Ph), 4.17-4.25 (m, 3H, 2'-H, 3'-H, 4'-H), 4.40-4.47 (m, 2H, -OCH $_2$ Ph), 4.52-4.70 (m, 7H, -OCH $_2$ Ph), 5.28 (d, 1H, 1'-H, $J_{1',2'} = 5.87$ Hz), 6.88-7.35 (m, 25H, Ph). ^{13}C -NMR (100 MHz, CDCl_3): δ 68.4 (5'-C), 71.1 (4'-C), 72.0, 72.6, 73.4, 74.4, 74.6 (PhCH $_2$ ×5), 78.0, 78.5, 78.7 (1', 2', 3'-C), 127.7-128.6 (Ph), 136.5, 136.8, 137.2, 138.0, 138.2 (ipso C of Ph×5), 154.0 (5-C). IR (neat) 3000 (Ph), 2850 cm^{-1} (CH).
- 9) ^1H -NMR (500 MHz, CDCl_3): δ 3.43 (dd, 1H, 3'-H, $J_{2',3'} = 6.23$ Hz, $J_{\text{gem}} = 10.12$ Hz), 3.50 (dd, 1H, 3'-H, $J_{2',3'} = 4.86$ Hz, $J_{\text{gem}} = 10.12$ Hz), 4.16 (ddd, 1H, 2'-H, $J_{1',2'} = 3.12$ Hz, $J_{2',3'} = 4.86$, 6.23 Hz), 4.40 (d, 1H, 1'-OCH $_2$ Ph, $J_{\text{gem}} = 11.84$ Hz), 4.44 (d, 1H, 1'-OCH $_2$ Ph, $J_{\text{gem}} = 11.84$ Hz), 4.49 (d, 1H, 2'-OCH $_2$ Ph, $J_{\text{gem}} = 11.72$ Hz), 4.54 (d, 1H, 2'-OCH $_2$ Ph, $J_{\text{gem}} = 11.72$ Hz), 4.69 (d, 1H, 3'-OCH $_2$ Ph, $J_{\text{gem}} = 6.47$ Hz), 4.72 (d, 1H, 3'-OCH $_2$ Ph, $J_{\text{gem}} = 6.47$ Hz), 5.17 (d, 1H, 1'-H, $J_{1',2'} = 3.12$ Hz), 7.17-7.36 (m, 15H, Ph), 12.74 (br, 1H, NH). ^{13}C -NMR (100 MHz, CDCl_3): δ 68.4 (3'-C), 71.9 (2'-C), 72.1 (3'-OCH $_2$ Ph), 73.6 (1' and 2'-OCH $_2$ Ph), 78.8 (1'-C), 127.6-128.9 (Ph×3), 136.7, 136.7, 137.3 (ipso C of Ph×3), 138.0 (5-C). IR (KBr) 3040 (Ph), 2880 cm^{-1} (CH).
- 10) The benzylalcohol was detected by GC-MS (Shimadzu GCMS-QP-2000A) in ca. 60% yield based on **2**.
- 11) J. -P. Praly, C. Di Stefano, G. Descotes, and R. Faure, *Tetrahedron Lett.*, **35**, 89 (1994).

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