## Note

## Photolysis of secondary azides of sugars\*<sup>,†</sup>

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The photolysis of primary azides  $(R-CH_2N_3)$  in sugar systems leads to nonmonomeric products, having elemental compositions corresponding to that of R-CH=NH, which, on treatment with water and a trace of acid, give the corresponding aldehydes, R-CHO, in high yield<sup>1-3</sup>. The procedure provides an excellent synthetic route for a wide range of  $\omega$ -aldehydo derivatives of protected and unprotected glycosides<sup>1-3</sup>, and for analogous derivatives of such polysaccharides as amylose<sup>4</sup>, starch, and cellulose<sup>5</sup>. The reaction presumably takes place by way of an intermediate nitrene (R-CH<sub>2</sub>N:) which rearranges by a 1,2-hydrogen migration to give the initial product isolated from the reaction<sup>6-8</sup>. It was considered that a similar process operating with secondary azides might provide a useful route to ketones in the sugar field, allowing preparation of keto derivatives without exposure of the precursor molecule to conventional oxidizing agents. The reaction was evaluated with 3-azido-3-deoxy-1,2:5,6-di-O-isopropylidene- $\alpha$ -D-glucofuranose<sup>9</sup> (1), a secondary azide obtainable in high yield from 1,2:5,6-di-O-isopropylidene- $\alpha$ -D-glucofuranose by the sequence: oxidation, reduction, p-toluenesulfonylation, and displacement by azide.



Irradiation of a solution of the azide 1 in benzene (or cyclohexane) with unfiltered light from a mercury arc led to decomposition of the starting material and the formation of a syrup that, by t.l.c. on silica gel, contained a nonmigrating component and a fast-moving component. The latter was isolated by column chromatography, and was identified as the anticipated 3-ketone<sup>10</sup> 2, characterized as its crystalline hydrate, 3. Presumably, the initial product of photolysis underwent hydrolysis during the exposure to silica gel, to give the ketone 2. The yield of 2 was

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low (15%) and a considerable proportion of the reaction product, apparently polymeric material, remained on the column. As the ketone 2 is somewhat unstable, an experiment was performed in which the product of photolysis of 1 in moist benzene was immediately treated with sodium borohydride, which reduces 2 stereospecifically to 1,2:5,6-di-O-isopropylidene- $\alpha$ -D-allofuranose<sup>11</sup> (4), a stable compound. The alcohol 4 was isolated crystalline in 18% yield.

Irradiation of methyl 2-azido-4,6-O-benzylidene-2-deoxy- $\alpha$ -D-altropyranoside<sup>12</sup> in cyclohexane gave a solid product whose elemental composition indicated an empirical formula of C<sub>14</sub>H<sub>17</sub>NO<sub>5</sub>, corresponding to that of an imino derivative (RR'C=NH), and the i.r. absorption at 6.0  $\mu$ m indicated the presence of C=N bonds. However, n.m.r. spectra of the product in various solvents were complex and were clearly inconsistent with a monomeric structure. The exact molecular formula was not determined. Very similar results were observed when methyl 3,4,6-tri-O-acetyl-2azido-2-deoxy- $\alpha$ -D-altropyranoside was irradiated. Irradiation of methyl 2-azido-2deoxy- $\alpha$ -D-altropyranoside<sup>12</sup> led to a product that had only about half the nitrogen content calculated for the polymeric imine structure; some hydrolysis had evidently occurred, as indicated also by an i.r. absorption at 5.8  $\mu$ m (carbonyl). These products were not further characterized.

It is evident from the foregoing results that photolysis of secondary azides of sugars does, indeed, lead to carbonyl derivatives, probably by way of intermediate, polymeric imines, but the yield of ketone is low. Although the yields in such conversions as  $1\rightarrow 2$  might be improved somewhat by alteration of the experimental conditions, it is doubtful that this photochemical method will be so attractive a synthetic procedure for keto sugars as is the photolysis of primary azides for the synthesis of aldehydo sugars. Presumably, the 1,2-hydrogen migration, postulated for conversion of a nitrene intermediate into an imine, is a favored process with the primary azides. With the secondary azides, there are probably competing processes, such as  $\delta$ -hydrogen abstraction<sup>8</sup>, that divert a large proportion of the initial intermediate into products that do not give the ketone upon treatment with water.

## **EXPERIMENTAL**

General methods. — Melting points were determined with a Thomas-Hoover "Unimelt" apparatus and are uncorrected. Specific rotations were determined in a 2-dm polarimeter tube. I.r. spectra were recorded with a Perkin-Elmer Model 137 "Infracord" i.r. spectrophotometer. Elemental analyses were performed by W. N. Rond. T.I.c. was conducted on Silica Gel G (E. Merck, Darmstadt, Germany) activated at 110°, with 4:1 dichloromethane-ethyl acetate as developer, and indication was effected with sulfuric acid. Irradiations were conducted at room temperature, under nitrogen, with unfiltered light from a mercury arc<sup>13</sup>, and the reactions were monitored by periodic removal of a small sample of the solution and examination for disappearance of the starting material by t.l.c. and i.r. spectroscopy (4.75  $\mu$ m, N<sub>3</sub>).

Photochemical conversion of 3-azido-3-deoxy-1,2:5,6-di-O-isopropylidene-a-D-

glucofuranose (1) into 1,2:5,6-di-O-isopropylidene- $\alpha$ -D-ribo-hexofuranos-3-ulose (2). — A solution of the azide<sup>9</sup> 1 (528 mg) in benzene (180 ml) was irradiated for 1 h and then evaporated under diminished pressure to a syrup (412 mg). T.l.c. of the product showed a component at the base line and a component that showed migration characteristics indistinguishable from those of the ketone 2; the starting azide 1 was absent. The product was placed on a column (1 × 20 cm) containing 25 g of silica gel (No. 7734, Merck) and the column was eluted with 9:1 dichloromethane-ethyl acetate. The faster-moving component was eluted in effluent fractions between 175 and 300 ml. Evaporation of these fractions gave a syrup that crystallized from a mixture of water-saturated ether and pentane to give the crystalline hydrate (3) of 1,2:5,6-di-O-isopropylidene- $\alpha$ -D-ribo-hexofuranos-3-ulose; yield 76 mg (15%), m.p. 110–112°, mixed m.p. (with authentic 3) 110–112°,  $[\alpha]_D^{20} + 44^\circ$  (c 1, chloroform) (lit.<sup>10</sup> m.p. 112–114°,  $[\alpha]_D + 44.5^\circ$  in chloroform).

Similar results were observed when cyclohexane or p-dioxane-water was used as the solvent for photolysis.

In a second experiment, the azide 1 (392 mg) in water-saturated benzene (180 ml) was irradiated as before for 1 h, and the mixture was then evaporated to a syrup. Sodium borohydride (400 mg) was added to a solution of the syrup in 70% aqueous ethanol, and the mixture was stirred for 1 h. Water (40 ml) was then added, and the solution was extracted with six 20-ml portions of ethyl acetate. The extract was dried (magnesium sulfate) and evaporated to a syrup (136 mg) that, by t.l.c., showed a nonmigrating component and a component that migrated as the allose derivative 4. The product was resolved by chromatography on a column containing 10 g of silica gel (No. 7734, Merck) by elution with 9:1 dichloromethane-ethyl acetate. Fractions (70–130 ml) containing the faster-moving component (by t.l.c.) were evaporated to a solid. Recrystallization from benzene-petroleum ether (b.p. 30–50°) gave 1,2:5,6-di-O-isopropylidene- $\alpha$ -D-allofuranose (4) (65 mg, 18% from the azide 1), m.p. 76–77°, mixed m.p. 76–77°,  $[\alpha]_D^{20} + 37.4^\circ$  (c 0.5, water); lit.<sup>11</sup> m.p. 76–77°,  $[\alpha]_D^{21} + 37.7^\circ$  (water).

Methyl 3,4,6-tri-O-acetyl-2-azido-2-deoxy- $\alpha$ -D-altropyranoside. — Acetylation of methyl 2-azido-2-deoxy- $\alpha$ -D-altropyranoside<sup>12</sup> with acetic anhydride in pyridine in the usual way gave the title compound as a distillable syrup, b.p. 150°/0.2 torr,  $[\alpha]_{\rm D}^{20}$  + 60.2° (c 1.2, chloroform).

Anal. Calc. for C<sub>13</sub>H<sub>19</sub>N<sub>3</sub>O<sub>8</sub>: C, 45.22; H, 5.51; N, 12.17. Found: C, 45.29; H, 5.53; N, 12.10.

Photolysis of derivatives of methyl 2-azido-2-deoxy- $\alpha$ -D-altropyranoside. — A. Methyl 2-azido-4,6-O-benzylidene-2-deoxy- $\alpha$ -D-altropyranoside<sup>12</sup> (500 mg) in cyclohexane (180 ml) was irradiated until the starting material disappeared (85 min), and the solution was evaporated. The resultant solid was dissolved in the minimal volume of chloroform, and hexane was added, to precipitate an amorphous solid (295 mg),  $\lambda_{max}^{KBr}$  6.0  $\mu$ m (C=N) that did not migrate in t.l.c.

Anal. Calc. for C<sub>14</sub>H<sub>17</sub>NO<sub>5</sub>: C, 60.22; H, 6.09; N, 5.02. Found: C, 59.96; H, 6.13; N, 4.87.

B. Methyl 3,4,6-tri-O-acetyl-2-azido-2-deoxy- $\alpha$ -D-altropyranoside (575 mg) in cyclohexane (180 ml) was irradiated as before. The starting material had all decomposed after 100 min. The product was isolated by the procedure used for A, to give an amorphous solid (213 mg),  $\lambda_{\text{max}}^{\text{KBr}}$  6.0 (C=N) and 5.7  $\mu$ m (C=O), that did not migrate in t.l.c. (Found: C, 50.57; H, 6.12; N, 5.18. C<sub>13</sub>H<sub>19</sub>NO<sub>8</sub> requires C, 49.21; H, 6.00; N, 4.42.)

C. A solution of methyl 2-azido-2-deoxy- $\alpha$ -D-altropyranoside<sup>12</sup> (200 mg) in 1:1 *p*-dioxane-benzene (180 ml) was irradiated until the starting material had all decomposed (105 min). The solution was evaporated to a syrup that was dissolved in ethanol. Hexane was added to precipitate an amorphous solid, yield 94 mg;  $\lambda_{max}^{KBr}$  5.8 (C=O) and 6.0  $\mu$ m (C=N). (Found: C, 51.58; H, 6.81; N, 4.64.)

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