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THE ACETYL GROUP MIGRATIONS IN D-GLUCOSE DIETHYL THIOACETYL TETRAACETATE[1]

By R. U. Lemieux and H. F. Bauer

ABSTRACT

The D-glucose diethyl thioacetal tetraacetate prepared by Wolfrom and associates both by detritylation of 6-*O*-trityl-D-glucose diethyl thioacetal tetraacetate and mercaptalation of 2,3,4,6-tetra-*O*-acetyl-β-D-glucose was obtained by direct acetylation of D-glucose diethyl thioacetal with acetic anhydride and sodium acetate. Methylation of the tetraacetate followed by deacetylation and demercaptalation gave only 2-*O*-methyl glucose and methyl β-D-glucopyranoside.

Acetylation of D-glucose diethyl thioacetal (I) with acetic anhydride and sodium acetate on the steam bath for a half hour results in the formation of a tetra-*O*-acetyl derivative (II) which can be readily isolated in 10–15% yield. The formation of II is analogous to the formation of the substance believed to be 3,4,5,6-tetra-*O*-benzoyl-D-glucose diethyl thioacetal on reaction of D-glucose diethyl thioacetal with benzoyl chloride in aqueous alkali (1). We have found that the tetraacetate (II) behaves in a manner similar to the tetrabenzoate (2) in that it undergoes methylation at the C2-position on treatment with methyl iodide and silver oxide. Deacetylation of the product formed on the methylation of the tetraacetate (II) gave a 56% yield of 2-*O*-methyl-D-glucose diethyl thioacetal (III). The material in the mother liquor was deacetylated and demercaptalated. The only monomethyl derivative of glucose other than 2-*O*-methyl glucose which could be identified in the product by application of the method developed by the authors for identifying mono-*O*-methylglucoses (7) was methyl β-D-glucopyranoside. The formation of the glucoside is attributable to the ability of silver oxide to bring about the demercaptalation of thioacetals (4).

The tetraacetate (II) was found to be identical with the compound prepared by Wolfrom and associates (12) both by detritylation of 6-*O*-trityl-D-glucose diethyl thioacetal tetraacetate (IV) and by mercaptalation of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose (V) with ethanethiol containing zinc chloride. Our methylation experiments suggest that compound II is 3,4,5,6-tetra-*O*-acetyl-D-glucose diethyl thioacetal. However, Wolfrom and co-workers have shown (12) that partial demercaptalation of II yields ethyl tetra-*O*-acetyl-α-D-1-thioglucofuranoside (VI). Thus, the free hydroxyl group in II may be at positions 2 or 4. The tetraacetate (II) (and perhaps the tetrabenzoate of Brigl and Mühlschlegel (1)) may undergo preferential methylation at the C2-position for the same reason that D-glucose diethyl thioacetal undergoes preferential methylation at this position (8). Wolfrom and Anno (10) have shown that acetylation of D-glucosamine diethyl thioacetal with acetic anhydride in pyridine has yielded (11) a crystalline tetraacetate. Considering the ease with which amines can be acetylated, this substance, which is closely

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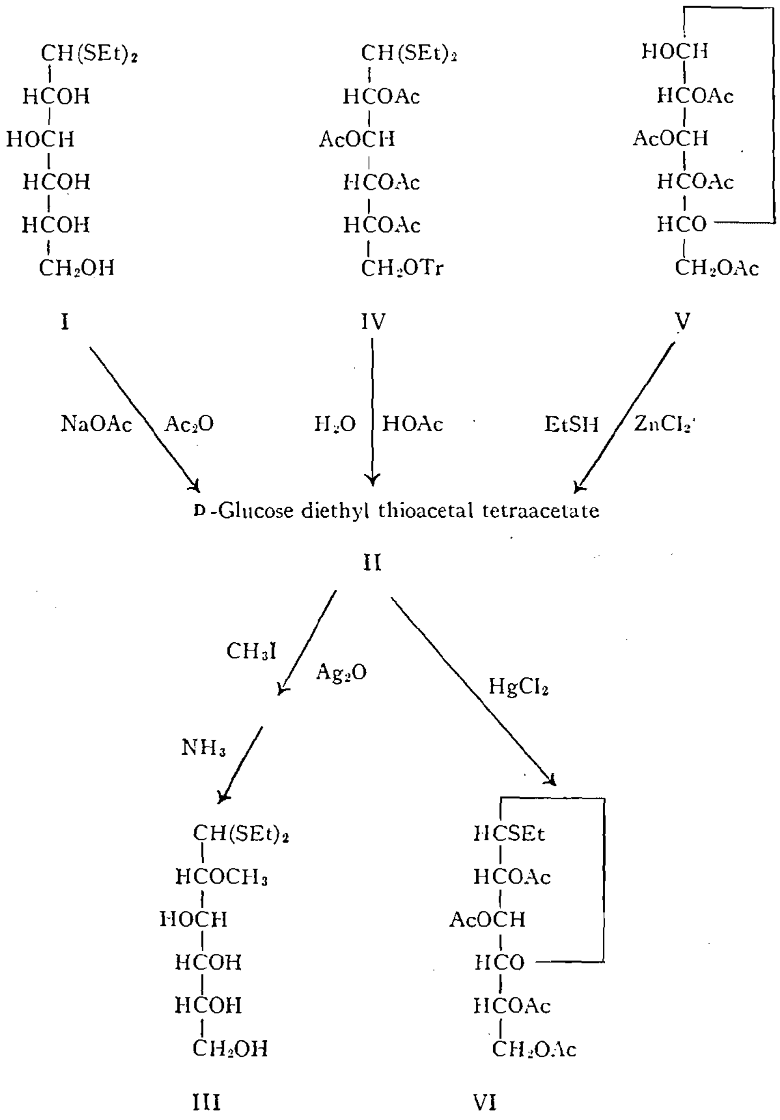

related to the tetraacetate (II) of D-glucose diethyl thioacetal, almost certainly possesses a 2-*N*-acetyl group. It is conceivable that the two tetraacetyl derivatives display resistance to acetylation for the same reason. It is of interest to note that an orthoacid structure could account for the resistance of these compounds toward acetylation. In this respect, it is noteworthy that Doerschuk (3) has confirmed the opinion of Fischer (5) that acyl group migrations are intramolecular and proceed by way of orthoacid intermediates.

In conclusion, the present data show that the tetraacetate (II) is a labile compound which can react as if either position 2 or position 4 were open. The position of the free hydroxyl group remains unknown.

EXPERIMENTAL

The rotations were measured at 22–25°C.

*Tetra-O-acetyl-*D*-glucose Diethyl Thioacetal* (II)

A mixture of D-glucose diethyl thioacetal (4), 5 gm., acetic anhydride, 50 ml., and sodium acetate, 5 gm., was heated on the steam bath for 30 min. The solution was stirred with ice water to decompose the anhydride and the mixture was extracted with chloroform. The chloroform solution was washed with aqueous sodium bicarbonate solution and water, dried, and evaporated to a sirup. The sirup readily yielded a crystalline product on being scratched in alcohol. Recrystallization from ethanol gave 1.22 gm. of material, m.p. 117–118°C., $[\alpha]_D$ −23° (*c*, 4 in chloroform), which did not depress the melting point of the tetra-*O*-acetyl-D-glucose diethyl thioacetal of same physical constants prepared by mercaptalation of 2,3,4,6-tetra-*O*-acetyl-β-D-glucose as reported by Wolfrom and co-workers (12). Calc. for $C_{10}H_{18}O_5S_2(CH_3CO)_4$: acetyl, 37.8; S, 14.1%. Found: acetyl, 36.6; S, 13.9%. The substance possessed an absorption band at 3425 cm.$^{-1}$ which is characteristic of hydroxyl groups.

Methylation of the Tetraacetate (II)

The tetraacetate (II), 1 gm., was shaken at room temperature with 5 ml. of dry dioxane, 10 ml. of methyl iodide, 1 gm. of freshly prepared silver oxide, and 1 gm. of Drierite. After two hours, 1 gm. of silver oxide and 0.5 gm. of Drierite were added and the shaking was continued for four hours. The silver salts were collected and washed with methanol. The filtrate was evaporated to a sirup which was dissolved in 30 ml. of saturated methanolic ammonia solution. After standing overnight at 0°C., the solution was evaporated to a crystalline residue which was triturated with ether. Recrystallization from ethanol gave 0.34 gm., 56% yield, of a substance, m.p. 156–157°, $[\alpha]_D$ −25.5° (*c*, 2 in pyridine), which did not depress the melting point of an authentic sample of 2-*O*-methyl-D-glucose diethyl thioacetal (9) of same physical constants.

The mother liquors from the above isolation of 2-*O*-methyl-D-glucose diethyl thioacetal were evaporated to a sirup which was heated for 30 min. on a steam bath with 25 ml. of saturated aqueous mercuric chloride solution in 25 ml. of water. The clarified solution was deionized by using hydrogen sulphide to precipitate the mercuric ions and Amberlite IR4B to remove the hydrochloric acid. Evaporation gave 0.30 gm. of sirup which was found to contain monomethylglucoses as the main component and small amounts of glucose and di-*O*-methylglucoses. The mono-*O*-methylglucose fraction was isolated by preparative paper chromatography (7). The material crystallized after some time. Recrystallization from ethanol gave a substance which was identified as methyl β-D-glucopyranoside by its melting point (110–111°C. with a crystalline transformation at 104–105°C. (6)), specific rotation (−33.1° (*c*,1 in water)), mixed melting point (undepressed) and infrared spectrum (identical to that of the authentic sample). 2-*O*-methyl-D-glucose was the only mono-*O*-methyl-D-glucose which could be identified in the mother liquors by the procedure of Lemieux and Bauer (7).

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