Preliminary communication

Isolation of *aldehydo* and septanoside derivatives from the acid-catalyzed reaction of D-glucose and some of its derivatives with acetone–alcohol

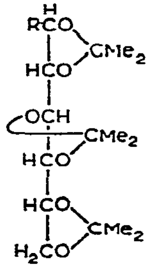
J. D. STEVENS
School of Chemistry, The University of New South Wales, Kensington, N. S. W. 2033 (Australia)

(Received November 23rd, 1971)

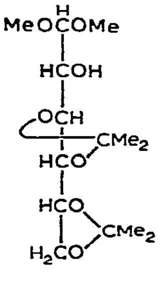
Acid-catalyzed reaction of D-glucose with acetone–methanol gives rise to a number of products, the yields of which are dependent upon the reaction time and the composition of the acetone–methanol. Partitioning of the products between chloroform and water gives a useful preliminary separation. The eight major products in the chloroform solution are numbered **1** to **8** according to the order in which they are eluted from a g.l.c. column of polyester (LAC-IR-296).

Separation of the chloroform-soluble products was achieved by chromatography on a column of silicic acid. Compound **1**, a mobile oil having $[\alpha]_D^{22}$ +76.6° (*c* 1.4, chloroform), was eluted first. Its n.m.r. spectrum showed the presence of one methoxyl group and three *O*-isopropylidene groups, and the i.r. spectrum showed no absorption in the 3-μm region. Mild, acid-catalyzed hydrolysis of **1** yielded a diol, and the n.m.r. spectrum of the diol diacetate showed the acetoxyl groups to be on C-5 and C-6 of D-glucose. Compound **1** therefore contains a 5,6-*O*-isopropylidene group (confirmed by a strong peak of 101 mass units in the mass spectrum[1]), and it is formulated as 1,2:3,4:5,6-tri-*O*-isopropylidene-1-methoxy-D-glucitol (**1a**). Although **1** may be prepared directly from D-glucose, a more satisfactory preparation involves treatment of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (100 g) with a mixture of acetone (900 ml), methanol (100 ml), and sulfuric acid (40 ml). Compound **1** is the product first formed in this reaction, and isolation (by extraction into light petroleum from water) after 4 h, followed by re-treatment of the recovered starting-material gave **1** in 30% yield.

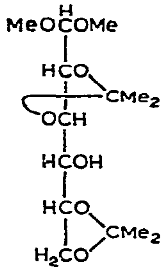
The concentration of compounds **2** and **5** in the reaction mixture reached a maximum after 4 days at room temperature. They were isolated by extraction from water into 1:2 (v/v) benzene–light petroleum, followed by chromatography on alumina. Further chromatography, with silicic acid, gave crystalline **2** and **5** [64 g and 43 g, respectively, from 1 kg of D-glucose in 15 liters of 1:4 (v/v) methanol–acetone containing 4% (v/v) of conc. sulfuric acid], identified as the previously reported[2] 2,3:4,5-diisopropylidene acetals of methyl α- and β-D-glucoseptanoside, respectively. Isolation of **2** and **5** from this modified, Fischer glycosidation reaction is the first instance of the isolation of septanoside derivatives starting from an unsubstituted sugar, and the procedure provides a practical method of preparation.



1a, R = OMe
1b, R = OEt
1c, R = OCHMe$_2$
1d, R = OCMe$_3$

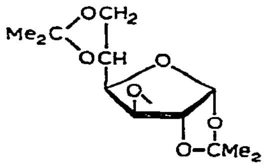


4



6

9, R =



In acetone–methanol, compound 3 is formed in minor amounts only. Reaction of D-glucose with an acidified mixture of methanol and 2,2-dimethoxypropane for a short time gives a higher concentration of this component. Chromatography on silicic acid gave 3 as a solid having m.p. 48°, $[\alpha]_D^{22}$ −52.4° (*c*, 1.1, chloroform). The mass, n.m.r., and i.r. spectra of 3 showed that it contains one methoxyl group and three *O*-isopropylidene groups, and is devoid of hydroxyl groups. As the mass spectrum (showing a strong peak of 101 mass units) is almost identical with that of 1, compound 3 is formulated as the C-1 configurational isomer of 1, and application of Hudson's rules of isorotation to 1 and 3 led to assignment of the *S* configuration to C-1 of 1. An X-ray crystallographic study of the crystalline, *tert*-butyl analog of 1, namely 1d {$[\alpha]_D^{22}$ +86.5° (*c*, 0.905, chloroform)} confirmed this assignment[3].

Compounds 4 and 6 were respectively identified[4,5] as the 3,4:5,6- and 2,3:5,6-diisopropylidene acetals of D-glucose dimethyl acetal. The benzoates of 4 and 6 were separated by fractional recrystallization, to give yields of 23% of the benzoate of 4 and 37.6% of the benzoate of 6 from a reaction involving the addition of 200 ml of 2,2-dimethoxypropane to a solution of 20 g of D-glucose in 300 ml of methanol containing 2% (v/v) of sulfuric acid. Compounds 4 and 6 were isolated after 2 h at 25°.

By using g.l.c., compound 7 was identified as 1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose[2], and compound 8 as 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose.

Treatment of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (8) with acidified mixtures of acetone with, respectively, ethanol, isopropyl alcohol, or *tert*-butyl alcohol gave the analogs of compound **1** (**1b**, **1c**, and **1d**, respectively). The formation of **1c** and **1d** suggested that any alcohol should be capable of reacting with **8**, including **8** itself. Such a product, **9**, (obtained in 6.6% yield by treating 40 g of **8** with 100 ml of acidified acetone for 4 h) had, in fact, been isolated earlier[6]; it had been called isopropylidene-bis(diisopropylidene-D-glucose), but its structure had not been determined. On the basis of its n.m.r. and mass spectra, and of selective acid hydrolysis of the two 5,6-*O*-isopropylidene groups, **9** is now formulated as 1-(3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranos-3-yloxy)-1,2:3,4:5,6-tri-*O*-isopropylidene-D-glucitol. Its optical rotation, $[\alpha]_D^{22}$ +45.7° (*c*, 1.3, chloroform), is consistent with the *S* configuration at C-1.

REFERENCES

1 D. C. De Jongh and K. Biemann, *J. Amer. Chem. Soc.*, 86 (1964) 67.
2 J. D. Stevens, *Chem. Commun.*, (1969) 1140.
3 D. C. Craig, N. C. Stephenson, and J. D. Stevens, unpublished results.
4 E. J. C. Curtis and J. K. N. Jones, *Can. J. Chem.*, 38 (1960) 890.
5 B. D. Kohn and P. Kohn, *J. Org. Chem.*, 28 (1963) 1037.
6 C. L. Mehltretter, B. H. Alexander, R. L. Mellies, and C. E. Rist, *J. Amer. Chem. Soc.*, 73 (1951) 2424.