[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF WISCONSIN]

1,2,3,4-Tetraacetyl-α-D-glucopyranose

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The synthesis of 1,2,3,4-tetraacetyl-β-D-glucopyranose from the corresponding 6-trityl compound by Helferich and Klein[1] made available a valuable intermediate for the synthesis of several disaccharides, glucose-6-phosphate[2] and certain related compounds. The preparation is given in "Organic Syntheses"[3] and was further improved by a new procedure[2] for crystallizing the product involving the use of di-*n*-butyl ether.

A parallel synthesis from tetraacetyl-6-triphenylmethyl-α-D-glucose has now yielded 1,2,3,4-tetraacetyl-α-D-glucopyranose for the first time in pure crystalline form. Although Reynolds and Evans[4] successfully employed the compound for the synthesis of α-gentiobiose octaacetate, their specimen was a sirup for which no analytical or rotational data were reported.

Butyl ether has been found to facilitate the crystallization of the hexose tetraacetates as well as of a number of other carbohydrate derivatives.

The structure of the new tetraacetate was confirmed by tritylation which gave the original tetraacetyl-6-triphenylmethyl-α-D-glucose,[5] and by condensation with acetobromoglucose to α-gentiobiose octaacetate. A molecular rotation in chloroform of 41,400° was found for 1,2,3,4-tetraacetyl-α-D-glucopyranose, whereas the corresponding figure for the known β-isomer is 4,200°. The numerical difference of 37,200 (2 A. value) is in the middle of the range (33,000 to 40,000 with an average of 36,000 to 37,000) predicted by Hudson's Rules of Isorotation[6] for pairs of acetylated sugars differing only in the configuration of the acetyl group on carbon atom 1.

The preparation of acetylated 6-glycosido-α-glucose compounds should be facilitated by the availability of the α-tetraacetate in crystalline form.

Experimental

1,2,3,4-Tetraacetyl-α-D-glucopyranose.—6-Trityl-tetraacetyl-α-D-glucopyranose obtained as a by-product in the preparation of the corresponding β-tetraacetate[3] was recrystallized from absolute ethanol until m. p. and rotation were constant.[7] A quantity of 2.7 g. of this 6-trityl-tetraacetyl-α-D-glucopyranose was dissolved in glacial acetic acid (12 cc.) and to the cooled solution 32% hydrobromic acid in glacial acetic acid (1 cc.) was added; after one minute the precipitated triphenylbromomethane was filtered off and washed with acetic acid (3 cc.). The filtrate was immediately poured into ice water and chloroform; the chloroform extract was washed three times with ice water, dried over sodium sulfate and evaporated to a light sirup. The cautious addition of dibutyl ether and scratching caused the compound to crystallize in small platelets. When filtered, washed with butyl ether and dried *in vacuo* the product weighed 0.90 g. (56%) and melted at about 99°. One recrystallization from chloroform by addition of butyl ether brought the substance to constant m. p. 102–103° (cor.) and rotation: $[\alpha]^{26}\mathrm{D}$ +119 ± 1° (c = 1.5, in $CHCl_3$).

Anal. Calcd. for $C_{14}H_{20}O_{10}$: C, 48.3; H, 5.79. Found: C, 48.0; H, 5.84.

Tritylation of 1,2,3,4-Tetraacetyl-α-D-glucopyranose.—To a solution of 0.33 g. of tetraacetyl-α-D-glucose in anhydrous pyridine (2 cc.) 0.28 g. (1.2 molar equivalents) of trityl chloride was added and the mixture was shaken until the trityl chloride dissolved. After standing overnight at room temperature, the solution was cooled to 0° and a small chip of ice was added. After one hour, more chipped ice was added while stirring. The product which crystallized during the next half hour was filtered off, washed with water and dried on a clay plate. When recrystallized twice from absolute ethanol and dried over calcium chloride, 0.3 g. of tetraacetyl-6-trityl-α-D-glucose was obtained: m. p. 125–128°.

α-Gentiobiose Octaacetate.—A mixture of "Drierite"[8] (7.0 g.), silver oxide[1] (2.0 g.) and 1,2,3,4-tetraacetyl-α-D-glucopyranose (2.7 g.) in anhydrous alcohol-free chloroform (7 cc.) was stirred for one hour in a three-necked flask fitted with a mercury-sealed stirrer, a dropping funnel and a drying tube. After the addition of 0.3 g. of iodine a solution of acetobromoglucose (3.2 g.) in anhydrous chloroform (10 cc.) was added dropwise during the course of one hour and the stirring was continued for eighteen hours. The insoluble materials were removed by filtration through a precoated funnel and washed thoroughly with chloroform. The chloroform was evaporated under reduced pressure to a sirup from which α-gentiobiose octaacetate crystallized when absolute ethanol was added. When recrystallized twice from absolute ethanol and dried, the product weighed 2.2 g. (42% of theoretical); it melted at 190–191° (cor.) and had $[\alpha]^{26}\mathrm{D}$ +54.3 ± 1° (c = 2.1, in $CHCl_3$). When mixed with the α-gentiobiose octaacetate (m. p. 188–189.5°) produced by Hudson and Johnson[9] from the corresponding β compound, by treatment with zinc chloride and acetic anhydride, the melting point was 188–190° (cor.).

Summary

The use of dibutyl ether as a crystallizing agent made it possible to prepare tetraacetyl-α-D-glucopyranose as pure crystals, m. p. 102–103° (cor.) and with a specific rotation in chloroform $[\alpha]^{26}\mathrm{D}$ + 119 ± 1°. The structure of the compound was confirmed by its conversion to known compounds.

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[1] B. Helferich and W. Klein, *Ann.*, **450**, 219 (1926).

[2] H. A. Lardy and H. O. L. Fischer, *J. Biol. Chem.*, **164**, 513 (1946).

[3] "Organic Syntheses," **22**, 56 (1942).

[4] D. Reynolds and W. L. Evans, THIS JOURNAL, **60**, 2559 (1938).

[5] B. Helferich, L. Moog and A. Junger, *Ber.*, **58**, 872 (1925).

[6] C. S. Hudson, THIS JOURNAL, **31**, 66 (1909).

[7] M. p. 130–132° (cor.) with sintering at 125°, $[\alpha]^{26}\mathrm{D}$ +102 ± 0.5° (c = 2, in $CHCl_3$). Helferich, *et al.*, see footnote 5, reported m. p. 129–131° $[\alpha]^{27}\mathrm{D}$ +97.8°.

[8] Preheated at 400° for three hours and held over phosphorus pentoxide.

[9] C. S. Hudson and J. M. Johnson, THIS JOURNAL, **39**, 1272 (1917). A specimen of their compound was generously supplied by Dr. Hudson.