moles of oxidant consumed per mole of substance, against time in hours.

Summary

1. Rules relating to the oxidation of cyclic triols by lead tetraacetate have been stated in an explicit form.

2. Standardized conditions for measuring the rates of oxidation of substances by lead tetraacetate have been described.

3. The degree of resemblance of the oxidation curves of substances related in structure and configuration to the methyl-D-glucopyranosides has been determined.

4. Evidence has been presented concerning the configurations of styracitol and polygalitol.

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[CONTRIBUTION FROM THE DIVISION OF CHEMISTRY, NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE, AND FROM THE DEPARTMENT OF PHARMACOLOGY, UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE]

Two Syntheses of Polygalitol (1,5-Anhydro-D-sorbitol)

BY NELSON K. RICHTMYER, C. JELLEFF CARR AND C. S. HUDSON

In a recent publication[1] on polygalitol and its relation to styracitol, it was stated that in view of the conflicting opinions and the lack of satisfactory evidence concerning the structure and configuration, especially of polygalitol, new methods would be applied to the further examination of these substances. Thus the oxidation of polygalitol and styracitol with periodic acid, followed by bromine water and strontium carbonate, to strontium D-hydroxymethyldiglycolate, proved that these anhydro hexitols possessed the same 1,5-ring; the D-configuration of polygalitol followed from the known D-configuration of styracitol.

There are eight possible 1,5-anhydro-D-hexitols. One of these, styracitol, has been synthesized previously by Zervas,[2] by the addition of hydrogen to the 1,2-ethylenic linkage of tetraacetylhydroxyglucal. The configuration of styracitol is limited, therefore, to that of 1,5-anhydro-D-mannitol or 1,5-anhydro-D-sorbitol. Definitive evidence has been presented by Zervas and Papadimitriou[3] that styracitol is 1,5-anhydro-D-mannitol.

The mother liquors from synthetic styracitol would be expected to contain the epimeric 1,5-anhydro-D-hexitol. Polygalitol has now been isolated in a 4% yield from the mother liquors remaining from the preparation of a large amount of styracitol for other purposes.[4] Polygalitol and styracitol, therefore, are epimeric, as Shinoda, Sato and Sato had claimed,[5] and accordingly polygalitol is to be represented as 1,5-anhydro-D-sorbitol.

Additional proof that polygalitol has the anhydro-D-sorbitol configuration is derived from the second synthesis in which D-glucose was transformed to polygalitol by a series of reactions which involved no change in the configuration of the second, third, fourth or fifth carbon atoms at any time. Acetobromoglucose was converted to octaacetyl-β,β-diglucosyl disulfide,[6] and this, in turn, to tetraacetyl-β-D-glucothiose.[7] When the latter —SH compound was shaken with Raney nickel in absolute alcohol, according to the general procedure of Bougault, Cattelain and Chabrier,[8] the sulfur atom was eliminated, and tetraacetylpolygalitol could be obtained from the resulting solution. By the same procedure the disulfide octaacetate underwent reductive cleavage and desulfurization, and tetraacetylpolygalitol was isolated in a 14% yield.

Experimental Part

Polygalitol from Tetraacetylhydroxyglucal.—The hydrogenation of 745 g. of tetraacetylhydroxyglucal was carried

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[1] Richtmyer and Hudson, THIS JOURNAL, **65**, 64 (1943).

[2] Zervas, *Ber.*, **63**, 1689 (1930).

[3] Zervas and Papadimitriou, *ibid.*, **73**, 174 (1940). Although we regard the evidence of Zervas and Papadimitriou as definitive, it is true that their conclusion is in disagreement with that of Asahina and Takimoto [*ibid.*, **64**, 1803 (1931)], who studied the problem by an entirely different method of experimentation. In a forthcoming article, Hockett and Conley will disprove the experimental results of Asahina and Takimoto, and show conclusively that styracitol is 1,5-anhydro-D-mannitol (private communication).

[4] Bell, Carr, Evans and Krantz, *J. Phys. Chem.*, **42**, 507 (1938); Dozois, Carr and Krantz, *J. Bact.*, **36**, 599 (1938); Carr and Forman, *J. Biol. Chem.*, **128**, 425 (1939); Krantz, Carr, Forman and Ellis, *J. Pharmacol.*, **67**, 187 (1939).

[5] Shinoda, Sato and Sato, *Ber.*, **65**, 1219 (1932).

[6] Wrede, *ibid.*, **52**, 1756 (1919).

[7] Wrede, *Z. physiol. Chem.*, **119**, 54 (1922).

[8] Bougault, Cattelain and Chabrier, *Compt. rend.*, **208**, 657 (1939). We are indebted to Mr. Theodore E. Perrine of this Institute for suggesting to us the use of this method. The desulfurizing action of Raney nickel upon organic sulfides, particularly in the development of the structural formula of biotin, has been described by du Vigneaud, Melville, Folkers, Wolf, Mozingo, Keresztesy and Harris [*J. Biol. Chem.*, **146**, 475 (1942)].

out, in small batches, according to the procedure of Zervas,[2] with a palladium catalyst. After deacetylation of the product there was obtained about 105 g. of crystalline styracitol, or 28% of the theoretical yield. The combined mother liquors from the styracitol crystallizations were kept in the laboratory for six years. At the end of that time 15 g. of a different substance had separated. This material was recrystallized from methyl alcohol as clusters of thin, more or less hexagonal plates which are typical of polygalitol. The melting point, 140–141°, and rotation, $[\alpha]^{20}\text{D}$ +42.4° in water (*c*, 2), identified it as polygalitol. The melting point was not depressed when the substance was mixed with an authentic sample of polygalitol, m. p. 141–142°, from *Polygala Senega*.

Anal. Calcd. for $C_6H_{12}O_5$: C, 43.90; H, 7.37. Found: C, 44.00; H, 7.36.

It is possible that the yield of polygalitol can be increased by the selection of different conditions of temperature, solvent and catalyst for the hydrogenation of tetraacetylhydroxyglucal.

Preparation of Glucothiose Derivatives.—Acetobromoglucose, prepared in an 85% yield by the method of Helferich and Günther,[9] was condensed with potassium ethyl xanthate according to Schneider, Gille and Eisfeld,[10] and the resulting **tetraacetylglucosyl ethyl xanthate** was isolated in an 85% yield. Degradation of this substance with sodium methylate to **sodium glucothiosate**[10] (not isolated), followed by oxidation with iodine and subsequent acetylation,[11] produced a 90% yield of **octaacetyl-β,β-diglucosyl disulfide**,[5] of m. p. 142–143°, and $[\alpha]^{20}\text{D}$ −156° in chloroform (*c*, 2). The rotation in chloroform has not been reported previously, but may be compared with the values $[\alpha]^{22}\text{D}$ −161° in acetylene tetrachloride and −185° in nitrobenzene.[11] Reduction of the disulfide derivative by aluminum amalgam was carried out according to Schneider and Bansa[11]; the amalgam appeared to be less active, so that two and one-half hours action was required. The yield was 4.1 g. from 5 g. of the disulfide. The product, **tetraacetyl-β-glucothiose,** was recrystallized from ether–isopentane in clusters of thin plates which melted at 74–75°. The melting point is in agreement with that reported originally by Wrede[7]; the value 113–114°, given by Schneider and Bansa,[11] may be that of a dimorphic modification. In 90% ethyl alcohol (*c*, 1.5), at 20°, the compound showed mutarotation, $[\alpha]^{20}\text{D}$ −8.3°, after five minutes, changing to +47.0 (constant) after 12 weeks. Wrede reported $[\alpha]^{15}\text{D}$ $-13.57 \rightarrow -6.78°$ in seven days; Schneider and Bansa reported $[\alpha]^{20}\text{D}$ $-6.04° \rightarrow +37.0°$ after twenty-one days.

Tetraacetylpolygalitol from Octaacetyl-β,β-diglucosyl Disulfide.—A mixture of 4 g. of the disulfide, 12 g. of Raney nickel and 200 cc. of absolute alcohol was shaken for ten days at room temperature. The nickel was removed by centrifugation, and the solution concentrated *in vacuo* to a sirup which was dissolved in ether and filtered from a small amount of flocculent precipitate. The ether was removed *in vacuo* and the residual sirup was extracted by shaking it several times with isopentane. As the isopentane evaporated it deposited clusters of acicular prisms resembling tetraacetylpolygalitol. The crystals were separated from adhering sirup and recrystallized from a mixture of ether and isopentane. The yield was 0.5 g. The product showed $[\alpha]^{20}\text{D}$ +38.9° in chloroform (*c*, 2), and a melting point of 73–74° in agreement with the values reported previously for tetraacetylpolygalitol.[1] A mixed melting point showed no depression.

Anal. Calcd. for $C_{14}H_{20}O_9$: C, 50.60; H, 6.07. Found: C, 50.71; H, 6.10.

Tetraacetylpolygalitol from Tetraacetyl-β-glucothiose.—The desulfurization of 1 g. of the tetraacetylglucothiose by 2.4 g. of Raney nickel was carried out as above. Tetraacetylpolygalitol was isolated in small yield, and identified by melting point and mixed melting point.

Thanks are expressed to Dr. Arthur T. Ness of this Laboratory, for carrying out the microanalyses.

Summary

The configuration of polygalitol as 1,5-anhydro-D-sorbitol has been established conclusively by two syntheses. In the first synthesis, polygalitol was shown to be the epimer of styracitol (1,5-anhydro-D-mannitol) by the isolation of both substances from the deacetylated products resulting from the hydrogenation of tetraacetylhydroxyglucal. In the second synthesis, tetraacetylpolygalitol was obtained simply by the desulfurization of tetraacetyl-β-D-glucothiose with Raney nickel.

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[9] As described by F. J. Bates and Associates, in "Polarimetry, Saccharimetry and the Sugars," United States Government Printing Office, Washington, D. C., 1942, p. 500.

[10] Schneider, Gille and Eisfeld, *Ber.*, **61**, 1244 (1928).

[11] Schneider and Bansa, *ibid.*, **64**, 1321 (1931).