under reduced pressure to dryness. The friable solid so produced was further dried in an Abderhalden pistol over potassium hydroxide; yield 17.2 g., m. p. 161° (sinters). *Anal.* Calcd. for $C_{41}H_{32}O_{26}$: C, 52.3; H, 3.43. Found: C, 52.3; H, 3.59. The optical rotation in ethyl acetate solution was determined, $\alpha^{23}D$ $-72.38°$ ($c = 2$).

Penta-(triacetylgalloyl)-*d*-glucose Diethyl Mercaptal.—Glucose diethyl mercaptal was made by the method of Fischer[5] by treatment of anhydrous *d*-glucose with ethyl mercaptan in the presence of cold aqueous hydrochloric acid: 11.45 g. of anhydrous, powdered *d*-glucose diethyl mercaptal was treated with 72 g. of triacetylgalloyl chloride in quinoline and chloroform exactly as described for the *d*-mannose derivative. The precipitation of the coupled product was made by addition to 90–100° petroleum ether rather than methanol; yield 65.5 g. of a white, amorphous, highly hygroscopic powder, m. p. 82° (sinters). The compound gave no color with dilute ferric alum solution. *Anal.* Calcd. for $C_{75}H_{72}O_{40}S_2$: S, 3.82. Found: S, 3.78 The optical rotation in chloroform solution was found: $\alpha^{22}D$ $+18.75°$ ($c = 2$).

***d*-Glucose Diethyl Mercaptal Pentagallate.**—This ester was made from 42.8 g. of the corresponding acetyl derivative following the procedure outlined for *d*-mannose pentagallate. During the deacetylation there was no odor of mercaptan, indicating that the mercaptal linkage was stable under the conditions of hydrolysis; yield 22.4 g. of light tan friable solid, m. p. 167° (sinters), which gave a positive test with reagent gelatine and a deep blue color with alcoholic ferric alum solution. *Anal.* Calcd. for $C_{45}H_{42}O_{26}S_2$: S, 6.03. Found: S, 5.91. The optical rotation in neutral ethyl acetate was determined: $\alpha^{23}D$ $+11.13°$ ($c = 2$)

Aldehydo-*d*-glucose Pentagallate.—The usual methods of demercaptalization using heavy metal salts were not attempted since heavy metal ions form insoluble precipitates with tannins; 4.25 g. (0.004 mole) of *d*-glucose diethyl mercaptal pentagallate was taken up in 100 cc. of water and 20 cc. of 1 *N* sulfuric acid and allowed to stand for two days. The yellow homogeneous solution smelled strongly of ethyl mercaptan. Oxygen-free nitrogen was passed through the solution for six days at room temperature at the end of which time there was no odor of mercaptan. The aqueous solution was extracted with neutral ethyl acetate, the ethyl acetate solution was washed with water and dried over anhydrous sodium sulfate. After filtering, the ethyl acetate solution was dried *in vacuo* and the residue was again taken up in ethyl acetate, filtered, and reduced to dryness. The product, after drying in an Aberhalden pistol, was a pale tan friable solid which was water soluble, gave a blue-black color with dilute ferric alum solution and a positive test with reagent gelatine; yield, 3.6 g., m. p. 113° (sinters). *Anal.* Calcd. for $C_{41}H_{32}O_{26}$: C, 52.3; H, 3.43. Found: C, 52.0; H, 3.61. The optical rotation in ethyl acetate solution was determined: $\alpha^{20}D$ $+10.13°$ ($c = 2$).

Summary

The preparations of β-*d*-glucose pentagallate, *d*-mannose pentagallate, *d*-glucose diethylmercaptal pentagallate, and aldehydo-*d*-glucose pentagallate have been accomplished.

All four are transparent vitreous solids that cannot be crystallized. However, each one has been adequately characterized.

Each is a very good tanning material and forms leather strictly comparable, both for quality and color, to that given by natural gallotannin.

CHAPEL HILL, NORTH CAROLINA RECEIVED MAY 3, 1943

[5] Fischer, *Ber.*, **27**, 674 (1894).

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 284]

Lead Tetraacetate Oxidations in the Sugar Group. IV.[1] The Rates of Oxidation of Trehalose, Levoglucosan, α-Methyl-L-sorbopyranoside, Polygalitol and Styracitol in Glacial Acetic Acid[2]

BY ROBERT C. HOCKETT, MARGARET T. DIENES AND HUGH E. RAMSDEN

Criegee's observation that *cis*-1,2-glycols are more rapidly oxidized by lead tetraacetate than *trans* glycols[3] led the senior author and McClenahan[4] to investigate correlations between oxidation rates and configurations in a series of pyranosides which contained α,β,γ-triol structures with fixed spatial relationships among the hydroxyl groups. The findings of this research are reiterated below in a more explicit form for the sake of easy reference in subsequent publications:

(1) Ultimately at least two moles of lead tetraacetate are consumed by a vicinal triol. Side reactions, such as the oxidation of formic acid, often prevent the consumption of oxidant from levelling off sharply at two moles.

(2) If two of the three hydroxyl groups bear a

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[1] Number III of this series, THIS JOURNAL, **65**, 403 (1943).

[2] The material in this paper is taken from theses submitted by Margaret T. Dienes and Hugh E. Ramsden in partial fulfillment of the requirements for the degree of Bachelor of Science in May, 1940, and in February, 1943, respectively. A similar paper was read before the Division of Organic Chemistry at the Detroit meeting of the American Chemical Society in September, 1940.

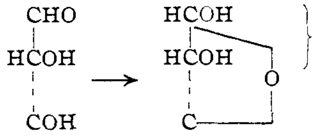
[3] Criegee, *Ann.*, **507**, 159 (1933).

[4] Hockett and McClenahan, THIS JOURNAL, **61**, 1667 (1939).

cis relation to each other in space (and are on adjacent carbon atoms) the structure is oxidized more rapidly than if all hydroxyl groups are *trans* with respect to their neighbors.

(3) An α-hydroxyaldehyde is attacked by lead tetraacetate, but the rate of oxidation is often low.

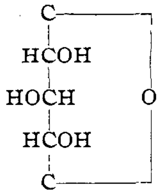
(4) An α-hydroxyaldehyde will be relatively rapidly oxidized if another hydroxyl group in a position γ or δ to the carbonyl permits formation of a pseudoglycol structure by cyclic hemiacetalization.



α-Hydroxy cyclic hemiacetal
(rapidly oxidized)

It is clear that if the space relations among the various hydroxyl groups are the major factor in determining oxidation rates, and if other influences are relatively unimportant, the four observations stated above will provide a powerful tool for the solution of problems of configuration in certain molecules. In particular, it should be possible to distinguish clearly and easily between the pyranosides containing a *trans–trans* configuration within the ring and those which have one or more pairs of hydroxyl groups in a *cis* relation. It should be emphasized that isolation of the final products of oxidation, while useful for many purposes, will not give any information concerning the original configurations of those carbon atoms which are eliminated or lose their asymmetry in the oxidation.[5]

Nevertheless, it seems unwise to base conclusions concerning the structures of compounds wholly upon such rate-of-oxidation curves until a sufficient background has been provided by the study of the behavior of substances with known configurations. The purpose of the present study was to record the oxidation rates of a number of sugar derivatives containing the following *trans–trans* configuration



If space relations are the dominant influence, these substances should all give curves of a very similar character. No breaks in the curves would be expected since the initial rate of cleavage is probably the rate determining step (see (1), (2) and (3)). The graph of Fig. 1 shows the extent to which six such substances resemble each other (I, II, III, IV, V and VI). The three compounds for which oxidation curves were published previously[4] have been restudied at the concentration and with the molar proportion of oxidant which have now been adopted as standard. Careful control of the water content of the solutions has also been established since the first publications were made.

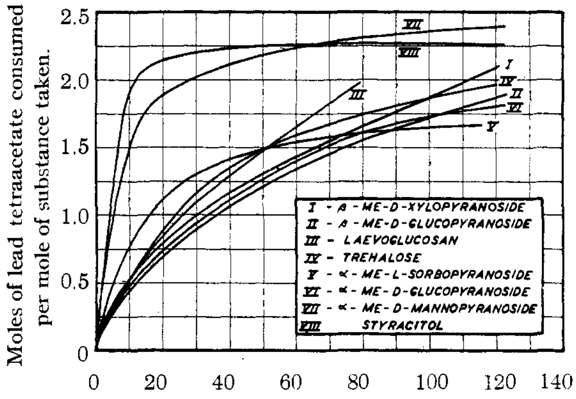
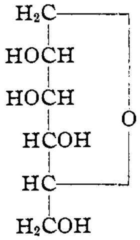
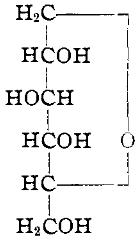


Fig. 1.—Oxidation of sugar derivatives by lead tetraacetate in dry acetic acid: 0.00025 mole substance in 100 cc., molar ratio of $Pb(OAc)_4$ to substance is 15.2/1; water less than 0.05%.

The structures of polygalitol and styracitol must be considered unsolved problems at this writing. The Zervas[6] synthesis of the latter should produce either a 1,5-anhydro-D-mannitol or a 1,5-anhydro-D-sorbitol.



A



B

Researches directed toward choice between these alternatives have yielded contradictory results.[6,7,8,9,10] The present method would seem

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(5) *Cf.* Jackson and Hudson, THIS JOURNAL, **61**, 1530 (1939); *ibid.*, **62**, 958 (1940).

(6) Zervas, *Ber.*, **63**, 1689 (1930).

(7) Asahina and Takimoto, *ibid.*, **64**, 1803 (1931).

(8) Freudenberg and Rogers, THIS JOURNAL, **59**, 1602 (1937).

(9) Freudenberg and Sheehan, *ibid.*, **62**, 559 (1940).

(10) Zervas and Papadimitriou, *Ber.*, **73**, 174 (1940).

well-adapted to the solution of such a question as this, once it has become established as invariably reliable. Freudenberg and Rogers[8] applied essentially this procedure in their attempt to solve the problem but full data concerning related substances were not then available for comparison. In the paper of Freudenberg and Sheehan,[9] the original conclusion was reversed.

Figure 2 shows a very notable resemblance between the oxidation curves of α-methyl-D-mannopyranoside and styracitol, strongly suggesting that the latter is a 1,5-mannitan (A). However, because of the contradictory nature of the other data which have accumulated, we are seeking further evidence concerning the structure of styracitol in order to test whether the oxidation curves can be depended upon to answer such a question correctly.

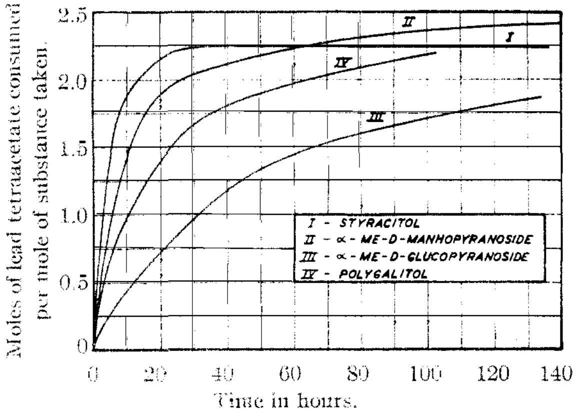

Fig. 2.—Oxidation of sugar derivatives by lead tetraacetate in dry acetic acid: 0.00025 mole substance in 100 cc.; ratio of $Pb(OAc)_4$ to substance, 15.2/1; water less than 0.05%.

The position of polygalitol remains uncertain. Its oxidation curve lies in such a position that no safe conclusion can be drawn as to whether it belongs to the mannopyranoside or glucopyranoside family.[11]

We wish to thank Dr. J. C. Krantz and C. J. Carr, of the Department of Pharmacology, University of Maryland Medical School, for samples of styracitol and polygalitol, Dr. C. S. Hudson and Dr. N. K. Richtmyer of the National Institute of Health for polygalitol samples, Miss Maryalice Conley of this Laboratory for samples of synthetic styracitol and for measurements of its rate of oxidation under strictly anhydrous conditions, and the Bureau of Chemistry and Soils, United States Department of Agriculture, for a sample of L-sorbose.

Experimental Part

Preparation of Acetic Acid.—Criegee and Buchner,[12] as well as Baer, Grosheintz and H. O. L. Fischer[13] have shown the powerful influence of water upon the speed of oxidations by lead tetraacetate. Hence it seemed wise to make a more careful control of the water content of the glacial acetic acid used as an oxidation medium. The practice has been adopted of rendering U. S. P. acetic acid aldehyde-free by boiling with chromic acid, fractionating through an efficient column and then titrating for water-content by the Almy, Griffin and Wilcox[14] modification of Karl Fischer's[15] method. The acid prepared as described usually contains very nearly 0.60% water which is sufficient to have a small but observable effect on oxidation rates. The water is removed by adding the calculated quantity of acetic anhydride and boiling under reflux for three hours in an apparatus protected from the atmosphere. The boiling is necessary to complete the reaction within a reasonable time. Subsequent titration usually shows from 0 to 0.05% water. This specially dried acetic acid is used both for making standard lead tetraacetate solutions and as a reaction medium. The standard solution is dispensed from an all-glass automatic buret with a two-liter reservoir and efficient protection from atmospheric moisture.

Samples.—The substances used all conformed closely to the rotations and melting points recorded in the literature, and were finely powdered and dried at 60° in a vacuum oven before use.

Procedure.—It is desirable to use as large an excess of oxidizing agent as possible in making rate measurements in order that reactions may be pseudo-unimolecular. Since the concentration of oxidant is limited by the solubility of lead tetraacetate and the weight of sample by the practical considerations attendant upon weighing and handling, the conditions for rate of oxidation measurements have been standardized as follows: (1) The lead tetraacetate solution is made about one-tenth normal. (2) The sample is 0.00025 mole. (3) The volume of standard solution containing 0.0038 mole $Pb(OCOCH_3)_4$ is calculated (a 15.2/1 ratio of oxidant to sample). (4) The sample in a 100-cc. volumetric flask is dissolved in a volume of special acetic acid equivalent to 99 cc. minus the volume of standard solution which is to be added. (5) The calculated volume of standard lead tetraacetate solution is added rapidly from an all-glass buret. The time is noted from the first contact of oxidizing agent with substrate. (6) The solution is made up to 100 cc. with special acetic acid and placed in a thermostat at 25°. (7) Samples are removed at noted time intervals with a 10-cc. pipet and dropped into 25-cc. volumes of a solution containing about one-half gram of sodium iodide and five grams of sodium acetate. (8) The liberated iodine is titrated with 0.0200 *N* sodium thiosulfate. (9) The results are plotted as the ratio of

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(11) Cf. Richtmyer and Hudson, THIS JOURNAL, **65**, 64 (1943).

(12) Criegee and Buchner, *Ber.*, **73**, 563 (1940).

(13) Baer, Grosheintz and Fischer, THIS JOURNAL, **61**, 2607, 3379 (1939).

(14) Almy, Griffin and Wilcox, *Ind. Eng. Chem., Anal. Ed.*, **12**, 392 (1940).

(15) Fischer, *Angew. Chem.*, **48**, 394 (1935).

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.

CAMBRIDGE, MASS. RECEIVED MARCH 17, 1943

[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)].