panied by decomposition, as disclosed by an evolution of gas (water vapor) from the mass.

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THE REACTIVITY OF THE METHYLATED SUGARS. I. THE ACTION OF ALKALINE HYDROGEN PEROXIDE SOLUTION ON TETRAMETHYL-*d*-GLUCOSE

By Edwin Lysle Gustus[1] with W. Lee Lewis

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The methylated sugars, because of the replacement of a labile hydrogen by a non-polar methyl group, would seem to offer an opportunity for direct experimental evidence of the validity of certain theories offered in explanation of the reactivity of the simple sugars.

Thus Nef[2] and his students extended the conceptions of Lobry de Bruyn,[3] Wohl and Neuberg[4] and Fischer[5] to a comprehensive explanation not only of the reciprocal interconversion of sugars under the influence of mild alkalies, but to the formation of isomeric ketoses, and various ene-diols whose subsequent dissociation led to the formation, in the presence of oxidizing agents, of the several acids containing from one to six carbon atoms, found experimentally. Nef believed that these intermediate ene-diols formed by a process of selective addition and loss of water.[2a,6] In the presence of alkaline oxidizing agents, dissociation took place at the point of unsaturation into active aldehydic forms, which could either oxidize to the corresponding acids or rearrange to form ordinary aldehydes. These latter, in turn, might give rise to similar ene-diols, thus repeating the process.

Illustrating with *d*-glucose and the 1,2-ene-diol common to *d*-glucose, *d*-mannose and *d*-fructose

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[1] Abstracted from a dissertation submitted by Edwin Lysle Gustus to the Graduate School of Northwestern University, in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

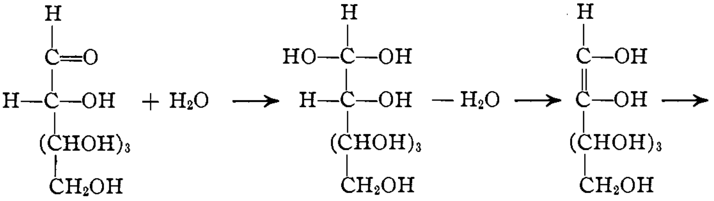
[2] (a) Nef, *Ann.*, **357**, 214 (1907); (b) **376**, 1 (1910); (c) **403**, 204 (1913). (d) Anderson, *Am. Chem. J.*, **42**, 401 (1909). (e) Lewis, *ibid.*, **42**, 301 (1909). (f) Glattfeld, *ibid.*, **50**, 135 (1913). (g) Lewis and Buckborough, This Journal, **36**, 2385 (1914). (h) Jensen and Upson, *ibid.*, **47**, 3023 (1925).

[3] Lobry de Bruyn and Van Ekenstein, *Rec. trav. chim.*, **14**, 156, 203, 213 (1895); **16**, 162, 259, 262, 278 (1897); **19**, 1 (1900).

[4] Wohl and Neuberg, *Ber.*, **33**, 3099 (1900).

[5] Fischer, *Ber.*, **28**, 1149 (1895).

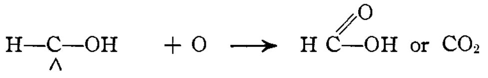
[6] Spoehr, *Am. Chem. J.*, **43**, 228 (1910).



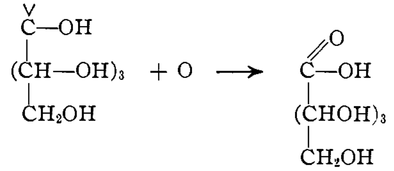
I d-Glucose aldehyde

II *d*-Glucose aldehydrate

III 1,2-Ene-diol



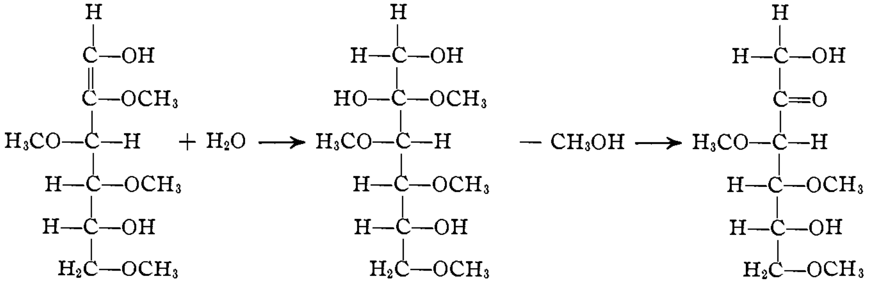
Active formaldehyde



Active *d*-arabinose

d-Arabonic acid

If this mechanism is correct in detail, there would seem to be no reason for the well-known greater stability[7] of the methylated sugars. Methylated sugars under the influence of alkalies should undergo the reciprocal conversion characteristic of the simple sugars, and should give on oxidation in alkaline media, the analogous acids containing from one to six carbon atoms. Thus, 2,3,4,6-tetramethyl-glucose[8] should add water to form its aldehydrate and, by selective dehydration, give the 1,2-ene-diol (IV) common to tetramethyl-*d*-glucose and tetramethyl-*d*-mannose. This in turn could add water to form V, which being an unstable non-cyclic hemi-acetal would lose methyl alcohol readily, leading to 3,4,6-trimethyl-*d*-levulose.



IV V VI

The process of ene-diol formation could then continue exactly as with

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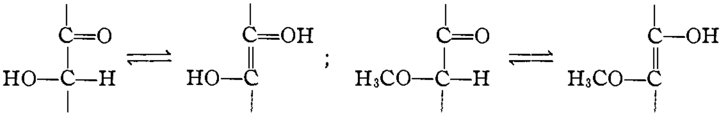
[7] (a) Purdie and Irvine, *J. Chem. Soc.*, **85**, 1060 (1904). (b) Irvine and Cameron, *ibid.*, **85**, 1077 (1904).

[8] (a) Hirst, *ibid.*, **128**, 350 (1926). (b) Charlton, Haworth and Peat, *ibid.*, **129**, 89 (1926).

the simple sugars, except that methyl alcohol would split off from the resulting hemi-acetals instead of water from a hydrated ketone.

This is inconsistent with the known stability of methylated sugars to alkalies, Fehling's solution, mineral acids and fermentation. Moreover, we have found that when *n*-tetramethyl-glucose is oxidized with alkaline hydrogen peroxide, there are formed predominantly acids of one and of five carbon atoms, that is, formic acid, carbonic acid and a methylated *d*-arabonic acid. This points strongly to the conclusion that such a methylated hexose forms only as 1,2-ene-diol, further enolization meeting with resistance at the point of the first methylated hydroxyl group.[9]

A slight modification of Nef's theory will, however, bring all of the experimental facts into harmony. If the conception of selective addition and loss of water in the ene-diol formation be replaced by a simple assumption of keto-enol tautomerism, it will be found that the reciprocal conversion of simple sugars under the influence of mild alkalies and the progressive enolization find ready and simple explanation.



$$\begin{array}{c} | \\ C{=}O \\ | \\ HO{-}C{-}H \\ | \end{array} \rightleftharpoons \begin{array}{c} | \\ C{=}OH \\ \| \\ HO{-}C \\ | \end{array} ; \quad \begin{array}{c} | \\ C{=}O \\ | \\ H_3CO{-}C{-}H \\ | \end{array} \rightleftharpoons \begin{array}{c} | \\ C{-}OH \\ \| \\ H_3CO{-}C \\ | \end{array}$$

Furthermore, the methylated ene-diol common to tetramethyl-glucose and tetramethyl-mannose (IV) cannot further enolize, as it is not probable that the methyl group joined through oxygen to the second carbon atom will leave its position to unite directly with Carbon 1.

Certain deductions as to the action of alkalies on methylated sugars become apparent at once if the accepted theory of common ene-diols, as modified, is the correct explanation of the Lobry de Bruyn reaction. Tetramethyl-*d*-mannose and tetramethyl-*d*-glucose should undergo reciprocal conversion in mild alkalies, but the analogous keto sugar cannot form. This we have experimentally confirmed in this Laboratory,[10] the so-called normal forms of the tetramethylated aldoses resulting in each case.

Nef sought carefully in his earlier work for proof of the presence of 1,2-ene-diols, giving pentonic acids in an alkaline oxidizing medium. These latter were subsequently found by Glattfeld[2f] and Upson.[2h]

It is worthy of mention, however, that the large amount of methylated *d*-arabonic acid found in the present study also further confirms Nef's premise.

The dissociation of the 1,2-ene-diol of 2,3,4,6-tetramethyl-glucose should give on oxidation, in addition to formic and carbonic acids, 2,3,5-trimethyl-*d*-arabonic acid.

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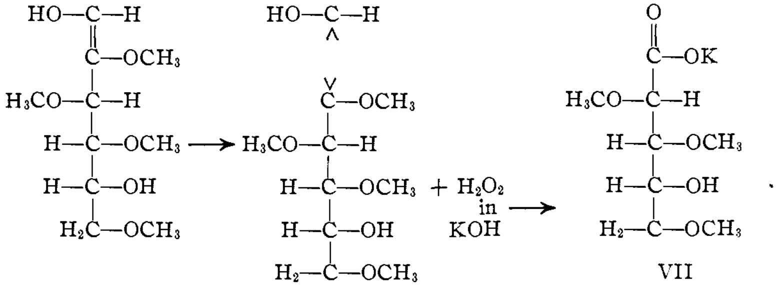
[9] (a) Zemplén and Braun, *Ber.*, **58**, 2566 (1925). (b) Sobotka, *J. Biol. Chem.*, **69**, 267 (1926).

[10] Unpublished work of Wolfrom and Green.


VII

There resulted, however, in the present instance, a dimethylpentonic lactone. Methyl alcohol was found in the distillate after acidification of the original oxidation reaction mixture, which suggests that the loss of methyl alcohol occurred on lactonization.[11]

The structure of this acid will be carefully studied because of its bearing upon the position of the methyl groups in normal tetramethyl-glucose.[12]

Experimental Part

The Preparation of Tetramethyl-glucose.—The methyl glucoside of 2,3,4,6-tetramethyl-glucose was prepared by the method of Haworth:[13] In this manner 322 g. was obtained from 600 g. of anhydrous glucose; yield, 38.7%. The product was a limpid, light straw-colored liquid; b. p., 115–117°, at 15 mm. The glucoside was hydrolyzed in a 7% aqueous solution containing 7% of hydrogen chloride, heated in a water-bath at 70° for eight hours. At the end of this period, the temperature of the bath was raised to 80° for five hours, after which the *dextro* rotation did not rise even on raising the bath to the boiling temperature. The solution was cooled, partly neutralized with sodium carbonate, finished with a slight excess of barium carbonate, clarified with charcoal, filtered and evaporated at 30° with an air blast to a crystalline mass. Drying was completed on large pieces of plate glass, and the light brown material powdered in a mortar. The tetramethyl-glucose was extracted with ether in a large Soxhlet extractor and recrystallized from low-boiling petroleum ether containing 5 cc. of ethyl ether per liter. This latter operation is best carried out in a continuous siphon extractor.

There was thus obtained from the 322 g. of 2,3,4,6-tetramethyl glucoside 242 g. of crystalline tetramethyl-glucose; yield, 80%. The product consisted of colorless needles; m. p., 88–89° (uncorr.); $[\alpha]_D^{20} = +83.4$; 0.5045 g. of substance dissolved in water, and the solution made up to 10.09 cc. at 20° (that is, "c" = 5), gave $\alpha = +4.17°$ in a 1-dcm. tube.

Anal. Subs., 0.1006, 0.2010: CO_2, 0.1878, 0.3726; H_2O, 0.0775, 0.1568. Calcd. for $C_{10}H_{20}O_6$: C, 50.83; H, 8.53. Found: C, 50.91, 50.55; H, 8.63, 8.67.

Preliminary Study of Optimum Conditions of Oxidation.—Two sets of preliminary oxidation runs were made on small amounts of tetramethyl-glucose. The first set consisted of four flasks, in each of which was placed 0.01 mole of tetramethyl-glucose, 0.065 mole of hydrogen peroxide, that is, 74 cc. of 3% solution, and 0.077 mole of potassium hydroxide. The sugar was dissolved in the hydrogen peroxide and added with vigorous shaking over a period of ten minutes to 100 cc. of a solution containing 4.3

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[11] Denham and Woodhouse, *J. Chem. Soc.*, **111**, 246 (1917).

[12] Hudson, THIS JOURNAL, **48**, 1435 (1926).

[13] Haworth, *J. Chem. Soc.*, **107**, 8 (1915).

g. of potassium hydroxide. The total volume of the combined solutions was then increased to 200 cc. with water.

The second series of flasks was prepared with double the concentration of hydrogen peroxide. In this case there was used 0.01 mole of tetramethyl-glucose, 0.13 mole of hydrogen peroxide, 148 cc. of 3% solution and 0.077 mole of potassium hydroxide, made up to 200 cc. The flasks were stoppered with soda lime tubes, and set aside at room temperature. Daily tests were made with starch-potassium iodide paper to insure the presence of hydrogen peroxide, and frequent qualitative tests for reducing sugar with Fehling's solution. Quantitative determinations were made on the twenty-sixth and thirty-eighth days by a modified Munson and Walker method, continuing the boiling of the solution ten minutes. After 38 days the hydrogen peroxide gave but a faint test in any flask, while the flasks had lost roughly but 85% of their reducing power. The preliminary tests were repeated at 45° and at 60°. While proceeding somewhat more rapidly at first at the latter temperature, it took as long to oxidize the methylated glucose completely as at 45° due to the decomposition of the hydrogen peroxide at the higher temperature. The time of oxidation was five days.

Oxidation of the Methylated Glucose.—Eight 2-liter, short-necked, round-bottomed Pyrex flasks were fitted with rubber stoppers carrying thermometers extending to the bottom of the flasks, and with soda lime tubes. Each flask was ultimately to contain tetramethyl-glucose, hydrogen peroxide and alkali, in the ratio of 0.01 mole of sugar, 0.13 mole of hydrogen peroxide and 0.077 mole of potassium hydroxide. Twenty-five g. of pure tetramethyl-glucose was dissolved in 780 cc. of 3% hydrogen peroxide solution, and added to 126.5 cc. of special potassium hydroxide solution containing 0.1809 g. per cc. The volume was then made up to 1000 cc. with water, and held at 45° for five days. At the end of the period, the flasks showed slight tests for hydrogen peroxide and the remaining portion of the oxidizing solution (780 cc. of 3% hydrogen peroxide solution, and 126.5 cc. of the special potassium hydroxide solution) was added to each flask. Periodic tests were made for hydrogen peroxide and quantitative determinations of reducing power. At the end of five days' further holding at 45°, the hydrogen peroxide test having become very faint and slight reduction still being present, 100 cc. of 30% hydrogen peroxide was added to each flask. At the expiration of six days more, hydrogen peroxide and reducing sugar had disappeared. Four-tenths g. of a flocculent, white precipitate was collected from the flasks at this point; this proved, on analysis, to be barium phosphate.

Determination of the Volatile Acids.—Carbon dioxide was determined by the modified method of Knorr.[14] Two samples of 400 cc. were taken from a typical flask and concentrated to 125 cc. Calculated to 100 g. of tetramethyl-glucose, the determinations gave 13.41 and 13.42 g. of carbon dioxide, respectively, or a total of 24.22 g. for the net 180.52 g. of tetramethyl-glucose oxidized.

Formic acid was determined by adding hydrochloric acid to the flasks and distilling at 70° under 25 mm. pressure. The salt cake was dissolved by warming in 200 cc. of water and repeatedly distilled under reduced pressure until tests of the distillates showed no hydrochloric acid. The combined distillates from each flask were titrated for total acidity, and for formic acid, by Jones'[15] method, as modified by Klein.[16] This was checked by the gravimetric method of Fincke.[17] Hydrogen chloride was deter-

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[14] Leach, "Food Inspection and Analysis," John Wiley and Sons, New York, **1913**, 3rd ed., p. 338.

[15] Jones, *Am. Chem. J.*, **17**, 539 (1895).

[16] Klein, *Ber.*, **39**, 2640 (1906).

[17] Fincke, *Z. Nahr. Genussm.*, **21**, 1 (1911).

mined volumetrically by Volhard's method.[18] Control analyses of known mixtures showed that the methods of Jones and Fincke for formic acid agree within the experimental error and that dil. formic acid does not interfere with the Volhard method for hydrogen chloride. This method of separating volatile and non-volatile acids, however, is not sharp, as traces of a solid organic acid carry over in the distillate, making total acidity and formic acid by the Jones method high. The total net 180.52 g. of tetramethyl-glucose yielded 60.98 g. of formic acid.

The Non-Volatile Acids.—The non-volatile acids were taken up from the salt cake by repeated extractions with boiling absolute alcohol. The alcohol was removed by distillation under reduced pressure, yielding a total of 93.27 g. of light brown, mobile gums. On standing for a week the gum crystallized to a solid cake. The crystals were extracted with boiling petroleum ether in a continuous extractor equipped with a stirrer. After recrystallization from petroleum ether, and drying in a vacuum desiccator, there was thus obtained 14.1 g. of long, colorless needles, melting sharply at 77° (corr.). The crystals are biaxial, optically positive with a small optical angle; α, 1.475; γ, 1.526; $[\alpha]^{20}_{D} = +86.6$; 0.5045 g. of substance dissolved and diluted to 10.1 cc. with water gave $\alpha = +4.33$ in a 1-dcm. tube; $[\alpha]^{20}_{D} = +65.2$; 0.5045 g. dissolved and diluted to 10.1 cc. with chloroform gave $\alpha = +3.26$ in a 1-dcm. tube. A highly purified sample showed the following slow change in water, indicating a 1,4-acid lactone; 0.5005 g. of substance dissolved and diluted to 10.01 cc.

Interval, hours	α, 1-dcm. tube	$[\alpha]^{20}_{D}$	Interval, hours	α, 1-dcm. tube	$[\alpha]^{20}_{D}$
0.3	+4.45	+89	92.0	3.98	79.6
3.0	4.39	87.8	190.0	3.85	77.0
21.0	4.30	86.0	163.0	3.77	75.4
45.0	4.20	84.0	237.0	3.59	71.8
70.0	4.07	81.4			

Methoxyl was determined by the Zeisel method as modified by Hewitt and Moore.[19]

Anal. Subs., 0.1378, 0.1236: AgI, 0.3732, 0.3314. Calcd. for $C_5H_6O_3(OCH_3)_2$: OCH_3, 35.2. Found: 35.7, 35.4.

Anal. Subs., 0.2001, 0.1567, 0.1762: CO_2, 0.3497, 0.2734, 0.3074; H_2O, 0.1237, 0.0972, 0.1122. Calcd. for $C_7H_{12}O_5$: H, 6.88; C, 47.73. Found: H, 6.87, 6.89, 7.07; C, 47.66, 47.57, 47.58.

The *p*-bromophenylhydrazide was prepared from 1.5174 g. of the material, 5.77 g. (3 molecular proportions) of *p*-bromophenylhydrazine hydrochloride, 2.12 g. (3 molecular proportions) of anhydrous sodium acetate and 25 cc. of water heated in a sealed tube to 140° for three and a half hours. The aqueous layer was separated from the thick, red, oily hydrazide, which was purified by taking up in ether, washing repeatedly with 2% acetic acid solution and finally with distilled water. After drying with calcium chloride, ether was removed under reduced pressure, leaving 0.785 g. of a thick, reddish-brown sirup; yield, 25%.

Anal. Subs., 0.2196: N_2, 13.78 cc. Calcd. for $C_{13}H_{19}O_5N_2Br$: N, 7.72. Found: 7.85.

By titration with 0.0093 *N* barium hydroxide, 0.0774 g. in boiling water required 48.40 cc.; calcd. for dimethyl arabonolactone, 47.29 cc. The slow disappearance of the color in the cold and the rapid disappearance in hot solution suggested a stable lactone ring. The freezing-point method, in acetic acid, gave a molecular weight of 172; calcd. for $C_7H_{12}O_5$, 176.

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[18] Volhard, *Ann.*, **190**, 1 (1878).

[19] Hewitt and Moore, *J. Chem. Soc.*, **81**, 318 (1902).

These data show the substance to be a dimethylated lactone of a pentonic acid.

Methyl alcohol was sought in the distillate from the acidified solution of the potassium salts of the acids resulting from the oxidation. Two liters were distilled through a 50cc. column. The first 250 cc. gave strong tests for methyl alcohol by both the resorcinol and gallic acid tests.[20] The 250 cc. was further fractionated and gave a methyl 2,5-dinitrobenzoate, melting correctly at 107–108°, and showing no depression with a known specimen of methyl 2,5-dinitrobenzoate.

The residual non-volatile gums were taken up in acetone, chilled and a small amount of a yellow, wax-like substance was filtered off. It changed to a colorless liquid below 100°, was soluble in warm absolute alcohol and insoluble in cold. On attempted recrystallization from acetone-alcohol, a few yellow crystals as bunched cubes, melting at 113° and giving the nitroprusside test for sulfur, were obtained. A very small amount of a second crystalline substance in the form of colorless needles was isolated from the wax and melted sharply at 121°; it contained no sulfur. Further identification of the two crystalline forms was abandoned.

The residual 0.8328 g. of light yellow, waxy gum was purified by solution in hot acetone-alcohol from which it came down as a flocculent precipitate on cooling. After holding under reduced pressure for 20 minutes at the melting point 60°, it was analyzed by the micro-combustion method of Wise.[21]

Anal. Subs., 0.01594, 0.01531: CO_2, 0.04142, 0.04019; H_2O, 0.01835, 0.01775. Calcd. for $C_{12}H_{26}S$: C, 71.19; H, 12.96. Found: C, 70.87, 71.58; H, 12.79, 12.89.

Anal. (Carius). Subs., 0.03035: $BaSO_4$, 0.03393. Calcd. for $C_{12}H_{26}S$: S, 15.84. Found: S, 15.36.

The substance was without optical effect and is obviously not an oxidation product of tetramethyl-glucose.

The residual gums now appeared as a dark, viscid sirup weighing 74.63 g. Titration in cold and finally in hot aqueous solution gave evidence of lactones and an average molecular weight of 186, assuming all acids present to be monobasic. After a thorough preliminary study of the use of alkaloids in separating the gum, 69.69 g. was dissolved in 100 cc. of water and boiled while stirring with 155 g. of anhydrous brucine, being 5% in excess of that calculated. The alkaloid dissolved in three hours. The solution was cooled, filtered and evaporated to dryness under reduced pressure. It was dissolved in alcohol and the evaporation repeated in order to remove all water. Two and a half g. of brucine salts from the preliminary tests was now added and the whole refluxed with 500 cc. of dry acetone. The light brown powder which remained was filtered off and again refluxed with 300 cc. of dry acetone. The insoluble powder was collected on a filter, dried on a porous plate and finally in a desiccator; yield, 64.40 g.; m. p., 153–155° (uncorr.).

Anal. (Kjeldahl). Subs., 2.0552, 1.6363: 26.39, 21.33 cc. of 0.2700 *N* acid. Calcd. for $C_{30}H_{40}O_{10}N_2$: N, 4.76. Found: 4.86, 4.94.

Since the brucine salts could not be recrystallized, they were dissolved in a liter of water and the brucine removed with barium hydroxide solution; the barium was removed with dil. sulfuric acid. The residue, after distillation under reduced pressure, re-solution in alcohol and evaporation, consisted of a light brown gum which formed a solid cake of crystals. They were mixed with washed, ignited sand and extracted with petroleum ether in a Jackson extractor.[22] After recrystallization in this manner,

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[20] Mulliken, "Identification of Pure Organic Compounds," John Wiley and Sons, New York, **1904**, vol. I, p. 171.

[21] Wise, This Journal, **39**, 2055 (1917).

[22] Jackson and Zanetti, *Am. Chem. J.*, **38**, 461 (1907).

there was obtained 15.26 g. of substance, melting sharply at 77–78° (uncorr.). A mixed melting point with the dimethyl *d*-arabonolactone previously isolated, showed no change.

Anal. Subs., 0.1961, 0.1753: CO_2, 0.3424, 0.3068; H_2O, 0.1227, 0.1069. Calcd. for $C_7H_{12}O_5$: C, 47.73; H, 6.88. Found: C, 47.61, 47.73; H, 6.95, 6.78.

The acetone-soluble residual brucine salts were freed from brucine in the usual manner, evaporated to dryness, dissolved in alcohol and again evaporated in a vacuum. The recovered gums weighed 46.78 g. and titrated for an average molecular weight of monobasic acids of 163.3. After repeated efforts to fractionate the gums with alkaloids, which reduced the material to 39.38 g., they were esterified according to the method of Hirst and Purves.[23] The product was resolved after seven fractionations, using a column and mercury pump, into 19.56 g. of tarry residue and three fractions: A, 1.3 g., b. p. 74–81°; B, 8.2 g., b. p. 85–86.5°; C, 2.6 g., b. p. 88–98°, at a pressure of 0.5 mm. The fractions were at first colorless, turning light yellow on standing. The specific rotations in chloroform were $[\alpha]^{20}_D = +12.5$, $+26$ and $+30.7$; n^{20}_D, A, 1.4370; B, 1.4411; C, 1.4425. The molecular weight of Fraction B was determined by saponification, and the methoxyl content in the usual manner.

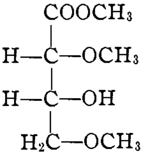
Mol. wt. Subs., 0.2043, 0.2426: 68.41, 80.37 cc. of 0.01776 *N* $Ba(OH)_2$. Found: mol. wt., 168, 170 (calcd. as a monobasic acid).

Anal. Subs., 0.2581, 0.1743: AgI, 0.9532, 0.6433. Found: OCH_3, 48.76, 48.74.

A combustion analysis was carried out using the modifications of Reimer,[24] and Levene and Bieber.[25]

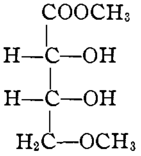
Anal. Subs., 0.1846, 0.1565: CO_2, 0.3136, 0.2647; H_2O, 0.1245, 0.1049. Found: C, 46.33, 46.13; H, 7.49, 7.45.

These results suggest that Fraction B is a mixture of the methyl esters of a mono- and a dimethylated tetronic acid, possibly *d*-erythronic. The following structures are suggested.



$$\begin{array}{c}\mathrm{COOCH_3}\\|\\\mathrm{H{-}C{-}OCH_3}\\|\\\mathrm{H{-}C{-}OH}\\|\\\mathrm{H_2C{-}OCH_3}\end{array}$$

Methyl ester of 2,4-dimethyl *d*-erythronic acid; C, 47.19; H, 7.87; OCH_3, 52.25; mol. wt., 178.



$$\begin{array}{c}\mathrm{COOCH_3}\\|\\\mathrm{H{-}C{-}OH}\\|\\\mathrm{H{-}C{-}OH}\\|\\\mathrm{H_2C{-}OCH_3}\end{array}$$

Methyl ester of 4-methyl *d*-erythronic acid. C, 43.90; H, 7.32; OCH_3, 37.81; mol. wt., 164.

The residue from the distillation was dissolved in chloroform and evaporated under reduced pressure on ignited sand. It was then extracted for two days in a Jackson extractor with 60–70° petroleum ether containing 5 cc. of chloroform per liter. There were thus obtained an oil and 1.75 g. of purified crystals; m. p., 77–78° (uncorr.). The melting point did not change on mixing some of the substance with our dimethyl *d*-arabonolactone.

Anal. Subs., 0.1761, 0.1192: CO_2, 0.3091, 0.2093; H_2O, 0.1080, 0.0744. Calcd. for $C_7H_{12}O_5$: C, 47.73; H, 6.88. Found: C, 47.87, 47.87; H, 6.82, 6.94.

The oily portion of the extract boiled at 135–155° at 0.5 mm.; yield, 6.48 g.; $[\alpha]^{20}_D = +46.5$; 0.4075 g. substance made up to 10.09 cc. in chloroform gave $\alpha = +1.88$ in a 1-dcm. tube; n^{20}_D, 1.4655.

Anal. Subs., 0.1657, 0.1623: CO_2, 0.2948, 0.2887; H_2O, 0.1017, 0.1000. Found:

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[23] Hirst and Purves, *J. Chem. Soc.*, **123**, 1357 (1923).

[24] Reimer, THIS JOURNAL, **37**, 1636 (1915).

[25] Levene and Bieber, *ibid.*, **40**, 460 (1918).

C, 48.52, 48.52; H, 6.82, 6.85. Subs., 0.1950, 0.2581: AgI, 0.5735, 0.7623. Found: OCH_3, 38.84, 38.99.

Considering the material as a monobasic acid, the following results were obtained by saponification.

Mol. wt. Subs., 0.2101, 0.2153: 65.21, 67.74 cc. of 0.01776 *N* $Ba(OH)_2$. Found: mol. wt., 181, 180.

The results indicate a mixture. The high molecular weight and low methoxyl content indicate a mixture of methyl esters of acids having a five- or six-carbon chain.

Ordinarily it is believed that the methoxyl groups are very firmly attached to the methylated sugar chain. Denham and Woodhouse[26] have observed demethylation during acetolysis of methylated celluloses.

The residual 9.8 g. of stiff black tar was lost in further attempts to resolve it by solvents and by esterification. Titration indicated a mixture of higher free acids and their lactones.

The foregoing experimental work definitely shows that tetramethylglucose, on oxidation with alkaline hydrogen peroxide solution, gives mainly the products to be expected from the oxidation of the dissociated 1,2-ene-diol of the sugar.

In the case of the unmethylated sugars, the vigorous oxidizing action of alkaline hydrogen peroxide solution seems to cause such destruction of the sugar molecule that other less vigorous agents have been largely employed. Alkaline hydrogen peroxide solution gives with glucose[27] a very large amount of formic acid, showing a rather complete burning of the sugar chain.

Less vigorous oxidizing agents have been used in the hope of obtaining a more nearly complete picture of the mechanism of oxidation, by leaving intact the higher acids in sufficient quantities to be isolated and identified. The most recent work in this direction is the work of Jensen and Upson,[2h] who oxidized glucose with copper carbonate in sodium carbonate solution. The oxidizing solution is a modification of Soldaini's reagent.[28]

The results of their experiments will be quoted in the authors' own words. "The oxidation products from 200 g. of *d*-glucose, excluding carbon dioxide, amounted to 142 g. in which the following substances were identified: formic acid, 30.86 g.; glycolic acid, 15.3 g.; mannonic acid, small amount; glunonic acid, 1–2 g.; arabonic acid, 6 g., isolated as the brucine salt; erythronic acid, isolated in the form of the brucine salt and identified as the lactone, 3.6 g.; *dl*-glycerinic acid, 6.2 g., isolated in the form of brucine salts; *d*-threonic acid, trace."

A summary of the products isolated from the oxidation of tetramethyl-

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[26] Denham and Woodhouse, *J. Chem. Soc.*, **103**, 1737 (1913).

[27] Ref. 6, p. 231.

[28] Soldaini, *Gazz. chim. ital.*, **6**, 322 (1876).

glucose by alkaline hydrogen peroxide solution, as determined in the present study, is given below for purposes of comparison.

Oxidation of 180.52 g. of tetramethyl-glucose gave 24.22 g. of carbon dioxide, 60.98 g. of formic acid (Fincke method), and 92.65 g. of non-volatile material. In the latter material there were identified 31.11 g. of dimethyl *d*-arabonolactone; 12.08 g. of methyl esters of methylated tetronic acids, of which 8.19 g. was shown to be a probable mixture of the methyl esters of monomethyl and dimethyl *d*-erythronic acids; 6.48 g. of a mixture of methyl esters of demethylated hexonic and pentonic acids. No non-volatile acids with a shorter chain than four carbon atoms were isolated; the composite non-volatile acids never showed molecular weights below 160 to 120 and were completely soluble in alkali.

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Summary

1. On oxidizing tetramethyl-glucose with an alkaline solution of hydrogen peroxide, there were obtained from 100 g. of the sugar, 13.42 g. of carbon dioxide, 33.78 g. of formic acid and 51.33 g. of non-volatile gums. The latter yielded, per 100 g. of original methylated sugar, 17.24 g. of dimethyl *d*-arabonolactone, 6.7 g. of methyl esters of methylated tetronic acids (of which 4.5 g. is believed to be a mixture of mono- and dimethyl *d*-erythronic acids), and 3.59 g. of demethylated hexonic and pentonic acids.

2. It is suggested that this indicates the oxidation of a 1,2-ene-diol, together with some destruction of the sugar because of the strong oxidizing conditions employed.

3. The accepted stability of the methylated sugars and the above indications of 1,2-ene-diol formation find ready explanation by assuming that the enolization of sugars takes place, not through the selective addition and loss of water as suggested by Nef but rather through a simple keto-enol tautomerism. With this modification, the experimental results, which follow closely the predictable blocking effect of the methyl groups on enolization, are strongly confirmatory of the enolization theory of sugar reactivity.

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