decrease being somewhat higher at the lower contact times.

Addition of water vapor, by dehydration of ethyl alcohol, in ratios of 0–1 moles per mole of heptane, preferentially retarded the formation of aromatics so that with 0.5 mole or more per mole of heptane the olefin–aromatic ratio was greater than 1. Under the more favorable conditions found in the direct addition of water, a ratio of 4.8 was obtained with a total olefin–aromatic conversion of 16.4 wt. per cent. of the charge per pass; the toluene–heptene yield amounted to 82% of the heptane decomposed.

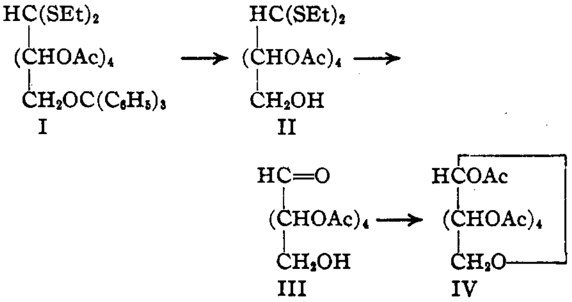
CHICAGO, ILLINOIS RECEIVED APRIL 24, 1944.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

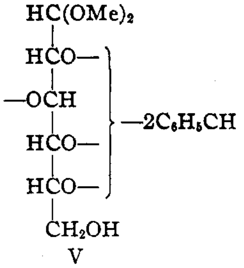
Ring Closure Studies in the D-Glucose Structure

BY M. L. WOLFROM, S. W. WAISBROT, D. I. WEISBLAT AND A. THOMPSON[1]

In the D-galactose structure, Micheel and coworkers[2] have synthesized derivatives containing the 1,6 or heptanoside ring. The best starting point for these important syntheses was the tetraacetate (I) of the 6-triphenylmethyl (trityl) ether of D-galactose diethyl mercaptal,[3] from which D-galactoheptanose pentaacetate (IV) was obtained by the step-wise removal of the ether and thioacetal groups on the terminal positions of the D-galactose molecule with subsequent acetylation.

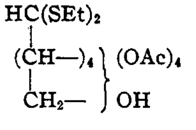


$$\begin{array}{l} HC(SEt)_2 \\ | \\ (CHOAc)_4 \\ | \\ CH_2OC(C_6H_5)_3 \\ \text{I} \end{array} \longrightarrow \begin{array}{l} HC(SEt)_2 \\ | \\ (CHOAc)_4 \\ | \\ CH_2OH \\ \text{II} \end{array} \longrightarrow \begin{array}{l} HC{=}O \\ | \\ (CHOAc)_4 \\ | \\ CH_2OH \\ \text{III} \end{array} \longrightarrow \begin{array}{l} HCOAc \\ | \\ (CHOAc)_4 \\ | \\ CH_2O \\ \text{IV} \end{array}$$



$$\left.\begin{array}{l} HC(OMe)_2 \\ | \\ HCO- \\ | \\ -OCH \\ | \\ HCO- \\ | \\ HCO- \\ | \\ CH_2OH \end{array}\right\} -2C_6H_5CH$$

V



$$\begin{array}{l} HC(SEt)_2 \\ | \\ (CH-)_4 \\ | \\ CH_2- \end{array} \begin{array}{l} \left.\right\} (OAc)_4 \\ \left.\right\} OH \end{array}$$

IIa

The initial derivatives corresponding to I and II in the D-glucose structure have not hitherto been available because of crystallization difficulties. We have now succeeded in synthesizing the 6-triphenylmethyl ether of D-glucose diethyl mercaptal tetraacetate, from which a crystalline D-glucose diethyl mercaptal tetraacetate (m. p. 117°; spec. rot. −25°, $CHCl_3$, D line) was obtained on removal of the triphenylmethyl group with dilute acetic acid according to the procedure of Kuhn and co-workers.[4] Previously reported work[5] from this Laboratory conclusively demonstrates that D-glucose diethyl mercaptal tritylates in the sixth position. Thus structure I is assured for the triphenylmethyl ether of D-glucose diethyl mercaptal tetraacetate. The same diethyl mercaptal tetraacetate (m. p. 117°; spec. rot. −25°, $CHCl_3$, D line) was obtained by mercaptalation of D-glucose 2,3,4,6-tetraacetate. If no acetyl migration had occurred, the 2,3,4,5-tetraacetate should have been obtained from I and a different 2,3,4,6-tetraacetate from D-glucose 2,3,4,6-tetraacetate. Since the two products were alike, it is apparent that an acetyl migration had occurred and the position of the unsubstituted hydroxyl group in this D-glucose diethyl mercaptal tetraacetate (IIa) is unknown. A similar shift is known[6] to occur when D-glucopyranose tetrabenzoate is mercaptalated. Evidence was obtained in this case that the isolated reaction product, also formed by the mercaptalation of D-glucofuranose pentabenzoate, carried the unsubstituted hydroxyl on carbon two of the D-glucose chain.[6a]

Demercaptalation of the D-glucose diethyl mercaptal tetraacetate with mercuric chloride and cadmium carbonate in moist acetone[7] led to the isolation of the ethyl α-thio-D-glucoside tetraacetate of Schneider and Sepp.[8] A furanoside structure for the parent, unacetylated substance has been favored[8b,9] but not rigorously proved. The substance was accordingly subjected to periodate oxidation.[10] If a furanoside ring were present, the substance would oxidize uniquely to

---

[1] Research Foundation Postdoctoral Fellow of the Graduate School.

[2] F. Micheel and F. Suckfüll, *Ann.*, **502**, 85 (1933); **507**, 138 (1933); *Ber.*, **66B**, 1957 (1933).

[3] F. Micheel and W. Spruck, *Ber.*, **67B**, 1665 (1934); M. L. Wolfrom and J. L. Quinn, THIS JOURNAL, **57**, 713 (1935).

[4] R. Kuhn, H. Rudy and F. Weygand, *Ber.*, **69B**, 1543 (1936).

[5] M. L. Wolfrom and C. C. Christman, THIS JOURNAL, **57**, 713 (1935).

[6] P. Brigl and R. Schinle, *Ber.*, **65B**, 1890 (1932).

(6a) P. Brigl and R. Schinle, *ibid.*, **63B**, 2884 (1930).

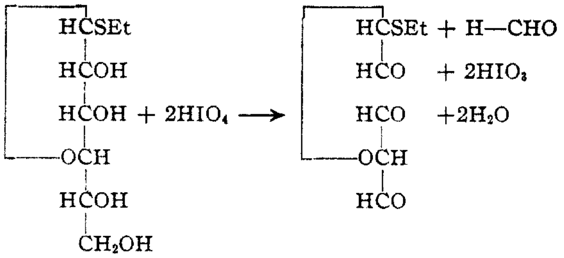
[7] M. L. Wolfrom, THIS JOURNAL, **51**, 2188 (1929).

[8] (a) W. Schneider and Johanna Sepp, *Ber.*, **49**, 2054 (1916); (b) J. W. Green and E. Pacsu, THIS JOURNAL, **59**, 1205 (1937).

[9] E. Pacsu and E. J. Wilson, Jr., THIS JOURNAL, **61**, 1450, 1930 (1939); P. Brigl, K. Gronemeir and A. Schulz, *Ber.*, **72B**, 1052 (1939).

[10] E. L. Jackson and C. S. Hudson, THIS JOURNAL, **59**, 994 (1937); **62**, 958 (1940); R. M. Hann, W. D. Maclay and C. S. Hudson, *ibid.*, **61**, 2432 (1939); P. Fleury and Jean Courtois; *Compt. rend.*, **214**, 366 (1942); *Bull. soc. chim.*, [5] **10**, 245 (1943).

consume two moles of oxidant with the production of one mole of formaldehyde and no formic acid.



The data of Table I show that the substance fulfills the above conditions and a furanoside structure for this thioglucoside is therefore established.

Another method of approach to the synthesis of a 1,6-ring in the D-glucose structure was then attempted. An effort was made to close such a ring by the loss of one mole of methanol from (2,3,4,5)-O-dibenzylidene-D-glucose dimethyl acetal (V), the structure of which can be considered as established with considerable certainty by previous work from this Laboratory[11] with the analogous diethyl acetal.

TABLE I

OXIDATION OF THE ETHYL α-THIO-D-GLUCOSIDE (0.005 M) OF SCHNEIDER AND SEPP[8] BY SODIUM METAPERIODATE (0.025 M) AT 25°

Time, minutes	Moles oxidant consumed	Moles formaldehyde formed	Moles acid formed
9	2.14		
15		0.88	
18	2.16		
28			0.00
31	2.14		
36			0.00
54	2.18		
60		0.86	
64			0.08

Unfortunately, this approach was unsuccessful. It is to be noted further that Christman has shown[5] in this Laboratory that the normal form (generally considered to be pyranoid) of D-glucose tetrabenzoate was produced on hydrolysis of the terminal groups of 6-iodo-D-glucose diethyl mercaptal tetrabenzoate.

Further work is in progress in this Laboratory on the attempted synthesis of <1,6> rings in the D-glucose series by the application of methylation techniques.

Experimental

6-O-Triphenylmethyl-D-glucose Diethyl Mercaptal Tetraacetate (I).—Well-dried D-glucose diethyl mercaptal (100 g.) was dissolved in 390 cc. of dry pyridine, 100 g. of triphenylmethyl (trityl) chloride was added and the solution was allowed to stand for three hours. Acetic anhydride (350 cc.) was then added and the solution kept overnight at room temperature. At the end of this period the solution was poured into an excess of ice and water. The separated sirup hardened on standing and was crystallized from ethanol; yield 175 g., m. p. 93–95°. Pure material was obtained on repeated purification from ethanol and from ether; m. p. 97–99°, spec. rot. +20° (19°, *c* 4.5, U. S. P. $CHCl_3$, D line).

Anal. Calcd. for $C_{29}H_{32}O_5S_2(CH_3CO)_4$: C, 63.78; H, 6.36; S, 9.20; CH_3CO, 5.74 cc. 0.1 *N* NaOH per 100 mg. Found: C, 63.70; H, 6.20; S, 9.25; CH_3CO, 5.74 cc.

D-Glucose Diethyl Mercaptal Tetraacetate (IIa).—The general detritylation procedure described by Kuhn and coworkers[4] was adapted to the compound in hand. To a boiling solution of 6-O-triphenylmethyl-D-glucose diethyl mercaptal tetraacetate (50 g.) in glacial acetic acid (80 cc.) was added 20 cc. of water and refluxing was maintained for four hours. The triphenylmethanol (17.5 g., 94% of theory) that separated on cooling was removed by filtration. The filtrate was concentrated under reduced pressure to a sirup which was crystallized from ether by the addition of petroleum ether; yield 6.5 g., m. p. 112–114°. Pure material was obtained on further crystallization from 50% ethanol and from ether–petroleum ether; m. p. 117°, spec. rot. −25° (25°, *c* 4, abs. $CHCl_3$, D line). The substance crystallized in the form of elongated prisms that did not reduce Fehling solution.

Anal. Calcd. for $C_{10}H_{18}O_5S_2(CH_3CO)_4$: C, 47.58; H, 6.65; S, 14.11; CH_3CO, 8.80 cc. of 0.1 *N* NaOH per 100 mg. Found: C, 47.03; H, 6.86; S, 14.20; CH_3CO, 8.91 cc.; $(C_6H_5)_3C$,[12] absent.

This substance also was obtained on mercaptalation of the D-glucose tetraacetate of Fischer and Delbrück[13] according to the general procedure of Wolfrom and Thompson.[14] D-Glucose tetraacetate (5 g.) and anhydrous sodium sulfate (5 g.) were added with shaking to a cooled (ice–salt-bath) solution of 2 g. of freshly fused zinc chloride in 20 cc. of ethyl mercaptan, previously dried over anhydrous calcium sulfate (Drierite). The tube was then sealed and maintained in the freezing mixture for five hours, whereupon the contents of the tube were poured into 50 cc. of a saturated aqueous solution of sodium bicarbonate. The precipitate formed was removed by filtration and transferred to a beaker for extraction with warm chloroform. The filtrate also was extracted with chloroform and the combined extracts were dried and concentrated to a sirup under reduced pressure. The dried sirup crystallized slowly upon long standing. Pure material was obtained on recrystallization from ethanol by the addition of water; yield 1.0 g., identified as the D-glucose diethyl mercaptal tetraacetate (IIa) above by melting point (116–117°), mixed melting point (undepressed) and specific rotation (−25°, $CHCl_3$, D line).

Conversion of D-Glucose Diethyl Mercaptal Tetraacetate to the Ethyl α-Thio-D-glucoside Tetraacetate of Schneider and Sepp.[8]—The above-described D-glucose diethyl mercaptal tetraacetate (20 g.) was added to a mixture of powdered cadmium carbonate (50 g.), mercuric chloride (40 g.), acetone (200 cc.) and water (8 cc.). The mixture was stirred mechanically for twelve hours at room temperature, after which the solution was filtered onto 10 g. of cadmium carbonate. The acetone was removed under reduced pressure in the presence of the cadmium carbonate and the residue was extracted with warm chloroform. The chloroform extract was washed with water until free of halides. The sirup obtained on chloroform removal under reduced pressure was crystallized from 50% ethanol; yield 9 g., m. p. 55–57°. Pure material was obtained on further crystallization from the same solvent;

---

[11] (a) M. L. Wolfrom and L. J. Tanghe, THIS JOURNAL, **59**, 1597 (1937); (b) M. L. Wolfrom, L. J. Tanghe, R. W. George and S. W. Waisbrot, *ibid.*, **60**, 132 (1938).

[12] Method of F. Valentin, *Coll. Czechoslov. Chem. Commun.*, **3**, 499 (1931).

[13] E. Fischer and K. Delbrück, *Ber.*, **42**, 2776 (1909); E. Fischer and K. Hess, *ibid.*, **45**, 914 (1912).

[14] M. L. Wolfrom and A. Thompson, THIS JOURNAL, **56**, 880 (1934).

m. p. 63–64° (unchanged on admixture with an authentic sample), spec. rot. +156° (22°, *c* 1.5, abs. EtOH, D line). For this ethyl α-thio-D-glucoside tetraacetate, Schneider and Sepp[8] recorded the constants: m. p. 63°, spec. rot. +155° (20°, EtOH, D line).

Anal. Calcd. for $C_{16}H_{24}O_9S$: C, 48.98; H, 6.17. Found: C, 49.17; H, 6.00.

Oxidation of the Ethyl α-Thio-D-glucoside of Schneider and Sepp[8] by Sodium Metaperiodate.—The parent substance of the above-described tetraacetate was oxidized in dilute solution and at room temperature with an excess of sodium metaperiodate. The reaction was followed with time and the results are tabulated in Table I. The formaldehyde was assayed by the dimedon procedure[15] and the acidity was that titratable with methyl red indicator. The results tabulated represent the initial phases of the reaction. On long standing, further oxidation occurs with this substance under these conditions.

(2,3,4,5)-O-Dibenzylidene-D-glucose Dimethyl Acetal (V).—(2,3,4,5)-O-Dibenzylidene-D-glucose diethyl mercaptal[11] (20 g.) was added to a suspension of 24 g. of cadmium carbonate in 300 cc. of absolute methanol and to this was added a solution of 100 cc. of methanol containing 56 g. of mercuric chloride. The mixture was then refluxed for twelve hours with constant stirring, whereupon the mixture was filtered and the solids washed with warm methanol. The filtrate was then poured into a mixture of 500 cc. each of chloroform and water and the chloroform layer was washed free of halides with water, treated with decolorizing charcoal and dried with Drierite and cadmium carbonate. The residue obtained on solvent removal was crystallized from 50% methanol; yield 15 g., m. p. 177–178°. Pure material was obtained on further crystallization from the same solvent; m. p. 183–184°, spec. rot. +14° (25°, *c* 4, $CHCl_3$, D line).

Anal. Calcd. for $C_6H_8O_6(C_6H_5CH)_2(OCH_3)_2$: OCH_3, 15.42; C_6H_5CH, 44.79. Found: OCH_3, 15.25; C_6H_5CH,[16] 44.53.

(2,3,4,5)-O-Dibenzylidene-D-glucose dimethyl acetal was treated at room temperature with essentially anhydrous methanol containing 0.05% dry hydrogen chloride. A gradual change in rotation occurred, with the liberation of benzaldehyde. No crystalline product was isolated from the reaction.

The assistance of Mr. Irving Auerbach in a portion of this work is acknowledged. One of us (A. T.) acknowledges a stipend from the funds of The Ohio State University Research Fonndation administered by the Graduate School.

Summary

1. The synthesis in crystalline form of 6-O-triphenylmethyl-D-glucose diethyl mercaptal tetraacetate (I), D-glucose diethyl mercaptal tetraacetate (IIa) and (2,3,4,5)-O-dibenzylidene-D-glucose dimethyl acetal (V) is reported.

2. IIa was formed by the detritylation of I and by the mercaptalation of D-glucose 2,3,4,6-tetraacetate.

3. Demercaptalation of IIa yielded the ethyl α-thio-D-glucoside tetraacetate of Schneider and Sepp.[8]

4. It is conclusively demonstrated by periodate oxidation that the ethyl α-thio-D-glucoside of Schneider and Sepp[8] has a furanoside structure.

5. V lost benzaldehyde on treatment with methanol containing 0.05% hydrogen chloride.

---

[15] D. Vorländer, C. Ihle and H. Volkholz, *Z. anal. Chem.*, **77**, 321 (1929).

[16] Method of W. Alberda van Ekenstein and J. J. Blanksma, *Rec. trav. chim.*, **25**, 153 (1906).

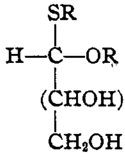
COLUMBUS, OHIO RECEIVED SEPTEMBER 1, 1944

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Reactivity of the Monothioacetals of Glucose and Galactose in Relation to Furanoside Synthesis[1]

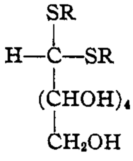
BY M. L. WOLFROM, D. I. WEISBLAT AND A. R. HANZE

The synthesis of the crystalline monothioacetals (I) of D-galactose[2] and of D-glucose[3] has been reported from this Laboratory. Since these compounds have been postulated by Green and Pacsu[4] as intermediates in the reaction of sugar mercaptals or thioacetals (II) with mercuric chloride in alcohol containing yellow mercuric oxide, their behavior under such conditions and under other ring closure conditions is of interest. The behavior of the acetals (III) and mercaptals under similar conditions was also studied in order to compare their reactivity with that of the monothioacetals.



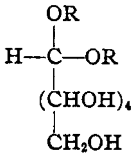
$$\begin{array}{c} SR \\ | \\ H-C-OR \\ | \\ (CHOH)_4 \\ | \\ CH_2OH \end{array}$$

I



$$\begin{array}{c} SR \\ | \\ H-C-SR \\ | \\ (CHOH)_4 \\ | \\ CH_2OH \end{array}$$

II



$$\begin{array}{c} OR \\ | \\ H-C-OR \\ | \\ (CHOH)_4 \\ | \\ CH_2OH \end{array}$$

III

When the monothioacetals were placed in dilute hydrochloric acid (0.05%) or in alcohols containing dry hydrogen chloride (0.05%), a reaction took place which proceeded at 25° with a speed suitable for polarimetric observation. The polarimetric data which we have obtained for D-glucose S-ethyl O-methyl monothioacetal and for D-galactose diethyl monothioacetal under such conditions are diagrammed in Figs. 1 and 2. The plots (Fig. 2) of the polarimetric data for the two compounds in alcohols containing dry hydrogen chloride yield continuous exponential curves. In dilute hydrochloric acid (Fig. 1)

---

[1] Presented before the Division of Sugar Chemistry and Technology at the 101st meeting of the American Chemical Society, St. Louis, Missouri, April 10, 1941.

[2] M. L. Wolfrom and D. I. Weisblat, THIS JOURNAL, **62**, 878 (1940).

[3] M. L. Wolfrom, D. I. Weisblat and A. R. Hanze, *ibid.*, **62**, 3246 (1940).

[4] J. W. Green and E. Pacsu, *ibid.*, **60**, 2288 (1938); E. Pacsu, *ibid.*, **61**, 1671 (1939).