

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

Aldehydo Derivatives of Dibenzylideneglucose

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For the past two years we have been concerned in this Laboratory with the investigation of the nature of the reaction between glucose diethyl mercaptal 6-benzoate and benzaldehyde in the presence of zinc chloride. It was then with considerable interest that we noted the excellent publication of Papadakis¹ which was concerned in part with the same subject. The speed of this reaction is profoundly affected by the nature of the zinc chloride used; in fact, it would almost appear from our results that some impurity in the zinc chloride is exerting a definite influence. It is apparent from the published results of Papadakis that the zinc chloride used by him was of such a type as to mask completely the truly complex nature of the reaction.

The structure of glucose diethyl mercaptal 6-benzoate may be considered as established by the work of Brigl and Grüner² who first prepared this substance. A detailed polarimetric study of the reaction between this compound and benzaldehyde-zinc chloride (Fig. 1) at room temperature (25°, approximately) showed that there was a rapid initial reaction accompanied by a rotation drop, followed by a slower secondary reaction in which there was a gradual rise in rotation. By sampling the reaction mixture at various time intervals it was possible to obtain a correlation between the rotation of the reaction mixture and the nature and yield of the crystalline reaction products. The results of this study are summarized in Table I and in curve B of Fig. 1.

The first sample (Table I) was found to be a mixture of starting material and dibenzylideneglucose diethyl mercaptal 6-benzoate. From the second to the ninth samples, inclusive, the main product was dibenzylideneglucose diethyl mercaptal 6-benzoate, the maximum yield of this compound making its appearance at the point of minimum rotation of the reaction mixture. From the tenth sample there was isolated a non-reducing dibenzylideneglucose 6-benzoate (m. p. 160-160.5°; $[\alpha]^{25}_{D(3)} + 15^\circ$, CHCl_3), apparently identical with the one recorded by Papadakis (m. p. 156°), who

(1) P. E. Papadakis, *THIS JOURNAL*, **59**, 841 (1937).(2) P. Brigl and H. Grüner, *Ann.*, **495**, 60 (1932).

(3) All rotations are herein recorded to the D-line of sodium light.

unfortunately cited no rotations in the description of his compounds.

There was found to be a wide variation in the catalytic activity of different samples of zinc chloride, as may be noted in Fig. 1. Curves A, B and D of Fig. 1 were obtained with different samples of "C. P." zinc chloride. In curve A the rise in rotation after reaching the minimum is very slow. Curve D shows the results with a sample of zinc chloride having a relatively high reactivity.

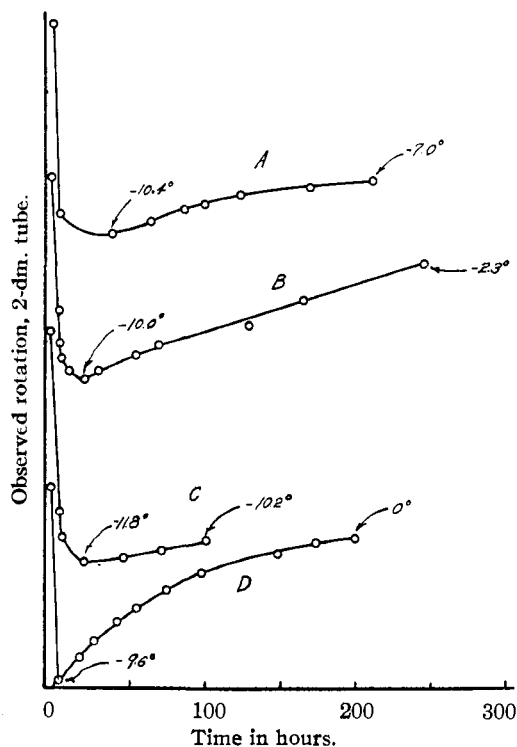


Fig. 1.—Polarimetric course of the reaction between *D*-glucose diethyl mercaptal 6-benzoate (0.2 mole, 78 g.), benzaldehyde (8 mole, 624 g.) and different samples of zinc chloride (100 g.) at room temperature (25°, approx.). Initial observed rotation, before addition of zinc chloride, was +3.2° (2-dm. tube) for all experiments.

The rate of reaction using a sample of "commercial" zinc chloride is shown in curve C. In this case the rise in rotation after passing through the minimum is very sluggish. In one instance before this polarimetric study was begun, a good yield of dibenzylideneglucose 6-benzoate was obtained in as short a time as thirty-six hours. This reaction

must have been much faster than any shown in Fig. 1, since dibenzylidene-glucose 6-benzoate does not make its appearance until the rotation of the reaction mixture, after passing through a levorotatory minimum, rises nearly to zero. Another but less probable explanation is that nuclei of the mercaptalated product were not then available. Papadakis¹ records the preparation of the dibenzylidene-glucose 6-benzoate, under practically identical conditions, in as short a time as two hours, giving evidence of a still wider range in the catalytic activity of different samples of zinc chloride.

In view of these facts, the reaction between glucose diethyl mercaptal 6-benzoate and benzaldehyde in the presence of zinc chloride can be followed polarimetrically to good advantage. To obtain dibenzylidene-glucose diethyl mercaptal 6-benzoate the reaction is interrupted at or shortly after the minimum rotation is attained, whereas if the non-reducing dibenzylidene-glucose 6-benzoate is desired, the reaction is not interrupted until the rotation has risen almost to zero.

In connection with this reaction study, it is of interest to note that both dibenzylidene-*aldehydo*-glucose 6-benzoate (see below) and its diethyl mercaptal are transformed to the non-reducing dibenzylidene-glucose 6-benzoate under the reaction conditions. Accordingly, the former is also a probable intermediate in the reaction and we may list the probable sequence of changes as follows: glucose diethyl mercaptal 6-benzoate \rightarrow dibenzylidene-glucose diethyl mercaptal 6-benzoate \rightarrow dibenzylidene-*aldehydo*-glucose 6-benzoate \rightarrow dibenzylidene-glucose 6-benzoate (non-reducing).

Removal of the benzoate group from the dibenzylidene-glucose 6-benzoate produced a non-reducing dibenzylidene-glucose (m. p. 163–165°; $[\alpha]_D^{24} + 35^\circ$, pyridine), undoubtedly identical with the product described by Papadakis¹ (m. p. 163°). Rebenzoylation of this compound produced the original 6-benzoate.

Demercaptalation of the dibenzylidene-glucose diethyl mercaptal 6-benzoate with mercuric chloride and cadmium carbonate in moist acetone⁴ produced the crystalline dibenzylidene-*aldehydo*-glucose 6-benzoate. This compound is of particular interest to this Laboratory as it represents an open-chain structure in the sugar cyclic acetals. Cyclic acetals of similar aldehyde structure have

been reported by Hixon and collaborators⁵ for some acetylated chloral sugar derivatives. The compound obtained by us showed the characteristic properties of the aldehyde structure. Thus it was reducing; it gave a positive Schiff aldehyde test; mutarotated in hydroxylated solvents⁶ and yielded a crystalline thiosemicarbazone.

Removal of the benzoate group from dibenzylidene-glucose diethyl mercaptal 6-benzoate produced the dibenzylidene-glucose diethyl mercaptal (VII) with the sixth position free, demonstrated by the formation of the original compound on rebenzoylation. Demercaptalation of this substance yielded a reducing dibenzylidene-glucose (VIII). This compound resisted crystallization but was characterized by a crystalline thiosemicarbazone. This dibenzylidene-glucose is of particular interest as a heptanoside is its only possible ring structure, if benzylidene shifts are excluded. So far heptanosides have been characterized only in the galactose series.⁷

Experimental

Dibenzylidene-*d*-glucose Diethyl Mercaptal 6-Benzoate (II).—Glucose diethyl mercaptal 6-benzoate⁸ (78 g.) was dissolved in eight parts (624 g.) of benzaldehyde in a three-necked flask provided with a thermometer and a mercury-sealed glass stirrer. The material was dissolved by heating to about 50°, the solution cooled to room temperature and 90–100 g. of freshly fused and finely ground zinc chloride was added quickly with rapid stirring. A temperature rise of 5–10° was observed during the next few minutes and the zinc chloride gradually dissolved. Solution of the zinc chloride was nearly complete after one hour, but the stirring was continued overnight.

The rotation of the solution was followed polarimetrically and when the observed rotation in a 2-dm. tube was approximately -10° , 3.5 l. of water was added. The time required to attain this rotation varied enormously with different samples of zinc chloride. With this particular sample of zinc chloride, the solution stood for four days at room temperature. The mixture was transferred to a three-necked flask containing a still-head in each side-neck and equipped with a dropping funnel, thermometer and capillary tubing in the central neck. The benzaldehyde was distilled under reduced pressure into ice-cooled receivers and the temperature of the water-bath was adjusted so that the temperature inside the distilling flask was maintained slightly below 30°. Water was added occasionally to maintain constant volume. During the course of seven hours about 5 l. of distillate was collected and further distillation did not yield any more benzaldehyde. With

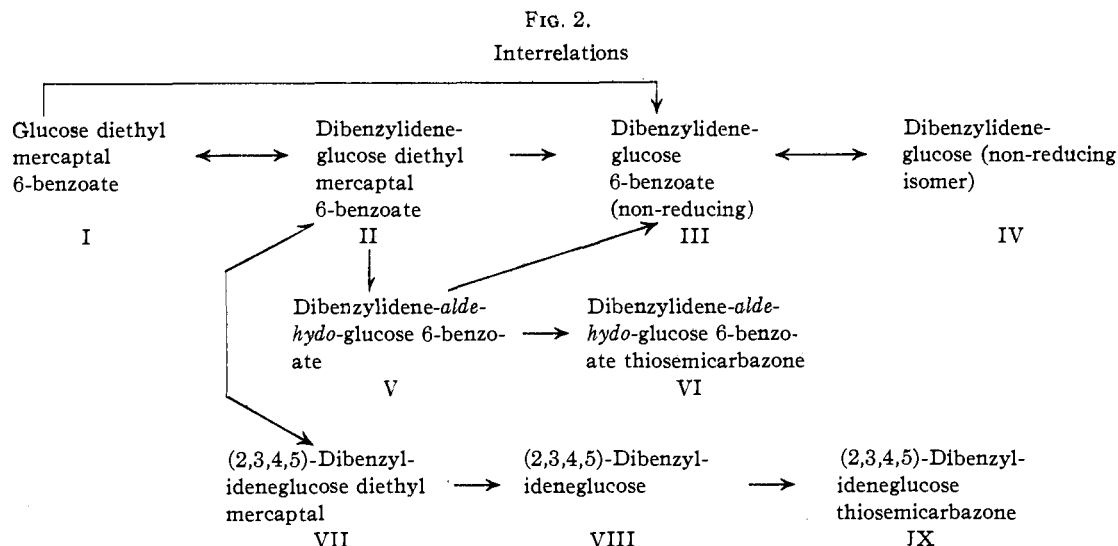
(5) Anne White and R. M. Hixon, *ibid.*, **55**, 2438 (1933).

(6) M. L. Wolfrom, *ibid.*, **53**, 2275 (1931).

(7) F. Micheel and F. Suckfüll, *Ann.*, **502**, 85 (1933); *ibid.*, **507**, 138 (1933); *Ber.*, **66**, 1957 (1933); F. Micheel and W. Spruck, *ibid.*, **67**, 1665 (1934).

(8) P. Brigl and W. Zerrweck, *Z. physiol. Chem.*, **229**, 117 (1934); T. Lieser and R. Schweizer, *Ann.*, **519**, 271 (1935).

(4) M. L. Wolfrom, *THIS JOURNAL*, **51**, 2188 (1929).



the removal of the benzaldehyde the reaction product separated out as a thick sirup on the walls of the flask. The water was removed by decantation and the residue dissolved in 2 l. of ether, filtered, concentrated to about 250 cc. and cooled, using finally an ice-salt bath. The crystals were removed by filtration and washed with cold ether; yield 23 g.; m. p. 128–129°. Pure material was obtained on several recrystallizations from 30–35 parts of hot 95% ethanol; m. p. 130.5–131.5°; $[\alpha]^{23} -15.5^\circ$ (*c*, 4; CHCl_3); $[\alpha]^{23} -11^\circ$ (*c*, 4; initial; benzaldehyde). The substance was insoluble in water, moderately soluble in alcohol, ether and hot petroleum ether, and was very soluble in chloroform, benzene and acetone.

Anal. Calcd. for $\text{C}_{24}\text{H}_{20}\text{O}_8\text{S}_2(\text{COC}_6\text{H}_5)$: C, 65.7; H, 6.06; S, 11.31; $\text{C}_6\text{H}_5\text{CO}$, 18.5. Found: C, 66.1; H, 6.08; S, 11.21; $\text{C}_6\text{H}_5\text{CO}$, 18.3.

Benzoyl determinations were performed by refluxing the substance (0.3 g.) with 10 cc. of 0.5 *N* sodium ethylate in a Pyrex flask equipped with ground glass joints for four hours and back titrating with 0.1 *N* hydrochloric acid, using phenolphthalein indicator. A blank run under the same conditions was found to be negligible.

Removal of the benzylidene groups from dibenzylidene-glucose diethyl mercaptal 6-benzoate produced the original glucose diethyl mercaptal 6-benzoate. Dibenzylidene-glucose diethyl mercaptal 6-benzoate (0.5 g.) was refluxed for two hours with a solution of 7 cc. of glacial acetic acid in 10 cc. of water. At the end of this period the material was dissolved completely. The solvent was removed under reduced pressure and several additions of water were made to the residue and removed by distillation. The crystalline residue was recrystallized from ether; yield 0.13 g.; m. p. not depressed on admixture with an authentic specimen of glucose diethyl mercaptal 6-benzoate (m. p. 111–112°).

Preparation of Dibenzylidene-*d*-glucose 6-Benzoate (III) from I.—This substance was prepared from glucose diethyl mercaptal 6-benzoate and isolated as described for the synthesis of dibenzylidene-glucose diethyl mercaptal 6-benzoate except for the difference in the time of reaction. The reaction was followed polarimetrically. The rotation

increased in the levo direction, passed through a levorotatory minimum, and then slowly increased in dextrorotation until it became nearly zero (Fig. 1). At this point the solution was worked up. The rate at which these polarimetric changes took place varied enormously with different samples of zinc chloride. The yield was variable, the maximum obtained being 1.9 g. from 4.0 g. of starting material; m. p. 156–156.5°. Pure material was obtained on recrystallization from ethanol (100 parts); m. p. 160–160.5°; $[\alpha]^{26} +15^\circ$ (*c*, 4; CHCl_3); $[\alpha]^{25} +18^\circ$ (*c*, 4; CHCl_2); $[\alpha]^{25} +20^\circ$ (*c*, 4; benzaldehyde).

In ethanol solution the substance did not reduce Fehling's solution and in pyridine solution it showed no reduction toward Tollens' reagent. It was recovered unchanged on attempted reaction with thiosemicarbazide. The solubilities of the substance were similar to those given for dibenzylidene-glucose diethyl mercaptal 6-benzoate. Papadakis¹ recorded the melting point of 156° for this substance.

Anal. Calcd. for $\text{C}_{20}\text{H}_{16}\text{O}_8(\text{COC}_6\text{H}_5)$: C, 70.4; H, 5.26; $\text{C}_6\text{H}_5\text{CO}$, 22.8; mol. wt., 460. Found: C, 70.4; H, 5.16; $\text{C}_6\text{H}_5\text{CO}$, 23.5; mol. wt. (Rast), 430; S, absent.

Preparation of Dibenzylidene-*d*-glucose 6-Benzoate (III) from Dibenzylidene-*d*-glucose Diethyl Mercaptal 6-Benzoate (II).—One gram of dibenzylidene-glucose diethyl mercaptal 6-benzoate was dissolved in 25 cc. of benzaldehyde and to the solution was added 0.96 g. of freshly fused and finely ground zinc chloride. The latter dissolved readily upon stirring under a mercury seal for a few minutes. The rotation of the reaction mixture in a 1-dm. tube showed a gradual increase from an observed rotation of -0.55° to $+0.13^\circ$, being constant after three days. The solution was diluted with 100 cc. of ether and was washed free of zinc chloride. The ethereal solution was concentrated and after adding water the benzaldehyde was distilled out under diminished pressure, maintaining a constant volume of water in the flask. The water was decanted and the oily residue was dissolved in 100 cc. of ether under reflux. The ethereal solution was dried and concentrated to about 5 cc., when crystals began to separate; yield 0.16 g.; m. p. 156–157°. Pure material was obtained

TABLE I
NATURE OF THE REACTION PRODUCTS FROM *d*-GLUCOSE DIETHYL MERCAPTAL 6-BENZOATE IN BENZALDEHYDE-ZINC CHLORIDE AT 25°^a

| Sample number | Reaction time, hours | Observed rotation, 2-dm. tube, deg. | Weight ^c crude ^d product, g. | Crystalline product | | | Residual sirup [α], CHCl ₃ , deg. |
|---------------|----------------------|-------------------------------------|--|---------------------|------------|--|--|
| | | | | Weight, g. | M. p., °C. | [α], CHCl ₃ , deg. | |
| 1 | 1 | +3.25 ^b -5.50 | | | | | - 7.0 |
| | | | | 0.15 | 104-107 | | |
| | | | | 1.08 | 107-109 | +39.8 | |
| | | | | 0.55 | 116-120 | - 8.5 | |
| 2 | 5 | -8.57 | 11.0 | .01 | 152-154 | | -13.3 |
| | | | | 2.4 | 93-100 | + 2.2 | |
| 3 | 10 | -9.37 | 15.0 | 1.5 | 124-125 | -14.8 | -14.9 |
| 4 | 21 | -9.95 | 17.7 | 2.3 | 127-128 | -14.6 | -17.7 |
| 5 | 34 | -9.12 | 16.4 | 2.1 | 126-127 | -14.9 | -16.3 |
| 6 | 45 | -8.80 | 14.8 | 2.0 | 122-123 | -14.6 | -14.0 |
| 7 | 70 | -7.74 | 16.2 | 1.8 | 127-128 | -14.3 | -13.1 |
| 8 | 118 | -5.85 | 16.7 | 2.0 | 122-124 | -13.6 | - 6.8 |
| 9 | 166 | -4.73 | 14.6 | 2.1 | 108-112 | -10.7 | - 9.0 |
| 10 | 243 | -2.34 | 15.3 | 0.90 | 155-157 | +16.6 | - 6.4 |
| | | | | .89 | 130-160 | +14.5 | |

^a Approximate average room temperature. ^b Before addition of the zinc chloride. ^c All weights are calculated to the basis of 10 g. of starting material. ^d Not entirely benzaldehyde free.

on one recrystallization from ethanol; m. p. 158-159° (mixed m. p. unchanged); [α]²⁴ +15° (c, 2; CHCl₃; 2-dm. semimicro tube); negative Fehling's reduction. The substance was therefore dibenzylidene-glucose 6-benzoate (non-reducing isomer), III.

Study of the Reaction between *d*-Glucose Diethyl Mercaptal 6-Benzoate (I) and Benzaldehyde in the Presence of Zinc Chloride.—A detailed polarimetric study of the reaction (Fig. 1) showed that there was a rapid initial change accompanied by a drop in rotation, followed by a slow secondary reaction in which there was a gradual rise in rotation. By sampling the mixture at various time intervals it was possible to obtain a correlation between the rotation of the reaction mixture and the nature and yield of the reaction products. An amount of 78 g. of glucose diethyl mercaptal 6-benzoate was dissolved in eight parts (624 g.) of benzaldehyde and the initial rotation observed. The zinc chloride (100 g.) was then added. Eighty-gram portions (one-tenth of the total) of the reaction mixture were worked up as previously described, at various time intervals, the first being removed after one hour and the last after ten days. Numerous polarimetric readings were taken during this time. The results are summarized in Table I and in curve B of Fig. 1. The yields obtained from this 78-g. run have been recalculated to the basis of grams of product isolated from 10 g. of starting material.

The first sample was found to consist of a mixture of starting material and dibenzylidene-glucose diethyl mercaptal 6-benzoate. From the second to the ninth samples, the main product was dibenzylidene-glucose diethyl mercaptal 6-benzoate, the maximum yield of this compound making its appearance at the point of minimum rotation of the reaction mixture. From the tenth sample there was isolated the non-reducing dibenzylidene-glucose 6-benzoate.

Dibenzylidene-aldehyde-*d*-glucose 6-Benzoate (V).—To a mixture of 10 g. of dibenzylidene-glucose diethyl mercaptal 6-benzoate, 20 g. of finely ground cadmium carbonate and 20 g. of mercuric chloride, were added 75 cc. of

acetone and 1.5 cc. of water. The mixture was stirred vigorously for four hours, adding 1 g. of fresh cadmium carbonate each hour. A further 40 cc. of acetone was then added and the mixture filtered into a flask containing a small amount of fresh cadmium carbonate. The residue was extracted by stirring with 100 cc. of acetone and the combined filtrates were concentrated nearly to dryness under reduced pressure at 40° in the presence of cadmium carbonate. The residue was extracted five times with 50-cc. portions of chloroform (free from alcohol, acid and chlorides) and the chloroform was washed repeatedly (seven times) with 100-cc. portions of water until chloride free. A little cadmium carbonate and Drierite were added to the turbid chloroform solution, and after a few minutes the mixture was filtered and the solvent removed under diminished pressure; yield 6.6 g. of crystalline product; free from sulfur and chloride; m. p. 180-183°. The substance was obtained pure on recrystallization from 20 to 25 parts of trichloroethylene (acid free); m. p. 185-187°; [α]²⁸ +43° (c, 4; CHCl₂-CHCl₂, acid free; no mutarotation). Recrystallization of the substance from toluene or from glacial acetic acid gave products of lower melting point, but with rotations unchanged.

An ethanol solution of the substance exhibited Fehling's reduction and a pyridine solution reduced Tollens' reagent. The compound gave a positive Schiff aldehyde test. Its aldehyde nature was also shown by its lack of mutarotation in *sym*-tetrachloroethane and its definite mutarotation in chloroform containing ethanol (U. S. P.): [α]²³ +51° (extrapolated) \rightarrow +14° (twenty hours). That this mutarotation was not due to an isomerization to the non-reducing isomer III ([α] +15°, CHCl₃; [α] +18°, CHCl₂-CHCl₂) was shown by recovering the equilibrated material and determining its rotation in *sym*-tetrachloroethane. This was found to be [α]²² +42.5° (c, 3).

The substance was very soluble in chloroform and pyridine, moderately so in alcohol and ether and was insoluble in water and petroleum ether.

Anal. Calcd. for $C_{27}H_{24}O_7$: C, 70.4; H, 5.26. Found: C, 70.0; H, 5.28.

Isomerization of Dibenzylidene-aldehydo-d-glucose 6-Benzoate (V) by Benzaldehyde and Zinc Chloride.—Dibenzylidene-aldehydo-glucose 6-benzoate (0.5 g.) was dissolved in 10 cc. of warm (45°) benzaldehyde and after cooling to room temperature, 1.3 g. of freshly fused and finely ground zinc chloride was added. Nearly all the zinc chloride dissolved after shaking for a few minutes. After standing at room temperature for two days, 50 cc. of ether was added and the zinc chloride was washed out with water. The ether was removed by distillation, water was added and the benzaldehyde was distilled out under diminished pressure, maintaining a constant volume of water in the flask. The residue was dissolved in 75 cc. of ether, dried and concentrated to 10 cc. to effect crystallization; yield 0.13 g.; m. p. 155–156°. Pure material was obtained on one recrystallization from 95% ethanol; $[\alpha]^{23} +15^\circ$, $CHCl_3$; m. p. 159–160° (mixed melting point unchanged); negative Fehling's reduction. The dibenzylidene-aldehydo-d-glucose 6-benzoate had thus been isomerized to its non-reducing isomer.

Dibenzylidene-aldehydo-d-glucose 6-Benzoate Thiosemicarbazone (VI).—Dibenzylidene-aldehydo-glucose 6-benzoate (2 g.) was dissolved in 300 cc. of hot absolute ethanol, cooled slightly, and a warm solution of 0.8 g. of thiosemicarbazide in 30 cc. of glacial acetic acid and 70 cc. of absolute ethanol, was added. The solution was cooled rapidly to room temperature and water (330 cc.) was added to a slight permanent turbidity. Crystallization was soon effected and was completed at ice-box temperature. The crystals were removed by filtration and washed with cold, dilute alcohol; yield 2.24 g.; m. p. 183–184° (dec.). Pure material was obtained on recrystallization from 80% ethanol; m. p. 191–192° (dec.); mixed melting point with starting material (m. p. 185–187°); 169–170°; $[\alpha]^{24} +47 \rightarrow +40^\circ$ (c, 2; U. S. P. $CHCl_3$). The small mutarotation of this substance in U. S. P. chloroform is unusual. That it did not represent hydrolysis or a permanent isomeric change was indicated by repeated recoveries of unchanged material from the equilibrated chloroform solutions.

The substance crystallized in plates, sometimes in the form of rosetts. It was very soluble in acetone, moderately so in alcohol, chloroform and benzene, and was insoluble in water, ether and petroleum ether.

Anal. Calcd. for $C_{28}H_{27}O_6N_3S$: S, 6.01. Found: S, 5.98.

(2,3,4,5)-Dibenzylidene-d-glucose Diethyl Mercaptal (VII).—Dibenzylidene-glucose diethyl mercaptal 6-benzoate (20 g.) was refluxed for five hours with 500 cc. of 0.5 N sodium ethylate solution. The cooled reaction mixture was poured into 5 l. of water and neutralized to phenolphthalein with hydrochloric acid. On standing overnight, the product collected at the surface and was removed by filtration, washed thoroughly with water and recrystallized from 200 cc. of 95% ethanol; yield 13.5 g.; m. p. 159.5–160.5°. Further recrystallizations from twenty parts of boiling 95% ethanol did not change the melting point. The rotation of the substance was $[\alpha]^{24} -17^\circ$ (c, 4; $CHCl_3$).

The substance was insoluble in water, slightly so in alco-

hol, ether and petroleum ether, and was very soluble in chloroform, acetone and benzene.

Anal. Calcd. for $C_{24}H_{30}O_6S_2$: C, 62.3; H, 6.54; S, 13.87. Found: C, 62.4; H, 6.87; S, 13.86.

Rebenzoylation of the compound produced the original 6-benzoate. Dibenzylidene-glucose diethyl mercaptal (44 mg.) was benzoylated with pyridine (1 cc.) and benzoyl chloride (75 mg.) by heating at 50–60° for two hours. Chloroform was added to the cooled solution and the pyridine was removed by washing with dilute sulfuric acid. The residue obtained after solvent removal was crystallized from 95% ethanol; yield 32 mg.; m. p. 131–132° (mixed m. p. unchanged).

(2,3,4,5)-Dibenzylidene-d-glucose Thiosemicarbazone (IX).—Dibenzylidene-glucose diethyl mercaptal (3.0 g.) was demercaptalated with mercuric chloride and cadmium carbonate in moist acetone as described for the synthesis of dibenzylidene-aldehydo-d-glucose 6-benzoate, except that the reaction time was shortened to ninety minutes. The final residue from the chloroform extract was an amorphous powder which resisted crystallization; yield 1.7 g. The substance was reducing and was characterized as its crystalline thiosemicarbazone.

The crude dibenzylidene-glucose (1.5 g.) was dissolved in 50 cc. of hot ethanol, filtered and cooled to room temperature. A warm solution of thiosemicarbazide (0.77 g.) in 15 cc. of water was added in small portions to the dibenzylidene-glucose solution and an additional 15 cc. of water was added to produce a permanent turbidity. The mixture was kept at room temperature for sixteen hours with occasional additions of more water until a turbidity was no longer produced. A total of approximately 45 cc. of water was thus added. The product was removed by filtration; yield 1.5 g.; m. p. 205–207° (dec.). Pure material was obtained on recrystallization from approximately 100 parts of isopropyl alcohol; m. p. 223–224° (dec.); $[\alpha]^{24} +91^\circ$ (c, 4; pyridine; no mutarotation).

The substance was readily soluble in acetone, pyridine and dioxane, was slightly soluble in alcohol, chloroform, benzene and ether, and was insoluble in water.

Anal. Calcd. for $C_{27}H_{28}O_6N_3S$: S, 7.46. Found: S, 7.27.

Preparation of Dibenzylidene-d-glucose (Non-reducing Isomer), IV.—This substance was prepared from its 6-benzoate (3.8 g.) as described for the preparation of dibenzylidene-glucose diethyl mercaptal; yield 2.8 g.; m. p. 157–160°. Pure material was obtained on recrystallization from 50 parts of methanol containing 0.5 cc. of 6 N ammonium hydroxide per 100 cc.; m. p. 163–165°; $[\alpha]^{24} +35^\circ$ (c, 4; pyridine). Recrystallization in the absence of a trace of alkalinity gave products of low and variable melting point. Papadakis¹ records the melting point of 163° for this substance.

The compound was very soluble in pyridine and dioxane, moderately soluble in acetone, slightly so in ether and alcohol and was insoluble in water. In ethanol solution it did not reduce Fehling's solution and in pyridine solution it showed no reduction toward Tollens' reagent.

Anal. Calcd. for $C_{26}H_{26}O_6$: C, 67.37; H, 5.67. Found: C, 67.02; H, 5.79.

Rebenzoylation of the compound produced the original

6-benzoate. Benzoylation of 45 mg. of the substance was effected as described for the rebenzoylation of dibenzylidene-glucose diethyl mercaptal and the product was crystallized from ethanol; yield 39 mg.; m. p. 159–160° (mixed m. p. unchanged).

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Summary

1. The reaction between *d*-glucose diethyl mercaptal 6-benzoate (I) and benzaldehyde-zinc chloride has been shown to vary in speed with the sample of zinc chloride used but always to consist of the rapid formation of dibenzylidene-*d*-glucose diethyl mercaptal 6-benzoate (II), followed by the relatively slow formation of the non-reducing dibenzylidene-*d*-glucose 6-benzoate (III) of Papadakis.

2. The demonstrated formation of III from II and from dibenzylidene-*aldehydo-d*-glucose 6-ben-

zoate (V) makes probable the consecutive changes $I \rightarrow II \rightarrow V \rightarrow III$.

3. Removal of the benzylidene groups from II produces I.

4. Rebenzoylation of the non-reducing dibenzylidene-*d*-glucose (IV) of Papadakis yields III.

5. Demercaptalation of II gives V, which forms a thiosemicarbazone and is isomeric with III.

6. Debenzoylation of II produces (2,3,4,5)-dibenzylidene-*d*-glucose diethyl mercaptal (VII), which forms II on rebenzoylation.

7. Demercaptalation of VII yields an amorphous, reducing (2,3,4,5)-dibenzylidene-*d*-glucose (VIII), characterized by its thiosemicarbazone (IX).

8. With the exception of VIII, all compounds herein reported have been obtained in crystalline condition and their constants determined.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FORDHAM UNIVERSITY]

The Chemistry of Naturally Occurring Monohydrohexitols¹

BY WERNER FREUDENBERG AND E. F. ROGERS

In the course of some studies on the structure and configuration of synthetic anhydrohexitols, a literature search covering occurrence, properties and structure of natural monoanhydrohexitols was essential for comparison. The results are summarized in Table I.

Both on oxidation with sodium hypobromite yield products which give the same 1,5-anhydrofructosazone,^{9,3,10} while hydrogen peroxide forms hexoses identified as glucosazone. Hence, styracitol and polygalitol have identical ring structure and are epimeric. The synthesis of the former,

TABLE I
NATURAL ANHYDROHEXITOLS, C₆H₁₂O₅, REPORTED IN LITERATURE

| Name | Author | Source | Free alcohol | | Acetyl der., M. p., °C. | Dibenzal der. | |
|-----------------|----------------------------------|-----------------------|--------------|----------|----------------------------|---------------|----------|
| | | | M. p., °C. | Sp. rot. | | M. p., °C. | Sp. rot. |
| Styracitol | Asahina ² | <i>Styrax obassia</i> | 155 | -49° | 66 | 163-165 | -148.7° |
| | | | | | | 192-193 | -80.5° |
| Polygalitol | Shinoda ³ | <i>Polyg. ten.</i> | | | | | |
| | Chodat ⁴ | <i>P. amara</i> | 143 | +43° | 73-75 | ... | ... |
| | Piccard ⁵ | <i>P. vulgaris</i> | | | | | |
| Aceritol | Perkin ⁶ | <i>Acer ginnala</i> | 142 | +39° | 74-75 | ... | ... |
| Viburnitol | Hérissey and Poirot ⁷ | <i>Viburnum tinus</i> | 180-181 | -49° | ... | ... | ... |
| Anhydromannitan | Haas and Hill ⁸ | <i>Pelvetia can.</i> | ... | ... | ... | 165-168 | ... |

Of these compounds structural formulas have only been assigned to styracitol and polygalitol.

(1) Reported before the Organic Division, A. C. S. Meeting, Chapel Hill, N. C., April, 1937.

(2) Asahina and Takimoto, *Ber.*, **64**, 1803 (1931).

(3) Shinoda, Sato and Sato, *ibid.*, **65**, 1219 (1932).

(4) Chodat, *Arch. sci. phys. nat.*, [3] **20**, 599 (1888).

(5) Piccard, *Bull. soc. chim. biol.*, **9**, 692 (1927).

(6) Perkin and Uyeda, *J. Chem. Soc.*, **121**, 66 (1922).

(7) Hérissey and Poirot, *Compt. rend.*, **203**, 148 (1936).

(8) Haas and Hill, *Biochem. J.*, **23**, 1000 (1929).

as carried out by Zervas,¹¹ involved hydrogenation of 2-oxyglucal acetate (I) and subsequent deacetylation of the reduced acetyl product. The conclusion, therefore, that the synthetic product was 1,5-anhydrosorbitol (II) found general acceptance. As a consequence polygalitol was given

(9) Asahina, *Ber.*, **45**, 2365 (1912).

(10) Bergmann and Zervas, *ibid.*, **64**, 1436, 2032 (1931).

(11) Zervas, *ibid.*, **63**, 1689 (1930).