washed with that same solvent and dried *in vacuo;* formyl found: 29.5 (equivalent to a degree of substitution of 2.3 formyl groups per anhydroglucose unit). This small increase in formyl content indicates that in other formylations ethanolysis during precipitation and washing is not a factor in preventing complete substitution of hydroxyl groups with formyl.

Thirty grams of air-dried starch was formylated for 4 hr. in 300 ml. of formic acid. Benzene (200 ml.) was added in 50-ml. portions and removed by distillation *in vacuo.* Bumping occurred and the viscous paste containing the partially formylated starch did not mix well with the benzene. After the surface layer of benzene disappeared, 150 ml. of anhydrous formic acid was added, and the mixture was allowed to stand overnight. The formate then isolated contained 24.8% formyl, not significantly higher than if no benzene distillation had been used.

Reaction of Dry Starch with Anhydrous Formic Acid.—To 300 ml. of anhydrous formic acid was added gradually 30 g. of corn starch which had been dried overnight at 110° *in vacuo* in the presence of Drierite. Samples precipitated in ethanol after varying time intervals gave these analyses:

Time, hours	Formyl, %
2	18.7
5	21.7
7.75	22.6
24	24.8
48	25.4

Thirty grams of corn starch was formylated as above. One hundred milliliters of the mixture was precipitated after 24 hr. To the remainder 25 ml. of water was added and reaction was continued for 27 hr. longer. The remainder was then precipitated. The analysis of these products was: 24-hr. product, 26.1% formyl; 51-hr. product, 18.9% formyl.

The starch formates are soluble in pyridine and in formic acid but not in the other common organic solvents tested.

Optical Rotation of Starch Formates.—The rotation of a formyl ester with 1.3 formyl groups per C_6 (19.0% formyl) was $[\alpha]^{25}D$ +180.6° (pyridine, *c* = 1). A formate containing 2.1 formyl per C_6 (27.7% formyl) had $[\alpha]^{25}D$ +166.5° (pyridine, *c* 1).

Oxidation of Starch Formate with Periodate.—Samples of starch formate were treated with an excess of sodium periodate. After 24 hr., analysis for excess periodate was carried out.[10] Data are summarized below.

		Starch formate	
Formyl/C_6 unit	Wt. sample, g.	Periodate consumed (millimole)	Millimoles periodate per millimole repeating unit
2.10	0.3050	0.21	0.15
1.16	.1449	.80	1.08

Carbanilation of Starch Formate.—To 19.0 g. of oven-dried starch formate (18.8% formyl, 1.28 formyl per C_6) in 125 ml. of dry pyridine was added 35 g. of phenyl isocyanate, and the mixture was heated for 6 hr. at 100°. The ester, isolated by precipitation with ethanol, had 5.99% N; calcd. 5.94% N. Similar preparation of other mixed esters from starch formates indicates that formyl esters are produced and that the formic acid is not held merely by sorption or solvation onto the carbohydrate.

Acknowledgment.—The authors are indebted to T. A. McGuire and C. H. Van Etten for assistance with the formyl analyses. The use of trade names in this paper does not necessarily constitute endorsement of these products or of the manufacturers thereof.

[10] Jackson (Adams, Editor-in-Chief), "Organic Reactions," Vol. II, John Wiley and Sons, New York, N. Y., 1944, pp. 341–375.

PEORIA, ILLINOIS

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH PUBLIC HEALTH SERVICE]

1,2:3,5-Di-*O*-benzylidene-α-D-glucose

BY HARRY B. WOOD, JR., HARRY W. DIEHL AND HEWITT G. FLETCHER, JR.

RECEIVED JANUARY 31, 1957

Condensation of D-glucose with benzaldehyde in the presence of zinc chloride–acetic acid gives a di-*O*-benzylidene-D-glucose identical with a substance which earlier authors obtained through successive benzylidenation and debenzoylation of 6-*O*-benzoyl-D-glucose diethyl dithioacetal. Evidence is presented showing the acetal to be 1,2:3,5-di-*O*-benzylidene-α-D-glucose.

In 1937, Papadakis[1] published a study of the behavior of 6-*O*-benzoyl-D-glucose diethyl dithioacetal with benzaldehyde in the presence of zinc chloride. Under the conditions which this author employed, the thioethyl groups were lost and a non-reducing *O*-benzoyl-di-*O*-benzylidene-D-glucose was obtained as the sole reaction product. Deacylation of the latter compound afforded a di-*O*-benzylidene-D-glucose, m.p. 163°, which was oxidized to a di-*O*-benzylidene-D-glucuronic acid, thus demonstrating that the di-*O*-benzylidene-D-glucose was unsubstituted at C_6 and that the benzoyl group in the starting material had not wandered in the process of cyclic acetal formation.[2]

In the same year Wolfrom and Tanghe[3] reported a more extensive study of the benzylidenation of 6-*O*-benzoyl-D-glucose diethyl dithioacetal. These authors were able to isolate a 6-*O*-benzoyl-di-*O*-benzylidene-D-glucose diethyl dithioacetal as an intermediate which, on further treatment with benzaldehyde and zinc chloride, afforded a non-reducing *O*-benzoyl-di-*O*-benzylidene-D-glucose melting at 160–160.5°. Debenzoylation gave a di-*O*-benzylidene-D-glucose melting at 163–165°. That Wolfrom and Tanghe's di-*O*-benzylidene-D-glucose and its benzoate were identical with the corresponding compounds prepared by Papadakis seems quite certain although the latter author unfortunately failed to report the rotations of his substances.

Recent investigations in this Laboratory have demonstrated, through experiments in the D-ribose

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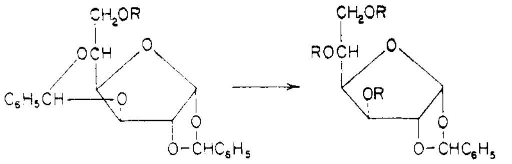
(1) P. Papadakis, THIS JOURNAL, **59**, 841 (1937).

(2) Normally, O → O acyl migrations progress toward, rather than away from primary positions although migrations in the opposite direction under acidic and somewhat violent conditions have been observed: R. C. Hockett, H. G. Fletcher, Jr., E. L. Sheffield and R. M. Goepp, Jr., THIS JOURNAL, **68**, 927 (1946); R. C. Hockett, H. G. Fletcher, Jr., E. L. Sheffield, R. M. Goepp, Jr., and S. Soltzberg, *ibid.*, **68**, 930 (1946).

(3) M. L. Wolfrom and L. J. Tanghe, *ibid.*, **59**, 1597 (1937).

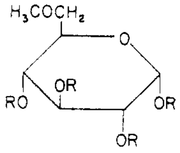
series,[4,5] that condensations of sugars with benzaldehyde in the presence of zinc chloride–acetic acid may give somewhat different results from those obtained when zinc chloride alone is the condensing agent.[6] In the D-glucose series we have shown[7] that benzylidenation with zinc chloride alone affords, in addition to the previously known substances 4,6-*O*-benzylidene-D-glucose[8] and 1,2-*O*-benzylidene-α-D-glucofuranose,[9] 1,2:4,6-di-*O*-benzylidene-α-D-glucose. It was of interest, therefore, to examine the behavior of D-glucose with benzaldehyde in the presence of zinc chloride–acetic acid. Under the conditions employed only two crystalline products, the known 1,2-*O*-benzylidene-α-D-glucofuranose and a di-*O*-benzylidene-D-glucose, were obtained—both in relatively low yield. Comparison of our di-*O*-benzylidene-D-glucose and its benzoate with the corresponding substances kindly provided by Professor Wolfrom showed identity in both cases.



I, R = —H
VII, R = —H

II, R = $\text{—}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{CH}_3$
VIII, R = $\text{—}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{C}_6\text{H}_5$

III, R = $\text{—}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{C}_6\text{H}_5$
IV, R = —CH_3



V, R = —H
VI, R = $\text{—}\overset{\text{O}}{\overset{\|}{\text{C}}}\text{—C}_6\text{H}_5$

The structure of the di-*O*-benzylidene-D-glucose has now been elucidated in the following simple manner. Methylation afforded a crystalline methyl ether (IV); hydrogenolysis of the latter furnished 6-*O*-methyl-D-glucose (V) which was further characterized as its tetrabenzoate VI. Carbon six in the starting material is, therefore, unsubstituted. Partial hydrogenolysis, facilitated by use of a solvent in which a mono-*O*-benzylidenehexose is sparingly soluble,[7] led to the isolation of the known[9] 1,2-*O*-benzylidene-α-D-glucofuranose (VII). It is apparent, then, that the diacetal is 1,2:3,5-di-*O*-benzylidene-α-D-glucose (I), a furanose derivative in contrast to the isomeric di-*O*-benzylidene-D-glucopyranose reported earlier.[7]

In passing, we would like to observe that the apparent marked variability in catalytic activity of zinc chloride in benzylidenations[3] may actually be due to variations in the benzoic acid content of benzaldehyde since one would expect a zinc chloride–benzoic acid complex to resemble zinc chloride–acetic acid as a catalyst in acetal formation.

Experimental[10]

1,2:3,5-Di-*O*-benzylidene-α-D-glucose (I).—A mixture of 10 g. of powdered, anhydrous D-glucose, 20 g. of freshly fused zinc chloride, 60 ml. of benzaldehyde and 7.7 ml. of glacial acetic acid was shaken at 26° for 17 hr. The light straw-colored solution was then poured with stirring into 200 ml. of ice and water. Three 100-ml. ether extractions of the resulting mixture were combined, washed with water and sodium bicarbonate solution, dried over sodium sulfate, treated with 1 g. of decolorizing carbon and filtered. The filtrate was concentrated, finally at 0.5 mm. and 60° (bath). From 20 ml. of ethanol the product crystallized and, after several days at −5°, was filtered off. The minute prisms (3.1 g., 16%) melted at 141–147° and showed $[\alpha]^{20}\text{D}$ +34.0 in pyridine (*c* 0.85). Recrystallization, first from 25 ml. of hot ethanol using 0.5 g. of decolorizing carbon, and then from ethyl acetate, gave pure 1,2:3,5-di-*O*-benzylidene-α-D-glucose melting at 160–161° and rotating $[\alpha]^{20}\text{D}$ +34.8° (pyridine, *c* 1.07) and $[\alpha]^{20}\text{D}$ +40° (CHCl_3, *c* 1.0). Wolfrom and Tanghe[3] recorded m.p. 163–165° and $[\alpha]^{24}\text{D}$ + 35° (pyridine) for their non-reducing di-*O*-benzylidene-D-glucose. Mixed with a sample prepared by Wolfrom and Tanghe, our product melted at 161–164°.

Anal. Calcd. for $\text{C}_{20}\text{H}_{20}\text{O}_6$: C, 67.40; H, 5.66. Found: C, 67.13; H, 5.71.

From the original mother liquor there was obtained, in addition to a small quantity of 1,2:3,5-di-*O*-benzylidene-α-D-glucose, 0.51 g. of **1,2-*O*-benzylidene-α-D-glucofuranose,** m.p. 174–175°, $[\alpha]^{20}\text{D}$ +11.5° (*c* 1, MeOH) and $[\alpha]^{20}\text{D}$ +27.9° (*c* 1.05, pyridine).

6-*O*-Acetyl-1,2:3,5-di-*O*-benzylidene-α-D-glucose (II).—One-half gram of 1,2:3,5-di-*O*-benzylidene-α-D-glucose was acetylated with acetic anhydride in pyridine in the usual fashion to yield, from ethanol, needles (0.4 g., 72%) melting at 144–145° and rotating $[\alpha]^{20}\text{D}$ +28.6° (CHCl_3, *c* 0.86).

Anal. Calcd. for $\text{C}_{22}\text{H}_{22}\text{O}_7$: C, 66.32; H, 5.57. Found: C, 66.23; H, 5.85.

6-*O*-Benzoyl-1,2:3,5-di-*O*-benzylidene-α-D-glucose (III).—One-half gram of 1,2:3,5-di-*O*-benzylidene-α-D-glucose was benzoylated in normal fashion using benzoyl chloride in pyridine to give a crude crystalline product which, recrystallized from 35 ml. of hot absolute ethanol, weighed 0.47 g. (73%), melted at 157–158° and rotated $[\alpha]^{20}\text{D}$ +12.9° (CHCl_3, *c* 1.1).

Anal. Calcd. for $\text{C}_{27}\text{H}_{24}\text{O}_7$: C, 70.42; H, 5.25. Found: C, 70.60; H, 5.33.

Papadakis[1] reported m.p. 156° while Wolfrom and Tanghe[3] reported m.p. 160–160.5° and $[\alpha]^{26}\text{D}$ +15° (CHCl_3) for this substance. Mixed with a sample of the product of these latter authors, our material melted at 158–161°.

1,2:3,5-Di-*O*-benzylidene-6-*O*-methyl-α-D-glucose (IV).—Two grams of 1,2:3,5-di-*O*-benzylidene-α-D-glucose was dissolved in a mixture of 20 ml. of methyl iodide and 10 ml. of dioxane. To the boiling, well-stirred solution 1-g. portions of silver oxide were added at half-hour intervals until 6 g. had been used. After a further hour of stirring and boiling, the solution was cooled, filtered and then concentrated *in vacuo*, the temperature of the material not exceeding 40° at any time. Crystallization was spontaneous: 2.06 g. The product was dissolved in ethanol, decolorized with carbon and crystallized by the addition of pentane. A second recrystallization from cold ether afforded pure material (1.2 g., 58%) melting at 98–100° and rotating $[\alpha]^{20}\text{D}$ +25.2° in chloroform (*c* 1).

Anal. Calcd. for $\text{C}_{21}\text{H}_{22}\text{O}_6$: C, 68.09; H, 5.99. Found: C, 67.81; H, 5.93.

6-*O*-Methyl-α-D-glucose (V).—One gram of 1,2:3,5-di-*O*-benzylidene-6-*O*-methyl-α-D-glucose (IV) was hydrogenolyzed in the customary fashion using 0.5 g. of palladium black suspended in 25 ml. of absolute ethanol. After removal of the catalyst and the solvent the product crystallized: 0.45 g. (86%), m.p. 137–144°. Two recrystallizations from hot absolute ethanol gave pure material (0.22 g.) which was chromatographically homogeneous: m.p. 142–143°, $[\alpha]^{20}\text{D}$ +99° (2 min.) → +56° (19 hr., equil.)

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[4] H. B. Wood, Jr., H. W. Diehl and H. G. Fletcher, Jr., This Journal, **78**, 4715 (1956).

[5] E. Vis and H. G. Fletcher, Jr., *ibid.*, **79**, 1182 (1957).

[6] Compare G. R. Barker and J. W. Spoors, *J. Chem. Soc.*, 1192 (1956).

[7] H. B. Wood, Jr., H. W. Diehl and H. G. Fletcher, Jr., This Journal, **78**, 4715 (1956).

[8] L. Zervas, *Ber.*, **64**, 2289 (1931).

[9] J. C. Sowden and D. J. Kuenne, This Journal, **74**, 686 (1952); see also B. Helferich and A. Porck, *Ann.*, **582**, 233 (1953).

[10] Melting points are corrected.

(*c* 0.94, water). For 6-*O*-methyl-α-D-glucose Bell[11] reported m.p. 145° and $[\alpha]^{15}_{\mathrm{D}}$ +110° → 55° (H_2O). Addition of 90 mg. of this material to a mixture of benzoyl chloride and pyridine which previously had been cooled to 0° led, after the usual manipulations, to the isolation, from ethanol-pentane, of 220 mg. of crystalline material. Recrystallization from hot pentane afforded, with little loss, a product melting at 157–159° and rotating $[\alpha]^{20}_{\mathrm{D}}$ +126.5° (*c* 1.1, $CHCl_3$).

Anal. Calcd. for $C_{35}H_{30}O_{10}$: C, 68.84; H, 4.95. Found: C, 68.81; H, 4.81.

Ohle and Tessmar[12] recorded m.p. 154° and $[\alpha]_{\mathrm{D}}$ +120.6° ($CHCl_3$) for 1,2,3,4-tetra-*O*-benzoyl-6-*O*-methyl-α-D-glucose (VI).

1,2-*O*-Benzylidene-α-D-glucofuranose (VII) from 1,2:3,5-Di-*O*-benzylidene-α-D-glucose (I).—A sample (0.5 g.) of palladium black catalyst was suspended in 50 ml. of ethyl acetate and saturated with hydrogen at room temperature and a pressure very slightly in excess of atmospheric. The ethyl acetate was then decanted and a solution of 2.0 g. of 1,2:3,5-di-*O*-benzylidene-α-D-glucose in 30 ml. of warm ethyl acetate added. The reduction was carried out in normal fashion and halted after 17 hr. when approximately two molar equivalents of hydrogen had been consumed. The product, which had precipitated in the course of the reaction, was removed with the catalyst and then extracted from the latter with 10 ml. of hot dioxane. Concentration of the dioxane solution gave a crystalline mass which was washed with a little water (to remove D-glucose) and dried: 0.65 g. (43%), m.p. 172–174°. Recrystallized successively from methyl ethyl ketone and from hot ethyl acetate (carbon treatment) the cyclic acetal (0.3 g.) was obtained as needles, m.p. 176–177°, $[\alpha]^{20}_{\mathrm{D}}$ +27.9° ($CHCl_3$, *c* 1) and $[\alpha]^{20}_{\mathrm{D}}$ +11.9° (MeOH, *c* 0.8). Sowden and Kuenne[9] reported m.p. 176–177° and $[\alpha]^{20}_{\mathrm{D}}$ +10.5° (MeOH) for 1,2-*O*-benzylidene-α-D-glucofuranose; admixture with authentic material prepared by the method of Sowden and Kuenne[9] caused no depression of melting point.

Benzoylation of a sample (0.1 g.) of our mono-*O*-benzylidene-D-glucose, prepared as described above, afforded, after recrystallization from ethanol, 0.13 g. of handsome needles melting at 112–114° either alone or in admixture with a sample of 3,5,6-tri-*O*-benzoyl-1,2-*O*-benzylidene-α-D-glucose (VIII) kindly provided by Dr. Sowden.[13] In chloroform (*c* 1) we found a rotation of −62.7°; the earlier authors reported $[\alpha]^{25}_{\mathrm{D}}$ −62.7° in this solvent.

Acknowledgments–We wish to thank Dr. M. L. Wolfrom and Dr. J. C. Sowden for samples of products for comparison purposes. Analytical data were obtained by the Institutes' Microanalytical Laboratory under the direction of Dr. W. C. Alford.

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[11] D. J. Bell, *J. Chem. Soc.*, 859 (1936).

[12] H. Ohle and K. Tessmar, *Ber.*, **71**, 1843 (1929).

[13] This value, slightly but significantly higher than that reported earlier (ref. 9), is considered both by the present authors and Dr. Sowden as the preferred figure for the melting point of 3,5,6-tri-*O*-benzoyl-1,2-*O*-benzylidene-α-D-glucofuranose.

BETHESDA 14, MD.

[CONTRIBUTION FROM NATIONAL BUREAU OF STANDARDS, DIVISION OF CHEMISTRY]

Structure of 5-Aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose[1]

BY ROBERT SCHAFFER AND HORACE S. ISBELL

RECEIVED MARCH 6, 1957

Crystalline dimeric 5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose was shown to be bis-(5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose) 5,5′:3′,5-cyclic acetal. The following crystalline derivatives were prepared: 5′-*O*-acetyl-[bis-(5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose) 5,5′:3′,5-cyclic acetal], 3,5′-di-*O*-acetyl-[bis-(5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose) 5,5′:3′,5-cyclic acetal] and 5′-*O*-acetyl-3-*O*-mesyl-[bis-(5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose) 5,5′:3′,5-cyclic acetal]. The parent compound and the derivatives have an acetal structure at carbon 5 and a hemiacetal structure at carbon 5′. Both carbon 5 and carbon 5′ are asymmetric and four modifications of each substance are possible. The diacetate differs from the somewhat analogous diacetyl derivatives of Späth and co-workers in that it does not undergo hydrogenolysis with elimination of the hemiacetal acetate group. The two acetyl groups, however, differ in stability, in agreement with the two types of acetyl groups shown in the assigned structure.

Crystalline 5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose was prepared in this Laboratory as a raw material for the synthesis of D-glucose-6-C^{14}.[2] The substance was crystallized in the form of a hydrate from water and in the anhydrous form from benzene. The anhydrous product appears to be the same as a crystalline substance reported by Brocca and Dansi,[3] who concluded that the substance was a monomer. Molecular weight determinations reported by the present authors showed that both the hydrate and the anhydrous compound are dimers.[2] The importance of the 5-aldo-derivative for synthetic purposes and the existence of unusual chemical properties to be reported later led us to undertake a more detailed study of its structure.

By acetylation with acetic anhydride and pyridine at low temperature, Brocca and Dansi obtained from their product an amorphous material that was assumed to be 3-*O*-acetyl-5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose. In the present study a crystalline acetate was obtained by the same method. The molecular weight and analysis of this product show that it is a dimer having two acetyl groups.

The monomeric form of 5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose (I) would have a free aldehyde group. The infrared spectrum[4] of the crystalline substance, however, showed no absorption corresponding to a free aldehyde group. Hence the aldehyde group must be masked, presumably by formation of a dimer. Structures IIa and IIIa fulfill the requirements that the aldehyde groups be masked and that two hydroxyls be available for acetylation.

The 8-membered ring structure IIa is like one

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[1] This work was conducted as part of a project on the development of methods for the synthesis of radioactive carbohydrates, sponsored by the Division of Research of the Atomic Energy Commission.

[2] R. Schaffer and H. S. Isbell, *J. Research Natl. Bur. Standards*, **56**, 191 (1956).

[3] V. Brocca and A. Dansi, *Ann. chim.* (*Rome*), **44**, 120 (1954).

[4] H. S. Isbell, R. Schaffer and J. Stewart, unpublished work.