(*c* 0.94, water). For 6-*O*-methyl-α-D-glucose Bell[11] reported m.p. 145° and $[\alpha]^{16}_{\text{D}}$ +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 $[\alpha]^{20}_{\text{D}}$ +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 $[\alpha]_{\text{D}}$ +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°, $[\alpha]^{20}_{\text{D}}$ +27.9° ($CHCl_3$, *c* 1) and $[\alpha]^{20}_{\text{D}}$ +11.9° (MeOH, *c* 0.8). Sowden and Kuenne[9] reported m.p. 176–177° and $[\alpha]^{20}_{\text{D}}$ +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 $[\alpha]^{25}_{\text{D}}$ −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.

BETHESDA 14, MD.

---

[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.

[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

---

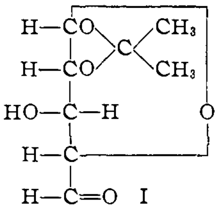
[1] This work was conducted as part of a project on the development of methods for the synthesis of radioactive carbohydrates, sponsored by the Division of Research of the Atomic Energy Commission.

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

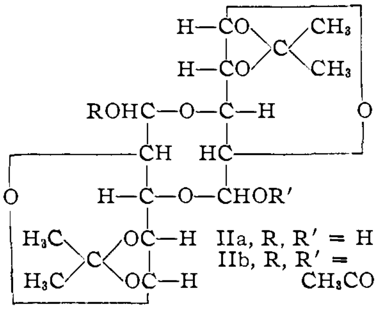
[3] V. Brocca and A. Dansi, *Ann. chim.* (*Rome*), **44**, 120 (1954).

[4] H. S. Isbell, R. Schaffer and J. Stewart, unpublished work.

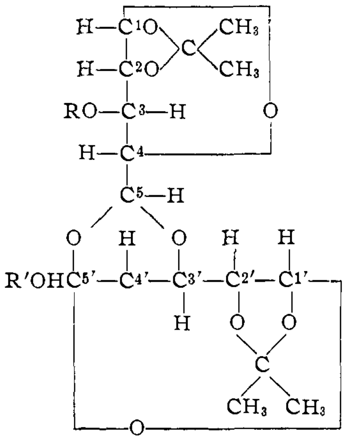
proposed by Bergmann and co-workers[5,6] for certain dimers of β-hydroxy-aldehydes. Subsequent work by Späth and co-workers,[7-9] however, established that β-hydroxy-aldehydes in general have the 6-membered ring structure IVa. Structure IIIa is of the same type, but is more restricted on account of the presence of several fused rings.



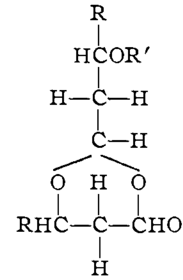
I



IIa, R, R' = H
IIb, R, R' = CH_3CO



IIIa, R,R' = H
IIIb, R,R' = CH_3CO
IIIc, R = H; R' = CH_3CO
IIId, R = Ms; R' = CH_3CO



IVa, R = alkyl; R' = H
IVb, R = alkyl; R' = CH_3CO

Späth and co-workers established structure IVa for the dimeric β-hydroxy-aldehydes by showing that the diacetyl derivatives IVb undergo hydrogenolysis with elimination of the hemiacetal acetate group to give the corresponding 1,3-dioxane derivatives in which hydrogen has been substituted for OR′ at carbon 4 of the ring.

Application of the hydrogenolysis procedure in the present case was not successful with either palladium black catalyst[10] in acetic acid or "S-palladium black."[11] It seems possible that the furanose ring fused to the 1,3-dioxane ring in IIIb, a structural feature not present in the acetylated 4-hydroxy-1,3-dioxane derivatives that undergo hydrogenolysis, constitutes a sufficient structural alteration to preclude hydrogenolysis under the conditions used.

Since the structure could not be determined by hydrogenolysis, attention was directed to other methods. Substance IIa has two hemiacetal hydroxyls and no alcoholic hydroxyl, but IIIa has one hemiacetal hydroxyl and one alcoholic hydroxyl. Aside from differences that might arise from the conformation of the 8-membered ring, the two hemiacetal hydroxyls of IIa are alike, and one would not expect the two groups to react at widely different rates, or the corresponding acetyl groups to have widely different properties.

To ascertain whether there was a difference in the reaction rates for the two hydroxyls, a sample of dimeric 5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose was acetylated for a short reaction time, and a crystalline product was isolated. The analysis and molecular weight showed that the compound is a dimer substituted with one acetyl group. Its infrared spectrum showed no aldehydic carbonyl absorption[4] and it did not react with phenylhydrazine. Hence all aldehyde groups must be blocked. With methanesulfonyl chloride the monoacetate gave a crystalline mesyl derivative. The analysis showed that the material corresponds to a dimer with one mesyl and one acetyl group. Its infrared spectrum showed no carbonyl absorption.[4] The method of preparation and the stability of the mesyl group in aqueous and alcoholic solution lead to the assignment of the mesyl group to a carbon in the alcoholic state of oxidation rather than in the hemiacetal state. This requires that the substance be IIId and the parent monoacetate be IIIc. The diacetate would then be IIIb.

To confirm the structure of the diacetate, the rate of hydrolysis of the acetyl groups was studied. The results given in the semi-log plot of Fig. 1 clearly show the presence of two types of acetyl groups. The graphical analysis of the data shows that the half-time for the hydrolysis of one acetyl group is 7 or 8 times that for the other. This difference in stability is consistent with structure IIIb but is not in accord with structure IIb. Thus IIa is clearly eliminated as a possibility, and IIIa can be considered the structure of the anhydrous dimer.

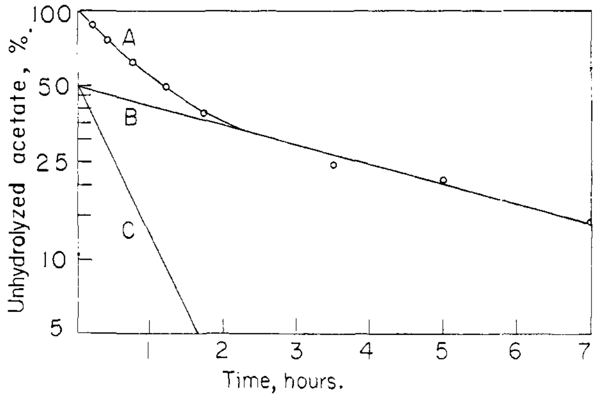


Fig. 1.—Hydrolysis of IIIb in 0.05 *N* hydrochloric acid at 80°: A, experimental curve; B, extrapolated curve for less reactive acetyl group; C, calculated curve for more reactive acetyl group.

---

(5) M. Bergmann, M. Miekeley and E. von Lippmann, *Ber.*, **62**, 1467 (1929).

(6) M. Bergmann and M. Miekeley, *ibid.*, **62**, 2297 (1929).

(7) E. Späth and H. Schmid, *ibid.*, **74**, 859 (1941).

(8) E. Späth, R. Lorenz and E. Freund, *ibid.*, **76**, 57, 1196 (1943); **77**, 354 (1944).

(9) E. Späth and I. v. Szilágyi, *ibid.*, **76**, 949 (1943).

(10) J. Tausz and N. von Putnoky, *ibid.*, **52**, 1573 (1919).

(11) V. K. Kindler, E. Schärfe and P. Henrich, *Ann.*, **565**, 51 (1949).

Official nomenclature rules[12] are inadequate for naming the compounds but for the present the following names are suggested: IIIa is bis-(5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose) 5,5′:3′,5-cyclic acetal, IIIb is 3,5′-di-*O*-acetyl-[bis-(5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose) 5,5′:3′,5-cyclic acetal], IIIc is 5′-*O*-acetyl-[bis-(5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose) 5,5′:3′,5-cyclic acetal] and IIId is 5′-*O*-acetyl-3-*O*-mesyl-[bis-(5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose) 5,5′:3′,5-cyclic acetal].

Different configurations for carbons 5 and 5′ would give rise to four isomers. Consideration of the configuration of the present compound and the conformation of the cyclic acetal ring will be deferred for inclusion in a study of the infrared spectra now in progress.[4]

Experimental

Bis-(5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose) 5,5′:3′,5-Cyclic Acetal (IIIa).—This substance, previously called 1,2-*O*-isopropylidene-D-*xylo*-dialdo-pentofuranose, was obtained by oxidation of 1,2-*O*-isopropylidene-D-glucofuranose with sodium metaperiodate, and crystallization of the product by the method described previously.[2] The hydrate (crystallized first) was converted to the anhydrous form by crystallization from benzene.

Acetylation of IIIa to 5′-*O*-Acetyl-[bis-(5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose) 5,5′:3′,5-Cyclic Acetal] (IIIc).—One gram of finely powdered anhydrous IIa was stirred vigorously at 0° with a mixture consisting of 5 ml. of acetic anhydride and 7 ml. of pyridine. After 8 to 10 minutes the reaction mixture was poured into 200 ml. of cracked ice. The product was extracted with chloroform. Then the chloroform solution was extracted twice with aqueous sodium bicarbonate and six times with copper sulfate solution. Finally the chloroform was evaporated, and subsequently the product was crystallized from carbon tetrachloride. The crystals, fine elongated prisms, weighed 0.54 g. and contained approximately 1.5 moles of carbon tetrachloride per mole of the product. They melted at 96–98°, solidified at 102°, and melted again at 175–176°. Recrystallization from ethanol and water (1:2) yielded a product that crystallized in large needles without solvent of crystallization; m.p. 175–176°, and $[\alpha]^{25}$D +37.8° (*c* 0.7, ethanol).

Anal. Calcd. for $C_{18}H_{26}O_{11}$: C, 51.7; H, 6.3. Found: C, 51.3; H, 6.5.

The unsolvated product had a molecular weight of 393 in benzene by the Beckmann freezing point method, and an equivalent weight of 418 by an acetyl-group determination.[13] The calculated molecular weight for the mono-acetylated dimer is 418.

After refluxing IIIc and 2,4-dinitrophenylhydrazine in ethanol for 17 hours, each of the materials was isolated unreacted.

Acetylation of IIIa to 3,5′-Di-*O*-acetyl-[bis-(5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose) 5,5′:3′,5-Cyclic Acetal] (IIIb).—A 2.5-g. sample of anhydrous IIIa was stirred for 2.5 hours at 0° with a mixture of 12.5 ml. of acetic anhydride and 17 ml. of pyridine. The reaction mixture was poured into ice-water and extracted as described above. The chloroform was evaporated, and the residue was crystallized from ethanol. The crystals weighed 3 g. They contained 0.5 mole of ethanol per mole of dimer, and melted at 113.5–115° with the evolution of gas; $[\alpha]^{20}$D +44.2° (*c* 2, ethanol).

Anal. Calcd. for $C_{20}H_{28}O_{12}\cdot{}^1/_2C_2H_5OH$: C, 52.1; H, 6.4. Found: C, 51.7; H, 6.4.

The molecular weight in benzene by the Beckmann freezing point method was 321. For the diacetylated dimer with one-half mole of ethanol of solvation the calculated value is 322. The equivalent weight by acetyl analysis was 251, and the calculated value is 242.

The product crystallized from carbon tetrachloride with approximately 0.5 mole of solvent per mole of dimer; m.p. 122–125°.

The unreacted diacetate was recovered unchanged after refluxing 18 hours with phenylhydrazine and with 2,4-dinitrophenylhydrazine.

Mesylation of IIIc to 5′-*O*-Acetyl-3-*O*-mesyl-[bis-(5-aldo-1,2-*O*-isopropylidene-D-*xylo*-pentofuranose) 5,5′:3′,5-Cyclic Acetal] (IIId).—A solution of 0.209 g. of IIIc and 5 ml. of ice-cold anhydrous pyridine was treated for 20 hours at 0° with 0.35 ml. of methanesulfonyl chloride in 5 ml. of pyridine. About 0.5 ml. of water was then added dropwise. After one hour the mixture was taken up in chloroform, and extracted two times with sodium bicarbonate solution and six times with copper sulfate solution. The chloroform was then evaporated, and the product was dissolved in carbon tetrachloride from which it separated, with solvent of crystallization, in pointed leaflets weighing 0.27 g.; m.p. 92–93.5° with the evolution of gas, and $[\alpha]^{20}$D +35° (*c* 0.4, carbon tetrachloride). For analysis a sample was dissolved in boiling xylene, the solution concentrated to dryness, the product recrystallized from carbon tetrachloride, and then dried under vacuum over boiling ethanol.

Anal. Calcd. for $C_{19}H_{28}O_{13}S\cdot CCl_4$: C, 36.9; H, 4.3; S, 4.9; Cl, 21.8. Found: C, 37.1; H, 4.4; S, 4.9; Cl, 20.2.

The low chloride value can be explained by loss on drying of about ten mole per cent. of carbon tetrachloride.

Attempted Hydrogenolysis of IIIb.—In a Parr hydrogenation apparatus 0.59 g. of IIIb in 10 ml. of glacial acetic acid and 0.62 g. of palladium black[10] were shaken under an atmosphere of hydrogen for 5 days. The slightly yellow solution was filtered, concentrated to dryness under vacuum several times with intermittent additions of ethanol, and then dissolved in ethanol. This solution was filtered through decolorizing carbon, concentrated to a 2-ml. volume, and a few drops of water and some seed crystals of IIIb were added. About 0.27 g. of crystalline IIIb was isolated leaving a sirupy residue of about the same weight with an $[\alpha]^{20}$D of +30°. No additional crystallization could be induced.

In another attempt 1.0 g. of the diacetate in 60 ml. of ethanol, and 1 g. of "S-palladium black"[11] were shaken in an atmosphere of hydrogen for 20 hours. After filtration and concentration of the solution, substantially all of the diacetate was recovered unchanged. Glacial acetic acid also was employed as solvent with the "S-palladium black" catalyst, but with the same result.

Acid Hydrolysis of the Diacetate IIIb.—Aliquots of 2 ml. of a stock solution of 0.497 g. of IIIb in 25 ml. of peroxide-free distilled dioxane were transferred to each of several test-tubes. The tubes were placed in a bath at 80 ± 1°, and 2-ml. portions of aqueous 0.1 *N* hydrochloric acid (previously heated to 80°) were added. The tubes were then fitted with reflux condensers. A series of blank samples were set up similarly using 2-ml. aliquots of a solution of 0.388 g. of IIIa in 25 ml. of dioxane and of the aqueous hydrochloric acid. Periodically a sample, or a blank, was removed, cooled in ice-water, and titrated to the phenolphthalein end-point with standard sodium hydroxide. In the blank runs acid formation in excess of the hydrochloric acid initially introduced increased uniformly with time, and amounted after three hours to about the equivalent of one-twentieth of the total hydrolyzable acetate, and to about one-tenth after seven hours. This correction served to reduce the net titers for the liberated acetyl groups at those times by only 3 and 6%, respectively. The results of the experiment are given in Fig. 1, where the curve representing the unsaponified acetate plotted against time was graphically analyzed into two linear curves showing the rates of hydrolysis for the two acetyl groups. The half-time for the rapidly split acetyl group is approximately 0.5 hour and for the slower approximate 3.5 to 4 hours.

The authors express their appreciation to R. A. Paulson and L. Tregoning of the Bureau for the microanalyses.

WASHINGTON 25, D. C.

---

[12] *Chem. Eng. News*, **31**, 1776 (1953).

[13] D. H. Brauns, THIS JOURNAL, **47**, 1294 (1925).