531. 2 : 4-3 : 5-*Diethylidene* aldehydo-L-*Xylose and its Derivatives.*

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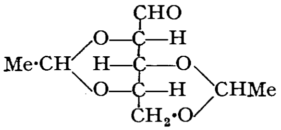
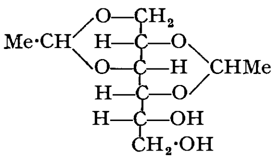
2 : 4-3 : 5-Diethylidene *aldehydo*-L-xylose has been prepared by an improved method and has been converted into three crystalline derivatives. It has been shown to exist as a monomer in the crystalline state and also in solution in benzene, dioxan, and water. Measurements have been made of the specific rotations and ultra-violet absorption spectra of its solutions in different solvents.

In order to explain certain anomalous optical-rotation measurements made during the course of unsuccessful attempts to prepare cyclic acetals by condensing *aldehydo*-sugars with polyhydroxy-compounds, it became necessary to study the physical and chemical properties of 2 : 4-3 : 5-diethylidene *aldehydo*-L-xylose (I) reported in this paper. This work was focussed mainly on the stability and hydration of the compound, and on its possible existence in a polymeric form, such as that postulated by Gätzi and Reichstein (*Helv. Chim. Acta*, 1938, **21**, 914) and by English and Griswold (*J. Amer. Chem. Soc.*, 1945, **67**, 2039) for 2 : 3-4 : 5-di*iso*propylidene *aldehydo*-arabinose.

2 : 4-3 : 5-Diethylidene *aldehydo*-L-xylose can be prepared conveniently by the action of a glycol-splitting oxidising agent on 1 : 3-2 : 4-diethylidene D-sorbitol (II), which results from the controlled hydrolysis of 1 : 3-2 : 4-5 : 6-triethylidene sorbitol (Appel, *J.*, 1935, 425; Gätzi and Reichstein, *Helv. Chim. Acta*, 1938, **21**, 86; Bourne and Wiggins, *J.*, 1948, 1933), and also from the partial ethylidenation of sorbitol (Hockett and Schaefer, *J. Amer. Chem. Soc.*, 1947, **69**, 849). Hockett and Schaefer (*loc. cit.*) recommended that this oxidation should be effected by adding a hot solution of lead tetra-acetate in glacial acetic acid to an aqueous solution of 1 : 3-2 : 4-diethylidene sorbitol, thus avoiding the formation of a by-product [possibly a condensation product of 2 : 4-3 : 5-diethylidene *aldehydo*-L-xylose with unchanged 1 : 3-2 : 4-diethylidene sorbitol (Hockett and Nickerson, Abs. Amer. Chem. Soc. Meeting, Memphis, April 1942)] which arises in a glacial acetic acid–benzene solvent; even so, extensive recrystallisation of the diethylidene *aldehydo*-L-xylose was necessary. We have found that the xylose diacetal is obtained in good yield (80%), and virtually pure, even before recrystallisation, when the oxidation is conducted with sodium metaperiodate in water.


(I)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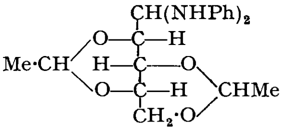
(III)

Although the diethylidene *aldehydo*-L-xylose thus prepared, and its crystalline oxime, had physical constants almost identical with those reported by Hockett and Schaefer (*loc. cit.*), this was not the case for its bisdimedone derivative, but the bisdimedone compound obtained by the American workers was not analytically pure. In its property of forming a water-insoluble crystalline bisdimedone derivative, 2 : 4-3 : 5-diethylidene *aldehydo*-L-xylose resembles 2 : 3-4 : 5-di*iso*propylidene *aldehydo*-D-arabinose (Bourne, McSweeney, Stacey, and Wiggins, *J.*, 1952, 1408) and 2 : 3-4 : 5-di*iso*propylidene *aldehydo*-L-xylose (Bourne, McSweeney, and Wiggins, *J.*, in the press), but differs from xylose itself, which does not react with dimedone under the same conditions. Thus it appears that the existence of a pyranose ring system precludes the formation of a dimedone derivative although not that of the mercaptal of xylose (cf. Wolfrom, Newlin, and Stahly, *J. Amer. Chem. Soc.*, 1931, **53**, 4379). The ready reaction of 2 : 4-3 : 5-diethylidene *aldehydo*-L-xylose with dimedone explains why the formaldehyde produced when 1 : 3-2 : 4-diethylidene sorbitol is oxidised with periodate can be determined with dimedone only after it has been purified by distillation in steam (Bourne, Bruce, and Stacey, unpublished work).

The crystalline product obtained when diethylidene *aldehydo*-L-xylose was heated with an excess of aniline in methanol gave the correct analysis for compound (III), *i.e.*, it contained two aniline residues for one xylose unit. This compound slowly darkened on storage, presumably owing to the liberation of aniline; the observed slow decrease in the optical rotation of an alcoholic solution could be attributed to the same cause. This rather unusual mode of condensation between a sugar and an amine finds a parallel in the reactions of simple aldehydes (cf. Hickinbottom, "Reactions of Organic Compounds," Longmans, Green, and Co., 1942, p. 135), and also in the fact that glucose condenses with one mol. of *o*-phenylenediamine to give a cyclic product in which $C_{(1)}$ of the hexose is united to both amino-groups (cf. Pigman and Goepp, "Chemistry of the Carbohydrates," Academic Press Inc., 1948, p. 380).

Optical rotations of 2 : 4-3 : 5-*diethylidene* aldehydo-L-*xylose in various solvents at room temperature.*

	$[\alpha]_D$			$[\alpha]_D$	
Solvent	Initial	At equilm.	Solvent	Initial	At equilm.
Benzene (dry)	−138°	−138°	Chloroform (not dried)	−69°	−9°
Benzene (not dried) ...	−135	−46	Water	−13	−13
Pyridine (dry)	−97	−97	Chloroform (98%)–ethanol (2%)	−24	−18

The optical rotations of 2 : 4-3 : 5-diethylidene *aldehydo*-L-xylose in different solvents showed considerable variations (see Table); for example, the values of $[\alpha]_D$ in dry benzene and water were −138° and −13°, respectively. The possibility that these differences were due to polymerisation effects was eliminated when cryoscopic measurements in benzene, dioxan, and water revealed that the solute was monomeric in each case; a similar result was obtained from crystallographic data for the solid. Nor were the rotational effects attributable to hydrolysis of the ethylidene residues, because diethylidene *aldehydo*-L-xylose still afforded its characteristic dimedone derivative after it had been kept in aqueous solution for 18 hours. Thus it appeared that the factor responsible was the addition of hydroxylic compounds to the carbonyl group of the xylose moiety; such additions are known to occur with other *aldehydo*-sugars (see, *e.g.*, Wolfrom, *J. Amer. Chem. Soc.*, 1931, **53**, 2275; Wolfrom, Konigsberg, and Weisblat, *ibid.*, 1939, **61**, 574; Ness, Hann, and Hudson, *ibid.*, 1944, **66**, 665; Stacey and Turton, *J.*, 1946, 661). In these circumstances the equilibrium value of $[\alpha]_D$ attained in a non-polar solvent which had not been dried should have been dependent on the proportion of the hydroxylic impurity present, and it was demonstrated that the addition of water or alcohol to such equilibrated solutions did, in fact, cause further changes in $[\alpha]_D$.

These conclusions were in harmony with the ultra-violet absorption spectra of solutions of 2 : 4-3 : 5-diethylidene *aldehydo*-L-xylose. A fresh solution in dry chloroform had $\lambda_{max.}$ at 2900 Å, the characteristic position for a carbonyl group, but the spectrum changed as the solution was stored, and, after 50 hours, had $\lambda_{max.}$ at 2530 Å. Aqueous and alcoholic solutions had $\lambda_{max.}$ at 2420 and 2550 Å, respectively, compared with 2500 Å for a solution of 1 : 3-2 : 4-diethylidene sorbitol in a chloroform (98%)–ethanol (2%) mixture.

EXPERIMENTAL

2 : 4-3 : 5-*Diethylidene* aldehydo-L-*Xylose.*—An aqueous solution (290 c.c.) of sodium metaperiodate (22 g.) was added slowly to a stirred solution (70 c.c.) of 1 : 3-2 : 4-diethylidene sorbitol (20·0 g.), which had been prepared from 1 : 3-2 : 4-5 : 6-triethylidene sorbitol by partial hydrolysis with acid (cf. Appel, *loc. cit.*; Bourne and Wiggins, *loc. cit.*). The stirring was continued for 2 hours before the solution was evaporated at 30°/15 mm.; the residue was extracted with chloroform. Evaporation of the extracts gave 2 : 4-3 : 5-diethylidene *aldehydo*-L-xylose (13·7 g.), m. p. 160—162°. Recrystallised from dioxan, the product (7·0 g.) had m. p. 160—161°, $[\alpha]_D^{22}$ $-12{\cdot}8°$ (*c*, 2·2 in water) (Found : C, 53·4; H, 7·0. Calc. for $C_9H_{14}O_5$: C, 53·5; H, 7·0%). Hockett and Schaefer (*loc. cit.*) recorded m. p. 162—163°, $[\alpha]_D^{20}$ $-12{\cdot}4°$ (*c*, 2·9 in water).

Bisdimedone Derivative of 2 : 4-3 : 5-*Diethylidene* aldehydo-L-*Xylose.*—The addition of a hot saturated aqueous solution of dimedone (0·138 g.) to a solution of 2 : 4-3 : 5-diethylidene *aldehydo*-L-xylose (0·090 g.) in water (2·0 c.c.) gave immediately a white precipitate, which was collected by filtration after 6 hours. Recrystallised twice from aqueous alcohol, it afforded the bisdimedone derivative (0·115 g.), m. p. 223—224° (decomp.), $[\alpha]_D^{16}$ $+9{\cdot}5°$ (*c*, 1·2 in ethyl alcohol) (Found : C, 64·5; H, 7·5. Calc. for $C_{25}H_{36}O_8$: C, 64·6; H, 7·8%). Hockett and Schaefer (*loc. cit.*) recorded m. p. 196—199° (decomp.), $[\alpha]_D^{20}$ $+40{\cdot}3°$ (*c*, 1·2 in chloroform).

In a second experiment, an aqueous solution (10 c.c.) of 2 : 4-3 : 5-diethylidene *aldehydo*-L-xylose (0·486 g.) was kept at room temperature for 18 hours before being freeze-dried. The residue, treated with dimedone as before, gave the bisdimedone derivative (55% yield), m. p. 224—225° alone or on admixture with the above specimen.

2 : 4-3 : 5-*Diethylidene* aldehydo-L-*Xylose Oxime.*—A solution (6·0 c.c.) of 2 : 4-3 : 5-diethylidene *aldehydo*-L-xylose (0·300 g.), hydroxylamine hydrochloride (0·300 g.), and sodium acetate (0·3 g.) in aqueous methanol (25% of water, by volume) was refluxed gently for 20 minutes, and then water was added until a faint turbidity developed. The clusters of needles which separated when the solution was kept at 0° for 2 days were recrystallised from ethyl alcohol, to give the oxime (0·077 g.), m. p. 255—256°, $[\alpha]_D^{19}$ $-97{\cdot}0°$ (*c*, 1·3 in pyridine) (Found : C, 49·9; H, 6·9. Calc. for $C_9H_{15}O_5N$: C, 49·8; H, 7·0%). Hockett and Schaefer (*loc. cit.*) reported m. p. 256—257°, $[\alpha]_D^{20}$ $-97{\cdot}8°$ (*c*, 1·6 in pyridine).

2 : 4-3 : 5-*Diethylidene* 1 : 1-*Bis*-C-*anilino*-1-*deoxy*-L-*xylitol.*—2 : 4-3 : 5-Diethylidene *aldehydo*-L-xylose (0·140 g.) was heated with aniline (0·25 c.c.) in dry methanol (7·0 c.c.) at 60° (bath-temp.) for 30 minutes. The solution was concentrated at 12 mm. until crystallisation commenced. After being washed with ether, the crystalline product (0·190 g.) had m. p. 98°. Recrystallised four times from methanol, it gave the 1 : 1-*bis*-C-*anilino*-compound, m. p. 103—104° (decomp.), $[\alpha]_D^{18}$ $-33{\cdot}3°$ (*c*, 0·15 in ethyl alcohol), slowly decreasing after 2 hours (Found : C, 67·9; H, 7·1; N, 7·7. $C_{21}H_{26}O_4N_2$ requires C, 68·1; H, 7·1; N, 7·6%).

Determination of the Molecular Weight of 2 : 4-3 : 5-*Diethylidene* aldehydo-L-*Xylose.*—(a) *Crystallographic method* (With Mr. P. CUCKA). By *X*-ray diffraction on a single crystal, 2 : 4-3 : 5-diethylidene *aldehydo*-L-xylose was found to be monoclinic with the following lattice parameters : *a*, 9·97; *b*, 8·48; *c*, 5·96 Å; β, 90°. The density was 1·346 g./c.c. Since the compound was asymmetric and optically active, the unit cell must have contained at least two molecules. From these figures the molecular weight was calculated to be 204, or possibly 102, the latter figure being incompatible with the fact that the compound was a xylose derivative (Calc. for $C_9H_{14}O_5$: *M*, 202).

(b) *Cryoscopic method.* The solvents used in three separate determinations by the Beckmann method were benzene ("AnalaR"), dioxan, and water, the two organic solvents having been fractionally distilled over metallic sodium. The molecular weight of the xylose derivative was calculated to be 209 in benzene, 205 in dioxan, and 185 in water. The fact that 2 : 4-3 : 5-diethylidene *aldehydo*-L-xylose forms a hydrate in aqueous solution did not materially influence the determinations made in this solvent, because the weight of solute used in the calculations was that of the anhydrous crystalline material actually introduced, and the molar concentration of the solution was altered to a negligible extent by hydrate formation.

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