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The Acetolysis of Trimethylene-D-sorbitol. 2,4-Methylene-D-sorbitol and 1,3:2,4-Dimethylene-D-sorbitol

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Recently[1] we have shown that the limited acetolysis of the trimethylene-D-mannitol of Schulz and Tollens yields a compound to which has been tentatively assigned the structure 1,6-diacetyl-3,4-di-(acetoxymethyl) - 2,5 - methylene - D - mannitol. This structure seems highly probable since the saponification of the acetolysis product yields a 2,5-methylene-D-mannitol, a fact which we take to indicate that the acetal linkages of trimethylene - D - mannitol which are formed through secondary hydroxyl groups are relatively more stable to acetolysis than those formed through primary hydroxyl groups. The acetolysis apparently proceeds with rapid rupture of the acetal linkages at positions one and six and the 3,4-di-(hydroxymethyl) - 2,5 - methylene - D - mannitol which is assumed to be formed is immediately acetylated to produce 1,6-diacetyl-3,4-di-(acetoxymethyl)-2,5-methylene-D-mannitol. In view of the unusual nature of the acetolysis reaction, and particularly since the acetolysis product and the 2,5-methylene-D-mannitol derived from it contain the rare C_5O_2 dioxepane ring as an integral part of their structures, it seemed of interest to study the acetolysis of the known trimethylene-D-sorbitol.[2] In the course of preparation of a supply of this material we isolated from the mother liquor a dimethylene-D-sorbitol, a new substance, which melted at 174–175° and rotated $[\alpha]^{20}D$ $-29.6°$ in water, and the investigation was extended to include the acetolysis and proof of structure of this diacetal.

Considering first the trimethylene-D-sorbitol, it is obvious that its acetal linkages must be formed through four secondary and two primary hydroxyl groups. From our previous experience it was anticipated that upon limited acetolysis it would yield a diacetyl-di-(acetoxymethyl)-monomethylene-D-sorbitol; it was found that the acetolysis of trimethylene-D-sorbitol by an ice-cold 1% sulfuric acid acetylating solution for five minutes gave a 51% yield of a crystalline reaction product (m. p. 111–112°; $[\alpha]^{20}D$ $+29.8°$ in chloroform), the composition of which agreed with that of the expected substance. The compound was saponified by the method of Kunz[3] with the consumption of four molecular equivalents of sodium hydroxide, and the saponification product proved to be a crystalline monomethylene-D-sorbitol (m. p. 163–164°; $[\alpha]^{20}D$ $-9.8°$ in water). Oxidation of this product with sodium periodate (and other glycol-splitting reagents) reduced one molecular equivalent of the oxidant and proved that only a single glycol grouping is present in the monomethylene-D-sorbitol. At this stage of the study the experimental results in the case of trimethylene-D-sorbitol are thus closely parallel with those previously reported for the isomeric trimethylene-D-mannitol. However, the periodate oxidation of the 2,5-methylene-D-mannitol proceeded without the production of acid or formaldehyde, thereby confirming the structure assigned to it, whereas 0.86 of a molecular equivalent of formaldehyde was isolated as the crystalline dimethone derivative from the oxidized solution of the monomethylene-D-sorbitol. One hydroxyl group of the glycol grouping of methylene-D-sorbitol is therefore primary in character and the structure of the acetal cannot be 2,5 but is limited to that of 2,4 or 3,5-methylene-D-sorbitol. A choice between these two possibilities could be readily made; the oxidation of 2,4-methylene-D-sorbitol (III) with glycol-splitting reagents would yield 2,4-methylene-L-xylose, which upon reduction would be converted to 2,4-methylene-xylitol (IV) of *meso* con-

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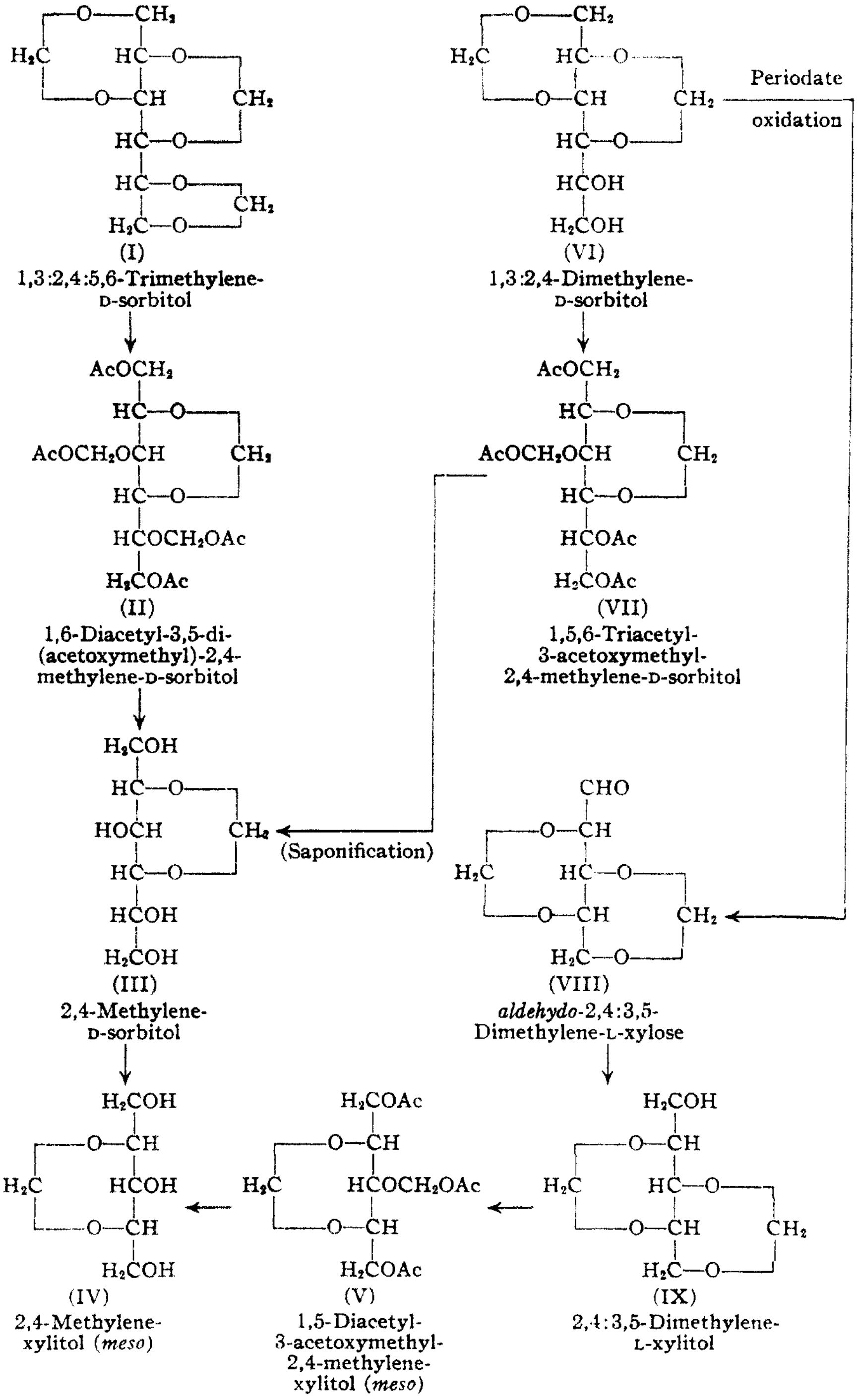
[1] Ness, Hann and Hudson, THIS JOURNAL, 65, 2215 (1943).

[2] Schulz and Tollens, *Ann.*, 289, 23 (1896).

[3] Kunz, THIS JOURNAL, 48, 1982 (1926).



figuration and therefore optically inactive; on the other hand, the oxidation of 3,5-methylene-D-sorbitol would produce 2,4-methylene-D-arabinose, reducible to 2,4-methylene-D-arabitol, the formula of which represents an optically-active system. To decide the question, methylene-D-sorbitol was oxidized by aqueous per-iodic acid; the oxidation was complete in fifteen minutes and the oxidized solution, which had changed in rotation $[\alpha]^{20}\mathrm{D}$ from an original value of $-9.8°$ (calculated as 2,4-methylene-D-sorbitol) to $-17.6°$ (calculated as 2,4-methylene-pentose), was found to be strongly reducing to Fehling solution; removal of the acids and the solvent left the colorless sirupy oxidation product, which did not crystallize; this sirup was reduced in aqueous solution at 100° for six hours with Raney nickel and hydrogen under a pressure of 133 atmospheres. The crystalline reduction product (m. p. 108–109°), which did not reduce Fehling solution and had the composition of a monomethylene-pentitol, was optically inactive in aqueous solution, from which fact the conclusion was drawn that it is the *meso* 2,4-methylenexylitol rather than the 2,4-methylene-D-arabitol. Exact proof of this conclusion was obtained through the preparation of authentic 2,4-methylene-xylitol from xylitol, as described in the accompanying article[4]; the substances from the two sources are identical. The production of 2,4-methylene-xylitol (IV) from the monomethylenesorbitol limits the structure of the latter to 2,4-methylene-D-sorbitol (III) and this conclusion makes it probable that trimethylene-D-sorbitol is 1,3:2,4:5,6-trimethylene-D-sorbitol (I) (since a 1,5- or 1,6-acetal ring is highly improbable) and that the intermediate product obtained by the acetolysis of trimethylene-D-sorbitol is 1,6-diacetyl-3,5-di-(acetoxymethyl)-2,4-methylene-D-sorbitol (II).

Considering next the dimethylene-D-sorbitol of m. p. 174–175° and rotation $[\alpha]^{20}\mathrm{D}$ $-29.6°$ in water, it was found that upon oxidation in dilute

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(4) Hann, Ness and Hudson, THIS JOURNAL, **66**, 670 (1944).

aqueous solution with sodium periodate, only slightly more than one molecular equivalent of oxidant was consumed, and the yield of crystalline formal-dimethone from the oxidized solution corresponded to 0.98 molecular equivalent of formaldehyde. In further experiments, the other oxidation product, which proved to be an *aldehydo*-dimethylene-pentose monohydrate, crystallized spontaneously from the oxidation mixture; the compound, which rotated $[\alpha]^{20}{\rm D}$ −33.9° in water and melted at 175–180° after previous sintering at 150°, was converted upon sublimation to the anhydrous dimethylene-pentose, which melted at 189–192° and rotated −38.7° in aqueous solution; it was characterized as the crystalline oxime, a substance which melted with decomposition at 227–228° and showed the unusually high rotations $[\alpha]^{20}{\rm D}$ −272° in pyridine and −215° in water. The structure of the *aldehydo*-dimethylene-pentose is limited by reason of the genesis of the substance from dimethylene-D-sorbitol to *aldehydo*-2,3,4,5-dimethylene-L-xylose or *aldehydo*-2,3,4,5-dimethylene-D-arabinose. Conclusive proof that it is the former compound was obtained in the following manner: upon reduction with hydrogen and Raney nickel it is converted to a crystalline dimethylene-pentitol melting at 217–219° and rotating $[\alpha]^{20}{\rm D}$ −25.3° in aqueous solution; this pentitol diacetal is transformed by limited acetolysis to the 1,5-diacetyl-3-acetoxymethyl-2,4-methylene-xylitol (*meso*) (V) that is obtained by the limited acetolysis of the 2,4:3,5-dimethylene-D,L-xylitol which is described in the accompanying communication.[4] This result is definitive proof that the optically active pentitol diacetal ($[\alpha]^{20}{\rm D}$ −25.3°) is 2,4:3,5-dimethylene-L-xylitol (IX); it follows that the *aldehydo*-dimethylene-pentose and the dimethylene-D-sorbitol from which it is derived must be *aldehydo*-2,4:3,5-dimethylene-L-xylose (VIII) and 1,3:2,4-dimethylene-D-sorbitol (VI), respectively.

The formation of an optically inactive acetolysis product (1,5-diacetyl-3-acetoxymethyl-2,4-methylene-xylitol, *meso* structure (V)) from the optically active 2,4:3,5-dimethylene-L-xylitol (IX) is additional evidence supporting our previously expressed view that the limited acetolysis of methylene sugar alcohol acetals takes place initially through a rupture of the acetal linkage at a primary hydroxyl group; had the acetal rupture of (IX) occurred at any other position than carbon five the acetolysis product would be expected to possess optical rotatory power.

Confirmatory evidence for the assigned structure of 1,3:2,4-dimethylene-D-sorbitol (VI) was also obtained through its acetolysis to form the expected 1,5,6-triacetyl-3-acetoxymethyl-2,4-methylene-D-sorbitol (VII), a compound which is saponified by sodium methylate with the production of the previously isolated 2,4-methylene-D-sorbitol (III).

The fact that 1,3:2,4-dimethylene-D-sorbitol (VI) is obtained from the reaction mixture employed for the preparation of trimethylene-D-sorbitol, suggests that it is a precursor of the latter compound; support for this inference was attained when it was found that upon treatment with formaldehyde and hydrochloric acid the crystalline diacetal was converted in 85% yield into the triacetal; this experimental result also offers further support for the previously expressed view that the triacetal is 1,3:2,4:5,6-trimethylene-D-sorbitol (I). Apparently the rare C_5O_2 dioxepane ring that is present in 1,3:2,5:4,6-trimethylene-D-mannitol is absent from the structure of the isomeric trimethylene-D-sorbitol. The two substances are structural rather than stereoisomers, and in view of this result it seems obvious that the methylene derivatives of the other hexitols should be investigated similarly.

Experimental

I. Substances Derived from Trimethylene-D-sorbitol

1,3:2,4:5,6-Trimethylene-D-sorbitol (I) and 1,3:2,4-Dimethylene-D-sorbitol (VI) from D-Sorbitol, Formaldehyde and Concentrated Hydrochloric Acid.—A solution of 200 g. of D-sorbitol in a mixture of 300 cc. of 37% aqueous formaldehyde and 200 cc. of concentrated hydrochloric acid was heated at 50° for four days; after cooling the reaction mixture to 5° for several hours the trimethylene-D-sorbitol which had crystallized was separated by filtration and the filtrate was again heated at 50° for several days; no further deposition of triacetal occurred and the solution was employed for the isolation of 1,3:2,4-dimethylene-D-sorbitol as described in the following paragraph. The trimethylene-D-sorbitol, which was obtained in a yield of 162 g. (68%), was recrystallized from 20 parts of water or 50% alcohol as long rods which melted at 212–216° and rotated $[\alpha]^{20}{\rm D}$ −30.8° in chloroform (*c*, 1.2).[5] Schulz and Tollens[2] record a melting point of 206° and rotations $[\alpha]^{20}{\rm D}$ −30.3° (*c*, 2.58) and −29.3° (*c*, 4.578) in chloroform.

The mother liquor of the triacetal preparation was neutralized with sodium carbonate, the sodium chloride which precipitated was separated by filtration, and the filtrate was concentrated *in vacuo* to dryness; the dry residue was extracted with two 200-cc. portions of hot absolute alcohol and the extract upon cooling deposited 35 g. of fine needles (m. p. 150–168°) which after several recrystallizations from 40 parts of acetone yielded 19.0 g. of pure 1,3:2,4-dimethylene-D-sorbitol melting at 174–175° and rotating $[\alpha]^{20}{\rm D}$ −29.6° in water (*c*, 1.47). The yield was 8% based on the D-sorbitol used or 26% based on the D-sorbitol which did not form trimethylene-D-sorbitol. The diacetal is soluble in cold water, dioxane, pyridine and acetic acid, in warm methyl and ethyl alcohols and practically insoluble in ether, carbon tetrachloride and chloroform.

Anal. Calcd. for $C_8H_{14}O_6$: C, 46.60; H, 6.84. Found: C, 46.66; H, 6.92.

1,6-Diacetyl-3,5-di-(acetoxymethyl)-2,4-methylene-D-sorbitol (II).—Eighty grams of dried and powdered trimethylene-D-sorbitol was added to a rapidly stirred ice-cold mixture of 175 cc. of acetic anhydride, 75 cc. of glacial acetic acid and 2.5 cc. of concentrated sulfuric acid; solution of the triacetal was rapid and after five minutes the reaction mixture was poured into 3 liters of vigorously stirred ice water. The acetolysis product crystallized and after two hours the crystalline product was separated by

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[5] All the crystalline compounds described in the experimental part were recrystallized to constant melting point and specific rotation; *c* is the concentration in grams in 100 cc. of solution; the tube length was 4 dm.; all melting points were determined with the stem of the calibrated thermometer immersed in the rapidly stirred bath.

filtration, washed with cold water and air dried. The yield was 80 g. (52%). The compound was recrystallized from 12 parts of alcohol as long needles which melted at 111–112° and rotated $[\alpha]^{20}\mathrm{D}$ +29.8° in chloroform (*c*, 1.20). It is soluble in acetone, chloroform, benzene, acetic acid and pyridine and practically insoluble in water, ether and cold methyl and ethyl alcohols.

Anal. Calcd. for $C_{17}H_{26}O_{12}$: C, 48.34; H, 6.20; saponification, 0.1452 g. substance requires 13.75 cc. 0.1 *N* NaOH (4 saponifiable groups). Found: C, 48.41; H, 6.10; saponification, 0.1452 g. substance consumed 13.75 cc. 0.1 *N* NaOH.

2,4-Methylene-D-sorbitol (III).—A solution of 10 g. of 1,6-diacetyl-3,5-di-(acetoxymethyl)-2,4-methylene-D-sorbitol in 100 cc. of chloroform was cooled in an ice-bath and 10 cc. of 0.2 *N* sodium methylate solution was added; upon standing at 5° for eighteen hours, 4.6 g. (quantitative) of 2,4-methylene-D-sorbitol crystallized from the reaction mixture. The acetal was recrystallized from 20 parts of alcohol in the form of fine needles which melted at 163–164° and rotated $[\alpha]^{20}\mathrm{D}$ −9.8° in aqueous solution (*c*, 1.30). It is readily soluble in water, hot methyl and ethyl alcohols and practically insoluble in chloroform, acetone and ether.

Anal. Calcd. for $C_7H_{14}O_6$: C, 43.29; H, 7.27. Found: C, 43.27; H, 7.25.

1,3,5,6-Tetraacetyl-2,4-methylene-D-sorbitol.—A solution of 2.0 g. of 2,4-methylene-D-sorbitol in a mixture of 15 cc. of acetic anhydride and 10 cc. of pyridine was allowed to stand for forty-eight hours at 25° and then poured into ice-water; the precipitated tetraacetyl derivative, which is soluble in chloroform, acetone, acetic acid, pyridine and benzene and practically insoluble in water and cold methyl and ethyl alcohols, was recrystallized from 10 parts of alcohol as prismatic needles melting at 150–151° and rotating $[\alpha]^{20}\mathrm{D}$ −1.5° in chloroform (*c*, 1.40). The yield was 3.6 g. (94%).

Anal. Calcd. for $C_{15}H_{22}O_{10}$: C, 49.72; H, 6.12; CH_3CO, 47.5. Found: C, 49.80; H, 6.03; CH_3CO, 47.3.

Lead Tetraacetate Oxidation of 2,4-Methylene-D-sorbitol.—To a solution of 0.1018 g. of 2,4-methylene-D-sorbitol in 15 cc. of glacial acetic acid, 30 cc. (3.32 molecular equivalents) of 0.0581 *M* lead tetraacetate glacial acetic acid solution was added and the volume was adjusted to 50 cc. with glacial acetic acid, all operations being conducted at 25°. Analysis of 5 cc. subsamples at one, three and nineteen hours indicated that 0.67, 1.00 and 1.04 molecular equivalents, respectively, of oxidant had been consumed. The analytical data indicate that 2,4-methylene-D-sorbitol contains a single glycol grouping as a portion of its structure.

Per-iodic Acid Oxidation of 2,4-Methylene-D-sorbitol.—A solution of 1.0036 g. of 2,4-methylene-D-sorbitol in 25 cc. of water was cooled to 5° and 15 cc. (1.79 molecular equivalents) of 0.616 *M* per-iodic acid was added; the solution was allowed to warm to 20° and the volume was adjusted to 50 cc. with water. Analysis of 5 cc. aliquots at twenty, forty and sixty minutes showed that 1.04 molecular equivalents of oxidant had been consumed and no further oxidation was noted after twenty and two hundred sixty hours. After titration, the first three aliquots were combined and poured into 200 cc. of 0.4% dimethone solution; the precipitate of formal-dimethone (m. p. 189–190°) which deposited on keeping the mixture at 5° for eighteen hours, weighed 0.387 g. and represented 85% of that expected from the production of one molecular equivalent of formaldehyde as an oxidation product. The results of the oxidation show that the glycol grouping of 2,4-methylene-D-sorbitol must contain a primary alcohol group since the analytical findings agree with the reaction course $C_5H_9O_4{\cdot}CHOH{\cdot}CH_2OH + HIO_4 = C_5H_9O_4{\cdot}CHO + HCHO + H_2O + HIO_3$. Although the analyses mentioned above show that the oxidation was complete within twenty minutes under the experimental conditions, the specific rotation $[\alpha]^{20}\mathrm{D}$ of the solution (calculated on its presumed content of methylene-pentose) showed values of −17.6, −14.5, −6.2, −3.1° and a constant value of −2.6° at the expiration of fifteen and sixty minutes, four, twenty and ninety-two hours, respectively; these changes in rotatory power are presumably due to the change of the *aldehydo* form of the methylene-pentose to the equilibrium mixture of its α and β cyclic forms (probably α- and β-2,4-methylene-L-xylopyranose).

Sodium Periodate Oxidation of 2,4-Methylene-D-sorbitol.—The oxidation of 1.0045 g. of 2,4-methylene-D-sorbitol with 15 cc. (1.65 molecular equivalents) of 0.570 *M* sodium periodate was conducted by the same procedure employed in the per-iodic acid oxidation. The analytical results showed that 1.01, 1.03 and 1.02 molecular equivalents of oxidant had been consumed at the end of twenty, forty and sixty minutes, respectively, and the formal-dimethone recovered was 86% of that expected for the production of one molecular equivalent of formaldehyde. The specific rotation $[\alpha]^{20}\mathrm{D}$ of the oxidized solution remained constant at −18.4° for three hours and thereafter showed values of −15.3, −11.9, −4.1, −3.6 and −2.6° at the expiration of nineteen, forty-three, one hundred eighty-seven, two hundred twelve and two hundred eighty-three hours, respectively, the reduced rate of mutarotation in this case being probably due to the lower hydrogen-ion concentration.

2,4-Methylene-xylitol (IV) from 2,4-Methylene-D-sorbitol (III).—A solution of 5.0 g. of 2,4-methylene-D-sorbitol in 50 cc. of water was cooled to 5° and 50 cc. (1.20 molecular equivalents) of 0.616 *M* aqueous per-iodic acid was added; the reaction mixture was allowed to stand at 25° for eighteen hours, cold saturated barium hydroxide solution was added in slight excess, the precipitated barium iodate and periodate were separated by filtration and the filtrate was concentrated *in vacuo* to a dry sirup in the presence of barium carbonate. The sirup was extracted with 50 cc. of warm water and the extract, which was reducing to Fehling solution, was transferred to a bomb and agitated at 100° for six hours with Raney nickel and hydrogen under a pressure of 133 atmospheres. The catalyst was separated by filtration and the filtrate, upon concentration *in vacuo*, deposited a crystalline residue (4.2 g.; quantitative) which was recrystallized from 5 parts of alcohol and yielded 2.9 g. of the 2,4-methylene-xylitol (m. p. 108–109°) which is described in the accompanying communication.[4] The isolation and identification of this methylene-pentitol is a definitive proof that the methylene-D-sorbitol from which it is derived is 2,4-methylene-D-sorbitol.

Anal. Calcd. for $C_6H_{12}O_5$: C, 43.90; H, 7.37. Found: C, 43.82; H, 7.35.

II. Substances Derived from 1,3:2,4-Dimethylene-D-sorbitol

5,6-Diacetyl-1,3:2,4-dimethylene-D-sorbitol.—A solution of 1.0 g. of the previously described 1,3:2,4-dimethylene-D-sorbitol in a mixture of 10 cc. of acetic anhydride and 10 cc. of pyridine was allowed to stand at 25° for seventy-two hours and then poured into 600 cc. of ice water; the solution was extracted with chloroform and the washed and dried extract was concentrated *in vacuo* to a crystalline residue which upon crystallization from 10 parts of alcohol formed plates melting at 135–136° and rotating $[\alpha]^{20}\mathrm{D}$ −12.8° in chloroform (*c*, 1.08). The compound is soluble in acetone, benzene, chloroform, acetic acid and ethyl acetate and insoluble in water. The yield was 1.2 g. (86%).

Anal. Calcd. for $C_{12}H_{18}O_8$: C, 49.65; H, 6.25; CH_3CO, 29.7. Found: C, 49.60; H, 6.27; CH_3CO, 29.8.

5,6-Dibenzoyl-1,3:2,4-dimethylene-D-sorbitol.—The dibenzoate was obtained by the action of benzoyl chloride on 1,3:2,4-dimethylene-D-sorbitol in pyridine solution. The yield was 2.1 g. (quantitative). The compound deposited from its solution in 10 parts of alcohol in the form of needles melting at 134–135° and rotating $[\alpha]^{20}\mathrm{D}$ −54.8° in chloroform (*c*, 1.08); it is soluble in pyridine, acetic acid, acetone and ethyl acetate and insoluble in water.

Anal. Calcd. for $C_{22}H_{22}O_8$: C, 63.76; H, 5.35; C_6H_5CO, 50.7. Found: C, 63.61; H, 5.37; C_6H_5CO, 50.8.

Sodium Periodate Oxidation of 1,3:2,4-Dimethylene-D-sorbitol (VI).—A solution of 1.0619 g. of 1,3:2,4-dimethylene-D-sorbitol in 20 cc. of water was cooled to 5° and 25 cc. (2.10 molecular equivalents) of 0.432 *M* aqueous sodium periodate was added; the mixture was allowed to warm to 25° and the volume was adjusted to 50 cc. with water. Analysis of 5-cc. aliquots at the expiration of twenty minutes, two and twenty hours indicated that 1.00, 1.03 and 1.04 molecular equivalents, respectively, of sodium periodate had been reduced. After titration, the first two aliquots were poured into 200 cc. of 0.4% dimethone solution and the mixture, upon preservation at 5° for forty-eight hours, deposited 0.2124 g. of formal-dimethone, which is 98% of that expected if one molecular equivalent of formaldehyde was produced as a product of the oxidation. These analyses prove that the dimethylene-D-sorbitol contains a terminal glycol grouping as a part of its structure. They indicate that the dimethylene-acetal was oxidized with the formation of formaldehyde and an *aldehydo*-dimethylene-pentose. Support for this assumption was obtained when it was noted that the specific rotation, $[\alpha]^{20}\mathrm{D}$ −37.1° (calculated as *aldehydo*-dimethylene-pentose), of the oxidized solution did not change in value even on standing for one-hundred twenty hours, an observation which would be expected only in the absence of a ring form of the sugar (compare the rotation changes of the oxidized solution of 2,4-methylene-D-sorbitol which presumably contains 2,4-methylene-L-xylose, a sugar capable of existing in α and β cyclic forms).

***aldehydo*-2,4:3,5-Dimethylene-L-xylose Monohydrate from 1,3:2,4-Dimethylene-D-sorbitol (VI).**—A solution of 5.0 g. of 1,3:2,4-dimethylene-D-sorbitol in 50 cc. of water was cooled to 5° and 75 cc. (1.3 molecular equivalents) of 0.432 *M* aqueous sodium periodate was added. Within thirty minutes small needles started to deposit in the solution and after the mixture had been allowed to stand in the refrigerator for eighteen hours they were separated by filtration. The yield was 2.6 g. (56%). The product was recrystallized from 10 parts of water as needles which rotated $[\alpha]^{20}\mathrm{D}$ −33.9° in aqueous solution (*c*, 0.82) and melted at 175–180° after prior sintering at 150°. The substance is soluble in warm water and acetic acid and practically insoluble in warm methyl and ethyl alcohols, chloroform, acetone and dioxane.

Anal. Calcd. for $C_7H_{10}O_5 \cdot H_2O$: C, 43.75; H, 6.30. Found: C, 43.78; H, 6.34.

***aldehydo*-2,4:3,5-Dimethylene-L-xylose (VIII).**—A sample of 0.5 g. of *aldehydo*-2,4:3,5-dimethylene-L-xylose monohydrate was sublimed in a vacuum at 140–145°; the sublimate of fine needles showed a melting point of 189–192° and a specific rotation $[\alpha]^{20}\mathrm{D}$ −38.7° in water (*c*, 0.44); no mutarotation was observed in twenty-four hours.

Anal. Calcd. for $C_7H_{10}O_5$: C, 48.27; H, 5.79. Found: C, 48.02; H, 5.92.

Oxime of *aldehydo*-2,4:3,5-Dimethylene-L-xylose.—A mixture of 1.0 g. *aldehydo*-2,4:3,5-dimethylene-L-xylose monohydrate, 1.0 g. of hydroxylamine hydrochloride, 1.0 g. of fused sodium acetate, 25 cc. of methyl alcohol and 5 cc. of water was refluxed for twenty minutes. Upon standing at 5° for several days the solution deposited 0.8 g. (80%) of product, which upon recrystallization from 100 parts of alcohol yielded small lath-like crystals which melted at 227–228° and rotated $[\alpha]^{20}\mathrm{D}$ −272° in pyridine (*c*, 0.50). Because the magnitude of this rotation is unusual for this type of compound, its rotation was also determined in aqueous solution (*c*, 0.31); it was found to be $[\alpha]^{20}\mathrm{D}$ −215.0°. The oxime is soluble in pyridine, hot water and hot alcohol and practically insoluble in cold alcohol, acetone and chloroform.

Anal. Calcd. for $C_7H_{11}O_5N$: C, 44.44; H, 5.86; N, 7.40. Found: C, 44.43; H, 5.86; N, 7.45.

2,4:3,5-Dimethylene-L-xylitol (IX) from *aldehydo*-2,4:3,5-Dimethylene-L-xylose Monohydrate.—A solution of 6.0 g. of 2,4:3,5-dimethylene-L-xylose monohydrate in 200 cc. of water was agitated in a bomb at 25° for eighteen hours with Raney nickel and hydrogen at a pressure of 133 atmospheres; the catalyst was separated by filtration and the filtrate was concentrated *in vacuo* to a crystalline mass (5.0 g.; 91%) which was recrystallized from 50 parts of alcohol; the 2,4:3,5-dimethylene-L-xylitol crystallized in needles which melted at 217–219° and rotated $[\alpha]^{20}\mathrm{D}$ −25.3° in aqueous solution (*c*, 1.09). The compound is one component of the crystalline 2,4:3,5-dimethylene-D,L-xylitol which is described in the accompanying communication.[4] A more detailed comparison of these two substances is made in that article.

Anal. Calcd. for $C_7H_{12}O_5$: C, 47.72; H, 6.87. Found: C, 47.64; H, 6.83.

1-Acetyl-2,4:3,5-dimethylene-L-xylitol.—This compound was prepared by the acetylation of 2,4:3,5-dimethylene-L-xylitol (1.0 g.) in pyridine solution (10 cc.) by acetic anhydride (10 cc.). The yield was 1.0 g. (83%). It was recrystallized from 12 parts of alcohol in the form of rods which melted at 153–154° and rotated $[\alpha]^{20}\mathrm{D}$ +2.8° in chloroform (*c*, 0.96); it is soluble in acetone, ethyl acetate, carbon tetrachloride and acetic acid and practically insoluble in water. A microscopic optical crystallographic examination by Mr. George L. Keenan, of the Food and Drug Administration, Federal Security Agency, showed that in parallel polarized light (crossed nicols) the extinction was parallel and the elongation negative, the refractive indices being n_α = 1.484, n_β = 1.504 and n_γ = 1.524, all ±0.002.

Anal. Calcd. for $C_9H_{14}O_6$: C, 49.54; H, 6.47; CH_3CO, 19.7. Found: C, 49.58; H, 6.48; CH_3CO, 19.7.

1,5-Diacetyl-3-acetoxymethyl-2,4-methylene-xylitol (V) from 2,4:3,5-Dimethylene-L-xylitol (IX).—A suspension of 1.0 g. of 2,4:3,5-dimethylene-L-xylitol in a mixture of 7.0 cc. of acetic anhydride and 3.0 cc. of glacial acetic acid was cooled to 0° and 10 cc. of an acetylating solution (prepared as described for the acetolysis of trimethylene-D-sorbitol) cooled to 0° was added; the mixture was agitated until solution of the alcohol diacetal was complete (ten minutes) and after a further five minutes it was poured into 400 cc. of ice water. The solution was nearly neutralized by the addition of 35 g. of sodium bicarbonate and extracted with three 50 cc. portions of chloroform; the washed and dried extract was concentrated to a crystalline residue (1.4 g.; 78%; m.p. 138–145°) which was recrystallized from 30 parts of hot water and yielded 0.8 g. of pure 1,5-diacetyl-3-acetoxymethyl-2,4-methylene-xylitol melting at 139–140° and devoid of rotation in aqueous solution (*c*, 0.92). A mixed melting point with the compound prepared by the acetolysis of 2,4:3,5-dimethylene-D,L-xylitol[4] also showed 139–140°, a result which was anticipated since the acetolysis of either the optically active (IX) or racemic form of the diacetal according to the acetolysis mechanism which has been proposed should yield the *meso* 1,5-diacetyl-3-acetoxymethyl-2,4-methylene-xylitol (V).

1,5,6-Triacetyl-3-acetoxymethyl-2,4-methylene-D-sorbitol (VII) from 1,3:2,4-Dimethylene-D-sorbitol (VI).—A solution of 1.0 g. of 1,3:2,4-dimethylene-D-sorbitol in 5 cc. of an ice-cold 1% sulfuric acid acetylating mixture was allowed to stand at 0° for five minutes and then poured into 200 cc. of ice-water; the flocculent precipitate which formed (0.6 g.; 32%) was separated by filtration and recrystallized from 7 parts of alcohol. The compound, which crystallized as fine needles, melted at 94–95° and rotated $[\alpha]^{20}\mathrm{D}$ +11.0° in chloroform (*c*, 1.04); it is readily soluble in acetone, ethyl acetate, acetic acid, pyridine and warm methyl and ethyl alcohols and practically insoluble in water.

Anal. Calcd. for $C_{16}H_{24}O_{11}$: C, 48.98; H, 6.16; saponification, 0.1139 g. substance requires 11.61 cc. 0.1 *N* NaOH (4 saponifiable groups). Found: C, 49.05; H, 6.21; saponification, 0.1139 g. substance consumed 11.58 cc. 0.1 *N* NaOH.

2,4-Methylene-D-sorbitol (III) from 1,5,6-Triacetyl-3-acetoxymethyl-2,4-methylene-D-sorbitol (VII).—To an ice-cold solution of 2.0 g. of 1,5,6-triacetyl-3-acetoxymethyl-2,4-methylene-D-sorbitol in 30 cc. of chloroform, 5 cc. of 0.2 *N* sodium methylate solution was added and the reaction mixture was allowed to stand at 5° for seventy-two hours; the precipitate which had deposited was separated by filtration and recrystallized from 20 parts of alcohol; the needles which formed showed a melting point of 163–

164° and a specific rotation $[\alpha]^{20}\text{D}$ −9.7° in aqueous solution, these data being in agreement with those previously found for the 2,4-methylene-D-sorbitol obtained by the saponification of 1,6-diacetyl-3,5-di-(acetoxymethyl)-2,4-methylene-D-sorbitol (II). A mixed melting point determination with 2,4-methylene-D-sorbitol from this source showed no depression.

1,3:2,4:5,6-Trimethylene-D-sorbitol (I) from 1,3:2,4-Dimethylene-D-sorbitol (VI).—A solution of 1.0 g. of 1,3:2,4-dimethylene-D-sorbitol (VI) in a mixture of 1.0 cc. of concentrated hydrochloric acid and 1.0 cc. of 37% aqueous formaldehyde was warmed to 50°; within thirty minutes crystallization of needles was noted and after forty-eight hours the mixture was cooled to 5°, the needles were separated by filtration, washed with ice-cold 50% alcohol, and dried. The yield was 0.90 g. (85%). The product, after recrystallization from 20 parts of 50% alcohol, showed a melting point of 210–214° and a mixed melting point determination with authentic trimethylene-D-sorbitol showed no depression.

Summary

The condensation of D-sorbitol with formaldehyde under the influence of concentrated hydrochloric acid yields, in addition to the known trimethylene-D-sorbitol of Schulz and Tollens, a new crystalline dimethylene-D-sorbitol. The limited acetolysis of the known trimethylene-D-sorbitol yields a diacetyl-di-(acetoxymethyl)-methylene-hexitol, which upon saponification is transformed into a crystalline methylene-D-sorbitol that can be only 2,4-methylene-D-sorbitol since it is converted by periodate oxidation and subsequent reduction to 2,4-methylene-xylitol of proved structure.

The new dimethylene-D-sorbitol can be only 1,3:2,4-dimethylene-D-sorbitol since upon periodate oxidation it yields an *aldehydo*-2,4:3,5-dimethylene-L-xylose which is successively converted to 2,4:3,5-dimethylene-L-xylitol, 1,5-diacetyl-3-acetoxymethyl-2,4-methylene-xylitol and 2,4-methylene-xylitol by known reactions.

The fact that the limited acetolysis of 2,4:3,5-dimethylene-L-xylitol forms a compound of *meso* structure rather than one possessing optical activity is cited as evidence supporting the previously proposed acetolysis mechanism based on the hypothesis that the acetal linkages of methylene acetals which are formed through primary alcoholic groups are more easily ruptured than those formed through secondary alcoholic groups; this experimental corroboration allows assignment of the structures of 1,6-diacetyl-3,5-di-(acetoxymethyl)-2,4-methylene-D-sorbitol and 1,5,6-triacetyl-3-(acetoxymethyl)-2,4-methylene-D-sorbitol, respectively, to the acetolysis products of trimethylene-D-sorbitol and 1,3:2,4-dimethylene-D-sorbitol.

In view of the present experimental results, and particularly the conclusive establishment of the presence of the 2,4-acetal linkage, it seems highly probable that the trimethylene-D-sorbitol of Schulz and Tollens is 1,3:2,4:5,6-trimethylene-D-sorbitol, the rare C_5O_2 dioxepane ring that is present in 1,3:2,5:4,6-trimethylene-D-mannitol being absent from the structure of the isomeric trimethylene-D-sorbitol.

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2,4:3,5-Dimethylene-D,L-xylitol and 2,4-Methylene-xylitol

BY RAYMOND M. HANN, A. T. NESS AND C. S. HUDSON

In the course of the study of the acetolysis of trimethylene-D-sorbitol that is described in the accompanying article[1] there was obtained by degradative reactions a monomethylene-pentitol (m. p. 108–109°) the structure and configuration of which needed to be established. In configuration it is limited to a monomethylene derivative of xylitol or D-arabitol by reason of its origin. In aqueous solution no optical rotation was detected, which indicated the probability that the compound is a monomethylene-xylitol of *meso* structure since all structures for a monomethylene-D-arabitol represent optically active systems. The direct identification of its constituent pentitol through acid hydrolysis seemed of little attraction because of the experimental difficulties that are often encountered in attempts to hydrolyze methylene cyclic acetals. Accordingly, it was sought to produce the substance by condensing formaldehyde with xylitol, a procedure which, if successful, would establish the identity of its constituent pentitol and might also lead to a less laborious method for obtaining it.

There appears to be no recorded combination of formaldehyde with xylitol, although dibenzylidene[2] and di-isopropylidene xylitols[3] are known. A crystalline dimethylene-xylitol (m. p. 201–202°) was obtained in 91% yield by the reaction of xylitol with 37% aqueous formaldehyde and concentrated hydrochloric acid for two hours at 50°. One of the methylene groups in this dimethylene-xylitol is readily removable, as will be described, and the resulting monomethylene-xylitol proved to be identical with the monomethylene-pentitol (m. p. 108–109°) which was obtained from trimethylene-D-sorbitol. This monomethylene-xylitol does not react with sodium periodate and thus it contains no α-glycol group;

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[1] Ness, Hann and Hudson, THIS JOURNAL, **66**, 665 (1944).

[2] (a) L. de Bruyn and van Ekenstein, *Rec. trav. chim.*, **18**, 151 (1899); (b) Wolfrom and Kohn, THIS JOURNAL, **64**, 1739 (1942).

[3] (a) Tipson and Cretcher, *J. Org. Chem.*, **8**, 95 (1943); (b) Hann, Ness and Hudson, THIS JOURNAL, **66**, 73 (1944).