

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

ALDEHYDO-*d*-XYLOSE TETRA-ACETATE AND THE
MERCAPTALS OF XYLOSE AND MALTOSE¹

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In continuation of the studies being made in this Laboratory on the open-chain forms of sugar acetates, we wish to report the synthesis of the crystalline free aldehyde form of xylose acetate, which we will designate aldehydo-*d*-xylose tetra-acetate. This substance differs widely in properties from the two known cyclic forms of xylose tetra-acetate, as the data of Table I show.

TABLE I
PROPERTIES OF THE THREE TETRA-ACETATES OF *d*-XYLOSE

Form	M. p., °C.	$[\alpha]_D$, Chloroform
α	59	+89°
β	128	-25
Aldehydo	87-89	-16

β -Xylose tetra-acetate was first prepared in crystalline condition by Stone² and was studied further by Dale³ and by Hudson and Johnson.⁴ The latter workers also synthesized crystalline α -xylose tetra-acetate. The rotation of aldehydo-xylose tetra-acetate was found to be stable in alcohol-free chloroform and showed a small change in rotation in methyl alcohol solution ($[\alpha]_D +4^\circ \rightarrow +12.5^\circ$). We have shown that this rotation change in hydroxylated solvents is due to hemi-acetal formation in the solution.⁵ The substance readily gave the Schiff aldehyde test and reduced Fehling's solution.

The aldehydo sugar acetates synthesized in crystalline condition in this Laboratory⁶ are tabulated in Table II.

TABLE II
ALDEHYDO SUGAR ACETATES

Derivative	M. p., °C.	$[\alpha]_D$, Chloroform
<i>d</i> -Glucose penta-acetate	116-118	- 4.5
<i>d</i> -Galactose penta-acetate	121	-25
<i>l</i> -Arabinose tetra-acetate	114	-65
<i>d</i> -Xylose tetra-acetate	87-89	-16

¹ Presented before the Sugar Division at the Eighty-second Meeting of the American Chemical Society, Buffalo, New York, August 31-Sept. 4, 1931.

² W. E. Stone, *Am. Chem. J.*, **15**, 653 (1893).

³ J. K. Dale, *THIS JOURNAL*, **37**, 2745 (1915).

⁴ C. S. Hudson and J. M. Johnson, *ibid.*, **37**, 2748 (1915).

⁵ M. L. Wolfrom, *ibid.*, **53**, 2275 (1931).

⁶ M. L. Wolfrom, *ibid.*, **51**, 2188 (1929); **52**, 2464 (1930); M. L. Wolfrom and Mildred R. Newlin, *ibid.*, **52**, 3619 (1930).

The method used in synthesizing the xylose compound was similar to that used for the others. Xylose ethyl mercaptal tetra-acetate was synthesized and the thio-ethoxyl groups replaced by an oxygen atom through reaction with mercuric chloride⁷ and water under controlled conditions. Previous workers had failed to obtain mercaptals of xylose.⁸ The methods used by these workers for isolating sugar mercaptals depended upon the low water solubility of these substances. We found that the ethyl mercaptal of xylose was highly soluble in water but could be isolated in crystalline condition by suitable modifications in procedure. Xylose ethyl mercaptal is readily soluble in water and in all common organic solvents except petroleum ether. Its solubilities are thus similar to those of the methylated sugars and differ sharply from those of other sugar mercaptals. Xylose ethyl mercaptal tetra-acetate was synthesized in crystalline condition from the mercaptal.

The method used for preparing xylose mercaptal was extended to maltose and the ethyl mercaptal octa-acetate of this sugar was obtained in crystalline condition. We believe that this represents the first mercaptal derivative of a disaccharide to be recorded.

Further work on the synthesis and reactivity of the free aldehyde forms of sugar acetates is in progress in this Laboratory.

Experimental

d-Xylose-ethylmercaptal.⁹—The synthesis of the ethyl mercaptal of *d*-xylose and its isolation in the pure crystalline state was first accomplished indirectly by converting xylose to the mercaptal acetate, and then removing the acetyl groups from that derivative. Following Fischer's general procedure, 10 g. of xylose was dissolved in 12 cc. of concentrated hydrochloric acid (sp. gr. 1.19) and 12 cc. of technical ethyl mercaptan added. The mixture was shaken vigorously in a glass-stoppered bottle until the layers disappeared. As the reaction proceeded it became necessary to cool the mixture occasionally in ice water and to release the pressure. When there was no further evolution of heat, the bottle was packed in ice and salt and allowed to stand for half an hour. The reaction mixture was then treated with solid lead carbonate to neutralize the hydrochloric acid. When the solution no longer showed an acid color with litmus it was filtered, and the filtrate saturated with hydrogen sulfide, aerated and filtered. The solution was neutralized with silver carbonate, the insoluble silver chloride being removed by filtration. Dissolved silver was precipitated by a second treatment with hydrogen sulfide. The slightly yellow solution obtained on filtration was concentrated under reduced pressure at 35–40°. The resulting sirup was dried by repeated additions of absolute ethyl alcohol followed by distillation under reduced pressure.

Acetylation of this sirup was accomplished by dissolving it in 35 cc. of dry pyridine at room temperature, and adding to the solution, cooled in ice water, 70 cc. of acetic anhydride. The mixture was held at zero for ten minutes and then allowed to stand

⁷ Cf. P. A. Levene and G. M. Meyer, *J. Biol. Chem.*, **69**, 175 (1926); **74**, 695 (1927).

⁸ E. Fischer, *Ber.*, **27**, 673 (1894); W. T. Lawrence, *ibid.*, **29**, 547 (1896).

⁹ All of the experimental work on the xylose compounds described was performed by Mildred R. Newlin in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry at the Ohio State University.

overnight. It was then poured into a liter of ice water. The thin yellow sirup which separated became encrusted with a layer of crystals after standing for four days at room temperature. The semi-solid substance was recrystallized twice by dissolving in methyl alcohol, adding water to opalescence, and allowing the material to stand in the ice box until it no longer became milky on the further addition of water. In this way 3.5 g. of xylose-ethylmercaptal tetra-acetate was obtained, melting at 46–48° (corr.)

Two grams of the acetate was dissolved in 20 cc. of absolute methyl alcohol and anhydrous ammonia bubbled through the solution for ten to fifteen minutes. The solution was then placed in the ice box for twenty-four hours. The material was evaporated to small volume under reduced pressure at 30–35°. The concentrate was dissolved in 6–8 cc. of warm ethyl acetate and the solution cooled in ice and salt. The xylose-ethylmercaptal separated as small, colorless, flaky crystals with melting point 63–65° (corr.).

Further preparation of the mercaptal was carried out by using these crystals to nucleate the sirup resulting from the concentration of the neutralized reaction mixture obtained in the manner described above. The seeded sirup was then run down in a vacuum desiccator at room temperature until all the alcohol was evaporated. In this way 60 g. of crude crystalline mercaptal was obtained from 50 g. of xylose, a yield of 70%. The crude mercaptal was recrystallized by cooling a warm, nearly saturated water solution in ice water and nucleating. Only small amounts, 4–5 g., could be treated in this way successfully because of the great solubility of the crystals in the mother liquor and the consequent need for rapid filtration and washing with ice water. The crystals were dried at room temperature in a vacuum desiccator. Recrystallization was also carried out by dissolving the mercaptal in a minimum amount of warm absolute alcohol, cooling in ice and salt and adding petroleum ether. This method has the advantage that the crystals do not redissolve in the mother liquor. In either case only about half the solute crystallized in the first crop.

After three recrystallizations from water, the substance melted at 63–65° and the specific rotation in water at 24° was -31.2° (0.4011 g. subs. in 10.02 cc. of water soln., 1.0-dm. tube, $\alpha_D -1.25^\circ$). The melting point was not changed by two more recrystallizations, and the specific rotation at 25° was then -30.8° (0.4008 g. subs. in 10.02 cc. of water soln., 1.0-dm. tube, $\alpha_D -1.23^\circ$). This mercaptal crystallized as colorless, square plates characterized by marked solubility in a variety of solvents. It dissolved readily in water, ethyl alcohol, methyl alcohol, acetone, chloroform and ethyl acetate at room temperature; it was slowly soluble in warm ether and benzene, and very slightly soluble in warm petroleum ether.

Anal. Subs., 0.2515: BaSO₄, 0.4568. Calcd. for C₅H₁₀O₄(SC₂H₅)₂: S, 24.98. Found: S, 24.97.

d-Xylose-ethylmercaptal Tetraacetate.—Twenty-five grams of crystalline xylose-ethylmercaptal was dissolved in 90 cc. of dry pyridine at room temperature and cooled to zero in ice water. To the solution was gradually added 180 cc. of acetic anhydride. The mixture was kept at zero for ten minutes and allowed to stand overnight. It was then poured into two liters of ice water. The addition of some of the crystalline material previously obtained caused the insoluble oil to crystallize in about five minutes. The crude material was filtered off and immediately recrystallized twice, as the impurities cause it to melt readily at room temperature. Recrystallization was effected by dissolving the substance in methyl alcohol, surrounding the beaker with ice and salt, and slowly adding water, nucleating the mixture when the cloudiness became permanent. After two recrystallizations a yield of 39 g., or 95%, was obtained, with melting point 40–42°.

Xylose-ethylmercaptal tetraacetate was practically insoluble in cold water and pe-

trolem ether, but was readily soluble in the latter when warmed. It was very soluble in methyl alcohol, ethyl alcohol, chloroform and acetone. After four recrystallizations in the manner described, the melting point was 46–48° (corr.) and the specific rotation in chloroform at 23° was +12.5° (0.4006 g. subs. in 10.02 cc. of U. S. P. chloroform soln., 1.0-dm. tube, $\alpha_D +0.50^\circ$). After two more recrystallizations the substance showed no change in melting point and gave a specific rotation at the same temperature of +13.0° (0.4006 g. subs. in 10.02 cc. of U. S. P. chloroform soln., 1.0-dm. tube, $\alpha_D +0.52^\circ$).

Anal. Subs., 0.2505, 0.2508: BaSO₄, 0.2776, 0.2743. Subs., 0.1000: 9.60 cc. 0.1 *N* NaOH. Calcd. for C₅H₈O₄(SC₂H₅)₂(COCH₃)₄: S, 15.11; cc. of 0.1 *N* NaOH, 9.43. Found: S, 15.21, 15.03.

Aldehyde-*d*-xylose Tetraacetate.—To remove the mercapto groups 10 g. (1 mol.) of xylose-ethylmercaptal tetraacetate was dissolved in 36 cc. of acetone and 6 cc. of water added. To this solution, held in a three-necked flask equipped with a reflux condenser and a mechanical stirrer, were added 20 g. of finely powdered, alkali-free cadmium carbonate and a solution of 24 g. (3.6 mols) of mercuric chloride in 36 cc. of acetone. Rapid stirring was maintained for twelve hours. The reaction mixture was then heated in a water-bath to 50° and held at this temperature for fifteen minutes. The temperature was then increased to 60° and the material refluxed for fifteen minutes. The solution was cooled and filtered, a small amount of cadmium carbonate being placed in the filter flask. The filtrate was concentrated under reduced pressure at 30–35° in the presence of excess cadmium carbonate. The residue was dried by repeatedly adding acetone and distilling off under reduced pressure. It was then extracted with warm chloroform and the extract treated with sodium sulfate and norite for a short time. The filtered solution was evaporated to dryness at room temperature in a vacuum desiccator. The sirup first obtained in this manner required three days to become crystalline. Thereafter the sirup was nucleated at this point and crystallization took place in about twelve hours. In this way 5.5 g. of crude semi-solid material was obtained. This was recrystallized by dissolving in warm anhydrous ether and cooling the solution in ice and salt. The crystalline product amounted to 1.1 g. with melting point 85–87°.

The once recrystallized material showed a stable specific rotation in alcohol-free chloroform of –15.5° at 26° (0.4010 g. subs. in 10.00 cc. of chloroform soln., 1.0-dm. tube $\alpha_D -0.62^\circ$). After three recrystallizations the melting point was 87–89° and the specific rotation at 26° was –15.9° (0.4015 g. subs. in 10.00 cc. of chloroform soln., 1.0-dm. tube, $\alpha_D -0.64^\circ$). Two more recrystallizations did not alter the melting point. In methyl alcohol the material showed an initial specific rotation of +3.7°. This value changed slowly in the dextro direction reaching a maximum of +12.5° in about two days. The substance crystallized in colorless, prismatic needles. A cold aqueous solution reacted with Schiff's reagent to produce a faint pink color in a minute and a half. It reacted immediately with hot Fehling's solution. It was slowly soluble in cold water and ethyl alcohol and ether, and readily soluble in methyl alcohol, acetone and chloroform. It was only slightly soluble in petroleum ether.

Anal. Subs., 0.1000: 12.42 cc. 0.1 *N* NaOH. Subs., 0.1000: 12.53 cc. of 0.1 *N* NaOH. Subs., 0.2097: H₂O, 0.1105; CO₂: 0.3757. Calcd. for C₅H₈O₅(COCH₃)₄: cc. of 0.1 *N* NaOH, 12.57; H, 5.69; C, 49.04. Found: H, 5.87; C, 48.87; S, absent.

Maltose-ethylmercaptal Octa-acetate.¹⁰—Fifty grams of maltose was placed in a large glass-stoppered bottle and dissolved at room temperature in 85 cc. of concentrated hydrochloric acid (sp. gr. 1.19). The solution was cooled to 0° and 35 cc. of technical ethyl mercaptan added. After five hours' standing at 0° with occasional shaking, no

¹⁰ Experimental work performed by Eldon E. Stahly in partial fulfilment of the requirements for the degree of Master of Science at The Ohio State University.

reduction of Fehling's solution could be observed. The solution was then diluted to 500 cc. with ice water and an excess of lead carbonate was added. After reaction the mixture was filtered. The filtrate was treated with hydrogen sulfide, aerated and filtered. The solution was then neutralized with silver carbonate, filtered and dissolved silver removed by a second treatment with hydrogen sulfide. The colorless solution was concentrated under reduced pressure and the resulting sirup dried by repeated additions of absolute ethyl alcohol followed by distillation under reduced pressure.

The crude maltose ethylmercaptal sirup so obtained was dissolved in 270 cc. of pyridine, the solution cooled to 0°, 135 cc. of acetic anhydride added and the mixture maintained at 0° for one hour. The solution was then left at room temperature for several days. At the end of this period the solution was poured into 6 liters of ice water and kept overnight in the ice box. The water was poured off of the sirup so obtained and the sirup dissolved in about 500 cc. of methanol. The solution was decolorized with norite, filtered and water added to the filtrate to incipient opalescence. Crystals separated on standing. This crude material was recrystallized two more times in the same manner; yield, 22 g., m. p. 121-122°; $[\alpha]_D^{25} +88.3^\circ$ in U. S. P. chloroform solution (0.3994 g. subs., 10.12 cc. U. S. P. chloroform solution, $\alpha_D +3.52^\circ$, 1-dm. tube). After three more recrystallizations a yield of 20 g. of material was obtained melting at 122-122.5°; $[\alpha]_D^{25} +87.5^\circ$ (0.4002 g. subs., 10.00 cc. U. S. P. chloroform solution, $\alpha_D +3.50^\circ$, 1-dm. tube). The crystals were prismatic needles and were fairly soluble in methyl alcohol and ether, less soluble in ethyl alcohol, readily so in chloroform, acetone, ethyl acetate and benzene and were practically insoluble in water and petroleum ether.

Anal. Subs., 0.2498, 0.2510: BaSO₄, 0.1454, 0.1470. Subs., 0.1940, 0.1979: 19.90, 20.10 cc. of 0.1 *N* NaOH. Calcd. for C₁₂H₁₄O₁₀(SC₂H₅)₂(COCH₃)₄: S, 8.17; 10.20 cc. of 0.1 *N* NaOH per 100 mg. Found: S, 8.00, 8.05; 10.25, 10.16 cc. of 0.1 *N* NaOH per 100 mg.

A more rapid method for removing the acidity of the mercaptal reaction mixture was successfully used. Ice was added to the reaction mixture and concentrated ammonium hydroxide until the solution was basic to litmus, the low temperature being maintained by suitable additions of ice. The solution was then evaporated under reduced pressure to a low volume and the ammonium chloride that separated removed by filtration and washed with methanol. The filtrate was then concentrated to a sirupy magma, dried and acetylated without removal of the remaining ammonium chloride. Work is now in progress in this Laboratory on obtaining the open-chain acetate of maltose.

We wish to acknowledge our indebtedness to the Federal Phosphorus Company of Birmingham, Alabama, for furnishing the xylose used in this investigation.

Summary

1. A new form of *d*-xylose tetra-acetate has been synthesized in pure crystalline condition.
2. Evidence is presented that this substance possesses the free aldehyde structure.
3. The synthesis in pure crystalline condition is reported for xylose ethylmercaptal and its tetra-acetate and for maltose ethylmercaptal octa-acetate.