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

Monothioacetals of Galactose

BY M. L. WOLFROM AND D. I. WEISBLAT

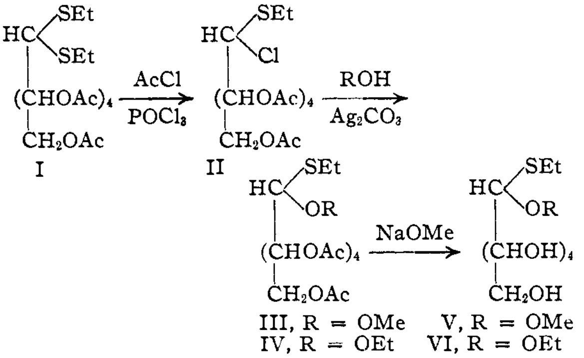
Geuther and Bachmann[1] treated the diethyl acetal of acetaldehyde with phosphorus pentachloride and obtained the 1-chloro-1-ethoxyethane (α-monochlorodiethyl ether), previously synthesized by Wurtz and Frapolli[2] from acetaldehyde, ethanol and hydrogen chloride. Blaise[3] and recently Post[4] postulated the probable formation of this same halogen compound in the reaction of acetaldehyde diethyl acetal with benzoyl chloride.

As thioacetals and acetals of the simple alcohols are available in the sugar series, we were interested in the possible extension of the above reactions to these carbohydrate derivatives. We have found that galactose dimethyl acetal reacts readily with acetyl chloride with the replacement of one methoxyl group by chlorine to form 1-chloro-1-methoxy-galactose pentaacetate. This general type of derivative is the open chain analog of the well-known acetohalogen sugars. Such a derivative had been prepared in the arabinose series by Montgomery, Hann and Hudson[5] through halogen replacement of the 1-acetate in the two isomeric *aldehydo*-1-methoxy-arabinose pentaacetates obtained by the acetolysis of the methyl arabinopyranosides. A corresponding galactose derivative had been obtained in this Laboratory[6] by halogen replacement of the 1-acetate in 1-ethoxy-galactose hexaacetate obtained by the acetylation of *aldehydo*-galactose pentaacetate ethyl hemiacetal.

We have found that galactose diethyl mercaptal pentaacetate (I) reacts with a mixture of acetyl chloride and phosphorus oxychloride to replace one ethylmercapto group with chlorine. The resulting *aldehydo*-1-chloro-1-ethylmercapto-galactose pentaacetate (II) reacts with methanol or ethanol to produce the monothioacetal pentaacetate (III and IV) from which the monothioacetals (V and VI) can be obtained by saponification. No evidence was obtained for the presence of more than one form of these derivatives in any of our reactions, although such a result is a possibility on stereochemical grounds. The halogen in the above halogen compounds is extremely reactive and the halogen derivatives are difficult to obtain in pure form. Montgomery, Hann and Hudson[5] likewise report the same experience with the arabinose derivative which they also used for acetal synthesis.

These monothioacetals of galactose and their pentaacetates are beautifully crystalline substances and are formed in high yield from the chloro compound. Such mixed oxygen, sulfur acetals have been postulated by Green and Pacsu[7] as a probable intermediate in the reaction of sugar mercaptals with mercuric chloride in alcoholic solution in the presence of mercuric oxide.

Work is in progress in this Laboratory on the extension of these reactions to other sugar structures and on the study of the behavior of the monothioacetals under ring-closure conditions.



Experimental

***aldehydo*-1-Chloro-1-ethylmercapto-*d*-galactose Pentaacetate (II).**—*d*-Galactose diethyl mercaptal pentaacetate[8] (30 g.) was dissolved in 20 cc. of freshly distilled acetyl chloride and the solution heated to boiling. Phosphorus oxychloride (10 cc.) was added to the boiling solution under reflux until a reddish-brown coloration began to develop (two to five minutes). The flask was then stoppered, quickly immersed in an ice-bath and the whole placed in an icebox. Crystallization in rosets of small needles began in a few hours and after standing overnight at icebox temperature the crystals were removed by filtration and washed thoroughly with a mixture of petroleum ether (5 parts) and ether (1 part). This crude material was re-

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[1] A. Geuther and A. Bachmann, *Ann.*, **218**, 38 (1883).

[2] A. Wurtz and A. Frapolli, *Ann. chim. phys.*, [3] **56**, 139 (1859).

[3] E. E. Blaise, *Compt. rend.*, **140**, 66 (1905).

[4] H. W. Post, *J. Org. Chem.*, **1**, 231 (1936).

[5] Edna M. Montgomery, R. M. Hann and C. S. Hudson, THIS JOURNAL, **59**, 1124 (1937).

[6] M. L. Wolfrom and M. Konigsberg, *ibid.*, **60**, 288 (1938).

[7] J. W. Green and E. Pacsu, *ibid.*, **60**, 2288 (1938).

[8] M. L. Wolfrom, *ibid.*, **52**, 2464 (1930).

crystallized rapidly from benzene by the addition of anhydrous ether; yield 13–18 g., m. p. 108–111°. The material at this stage of purity still decomposed rapidly and evolved ethyl mercaptan. After two more recrystallizations from four parts of benzene by the addition of approximately seven parts of dry ether, pure material was obtained; yield 7–7.5 g., m. p. 111–113°, spec. rot. −27° (22°, *c* 3.7, abs. $CHCl_3$).[9] Due to the instability of the compound, the constants recorded are probably not quite the maximum.

In absolute chloroform the rotation changed slowly in the *dextro* direction. In one experiment the specific rotation was −13° after fifteen hours. At this point the solution had darkened somewhat and an odor of ethyl mercaptan was distinctly noticeable. It is believed that this mutarotation represents decomposition, probably by reaction with traces of moisture.

The substance was readily soluble in the common organic solvents but was practically insoluble in cold ether, petroleum ether and water. It reduced Fehling's solution and evolved ethyl mercaptan on boiling with dilute alkali or acid. The substance was found to be stable only when kept in a vacuum desiccator over soda lime. An investigation of mother liquors yielded no other definite substance or any methanol reaction product different from that described below (III).

Anal. Calcd. for $C_8H_{12}O_5(CH_3CO)_5SCl$: Cl, 7.5; saponification value (six equivalents), 12.8 cc. 0.1 *N* NaOH per 100 mg. Found: Cl, 6.9; saponification value, 12.9 cc.

***d*-Galactose S-Ethyl O-Methyl Monothioacetal Pentaacetate** (III).—*aldehydo*-1-Chloro-1-ethylmercapto-*d*-galactose pentaacetate (II, 10 g.) was added to a previously cooled suspension of 20 g. of Drierite (anhydrous calcium sulfate) and 10 g. of silver carbonate in 50 cc. of anhydrous methanol in a three-necked flask equipped with a mercury-sealed mechanical stirrer and a drying tube. The reaction was then allowed to run at room temperature for approximately sixteen hours. The inorganic salts were removed by filtration through a bed of Super-cel (Johns-Manville) and the clear, colorless filtrate was made just opalescent with water. The product crystallized on standing at icebox temperature; yield 5.6 g., m. p. 114–117°, spec. rot. +42.5° (abs. $CHCl_3$). Pure material was obtained on recrystallization (92–95% return) from five parts of hot methanol containing a few drops of pyridine; m. p. 119–120°, spec. rot. +42.5° (19°; *c*, 3.3; abs. $CHCl_3$).

The substance crystallized in beautiful diamond-shaped plates and was readily soluble in chloroform, ether, acetone and warm alcohol but was practically insoluble in water and petroleum ether. It showed no reduction toward hot Fehling's solution and evolved ethyl mercaptan on heating with dilute hydrochloric acid.

Anal. Calcd. for $C_9H_{15}O_6(CH_3CO)_5S$: S, 6.87; CH_3CO, 10.7 cc. 0.1 *N* NaOH per 100 mg. Found: S, 7.08; CH_3CO, 10.8 cc.

***d*-Galactose Diethyl Monothioacetal Pentaacetate** (IV).—This substance was synthesized from *aldehydo*-1·chloro-1-ethylmercapto-*d*-galactose pentaacetate (II, 10 g.) exactly as described for the synthesis of the corresponding methoxy compound (III) except that 60 cc. of absolute ethanol was substituted for the methanol. The product was isolated from the reaction mixture in the same manner; yield 5.3 g., m. p. 102–102.5°, spec. rot. +50° (abs. $CHCl_3$). Pure material was obtained on recrystallization (93–95% return) from six parts of hot absolute ethanol containing a few drops of pyridine; m. p. 104–105°, spec. rot. +50° (20°; *c*, 3.5; abs. $CHCl_3$).

The substance crystallized in beautiful prisms and exhibited properties and solubilities similar to those of the corresponding methoxy compound (III).

Anal. Calcd. for $C_{10}H_{17}O_6(CH_3CO)_5S$: S, 6.67; CH_3CO, 10.4 cc. 0.1 *N* NaOH per 100 mg. Found: S, 6.62; CH_3CO, 10.4 cc.

***d*-Galactose S-Ethyl O-Methyl Monothioacetal** (V).—*d*-Galactose S-ethyl O-methyl monothioacetal pentaacetate (III, 8.5 g.) was dissolved at room temperature in 20 cc. of anhydrous methanol, 4 cc. of 0.2 *N* sodium methylate added and the solution cooled rapidly in an ice-bath. Crystallization occurred immediately upon shaking. After a few hours of standing the crystalline material was removed by filtration and washed thoroughly with ether; yield 4.6 g. (98%), m. p. 144–146°, spec. rot. +48° (H_2O). Pure material was obtained on recrystallization (90–95% return) from six parts of hot anhydrous methanol; m. p. 146–147°, spec. rot. +50° (20°; *c*, 3; H_2O).

The substance crystallized in the form of elongated prisms. It showed no reduction toward hot Fehling's solution but on acid hydrolysis ethyl mercaptan was liberated and the hydrolyzate was reducing. The material was soluble in water and warm methanol and was practically insoluble in ether, acetone and chloroform.

Anal. Calcd. for $C_9H_{20}O_6S$: C, 42.13; H, 7.87; S, 12.51. Found: C, 41.86; H, 7.70; S, 12.28.

***d*-Galactose Diethyl Monothioacetal** (VI).—*d*-Galactose diethyl monothioacetal pentaacetate (IV, 9.6 g.) was dissolved in 30 cc. of warm ethanol and to the warm solution 5 cc. of 0.2 *N* sodium methylate was added. The solution was immediately immersed in an ice-bath and crystallization began immediately. After a few hours of standing the material was removed by filtration and washed with ether; yield 5.2 g. (93%), m. p. 155–156°, spec. rot. +53° (20°; *c*, 3; H_2O). The product was pure and identical constants were obtained on material after four recrystallizations from 14 parts of hot absolute ethanol from which it could be obtained in 94% return.

The substance crystallized in elongated prisms exhibiting a beautiful pearly luster and showed properties and solubilities similar to those of the corresponding methoxy compound (V).

Anal. Calcd. for $C_{10}H_{22}O_6S$: S, 11.86. Found: S, 11.82.

***aldehydo*-1-Chloro-1-methoxy-*d*-galactose Pentaacetate.**—*d*·Galactose dimethyl acetal pentaacetate[10] (1 g.) was dissolved in 3.5 cc. of boiling, freshly distilled acetyl chloride and the stoppered container placed in the icebox, whereupon the product crystallized. After several hours the product was removed by filtration and washed with ether; yield 0.9 g., m. p. 140–145°. Pure material was obtained on recrystallization from dry benzene by the addi-

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(9) All specific rotations are recorded to the D-line of sodium light; 22° is the temperature; *c* is the concentration in g. per 100 cc.

(10) M. L. Wolfrom, L. J. Tanghe, R. W. George and S. W. Waisbrot, THIS JOURNAL, **60**, 132 (1938); H. A. Campbell and K. P. Link, *J. Biol. Chem.*, **122**, 635 (1938).

tion of ligroin; m. p. 155–156°; spec. rot. $-38° \longrightarrow +15°$ (25°; *c*, 5; abs. $CHCl_3$, 24 hrs.); spec. rot. $-53° \longrightarrow -42.5°$ (26°; *c*, 5; dry benzene; 10 hrs.).

Anal. Calcd. for $C_7H_{10}O_6(CH_3CO)_5Cl$: Cl, 8.04; saponification value (six equivalents), 13.6 cc. 0.1 *N* NaOH per 100 mg. Found: Cl, 7.96; saponification value, 13.7 cc.

We are indebted to Mr. John Walker (W. P. A. Project 18062) for assistance rendered in the analytical determinations. We also acknowledge the assistance of Mr. Irving Auerbach (N. Y. A. Project O. S. U. 167).

Summary

1. *aldehydo*-1-Chloro-1-methoxy-*d*-galactose pentaacetate was synthesized by the action of acetyl chloride upon *d*-galactose dimethyl acetal pentaacetate.

2. *aldehydo*-1-Chloro-1-ethylmercapto-*d*-galactose pentaacetate (II) was synthesized by the action of a mixture of acetyl chloride and phosphorus oxychloride upon *d*-galactose diethyl mercaptal pentaacetate.

3. *d*-Galactose diethyl monothioacetal and *d*-galactose S-ethyl O-methyl monothioacetal and their pentaacetates have been synthesized from II.

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The Thermal Decomposition of Diacetyl

BY W. D. WALTERS

In a previous investigation[1] the rate of decomposition of diacetyl in the range 424–470° was obtained by pressure measurements and the products of the reaction analyzed. Since diacetyl can be determined quantitatively by conversion to dimethylglyoxime, which, on addition of a nickel salt, precipitates as nickel dimethylglyoxime, it is possible to analyze for the amount of diacetyl remaining after the decomposition has been allowed to proceed for a definite time. The present work was undertaken to investigate the kinetics of the decomposition by this method, thereby avoiding any assumptions regarding the relation between the pressure increase and the amount of decomposition. The effect of propylene on the rate of decomposition and the variation of the ketene concentration during the decomposition also were studied.

Experimental

The diacetyl, obtained from the Eastman Kodak Company, was dried over calcium sulfate and purified by four fractional distillations under vacuum, the middle two-thirds being used for each subsequent operation. The diacetyl used in this investigation was analyzed quantitatively, as indicated later, and found to be pure within the limits of error of the method, ±0.1%. The diacetyl was protected from light and between runs kept at −80°. The propylene, obtained from the Ohio Chemical Company, was of 99.5% purity.

The cylindrical Pyrex vessel, 75 × 120 mm., was contained in a furnace similar in design to the one previously used.[1] By means of a chromel–alumel thermocouple located at the center of the reaction vessel, the temperature was determined to within 0.1°. A temperature control of ±0.25° was obtained by causing light reflected from the mirror of a galvanometer in the thermocouple-potentiometer circuit to fall on a photoelectric cell, which controlled additional heating current. All thermocouples were standardized at the boiling point of sulfur and the absolute accuracy of the temperatures measured should be at least ±0.5°. In runs 29–50 inclusive, from which the activation energy was determined, a new thermocouple, standardized before use at the sulfur boiling point and after use against a standard thermocouple, was used every day.[2]

In order to obtain a pressure of diacetyl in the reaction vessel higher than its vapor pressure at room temperature, a small side arm was connected to the line leading from the storage bulb to the reaction vessel. This T-section was separated by a stopcock I from the reaction vessel and separated by another stopcock II from the line leading to the storage bulb. To introduce a sample into the reaction bulb, stopcock I was closed and stopcock II opened. Using dry-ice–acetone mixture the desired amount of diacetyl was condensed in the lower part of the side arm. After stopcock II was closed and I opened, the dry-ice-bath was replaced by a heated liquid-bath, vaporizing the diacetyl within fifteen seconds. The external tubing adjacent to the reaction bulb was heated with resistance wire to approximately 85° to prevent condensation of diacetyl. Stopcocks I and II which were also heated were "no-lube" stopcocks ground for high vacuum, and to these it was necessary to apply only a small amount of high vacuum grease. The diacetyl storage bulb was fitted with a small stopcock and ground glass joint so that it could be removed, the grease wiped off the

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[1] Rice and Walters, *J. Chem. Phys.*, **7**, 1015 (1939).

[2] Roeser and Wensel, *Bur. Standards J. Research*, **14**, 277 (1935).