

Anal. Calcd. for $C_{17}H_{28}O_8N_2$: N, 13.15. Found: N, 13.13.

Summary

β' -Diethylaminoethyl β -aminocrotonate has been synthesized from ethyl acetoacetate through

the sequence: ethyl acetoacetate \rightarrow β -chloro-crotonyl chloride \rightarrow β' -diethylaminoethyl β -chlorocrotonate \rightarrow β' -diethylaminoethyl β -aminocrotonate. This ester possessed no local anesthetic activity.

URBANA, ILLINOIS

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

Esters of the Aldehydrol Form of Sugars. II

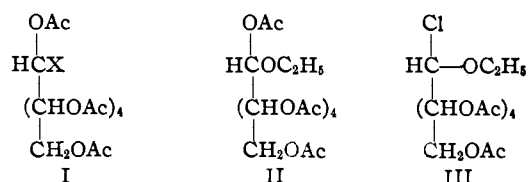
BY M. L. WOLFROM AND M. KONIGSBERG

Crystalline substances that may be considered as esters of the aldehydrol forms of the aldoses have been reported from this Laboratory and from others.¹ Felton and Freudenberg² obtained *aldehydo*-1-bromo-*l*-arabinose pentaacetate as a by-product in the large scale preparation of acetobromo-*l*-arabinose. Montgomery, Hann and Hudson³ have reported a number of novel derivatives of *d*-arabinose of this same general type, obtained by the hydrolysis of the acetylated methyl-*d*-arabinosides under acetylating conditions.

We have continued our studies in the preparation from *aldehydo*-acetates of esters of the aldehydrol forms of the aldoses. We wish to report herein the extension to the *d*-glucose and *l*-arabinose series of the *aldehydo*-acetohalogen compounds (I) previously reported for *d*-galactose.^{1a} The sugar derivatives of this type now known are tabulated in Table I. Similar carbonyl acyl halide addition compounds of the common, non-carbohydrate aldehydes have been studied extensively by Adams and co-workers.⁴

We have found acetylating conditions wherein it is possible to acetylate the ethyl hemiacetal of *aldehydo*-*d*-galactose pentaacetate⁵ and obtain the crystalline *aldehydo*-1-ethoxy-*d*-galactose hexaacetate (II). Replacement of the acetate on the aldehydic carbon with chlorine was feasible and produced the *aldehydo*-1-chloro-1-ethoxy-*d*-galactose pentaacetate (III). These substances are of

interest as the acyclic analogs of structures which have been of importance in the chemistry of the cyclic forms of the sugars.



Experimental

Preparation of *aldehydo*-1-Bromo-*l*-arabinose Pentaacetate.—*aldehydo*-*l*-Arabinose tetraacetate⁶ (5 g.) was dissolved in 25 cc. of acetyl bromide and the solution, after standing at room temperature for one hour, was poured into 100 cc. of ice and water. A colorless, crystalline product separated that was removed by filtration, after an hour of standing, and was washed with cold water; yield 6.5 g. Pure material was obtained on recrystallization from ether; m. p. 130-131°; $[\alpha]^{25} -134^\circ$ (*c*, 4; CHCl_3 , alcohol free; no mutarotation).⁷ For the crystalline substance which they called pentaacetylbrotoarabinose, Felton and Freudenberg² recorded the constants: m. p. 132°; $[\alpha]^{25} -135^\circ$.

Synthesis of Other Acyclic Acetohalogen Compounds of *l*-Arabinose and *d*-Glucose.—These compounds were synthesized in crystalline condition by the following general procedure. The solution of 5 g. of the *aldehydo*-acetate in 50 cc. of the acyl halide was allowed to stand at room temperature for twenty-four hours, whereupon it was poured into 800 cc. of ice and water and the crystalline precipitate was removed by filtration and washed with cold water; yield, 4 to 6.5 g. The chloroacetates were recrystallized from absolute ethanol and the bromoacetate from ordinary ether. The properties of the purified compounds are tabulated in Table II.

***aldehydo*-1-Ethoxy-*d*-galactose Hexaacetate (II).**—Acetic anhydride (250 cc.) was added slowly to a solution of 10 g. of *aldehydo*-galactose pentaacetate ethyl hemiacetal⁵ in 125 cc. of pyridine, previously cooled to 0°. The mixture was kept at 0° for thirty minutes and then at ice-box temperature for eighteen hours, whereupon it was poured

(1) (a) M. L. Wolfrom, *THIS JOURNAL*, **57**, 2498 (1935); (b) F. Michael, H. Ruhkopf and F. Suckfüll, *Ber.*, **68**, 1523 (1935); (c) N. W. Pirie, *Biochem. J.*, **30**, 374 (1936).

(2) G. E. Felton and W. Freudenberg, *THIS JOURNAL*, **57**, 1637 (1935).

(3) Edna M. Montgomery, R. M. Hann and C. S. Hudson, *ibid.*, **59**, 1124 (1937).

(4) R. Adams and E. H. Vollweiler, *ibid.*, **40**, 1732 (1918); H. B. French with R. Adams, *ibid.*, **43**, 651 (1921); L. H. Ulich with R. Adams, *ibid.*, **43**, 660 (1921).

(5) M. L. Wolfrom, *ibid.*, **52**, 2464 (1930).

(6) M. L. Wolfrom and Mildred R. Newlin, *ibid.*, **52**, 3619 (1930).

(7) All rotations are recorded to the D-line of sodium light.

TABLE I

Sugar	<i>aldehydo</i> -ACETOHALOGEN COMPOUNDS		M. p., °C.	Iodide [α] ^a
	Chloride M. p., °C.	[α] ^a		
<i>l</i> -Arabinose	109-110	-96°	130-131	-134°
<i>d</i> -Glucose	105-106	-49°	129-130	-79°
<i>d</i> -Galactose	174-175	-44°	179-181	-79°
			152-153	-111°

^a Measured in chloroform (alcohol-free) solution. See ref. 7.

TABLE II

aldehydo-ACETOHALOGEN COMPOUNDS OF *d*-GLUCOSE AND *l*-ARABINOSE

Compound	<i>aldehydo</i> -1-Chloro- <i>l</i> -arabi- nose pentaacetate	<i>aldehydo</i> -1-Chloro- <i>d</i> -glu- cose hexaacetate	<i>aldehydo</i> -1-Bromo- <i>d</i> -glu- cose hexaacetate
Formula	C ₈ H ₈ O ₈ (CH ₃ CO) ₅ Cl	C ₈ H ₇ O ₈ (CH ₃ CO) ₆ Cl	C ₈ H ₇ O ₈ (CH ₃ CO) ₆ Br
M. p., °C.	109-110	105-106	129-130
(α) ²⁵ D, CHCl ₃ (alc.-free), c, 4	-96°	-49°	-79°
Halogen analyses, %	Calcd. Cl, 8.94	Cl, 7.56	Br, 15.57
	Found Cl, 8.88	Cl, 7.55	Br, 15.61
Sap. value, cc. of 0.1 N NaOH per 100 mg.	Calcd. ^a 15.1	14.9	13.6
	Found 15.1	14.8	13.5

^a Calcd. as six equivalents for the pentaacetate and as seven equivalents for the hexaacetates.

into 2 l. of ice and water. Crystallization began after a few minutes and the product was removed by filtration and washed with cold water; yield 6.3 g. A further quantity (3.5 g.) was obtained on extraction of the filtrate with chloroform and washing of the chloroform extract with cold 5% sulfuric acid, cold sodium bicarbonate solution, and finally with water, followed by drying and solvent removal.

After one recrystallization from ethanol by the addition of water, different preparations melted at various points between 80 and 90° and showed rotations in chloroform solution varying between [α] +2 to +7°. On repeated crystallization a substance was obtained with the constants: m. p. 97°; [α]²⁵ +3.4° (c, 4; CHCl₃; no mutarotation); [α]²⁵ +10° (c, 5; EtOH; no mutarotation). The substance is very soluble in ether, alcohol, acetone, chloroform and benzene and is moderately soluble in warm water.

Anal. Calcd. for C₈H₇O₈(CH₃CO)₆OC₂H₅: OC₂H₅, 9.42; CH₃CO, 12.55 cc. 0.1 N NaOH per 100 mg. Found: OC₂H₅, 9.64; CH₃CO, 12.56 cc.

aldehydo-1-Chloro-1-ethoxy-*d*-galactose Pentaacetate (III).—*aldehydo*-1-Ethoxy-galactose hexaacetate (10 g.) was dissolved in 200 cc. of anhydrous ether previously saturated with dry hydrogen chloride and the solution was kept at ice-box temperature for eighteen hours, whereupon the crystalline reaction product that had separated was removed by filtration and washed with anhydrous ether; yield 6 g.; m. p. 135-138°. Pure material was obtained by refluxing the product for several hours with several portions of anhydrous ether; m. p. 142-143°; [α]²⁵ -56° → +25° (c, 4; CHCl₃, alcohol free). The time re-

quired to attain mutarotation equilibrium varied from two to six hours with different preparations. The nature of this mutarotation is under investigation.

The pure material is insoluble in ether and in water and is stable in the air. It is soluble in chloroform, alcohol, benzene and acetone.

Anal. Calcd. for C₈H₇O₈(CH₃CO)₆(OC₂H₅)Cl: Cl, 7.79; saponification value (six equivalents): 13.2 cc. 0.1 N NaOH per 100 mg. Found: Cl, 7.67; saponification value, 13.2 cc.

Acknowledgment is made to Mr. Frank L. Steahly for assistance in the analytical determinations.

Summary

1. *aldehydo*-1-Chloro-*l*-arabinose pentaacetate and the chloride and bromide forms (I) of *aldehydo*-*d*-glucose hexaacetate 1-halide have been synthesized in crystalline form.

2. The structure of the *aldehydo*-1-bromo-*l*-arabinose pentaacetate of Felton and Freudenberg has been confirmed by its synthesis from *aldehydo*-*l*-arabinose tetraacetate.

3. The 1-ethoxy (II) and 1-chloro (III) forms of *aldehydo*-*d*-galactose hexaacetate have been synthesized in crystalline form from *aldehydo*-*d*-galactose pentaacetate ethyl hemiacetal.

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