

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

HEMI-ACETALS OF ALDEHYDO-GALACTOSE PENTAACETATE AND THEIR OPTICAL PROPERTIES

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The open-chain or aldehydo form of galactose pentaacetate forms a crystalline addition compound with one mole of ethyl alcohol.¹ Brigl and Muehlschlegel² have reported a similar compound for aldehydo-glucose pentabenzoate. In the case of the galactose compound, we have produced evidence³ that the substance is a true hemi-acetal of unusual stability. Such a compound is thus the open-chain analog of the glycosides which are monocyclic acetals. In view of the great amount of research which has been done on the latter compounds, it was considered of interest to study the corresponding open-chain galactose compounds in somewhat more detail. Accordingly the hemi-acetals of aldehydo-galactose pentaacetate with a number of aliphatic alcohols will now be reported. That the carbonyl group in the sugar acetate used possesses the power of adding an alcohol of relatively large molecular weight is shown by the successful preparation of a compound with cyclohexanol.

The ethyl hemi-acetal showed a mutarotation curve in chloroform (alcohol-free) which passed through a minimum and was thus indicative of a three-membered equilibrium. This was explained³ by the following equation, the carbonyl carbon atom being asymmetric in the hemi-acetal and so existing in two forms

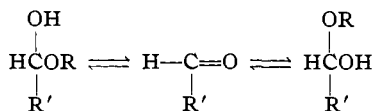


Figure 1 shows that a similar type of curve is obtained for the other hemi-acetals now prepared. It is to be noted that as the molecular weight of the alcohol increases, the dissociation in chloroform solution is more rapid, this being indicated by the steepness of the first part of the curve.

The investigation of the optical properties of these hemi-acetals has a direct bearing upon the theory of sugar mutarotation because the open-chain form of the sugar or its aldehydrol is postulated as the most probable intermediate in this reaction.⁴ From the standpoint of organic structural theory, the mutarotation of an aldehydo hemi-acetal in its own alcohol is

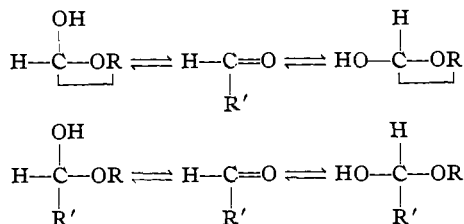
¹ Wolfrom, *THIS JOURNAL*, **52**, 2464 (1930).

² Brigl and Muehlschlegel, *Ber.*, **63**, 1551 (1930).

³ Wolfrom, *THIS JOURNAL*, **53**, 2275 (1931).

⁴ Lowry, "Rapports sur les Hydrates de Carbone. Dixième Conférence de l'Union Internationale de Chimie," Liège, 1930, p. 79.

quite analogous to the mutarotation of a sugar (a cyclic hemi-acetal) in water as the following formulas show



Of the hemi-acetals prepared, only the methanol compound possessed a solubility in its corresponding alcohol suitable for polarimetric observation at room temperature. Figure 2 shows that this compound in methanol exhibits a typical sugar mutarotation curve and the data of Table I place the reaction as apparently monomolecular. In view of the low rotations and the long time involved, the slight deviation from constancy of the values obtained is within the limits of experimental error. The presence of the intermediate aldehyde in methanol solution is thus undetectable by polarimetric measurement, while in chloroform solution an intermediate form is easily detectable. It appears reasonable that the intermediate is the same in both cases but that the concentration of the intermediate form is much greater in the chloroform solution.

In the course of this work it was necessary to prepare considerable quantities of aldehydo-galactose pentaacetate and a somewhat simplified method of preparation for this substance was devised.

Experimental

Preparation of Aldehydo-galactose Pentaacetate.—The mercaptal groups were removed from galactose ethyl mercaptal with mercuric chloride in acetone solution to which had been added only 25 cc. of water for 50 g. of the acetylated mercaptal, the proportions of the other reagents being the same as previously reported.¹ The evapo-

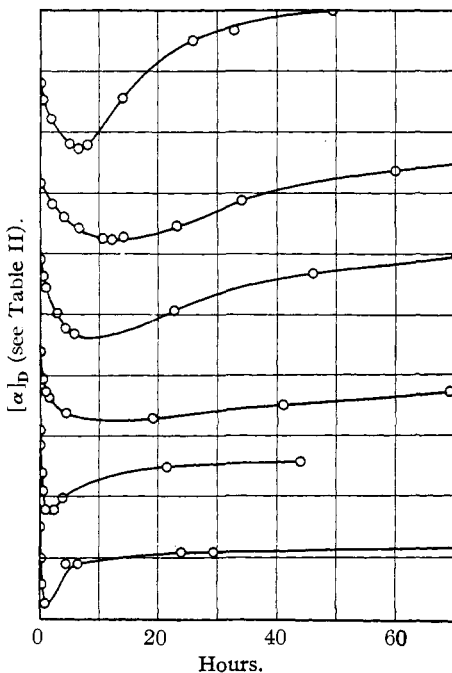


Fig. 1.—Mutarotation of several hemi-acetals of aldehydo-galactose pentaacetate in chloroform (alcohol-free). Order, from top to bottom: methyl, ethyl, *n*-propyl, isopropyl, isobutyl, cyclohexanol.

TABLE I
MUTAROTATION OF THE METHYL HEMI-ACETAL OF ALDEHYDO-GALACTOSE PENTA-
ACETATE IN METHANOL
 l , 4-dm.; λ 5892 Å.; t , 24°; c , 2.006

t , min.	α , degrees	$[\alpha]_D$, degrees	k
0	..	0.0 ^a	
60	+0.05	+ 0.6	6.6×10^{-4}
120	.09	1.1	6.2
255	.18	2.3	6.4
375	.25	3.1	6.0
450	.30	3.8	6.3
570	.34	4.3	5.8
735	.41	5.1	5.5
1320	.65	8.1	5.7
2190	.84	10.5	5.2
2940	.99	12.4	5.6
73 hrs.	1.09	13.6	
121	1.23	15.4	
173	1.22	15.3	

^a Interpolated.

$$k = 1/t \ln_e \frac{\alpha_0 - \alpha_\infty}{\alpha t - \alpha_\infty} \quad \alpha_0 = 0; \alpha_\infty = 15.4; t \text{ in minutes.}$$

rated reaction mixture was dried by repeated additions of acetone followed by evaporation under reduced pressure. The residue was extracted with hot carbon tetrachloride, filtered hot and allowed to cool for the first crop of crystals. A second crop was obtained by evaporation of the mother liquor under reduced pressure. This crude product was

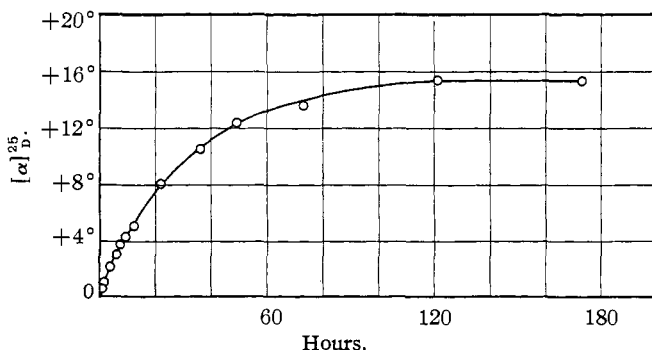


Fig. 2.—Mutarotation of the methyl hemi-acetal of aldehydo-galactose pentaacetate in methanol solution.

recrystallized by dissolving in a small amount of boiling acetone (carboraffin) cooled to room temperature and half the volume of alcohol-free ether added. Petroleum ether was then added until crystallization was initiated, an excess being avoided. After three crystallizations a yield of 11 g. of pure product (m. p. 120–121°) was obtained from 50 g. of the acetylated mercaptal. A much higher yield of slightly less pure product was

⁵ Hudson, THIS JOURNAL, 26, 1065 (1904).

readily obtainable, such material being satisfactory for the further synthetic experiments reported below.

Hemi-acetal Synthesis.—The hemi-acetals were prepared by recrystallization to constant melting point of aldehydo-galactose pentaacetate from the purified, anhydrous alcohols. For removal of the mother liquor, the filtered crystals were washed first with the cold alcohol and then with cold ether, the substances being insoluble in the latter solvent. In the case of the methyl hemi-acetal, the ether washing was omitted. A special procedure was required for the preparation of the cyclohexanol hemi-acetal. The aldehydo-galactose pentaacetate was dissolved in the least amount of cyclohexanol by warming to 80°. The solution was then quickly chilled by immersing the flask in ice water and was then treated with twice its volume of an equal mixture of absolute ethyl ether and petroleum ether. This procedure effected a good crystallization of the cyclohexanol compound. The filtered product was washed with a cold equal mixture of absolute ether and petroleum ether. The hemi-acetals prepared are shown in Table II, the ethyl compound having been reported previously. The mutarotation of the substances in alcohol-free chloroform is shown in Fig. 1.

TABLE II
HEMI-ACETALS OF ALDEHYDO-GALACTOSE PENTAACETATE, PROPERTIES AND ANALYSES

Hemi-acetal	M. p., °C.	[α] _D ²⁵ CHCl ₃ (alcohol-free)			Acetyl value (cc. 0.1 <i>N</i> NaOH per 100 mg. subs.)	
		Initial	Minimum	Final	Calcd.	Found
Methyl	123	+3.0	- 7.7	+15°	11.8	11.7
Ethyl	133	+1.5	- 7.5	+ 6	11.4	11.4
<i>n</i> -Propyl	130	+4.2	- 8.2	+ 4.5	11.1	11.1
Isopropyl	144	-1	-12	- 7	11.1	10.9
Isobutyl	123	+6	- 7	+ 1	10.8	10.7
Cyclohexanol	136	0	-12	- 3	10.2	10.4

The calculated acetyl value for aldehydo-galactose pentaacetate is 12.8 cc. of 0.1 *N* sodium hydroxide per 100 mg. A methoxyl (Zeisel) determination on the methyl hemi-acetal gave the following result: Subs., 0.3019; AgI, 0.1613. Calcd. for C₁₆H₂₈O₁₁-(OCH₃): OCH₃, 7.35. Found: OCH₃, 7.06.

Summary

1. The following hemi-acetals of aldehydo-galactose pentaacetate have been synthesized in crystalline condition: methyl, *n*-propyl, isopropyl, isobutyl, cyclohexanol.

2. The optical properties of these compounds have been investigated and it has been shown that their behavior supports the open chain intermediate theory of sugar mutarotation.

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