dilute (10%) sodium hydroxide was reduced by the addition of 0.5 g. of sodium hydrosulfite, there resulted a pale yellow vat, which dyed cotton a peach red, fairly stable to laundering but fugitive to light.

Summary

1. 6-Acetoxyretene is readily nitrated to a crystalline mononitro derivative, which can be reduced to the corresponding amine.

2. Retene ketone (1-methyl-7-isopropylfluorenone) likewise yields a mononitro derivative by direct nitration, and this nitro derivative also is easily reduced to the amine.

3. Retene ketone, in anhydrous media, gives the oxime which, by phosphorus pentachloride, is rearranged to a phenanthridone.

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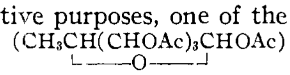
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Free Aldehyde Form of Fucose Tetraacetate

BY M. L. WOLFROM AND J. A. ORSINO

The methods previously employed in this Laboratory for the synthesis of non-cyclic sugar acetates[1] have now been extended to the methylpentose *l*-fucose. This substance has the configuration of *l*-galactose and may be named *l*-galactomethylose. The open chain or aldehydo-galactose pentaacetate ($CH_2OAc(CHOAc)_4CHO$) differed from the other open chain acetates in that it formed well-defined carbonyl addition compounds.[2] The same property has been found for the corresponding fucose compound ($CH_3(CHOAc)_4CHO$). Aldehydo-*l*-fucose tetraacetate shows an unusually low solubility in all solvents. This same property is shown by the corresponding open chain tetraacetate of galactose, recently prepared by Micheel and Suckfuell,[3] in which the terminal methyl group of fucose is replaced by a primary alcohol group. This low solubility of the fucose acetate made its isolation quite a different problem from that of the other open chain sugar acetates.

For comparative purposes, one of the ring acetates of fucose was also synthesized.



$$(CH_3\underbrace{CH(CHOAc)_3CHOAc}_{O})$$

Experimental

l-Fucose Ethyl Mercaptal Tetraacetate.—The fucose used in this work was prepared from seaweed by the excellent method of Clark.[4] Twenty-five grams of fucose ethyl mercaptal[5] was dissolved in 150 cc. of pyridine and 225 cc. of acetic anhydride added. The mixture was held at 0° for one hour and then at room temperature for eighteen hours. The solution was then poured into five liters of ice water, whereupon the acetate crystallized immediately. This was filtered and washed with cold water. Pure material was obtained by dissolving the product in 150 cc. of hot methanol and adding water to opalescence; yield, 35 g. or 87%; lustrous plates soluble in warm water and warm petroleum ether, and very soluble in other common organic solvents.

Anal. Calcd. for $C_6H_8O_4(SC_2H_5)_2(COCH_3)_4$: S, 14.62; acetyl, 9.13 cc. 0.1 *N* NaOH per 100 mg. Found: S, 14.56; acetyl, 9.13 cc.

Aldehydo-l-fucose Tetraacetate.—Fifteen grams of fucose ethyl mercaptal tetraacetate was dissolved in 60 cc. of acetone in a three-necked flask equipped with a mechanical stirrer, a condenser and a dropping funnel. Thirty grams of finely powdered cadmium carbonate and 7.5 cc. of water were added, and under vigorous stirring a solution of 30 g. of mercuric chloride in 60 cc. of acetone was added drop by drop. After twenty hours of constant stirring the reaction mixture was heated at a bath temperature of 50° for fifteen minutes and finally refluxed at 60° for the same length of time. The mixture was then rapidly filtered while still warm. White crystals of aldehydo-*l*-fucose tetraacetate separated almost immediately. The crystallization was completed by standing overnight in the ice box and the product filtered and washed with cold acetone; yield, 9.6 g. of crude material.

Pure material was obtained by dissolving the crude product in acetylene tetrachloride, adding carboraffin and filtering. Petroleum ether was added to the filtrate to incipient crystallization, and the solution placed in the ice box overnight to complete the crystallization. The white crystals produced by this procedure were filtered under suction and washed with petroleum ether; yield, 7.8 g.

The substance showed a constant rotation in acetylene tetrachloride solution but mutarotated slowly in methanol, changing from a specific rotation of +22 to +9° in about four days at room temperature. It is sparingly soluble in methanol, ethyl acetate and in acetone; almost insoluble in ether, ethanol and chloroform, and is insoluble in water, petroleum ether, benzene and carbon tetrachloride. It dissolves quite readily in pyridine and warm acetylene

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[1] M. L. Wolfrom, THIS JOURNAL, **51**, 2188 (1929); **52**, 2464 (1930); M. L. Wolfrom and Mildred R. Newlin, *ibid.*, **52**, 3619 (1930); **53**, 4379 (1931).

[2] M. L. Wolfrom, *ibid.*, **53**, 2275 (1931); M. L. Wolfrom and W. M. Morgan, *ibid.*, **54**, 3390 (1932).

[3] F. Micheel and F. Suckfuell, *Ann.*, **502**, 85 (1933).

[4] E. P. Clark, *J. Biol. Chem.*, **54**, 65 (1922).

[5] E. Votoček and V. Veselý, *Z. Zuckerind. Böhmen*, **40**, 207 (1916).

tetrachloride, in hot water, hot methyl or ethyl alcohol. The substance crystallizes from hot acetone in the form of six-sided plates. It gives a positive Schiff test in two minutes and reacts with Fehling's solution immediately on heating.

Anal. Calcd. for $C_6H_8O_5(COCH_3)_4$: C, 50.58; H, 6.07; acetyl, 12.0 cc. of 0.1 *N* NaOH per 100 mg. Found: C, 50.32; H, 6.28; acetyl, 12.0 cc.

Aldehydo-*l*-fucose Tetraacetate Ethyl Hemi-acetal.—Two grams of aldehydo-*l*-fucose tetraacetate was dissolved in 50 cc. of hot absolute ethanol and the solution filtered. The solution was concentrated in a vacuum desiccator to about 10 cc. and the white crystalline mass separated from the mother liquor. After one recrystallization from hot absolute ethanol the substance softened at 120–121°, solidified on further heating and melted sharply at 170°. This double melting point was undoubtedly due to decomposition into ethanol and the high melting aldehydo-fucose tetraacetate. Further crystallizations did not alter the behavior of the compound on heating. The purified substance mutarotated slowly in ethanol, changing from $[\alpha]_D$ −3.4° (*c*, 1.7) to a constant maximum of $[\alpha]_D$ +3.4° in seventy hours at room temperature. In alcohol-free chloroform the observed rotation after four minutes was $[\alpha]_D$ −25.8°. The extrapolated initial value was $[\alpha]_D$ −32°, changing rapidly and continuously to a maximum of $[\alpha]_D$ +27.8° in about seven hours.

The substance dissolves readily in chloroform and acetone, hot water and hot alcohol. It is sparingly soluble in ether and is insoluble in petroleum ether and cold water.

Anal. Calcd. for $C_8H_{14}O_6(COCH_3)_4$: C, 50.76; H, 6.95; acetyl, 10.6 cc. 0.1 *N* NaOH per 100 mg. Found: C, 50.31; H, 7.17; acetyl, 10.6 cc.

Aldehydo-*l*-fucose Tetraacetate Aldehydrol.—This compound was made by dissolving 1.5 g. of aldehydo-fucose tetraacetate ethyl hemi-acetal in boiling water, filtering and allowing to stand overnight in the ice box to crystallize; yield, 1.1 g., m. p. 160–161°. Further recrystallizations from boiling water did not change the melting point. No suitable inert solvent was found for determining its rotation. It crystallizes from water in well-defined tabular prisms which are slightly soluble in hot acetone but dissolve readily in hot alcohol. At room temperature it is insoluble in water, alcohol, chloroform, acetylene tetrachloride, acetone and ether.

Anal. Calcd. for $C_6H_8O_5(COCH_3)_4H_2O$: C, 47.97; H, 6.33; acetyl, 11.4 cc. 0.1 *N* NaOH per 100 mg. Found: C, 47.78; H, 6.64; acetyl, 11.5 cc.

Aldehydo-*l*-fucose Semicarbazone Tetraacetate.—One gram of aldehydo-*l*-fucose tetraacetate (one mol) was dissolved in 70 cc. of boiling water and the solution filtered. An intimate mixture of 0.33 g. of semicarbazide hydrochloride (one mol) and 0.29 g. of potassium acetate (one mol) was added to the solution while this was still hot. A copious crystalline precipitate of the semicarbazone formed almost immediately. The mixture was held overnight at ice box temperature to complete the crystallization, filtered and washed with water; yield, 1.0 g., m. p. 215° (dec.). The crystals show a five-sided face in both a tabular and elongated habit. The substance is very slightly soluble in alcohol and acetone. It is insoluble in ether and cold water, but dissolves readily in chloroform and with difficulty in hot water.

Anal. Calcd. for $C_7H_{11}O_5N_3(COCH_3)_4$: N, 10.79; acetyl, 10.3 cc. 0.1 *N* NaOH per 100 mg.; mol. wt., 389.2. Found: N, 10.89; acetyl, 10.3 cc.; mol. wt., 427 (Rast method).

α-*l*-Fucose Tetraacetate.—Ten grams of *l*-fucose was added to a mixture of 70 g. of pyridine and 50 g. of acetic anhydride, previously cooled to 0°. The mixture was kept at this temperature or below until all the sugar had dissolved and was then held at room temperature for twenty-four hours. The solution was then poured into 500 cc. of ice water, whereupon a low yield of sirup separated. The whole mixture was extracted with chloroform. The extract was washed with a saturated aqueous solution of sodium bisulfate to remove the pyridine, dried over calcium chloride, decolorizing carbon added and filtered. The chloroform was removed in a vacuum desiccator and the brown sirup obtained was crystallized by stirring with small portions of ether. A larger quantity of ether was added and the crystals were filtered immediately by suction and washed with cold ether; yield, 7.5 g., m. p. 92–93°. The substance was purified by dissolving in about 100 cc. of ether, filtering (carboraffin) and evaporating to about half volume in a vacuum desiccator. The crystals which formed were rapidly filtered under suction and washed with cold ether.

α-*l*-Fucose tetraacetate crystallizes from chloroform solution on slow evaporation in large square crystals measuring nearly one centimeter on a side. It is very soluble in alcohol, acetone and chloroform, less soluble in cold ether and insoluble in petroleum ether.

Anal. Calcd. for $C_6H_8O_5(COCH_3)_4$: C, 50.58; H, 6.07; acetyl, 12.04 cc. 0.1 *N* NaOH per 100 mg. Found: C, 50.83; H, 6.31; acetyl, 12.17 cc.

Table I

Acetates of Fucose

Name	M. p.,[a] °C.	Rotation[a] $[\alpha]_D$	Solvent	*c*[b]	Temp., °C.
α-*l*-Fucose tetraacetate (I)	92	−120°	$CHCl_3$	1.8	34
Aldehydo-*l*-fucose tetraacetate (II)	166–167	+ 40	$(CHCl_2)_2$	1.6	25
Ethyl hemi-acetal of II	120–121	− 32[d]	$CHCl_3$[c]	1.5	29
Ethyl mercaptal of II	99–100	+ 5	$CHCl_3$	3.8	25
Aldehydrol of II	160–161	...			
Semicarbazone of II	215 (dec.)	...			

[a] All melting points and rotations are those determined after recrystallization to constancy. [b] *c* = g. subs. per 100 cc. soln. [c] Alcohol-free. [d] Initial.

Acknowledgment is gratefully made to Mr. Edward E. Glasser for assistance in the preparation of the fucose used in this investigation.

Summary

1. The free aldehyde form of fucose tetraacetate has been synthesized in pure crystalline condition.

2. The aldehydrol, ethyl hemi-acetal, semi-

carbazone and ethyl mercaptal of the above aldehyde have been synthesized in crystalline form.

3. The free aldehyde form of fucose tetraacetate is similar to the corresponding compound of galactose in its ability to form stable carbonyl addition compounds with water and alcohol.

4. *α-l*-Fucose tetraacetate has been synthesized in crystalline condition.

COLUMBUS, OHIO RECEIVED JANUARY 15, 1934

[CONTRIBUTION FROM THE INSECTICIDE DIVISION, BUREAU OF CHEMISTRY AND SOILS]

Toxicarol. V. 7-Hydroxytoxicarol and Related Compounds

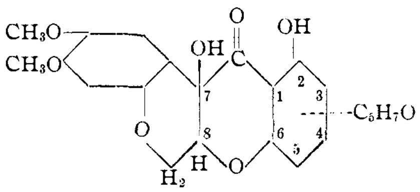
BY E. P. CLARK

Recently Butenandt and Hilgetag[1] described a substance, designated as toxicarol hydrate, which they obtained by the action of alcoholic alkali upon toxicarol. It was characterized as yellow prisms which melted at 223.5° and gave a green color with ferric chloride. It was stable toward alcoholic alkali, but when boiled with alcoholic hydrochloric acid it was readily converted to dehydrotoxicarol. The authors tentatively assumed, as the name implies, that toxicarol reacted additively with a molecule of water to form the compound $C_{23}H_{24}O_8$.

Continuing their study of the substance, they hydrogenated the reaction mixture with palladium-charcoal and hydrogen and obtained a new compound which melted at 217.5°. The same material was also obtained by treating dihydrotoxicarol with alcoholic alkali. From analogy, this should have the formula $C_{23}H_{26}O_8$. Strangely enough, however, they suggested $C_{21}H_{24}O_7$ as its formula, notwithstanding that a methoxyl determination would have given decisive information as to which was correct.

Finally, in a more recent communication[2] in which they again reported the preparation and analysis of the compound and designated the substance as dihydrotoxicarol hydrate, two formulas, $C_{23}H_{26}O_8$ and $C_{23}H_{24}O_8$, were proposed. In this case their analytical data definitely agreed with the latter formula. Thus, from these prefatory statements it is evident that the nature of the two compounds is greatly in need of clarification.

Information necessary for this purpose is available, largely as a result of work already reported or in progress, and consists of a correlation of studies involving the preparation of the compounds by different methods and a consideration of their reactions. The conclusion derived from these data is that toxicarol hydrate is 7-hydroxytoxicarol,[3] $C_{23}H_{22}O_8$, represented by formula I, and dihydrotoxicarol hydrate is 7-hydroxydihydrotoxicarol, $C_{23}H_{24}O_8$.



I 7-Hydroxytoxicarol

The evidence supporting this statement follows In addition to clarifying the point under consideration it is also important because of its bearing upon the structure of toxicarol.

The reaction described by Butenandt and Hilgetag is undoubtedly one of atmospheric oxidation and is the same as that described by Takei, Miyajima and Ono[4] in which tephrosin and isotephrosin are formed from deguelin. As evidence of this the following is pertinent. The action of alcoholic alkali upon toxicarol produces 7-hydroxytoxicarol (toxicarol hydrate) as reported, but the yields and the purity of the product vary with the conditions of the experiment. For example, occasionally shaking the alkaline reaction mixture results in larger yields and a purer product than is obtained when this is not done. From the preparative standpoint, a better procedure is to stir rapidly an alkaline benzene-99% alcoholic solution of toxicarol for five hours, then allow it to stand until the next day. These conditions give some dehydrotoxicarol and a good yield of 7-hydroxytoxicarol, but because of the insolubility of the dehydro compound it may be separated readily from the main product.

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(1) Butenandt and Hilgetag, *Ann.*, **495**, 173 (1932).

(2) Butenandt, *ibid.*, **506**, 158 (1933).

(3) The numbering system is that previously employed in considering deguelin and tephrosin [THIS JOURNAL, **54**, 3000 (1932)].

(4) Takei, Miyajima and Ono, *Chem. Abs.*, **27**, 2954 (1933).