Dimesitylphenylfuran is made by dehydration of the saturated diketone. It is not oxidized by the nitric–acetic acid reagent.

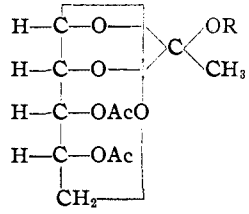
CHARLOTTESVILLE, VIRGINIA RECEIVED AUGUST 30, 1939

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

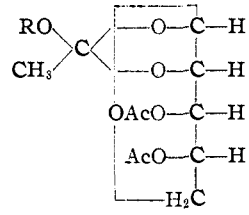
The Preparation of *d*- and *l*-Ribosidodihydroxyacetone Tetraacetates with an Orthoester Structure

BY CLARENCE W. KLINGENSMITH AND WILLIAM LLOYD EVANS

In a previous communication[1] the synthesis of the first pairs of disaccharide antipodes, β-*d*- and β-*l*-arabinosidodihydroxyacetone tetraacetates and β-*d*- and β-*l*-xylosidodihydroxyacetone tetraacetates, and the synthesis of the first disaccharide racemate, β-*d*,β-*l*-arabinosidodihydroxyacetone tetraacetate were reported. In this communication another pair of antipodes containing *d*- and *l*-ribose and dihydroxyacetone is reported. The behavior of this pair of ribose derivatives as well as the synthesis of methyl-*d*-riboside triacetate (II) with an orthoester structure by Levene and Tipson[2] indicates that the orthoester structures, (I) and (III), should be assigned to them.



I. R = $AcOCH_2COCH_2$-. II. R = CH_3-.



III. R = $AcOCH_2COCH_2$-.

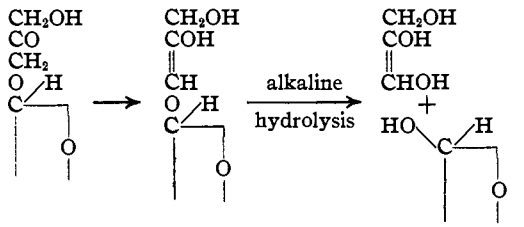
In conformity to the nomenclature proposed by Haworth, Hirst and Stacy[3] for methylglycoside acetates with an orthoester structure, our compounds are named diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate (I) and diacetyl *l*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate (III).

Methylglycoside acetates with an orthoester structure were first obtained by Fischer, Bergmann and Rabe,[4] and the nature of their structures was first explained by Bott, Haworth and Hirst[5] and independently by Freudenberg and Scholz.[6] This type of methylglycoside acetate has been obtained with rhamnose,[4,7] mannose,[5,8,9] lyxose,[10] maltose,[6,11] 4-[β-*d*-glucosido]-*d*-mannose,[12] ribose,[2] *d*-α-glucoheptose,[3] turanose,[13] fructose,[14] and talose,[15] and is characterized by (a) one acetyl group that is stable to alkaline hydrolysis and (b) extreme sensitivity to acids.

The orthoester structures of diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate and diacetyl *l*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate differ from the orthoester structure of the methylglycoside acetates in that the acetoxyacetonyl group, $AcOCH_2COCH_2$-, of the former is substituted for the methyl group of the latter. The presence of the acetoxyacetonyl group made it impossible for us to demonstrate the stability of one acetyl group to alkaline hydrolysis in contrast to the removal of the other three normal acetyl groups. In an acetyl determination by the method of Kunz and Hudson,[16] diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate gave a value that was 9.4% higher than the theoretical value for four groups or 46% higher than the theoretical value for three groups. Kreider and Evans[17] previously reported that the acetyl values of oligosaccharide acetates that contained dihydroxyacetone were about 10% high by the method of Kunz and Hudson. Bernier[18] also obtained high acetyl values with dihydroxyacetone monoacetate. These high values are in accord with

(1) L. C. Kreider and W. L. Evans, THIS JOURNAL, **58**, 797 (1936).
(2) P. A. Levene and R. S. Tipson, *J. Biol. Chem.*, **92**, 109 (1931).
(3) W. N. Haworth, E. L. Hirst and M. Stacy, *J. Chem. Soc.*, 2864 (1931).
(4) E. Fischer, M. Bergmann and A. Rabe, *Ber.*, **53**, 2362 (1920).
(5) H. G. Bott, W. N. Haworth and E. L. Hirst, *J. Chem. Soc.*, 1395 (1930).
(6) K. Freudenberg and H. Scholz, *Ber.*, **63**, 1969 (1930).
(7) W. N. Haworth, E. L. Hirst and E. J. Miller, *J. Chem. Soc.*, 2469 (1929).
(8) J. K. Dale, THIS JOURNAL, **46**, 1046 (1924).
(9) P. A. Levene and H. Sobotka, *J. Biol. Chem.*, **67**, 771 (1926).
(10) P. A. Levene and M. L. Wolfrom, *ibid.*, **78**, 525; **79**, 471 (1928).
(11) K. Freudenberg, H. Hochstetter and H. Engels, *Ber.*, **58**, 666 (1925).
(12) H. S. Isbell, *Bur. Standards J. Research*, **7**, 1115 (1931).
(13) E. Pacsu, THIS JOURNAL, **55**, 2451 (1933).
(14) E. Pacsu, *ibid.*, **57**, 745 (1935).
(15) W. W. Pigman and H. S. Isbell, *Bur. Standards J. Research*, **9**, 189 (1937).
(16) A. Kunz and C. S. Hudson, THIS JOURNAL, **48**, 1978 (1926).
(17) L. C. Kreider and W. L. Evans, *ibid.*, **58**, 1661 (1936).
(18) C. L. Bernier, Master's Thesis, The Ohio State University 1932.

the work of Evans and Cornthwaite,[19] who found that dihydroxyacetone in alkaline solution was converted into lactic, acetic, and formic acids as well as other substances. The fact that our acetyl value by the Kunz and Hudson method was abnormally high for three groups can be accounted for on the basis of the findings of Gehman, Kreider, and Evans.[20] They presented evidence to show that the dihydroxyacetone portion of oligosaccharides (IV) containing dihydroxyacetone was susceptible to alkaline hydrolysis by virtue of their possible rearrangement to the enediol structure (V).

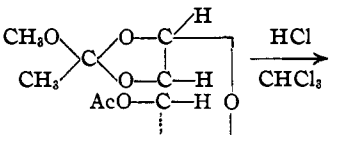


IV V

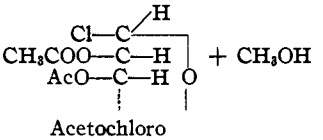
In an analogous manner, the *d*-ribose-1,2-ortho-3′-hydroxyacetonyl acetate (VI), formed by the removal of the three normal acetyl groups in the alkaline hydrolysis (Kunz and Hudson acetyl determination) of diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate (I), may rearrange to the enediol structure (VII). This may then undergo alkaline hydrolysis to the trioseenediol (VIII), the precursor of lactic acid and *d*-ribose-1,2-orthoacetic acid (IX), which may suffer further hydrolysis to *d*-ribose (XI) by first rearranging to 2-monoacetyl-*d*-ribose (X).

The rearrangement of *d*-ribose-1,2-orthoacetic acid (IX) to 2-monoacetyl-*d*-ribose (X) is in harmony with the evidence presented by Pigman and Isbell[15] to show that orthoacid derivatives are unstable to alkali.

The behavior of diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate and diacetyl *l*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate in dry alcohol-free chloroform containing dry hydrogen chloride was analogous to the behavior of the methylglycoside acetates with an orthoester structure. Isbell[12,15] observed that the rotations of 4-[β-*d*-glucosido]-methyl-*d*-mannoside heptaacetate and of methyl-*d*-taloside tetraacetate with orthoester structures changed rapidly in chloroform solution containing dry hydrogen chloride and that acetochloro-4-[β-*d*-glucosido]-*d*-mannose and acetochloro-*d*-talose were formed.

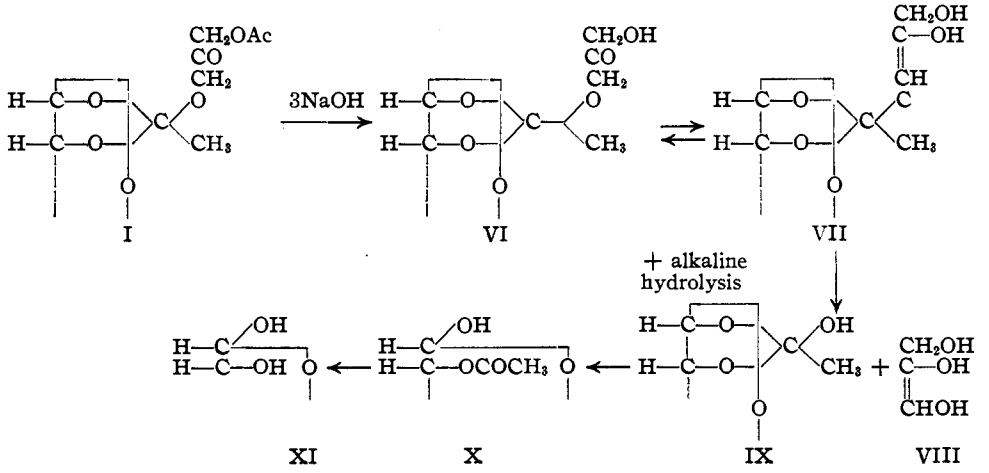


Methylglycoside acetate with an orthoester structure



Acetochloro derivative

A similar rotation change occurred with our ribose derivatives, (I) and (III), and evidence that the acetochlororiboses were formed was observed. Furthermore, the isomeric compound, the β-*d*-arabinosidodihydroxyacetone tetraacetate of Kreider and Evans,[1] which does not possess an orthoester structure, showed no reaction with hydro-



I VI VII

XI X IX VIII

(19) W. L. Evans and W. R. Cornthwaite, THIS JOURNAL, **50**, 486 (1928).

(20) H. Gehman, L. C. Kreider and W. L. Evans, *ibid.*, **58**, 2388 (1936).

gen chloride in chloroform solution. Hence, it is concluded that the behavior of the ribose derivatives, (I) and (III), is to be attributed to an orthoester structure.

The possibility that diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate and diacetyl *l*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate contain β-biosidic links was also eliminated by the fact that the calculated specific rotations of β-*d*-ribosidodihydroxyacetone tetraacetate (unknown compound) and β-*l*-ribosidodihydroxyacetone tetraacetate (unknown compound) are −112.3 and +112.3°, respectively, which are in complete disagreement with the observed specific rotations of −11.6 and +11.8°. These rotations were calculated from the value of A as given by Kreider and Evans[1] and from the value of B which was calculated from the rotatory values of the individual asymmetric carbon atoms of a pentose tetraacetate which were obtained by a method analogous to that of Isbell.[21]

A racemate, diacetyl *d,l*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate, also is described. Other compounds which are reported in the literature for the first time are *l*-ribose tetraacetate, *d,l*-ribose tetraacetate and acetobromo-*l*-ribose.

Experimental Part

Preparation of Known Starting Materials.—*d*- and *l*-ribose were prepared from *d*- and *l*-arabinose, respectively, according to the directions of Karrer, *et al.*[22] The *d*-ribose, which was recrystallized once from absolute ethanol, was acetylated by the procedure of Levene and Tipson[2] to *d*-ribose tetraacetate, m. p. 109.5–110.0° (corr.), $[\alpha]^{28}D$ −56.0° (*c*,[23] 3.0; pure chloroform). A product with these same constants was obtained by the acetylation of a sample of *d*-ribose that had been purified by conversion to *d*-ribose *p*-bromophenylhydrazone, m. p. 165.0–165.5° (corr.), and subsequent hydrolysis with benzaldehyde according to the procedure given by Karrer.[22] The values of *d*-ribose tetraacetate as reported by Levene and Tipson[3] are given here for comparison: m. p. 110°, $[\alpha]^{25}D$ −52.0° (chloroform). Acetobromo-*d*-ribose, m. p. 94.5–95.5° (corr.), $[\alpha]^{25}D$ −223.9° (*c*, 3.0; pure chloroform), was obtained from the tetraacetate according to the directions of Levene and Tipson.[2] The values of acetobromo-*d*-ribose as given in the literature[2] are presented here for comparison: m. p. 96°, $[\alpha]^{25}D$ −209.3° (*c*, 2; chloroform). Dihydroxyacetone monoacetate was prepared by the method of Fischer, Baer and Feldmann.[24] The silver carbonate was prepared as in the previous communication.[1] The Drierite used as the internal desiccant was finely powdered and preheated at 235° for two hours. The benzene used as the reaction medium and the solvent for the acetobromo riboses was thiophene-free, dried and distilled over sodium and preserved over Drierite.

l-Ribose Tetraacetate.—This compound was prepared from *l*-ribose (once recrystallized from absolute ethanol), according to the procedure used by Levene and Tipson[2] in the preparation of *d*-ribose tetraacetate. After two recrystallizations from ethanol (95%), the melting point, m. p. 109.5–110.0° (corr.), and specific rotation, $[\alpha]^{30}D$ +56.0° (*c*, 3.5; pure chloroform), were constant. The yield of the pure crystalline product was 58% of the theoretical. The acetylation of a sample of *l*-ribose that was purified by conversion to *l*-ribose *p*-bromophenylhydrazone, m. p. 165.0–165.5° (corr.), and subsequent hydrolysis with benzaldehyde by the procedure of Karrer[22] gave a product with the same constants.

Anal. Calcd. for $C_5H_6O_5(COCH_3)_4$: acetyl, 12.58 ml. of 0.1 *N* NaOH per 100 mg. Found: acetyl, 12.60 ml.

d,l-Ribose Tetraacetate.—Equal portions (200 mg.) of *d*-ribose tetraacetate and *l*-ribose tetraacetate were dissolved in warm ethanol (95%). Upon cooling the solution, crystallization took place. The product melted at 90.5° (corr.). The observed rotation in a 2-dm. micro polarimeter tube was ±0.0° (*c*, 2.4; pure chloroform). The melting point of each constituent taken separately was 109.5–110.0°, a mixed melting point of the two active isomers was 84.5–86.5° (corr.), and a mixed melting point of the racemic modification and a small amount of either active isomer was 88.0–90.0° (corr.). These facts seem to indicate that the racemic modification is a molecular compound.

Acetobromo-l-ribose.—This compound was prepared essentially according to the procedure of Levene and Tipson[2] for the preparation of acetobromo-*d*-ribose except that *l*-ribose tetraacetate was substituted for *d*-ribose tetraacetate. The yield was 69–75% of the theoretical based on the *l*-ribose tetraacetate as compared with the 60% yield reported by Levene and Tipson. This higher yield was attributed to the fact that the solution of the *l*-ribose tetraacetate in the acetic acid–hydrogen bromide reagent was allowed to stand at room temperature (20–25°) for two hours rather than for one hour. The product was recrystallized once from ether and petroleum ether: m. p. 94.5–95.5° (corr.), $[\alpha]^{23}D$ +224.8° (*c*, 3.1; pure chloroform).

Anal. Calcd. for $C_{11}H_{15}O_7Br$: Br, 23.58. Found: Br, 23.68.

Diacetyl d-Ribose-1,2-ortho-3′-acetoxyacetonyl Acetate.—This compound was prepared from acetobromo-*d*-ribose and dihydroxyacetone monoacetate essentially according to the directions of Kreider and Evans[1] for the preparation of β-*d*-arabinosidodihydroxyacetone tetraacetate. After the manner of Reynolds and Evans[25] the acetobromo-*d*-ribose was dissolved in benzene and dropped into the reaction flask over a period of forty-five minutes rather than adding the solid substance portion-wise. Iodine (1 mole) was used as a catalyst after the manner of Helferich, Bohm and Winkler.[26] The yield was 18–20%

(21) H. S. Isbell, *Bur. Standards J. Research*, **3**, 1041 (1929).

(22) P. Karrer, *et al.*, *Helv. Chim. Acta*, **18**, 1435 (1935).

(23) In this paper, *c* represents the concentration in grams per 100 ml. of solution.

(24) H. O. L. Fischer, E. Baer and L. Feldmann, *Ber.*, **63**, 1732 (1930).

(25) D. D. Reynolds and W. L. Evans, THIS JOURNAL, **60**, 2559 (1938).

(26) B. Helferich, E. Bohm and S. Winkler, *Ber.*, **63**, 990 (1930).

of the theoretical based on the acetobromo-*d*-ribose. The crude product was recrystallized to constant melting point and rotation by dissolving in pure chloroform or benzene, decolorizing with Carboraffin, evaporating to a thin sirup and adding 10–15 volumes of dry alcohol-free ether. It crystallized in needle-like clusters; m. p. 97.0–98.0° (corr.), $[\alpha]^{24}D$ −11.6° (*c*, 1.8; pure chloroform).

Anal. Calcd. for $C_8H_{10}O_7(COCH_3)_4$: acetyl, 10.26 ml. of 0.1 *N* NaOH per 100 mg. Found: acetyl (Freudenberg[27]), 10.25 ml.

This substance was soluble in chloroform, acetone, and benzene; moderately soluble in alcohol; and slightly soluble in ether and water. It was very sensitive to hydrogen chloride in chloroform solution. When 0.2075 g. was dissolved in 15.08 ml. of dry alcohol-free chloroform containing 0.011 g. of dry hydrogen chloride, the first rotation observed in a 2-dm. tube six minutes after dissolution was −3.03°. On the basis of a specific rotation of −11.6°, the initial rotation in chloroform alone was calculated to be −0.32°, indicating that a very rapid rotation change had taken place. No further change in rotation was observed even after standing for fifteen minutes. The hydrogen chloride was then removed from the solution by shaking with silver carbonate, after first adding a few grams of powdered Drierite to remove the water formed by the neutralization reaction. The solid materials were removed by filtration. Upon evaporating the solvent from the filtrate a sirup was obtained which could not be brought to crystallization. The sirup gave a positive test for halogen and evolved acid fumes after standing several weeks at room temperature which indicated the presence of acetochloro-*d*-ribose.

Diacetyl *l*-Ribose-1,2-ortho-3′-acetoxyacetonyl Acetate.—This compound was prepared and purified in exactly the same manner as the *d*-isomer except that acetobromo-*l*-ribose was substituted for acetobromo-*d*-ribose: yield, 18–20% of the theoretical, m. p. 97.0–98.0° (corr.), $[\alpha]^{25}D$ +11.8° (*c*, 3.2; pure chloroform). It crystallized in needle-like clusters.

Anal. Calcd. for $C_8H_{10}O_7(COCH_3)_4$: acetyl, 10.26 ml. of 0.1 *N* NaOH per 100 mg. Found: acetyl (Freudenberg[27]), 10.10 ml.

This substance was soluble in chloroform, acetone, and benzene, moderately soluble in alcohol, and slightly soluble in ether and water. The behavior of this compound in chloroform solution containing hydrogen chloride was analogous to the *d*-isomer. When 0.5211 g. was dissolved in 25.72 ml. of dry alcohol-free chloroform containing 0.162 g. of dry hydrogen chloride, the first rotation observed in a 4-dm. tube five minutes after dissolution was +9.45°. On the basis of a specific rotation of +11.8°, the initial rotation in chloroform alone was calculated to be +0.95°, indicating that a rapid rotation change had occurred. After removing the hydrogen chloride and the solvent as described in the case of the *d*-isomer, a sirup was obtained which could not be brought to crystallization. The sirup gave a positive test for halogen and evolved acid fumes after standing for a few weeks. The behavior of this sirup was indicative of the presence of acetochloro-*l*-ribose.

Diacetyl *d,l*-Ribose-1,2-ortho-3′-acetoxyacetonyl Acetate.—Equal portions (52 mg.) of the two isomers were dissolved in benzene and evaporated to a thin sirup. Upon adding a large volume of anhydrous ether, crystallization took place. The product melted at 124.5–125.0° (corr.). The melting point of the constituents taken separately was 97.0–98.0°. The observed rotation in a 2-dm. micro polarimeter tube was ±0.0° (*c*, 1.7; pure chloroform). These facts indicate that a true racemate was formed.

Acknowledgment.—The authors wish to thank H. J. Dauben, who prepared a large part of the *l*-ribose that was used in this work.

Summary

1. The preparation of the following pair of disaccharide antipodes in crystalline condition is described: diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate and diacetyl *l*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate. The racemate, diacetyl *d,l*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate is also described.

2. These are the first examples of orthoester derivatives which contain a group other than the methyl and ethyl groups as a part of the ortho structure.

3. A possible explanation for the high acetyl values of diacetyl *d*-ribose-1,2-ortho-3′-acetoxyacetonyl acetate by the Kunz and Hudson method is presented.

4. *l*-Ribose tetraacetate and acetobromo-*l*-ribose are reported for the first time. The racemate, *d,l*-ribose tetraacetate, is described.

COLUMBUS, OHIO RECEIVED AUGUST 21, 1939

(27) K. Freudenberg and M. Harder, *Ann.*, **433**, 230 (1923).