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Reaction of Ethyl 5-*O*-Benzoyl-1-thio- β -L-arabinoside with Silver Benzoate and with Mercuric Acetate

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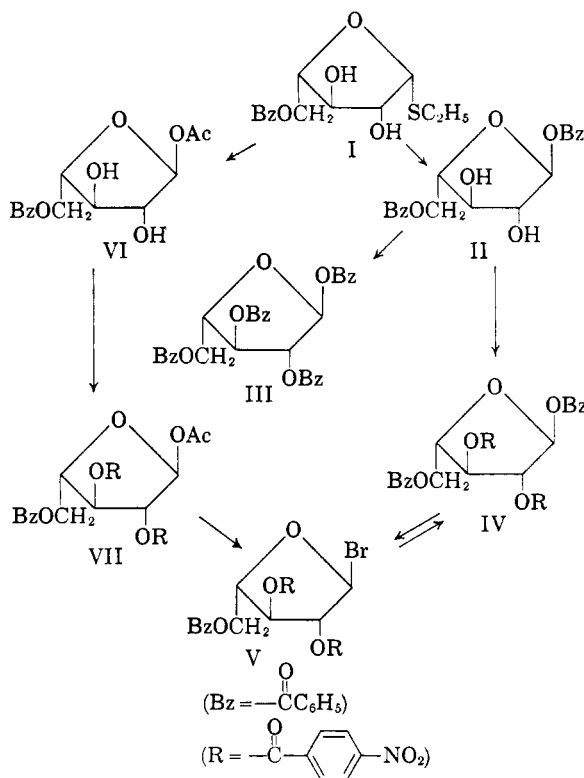
Ethyl 5-*O*-benzoyl-1-thio- β -L-arabinoside (I) reacts in boiling acetonitrile solution with silver benzoate to give 1,5-di-*O*-benzoyl- α -L-arabinose (II). The structure of this product is shown through conversion to 1,5-di-*O*-benzoyl-2,3-di-*O*-*p*-nitrobenzoyl- α -L-arabinose (IV) and 5-*O*-benzoyl-2,3-*O*-di-*p*-nitrobenzoyl- α -L-arabinosyl bromide (V) and through conversion of V to IV by silver benzoate.

With mercuric acetate in acetonitrile at room temperature ethyl 5-*O*-benzoyl-1-thio- β -L-arabinoside (I) is transformed to 1-*O*-acetyl-5-*O*-benzoyl- α -L-arabinose (VI). The nature of this product is clarified through its behavior with periodate, stability in aqueous pyridine and conversion through 1-*O*-acetyl-5-*O*-benzoyl-2,3-di-*O*-*p*-nitrobenzoyl- α -L-arabinose (VII) to V.

In recent communications it has been shown that aldose dialkyl dithioacetals^{2,3} and an alkyl 1-thioaldopyranoside² react with the silver salts of various carboxylic acids to give 1-*O*-acylaldoses. Likewise, 5-*O*-benzoyl-2-deoxy-D-ribose diisopropyl dithioacetal has been found to condense with chloromercuri-6-benzamidopurine to give (after removal of the protecting groups) 2'-deoxyadenosine and its anomer.⁴ We have now extended this investigation to a representative of a third class of 1-thioaldose derivatives, an alkyl 1-thioaldofuranoside.

Ethyl 5-*O*-benzoyl-1-thio- β -L-arabinoside (I) was prepared through partial demercaptalation of 5-*O*-benzoyl-L-arabinose diethyl dithioacetal using the process which Reist, Hart, Goodman and Baker⁵ described for its enantiomorph. Condensation of this substance with silver benzoate in boiling acetonitrile led to the isolation in 33% yield of a crystalline di-*O*-benzoylpentose. The ring structure of this substance was demonstrated through benzylation which gave α -L-arabinofuranose tetrabenzoate (III). That the newly introduced benzoyl group was located at C₁ was ascertained through *p*-nitrobenzylation to the crystalline ester IV and conversion of this with hydrogen bromide to a crystalline *O*-benzoyl-di-*O*-*p*-nitrobenzoyl-L-arabinosyl bromide (V), the loss of one benzoyl group in the last step clearly indicating its location at C₁.

Since the reaction of ethyl 1-thio- β -D-glucopyranoside with silver mesitoate is not stereospecific,² giving both anomeric 1-*O*-mesitoyl-D-glucopyranoses, it is not possible to decide *a priori* whether II is an α - or a β -anomer. However, condensation of



the bromide V with silver benzoate should give the *trans*, or α -L-, ester IV regardless of the anomeric configuration of the bromide.⁶ This condensation was carried out and the crystalline product found to be identical with that obtained from the *p*-nitrobenzylation of the 1,5-di-*O*-benzoyl-L-arabinose. The latter is, therefore, the α -L-anomer depicted by II.

It is of interest to contrast the behavior of ethyl 5-*O*-benzoyl-1-thio- β -L-arabinofuranoside (I) with that of ethyl 1-thio- β -D-glucopyranoside toward silver benzoate.² With the furanoside, one hour in boiling acetonitrile with an excess of silver benzoate served to give, as stated earlier, a 33%

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(2) C. Pedersen and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **82**, 3215 (1960).

(3) C. Pedersen, H. W. Diehl and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **82**, 3425 (1960).

(4) C. Pedersen and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **82**, 5210 (1960).

(5) E. J. Reist, P. A. Hart, L. Goodman and B. R. Baker, *J. Am. Chem. Soc.*, **81**, 5176 (1959).

(6) R. S. Tipson, *J. Biol. Chem.*, **130**, 55 (1939).

yield of the *trans* product II. Three hours in boiling acetonitrile with an excess of silver benzoate was required to desulfurize the 1-thiopyranoside and the product, 1-*O*-benzoyl- β -D-glucopyranose (isolated as its tetraacetate), was obtained in only 6.2% yield. The role, if any, of neighboring groups in this type of reaction is not known although it should be observed that ethyl 1-thio- β -D-glucopyranoside is a *trans*-glycoside while I is a *cis*-glycoside. However, it seems from the present work that alkyl 1-thioaldofuranosides may be more reactive toward silver benzoate than alkyl 1-thioaldopyranosides.

In the condensation of ethyl 1-thio- β -D-glucopyranoside with silver benzoate 2-*O*-benzoyl-D-glucose as its tetraacetate was isolated² in 5% yield and evidence found for the formation of a trace of free D-glucose. Both anomeric 1-*O*-benzoyl-D-glucopyranoses had doubtless been formed, the *cis* ester, however, undergoing acyl migration under the conditions of the reaction. With the more stable mesitoyl group, both anomeric 1-*O*-mesityl-D-glucopyranoses were isolated.² A considerable quantity of crystalline by-product was found after the formation of the *trans* ester 1,5-di-*O*-benzoyl- α -L-arabinose (II). This proved to be heterogeneous and efforts to resolve the mixture were unsatisfactory; it seems likely that products derived from the migration of the 1-*O*-benzoyl group of 1,5-di-*O*-benzoyl- β -L-arabinose may have been present.

In contrast to silver benzoate, mercuric acetate reacts rapidly with ethyl 5-*O*-benzoyl-1-thio- β -L-arabinoside (I) in acetonitrile at room temperature to give, in 34% yield, a mono-*O*-acetyl-mono-*O*-benzoyl-L-arabinose. This ester reduced 1.03 molar equivalents of sodium metaperiodate at room temperature during twenty-four hours and was stable in 20% aqueous pyridine. These facts, together with the analogy provided by II, indicate the *trans* ester structure VI.⁷ *p*-Nitrobenzoylation of VI gave an *O*-acetyl-*O*-benzoyl-di-*O*-*p*-nitrobenzoyl-L-arabinose which was converted to the bromide V, identical with that obtained from IV.

The rotation of the 5-*O*-benzoyl-2,3-di-*O*-*p*-nitrobenzoyl-L-arabinosyl bromide (V), $[\alpha]_D^{20} -40.0^\circ$ in chloroform, indicates that it is probably the α -L-anomer V. It may be noted that Ness and Fletcher⁸ found 2,3,5-tri-*O*-benzoyl- α -D-arabinosyl bromide to be the predominant anomer formed when methyl α -D-arabinofuranoside tribenzoate is treated with hydrogen bromide.⁹

(7) The *cis* ester 1,3,5-tri-*O*-benzoyl- α -D-ribose is readily converted to 2,3,5-tri-*O*-benzoyl-D-ribose by aqueous pyridine: R. K. Ness and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **78**, 4710 (1956). For a general discussion of this rearrangement see H. G. Fletcher, Jr., *Record Chem. Progr. Kresge-Hooker Sci. Libr.*, **19**, 147 (1958).

(8) R. K. Ness and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **80**, 2007 (1958).

(9) The "normal" anomer in the arabinopyranose series is, however, β .

EXPERIMENTAL¹⁰

1,5-Di-*O*-benzoyl- α -L-arabinose (II) from ethyl 5-*O*-benzoyl-1-thio- β -L-arabinoside (I). To a solution of 2.00 g. of ethyl 5-*O*-benzoyl-1-thio- β -L-arabinoside¹¹ in 30 ml. of acetonitrile was added 3.08 g. (2.01 molar equivalents) of silver benzoate. The mixture was refluxed and stirred for 1 hr. and then cooled and filtered, the solid being washed several times with fresh acetonitrile. Solvent was removed from the combined filtrate and washings and the residue dissolved in dichloromethane. After filtration through decolorizing carbon the solution was concentrated to give 2.84 g. of brownish sirup which was dissolved in 50 ml. of benzene and adsorbed on a column of 50 g. of alumina ("Woelm," Grade III, acid-washed). Elution with 500 ml. of benzene, followed by removal of solvent, afforded 879 mg. of sirup which crystallized spontaneously. Recrystallized twice from a mixture of ether and pentane, the nearly pure product (470 mg., 20%) melted at 111–115° and had $[\alpha]_D^{20} -31.2^\circ$ in chloroform. Two further recrystallizations from the same solvent mixture gave pure 1,5-di-*O*-benzoyl- α -L-arabinose; m.p. 113–115°, $[\alpha]_D^{20} -34.4^\circ$ (CHCl₃, *c* 1.21).

Anal. Calcd. for C₁₉H₁₈O₇ (358.33): C, 63.68; H, 5.07. Found: C, 63.33; H, 5.19.

Further elution of the alumina with benzene-ether (1:1, 500 ml.) gave a second fraction (1.1 g.) which, from ether-pentane afforded 800 mg. of crystalline material melting as 95–105° and rotating $[\alpha]_D^{20} +36.1^\circ$ in chloroform. Attempts to obtain a homogeneous product from this were unsuccessful. A sample (100 mg.) was *p*-nitrobenzoylated to give 73 mg. of 1,5-di-*O*-benzoyl-2,3-di-*p*-nitrobenzoyl- α -L-arabinose identical with the ester prepared from pure 1,5-di-*O*-benzoyl- α -L-arabinose as described later in this paper. The total yield of 1,5-di-*O*-benzoyl- α -L-arabinose in this reaction is therefore at least 33%.

α -L-Arabinofuranose tetrabenzoate (III) from 1,5-di-*O*-benzoyl- α -L-arabinose (II). Pure 1,5-di-*O*-benzoyl- α -L-arabinose (120 mg.) was benzoylated in the usual manner with benzoyl chloride (0.30 ml.) in pyridine (1 ml.) to give, after removal of the reagents, a sirup which, from ether-pentane solution, afforded 150 mg. (79%) of α -L-arabinofuranose tetrabenzoate, melting at 114–118°. After recrystallization from ethanol it melted at 115–118° and showed $[\alpha]_D^{20} -28.1^\circ$ (CHCl₃, *c* 1.06). An authentic sample of α -L-arabinofuranose tetrabenzoate, prepared through the condensation of 2,3,5-tri-*O*-benzoyl- α -L-arabinosyl bromide with silver benzoate as described earlier by Ness and Fletcher⁸ for its enantiomorph, showed m.p. 115–117° and $[\alpha]_D^{20} -28.5^\circ$ (CHCl₃, *c* 1.56). A mixed melting point was undepressed.

Anal. Calcd. for C₃₂H₂₆O₈ (566.54): C, 69.96; H, 4.63. Found: C, 69.99; H, 4.72.

1,5-Di-*O*-benzoyl-2,3-di-*O*-*p*-nitrobenzoyl- α -L-arabinose (IV). Pure 1,5-di-*O*-benzoyl- α -L-arabinose (110 mg.) was added to a solution of 200 mg. of *p*-nitrobenzoyl chloride in 2 ml. of pyridine. The mixture was kept at room temperature for 3 hr. and a crystalline mass then precipitated through the addition of ca. 15 ml. of water. The crude product was washed successively with water and methanol; recrystallization from benzene-pentane then afforded 190 mg. (94%) of fine needles melting at 170–172°. After one further recrystallization the ester melted at 171–172° and showed $[\alpha]_D^{20} -9.6^\circ$ in chloroform (*c* 1.09).

Anal. Calcd. for C₃₃H₂₄N₂O₁₃ (656.54): C, 60.37; H, 3.68; N, 4.27. Found: C, 60.56; H, 3.86; N, 4.18.

5-*O*-Benzoyl-2,3-di-*O*-*p*-nitrobenzoyl- α -L-arabinosyl bromide (V) from 1,5-di-*O*-benzoyl-2,3-di-*O*-*p*-nitrobenzoyl- α -L-arabinose (IV). 1,5-Di-*O*-benzoyl-2,3-di-*O*-*p*-nitrobenzoyl- α -L-arabinose (100 mg.) was dissolved in 5 ml. of dichloro-

(10) Melting points are corrected.

(11) Using the method of Reist, Hart, Goodman, and Baker (ref. 5), the yields of this compound varied unaccountably from 30–67%.

methane and the solution treated with 1 ml. of a 30% solution of hydrogen bromide in glacial acetic acid. The reaction mixture was kept at room temperature for 30 min., diluted with dichloromethane and washed successively with water, saturated aqueous sodium bicarbonate and water. Moisture was removed with granular sodium sulfate and the solution, after filtration through decolorizing carbon, concentrated *in vacuo*. Dissolved in a mixture of benzene and pentane (1:1), the residue crystallized as short needles: 57 mg. (61%), m.p. 160–161°. Recrystallization failed to change this value. The pure bromide showed $[\alpha]_D^{20} -40.0^\circ$ in U.S.P. chloroform (*c* 0.73) and could be recovered unchanged from this solvent.

Anal. Calcd. for $C_{25}H_{19}BrN_2O_{11}$ (615.35): C, 50.75; H, 3.11; N, 4.56; Br, 12.99. Found: C, 50.95; H, 3.05; N, 4.74; Br, 12.68.

1,5-Di-O-benzoyl-2,3-di-O-p-nitrobenzoyl- α -L-arabinose (IV) from 5-O-benzoyl-2,3-di-O-p-nitrobenzoyl- α -L-arabinosyl bromide (V). A solution of the bromide V (76 mg.) in 10 ml. of dry benzene was stirred with 150 mg. of silver benzoate for 30 min. at room temperature. The mixture was then filtered through decolorizing carbon, the filtrate evaporated *in vacuo* and the residue crystallized from benzene-pentane to give 51 mg. (62%) of 1,5-di-O-benzoyl-2,3-di-O-p-nitrobenzoyl- α -L-arabinose, melting at 169–170°; the substance failed to depress the melting point of a sample prepared through the *p*-nitrobenzoylation of 1,5-di-O-benzoyl- α -L-arabinose.

1-O-Acetyl-5-O-benzoyl- α -L-arabinose (VI) from ethyl 5-O-benzoyl-1-thio- β -L-arabinoside (I). To a stirred solution of 5.0 g. of ethyl 5-O-benzoyl-1-thio- β -L-arabinoside in 125 ml. of acetonitrile was added 5.90 g. (1.1 molar equivalents) of mercuric acetate. The salt dissolved within a few minutes and then a precipitate began to form. The mixture was stirred for 2 hr., filtered and the filtrate concentrated *in vacuo*. After solution in dichloromethane the residue was treated with hydrogen sulfide and the solution filtered through decolorizing carbon. Evaporation of the filtrate afforded a partly crystalline mass (5.53 g.) which was recrystallized from 50 ml. of ether to yield 2.12 g. of crude 1-O-acetyl-5-O-benzoyl- α -L-arabinose. After two recrystallizations from a mixture of ethyl acetate and pentane the pure ester (1.70 g., 34%) was obtained as plates melting at 117–118°, $[\alpha]_D^{20} -49.3^\circ$ (*c* 0.53). The substance failed to mutarotate in 20% aqueous pyridine and could be recovered unchanged after 24 hr. in this solvent mixture. In

aqueous solution it reduced 1.03 molar equivalents of sodium periodate in 24 hr. at room temperature.

Anal. Calcd. for $C_{14}H_{16}O_7$ (296.27): C, 56.75; H, 5.44. Found: C, 56.77; H, 5.47.

1-O-Acetyl-5-O-benzoyl-2,3-di-O-p-nitrobenzoyl- α -L-arabinose (VII). To a solution of 1.25 g. of *p*-nitrobenzoyl chloride in 10 ml. of pyridine was added 500 mg. of 1-O-acetyl-5-O-benzoyl- α -L-arabinose. After standing at room temperature overnight the mixture was diluted with water and the product extracted with dichloromethane. The extract was washed successively with 3*N* sulfuric acid, saturated aqueous sodium bicarbonate and water. Moisture was removed with granular sodium sulfate and the solution filtered through decolorizing carbon. Removal of solvent left an amorphous residue; dissolved in a mixture of benzene (10 ml.) and pentane (10 ml.) this yielded 750 mg. (75%) of 1-O-acetyl-5-O-benzoyl-2,3-di-O-p-nitrobenzoyl- α -L-arabinose as very pale yellow prisms melting at 149–151°, $[\alpha]_D^{20} +38.6^\circ$ in chloroform. A further recrystallization failed to change this melting point but raised the rotation to $[\alpha]_D^{20} +39.7^\circ$ ($CHCl_3$, *c* 0.82).

Anal. Calcd. for $C_{28}H_{22}N_2O_{13}$ (594.48): C, 56.57; H, 3.73; N, 4.71. Found: C, 56.83; H, 3.65; N, 4.70.

5-O-Benzoyl-2,3-di-O-p-nitrobenzoyl- α -L-arabinosyl bromide (V) from 1-O-acetyl-5-O-benzoyl-2,3-di-O-p-nitrobenzoyl- α -L-arabinose (VII). 1-O-Acetyl-5-O-benzoyl-2,3-di-O-p-nitrobenzoyl- α -L-arabinose (295 mg.) was dissolved in 8 ml. of dichloromethane and 2 ml. of a 30% solution of hydrogen bromide in glacial acetic acid added. Mutarotation ceased after 3 min. at 20°; after 23 min. the solution was diluted with 15 ml. of dichloromethane and washed successively with water, saturated aqueous sodium bicarbonate and water. Moisture was removed with granular sodium sulfate, the solution filtered through decolorizing carbon and solvent removed *in vacuo*. From its solution in a mixture of 10 ml. of benzene and 10 ml. of pentane the residue afforded 230 mg. (75%) of 5-O-benzoyl-2,3-di-O-p-nitrobenzoyl- α -L-arabinosyl bromide melting at 160–161° either alone or in admixture with a sample prepared as described earlier from 1,5-di-O-benzoyl-2,3-di-O-p-nitrobenzoyl- α -L-arabinose.

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Contributions to the Study of Marine Products.

L. Phospholipids of Sponges^{1,2}

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The phospholipid fractions of two sponges, *Lissodendoryx isodyctialis* and *Speciospongia vesparia*, have been isolated and characterized. That from *L. isodyctialis* was found to consist of sphingosine phosphate fatty acid esters, free of choline and sugars; the other, from *S. vesparia*, was a lecithin containing aldehyde in an enol ether linkage.

The study of the phospholipids of marine invertebrates has been continued as an extension of

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our comparative studies on the composition and evolution of the lipids of these organisms. In the previous report⁵ the importance of isolation fol-

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