Preparation and Properties of 3,5-Di-*O*-*p*-anisoyl-1,2-dideoxy-D-*erythro*-pentofuranos-1-ene. Various *p*-Anisoylated Derivatives of D-Ribofuranose[1a]

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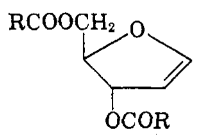
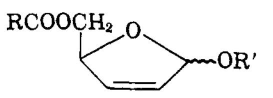
A di-*O*-*p*-anisoyl derivative of 1,2-dideoxy-D-*erythro*-pentofuranos-1-ene has been synthesized and compared with the previously known di-*O*-benzoyl derivative particularly in regard to its reactivity with methanol and with water. Theoretical considerations suggest that the more nucleophilic the substituent at C-3, the less readily it will be eliminated with simultaneous migration of the double bond from C-1 to C-2. Although this was observed, its elimination was not sufficiently retarded to allow the direct addition of methanol or water to the double bond of the glycal under the conditions employed.

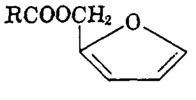
Recently 3,5-di-*O*-benzoyl-1,2-dideoxy-D-*erythro*-pentofuranos-1-ene (1,4-anhydro-3,5-di-*O*-benzoyl-2-deoxy-D-*erythro*-pentose-1-enol) (Ia),[2] the first known glycal derivative that possessed a furanose structure, was prepared and found to be extremely labile. It reacted at room temperature with methanol to form an unsaturated glycoside with the elimination of the benzoyloxy group at C-3 (Ia → IIa) and with water to form furfuryl benzoate (IIIa).



Ia, R = phenyl
b, R = *p*-methoxyphenyl



IIa, R = phenyl; R' = CH_3
b, R = *p*-methoxyphenyl; R' = H
c, R = *p*-methoxyphenyl; R' = CH_3
d, R = phenyl; R' = H

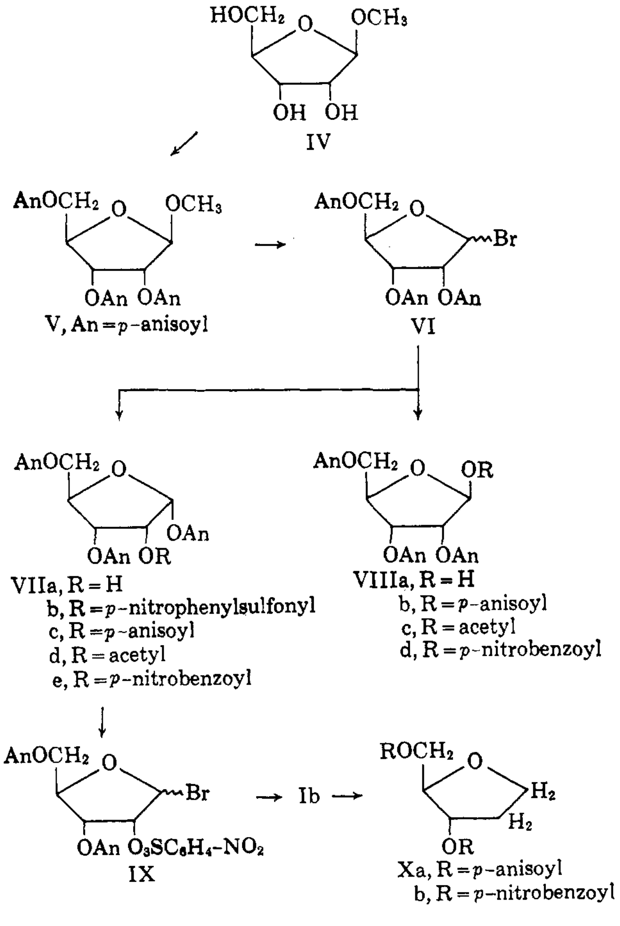


IIIa, R = phenyl
b, R = *p*-methoxyphenyl

Prevention of this elimination should increase the possibility of a normal addition to the double bond similar to the addition of purines to 2,3-dihydro-4H-pyrane,[3] 2,3-dihydrofuran,[4] and their derivatives as reported by Robins and co-workers. Such an addition would yield 2-deoxy-D-*erythro*-pentose derivatives. It was anticipated that the greater the nucleophilicity of the substituent at C-3 (of I), the less would be the tendency to form unsaturated products. Therefore, 3,5-di-*O*-*p*-anisoyl-1,2-dideoxy-D-*erythro*-pentofuranos-1-ene (Ib) was synthesized and some of its properties were investigated.

The glycal Ib was prepared by the following route: methyl β-D-ribofuranoside[5,6] (IV) → methyl 2,3,5-tri-*O*-*p*-anisoyl-β-D-ribofuranoside[7] (V) → sirupy 2,3,5-tri-*O*-*p*-anisoyl-D-ribofuranosyl bromide (VI) → 1,3,5-tri-*O*-*p*-anisoyl-α-D-ribofuranose (VIIa) [and 2,3,5-tri-*O*-*p*-anisoyl-β-D-ribofuranose (VIIIa)] → 1,3,5-tri-*O*-*p*-anisoyl-2-*O*-*p*-nitrophenylsulfonyl-α-D-ribofuranose (VIIb) → 3,5-di-*O*-*p*-anisoyl-2-*O*-*p*-nitrophenylsulfonyl-D-ribofuranosyl bromide (IX) → Ib (see Scheme I).

SCHEME I



That VIIa had a free hydroxyl group at a position other than C-1 was demonstrated by treatment of its *p*-nitrophenylsulfonyl derivative VIIb with hydrogen bromide and acetic acid to form the bromide IX with the loss of *p*-anisic acid. Because of the eventual formation of the glycal Ib from VIIb and because of

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[1] (a) Presented in part at the Meeting-in-miniature held jointly by the Chemical Society of Washington and the Maryland Section of the American Chemical Society, May 1, 1964. (b) Chemical Foundation Fellow, 1963–1965.

[2] R. K. Ness and H. G. Fletcher, Jr., *J. Org. Chem.*, **28**, 435 (1963).

[3] R. K. Robins, E. F. Godefroi, E. C. Taylor, L. R.Lewis, and A. Jackson, *J. Am. Chem. Soc.*, **83**, 2574 (1961).

[4] L. R. Lewis, F. H. Schneider, and R. K. Robins, *J. Org. Chem.*, **26**, 3837 (1961).

[5] I. Augestad and E. Berner, *Acta Chem. Scand.*, **10**, 911 (1956).

[6] R. Barker and H. G. Fletcher, Jr., *J. Org. Chem.*, **26**, 4605 (1961).

[7] L. J. Haynes, N. A. Hughes, G. W. Kenner, and A. Todd, *J. Chem. Soc.*, 3727 (1957). Although these workers did not specify the anomeric configuration, the present preparation of V from crystalline methyl β-D-ribofuranoside reveals V to be the β-derivative.

the analogy of the formation and properties of VIIa to those of 1,3,5-tri-*O*-benzoyl-α-D-ribofuranose,[8,9] the hydroxyl group was assigned to C-2.[10] The migration of an acyl group from C-2 to C-1 during hydrolysis of an acylated halide under acid or neutral conditions is now a commonly observed phenomenon.[11–13] The migration occurs in the reverse direction (C-1 to C-2) if the substance, which possesses a hydroxyl group at C-2 *cis* to the acyloxy group at C-1, is dissolved in aqueous pyridine,[9] in methanolic ammonia,[14a] or even in dried acetone.[14b] In aqueous pyridine VIIa was readily converted to VIIIa. Thus VIIa has the *cis* configuration at C-1 and C-2 and is an α-derivative. The structure of VIIIa was shown to be a 1-hydroxy β-compound by acetylation in good yield to the already known 1-*O*-acetyl-2,3,5-tri-*O*-*p*-anisoyl-β-D-ribofuranose (VIIIc) of Haynes[7] and co-workers and by the preparation of VIIIc from the reaction of silver acetate and VI. This latter reaction would be expected to form a β-*trans* product.[15] Rotatory considerations[16] of the *p*-anisoylation products of VIIa and VIIIa substantiate these anomeric assignments, the product VIIc (from VIIa) being more dextrorotatory than the product VIIIb (from VIIIa).

The structure of the glycal Ib was demonstrated by (a) its rapid decolorization of bromine–carbon tetrachloride; (b) its conversion on hydrogenation to 1,4-anhydro-3,5-di-*O*-*p*-anisoyl-2-deoxy-D-*erythro*-pentitol (Xa), which afforded, on replacement of its *p*-anisoyl groups by *p*-nitrobenzoyl groups, the known 1,4-anhydro-2-deoxy-D-*erythro*-pentitol di-*p*-nitrobenzoate (Xb)[17]; and (c) its n.m.r. spectrum which is similar to that of Ia[2] except for differences due to the presence of the methoxyl groups.

Methyl 5-*O*-*p*-anisoyl-2,3-dideoxy-D-*glycero*-pentofuranosid-2-ene (IIc) was obtained (along with furfuryl *p*-anisoate IIIb) in crystalline form from a methanolic solution of Ib. The structure of IIc was deduced from (a) its n.m.r. spectrum, which is similar to that of IIa[2] except for differences due to the presence of the methoxyl groups on the benzene ring; (b) its rapid decolorization of bromine–carbon tetrachloride; and (c) its gradual decomposition at room temperature to IIIb.

From the reaction of Ib and water, a 93% yield of *p*-anisic acid was obtained. Thin layer chromatography of the remaining sirupy product revealed two spots—the faster one corresponding to IIIb. When the sirupy product whose infrared spectrum showed hydroxyl absorption[18] at 3500 cm.$^{-1}$ was methylated (no longer absorbing at 3500 cm.$^{-1}$) and chromatographed (thin layer) on silica gel, two spots were again observed, this time corresponding to IIc and IIIb. From this methylation product, IIc was actually isolated, albeit in low yield. The isolation of IIc from the methylation reaction strongly indicates that the product from the reaction of Ib and water consisted of IIIb and 5-*O*-*p*-anisoyl-2,3-dideoxy-D-*glycero*-pentofuranos-2-ene (IIb).

The first-order reaction rates of the reactions of Ia and of Ib with methanol and with water were calculated from polarimetric measurements and are tabulated in Table I. The rates for the benzoylated glycal Ia were found to be double those for the *p*-anisoylated glycal Ib. This observation is in agreement with the prediction that the greater the nucleophilic character of the substituent at C-3 the less readily would it be eliminated. Chromatography of all of the reaction products from Ib revealed no organic products other than *p*-anisic acid, IIc, IIb, or IIIb. Thus the retardation attributable to the *p*-anisoyloxy group at C-3 was not sufficient to allow direct addition to the double bond to occur under the conditions employed.

TABLE I

THE FIRST-ORDER RATE CONSTANTS FOR THE REACTIONS OF THE GLYCAL DERIVATIVES Ia AND Ib WITH METHANOL AND WITH WATER

	Rate constant × 10^2, ln, min.	
Reaction media	Ia[a]	Ib
Methanol–dichloromethane	1.4	0.65
	1.2	
Methanol–dichloromethane–*p*-toluenesulfonic acid		3–4
Water–acetone	1.1	0.53
	1.0	
Water–acetone–pyridine	1.1	
Water–acetone–acetic acid	1.4	

[a] Calculated from previously observed polarimetric data; *cf.* ref. 2.

Since no evidence for the formation of 2-deoxy-D-*erythro*-pentofuranosides was obtained in the reactions of Ib with methanol or with water, the acidic conditions of Robins and co-workers[4] were used for the methanol reaction. Even in the presence of *p*-toluenesulfonic acid, no formation of 2-deoxy-D-*erythro*-pentosides was detected by thin layer chromatography.

The data listed in Table I also reveal a fivefold increase in the reactivity of Ib with methanol when *p*-toluenesulfonic acid is present. In a previous qualitative interpretation[2] of the polarimetric data of Ia with water alone or in the presence of pyridine or acetic acid, no definite acid or base catalysis was observed. Calculations of the first-order rate constants for the three conditions, however, show the rate may be very slightly increased by the presence of the acetic acid. The reactions of Ia or Ib whereby the substituent at C-3 is eliminated thus appear to be acid catalyzed.

In passing we may note that Haynes, Hughes, Kenner, and Todd[7] had observed an increased neighboring group participation role for the *p*-anisoyl group at C-2, in directing a nucleophile into the *trans* 1-position, over that of the benzoyl group at C-2, but because of a lack

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(8) R. K. Ness and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **76**, 1663 (1954)

(9) R. K. Ness and H. G. Fletcher, Jr., *ibid.*, **78**, 4710 (1956).

(10) Acetylation of VIIa gave the same substance which Haynes and co-workers[7] had obtained in low yield and tentatively described as 2-*O*-acetyl-1,3,5-tri-*O*-*p*-anisoyl-D-ribofuranose.

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

(12) W. M. Corbett, J. Kidd, and A. M. Liddle, *J. Chem. Soc.*, 616 (1960), and references cited therein.

(13) (a) B. Helferich and J. Zirner, *Ber.*, **95**, 2604 (1962); (b) *ibid.*, **96**, 385 (1963).

(14) (a) H. B. Wood, Jr., and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **78**, 2849 (1956); (b) C. P. J. Glaudemans and H. G. Fletcher, Jr., *J. Org. Chem.*, **29**, 3286 (1964).

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

(16) C. S. Hudson, *J. Am. Chem. Soc.*, **31**, 66 (1909).

(17) A. K. Bhattacharya, R. K. Ness, and H. G. Fletcher, Jr., *J. Org. Chem.*, **28**, 428 (1963).

(18) During the earlier investigation[2] in which Ia reacted with water, it was observed that the sirupy product showed hydroxyl absorption but otherwise its spectrum was identical with that of IIIa. Most probably 5-*O*-benzoyl-2,3-dideoxy-D-*glycero*-pentofuranos-2-ene (IId) was present as well as IIIa.

of consistency in the proportions of anomers formed concluded that the use of *p*-anisoyl derivatives offered no real advantage over that of benzoylated compounds. Similarly, we noted no advantage in the use of the *p*-anisoylated bromide VI, over that of the corresponding benzoylated bromide, in the preparation of 1,3,5-tri-O-acylated D-ribose compounds. In fact the yield of the benzoylated derivative,[8,9] 1,3,5-tri-*O*-benzoyl-α-D-ribose, appears to be superior to that of its *p*-anisoyl analog, VIIa.

Experimental[19]

Methyl 2,3,5-Tri-*O*-*p*-anisoyl-β-D-ribofuranoside (V).—Crystalline methyl β-D-ribofuranoside[6] (IV, 5.0 g.) was acylated in 30 ml. of dry pyridine by the addition of 22 g. of *p*-anisoyl chloride at 0°. After 2 hr. at room temperature, the product was isolated in the usual manner and crystallized from ethanol: 15.2 g. (87.4%), m.p. 82–86°. Two recrystallizations from the same solvent gave needles of pure V: 11.4 g., m.p. 87–88°, $[\alpha]^{20}\mathrm{D}$ +109.2° (*c* 1.38, chloroform); lit.[7] m.p. 86–88°, $[\alpha]^{20}\mathrm{D}$ +109.5° (chloroform).

1,3,5-Tri-*O*-*p*-anisoyl-α-D-ribofuranose (VIIa) *via* **2,3,5-Tri-*O*-*p*-anisoyl-D-ribofuranosyl Bromide (VI).**—Hydrogen bromide in glacial acetic acid (12 ml., 32%) was added to a solution of 15.0 g. of V in 10 ml. of dichloromethane. After 10 min., 100 ml. of dichloromethane was added and the solution was washed with ice–water and with cold sodium bicarbonate solution. Moisture was removed (magnesium sulfate) and evaporation of solvent under reduced pressure gave the crude bromide VI. To the solution of VI in 50 ml. of acetone was added 7 ml. of water. Thirty minutes later, dichloromethane (100 ml.) was added and the solution was washed with water and with saturated sodium bicarbonate solution and dried with magnesium sulfate. After displacement of solvent, the product was crystallized from cold ethyl ether (50 ml.): 5.4 g. (38%), m.p. 116–117°. Two recrystallizations from ethanol gave pure VIIa: 4.3 g. (28%), m.p. 126–127°, $[\alpha]^{20}\mathrm{D}$ +90.2° (*c* 1.9, chloroform).

Anal. Calcd. for $C_{29}H_{28}O_{11}$ (552.5): C, 63.04; H, 5.11. Found: C, 62.81; H, 5.17.

2,3,5-Tri-*O*-*p*-anisoyl-β-D-ribofuranose (VIIIa).—The ethereal mother liquor from the above preparation of VIIa gave upon concentration a sirup which crystallized spontaneously after several days at room temperature. The crystalline magma was washed with several small portions of ethyl ether. The crystals were dissolved in 100 ml. of ethyl ether and the solution, upon the slow addition of 200 ml. of pentane, deposited crystalline VIIIa: m.p. 110–111°, $[\alpha]^{20}\mathrm{D}$ +105.1° (*c* 2.6, chloroform).

Anal. Calcd. for $C_{29}H_{28}O_{11}$ (552.5): C, 63.04; H, 5.11. Found: C, 63.39; H, 5.23.

Conversion of VIIa to VIIIa.—Compound VIIa (0.1020 g.) in 5.00 ml. of dry pyridine in a 1.5-dm. tube at 20° showed $\alpha^{20}\mathrm{D}$ +1.79°, no mutarotation being observed after 2 hr. At zero time, 1.00 ml. of water at 0°[20] was added: $\alpha^{20}\mathrm{D}$ +1.512 (5.0 min.), +1.514 (10.0), +1.554 (30), +1.672 (160), +1.786 (380), +1.896 (1320), and +1.924° (1680, constant). The solvent was removed *in vacuo* and the resulting sirup was dissolved in 5 ml. of ethyl ether and then 10 ml. of petroleum ether was added. After standing overnight in the refrigerator, VIIIa crystallized: 0.0822 g. (80.6%), m.p. 110–111°, m.p. (mixed with VIIIa prepared above) 110–111°, $[\alpha]^{20}\mathrm{D}$ +102.2° (*c* 1.18, chloroform).

1,2,3,5-Tetra-*O*-*p*-anisoyl-α-D-ribofuranose (VIIc).—Compound VIIa (1.20 g.) was added to a cold solution (0°) of pyridine (15 ml.) and *p*-anisoyl chloride (0.6 g.). After 5 min. at 0° and 16 hr. at 22°, the reaction mixture was worked up in the usual manner. From ethanol, crystals of VIIc slowly formed: 1.25 g. (83.8%), m.p. 120–122°, $[\alpha]^{20}\mathrm{D}$ +105.8° (*c* 1.3, chloroform).

Anal. Calcd. for $C_{37}H_{34}O_{13}$ (686.6): C, 64.72; H, 4.99. Found: C, 64.60; H, 4.91.

1,2,3,5-Tetra-*O*-*p*-anisoyl-β-D-ribofuranose (VIIIb).—Compound VIIIa (1.00 g.) was anisoylated in a manner similar to the above preparation of VIIc yielding a sirup which crystallized spontaneously from ethanol: m.p. 140–142°. A recrystallization from ethanol gave needles of pure VIIIb: 0.96 g. (77%), m.p. 142–143°, $[\alpha]^{20}\mathrm{D}$ +42.0° (*c* 1.87, chloroform).

Anal. Calcd. for $C_{37}H_{34}O_{13}$ (686.6): C, 64.72; H, 4.99. Found: C, 64.57; H, 5.25.

2-*O*-Acetyl-1,3,5-tri-*O*-*p*-anisoyl-α-D-ribofuranose (VIId).—Compound VIIa (0.25 g.) was acetylated by addition to a cold (0°) solution of 10 ml. of dry pyridine and 10 ml. of acetic anhydride. After 5 min. at 0° and 4 hr. at 25°, the reaction mixture was poured into 100 ml. of ice and water, yielding 0.18 g. of crystalline material (m.p. 89–94°). One recrystallization from ethanol gave 0.14 g. (53%) of pure VIId: m.p. 117–119° (unchanged by another recrystallization), $[\alpha]^{20}\mathrm{D}$ +80.2° (*c* 1.3, chloroform). Haynes, *et al.*,[7] tentatively identified one of their products as 2-*O*-acetyl-1,3,5-tri-*O*-*p*-anisoyl-D-ribofuranose: m.p. 117–119°, $[\alpha]^{20}\mathrm{D}$ +80.5° (chloroform).

Anal. Calcd. for $C_{31}H_{30}O_{12}$ (594.6): C, 62.62; H, 5.09. Found: C, 62.59; H, 5.15.

1-*O*-Acetyl-2,3,5-tri-*O*-*p*-anisoyl-β-D-ribofuranose (VIIIc). **A. From VIIIa.**—Acetylation of 1.15 g. of VIIIa with 10 ml. of dry pyridine and 10 ml. of acetic anhydride for 4 hr. at 25° followed by the usual isolation procedure gave, from 20 ml. of ethanol, needles of VIIIc: 0.84 g. (68%), m.p. 117–120°. Two recrystallizations from ethanol afforded pure VIIIc: m.p. 123–124°, $[\alpha]^{20}\mathrm{D}$ +82.9° (*c* 1.9, chloroform); lit.[7] m.p. 123–125°, $[\alpha]^{20}\mathrm{D}$ +84.4° (chloroform).

B. From VI.—Compound VI, prepared from 2.54 g. of V, in 30 ml. of benzene was stirred with 2.5 g. of silver acetate for 18 hr. After filtration and removal of solvent, 1.72 g. (from 40 ml. of ethanol) (64.6%) of VIIIc (m.p. 118–121°) was obtained. Recrystallization from ethanol gave pure VIIIc: 1.44 g., m.p. 123–124°.

1,3,5-Tri-*O*-*p*-anisoyl-2-*O*-(*p*-nitrobenzoyl)-α-D-ribofuranose (VIIe).—The reaction of 1.8 g. of VIIa with 0.6 g. of *p*-nitrobenzoyl chloride in 25 ml. of dry pyridine for 5 min. at 0° and 4 hr. at 22° gave, after isolation in the usual manner, a yellow sirup. Crystals formed when the sirup was dissolved in ethanol and the solution was left overnight at 5°: 1.9 g. (83%), m.p. 126–134°. After three recrystallizations from ethanol, pure VIIe was obtained: m.p. 130–137°, $[\alpha]^{20}\mathrm{D}$ +62.5° (*c* 5.8, chloroform).

Anal. Calcd. for $C_{36}H_{31}O_{14}N$ (701.6): C, 61.62; H, 4.45; N, 1.99. Found: C, 61.34; H, 4.64; N, 2.01.

2,3,5-Tri-*O*-*p*-anisoyl-1-*O*-(*p*-nitrobenzoyl)-β-D-ribofuranose (VIIId).—Compound VIIIa (0.230 g.) was added to a solution of 10 ml. of pyridine and 0.120 g. of *p*-nitrobenzoyl chloride at 0°. After a few min. at 0° and 24 hr. at 22°, the reaction mixture was worked up in the usual manner. From 70 ml. of ethanol, 0.230 g. (78.8%) of crystals melting at 151–152° was obtained. A recrystallization from 1:9 acetone–ethanol did not alter the melting point: $[\alpha]^{20}\mathrm{D}$ +35.3° (*c* 1.47 chloroform).

Anal. Calcd. for $C_{36}H_{31}O_{14}N$ (701.6): C, 61.62; H, 4.45; N, 1.99. Found: C, 61.69; H, 4.69; N, 2.13.

1,3,5-Tri-*O*-*p*-anisoyl-2-*O*-(*p*-nitrophenylsulfonyl)-β-D-ribofuranose (VIIb).—Compound VIIa (5.4 g.) was added to a solution of 2 g. of *p*-nitrobenzenesulfonyl chloride in 20 ml. of dry pyridine at 0°. After standing at room temperature overnight, the excess of reagent was decomposed with a little ice and the product was worked up as for V to yield frothy, sirupy VIIb: 5.9 g. (82%), $[\alpha]^{20}\mathrm{D}$ +65.8° (*c* 0.76, chloroform). The product was homogeneous on silica gel G[21] by thin layer chromatography and showed no hydroxyl absorption in the 3500-cm.$^{-1}$ region.

3,5-Di-*O*-*p*-anisoyl-2-*O*-(*p*-nitrophenylsulfonyl)-D-ribofuranosyl Bromide (IX).—Sirupy VIIb (5.9 g.) in 20 ml. of glacial acetic acid was treated 1 hr. with 20 ml. of 32% hydrogen bromide in acetic acid. Dichloromethane was added and the solution was washed with ice–water and cold sodium bicarbonate solution, dried (magnesium sulfate), and concentrated *in vacuo* to a yellowish brown sirup, which crystallized from 100 ml. of ethyl ether: 4.1 g. (77%), m.p. 115–117°. Two recrystallizations from 115 ml. of dichloromethane–ethyl ether (3:20) gave the pure crystalline IX: 3.5 g., m.p. 116–117°, $[\alpha]^{20}\mathrm{D}$ +24.9°[22] (*c* 1.5, dichloromethane).

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[19] All melting points are corrected and were taken in open capillaries unless otherwise stated.

[20] The use of water at 0° does not completely compensate for the slight exothermic character of the dissolution of water in anhydrous pyridine. In a blank, the temperature rose to 24°.

[21] Brinkmann Instruments, Inc., Great Neck, L. I., N. Y., distributors for E. Merck AG, Darmstadt, Germany.

[22] *Comparison of this rotation with the +17° of the benzoylated analog* [R. K. Ness, *J. Org. Chem.*, **27**, 1155 (1962)], which is known to possess the β-configuration, suggests that compound IX too possesses the β-configuration.

Anal. Calcd. for $C_{27}H_{24}BrNO_{12}S$ (666.5): C, 48.66; H, 3.63; Br, 11.99; N, 2.01; S, 4.81. Found: C, 48.70; H, 3.68; Br, 12.18; N, 2.32; S, 4.90.

3,5-Di-*O*-*p*-anisoyl-1,2-dideoxy-D-*erythro*-pentofuranos-1-ene (Ib).—Crystalline IX (3.5 g.) was added with stirring to a solution of 3.5 g. of sodium iodide in 30 ml. of acetone at 5°. The bromide dissolved promptly and a brown coloration became immediately apparent. After 4 hr. at 5°, the reaction mixture was filtered and the residue (1.87 g.) was washed with 20 ml. of acetone. The combined filtrate and washings were concentrated to dryness at room temperature and under reduced pressure. Benzene (100 ml.) was added and the resulting solution was washed with saturated sodium bicarbonate solution containing sodium thiosulfate. After drying (magnesium sulfate) the solution (negative to Beilstein test) was concentrated under reduced pressure (35°) to 2.2 g. of a pale yellow sirup. Crude Ib crystallized from ethyl ether and pentane: m.p. 80–87°. Two recrystallizations from the same solvent and the use of activated charcoal gave 1.37 g. (67.8%) of pure Ib: m.p. 85–87°, $[\alpha]^{20}_{D}$ +287° (*c* 0.36, dichloromethane). This compound rapidly decolorized bromine in carbon tetrachloride.

Anal. Calcd. for $C_{21}H_{20}O_7$ (384.4): C, 65.61; H, 5.24. Found: C, 65.62; H, 5.52.

N.m.r.[23] of Ib: aromatic OCH_3, 3.86 p.p.m. (s) [6]; C-5, 4.50 and 4.58 (unequal peaks) [2]; C-4, 4.8 (c) [1]; C-3, 5.34 (t) [1]; C-2, 5.98 (t) [1]; C-1, 6.74 (d) [1]; aromatic ring, 6.86, 7.00, 7.95 and 8.09 (q) [8].

Hydrogenation of Ib.—Pure Ib (190.7 mg.) was added to a hydrogen-saturated suspension 0.26 g. of 5% palladium on charcoal (previously saturated with hydrogen in dioxane and washed with the same solvent) in 10 ml. of dioxane (dried over Molecular Sieve 5A).[24] After 10 min. and approximately 12-ml. uptake of hydrogen, the catalyst was removed by filtration. The filtrate on concentration afforded 185.2 mg. of a sirup. From ethyl ether–hexane, 154.6 mg. of crude 1,4-anhydro-3,5-di-*O*-*p*-anisoyl-2-deoxy-D-*erythro*-pentitol (Xa) melting at 63–65° was obtained. A recrystallization from the same solvents gave pure Xa: 104 mg. (54.2%), m.p. 80–81°, $[\alpha]^{20}_{D}$ +71.1° (*c* 1.7, chloroform).

Anal. Calcd. for $C_{21}H_{22}O_7$ (386.4): C, 65.27; H, 5.74. Found: C, 65.50; H, 5.52.

Compound Xa (49.7 mg.) was deacylated in 3 ml. of methanol with 0.5 ml. of 1.75 *N* barium methoxide. After 2 hr., the basic solution was neutralized with carbon dioxide and evaporated to dryness. An aqueous solution of the residue was extracted with dichloromethane and the aqueous layer was then concentrated to dryness. After further drying by evaporation of pyridine therefrom, the material was *p*-nitrobenzoylated (5 ml. of dry pyridine, 40.2 mg. of *p*-nitrobenzoyl chloride, 4 hr., <25°) to yield 37.8 mg. of sirup, which from ethanol gave a small amount of pure 1,4-anhydro-2-deoxy-3,5-di-*O*-(*p*-nitrobenzoyl)-D-*erythro*-pentitol (Xb): m.p. 132–134°, m.m.p. (with authentic Xb)[17] 132–134° (Kofler).

Methyl 5-*O*-*p*-Anisoyl-2,3-dideoxy-D-*glycero*-pentofuranosid-2-ene (IIc). A. Reaction of Ib with Methanol in Dichloromethane.—To a solution of 0.6727 g. of Ib in 10 ml. of dichloromethane was added 20 ml. of methanol. After 22 hr., the reaction mixture was evaporated under reduced pressure. The solution of the resulting sirup in 50 ml. of dichloromethane was extracted with sodium bicarbonate solution. Acidification of the aqueous extract with 3 *N* hydrochloric acid precipitated 0.2184 g. (82.1%) of *p*-anisic acid: m.p. 183–184° (lit.[25] m.p. 184.2°). The organic layer upon evaporation yielded 0.42 g. of sirup, which from 4 ml. of ethyl ether and 20 ml. of pentane afforded crystals of IIc: 0.264 g. (58.4%), m.p. 86–88°. Two recrystallizations from the same solvents gave the pure substance: m.p. 88–90°, $[\alpha]^{20}_{D}$ −72.9° (*c* 2.2, chloroform).

Anal. Calcd. for $C_{14}H_{16}O_5$ (264.3): C, 63.63; H, 6.10. Found: C, 63.70; H, 6.04.

N.m.r.[23] of IIc: aliphatic OCH_3, 3.41 p.p.m. (s) [3]; aromatic OCH_3, 3.87 (s) [3]; C-5, 4.37 and 4.45 (unequal peaks) [2]; C-4, 5.2 (c) [1]; C-3 and C-2, 5.9 (c) [2]; C-1, 6.2 (d) [1]; aromatic ring, 6.87, 7.01, 7.95, and 8.09 (q) [4].

Pure crystalline IIc, on standing 2 months at room temperature, partially decomposed to IIIb as determined by thin layer chromatography.

A second experiment was observed polarimetrically [1.50-dm. tube, 20°, 0.1027 g. (0.267 mmole) of Ib in 2.00 ml. of dry dichloromethane with 4.00 ml. of methanol added at zero time] and the rate constants were calculated (see Table II).

TABLE II

Time, min.	Obsd. rotn., α_D, deg.	k, $\times 10^{-2}$, ln, min.
0	+7.28 (extrapolated)	..
9.0	6.83	0.62
11.0	6.71	0.64
14.0	6.55	0.65
17.0	6.43	0.62
19.0	6.34	0.62
23.0	6.11	0.65
30.0	5.78	0.65
35.0	5.57	0.65
50.0	4.85	0.68
100.0	3.22	0.66
210	0.97	0.66
360	−0.295	0.64
480	−0.759	0.64
1320	−1.15	..
1800	−1.15	..

From this run, 31.9 mg. (78.5%) of *p*-anisic acid and 51.2 mg. of a sirupy product were obtained. Crystallization from ethyl ether and pentane afforded 32.2 mg. (45.6%) of IIc: m.p. 88–90°. The filtrate on thin layer chromatography (silica gel G,[21] 2:1 hexane–ethyl ether) revealed two components after spraying with 10% sulfuric acid and heating; one migrated similarly to IIc and the other, to IIIb. After chromatography on silica gel and elution with 1:1 benzene–hexane followed by 1:1 benzene–ethyl ether, an oil (10.6 mg. 17.1%) was obtained whose infrared absorption spectrum was identical with that of authentic IIIb.

B. Reaction of Ib with Methanol in Dichloromethane with *p*-Toluenesulfonic Acid Added.—A solution of Ib (160.7 mg.) in 5.00 ml. of dry dichloromethane (dried over Molecular Sieve 4A[24]) in a 1.50-dm. polarimeter tube (α^{20}_{D} +13.09°) was treated with 5.00 ml. of methanol containing 0.885 mg. of anhydrous *p*-toluenesulfonic acid. The mutarotation of the solution was observed at 20° and the rate constants were calculated[26] (see Table III).

TABLE III

Time, min.	Obsd. rotn., α_D, deg.	k, $\times 10^{-2}$, ln, min.
0	+6.50 (extrapolated)	...
1.0	6.34	2.0
2.4	5.90	3.4
4.8	5.35	3.3
6.5	4.95	3.4
9.4	4.28	3.5
17.1	2.87	3.6
27.5	1.50	3.7
36.3	0.66	3.8
43.4	0.18	3.8
46.5	0.03	3.8
61.5	−0.56	3.9
81.8	−0.95	4.0
170	−1.00	3.1
180	−1.01	...
250	−0.88	...
1070	−0.01	...
1190	0.00	...

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(23) The spectrum was recorded on a Varian A-60 spectrometer employing deuteriochloroform as solvent with tetramethylsilane as an internal standard at 0 p.p.m. Letters in parentheses describe the corresponding peaks: s, singlet; d, doublet; t, triplet; c, complex multiplet; and q, quartet typical of *p*-substituted benzene compounds. Numbers in brackets refer to the relative areas of the peaks involved.

(24) Product of Linde Air Products Co., a division of Union Carbide and Carbon Corporation.

(25) A. Oppenheim and S. Pfaff, *Ber.*, **8**, 890 (1875).

(26) Calculations, based on the method of T. M. Lowry and G. F. Smith [*J. Phys. Chem.*, **33**, 9 (1929)], were similar to that employed by H. S. Isbell and W. W. Pigman [*J. Res. Natl. Bur. Std.*, **18**, 141 (1937)] except for the use of Naperian logarithms.

After 4 hr., 5.0 ml. of the reaction mixture was diluted with dichloromethane and washed with sodium bicarbonate solution. The organic layer was dried ($MgSO_4$); solvent was removed under reduced pressure. The resulting sirup,[27] from 5 ml. of ethyl ether and 5 ml. of pentane, furnished 15.9 mg. of IIc: m.p. 88–89°, m.m.p. (with authentic IIc) 87–89°.

The remaining portion of the reaction mixture showed on thin layer chromatography only IIIb and *p*-anisic acid.[28]

TABLE IV

Time, min.	Obsd. rotn., α_D, deg.	*k*, × 10^{-2}, ln, min.
0	+14.68 (extrapolated)	. .
5.0	14.23	0.55
10.0	13.82	0.53
15.0	13.38	0.54
20.0	13.00	0.53
30.0	12.19	0.54
40.0	11.40	0.55
50	10.71	0.55
60	10.07	0.54
120	6.85	0.53
195	4.20	0.51
240	2.96	0.51
300	1.75	0.50
360	0.85	0.50
420	0.180	0.49
480	−0.439	0.50
540	−0.88	0.52
1680 (∞)	−1.90	. .

Reaction of Ib with Water.—The mutarotation of 0.2105 g. (0.549 mmoles) of Ib in 5 ml. of anhydrous acetone diluted with 1.00 ml. of water in a 1.50-dm. tube at 20° was observed and the rate constants were calculated (see Table IV).

After 48 hr., the reaction mixture was concentrated under reduced pressure to dryness. The residue in dichloromethane was washed with saturated sodium bicarbonate solution, which on acidification gave 71.6 mg. (93.3%) of *p*-anisic acid. The dichloromethane solution was dried over sodium sulfate and evaporated under reduced pressure to a pale yellow sirup: 128.4 mg., $[\alpha]^{20}_{D}$ −35.6° (*c* 0.79, dichloromethane). This sirup showed a definite hydroxyl band at 3500 cm.$^{-1}$ and two spots on thin layer chromatography (silica gel G[21]) with 4:1 benzene–ethyl ether; the faster moving spot being identical with that of IIIb. A portion of the crude sirup (72 mg.) was methylated by stirring its methyl iodide (10 ml.) solution with 4.2 g. of silver carbonate for 18 hr. After filtration of the solids, the filtrate and dichloromethane washings were combined, washed with water, and dried with sodium sulfate. Removal of the solvents under reduced pressure afforded a yellow sirup: 69.8 mg., $[\alpha]^{20}_{D}$ −31.9°[29] (*c* 0.7, dichloromethane), no absorption in the 3500-cm.$^{-1}$ region, two spots (thin layer chromatography, silica gel G[21] with 4:1 benzene–ethyl ether and with 1:1 ethyl ether–heptane) corresponding to IIc and IIIb. The sirup in 5 ml. of ethyl ether and 20 ml. of pentane yielded a few needles when stored overnight in the refrigerator: m.p. (Kofler) 84–86°; m.m.p. (Kofler) (with IIc) 84–86°; infrared absorption spectrum identical with that of IIc.

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[27] *Thin layer chromatography on silica gel G[21] revealed two spots corresponding to IIc and IIIb.*

[28] *p*-Anisic acid and other compounds with aromatic substituents were made more visible under ultraviolet light by the use of fluorescent zinc silicate in the silica gel G[21] [*cf.* M. E. Tate and C. T. Bishop, *Can. J. Chem.*, **41**, 1801 (1963)].

[29] This rotation corresponds to a 38% over-all yield of IIc from Ib assuming only the presence of IIc and IIIb.

Formation of 1,2-*O*-Isopropylidene-α-D-glucofuranose 5,6-Thionocarbonate by Rearrangement–Fragmentation of Bis(1,2-*O*-isopropylidene-3-*O*-thiocarbonyl-α-D-glucofuranose) Disulfide[1a]

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Selective hydrolysis of bis(1,2:5,6-di-*O*-isopropylidene-3-*O*-thiocarbonyl-α-D-glucofuranose) disulfide (I) removed the 5,6-*O*-isopropylidene radical and gave bis(1,2-*O*-isopropylidene-3-*O*-thiocarbonyl-α-D-glucofuranose) disulfide (II) as an amorphous product. Dissolution of II in pyridine gave equimolar amounts of 1,2-*O*-isopropylidene-α-D-glucofuranose 5,6-thionocarbonate (III), 1,2-*O*-isopropylidene-α-D-glucofuranose (VIII), carbon disulfide, and free sulfur. The structure of III is proved by its conversion into known compounds and by its independent synthesis.

In elucidating the behavior of dithiocarbonate groups in starch *O*-(*S*-sodium dithiocarbonate) esters (starch xanthates) and the oxidatively cross-linked products thereof, starch bis(*O*-thiocarbonyl) disulfides (starch xanthides), model compounds of glucose, were prepared for study of their chemical and physical properties. Unexpectedly a rearrangement–fragmentation of one of these compounds, namely bis(1,2-*O*-isopropylidene-3-*O*-thiocarbonyl-α-D-glucofuranose) disulfide (II), formed nearly equimolar amounts of 1,2-*O*-isopropylidene-α-D-glucofuranose 5,6-thionocarbonate (III) and 1,2-*O*-isopropylidene-α-D-glucofuranose (VIII). This report is concerned with the proof of structure of the cyclic thionocarbonate (III) (Scheme I).

The literature contains only a few reports of thionocarbonate derivatives of carbohydrate materials. Interestingly in each case, the thionocarbonate was an unexpected product. Thus Freudenberg and Wolf[2] reported that on long standing crystalline 2,3:5,6-di-*O*-isopropylidene-D-mannose 1-*O*-(*S*-methyl dithiocarbonate) gave bis(2,3:5,6-di-*O*-isopropylidene-D-mannose) 1-thionocarbonate. The structure of this com-

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[1] (a) Presented before Division of Carbohydrate Chemistry, 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964. (b) This is a laboratory of the Northern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture. Article is not copyrighted.

[2] K. Freudenberg and A. Wolf, *Ber.*, **60**, 232 (1927).