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Orthobenzoic Acid Derivatives of D-Ribopyranose. Preparation and Some Properties of 1,2-*O*-(1-Benzyloxybenzylidene)-α-D-ribopyranose and 1,2,4-*O*-Orthobenzoyl-α-D-ribopyranose

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Condensation of tri-*O*-benzoyl-β-D-ribopyranosyl bromide (I) with benzyl alcohol in the presence of quinoline, followed by alkaline debenzoylation, gives a crystalline 1,2-*O*-(1-benzyloxybenzylidene)-α-D-ribopyranose (III), an unusually labile derivative of orthobenzoic acid, the structure of which is confirmed by its consumption of one mole of periodate. With benzoyl chloride in pyridine at 40° this substance is converted to tri-*O*-benzoyl-β-D-ribopyranosyl chloride (VII). On standing or in the presence of a trace of acid the 1,2-*O*-(1-benzyloxybenzylidene)-α-D-ribopyranose (III) gives an orthobenzoyl-D-ribose (VI) which was characterized further through its monobenzoate V, monoacetate IV and monomethyl ether X. Methanolysis of the latter, followed by debenzoylation, afforded an amorphous methyl mono-*O*-methyl-D-riboside (XII) which was stable to periodate. Hydrolysis of XII to a mono-*O*-methyl-D-ribose and then condensation with *p*-bromophenylhydrazine gave the *p*-bromophenylosazone of a methyl-D-ribose. On the basis of these facts the orthoester is assigned the structure 1,2,4-*O*-orthobenzoyl-α-D-ribopyranose (VI).

In continuation of our studies on the chemistry of ribose and particularly of orthobenzoic acid derivatives of this sugar[1] an attempt was made to obtain 3,4-di-*O*-benzoyl-1,2-*O*-(1-benzyloxybenzylidene)-α-D-ribopyranose (II) through condensation of tri-*O*-benzoyl-β-D-ribopyranosyl bromide (I) with benzyl alcohol in the presence of quinoline. However, like its furanose analog[1] the substance was obtained only in amorphous form despite extensive chromatography. Alkaline debenzoylation of the sirupy material yielded a readily crystalline substance in 73% yield, based on the original bromide. Analysis of this new compound showed it to have the composition of a benzyl pentoside monobenzoate, one benzoyl group having resisted the action of the alkali as is characteristic of glycosides of orthoester structure.[2] Since the substance consumed one mole of periodate, structure III (1,2-*O*-(1-benzyloxybenzylidene)-α-D-ribopyranose) was assigned to it, although the configuration of the new asymmetric carbon atom in both II and III remains unknown.

1,2-*O*-(1-Benzyloxybenzylidene)-α-D-ribopyranose proved to have some interesting and unexpected properties. Benzoylation with benzoyl chloride in pyridine at 0° gave a dextrorotatory sirup, presumably the corresponding dibenzoate II. Benzoylation at 40°, however, furnished tri-*O*-benzoyl-β-D-ribopyranosyl chloride[3,4] (VII) in 60% yield. One would expect an *ortho* ester structure to be stable in a pyridine solution of benzoyl chloride; indeed, Helferich and his collaborators[5,6] have shown recently that 2,3-*O*-(1-benzyloxybenzylidene)-β-D-fructofuranose (XIII) gives the corresponding tribenzoate when treated with benzoyl chloride in pyridine although these authors did not specify the conditions employed.

Attempts to acylate III with benzoic anhydride and with acetic anhydride, to mesylate with methanesulfonyl chloride, to methylate with Purdie reagents and to hydrogenate over palladium failed to yield well-defined products and served only to emphasize the unusual instability of the substance. Indeed, while 1,2-*O*-(1-benzyloxybenzylidene)-α-D-ribopyranose (III) is stable to Fehling solution when pure, a sample which had been kept in a vial at room temperature for nearly three months was found to have changed to a clear, colorless oil giving a strong Fehling test. Attempts to crystallize the reducing component led to the isolation of a non-reducing substance which had the composition and molecular weight of an orthobenzoylribose. Polarimetric studies of the action of very dilute acid on solutions of 1,2-*O*-(1-benzyloxybenzylidene)-α-D-ribopyranose (III) in aqueous dioxane showed a rapid dextromutarotation followed by a rapid levomutarotation. Removal of acid at the point of maximum rotation led to the isolation of a crystalline substance which proved to be identical with the orthobenzoylribose isolated earlier. Conversion of III to the orthobenzoylribose through the action of calcium chloride, as was done by Helferich and Bottenbruch[5] in an analogous case in the fructofuranose series, led to the same substance but in poor yields. Eventually it was found that the orthobenzoylribose could be precipitated by the gradual addition of water to a solution of III in very faintly acidic aqueous acetone.

Attention was now turned to the structure of the new orthobenzoylribose. Its stability toward Fehling solution indicated substitution at C_1. Examination of mechanical models appeared to show that 1,2,4-*O*-orthobenzoyl-α-D-ribopyranose (VI) and the 1,3,4-isomer were sterically feasible. No orthobenzoylribofuranose appeared possible. The substance itself is more stable in storage than 1,2-*O*-(1-benzyloxybenzylidene)-α-D-ribopyranose (III); with benzoyl chloride in pyridine it gives a monobenzoate V in normal fashion. The formation of this benzoate, as well as of the corresponding acetate IV, confirms the presence of a free hydroxyl group. Treatment with methyl iodide and silver oxide gave a crystalline methyl ether which, re-

(1) R. K. Ness and H. G. Fletcher, Jr., THIS JOURNAL, **76**, 1663 (1954).

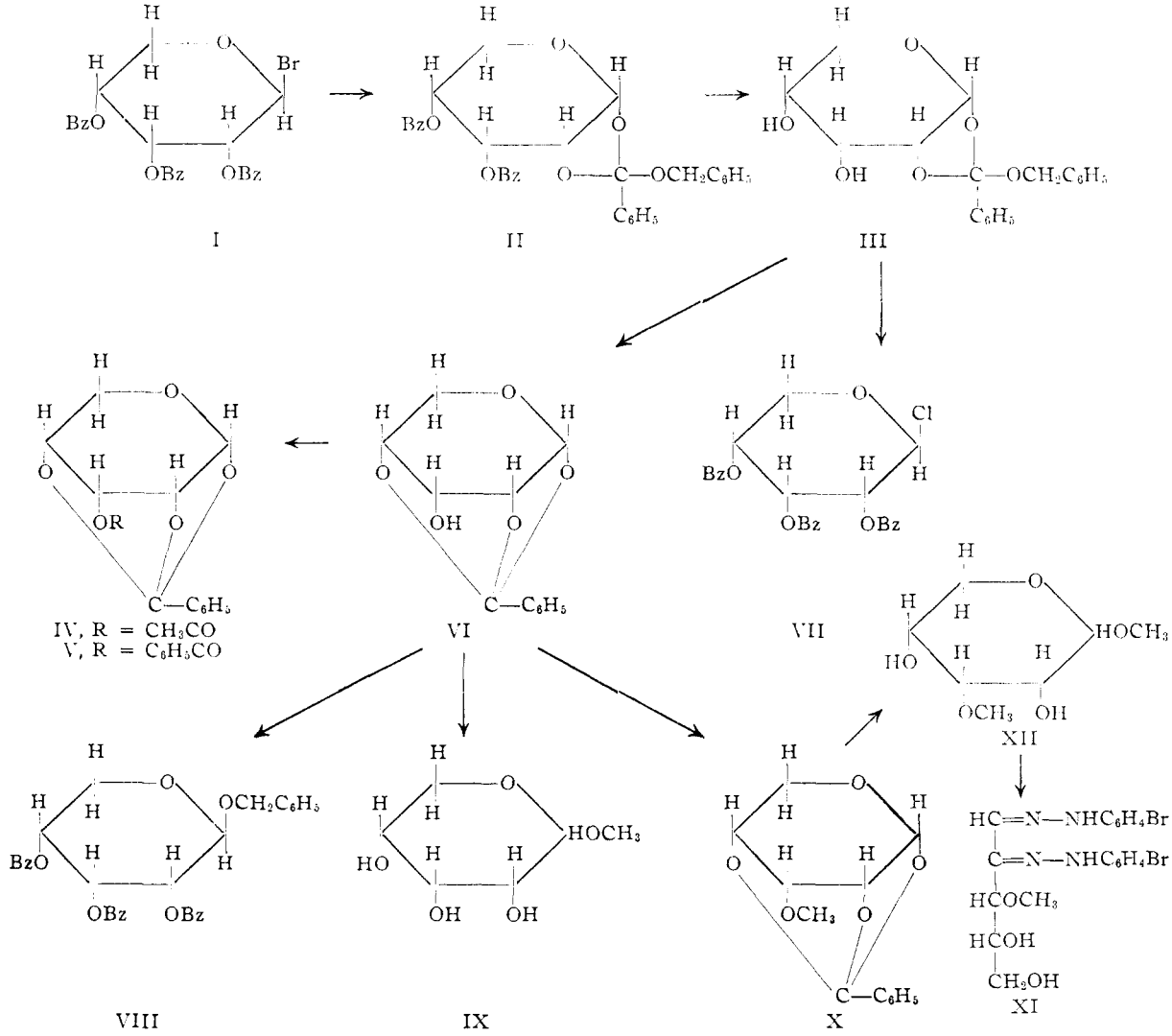
(2) See E. Pacsu, *Adv. Carbohydrate Chem.*, **1**, 78 (1945), for a review of carbohydrate orthoesters.

(3) R. K. Ness, H. G. Fletcher, Jr., and C. S. Hudson, THIS JOURNAL, **73**, 959 (1951).

(4) F. Micheel and H. Micheel [*Ber.*, **63**, 390 (1930); **65**, 253 (1932)] have observed that *cis*-acetohalogeno sugars react with tertiary amines to form salts while *trans*-acetohalogeno sugars are more stable in this regard. While the generality of this "rule" has been questioned [L. J. Haynes and A. R. Todd, *J. Chem. Soc.*, 303 (1950)] it is not surprising that tri-*O*-benzoyl-β-D-ribopyranosyl chloride (VII), a relatively unreactive *trans*-halide, is readily isolable from pyridine solution.

(5) B. Helferich and L. Bottenbruch, *Chem. Ber.*, **86**, 651 (1953).

(6) B. Helferich and W. Schulte-Hürmann, *ibid.*, **87**, 977 (1954).



fluxed with methanolic hydrogen chloride and then debenzoylated with barium methoxide, afforded a sirup which was stable toward sodium metaperiodate. Since similar methanolysis, followed by debenzoylation, of the unmethylated orthobenzoylribose led to a sirup which periodate analysis showed to be methyl D-ribopyranoside (IX), it seems most probable that the product here is methyl 3-methyl-D-ribopyranoside. However, a methyl 2-methyl-D-ribofuranoside also would be resistant to the action of periodate. In order to exclude this latter possibility, the methyl monomethyl-D-riboside (XII) was hydrolyzed to the free sugar and the *p*-bromophenylosazone made. This crystalline derivative retained the methyl group, showing that it could not have been attached at position 2.[7] The methyl group must, therefore, occupy position 3 and structure VI is assigned to the orthobenzoylribose.[8]

When 1,2-*O*-(1-benzyloxybenzylidene)-α-D-ribopyranose (III) is dissolved in benzyl alcohol and a trace of hydrogen bromide added, the rotation of

(7) The original intention was to convert the *p*-bromophenylosazone (XI) to the corresponding phenylosotriazole [*cf.* E. Hardegger, H. El Khadem and E. Schreier, *Helv. Chim. Acta*, **34**, 253 (1951)] and to confirm the position of the methyl group in the latter by periodate oxidation. However, the very small quantity of XI available and the poor yields involved in conversion to the osotriazole rendered this approach impracticable. The *p*-bromophenylosazone itself is a new substance, differing in its properties from the *p*-bromophenylosazone of 5-*O*-methyl-D-ribose reported by P. A. Levene and E. T. Stiller [*J. Biol. Chem.*, **104**, 299 (1934)] and, more recently, by D. M. Brown, D. I. Magrath and A. R. Todd [*J. Chem. Soc.*, 1442 (1954)].

(8) It might be expected that benzoylation of methyl 3-*O*-methyl-D-ribopyranoside (XII), followed by conversion to 2,4-di-*O*-benzoyl-3-*O*-methyl-D-ribopyranosyl bromide *via* hydrogen bromide and, finally, reduction with lithium aluminum hydride, would give 1,5-anhydro-3-*O*-methyl-D-ribitol, a *meso* substance. Actually, the amorphous product thus obtained is definitely dextrorotatory ($[\alpha]^{20}D$ +14.4° *in* alcohol) and, while its exact nature has not been elucidated, the sirup became reducing to Fehling solution after storage for some months in the refrigerator. It is interesting to note that tri-*O*-benzoyl-β-D-ribopyranosyl bromide gives, on reduction with lithium aluminum hydride, a sirup which, with acid, affords *benzaldehyde*, identified as its 2,4-dinitrophenylhydrazone. The same is true, but to a markedly lesser extent, of the α-anomer, tri-*O*-benzoyl-α-D-ribopyranosyl bromide, suggesting that a conventional neighboring group mechanism, involving the as yet unattacked 2-benzoyl group, may have led in these cases to the formation of a 1,2-*O*-benzylidene-α-D-ribopyranose.

the solution rapidly rises to a maximum and then falls to a negative value. The final product consumes periodate and gives, on benzoylation, benzyl β-D-ribopyranoside tribenzoate (VIII); it seems likely, then, that a benzyl 2- or 4-*O*-benzoyl-β-D-ribopyranoside is formed. The maximum observed in the mutarotation curve may possibly represent the formation of 1,2,4-*O*-orthobenzoyl-α-D-ribopyranose (VI) as an intermediate. However, when the latter is dissolved in benzyl alcohol and the solution treated with hydrogen chloride, a molar quantity of the acid appears to be necessary in order to bring the rotation to a minimum value. Benzoylation then affords benzyl β-D-ribopyranoside tribenzoate (VIII), albeit in low yield.

A convenient method for the preparation of the anomeric tri-*O*-benzoyl-D-ribopyranosyl bromides from D-ribose without the isolation of crystalline intermediates is described.

Acknowledgment.—We wish to thank Mr. Harry W. Diehl for assistance in some of the preparations and Mr. William M. Jones for infrared spectra measurements. Microanalyses were carried out in the Institute's Microanalytical Laboratory under the direction of Dr. W. C. Alford.

Experimental[9]

Tri-*O*-benzoyl-β-D-ribopyranosyl Bromide (I) from D-Ribose.—Thirty grams of pure D-ribose was added gradually to a well-stirred mixture of 360 ml. of dry pyridine and 120 ml. of benzoyl chloride, the temperature being maintained at 0–5°. The reaction mixture was allowed to stand at room temperature overnight and then 8 ml. of water added to destroy the excess of benzoyl chloride. After standing for 15 min. at room temperature the mixture was diluted with methylene chloride and washed successively with water, cold 3 *N* sulfuric acid and aqueous sodium bicarbonate. Moisture was removed with sodium sulfate and the solution concentrated *in vacuo* to a volume of about 300 ml. Acetic anhydride (5 ml.) and 100 ml. of hydrogen bromide in glacial acetic acid (32% w./w.) were added and the mixture left at room temperature for 2 hr. It was then poured into ice-water and methylene chloride and the solution washed twice with water and once with aqueous sodium bicarbonate. Moisture was again removed with sodium sulfate, the solution filtered through a thin layer of carbon and concentrated *in vacuo* (50° bath) to a crystalline magma. From a mixture of 290 ml. of ethyl acetate and 290 ml. of ether at 0° crystallization was rapid. After standing at −5° overnight the product (67.2 g., 64%) was removed. It melted at 153–154° dec. and was sufficiently pure for use in the following preparation. Addition of pentane to the mother liquor and storage at −5° overnight yielded 14.7 g. of crude tri-*O*-benzoyl-α-D-ribopyranosyl bromide[3] raising the total yield to 78%.

1,2-*O*-(1-Benzyloxybenzylidene)-α-D-ribopyranose (III).—Fifteen grams of tri-*O*-benzoyl-β-D-ribopyranosyl bromide (I), prepared as described above, was dissolved in 75 ml. of dry benzene and to this solution 9 ml. of freshly redistilled quinoline was added. Pure, anhydrous benzyl alcohol (75 ml.) then was added and, after 1.5 hr. at room temperature, the mixture was washed with water (3 × 100 ml.) and dried over sodium sulfate. The desiccant was removed and the solution concentrated *in vacuo*, finally at 80° (bath) and 0.3 mm. pressure. The residue, dissolved in chloroform (60 ml.) and cooled to 0°, was treated with 75 ml. of *ca.* 1.3 *N* sodium methoxide and left at 0° for 140 min. The solution was then diluted with methylene chloride, washed with water (2 × 300 ml.) and dried over Na_2SO_4. Solvent was removed *in vacuo*, the nearly colorless residue being finally held at 80° (bath) and 0.1 mm. pressure. From 18 ml. of acetone and 15 ml. of pentane at −5° the product (6.11 g., m.p. 101–103°) crystallized rapidly; a second crop (1.06 g., m.p. 99–102°) raised the total crude yield to 73%. Recrystallized from a mixture of 1.7 parts of acetone and 1.7 parts of pentane the product was obtained as clear quadrilateral plates melting at 103–104° and rotating +6.6° in chloroform (*c* 0.72) and +21° in dioxane (*c* 1.14). As described below the pure substance decomposes spontaneously to a sirupy mixture which contains 1,2,4-*O*-orthobenzoyl-α-D-ribopyranose and benzyl alcohol, although this action may be slowed greatly by storage at −5°.

Anal. Calcd. for $C_{19}H_{20}O_6$: C, 66.27; H, 5.85. Found: C, 66.20; H, 5.96.

A sample (115.1 mg.) of the product was dissolved in 5 ml. of pure dioxane. Saturated aqueous sodium bicarbonate (2 ml.), 0.45 *M* sodium metaperiodate (1.00 ml.) and sufficient water to make 25.0 ml. were then added. After 18 hr. at room temperature analysis of an aliquot showed the consumption of 1.12 molar equivalents of oxidant.

The infrared spectrum of the substance lacked the characteristic absorption peak at 5.70 to 5.76 μ associated with ester carbonyl.

Behavior of 1,2-*O*-(1-Benzyloxybenzylidene)-α-D-ribopyranose (III) with Benzyl Alcohol in the Presence of Hydrogen Bromide.—1,2-*O*-(1-Benzyloxybenzylidene)-α-D-ribopyranose (453.8 mg.), dissolved in pure benzyl alcohol (total volume 5.00 ml.), showed in a 1.5-dm. tube an observed rotation of +3.18°, corresponding to $[\alpha]^{20}D$ +23.4°. After 25 min. the rotation was unchanged. Four drops of a freshly prepared, dilute solution of hydrogen bromide in benzyl alcohol then was added causing the observed rotation to rise (1 min., +4.46°; 2 min., +4.07°) and then to fall rapidly, attaining constancy after 54 min. at −11.87°. Chloroform was added, the solution washed with aqueous sodium bicarbonate and dried over sodium sulfate. Solvent was removed *in vacuo* (80° bath and 0.1 mm.). Attempts to obtain the product in crystalline form failed. A sample (93.9 mg.) in aqueous, bicarbonate-buffered dioxane was found to consume 1.31 molar equivalents of periodate over a period of 18 hr.[10]

Another sample of the sirup was benzoylated with benzoyl chloride and pyridine in the usual manner to give crude benzyl β-D-ribopyranoside tribenzoate in *ca.* 55% yield. Recrystallized twice from ethanol this rotated −108° in chloroform (*c* 2.2) and melted at 142–144°. Mixed with authentic benzyl β-D-ribopyranoside tribenzoate[11] it melted at 143–144°. Pure benzyl β-D-ribopyranoside melts at 144–145° and rotates −108° in chloroform (*c* 1.28).[11]

Action of Benzoyl Chloride in Pyridine on 1,2-*O*-(1-Benzyloxybenzylidene)-α-D-ribopyranose (III).—One-half gram of 1,2-*O*-(1-benzyloxybenzylidene-α-D-ribopyranose was dissolved in 3 ml. of dry pyridine and the solution treated with 0.4 ml. (2.4 molar equivalents) of benzoyl chloride. The temperature did not rise above 40°. After 85 min. at 40° the reaction mixture was cooled, diluted with methylene chloride and washed successively with cold 3 *N* sulfuric acid and aqueous sodium bicarbonate. Moisture was removed with sodium sulfate, the solution filtered through a thin layer of carbon and, finally, concentrated *in vacuo* (35° bath) to a crystalline mass. From 1 ml. of acetone and 3.5 ml. of pentane there was obtained 420 mg. (60%) of product melting at 163–164° and rotating in chloroform −144° (*c* 0.62). The infrared spectrum was identical with that of tri-*O*-benzoyl-β-D-ribopyranosyl chloride for which a melting point of 162–163° and a rotation of −147° ($CHCl_3$) have been reported earlier.[3] A mixed melting point with authentic material showed no depression.

1,2,4-*O*-Orthobenzoyl-α-D-ribopyranose (VI) from 1,2-*O*-(1-Benzyloxybenzylidene)-α-D-ribopyranose (III). (a) By Spontaneous Decomposition.—When freshly prepared, 1,2-*O*-(1-benzyloxybenzylidene)-α-D-ribopyranose forms clear quadrilateral plates which are not affected by Fehling solution. A sample left for nearly three months in a vial at room temperature was found to have changed to a clear colorless sirup which reduced Fehling solution. Addition of ethylene chloride to the sirupy material caused the formation of a small quantity of fine needles, m.p. 132–144°. Recrystallization from acetone–pentane raised the melting point to 152–153°—a value unchanged upon admixture with

(9) Melting points are corrected. Unless otherwise specified rotations are specific rotations for the D-line of sodium at 20°, concentration being expressed in g. per 100 ml. of solution.

(10) A molecular weight of 344 ($C_{19}H_{20}O_6$ = benzyl riboside monobenzoate) was assumed.

(11) H. G. Fletcher, Jr., and R. K. Ness, THIS JOURNAL, **76**, 760 (1954).

1,2,4-*O*-orthobenzoyl-α-D-ribopyranose prepared as described immediately below.

(b) *Via* **Weakly Acidic Aqueous Acetone.**—Preliminary polarimetric studies of the action of exceedingly dilute acid on 1,2-*O*-(1-benzyloxybenzylidene)-α-D-ribopyranose in 18:7 dioxane–water (v./v.) showed a rapid dextromutarotation followed by a rapid levomutarotation. When the acid was removed at the point of maximum rotation (by passage through Duolite A-4), 1,2,4-*O*-orthobenzoyl-α-D-ribopyranose could be isolated in small yield. Consideration of the solubility of this product as well as that of benzyl alcohol, however, led to the development of the following exceedingly simple process which gave higher yields.

1,2-*O*-(1-Benzyloxybenzylidene)-α-D-ribopyranose (5.32 g.) was dissolved in 23.4 ml. of acetone and the solution diluted with 22 ml. of an "acid solution" which had been made by the addition of one drop of 0.1 *N* hydrochloric acid to 25 ml. of distilled water. Water then was added dropwise to the reaction mixture until the cloud-point was almost reached. The dropwise addition of water was continued over the course of approximately an hour[12] as the cloud-point receded and finally became constant; *i.e.*, the addition of further water caused a permanent turbidity. At this point (and sometimes earlier) needles were forming. The whole was left at −5° until crystallization had ceased. The product (1.38 g., 38%) melted at 150–151°. After sublimation *in vacuo* (130–140° bath, 0.05 mm.) and recrystallization from *n*-propyl alcohol the product melted at 151–152°. In chloroform it rotated +68.4° (*c* 0.61) and in 18:7 (v./v.) dioxane–water +75.2° (*c* 0.58).

Anal. Calcd. for $C_{12}H_{12}O_5$: C, 61.02; H, 5.12; mol. wt., 236. Found: C, 60.66; H, 5.26; mol. wt., 253 (Rast), 239 (Signer-Clark).

The product does not reduce Fehling solution although it is strongly reducing after brief treatment with dilute acid. The mother liquor from a run similar to that above was concentrated *in vacuo* to a sirup. At 80° (bath) and 0.1 mm. pressure this latter afforded a distillate which, treated with phenyl isocyanate, afforded crystals melting at 76–77° either alone or in admixture with authentic benzyl N-phenylcarbamate.

3-*O*-Acetyl-1,2,4-*O*-orthobenzoyl-α-D-ribopyranose (IV).—1,2,4-*O*-Orthobenzoyl-α-D-ribopyranose (122.7 mg.) was acetylated with acetic anhydride in pyridine in the usual manner to give from aqueous acetone needles (124.0 mg., 86%) which melted at 96–97°—a value unchanged after sublimation at 150° (bath) and <0.1 mm. pressure. In chloroform the ester rotates +83.5° (*c* 0.99). Dissolved in a little alcohol it failed to reduce Fehling solution.

Anal. Calcd. for $C_{14}H_{14}O_6$: C, 60.43; H, 5.07; CH_3CO, 15.47. Found: C, 60.43; H, 5.24; CH_3CO, 15.58.

3-*O*-Benzoyl-1,2,4-*O*-orthobenzoyl-α-D-ribopyranose (V).—1,2,4-*O*-Orthobenzoyl-D-ribopyranose (203.8 mg.) was benzoylated with benzoyl chloride in pyridine in the usual manner. Upon dilution of the reaction mixture the product (244.6 mg., 83%, m.p. 169–170°) crystallized spontaneously. From 13 ml. of warm absolute ethanol fine needles melting at 170–171° and rotating +78.1° (*c* 0.47) in chloroform were obtained.

Anal. Calcd. for $C_{19}H_{16}O_6$: C, 67.05; H, 4.74. Found: C, 66.88; H, 4.90.

Phenylmethanolysis of 1,2,4-*O*-Orthobenzoyl-α-D-ribopyranose (VI).—A solution of 402.5 mg. of 1,2,4-*O*-orthobenzoyl-α-D-ribopyranose in 3.0 ml. of dioxane was diluted to 10.0 ml. with benzyl alcohol and the resulting solution found to give an observed rotation of +3.98° in a 1.5-dm. tube at 20°. Hydrogen chloride in benzyl alcohol (3.84 *N*) was added dropwise until, with the addition of 16 drops (0.48 ml. or 1.1 molar equivalents of HCl), the observed rotation reached a minimum of −8.81°. Acid then was removed with silver carbonate, the silver salts were washed with dioxane, and the combined filtrate and washings concentrated *in vacuo*, the residue finally being held at 90° (bath) and 0.3 mm. The product was extracted once with cyclohexane to remove residual benzyl alcohol and then benzoylated in the usual fashion. From absolute ethanol the resulting product gave 174 mg. (18%) of crystalline material. After recrystallization from absolute alcohol it melted at 141–142°; mixed with authentic benzyl β-D-ribopyranoside tribenzoate it melted at 141–143°. In chloroform it rotated −106.8° (*c* 1.17). A specific rotation of −108° ($CHCl_3$) was reported earlier for this substance.[11]

Methanolysis of 1,2,4-*O*-Orthobenzoyl-α-D-ribopyranose (VI).—A solution of the orthoester (890 mg.) in 7.5 ml. of 1.5% (w./w.) of methanolic hydrogen chloride was refluxed four hours and then cooled and freed of acid with silver oxide. Concentration *in vacuo* gave a light brown sirup which was dissolved in 10 ml. of absolute alcohol and treated with 0.5 ml. of 1.5 *N* barium methoxide. After 17 hr. water was added and the solution deionized by passage through columns of Amberlite IR-120 and Duolite A-4. The neutral solution then was filtered through a little carbon and the methyl benzoate removed by extraction with methylene chloride. Concentration *in vacuo* gave a sirup which was dried by azeotroping absolute ethanol therefrom. The residue (33.4 mg.) was found to consume periodate, releasing formic acid in the process. Using the molecular weight of methyl riboside as a basis, the consumption of oxidant amounted in 72 hr. to 1.73 moles; the formic acid to 0.75 mole.

3-*O*-methyl-1,2,4-*O*-orthobenzoyl-α-D-ribopyranose (X).—The orthoester (4.00 g.) was dissolved in 40 ml. of methyl iodide and 6 g. of powdered Drierite added to the solution. With heating and vigorous stirring, 6 g. of silver oxide was added in five portions over a 2-hr. period and the mixture then refluxed a further hour. After the solids were removed by filtration through Super-cel and the solvents removed *in vacuo*, the product (4.31 g.) crystallized spontaneously. Recrystallized from 1:1 ether–pentane the methyl ether (2.79 g.) was obtained as stout, rod-like prisms. Remethylation of the material in the mother liquor raised the total yield to 3.60 g. (85%). Two recrystallizations from methylene chloride–pentane failed to change the original melting point of 103–105°. In chloroform the methyl ether rotated +84.3° (*c* 3.4).

Anal. Calcd. for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64; CH_3O, 12.40. Found: C, 62.20; H, 5.59; CH_3O, 12.28.

3-*O*-Methyl-D-ribose *p*-Bromophenylosazone (XI) from 3-*O*-Methyl-1,2,4-*O*-orthobenzoyl-α-D-ribopyranose (X).—A solution of the methylated orthoester (1.88 g.) in 15 ml. of methanolic hydrogen chloride (1.5%, w./w.) was refluxed 4 hr. Acid was removed with silver oxide, the solution concentrated *in vacuo* and the residue extracted three times with cyclohexane to remove methyl benzoate. Dissolved in 10 ml. of methanol, the material was completely debenzoylated by the addition of 0.5 ml. of 1.5 *N* barium methoxide. After standing overnight at room temperature the mixture was neutralized with carbon dioxide, filtered and concentrated *in vacuo* to give a sirup (910 mg.), a sample of which was stable to aqueous sodium metaperiodate over a period of 18 hr. at room temperature. Another sample of the sirupy methyl 3-*O*-methyl-D-ribopyranoside (162.1 mg.) was hydrolyzed by warming on the steam-bath for 45 min. with 1.0 ml. of *N* hydrochloric acid. Deionized with Duolite A-4, the solution was concentrated *in vacuo* and then converted to the *p*-bromophenylosazone according to the procedure of Brown, Magrath and Todd,[7] employing 4 ml. of 2 *N* acetic acid, 2 ml. of methyl Cellosolve and 530 mg. of *p*-bromophenylhydrazine and heating 3.5 hr. on a steam-bath. After cooling, the precipitate was removed, washed first with 2 *N* acetic acid, then with water and dried *in vacuo*. Dissolved in 75 ml. of warm benzene the crude product was chromatographed on 40 g. of activated alumina. The column of alumina was washed with (a) 100 ml. of benzene, (b) 200 ml. of 2% methanol in benzene (v./v.) and then (c) 200 ml. of 5% methanol in benzene. Concentration of the last-named eluent afforded 340 mg. of sirup which, from 15 ml. of warm benzene, gave rosettes of very fine needles (138 mg.). The material was purified by successive recrystallizations from 1:1 ethanol–water (*ca.* 40 parts), absolute ethanol and twice again from 1:1 ethanol–water. The pure yellow needles melted with decomposition at 195–196° when placed in the bath at 190° and heated at the rate of 4° per min. The substance in 3:2 absolute ethanol–pyridine (*c* 0.60) gave a rotation of +15° (15 min.) and +2° (18 hr., not equil.).

Anal. Calcd. for $C_{18}H_{20}O_3N_4Br_2$: C, 43.22; H, 4.03; N, 11.20; CH_3O, 6.20. Found: C, 43.42; H, 4.06; N, 11.27; CH_3O, 6.26.

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(12) The time varies with the *p*H of the solution, depending, of course, on the size of the original drop of acid.