[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH, U. S. PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH, EDUCATION AND WELFARE]

Preparation and Properties of 2,3,4-Tri-*O*-benzoyl-β-D-ribose

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The crystalline form of the levorotatory 2,3,4-tri-*O*-benzoyl-D-ribose previously described has been re-examined. From its mutarotation in aqueous dioxane, its preparation *via* the hydrogenolysis of benzyl tri-*O*-benzoyl-β-D-ribopyranoside, its benzoylation at low temperature to β-D-ribopyranose tetrabenzoate and, finally, through a study of the hydrolysis of the anomeric tri-*O*-benzoyl-D-ribopyranosyl bromides it has been shown to be 2,3,4-tri-*O*-benzoyl-β-D-ribose. A method has been developed whereby the substance can be prepared from crystalline D-ribose in high yield without the isolation of intermediates. Its dextrorotatory anomer 2,3,4-tri-*O*-benzoyl-α-D-ribose has been obtained in crystalline but impure form. The utility of either of the forms of 2,3,4-tri-*O*-benzoyl-D-ribose as stable, readily accessible precursors for the preparation of tri-*O*-benzoyl-β-D-ribopyranosyl bromide is discussed.

In an earlier paper from this Laboratory[1] the preparation of a crystalline 2,3,4-tri-*O*-benzoyl-D-ribose through the hydrolysis of tri-*O*-benzoyl-β-D-ribopyranosyl bromide was described[2]; this substance has now been examined in greater detail.

When first obtained in crystalline form 2,3,4-tri-*O*-benzoyl-D-ribose did not appear to mutarotate in chloroform ($[\alpha]^{20}$D $-42.2°$)[3] and for this reason the anomeric configuration of the compound was left unspecified in the earlier paper.[1,4] However, following an investigation of the analogous 2,3,4-tri-*O*-benzoyl-α-D-xylose,[5] reinvestigation of the ribose compound revealed that it mutarotates in aqueous dioxane (catalyzed with either acid or base) from -45.0 to $-39.0°$ and may, tentatively, be assigned the β-D-configuration. This assignment was confirmed in the following ways.

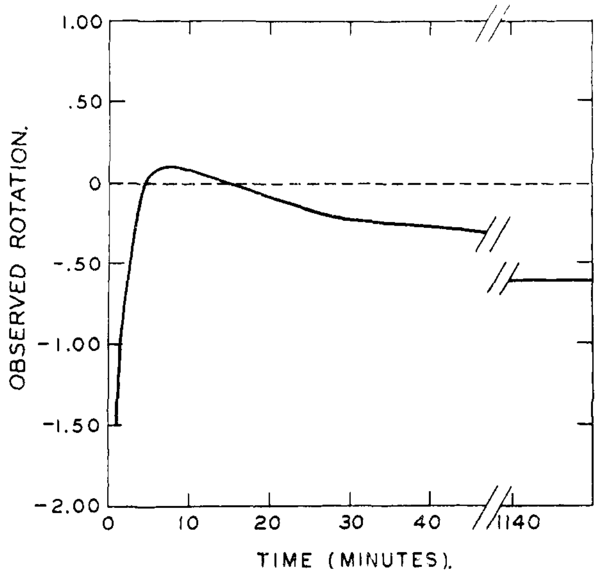
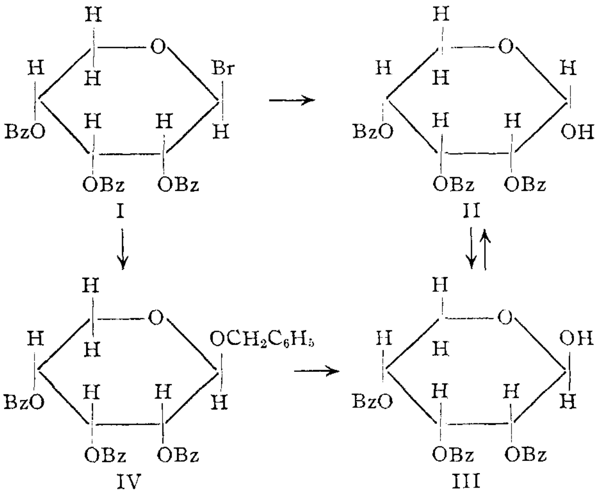


Fig. 1.—Reaction of tri-*O*-benzoyl-β-D-ribopyranosyl bromide with 18:7 dioxane–water (v./v.) at 20°.

First, the behavior of tri-*O*-benzoyl-β-D-ribopyranosyl bromide in aqueous dioxane was studied. On the basis of previous experience in other series[5,6] one would predict that the strongly levorotatory bromide I would hydrolyze to the more dextrorotatory 2,3,4-tri-*O*-benzoyl-α-D-ribose (II) and that the rotation would then become more negative as this latter compound came into equilibrium with its more levorotatory β-anomer III. As may be seen from Fig. 1 this prediction was confirmed by experiment. From the end rotation it is apparent that the β-anomer predominates in the equilibrium mixture. Furthermore it might be predicted that tri-*O*-benzoyl-α-D-ribopyranosyl bromide,[1] much less reactive than its anomer, would hydrolyze from its initial dextrorotation directly to a negative value since its rate of hydrolysis is probably less than the rate of mutarotation of the β-tribenzoate initially formed. This too was borne out by experiment.[7]



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[1] R. K. Ness, H. G. Fletcher, Jr., and C. S. Hudson, THIS JOURNAL, **73**, 959 (1951); see also R. Jeanloz, H. G. Fletcher, Jr., and C. S. Hudson, *ibid.*, **70**, 4055 (1948).

[2] L. Berger, U. V. Solmssen, F. Leonard, E. Wenis and J. Lee [*J. Org. Chem.*, **11**, 91 (1946)] hydrolyzed tri-*O*-benzoyl-*N*-phenyl-D-ribopyranosylamine and obtained what is probably 2,3,4-tri-*O*-benzoyl-D-ribose as an amorphous powder.

[3] Unless otherwise stated, rotations cited are specific rotations for the D-line of sodium at 20°, concentration being expressed in g. of substance per 100 ml. of solution. Melting points are corrected.

[4] It may be noted, however, that the amorphous 2,3,4-tri-*O*-benzoyl-D-ribose described by Jeanloz, Fletcher and Hudson (ref. 1) afforded, on methylation at +2°, a high yield of crystalline methyl β-D-ribopyranoside tribenzoate and therefore probably consisted largely of the β-anomer.

[5] H. G. Fletcher, Jr., THIS JOURNAL, **75**, 2624 (1953).

[6] R. K. Ness and H. G. Fletcher, Jr., *ibid.*, **75**, 2619 (1953).

[7] It is interesting to note that while the hydrolysis of tri-*O*-benzoyl-α-D-ribopyranosyl bromide in aqueous dioxane leads to a final rotation corresponding closely to the equilibrium rotation of 2,3,4-tri-*O*-benzoyl-D-ribose ($-39.0°$) its anomer gives a more dextrorotatory final rotation ($-31°$) which is unaffected by the addition of an excess of pyridine. A similar discrepancy is noted when aqueous acetone is used as a solvent for the hydrolysis of the β-bromide. At present these observations cannot be rationalized.

The second method used to throw light upon the anomeric configuration of the levorotatory 2,3,4-tri-*O*-benzoyl-D-ribose involved the hydrogenation of benzyl-β-D-ribopyranoside tribenzoate (IV). When treated with an excess of benzyl alcohol and hydrogen chloride D-ribose gave a crystalline benzyl D-riboside which, when subjected to periodate, consumed two moles of oxidant and produced one mole of formic acid. The periodate-oxidized material showed a rotation close to that shown by the analogous solution produced from benzyl β-D-arabinoside.[8] Benzyl α-D-arabinoside[8] when similarly oxidized gave an equal rotation of opposite sign. From Table I it may be seen that the differences between the molecular rotations of the benzyl and methyl β-D-pentopyranosides in the arabinose and ribose series are roughly equal. From these facts it is apparent that the new glycoside is benzyl β-D-ribopyranoside.

TABLE I

COMPARISON OF THE MOLECULAR ROTATIONS OF SOME BENZYL PENTOPYRANOSIDES

Pyranoside	Mol. wt.	$[\alpha]^{20}D$ (H_2O)	$[M]D$	Diff.
Methyl β-D-arabino-	164	−245.5°	−40,300	9900
Benzyl β-D-arabino-	240	−209[a]	−50,200	
Methyl β-D-ribo-	164	−105[b]	−17,200	9000
Benzyl β-D-ribo-	240	−109	−26,200	

[a] See ref. 8. [b] E. L. Jackson and C. S. Hudson, THIS JOURNAL, **63**, 1229 (1941).

Benzoylation of benzyl β-D-ribopyranoside readily gave a crystalline tribenzoate IV which could also be made through the action of benzyl alcohol on tri-*O*-benzoyl-β-D-ribopyranosyl bromide (I) in the absence of an acid acceptor. Following a technique developed by Ballou, Roseman and Link[9] benzyl β-D-ribopyranoside tribenzoate was hydrogenolyzed rapidly in dioxane solution using palladium black as a catalyst. The rotation of the resulting solution corresponded to that of 2,3,4-tri-*O*-benzoyl-β-D-ribose (III) and this compound was isolated in good yield.

Finally, benzoylation of 2,3,4-tri-*O*-benzoyl-β-D-ribose in pyridine at a low temperature afforded the known β-D-ribopyranose tetrabenzoate in high yield.

In previous work[1,10] tri-*O*-benzoyl-β-D-ribopyranosyl bromide (I) has been prepared from crystalline β-D-ribopyranose tetrabenzoate or the amorphous material which is the main product in its preparation. In this process the benzoyloxy group is cleaved from carbon one by the hydrogen bromide and the benzoic acid formed must be removed by shaking with aqueous sodium bicarbonate lest it interfere with the subsequent crystallization of the halide. The use of 2,3,4-tri-*O*-benzoyl-β-D-ribose for the preparation of the bromide avoids this difficulty and results in a simpler, more rapid preparation wherein the relatively reactive halide is not exposed to moisture. The tribenzoate is treated with hydrogen bromide in glacial acetic acid to which a small quantity of acetic anhydride has been added. When the reaction is complete the solvents are removed by codistilling with toluene and the product crystallized directly without transfer or exposure to water. The superiority of 2,3,4-tri-*O*-benzoyl-β-D-ribose as a precursor for the synthesis of tri-*O*-benzoyl-β-D-ribopyranosyl bromide[11] induced us to develop a more convenient method for its preparation. Since the tribenzoate could readily be made from β-D-ribopyranose tetrabenzoate without isolation of the intermediate bromide it seemed worthwhile to try a similar preparation directly from D-ribose. The sugar was benzoylated at a low temperature in pyridine and, after removal of excess reactants, the benzoate treated with hydrogen bromide–glacial acetic acid. Acid was then removed and the damp product, dissolved in methylene dichloride, hydrolyzed in aqueous acetone in the presence of an excess of silver carbonate. From aqueous ethanol there was thus obtained 81% of 2,3,4-tri-*O*-benzoyl-β-D-ribose. When ether, rather than aqueous ethanol, was added to the nearly solvent-free sirup obtained in the above process, crystallization was rapid but the product, in contrast to the β-isomer hitherto obtained, was dextrorotatory. In aqueous dioxane it mutarotated to the same end value as the β-isomer and with hydrogen bromide–glacial acetic acid–acetic anhydride gave tri-*O*-benzoyl-β-D-ribopyranosyl bromide in as good yield as the β-isomer. Attempts to obtain this dextrorotatory material in pure form failed because of the ease with which it mutarotated; on repeated recrystallization from non-aqueous solvents a maximum rotation of +11°[12] was attained. Evidently this is 2,3,4-tri-*O*-benzoyl-α-D-ribose (II), the initial product of the hydrolysis of tri-*O*-benzoyl-β-D-ribopyranosyl bromide (I), a supposition which is supported by the fact that under identical conditions it mutarotates at nearly the same rate as the β-anomer.[13]

While both the α- and β-forms of 2,3,4-tri-*O*-benzoyl-D-ribose crystallize as needles a third, prismatic form rotating −35.8° in chloroform was encountered in the latter part of this work. This did not mutarotate in aqueous dioxane (−38.8°) and gave tri-*O*-benzoyl-β-D-ribopyranosyl bromide in as high yield as did either of the two anomers; the substance is presumed to be a mixture of the α- and β-form of 2,3,4-tri-*O*-benzoyl-D-ribose. Its infrared spectrum appeared to be identical with that of pure 2,3,4-tri-*O*-benzoyl-β-D-ribose.

Experimental[3]

Reaction of Tri-*O*-benzoyl-β-D-ribopyranosyl Bromide (I) with Aqueous Dioxane at 20°.—Tri-*O*-benzoyl-β-D-ribopyranosyl bromide (0.3698 g., m.p. 156–158° with rapid heating) was dissolved in 18.00 ml. of dioxane which had just been distilled from lithium aluminum hydride. The solution was made up to 25.00 ml. with water and observed polarimetrically in a 1.5-dm. tube at 20°. The data ob-

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(8) H. G. Fletcher, Jr., and C. S. Hudson, THIS JOURNAL, **72**, 4173 (1950).

(9) C. E. Ballou, S. Roseman and K. P. Link, *ibid.*, **73**, 1140 (1951).

(10) R. Jeanloz, H. G. Fletcher, Jr., and C. S. Hudson, *ibid.*, **70**, 4052 (1948).

(11) Since the more stable α-bromide appears to be formed in low yield in the preparation as it was when β-D-ribopyranose tetrabenzoate was used this method is also doubtless more advantageous for obtaining this less accessible halide. For the synthesis of glycosides where no acid acceptor is used it is, of course, unnecessary to separate the anomeric bromides since each gives the same product although at different rates (ref. 1).

(12) It may be noted that the maximum rotation reached by tri-*O*-benzoyl-β-D-ribopyranosyl bromide in the course of its hydrolysis (Fig. 1) corresponds fairly closely to this specific rotation for 2,3,4-tri-*O*-benzoyl-α-D-ribose.

(13) C. S. Hudson, *Z. physik. Chem.*, **44**, 487 (1903).

tained are shown graphically in Fig. 1. On the basis of the theoretical quantity of 2,3,4-tri-*O*-benzoyl-D-ribose formed the maximum specific rotation attained was approximately +5° and the final equilibrium rotation was −31°. Addition of 1 ml. of pyridine to the solution after mutarotation had ceased caused no further mutarotation in 48 hours. From a similar rate measurement 2,3,4-tri-*O*-benzoyl-β-D-ribose was isolated in 72% yield and identified by melting point and mixed melting point with authentic material prepared from benzyl β-D-ribopyranoside tribenzoate as described below.

A parallel rate determination using 18:7 aqueous acetone gave a maximum specific rotation of +10° and a final rotation of −26°.

Reaction of Tri-*O*-benzoyl-α-D-ribopyranosyl Bromide with Aqueous Dioxane at 20°.—Tri-*O*-benzoyl-α-D-ribopyranosyl bromide[1] (153.3 mg.) was dissolved in 7.2 ml. of pure dioxane, the solution diluted to 10.0 ml. with water and observed in a 1.5-dm. tube at 20°. The addition of the water precipitated some of the starting material which slowly redissolved over the course of about 6 hours. After 22 days the rotation was found to be constant at an observed value of −0.79°, corresponding to a specific rotation (on the basis of complete hydrolysis to a tribenzoylpentose) of −39°.

2,3,4-Tri-*O*-benzoyl-β-D-ribose (III) from Crystalline β-D-Ribopyranose Tetrabenzoate.—2,3,4-Tri-*O*-benzoyl-β-D-ribose may readily be prepared from pure tri-*O*-benzoyl-β-D-ribopyranosyl bromide in a manner similar to that described in the earlier papers cited[1] but it is more convenient to start with β-D-ribopyranose tetrabenzoate and thus avoid the isolation of the relatively labile bromide. Ten grams of pure β-D-ribopyranose tetrabenzoate was dissolved in 20 ml. of methylene dichloride and the solution treated with 20 ml. of a solution of hydrogen bromide in glacial acetic acid (*ca.* 32% HBr). When mutarotation at 20° had virtually ceased (2 hours) the reaction mixture was poured on ice, diluted with more methylene dichloride and washed successively with water, aqueous sodium bicarbonate and water. The moist solution was then added to a mixture of 100 ml. of acetone, 2 ml. of water and 10 g. of powdered silver carbonate and the whole stirred vigorously for 0.5 hour. After filtration the solution was concentrated *in vacuo* at 50° to a sirup which, from a mixture of 80 ml. of ethanol and 55 ml. of water, gave 5.20 g. of fine needles melting at 136–138° and rotating −42.4° in chloroform. A second crop (1.55 g.) raised the total yield to 83%. Recrystallization from aqueous 66% (v./v.) ethanol afforded, with little loss, material melting at 135–137° and rotating −42.2° in chloroform (*c* 1.41). Further recrystallization failed to change these values. The substance mutarotates very slowly if at all in U.S.P. chloroform. In 18:7 (v./v.) dioxane–water (*c* 4.04) 2,3,4-tri-*O*-benzoyl-β-D-ribose shows a rotation of −45.0°; the addition of a trace of either acid or base causes the rotation to fall to −39.0°. When two drops of 41% aqueous hydrobromic acid was used as a catalyst mutarotation data were obtained from which an average first-order rate constant of 0.0065 (min., decadic logs, 20°) was calculated. In 18:7 (v./v.) acetone–water containing a trace of hydrobromic acid the substance mutarotates from −37.8° (2 min.) to −32.0° (*c* 2.52) in seven hours; in anhydrous pyridine it mutarotates from −53.8° to −45.0° (*c* 4.32) in three hours.

2,3,4-Tri-*O*-benzoyl-β-D-ribose (III) and Crude 2,3,4-Tri-*O*-benzoyl-α-D-ribose (II) from D-Ribose.—Twenty grams of powdered D-ribose was added gradually to a chilled, well-stirred mixture of 75 ml. of benzoyl chloride, 100 ml. of pyridine and 150 ml. of methylene dichloride at such a rate that the temperature of the mixture was maintained between +5 and +10°. When the addition was complete the mixture was held at room temperature for 0.5 hour and then at 40° for 0.5 hour. It was then washed with ice-water, cold 3 *N* sulfuric acid and aqueous sodium bicarbonate, dried with sodium sulfate and concentrated *in vacuo* to a thin, pale yellow sirup. The latter was treated with 150 ml. of methylene dichloride and 150 ml. of hydrogen bromide in glacial acetic acid (32% HBr) and, after 2.5 hours at room temperature, the resulting solution was washed successively with cold water and aqueous sodium bicarbonate. Without drying, it was poured into a cooled, well-stirred suspension of 75 g. of silver carbonate in a mixture of 300 ml. of acetone and 10 ml. of water. Stirring was continued for 0.5 hour at room temperature, the mixture was filtered through a thin layer of carbon and concentrated *in vacuo* at 40–45° to a thin sirup. Fifty ml. of absolute alcohol was evaporated from this sirup *in vacuo* and the pale yellow residue diluted with 150 ml. of ether. Crystallization was spontaneous. After 17 hours at −5° the crystalline mass was filtered: 36.1 g. (59%) rotating +5.6° in U.S.P. chloroform. From aqueous alcohol the material remaining in the mother liquor afforded a second crop (11 g.) rotating −39.2° (v./v.) dioxane–water and raising the total yield to 76%. In 18:7 dioxane–water (*c* 3.76) the first crop was without rotation; when two drops of 41% aqueous hydrobromic acid were added the rotation changed in a negative direction, attaining constancy in 11.4 hours with a rotation of −39.6°, essentially the same as the equilibrium rotation reached by 2,3,4-tri-*O*-benzoyl-β-D-ribose under similar conditions. The first order-rate constant for the mutarotation thus catalyzed, 0.0048 (min., decadic logs, 20°) may be compared with the constant of 0.0065 obtained above from the parallel mutarotation of the β-isomer.

When the solution used for the measurement of the mutarotation of the crude α-isomer was concentrated and the residue crystallized from aqueous alcohol pure 2,3,4-tri-*O*-benzoyl-β-D-ribose, melting at 136–137° and showing a rotation of −42.2° in chloroform, was isolated in 85% yield.

Five recrystallizations of the dextrorotatory first crop from cold acetone–pentane gave 0.55 g. of needles melting at 146–149° and showing +11° in chloroform (*c* 1.15).

Anal. Calcd. for $C_{26}H_{22}O_8$: C, 67.52; H, 4.80. Found: C, 67.63; H, 4.87.

Further attempts to purify the substance were abandoned because of the ease with which it mutarotated. The mother liquors afforded the β-isomer in good yield.

The second crop mentioned above appeared to be a new form of 2,3,4-tri-*O*-benzoyl-D-ribose. On recrystallization from aqueous alcohol it was obtained as stubby, rectangular prisms which melted at 118–120°, resolidified and melted again at 134–137°. In chloroform it rotated −35.8° (*c* 1.43) and in 18:7 (v./v.) dioxane–water (*c* 2.00) rotated −38.8°, no mutarotation being observed on the addition of 2 drops of 41% hydrobromic acid. With hydrogen bromide–glacial acetic acid–acetic anhydride it gave tri-*O*-benzoyl-β-D-ribopyranosyl bromide in essentially the same yield as the β- or crude α-isomer (see below) and is therefore tentatively considered to be a mixture of the α- and β-isomers.

Anal. Calcd. for $C_{26}H_{22}O_8$: C, 67.52; H, 4.80. Found: C, 67.43; H, 4.71.

β-D-Ribopyranose Tetrabenzoate from 2,3,4-Tri-*O*-benzoyl-β-D-ribose (III).—One gram of pure 2,3,4-tri-*O*-benzoyl-β-D-ribose was added to a mixture of 10 ml. of pyridine and 1 ml. of benzoyl chloride which had been chilled to 0°. After 10 minutes at 0° the mixture was warmed to room temperature and on the following day worked up in the usual manner to yield from 12 ml. of absolute ethanol 1.15 g. (94%) of product which melted at 130–131° either alone or in admixture with β-D-ribopyranose tetrabenzoate which had been prepared through the direct benzoylation of D-ribose.

Benzyl β-D-Ribopyranoside from D-Ribose.—A mixture of powdered D-ribose (7.5 g.), pure, anhydrous benzyl alcohol (30 ml.) and hydrogen chloride (1.5 g.) was stirred at room temperature until solution was complete (28 min.). The solution, kept at 20°, ceased to change in rotation after 28 hours and was then neutralized with 30 g. of silver carbonate. After washing the silver salts with 200 ml. of boiling ethanol the filtrate and washings were concentrated at 100° under 0.15 mm. pressure and the residue dissolved in a mixture of 20 ml. of ethyl acetate and 20 ml. of pentane. The fine needles (8.05 g., 67%) thus obtained were recrystallized once from 2.7 parts of absolute ethanol and twice from 5.4 parts of water to give pure benzyl β-D-ribopyranoside melting at 103–104° and rotating −109° in water (*c* 1.32).

Anal. Calcd. for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 59.97; H, 6.84.

Benzyl β-D-ribopyranoside is soluble in ethyl acetate, methanol, warm water and warm ethanol; it is sparingly soluble in cold water and cold ethanol.

A sample (0.5460 g.) of the new glycoside was dissolved in 10.00 ml. of 0.49 *M* sodium metaperiodate and the solution diluted to 25.00 ml. with water. After 24 hours analysis showed that 1.98 mole equivalents of oxidant had been consumed while 0.972 mole equivalent of formic acid had been formed. The oxidation mixture showed in a 1.5-dm. tube an observed rotation of −2.90°. An equal quantity of authentic benzyl β-D-arabinopyranoside, similarly oxidized, gave a rotation of −2.95° while its anomer, benzyl α-D-arabinopyranoside, rotated +2.95°.

Benzyl β-D-Ribopyranoside Tribenzoate (IV) (a) from Benzyl β-D-Ribopyranoside.—Benzyl β-D-ribopyranoside (0.46 g.) was benzoylated with pyridine and benzoyl chloride in the usual manner to yield from 10 ml. of ethanol 1.00 g. (95%) of clear, square plates melting at 143–144°. Recrystallization from warm absolute alcohol gave material melting at 144–145° and rotating −108° in chloroform (*c* 1.28). In pure dioxane the substance rotated −110.5° (*c* 4.80).

Anal. Calcd. for $C_{33}H_{28}O_8$: C, 71.73; H, 5.11. Found: C, 71.83; H, 5.21.

(b) **From Tri-*O*-benzoyl-β-D-ribopyranosyl Bromide (I).**—Pure tri-*O*-benzoyl-β-D-ribopyranosyl bromide (3.64 g.) was shaken with 18 ml. of pure, anhydrous benzyl alcohol at room temperature until solution was complete. After 18 hours the reaction mixture was diluted with methylene dichloride, washed successively with aqueous sodium bicarbonate and water, and concentrated at 95° and 0.2 mm. pressure. From *ca.* 10 ml. of absolute ethanol the colorless residue deposited 1.87 g. (49%) of crystalline material which melted at 143–144° either alone or in admixture with the benzyl β-D-ribopyranoside tribenzoate prepared in (a) above.

Hydrogenolysis of Benzyl β-D-Ribopyranoside Tribenzoate (IV).—Two grams of palladium black was suspended in 25.0 ml. of pure dioxane in a 1.5-dm. polarimeter tube and saturated with hydrogen at room temperature. Benzyl β-D-ribopyranoside tribenzoate (1.0027 g.) was then added and the suspension shaken with hydrogen. After 19 minutes the theoretical quantity of hydrogen had been absorbed and the solution, read over the settled catalyst, showed a rotation of −2.13°, corresponding to a specific rotation (based on the theoretical yield of tri-*O*-benzoylpentose) of −42.3°. The solution showed a slow dextromutarotation on standing. After removal of the catalyst and solvent there was obtained from aqueous alcohol 0.61 g. (73%) of 2,3,4-tri-*O*-benzoyl-β-D-ribose melting at 134–135°. Mixed with authentic material it melted at 136–137°. The product showed a rotation of −43.3° in chloroform (*c* 1.09).

Tri-*O*-benzoyl-β-D-ribopyranosyl Bromide (I) from 2,3,4-Tri-*O*-benzoyl-D-ribose.—Each of the three forms of 2,3,4-tri-*O*-benzoyl-D-ribose (the pure β-isomer, the impure, dextrorotatory α-isomer and the prismatic form) gave the same yield in this preparation. In a typical experiment 5.00 g. of impure 2,3,4-tri-*O*-benzoyl-α-D-ribose ($[\alpha]^{20}D$ +4.9° in chloroform) was dissolved in a mixture of 10 ml. of ethylene dichloride, 10 ml. of hydrogen bromide in glacial acetic acid (32% HBr) and 4 ml. of acetic anhydride. After 2.5 hours at room temperature a mixture of 30 ml. of toluene and 5 ml. of acetic anhydride was added and the solution concentrated *in vacuo* (40–45° bath) to a thin sirup which crystallized spontaneously. Ether (20 ml.) was added, the mixture cooled to −5° and then 20 ml. of pentane added as crystallization proceeded. The mixture of prisms and needles thus obtained (4.58 g., 81%) melted at 152–154° (dec., rapid heating) and rotated −178.8° in absolute chloroform (*c* 1.96). Recrystallization from 10 ml. of methylene dichloride and 10 ml. of pentane gave 2.51 g. of pure tri-*O*-benzoyl-β-D-ribopyranosyl bromide melting at 155–158° (dec.) and rotating −203° in absolute chloroform (*c* 2.25).

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BETHESDA, MARYLAND

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH, U. S. PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH, EDUCATION AND WELFARE]

New Benzoyl Derivatives of D-Ribofuranose and *aldehydo*-D-Ribose. The Preparation of Crystalline 2,3,5-Tri-*O*-benzoyl-β-D-ribose from D-Ribose[1]

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A method for the preparation of crystalline 2,3,5-tri-*O*-benzoyl-β-D-ribose from D-ribose in relatively high yield and without the isolation of intermediates is described. The structure of the new tribenzoate is demonstrated by its synthesis through the hydrogenolysis of benzyl β-D-ribofuranoside tribenzoate. Its anomeric configuration is assigned on the basis of methylation studies and on comparisons between its optical rotation and those of various closely related compounds. Acetylation of 2,3,5-tri-*O*-benzoyl-β-D-ribose affords crystalline 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribose; benzoylation gives β-D-ribofuranose tetrabenzoate which may also be prepared through the benzoylation of D-ribose in pyridine at an elevated temperature. The possible utility of 2,3,5-tri-*O*-benzoyl-β-D-ribose as a stable precursor for the synthesis of D-ribofuranosides is investigated through its use for the preparation of benzyl β-D-ribofuranoside tribenzoate. A second new D-ribose tetrabenzoate, *aldehydo*-D-ribose tetrabenzoate, has been prepared in crystalline form for comparison purposes.

In a recent paper[2] there has been described a procedure whereby the α- and β-D-xylofuranose tetrabenzoates may be prepared from D-xylose without the isolation of intermediates. In this procedure D-xylose is dissolved in methanol containing 1% of hydrogen chloride and the reaction halted when the yield of methyl D-xylofuranosides has reached a maximum. The amorphous mixture thus obtained is benzoylated in normal fashion and the mixture of benzoates treated with hydrogen bromide in glacial acetic acid. The benzoylated D-xylofuranosyl and D-xylopyranosyl bromides thus formed are then hydrolyzed and the pyranose portion very largely eliminated through the crystallization of 2,3,4-tri-*O*-benzoyl-α-D-xylose which is, indeed, the main product of these reactions. In the mother liquor the remaining amorphous 2,3,5-tri-*O*-benzoyl-D-xylose is benzoylated to give the crystalline, anomeric tetrabenzoates of D-xylofuranose in a total over-all yield of 33%. Application of this synthetic process to the D-ribose series has led to very different results which will now be described.

It is well known that while crystalline D-ribose exists in the pyranose form,[3] it appears to assume the furanose form with greater ease than the majority of sugars and, indeed, occurs in nature largely, if not wholly, as furanose derivatives.[4] In view of

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(1) A preliminary account of this work appeared in THIS JOURNAL, **75**, 3289 (1953).

(2) H. G. Fletcher, Jr., *ibid.*, **75**, 2624 (1953).

(3) R. Jeanloz, H. G. Fletcher, Jr., and C. S. Hudson, *ibid.*, **70**, 4052 (1948).

(4) See R. W. Jeanloz and H. G. Fletcher, Jr. [*Advances in Carbohydrate Chem.*, **6**, 135 (1951)] for a recent review of ribose chemistry.