inositol hexabenzoate melted at 216–217°. Mixed with a sample of racemic inositol hexabenzoate prepared in a similar fashion from authentic racemic inositol the material melted at 216–217°.[11]

Racemic inositol hexabenzoate is insoluble in pentane, very sparingly soluble in boiling alcohol and readily soluble in acetone and dioxane.

Anal. Calcd. for $C_{48}H_{36}O_{12}$: C, 71.63; H, 4.51. Found: C, 71.55; H, 4.48.

Müller[4] obtained a crystalline *iso*-inositol tetrabenzoate on heating *iso*-inositol with benzoyl chloride. Maquenne and C. Tanret[5] and later G. Tanret[7] reported a racemic inositol benzoate melting at 217°. Since our present hexabenzoate shows the same melting point it is presumed to be identical with theirs although their publications fail to give any details of preparation or analyses.

Summary

The previously recorded observation that *meso*-inositol may be converted by the successive actions of hydrogen chloride in glacial acetic acid solution and hot aqueous barium hydroxide into an isomer has been confirmed.

Comparison of this isomer and its hexaacetate and hexabenzoate with racemic inositol and its corresponding derivatives has shown that the isomer, originally called *iso*-inositol is, in fact, racemic inositol.

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[11] When heated rapidly to temperatures between 135 and 215° racemic inositol hexabenzoate melted and then resolidified. When heated slowly from 130 to 135° the clear prisms became opaque without losing their form and then melted at 216–217°.

[Contribution from the Chemistry Laboratory, Experimental Biology and Medicine Institute, National Institutes of Health]

1,5-Anhydroribitol

By R. Jeanloz,[1] Hewitt G. Fletcher, Jr., and C. S. Hudson

Stereochemical theory predicts the possible existence of four 1,5-anhydro-pentitols: 1,5-anhydro-D-arabitol, 1,5-anhydro-L-arabitol, 1,5-anhydroxylitol and 1,5-anhydroribitol. The syntheses of 1,5-anhydro-D-arabitol[2] and 1,5-anhydroxylitol[3] have recently been reported by this Laboratory. This communication will describe the synthesis of the fourth member of the series, 1,5-anhydroribitol, and a group of related derivatives encountered in the course of the research.

In previous syntheses of 1,5-anhydrides of sugar alcohols[2,3,4] reductive desulfurization of acetylated aryl 1-thioglycosides has been the method of choice. However, in view of the ease of preparation and crystallinity of the pentose benzoates and tribenzoylpentosyl bromides[3,5] and considering the marked instability of triacetylribopyranosyl bromide,[6] the path to an aryl 1-thio-D-ribopyranoside tribenzoate appeared more attractive than that to the corresponding acetate. Low temperature benzoylation of D-ribose indeed readily gave in 35% yield crystalline β-D-ribopyranose tetrabenzoate (I); the substance is provisionally assigned to the β-series because of its strong levorotation and the dextrorotation (+8.6°) of the amorphous mixture remaining in the mother liquor which presumably contains the α-anomer. Both this crystalline tetrabenzoate and the sirup remaining after removal of solvent from its mother liquor gave, when treated with a solution of hydrogen bromide in glacial acetic acid, an easily crystallized 2,3,4-tribenzoyl-β-D-ribopyranosyl bromide (II) which was strongly levorotatory (−199°) and could therefore tentatively be classed in the β-series.

The stability of 2,3,4-tribenzoyl-β-D-ribopyranosyl bromide stands in marked contrast to that of its acetyl analog; a once-recrystallized sample showed no decomposition after storage for six months in a closed container at room temperature. Its condensation with potassium 2-thionaphtholate[7,2] yielded an amorphous mixture which was separated by chromatography on alumina. Rechromatography of a weakly adsorbed, sulfur-containing, levorotatory fraction gave in 42% yield (based on the bromide) a sirup having the analysis of a 2′-naphthyl 2,3,4-tribenzoyl-1-thio-β-D-ribopyranoside (III); its rotation of −59° permits its tentative classification in the β-series.

Reductive desulfurization of 2′-naphthyl 2,3,4-tribenzoyl-1-thio-β-D-ribopyranoside in alcoholic solution with Raney nickel led to the isolation of crystalline 2,3,4-tribenzoyl-1,5-anhydroribitol (IV). Catalytic debenzoylation of this product gave 1,5-anhydroribitol (V). The optical inactivity of this pentitol anhydride as well as that of its tribenzoate and triacetate affords conclusive proof of the presence of a *meso*-tetrahydropyran structure and confirms the supposition that the preceding three intermediates are all pyranose derivatives. Further proof was obtained through periodate oxidation of the free anhydride; as expected, 1,5-anhydroribitol consumed on a molar

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[2] H. G. Fletcher, Jr., and C. S. Hudson, This Journal, **69**, 1672 (1947).

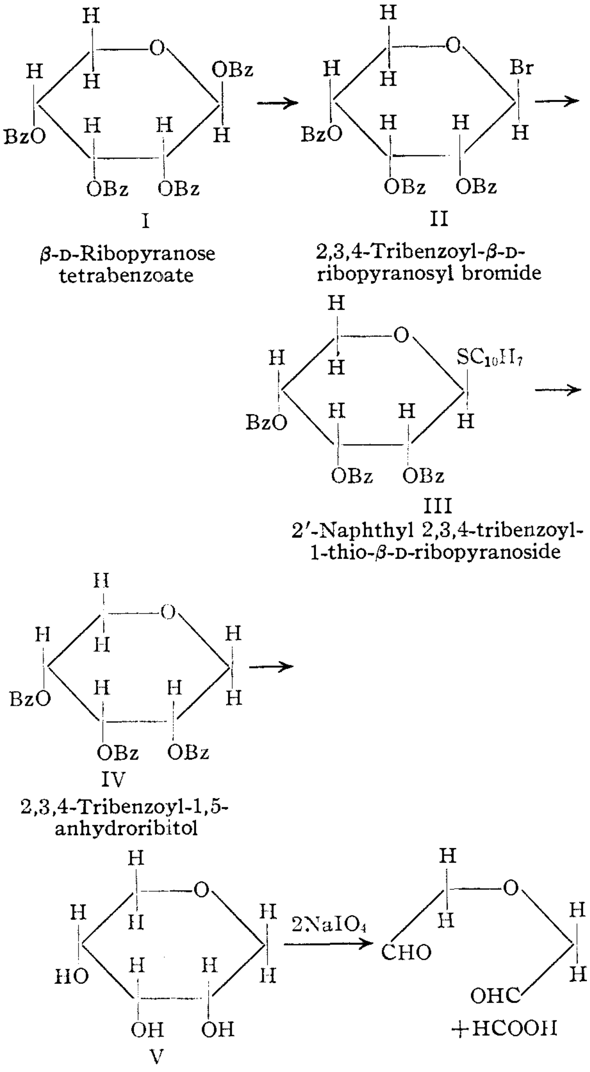
[3] H. G. Fletcher, Jr., and C. S. Hudson, *ibid.*, **69**, 921 (1947).

[4] H. G. Fletcher, Jr., and C. S. Hudson, *ibid.*, **70**, 310 (1948).

[5] H. G. Fletcher, Jr., and C. S. Hudson, *ibid.*, **69**, 1145 (1947).

[6] R. A. Baxter, A. C. McLean and F. S. Spring, *J. Chem. Soc.*, **523** (1948).

[7] W. T. Haskins, R. M. Hann and C. S. Hudson, This Journal, **69**, 1668 (1947).



I
β-D-Ribopyranose tetrabenzoate

II
2,3,4-Tribenzoyl-β-D-ribopyranosyl bromide

III
2′-Naphthyl 2,3,4-tribenzoyl-1-thio-β-D-ribopyranoside

IV
2,3,4-Tribenzoyl-1,5-anhydroribitol

V
1,5-Anhydroribitol

basis two moles of periodate with the simultaneous formation of one mole of formic acid.

Acknowledgment.—We are indebted to Mr. C. A. Kinser and Mrs. Margaret M. Ledyard for microanalyses.

Experimental[8]

β-D-Ribopyranose Tetrabenzoate.—Thirty grams of D-ribose (m. p. 91–92°, $[\alpha]^{20}\text{D}$ −20°) was added to a mixture of 120 ml. of pyridine, 115 ml. of benzoyl chloride and 230 ml. of ethylene dichloride which had been previously chilled to −20°. After agitation for approximately forty-five minutes at 0° the reaction mixture was left in the refrigerator overnight and then at room temperature for five hours. It was then poured on finely chipped ice and agitated vigorously. The non-aqueous layer was augmented with 230 ml. of ethylene dichloride and then washed successively twice with ice-cold 3 *N* sulfuric acid, twice with saturated sodium bicarbonate solution and, finally, thrice with water. The solution was then dried with sodium sulfate, filtered through decolorizing carbon and concentrated *in vacuo* (40–45° bath). The last traces of ethylene dichloride were removed from the resulting sirup by evaporation *in vacuo* therefrom of 300 ml. of absolute alcohol. The substantially solvent-free sirup (131.5 g.) was kneaded with a small quantity of alcohol, seeded[9] and left at room temperature. As crystallization progressed over the course of three days more alcohol was stirred into the mixture in order to improve its filtrability. The solid was then washed with 50 ml. of a 1:1 ether–alcohol mixture and, finally, with much absolute alcohol. The sirup obtained after removal of solvent from the mother liquors and washings showed a specific rotation of +8.6° ($CHCl_3$). One recrystallization of the crude β-D-ribopyranose tetrabenzoate from 75% aqueous acetic acid afforded 40.0 g. (35%, based on the ribose) of product melting at 129–131°. Further recrystallizations from 15 parts absolute ethanol and from a mixture of 10 parts ether with one part pentane afforded prismatic needles which melted at 131° and showed a rotation of −102° in chloroform (*c*, 0.964).

Anal. Calcd. for $C_{33}H_{26}O_9$: C, 69.96; H, 4.63. Found: C, 70.28; H, 4.79.

The substance is soluble in acetone, benzene, chloroform and glacial acetic acid; sparingly soluble in alcohol and ether and practically insoluble in pentane and water.

2,3,4-Tribenzoyl-β-D-ribopyranosyl Bromide.—Three grams of β-D-ribopyranose tetrabenzoate (m. p. 130–131°) was dissolved in 3 ml. of ethylene dichloride and the solution treated with 6 ml. of a chilled solution of glacial acetic acid containing 30% of hydrogen bromide. After standing for two hours at room temperature the reaction mixture was diluted with 30 ml. of dry toluene and concentrated *in vacuo* (40–45° bath). The resulting crystalline magma was dissolved in 100 ml. of a 3:1 mixture of ether and ethylene dichloride and washed twice with ice-cold aqueous sodium bicarbonate solution and three times with ice-water. After desiccation with sodium sulfate, the solution was concentrated *in vacuo* to 10 ml. and then diluted with a mixture of 20 ml. of ether and 50 ml. of pentane. On standing for several hours in the refrigerator, 2.37 g. (85%) of elongated prisms was removed by filtration, washed with ether and then with pentane; m. p. 148–150°. On concentration the mother liquor gave 0.10 g. of less pure material. Recrystallized from the same mixture of ethylene dichloride–ether–pentane, the substance melted at 151–153° and showed a rotation of −199° in chloroform (*c*, 1.352). The melting point on the Kofler block was 156-158° (cor.).

Anal. Calcd. for $C_{26}H_{21}O_7Br$: C, 59.44: H, 4.03; Br, 15.21. Found: C, 59.47; H, 4.08; Br, 15.34.

The sirup that was obtained by the removal of solvent from the mother liquor from the preparation of β-D-ribopyranose tetrabenzoate similarly gave a good yield of the bromine compound, which supports the view that it contained mainly the α-anomeric tetrabenzoate. Thus 30 g. of D-ribose afforded a total of 71 g. (68%) of 2,3,4-tribenzoyl-β-D-ribopyranosyl bromide. The substance is soluble in acetone, chloroform and benzene; sparingly soluble in ether and insoluble in pentane.

2′-Naphthyl 1-Thio-β-D-ribopyranoside Tribenzoate.—The procedure of Haskins, Hann and Hudson[7] was used. To a solution of 2 g. of 2,3,4-tribenzoyl-β-D-ribopyranosyl bromide in 20 ml. of chloroform a warm solution of 1.28 g. (100% excess) 2-thionaphthol in 5.55 ml. of 0.6874 *N* methanolic potassium hydroxide was added. The condensation was completed by boiling the solution one hour under an atmosphere of hydrogen to avoid the formation of 2-naphthyl disulfide. The reaction mixture was washed three times with ice-cold 5% sodium hydroxide, three times with water and then dried over sodium sulfate. Removal of the solvent *in vacuo* gave 2.33 g. of partially crystalline material which was dissolved in a mixture of 50 ml. of benzene and 150 ml. of petroleum ether and chromato-

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[8] Unless otherwise specified, melting points were taken with a calibrated Anschütz-type thermometer completely immersed in the bath liquid. Rotations are specific rotations for sodium light at 20°; concentration is expressed in g. of substance per 100 ml. of solution.

[9] Seed crystals were originally obtained from a sample of the sirup which had been partially precipitated from alcoholic solution by water and allowed to stand at 5° for fifteen days.

graphed on a column of 40 g. of neutralized alumina.[10] Elution with 200-ml. batches of various mixtures of petroleum ether and benzene and finally with pure benzene gave first a small quantity of 2-naphthyl disulfide and then a quantity of amorphous levorotatory, sulfur-containing material. Rechromatography of this latter gave sirupy 2′-naphthyl 1-thio-β-D-ribopyranoside tribenzoate rotating −59.0° in chloroform (*c*, 1.285).

Anal. Calcd. for $C_{36}H_{28}O_7S$: C, 71.27; H, 4.65; S, 5.28. Found: C, 71.68; H, 4.80; S, 5.32.

2,3,4-Tribenzoyl-1,5-anhydroribitol.—A solution of the amorphous 2′-naphthyl 1-thio-β-D-ribopyranoside (0.78 g.) in 15 ml. of absolute alcohol was treated with about 8 g. of freshly prepared Raney nickel[11] and the resulting suspension boiled for two hours. The nickel was removed by filtration and washed thoroughly with hot absolute alcohol and with acetone. The combined filtrate and washings were concentrated *in vacuo* to a sirup; solution of this in 10 ml. of absolute alcohol gave 0.34 g. (59%) of needle-like crystals melting at 155–156°. After two recrystallizations from 10 parts of ether the product melted at 156–157° and showed no rotation in chloroform solution. Chromatography of the mother liquor on alumina gave, on elution with 1:1 petroleum ether–benzene and benzene alone, 0.078 g. of almost equally pure material and raised the total yield to 0.418 g. (73%).

Anal. Calcd. for $C_{26}H_{22}O_7$: C, 69.94; H, 4.97. Found: C, 70.11; H, 5.05.

1,5-Anhydroribitol.—2,3,4-Tribenzoyl-1,5-anhydroribitol (0.33 g.) was debenzoylated catalytically with barium methylate in the usual manner to yield 0.089 g. (90%) of stubby prisms melting at 127–128°. After recrystallization, first from 4 and then from 8 parts of ether, the 1,5-anhydroribitol melted at 128–129° and showed no rotation in aqueous solution.

1,5-Anhydroribitol resembles 1,5-anhydro-D-arabitol[2] and 1,5-anhydroxylitol[3] in its solubility characteristics.

Anal. Calcd. for $C_5H_{10}O_4$: C, 44.78; H, 7.52. Found: C, 45.07; H, 7.29.

Sodium Metaperiodate Oxidation of 1,5-Anhydroribitol.—The technique of Jackson and Hudson[12] was employed. 1,5-Anhydroribitol (0.0572 g.) was dissolved in 2 ml. of water, treated with 3.0 ml. of 0.450 *M* sodium metaperiodate and the solution diluted to 10.0 ml. with water. After twenty-four hours at room temperature a 3.0 ml. sample was titrated for formic acid and residual oxidant. On a molar basis 1.95 moles of oxidant was consumed while 0.98 mole of formic acid was formed.

2,3,4-Triacetyl-1,5-anhydroribitol.—Forty milligrams of 1,5-anhydroribitol was dissolved in 0.5 ml. of pyridine, cooled to 0°, and treated with 0.3 ml. of acetic anhydride. After standing at 0° overnight and at room temperature for six hours the solution was treated with ice and the resulting sirup extracted with chloroform. The chloroform solution was then washed thrice with 3 *N* sulfuric acid, twice with aqueous sodium bicarbonate, thrice with water and finally dried over sodium sulfate. Removal of the desiccant and concentration *in vacuo* afforded 80 mg. of crystalline material; recrystallization from a mixture of one part of chloroform, five parts of ether and ten parts of pentane gave 73 mg. (94%) of rectangular plates melting at 132–133°. Recrystallization from absolute alcohol afforded material melting at 133–134° and showing no rotation in chloroform solution. Further recrystallization from a mixture of ether and pentane failed to change the melting point.

2,3,4-Triacetyl-1,5-anhydroribitol is readily soluble in acetone, warm alcohol and ether; insoluble in water and pentane.

Anal. Calcd. for $C_{11}H_{16}O_7$: C, 50.77; H, 6.20. Found: C, 50.85; H, 6.28.

Summary

Crystalline β-D-ribopyranose tetrabenzoate and 2,3,4-tribenzoyl-β-D-ribopyranosyl bromide have been prepared from D-ribose and the latter substance shown to be markedly more stable than its acetyl analog.

The condensation of 2,3,4-tribenzoyl-β-D-ribopyranosyl bromide with potassium 2-thionaphtholate has given 2′-naphthyl 2,3,4-tribenzoyl-1-thio-β-D-ribopyranoside. Reductive desulfurization of this latter substance with Raney nickel afforded 2,3,4-tribenzoyl-1,5-anhydroribitol, a *meso* substance.

Catalytic debenzoylation of 2,3,4-tribenzoyl-1,5-anhydroribitol gave 1,5-anhydroribitol which was further characterized as its crystalline triacetate.

The optical inactivity of 1,5-anhydroribitol and its esters as well as its behavior with sodium metaperiodate confirm its structure and configuration.

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[10] Merck (Darmstadt) Brockmann alumina was used. However, the alkalinity of commercial alumina tends to hydrolyze esters which may be adsorbed on it and in consequence either Merck-Brockmann or Alorco (grade F-20, 80-200 mesh) should be washed before use with 5% acetic acid and then with distilled water until the washings have a *p*H of 5.5-6.5. The adsorbent is then dried at 150-200° *in vacuo* for twenty-four hours.

[11] R. Mozingo, D. E. Wolf, S. A. Harris and K. Folkers, THIS JOURNAL, **65**, 1013 (1943).

[12] E. L. Jackson and C. S. Hudson, *ibid.*, **59**, 994 (1937).