[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF CALIFORNIA]

The Synthesis of Certain Benzylidene Derivatives of D-Ribose and Ribitol[1]

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Condensation of benzaldehyde with D-ribose di-*n*-propyl dithioacetal has led to the isolation of two products which have been shown to be 2,4-*O*-benzylidene-D-ribose di-*n*-propyl dithioacetal and 2,4:3,5-di-*O*-benzylidene-D-ribose di-*n*-propyl dithioacetal. These dithioacetals have been converted to the dimethyl acetals as well as to the corresponding substituted D-riboses and ribitols. The long known dibenzylideneribitol, useful for characterization of the pentitol, was shown to be 2,4:3,5-di-*O*-benzylidene-DL-ribitol.

A number of cyclic acetals of D-ribose and its derivatives have been described, and many of these compounds have proved to be of value as intermediates in the preparation of biologically important phosphorylated sugars. The acetals most frequently used for this purpose are those derived from benzaldehyde and acetone and in all instances where monobenzylidene compounds have been prepared, the acetal formed has been found to involve carbon atoms two and three of the D-ribose molecule.[3] A similar situation usually, but not always, occurs when acetone is used as the blocking group.[3b,4]

In all of the above-mentioned work, the condensation with acetone or benzaldehyde was carried out using either free D-ribose or a glycoside of D-ribose, and the complications arising from the preexisting ring affect considerably the nature of the acetal which is formed. Hence, an acyclic derivative of sugar appeared to be a suitable starting material for the preparation of derivatives unsubstituted in either the two or the three position. The most readily accessible acyclic derivatives of the sugars are the dithioacetals, and the present work describes the condensation products of benzaldehyde with D-ribose di-*n*-propyl dithioacetal, and their conversion into other derivatives of D-ribose and ribitol.

D-Ribose di-*n*-propyl dithioacetal (I)[5] was condensed with benzaldehyde under a variety of standard conditions, and in all instances, a dibenzylidene derivative (II) preponderated. The yield of monobenzylidene derivative was always low until conditions were developed under which the monosubstituted derivative precipitated from solution almost immediately after its formation. In this manner a monobenzylidene compound (III), contaminated only slightly with the dibenzylidene derivative from which it is readily separated, was obtained in a yield of about 75%.

This monobenzylidene D-ribose di-*n*-propyl dithioacetal was demercaptalated and the resulting aldehydo sugar (VI) was reduced with sodium borohydride to a crystalline monobenzylideneribitol (IX). This compound was unattacked by periodate, and neither it nor its triacetate (VIII) showed any optical activity; consequently, it must have the 2,4-*O*-benzylideneribitol structure, and the dithioacetal must be 2,4-*O*-benzylidene-D-ribose di-*n*-propyl dithioacetal. In the course of the present work, several derivatives were prepared of this dithioacetal, as well as of 2,4-*O*-benzylidene-D-ribose dimethyl acetal, and of 2,4-*O*-benzylideneribitol. Of these derivatives, 2,4-*O*-benzylidene-D-ribose dimethyl acetal (XI) is of interest in that it forms a moderately stable crystalline complex with mercuric chloride. From the analyses on the material one would infer that one mole of mercuric chloride combines with three moles of the acetal, but a definite conclusion would require further study of this unusual material. The acetal is readily recovered from the complex by treatment with pyridine to precipitate the mercuric chloride-pyridine complex.

As mentioned above, the first product obtained on condensation of benzaldehyde with D-ribose di-*n*-propyl dithioacetal was a crystalline 2,3,4,5-di-*O*-benzylidene-D-ribose di-*n*-propyl dithioacetal (II) and the structure of this compound was of interest. It seemed probable that one of the benzylidene groups occupied the two and four positions; indeed, reaction of 2,4-*O*-benzylidene-D-ribose di-*n*-propyl dithioacetal with benzaldehyde and acid led to the formation of the same dibenzylidene dithioacetal previously isolated. However, the possibility of rearrangements or of migration of the benzylidene group during the reaction could not be excluded and so an unequivocal proof of structure was sought.

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(1) Taken in part from a thesis submitted by D. J. J. Potgieter to the Graduate Division of the University of California, in partial fulfillment of the requirements of the Ph.D. degree.

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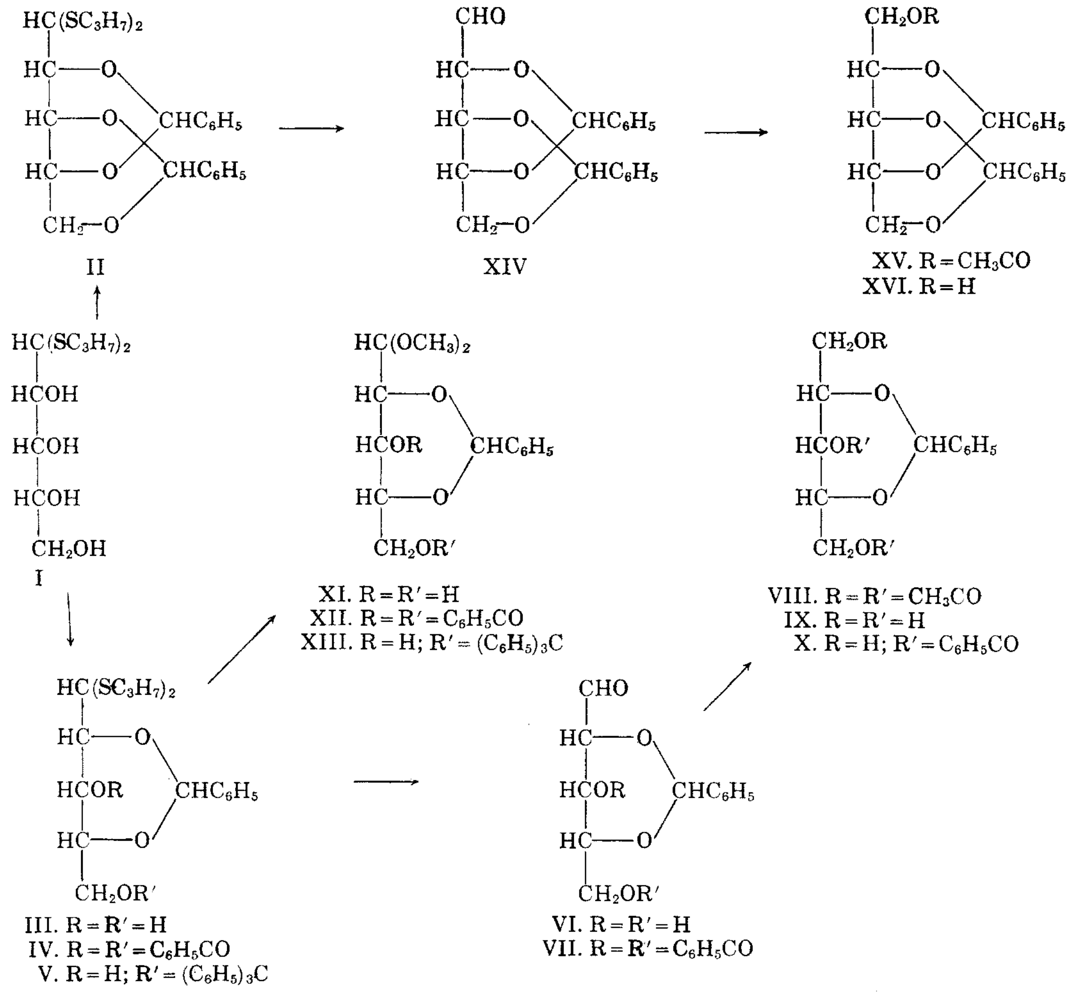
(3) See, for instance, (a) D. M. Brown, L. J. Haynes, and A. R. Todd, *J. Chem. Soc.*, 408, 3299 (1950); (b) G. R. Barker, T. M. Noone, D. C. C. Smith, and J. W. Spoors, *J. Chem. Soc.*, 1327 (1955); (c) G. R. Barker and J. W. Spoors, *J. Chem. Soc.*, 1192 (1956); and (d) H. B. Wood, Jr., H. W. Diehl, and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **78**, 4715 (1956).

(4) P. A. Levene and E. T. Stiller, *J. Biol. Chem.*, **102**, 187 (1933); G. R. Barker and J. W. Spoors, *J. Chem. Soc.*, 2656 (1956).

(5) H. Zinner, *Chem. Ber.*, **83**, 275 (1950).



II

XIV

XV. R = CH_3CO
XVI. R = H

I

XI. R = R′ = H
XII. R = R′ = C_6H_5CO
XIII. R = H; R′ = $(C_6H_5)_3C$

VIII. R = R′ = CH_3CO
IX. R = R′ = H
X. R = H; R′ = C_6H_5CO

III. R = R′ = H
IV. R = R′ = C_6H_5CO
V. R = H; R′ = $(C_6H_5)_3C$

VI. R = R′ = H
VII. R = R′ = C_6H_5CO

Demercaptalation of 2,3,4,5-di-*O*-benzylidene-D-ribose di-*n*-propyl dithioacetal, followed by sodium borohydride reduction led to the isolation of a crystalline 2,3,4,5-di-*O*-benzylidene-D-ribitol (XVI). This compound, which is most readily purified *via* its acetate (XV), has a melting point of 176–177°. This corresponds quite closely to the melting point of dibenzylideneribitol, the derivative which is widely used for the identification of ribitol.[6] Furthermore, it has been shown[7] that the latter dibenzylideneribitol has a free primary hydroxyl group and is therefore 2,3,4,5-di-*O*-benzylidene-DL-ribitol. The two compounds were shown to be structurally identical by comparison of their infrared spectra in chloroform solution.

The question of the actual position of the benzylidene groups in these two benzylideneribitols was finally resolved by relating them to the previously described 2,4-*O*-benzylideneribitol. Acid hydrolysis could, presumably, effect a conversion of the dibenzylideneribitol to a monobenzylideneribitol, and this technique has been used in similar structural studies, for instance in studies on benzylidene derivatives of D-glucitol.[8] However it was felt that the mildest conversion, which would entail the least likelihood of any migration of benzaldehyde during the reaction, would be a partial hydrogenolysis using palladium and hydrogen. Accordingly, a sample of 2,3,4,5-di-*O*-benzylidene-DL-ribitol was partially hydrogenated and from the products, along with unchanged starting material and ribitol, a sample of 2,4-*O*-benzylideneribitol (IX) was isolated. The benzaldehyde group removed must have occupied the 1,3 (or 3,5) position and hence the two ribitol derivatives must be 2,4:3,5-di-*O*-benzylidene-DL-ribitol and 2,4:3,5-di-*O*-benzylidene-D-ribitol (XVI), the latter having been derived from 2,4:3,5-di-*O*-benzylidene-D-ribose di-*n*-propyl dithioacetal (II).

A compound such as 2,4:3,5-di-*O*-benzylidene-D-ribose di-*n*-propyl dithioacetal has two new asym-

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[6] E. Fischer, *Ber.*, **26**, 633 (1893). As first reported, this dibenzylideneribitol melted at 164–165°. A few years ago, the late Dr. Raymond M. Hann of the National Institutes of Health obtained a melting point of 174–175° during the course of some unpublished structural studies on this compound. We thank Dr. N. K. Richtmyer for bringing this matter to our attention and for providing a sample of the material.

[7] R. Lukeš and J. Jarý, *Chem. Listy*, **49**, 1808 (1955); *Chem. Abstr.*, **50**, 9293 (1956).

[8] S. J. Angyal and J. V. Lawler, *J. Am. Chem. Soc.*, **66**, 837 (1944).

metric centers at the acetal carbon atoms and hence there can be four possible diastereoisomers of II. This type of isomerism has been fully described,[9] but more than one of the resulting isomers has been encountered only rarely. In the case of the well known *cis*- and *trans*-1,3-*O*-benzylideneglycerols, structural assignments have been made on the basis of intramolecular hydrogen bonding as revealed by infrared spectroscopy.[10] In compounds such as II, it is likely that the large phenyl groups would assume stable equatorial positions in the *trans*-decalin type of structure involved, and it is thus probable that the compound described represents an individual isomer and not a mixture.

A number of rules have been formulated[11] which are useful for predicting the structures of acetals of polyhydric alcohols. Assuming these rules to be applicable to other acyclic derivatives of carbohydrates, one would predict that D-ribose dithioacetals would form 2,4-mono-*O*-benzylidene derivatives and 2,4:3,5-di-*O*-benzylidene derivatives, a conclusion experimentally verified in the present work. With D-xylose dithioacetals, the recent experimental findings agree with the predicted 2,4:3,5-di-*O*-benzylidene structure[12] and not with the 2,3:4,5-structure claimed earlier.[13] The benzylidene derivative of L-arabinose diethyl dithioacetal has been shown to possess the 2,3:4,5-structure.[14]

EXPERIMENTAL[15]

2,4:3,5-Di-O-benzylidene-D-ribose di-n-propyl dithioacetal (II). Freshly fused zinc chloride (5 g.) was shaken with benzaldehyde (15 ml.) until most of the former had dissolved, and then D-ribose di-*n*-propyl dithioacetal[5] (1 g.) was added and the mixture shaken for 30 min. The mixture was poured into 100 ml. of hot, vigorously stirred petroleum ether (b.p. 60–70°), and the solution was decanted from the oily zinc chloride precipitate. Evaporation of the petroleum ether left an oily mass which crystallized when the benzaldehyde was distilled at oil pump pressure. Two recrystallizations from ethanol gave 1.1 g. (68%) of fine needles, m.p. 110.5–111.5°, $[\alpha]_D^{27}$ −61.5° (*c* 4, chloroform).

Anal. Calcd. for $C_{25}H_{32}O_4S_2$ (460.6): C, 65.18; H, 7.00; S, 13.92. Found: C, 64.73; H, 6.94; S, 13.92.

2,4-O-Benzylidene-D-ribose di-n-propyl dithioacetal (III). Benzaldehyde (3.6 ml., 36 mmoles) was added to a solution of D-ribose di-*n*-propyl dithioacetal (8.5 g., 30 mmoles) in 21 ml. of dioxane, and the solution cooled to 5–10°. To this solution was added a mixture of 32 ml. of concd. hydrochloric acid and 18 ml. of water, previously cooled to 5–10°, and this mixture was shaken vigorously, with occasional cooling in ice. Within 2 or 3 min. a precipitate had appeared and after 10 min. the product was filtered and washed with cold water. It was then dissolved in chloroform, and the solution washed with saturated aqueous sodium bicarbonate and then with water and dried over sodium sulfate. Removal of the solvent left fine needles which were recrystallized from benzene–petroleum ether (b.p. 60–70°). The product (8.8 g., 79%) had a m.p. of 101.5–102.5°, $[\alpha]_D^{24}$ −27.1° (*c* 4, methanol).

Anal. Calcd. for $C_{18}H_{28}O_4S_2$ (372.5): C, 58.03; H, 7.57; S, 17.21. Found: C, 57.86; H, 7.45; S, 17.05.

Evaporation of the mother liquors and crystallization from a minimum of ethanol gave approximately 1 g. of the abovementioned dibenzylidene derivative, m.p. 110.5–111.5°.

3,5-Di-O-benzoyl-2,4-O-benzylidene-D-ribose di-n-propyl dithioacetal (IV). The above monobenzylidene dithioacetal (5.6 g., 15 mmoles) was benzoylated in the cold with a mixture of 15 ml. of pyridine and 6 ml. of benzoyl chloride. After standing overnight at room temperature, the mixture was treated with a little water to destroy the excess benzoyl chloride and then poured into a liter of vigorously stirred ice water. The milky supernatent was decanted after 1 hr. and the gummy residue taken up in chloroform (250 ml.) and the solution washed successively with 50-ml. portions of *N* sulfuric acid, saturated aqueous sodium bicarbonate, and water. The solution was dried (sodium sulfate) and removal of the solvent gave a sirup which was crystallized from ethanol. Recrystallization from ethanol, using charcoal if necessary, gave 7.4 g. (85%) of material, m.p. 94–95°, $[\alpha]_D^{27}$ −9.6° (*c* 4, chloroform).

Anal. Calcd. for $C_{32}H_{36}O_6S_2$ (580.7): C, 66.17; H, 6.25. Found: C, 66.14; H, 6.12.

2,4-O-Benzylidene-5-O-trityl-D-ribose di-n-propyl dithioacetal (V). Trityl chloride (7.2 g., 26 mmoles) was dissolved in a solution of 9.3 g. (25 mmoles) of 2,4-*O*-benzylidene-D-ribose di-*n*-propyl dithioacetal in 25 ml. of dry pyridine. After 48 hr. at room temperature, the mixture was poured into 400 ml. of ice water and after 10 min. of stirring, the milky supernatent liquid was decanted. The gummy precipitate was dissolved in 250 ml. of chloroform and the solution washed with ice-cold 100-ml. portions of *N* sulfuric acid, saturated aqueous sodium bicarbonate, and water. After being dried (sodium sulfate) the solution was concentrated and the residue dissolved in warm methanol (50 ml.) and filtered from traces of insoluble material. Slow cooling gave crystals which were collected after 48 hr. at 0°; yield 13.4 g. (87%) m.p. 27–29° (sinters at 25°), $[\alpha]_D^{24}$ −8.8 (*c* 5.6, methanol).

Anal. Calcd. for $C_{37}H_{42}O_4S_2$ (614.8): C, 72.27; H, 6.88. Found: C, 72.1; H, 6.75.

2,4-O-Benzylidene-D-ribose (VI). A mixture of acetone (30 ml.), 2,4-*O*-benzylidene-D-ribose di-*n*-propyl dithioacetal (5.6 g., 15 mmoles), water (2 ml.), and yellow mercuric oxide (9.7 g., 45 mmoles) was stirred vigorously while a solution of 12.2 g. of mercuric chloride (45 mmoles) in 30 ml. of acetone was added over a period of 20 min. Stirring was continued for 2 hr. at room temperature followed by 0.75 hr. at 40°. The precipitate was removed by filtration and washed with acetone, a little yellow mercuric oxide was added to the filtrate and washings, and these were concentrated at 40°. The gummy residue was extracted with three 15-ml. portions of dioxane and the filtered solution concentrated. The resultant mixture was then extracted with

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[9] J. A. Mills, *Advances in Carbohydrate Chem.*, **10**, 1 (1955); R. J. Ferrier and W. G. Overend, *Quart. Rev.* (*London*), **13**, 265 (1959); B. Dobinson, A. B. Foster, and M. Stacey, *Tetrahedron Letters*, **1**, 1 (1959); H. Zinner and W. Thielebeule, *Chem. Ber.*, **93**, 2791 (1960).

[10] J. A. Brimacombe, A. B. Foster, and M. Stacey, *Chem. & Ind.* (*London*), 1228 (1958).

[11] S. A. Barker and E. J. Bourne, *Advances in Carbohydrate Chem.*, **7**, 137 (1952).

[12] E. J. C. Curtis and J. K. N. Jones, *Can. J. Chem.*, **38**, 1305 (1960).

[13] H. Zinner, G. Rembarz, H.-W. Linke, and G. Ulbricht, *Chem. Ber.*, **90**, 1761 (1957). This earlier structural assignment has now been revised to the correct 2,4:3,5-structure, and the benzylidene derivatives of D-ribose dithioacetals have been investigated; the results are substantially the same as recorded here [H. Zinner and E. Wittenburg, *Chem. Ber.*, **94**, 1298 (1961); H. Zinner and H. Schmandke, *Chem. Ber.*, **94**, 1304 (1961)].

[14] C. F. Huebner, R. A. Pankratz, and K. P. Link, *J. Am. Chem. Soc.*, **72**, 4811 (1950).

[15] Microanalyses were performed by the Microchemical Laboratory, University of California. All evaporations were at water aspirator pressure unless otherwise stated.

three 15-ml. portions of chloroform[16] and the filtered solution again concentrated. The sirup so obtained was dissolved in 100 ml. of dry methanol, and the solution treated with charcoal and filtered; aqueous ammonium hydroxide (*ca.* 0.1%) was added dropwise until the solution was very faintly alkaline. The resulting white precipitate of ammonium mercuric chloride complex was removed by filtration and washed with a little methanol, and the filtrate was concentrated. Three evaporations from 100-ml. portions of absolute ethanol, followed by three evaporations from 100-ml. portions of acetone, left a white hygroscopic glass which weighed 3.1 g. (84%) after drying *in vacuo* over phosphorus pentoxide at room temperature. All attempts to crystallize the compound failed, and the analysis indicates the presence of water which could not be entirely removed by drying.

Anal. Calcd. for $C_{12}H_{14}O_5 \cdot 1/3H_2O$ (244.2): C, 59.01; H, 6.05. Found: C, 59.00; H, 6.09.

3,5-Di-O-benzoyl-2,4-O-benzylidene-D-ribose (VII). In a three necked flask equipped with mercury-sealed stirrer and reflux condenser were placed 1.74 g. (3 mmoles) of 3,5-di-*O*-benzoyl-2,4-*O*-benzylidene-D-ribose di-*n*-propyl dithioacetal, 1.9 g. (9 mmoles) of yellow mercuric oxide, 20 ml. of acetone, and 3 ml. of water. The mixture was stirred vigorously under gentle reflux, while a solution of 2.0 g. (7.5 mmoles) of mercuric chloride in 10 ml. of acetone was added dropwise over a period of 5 min. Stirring and refluxing were continued for 1.5 hr., and the solids were then removed by filtration and washed with acetone. The filtrate and washings were concentrated, the resulting sirup was dissolved in chloroform (50 ml.) and this solution washed twice with 10% aqueous potassium iodide, and then twice with water. The dried (sodium sulfate) solution was concentrated and the sirup so obtained was dissolved in a minimum of hot ethanol. Addition of water gave crystals m.p. 109–110° (sinters at 104°). Recrystallization from ethanol-water gave 1.2 g. (81%) m.p. 110–112° (sinters at 104°) $[\alpha]^{27}_{\mathrm{D}}$ +52° (*c* 4, chloroform). The analyses indicated a mole of ethanol of crystallization or as part of a hemi-acetal, as has been observed for similar compounds.[17]

Anal. Calcd. for $C_{26}H_{22}O_7 \cdot C_2H_5OH$ (492.5): C, 68.28; H, 5.73. Found: C, 67.93; H, 5.85.

1,3,5-Tri-O-acetyl-2,4-O-benzylideneribitol (VIII). To a solution of 0.95 g. (4 mmoles) of 2,4-*O*-benzylidene-D ribose in 10 ml. of ethanol was added a solution of 0.15 g. (4 mmoles) of sodium borohydride in 5 ml. of water. After 1.75 hr. at room temperature, the solids were removed by filtration and washed with ethanol, and the combined filtrate and washings concentrated. The residue was dried by repeated evaporation of added ethanol and acetone. The residue was acetylated for 18 hr. at room temperature in a mixture of pyridine (10 ml.) and acetic anhydride (7 ml.). The acetate, which crystallized on pouring this mixture into crushed ice, was removed by filtration and recrystallized from 2-propanol giving 0.95 g. (67%) of m.p. 106–108°, with sintering from 102°, $[\alpha]^{27}_{\mathrm{D}}$ 0 ± 0.2° (*c* 4, chloroform). This material could also be obtained by Raney nickel reduction, rather than borohydride reduction, but considerable hydrogenolysis of the benzylidene group lowered the yield to 10%.

Anal. Calcd. for $C_{18}H_{22}O_8$ (366.3): C, 59.01; H, 6.05. Found: C, 58.99; H, 6.06.

2,4-O-Benzylideneribitol (IX). A solution of 1,3,5-tri-*O*-acetyl-2,4-*O*-benzylideneribitol (0.55 g., 1.5 mmoles) in 15 ml. of absolute ethanol was made basic by the addition of barium methoxide solution. After 1 hr. at room temperature, the solution was concentrated, and the residue treated with 25 ml. of chloroform and filtered hot. On cooling this solution, fine needles were obtained (0.30 g., two crops, 83%), m.p. 133.5–134.5°, $[\alpha]^{27}_{\mathrm{D}}$ 0 ± 0.2° (*c* 2, ethanol). No periodate was consumed in a period of 36 hr. when 0.1 mmole of the compound, in 5 ml. of ethanol, was treated with 10 ml. of 0.05*N* sodium metaperiodate.

Anal. Calcd. for $C_{12}H_{16}O_5$ (240.2): C, 59.98; H, 6.71. Found: C, 60.15; H, 6.72.

3,5-Di-O-benzoyl-2,4-O-benzylidene-D-ribitol (X). A solution of 2.46 g. (5 mmoles) of 3,5-di-*O*-benzoyl-2,4-*O*-benzylidene-D-ribose in 40 ml. of dioxane was diluted with water (*ca.* 15 ml.) until a faint opalescence appeared. A solution of 0.11 g. of sodium borohydride in 5 ml. of dioxane-water (1:1) was then added in one portion. After 5 min., the solution was concentrated and a chloroform solution of the residue was washed successively with water, *N* sulfuric acid, saturated aqueous sodium bicarbonate, and water. The solution was then dried (sodium sulfate) and concentrated; addition of ethanol followed by concentration gave crystalline material which after recrystallization from ethanol (4 parts) weighed 1.73 g. (77%) and showed m.p. 135–136°, and $[\alpha]^{27}_{\mathrm{D}}$ +1.2° (*c* 4, chloroform). A further 0.2 g. of material, m.p. 131–132° was obtained from the mother liquors.

Anal. Calcd. for $C_{26}H_{24}O_7$ (448.5): C, 69.63; H, 5.39. Found: C, 69.95; H, 5.60.

2,4-O-Benzylidene-D-ribose dimethyl acetal (XI). A dry three-necked flask, equipped with a mercury-sealed stirrer, reflux condenser with a calcium chloride tube, and a dropping funnel was charged with 1.86 g. (5 mmoles) of 2,4-*O*-benzylidene-D-ribose di-*n*-propyl dithioacetal, 3.24 g. (15 mmoles) of yellow mercuric oxide, 4 g. of anhydrous sodium sulfate, and 20 ml. of dry methanol. The flask was placed in a water bath maintained at 60°, and its contents were stirred vigorously while a solution of 3.4 g. (12.5 mmoles) of mercuric chloride in 20 ml. of dry methanol was added dropwise over a period of 5 min. After 1.25 hr. the hot reaction mixture was filtered through a thin layer of filter-aid[18] into a flask containing 5 ml. of pyridine, and the precipitate was washed with small portions of methanol. The filtrate, after cooling in ice for 1 hr. had deposited a crystalline pyridine–mercuric chloride complex which was removed by filtration and this filtrate was then concentrated. The resulting mixture was extracted with three 100-ml. portions of boiling petroleum ether and filtered hot. Slow cooling gave 1.24 g. of material, m.p. 90–93°, which after recrystallization from butyl ether weighed 1.12 g. (79%) and had a m.p. of 93–94° and $[\alpha]^{24}_{\mathrm{D}}$ +13.6° (*c* 4, methanol). No periodate was consumed over a 36-hr. period when 0.1 mmole of the compound, in 5 ml. of ethanol, was treated with 10 ml. of 0.05*N* sodium metaperiodate.

Anal. Calcd. for $C_{14}H_{20}O_6$ (284.3): C, 59.14; H, 7.09; OCH_3, 21.83. Found: C, 59.27; H, 6.86; OCH_3 21.63.

Mercuric chloride complex of 2,4-O-benzylidene-D-ribose dimethyl acetal. In the above demercaptalation experiment, the solids were filtered off after the reaction had been completed, the methanol solution concentrated, and the residue extracted with hot petroleum ether (b.p. 60–80°). On cooling, crystals were obtained which on recrystallization, from petroleum ether or butyl ether melted at 76–80° and showed $[\alpha]^{24}_{\mathrm{D}}$ +10.1° (*c* 4, methanol). The analyses of this material corresponded approximately to three moles of the acetal to one of mercuric chloride.

Anal. Calcd. for $3(C_{14}H_{20}O_6) \cdot HgCl_2$ (1124): C, 44.85; H, 5.38; Cl, 6.31; OCH_3, 16.56. Found: C, 45.13; H, 5.54; Cl, 6.89; OCH_3, 17.81.

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(16) Attempts to remove the mercuric chloride in the usual way by washing the chloroform solution with potassium iodide solution failed because the compound dissolved in the aqueous phase.

(17) M. L. Wolfrom, M. Konigsberg, and F. B. Moody, *J. Am. Chem. Soc.*, **62**, 2343 (1940).

(18) Alternatively, the mixture was filtered into a flask containing mercuric oxide and the filtrate concentrated. The residue was taken up in chloroform and the solution washed with 10% aqueous potassium iodide, followed by water; after being dried (sodium sulfate) the solution was taken to dryness and the residue crystallized from butyl ether. Although the yield was somewhat lower (65–70%), this method was less cumbersome.

2,4-*O*-Benzylidene-D-ribose dimethyl acetal could be recovered from the complex (0.83 g.) by dissolving in 2 ml. of dry methanol and adding 0.5 ml. of dry pyridine to precipitate the pyridine–mercuric chloride complex. After filtration, the filtrate was taken to dryness; a hot petroleum ether extract of the residue yielded crystals, m.p. 92–93°, which after recrystallization from butyl ether had a m.p. of 93–94°, undepressed on admixture with authentic acetal.

*3,5-Di-O-benzoyl-2,4-O-benzylidene-*D*-ribose dimethyl acetal* (XII). A mixture of 1.2 g. (2 mmoles) of 3,5-di-*O*-benzoyl-2,4-*O*-benzylidene-D-ribose di-*n*-propyl dithioacetal, 1.3 g. (6 mmoles) of yellow mercuric oxide, 3 g. of anhydrous sodium sulfate, and 30 ml. of dry methanol was placed in a three neck flask equipped with a mercury-sealed stirrer, reflux condenser, and dropping funnel. The contents were heated to reflux, and a solution of 1.36 g. (5 mmoles) of mercuric chloride in 10 ml. of dry methanol was added over a 5-min. period, and the refluxing and stirring were continued for 1.5 hr. The insolubles were then removed by filtration and washed with methanol, and the combined methanolic solutions were concentrated in the presence of a little mercuric oxide. The residue was extracted with three 10-ml. portions of chloroform and the filtered chloroform solution washed with 10% aqueous potassium iodide and then with water. The dried (sodium sulfate) solution was concentrated to dryness and the residue then triturated with ethanol to give fine needles. Recrystallization from ethanol gave an almost quantitative yield of the acetal, m.p. 132–133° (sinters at 131°), $[\alpha]^{27}_{D}$ +2° (*c* 4, chloroform).

Anal. Calcd. for $C_{28}H_{28}O_8$ (492.5): C, 68.28; H, 5.72; OCH_3, 12.60. Found: C, 68.08; H, 5.84; OCH_3, 13.25.

*2,4-O-Benzylidene-5-O-trityl-*D*-ribose dimethyl acetal* (XIII). Demercaptalation of 2,4-*O*-benzylidene-5-*O*-trityl-D-ribose di-*n*-propyl dithioacetal as described above for the 3,5-dibenzoate gave a 91% yield of a colorless glass which showed $[\alpha]^{24}_{D}$ +7.4 (*c* 4.7, methanol).

Anal. Calcd. for $C_{33}H_{34}O_6$ (526.6): C, 75.26; H, 6.51; OCH_3, 11.78. Found: C, 74.67; H, 6.61; OCH_3, 11.56.

*2,4:3,5-Di-O-benzylidene-*D*-ribose* (XIV). A sample of 2,4.3,5-di-*O*-benzylidene-D-ribose di-*n*-propyl dithioacetal was demercaptalated as described for the preparation of 3,5-di-*O*-benzoyl-2,4-*O*-benzylidene-D-ribose. The product, which readily forms a gel, was obtained in a yield of 73% from methanol by addition of water; m.p. 99–101° (sinters at 95°), $[\alpha]^{27}_{D}$ −29.7 (*c* 4, chloroform) after drying *in vacuo* at 80° over phosphorus pentoxide.

Anal. Calcd. for $C_{19}H_{18}O_5 \cdot 1/2H_2O$ (335.3): C, 68.04; H, 5.71. Found: C, 67.62; H, 5.94.

*1-O-Acetyl-2,4:3,5-di-O-benzylidene-*D*-ribitol* (XV). A sample of 2,4:3,5-di-*O*-benzylidene-D-ribose di-*n*-propyl dithioacetal (3.22 g., 7 mmoles) was demercaptalated as above; the product was dissolved in 30 ml. of warm dioxane and the solution diluted with 120 ml. of methanol. Ten milliliters of water containing 0.5 g. of sodium borohydride was then added and after 2 hr. the solvent was distilled and the gel-like residue dissolved in 100 ml. of chloroform; this solution was washed with 50-ml. portions of water (three times) and then dried (sodium sulfate). Removal of the solvent left 2.12 g. (92%) of material which was acetylated overnight in 10 ml. of pyridine containing 2 ml. of acetic anhydride. The product crystallized when the acetylation mixture was poured into water; the flexible needles so obtained weighed 2.18 g. (84%) after two recrystallizations from absolute alcohol and had a m.p. of 143–144° and $[\alpha]^{20}_{D}$ −57° (*c* 1.1, chloroform). For the racemate, Lukeš and Jarý reported[7] m.p. 136–137°.

Anal. Calcd. for $C_{21}H_{22}O_6$ (370.4): C, 68.08; H, 5.99. Found: C, 67.88; H, 6.06.

*2,4:3,5-Di-O-benzylidene-*D*-ribitol* (XVI). A sample of 1-*O*-acetyl-2,4:3,5-di-*O*-benzylidene-D-ribitol (1.85 g., 5 mmoles) in 100 ml. of warm dry methanol was treated with 1 ml. of 0.2*N* barium methoxide. After 2 hr. the solution was concentrated and the resulting gel dissolved in 50 ml. of dichloromethane; this solution was washed twice with water (25 ml.) and dried (sodium sulfate). Concentration of the solution left a solid which weighed 1.39 g. (84%) after crystallization from hot dioxane (30 ml.) by addition of hot hexane (80 ml.); the product had a m.p. of 176–177° and $[\alpha]^{27}_{D}$ −35.7° (*c* 4, chloroform), and its infrared spectrum in chloroform was identical with that of a sample of dibenzylideneribitol of m.p. 174–175°, prepared from ribitol.

Anal. Calcd. for $C_{19}H_{20}O_5$ (328.3): C, 69.50; H, 6.14. Found: C, 69.05; H, 6.02.

*Isolation of 2,4-O-benzylideneribitol from 2,4:3,5-dibenzylidene-*DL*-ribitol.* One gram of 2,4:3,5-di-*O*-benzylidene-DL-ribitol was reduced in 50 ml. of dioxane with 300 mg. of reduced and washed palladium black. After 4 hr., when the hydrogen uptake was approximately half of the theoretical maximum, the catalyst was removed by filtration and the solution concentrated to dryness. The residue was extracted with several portions (total 60 ml.) of hot chloroform and there remained 0.16 g. (35%) of ribitol, m.p. and mixed m.p. 102.5–103.5°. The chloroform layer was concentrated and the residue extracted with five 10-ml. portions of water; this residue was dissolved in chloroform and the solution filtered and concentrated to give 0.56 g. (56%) of starting dibenzylideneribitol.

The aqueous layer was concentrated to give 0.08 g. of a mixture of sirup and crystals. This was combined with another sample (0.06 g.) obtained from the reduction of a second 1-g. portion of dibenzylideneribitol, and chromatographed on a sheet of Whatman 3 *MM* paper, using acetone-water (4:1) as solvent. The material with an R_f of approximately 0.9, as seen with the aid of ultraviolet light, was eluted with acetone, and the acetone removed *in vacuo*. The residue was crystallized twice from chloroform to give 0.03 g. (2%) of material, m.p. 133–135°, undepressed on admixture with authentic 2,4-*O*-benzylideneribitol. The infrared spectra of the isolated material and of authentic material taken in Nujol were identical.

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