

Similarly, one could expect a dextran containing a large proportion of 1→4-linkages as the principal non-1→6-linkage to show a large negative rotational shift as compared to the value $-99,000^\circ$ for a dextran in which only 1,6-linked units are present.

Acknowledgments.—The authors would like to thank Drs. Allene Jeanes and R. L. Lohmar for many of the dextran samples used in this investigation.

PEORIA, ILLINOIS

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH]

1,5-Anhydro- β -D-ribofuranose and the "Monoacetone Anhydroriboses" of Levene and Stiller

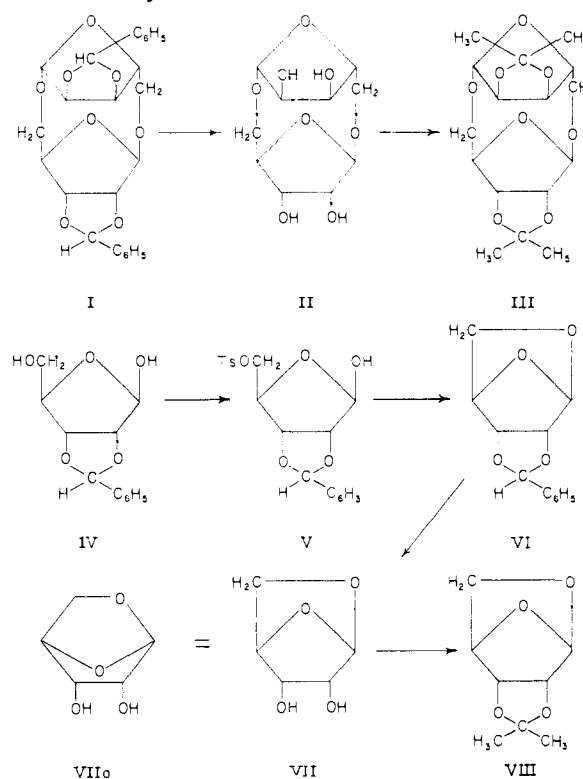
BY ERIK VIS¹ AND HEWITT G. FLETCHER, JR.

RECEIVED SEPTEMBER 26, 1956

Among the products arising from the condensation of D-ribose with benzaldehyde in the presence of zinc chloride-acetic acid has now been found an anhydrobenzylidene-pentose. The same substance has been synthesized through treatment of 2,3-*O*-benzylidene-5-*O*-*p*-tolylsulfonyl-D-ribofuranose with alkali, showing its structure to be 1,5-anhydro-2,3-*O*-benzylidene- β -D-ribofuranose. Hydrogenolysis afforded the parent 1,5-anhydro- β -D-ribofuranose (synonym: 1,4-anhydro- α -D-ribofuranose) in crystalline form. Condensation of this anhydride with acetone under mild conditions has given the 1,5-anhydro-2,3-*O*-isopropylidene- β -D-ribofuranose which Levene and Stiller reported as a by-product in the acetonation of D-ribose. Condensation of the known di- β -D-ribofuranose 1,5':1',5-dianhydride with acetone under mild conditions has given di-(2,3-*O*-isopropylidene- β -D-ribofuranose) 1,5':1',5-dianhydride which is probably identical with the second "monoacetone anhydroribose" mentioned by Levene and Stiller. Phenyl β -D-ribofuranoside and its tribenzoate are described.

In a recent paper from this Laboratory² the benzylidenation of D-ribose in the presence of zinc chloride-acetic acid as catalyst was shown to give rise to 2,3-*O*-benzylidene- β -D-ribofuranose (IV)³ and di-(2,3-*O*-benzylidene- β -D-ribofuranose) 1,5':1',5-dianhydride (I). Chromatography of this rather complex reaction mixture has now led to the isolation in 7% yield of a second crystalline substance having the composition of an anhydrobenzylidene-pentose. Hydrogenolysis afforded the parent anhydride which was further characterized through its dibenzoate. In contrast to the known dimolecular anhydride II obtained through the hydrogenolysis of I, the new substance proved to have the molecular weight of a monomeric anhydride. Like levoglucosan it was stable to Fehling solution but was converted rapidly to a reducing mixture on brief treatment with acid. Preliminary experiments showed that acid hydrolysis gave a sugar which migrated at the same rate as D-ribose on a paper chromatogram. When methylation preceded hydrolysis the product migrated at the same rate as 2,3-di-*O*-methyl-D-ribose. This evidence seemed to indicate that the anhydride might be 1,5-anhydro- β -D-ribofuranose (VII) and so its synthesis from 2,3-*O*-benzylidene- β -D-ribofuranose (IV) was attempted. Tosylation provided the monotosyl ester V⁴; treatment of this ester with sodium isopropoxide afforded 1,5-anhydro-2,3-*O*-benzylidene- β -D-ribofuranose (VI), identical with the product obtained through the benzylidenation of D-ribose. This identity was confirmed through conversion of the product VI thus made to the free anhydride VII and its dibenzoate. These latter

two substances were identical with those derived *via* the benzylidenation of D-ribose.



An unsubstituted, monomeric, non-reducing anhydropentose has not to our knowledge been reported before⁵ although Micheel and Micheel⁶ have described a substance to which they assigned a

(1) Chemical Foundation Fellow, 1956-1957.

(2) H. B. Wood, Jr., H. W. Diehl and H. G. Fletcher, Jr., THIS JOURNAL, **78**, 4715 (1956).

(3) This substance was found independently by G. R. Barker and J. W. Spoor, *J. Chem. Soc.*, 1192 (1956), who employed zinc chloride alone as a catalyst.

(4) In view of the relative reactivities of a primary hydroxyl group in a sugar and the hemiacetal hydroxyl in an aldose it seems reasonable to assume that the tosyl group here is at C₅.

(5) The dimeric anhydride II was originally assumed to be 1,5-anhydro- β -D-ribofuranose by its discoverers [H. Bredereck, M. Köthnig and E. Berger, *Ber.*, **73**, 956 (1940)] but later work showed clearly that the substance contained two D-ribose residues [G. R. Barker and M. V. Lock, *J. Chem. Soc.*, 23 (1950); R. W. Jeanloz, G. R. Barker and M. V. Lock, *Nature*, **167**, 42 (1951)].

(6) F. Micheel and H. Micheel, *Ber.*, **63**, 2861 (1930).

closely related structure. These authors studied the action of trimethylamine in absolute ethanol-benzene on 2,3,4-tri-*O*-acetyl-6-deoxy- α -L-mannopyranosyl bromide and succeeded in isolating a crystalline product which had the analysis and molecular weight of a di-*O*-acetylanhydrodeoxyhexose. The material, which was weakly reducing to Fehling solution, was considered to be 2,3-di-*O*-acetyl-1,4-anhydro-6-deoxy- β -L-mannopyranose. No further investigation of this interesting substance has been reported.

In 1933, Levene and Stiller⁷ found that the acetonation of *D*-ribose gave rise *inter alia* to two crystalline products having the composition of anhydroisopropylidene-pentoses. One of these melted at 61–62° and showed $[\alpha]^{28D} -64.35^\circ$ (methanol), $[\alpha]^{25D} -64.7^\circ$ (acetone) and $[\alpha]_D -59.4^\circ$ (water). Its molecular weight was close to that of a monomer and the substance was assumed to be 1,5-anhydro-2,3-*O*-isopropylidene- β -*D*-ribofuranose (VIII). We have now treated our anhydride VII with acetone in the presence of anhydrous copper sulfate at room temperature and obtained an isopropylidene derivative which melts at 60–61°. A mixed melting point with material prepared by Levene and Stiller's⁷ process was undepressed. If we assume that the ring structure of the anhydride VII was undisturbed in the course of the condensation we may conclude that Levene and Stiller were correct in their structural assignment (VIII).^{7a}

The second crystalline "monoacetone anhydroribose" obtained by Levene and Stiller⁷ was reported to melt at 93–94° but no further data were given. We have now condensed the dimeric anhydride of *D*-ribose (II) with acetone at room temperature in the presence of anhydrous copper sulfate and obtained a crystalline derivative having the double melting point 86–87°, 97–98°. Again assuming no unexpected rearrangements, our material is di-(2,3-*O*-isopropylidene- β -*D*-ribofuranose) 1,5':1',5-dianhydride (III) and is quite probably the substance which Levene and Stiller^{7,8} had in hand.

1,5-Anhydro- β -*D*-ribofuranose (VII) may equally well be regarded as a pyranose derivative: 1,4-anhydro- α -*D*-ribofuranose (VIIa). As is evident from the earlier discussion its ring structure is at present exceedingly rare or unique in the carbohydrate field, other non-reducing, monomeric anhydro-sugars being 1,6-anhydroglycopyranoses (or their ketose-derived equivalents),⁹ 1,6-anhydroglycofuranoses¹⁰ or 1,7-anhydroglycopyranose.^{11,12}

(7) P. A. Levene and E. T. Stiller, *J. Biol. Chem.*, **102**, 187 (1933); cf. P. A. Levene and R. S. Tipson, *ibid.*, **115**, 731 (1936).

(7a) NOTE ADDED IN PROOF, JANUARY 8, 1957.—Since the work described here was completed we have found that treatment of 2,3-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-*D*-ribose (m.p. 95–103°) with warm sodium isopropoxide likewise gives 1,5-anhydro-2,3-*O*-isopropylidene- β -*D*-ribofuranose, a fact which further supports Levene and Stiller's structure.

(8) The lability of the parent anhydrides to acid is such that their preparation through acid hydrolysis of the corresponding isopropylidene derivatives would almost certainly be impracticable.

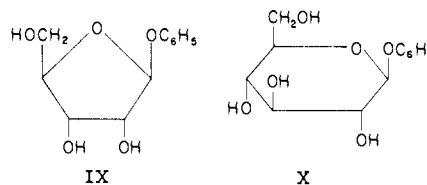
(9) See L. C. Stewart, E. Zissis and N. K. Richtmyer, *Chem. Ber.*, **89**, 535 (1956).

(10) See R. J. Dimler, *Advances in Carbohydrate Chem.*, **7**, 37 (1952).

(11) L. C. Stewart and N. K. Richtmyer, *THIS JOURNAL*, **77**, 424 (1955).

(12) Some years ago, in connection with studies of the structure of cellulose, considerable effort was directed toward the synthesis of 1,4-

In the course of the present research phenyl β -*D*-ribofuranoside (IX) and its tribenzoate were



made by methods developed earlier in this Laboratory.¹³ The anomeric configuration of the new glycoside IX was confirmed through observation of the final rotation resulting after periodate oxidation and comparison of this value with a similar one derived from the well-known phenyl β -*D*-glucopyranoside (X). As might be predicted from examination of formulas IX and X the rotations of equimolar solutions oxidized with periodate eventually were equal. With IX, a locked *cis*-diol, the oxidation was complete in three minutes while X, a *trans-trans*-triol, required six hours for oxidation. An attempt to synthesize 1,5-anhydro- β -*D*-ribofuranose (VII) through the action of strong alkali on phenyl β -*D*-ribofuranoside (IX) failed to yield a crystalline product.

Experimental¹⁴

1,5-Anhydro-2,3-*O*-benzylidene- β -*D*-ribofuranose (VI).—To a constantly stirred mixture of 50 g. of freshly fused and powdered zinc chloride, 50 ml. of glacial acetic acid and 500 ml. of freshly distilled benzaldehyde was added 10 g. of powdered *D*-ribose. The sugar was completely dissolved in 3 min.; after 1.5 hr. the mixture was cooled, treated with 280 ml. of pyridine and left at –5° until precipitation of the zinc chloride-pyridine complex was complete. The mass was filtered and the crystals washed with ether; concentration of the combined filtrate and washings *in vacuo* (finally at 0.5 mm. and 70° bath) afforded a sirup which was diluted to 200 ml. with pure ethyl acetate and chromatographed on 315 g. of alumina. The material was then eluted with pure ethyl acetate, and in the third 200-ml. portion of effluent 8.1 g. of sirupy material was found. From ether-pentane (ca. 1:2) at 0–5° there was obtained 3.15 g. of crystalline material melting at 90–130°; recrystallization from 55 ml. of ether gave 1.0 g. (7%) of nearly pure 1,5-anhydro-2,3-*O*-benzylidene- β -*D*-ribofuranose. Further recrystallization from absolute ethanol and carbon tetrachloride afforded material melting at 141–146°¹⁵ and rotating $[\alpha]^{20D} -56.6^\circ$ in chloroform (*c* 0.97).

Anal. Calcd. for C₁₂H₁₂O₄: C, 65.44; H, 5.49. Found: C, 65.45; H, 5.51.

The infrared absorption spectrum of this substance showed neither hydroxyl nor carbonyl absorption.

1,5-Anhydro- β -*D*-ribofuranose (VII).—The benzylidene derivative described above (644 mg.) was reduced at room temperature in methanol solution in the presence of palladium black. When the absorption of hydrogen had ceased the catalyst was removed and the solution concentrated to dryness. From 20 drops of absolute ethanol the product (325 mg., 84%) crystallized as an arboraceous mass melting at 107–109°. Recrystallized from 1:2 dioxane-isopropyl ether, the anhydride melted at 109–110°; further recryst-

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tallization from the same solvent mixture failed to change this melting range. The substance readily sublimes *in vacuo* (0.07 mm. and 90° bath). In water (*c* 0.83) the 1,5-anhydro- β -D-ribofuranose rotated $[\alpha]^{20}_D -78.8^\circ$.

Anal. Calcd. for $C_5H_8O_4$: C, 45.45; H, 6.10; mol. wt., 132. Found: C, 45.45; H, 6.19; mol. wt. (cryoscopic in water), 137.¹⁶

The product prepared as described above was stable to hot Fehling solution although it gave a strongly positive test after brief treatment with 6 *N* hydrochloric acid.

1,5-Anhydro-2,3-di-*O*-benzoyl- β -D-ribofuranose.—The anhydride VII (52.7 mg.) was benzoylated in conventional fashion to yield from absolute ethanol 82.8 mg. (61%) of needle-shaped crystals melting at 132–133° and rotating in chloroform $[\alpha]^{20}_D -58.9^\circ$ (*c* 1.8).

Anal. Calcd. for $C_{19}H_{16}O_6$: C, 67.05; H, 4.74. Found: C, 67.12; H, 4.76.

2,3-*O*-Benzylidene-5-*O*-*p*-tolylsulfonyl-D-ribofuranose (V).—A solution of 6.5 g. of 2,3-*O*-benzylidene- β -D-ribofuranose² in 10 ml. of pyridine was cooled to -70° and mixed with a solution of 5.8 g. (1.11 molar equivalents) of tosyl chloride in 10 ml. of pyridine. The resulting solution was held at 0° for 1 hr. and then at 25° for 4 hr. After cooling to 0° the mixture was treated with 5 ml. of saturated aqueous sodium bicarbonate; 30 min. later it was poured into 50 ml. of the same reagent. The crystalline precipitate was removed, washed thoroughly with aqueous sodium bicarbonate and dissolved in toluene. Concentration *in vacuo* afforded a sirup which was largely free of moisture and pyridine. From ethanol solution (after treatment with decolorizing carbon) the product (8.6 g., 80%) was precipitated by the addition of water. After three recrystallizations from ethanol-pentane and drying *in vacuo* at 0° the pure material melted at 93–94° and rotated in acetone (*c* 5.0), $[\alpha]^{20}_D +11.2^\circ$. In U.S.P. chloroform (*c* 8.0) a slight mutarotation was observed, $[\alpha]^{20}_D +2.06^\circ$ (10 min.) $\rightarrow +3.43^\circ$ (2 hr.) $\rightarrow +4.24^\circ$ (48 hr., constant). The substance is markedly unstable at room temperature, the odor of benzaldehyde being apparent after a few days.¹⁷

Anal. Calcd. for $C_{19}H_{20}O_7S$: C, 58.15; H, 5.14. Found: C, 58.26; H, 5.15.

1,5-Anhydro-2,3-*O*-benzylidene- β -D-ribofuranose (VI) from **2,3-*O*-Benzylidene-5-*O*-*p*-tolylsulfonyl-D-ribofuranose (V).**—A solution of 190 mg. of sodium in 35 ml. of 2-propanol mixed with a solution of 1.7 g. of 2,3-*O*-benzylidene-5-*O*-*p*-tolylsulfonyl-D-ribofuranose in 20 ml. of 2-propanol gave a white precipitate immediately. The mixture was held at 60° for 20 hr., diluted with benzene and ether and shaken twice with water. The organic layer, freed of water with sodium sulfate, was concentrated *in vacuo* and the resulting residue dissolved in methanol. The solution was treated with traces of calcium carbonate and charcoal, filtered and diluted with water. The crystals (737 mg., 77%) thus obtained melted at 98–110°; recrystallization from methanol gave material which melted at 115–119° and rotated in chloroform (*c* 2.15), $[\alpha]^{20}_D -49.8^\circ$. Subsequent sublimation at 0.03 mm. pressure and 70–90° (bath) followed by recrystallization from cyclohexane-pentane raised the m.p. to 121–125°. Mixed with a sample of the 1,5-anhydro-2,3-*O*-benzylidene- β -D-ribofuranose obtained through the benzylideneation of D-ribose, the material melted at 121–132°.

Hydrogenolysis of a sample (187.5 mg.) in methanol solution with palladium black as a catalyst gave 94.5 mg. (84%) of crystals melting at 102–106°. Sublimed at 0.03 mm. and 80–90° (bath) and then recrystallized from acetone-benzene, the product melted at 109–110° either alone or in admixture with a sample of 1,5-anhydro- β -D-ribofuranose derived *via* the benzylideneation of D-ribose as described earlier.

(16) We are indebted to Dr. Hans Keitel of the National Heart Institute for this measurement.

(17) Levene and Stiller (ref. 7) tosylated crude 2,3-*O*-isopropylidene-D-ribofuranose and obtained in small yield a ditosyl ester which J. A. Mills [*Advances in Carbohydrate Chem.*, **10**, 1 (1955)] has shown to be derived from 1,2-*O*-isopropylidene-D-ribofuranose. 2,3-*O*-Isopropylidene-5-*O*-tolylsulfonyl-D-ribose, the compound which Levene and Stiller sought, is, like its benzylidene analog described here, a markedly unstable substance and the failure of these authors to isolate it is readily understandable.

A sample of the 1,5-anhydro- β -D-ribofuranose made through the tosyl ester was benzoylated in the usual manner to give a product which, after two recrystallizations from ethanol, melted at 132–133° either alone or in admixture with 1,5-anhydro-2,3-di-*O*-benzoyl- β -D-ribofuranose derived through the benzylideneation of ribose.

1,5-Anhydro-2,3-*O*-isopropylidene- β -D-ribofuranose (VIII).—1,5-Anhydro- β -D-ribofuranose (VII, 6 mg.) was dissolved in 3 ml. of acetone and shaken for 24 hr. at 25° with anhydrous copper sulfate. After removal of the catalyst the solution was concentrated *in vacuo* and the resulting residue extracted with pentane. After concentration, the pentane extract gave, at 0°, 5 mg. of crystalline material, m.p. 60–61°. A mixed m.p. with material prepared by the method of Levene and Stiller⁷ and rotating $[\alpha]^{20}_D -62.9^\circ$ in methanol (*c* 0.088) was undepressed.

Di-(2,3-*O*-isopropylidene- β -D-ribofuranose) 1,5':1',5-Dianhydride (III).—The dimeric anhydride (II, 220 mg.) was shaken for 48 hr. at 25° with 25 ml. of acetone and 3 g. of anhydrous copper sulfate. The catalyst was then removed and the solution concentrated *in vacuo* to a semi-crystalline mass which was extracted with pentane. On concentration the pentane solution yielded 258 mg. (90%) of crystalline material melting at 93–96°. The product was then sublimed (0.02 mm., 90° bath) and recrystallized from aqueous methanol to yield a mixture of flat needles and plates which melted at 86–87°. On cooling it resolidified and then melted at 97–98°. The higher melting form could also be obtained directly from aqueous methanol or pentane. In chloroform (*c* 4.61) it showed $[\alpha]^{20}_D -49.0^\circ$.

Anal. Calcd. for $C_{16}H_{24}O_8$: C, 55.80; H, 7.03. Found: C, 56.04; H, 7.26.

Phenyl β -D-Ribofuranoside Tribenzoate.—A solution of 10 g. of 2,3,5-tri-*O*-benzoyl-D-ribofuranose¹³ in 28 ml. of dichloromethane was mixed with 2.8 ml. of acetic anhydride and 29 ml. of a 30% (w./w.) solution of hydrogen bromide in glacial acetic acid. After 30 min. at 0° and 90 min. at 25° the mixture was diluted with toluene and evaporated *in vacuo* at less than 50° (bath). This evaporation with toluene was repeated twice and the residual sirup then mixed with a solution of phenol (10 g.) in 20 ml. of 1,2-dimethoxyethane in which 550 mg. of sodium had been dissolved. After 1 hr. at 50° the mixture was cooled, diluted with ether-benzene and washed repeatedly with water. The organic layer was dried with sodium sulfate and concentrated *in vacuo*, finally at 80° and 0.03 mm. for 2 hr. The brown residue was dissolved in hot ethanol, decolorized with carbon and filtered; on cooling, the solution deposited needles melting at 125–130°. Several recrystallizations from aqueous ethanol and ethanol-pentane gave pure phenyl β -D-ribofuranoside tribenzoate melting at 132–133° and rotating $[\alpha]^{20}_D -7.8^\circ$ in acetone (*c* 0.94); yield 6.9 g. (59%).

Anal. Calcd. for $C_{32}H_{26}O_8$: C, 71.36; H, 4.87. Found: C, 71.61; H, 4.87.

Phenyl β -D-Ribofuranoside (IX).—A solution of phenyl β -D-ribofuranoside tribenzoate (4.1 g.) in 180 ml. of methanol was mixed with 3.5 ml. of 1.5 *N* barium methoxide. The mixture was kept at +5° for 18 hr. and then treated with 5 ml. of water and carbon dioxide until saturated. Solvent was removed *in vacuo* and the thick sirup dissolved in hot 1-propanol. The filtered solution was concentrated *in vacuo* and the residue recrystallized from 1-butanol-pentane. After a further recrystallization from 250 ml. of toluene the long needles (1.43 g., 83%) melted at 106–107° and rotated $[\alpha]^{20}_D -117.2^\circ$ in acetone (*c* 3.89) and $[\alpha]^{20}_D -99.0^\circ$ in water (*c* 1.77).

Anal. Calcd. for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24. Found: C, 58.36; H, 6.09.

Phenyl β -D-ribofuranoside (0.313 mM.) was treated with an excess of sodium metaperiodate and made up to a volume of 10.0 ml.; observed in a 1.5-dm. tube at 20° the rotation of the resulting solution became constant at a value of -1.68° after 3 min. In a parallel experiment with phenyl β -D-glucopyranoside (0.313 mM.) the rotation was found to attain constancy at a value of -1.68° after 6 hr..

Acknowledgment.—We are indebted to Mr. W. M. Jones for infrared spectra and to Mr. H. W.

Diehl for a supply of 2,3-*O*-benzylidene- β -D-ribofuranose and of 2,3,5-tri-*O*-benzoyl-D-ribose. Analyses were performed in the Institutes' Micro-

analytical Laboratory under the supervision of Dr. W. C. Alford. BETHESDA 14, Md.

[CONTRIBUTION FROM THE ORGANIC CHEMICAL RESEARCH SECTION AND THE VIRAL AND RICKETTSIAL RESEARCH SECTION, RESEARCH DIVISION, LEDERLE LABORATORIES, AMERICAN CYANAMID COMPANY]

Synthesis and Biological Properties of Certain 5,6-Dichlorobenzimidazole Ribosides

BY HENRY M. KISSMAN, RALPH G. CHILD AND MARTIN J. WEISS

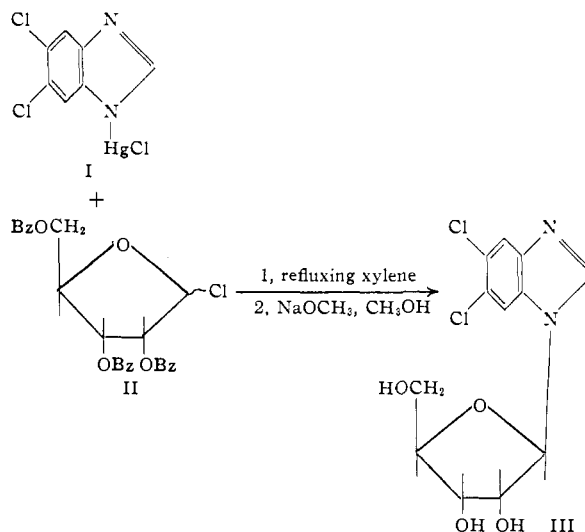
RECEIVED SEPTEMBER 21, 1956

The syntheses of 1- β -D-ribofuranosyl-5,6-dichlorobenzimidazole (DRB, III) a known¹ but hitherto undescribed compound and of the β - and α -anomers of 1-(5-deoxy-D-ribofuranosyl)-5,6-dichlorobenzimidazole (VI and VII, respectively) are reported. Evidence is presented showing that DRB does not inhibit the multiplication of the PR8 strain of influenza virus in mice. DRB and compounds VI and VII are also inactive against a variety of other viruses *in ovo*, in tissue culture and in mice.

The report by Tamm, *et al.*,¹ that 1- β -D-ribofuranosyl-5,6-dichlorobenzimidazole (III, DRB) inhibits influenza virus multiplication *in ovo* and in mice prompted us to test this and related compounds in our antiviral testing program.²

Compound II was unavailable to us and since experimental directions for its preparation have never been published, it was necessary to devise a synthesis. The only preparation of an N-glycoside of 5,6-dichlorobenzimidazole described in the literature is that of Weygand, Wacker and Wirth,³ who condensed acetobromoglucose with the silver salt of 5,6-dichlorobenzimidazole to obtain 1- β -D-glucopyranosyl-5,6-dichlorobenzimidazole in 34% yield. A similar experiment by Antaki and Petrow⁴ with the silver salt of 2-methyl-5,6-dichlorobenzimidazole failed. In our work we applied the "mercuric chloride method" which Davoll and Brown⁵ had developed for the synthesis of glycosides of benzimidazole and 5,6-dimethylbenzimidazole. The chloromercuri derivative I of 5,6-dichlorobenzimidazole³ was prepared according to the general procedure of these authors⁵ and was allowed to react in xylene suspension with an equivalent of the 1-chloro sugar (II) obtained⁶ from 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribofuranose (IV).^{6,7} The blocked condensation product was not isolated *per se* but was de-*O*-benzoylated with sodium methoxide in methanol⁸ to afford III as a crystalline solid, m.p. 215–216°, in 68% over-all yield from IV. While it is not possible to furnish

rigorous proof for the β -configuration of our product, this can be assumed from the high negative rotation value ($[\alpha]^{25}_D -63^\circ$ in pyridine¹⁰) and from analogy to results observed in the purine series by Baker and co-workers.¹¹ These authors found that in a condensation of a 1-chloro sugar with a chloromercuripurine, the entering purine moiety assumes a configuration *trans* to the 2-acyloxy group of the sugar (" C_1-C_2 *trans* rule").



Since 1,2,3-tri-*O*-acetyl-5-deoxy-D-ribofuranose (V)¹² was readily available in our laboratory, it was of interest to prepare 1-(5-deoxy- β -D-ribofuranosyl)-5,6-dichlorobenzimidazole (VI) as an analog of III. The synthesis was effected by condensing I with 2,3-di-*O*-acetyl-5-deoxy-D-ribofuranosyl chloride in refluxing xylene. The gummy reaction product was deblocked with methanolic sodium methoxide⁸ to give a mixture of solids. This mixture was resolved into two crystalline compounds

(10) The rotation of β -ribazole, which is the corresponding 5,6-dimethylbenzimidazole derivative, is $[\alpha]^{25}_D -45^\circ$ in pyridine; F. Weygand and F. Wirth, *Chem. Ber.*, **85**, 1000 (1952). The rotation of α -ribazole is $[\alpha]^{25}_D +9.9^\circ$ in pyridine; N. G. Brink and K. Folkers, *This Journal*, **74**, 2856 (1952).

(11) B. R. Baker, J. P. Joseph, R. E. Schaub and J. H. Williams, *J. Org. Chem.*, **19**, 1786 (1954).

(12) H. M. Kissman and B. R. Baker, to be published.

(1) (a) I. Tamm, K. Folkers, C. Shunk and F. L. Horsfall, Jr., *J. Exptl. Med.*, **99**, 227 (1954); (b) I. Tamm and D. A. Tyrrell, *ibid.*, **100**, 541 (1954).

(2) It may be noted that other benzimidazole derivatives have been reported to exhibit similar properties; cf. I. Tamm, *et al.*, *ibid.*, **98**, 245 (1953); *J. Bact.*, **72**, 42, 54, 59 (1956). Furthermore, DRB and a trichlorobenzimidazole riboside have been reported to inhibit mumps virus multiplication *in ovo*. I. Tamm, *Science*, **120**, 847 (1954); cf. F. L. Horsfall, Jr., *Bull. N. Y. Acad. Med.*, **31**, 783 (1955).

(3) F. Weygand, A. Wacker and F. Wirth, *Z. Naturforsch.*, **6b**, 25 (1951).

(4) H. Antaki and V. Petrow, *J. Chem. Soc.*, 2873 (1951).

(5) J. Davoll and G. B. Brown, *This Journal*, **73**, 5781 (1951).

(6) H. M. Kissman, C. Pidacks and B. R. Baker, *ibid.*, **77**, 18 (1955).

(7) R. K. Ness, H. W. Diehl and H. G. Fletcher, Jr., *ibid.*, **76**, 763 (1954).

(8) G. Zemplén and E. Pacsu, *Ber.*, **62**, 1613 (1929).

(9) As far as could be ascertained, physical characteristics of III have never been published.