When a 2.5 x 10^{-5} M aqueous solution of the product was titrated at 25° with sodium periodate[13] the uptake of periodate (2 molar equiv) was the same as that by the same volume of a 5 x 10^{-5} M solution of inosine. A difference of 5% would have been detectable under these conditions. The time required (30 min) for complete reaction with periodate was the same for both nucleosides.

(13) R. L. Metzenberg and H. K. Mitchell, *J. Am. Chem. Soc.*, **76**, 4187 (1954).

Attempted Synthesis of a 3-Deoxy-3-phthalimido-D-ribopyranose Derivative. Formation of Furanose Derivatives

JOSEPH P. JOSEPH AND MARTIN J. WEISS

Organic Chemical Research Section, Lederle Laboratories Division, American Cyanamid Company, Pearl River, New York

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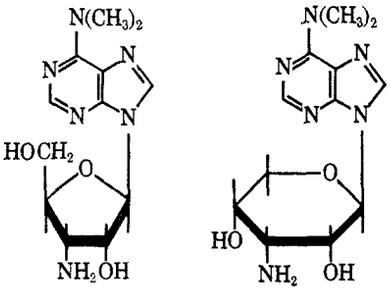
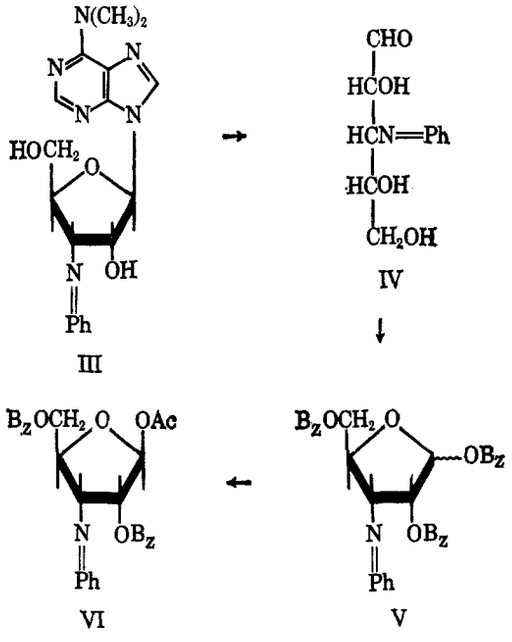
Analogs of the aminonucleoside I[1] derived from the antibiotic puromycin are of interest because of the antitumor[2] and trypanocidal[3] properties exhibited by I in experimental animals. As part of our program for the synthesis of aminonucleoside analogs, we undertook to prepare the 9β-3-amino-3-deoxy-D-ribopyranosyl derivative (II) of 6-dimethylaminopurine. Although our attention was diverted to other areas before the synthesis of II could be successfully achieved, several observations which were made during this study appear worthy of note.



I II

In principle, the synthesis of II requires the preparation of a suitably blocked derivative of 3-aminoribopyranose, its conversion to a 1-halo sugar, and condensation of this halogenose with a chloromercuripurine derivative. At the inception of our study, it seemed likely that the required 3-aminoribopyranose could be prepared by procedures analogous to those reported for the preparation of ribopyranose derivatives. Of particular interest was the procedure of Jeanloz, Fletcher, and Hudson,[4] whereby ribose was benzoylated at low temperature in pyridine solution to give a high yield of ribopyranose tetrabenzoate anomers. Since it had already been indicated[5] that N-phthaloyl amino sugar derivatives were best suited for the transformations required to produce aminonucleosides, our work was directed towards the preparation of a 3-phthalimidoribopyranoside and required as starting material 3-phthalimido-3-deoxy-D-ribose (IV). This compound was obtained by acid-catalyzed cleavage of the N-phthaloylaminonucleoside III.[5] After some study (see the Experimental Section), it was found that hydrolytic cleavage could best be achieved (79% yield) by a 15-min treatment of a suspension of III with Amberlite IR-120[6] [H] resin at reflux temperature.[7]

Benzoylation of IV according to the procedure of Jeanloz, Fletcher, and Hudson[4] gave amorphous tribenzoate (V) in 79% crude yield. Acetolysis of this crude product afforded a mixture from which it was possible to isolate crystalline material in 61% yield. This product, after further purification, was then identified as the known[5,8] 1-*O*-acetyl-2,5-di-*O*-benzoyl-3-deoxy-3-phthalimido-β-D-ribofuranose (VI). Thus, contrary to experience with ribose itself,[4] 3-phthalimidoribose affords on benzoylation, at least as the major product, a structure having the furanoid configuration.



Ph = phthaloyl; Bz = benzoyl

As an alternative approach, we next investigated the product that might be obtained on acetonation of IV. Conceivably, acetonation could lead to the furanoside VII or the pyranoside VIII, or a mixture of both. When 3-phthalimidoribose (IV) was treated with acetone in the presence of copper sulfate and ethanesulfonic acid,[9] there was obtained an 85% yield of a crystalline isopropylidene derivative of unknown ring size. In order to determine the ring configuration, the isopropylidene derivative was dephthaloylated[8] by treatment with butylamine in refluxing methanol. The re-

(1) B. R. Baker, J. P. Joseph, and J. H. Williams, *J. Am. Chem. Soc.*, **77**, 1 (1955).

(2) P. L. Bennett, S. L. Halliday, J. J. Oleson, and J. H. Williams, "Antibiotics Annual, 1954–1955," Medical Encyclopedia, Inc., New York, N. Y., 1954, pp 766–769.

(3) R. I. Hewitt, A. R. Gumble, W. S. Wallace, and J. H. Williams, *Antibiot. Chemotherapy*, **4**, 1222 (1954).

(4) R. Jeanloz, H. G. Fletcher, Jr., and C. S. Hudson, *J. Am. Chem. Soc.*, **70**, 4052 (1948).

(5) B. R. Baker, J. P. Joseph, and R. E. Schaub, *ibid.*, **77**, 5905 (1955).

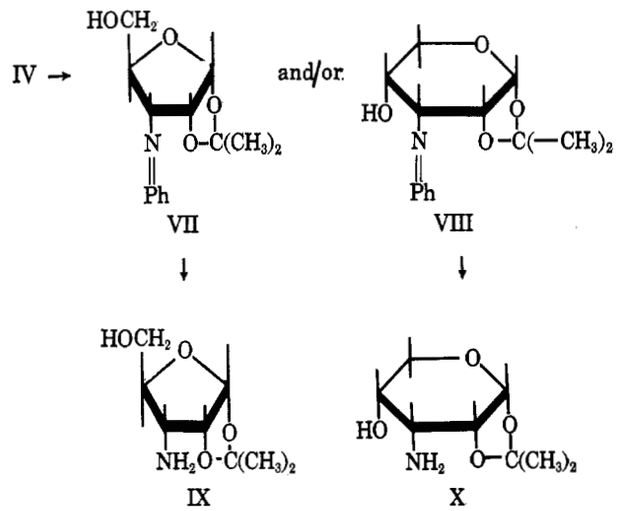
(6) Amberlite IR-120 is the trademark of the Rohm and Haas Co.

(7) This procedure was based on that used by J. X. Khym, D. G. Doherty, and W. E. Cohn [*J. Am. Chem. Soc.*, **76**, 5523 (1954)] for the cleavage of ribose 5-phosphate from adenosine 5′-phosphate.

(8) L. Goldman and J. W. Marsico, *J. Med. Chem.*, **6**, 413 (1963).

(9) Method of B. R. Baker and R. E. Schaub, *J. Am. Chem. Soc.*, **77**, 5900 (1955).

sulting crystalline free amine did not consume any periodate, indicating a furanoid structure (IX) for it and the precursor phthalimido derivative (VII).



Ph = phthaloyl

Experimental Section[10]

3-Deoxy-3-phthalimido-D-ribose (IV). A.[7]—In 5 ml of ethanol, 500 mg of pulverized N-phthaloylaminonucleoside III[5] was suspended and 15 ml of distilled water was added with 1.0 g of reactivated Dowex 50[11] [H] cation-exchange resin. The mixture was refluxed for 15 min, during which time all solid dissolved, and was then filtered while hot. The filtrate was evaporated to dryness *in vacuo* from a water bath at 50° leaving a gummy solid, mp 125–135°. This product was triturated with 1 ml of absolute ethanol and dried. The resulting crystalline 3-deoxy-3-phthalimido-D-ribose (IV) weighed 150 mg (45%) and had mp 150–153° dec, with previous shrinking at 148°. A sample was submitted for analysis without further purification because decomposition was noted during attempts to recrystallize this material from ethanol: $[\alpha]^{25}D$ +40.0° (0.5% in 2-methoxyethanol).

Anal. Calcd for $C_{13}H_{13}NO_6$: C, 55.9; H, 4.70; N, 5.02. Found: C, 56.1; H, 5.08; N, 4.80.

In another experiment where the reflux time was 30 min, there was obtained a 60% yield of material IV, mp 138–140° dec, which decomposed on recrystallization, but after trituration with ethanol melted at 150–153° dec. A 50% yield was obtained after 1 hr of reflux, mp 140–143° dec.

B.—In 50 ml of distilled water, 1.0 g of pulverized N-phthaloylaminonucleoside III[5] was suspended with 2.0 g of reactivated cation exchange resin Amberlite IR-120 [H]. The mixture was refluxed with stirring for 15 min to give a clear solution. The resin was removed by filtration through Celite[12] diatomaceous earth and the filtrate, which had a pH of approximately 3, was neutralized with Duolite A-4[13] anion-exchange resin. The solution was filtered and the filtrate was evaporated to dryness *in vacuo* (bath temperature 50°). There remained a white solid, 0.51 g (79%), mp 147–149° dec. On a larger scale, the product was not so pure.

1,2,5-Tri-*O*-benzoyl-3-deoxy-3-phthalimido-D-ribofuranose (V).—In 4 ml of reagent pyridine and 6 ml of methylene chloride cooled to 5°, 600 mg of 3-phthalimidoribose (IV) was dissolved. To this solution was added 0.82 ml of benzoyl chloride, and the reaction mixture was sealed from atmospheric moisture and kept at 5° for 3 days. It was then poured into 50 ml of ice–water and extracted with chloroform. The chloroform solution was washed with excess sodium bicarbonate solution and then water. It was dried over magnesium sulfate, filtered, and evaporated to dryness *in vacuo*. The residual gum was redissolved in anhydrous ether, clarified with decolorizing charcoal, and evaporated to dryness *in vacuo* leaving a pale yellow gum, 1.0 g (79%). A sample of this gum was submitted for analysis: λ_{max}^{KBr} 5.6 and 5.8 (phthalimido) and 7.9 μ (benzoate).

Anal. Calcd for $C_{34}H_{25}NO_9$: C, 69.1; H, 4.28; N, 2.37. Found: C, 66.8; H, 4.98; N, 2.63.

Acetolysis of 1,2,5-Tri-*O*-benzoyl-3-deoxy-3-phthalimido-D-ribofuranose (V). Formation of 1-*O*-Acetyl-2,5-di-*O*-benzoyl-3-deoxy-3-phthalimido-β-D-ribofuranose (VI).—In 7.2 ml of glacial acetic acid containing 0.8 ml of acetic anhydride there was dissolved 940 mg of crude 1,2,5-tri-*O*-benzoyl-3-deoxy-3-phthalimido-D-ribofuranose (V). The solution was cooled below 20° and 0.43 ml of concentrated sulfuric acid was added portionwise. After standing at room temperature overnight, the solution was poured into 50 ml of ice–water to give a white precipitate which was taken up in chloroform. The chloroform solution was washed with excess saturated sodium bicarbonate solution and then with water. After drying over magnesium sulfate, the chloroform solution was evaporated to dryness *in vacuo* leaving 760 mg (90%) of a gum. The gum was dissolved in 10 ml of ethanol and cooled overnight to give 510 mg (61%) of a white, crystalline solid, mp 120–122°, $[\alpha]^{26}D$ +89.50° (2% in chloroform). From 176 mg of this material, 109 mg (62%) of white needles, mp 135–138°, was obtained on recrystallization from absolute ethanol, $[\alpha]^{26}D$ +118° (2% in chloroform). The melting point suggested the possibility that this product was 1-*O*-acetyl-2,5-di-*O*-benzoyl-3-deoxy-3-phthalimido-β-D-ribofuranose (VI), mp 138–140°, $[\alpha]^{25}D$ +122° (chloroform), which had previously been prepared[5] by acetolysis of 6-dimethylamino-9-(2,5-di-*O*-benzoyl-3-deoxy-3-phthalimido-β-D-ribofuranosyl)-purine. The identity was confirmed by mixture melting point and infrared data.

3-Deoxy-1,2-*O*-isopropylidene-3-phthalimido-α-D-ribofuranose (VII).—In 173 ml of reagent acetone, 14.5 g of anhydrous reagent cupric sulfate and 3.09 g of 3-deoxy-3-phthalimido-D-ribose (IV) were suspended. The mixture was stirred magnetically and a solution containing 8.9 ml of ethanesulfonic acid[9] in 75 ml of reagent acetone was added dropwise rapidly. After stirring for 30 min, the copper sulfate was removed by filtration and the filtrate was poured into 600 ml of 5% sodium bicarbonate solution. The sodium bicarbonate mixture was extracted four times with chloroform (total 300 ml). The chloroform extracts were combined, washed with water, and dried over magnesium sulfate. After filtration and evaporation to dryness *in vacuo*, a gum remained. This gum was dissolved in 100 ml of dry ether, clarified with decolorizing charcoal, and filtered through Celite. On standing overnight at 5°, white crystals separated; these were collected by filtration and washed with ether. There was obtained 1.17 g of crystalline VII, mp 112–114°, $[\alpha]^{24}D$ +185° (1% in chloroform). From this filtrate an additional 1.8 g of crystalline solid, mp 100–105°, was obtained. Total yield of 3-decxy-1,2-*O*-isopropylidene-3-phthalimido-α-D-ribofuranose (VII) was 2.97 g (85%).

Anal. Calcd for $C_{16}H_{17}NO_6$: C, 60.1; H, 5.36; N, 4.39. Found: C, 59.9; H, 5.33; N, 4.39.

This material did not lend itself to recrystallization.

3-Amino-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (IX).—To a methanolic solution (10 ml) containing 0.5 g of 3-deoxy-1,2-*O*-isopropylidene-3-phthalimido-α-D-ribofuranose (VII) 1.57 ml of butylamine[8] was added. The solution was refluxed for 18 hr on a steam bath and then evaporated to dryness *in vacuo* leaving a solid and gum. After the addition of 10 ml of water, the solid separated and was collected by filtration and dried. Thus, 0.35 g (91%) of dibutylphthalamide, mp 115–117°, was obtained. This material was identified by mixture melting point with an authentic sample. The aqueous filtrate was evaporated to dryness *in vacuo* at 30° bath temperature leaving 350 mg of an oil and solid. This was dissolved in anhydrous ether at room temperature and the ether solution was concentrated to about 5 ml. After allowing the concentrate to evaporate slowly, 310 mg of white needles and a gum formed. The crystalline material was mechanically separated from the gum to give 185 mg of long needles, mp 62–65°. After two recrystallizations from petroleum ether (bp 90–100°) the melting point was 63–67°, $[\alpha]^{24}D$ +43.9° (0.5% in water). An analytical sample was obtained after drying for 3 hr at 78° and overnight at room temperature *in vacuo* over phosphorus pentoxide.

Anal. Calcd for $C_8H_{15}NO_4$: C, 50.8; H, 8.01; N, 7.41. Found: C, 51.0; H, 7.98; N, 7.53.

(10) Melting points are uncorrected.
(11) Dowex 50 is the trademark of the Dow Chemical Co.
(12) Celite is the trademark of the Johns-Manville Corp.
(13) Duolite A-4 is the trademark of the Chemical Process Co.

When treated with sodium metaperiodate (sodium bicarbonate buffer),[14] this product (IX) did not consume any oxidant.

Acknowledgments.—We wish to thank Dr. H. M. Kissman for helpful conversations, Mr. W. Fulmor and staff for the spectroscopic and polarimetric data, and Mr. L. Brancone and staff for the microanalyses.

(14) Procedure A described by M. J. Weiss and co-workers, *J. Am. Chem. Soc.*, **81**, 4050 (1959).

2,3-Dideoxy-DL-pentose

CHARLES C. PRICE AND RICHARD B. BALSLEY[1]

Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104

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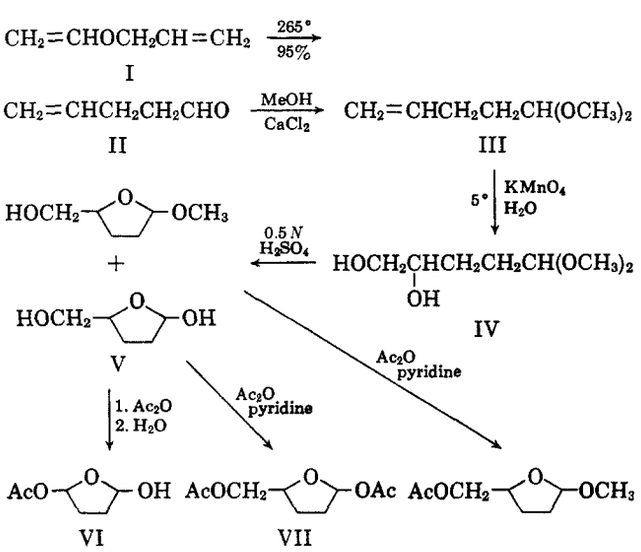
In view of the importance of ribose and 2-deoxyribose in biological systems, we wished to develop a more convenient and practical synthesis of 2,3-dideoxyribose (V) than that described from arabinose[2a] or of the phenylhydrazone from 2-deoxy-D-ribose.[2b] The racemic form is obtained by the Claisen rearrangement of allyl vinyl ether to 4-pentenal,[3,4] conversion to the methyl acetal, and permanganate oxidation.



The furanose ring system for the 5-acetate (VI) as well as the 1,5-diacetate (VII) is indicated by the chemical shifts for the 4 and 5 hydrogens in the nmr spectra.

Experimental Section

Allyl vinyl ether (I) was prepared by mercuric acetate catalyzed reaction of butyl vinyl ether with allyl alcohol, distilling the crude product directly from the reaction mixture held at 87°. After fractional distillation, material containing 70% I was obtained. This was washed with water to remove allyl alcohol and dried over sodium sulfate. Refractionation gave a 51% yield of 95% pure I (by vpc) and one more distillation produced 30% of 99.5% pure I, bp 66–67.2°, n^{20}D 1.4111.[5]

Allyl butyl acetal was isolated by careful fractionation of the initial residue in the above preparation, bp 70–71° (22 mm), n^{20}D 1.4144.

Anal. Calcd for $C_9H_{18}O_2$: C, 68.32; H, 11.47. Found: C, 68.26; H, 11.52.

4-Pentenal (II).—Conditions for optimum pyrolytic conversion of I to II were carefully explored. The best results (>97% conversion, >98% yield) were obtained by passing I through a 24 × 0.5 in. o.d. glass tube packed with 30–60 mesh, nonacid-washed Chromosorb W and maintained at 265°. A flow rate of 15 cc/min of dry nitrogen was maintained while 12 g/hr of I was passed through the column. The product which liquefied in a water-cooled condenser amounted to 97% of charged I and the purity (by vpc) ranged from 95 to 99% in twelve conversions. The column required cleaning about every four runs owing to accumulation of polymer. The redistilled II had bp 102–104°, n^{20}D 1.4165, d^{20} 0.851.[3]

The infrared spectrum showed bands at 3.27 (sh), 3.46 (31), 3.55 (34), 3.69 (29), 5.84 (90), 6.11 (26), 7.00 (sh), 7.12 (33), 7.22 (sh), 7.45 (sh), 9.5 (18), 10.06 (25), and 10.93 (33) μ (per cent absorbance). The nmr spectrum (neat) showed absorption for one hydrogen each at τ 0.8, at 4.2–5, at 5.3 (doublet, J = 5.5 cps), and at 5.42 (doublet J = 2.7 cps) and for four hydrogens at 7.7–7.9.

1,1-Dimethoxy-4-pentene (III) was prepared by adding 320 g of II (in 10-ml portions) to 300 g of anhydrous calcium chloride in 2 l. of absolute methanol at 0°. After standing for 36 hr at 25°, the product was extracted with petroleum ether (bp 30–60°) and distilled to provide 400 g (81%) of 99% pure III, bp 60.5–61.2° (49 mm), n^{20}D 1.4120, d^{20} 0.868.

Anal. Calcd for $C_7H_{14}O_2$: C, 64.57; H, 10.84. Found: C, 64.73; H, 10.63.

The infrared spectrum showed bands at 3.24 (69), 3.31 (50), 6.13 (18), 6.97 (37), 7.08 (15), 7.29 (31), 7.38 (30), 8.44 (51), 8.92 (94), 9.41 (90), 10.10 (39), 10.35 (35), and 11.00 (67) μ (per cent absorbance). The nmr spectrum (neat) showed absorption for one hydrogen each at τ 4.7–4.9, at 5.3 (doublet, J = 4.9 cps), at 5.5 (doublet, J = 2 cps), and at 6.0 (triplet, J = 4.9 cps), for six hydrogens at 7.1, and for four hydrogens at 8–8.6.

1,1-Dimethoxy-4,5-pentanediol (IV) was prepared from III essentially by the procedure described for the permanganate oxidation of acrolein diethyl acetal.[6] A solution of 79 g (0.5 mole) of potassium permanganate in 1800 ml of water was added dropwise over 4 hr to 65.1 g (0.5 mole) of III in 300 ml of water maintained at 5 ± 0.5°. The reaction mixture, which gelled, was allowed to stand overnight then heated at 95° for 1 hr. After filtration, the product was salted out with potassium carbonate. The orange oil was treated with activated charcoal and anhydrous magnesium sulfate and distilled to give 45% of IV, bp 103.8–103.9° (0.25 mm), n^{20}D 1.4518, d^{25} 1.079.

Anal. Calcd for $C_7H_{16}O_4$: C, 51.20; H, 9.82. Found: C, 50.73; H, 9.75.

The infrared spectrum showed bands at 2.94 (90), 3.44 (72), 6.95 (72), 7.25 (46), 7.35 (47), 8.41 (54), 8.52 (52), 8.86 (91), 9.45 (97), 10.34 (52), 10.91 (31), and 11.34 (35) μ (per cent absorbance). The nmr spectrum in deuteriochloroform showed an apparent quartet at τ 5.7–6.0 (3 H), broad absorption at 6.5–6.8 (3 H), a singlet at 6.95 (6 H), and broad absorption at 8.3–8.8 (4 H).

2,3-Dideoxypentose (V).—Hydrolysis of IV by 0.5 N sulfuric acid in a steam bath for 3 hr followed by neutralization, evaporation, and methanol extraction gave an amber syrup (~100% yield), n^{20}D 1.4704, giving a positive Benedict's test, undoubtedly a mixture of ring and stereo isomers.

The infrared spectrum showed bands at 2.94 (88), 3.40 (53), 6.92 (41), 7.38 (36), 7.81 (30), 7.99 (26), 8.25 (37), 8.81 (52), 9.10 (70), 9.5 (8.4), 10.12 (70), 11.19 (41), 11.6 (27), and 12.4 (21) μ (per cent absorbance).

The **dinitrophenylhydrazone** was prepared by the procedure of Richards,[7] as yellow needles from ethyl acetate: mp 134–135°.

Anal. Calcd for $C_{11}H_{14}N_4O_6$: C, 44.29; H, 4.73; N, 18.78. Found: C, 44.55; H, 4.85; N, 18.55.

(1) From a Ph.D. Dissertation by R. B. Balsley, University of Pennsylvania, 1964.

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