The filtrate from the 130 mg. was evaporated to dryness *in vacuo*. Acetylation of the residue with acetic anhydride in pyridine as described for X[3] gave a glass. Crystallization from ethyl acetate afforded 60 mg. (11%) of white crystals, m.p. 185–187°. A mixture with 6-dimethylamino-9-(3′-amino-3′-deoxy-β-D-ribofuranosyl)-purine triacetate obtained from puromycin[3] gave no depression in m.p. and both compounds had the same infrared spectra.

PEARL RIVER, NEW YORK

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

Puromycin. Synthetic Studies. X. A Novel Breakdown of the Purine Ring System

BY B. R. BAKER AND JOSEPH P. JOSEPH

RECEIVED JULY 19, 1954

6-Dimethylamino-9-(5′-methanesulfonyl-3′-amino-3′-deoxy-β-D-ribofuranosyl)-purine 2′,3′-carbonate (VI) has been found to quaternerize easily to V. The latter is very labile to 0.1 *N* base at 25°, hydrolyzing rapidly to 5′,N[4]-cyclo-3-(2′,3′-carbonyl-3′-amino-3′-deoxy-β-D-ribofuranosyl)-4-formamidoimidazole-5-(N,N-dimethyl)-carboxamidine methanesulfonate (IV) which in turn hydrolyzes more slowly to 5′,N[4]-cyclo-3-(2′,3′-carbonyl-3′-amino-3′-deoxy-β-D-ribofuranosyl)-4-aminoimidazole-5-carboxamide (VII). Biological implications are suggested for this sequence.

The total synthesis of the aminonucleoside, 6-dimethylamino-9-(3′-amino-3′-deoxy-β-D-ribofuranosyl)-purine (I), from D-xylose[1] and its partial synthesis from the antibiotic, puromycin,[2] have been described recently. Since the aminonucleoside I is highly active against the transplanted adenocarcinoma of the C_3H mouse[3] as well as *Trypanosoma equiperdum*[4] in mice, it was considered desirable to prepare some functional analogs of the aminonucleoside I by replacement of the 5′-hydroxyl with other groups (IX) *via* a 5′-mesylate. Although the general method of approach failed, a novel breakdown of the pyrimidine portion of the purine ring system was observed and is the subject of this paper.

The conversion of adenosine to its 5′-methylmercapto derivative *via* 2′,3′-isopropylidene-5′-tosyladenosine has been described by Satoh and Makino[5] as well as Baddiley, Trauth and Weygand.[6] A similar sequence with the aminonucleoside I was investigated. Reaction of I with carbobenzoxy chloride and triethylamine in dimethylformamide afforded the carbobenzoxy derivative II in 78% yield. Ring closure of II to the cyclic urethan III with elimination of benzyl alcohol proceeded smoothly in 93% yield with a catalytic amount of sodium methoxide in dimethylformamide.[7] The formation of this cyclic urethan III was substantiated by the hypsochromic shift of the carbonyl absorption of the carbobenzoxy group from 5.87 to 5.62 μ in the infrared as would be expected for a five-membered ring bearing a carbonyl. With the 2′- and 3′-groups now effectively blocked in III, the remaining 5′-hydroxyl was mesylated smoothly in pyridine at 3° to give VI in 80% yield as a crude gum insoluble in water and readily soluble in chloroform. However, after standing at room temperature for several days or, more efficiently, by refluxing in chloroform for two hours, the gum changed to an isomeric crystalline product, m.p. 283° dec., in 91% yield which was now insoluble in chloroform, but readily soluble in water. The salt-like character of this compound could be explained most readily by reaction of the 5′-mesylate with the 3-nitrogen of the purine ring to form a 3,5′-cyclonucleoside V. That the purine ring system had been further alkylated readily could be seen by the shift in the ultraviolet maximum in water from 275 mμ for an ordinary 9-nucleoside derivative of 6-dimethylaminopurine[8] such as I to 288 mμ.

Clark, Todd and Zussman[9] have described the formation of a similar quaternary salt when 2′,3′-isopropylidene-5′-tosyladenosine was heated at 100° in acetone or dioxane. Their proposed structure was beautifully substantiated by X-ray crystallographic analysis. Their results also serve to explain why only about 2% yield of 5′-methylmercaptoadenosine can be obtained from the 5′-tosylate.[5,6] The rate of monomolecular quaternization is obviously much more rapid than the bimolecular displacement reaction with mercaptide ion. Since the 6-dimethylaminopurine nucleoside (VI) appears to quaternerize even more rapidly than in the adenine series, the use of VI as an intermediate in displacement reactions could not possibly lead to useful yields of functional analogs of the aminonucleoside IX.

The usual routine measurement of the ultraviolet absorption spectra at *p*H 1, 7 and 14 on the quaternary salt V, showed an instability at *p*H 14. Within five minutes the initial peak at 230 mμ began to shift and in one hour was at 235 mμ. Then a slower shift to 272 mμ over 27 hours (Graph 1) gradually took place, thus indicating at least two break-down products. The quaternary salt V absorbed at 288 mμ at *p*H 1 and 7 showing that it could not protonate further which contrasts to an ordinary nucleoside such as I which will protonate in acid giving a hypsochromic shift of 7–8 mμ.[8]

(1) B. R. Baker, R. E. Schaub, J. P. Joseph and J. H. Williams, paper IX of this series, THIS JOURNAL, **77**, 12 (1955).

(2) B. R. Baker, J. P. Joseph and J. H. Williams, paper VII of this series, *ibid.*, **77**, 1 (1955).

(3) P. Lydick, S. Halladay and J. J. Oleson, to be published.

(4) R. I. Hewitt, A. Gumble, W. S. Wallace and J. H. Williams, *Am. J. Trop. Med.*, in press.

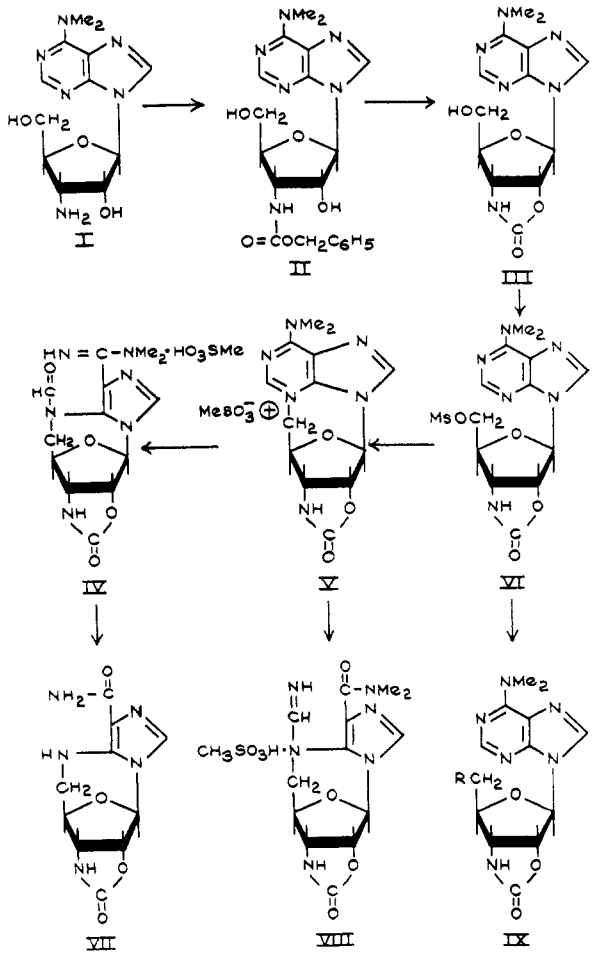
(5) K. Satoh and K. Makino, *Nature*, **167**, 238 (1951).

(6) J. Baddiley, O. Trauth and F. Weygand, *ibid.*, **167**, 359 (1951); J. Baddiley, *J. Chem. Soc.*, 1348 (1951); F. Weygand and O. Trauth, *Chem. Ber.*, **84**, 633 (1951).

(7) The base-catalyzed condensation of ethanolamine with ethyl carbonate to form 2-oxazolidone, which probably proceeds through ethyl N-(β-hydroxyethyl)-carbamate, has been described by A. H. Homeyer, U. S. Patent 2,399,118.

(8) B. R. Baker, R. E. Schaub and J. P. Joseph, paper II of this series, *J. Org. Chem.*, **19**, 638 (1954).

(9) V. M. Clark, A. R. Todd and S. Zussman, *J. Chem. Soc.*, 2952 (1951).



When the quaternary salt V was allowed to react with 0.1 *N* barium hydroxide for 30 minutes, no V could be recovered and a new salt, formed by the addition of the elements of water, was isolated in 31% yield. This hydrolysis product was obtained in 30% yield with 0.1 *N* barium hydroxide in five minutes and 40% of V was recovered. The hydrolytic compound has a new carbonyl band at 5.95 μ in addition to the cyclic urethan carbonyl at 5.67 μ, sulfonate at 8.50 μ and OH–NH absorption at 2.88, 3.05 and 3.25 μ in the infrared. In the ultraviolet the compound has a single peak at 278 (*p*H 1), 288 (*p*H 7) and 235 mμ (*p*H 14). The same change in ultraviolet on standing in base was noted as in the case of V, that is, a shift to 272 mμ complete in 27 hours. The fact that at *p*H 1 there was a shift to 278 from 288 mμ at *p*H 7 showed that this new salt-like compound could protonate further, that is, another basic center had been generated during hydrolysis of V.

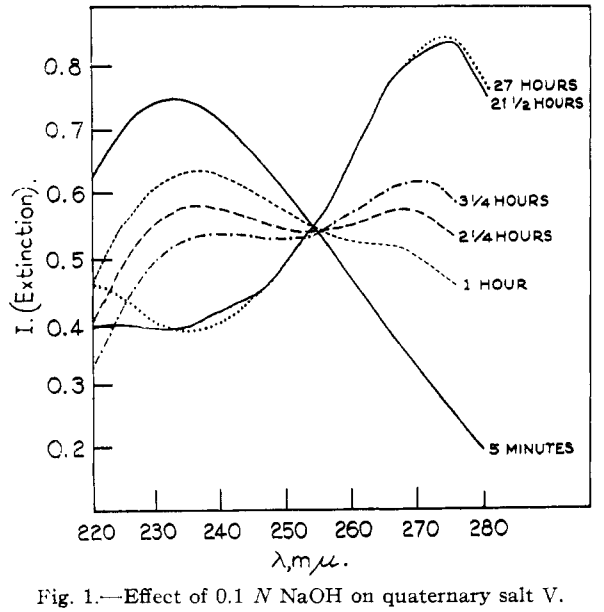


Fig. 1.—Effect of 0.1 *N* NaOH on quaternary salt V.

Two of the possible structures which could be formed during this reaction are (a) the formamidine VIII, if cleavage took place at the 1,6-bond of the purine or (b) the carboxamidine IV, formed if the 1,2-bond were cleaved. The proton of the methanesulfonic acid would no doubt be attached to the strongly basic amidine in either case. This allows the further acceptance of a proton by the imidazole ring with the resultant hypsochromic shift in the ultraviolet maximum in acid solution. The correct structure IV was determined readily by further reaction.

A solution of the quaternary salt V was allowed to stand in 0.1 *N* sodium hydroxide at room temperature until the ultraviolet change was complete. During this time the intermediate IV or VIII was further hydrolyzed and the solution deposited a crystalline product with the concurrent formation of dimethylamine. That the product has structure VII was substantiated by combustion and spectrophotometric data. The infrared spectrum indicated non-tertiary-amide absorption at 6.04 μ with companion band at 6.58 μ. The presence of the cyclic carbonate was still noted at 5.67 μ. The presence of C=N absorption at 6.17 and aromatic C=C at 6.31 μ indicated an imidazole ring. The ultraviolet spectra were in good agreement with that expected for a 1,N^4-disubstituted derivative of 4-aminoimidazole-5-carboxamide,[10] namely, $\lambda_{max}^{pH\ 1}$ 259 mμ (ϵ 12,200); $\lambda_{max}^{H_2O}$ 271 mμ (ϵ 10,600); $\lambda_{max}^{pH\ 14}$ 272 mμ (ϵ 12,300). The intermediate rapidly formed when the quaternary V is converted to VII could only have structure IV since VII cannot be obtained from the isomeric amidine VIII. Thus, the initial breakdown of the purine ring system occurs at the 1,2-linkage to give an N-formylcarboxamidine.

The great ease of cleavage of the quaternary V to an imidazole compared to the stability of the normal purine ring system[11] suggests that this sequence may have biological implications. Buchanan and Schulman[12] have presented strong evidence

(10) 4-Aminoimidazole-5-carboxamide hydrochloride was prepared by the method of E. Shaw and D. W. Woolley, *J. Biol. Chem.*, **181**, 89 (1949), and found to have $\lambda_{max}^{pH\ 1}$ 240 mμ (ϵ 9100), 262 mμ (ϵ 11,220), $\lambda_{max}^{pH\ 14}$ 278 mμ (ϵ 14,600).

(11) The purine ring system is stable to dilute aqueous ammonia at 180°; P. A. Levene and W. A. Jacobs, *Ber.*, **42**, 2469, 2474 (1909); **43**, 3150 (1910). The acid hydrolysis of adenine to 4-aminoimidazole-5-carboxamidine has been shown by L. F. Cavalieri, J. F. Tinker and G. B. Brown (THIS JOURNAL, **71**, 3973 (1949)), to require 6 *N* hydrochloric acid at 150° for 2 hours.

(12) J. M. Buchanan and M. P. Schulman, *J. Biol. Chem.*, **202**, 241 (1953).

that inosinic acid and 4-aminoimidazole-5-carboxamide ribotide are in an enzymatically reversible system *via* the intermediate N-formylimidazole wherein the *citrovorum* factor is acting as a coenzyme which accepts and donates formyl groups. It is interesting to speculate that compounds of type V and VII also are involved as intermediates in this reversible sequence of converting inosinic acid to 4-aminoimidazole-5-carboxamide ribotide.

When II was treated with 1 mole of methanesulfonyl chloride in pyridine at 3°, a 96% yield of crude 5'-mesylate was obtained as a glass. When boiled in chloroform this cyclized to 63% of 3,5'-cyclo-6-dimethylamino-9-(3'-carbobenzoxyamino-3'-deoxy-β-D-ribofuranosyl)-purine methanesulfonate, m.p. 106°. Treatment with hydrogen bromide in acetic acid caused rapid cleavage of the carbobenzoxy group[13] with formation of 74% of crystalline 3,5'-cyclo-6-dimethylamino-9-(3'-amino-3'-deoxy-β-D-ribofuranosyl)-purine bromide hydrobromide. The latter compound had no activity against *Trypanosoma equiperdum* or the transplanted adenocarcinoma of the C_3H mouse.[14] Thus, it can be stated that if the aminonucleoside II owes its biological activity to enzymatic transformation to an active compound, the process cannot proceed through the cyclonucleoside.

Acknowledgment.—The authors wish to thank L. Brancone and staff for the microanalyses and W. Fulmor and staff for the rotations and spectrophotometric data.

Experimental

6-Dimethylamino-9-(3'-carbobenzoxyamino-3'-deoxy-β-D-ribofuranosyl)-purine (II).—To a solution of 1.00 g. of I[2] and 1.0 cc. of triethylamine in 50 cc. of dimethylformamide cooled to 5° was added 0.65 cc. of 93% carbobenzoxy chloride. After being stirred for 15 minutes without cooling, the mixture was poured into 250 cc. of water. The product was collected and washed with water; yield 1.15 g. (78%), m.p. 192–194°. Recrystallization from methanol gave white crystals of unchanged m.p.; $[\alpha]^{24}D$ −19.6° (2% in pyridine); $\lambda_{max}^{nuj.}$ 5.87, 6.30 μ (–CONH); 2.98, 3.10, 3.19 μ (–OH and –NH); 6.18 μ (C=N).

Anal. Calcd. for $C_{20}H_{24}N_6O_5$: C, 56.1; H, 5.66; N, 19.6. Found: C, 55.7; H, 5.45; N, 19.6.

In larger runs the yields were lower (50–55%) and about 20% of III was then isolated by continuous chloroform extraction. Lower yields were obtained with longer or shorter reaction times. No appreciable yield was obtained with water and chloroform in place of the dimethylformamide.

6-Dimethylamino-9-(3'-amino-3'-deoxy-β-D-ribofuranosyl)-purine 2',3'-Carbonate (III).—A solution of 3.5 g. of II and 0.53 cc. of 1 *N* methanolic sodium methoxide in 20 cc. of dimethylformamide was heated on the steam-bath for 2 hours protected from moisture. Evaporation to dryness *in vacuo* gave a solid which was triturated with 5 cc. of absolute alcohol; yield, 2.3 g. (88%), m.p. 241–243° dec. Recrystallization from absolute alcohol gave white crystals, m.p. 245–246°, $[\alpha]^{24}D$ −92° (2% in pyridine); $\lambda_{max}^{nuj.}$ 5.62 μ (–CONH); 3.07, 3.15 μ (–OH and –NH); 6.23 μ (C=N); 8.48 μ (sulfonate).

Anal. Calcd. for $C_{13}H_{16}N_6O_4$: C, 48.8; H, 5.03; N, 26.2. Found: C, 49.1; H, 5.18; N, 26.4.

In other runs the yields were 88–93%. Without the sodium methoxide catalyst, no ring closure took place with the above conditions.

3,5'-Cyclo-6-dimethylamino-9-(3'-amino-3'-deoxy-β-D-ribofuranosyl)-purine 2',3'-Carbonate Methanesulfonate (V).—To a solution of 1.00 g. of III in 6 cc. of pyridine cooled in an ice-bath was added 0.36 cc. of methanesulfonyl chloride. After 18 hours at 5° in a closed flask, the mixture was poured into 30 cc. of ice-water and extracted with three 30-cc. portions of chloroform. The combined chloroform extracts, washed with aqueous sodium bicarbonate, then water, were dried with magnesium sulfate and evaporated to dryness *in vacuo* (bath 50°); yield 1.00 g. (80%) of VI as a gum, soluble in chloroform but insoluble in water.

The gum was dissolved in 25 cc. of chloroform and refluxed for 2 hours during which the product crystallized; yield 0.80 g., m.p. 278–280° dec. Evaporation of the filtrate gave an additional 0.11 g. (total 91%), m.p. 278–280° dec. Recrystallization of a sample from absolute alcohol afforded white crystals, m.p. 281–283° dec., $[\alpha]^{26}D$ −18.2° (2% in H_2O); $\lambda_{max}^{nuj.}$ 5.63 μ (C=O); 6.09, 6.18 μ (C=N); 8.43 μ (sulfonate); $\lambda_{max}^{H_2O}$ 288 mμ (ε 17,500), $\lambda_{max}^{pH\ 1}$ 288 mμ (ε 17,500), $\lambda_{max}^{pH\ 14}$ 230 mμ (ε 11,900) (see Graph 1).

Anal. Calcd. for $C_{14}H_{18}N_6O_6S$: C, 42.3; H, 4.55; N, 21.1. Found: C, 42.6; H, 4.35; N, 21.2.

5',N[4]-Cyclo-3-(2',3'-carbonyl-3'-amino-3'-deoxy-β-D-ribofuranosyl)-4-formamidoimidazole-5-(N,N-dimethyl)-carboxamidine Methanesulfonate (IV).—A solution of 500 mg. of V in 25 cc. of 0.1 *N* barium hydroxide was allowed to stand at room temperature for exactly 5 minutes, then it was neutralized with solid carbon dioxide. The filtered solution was evaporated to dryness *in vacuo*. A solution of the residue in 5 cc. of water was clarified by filtration and again evaporated to dryness *in vacuo*. The amorphous residue was dissolved in 5 cc. of hot absolute alcohol and filtered from a trace of inorganic material. Cooling gave 200 mg. (40%) of unchanged V in two crops, m.p. 283–285° dec., which were identified by mixed m.p. and infrared spectra. The final filtrate was evaporated to dryness *in vacuo*. Crystallization from 2 cc. of methanol by addition of 15 cc. of ethyl acetate gave 170 mg. (30%) of product, m.p. 223–225° dec. Recrystallization from methanol by concentration of a solution to about 1 cc. gave white crystals, m.p. 243–244° dec.; $\lambda_{max}^{nuj.}$ 5.67 μ (cyclic C=O); 5.95 μ (C=O of formyl); 6.19 (C=N); 2.88, 3.05, 3.25 μ (NH); 8.50 μ (sulfonate); 9.53 μ (C–O–C); $\lambda_{max}^{H_2O}$ 288 mμ (ε 10,900), $\lambda_{max}^{pH\ 1}$ 278 mμ (ε 10,250), $\lambda_{max}^{pH\ 14}$ 235 mμ (ε 14,300).

Anal. Calcd. for $C_{14}H_{20}N_6O_7S \cdot H_2O$: C, 38.7; H, 5.12; N, 19.3; S, 7.38; N–Me, 2.00. Found: C, 39.0; H, 5.60; N, 19.4; S, 7.95; N–Me, 2.06.

5',N[4]-Cyclo-3-(2',3'-carbonyl-3'-amino-3'-deoxy-β-D-ribofuranosyl)-4-aminoimidazole-5-carboxamide (VII).—A solution of 200 mg. of V in 10 cc. of 0.1 *N* sodium hydroxide was allowed to stand for 20 hours. At the end of this time there was a pronounced odor of dimethylamine and white crystals had separated. The product was collected and washed with 2 cc. of water; yield 50 mg., m.p. >300°. For analysis a sample was triturated with absolute alcohol, $[\alpha]^{25}D$ +78° (1% in 4:1 H_2O–pyridine); $\lambda_{max}^{nuj.}$ 2.85, 2.98 μ(NH); 5.67 μ (cyclic C=O); 6.04, 6.58 μ (–$CONH_2$); 6.17 μ (C=N); 6.31 μ (conj. C=C); $\lambda_{max}^{pH\ 1}$ 259 mμ (ε 12,200), $\lambda_{max}^{H_2O}$ 271 mμ (ε 10,600), $\lambda_{max}^{pH\ 14}$ 272 mμ (ε 12,300).

Anal. Calcd. for $C_{10}H_{11}N_5O_4$: C, 45.3; H, 4.18; N, 26.4. Found: C, 45.4; H, 4.47; N, 26.2.

An additional 12 mg. (total 47%) was isolated by concentration of the mother liquor *in vacuo*.

3,5'-Cyclo-6-dimethylamino-9-(3'-carbobenzoxyamino-3'-deoxy-β-D-ribofuranosyl)-purine Methanesulfonate.—To a solution of 3.90 g. of II in 24 cc. of reagent pyridine was added at 0–5° 0.78 cc. of methanesulfonyl chloride. After 4 days at 3° in a stoppered flask the mixture was poured into 120 cc. of ice-water, then extracted with chloroform (3 × 40 cc.). The combined extracts, washed with aqueous sodium bicarbonate, then water, were dried with magnesium sulfate. Evaporation to dryness *in vacuo* (bath 50°) left an oil which contained some pyridine. The residue was dissolved in 10 cc. of toluene and the evaporation repeated. The crude 5'-mesylate of II, which may have been partially quaternerized, weighed 4.44 g. (96%) and melted at 110–114° (cloudy).

A solution of 4.40 g. of this material was refluxed in 80 cc. of chloroform for 4 hours, then evaporated to dryness *in vacuo*. The residue was extracted with 20 cc., then 10 cc. of warm water. Each extract was decanted from the insoluble gum and clarified by filtration through Celite. The combined aqueous solutions were evaporated to dryness

(13) D. Ben-Ishai and A. Berger, *J. Org. Chem.*, **17**, 1564 (1952); R. A. Boissonnas and G. Preitner, *Helv. Chim. Acta*, **36**, 875 (1953).

(14) We wish to thank Dr. R. I. Hewitt and Dr. J. J. Oleson, respectively, for these assays.

in vacuo. The colorless glass was crystallized by solution in 10 cc. of absolute alcohol and addition of heptane to turbidity; yield 2.75 g. (63 or 60% based on II), m.p. 101–104°.

In a pilot run the yield was 52% over-all from II, m.p. 102–106°. Recrystallization from absolute ethanol–heptane gave hygroscopic white crystals, m.p. 103–106°. The analytical data showed that the compound was slightly hydrated.

Anal. Calcd. for $C_{21}H_{26}N_6O_7S$: C, 49.8; H, 5.20; N, 16.6. Found: C, 49.1; H, 5.58; N, 16.1.

The compound had $\lambda_{max}^{pH\ 1.7}$ 291 mμ (ε 16,600) and only end absorption in 0.1 *N* NaOH. The infrared spectrum (Nujol mull) showed OH–NH absorption at 2.83, 3.12 and 3.20 μ, –CONH– at 5.89 μ, C=N at 6.18 μ and sulfonate at 8.53 μ.

3,5′-Cyclo-6-dimethylamino-9-(3′-amino-3′-deoxy-β-D-ribofuranosyl)-purine Bromide Hydrobromide.—To a solution of 2.00 g. of the preceding carbobenzoxy derivative in 8.8 cc. of glacial acetic acid was added 3.3 cc. of 30% hydrogen bromide in acetic acid.[13] An amorphous solid began to separate after 10 minutes. After 1.5 hours the mixture was diluted with 10 cc. of dry ether. The solid was collected on a sintered-glass filter and washed with dry ether. The solvent wet solid was stirred immediately with 10 cc. of absolute alcohol on the filter, causing the amorphous solid to crystallize rapidly. The solvent was removed and the product washed thrice with acetone; yield 1.28 g. (74%) of white crystals, m.p. 216–218° dec., $[\alpha]^{24}D$ −53.9° (1.7% in H_2O).

Anal. Calcd. for $C_{12}H_{18}Br_2N_6O_2$: C, 32.9; H, 4.14; N, 19.2. Found: C, 33.0; H, 4.31; N, 18.9.

This compound had $\lambda_{max}^{pH\ 1.7}$ 290 mμ (ε 18,000), $\lambda_{max}^{pH\ 14}$ 275 mμ (ε 6470) (inflection) in the ultraviolet. The infrared spectrum (Nujol mull) showed OH–NH absorption at 2.92 μ, N^+ absorption at 3.75, 3.87, 4.10 and 5.04 μ and C=N absorption at 6.07 and 6.15 μ.

PEARL RIVER, NEW YORK

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

Puromycin. Synthetic Studies. XI. D-Ribofuranosyl Derivatives of 6-Dimethylaminopurine

BY HENRY M. KISSMAN, CHARLES PIDACKS AND B. R. BAKER

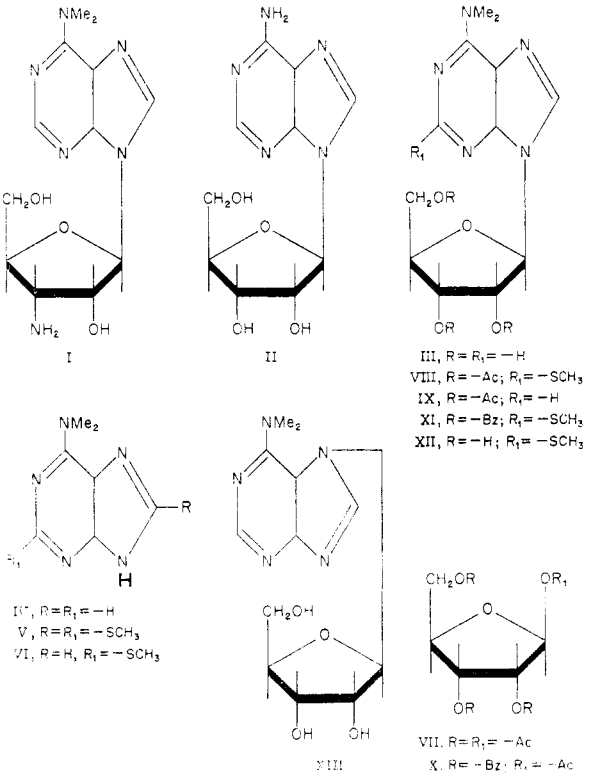
RECEIVED JULY 6, 1954

The puromycin analogs, 6-dimethylamino-9-β-D-ribofuranosylpurine (III), 2-methylmercapto-6-dimethylamino-9-β-D-ribofuranosylpurine (XII) and 6-dimethylamino-7-β-D-ribofuranosylpurine (XIII) have been synthesized. Tetra-*O*-acetyl-β-D-ribofuranose (VII), one of the two ribofuranose derivatives used for these syntheses, was separated from tetra-*O*-acetyl-D-ribopyranose by partition chromatography.

The aminonucleoside derived from the antibiotic puromycin has been shown[1] to be 6-dimethylamino-9-(3′-amino-3′-deoxy-β-D-ribofuranosyl)-purine (I). In view of the resemblance of this compound to adenosine (II) it seemed of interest to investigate whether the biological activities[1] of I were due to the presence of an amino function in the sugar moiety or to the methylation of the amino group on the purine nucleus. It was thought that a partial answer to this question might be found with the synthesis of the adenosine analog, 6-dimethylamino-9-β-D-ribofuranosylpurine (III).

Baker, Joseph and Schaub[2a] have studied the condensation of tetra-*O*-acetyl-α-D-glucopyranosyl bromide with the mercuric chloride salts[3] of 6-dimethylaminopurine (IV), 2,8-bis-methylmercapto-6-dimethylaminopurine (V) and 2-methylmercapto-6-dimethylaminopurine (VI). They were able to show by comparison of the ultraviolet spectra of the condensation products with those of unequivocally synthesized 7- and 9-alkyl substituted 6-dimethylaminopurines,[2b] that glucosidation took place in the 9-position only with the 2-methylmercapto derivative VI. The other two compounds (IV and V) yielded 7-glucosylpurine derivatives. Accordingly, it was decided to use the mercuric chloride salts of VI for the synthesis of III.

Todd and his co-workers have made extensive use of 1,2,3,5-tetra-*O*-acetyl-D-ribose (VII) in their elegant nucleoside syntheses.[4] Recently the prepara-



(1) B. R. Baker, J. P. Joseph and J. H. Williams, paper VII of this series, THIS JOURNAL, **76**, 2838 (1954). Compound I was active against *Trypanosoma equiperdum* in mice and also against the transplanted mammary adenocarcinoma of the C_3H mouse.

(2) (a) B. R. Baker, J. P. Joseph and R. E. Schaub, paper IV of this series, *J. Org. Chem.*, **19**, 1780 (1954); (b) B. R. Baker, R. E. Schaub and J. P. Joseph, *ibid.*, **19**, 638 (1954).

(3) J. Davoll and B. A. Lowy, THIS JOURNAL, **73**, 1650 (1951).

(4) The work of this group has been reviewed by G. W. Kenner, "Progress in the Chemistry of Organic Natural Products," Vol. VIII, Springer Verlag, Vienna, 1951, 108 ff.; *cf.* reference 6a.