after. When cool, the volatiles were removed, the residue dissolved in 5.5 l. of water, the whole washed with ether, and filtered. Upon acidification to *p*H 2.0 the aqueous phase afforded the substantially pure product, 262 g. (96.5%), m.p. 207–211°.

On recrystallization (9 parts methyl ethyl ketone), there was obtained 217 g. (83%), m.p. 217–218°.

The runs cited in the tables were purified similarly to that described above with the variations involved being specifically shown in the tables.

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9-Ribityl Derivatives of Guanine and 8-Azaguanine[1a]

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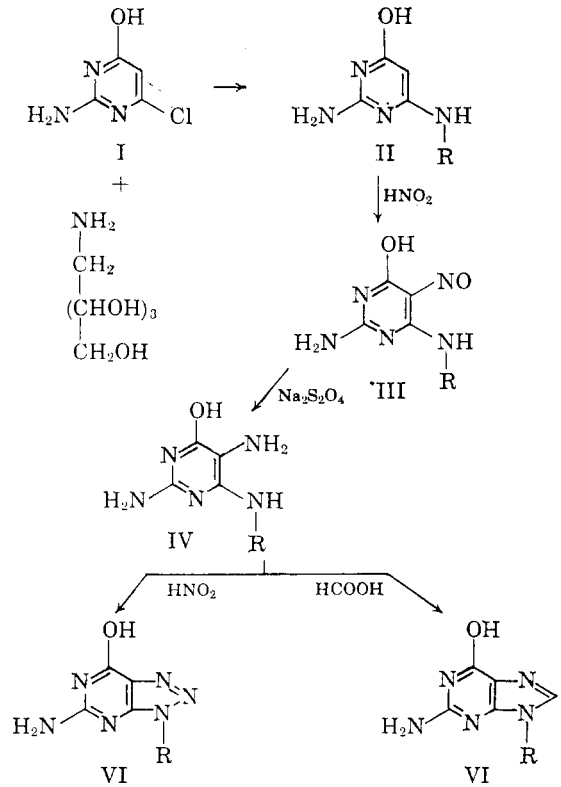
The biological transformation of a ribosyl derivative to the corresponding deoxyribosyl derivative might involve the intermediate formation of a ribityl derivative, rearrangement of which would then form the deoxy compound. Accordingly, 9-ribitylguanine was prepared as a possible biologically active intermediate, and an analog, 8-aza-9-ribitylguanine, was also prepared as a possible metabolic antagonist. During the course of this work, an enzyme requiring the vitamin B_{12} coenzyme has been observed to carry out a comparable intramolecular oxidation-reduction reaction on synthetic substrates—*e.g.*, cell-free extracts of *Aerobacter aerogenes* converted 1,2-propanediol and ethylene glycol to propionaldehyde and acetaldehyde, respectively.[2] These derivatives were synthesized through the indicated sequence of reactions (R = ribityl).

2 - Amino - 4,6 - dihydroxypyrimidine, prepared through the condensation of diethylmalonate and guanidine,[3] was treated with phosphorus oxychloride to form 2-amino-4,6-dichloropyrimidine.[4] Hydrolysis using one equivalent of sodium hydroxide in ethanol yielded 2-amino-4-chloro-6-hydroxypyrimidine[5] (I) which was subsequently condensed with ribitylamine[6] to form 2-amino-6-hydroxy-4-ribitylaminopyrimidine (II). Nitrosation of II



yielded the desired nitroso derivative III, which was then reduced with sodium hydrosulfite to produce an intermediate which proved to be difficult to isolate in a chemically pure state. Thus, the reduced reaction product, IV, was used directly without further purification to react with formic acid to form the 9-ribitylpurine V; or with nitrous acid to form the corresponding 8-aza-9-ribitylpurine VI.

9-Ribitylguanine possesses some activity in replacing purines as reversing agents for sulfonamide toxicity in *Lactobacillus arabinosus*, but it was ineffective in replacing guanine as a reversing agent for azaguanine toxicity. The ribityl derivative was not converted to the deoxyribosyl derivative by extracts of either *Escherichia coli* 9723 or *Lactobacillus leichmannii* ATCC 7830; however, these results do not preclude the possibility that a phosphorylated ribityl derivative might be an intermediate in the conversion of ribosyl to deoxyribosyl derivatives.

EXPERIMENTAL[7]

2-Amino-6-hydroxy-4-ribitylaminopyrimidine (II). A solution of 16.5 g. of 2-amino-4-chloro-6-hydroxypyrimidine and

(1)(a) After this manuscript had been accepted for publication an article appeared which described the syntheses of these analogs using a slightly different synthetic approach [J. Davoll and D. D. Evans, *J. Chem. Soc.*, 5041 (1960)]. (b) Predoctoral Fellow (CF-10,027) National Cancer Institute, United States Public Health Service.

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(4) E. Büttner, *Ber.*, **36**, 2227 (1903).

(5) H. S. Forrest, R. Hull, H. J. Rodda, and A. R. Todd, *J. Chem. Soc.*, 3 (1951).

(6) G. F. Maley and G. W. E. Plaut, *J. Biol. Chem.*, **234**, 641 (1959).

(7) All melting points are uncorrected. The authors are indebted to Mrs. J. Humphries for assistance with the microbial assays, and to J. D. Glass and C. Hedgcoth for the elemental analyses. Repeated attempts to obtain better nitrogen analyses failed; however, these results are in accord with those previously reported by other investigators[8] and are presumably due to the difficulty of burning these nitrogeneous compounds under the typical Dumas conditions. The ultraviolet spectra were determined using a Beckman DK-2 recording spectrophotometer.

ULTRAVIOLET SPECTRA OF SOME RIBITYL PURINES AND PYRIMIDINES

Compound	0.1N HCl			H_2O			0.1N NaOH		
	λ_{min}	λ_{max}	$\epsilon^a \times 10^{-4}$	λ_{min}	λ_{max}	$\epsilon^a \times 10^{-4}$	λ_{min}	λ_{max}	$\epsilon^a \times 10^{-4}$
2-Amino-6-hydroxy-4-ribitylamino-pyrimidine, II	232	267	1.89	242	268	1.69	240	264	1.67
2-Amino-6-hydroxy-5-nitroso-4-ribityl-aminopyrimidine, III	231	265	1.39	265	318	1.86	237	318	2.27
9-Ribitylguanine, V	227	254	1.17	225	252	1.12	232	268	1.05
8-Aza-9-ribitylguanine, VI	229	253	1.24	229	253	1.17	—[b]	—[b]	—[b]

[a] $\epsilon = \frac{\text{absorbance}}{\text{moles/liter}}$, calculated at λ_{max}. [b] Compound decomposes in alkaline solution.

17.8 g. of ribitylamine in 200 ml. of water was heated at 130–145° for 7 hr. in a sealed glass pressure bottle. The resulting clear yellow neutral solution was cooled to 0–5°, and the unchanged pyrimidine which precipitated was filtered and washed with a small portion of cold water. After the combined filtrates were decolorized with Darco, the solution was evaporated *in vacuo* to about one-third the original volume, ethanol was added to induce turbidity, and the solution was cooled overnight at 0–5°. The pale yellow solid which precipitated was filtered, washed with ethanol and dried. The addition of ethanol produced a second batch of product from the mother liquor. The combined crude material was then recrystallized from water giving 8.8 g. of product., m.p. 189–190°.

Anal. Calcd. for $C_9H_{16}N_4O_5$: C, 41.53; H, 6.20; N, 21.53. Found: C, 41.58; H, 6.28; N, 21.37.

2-Amino-6-hydroxy-5-nitroso-4-ribitylaminopyrimidine (III). To a stirred cold solution of 6.8 g. of 2-amino-6-hydroxy-4-ribitylaminopyrimidine and 6.8 g. of sodium nitrite in 300 ml. of water was added sufficient 4*N* acetic acid to make the solution about *pH* 4. After standing in the cold for 5–10 min., an orange product began to precipitate. After further cooling, the resulting product was filtered, washed with cold water and dried to yield 6.7 g. of material; which, after recrystallization from water melted between 219–220° dec.

Anal. Calcd. for $C_9H_{15}N_5O_6$: C, 37.37; H, 5.23; N, 24.21. Found: C, 37.07; H, 5.30; N, 23.61.

Reduction of 2-amino-6-hydroxy-5-nitroso-4-ribitylamino-pyrimidine (IV). A suspension of 1.5 g. of 2-amino-6-hydroxy-5-nitroso-4-ribitylaminopyrimidine in 30 ml. of water was heated over a steam bath, and to the hot stirred solution 2.5 g. of sodium hydrosulfite was added in small portions. When the clear red solution turned pale yellow it was cooled immediately in an ice bath, and the solution was adjusted to *p*H 3 with formic acid. After evaporation to dryness *in vacuo*, the residue was suspended in ethanol, and the ethanol was removed *in vacuo* to yield a yellow residue which was used directly in the subsequent condensation reactions.

2-Amino-6-hydroxy-9-ribitylpurine (9-Ribitylguanine) (V). The dry yellow residue from the reduction of 1.5 g. of 2-amino-6-hydroxy-5-nitroso-4-ribitylaminopyrimidine was suspended in 30 ml. of 98% formic acid, and the mixture was heated under reflux for about 8 hr. After cooling, some insoluble material precipitated which was removed and the filtrate was evaporated to dryness *in vacuo*. The resulting residue was dissolved in water and again evaporated to dryness *in vacuo* to remove the excess formic acid. The residue was crystallized twice from water to yield 0.9 g. of product, m.p. 290–291° dec.

Anal. Calcd. for $C_{10}H_{15}N_5O_5$: C, 42.10; H, 5.30; N, 24.55. Found: C, 41.70; H, 5.33; N, 23.79.

5-Amino-7-hydroxy-3-ribityl-v-triazolo[d]pyrimidine (8-aza-9-ribitylguanine (VI). The reduction of 1 g. of 2-amino-6-hydroxy-5-nitroso-4-ribitylaminopyrimidine was carried out in the manner previously described. After the addition of sodium hydrosulfite, the reaction mixture was cooled in an ice bath, the solution was adjusted to *p*H 3 with acetic acid, and 0.5 g. of sodium nitrite dissolved in 5 ml. of cold water was added dropwise while the reaction mixture was stirred at 0–5°. The addition required about 15 min., and stirring was continued for an additional hour at room temperature. The volume of the reaction mixture was reduced *in vacuo* to about 25 ml., ethanol was added to induce turbidity, and the solution was cooled overnight in a refrigerator. The inorganic precipitate was removed, the filtrate was further reduced in volume, ethanol was added, and the solution was placed in the refrigerator overnight. There was obtained 0.6 g. of crude product which was recrystallized repeatedly from water and ethanol, m.p. 268–269° dec.

Anal. Calcd. for $C_9H_{14}N_6O_5$: C, 37.76; H, 4.93; N, 29.36. Found: C, 37.55; H, 5.39; N, 28.62.

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1-Ethynyl-2-vinylbenzene[1a]

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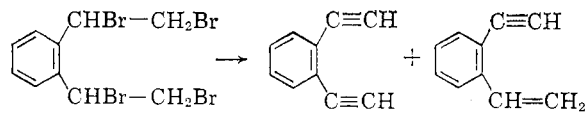
The recent report[2] of the isolation of a mixture of *o*-diethynylbenzene (II) and 1-ethynyl-2-vinylbenzene (III) from the reaction of *o*-bis(1,2-dibromoethyl)benzene (I) with sodium amide in liquid ammonia prompted the publication of an independent study of this reaction.



I II III

Treatment of the bromo compound I with commercial sodium amide[3] in liquid ammonia provided an inseparable mixture of II and III; however, use of sodium amide prepared *in situ* gave only III. That this product was pure was demonstrated

(1)(a) This work was conducted under Army Ordnance Contract DA-01-021-ORD-5135. (1)(b) Present address: Rohm & Haas Co., Research Laboratories, P. O. Box 219, Bristol, Pa.

(2) O. M. Behr, G. Eglinton, A. R. Galbraith and R. A. Raphael, *J. Chem. Soc.*, 3614 (1960).

(3) Obtained from Farchan Research Laboratories, Cleveland, Ohio.