2-Aza-adenosine (4-Amino-7-β-D-ribofuranosyl-7*H*-imidazo[4,5-*d*]-*v*-triazine)

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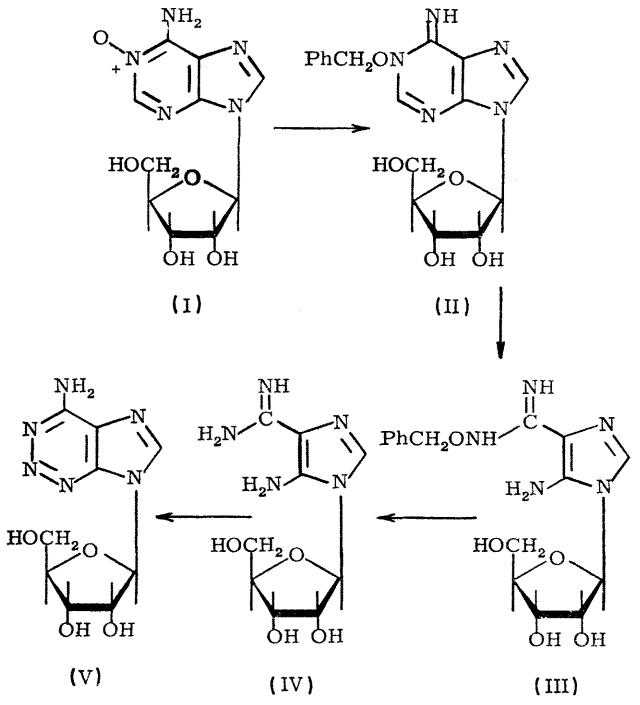
AZAPURINES[1] have shown anticancer activity and other interesting biological properties.[2] The ribonucleosides of certain 8-azapurines (*v*-triazolo[4,5-*d*]pyrimidines) have been prepared[3] and have shown biological activity as the intact nucleosides,[2,4] but the synthesis of a 2-azapurine (imidazo[4,5-*d*]-*v*-triazine) ribonucleoside has not previously been described.



We have prepared 2-aza-adenosine (4-amino-7-β-D ribofuranosyl-7*H*-imidazo[4,5-*d*]-*v*-triazine) conveniently from adenosine and found it to be a potent cytotoxic nucleoside. The reaction of adenosine 1-oxide[5] (I) with benzyl bromide in dimethylacetamide gave an 88% yield of 1-benzyloxyadenosine (II) [m.p. 157°].[6] Treatment of 1-benzyloxyadenosine (II) with methanolic ammonia (saturated at 0°) at 80° opened the pyrimidine ring and then caused deformylation of the resultant *N*-benzyloxy-5-formamido-1-β-D-ribofuranosylimidazole-4-carboxamidine to give 5-amino-*N*-benzyloxy-1-β-D-ribofuranosylimidazole-4-carboxamidine (III) [picrate m.p. 149°, resolidifies and melts at 167°].[7] Catalytic hydrogenation of the benzyloxy-group of (III) gave 5-amino-1-β-D-ribofuranosylimidazole-4-carboxamidine (IV), m.p. 174—175°. Compound (IV) was converted into 2-aza-adenosine (V) (69%) by treatment with sodium nitrite in aqueous acetic acid m.p. 260°.

2-Aza-adenosine was cytotoxic to human epidermoid carcinoma cells (No. 2) in culture at 0·05 μg./ml.† All the compounds described had satisfactory spectral properties, which will be given in detail in the full paper.

This work was supported by the C. F. Kettering Foundation and Chemotherapy, National Cancer Institute, National Institutes of Health.

(*Received, March 5th*, 1969; *Com.* 314.)

† We thank Dr. L. L. Bennett, jun., and Mrs. M. H. Vail for this result.

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[6] 1-Ethoxyadenosine has been prepared in a similar way. T. Fujii, C. C. Wu, T. Itaya, and S. Yamada, *Chem. and Ind.*, 1966, 1598.

[7] Under the same conditions 1-benzyladenosine is converted into *N*-benzyladenosine. See also N. J. Leonard, S. Achmatowicz, R. N. Loeppky, K. L. Carraway, W. A. H. Grimm, A. Szweykowska, H. Q. Hamzi, and F. Skoog, *Proc. Nat. Acad. Sci. U.S.A.*, 1966, **56**, 709.