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

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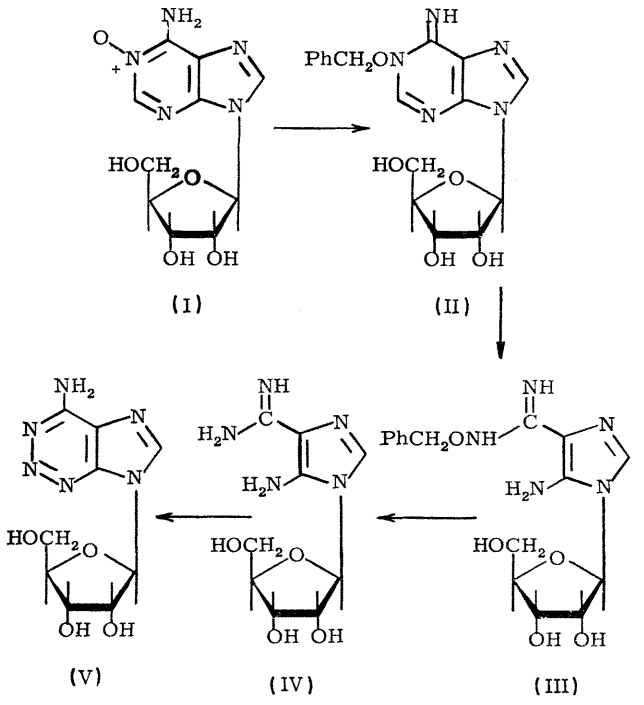
AZAPURINES[1] have shown anticancer activity and other interesting biological properties.[2] The ribonucleosides of certain 8-azapurines (*v*-triazolo[4,5-*d*]pyrimidines) have been prepared[3] and have shown biological activity as the intact nucleosides,[2,4] but the synthesis of a 2-azapurine (imidazo[4,5-*d*]-*v*-triazine) 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.

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[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.