A New Route to the 7-Methyl-8-azapurines[1] (1,2,3,4,6-Penta-azaindenes)

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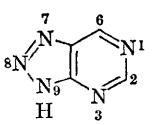
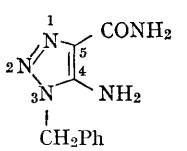
ALTHOUGH many 9-alkyl-8-azapurines are known, much difficulty has been encountered in preparing 8-azapurines (I) bearing an alkyl substituent in the 7-position. The most obvious synthesis of 7-methyl-8-azapurine, by the action of nitrous acid on 4-amino-5-methylaminopyrimidine, halts at the 5-nitrosamine stage,[2] and from the products of methylation of 8-azapurine, none of the 7-methyl derivative could be isolated.[2] A poor yield of a mixture of 7- and 9-glucosyl-8-azapurines was obtained in a Hofmann reaction on the diamide of 1-glucosyl-1,2,3-triazole-4,5-dicarboxylic acid.[3] Recently 2,6-dihydroxy-7-methyl-8-azapurine has been produced from barbituric acid in nine steps, passing through 2,4,6-trichloropyrimidine, 6-benzylamino-2,4-dihydroxypyrimidine (and its 5-nitroso-derivative) and giving 9-benzyl-2,6-dihydroxy-8-azapurine which was methylated and then debenzylated.[4]

A new, and more rapid, entry into the 7-methyl-8-azapurine series is now reported. 4-Amino-3-benzyl-1,2,3-triazole-5-carboxyamide (II), readily prepared from benzyl azide and cyanoacetamide, was methylated to 4-amino-3-benzyl-5-carbamoyl-1-methyl-1,2,3-triazolium toluene-*p*-sulphonate-m.p. 221° (75% yield). Hydrogenation of this over palladium gave 4-amino-1-methyl-1,2,3-triazole-5, carboxyamide, m.p. 174° (70%). Boiling with formamide converted the latter into 6-hydroxy-7-methyl-8-azapurine, m.p. 262° (70%) which, with phosphorus pentachloride in boiling phosphoryl chloride gave 6-chloro-7-methyl-8-azapurine, m.p. 133° (55%). The chlorine atom in this compound is highly labile, permitting preparation of the parent substances and many derivatives.



(I)



(II)

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[1] Although contrary to IUPAC nomenclature, "8-azapurine" is permitted as a trivial name because of its widespread use in biological work.

[2] A. Albert, *J. Chem. Soc.* (*B*), 1966, 427.
[3] J. Baddiley, J. G. Buchanan, and G. O. Osborne, *J. Chem. Soc.*, 1958, 1651.
[4] G. Nübel, and W. Pfleiderer, *Chem. Ber.*, 1965, **98**, 1060.
[5] J. R. E. Hoover and A. R. Day, *J. Amer. Chem. Soc.*, 1956, **78**, 5832.