A New Synthesis of Pteridines

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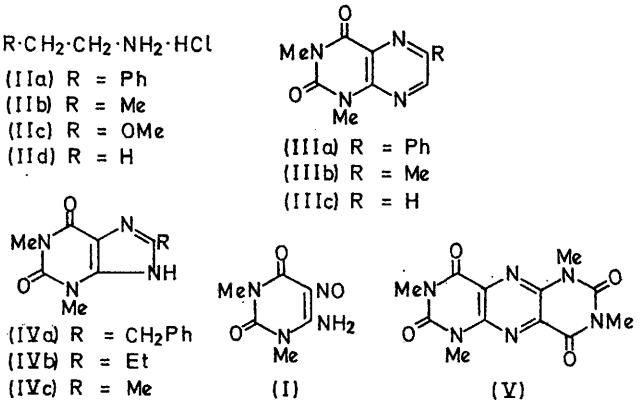
Summary Reaction of 4-amino-1,3-dimethyl-5-nitrosouracil with various amine salts led to the formation of the corresponding pteridines as well as purines.

THE condensation of 4-amino-5-nitrosopyrimidine with compounds which possess an active methylene group adjacent to a functional group was first developed by Timmis[1] as a route to pteridine formation. Further studies[2] demonstrated that purines are the sole products if the methylene component is not activated and the condensation with nitroso-group is intramolecular.



We now describe the ready formation of the corresponding pteridines as well as purines when a 4-amino-5-nitrosopyrimidine is fused with a suitable amine salt. The yield of pteridine increases in parallel with the activity of β-methylene group in the amine salt. Thus, fusion of 4-amino-1,3-dimethyl-5-nitrosouracil (I) with 2-phenylethylamine hydrochloride (IIa) at 180° led to 41% of 1,3-dimethyl-6-phenyl-lumazine (IIIa)† [m.p. 257—258° (lit.[3] m.p. 258—259°)] and 11% of 8-benzyltheophylline (IVa) [m.p. 298—299° (lit.[4] m.p. 298—300°)]; (I) and n-propylamine hydrochloride (IIb) yielded 19% of 6-methyl-1,3-dimethyl-lumazine (IIIb),[5] 37% of 8-ethyltheophylline (IVb),[6] and 25% of pyrimido-pteridine (V).[7]

The procedure involves the fusion of a mixture of thoroughly mixed pyrimidine and an excess of amine salt at 170—180°, followed by dilution with water and extraction with dichloromethane. After drying and removal of the solvent, the residue is chromatographed over neutral alumina. By this method, (I) with 2-methoxyethylamine hydrochloride (IIc) led to 1,3-dimethyl-lumazine (IIIc)[8] and pyrimido-pteridine (V).[7] These same products in addition to 8-methyltheophylline (IVc)[6] were obtained from the fusion of (I) and ethylamine hydrochloride (IId).

The formation of (V) from (I) by thermal or acid induced reaction has been reported in recent years.[7]

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† Satisfactory analysis, n.m.r., u.v., and i.r. spectral data are obtained for all the products.

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