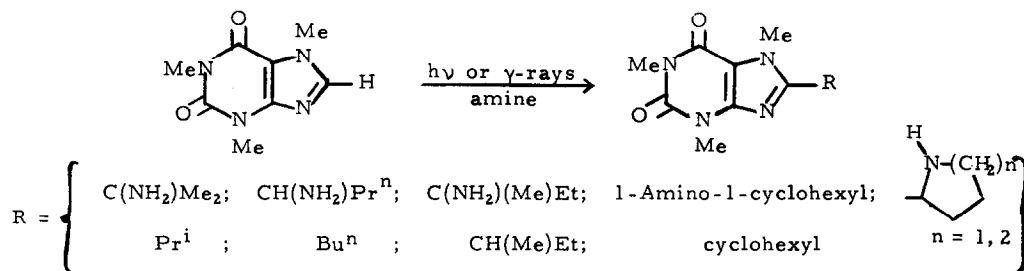


ULTRAVIOLET- AND RADIATION-INDUCED REACTIONS OF CAFFEINE WITH AMINES

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We have recently described the photochemical and γ -ray-induced reactions of purines and purine nucleosides with alcohols¹. These reactions resulted in the substitution of an α -hydroxyalkyl or an alkyl group for the hydrogen atom at C-6 or C-8 in the purine system^{1c}. Similarly, the photochemical reactions of caffeine and amino acids led to substitution at the 8-position of caffeine by the appropriate alkyl group². We report the ultraviolet- and γ -ray-induced reactions of caffeine with amines which lead to the substitution of an α -aminoalkyl or an alkyl group for the hydrogen atom at the purine 8-position. The addition of di-*t*-butyl peroxide gives higher yields of the appropriate 8-substituted caffeine (up to 65%). The major products isolated from the reactions of caffeine and aliphatic primary amines were the appropriate 8- α -aminoalkyl and 8-alkyl-caffeines (2-propyl, n-butyl, and 2-butyl), whereas cyclohexylamine and caffeine gave 8-(1'-amino-1'-cyclohexyl)-caffeine as the major product. Pyrrolidine and piperidine led to 8-(2'-pyrrolidinyl)- and 8-(2'-piperidyl)-caffeine, respectively. The reactions can be summarized as follows:



The photochemical reaction of 1-propylamine and purine has been reported recently³, and resulted in the substitution of a propyl group for the hydrogen at the purine 6-position.

In a typical experiment, a mixture of caffeine (500 mg), water (10 ml), piperidine (90 ml) and di-*t*-butyl peroxide (6 ml, added periodically in small portions) was irradiated* for 24 hr. to yield 8-(2'-piperidyl)-caffeine (440 mg; 65% based on reacted caffeine), m. p. 190-191°. γ -Ray initiation** led to the same product in 30% yield.

Products were isolated by chromatography on silica gel and identified by elemental analyses and their n. m. r. and mass spectra, as well as by comparison with authentic samples^{1c, 2}. In some cases extensive preparative tlc was required for the isolation of the 8- α -aminoalkylcaffeines.

Prof. J. N. Pitts kindly informed us that a similar investigation has been performed in his laboratory. We are indebted to Prof. Pitts for disclosing this information prior to publication.

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* Hanovia 450 W high-pressure mercury vapour lamp (Corex or Pyrex filter).

** ⁶⁰Co- γ -source Gammacell 220 (Atomic Energy of Canada, Ltd., Ottawa).