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A NEW REARRANGEMENT OF 3-ALKYL-6-BENZAMIDOPURINE

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As for the rearrangement of alkyl groups on the nuclear nitrogen of purine or pyrimidine base, only the migration to the extranuclear nitrogen has been described (1-12). For examples, 1-methyladenines(I) have been converted to the corresponding N^6-methyl derivatives (II) under alkaline conditions (1-5).

In the course of studies of alkylation of 6-benzamidopurine (III)*, we found the first example of an alkyl migration, IV→V and VI→VII, involving two intranuclear nitrogens as the reaction termini. Such rearrangement has never been described.

Treatment of III with benzyl bromide in N,N-dimethylformamide or -acetamide at 80-100° gave 3-benzyl-6-benzamidopurine (IV) and 9-benzyl-6-benzamidopurine (V)**, in contrast to the similar treatment of adenine giving rise mainly to 3-benzyl adenine. Prolonged heating of the reaction

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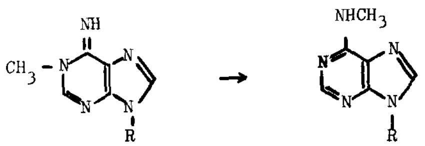
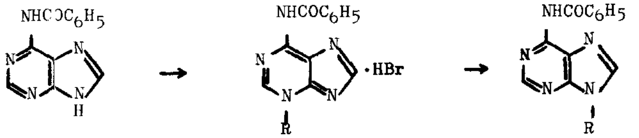
* Previously it was reported that phosphoribosylation (13), ribosylation and glucosylation (14) of III gave only the 9-substituted derivatives in contrast to adenine which gave the 3-and 9- substituted derivatives.

** In a similar reaction only the formation of IV was reported (15).



I II



III

IV R=$CH_2C_6H_5$

VI R=CH_2-CH=CH_2

V R=$CH_2C_6H_5$

VII R=CH_2-CH=CH_2

mixture increased the ratio of the yield of V to that of IV, indicating that the formation of V would have proceeded via IV. When IV was heated at 110-120° in N,N-dimethylformamide for 70 hr., V was isolated in 75% yield after silica gel chromatography [mp. 161°, λ_{max}^{pH1} 290 mμ (21,700), pH 7 281 mμ (18,200), pH 13 299 mμ (13,300)]: it was characterized by conversion to the known 9-benzyladenine (15). The free base of IV, however, did not undergo the rearrangement. In a pyridine solution IV was hardly converted to V. Neither the reverse rearrangement was observed under the above condition. Importance of the benzoyl group on N^6 for the successful rearrangement was demonstrated by the fact that 3-benzyladenine and its HBr salt did not rearrange. A similar rearrangement of VI to VII was also observed.

The rearrangement discussed above appears to involve the migration of a benzyl (allyl) group from N-3 to N-9. Experiments for elucidation of the mechanism of this rearrangement and also those with 3-ribosyl and -phosphoribosyl derivatives are in progress.

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