RING OPENING AND RECLOSURE OF THE ADENINE RING: SYNTHESIS, RING OPENING, AND REARRANGEMENT OF 7,9-DIALKYLADENINES

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7,9-Dialkyladenines (I) were synthesized from N^6-benzyloxy-9-alkyladenines (II) by alkylations with alkyl halides in N,N-dimethylacetamide (DMAc) followed by hydrogenolysis of the N^6-benzyloxy group using hydrogen and Raney Ni. 7,9-Dialkyladenines (I) thus obtained were found to be unstable in aqueous alkaline solution. Treatment of I with 0.5 N aqueous Na_2CO_3 or Amberlite CG-400 (OH^-) gave the ring-opened derivatives, N-alkyl-N-(4-alkylamino-6-amino-5-pyrimidinyl)formamides (III), and the pseudo-first-order rate constants for the ring opening of I at pH 9.84 (μ = 0.50) and 25°C were determined. Compounds III were also unstable in solution and equilibrated with the substances presumed to be N-[4,5-bis(alkylamino)-6-pyrimidinyl]formamides. The equilibrium constant for such a formyl transfer reaction of N-methyl-N-(4-methylamino-6-amino-5-pyrimidinyl)formamide at pH 9.84 and 25°C was also determined.

When refluxed with 1 N aqueous NaOH, III cyclized to give N^6,7-dialkyladenines (IV). The cyclization of III was also effected with NaH in DMAc at room temperature. Apart from the above stepwise conversion of I into IV, treatment of I with boiling 1 N aqueous NaOH was found to be a convenient one-step procedure for the rearrangement of I to IV.