SYNTHESES AND PROPERTIES OF FLAVINS (ISOALLOXAZINES)

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In continuation of our studies on the syntheses of the fused pyrimidines related to organisms, we describe several new synthetic approaches to flavins (isoalloxazines). Additionally, we wish to touch on the hydrolysis of flavins in both the ground and excited states.

Method A. Treatment of the Michael-type adducts of 6-(N-alkylanilino)uracils to diethyl azodicarboxylate (DAD) with lead tetraacetate in dioxane caused an oxidative rearrangement, followed by thermal or photolytic cyclization, to give the respective flavins.

Method B. Heating of 6-(N-alkylanilino)-5-nitrouracils with excess DAD at 130° in the presence of triphenylphosphine or pyridine as a basic catalyst gave directly the corresponding flavins without involving the oxidation process.

Method C. Dehydrogenation of 5-amino-6-(N-alkylanilino)uracils with DAD in alcohol gave the 5-imino intermediates, which were cyclized by the irradiation of the visible light to give the corresponding flavins.

Method D. Photolytic degradation of 6-(N-alkylanilino)-5-azidouracils, which were prepared by the reaction of 6-(N-alkylanilino)-5-hydrazinouracils with sodium nitrite in acetic acid, gave the flavins via the nitrene intermediates.

The reaction of 3,10-dialkylisoalloxazines thus obtained with benzyltrimethylammonium hydroxide in dimethylformamide or alcoholic potassium hydroxide in the dark (ground state) gave the corresponding spirohydantoins, while the reaction in the light (excited state) brought about the elimination of 10-alkyls to give 3-alkylalloxazines. The treatment of the spirohydantoins with concentrated sulfuric acid caused intramolecular dehydration to give the original flavins.