SYNTHESIS OF HETEROCYCLES VIA INTRAMOLECULAR CYCLIZATIONS OF N-SUBSTITUTED ENAMINO KETONES

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Intramolecualr arylations of N-substituted β-enamino ketones providing polycyclic N-heterocycles have been investigated. For the general synthesis of the starting enamino ketone derivatives, the key intermediate, 3,3a,4,5-tetrahydro-6-methoxy-2H-indole (4), was prepared by the Birch reduction of 6-methoxyindoline, which was conveniently obtained via the benzyne reaction of 3-chloro-4-methoxyphenethylamine (2). The subsequent reaction of the iminoenol ether (4) with the acyl chlorides or the alkyl halides produced a simple and direct synthesis of the N-substituted enamino ketones. N-Benzoyl, N-phenylacetyl, N-benzyl, and N-phenethyl derivatives of 1,2,3,3a,4,5-hexahydro-6H-indol-6-one so produced were subjected to intramolecular arylations to give the tetracyclic compounds, some of which were converted to alkaloids; these reactions are classified into five categories as follows:

(1) The synthesis of α-anhydrodihydrocaranine (12) and γ-lycorane (13) via photocyclization of 1,2,3,3a,4,5-hexahydro-1-(3,4-methylenedioxybenzoyl)-6H-indol-6-one (8).

(2) The synthesis of α-dihydrocaranone (16) and 1-epi-γ-dihydrocaranine (17) via the benzyne reaction of 1-(2-bromo-4,5-methylenedioxybenzyl)-1,2,3,3a,4,5-hexahydro-6H-indol-6-one (14).

(3) Photolysis of 1,2,3,3a,4,5-hexahydro-1-(2-iodo-4,5-dimethoxyphenylacetyl)-6H-indol-6-one (18) affording 3,3a,4,5-tetrahydro-10,11-dimethoxyindolo[7,1-ab][3]-banzazepine-1,7(2H,8H)-dione (19) and some photolysates involving the ketene intermediate (24).

(4) The synthesis of hexahydroapoerysopine dimethyl ether (36) via photolysis of 1-(2-iodo-4,5-dimethoxyphenethyl)-1,2,3,3a,4,5-hexahydro-6H-indol-6-one (30) or 6-bromo-1,2,3,3a,4,5-hexahydro-1-(3,4-dimethoxyphenethyl)-6H-indol-6-one (33).

(5) The reaction of 1,2,3,3a,4,5-hexahydro-1-(3,4-dimethoxyphenylacetyl)-6H-indol-6-one (20) with phosphoryl chloride leading to 3-chloro-3,4-dehydro-15,16-dimethoxyerythrinan-10-one (39).