SYNTHETIC STUDIES ON SOME INDOLE ALKALOIDS VIA FISCHER BASE TYPE INTERMEDIATES

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A study of the intramolecular cyclization of the 6-substituted 2-(2-methyl-3-indolyl)ethylamino-enamine derivatives promoted by a mixture of acetic acid and acetic anhydride is presented.

The cyclization takes place through a Fischer base type intermediate when an enamine system is carried two electron withdrawing groups such as ester, ketone, and nitrile groups on its 8 position to give a tetracyclic amide or a carbazole depending on the 8-substituents. When an enamine carries two ester groups, a tetracyclic vinylogous amide is formed with loss of one of the ester groups, while an enamine carries two nitrile groups, a tetracyclic conjugated diene is formed without loss of any substituent. When an enamine carries one or two ketonic groups, the overall reaction involves elimination of its ethanamine moiety to form a carbazole. Relative reactivity of 8-substituents toward the intramolecular cyclization can be defined as follows, ketone > nitrile > ester.

Using this cyclization a new synthesis of the key intermediates of the Aspidosperma indole alkaloids, vindoline and vodorosine, and a promising intermediate for the Strychnos and the Aspidospermatidine type indole alkaloids is accomplished. Moreover, a new synthesis of a pyridocarbazole alkaloid chromophore is established by employing the newly developed carbazole synthesis.