SYNTHETIC STUDIES ON SOME INDOLE ALKALOIDS VIA FISCHER BASE TYPE INTERMEDIATES

Seiichi Takano, Kohtaro Yuta, Susumi Hatakeyama,
Masaaki Sato, Kozo Shishido and Kunio Ogasawara

Pharmaceutical Institute, Tohoku University
Aobayama, Sendai 980, Japan

A study of the intramolecular cyclization of the β-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 β position to give a tetracyclic amide or a carbazole depending on the β-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 β-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 vidorosine, and a promissing 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.