HETEROCYCLES, Vol 14, No 1, 1980

APPLICATION OF THE DDQ OXIDATION TO THE SYNTHESIS OF OXIDIZED INDOLE ALKALOIDS

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DDQ is the only reagent for the selective oxidation of side chains at C-3 of indoles. This selective oxidation has now been applied to a synthetic work of oxidized indole alkaloids, pimprinine and a series of related oxazolylindoles, model compounds of fumitremorgin B, and neoechinulins.

When N-acetyltryptamine was heated under reflux in anhydrous THF with DDQ (2 equiv) under argon, pimprinine was directly formed and easily isolated by passing through a short alumina column though in a very poor yield. N-Benzoyltryptamine gave similarly the corresponding oxazolylindole, although the yield was still unsatisfactory. Better results were obtained in the oxidation of N-acyl derivatives of tryptophan methyl ester.

When a series of N-acyl derivatives of both tryptamine and tryptophan methyl ester were treated with DDQ (2 equiv) in THF-H_2O (9:1) under argon at room temperature, the corresponding β-keto products were readily isolated in good yields, except tryptophan methyl esters having electron-donative N-benzoyl and N-p-methoxybenzoyl groups, which gave the oxazolylindoles even in aqueous THF solutions.

The mechanism of these oxidations, which involves either the intramolecular nucleophilic attack of acyl groups to form the oxazolylindoles in anhydrous solvents or the intermolecular addition of water to form the β-keto products in aqueous solvents, are also discussed.

The DDQ oxidation of some model compounds for the synthesis of fumitremorgin B and a synthetic work of neoechinulin alkaloids are finally reported.