# NEW METHOD FOR THE INTRODUCTION OF OXYGEN FUNCTION TO THE AROMATIC RING OF INDOLINE ALKALOID

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In connection with the synthetic studies of indole alkaloids having oxygen function on the aromatic ring, a method for the introduction of oxygen function to the aromatic ring after the fundamental skeleton of the alkaloids had been constructed was examined.

Introduction of methoxy group to the 5-position of indolines: Initially, we examined a nucleophilic aromatic substitution of chloroindolines with methoxide anion and found that it was essential to activate aromatic ring by chromium tricarbonyl complex(CTC-complex) formation and methoxide anion by using crown ether. When CTC-5-chloro-1,3,3-trimethylindoline obtained in 50% yield from the corresponding indoline was treated with "naked" methoxide anion, CTC-5-methoxy-1,3,3-trimethylindoline was obtained in 93% yield. Removal of $Cr(CO)_3$ group from the CTC-complex with an excess of iodine in THF-10%HCl afforded free base in nearly quantitative yield.

Introduction of methoxy group to the 6-position of indolines: CTC-3,3-Dimethyl-indoline obtained from its free base in 89% yield was, after nitrogen protection by a bulky $^tBuMe_2Si$ group, treated with n-BuLi/TMEDA at -60° and quenched with an excess of acetaldehyde to afford secondary alcohol derivatives. Without purification, $Cr(CO)_3$ and the silyl protecting group were removed by iodine in the presence of camphor-sulfonic acid yielding a mixture of free indolines, which was converted to the N-acetyl derivatives(28, 62% from CTC-complex) by O,N-diacetylation followed by O-deacetylation. The ketones obtained by Jones oxidation of 28 could be separated using Lobar column into three isomers and they were assigned as 4-, 5- and 6-acetyl derivatives mainly by NMR technique. 1,6-Diacetyl-3,3-dimethylindoline(main product, 57%) and the 5-substituted isomer(16%) were converted to the corresponding 6-methoxy and 5-methoxy derivatives respectively by means of Baeyer-Villiger reaction. However, 4-Acetyl derivative(27%) was remained unaffected by per-acid treatment presumably because of steric hindrance due to methyl substituents in 3-position. The present method could be extended to 4a-methyl-1,2,3,4,4a,9a-hexahydrocarbazole affording 6-methoxy and 5-methoxy derivatives in the ratio of 7 : 1.