Selective Reactions of Active Methyl Groups on Pyridine and Quinoline Rings

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Site-selective reactions of various N-heteroaromatics having more than two active methyl groups were investigated. As one of typical examples, the following results were obtained on the reaction of 2,4-dimethylquinoline (1).

1) The reaction of 1 with ethyl benzoate in the presence of potassium amide gave 2-methyl-4-phenacylquinoline selectively. In contrast, when isopropylmagnesium bromide was used instead of potassium amide, the positional isomer, 4-methyl-2-phenacylquinoline was obtained as a sole product.

2) When 1 was treated with benzaldehyde in the presence of zinc dichloride and with selenium dioxide, selective formation of 4-methyl-2-styrylquinoline and 4-methyl-2-quinolinecarbaldehyde was observed, respectively.

3) The introduction of an N-oxide function into a quinoline ring facilitates the reactivity of the 2-methyl group of 1. Thus, the reaction of 2,4-dimethylquinoline 1-oxide with ethyl benzoate under basic conditions gave 4-methyl-2-phenacylquinoline 1-oxide exclusively.

In connection with these findings, the relative reactivity of methyl groups in the various N-heteroaromatics was estimated by means of the ^{1}H-NMR sepectroscopy. Furthermore, the site-selective reactions of 2,4-dimethylpyrimidine derivatives are briefly described.