ACYLATION OF ETHYL INDOLE-2-CARBOXYLATE

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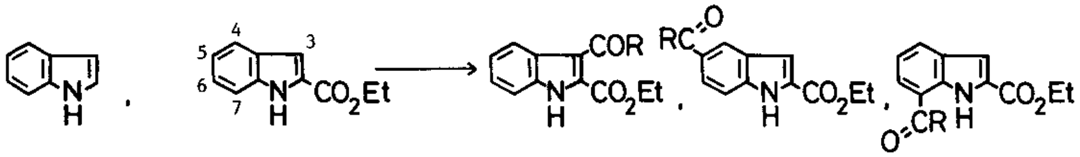
Acylation of indoles at the C-3 position is synthetically important reaction. However, the acylation of indole itself (1) cannot be carried out in strongly acidic condition, because 1 is labile in such condition. On the other hand, ethyl indole-2-carboxylate (2) is a stable equivalent of 1, and the acylation of 2 has not been studied. So we became interested for developing methods for the acylation of 2 under strongly acidic condition.

A. Mixed Anhydride Method: 2 was easily reacted with various carboxylic acids by using $(CF_3CO)_2O$ and H_3PO_4 to give 3-acylindoles (3). Weaker carboxylic acids tended to give better yields than stronger acids. Thus, the electronic effect in the carboxylic acid is critical for this reaction.

B. Friedel-Crafts Reaction: The reaction of 2 with various acid chlorides using $AlCl_3$ was found to proceed smoothly. Acid chlorides derived from weaker acids tended to give the C-3 acylated products (3), whereas acid chlorides derived from stronger acids tended to give the C-5 acylated products (4) accompanied by a small amount of the C-7 acylated products (5). In order to increase the regioselectivity, we further examined this reaction by changing molar ratio of $AlCl_3$, kinds of Lewis acid, and acylating reagent from acid chloride to anhydride. It is noteworthy that the Friedel-Crafts reaction of 2 catalyzed by $AlCl_3$ gave 5-acylated product in some cases, offering a new route for functionalization on benzene ring of indole nucleus.



(1) (2) (3) (4) (5)