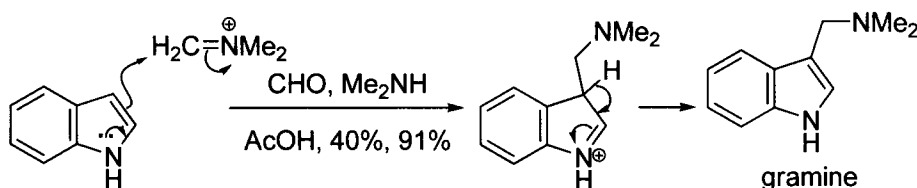
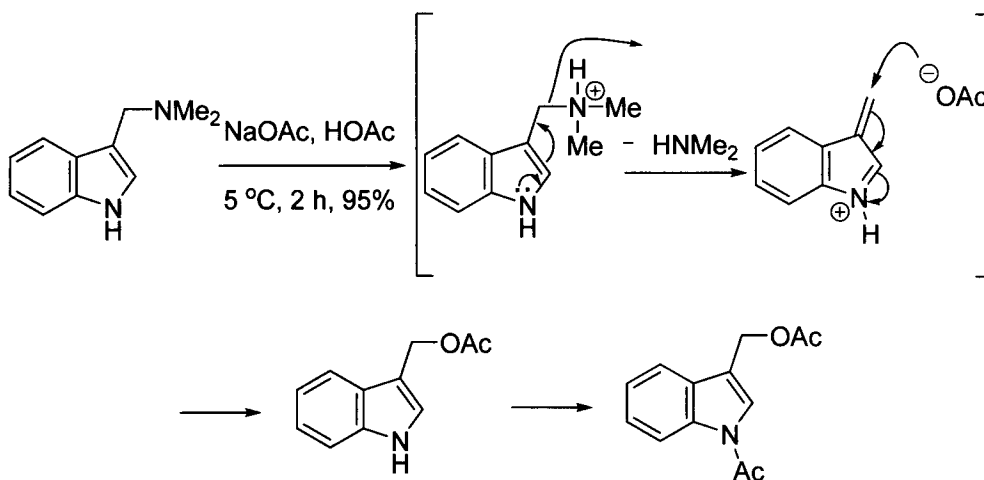


The Mannich condensation of indole results in the C-3 substitution in good yield.



The dimethylaminomethyl group in gramine resulting from the Mannich reaction is labile and readily undergoes elimination when a nucleophile is present to take part in a Michael addition. For example:



The preference for indole to undergo C3 electrophilic substitution has been applied to the synthesis of many drugs. One example is found in the synthesis of zafirlukast (Accolate), which is a potential drug used in the treatment of pulmonary disorders such as asthma. Zafirlukast acts by antagonizing the pharmacological actions of one or more of the arachidonic acid metabolites known as leukotrienes. In a process synthesis, a C3 electrophilic substitution was carried out between 5-nitroindole and the