Quadrant II – Transcript and Related Materials

Programme : Bachelor of Science (Third year)

Subject : Chemistry

Course Code : CHC 110

Course Title : Organic Chemistry

Unit : 1- Name Reaction and Rearrangements

Module Name : Reaction and mechanism: Knoevenagel

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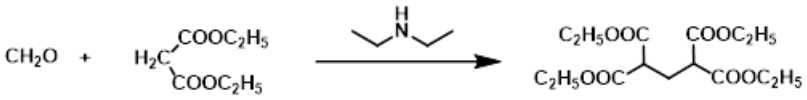
Notes

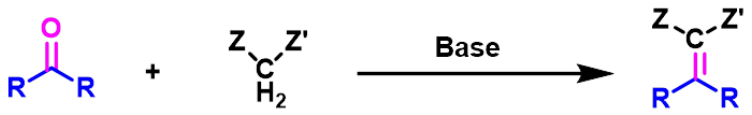
Knoevenagel Reaction

Emil Knoevenagel discovered a new type of carbon–carbon bond-forming reaction, which was published in Chemische Berichte in 1894. In the reaction of formaldehyde with diethyl malonate in the presence of diethylamine as a catalyst to form the bis adduct.



It is the condensation of aldehydes or ketones (usually not containing an alpha H atom) with compounds containing active methylene group to form α,β–unsaturated compounds. Catalysts usually used are pyridine, piperidine or diethylamine.

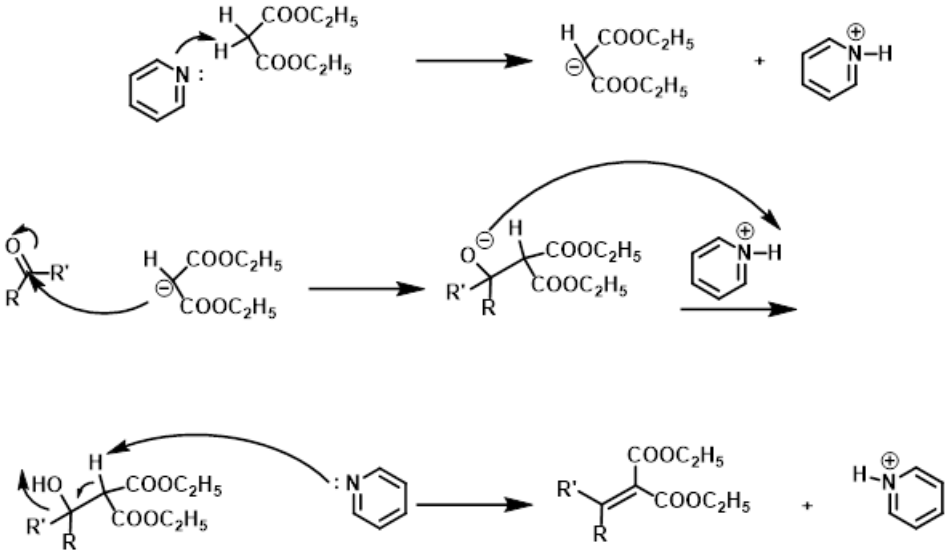
The general reaction maybe represented as:



The mechanism is as follows:

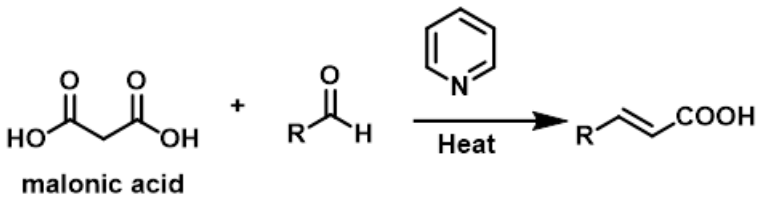
The base picks up the acidic hydrogen from the active methylene group to generate the enolate ion, which then attacks the electrophilic carbon of the

carbonyl group. This is followed by dehydration (elimination of beta hydrogen) that leads to the formation of the α, β unsaturated product.



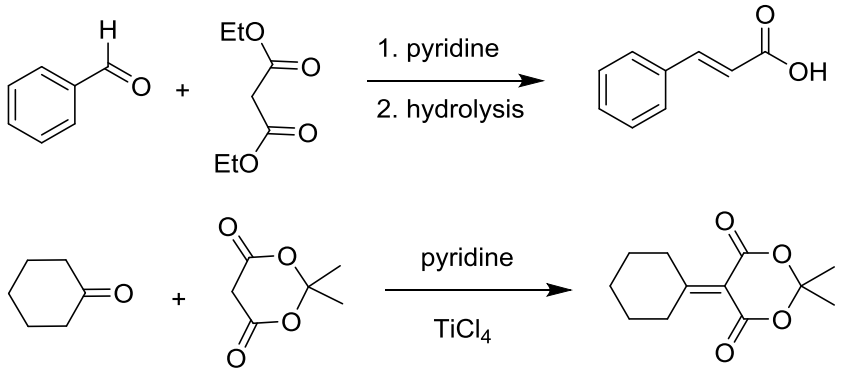
Doebner modification of Knoevenagel Reaction

Malonic acid is used as the active methylene compound, and treated with aldehyde in the presence of base. The product formed can lose a molecule of carbon dioxide in a subsequent step to give an α, β unsaturated carboxylic acid.



Application of Knoevenagel Reaction

It is used to prepare α, β unsaturated compounds as shown:



The Hantzsch pyridine synthesis, the Gewald reaction and the Feist–Benary furan synthesis all contain a Knoevenagel reaction step. It is is also used in the synthesis of an anti malarial drug Lumefantrine and biologically significant compounds like coumarin derivatives.