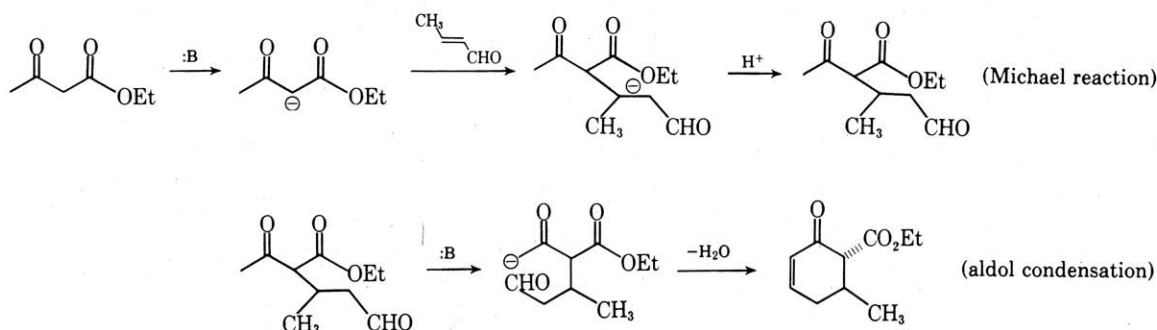


Example of the Robinson Annulation Procedure via Phase Transfer Catalysis— A Beginning Organic Synthesis Experiment

An important example of the synthetic use of intramolecular condensations is the Robinson annulation, a procedure that constructs a six-membered ring from the base-catalyzed Michael addition of activated methylene systems to, for example, an α, β unsaturated aldehyde, followed by aldol condensation¹:



A major problem of the sequence, rapid polymerization of α, β unsaturated aldehydes, under basic conditions, usually leads to unacceptable yields of the Robinson product.² It is well known that phase-transfer catalysis of carbanionic reactions leads to excellent results^{3,4}, and several experiments suitable for undergraduate laboratories have been recently described in *this Journal*.^{5,6} We have found that this procedure is well suited for the Robinson annulation of ethyl acetoacetate to selected α, β unsaturated aldehydes such as crotonaldehyde resulting in yields often exceeding 50% of the Robinson product. The procedure can be accomplished in a four-hour laboratory period and will be found to be a challenging synthetic procedure suitable for inclusion in undergraduate organic synthesis experiments.

Procedure

Caution: Because crotonaldehyde and other α, β unsaturated aldehydes are often lachrymal in nature, carry out this experiment in a hood or in a well-ventilated laboratory.

Place 60 mL of dry toluene, 19.1 mL (0.15 mol) ethyl acetoacetate, 0.68 g (0.015 mol) benzyl triethyl ammonium chloride, and 24.7 g (0.15 mol) of K_2CO_3 in a 500-mL round-bottom flask. Cool the heterogeneous mixture to 0–10 °C in an ice-water bath and begin stirring well with a magnetic stirring bar or mechanical stirrer (8). Fourteen milliliters (0.17 mol) of crotonaldehyde is then added dropwise from a connected addition funnel over 30 min. The solution, at this time, is brought to room temperature and stirred an additional 2 h. At the end of this time period, the mixture is filtered, and the filtrate is transferred to a 100-mL round-bottom flask equipped with a column packed with glass beads. The toluene is distilled off at room pressure, and the yellow residue is subjected to vacuum distillation. After a small forerun of unreacted ethyl acetoacetate (35 °C, 0.25 mm torr), the fraction boiling at 80–90 °C (0.25 mm torr) is collected as the Robinson annulation product 5-methyl-6-carboxyethyl-2 cyclohexenone; 16.9 g (54.5% yield); IR (thin film): 1695, 1725 cm^{-1} ($C=O$); NMR ($CDCl_3$): 5.9, 6.8 δ (m, 2H, vinylic); 4.1 δ (q, $CO_2CH_2CH_3$); 3.0 δ (d, 1H, $CHCO_2Et$); 2.0–2.4 δ (m, 3H, ring hydrogens); 1.3 δ (t, 3H, $-CO_2CH_2CH_3$); .95 δ (d, 3H, CH_3). Under the basic conditions of the experiment, epimerization occurs, and only one stereoisomer is obtained. We have found that best results are obtained using a mechanically stirred solution.

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