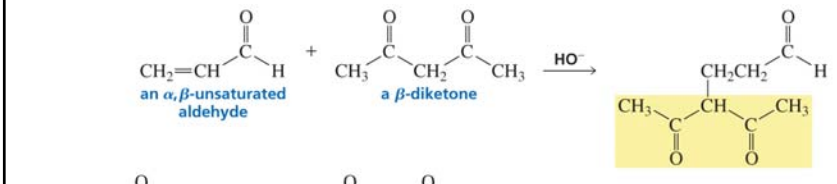
Disampaikan oleh : Dr. Sri Handayani
2013

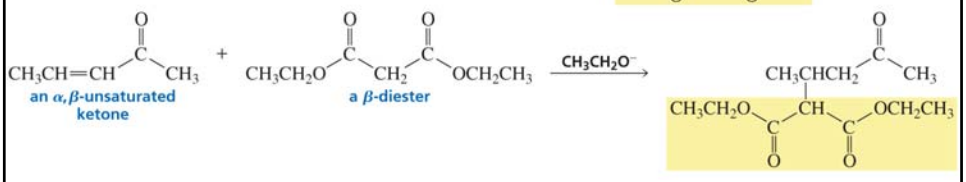
α-Carbonyl Nucleophiles

Michael and Stork reactions
Aldol condensation
Claisen condensation

The Michael Reaction

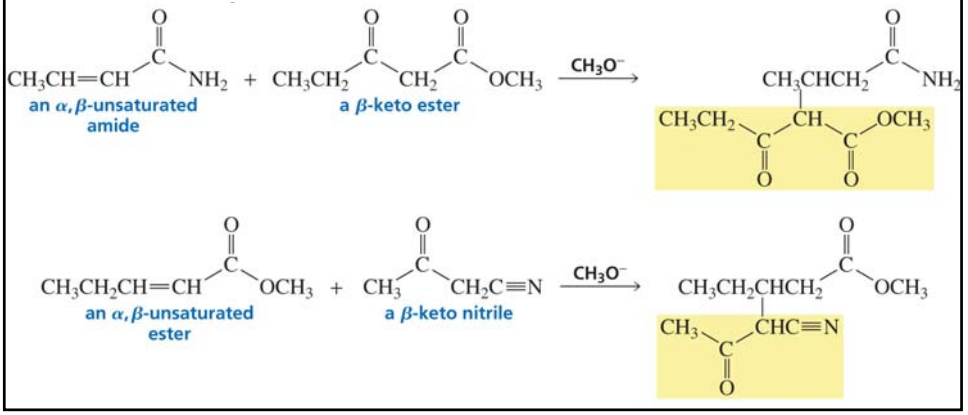
- Addition of any β-dicarbonyl compound to any α,β-unsaturated carbonyl compound, in the β position.



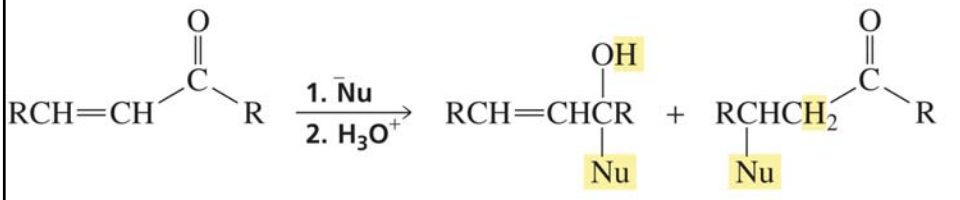


The Michael Reaction

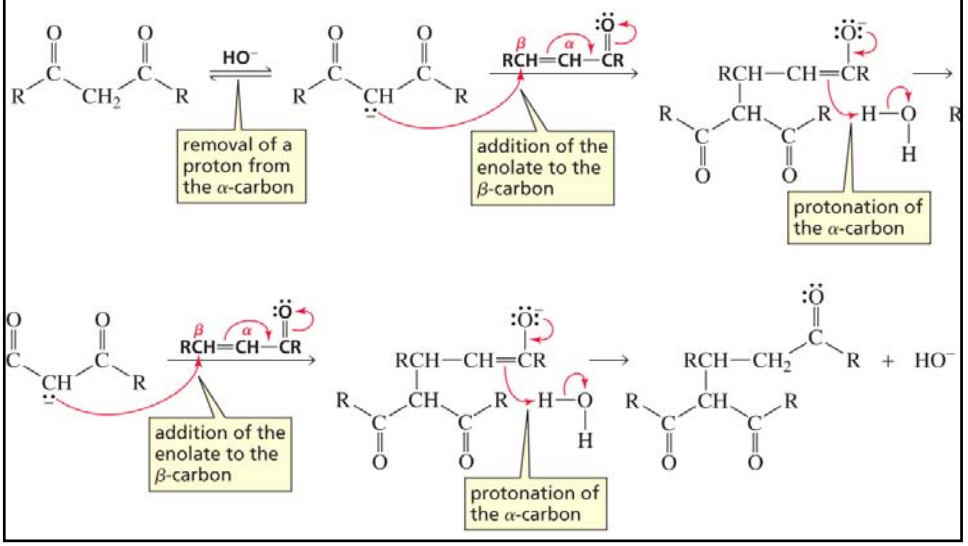
- Addition of any β-dicarbonyl compound to any α,β-unsaturated carbonyl compound, in



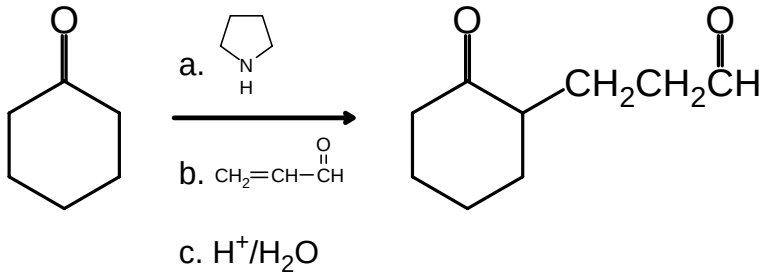
Generic "Michael" addition



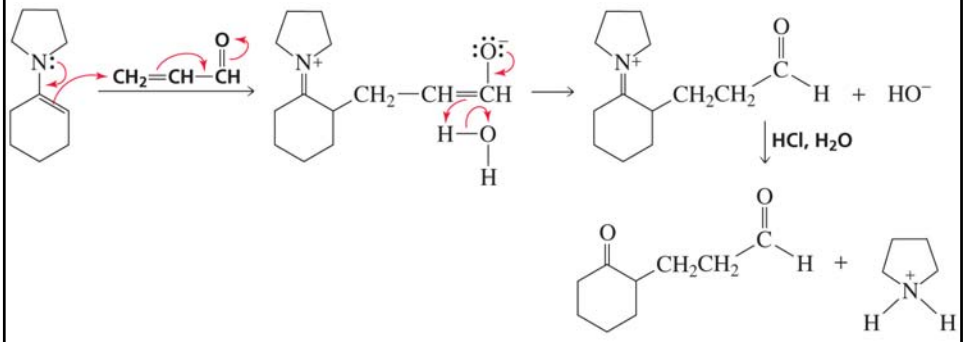
Mechanism of the Michael Reaction



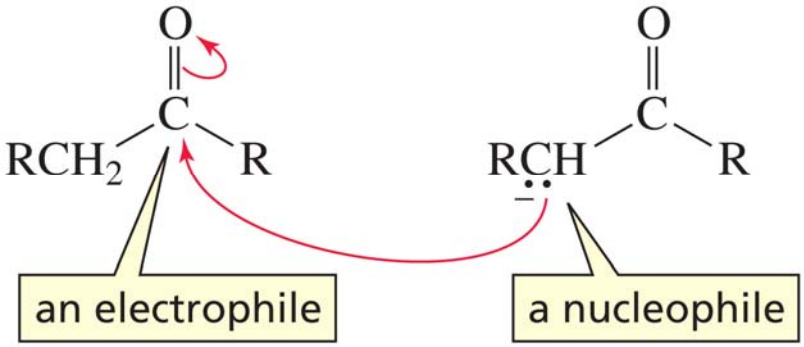
The Stork Enamine Reaction



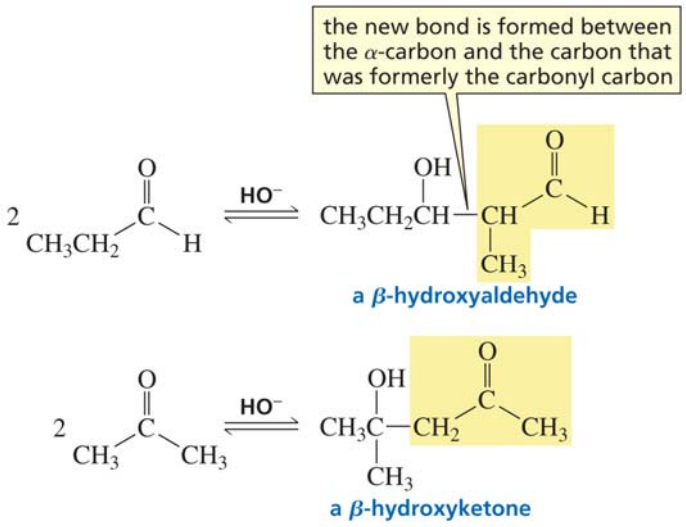
Mechanism of the Stork Enamine Reaction



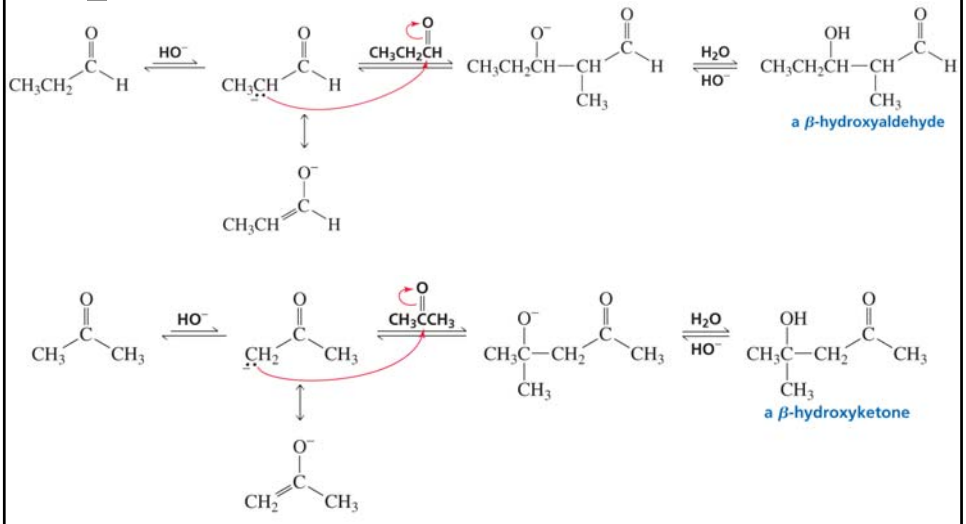
Enolates react with carbonyls



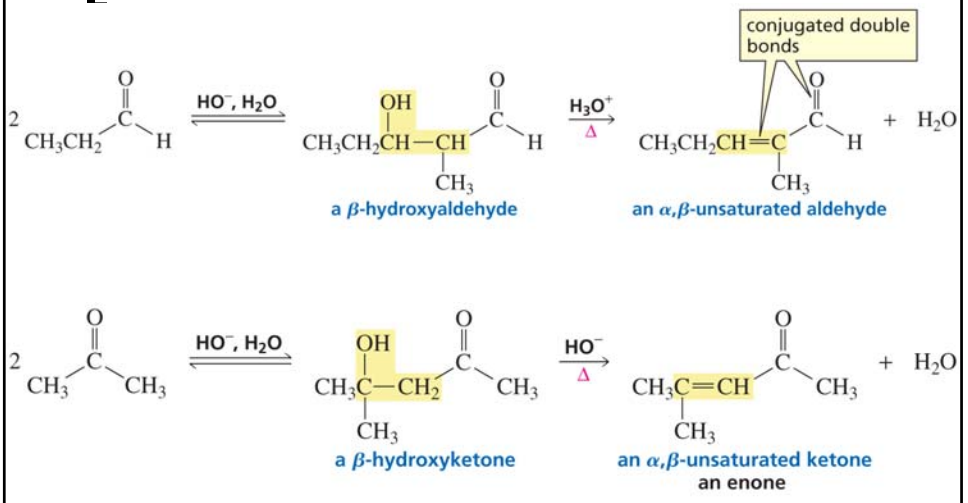
The Aldol addition and its products



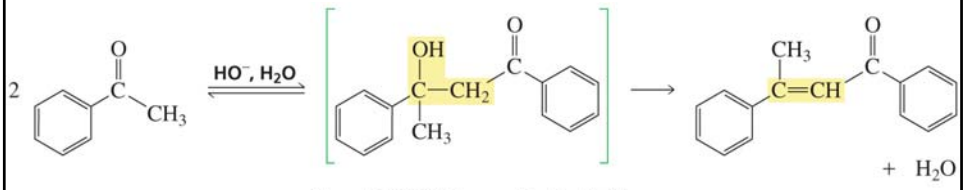
Mechanism of the Aldol reaction



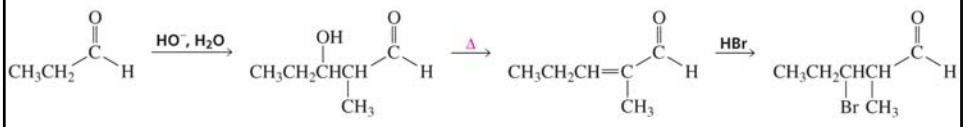
The Aldol condensation makes α,β-unsaturated carbonyls



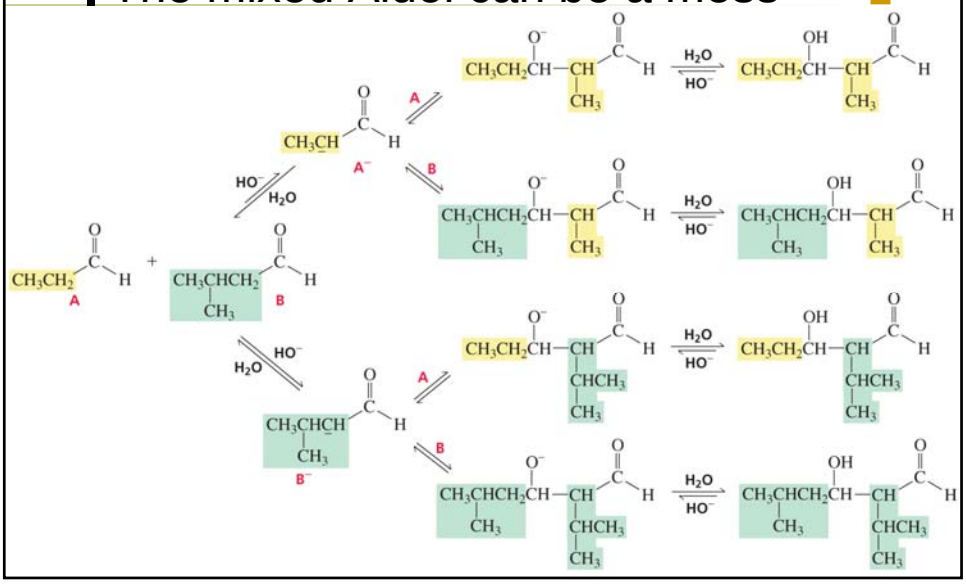
The Aldol intermediate is not always isolated



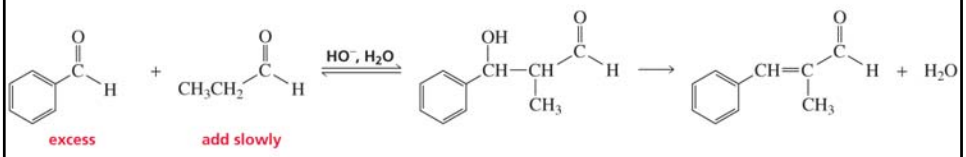
What's the mechanism?



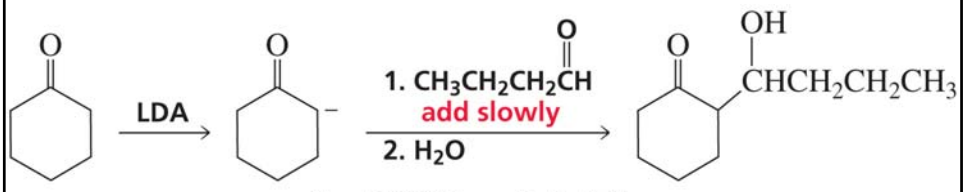
The mixed Aldol can be a mess



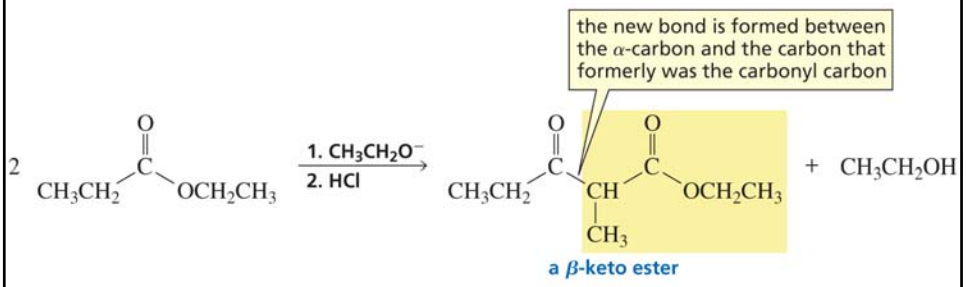
Mixed Aldol works if one has no α-hydrogens



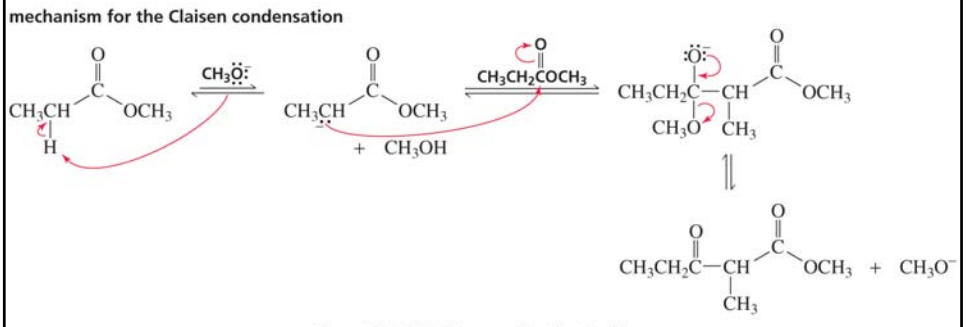
Mixed aldol works if enolate is pre-formed



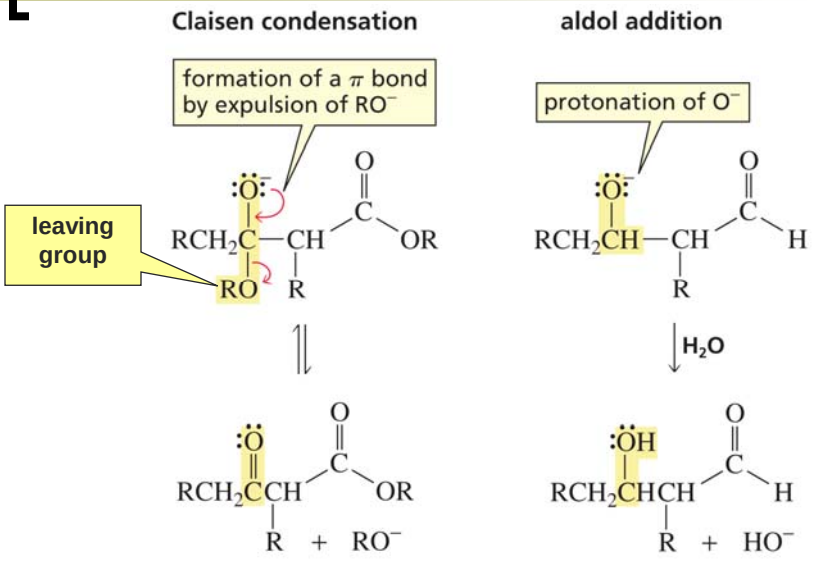
The Claisen condensation makes β-keto esters



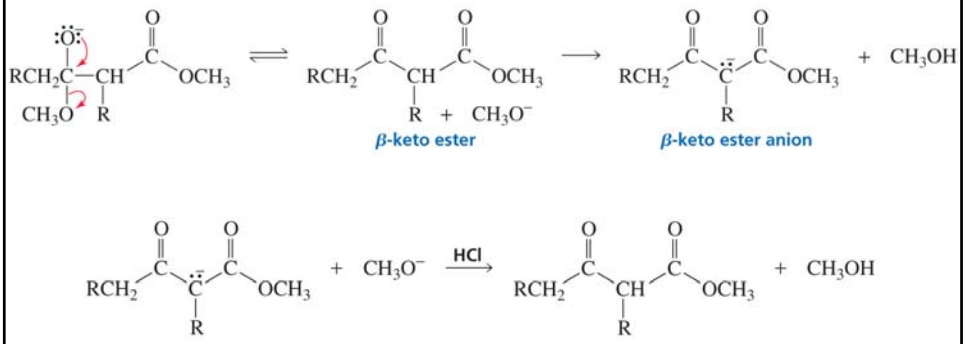
Mechanism



The essential difference between Aldol and Claisen

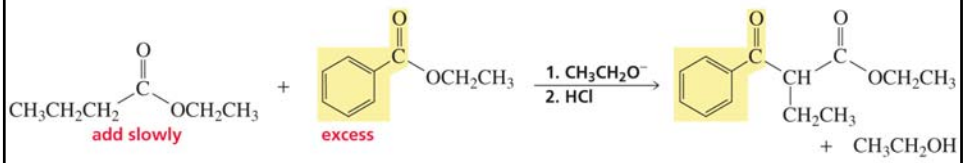


Why the Claisen only happens once: acidity of β-dicarbonyl

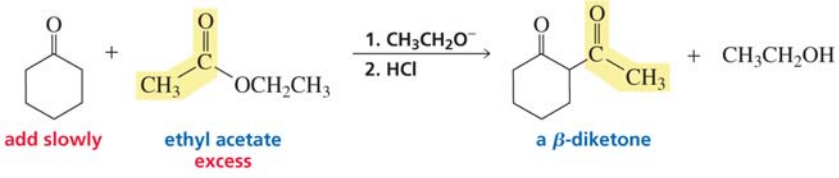


Mixed Claisen in which one component has no α-hydrogens

a mixed Claisen condensation



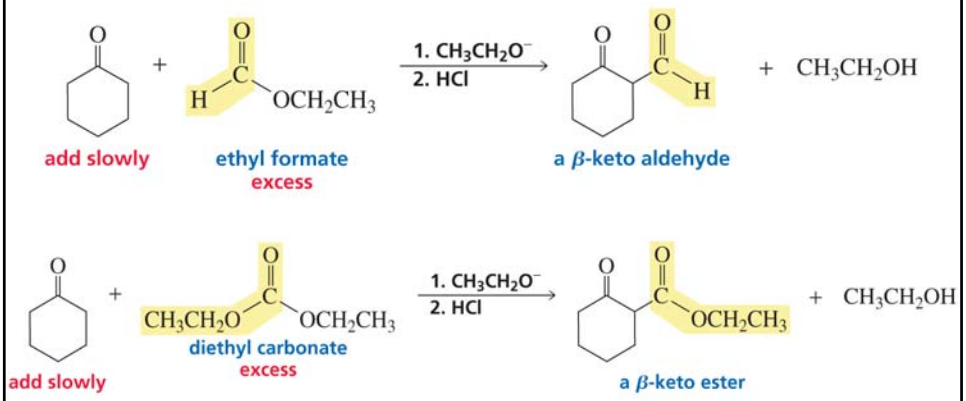
Mixed Claisen between ketone and ester



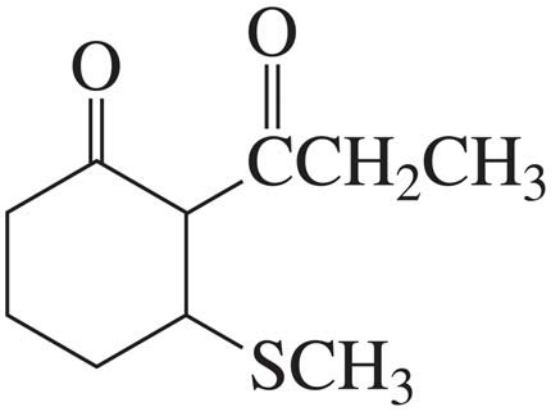
pK_a ~ 20 pK_a ~ 25

- Why don't we get Aldol with ester enolate nucleophile?

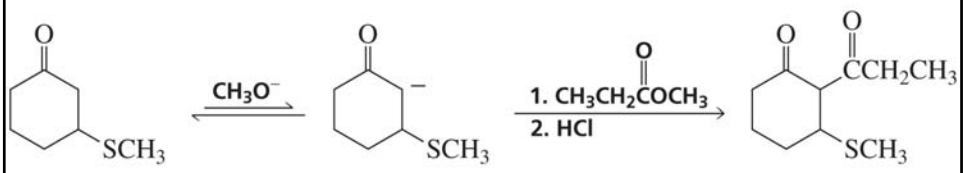
Mixed Claisen with formic or carbonate ester



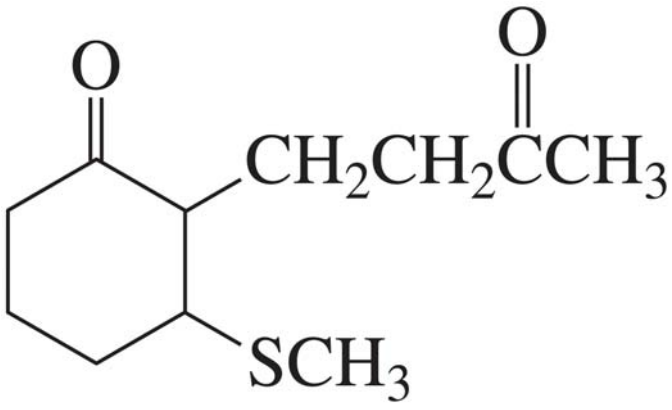
Synthesis problem, from cyclohexanone



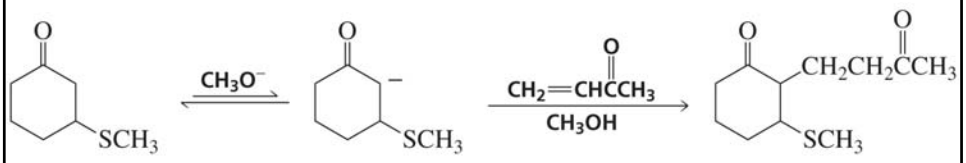
Solution



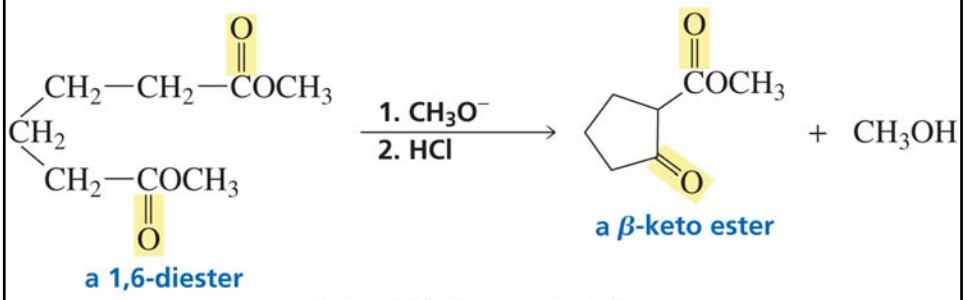
Synthesis problem, from cyclohexanone

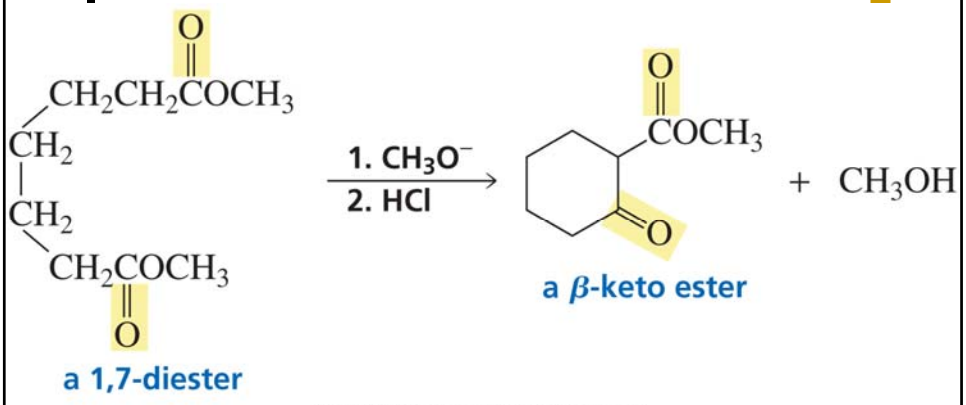


Solution



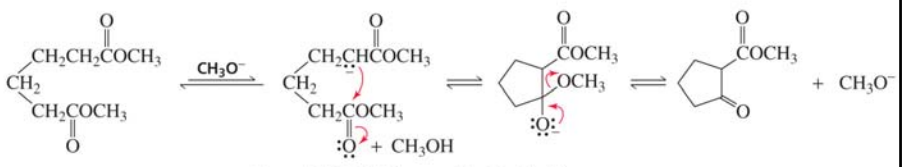
The Dieckmann Condensation: an intramolecular Claisen condensation



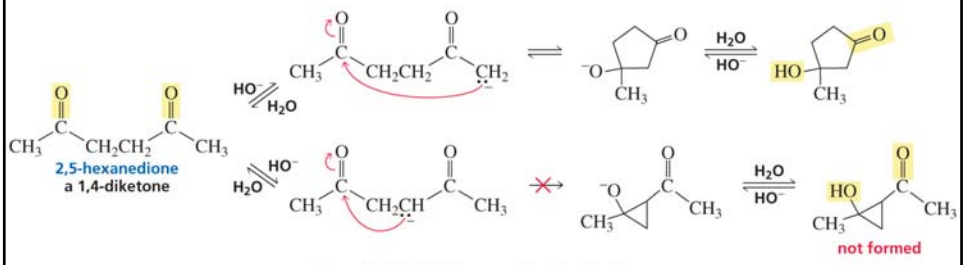


Mechanism

mechanism for the Dieckmann condensation



Intramolecular Aldol can give two possible ring sizes



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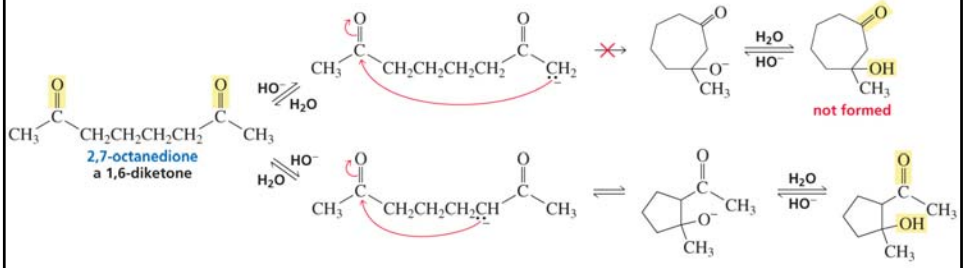
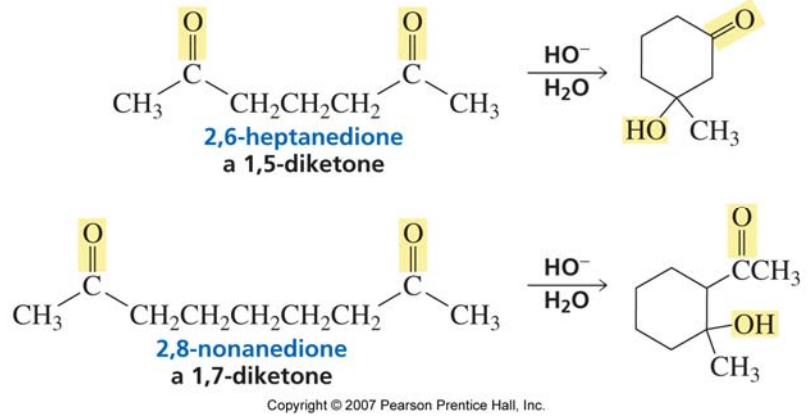
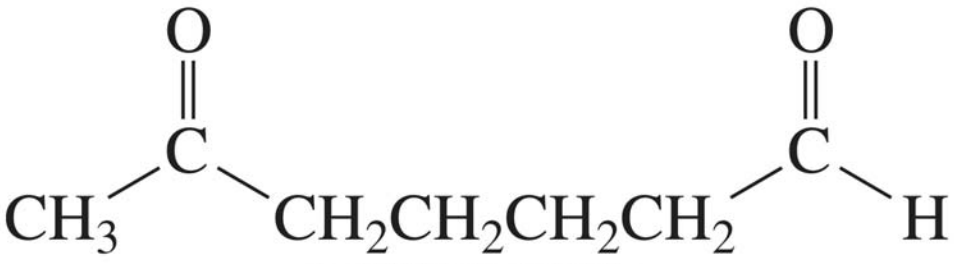
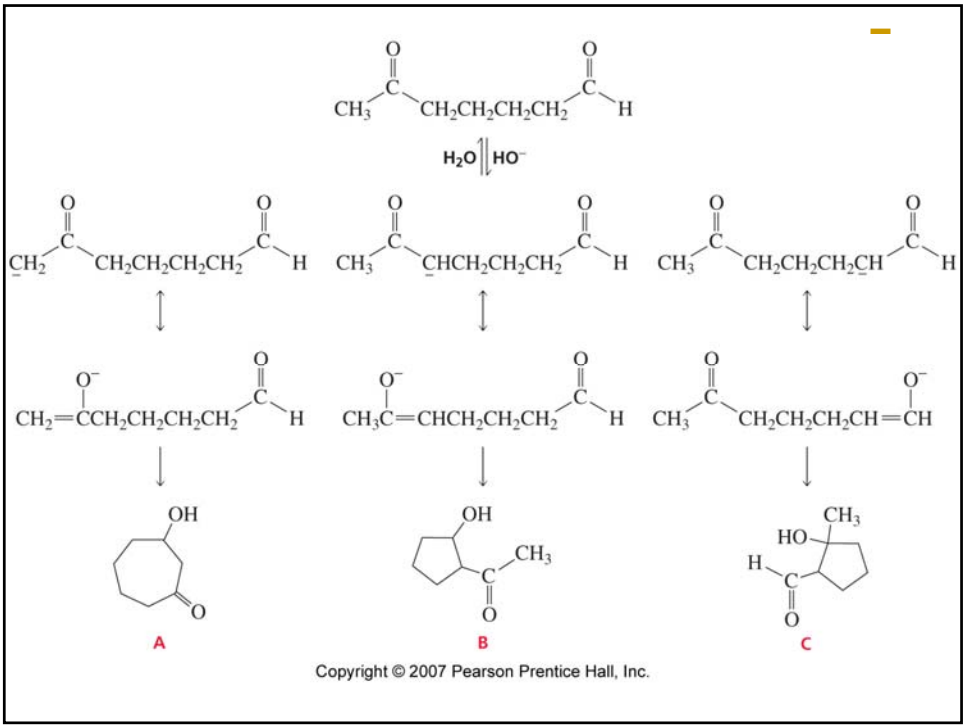


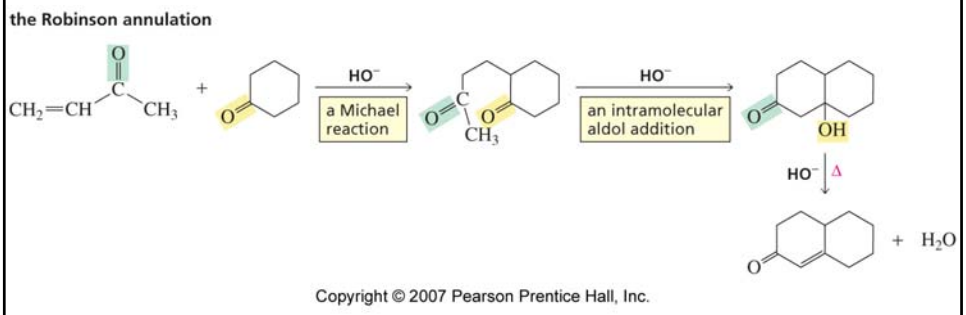
Six-membered rings are preferred





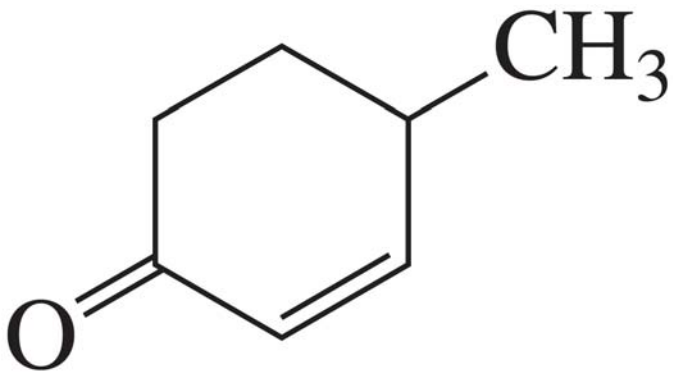


The Robinson Annulation: Michael Addition, then intramolecular Aldol condensation

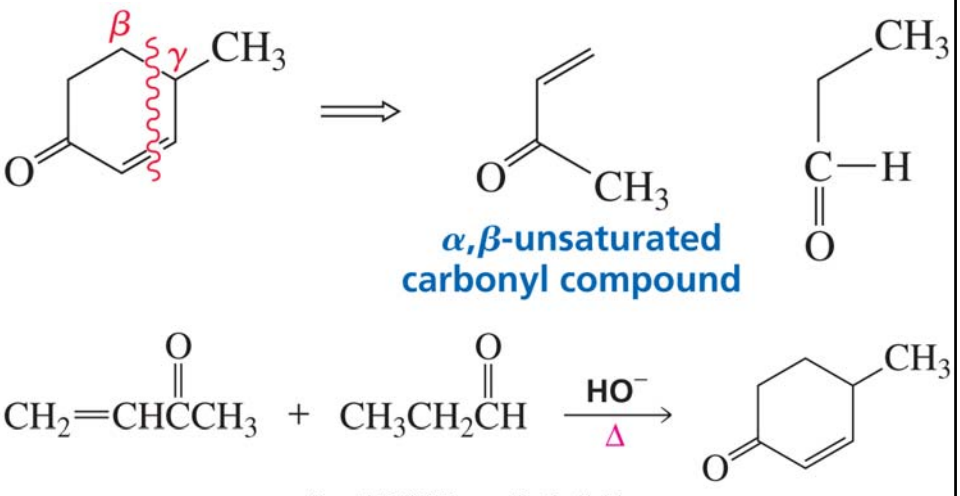


Retrosynthetic breakdown

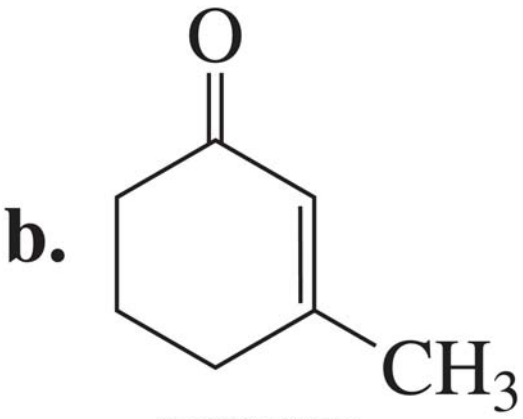
a.



Robinson retrosynthesis



Retrosynthetic breakdown



Robinson retrosynthesis