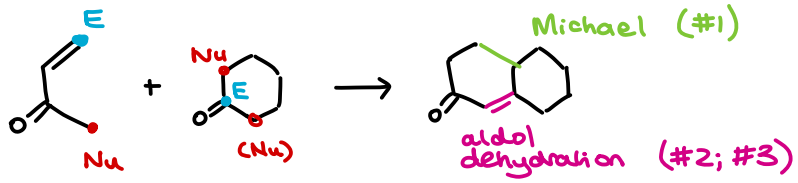
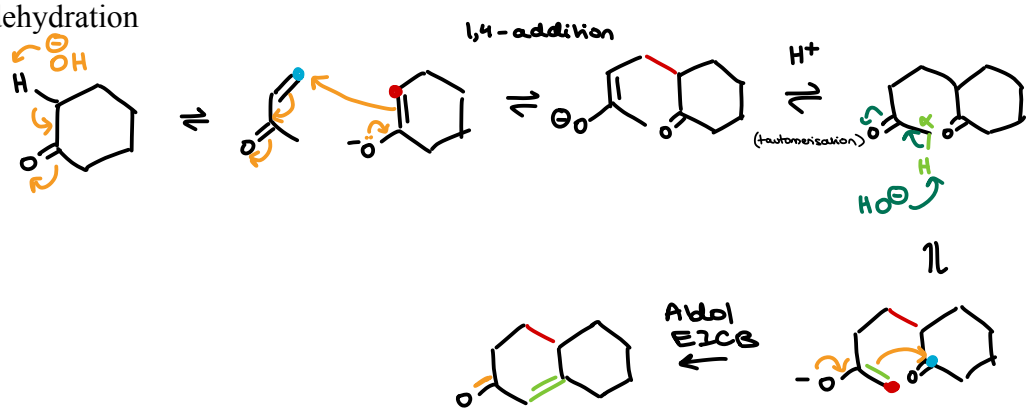


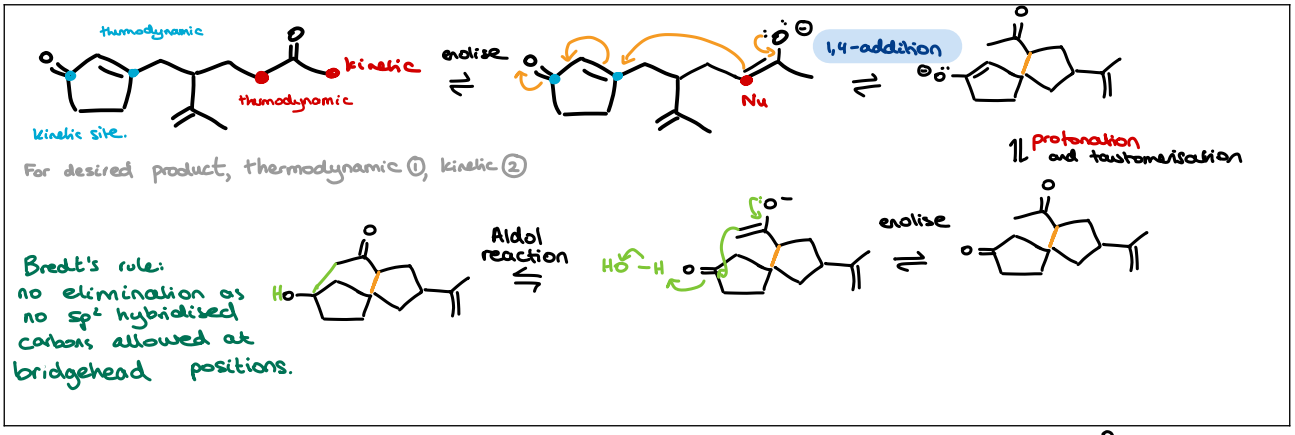
Robinson annulation – Michael Reaction + intramolecular aldol reaction

6-membered ring synthesis

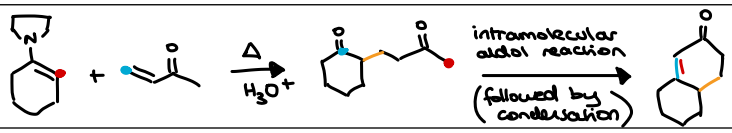
1. enolate formation
2. conjugate addition
3. aldol reaction
4. dehydration



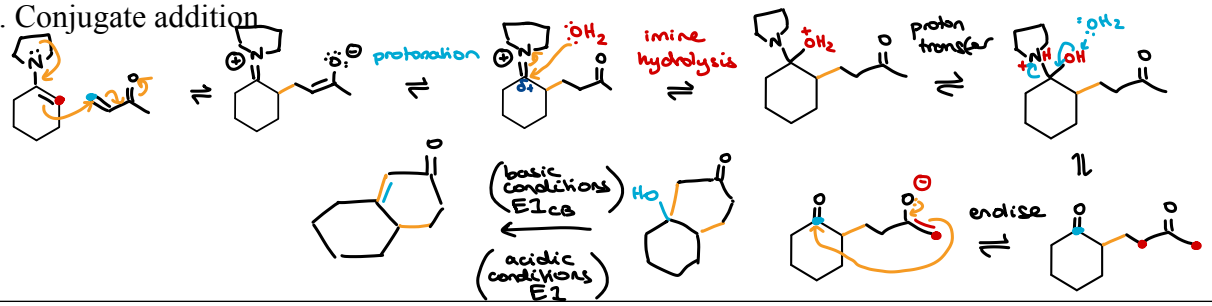
Intramolecular conjugate addition – always consider 5 and 6 membered rings



Enamine conjugate addition:



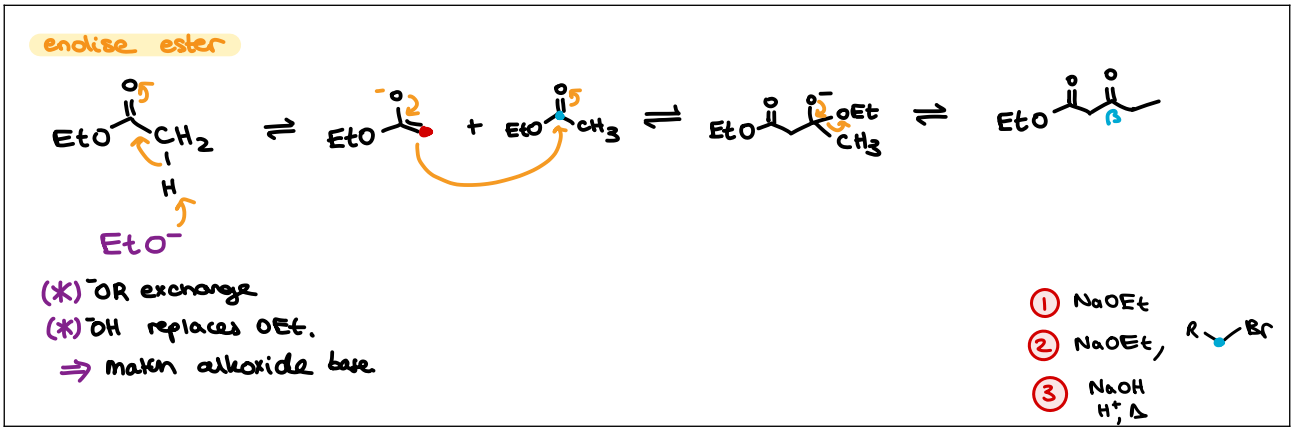
1. Enamine formation
2. Conjugate addition



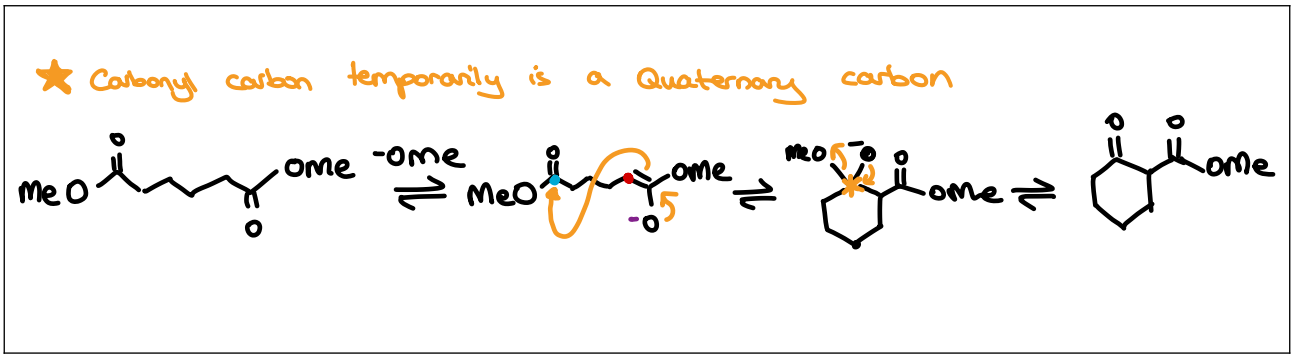
Claisen and Dieckmann condensations

Claisen – condensation between two esters

ester enolate + carbonyl → β ketoester



Dieckmann condensation (Intramolecular Di-ester condensation to form 5/6 membered rings)



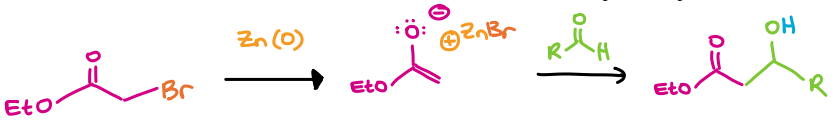
Reformatsky reaction

no base

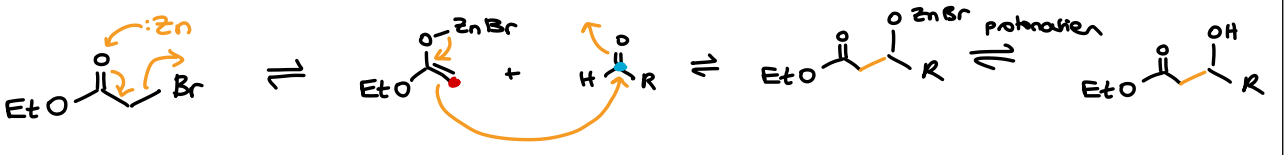
α-bromoester → zinc enolate → ß-hydroxy ester

aldehyde

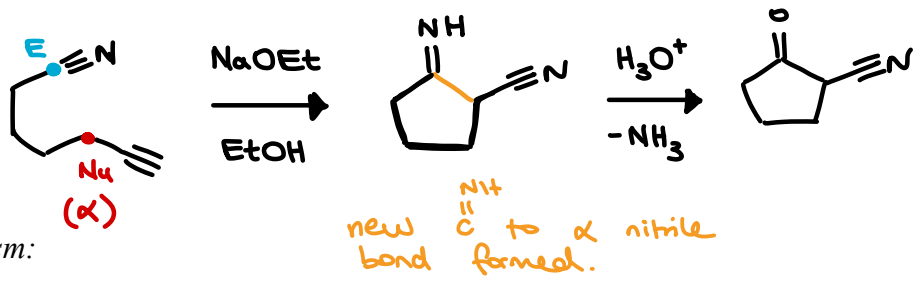
↙ doesn't work for ketones because of self-condensation.



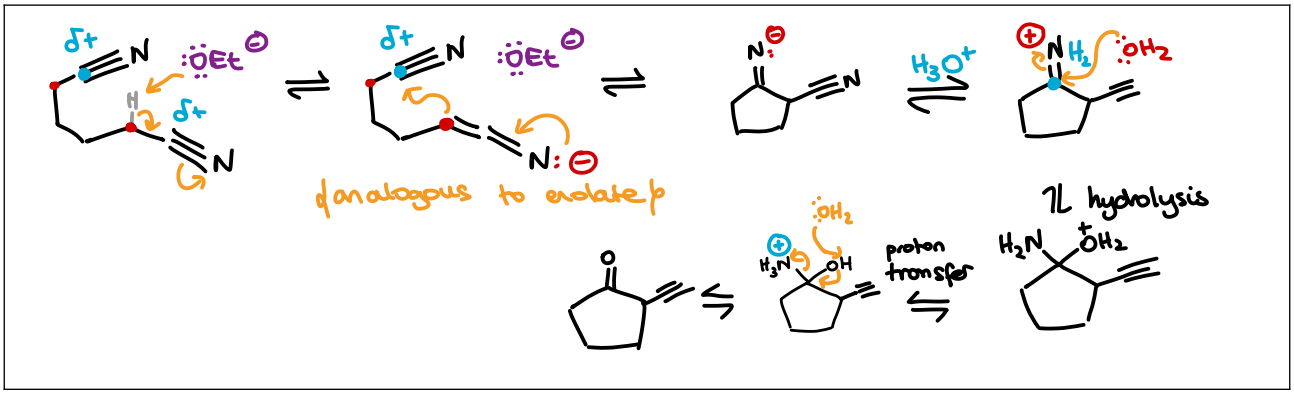
Mechanism



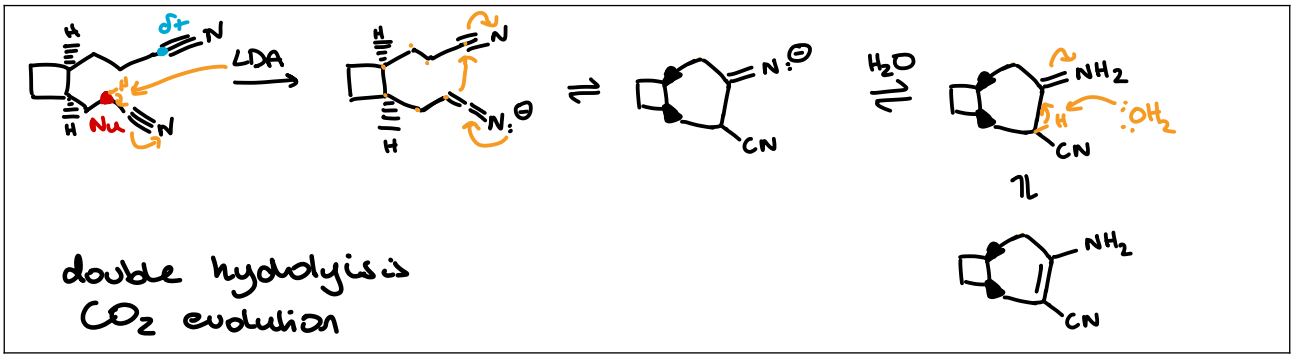
Thorpe reaction – Nitrile deprotonation:



Mechanism:

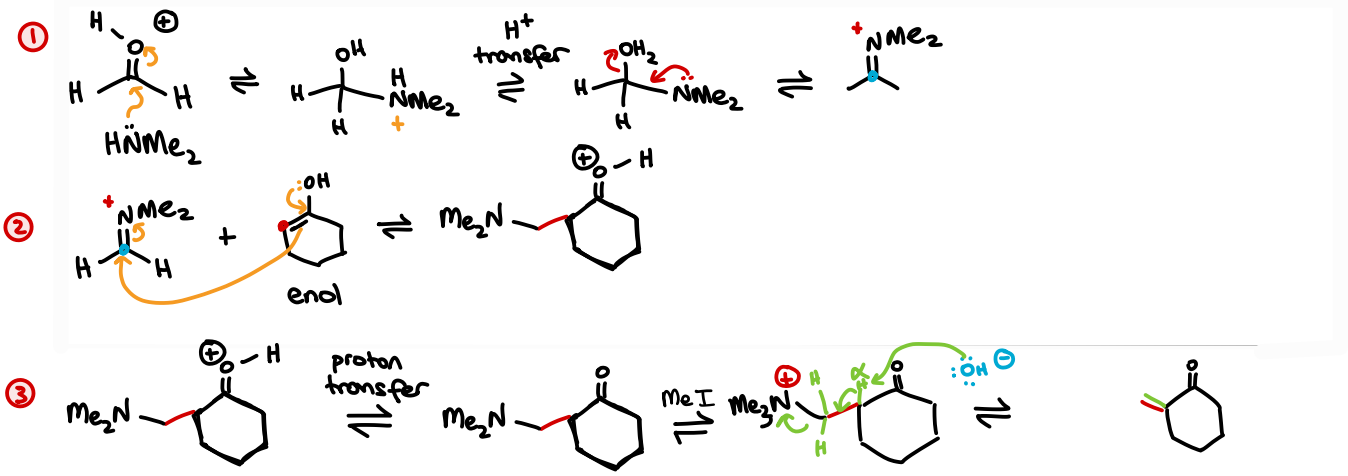


Example:

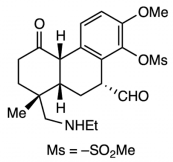


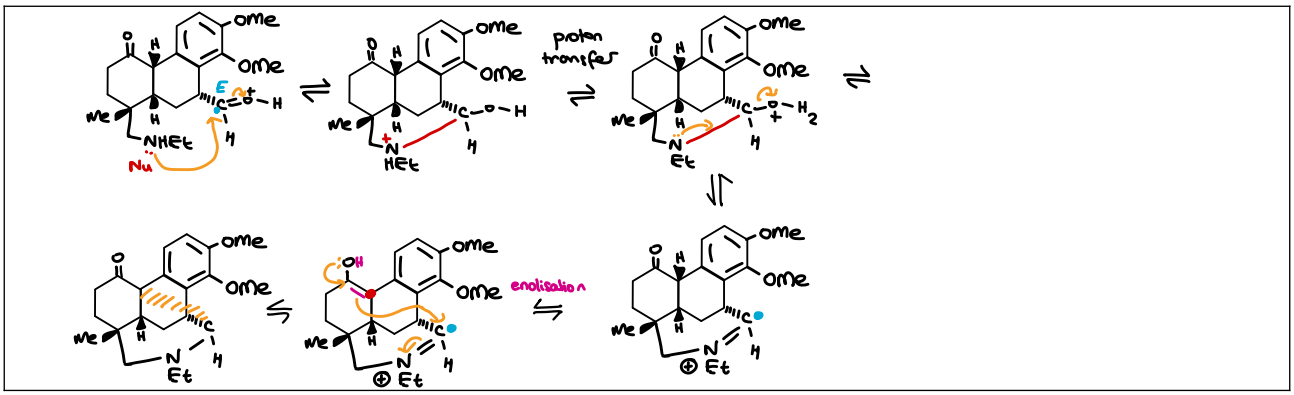
Mannich Reactions

1. Imine formation
2. Enol Addition
3. Elimination



Example: Mannich reaction of

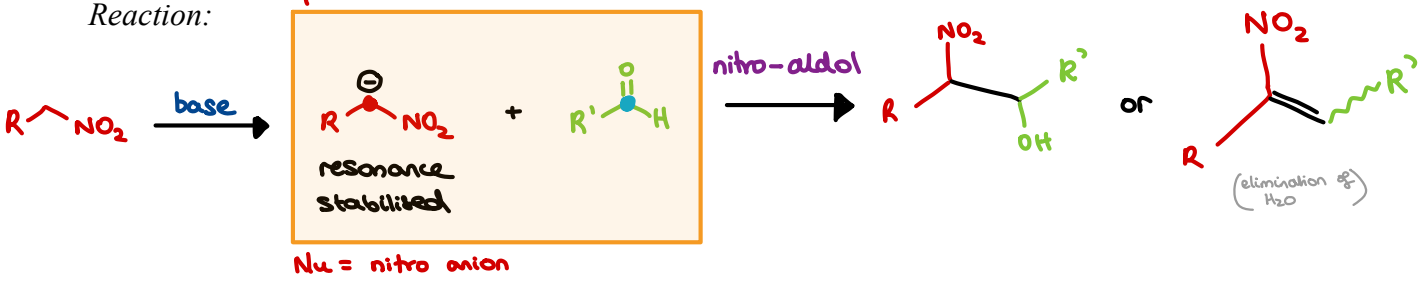




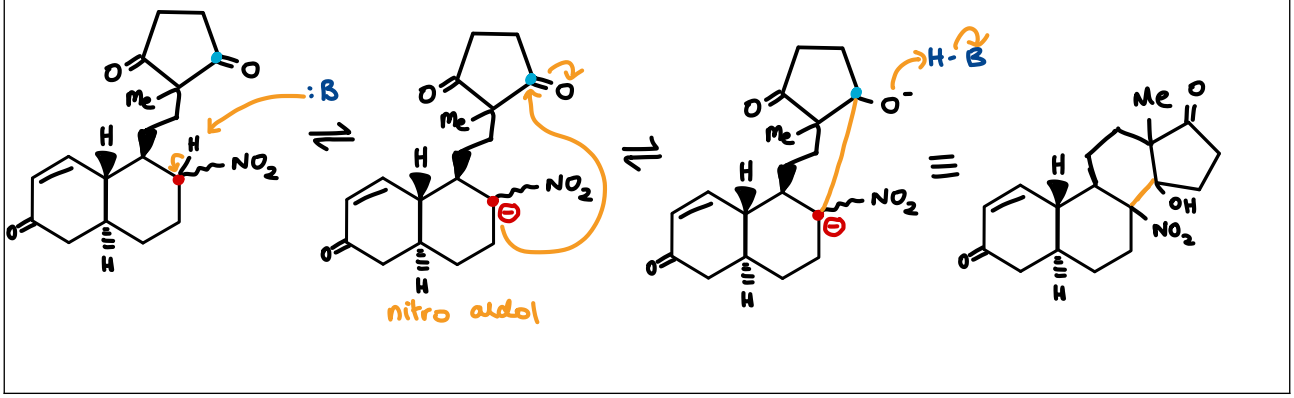
Nitroaldol (Henry) reaction

pKa ~21 ← self-condensation not possible.

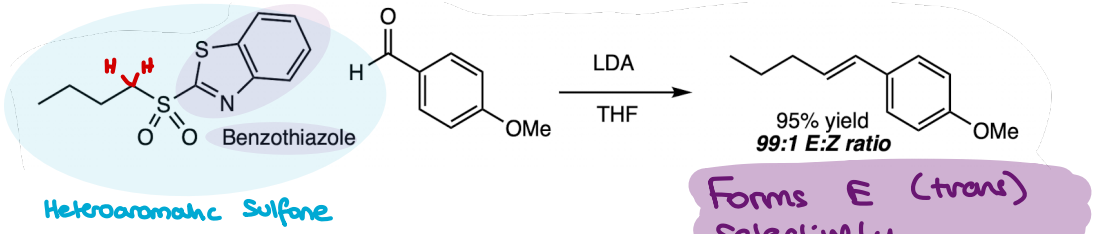
Reaction:



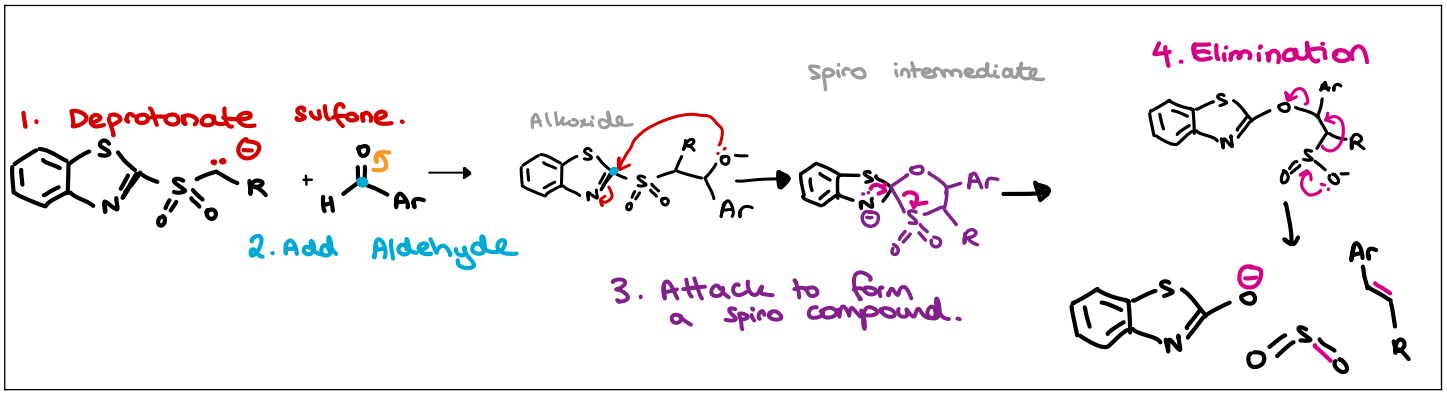
Mechanism:



Julia Reaction:



Mechanism:



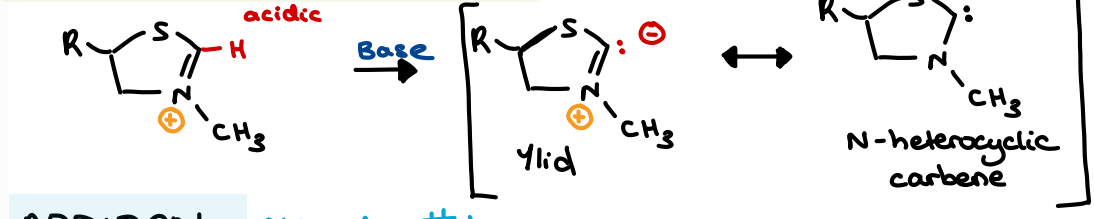
N-heterocyclic carbenes

Benzoin Condensation Umpolung using a thiazole (1-3 S, N). Acidic sp^2 carbon.

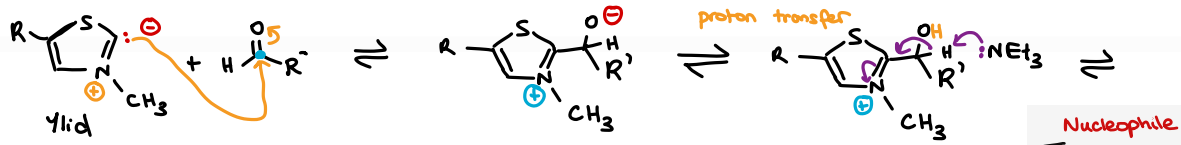
Ylide addition

1,2 or 1,4 addition → For synthesising α hydroxy ketone compounds → carbonyl + carbonyl.

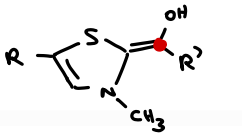
FORMATION OF CARBENE



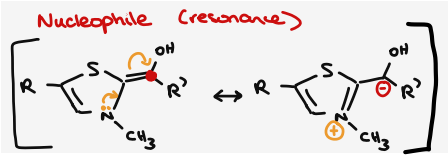
ADDITION Aldehyde #1



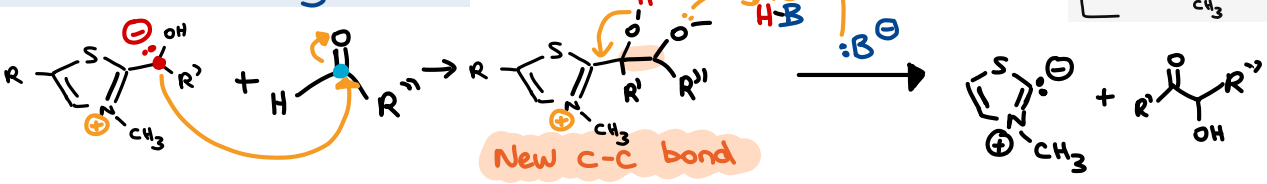
Nucleophilic
↳ Umpolung!!



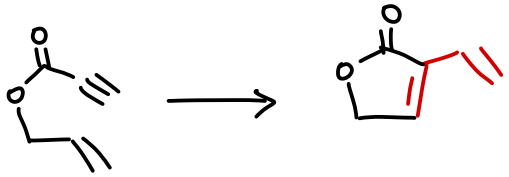
Nucleophile (resonance)



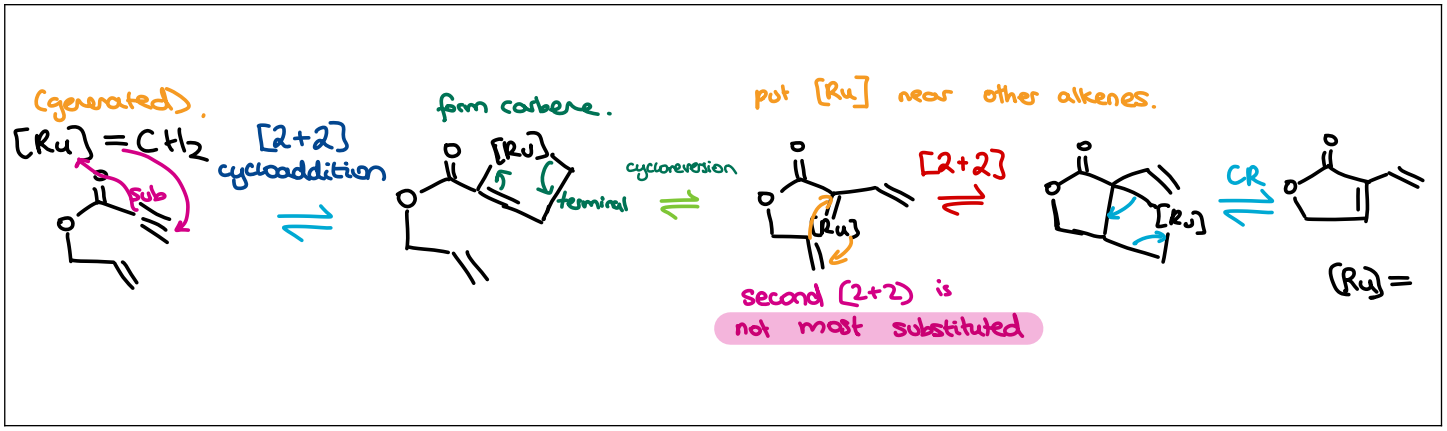
ADDITION Aldehyde #2



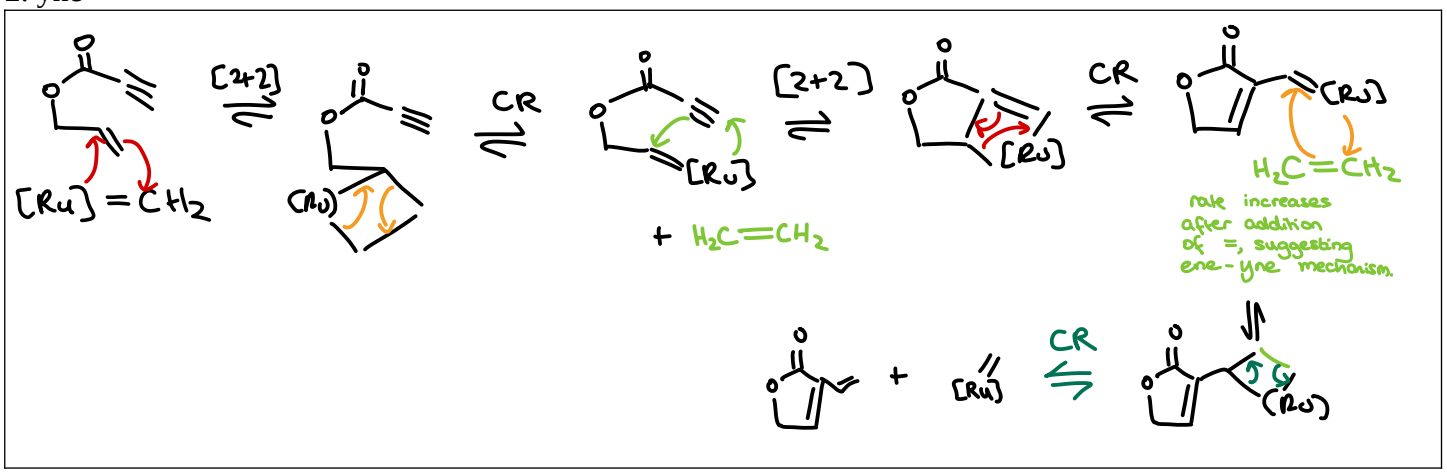
Enyne Metathesis



pathway 1:
1. yne
2. ene



pathway 2:
1. ene
2. yne



Example Ring-Closing Mechanism: