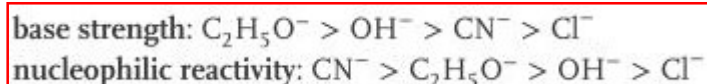
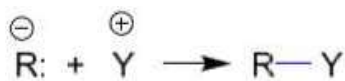
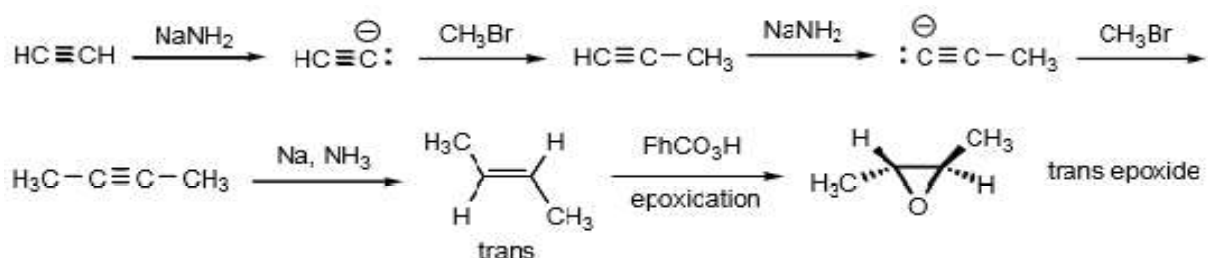
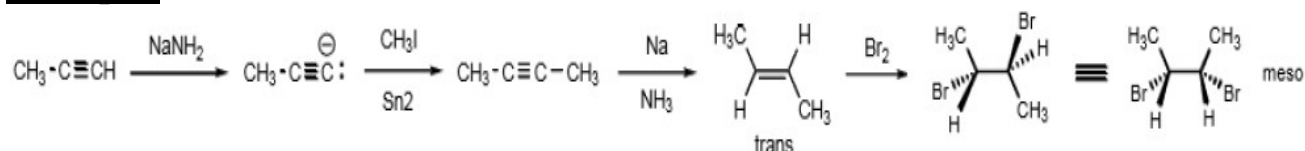
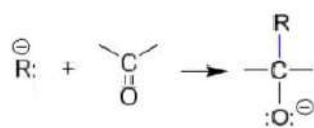
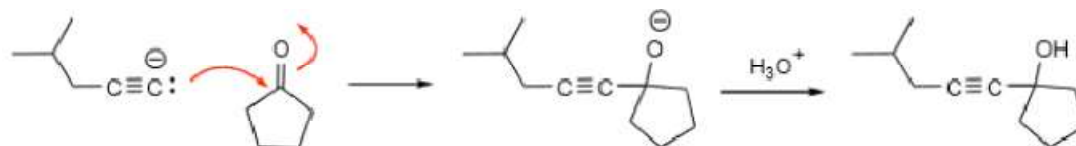
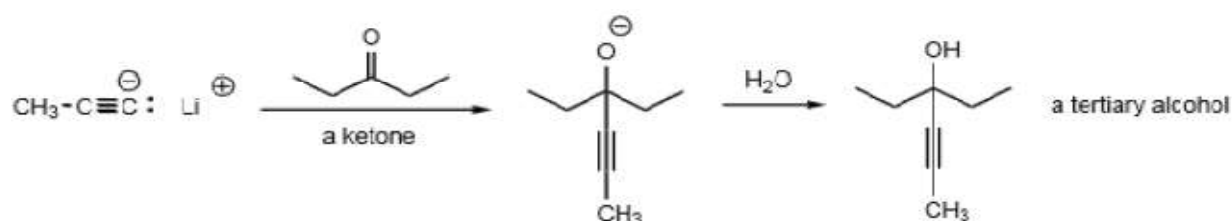


Reactions of carbanions:**1- Reaction with an Electrophile:****2- Reaction with Alkyl halides:(e.g. $\text{S}_{\text{N}}2$ reaction)****Example:** formation of the **epoxide**.**Example:** formation of **vicinal dihalides**.**3- Reaction with Carbonyl compounds:****Examples:** formation of **alcohol**.

Nucleophilic attack on the ketone gives the alkoxide ion, which is the conjugate base of the 3° alcohol.

3° alcohols are produced from the reaction between carbon nucleophiles and ketones.



The reaction of carbanions with carbonyl compounds includes:

A. Enolate Reactions with Carbonyl Groups:

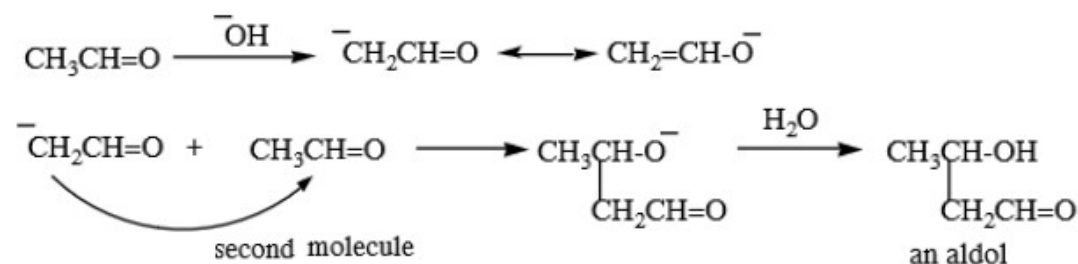
1- Aldol Condensation: (reactants are aldehydes & ketones)

An **aldehyde** or **ketone** that **has hydrogen next to the carbonyl group**, an **α -hydrogen**, can **form an enolate** in a **basic solution**, and the **enolate** can **react** by **nucleophilic addition** at the **carbonyl group** of **another molecule**. This process is an essential synthetic procedure known as the **Aldol Condensation**. The **final product** from **aliphatic aldehydes or ketones** contains both a **carbonyl** and an **alcohol group**. The **product** is called an **aldol**.

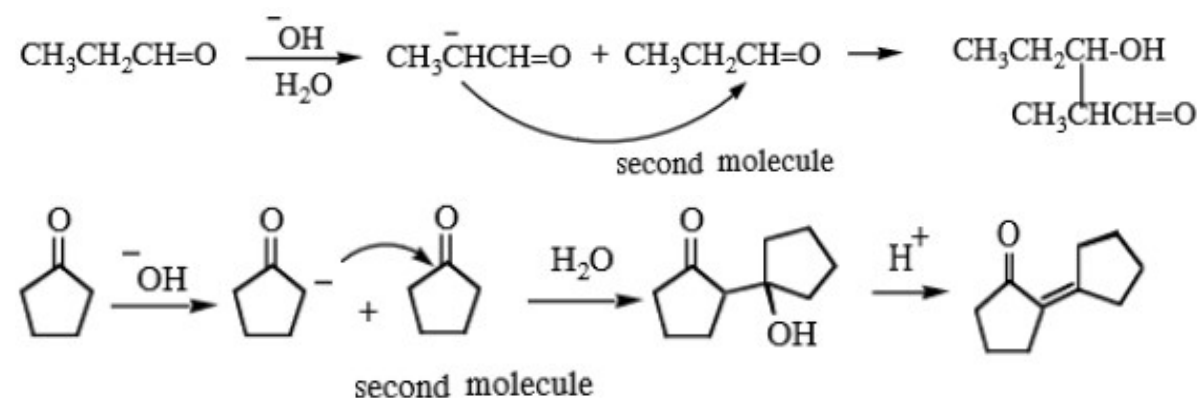
Conditions of the aldol condensation:

- 1- Two molecules of an aldehyde or ketone (at least one of them **contrasted α -hydrogens**).
- 2- Dilute base or dilute acid (**dil. NaOH**).
- 3- Form a **β -hydroxyaldehyde** or **β -hydroxyketone**.

Example:

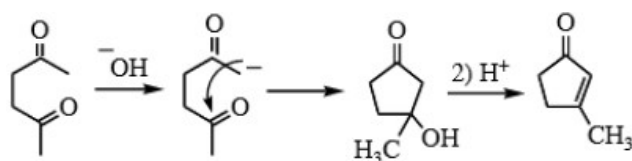


Examples:



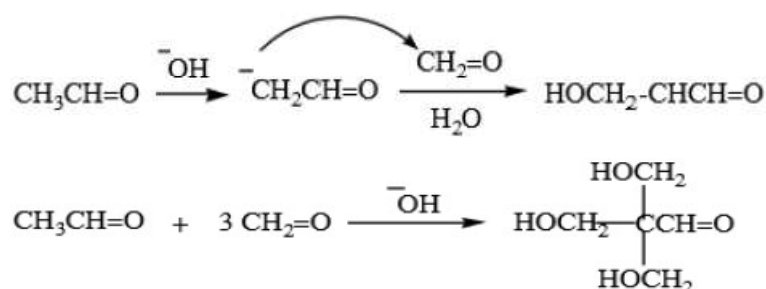
- The **aldol products react** readily with **acid** to undergo **dehydration** and give **α,β -unsaturated carbonyl compounds** that are also very useful in **synthetic organic and biological chemistry**.

Intramolecular aldol condensations are useful in the **formation** of **cyclic α,β -unsaturated ketones**.

Example:**Crossed-Aldol Condensation:**

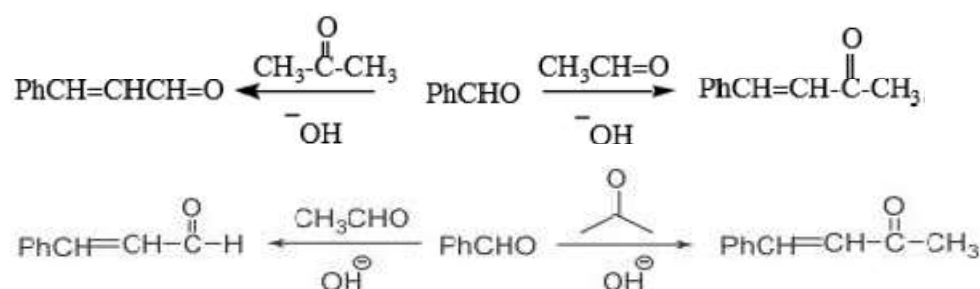
The main aldol condensation involves the reaction **between two aldehydes or ketones of the same structure**. However, the procedure can be modified so that the **enolate** can **react** with **another aldehyde** of a **different structure**. The requirement is that the **other aldehyde has to be more reactive than the first and it contains no α -hydrogens**.

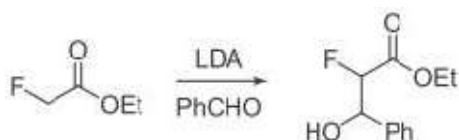
Formaldehyde ($\text{CH}_2\text{C}=\text{O}$), and **benzaldehyde ($\text{PhCH}=\text{O}$)**, both meet these requirements and are useful in this procedure called **crossed-aldol condensation**. All **three** of the **α -hydrogens** in **acetaldehyde** can **react** in a crossed-aldol condensation with **formaldehyde**.

Examples:

Aromatic ketones bearing **α -hydrogens** give aldol reaction products readily, but in this case, the **aldol product spontaneously loses water** to **form the unsaturated ketone**.

When **benzaldehyde** is used in the **crossed-aldol condensation** the final product is the **unsaturated aldehyde or ketone**. **Conjugation of the double bond with the aromatic ring** is the reason for the spontaneous dehydration.

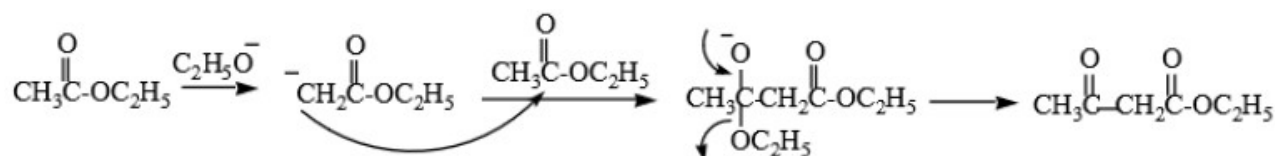
Examples:



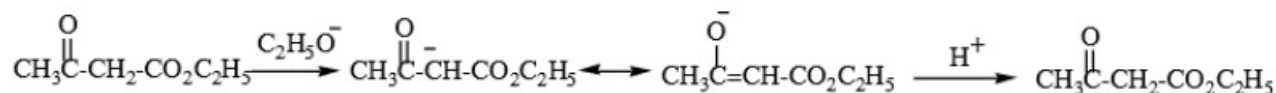
2- Claisen Condensation: (reactants are esters)

Esters give an **aldol** type reaction. The **α -hydrogen** of the **ester** is **removed** by the **base** to give the **enolate**. The **enolate reacts** with another molecule of the **ester** in an **addition-elimination reaction** characteristic of esters, which appears as **displacement** of the **alkoxide**. The resulting **product** is a **B-ketoester**.

Example:



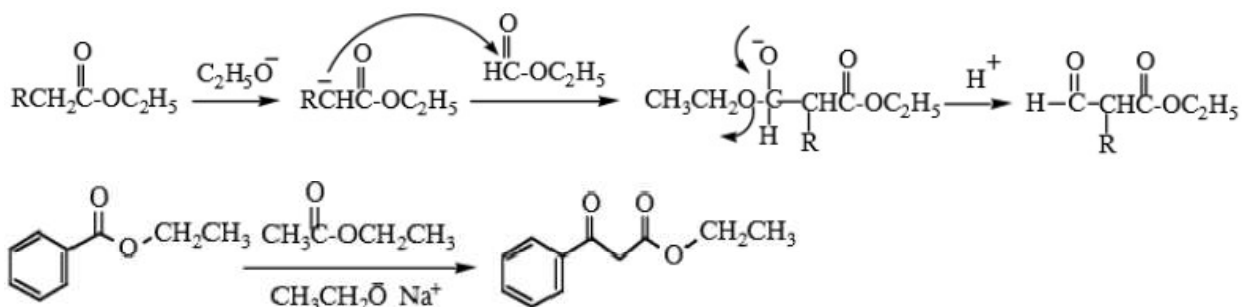
The **α -hydrogens** in the product **B-ketoester** are **more acidic** than the **α -hydrogens** in the **starting ester**. Thus a **new enolate** is formed that is **more stable** than the **first enolate**, thus helping the reaction go to completion.

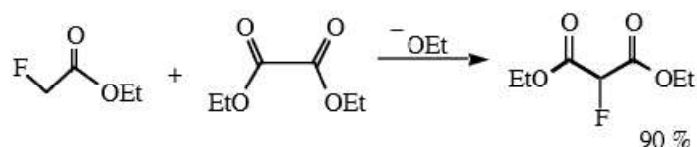
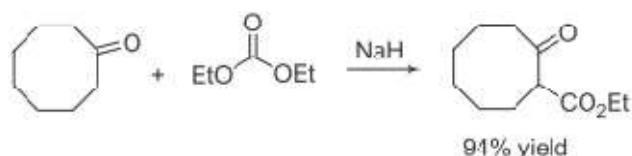
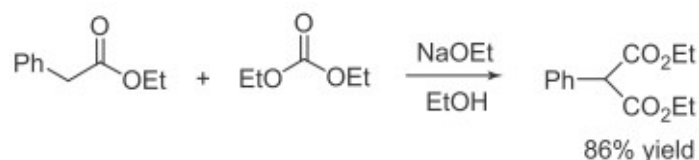


Crossed-Claisen condensation: Occurs when a **highly reactive ester** with **no α -hydrogens** reacts with the **enolate** derived from **another ester**. **Ethyl benzoate** and **ethyl formate** are two frequently used esters that have **no α -hydrogens**.



Examples:

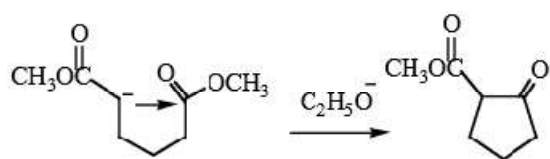




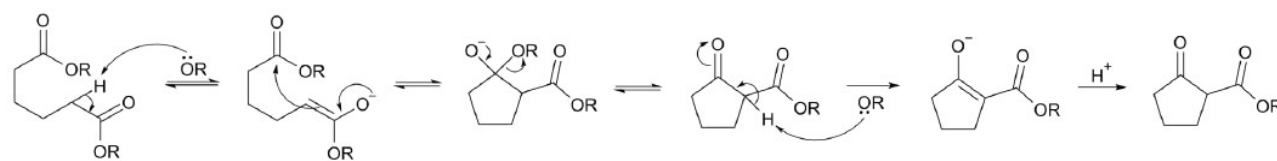
3- Dieckmann condensation: (reactants are diesters)

Is the **intramolecular chemical reaction** of **diesters** with the **base** to give **β -keto esters**. Is **intramolecular Claisen condensation** and is useful for the **preparation** of **five** and **six-membered rings**.

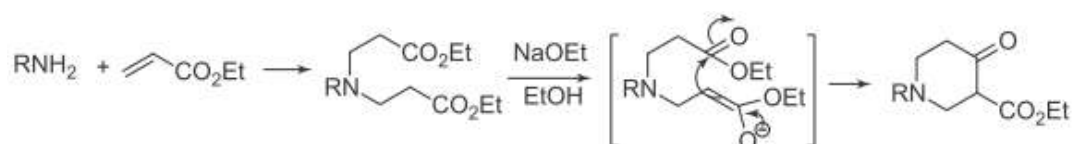
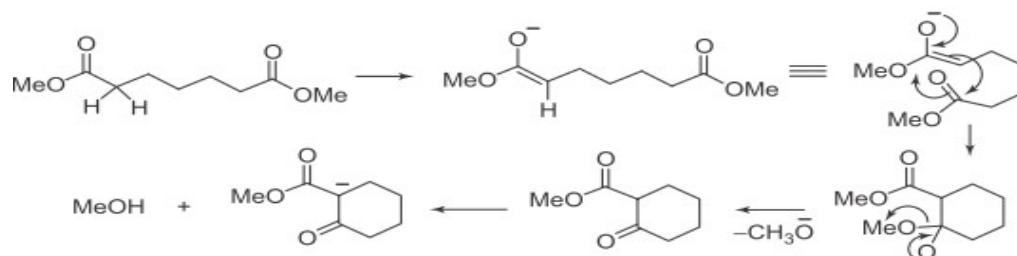
Example:



Mechanism: Deprotonation of an ester at the α -position generates an **enolate ion** which then undergoes a **5-exo-trig** nucleophilic attack to give a cyclic enol. Protonation with a **Brønsted-Lowry acid** (H_3O^+ for example) re-forms the β -keto ester.



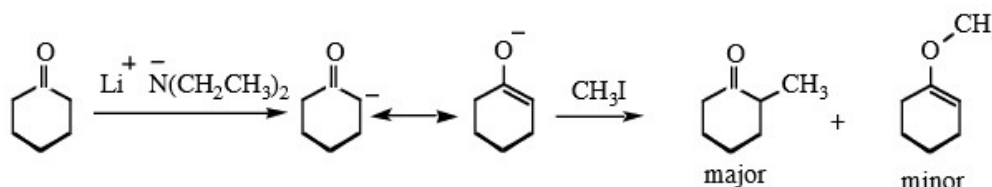
Examples:



B- Enolate Anion Alkylation Reactions

General Reaction: when **strong anhydrous bases** such as (**sodium hydride, sodamide, or lithium diethylamide $\text{LiN}(\text{C}_2\text{H}_5)_2$**), are used to prepare the **enolate anions** at **low temperatures**, the resulting **enolate** reacts very slowly with **carbonyl groups** and can be used as **nucleophiles** in the $\text{S}_{\text{N}}2$ reaction with **primary alkyl halides**. In the **resonance stabilized enolate**, a **negative charge** exists on **both a carbon** and an **oxygen**. **Both** sites are possible **nucleophiles** in the reaction but the **carbon nucleophile** predominates because it is a **stronger nucleophile**, but **minor products** from **O-alkylation** are found.

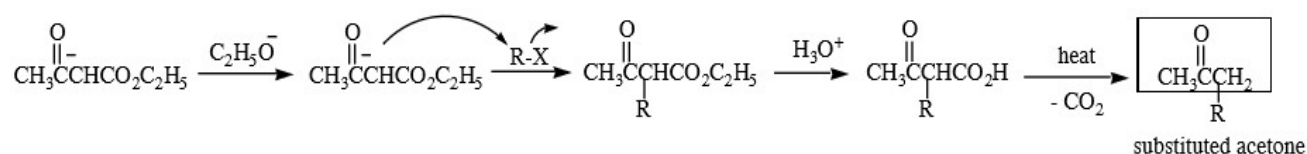
Example:



1- Reaction of Ethyl Acetoacetate with alkyl halides:

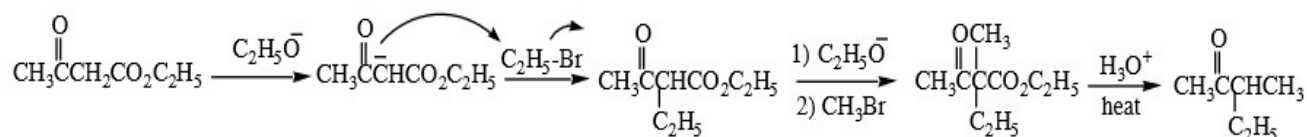
The **α -hydrogens** of **ethyl acetoacetate** are **acidic** enough ($\text{pK}_a = 11$) to be **removed** by a **variety of bases**. The **enolate anion** can be used to **displace a halogen** in an **alkyl halide**. **Hydrolysis** of the **product** gives a **B-ketoacid** which **loses CO_2** by **mild heating**. A **derivative of acetone** is the **final product**.

Example:



Double alkylation of **ethyl acetoacetate** in **sequential steps** can provide a synthesis of **highly branched derivatives** of **acetone after hydrolysis**.

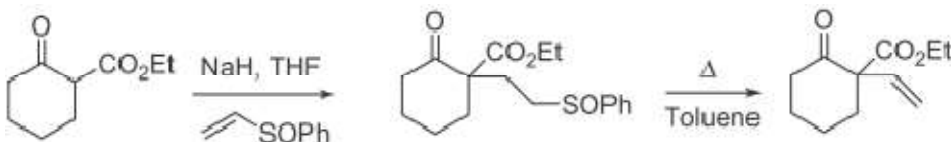
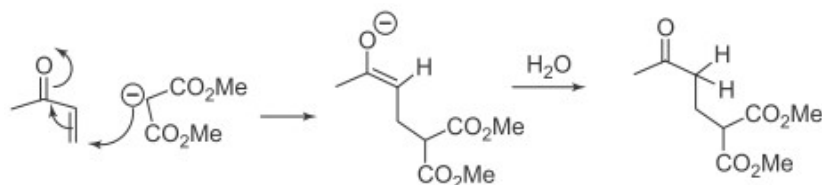
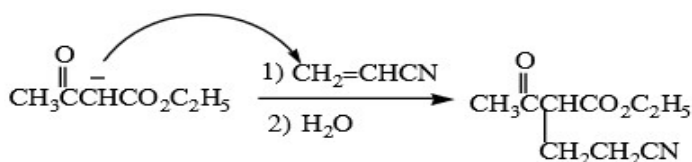
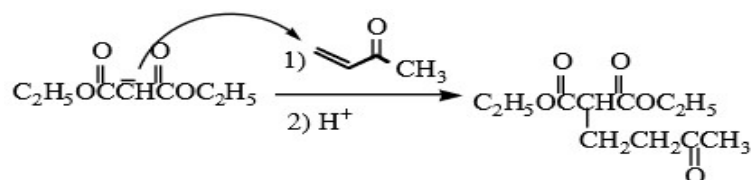
Example:



2- The Michael Reaction: (Enolate Addition) (reactants are α,β -unsaturated compounds)

Enolates may also be **alkylated** with **α,β -unsaturated carbonyl substrates**. The **enolate adds** in the **1,4 fashion** to **give a unit extended by three carbon atoms** in a process known as the **Michael reaction**. Many **α,β -unsaturated carbonyl** systems may be **prepared** by the **dehydration of aldol products**. E.g. **methyl vinyl ketone** and **acrylonitrile**, two common units in the reaction.

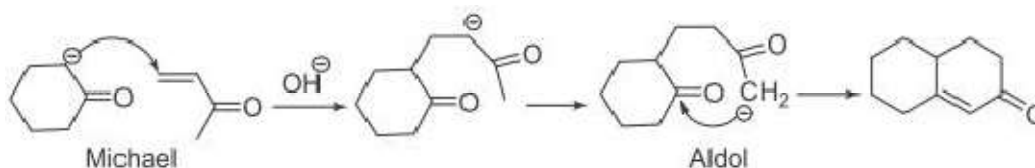
Examples:



3- Robinson Ring-forming Reaction: (reactants are α,β -unsaturated carbonyl compounds)

A **unique reaction** that **produces a new ring containing an α,β - unsaturated ketone** is the **Robinson reaction**. When an **enolate** derived from a **ketone reacts** with **methyl vinyl ketone**, the **enolate adds** in the **Michael reaction**, and then a second enolate in the ketone product is **formed** that **cyclizes** in an **Aldol condensation** to give the final product.

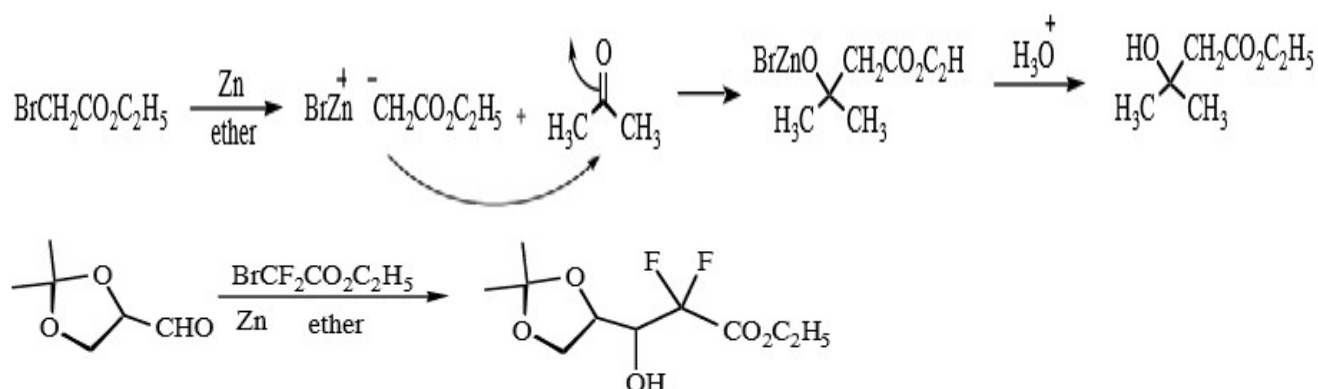
Example:



4- Reformatsky Reaction: (reactants are α -bromine)

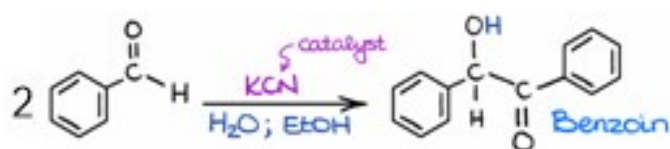
Instead of forming the enolate from an α -hydrogen, an α -bromine atom can also be used. **Zinc reacts** with **ethyl α -bromoacetate** to form a **zinc enolate** that **reacts** at the **carbonyl function of aldehydes and ketones** to **produce α,β -hydroxyester**. The method is made easier by the **addition** of the **bromoester** to a **mixture of zinc and the carbonyl compound**.

Examples:

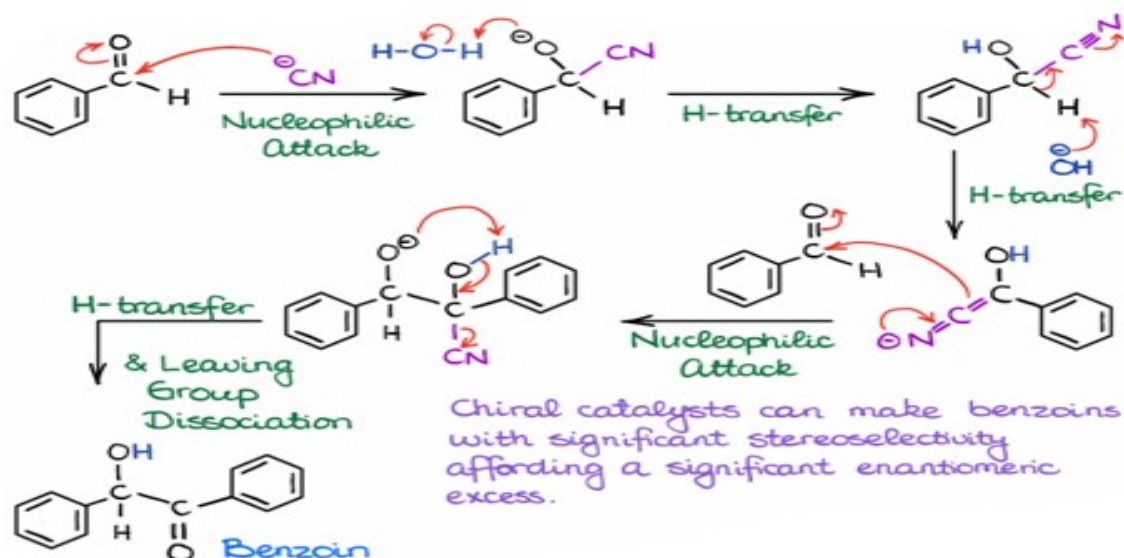


Note: Ethyl bromodifluoroacetate is used frequently in Reformatsky procedures to **give high yields** of **alcohol** products.

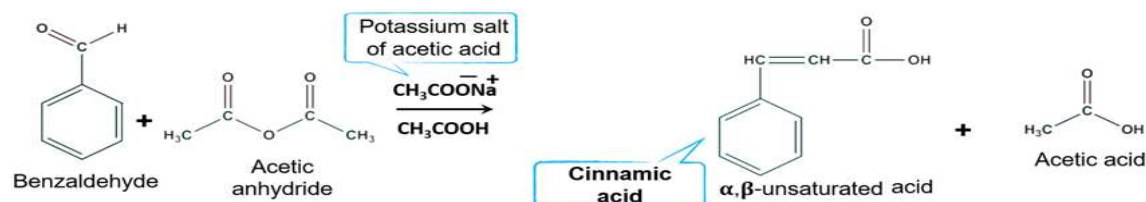
5- Benzoin condensation:



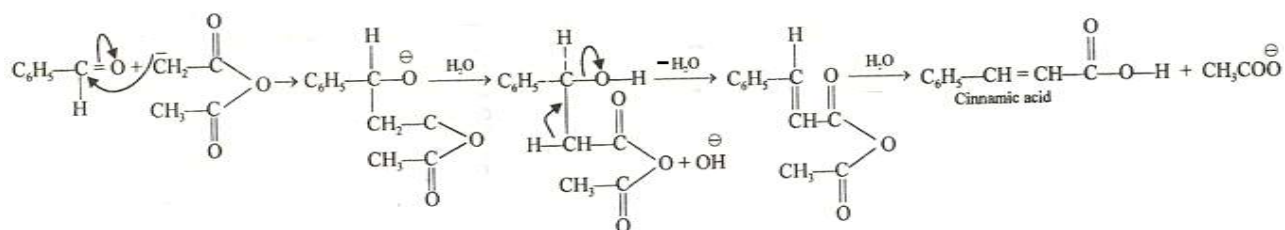
Mechanism: steps 1-5: as in others, step 6: loss CN^- .



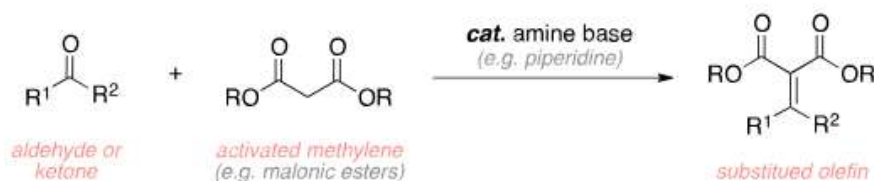
6- Perkins reaction: (reactants are anhydride compounds)



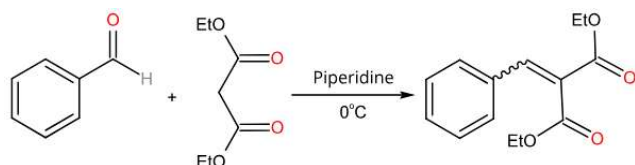
Mechanism: steps 1-2: as in others, step 3: protonation of the alkoxide ion to form an aldol-type compound, step 4: dehydration, the hydroxyl group, and neighboring hydrogen are removed as water, step 5: hydration.



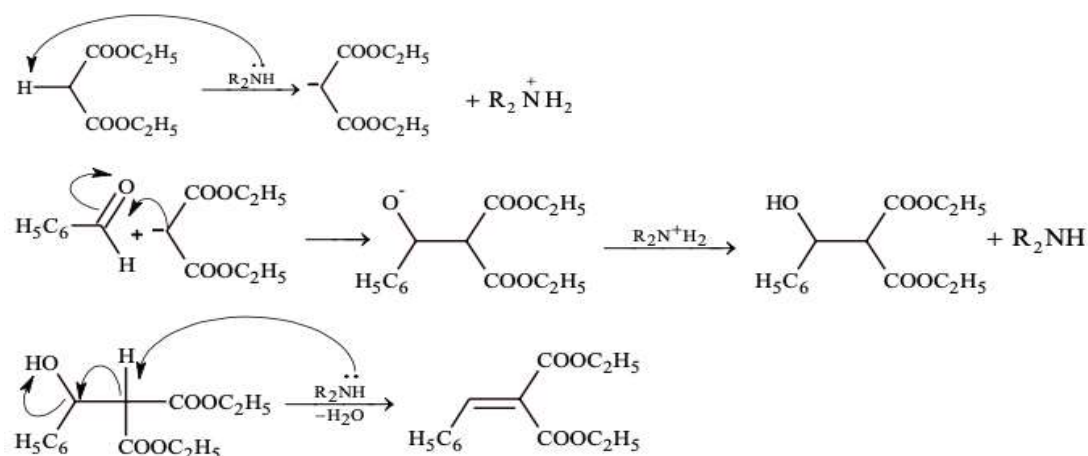
7- Knoevenagel reaction: (reactants are diethyl malonate)



Example:

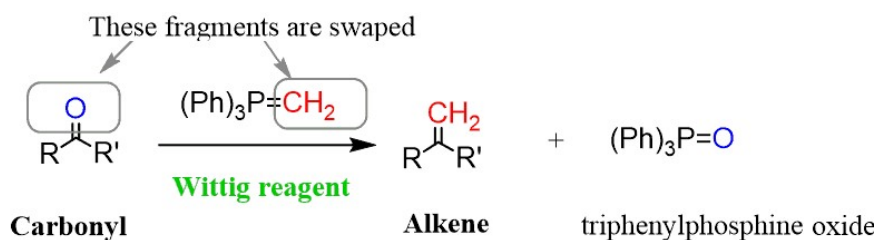


Mechanism: steps 1-2 as in other reactions, step 3: protonation: - alkoxide accepts a proton to form a hydroxyl compound, step 4: involves dehydration.

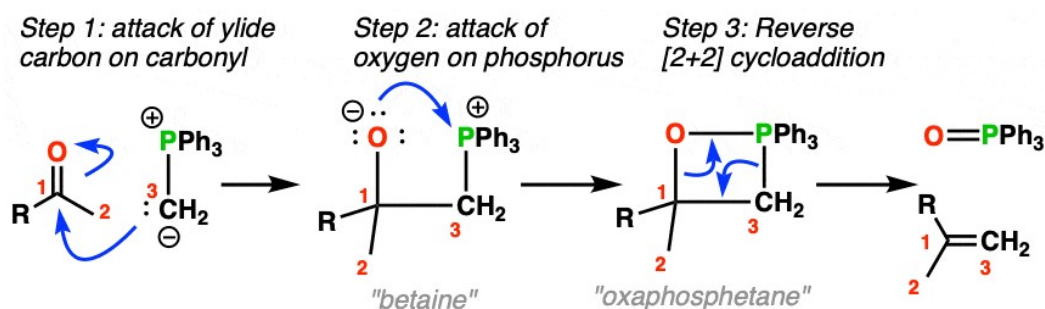


8- Witting's reaction: (reactants are phosphorous ylides $(\text{Ph})_3\text{P}=\text{CR}_2$)

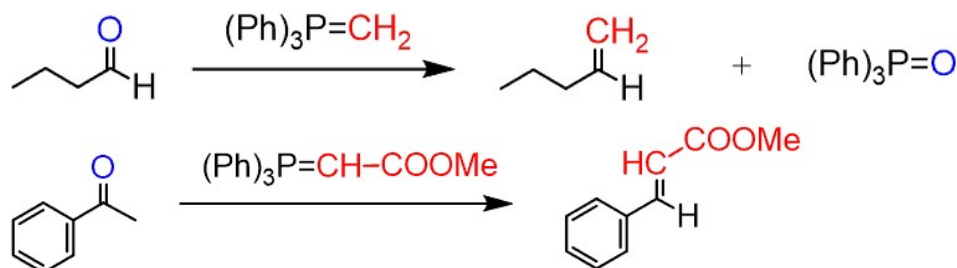
The reaction occurs between an **aldehyde/ketone** and **phosphorous ylides** to form substituted alkenes.



Mechanism:



Examples:



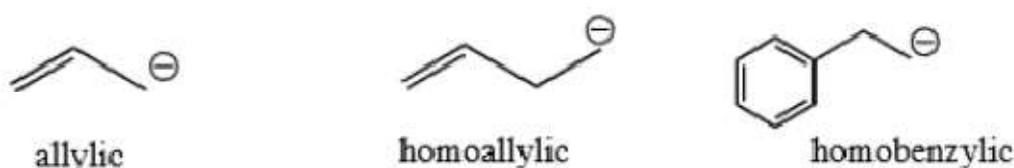
4- Rearrangements of Carbanions:



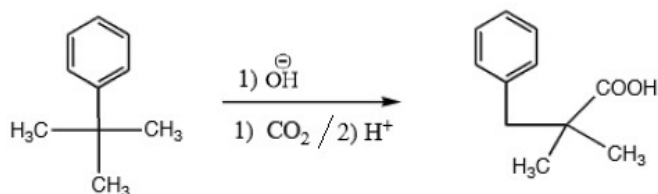
Includes of:

A. Homoallylic & Homobenzylic rearrangements:

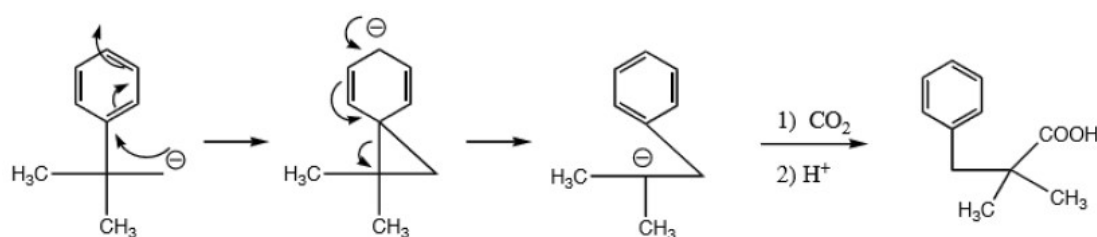
The structures below represent **allylic**, **homoallylic**, and **homobenzylic**. The "**homo**" means that there is one additional carbon atom. Some interesting rearrangements occur with the homoallylic systems.



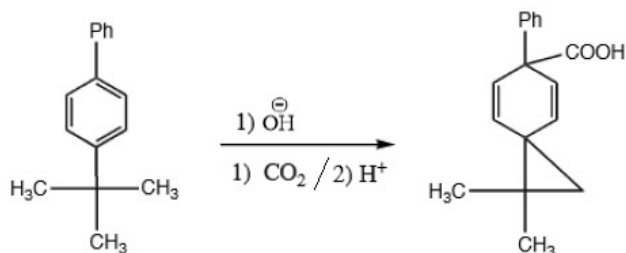
Example: shows a **homobenzylic rearrangement** where the **carbanion** interacts with the **aromatic ring**. The **carbanion** appears to be **inserted between the ring and the carbon-containing the two methyl groups**. The **mechanism of the rearrangement is proven by the isolation of the cyclopropane structure** when a **para phenyl group is present**.



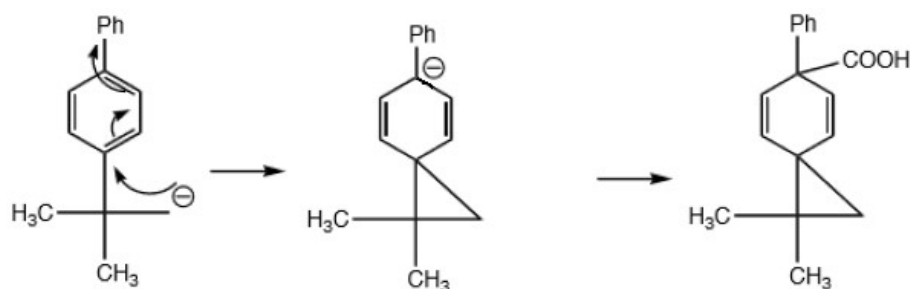
Mechanism:



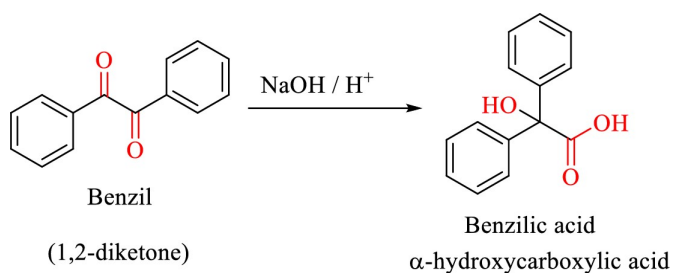
Example:

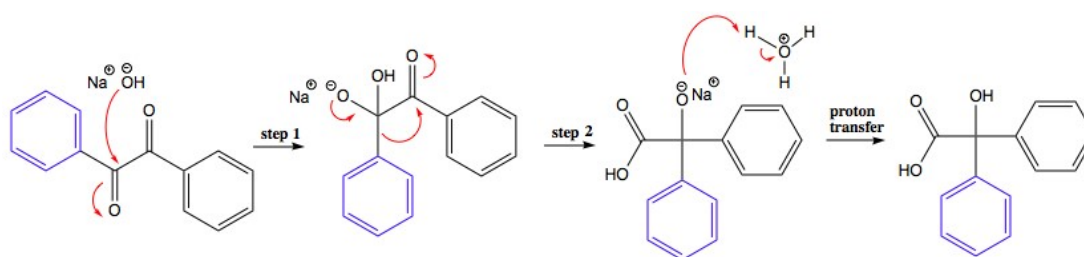
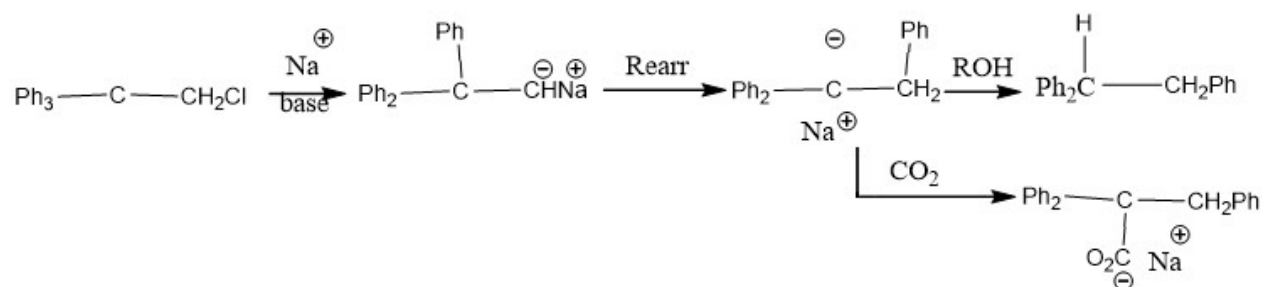
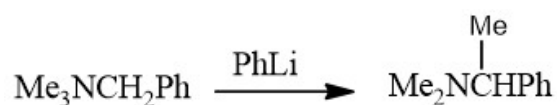
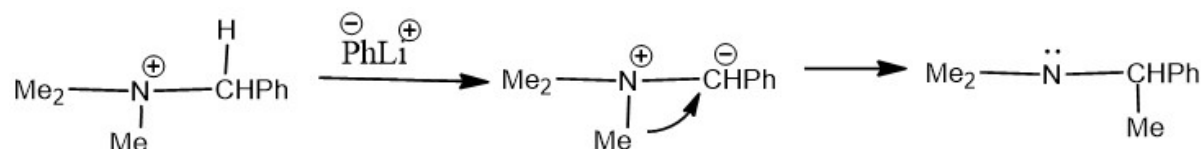
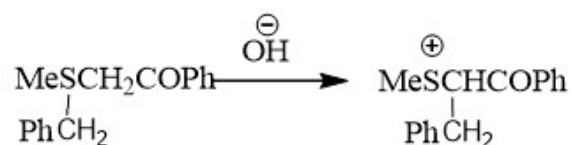
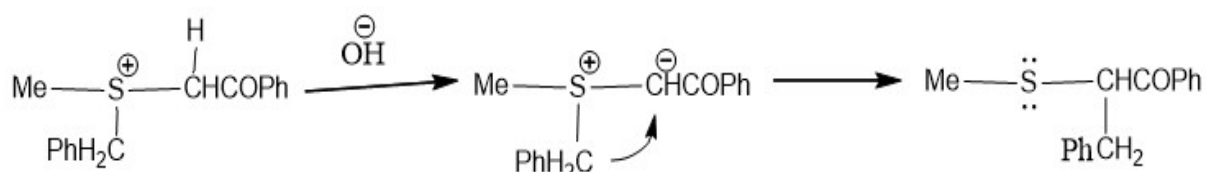


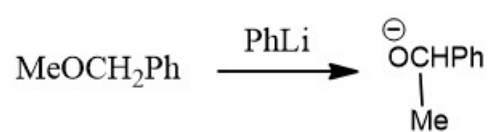
Mechanism:



B. Benzil-Benzilic acid rearrangement:



Mechanism:**C.1, 2 aryls shift an adjacent carbon atom (carbon 1):****D.1, 2 alkyls shift from N to carbanion:****Example:****Mechanism:****E.1, 2 alkyls shift from S to carbanion:****Example:****Mechanism:****F.1, 2 alkyls shift from O to carbanion:**

Example:**Mechanism:**