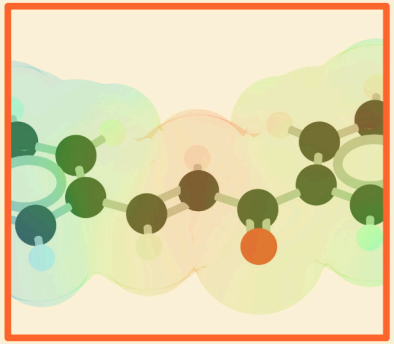
HIGHLIGHTS

- The aldol addition joins two molecules through the formation of a C–C bond and gives either a ß-hydroxy aldehyde or ketone.
- The aldol condensation forms a C=C bond through the elimination of water. It gives either an enal or enone.
- Both reactions can be promoted by acid or base.
- The crossed, or mixed, aldol reaction couples two different molecules together. It can give a mixture of compounds unless you control the addition - the simplest method limits you to forming a single nucleophile & coupling it to a more electrophilic aldehyde or ketone.



The aldol addition is one of the most useful reactions in synthesis. The aldol condensation is a reliable method for the formation of activated alkenes.

The aldol addition uses either an enolate or enol as the nucleophile & this attacks an electrophilic aldehyde or ketone. After proton transfer this leads to a ß-hydroxy aldehyde or ketone. Under both acidic or basic conditions, the reaction can proceed further giving the aldol condensation. This involves dehydration to an enal or enone.

When the aldol reaction occurs between different aldehydes or ketones in the crossed aldol reaction, it is necessary to control the addition or a mixture is formed. The simplest strategy involves having a single reactant with α-protons so only one of the coupling partners forms a nucleophilic enolate or enol. The other coupling partner must be more electrophilic than the first to prevent competitive self-condensation.

CHEMISTRY CLASSICS

THE ALDOL REACTION

SIMPLE ADDITION AND CONDENSATION

The Aldol Reaction

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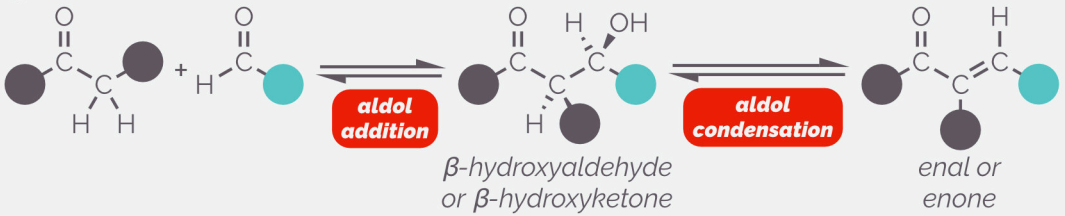
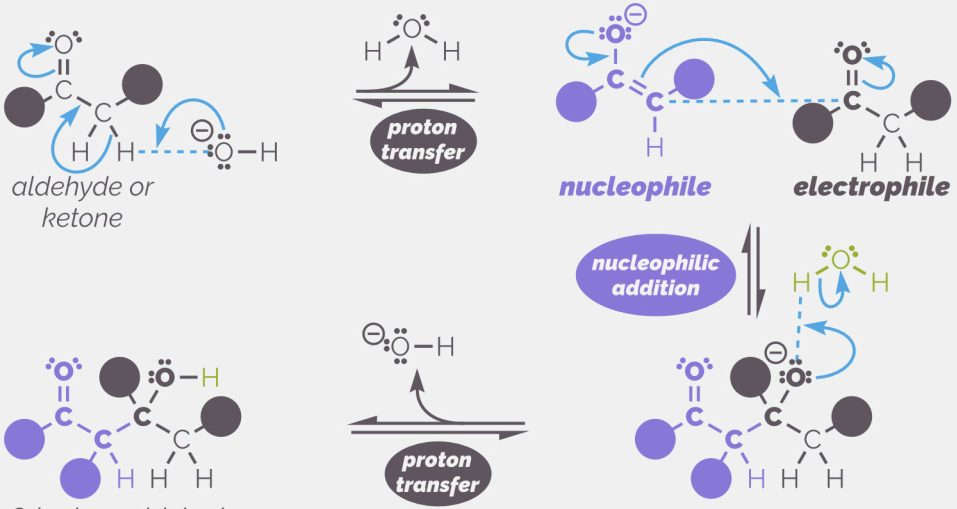
1. The aldol addition & condensation

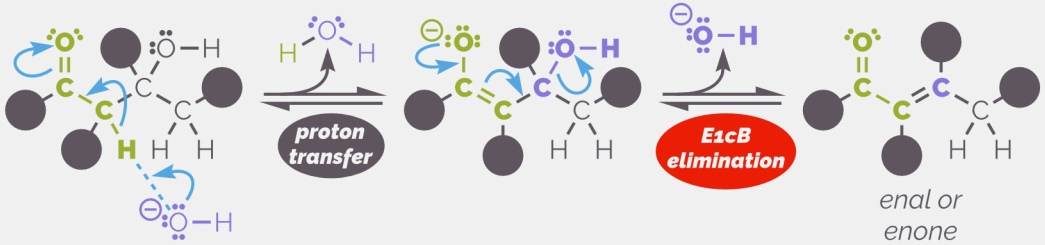


Example of nucleophilic addition to carbonyl **HERE** & enol/enolate chemistry **HERE**

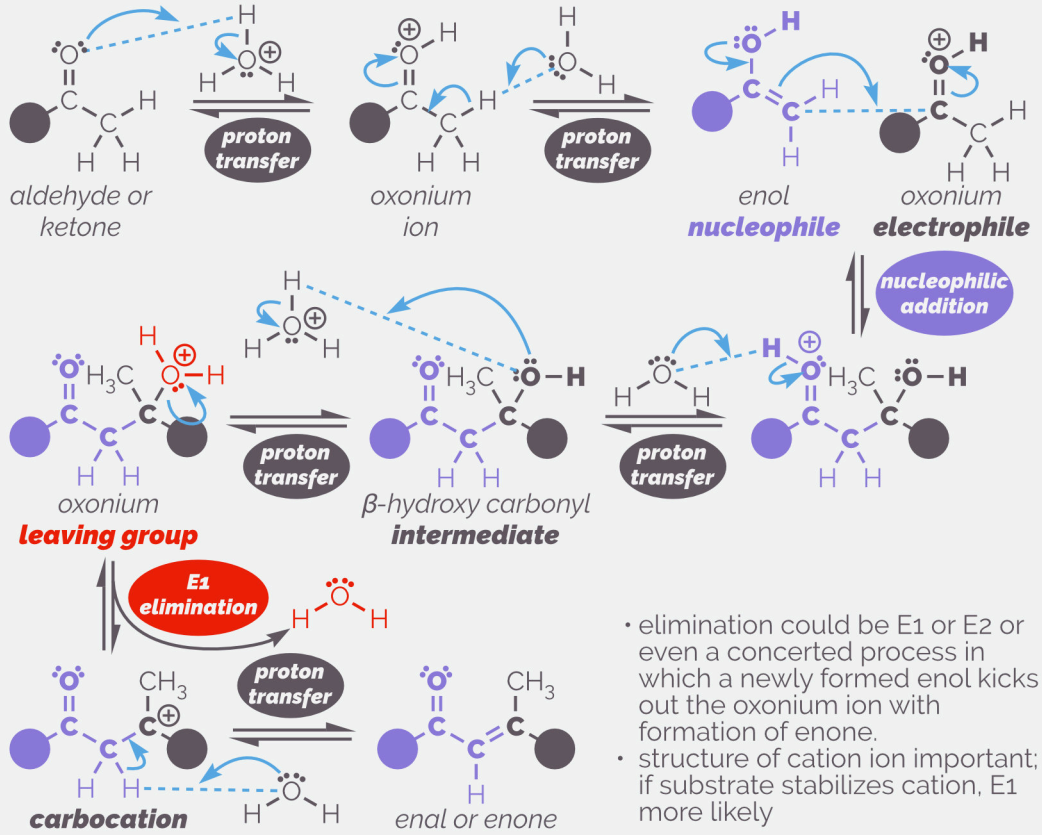
2. Mechanism of base-promoted aldol addition



3. Mechanism of base-catalyzed aldol condensation

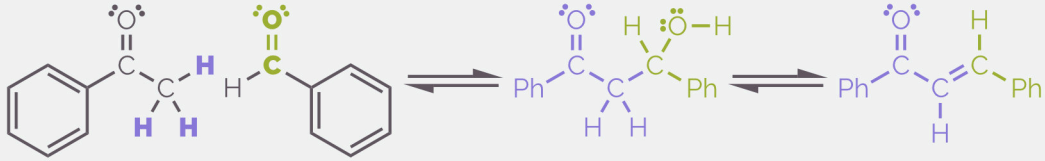


4. Mechanism of acid-catalyzed aldol reaction



- elimination could be E1 or E2 or even a concerted process in which a newly formed enol kicks out the oxonium ion with formation of enone.
- structure of cation ion important; if substrate stabilizes cation, E1 more likely

5. The crossed (or mixed) aldol (substrate control)



There are multiple strategies to control a crossed aldol. The simplest ensures that only one nucleophile is formed & that the other molecule is more electrophilic.