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CHEMISTRY
Paper 9: Organic Chemistry-III (Reaction Mechanism-2)
Module NO. 21: Benzoin Condensation and Stobbe Condensation

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1. Learning Outcomes

After studying this module, you shall be able to:

- Know what are Benzoin condensation and Stobbe condensation reactions
- Learn mechanism of Benzoin and Stobbe condensation reactions
- Know about the role of CN^- ion in Benzoin condensation
- Identify the products of reduction and oxidation of Benzoin condensation
- Understand the product formation in Benzoin and Stobbe condensation.

2. Introduction

A condensation reaction, also commonly referred to as dehydration synthesis, is a chemical reaction in which two molecules or moieties (functional groups) combine to form a larger molecule, together with the loss of a small molecule. Generally the small molecules lost are water, hydrogen chloride, methanol, or acetic acid but most commonly in a biological reaction it is water.

In organic synthesis, by far the most important activating groups are the carbonyl and carboxylic ester groups. Removal of a proton from the α -carbon atom of a carbonyl compound with base produces the corresponding α -carbanion, which are resonance stabilized via enolate anion. These enolate ions are involved in base catalysed reactions of carbonyl compounds.

Amongst these base catalysed reactions, the Stobbe reaction between dialkyl succinate and aldehyde or a ketone is a good method for making carbon-carbon bonds.

Another important reaction for C-C bond formation is Benzoin condensation, in which aromatic aldehydes (with no α -hydrogens) in the presence of CN^- condensed to form

benzoin. In majority of simple cases, as a result of this reaction, double the number of carbon atoms are present in the final product as compared to the starting molecule.

3. Benzoin Condensation

The **benzoin condensation** is a reaction (often called a condensation reaction, for historical reasons) between two aromatic aldehydes, particularly benzaldehyde. The reaction is catalyzed by a nucleophile such as the cyanide anion or an N-heterocyclic carbene. The reaction product is an aromatic acyloin with benzoin as the parent compound.

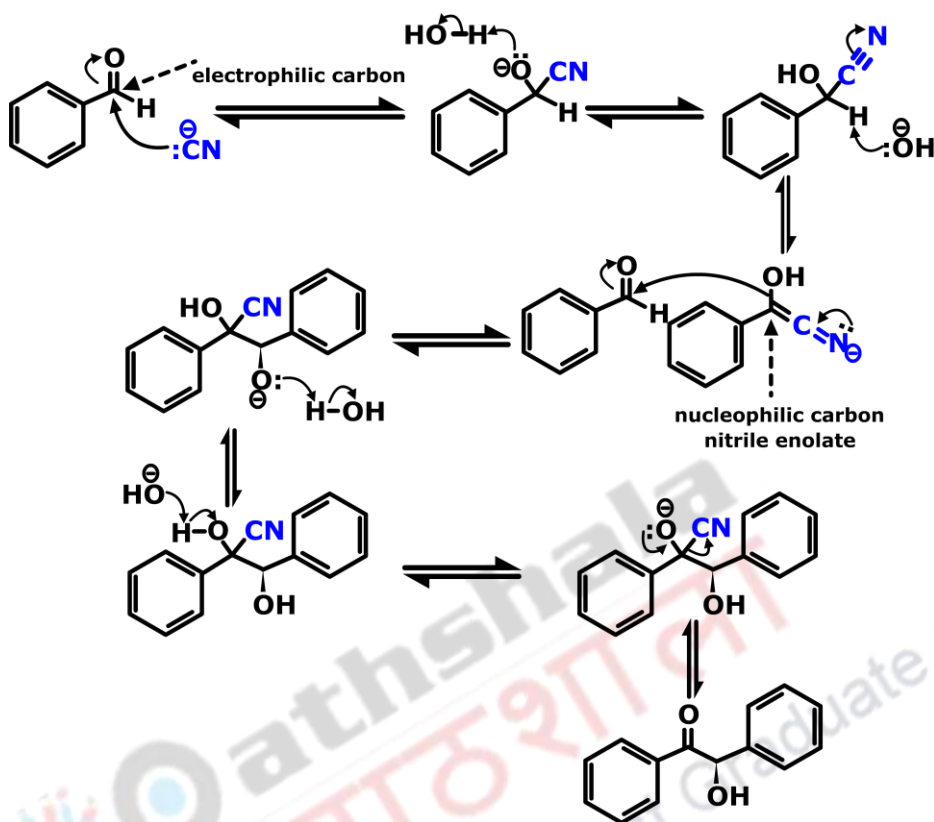


An early version of the reaction was developed in 1832 by *Justus von Liebig* and *Friedrich Woehler* during their research on bitter almond oil. The catalytic version of the reaction was developed by *Nikolay Zinin* in the late 1830s, and the reaction mechanism for this organic reaction was proposed in 1903 by *A. J. Lapworth*.

3.1 Mechanism of Benzoin Condensation

In the first step, the cyanide anion (as sodium cyanide) attacks the carbonyl carbon of the aldehyde in a nucleophilic addition. Rearrangement of the intermediate results in polarity reversal of the carbonyl group, which then adds to the carbonyl group of the other aromatic aldehyde (instead of H^+ transfer as that of Cannizzaro reaction). Proton transfer and elimination of the cyanide ion results in benzoin as the product.

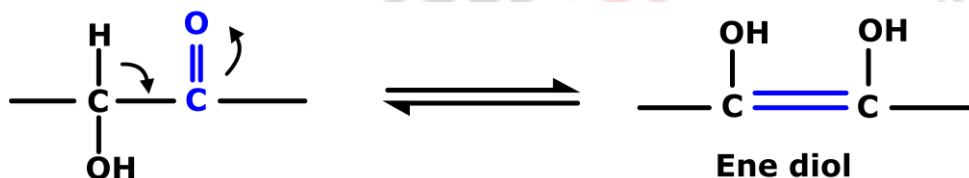
Mechanism involved:



3.2 Characteristics of Benzoin Condensation

- This reaction is completely reversible, the reversibility is indicated by the fact that benzoin is heated with another aromatic aldehyde mixed products are obtained.
- Cyanide ion catalyzes the reaction because:
 - It is good nucleophile
 - It is good leaving group
 - It increases the acidity of the C-H bond and stabilizes the carbanion that results from the loss of proton from C.

- The benzoin condensation is in effect a dimerization and not a condensation because a small molecule like water is not released in this reaction. For this reason the reaction is also called a **benzoin addition**.
- In this reaction, the two aldehydes serve different purposes; one aldehyde donates a proton and one aldehyde accepts a proton. In this way it is possible to synthesize mixed benzoin, i.e. products with different groups on each half of the product.
- Rate law of Benzoin condensation, $r = [\text{ArCHO}]^2 [\text{CN}^-]$
- Benzoin is colorless solid (M.P. 157 C) which assumed to tautomerise to ene diol.

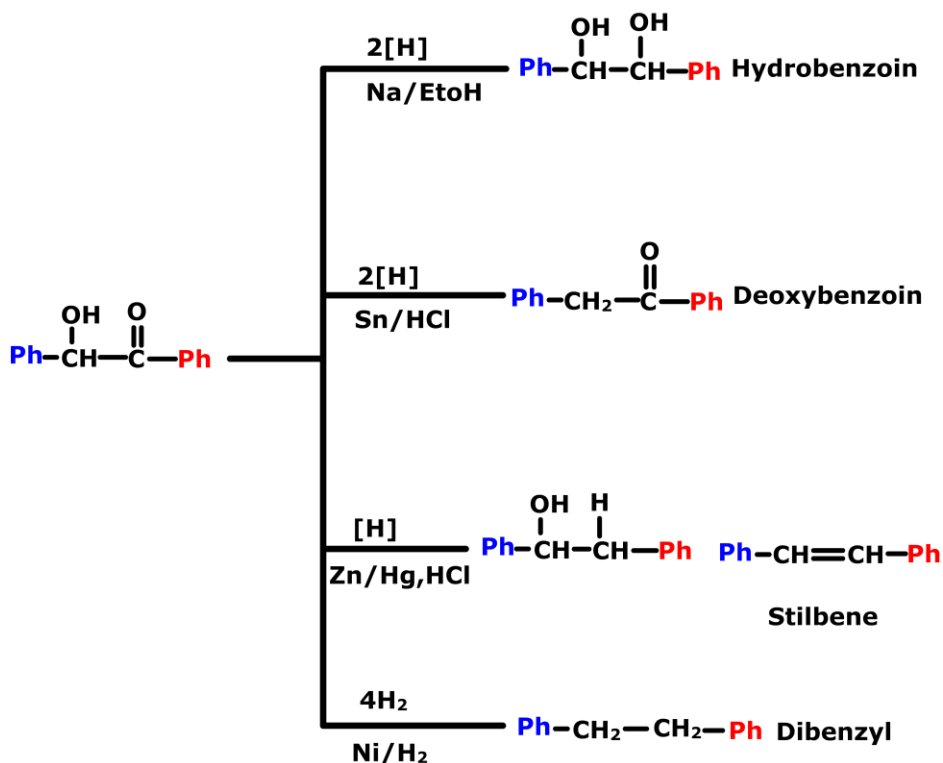


3.3 Reactions of Benzoin

3.3.1. Reduction of Benzoin:

Benzoin is sensitive to reduction and can be reduced to different products using different reaction conditions and catalysts.

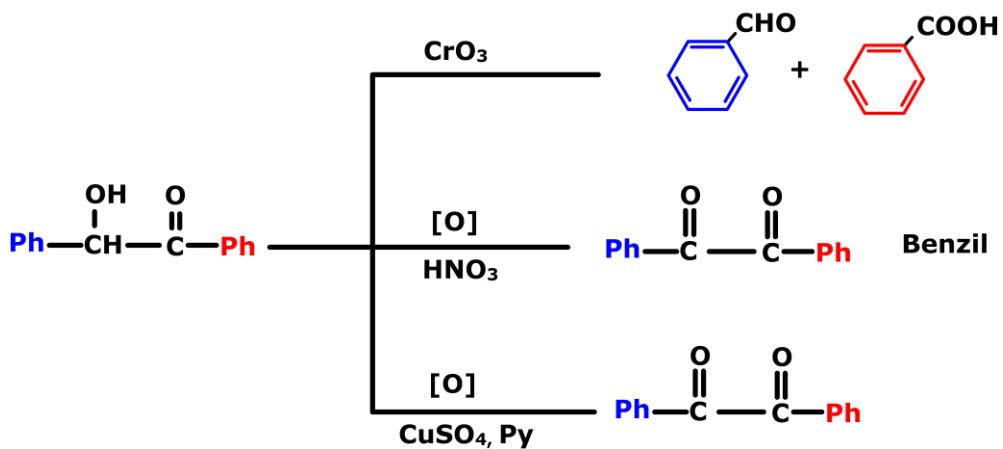
- Reduction with Na/ EtOH gives hydrobenzoin.
- Reduction with Sn/HCl results in the formation of Deoxybenzoin.
- Clemmensen reduction results in stilbene.
- Complete reduction product dibenzyl is obtained on reducing in the presence of Ni catalyst.



3.3.2. Oxidation of Benzoin:

Benzoin can be easily oxidised using various oxidising agents. One of the most important product of benzoin oxidation is benzil.

- (i) Oxidation with CrO_3 results in the formation of an aromatic aldehyde and one benzoin acid derivative.
- (ii) Oxidation of benzoin with nitric acid gives benzil.
- (iii) And benzoin oxidation



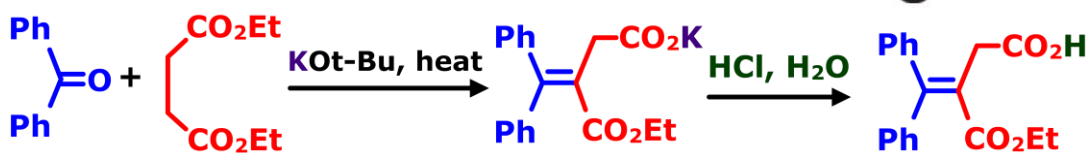
4. Stobbe Condensation

The condensation reaction of aldehyde or ketone with succinic ester in the presence of basic catalyst like sodium hydroxide or potassium tertiary butoxide to form alkylidene succinic acid is known as Stobbe condensation.

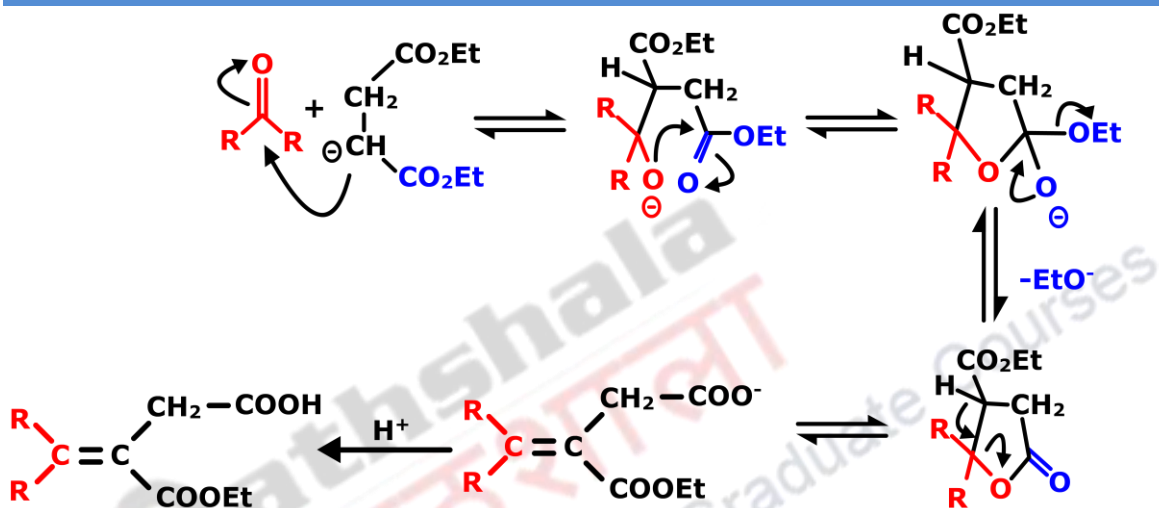
The reaction is specific for succinic ester although the carbonyl compound may be varied over a wide range. The carbonyl compounds which may be used are:

- Aliphatic and α,β -unsaturated aldehydes
- Aliphatic, aromatic, alicyclic and cyanoketones are also ketoesters.

However, ketones are more often used than aldehydes. In practice, the reaction mixture – ketone, diethyl succinate and ether solution of sodium ethoxide- is allowed to stand at room temperature for several days and then the product is recovered by acidification. The yield is improved and the reaction time is reduced on using potassium tertiary butoxide and tertiary butyl alcohol as base.



4.1 Mechanism of Stobbe Condensation



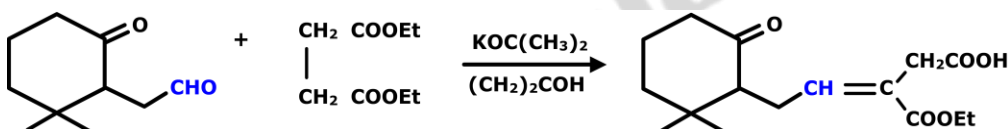
4.2 Characteristics of Stobbe Condensation

- This reaction is limited to α - ω diester ester groups at the 1st carbon and the last carbon.
- The reaction goes via a lactone intermediate which, on subsequent base-catalyzed elimination, causes almost irreversible ring opening to produce a salt of unsaturated esters. The lactone intermediate has been isolated and provides the support for the mechanism.
- Esters where only one α - hydrogen is present cannot undergo irreversible ring opening in the last step, which actually drives the reaction in the forward direction. In case of these esters, only the lactone intermediate has been isolated.

- If only one α - carbon has two α - hydrogens, then reaction can proceed to the last step.

4.3 Few Examples of Stobbe Condensation

Stobbe condensation has been used to prepare a large number of varieties of unsaturated and saturated acids. The condensation has also been useful for the synthesis of many types of polycyclic ring systems. It has also been used during the synthesis of estrone. Some synthetic applications are listed below



New reaction added

5. Summary

- Benzoin condensation involves condensation of two aromatic aldehydes (with no α - hydrogens) in the presence of CN^- to form benzoin.
- This reaction is completely reversible.
- Cyanide ion catalyses the reaction because it acts as a good nucleophile as well as good leaving group. It also increases the acidity of the C-H bond and stabilises the carbanion that results from the loss of proton.
- Benzoin condensation is a 3rd order reaction.
- Benzoin can be easily oxidised and reduced. One of the important oxidised product is benzil.

- Stobbe condensation involves reaction of aldehyde or ketone with succinic ester in the presence of basic catalyst like sodium hydroxide or potassium tertiary butoxide to form alkylidene succinic acid.
- This reaction limited to α - ω diester ester group at 1st carbon and last carbon.

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