

THIS PDF NOTE WAS FOUND ON INTERNET.I DON'T BEHOLD THE COPYRIGHT OF THIS MATERIAL. IF SOMEONE THINKS THAT THIS MATERIAL SHOULDN'T BE HERE, PLEASE EMAIL AT

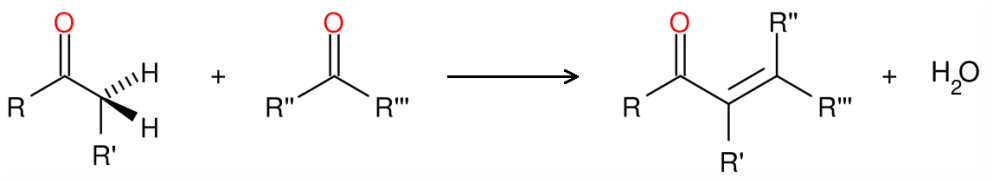
joyoshish@gmail.com AND THE MATERIAL WILL BE IMMEDIATELY REMOVED (ONLY FOR COPYRIGHT ISSUES).

Joyoshish Saha

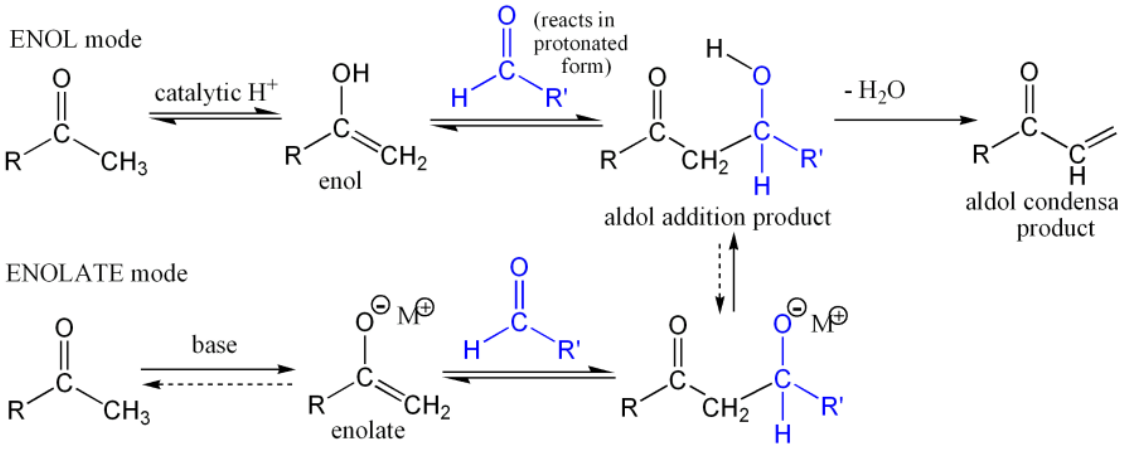


Downloaded from https://plustwopcm.blogspot.in/
Visit the blog to get helpful notes for your 10+2 preparation.

An aldol condensation is an organic reaction in which an enol or an enolate ion reacts with a carbonyl compound to form a β-hydroxyaldehyde or β-hydroxyketone, followed by a dehydration to give a conjugated enone.



Aldol condensations are important in organic synthesis, providing a good way to form carbon–carbon bonds. For example, the Robinson annulation reaction sequence features an aldol condensation; the Wieland-Miescher ketone product is an important starting material for many organic syntheses. Aldol condensations are also commonly discussed in university level organic chemistry classes as a good bond-forming reaction that demonstrates important reaction mechanisms.[In its usual form, it involves the nucleophilic addition of a ketone enolate to an aldehyde to form a β-hydroxy ketone, or "aldol" (aldehyde + alcohol), a structural unit found in many naturally occurring molecules and pharmaceuticals.



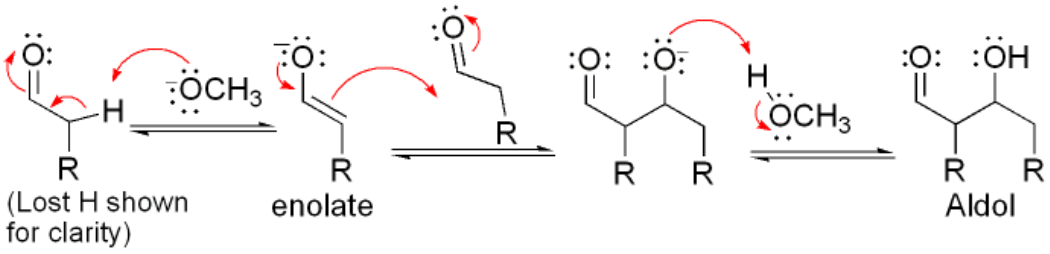
The name aldol condensation is also commonly used, especially in biochemistry, to refer to just the first (addition) stage of the process—the aldol reaction itself—as catalyzed by aldolases. However, the aldol reaction is not formally a condensation reaction because it does not involve the loss of a small molecule.

The reaction between an aldehyde/ketone and a carbonyl compound lacking an alpha-hydrogen (cross aldol condensation) is called the Claisen-Schmidt condensation. This reaction is named after two of its pioneering investigators Rainer Ludwig Claisen and J. G. Schmidt, who independently published on this topic in 1880 and 1881. An example is the synthesis of dibenzylideneacetone.

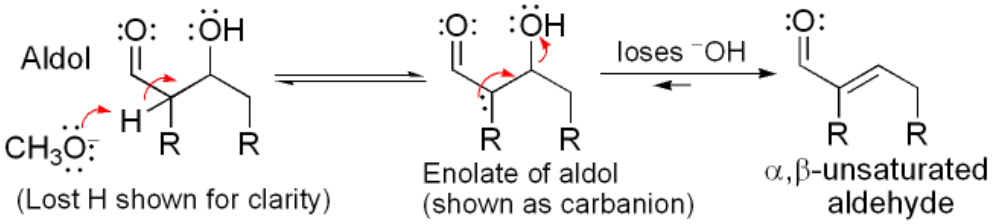
Mechanism

The first part of this reaction is an aldol reaction, the second part a dehydration—an elimination reaction(Involves removal of a water molecule or an alcohol molecule). Dehydration may be accompanied by decarboxylation when an activated carboxyl group is present. The aldol addition product can be dehydrated via two mechanisms; a strongbase like potassium t butoxide, potassium hydroxide or sodium hydride in an enolate mechanism, or in an acid-catalyzed enol mechanism.

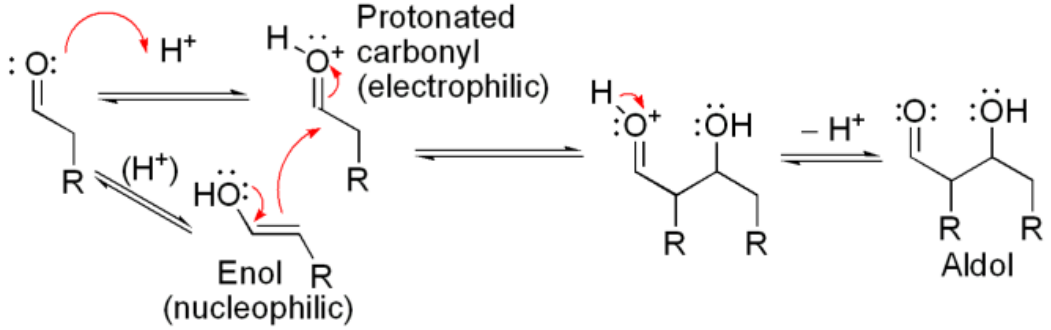
Base catalyzed aldol reaction (shown using $^{-}OCH_3$ as base)



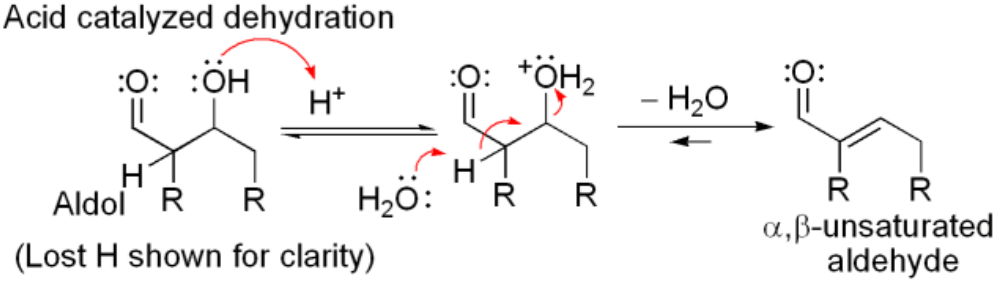
Base catalyzed dehydration (sometimes written as a single step)



Acid catalyzed aldol reaction

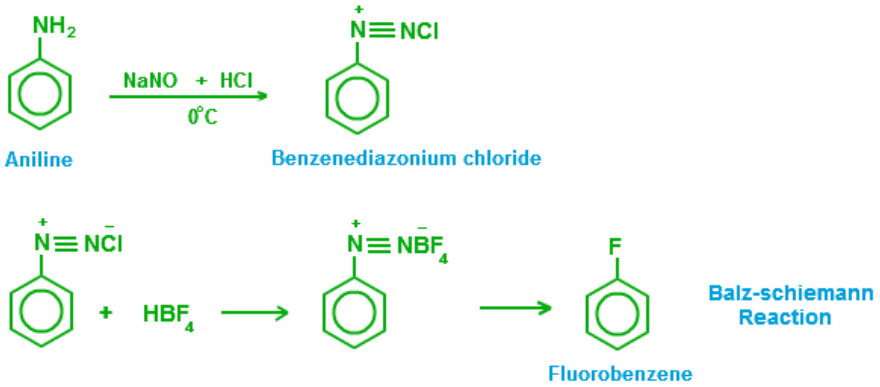


Acid catalyzed dehydration



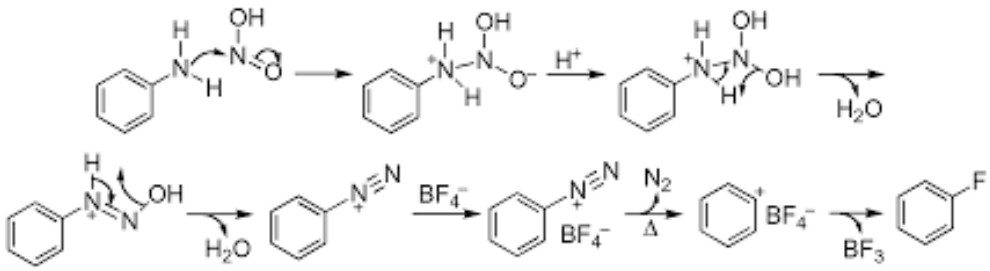
Balz–Schiemann Reaction

The Schiemann reaction (also called the Balz–Schiemann reaction) is a chemical reaction in which anilines are transformed to aryl fluorides via diazonium fluoroborates . Named after the German chemists Günther Schiemann and Günther Balz, this reaction is the preferred route to fluorobenzene. acid.



Fluoroarenes (aryl fluorides) cannot be prepared by the direct fluorination of aromatic hydrocarbon ,since the reaction is very violent and cannot be easily controlled. These can however be easily prepared by Balz–Schiemann reaction. in this reaction the aromatic primary amine is first diazotized with NaNO2 in the presence of HBF4 (Fluoroboric acid) at 273-278 K and the aryl diazonium tetrafluroborate yhus formed is heated to give the corresponding aryl fluoride.

Mechanism



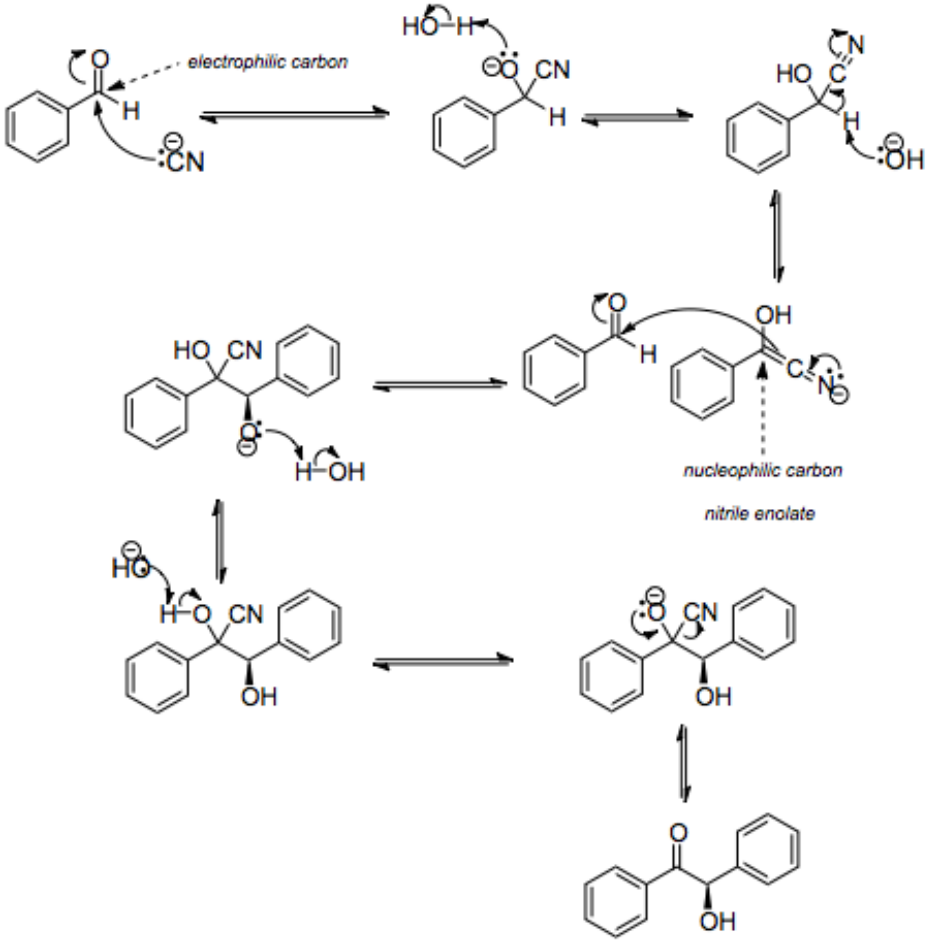
Benzoin condensation

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.

The Benzoin Condensation is a coupling reaction between two aldehydes that allows the preparation of α-hydroxyketones. The first methods were only suitable for the conversion of aromatic aldehydes.

Mechanism of Benzoin Condensation

In the first step in this reaction, the cyanide anion (as sodium cyanide) reacts with the aldehyde in a nucleophilic addition. Rearrangement of the intermediate results in polarity reversal of the carbonyl group, which then adds to the second carbonyl group in a second nucleophilic addition. Proton transfer and elimination of the cyanide ion affords benzoin as the product. This is a reversible reaction.



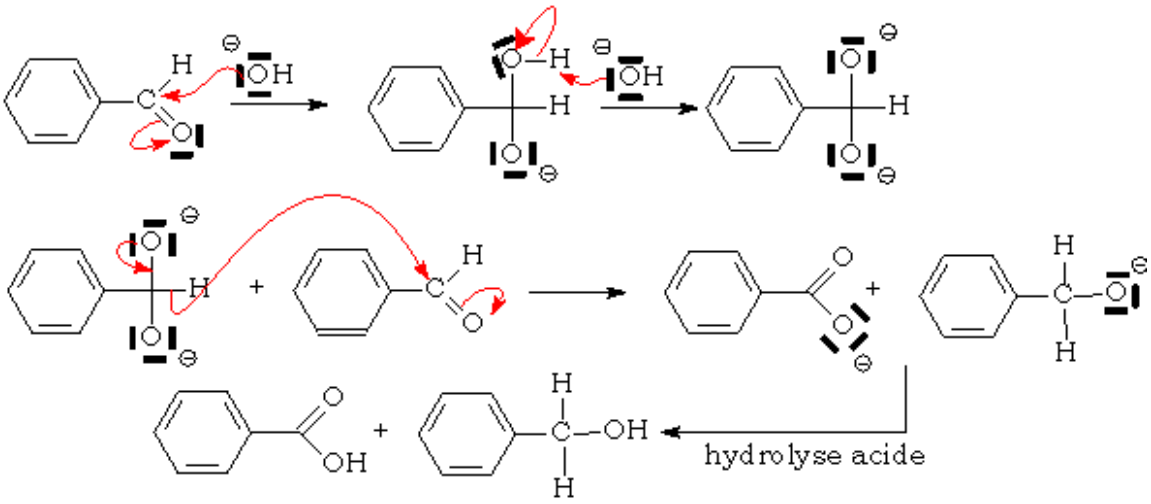
Mechanism of Benzoin condensation

The cyanide ion serves three different purposes in the course of this reaction. It acts as a nucleophile, facilitates proton abstraction, and is also the leaving group in the final step. 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. 4-Dimethylaminobenzaldehyde is an efficient proton donor while benzaldehyde is both a proton acceptor and donor. In this way it is possible to synthesise mixed benzoins, i.e. products with different groups on each half of the product.

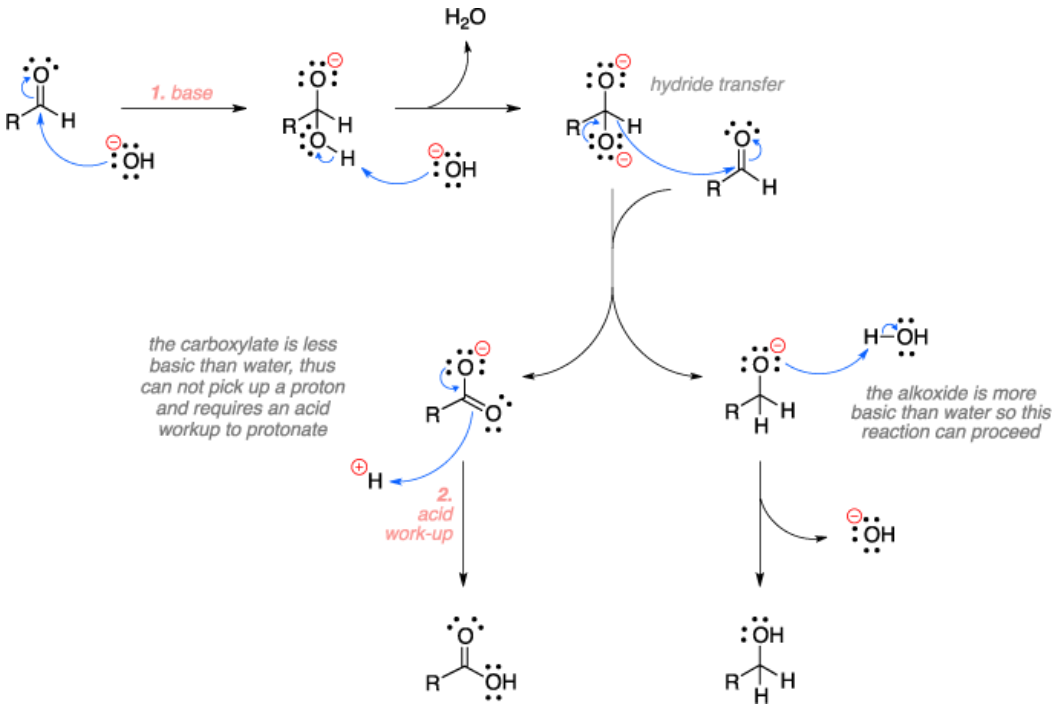
Cannizzaro reaction

The Cannizzaro reaction is a redox reaction in which two molecules of an aldehyde are reacted to produce a primary alcohol and a carboxylic acid using a hydroxide base. The reaction begins with hydroxide attack on the carbonyl carbon followed by deprotonation to give a dianion. This unstable intermediate releases a hydride anion which attacks another molecule of aldehyde. In this process the dianion converts to a carboxylate anion and the aldehyde to an alkoxide. The alkoxide then picks up a proton from water to provide the alcohol final product, while the caboxylate is converted to the carboxylic acid product after acid work-up.

1. Benzaldehyde (Aromatic Aldehyde do not have α hydrogen)



2. Aliphatic Aldehyde do not have α hydrogen

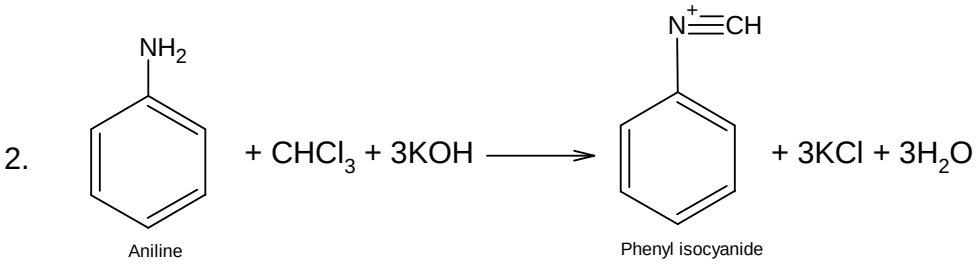


Carbylamine reaction

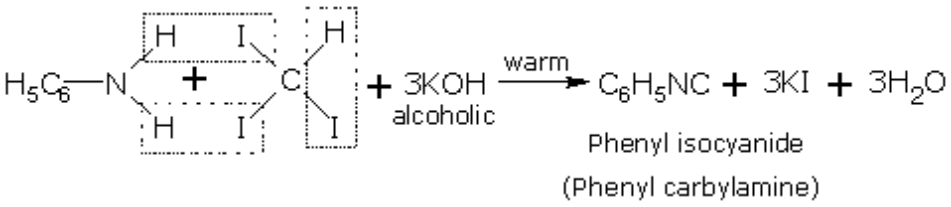
When a primary amine (Aliphatic or Aromatic) is warmed with chloroform or alcoholic KOH it forms an isocynide or carbylamines having offensive smell. This reaction is called carbylamines reaction .

1. $CH_3CH_2NH_2 + CHCl_3 + 3KOH \xrightarrow{\text{alcoholic}} CH_3CH_2NC + 3KCl + 3H_2O$

Ethyl Amine — Ethyl isocyanide

2. 

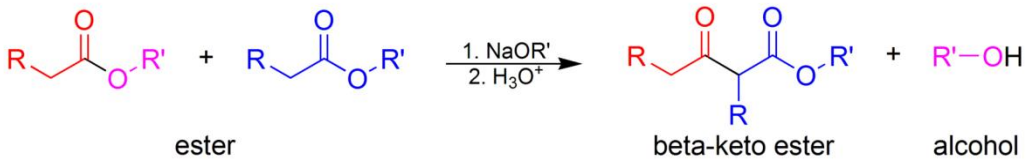
Aniline — Phenyl isocyanide



Phenyl isocyanide
(Phenyl carbylamine)

Claisen Condensation

The Claisen condensation (not to be confused with the Claisen rearrangement) is a carbon–carbon bond forming reaction that occurs between two esters or one ester and another carbonyl compound in the presence of a strong base, resulting in a β-keto ester or a β-diketone. It is named after Rainer Ludwig Claisen, who first published his work on the reaction in 1887



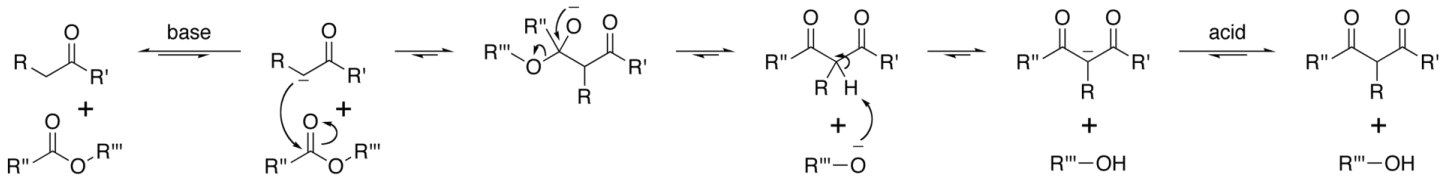
At least one of the reagents must be enolizable (have an α-proton and be able to undergo deprotonation to form the enolate anion). There are a number of different combinations of enolizable and nonenolizable carbonyl compounds that form a few different types of Claisen condensations.

The base used must not interfere with the reaction by undergoing nucleophilic substitution or addition with a carbonyl carbon. For this reason, the conjugate sodium alkoxide base of the alcohol formed (e.g. sodium ethoxide if ethanol is formed) is often used, since the alkoxide is regenerated. In mixed Claisen condensations, a non-nucleophilic base such as lithium diisopropylamide, or LDA, may be used, since only one compound is enolizable. LDA is not commonly used in the classic Claisen or Dieckmann condensations due to enolization of the electrophilic ester.

The alkoxy portion of the ester must be a relatively good leaving group. Methyl and ethyl esters, which yields methoxide and ethoxide, respectively, are commonly used.

Mechanism

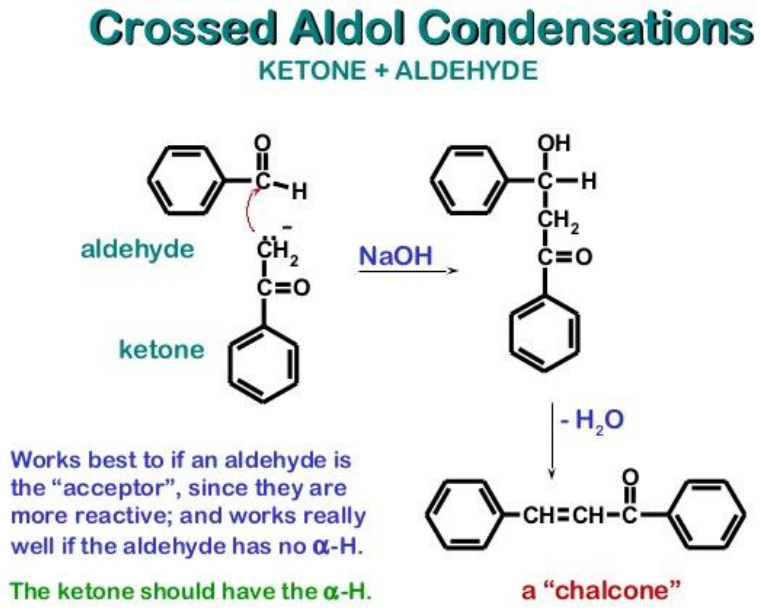
In the first step of the mechanism, an α-proton is removed by a strong base, resulting in the formation of an enolate anion, which is made relatively stable by the delocalization of electrons. Next, the carbonyl carbon of the (other) ester is nucleophilically attacked by the enolate anion. The alkoxy group is then eliminated (resulting in (re)generation of the alkoxide), and the alkoxide removes the newly formed doubly α-proton to form a new, highly resonance-stabilized enolate anion. Aqueous acid (e.g. sulfuric acid or phosphoric acid) is added in the final step to neutralize the enolate and any base still present. The newly formed β-keto ester or β-diketone is then isolated. Note that the reaction requires a stoichiometric amount of base as the removal of the doubly α-proton thermodynamically drives the otherwise endergonic reaction. That is, Claisen condensation does not work with substrates having only one α-hydrogen because of the driving force effect of deprotonation of the β-keto ester in the last step.

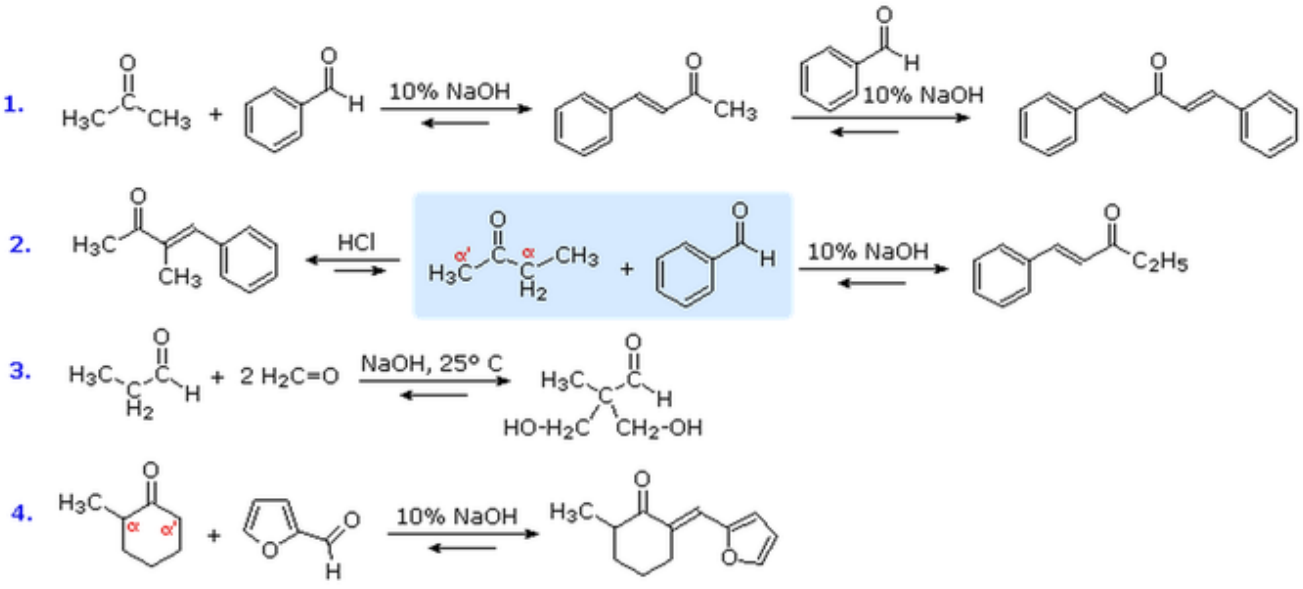


Crossed Aldol Reactions

In a crossed aldol reaction, two different carbonyl compounds are applied. If both carbonyl compounds contain an α hydrogen atom, both may act as electrophilic carbonyl compound, as well as nucleophilic enol or enolate. In addition, each enol may nucleophilically attack the two different carbonyl compounds. As a result, such a crossed aldol reaction yields four different products. Therefore, crossed aldol reactions of this kind are synthetically less valuable. The starting products depicted in the illustration are symmetric ketones. If this were not the case additional products would be possible, due to the problem of regioselectivity.

If a starting product does not contain any α hydrogen atom, the variety of possible products is reduced to two, as this starting product can only act as an electrophilic carbonyl compound, though it cannot act as a nucleophilic enolate. Benzaldehyde, which contains no α hydrogen atoms, is such an aldehyde.



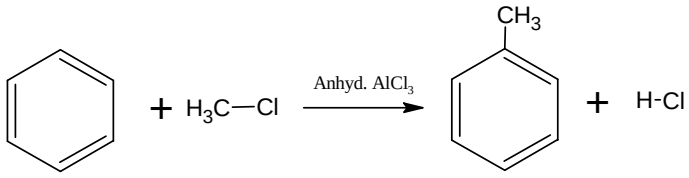


Friedel Craft Reaction

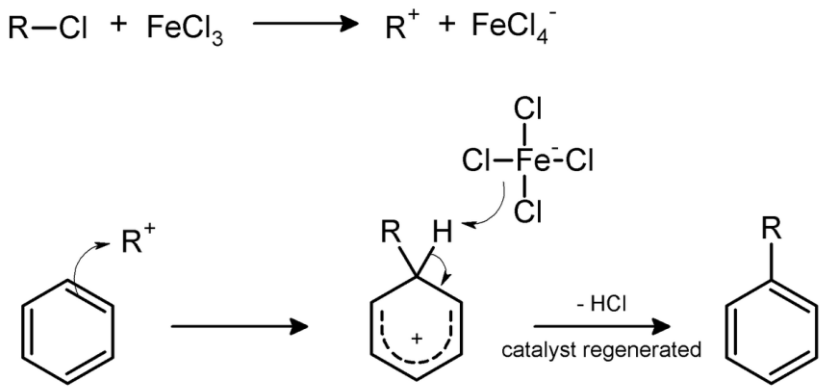
The reaction used for the introduction of alkyl or an acyl group into an aromatic compound in the presence of lewis acid catalyst. The most commonly used lewis acid catalyst is anhydrous $AlCl_3$ while other catalyst which have been used are BF_3,$FeCl_3$, $SnCl_4$ etc.

(a) Friedel Craft Alkylation

Benzene and other aromatic compound react with alkyl halide in the presence of anhydrous aluminium chloride to form alkyl benzenes.



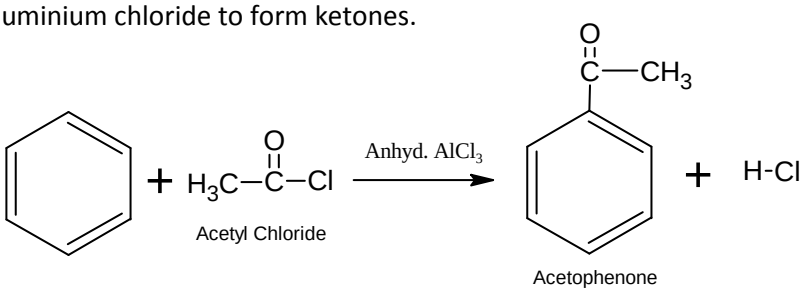
Mechanism:-



This reaction has one big disadvantage, namely that the product is more nucleophilic than the reactant due to the electron donating alkyl-chain. Therefore, another hydrogen is substituted with an alkyl-chain, which leads to overalkylation of the molecule. Also, if the chloride is not on a tertiary carbon or secondary carbon, then the carbocation formed (R+) will undergo a carbocation rearrangement reaction.

(b) Friedel Craft Acylation:-

Benzene and other aromatic compound react with acid halide or acid anhydride in the presence of anhydrous aluminium chloride to form ketones.

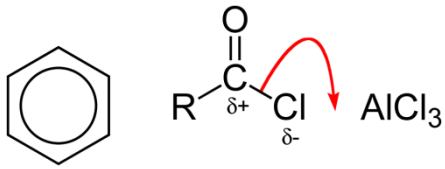


Mechanism of Friedel - Crafts Reaction

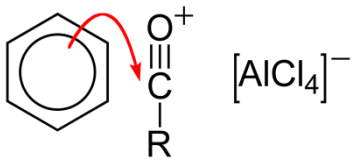
Mechanism:-

Friedel–Crafts acylation is the acylation of aromatic rings with an acyl chloride using a strong Lewis acid catalyst. Friedel–Crafts acylation is also possible with acid anhydrides. Reaction conditions are similar to the Friedel–Crafts alkylation mentioned above. This reaction has several advantages over the alkylation reaction. Due to the electron-withdrawing effect of the carbonyl group, the ketone product is always less reactive than the original molecule, so multiple acylations do not occur. Also, there are no carbocation rearrangements, as the carbonium ion is stabilized by a resonance structure in which the positive charge is on the oxygen.

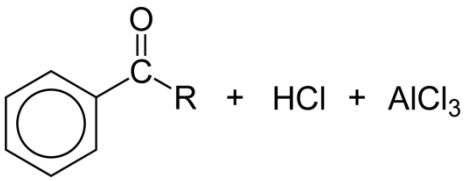
In a simple mechanistic view, the first step consists of dissociation of a chloride ion to form an acyl cation (acylium ion)



In some cases, the Lewis acid binds to the oxygen of the acyl chloride to form an adduct. Regardless, the resulting acylium ion or a related adduct is subject to nucleophilic attack by the arene:



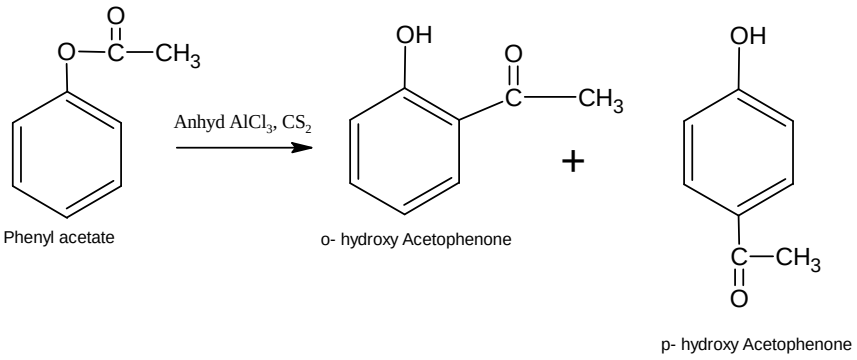
Finally, chloride anion (or AlCl4−) deprotonates the ring (an arenium ion) to form HCl, and the AlCl3 catalyst is regenerated:

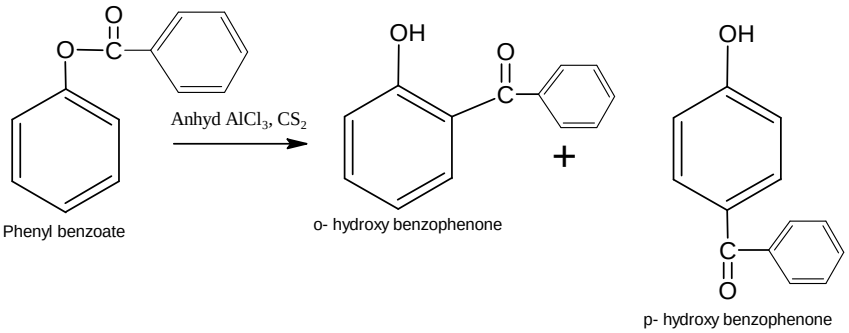


If desired, the resulting ketone can be subsequently reduced to the corresponding alkane substituent by either Wolff–Kishner reduction or Clemmensen reduction. The net result is the same as the Friedel–Crafts alkylation except that rearrangement is not possible

Fries Rearrangement

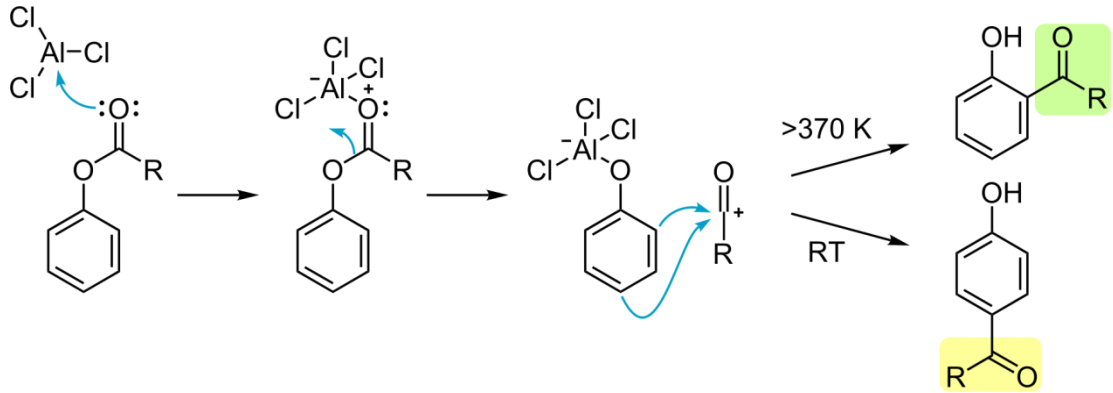
Phenyl esters (phenyl acetate,phenyl benzoate etc.) on heating with anhydrous $AlCl_3$ in the presence of CS_2 as solvent undergo a rearrangement in which the acyl group (acetyl , benzoyl etc.) group migrates from the phenolic oxygen atom to the ortho and para position of the benzene ring to give a mixture of o and p hydroxy ketones. this reaction is called fries rearrangement.





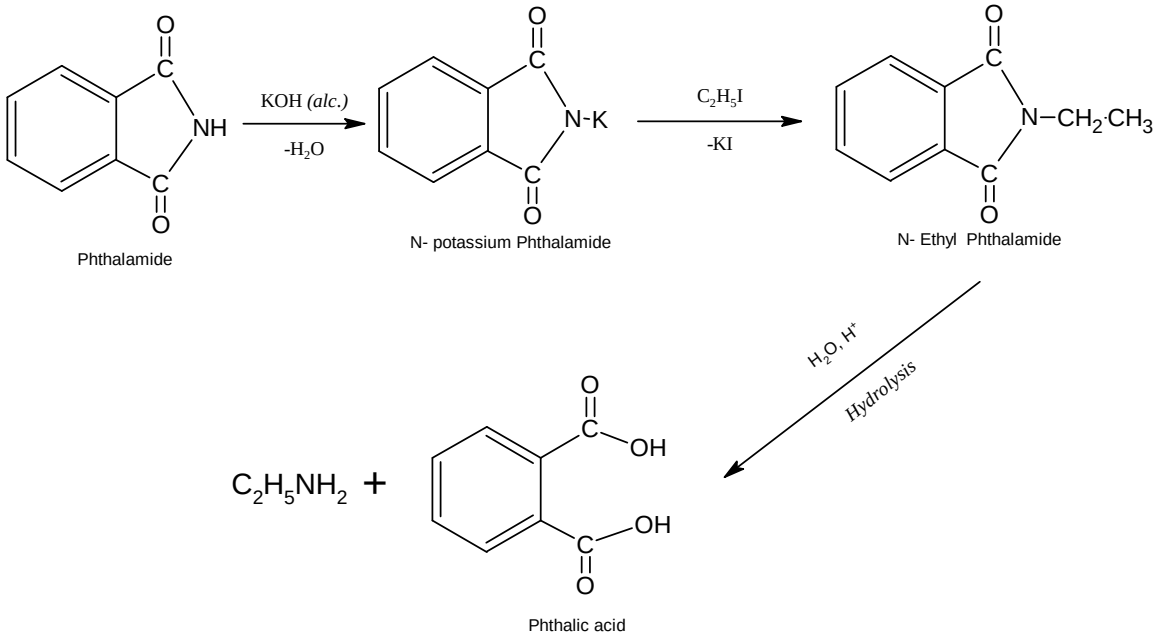
Mechanism :-

Despite many efforts, a definitive reaction mechanism for the Fries rearrangement has not been determined. Evidence for inter- and intramolecular mechanisms have been obtained by crossover experiments with mixed reactants. Reaction progress is not dependent on solvent or substrate. A widely accepted mechanism involves a carbocation intermediate.

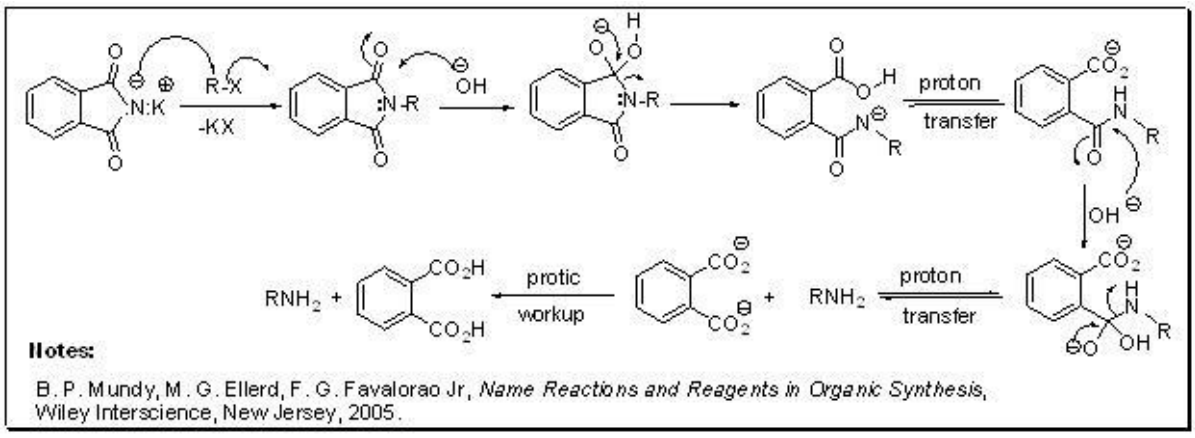


Garbriel Phthalamide Synthesis

In this reaction phthalamide is converted into its potassium salt by treating it with alcoholic potassium hydroxide. Then potassium phthalamide is heated with an alkyl halide to yield an N – Alkyl phthalamide which is hydrolysed to phthalic acid and primary amine by heating with HCl and KOH solution.

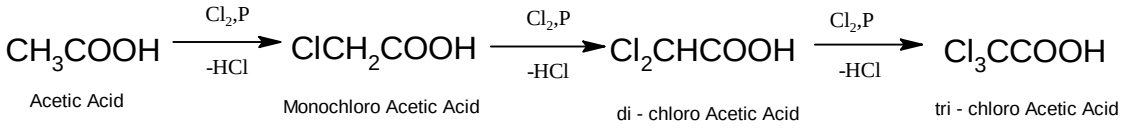


Mechanism:-



Hell–Volhard–Zelinsky Halogenation

The Reaction of Aliphatic carboxylic acid containg α hydrogens with Cl2 or Br2 in the presence of small amount of red phosphorus to give α halo acids is called Hell–Volhard–Zelinsky (H.V.Z.) reaction. with the excess of halogen all the αhydrogen atoms of an aliphatic carboxylic acid is replaced by halogen atoms.



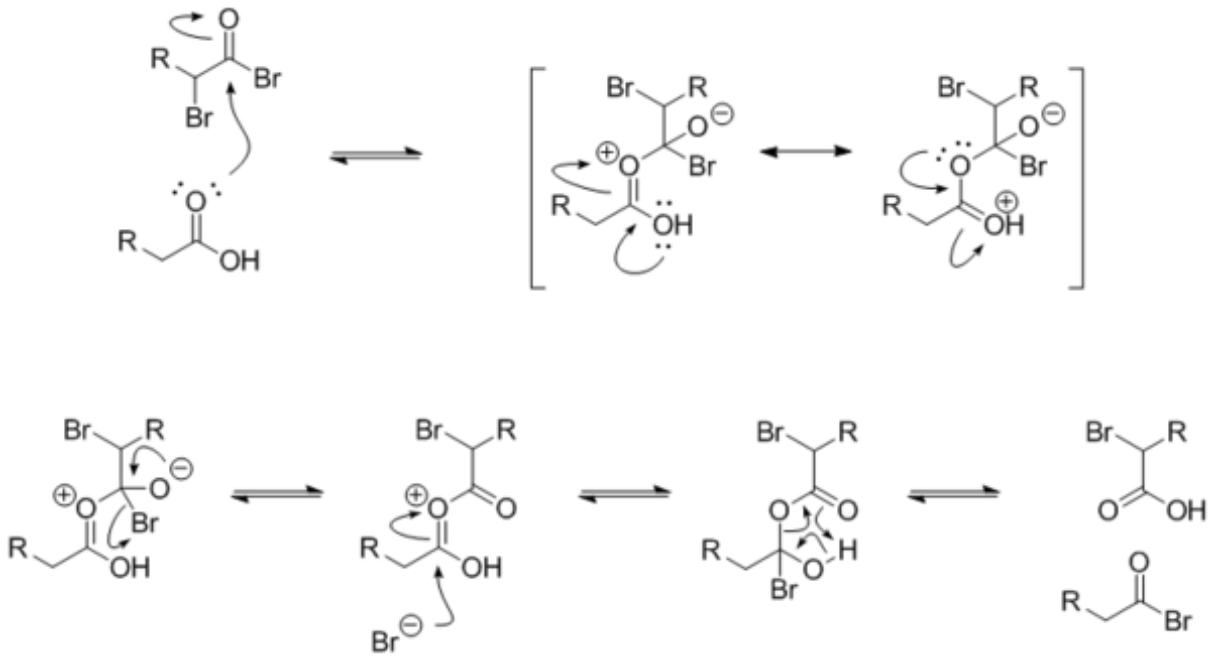
Mechanism :-

Unlike other halogenation reactions, this reaction takes place in the absence of a halogen carrier. The reaction is initiated by addition of a catalytic amount of PBr3, after which one molar equivalent of Br2 is added. PBr3 replaces the carboxylic OH with a bromide, resulting in a carboxylic acid bromide. The acyl bromide can then tautomerize to an enol, which will readily react with the Br2 to brominate a second time at the α position.

In neutral to slightly acidic aqueous solution, hydrolysis of the α-bromo acyl bromide occurs spontaneously, yielding the α-bromo carboxylic acid in an example of a nucleophilic acyl substitution. If an aqueous solution is desirable, a full molar equivalent of PBr3 must be used as the catalytic chain is disrupted.

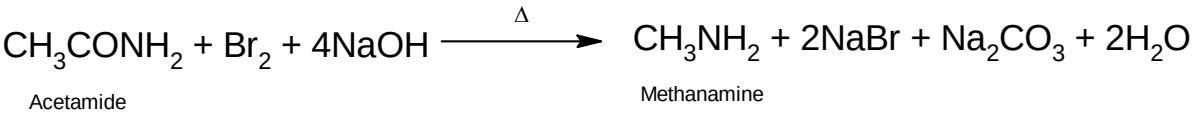
If little nucleophilic solvent is present, reaction of the α-bromo acyl bromide with the carboxylic acid yields the α-bromo carboxylic acid product and regenerates the acyl bromide intermediate. In practice a molar equivalent of PBr3 is often used anyway to overcome the slow reaction kinetics.

The mechanism for the exchange between an alkanoyl bromide and a carboxylic acid is below. The α-bromoalkanoyl bromide has a strongly electrophilic carbonyl carbon because of the electron-withdrawing effects of the two bromides.

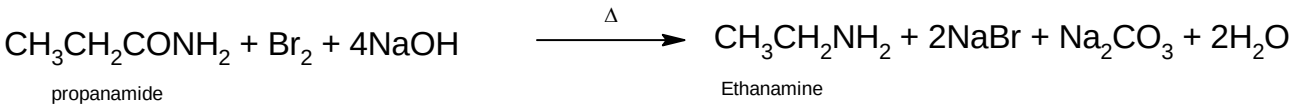


Hofmann Bromamide Reaction

The Conversion of a primary amide to a primary amine containing one carbon atom less than the original amide on heating with the mixture of Br2 in the presence of NaOH or KOH (ie. NaOBr, KOBr) is called Hofmann Bromamide reaction or Hofmann degradation of amide.

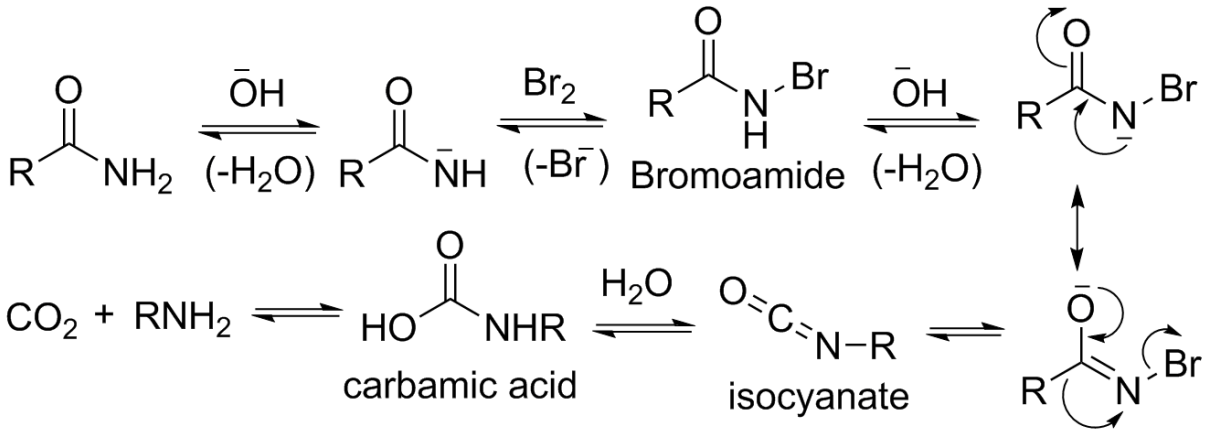


Acetamide — Methanamine



propanamide — Ethanamine

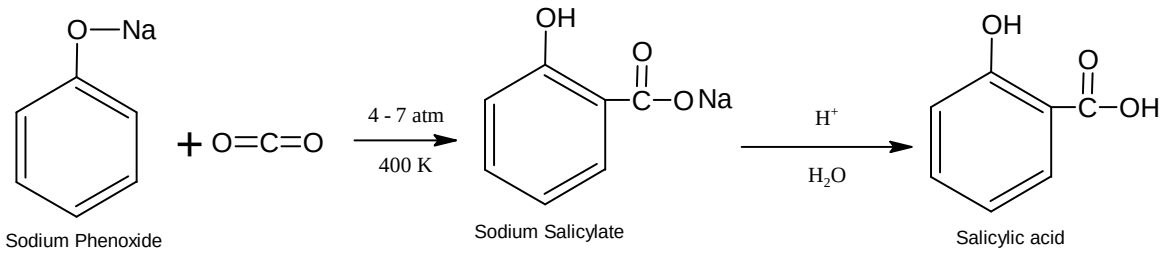
Mechanism:-



Kolbe Schmitt Reaction

Sodium Phenoxide reacts with carbon dioxide under pressure (4-7) atmosphere at 400 K to form sodium salicylate which on acidification with mineral acid gives salicylic acid. This reaction is called Kolbe reaction.

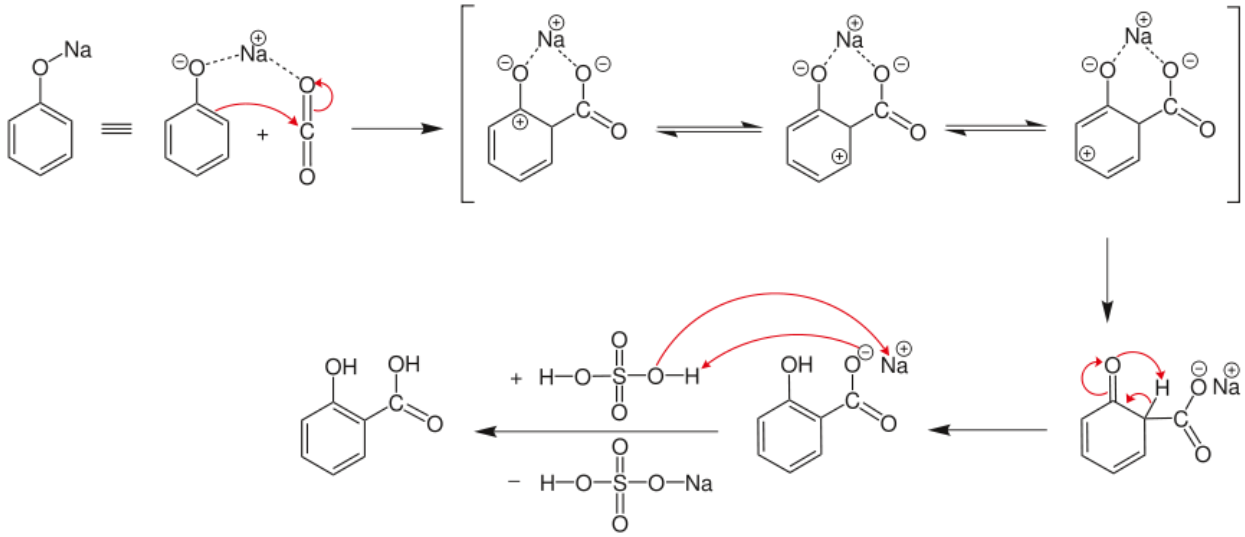
The Kolbe–Schmitt reaction or Kolbe process (named after Hermann Kolbe and Rudolf Schmitt) is a carboxylation chemical reaction that proceeds by heating sodium phenolate (the sodium salt of phenol) with carbon dioxide under pressure (100 atm, 125 °C), then treating the product with sulfuric acid. The final product is an aromatic hydroxy acid which is also known as salicylic acid(the precursor to aspirin)



Sodium Phenoxide — Sodium Salicylate — Salicylic acid

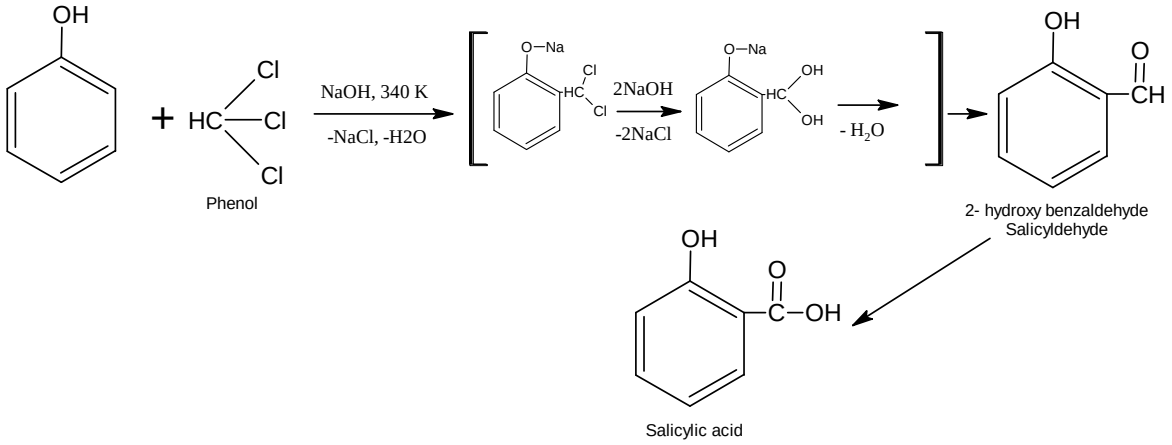
Mechanism

The Kolbe–Schmitt reaction proceeds via the nucleophile addition of a phenoxide, classically sodium phenoxide ($NaOC_6H_5$), to carbon dioxide to give the salicylate. The final step is reaction of the salicylate with acid to form the desired salicylic acid.

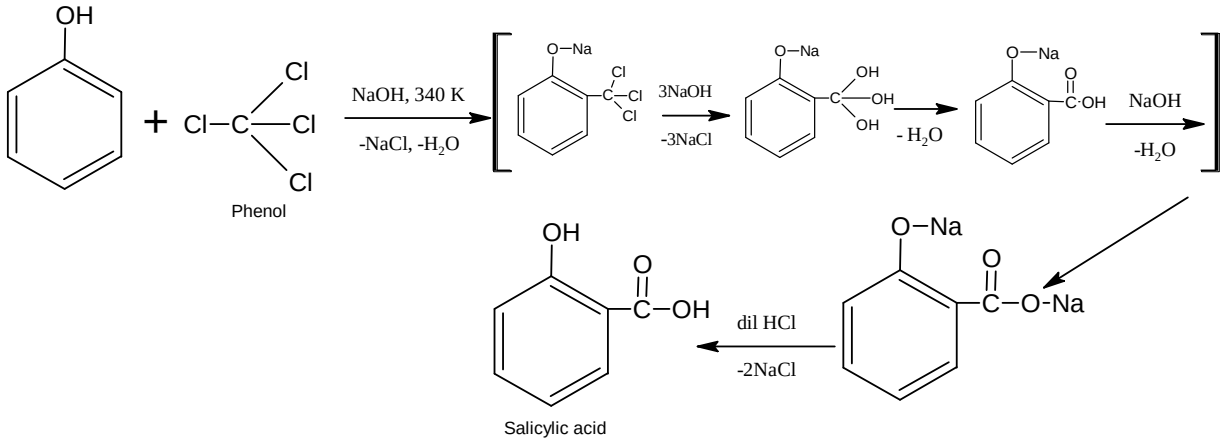


Reimer Tiemann Reaction

Treatment of Phenol with Chlorform in the presence of aqueous sodium or potassium hydroxide at 340K followed by hydrolysis of the resulting product gives 2 hydroxy benzaldehyde (salicylaldhyde) . This reaction is called Reimer Tiemann reaction.



Instead of chloroform carbon tetrachloride is used ,salicylic acid is formed



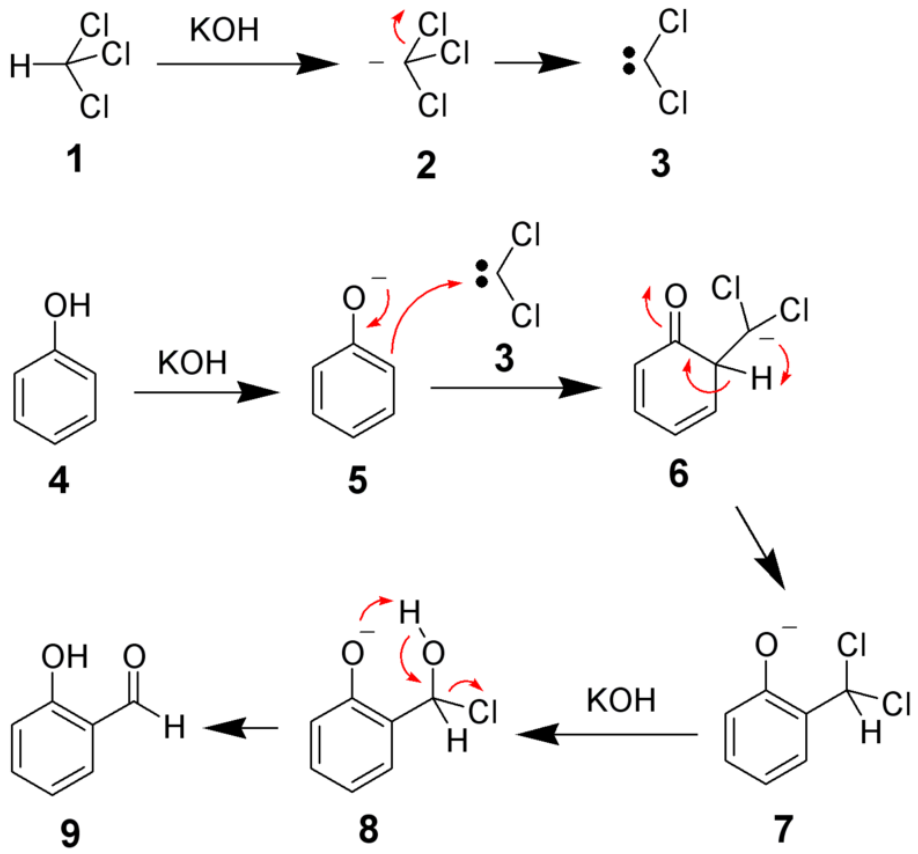
Reaction mechanism

Chloroform (1) is deprotonated by strong base (normally hydroxide) to form the chloroform carbanion (2) which will quickly alpha-eliminate to give dichlorocarbene (3); this is the principle reactive species. The hydroxide will also deprotonate the phenol (4) to give a negatively charged phenolate (5). The negative charge is delocalised into the aromatic ring, making it far more nucleophilic and increases its ortho selectivity. Nucelophilic attack of the dichlorocarbene

from the ortho position gives an intermediate dichloromethyl substituted phenol (7). After basic hydrolysis, the desired product (9) is formed.

Hydroxides are not readily soluble in the chloroform, thus the reaction is generally carried out in a biphasic solvent system. In the simplest sense this consists of an aqueous hydroxide solution and an organic phase containing the chloroform. The two reagents are therefore separated and must be brought together for the reaction to take place. This can be achieved by rapid mixing, phase-transfer catalysts, or an emulsifying agent (the use of 1,4-Dioxane as a solvent is an example).

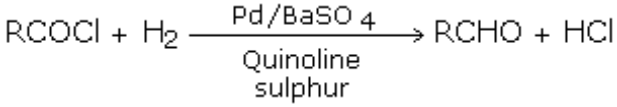
The reaction typically needs to be heated to initiate the process, however once started the Reimer-Tiemann Reaction can be highly exothermic; this combination makes it prone to thermal runaways.



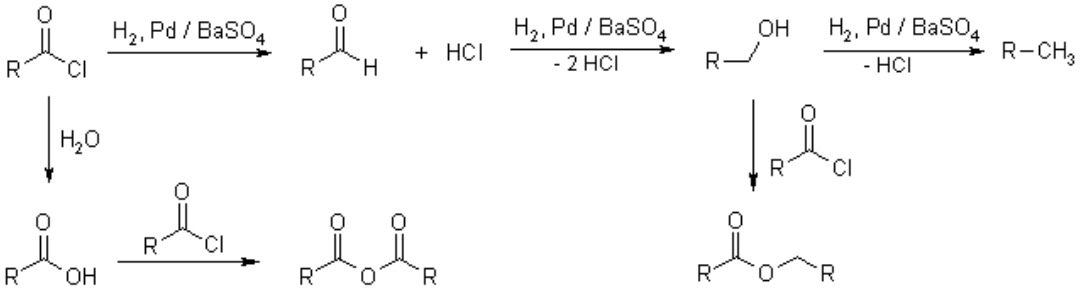
Rosenmund Reduction

The Rosenmund reduction is a hydrogenation process in which an acyl chloride is selectively reduced to an aldehyde. The reaction was named after Karl Wilhelm Rosenmund who first reported it in 1918

The reaction is catalysed by palladium on barium sulfate, which is sometimes called the Rosenmund catalyst. Barium sulfate has a low surface area which reduces the activity of the palladium, preventing over-reduction. However for certain reactive acyl chlorides the activity must be reduced further, by the addition of a poison. Originally this was thioquinanthrene although thiourea[2] has also been used. Deactivation is required because the system must reduce the acyl chloride but not the subsequent aldehyde. If further reduction does take place it will create a primary alcohol which would then react with the remaining acyl chloride to form an ester.

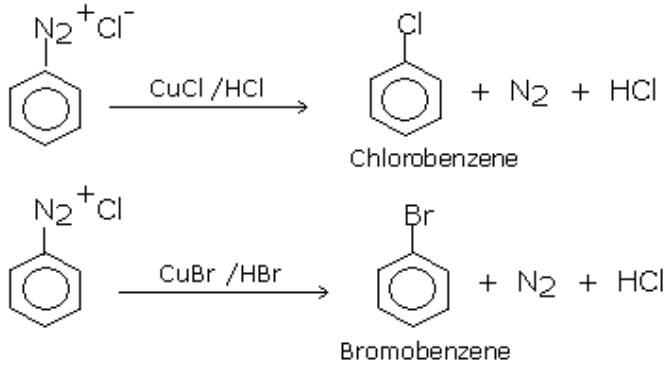


Mechanism



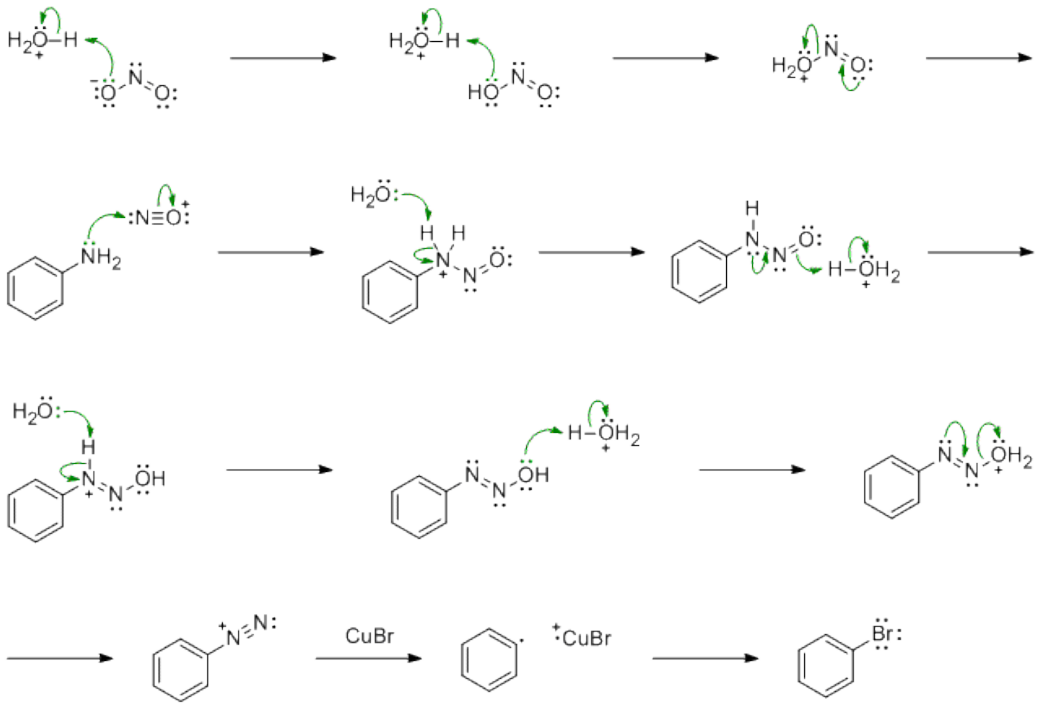
Sandmeyer reaction

The Sandmeyer reaction is a chemical reaction used to synthesize aryl halides from aryl diazonium salts. It is named after the Swiss chemist Traugott Sandmeyer. The reaction is a method for substitution of an aromatic amino group via preparation of its diazonium salt followed by its displacement with a nucleophile, often catalyzed by copper(I) salts. The nucleophile can include halideanions, cyanide, thiols, water, and others. The reaction does not proceed well with the fluoride anion, but fluorination can be carried out using tetrafluoroborate anions (Balz–Schiemann reaction)

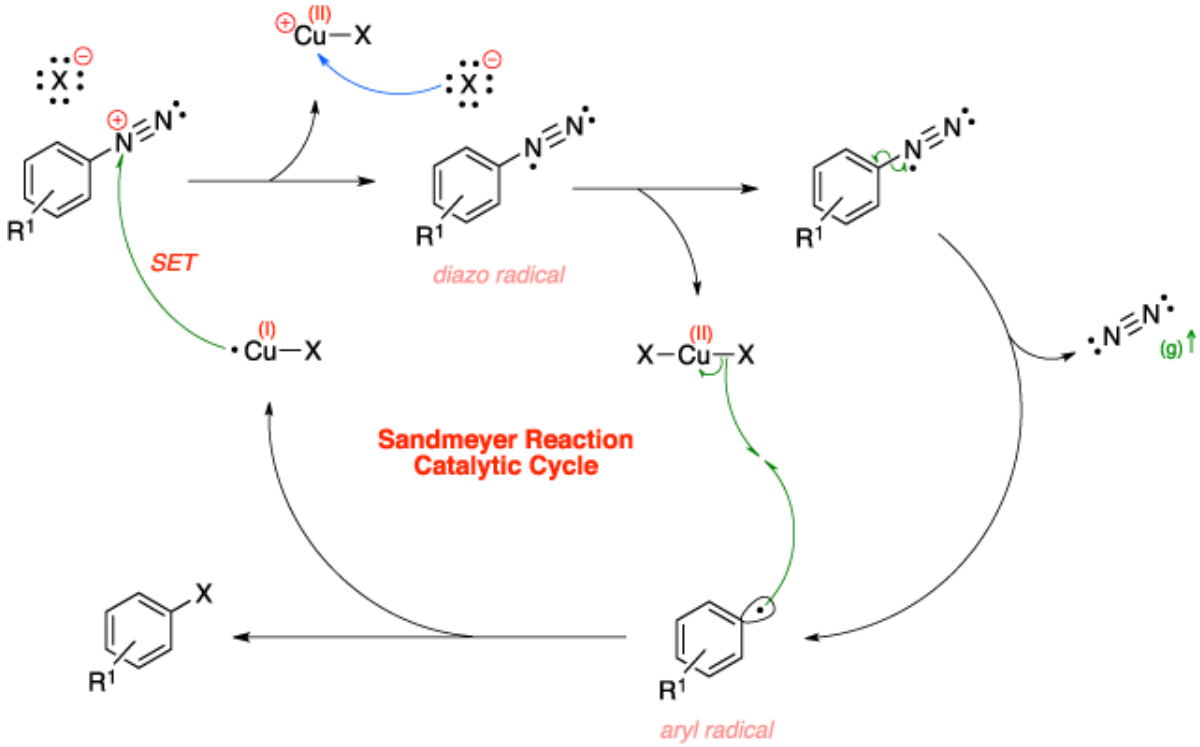


Reaction Mechanism

The nitrous acid is usually prepared in situ from sodium nitrite and an acid. Following a 2nd protonation step, one equivalent of water is lost to form nitrogen monoxide cation i.e. the "Nitronium ion" electrophile.

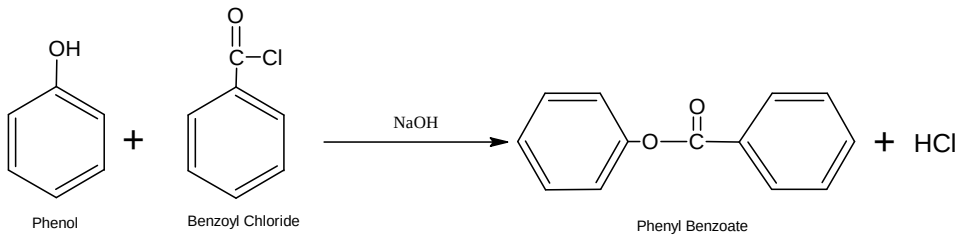


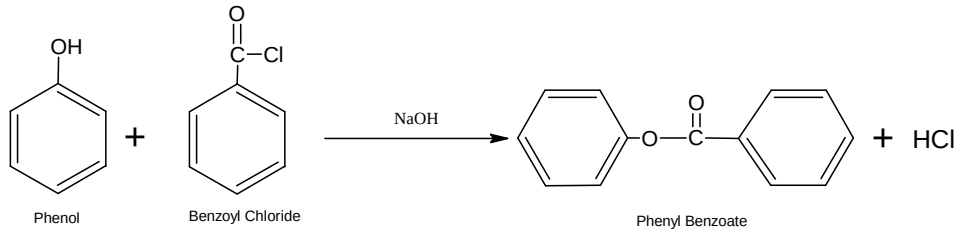
Mechanism of Sandmeyer Reaction



Schotten Baumann Reaction

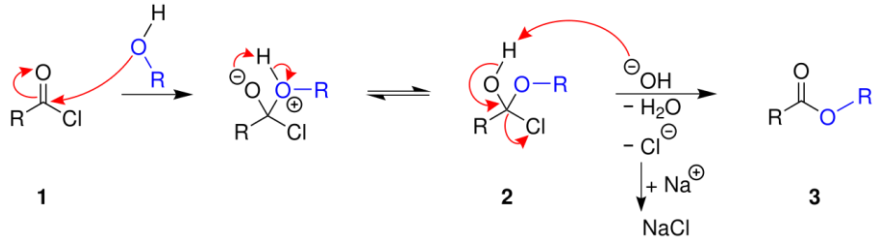
The Process of benzoylation of compounds containing active hydrogen such as phenol, Aniline, Alcohol etc. with benzoyl chloride in the presence of aqueous NaOH is called Schotten Baumann reaction



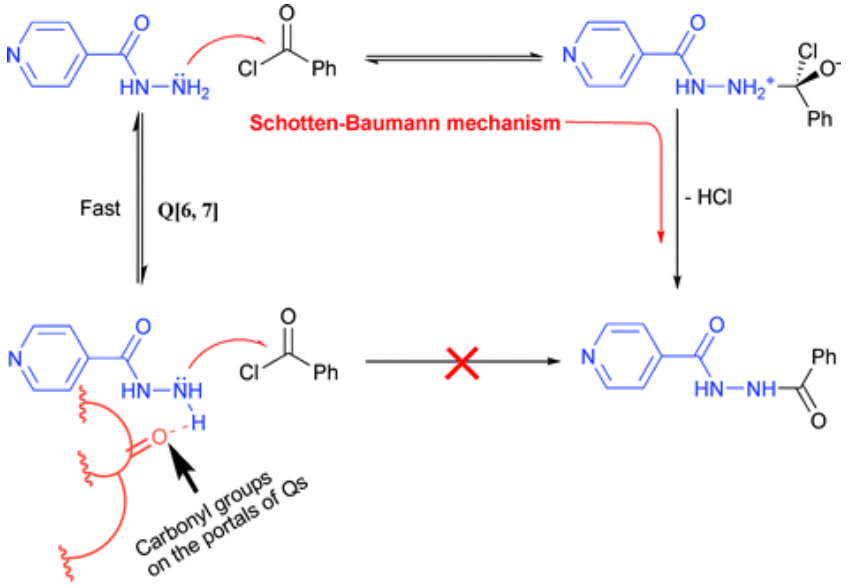


Schotten Baumann Reaction Mechanism

Aliphatic Compound



Aromatic Compound



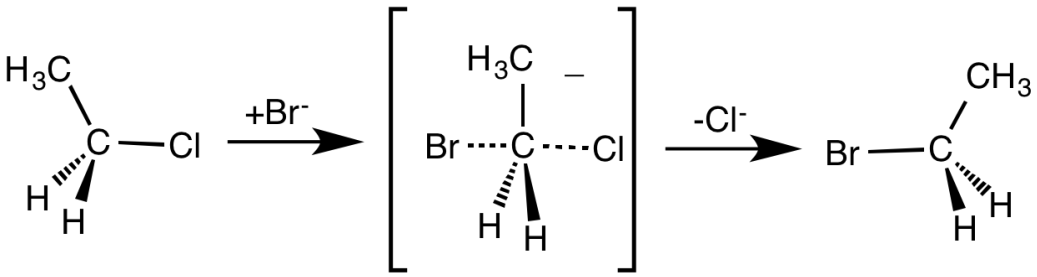
Substitution Nucleophelic Bimolecular Reaction (SN^2)

The S_N2 reaction is a type of reaction mechanism that is common in organic chemistry. In this mechanism, one bond is broken and one bond is formed synchronously, i.e., in one step. S_N2 is a kind of nucleophilic substitution reaction mechanism. Since two reacting species are involved in the slow (rate determining) step, this leads to the term substitution nucleophilic (bi-molecular) or S_N2, the other major kind is S_N1. Many other more specialized mechanisms describe substitution reactions.The reaction type is so common that it has other names, e.g. "bimolecular nucleophilic substitution", or, among inorganic chemists, "associative substitution" or "interchange mechanism".

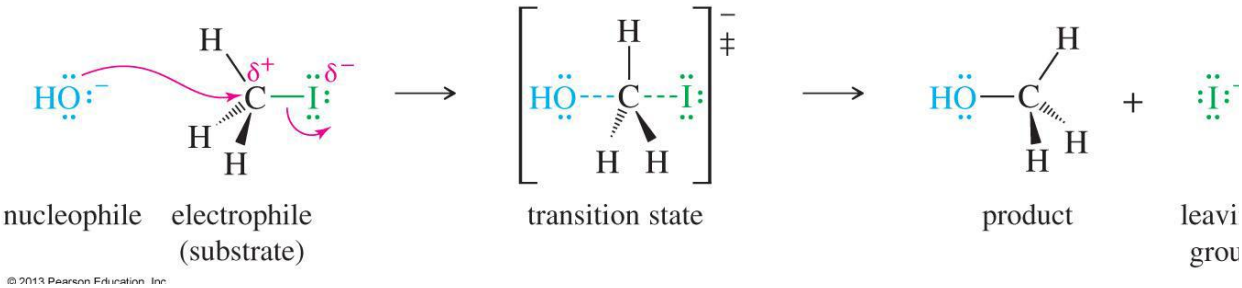
The reaction most often occurs at an aliphatic sp^3 carbon center with an electronegative, stable leaving group attached to it (often denoted X), which is frequently a halide atom. The breaking of the C–X bond and the formation of the new bond (often denoted C–Y or C–Nu) occur simultaneously through a transition state in which a carbon under nucleophilic attack is pentacoordinate, and approximately sp2hybridised. The nucleophile attacks the carbon at 180° to the leaving group, since this provides the best overlap between the nucleophile's lone pair and the C–X σ* antibonding orbital. The leaving group is then pushed off the opposite side and the product is formed withinversion of the tetrahedral geometry at the central atom.

If the substrate under nucleophilic attack is chiral, this often leads to inversion of configuration (stereochemistry), called a Walden inversion.

In an example of the SN^2 reaction, the attack of Br^- (the nucleophile) on an ethyl chloride (the electrophile) results in ethyl bromide, withchloride ejected as the leaving group.:

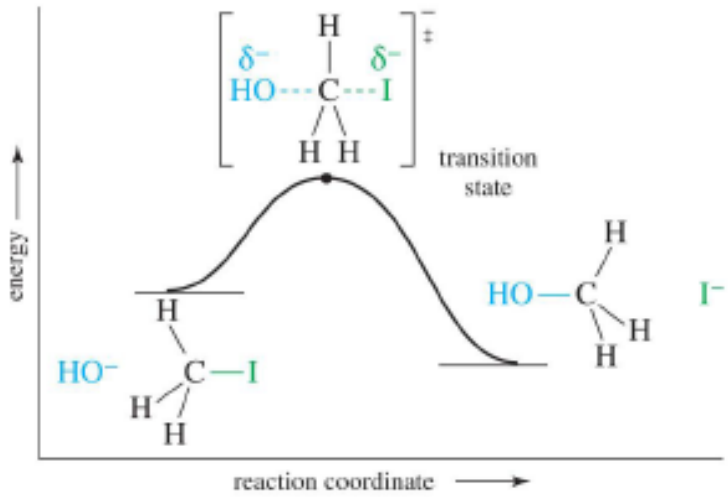


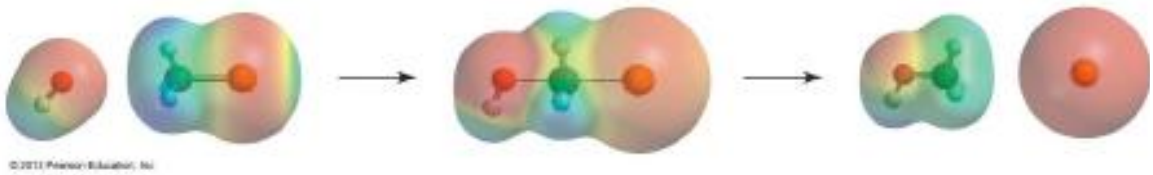
SN^2 attack occurs if the backside route of attack is not sterically hindered by substituents on the substrate. Therefore, this mechanismusually occurs at an unhindered primary carbon centre. If there is steric crowding on the substrate near the leaving group, such as at a tertiary carbon centre, the substitution will involve an SN^1 rather than an SN^2 mechanism, (an SN^1 would also be more likely in this case because a sufficiently stable carbocationintermediary could be formed).



The reaction is said to be concerted, taking place in a single step with the new bond forming as the old bond is breaking.

The transition state is a point of highest energy (not an intermediate).



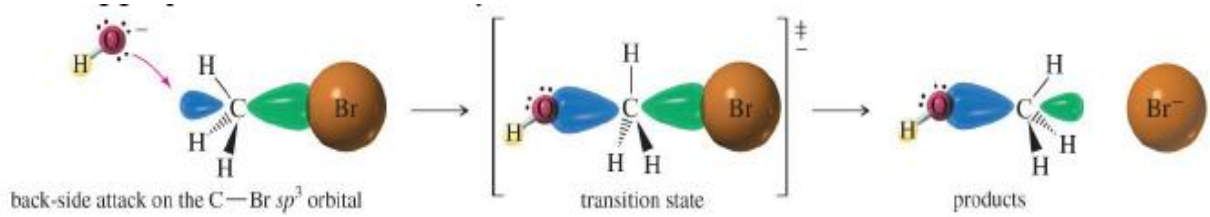


Stereochemistry of the SN^2 Reaction

A nucleophile donates its electron density into (attacks) the small back lobe of the sp^3 hybridized C-X bond, since the leaving group itself blocks attack from any other direction. This is called back side attack. The SN^2 reaction is called a stereospecific reaction since a certain stereoisomer reacts to give one specific stereoisomer as product.

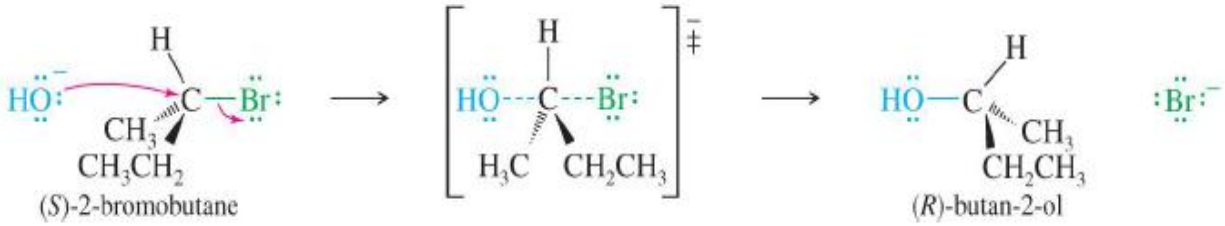
SN^2 reactions always proceed with inversion of Configuration also known as walden inversion.

Mechanism of Substitution Nucleophelic Bimolecular Reaction (SN^2)





The product has its stereochemistry inverted by an S_N2 reaction.

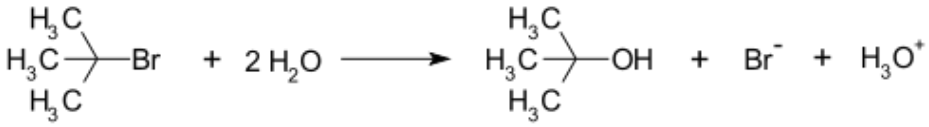


Substitution Nucleophelic Unimolecular Reaction (SN^1)

The SN^1 reaction is a substitution reaction in organic chemistry. "S_N" stands for nucleophilic substitution and the "1" represents the fact that the rate-determining step is unimolecular. Thus, the rate equation is often shown as having first-order dependence on electrophile and zero-order dependence on nucleophile. This relationship holds for situations where the amount of nucleophile is much greater than that of the carbocation intermediate. Instead, the rate equation may be more accurately described using steady-state kinetics. The reaction involves a carbocation intermediate and is commonly seen in reactions of secondary or tertiary alkyl halides under strongly basic conditions or, under strongly acidic conditions, with secondary or tertiary alcohols. With primary alkyl halides, the alternative SN^2 reaction occurs. In inorganic chemistry, the SN^1 reaction is often known as the dissociative mechanism. This dissociation pathway is well-described by the cis effect. A reaction mechanism was first proposed by Christopher Ingold et al. in 1940. This reaction does not depend much on the strength of the nucleophile unlike the SN^2 mechanism.

Mechanism

An example of a reaction taking place with an S_N1 reaction mechanism is the hydrolysis of tert-butyl bromide with water forming tert-butanol:

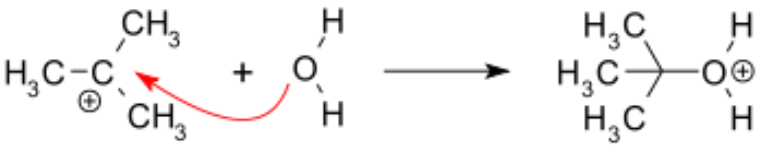


This SN^1 reaction takes place in three steps:

- Formation of a tert-butyl carbocation by separation of a leaving group (a bromide anion) from the carbon atom: this step is slow and reversible.



- Nucleophilic attack: the carbocation reacts with the nucleophile. If the nucleophile is a neutral molecule (i.e. a solvent) a third step is required to complete the reaction. When the solvent is water, the intermediate is an oxonium ion. This reaction step is fast.

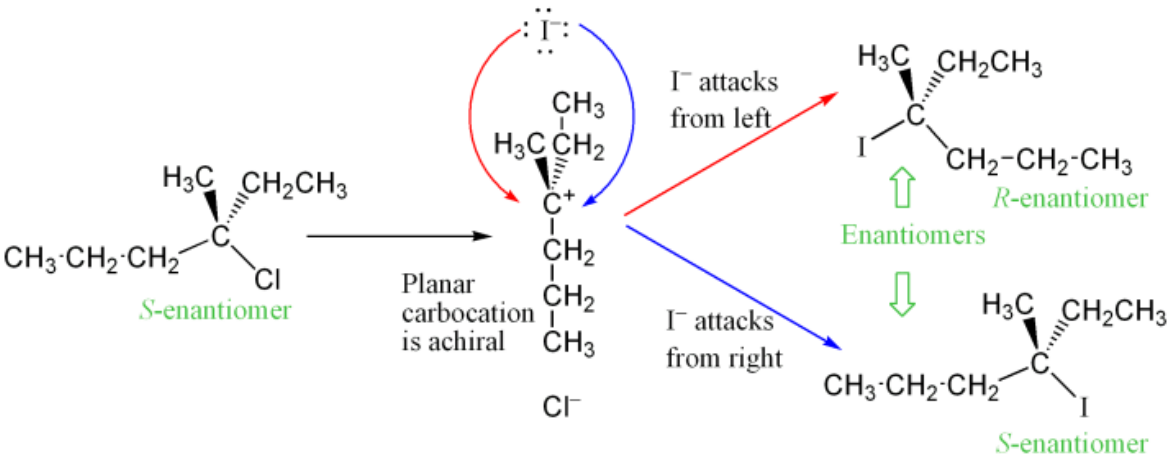


- Deprotonation: Removal of a proton on the protonated nucleophile by water acting as a base forming the alcohol and a hydronium ion. This reaction step is fast.



Stereochemistry

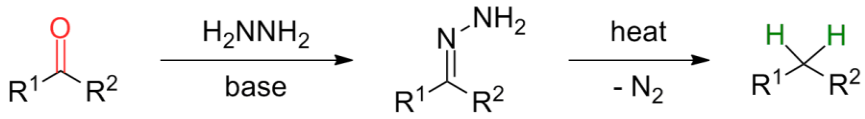
The carbocation intermediate formed in the reaction's rate limiting step is an sp^2 hybridized carbon with trigonal planar molecular geometry. This allows two different avenues for the nucleophilic attack, one on either side of the planar molecule. If neither avenue is preferentially favored, these two avenues occur equally, yielding a racemic mix of enantiomers if the reaction takes place at a stereocenter.[6] This is illustrated below in the S_N1 reaction of S-3-chloro-3-methylhexane with an iodide ion, which yields a racemic mixture of 3-iodo-3-methylhexane:



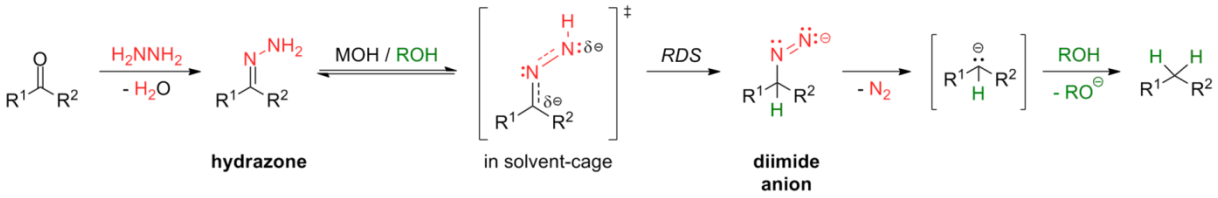
However, an excess of one stereoisomer can be observed, as the leaving group can remain in proximity to the carbocation intermediate for a short time and block nucleophilic attack. This stands in contrast to the SN^2 mechanism, which is a stereospecific mechanism where stereochemistry is always inverted as the nucleophile comes in from the rear side of the leaving group.

Wolf – Kishner Reaction

The Wolff–Kishner reduction is a reaction used in organic chemistry to convert carbonyl functionalities into methylene groups. In the context of complex molecule synthesis, it is most frequently employed to remove a carbonyl group after it has served its synthetic purpose of activating an intermediate in a preceding step. As such, there is no obvious retron for this reaction. Originally reported byNikolai Kischner in 1911 and Ludwig Wolff in 1912, it has been applied to the total synthesis of scopadulcic acid B, aspidospermidine and dysidiolide.



In general, the reaction mechanism first involves the in situ generation of a hydrazone by condensation of hydrazine with the ketone or aldehyde substrate. Sometimes it is however advantageous to use a pre-formed hydrazone as substrate (see modifications). The hydrazone is deprotonated by alkoxide base followed by a concerted, rate-determining step in which a diimide anion is formed. Collapse of this alkyldiimde with loss of N2 leads to formation of an alkylanion which can be protonated by solvent to give the desired product.



Mechanism of Wolf – Kishner Reaction

The mechanism of the Wolff–Kishner reduction has been studied by Szmant and coworkers. According to Szmant's research, the first step in this reaction is the formation of a hydrazone anion 1 by deprotonation of the terminal nitrogen by MOH. If semicarbazones are used as substrates, initial conversion into the corresponding hydrazone is followed by deprotonation. A range of mechanistic data suggests that the rate-determining step involves formation of a new carbon–hydrogen bond at the carbon terminal in the delocalized hydrazone anion. This proton capture takes place in a concerted fashion with a solvent-induced abstraction of the second proton at the nitrogen terminal. Szmant's finding that this reaction is first order in both hydroxide ion and ketone hydrazone supports this mechanistic proposal. Several molecules of solvent have to be involved in this process in order to allow for a concerted process. A detailed Hammett analysisof aryl aldehydes, methyl aryl ketones and diaryl ketones showed a non-linear relationship which the authors attribute to the complexity of the rate-determining step. Mildy electron-withdrawing substituents favor carbon-hydrogen bond formation, but highly electron-withdrawing substitutents will decrease the negative charge at the terminal nitrogen and in turn favor a bigger and harder solvation shell that will render breaking of the N-H bond more

difficult. The exceptionally high negative entropy of activation values observed can be explained by the high degree of organization in the proposed transition state.

It was furthermore found that the rate of the reaction depends on the concentration of the hydroxylic solvent and on the cation in the alkoxide catalyst. The presence of crown ether in the reaction medium can increase the reactivity of the hydrazone anion 1 by dissociating the ion pair and therefore enhance the reaction rate. The final step of the Wolff–Kishner reduction is the collapse of the diimide anion 2 in the presence of a proton source to give the hydrocarbon via loss of dinitrogen. Taber showed experimental evidence for the intermediacy of a sp3-hybridized carbanion 3 during this last step, distinguishing it from a mechanism in which dinitrogen is lost by a free-radical pathway. The overall driving force of the reaction is the evolution of nitrogen gas from the reaction mixture.

