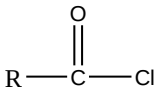
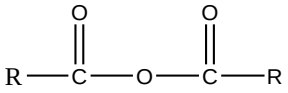
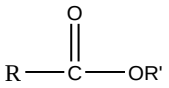
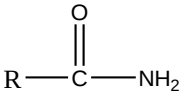
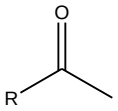
Course Content Developed By:	Dr. Satish Kumar
Institution Name	Govt. Degree College, (Boys) Udhampur
Department	Department of Higher Education UT of Jammu and Kashmir
Syllabus	Jammu University and B.Sc. Honours - Cluster University of Jammu
Unit	Carboxylic acid Derivatives
Syllabus	**Carboxylic acid Derivatives:** **Cluster University (Honours) :**Preparation and reactions of acid chlorides, anhydrides, esters and amides; Comparative study of nucleophilic substitution at acyl group., Claisen condensation, Dieckmann and Reformatsky reactions, Hofmann-bromamide degradation and Curtius rearrangement. **Cluster University, Jammu University and Autonomous College (UG-General):** **Preparation:** Acid chlorides, Anhydrides, Esters and Amides from acids and their interconversion. **Reactions**: Comparative study of nucleophilicity of acyl derivatives. Reformatsky Reaction, Perkin condensation.

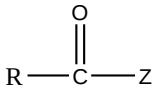
Carboxylic Acid derivatives (Acyl Derivatives)

This section deals with four categories of organic compounds which are related to carboxylic acids. The important carboxylic acid derivatives or simply acyl derivatives are:

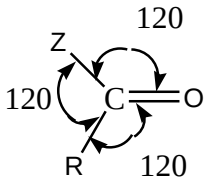
1. Acid chlorides or Acyl halide 
2. Acid anhydride 
3. Esters 
4. Amides 

These compounds are obtained by replacement of –OH part of –COOH group of carboxylic acid by –X, -OCOR', -OR' and $–NH_2$ respectively are collectively called functional derivatives of Carboxylic Acids or simply derivatives of carboxylic acids since all these on hydrolysis give back the parent acid. The common structural feature is the acyl group 

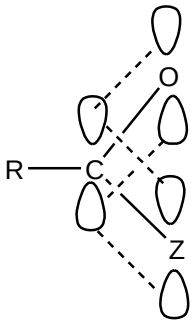
Electronic Structure of acid derivative

The general electronic structure of acid derivatives is  where Z = X, OCOR', OR', NH_2; R and R' may be same or different alkyl or acyl groups or even Hydrogen atom.

In all these acid derivatives, the carbonyl carbon is sp^2 hybridized with all three atoms joining with carbon aton in one plane having bong angle approximately 120.

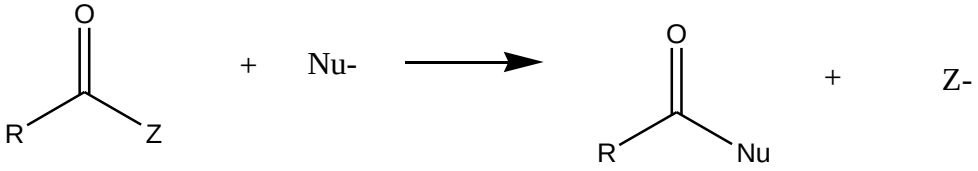


Further the group Z (Cl inacid chlorides, O in esters and anhydrides, N in amides) is directly linked to the carbonyl carbon has atleast one lone pair of electrons in a p-orbital. This p-orbital on Cand O-atoms of carbonyl group to provide additional bonding as shown in figure

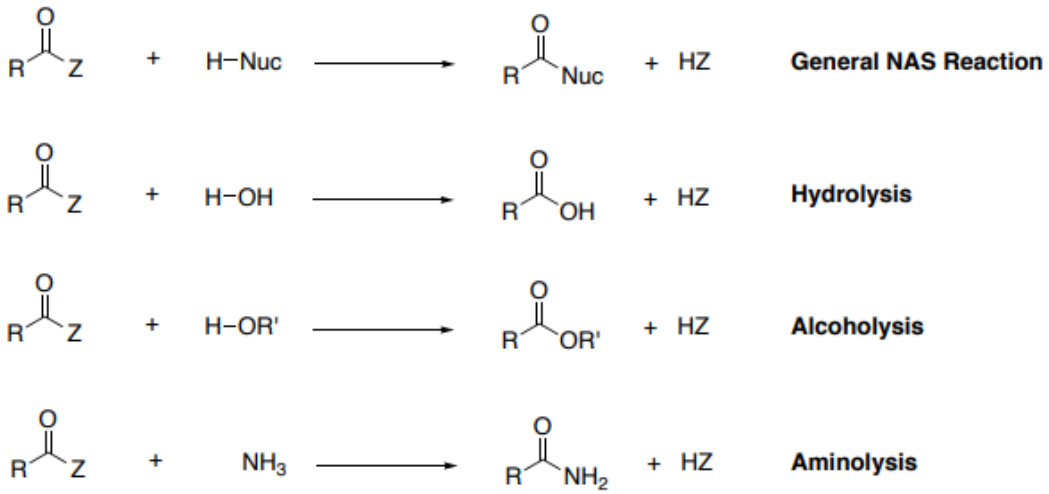


Nucleophilic Acyl Substitution

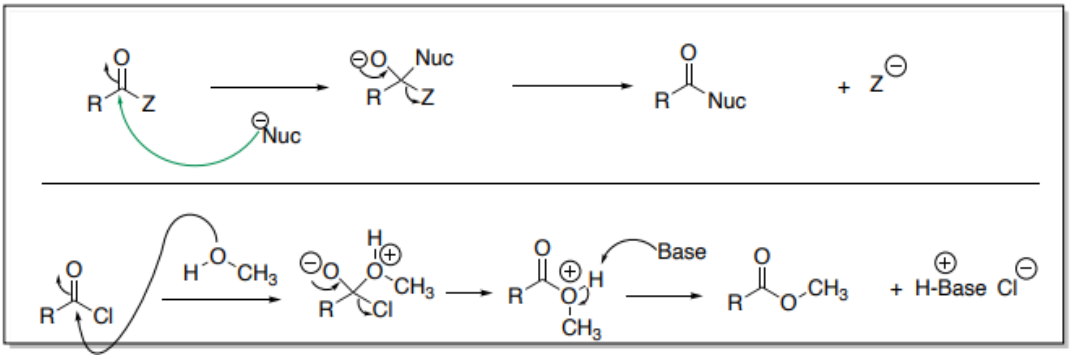
Nearly all the chemistry of carboxylic acid derivatives involves the addition of a nucleophile to the carbonyl carbon followed by loss of a leaving group to affect a nucleophilic substitution on the acyl carbon. This is a two step process. If the acid derivative is represented by the general formula R-CO-Z (where Z = -Cl,-OCOR', -OR', -NH_2), then their nucleophilic substitution reaction can be shown by equation,



Reaction Types: The nucleophilic acyl substitution with weak nucleophiles can be classified into various reaction types depending on what kind of nucleophile is adding.



The mechanism is shown below with a typical example of base catalysed ester formation from acyl chloride

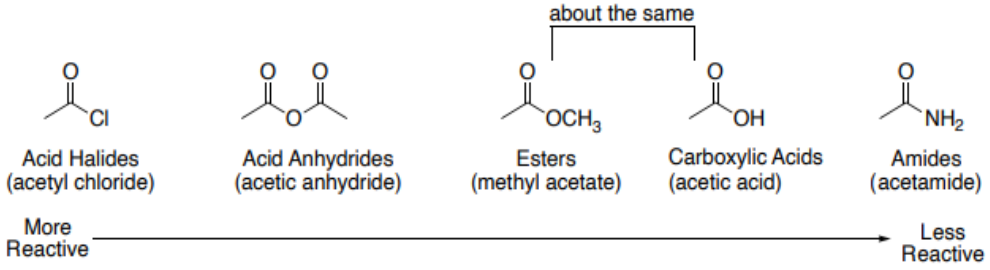


In the first step, during addition of nucleophile, the trigonal carbon of the acyl group is converted to the tetrahedral carbon in the intermediatewhich is susceptible to steric hinderance for bulky groups around carbonyl carbon. Further, this addition step will be retarted by electron releasing substituents intensifying negative charge in the intermediate and facilitated by electron withdrawing groups which tend to disperse negative charge in the intermediate.

In second step, reorganisation of electrons occurs leading to the formation of the substitution product with elimination of the group Z^-. The ease with which Z- is expelled depends upon its basicity; weaker the base, better is the leaving group. In the nucleophilic acyl substitution of acid chlorides, anhydrides, esters and amides, the leaving group Z- are Cl-, RCOO-, RO- and NH_2- respectively. As we know Cl- is a weak base, RCOO- is moderately strong base, RO- is stronger and NH_2- is the strongest base. In other words Cl- is a very good leaving groupwhile NH_2- is a bad leaving group. In contrast, if aldehydes and ketones were to undergo nucleophilic sustitution reaction, it would involve the removal of hydride ion (H- ion) or alkide ion (R- ion). Since these are the strogest bases, therefore, aldehydes and ketones donot undergo nucleophilic substitution reactions

Relative stability of Acid derivatives:

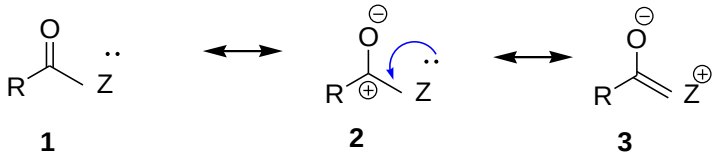
From the most reactive to the least reactive: acid halides, anhydrides, esters, and amides are arranged as given below



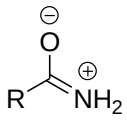
The order of reactivity can be explained partly

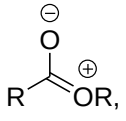
(i) On the stability of the resonance structure of acid derivatives and
(ii) Partly on the ability of the leaving groups to depart

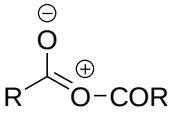
I The acid dereivatives may be regarded as a resonance hybrid of the following three structures:

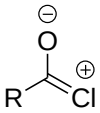


Structure 3 makes a significant contribution towards the resonance hybrid because it involves dispersal of positive charge from the carbonyl carbon. More the contribution of structure 3, more the stability of acid derivative and lesser is its reactivity towards nuclephilic acyl substitution reaction. The extent of cotribution of structure 3 towards resonance hybrid depends upon the electronegativity of the atom directly attached with carbonyl carbon. As O is more electrnegative than N, therefore contribution of structure 3a is significant in case of amides than structure 3b in case of esters and 3c in case of anhydrides.

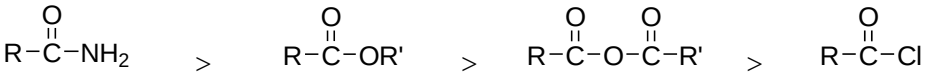

3a


3b

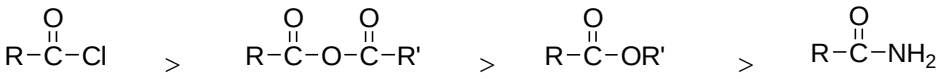

3c


3d

In structure 3c, -I effect of carbonyl group intensify positive charge on oxygen, therefore structure 3b is more stable than 3c. The contribution of structure 3d towards resonance hybrid is the lowest because lone pair is present in orbital of different size ie 3p-orbital. Therefore the overlap is poor and contribution towards the resonce hybrid of acid chloride is much lower. It follows the stability of the resonance structures of acid derivatives decreases in the order:



Consequently, their reactivity towards nucleophilic acyl substitution reaction decreases in the reverse order:



II The order of reactivity can also be explained on the ability of the leaving groups to depart. The better the leaving group, more is the reactivity of the acid derivative. The leaving group ability of different groups depends upon their relative basicities. In nucleophile acyl substitution reactions, the leaving groups are: Cl- (in acid chlorides), RCOO- (in Anhydrides), R'O- (in esters) and NH_2^- (in amides). Their relative basicities decrease in the order

NH_2^- > R'O- > R'COO- > Cl-

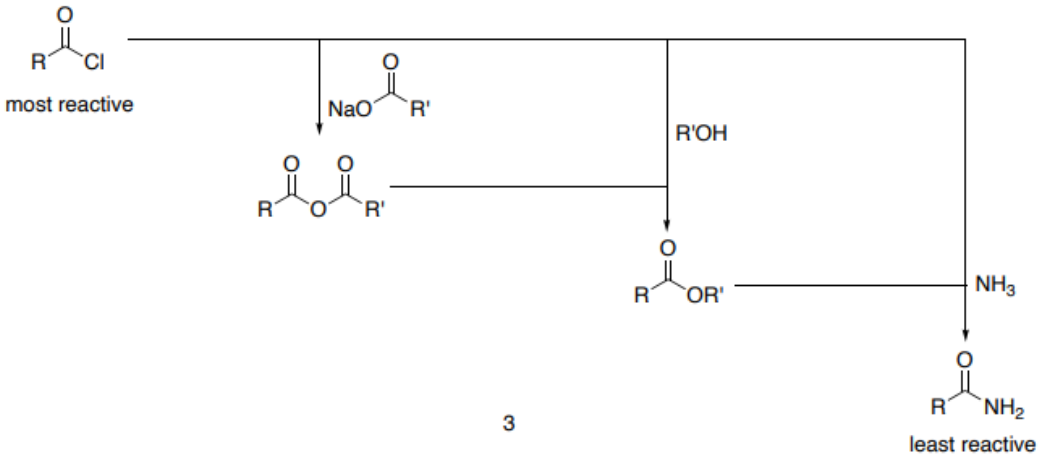
Since a stronger base is a poor leaving group, therefore, the ease with which these leaving groups depart decreases in the reverse order, ie Cl- > R'COO- > R'O- > NH_2-.

Consequently, the relative reactivities of all these acid derivatives decreases in the order:

Acid chlorides > anhydride > ester > amide

Interconversions of acid derivatives by nucleophilic acyl substitution:

Due to large difference in the reactivity of acid derivatives, It is generally easy to go from a more reactive carboxylic acid derivative to a less reactive one. It is very difficult to go the other direction.



The possible conversions that can be carried out are summerised below:

Acid chlorides--------→Anhydrde--------→ Esters ----- → Amides

Acid chlorides ←-----X--- Anhydride -------→Esters ----→ Amides

Acid chlorides and anhydrides ←----X-----Esters -------→ Amides

Preparation and reactions of Acid Derivatives

1. Acid chlorides

Nomenclature: the name of acid chlorides are obtained by replacing terminal *–ic acid* from common or IUPAC name of parent acid by suffix *–yl chloride*. For example

Structural formula	Common name	IUPAC name
HCOCl	Formyl chloride	Methanoyl chloride
CH_3COCl	Acetyl chloride	Ethanoyl chloride
CH_3CH_2Cl	Propionyl chloride	Propanoyl chloride
C_6H_5COCl	Benzoyl chloride	Benzene carbonyl chloride

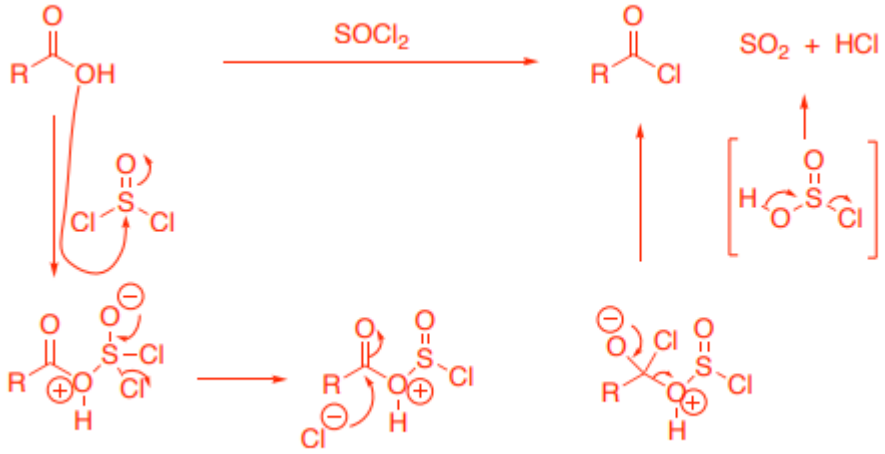
Methods of formation:

As the acid chlorides are the most reactive of the common acid derivatives, they cannot be prepared by reaction of esters, acids or amides. However these can be prepared conveniently from carboxyli acid with thionyl chloride, PCl_3 or PCl_5

$$RCOOH + SOCl_2 \longrightarrow RCOCl + SO_2 + HCl$$

$$RCOOH + PCl_5 \longrightarrow RCOCl + POCl_3 + HCl$$

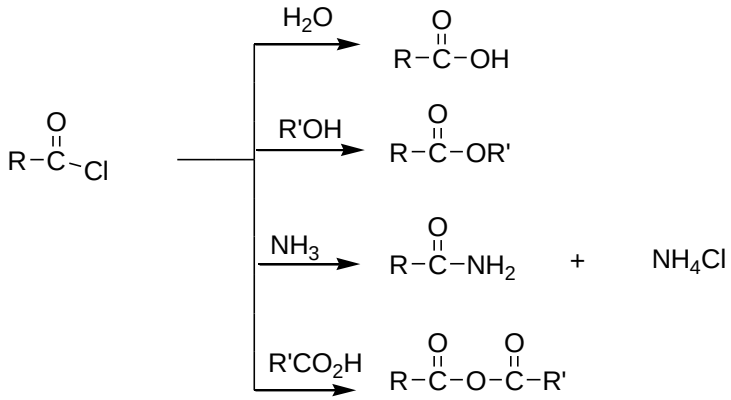
The mechanism using thionyl chloride is given below:



Chemical reactions :

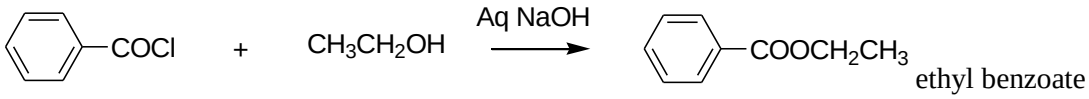
1 **Nucleophilic acyl substitution reactions:**

Acid chloride are the most reactive of all the derivatives of carboxylic acids. Both aliphatic and aromatic acid chloridesreadily undergo a number of nucleophilic acyl substitution reactions even with weak nucleophiles such as water, alcohols, amines and carboxylic acids to give carboxylic acids, esters, amides and anhydrides respectively



All these reactions are regarded as **acylation reactions** because in all these reactions, the hydrogen atom of water, alcohols, phenols, ammonia and carboxylic acids is replaced by an acyl group. Thus acid chlorides may be regarded as *acylating reagent*s.

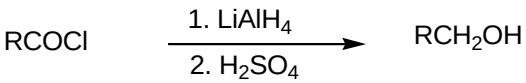
The reaction of an aromatic acyl chloride with an alcohol or a phenol or an amineis usually carried out in presence of a base such as aq. NaOH or pyridine. The reaction is called as **Schotten Baumann reaction**.



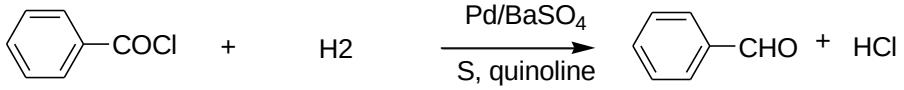
ethyl benzoate

1 Reduction:

Acid chlorides react smoothly with $LiAlH_4$ to give corresponding primary alcohols

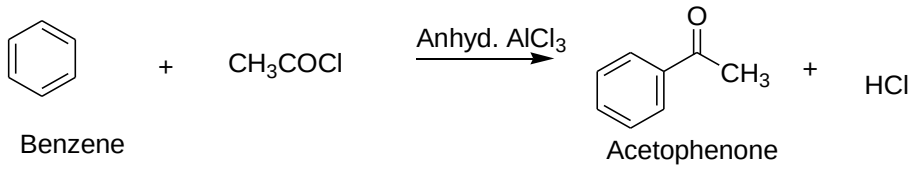


Acid chlorides are easily reduced to corresponding aldehydes with hydrogen in presence of palladium deposited over $BaSO_4$. The reduction is known as **Rosenmund reduction** is a good preparative method for aldehydes



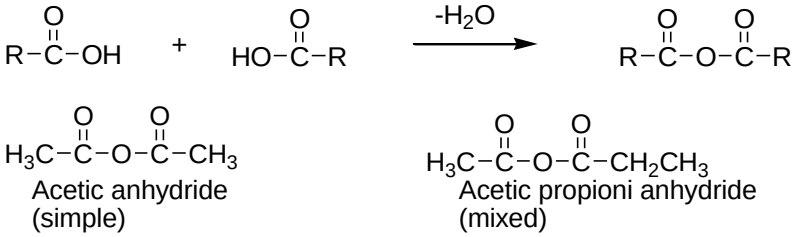
1. **Freidel-Craft acylation:**

Acyl chlorides react with aromatic compounds in presence of a Lewis acid catalyst such as anhyd. $AlCl_3$ undergoing aromatic electrophilic substitution reaction to form aromatic ketones. For example benzene on treatment with acetyl chloride gives acetophenone.

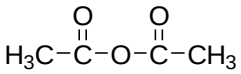
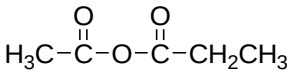
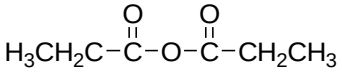
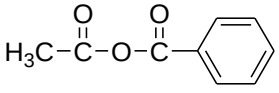


2 Acid Anhydrides

Acid Anhydrides are formally derived by removal of one molecule of water from two molecules of carboxylic acids. Acid anhydride may be simple (symmetrical) or mixed (unsymmetrical)

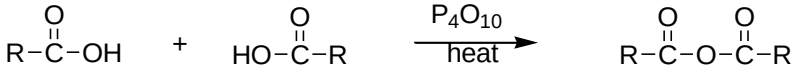


Nomenclature: Acid anhydrides are named by replacing the word *acid* from the name of parent carboxylic acid by the word *anhydride*. In case of mixed anhydrides, the names of two parent acids are written in alphabetical order and the word anhydride is added only once. For example

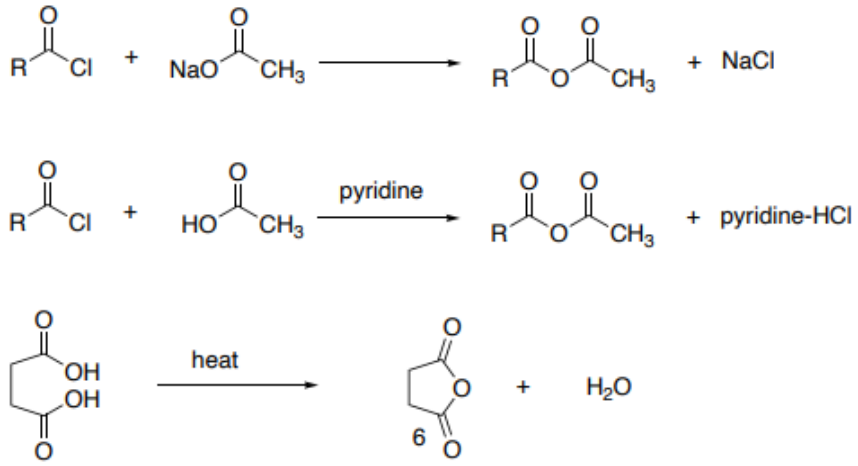
Structural formula	Common name	IUPAC name
	Acetic anhydride	Ethanoic anhydride
	Acetic propionic anhydride	Ethanoic propanoic anhydride
	Prpionic anhydride	Propanoic anhydride
	Acetic benzoic anhydride	Benzoic ethanoic anhydride

Preparation of Acid Anhydrides :

a. **From carboxylic acids**: Simple acid anhydides are obtained by heating carboxylic acids with phosphorous pentoxide(P_4O_{10})

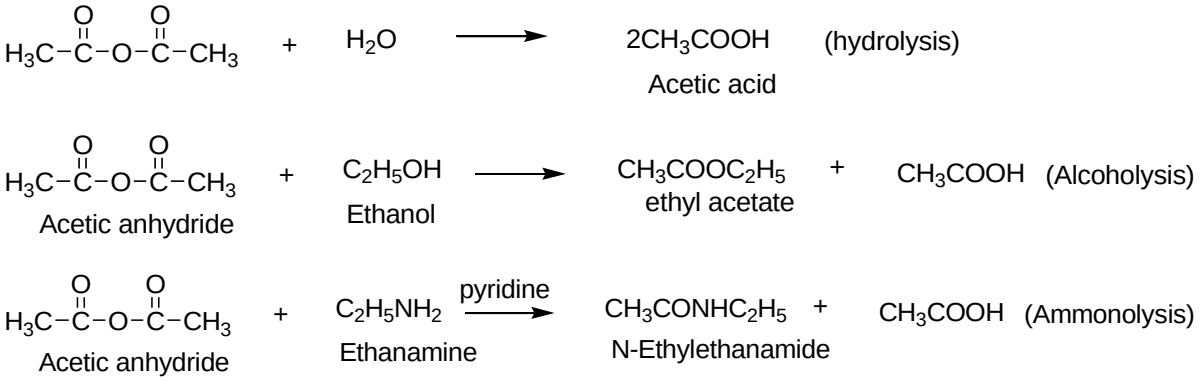


b. **From acid chloride**: Both symmetrical and mixed anhydrides may be prepared by treating acid chloride with a carboxylic acid i.p.o. a base such as pyridine. For example



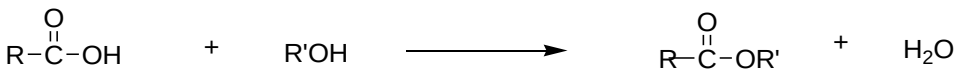
Chemical reactions:

Like acid chlorides, acid anhydride undergo acyl nucleophilic substitution reactions. However, they are less reactive than the corresponding acyl halides. Important nucleophilic acyl substitution reactions are hydrolysis, alcoholysis, and ammonolysis of anhydrides

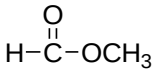
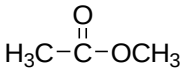
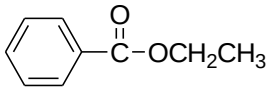
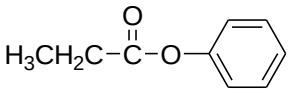


3 Esters

An ester is the product of a condensation reaction between acarboxylic acid and an alcohol.

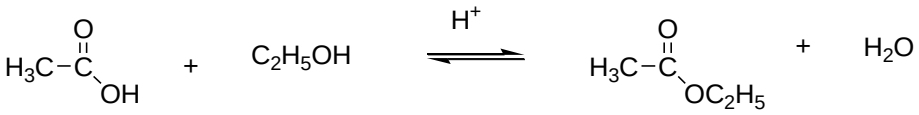


Nomenclature: Esters are named by writing the name of the alkyl or the aryl group (of the OR' part of the molecule) before the common name or IUPAC name of the parent acid with its terminal *ic acid* replaced by *ate*. For example

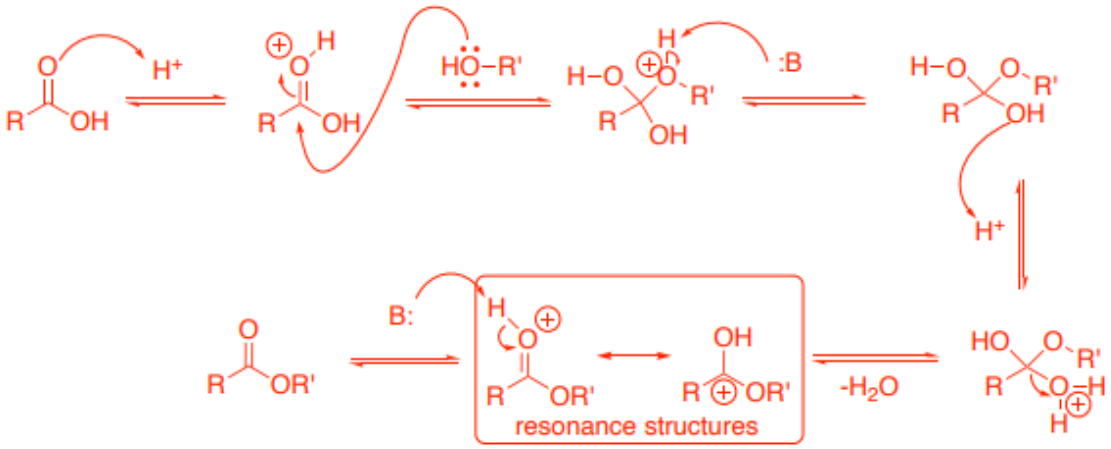
Ester	Common name	IUPAC name
	Methyl formate	Methyl methanoate
	Methyl acetate	Methyl ethanoate
	Ethyl benzoate	Ethyl benzoate
	Phenyl propionate	Phenyl propanoate

Preparation of Esters

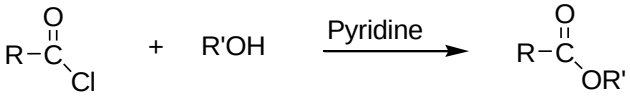
By action of alcohols on carboxylic acid (Esterification): Esters are generally prepared by heating carboxylic acids with alcohols in presence of a mineral acid



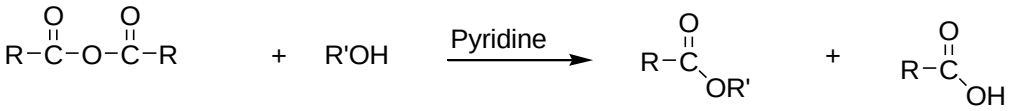
With a large excess of alcohol and an acid catalyst, a Fischer Ester synthesis can be undertaken. This is limited to cheap readily available alcohols like methanol and ethanol. Water can be removed from the reaction by azeotropic distillation with a suitable solvent, such as benzene, thereby driving the reaction to completion. Reaction Mechanism for Fischer Esterification is as given below:



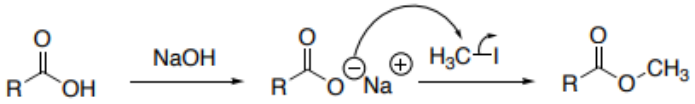
By reaction of acid chlorides or acid anhydride with alcohols: Other esters are more easily prepared from the acid chloride. Usually the reaction is carried out in pyridine, which forms a salt wth HCl generated and prevents the solution from becoming acidic.



Tertiary alcohols which donot react under the conditions of above method, are best prepared from acid chlorides and alcohols. An anhydride can also be used in place of an acid chloride

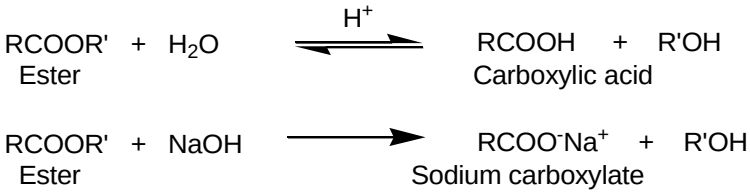


By reaction of an alkyl halide with salt of a carboxylic acid: The deprotonated acid will react with methyl or primary alkyl halides via an S_N2 reaction.



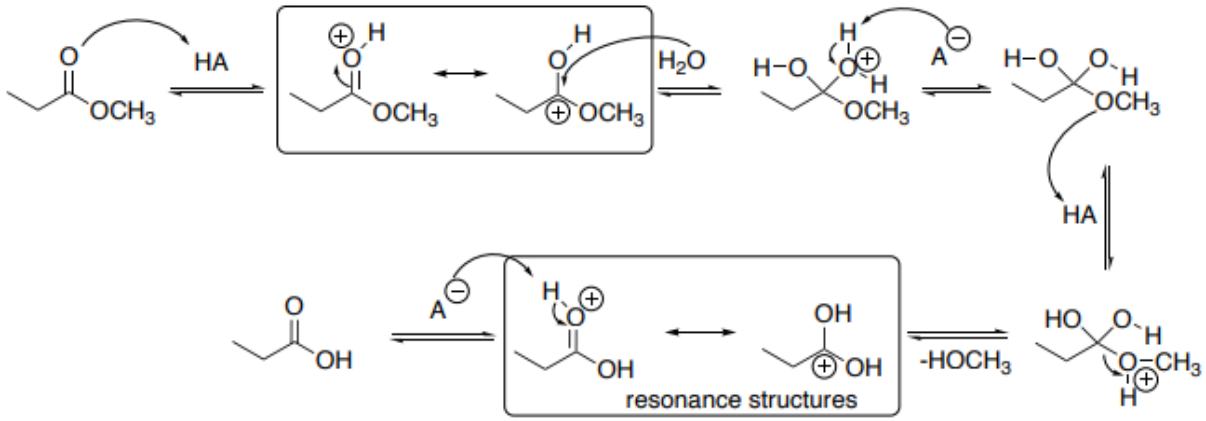
Chemical reactions: Like other acid derivatives, esters can also undergo nucleophilic acyl substitution reaction. However they are less reactive than both acid chlorides and anhydrides. Some typical reactions of esters are:

Hydrolysis: Esters react with water to give the parent acids inthe presence of strong acids or strong bases

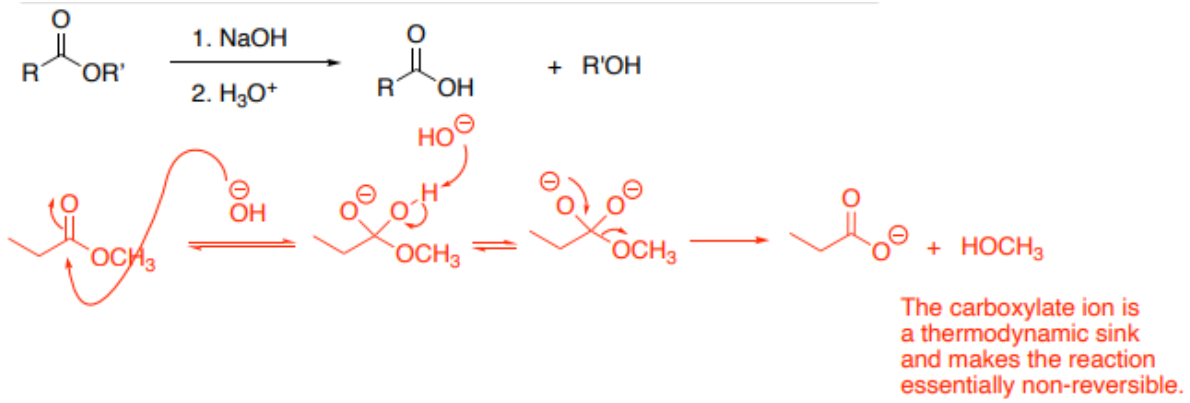


The acid catalysed hydrolysis of esters is the reverse of the Fischer esterification and all the steps are reversible. In contrast, hydrolysis in aqueous alkaline solution is irreversible because of the conversion of carboxylic acid to aresonance-stabilized carboxylate anion.

Mechanism for Acid Catalyzed Hydrolysis:



Saponification: Since soaps are sodium salts of higher fatty acids, therefore, alkaline hydrolysis of esters is commonly called *saponification*. The mechanism of base catalysed hydrolysis of esters (saponification) is as follows;



<u>Alcoholysis or trans-esterification</u>: (Conversion to other esters): When an ester is treated with excess of another alcohol (R"OH) in presence of an acid (H_2SO_4 or HCl) or a base (R"Ona) as catalyst, it gives another ester. This reaction involving replacement of the alkoxy part of the ester by the alkoxy part of the alcohol taken in excess is called **trans-esterification**. Thus,

$$\underset{\text{Ester}}{RCOOR'} + \underset{\text{(excess)}}{R''OH} \xrightleftharpoons{H^+ \text{ or } R''ONa} RCOOR'' + R'OH$$

For example

$$\underset{\text{Glyceryl tripalmitate}}{\begin{matrix}CH_2O-COC_{15}H_{31}\\ CHO-COC_{15}H_{31}\\ CH_2O-COC_{15}H_{31}\end{matrix}} + \underset{\text{(excess)}}{3CH_3CH_2OH} \xrightleftharpoons{H^+ \text{ or } CH_3CH_2O^-} \underset{\text{Glycerol}}{\begin{matrix}CH_2OH\\ CHOH\\ CH_2OH\end{matrix}} + \underset{\text{Ethyl palmitate}}{3C_{15}H_{31}COOCH_2CH_3}$$

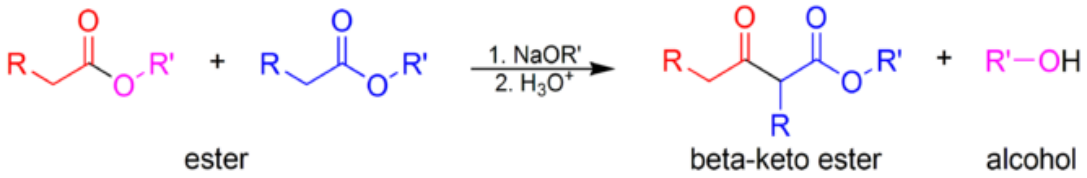
Ammonolysis (Conversion to amides): Esters react with ammonia, primaryand secondry amines to form amides.

$$RCOOR' + NH_3 \dashrightarrow RCONH_2 + R'OH$$

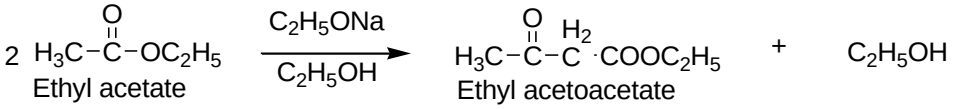
Eg $CH_3COOC_2H_5 + NH_3 \dashrightarrow CH_3CONH_2 + C_2H_5OH$

<u>Claisen Condensation</u>

The **Claisen condensation** 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 basesuch as sodium alkoxide 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.

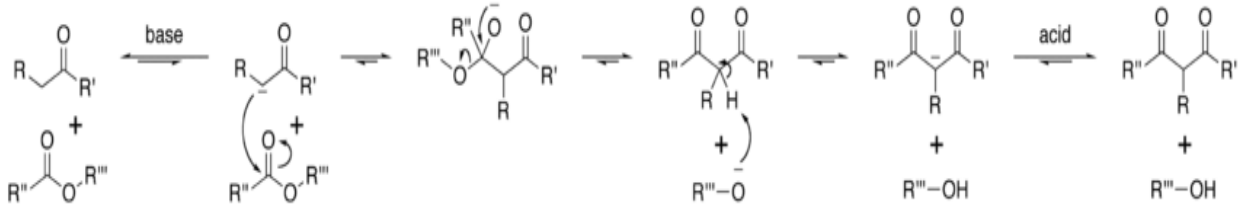


For example



Mechanism

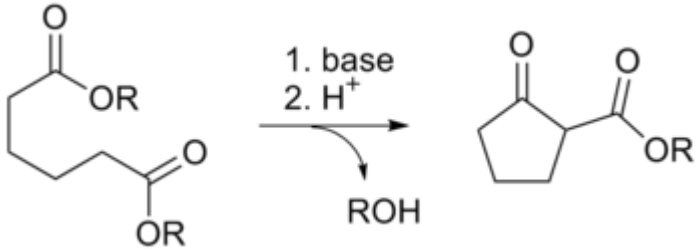
The mechanism of the reaction is similar to Claisen-Schmidt reaction and occurs through the intermediate formation of a carbanion.



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.

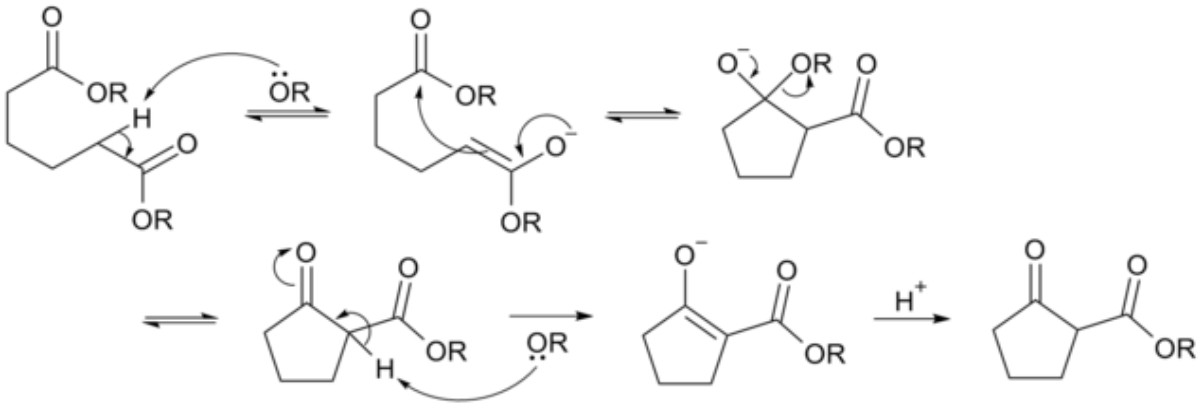
Dieckmann condensation

The **Dieckmann condensation** is the intramolecular chemical reaction of diesters with base to give β-keto esters. It is named after the German chemist Walter Dieckmann (1869–1925). The equivalent intermolecular reaction is the Claisen condensation.



Reaction Mechanism

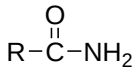
Deprotonation of an ester at the α-position generates an enolate ion which then undergoes a 5-exo-trig nucleophilic attack to give a cyclic enol. Protonation with a Brønsted-Lowry acid (H_3O^+ for example) re-forms the β-keto ester.



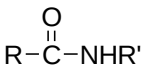
Due to the steric stability of five- and six-membered rings, these structures will preferentially be formed. 1,6 diesters will form five-membered cyclic β-keto esters, while 1,7 diesters will form six-membered β-keto esters.

4 Amides

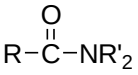
Amides are the derivatives of acids in which –OH part of the –COOH group is replaced by $–NH_2$, -NHR' or $–NR'_2$ groups. They are classified as primary (1°), secondry (2°) and tertiary (3°) amides respectively.



primary (1°)amide



secondry (2°)amide



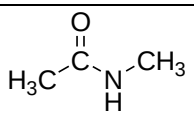
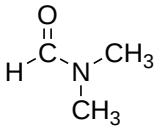
tertiary (3°)amide

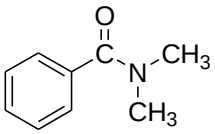
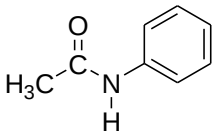
Nomenclature

Primary amides are named by replacing the suffix ic acid from the common name or oic acid from IUPAC nameof the parent acid by the suffix amide. For example,

Amide	Common name	IUPAC name
$HCONH_2$	Formamide	Methanamide
CH_3CONH_2	Acetamide	Ethanamide
$CH_3CH_2CONH_2$	Propionamide	Propanamide
$C_6H_5CONH_2$	Benzamide	Benzamide

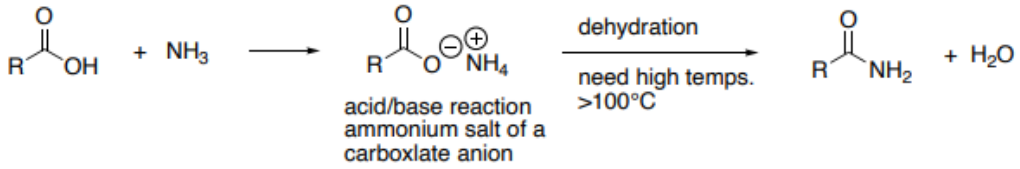
Secondry and tertiary amides are named by adding the prefix N-alkyl or N,N-dialky before the above names. For example,

Amide	Common name	IUPAC name
	N-Methylacetamide	N-Methylethanamide
	N,N-Dimethylformamide	N,N-Dimethylmethanamide

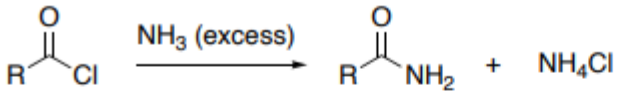
	N,N-Dimethylbanzamide	N,N-Dimethylbanzamide
	Acetanilide	N-Phenylacetamide

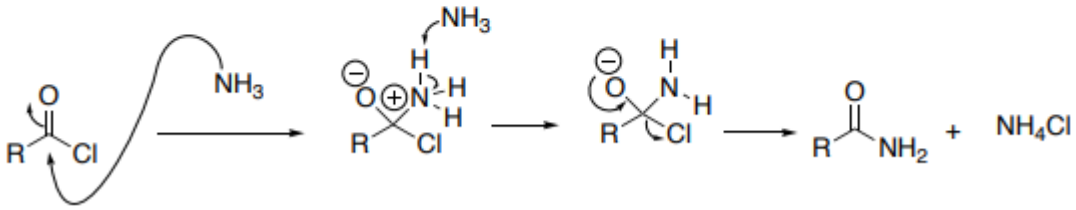
Preparation of Amides

It is very difficult to prepare amides directly from carboxylic acids. This is because the acid and the amine will simply do an acid-base reaction to make an ammonium cation and a carboxylate anion. The most convenient way to make amides is by reacting an acid chloride with ammonia, a primary or a scecondary amine.

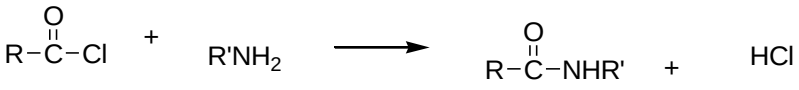


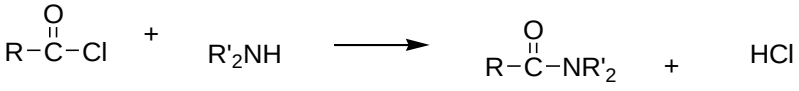
Amides from acid chlorides and amines are quite fast.





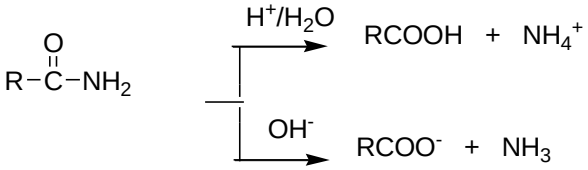
Secondry and tertiary amides are often prepared by treating an acid chloride with aprimary or secondry amine.



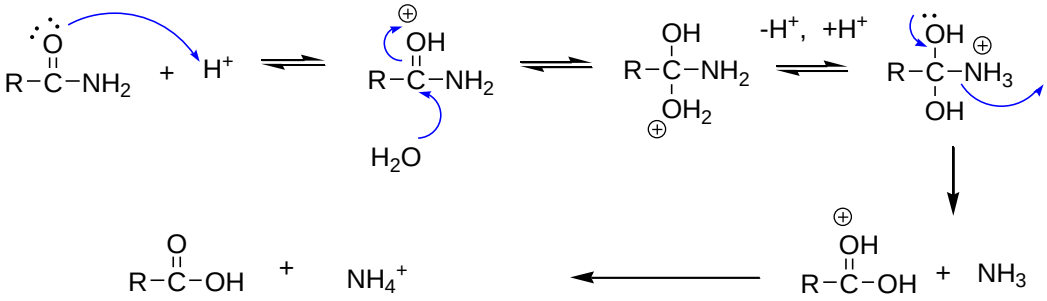


Chemical reactions

Reactions with nucleophiles: The hydrolysis of amides, like that of esters, is catalysed by both acids and bases.



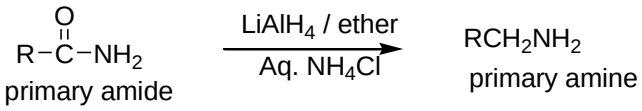
The mechanism of acidic or basic hydrolysis of amides is similar to that of esters except that in case of esters, a mole of alcohol is removed while in amides, a molecule of NH_3 is lost. The mechanism of acid catalysed hydrolysis of amides is as shown below:



Dehydration: On heating with dehydrating agents such as P_2O_5, $POCl_3$, $SOCl_2$ etc amides undergo dehydration to form alkyl cyanide.

$$3\ R\text{-}CO\text{-}NH_2 + P_2O_5 \dashrightarrow 3R\text{-}CN + 2H_3PO_4$$

Reduction: Amides are reduced to the corresponding amines with lithium aluminium hydride (LAH). Thus



Hofmann bromamide degradation reaction

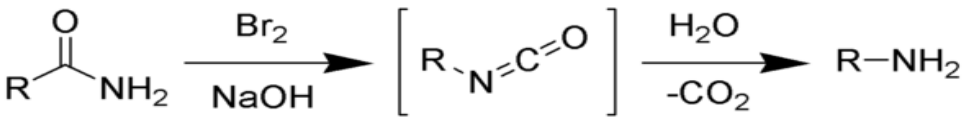
When a primary amide is treated with bromine in an aqueous or ethanolic solution of sodium hydroxide, degradation of amide takes place leading to the formation of primary amine. This reaction involving degradation of amide and is popularly known as Hoffmann bromamide degradation reaction. The primary amine thus formed contains one carbon less than the number of carbon atoms in that amide.

$$RCONH_2 + Br_2 + 4NaOH \rightarrow R\text{-}NH_2 + Na_2CO_3 + 2NaBr + 2H_2O$$

For example,

$$CH_3CH_2\text{-}CO\text{-}NH_2 + Br_2 + 4NaOH \dashrightarrow CH_3CH_2NH_2 + Na_2CO_3 + 2NaBr + 2H_2O$$

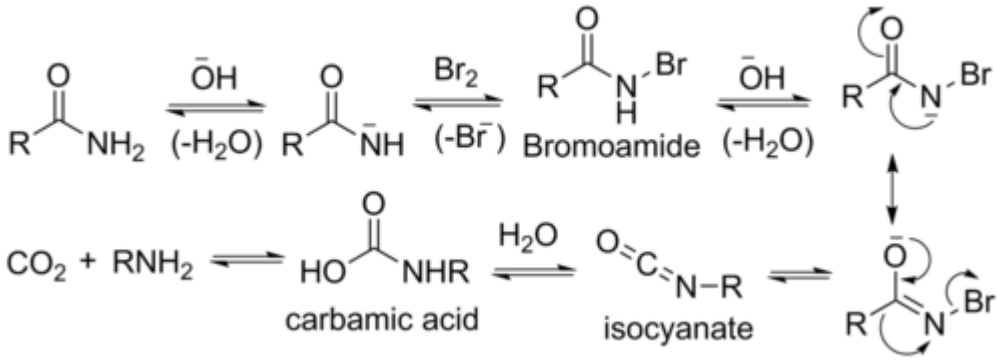
Porpanamide Ethanamine



Mechanism

The reaction of bromine with sodium hydroxide forms sodium hypobromite *in situ*, which transforms the primary amide into an intermediate isocyanate. The formation of an intermediate nitrene is not

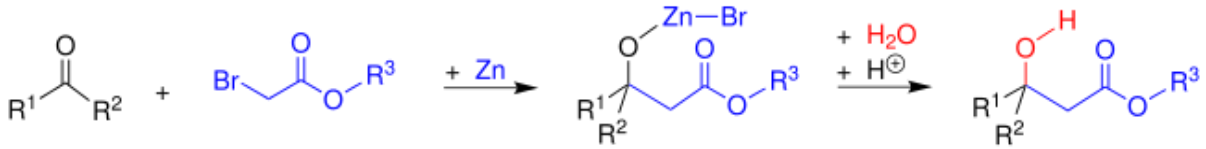
possible because it implies also the formation of a hydroxamic acid as a byproduct, which has never been observed. The intermediate isocyanate is hydrolyzed to a primary amine, giving off carbon dioxide.



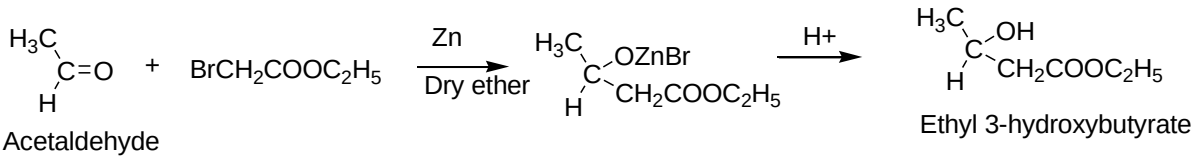
Some Named reactions involving Acid Derivatives

Reformatsky reaction

The **Reformatsky reaction** (sometimes spelled **Reformatskii reaction**) is an organic reaction which condenses aldehydes or ketones with α-halo esters using metallic zinc to form β-hydroxy-esters:



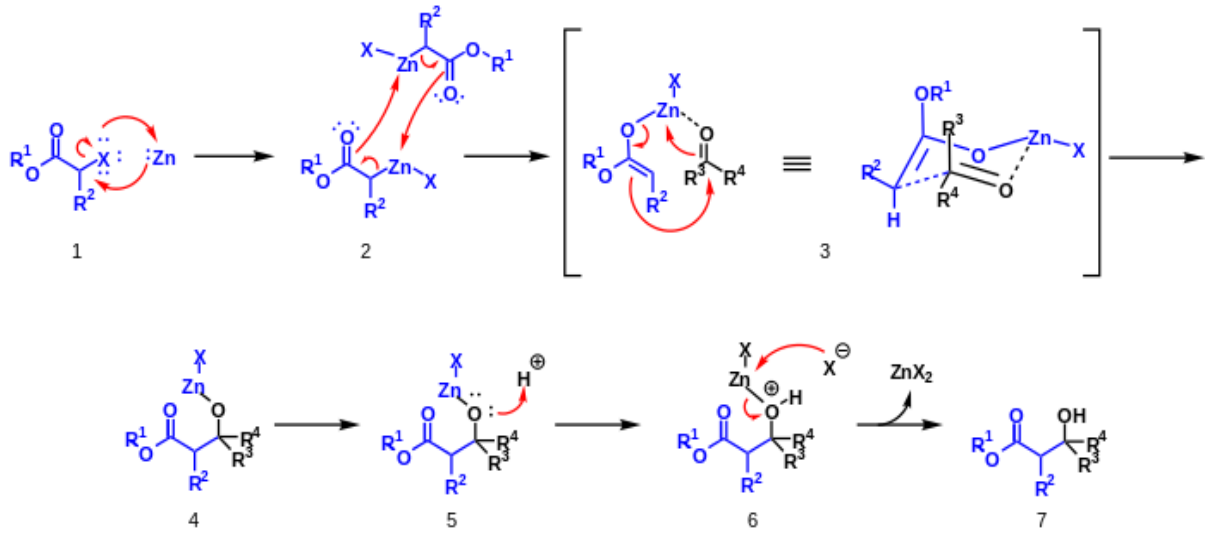
For example



The organozinc reagent, also called a 'Reformatsky enolate', is prepared by treating an alpha-halo ester with zinc dust. Reformatsky enolates are less reactive than lithium enolates or Grignard reagents and hence nucleophilic addition to the ester group does not occur. The reaction was discovered by Sergey Nikolaevich Reformatsky.

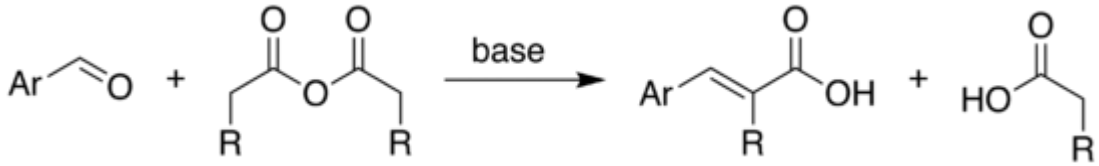
Reaction Mechanism

Zinc metal is inserted into the carbon-halogen bond of the α-haloester by oxidative addition **1**. This compound dimerizes and rearranges to form two zinc enolates **2**. The oxygen on an aldehyde or ketone coordinates to the zinc to form the six-member chair like transition state **3**. A rearrangement occurs in which zinc switches to the aldehyde or ketone oxygen and a carbon-carbon bond is formed **4**. Acid workup **5**,**6** removes zinc to yield zinc(II) salts and a β-hydroxy-ester **7**.

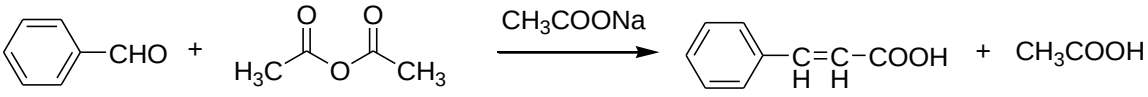


Perkin reaction

The **Perkin reaction** is an organic reaction developed by English chemist William Henry Perkin. In This reaction aromatic aldehyde condense with an acid anhydride to yields an α,β-unsaturated aromatic acid in the presence of an alkali salt of the acid. The alkali salt acts as a base catalyst. Other bases such as sodium carbonate, quinoline, pyridine and triethylamine can also be used.

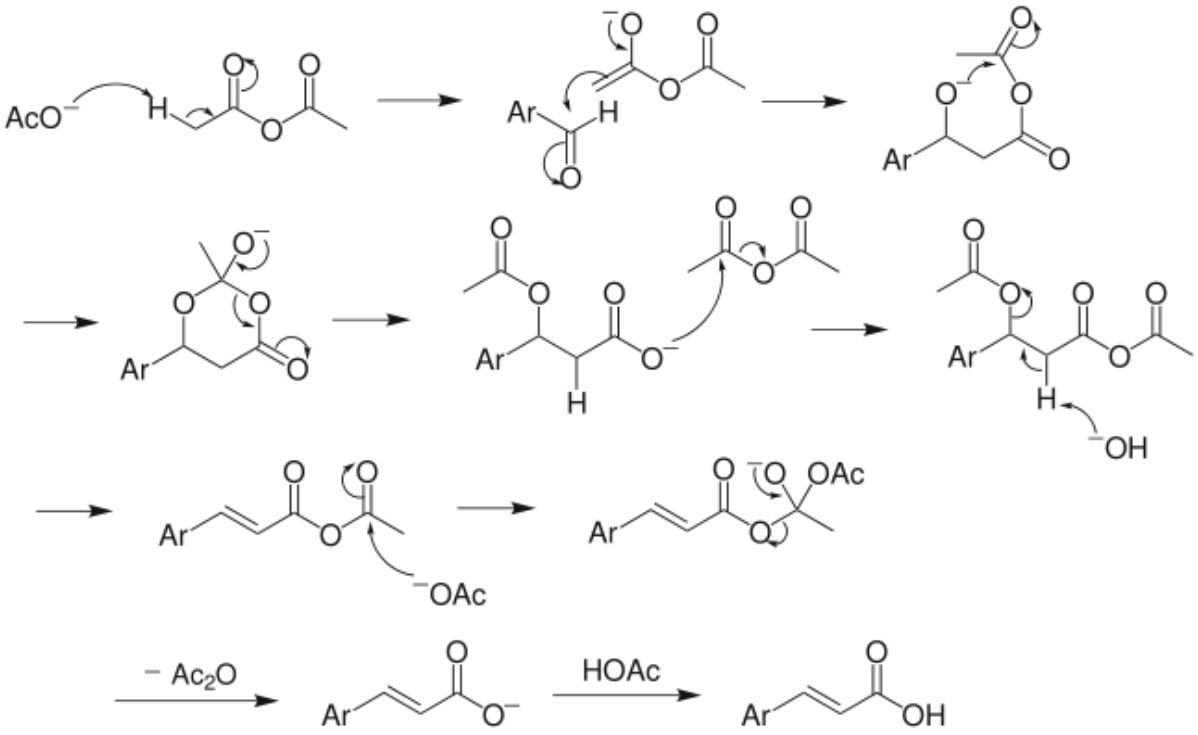


For example



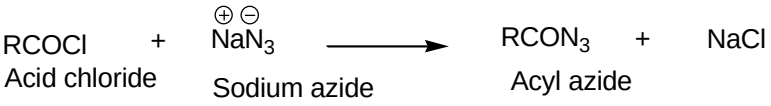
Benzaldehyde | Acetic anhydride | Cinnamic acid

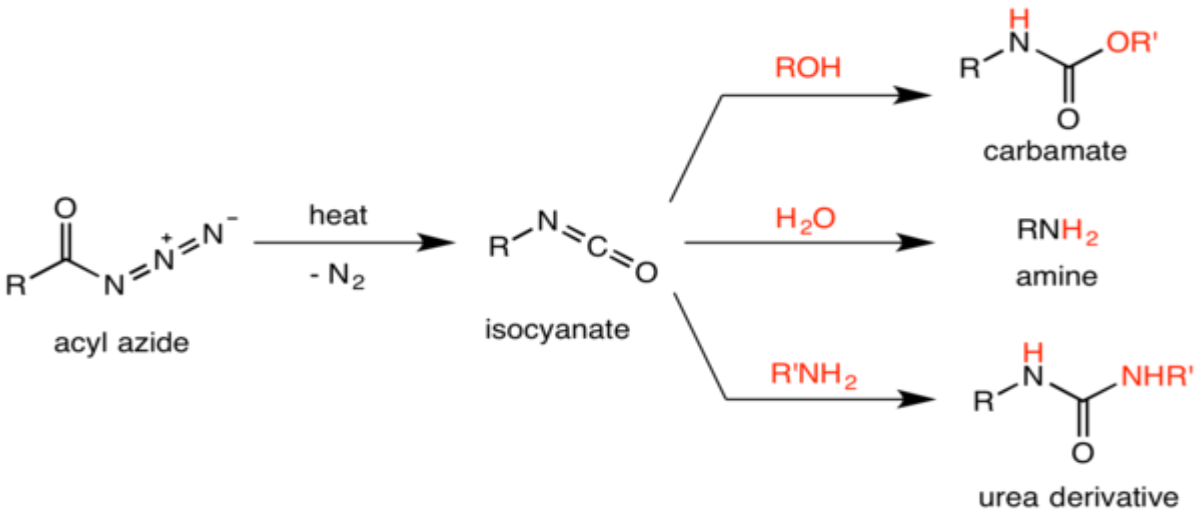
Reaction Mechanism: The function of the base is to abstract an α-hydrogen atom of the anhydride to generate a carbanion which then attacks the carbonyl carbon of the aldehyde to give an anion. Protonation of the anion followed by removal of water produces an unsaturated anhydride which is finally hydrolysed to form the unsaturated acid. The mechanism is as given below



Curtius rearrangement

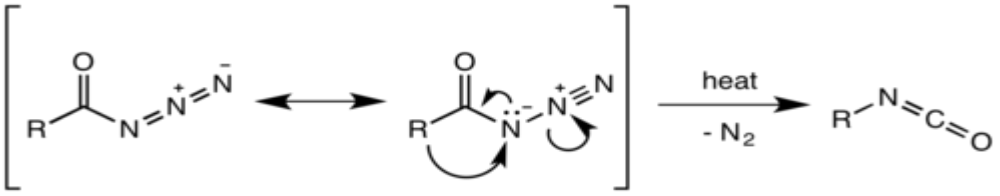
The **Curtius rearrangement** (or **Curtius reaction** or **Curtius degradation**), first defined by Theodor Curtius in 1885, is the thermal decomposition of an acyl azide to an isocyanate with loss of nitrogen gas. The isocyanate then undergoes attack by a variety of nucleophiles such as water, alcohols and amines, to yield a primary amine, carbamate or urea derivative respectively. The acyl azides are prepared from acyl chloride on treatment with sodium azide.





Reaction Mechanism

It was believed that the Curtius rearrangement was a two-step process, with the loss of nitrogen gas forming an acyl nitrene, followed by migration of the R-group to give the isocyanate. However, recent research has indicated that the thermal decomposition is a concerted process, with both steps happening together, due to the absence of any nitrene insertion or addition byproducts observed or isolated in the reaction. Thermodynamic calculations also support a concerted mechanism.



The migration occurs with full retention of configuration at the R-group. The migratory aptitude of the R-group is roughly tertiary > secondary ~ aryl > primary. The isocyanate formed can then be hydrolyzed to give a primary amine, or undergo nucleophilic attack with alcohols and amines to form carbamates and urea derivatives respectively.

-------ooo-------ooo-------

References:

1. Advanced Organic chemistry, Reactions, Mechanism and structure by March, J.(Wiley eastern publishers)
2. Organic chemistry by Morrison and Boyd (Prentice Hall publishers)
3. Organic chemistry by Carey (McGraw Hill publishers)
4. Organic chemistry vol II by Mukherjee, Singh and Kapoor (New Age international publishers)
5. Organic chemistry by Solomons and Fryhle (Wiley india edition)