

## II. CARBOXYLIC ACIDS AND DERIVATIVES

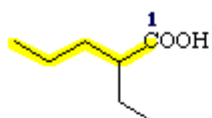
One of the more complex oxygenated alkane is the carboxylated alkane. Carboxylated alkanes have a double bond O (= O) and have an OH on the primary carbon ( $1^{\circ}$  C) of the parent chain. These two groups are on the  $1^{\circ}$  C because carboxylic acids are oxidized aldehydes. Carbon backbone filled with hydrogen. Primary carbon has a substituted carboxylate group. Carboxylate group is a double bond O (= O) and a hydroxyl group (OH).

### Nomenclature carboxylic acid

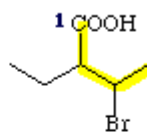
Simple carboxylic acids are named as derivatives of the parent alkane, using the suffix *-oic acid*

1. Select the longest continuous carbon chain, containing the carboxylic acid group, and derive the parent name by replacing the -e ending with -oic acid.
2. Number the carbon chain, beginning at the end nearest to the carboxylic acid group.
3. Number the substituents and write the name, listing substituents alphabetically.
4. Carboxylic acid substituents attached to rings are named using the suffix -carboxylic acid.

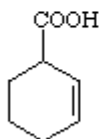
Several simple examples are shown below:



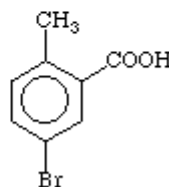
**2-ethylpentanoic acid**



**3-bromo-2-ethylbutanoic acid**



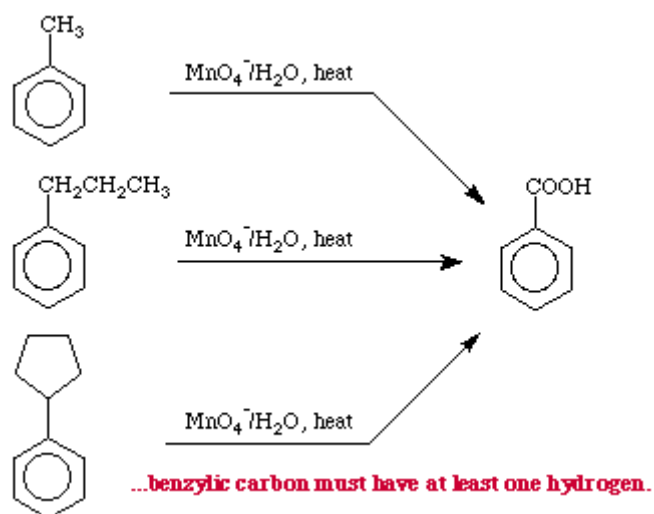
**2-cyclohexenecarboxylic acid**



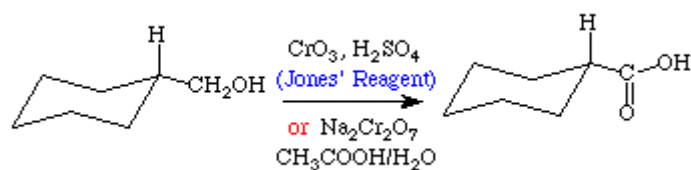
**5-bromo-2-methylbenzoic acid**

## Reactions which Yield Carboxylic Acids

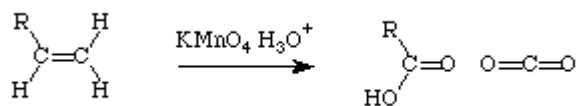
### Oxidation of Aromatic Side-Chains with Neutral Permanganate



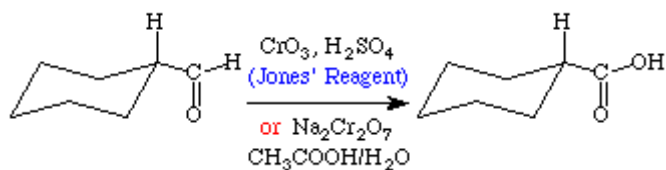
Warm, neutral permanganate anion will oxidize aromatic side-chains which **contain at least one benzylic hydrogen** to the corresponding carboxylic acid.



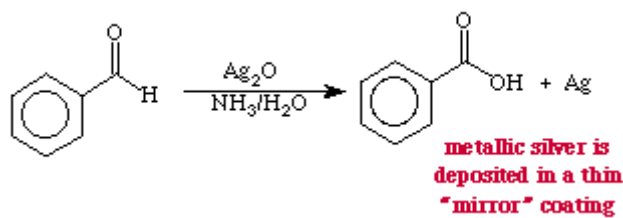
Primary alcohols can be oxidized smoothly to the corresponding carboxylic acid with either  $\text{CrO}_3/\text{H}_2\text{SO}_4$  or sodium dichromate.



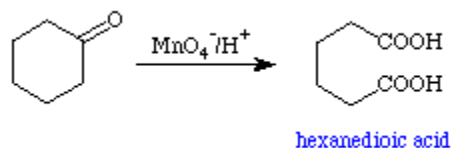
Acidic  $\text{MnO}_4^-$  will oxidize an alkene bearing at least one alkyl or aryl substituent to the corresponding carboxylic acid. Terminal alkenes are converted to  $\text{CO}_2$  under these conditions.



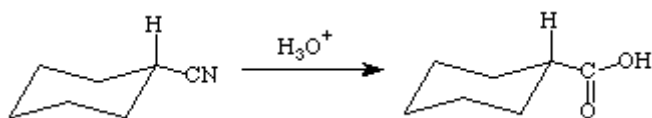
Aldehydes are smoothly oxidized to the corresponding carboxylic acid with either  $\text{CrO}_3/\text{H}_2\text{SO}_4$  or sodium dichromate.



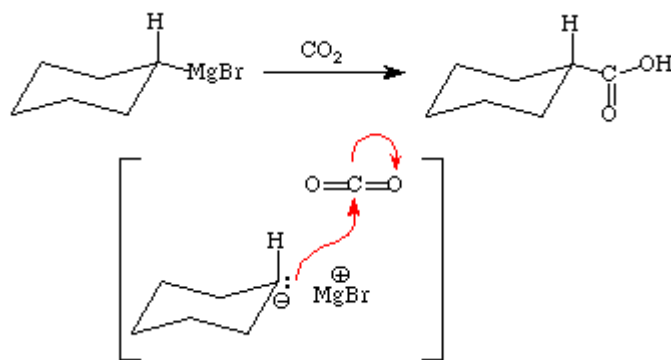
Aldehydes (but not ketones) are oxidized by  $\text{Ag}_2\text{O}$  in aqueous ammonia to give the carboxylic acid and metallic silver. This is used as a qualitative test for aldehydes since the silver metal is deposited in a thin film, forming a "silver mirror" (the Tollens test).



Acidic  $\text{MnO}_4^-$  will oxidize a ketone to the corresponding carboxylic acid, in this case, splitting the ring. The reaction is slower than the oxidation of alkenes, allowing disubstituted alkene carbons to be oxidized to the ketone, without significant over-oxidation.



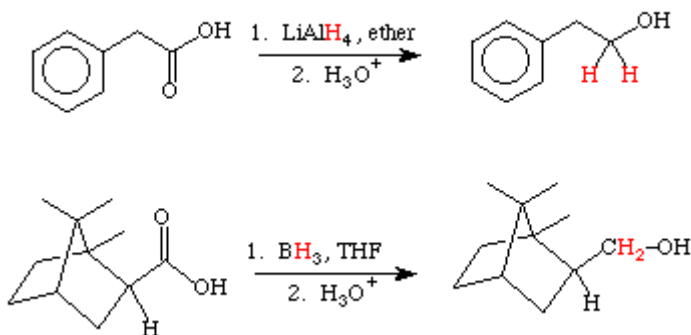
Nitriles can be hydrolyzed to the corresponding carboxylic acids. Typically, vigorous conditions are required (heat and concentrated acid).



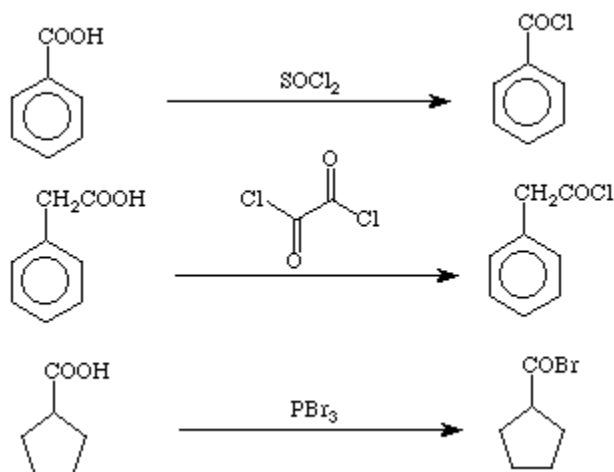
Grignard reagents react with  $\text{CO}_2$  to yield carboxylic acids. This is an important method for the preparation of carboxylic acids and yields are generally good.

### Reactions of Carboxylic Acids

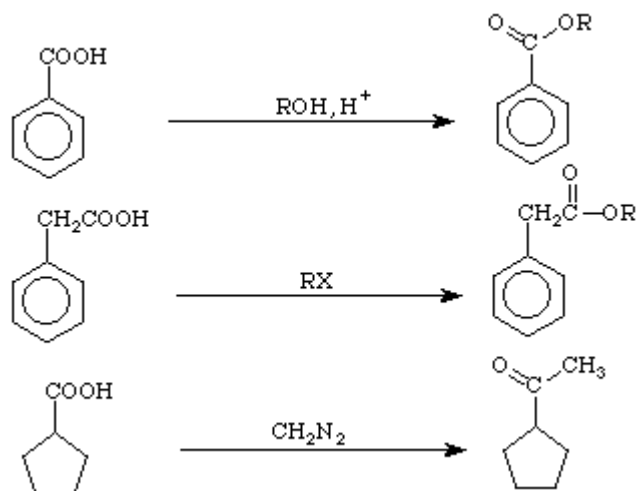
Carboxylic acids can be reduced to primary alcohols with  $\text{LiAlH}_4$ , or with  $\text{BH}_3$ , followed by work-up with aqueous acid. In the reduction with  $\text{LiAlH}_4$ , an intermediate aldehyde is formed, which is rapidly reduced to give the primary alcohol.



Carboxylic acids can be converted into acid halides by reaction with  $\text{SOCl}_2$ , phosgene, or  $\text{PBr}_3$ .

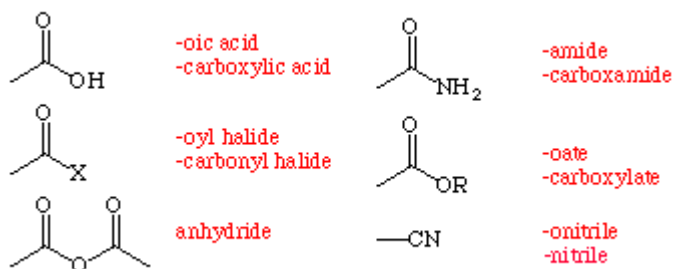


Carboxylic acids can be converted into esters by reaction with the corresponding alcohol in the presence of an acid catalyst (Fischer esterification), by alkylation of the carboxylate anion with an alkyl halide in an  $S_N2$  reaction, or by reaction with diazomethane (methyl esters only).



### Carboxylic Acid Derivatives

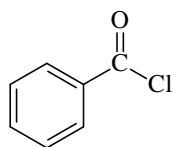
Carboxylic acid derivatives can be converted to the carboxylic acid by acidic or basic hydrolysis. Some carboxylic acid derivatives are given below :



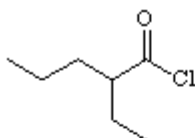
## Acyl Halides

- More reactive than acids; the halogen withdraws  $e^-$  density from carbonyl.
- Named by replacing *-ic acid* with *-yl halide*.
- Simple acid halides are named by identifying the acyl group, using the suffix *-oyl* followed by the halogen.
  1. Select the longest continuous carbon chain, containing the acyl group, and derive the parent name by replacing the *-e* ending with *-oyl*, then append the halogen.
  2. Number the carbon chain, beginning at the end nearest to the acyl group.
  3. Number the substituents and write the name, listing substituents alphabetically.
  4. Acid halide substituents attached to rings are named using the suffix *-carbonyl*.

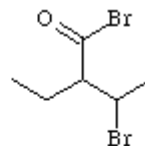
Several simple examples are shown below:



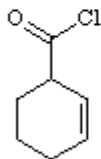
Benzoyl chloride



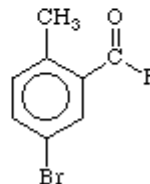
2-ethylpentanoyl chloride



3-bromo-2-ethylbutanoyl bromide

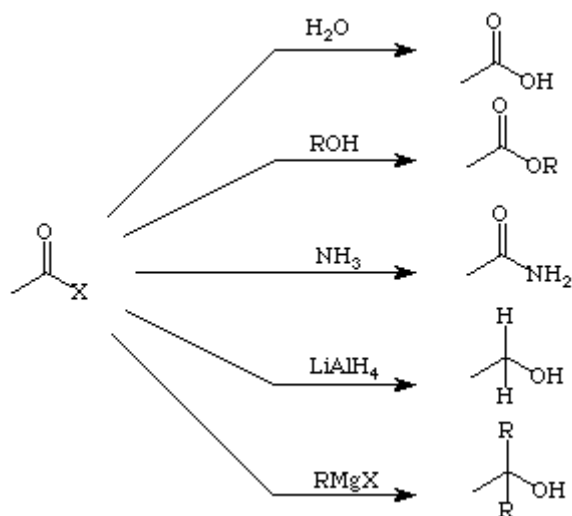


2-cyclohexenecarbonyl chloride

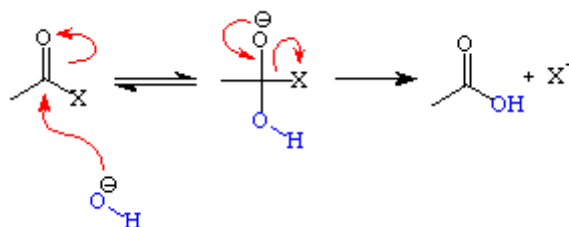


5-bromo-2-methylbenzoyl fluoride

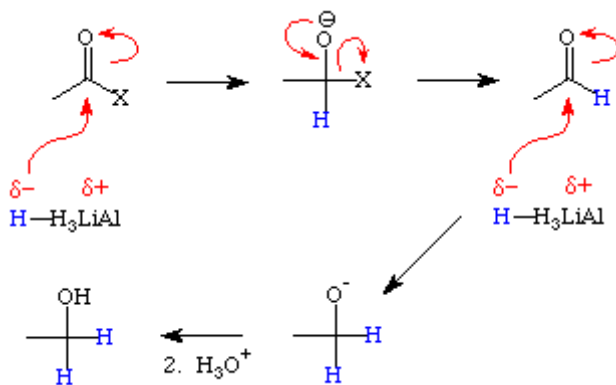
Acid halides are the most reactive acyl derivatives, and can be readily converted into carboxylic acids, esters and amides, by simple reaction with the appropriate nucleophile. The reaction involves an addition-elimination mechanism, as shown below:



Reaction of acid halides with Grignard reagents, or reduction with  $\text{LiAlH}_4$ , leads to the incorporation of **two moles** of Grignard (or hydride), in a mechanism which involves an intermediate aldehyde or ketone, as shown below for hydride reduction.

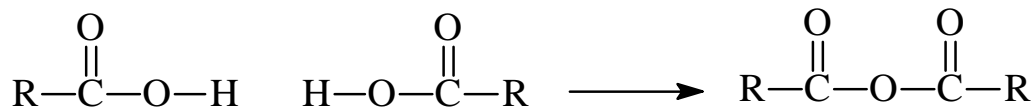


When a bulky reducing agent, such as lithium tri-tert-butoxyaluminum hydride is utilized, the reduction of acyl halides can be stopped at the intermediate aldehyde.



## Acid Anhydrides

- Two molecules of acid combine with the loss of water to form the anhydride.
- Anhydrides are more reactive than acids, but less reactive than acid chlorides.
- A carboxylate ion is the leaving group in nucleophilic acyl substitution reactions.

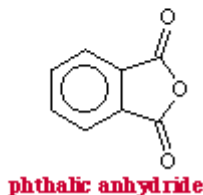
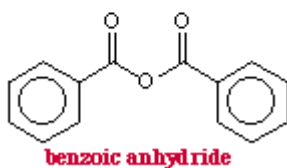
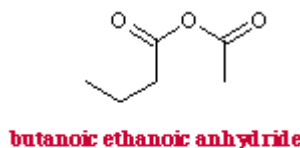
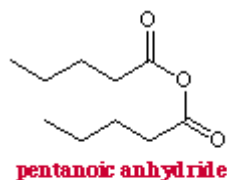


## Nomenclature acid anhydrides

Simple acid anhydrides are named by replacing the ending "acid" with "anhydride".

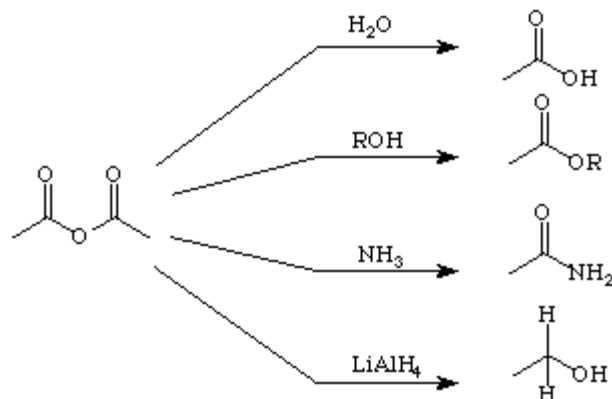
1. Select the longest continuous carbon chain, containing the carboxylic acid group, and derive the parent name by replacing the -e ending with -oic anhydride.
2. Number the carbon chain, beginning at the end nearest to the acyl group.
3. Number the substituents and write the name, listing substituents alphabetically.

Several simple examples are shown below:

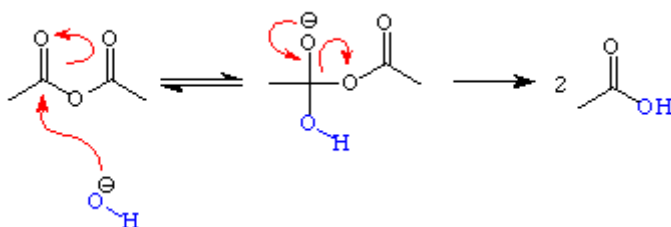


Acid halides are the next most reactive acyl derivatives, and can be readily converted into carboxylic acids, esters and amides, by simple reaction with the appropriate nucleophile.

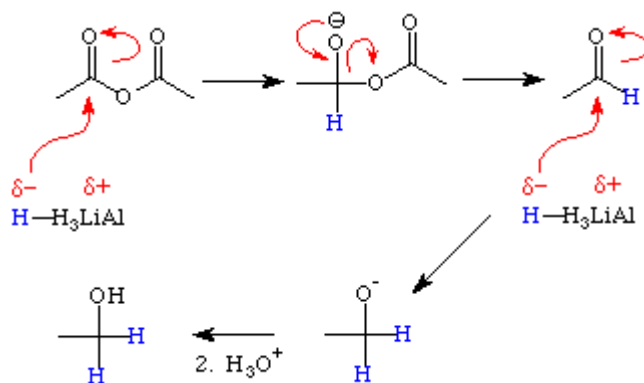




The reaction involves an addition-elimination mechanism, as shown below:



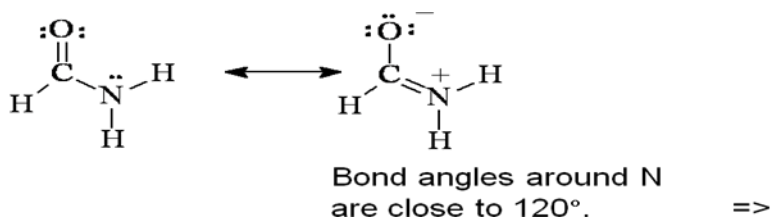
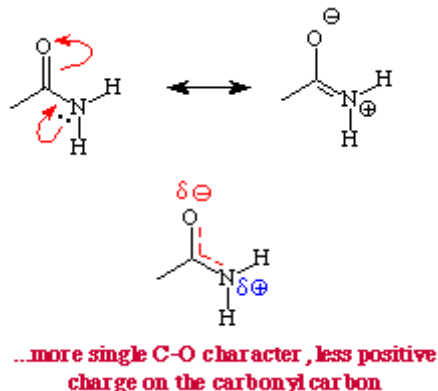
As with acid halides, reduction of anhydrides with  $\text{LiAlH}_4$  results in the addition of **two moles** of hydride, forming the primary alcohol.



## Amides

Product of the reaction of a carboxylic acid and ammonia or an amine. Not basic because the lone pair on nitrogen is delocalized by resonance. Amides are relatively unreactive in acyl transfer reactions, largely because the electrons from the adjacent nitrogen participate in

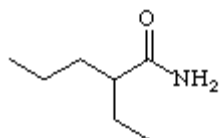
resonance delocalization with the adjacent carbonyl, making the carbonyl carbon significantly less electropositive.



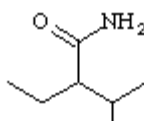
**Simple amides are named by replacing the ending -oic acid with -amide .**

1. Select the longest continuous carbon chain, containing the acyl group, and derive the parent name by replacing the -e ending with -amide.
2. Number the carbon chain, beginning at the end nearest to the acyl group.
3. Number the substituents and write the name, listing substituents alphabetically.
4. Acid halide substituents attached to rings are named using the suffix -carboxamide.
5. If the nitrogen atom is further substituted, the substituents are preceded by N- to indicate that they are attached to the nitrogen.

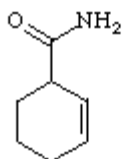
Several simple examples are shown below:



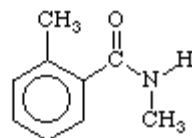
**2-ethylpentanamide**



**3-bromo-2-ethylbutanamide**



**2-cyclohexanecarboxamide**



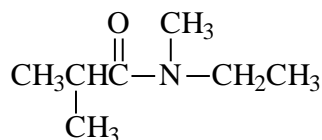
**N-methyl-5-bromo-2-methylbenzamide**

### Classes of Amides

- 1° amide has one C-N bond (two N-H).
- 2° amide or *N*-substituted amide has two C-N bonds (one N-H).
- 3° amide or *N,N*-disubstituted amide has three C-N bonds (no N-H).

### Nomenclature amides

- For 1° amide, drop *-ic* or *-oic acid* from the carboxylic acid name, add *-amide*.
- For 2° and 3° amides, the alkyl groups bonded to nitrogen are named with *N-* to indicate their position.

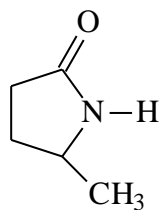


*N*-ethyl-*N*,2-dimethylpropanamide

*N*-ethyl-*N*-methylisobutyramide

### Cyclic Amides

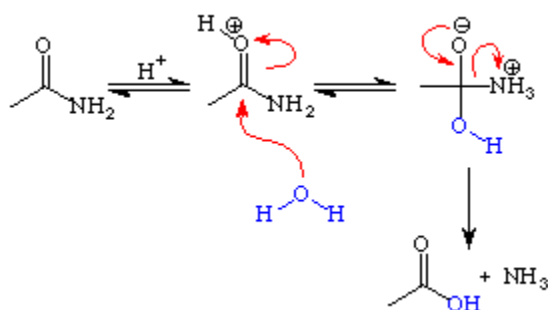
- Reaction of  $-\text{NH}_2$  and  $-\text{COOH}$  on same molecule produces a cyclic amide, lactam.
- To name, add word *lactam* to the IUPAC acid name or replace the *-ic acid* of common name with *-olactam*.



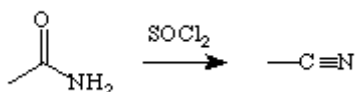
4-aminopentanoic acid lactam

$\gamma$ -valerolactam

Amides undergo **acid-catalyzed** hydrolysis to give carboxylic acids by the addition-elimination mechanism shown below:



Unsubstituted amides also undergo **dehydration** in the presence of  $\text{SOCl}_2$  to give the corresponding nitrile.

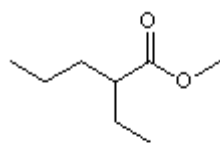


## Ester

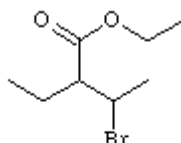
Simple carboxylate esters are named as derivatives of the carboxylic acid, by changing the suffix *-oic acid* to *-oate*, and naming the alcohol portion *first*.

1. Select the longest continuous carbon chain, containing the acyl group, and derive the parent name by replacing the *-e* ending with *-oate*, then append the the alcohol to the front of the name.
2. Number the carbon chain, beginning at the end nearest to the acyl group.
3. Number the substituents and write the name, listing substituents alphabetically.
4. Acid halide substituents attached to rings are named using the suffix *-carboxylate*.

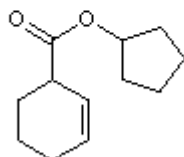
Several simple examples are shown below:



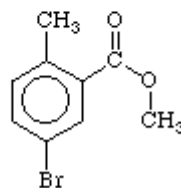
**methyl 2-ethylpentanoate**



**ethyl 3-bromo-2-ethylbutanoate**

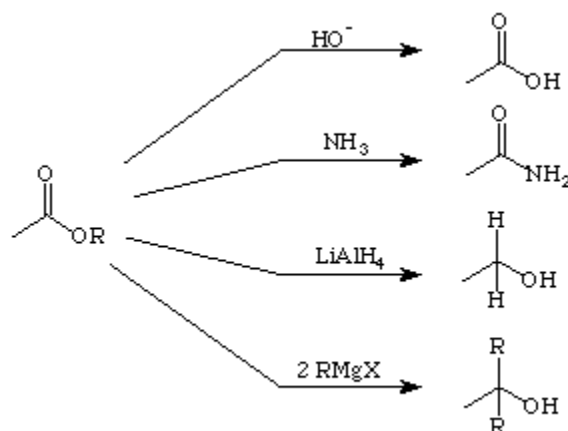


**cyclopentyl 2-cyclohexene-1-carboxylate**

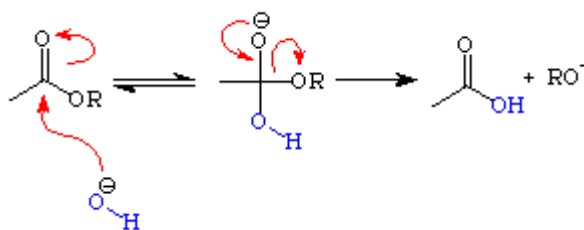


**methyl 5-bromo-2-methylbenzoate**

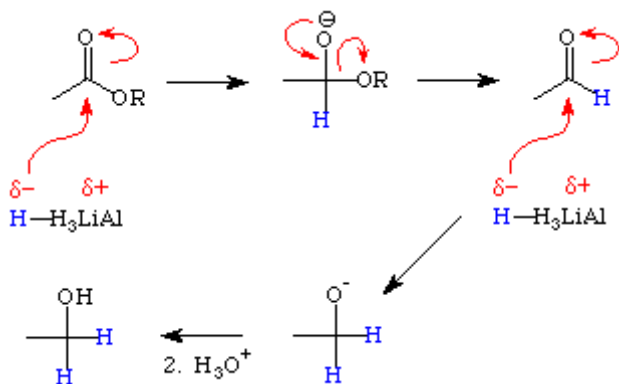
Carboxylate esters can be readily converted into carboxylic acids and amides, by simple reaction with the appropriate nucleophile.



The reaction involves an addition-elimination mechanism, as shown below:

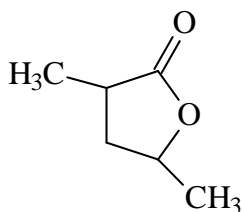


Reaction of esters with Grignard reagents, or reduction with  $\text{LiAlH}_4$ , leads to the incorporation of **two moles** of Grignard (or hydride), in a mechanism which involves an intermediate aldehyde or ketone, as shown below for hydride reduction.



### Cyclic Esters

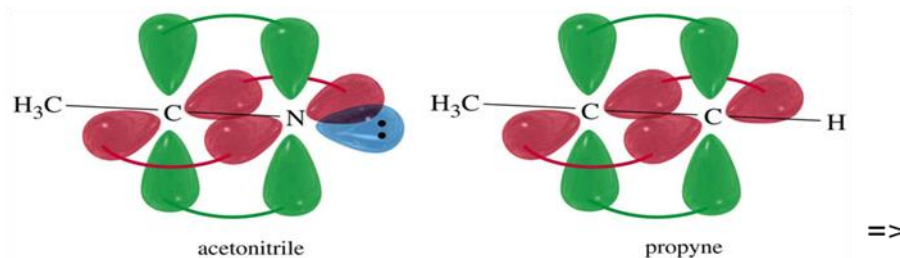
Reaction of  $-\text{OH}$  and  $-\text{COOH}$  on same molecule produces a cyclic ester, lactone. To name, add word *lactone* to the IUPAC acid name or replace the *-ic acid* of common name with *-olactone*.



4-hydroxy-2-methylpentanoic acid lactone  
 $\alpha$ -methyl- $\gamma$ -valerolactone

### Nitriles

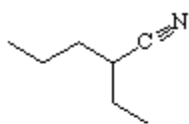
- $-\text{C}\equiv\text{N}$  can be hydrolyzed to carboxylic acid, so nitriles are acid derivatives.
- Nitrogen is *sp* hybridized, lone pair tightly held, so not very basic ( $\text{p}K_b$  about 24).



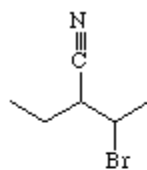
**Simple nitriles are named as derivatives of the parent alkane, using the suffix *-nitrile* to *-oate*, and naming the alcohol portion *first*.**

1. Select the longest continuous carbon chain, containing the nitrile, and derive the parent name by appending **-nitrile**.
2. Number the carbon chain, beginning at the end nearest to the nitrile group.
3. Number the substituents and write the name, listing substituents alphabetically.
4. Acid halide substituents attached to rings are named using the suffix *-carbonitrile*.

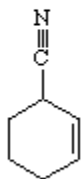
Several simple examples are shown below:



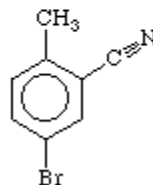
**2-ethylpentanenitrile**



**3-bromo-2-ethylbutanenitrile**



**2-cyclohexenecarbonitrile**



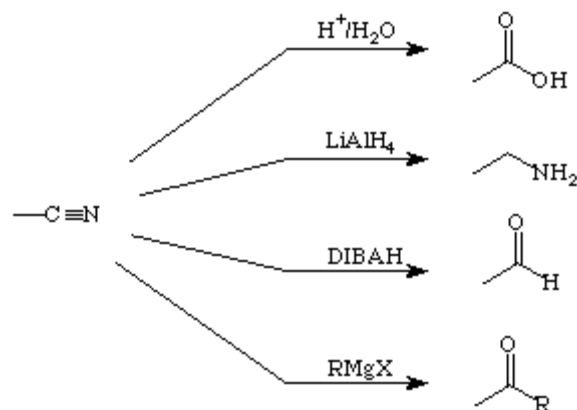
**5-bromo-2-methylbenzonitrile**



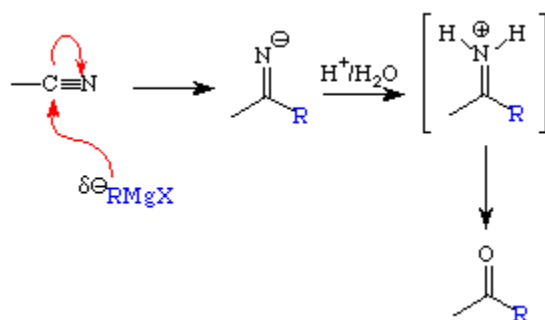
5-bromohexanenitrile

$\delta$ -bromocapronitrile

Nitriles can be hydrolyzed to carboxylic acids, converted into ketones by reaction with Grignard reagents, reduced to primary amines with  $\text{LiAlH}_4$  and partially reduced to aldehydes using DIBALH (diisobutylaluminum hydride).

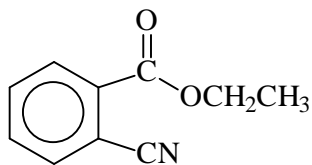


The reaction with Grignard reagent is typical of these latter reactions and involves nucleophilic attack on the nitrile carbon to give an anionic intermediate which is resistant to further attack, and undergoes hydrolysis to give a ketone, as shown below.



### Multifunctional Compounds

- The functional group with the highest priority determines the parent name.
- Acid > ester > amide > nitrile > aldehyde > ketone > alcohol > amine > alkane > alkene > alkane.



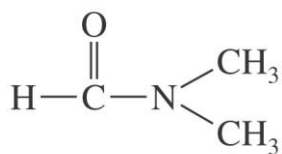
ethyl *o*-cyanobenzoate



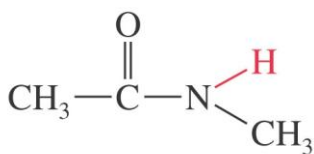
## Physical properties

### Melting Points

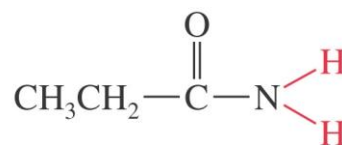
- Amides have very high melting points.
- Melting points increase with increasing number of N-H bonds.



m.p.  $-61^{\circ}\text{C}$



m.p.  $28^{\circ}\text{C}$

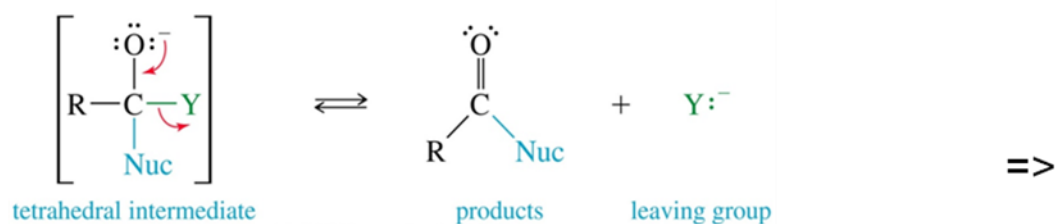
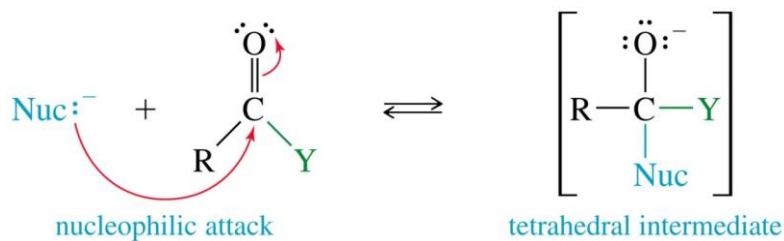


m.p.  $79^{\circ}\text{C}$

### Solubility

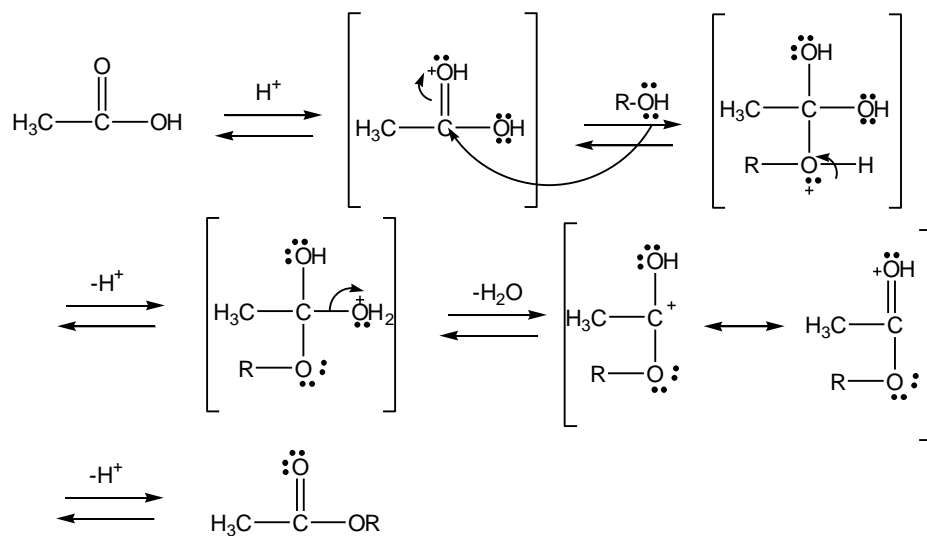
- Acid chlorides and anhydrides are too reactive to be used with water or alcohol.
- Esters, 3° amides, and nitriles are good polar aprotic solvents.
- Solvents commonly used in organic reactions: Ethyl acetate; Dimethylformamide (DMF) Acetonitrile

## Interconversion of Acid Derivatives



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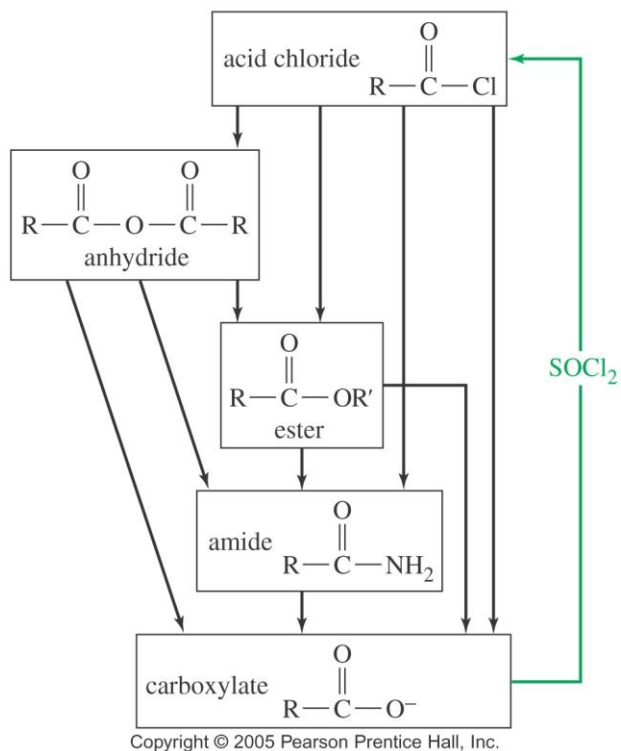
## Example mechanism of esterification



## Reactivity

<i>Reactivity</i>	<i>Derivative</i>	<i>Leaving group</i>	<i>Basicity</i>
more reactive	acid chloride $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{Cl}$	$\text{Cl}^-$	less basic
	anhydride $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}$	$-\text{O}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}$	
	ester $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\text{R}'$	$-\text{O}-\text{R}'$	
	amide $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$	$-\text{NH}_2$	
less reactive	carboxylate $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}^-$	—	more basic

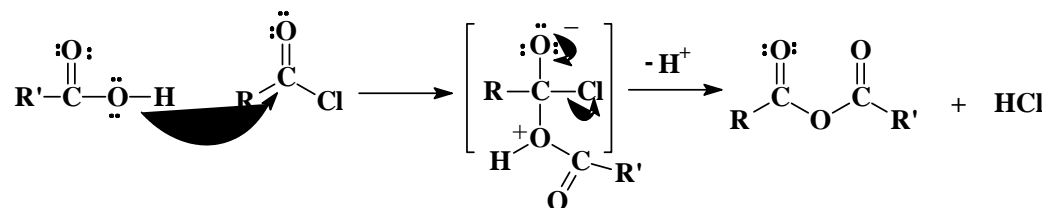
## Interconversion of Derivatives



More reactive derivatives can be converted to less reactive derivatives.

### Acid Chloride to Anhydride

- Acid *or* carboxylate ion attacks the C=O.
- Tetrahedral intermediate forms.
- Chloride ion leaves, C=O is restored,  $\text{H}^+$  is abstracted.



## Acid Chloride to Ester

- Alcohol attacks the C=O.
- Tetrahedral intermediate forms.
- Chloride ion leaves, C=O is restored, H<sup>+</sup> is abstracted.

