



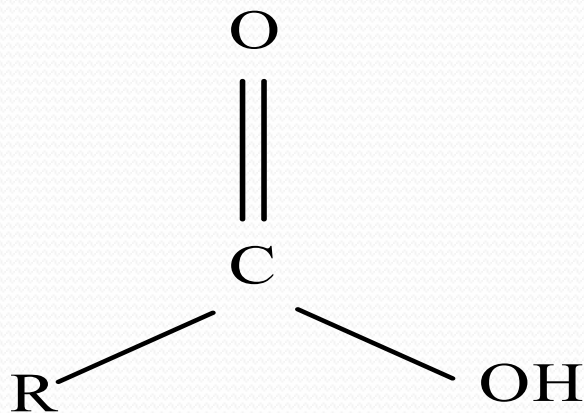
CARBOXYLIC ACIDS AND THEIR DERIVATIVES

Carboxylic Acids

- Carboxylic acid and their derivatives are the most abundant organic compounds present in living organisms and synthesized in laboratory.
- Carboxylic acids are present in many industrial processes and most biological processes.
- Abundant in nature from oxidation of aldehydes and alcohols in metabolism.
 - Acetic acid, $\text{CH}_3\text{CO}_2\text{H}$, - vinegar.
 - Butanoic acid, $\text{CH}_3\text{CH}_2\text{CH}_2\text{CO}_2\text{H}$ (rancid butter).
 - Long-chain aliphatic acids from the breakdown of fats.

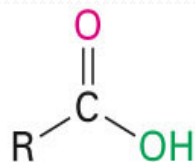
Carboxylic Acid Structure

- The functional group of a carboxylic acid is a carboxyl group.
- The general formula of an aliphatic carboxylic acid is RCO_2H ; that of an aromatic carboxylic acid is ArCO_2H

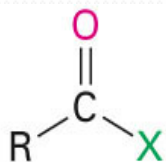


Derivatives Of Carboxylic Acids

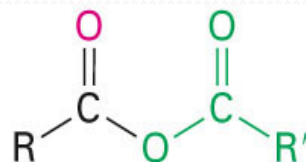
The different kinds of carboxylic acid derivatives are;



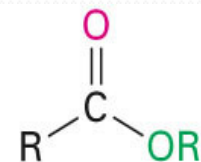
Carboxylic acid



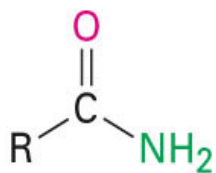
Acid halide
(X = Cl, Br)



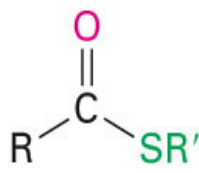
Acid anhydride



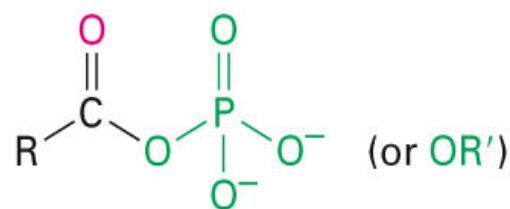
Ester



Amide



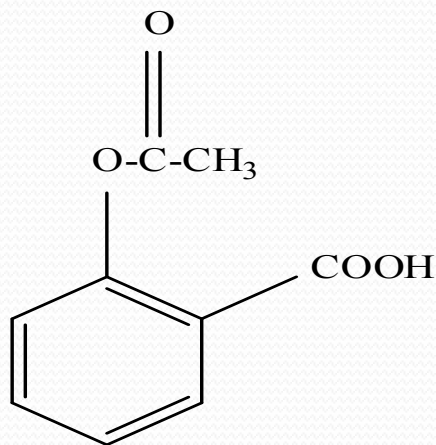
Thioester



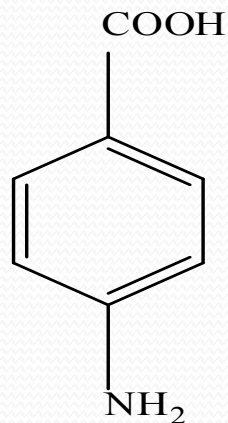
Acyl phosphate

Importance Of Carboxylic Acids

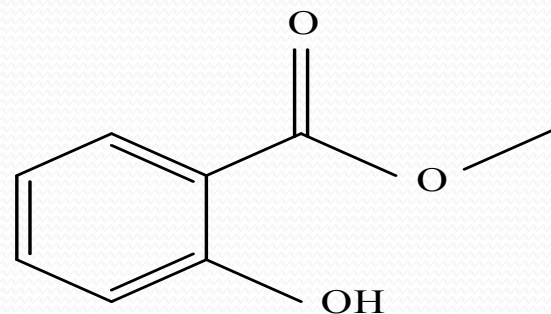
- Aspirin is one of the safest and widely used drugs.
- *p*-Aminobenzoic acid (PABA) - sunblock creams.
- Penicillins an antibiotic, are large group of carboxylic acid derivatives.
- Methyl salicylate – an aromatic component of heat rub.



Aspirin



p-Aminobenzoic acid
PABA

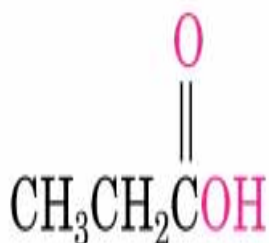


Methyl Salicylate

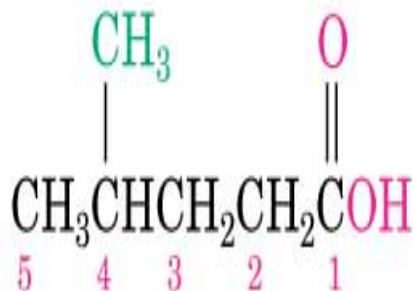
Naming Carboxylic Acids And Derivatives

Carboxylic Acids, RCO_2H .

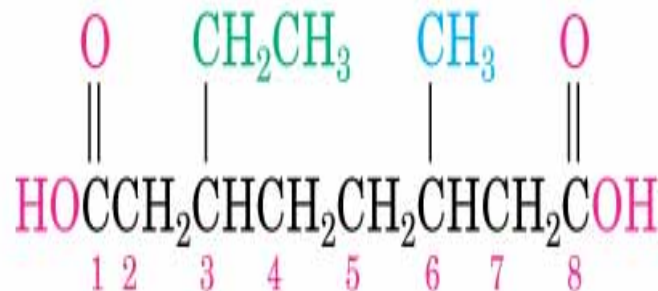
- If derived from open-chain alkanes, replace the terminal -e of the alkane name with -oic acid.
- The $-\text{COOH}$ carbon atom is always numbered C1.



Propanoic acid
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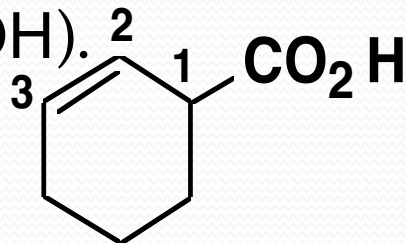
4-Methylpentanoic acid



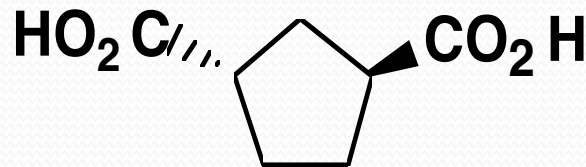
3-Ethyl-6-methyloctanedioic acid

Naming Carboxylic Acids And Derivatives

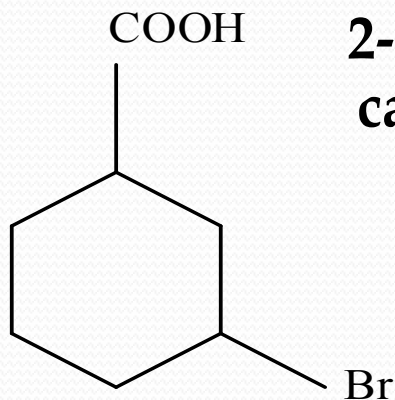
- Compounds with $\text{—CO}_2\text{H}$ bonded to a ring are named using the suffix *-carboxylic acid*.
- The CO_2H carbon is not itself numbered in this system.
- Use common names for formic acid (HCOOH) and acetic acid (CH_3COOH).



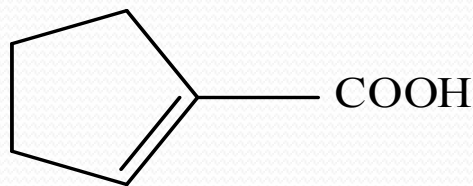
**2-Cyclohexene-
carboxylic acid**



**trans-1,3-Cyclopentane-
dicarboxylic acid**



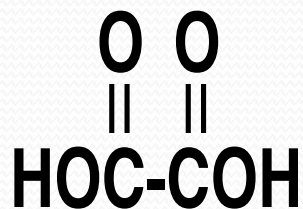
**3-Bromocyclohexane
carboxylic acid**



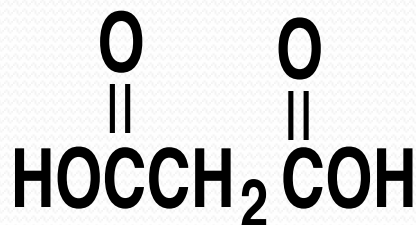
Cyclopent-1-ene-1-carboxylic acid

Naming Carboxylic Acids

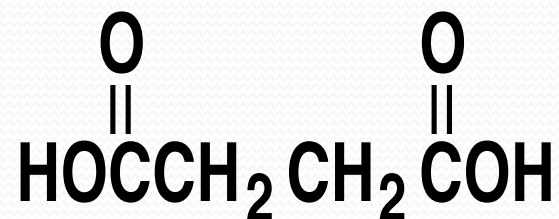
Dicarboxylic acids: add the suffix -dioic acid to the name of the parent alkane containing both carboxyl groups.



Ethanedioic acid
(Oxalic acid)



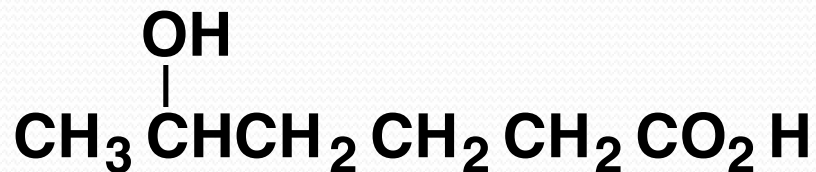
Propanedioic acid
(Malonic acid)



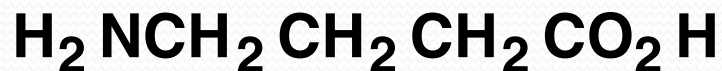
Butanedioic acid
(Succinic acid)

Naming Carboxylic Acids

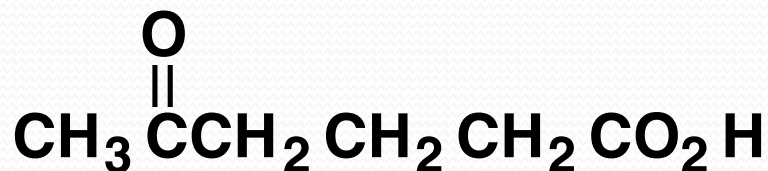
The carboxyl group takes precedence over most other functional groups.



5-Hydroxyhexanoic acid



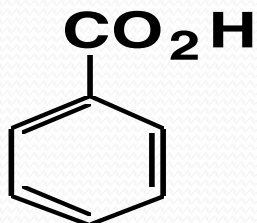
4-Aminobutanoic acid



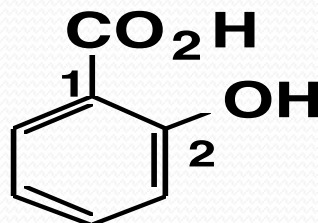
5-Oxohexanoic acid

Naming Carboxylic Acids

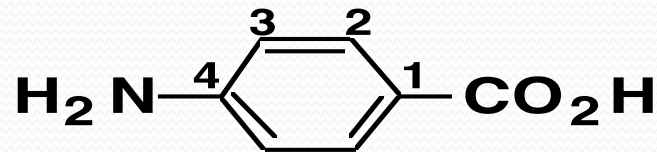
- The simplest aromatic carboxylic acid is benzoic acid. Derivatives are named using numbers to show the location of substituent's relative to the carboxyl group.



Benzoic acid

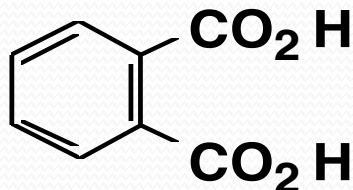


2-Hydroxybenzoic acid
(Salicylic acid)



4-Aminobenzoic acid

- Aromatic dicarboxylic acids are named by adding the words "dicarboxylic acid" to "benzene."



1,2-Benzenedicarboxylic acid
(Phthalic acid)



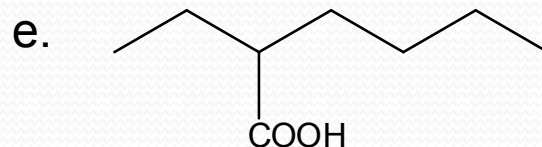
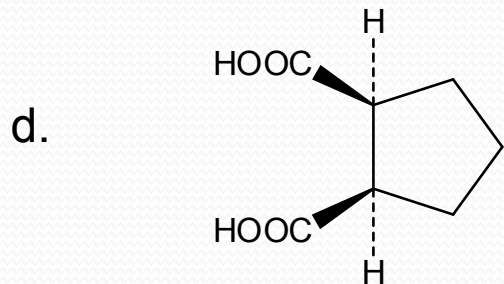
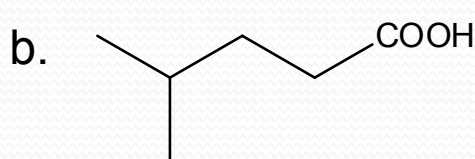
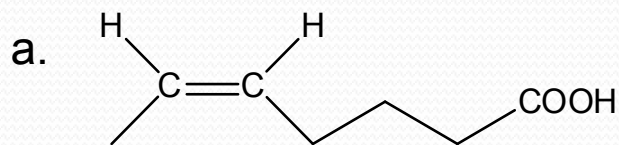
1,4-Benzenedicarboxylic acid
(Terephthalic acid)

Practice Examples

1. Draw the structures corresponding to the following names:

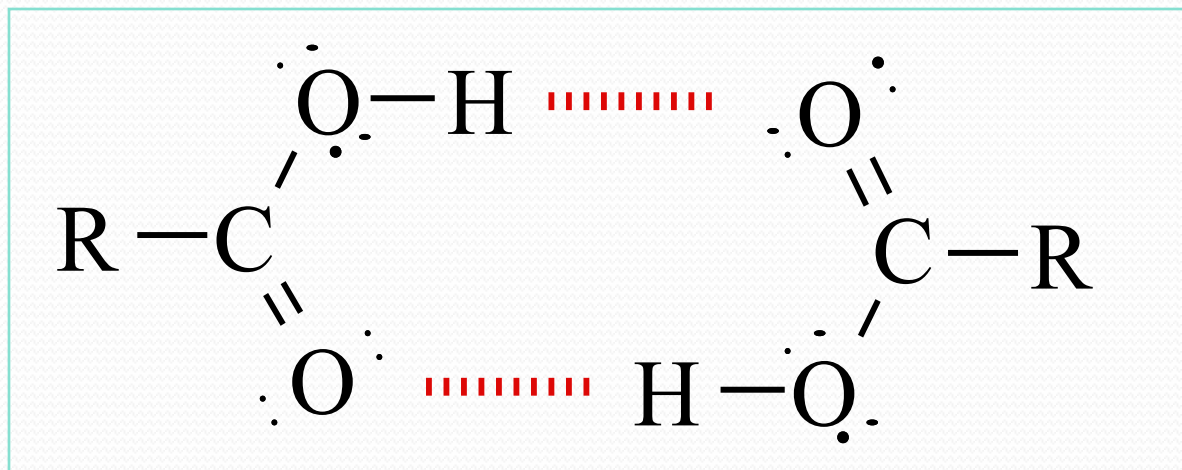
- 2,3-Dimethylhexanoic acid.
- 0-Hydroxybenzoic acid.
- Trans-Cyclobutane-1,2-dicarboxylic acid.
- 4-Methylpentanoic acid.

2. Give the IUPAC names for the following carboxylic acids.



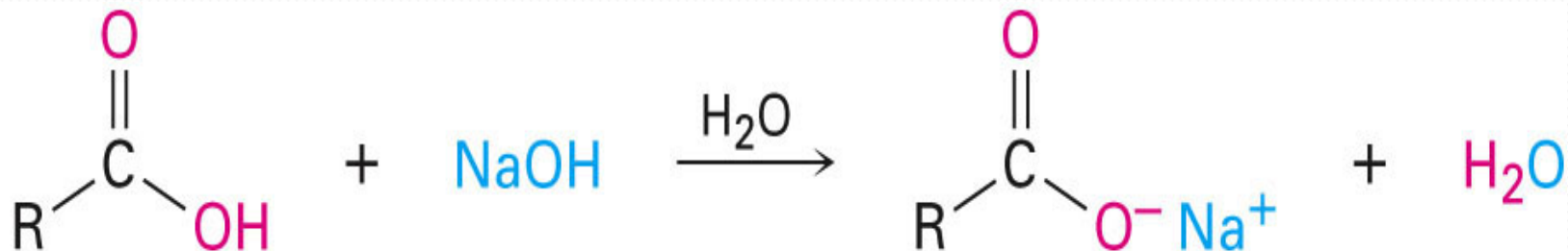
Physical Properties

- Carboxyl carbon sp^2 hybridized: carboxylic acid groups are planar with C–C=O and O=C–O bond angles of approximately 120° .
- Carboxylic acids form hydrogen bonds, existing as cyclic dimers held together by two hydrogen bonds.
- Strong hydrogen bonding causes much higher boiling points than the corresponding alcohols.



Acidity Of Carboxylic Acids

- Carboxylic acids are proton donors toward weak and strong bases, producing metal carboxylate salts, $\text{RCO}_2^- \text{M}^+$.
- Carboxylic acids with more than six carbons are only slightly soluble in water, but their conjugate base salts are water-soluble.



**A carboxylic acid
(water-insoluble)**

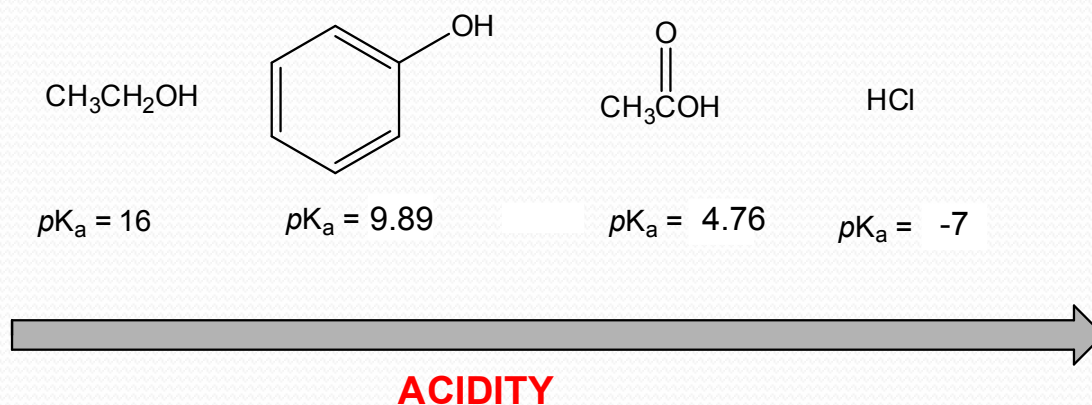
**A carboxylic acid salt
(water-soluble)**

Acidity Of Carboxylic Acids

- Carboxylic acids transfer a proton to water to give H_3O^+ and carboxylate anions, RCO_2^- .
- The carboxylate anion is resonance stabilized.
- The acidity constant, K_a , is about 10^{-5} for a typical carboxylic acid ($\text{p}K_a \sim 5$).

Acidity of Carboxylic acids

- Carboxylic acids are much stronger than alcohols and phenols.
- Carboxylic acids are much weaker than mineral acids (HCl).

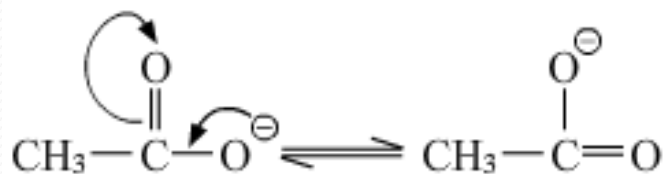
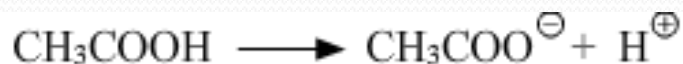


Acidity of Carboxylic acids

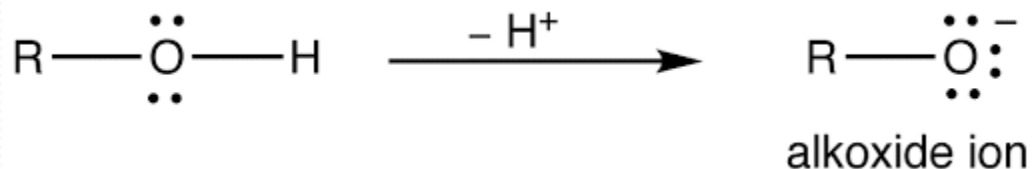
Carboxylic acids are much more acidic than alcohols.

A carboxylate anion is more stable than the alkoxide ion.

The carboxylate anion is resonance stabilized, as the negative charge is spread out over both the oxygen atoms.

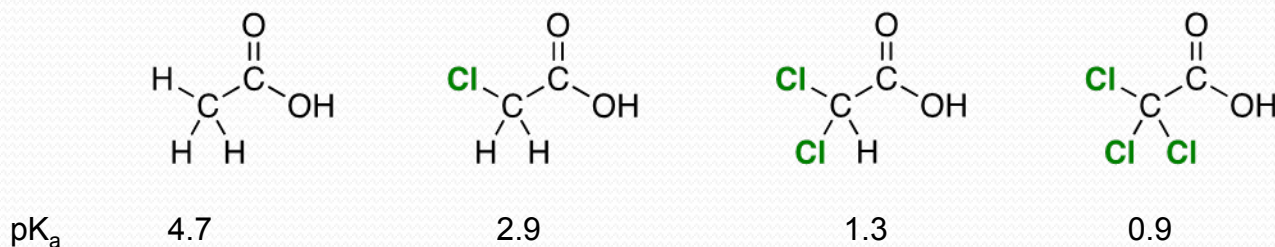
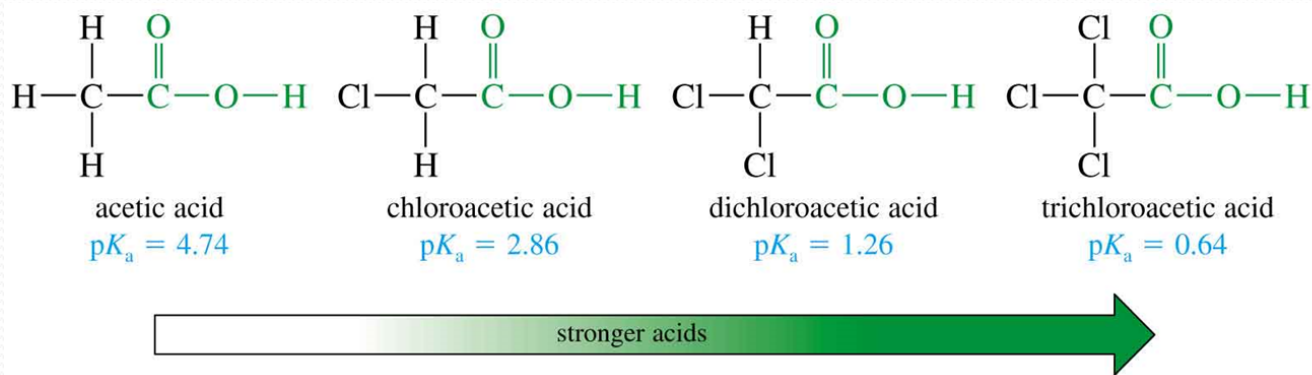


Resonating structure of carboxylate ion.



Acidity of Carboxylic acids

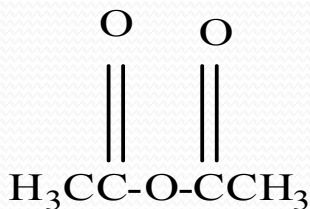
- The presence of electron-withdrawing substituents increases the acidity.
- The acid strength of some carboxylic acids.



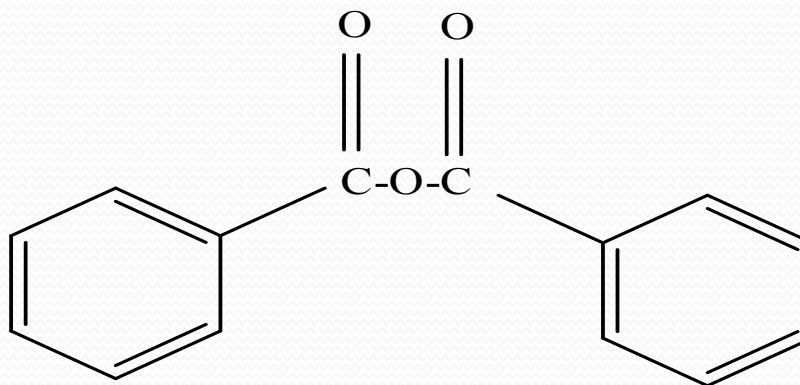
Derivatives Of Carboxylic Acids

Anhydrides: $\text{RCO}_2\text{CO R}'$

- Anhydrides are named by replacing the word acid with anhydride.



Acetic anhydride

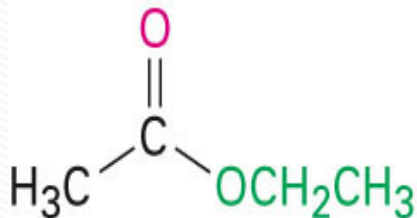


Benzoic anhydride

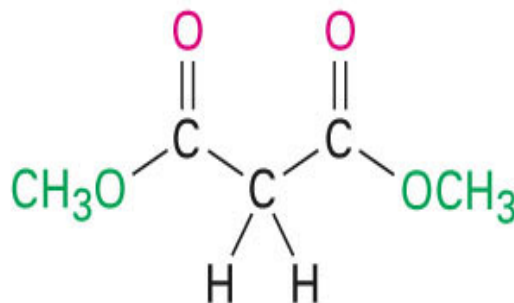
Derivatives Of Carboxylic Acids

Esters: RCOOR'

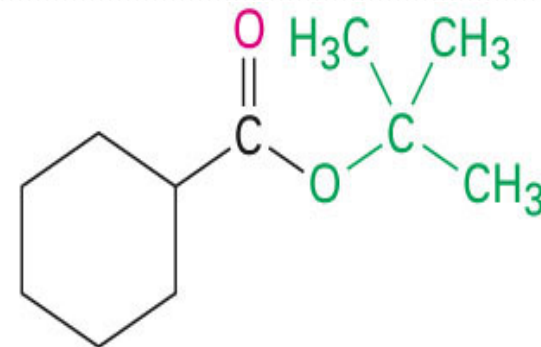
- In naming esters, *-ic acid* ending is replaced by *-ate*.



Ethyl acetate



Dimethyl malonate

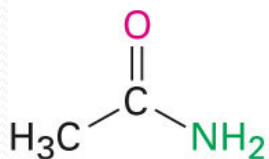


***tert*-Butyl cyclohexane-carboxylate**

Derivatives Of Carboxylic Acids

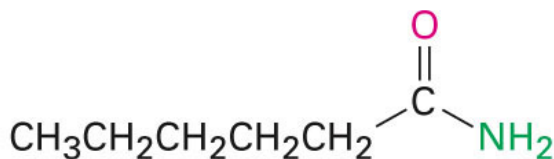
Amides: RCONH_2

- Amides with an unsubstituted $-\text{NH}_2$ group are named by replacing the $-\text{oic acid}$ or $-\text{ic acid}$ ending with $-\text{amide}$, or by replacing the $-\text{carboxylic acid}$ with $-\text{carboxamide}$.

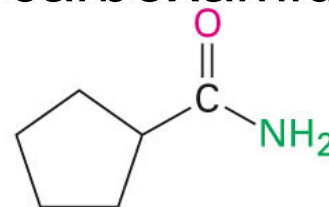


Acetamide

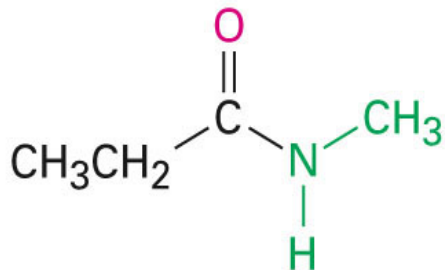
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Hexanamide

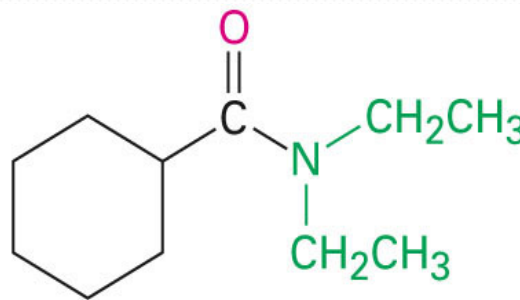


**Cyclopentane-
carboxamide**



***N*-Methylpropanamide**

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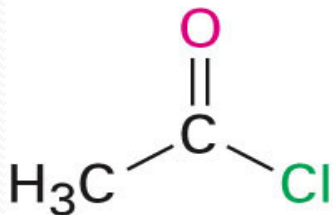


***N,N*-Diethylcyclohexanecarboxamide**

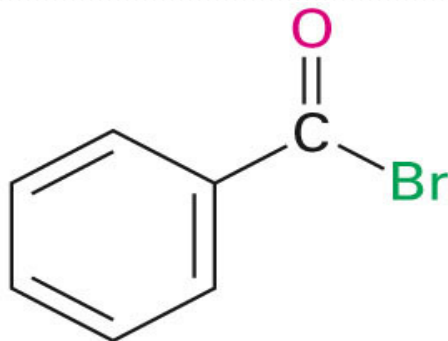
Derivatives Of Carboxylic Acids

Acid Chlorides: RCOCl

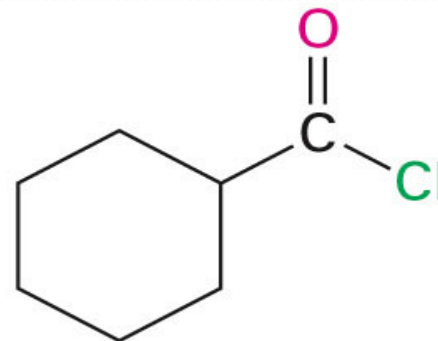
- The acyl group name is derived from acid name by replacing the *-ic acid* ending with *-yl*, or the *-carboxylic acid* ending with *-carbonyl*.



**Acetyl
chloride**



**Benzoyl
bromide**



**Cyclohexanecarbonyl
chloride**

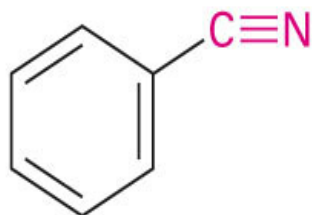
Derivatives Of Carboxylic Acids

Nitriles: $R-C\equiv N$

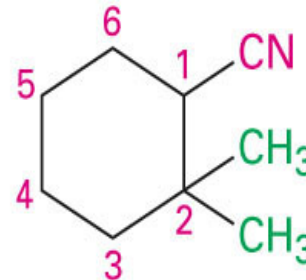
- Compounds containing $-CN$ functional group are called nitriles. Nitriles are named by replacing the *-ic acid* or *-oic acid* ending with *-onitrile*, or by replacing the *-carboxylic acid* ending with *-carbonitrile*.



Acetonitrile
(from acetic acid)



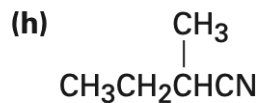
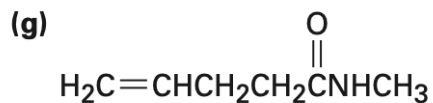
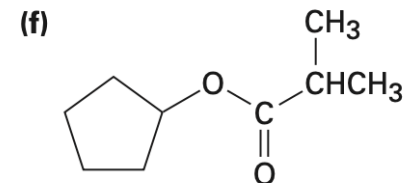
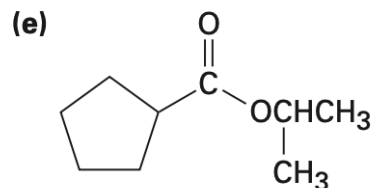
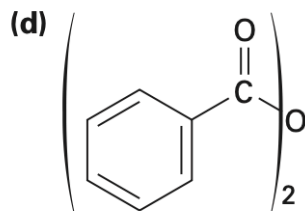
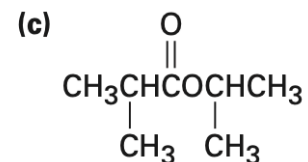
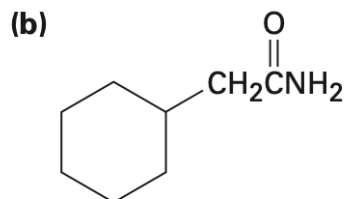
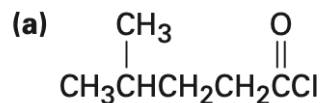
Benzonitrile
(from benzoic acid)



2,2-Dimethylcyclohexanecarbonitrile
(from 2,2-dimethylcyclohexane-carboxylic acid)

Problem 10.3

Give IUPAC names for the following acyl derivatives:

**Problem 10.4**

Draw structures corresponding to the following names:

(a) 2,2-Dimethylpropanoyl chloride

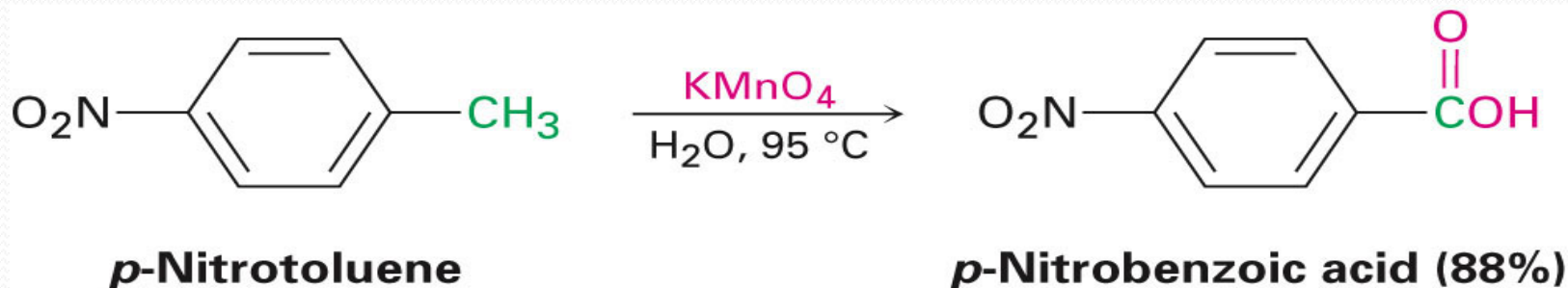
(b) *N*-Methylbenzamide

(c) 5,5-Dimethylhexanenitrile

(d) *tert*-Butyl butanoate(e) *trans*-2-Methylcyclohexanecarboxamide(f) *p*-Methylbenzoic anhydride(g) *cis*-3-Methylcyclohexanecarbonyl bromide(h) *p*-Bromobenzonitrile

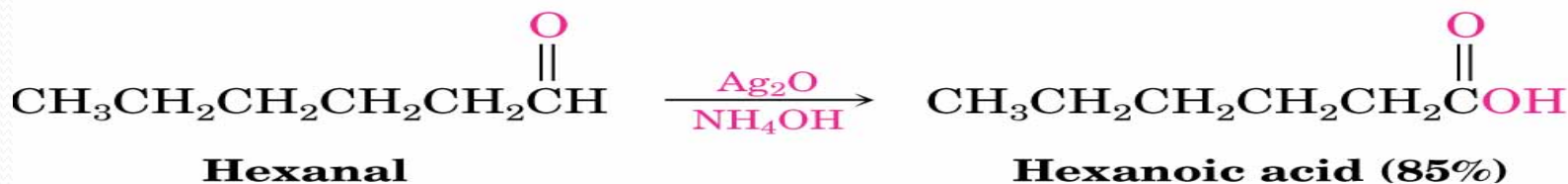
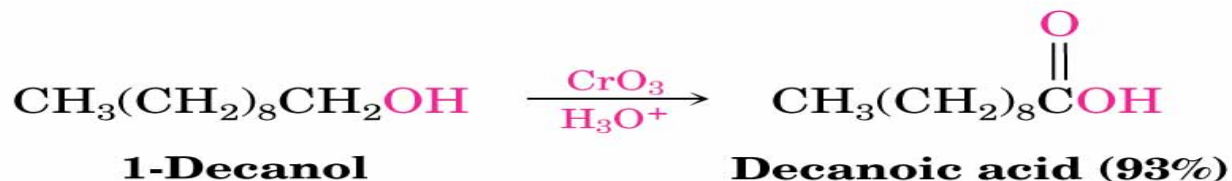
Synthesis Of Carboxylic Acids

- A substituted alkyl benzene can be oxidized with KMnO_4 to give substituted benzoic acid.



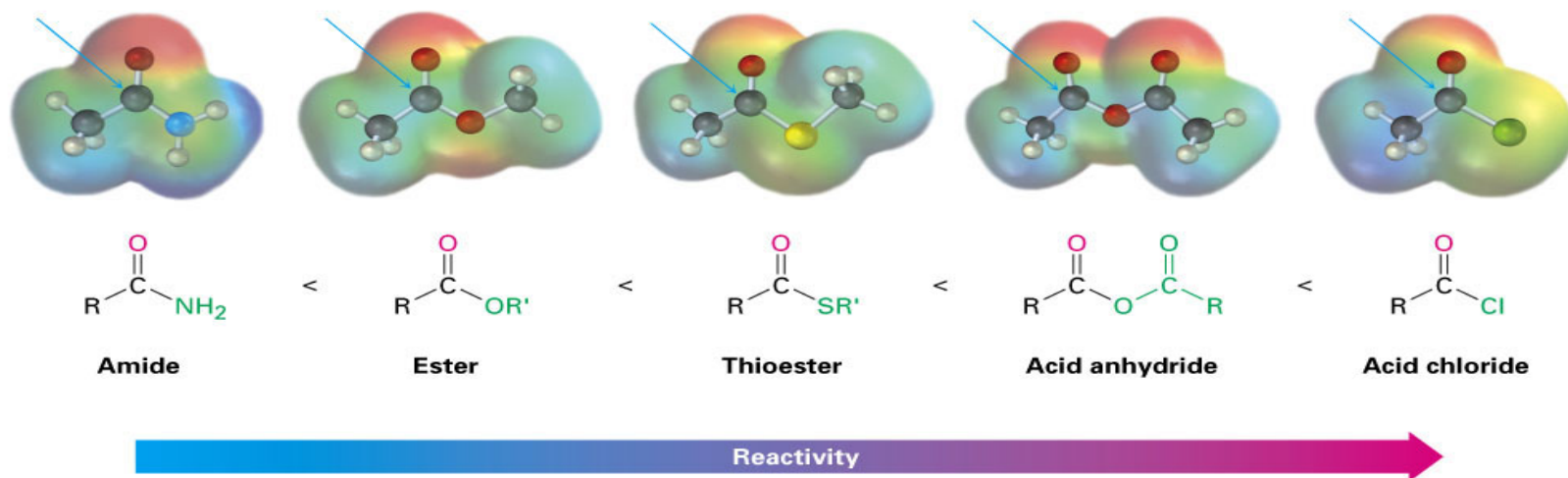
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- Primary alcohols and aldehydes can be oxidized to give carboxylic acids.



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Reactivity



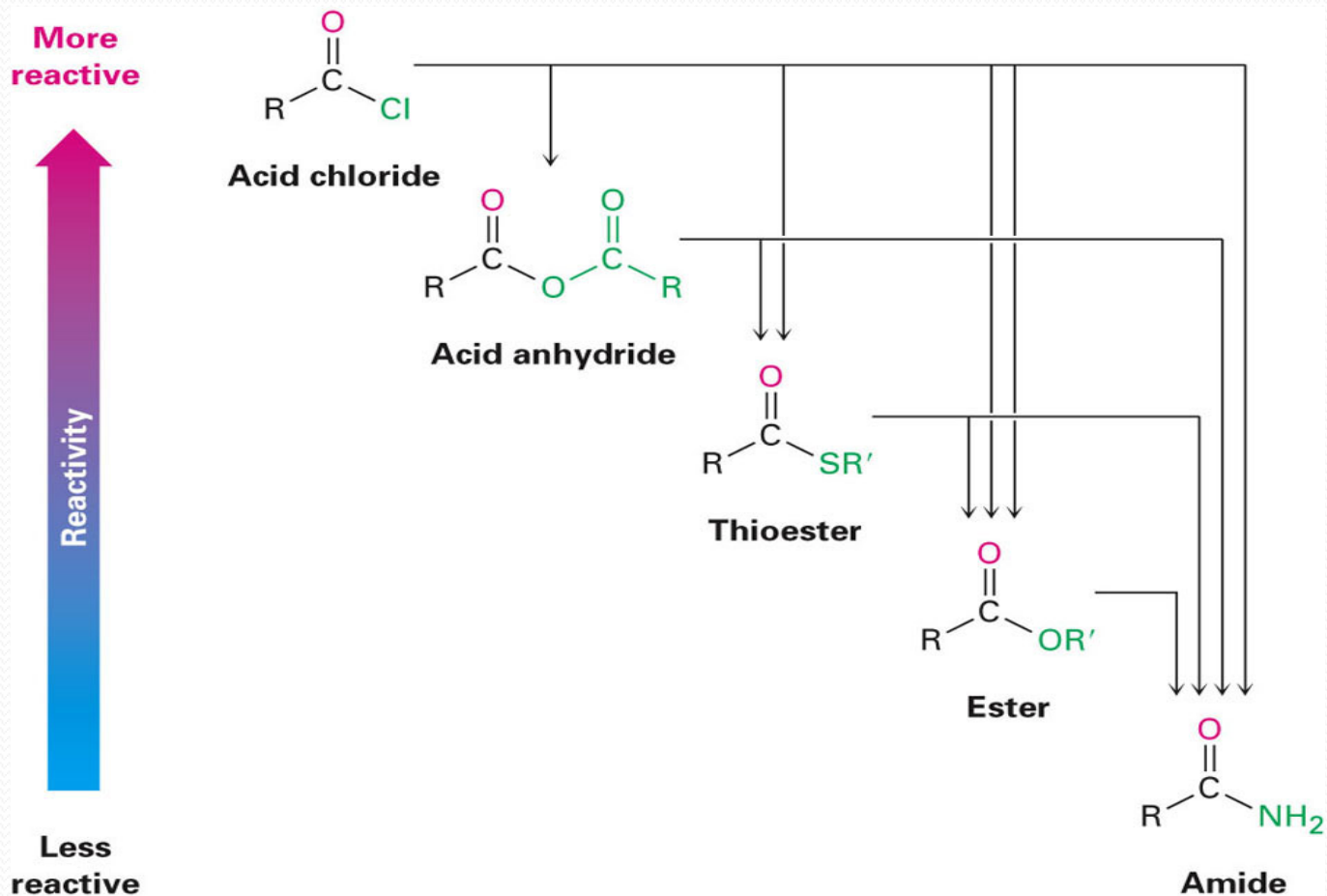
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- A consequence of the reactivity differences, it's possible to convert a more reactive derivative into a less reactive one.

Example: Acid chlorides can be converted into esters and amides, but esters and amides cannot be converted into acid chlorides.

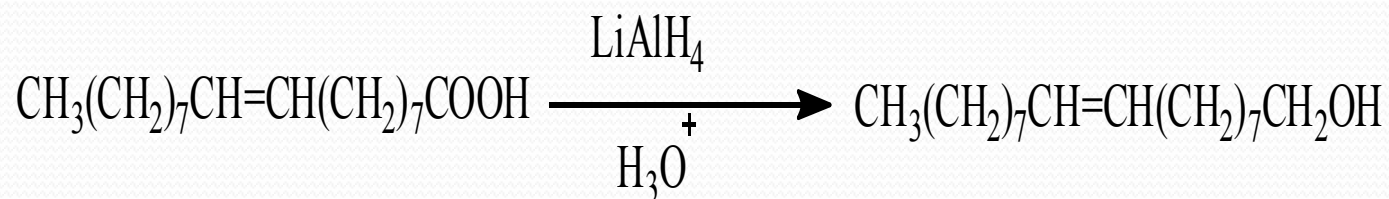
Reactivity

This reactivity order is useful to keep track on large number of reactions.



Reactions Of Carboxylic Acids

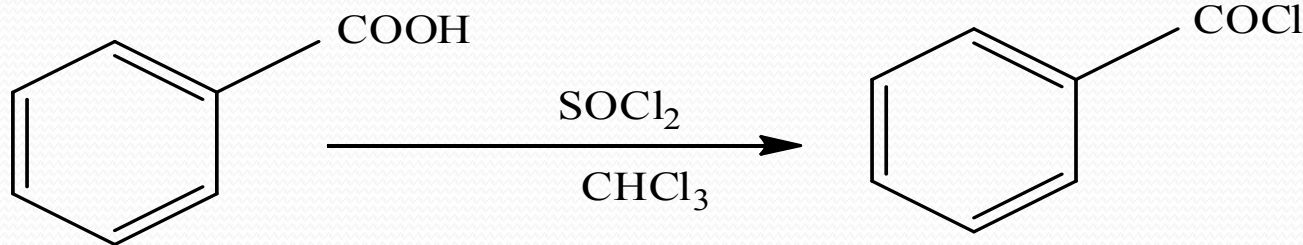
1. Conversion of Acids into Alcohols by Reduction:
Carboxylic acids are reduced by LiAlH_4 to yield primary alcohols.



Oleic acid

cis-Octadec-9-en-1-ol

2. Conversion of Acids into acid chlorides:
Carboxylic acids react with SOCl_2 to form acid chlorides.

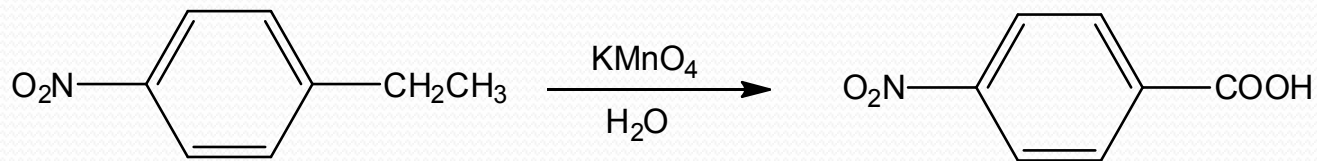


Benzoic acid

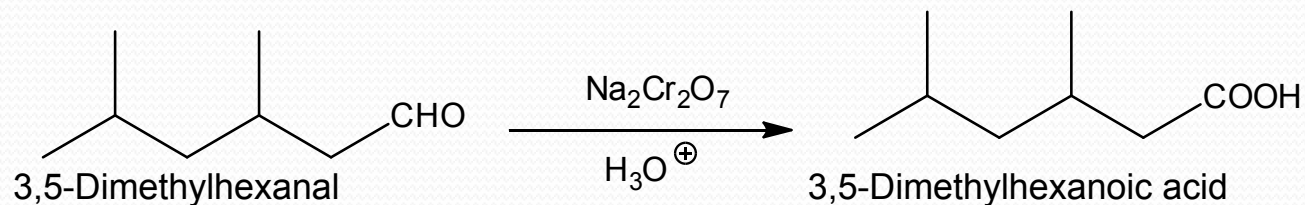
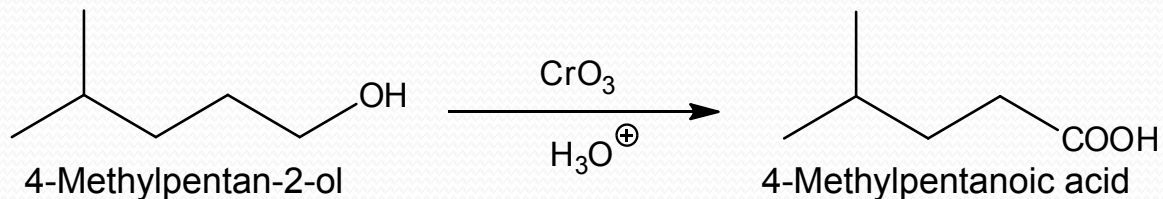
Benzoyl chloride

Synthesis of Carboxylic acids

1. A substituted alkyl benzene can be oxidized with KMnO_4 to give a substituted benzoic acid.



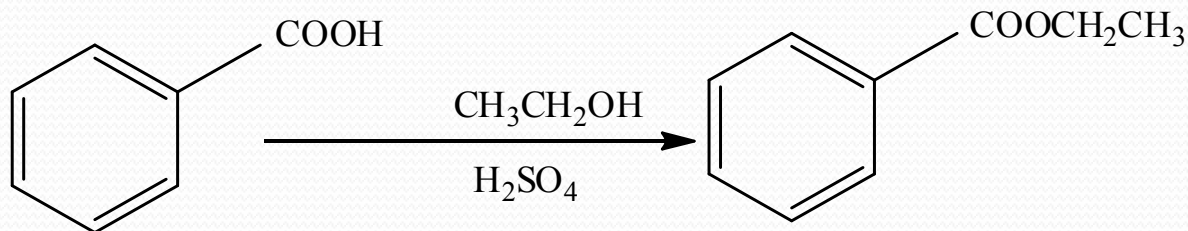
2. Primary alcohols and aldehydes can be oxidized with aqueous CrO_3 or $\text{Na}_2\text{Cr}_2\text{O}_7$ to give carboxylic acids.



Reactions Of Carboxylic Acids

1. Conversion of acids into esters: Esterification reaction

Carboxylic acids react with alcohols in presence of an acid catalyst to form esters.



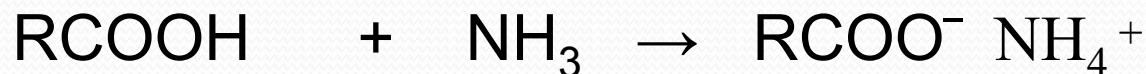
Benzoic acid

Ethyl benzoate

2. Conversion Of acids into amides:

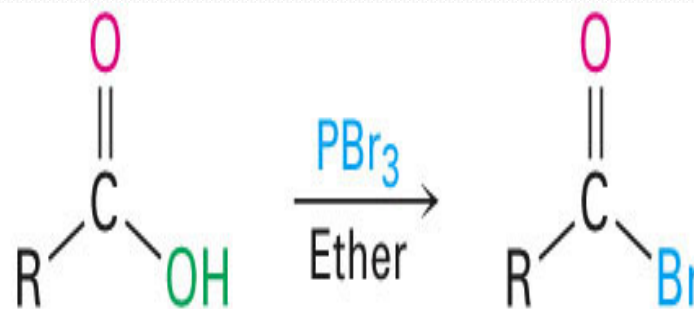
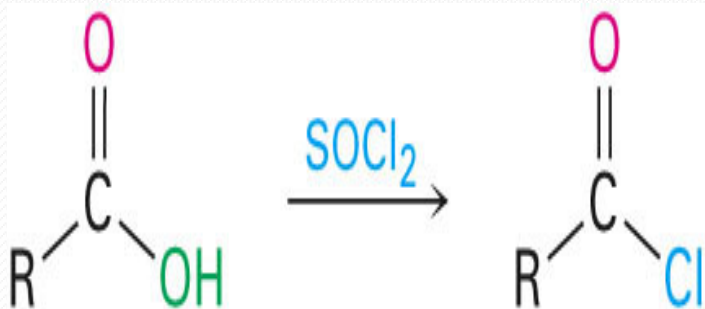
Amides are difficult to prepare directly from carboxylic acids.

Acids convert into carboxylate anions.



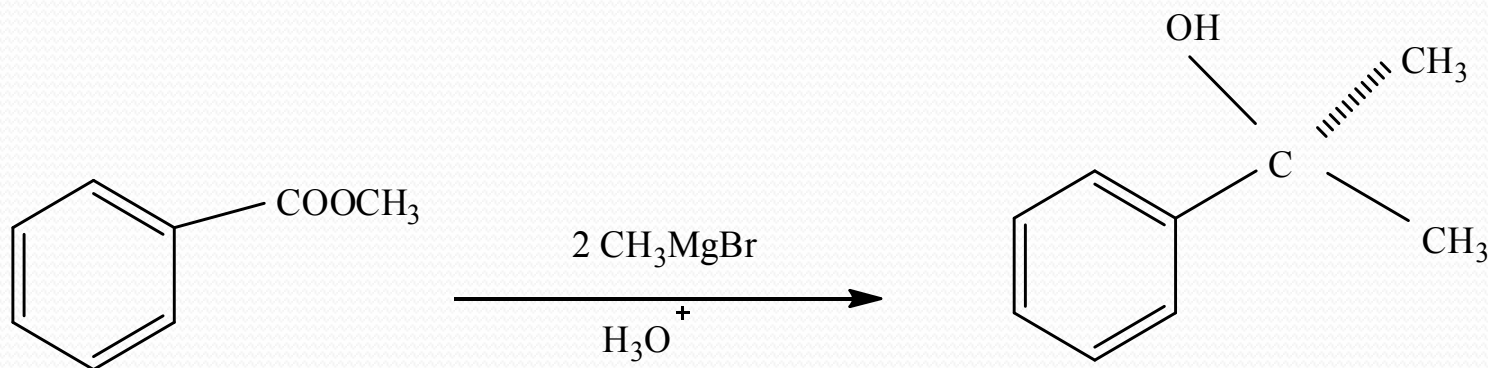
Chemistry Of Acid Halides

- Acid chlorides are prepared from carboxylic acids by reaction with SOCl_2 .
- Reaction of a carboxylic acid with PBr_3 yields the acid bromide.



Chemistry of Esters

- Esters react with Grignard reagent to form alcohols.
- Methyl benzoate reacts with 2 equivalents of CH_3MgBr yield 2-phenyl-propan-2-ol.

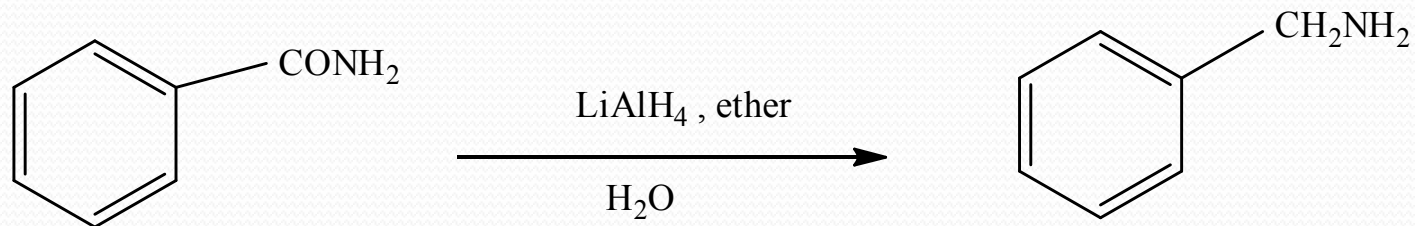


Methyl benzoate

2-Phenylpropan-2-ol

Chemistry Of Amides

- Amides are reduced by LiAlH_4 , to form amines.

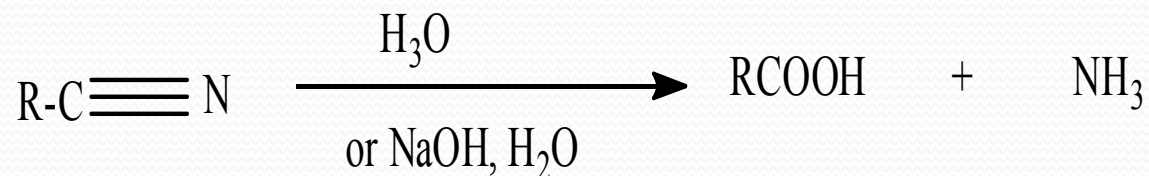


Benzamide

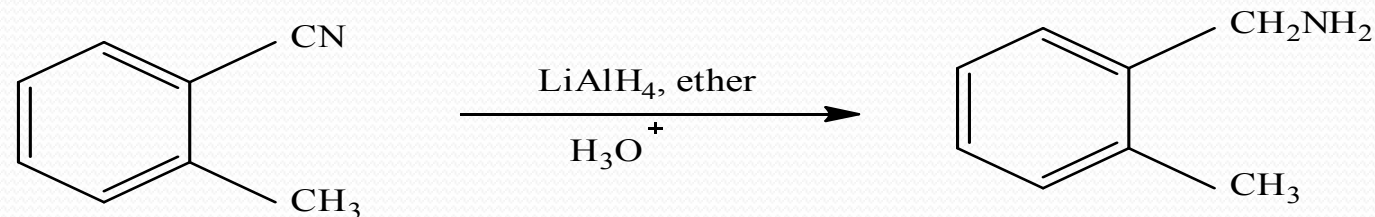
Benzylamine

Chemistry Of Nitriles

- Nitriles are hydrolyzed in acidic or basic solution yield carboxylic acids.



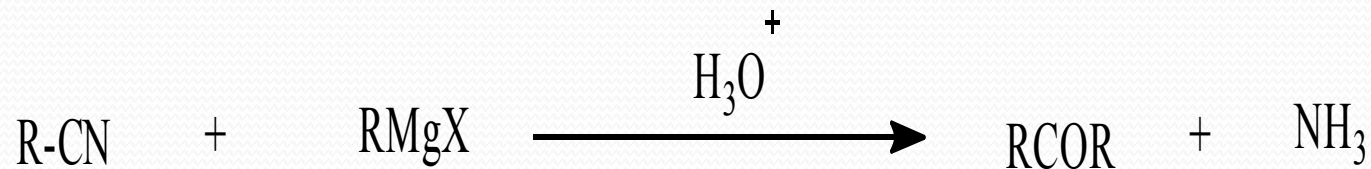
- Reduction of nitrile with LiAlH_4 gives a primary amine.



o-Methylbenzonitrile

o-Methylbenzylamine

- Nitriles react with RMgX , to give ketones.



Practice Examples

- Order the compounds in each of the following sets with respect to increasing acidity.
 - Acetic acid, chloroacetic acid and trifluoroacetic acid.
 - Benzoic acid, p-bromobenzoic acid and p-nitroacetic acid.
 - Acetic acid, phenol and cyclohexanol.

2. Predict the product of reaction of benzoic acid with each of the following reagents.

- LiAlH_4
- SOCl_2
- $\text{CH}_3\text{CH}_2\text{OH} / \text{H}^+$
- $\text{CH}_3\text{NH}_2 / \text{DCC}$

3. Identify A,B,C and D in the following organic synthesis.

