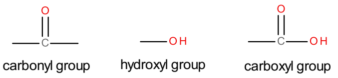
Carboxylic Acids

- The functional group of carboxylic acids consists of a C=O with -OH bonded to the same carbon.
- Carboxyl group is usually written -COOH.
- Aliphatic acids have an alkyl group bonded to -COOH.
- Aromatic acids have an aryl group.
- Fatty acids are long-chain aliphatic acids.

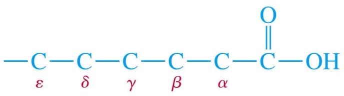
Structure

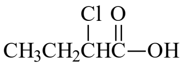
- The functional group present in a carboxylic acid is a combination of a carbonyl group and a hydroxyl group; however, the resulting carboxyl group (-COOH) possesses properties that are unlike those present in aldehydes/ketones and alcohols.



Common Names

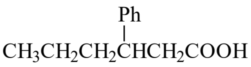
- Many aliphatic acids have historical names.
- Positions of substituents on the chain are labeled with Greek letters.





$CH_3CH_2\overset{Cl}{C}H\overset{O}{C}-OH$

α-chlorobutyric acid

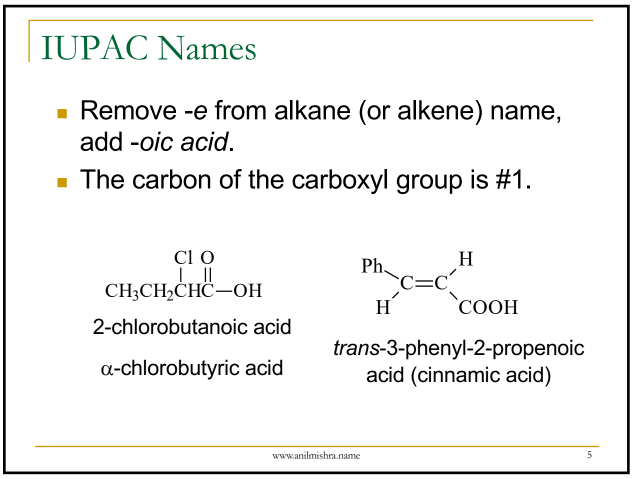


$CH_3CH_2CH_2\overset{Ph}{C}HCH_2COOH$

β-phenylcaproic acid

Naming Carboxylic Acids

Formula	IUPAC	Common
	alkan -oic acid	prefix – ic acid
HCOOH	methanoic acid	formic acid
CH_3COOH	ethanoic acid	acetic acid
CH_3CH_2COOH	propanoic acid	propionic acid
$CH_3CH_2CH_2COOH$	butanoic acid	butyric acid



IUPAC Names

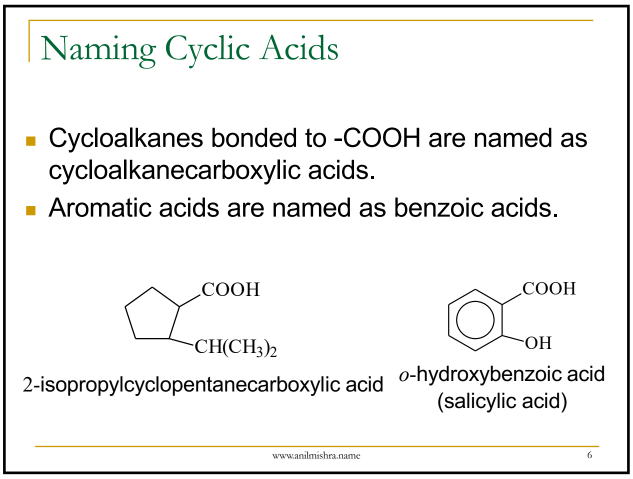
- Remove -*e* from alkane (or alkene) name, add -*oic acid*.
- The carbon of the carboxyl group is #1.

$CH_3CH_2\overset{\overset{Cl}{|}}{C}H\overset{\overset{O}{\|}}{C}-OH$

2-chlorobutanoic acid

α-chlorobutyric acid

trans-3-phenyl-2-propenoic acid (cinnamic acid)

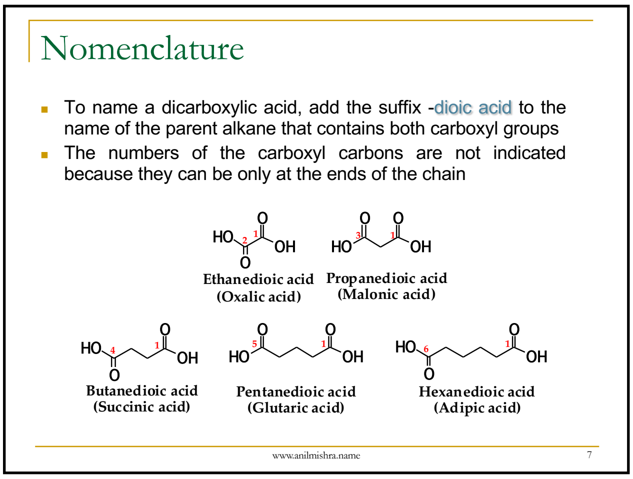


Naming Cyclic Acids

- Cycloalkanes bonded to -COOH are named as cycloalkanecarboxylic acids.
- Aromatic acids are named as benzoic acids.

2-isopropylcyclopentanecarboxylic acid

o-hydroxybenzoic acid (salicylic acid)



Nomenclature

- To name a dicarboxylic acid, add the suffix -dioic acid to the name of the parent alkane that contains both carboxyl groups
- The numbers of the carboxyl carbons are not indicated because they can be only at the ends of the chain

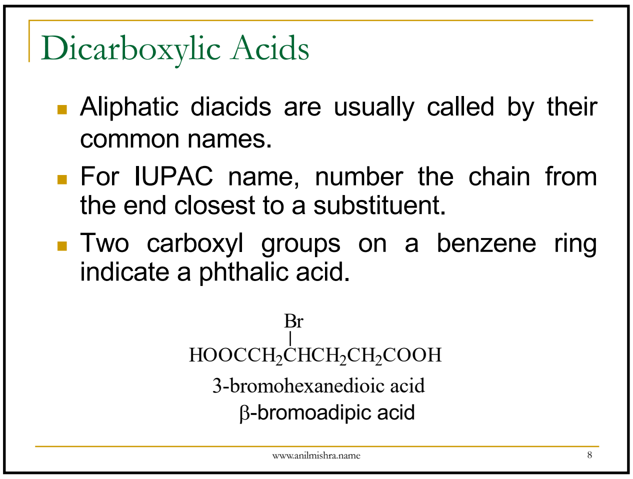
Ethanedioic acid (Oxalic acid)

Propanedioic acid (Malonic acid)

Butanedioic acid (Succinic acid)

Pentanedioic acid (Glutaric acid)

Hexanedioic acid (Adipic acid)



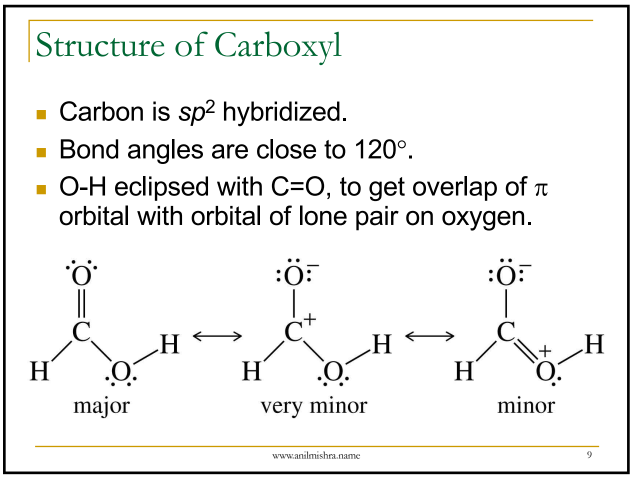
Dicarboxylic Acids

- Aliphatic diacids are usually called by their common names.
- For IUPAC name, number the chain from the end closest to a substituent.
- Two carboxyl groups on a benzene ring indicate a phthalic acid.

$HOOCCH_2\overset{\overset{Br}{|}}{C}HCH_2CH_2COOH$

3-bromohexanedioic acid

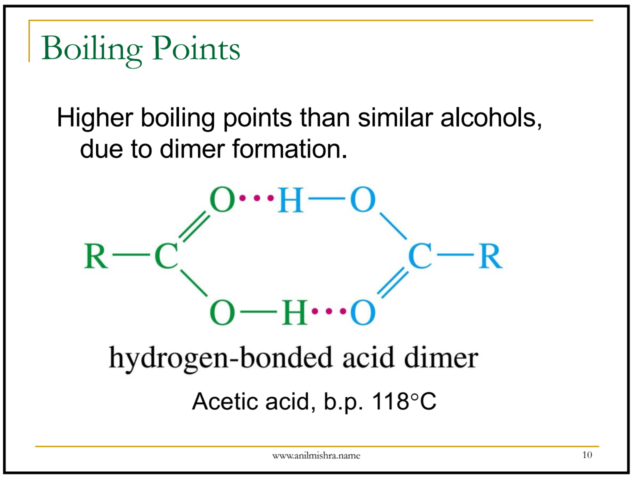
β-bromoadipic acid



Structure of Carboxyl

- Carbon is *sp*^{2} hybridized.
- Bond angles are close to 120°.
- O-H eclipsed with C=O, to get overlap of π orbital with orbital of lone pair on oxygen.

major ⟷ very minor ⟷ minor

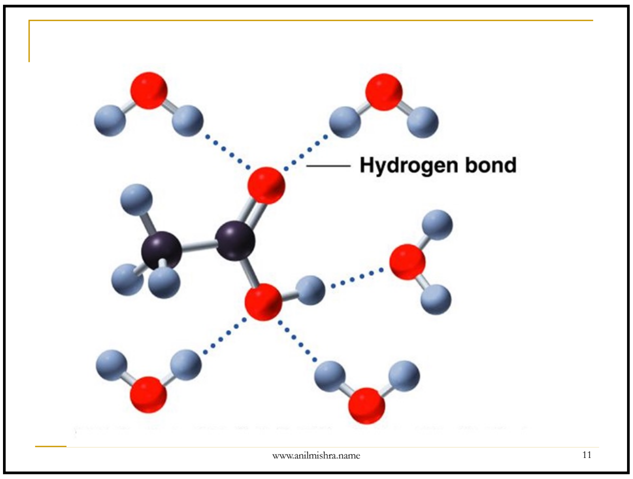


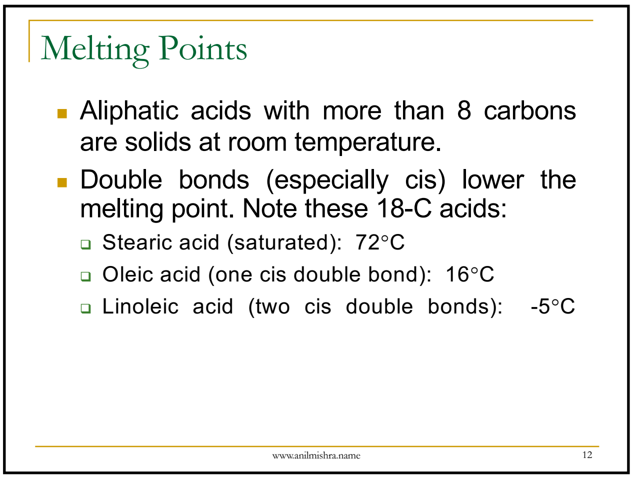
Boiling Points

Higher boiling points than similar alcohols, due to dimer formation.

hydrogen-bonded acid dimer

Acetic acid, b.p. 118°C





Melting Points

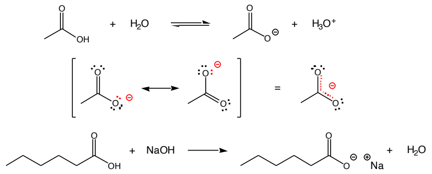
- Aliphatic acids with more than 8 carbons are solids at room temperature.
- Double bonds (especially cis) lower the melting point. Note these 18-C acids:
  - Stearic acid (saturated): 72°C
  - Oleic acid (one cis double bond): 16°C
  - Linoleic acid (two cis double bonds): -5°C

Solubility

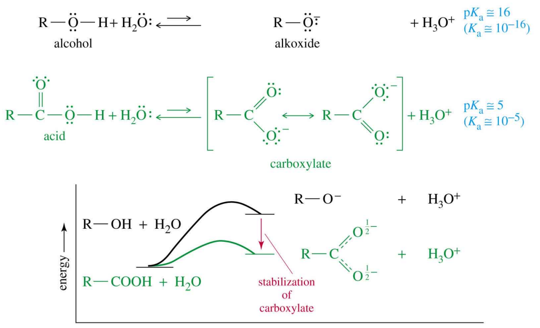
- Water solubility decreases with the length of the carbon chain.
- Up to 4 carbons, acid is miscible in water.
- More soluble in alcohol.
- Also soluble in relatively nonpolar solvents like chloroform because it dissolves as a dimer.

Acidity and Salts of Carboxylic Acids

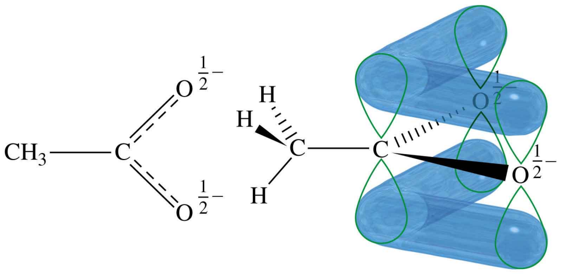
- Carboxylic acids are weak acids (partially ionize in water)
- They are stronger acids than alcohols, or even phenols, due to the high stability of their conjugate bases (resonance)
- Carboxylic acids are neutralized by bases to form salts
- Salts of carboxylic acids are useful because they are solids at room temperature, and most are soluble in water



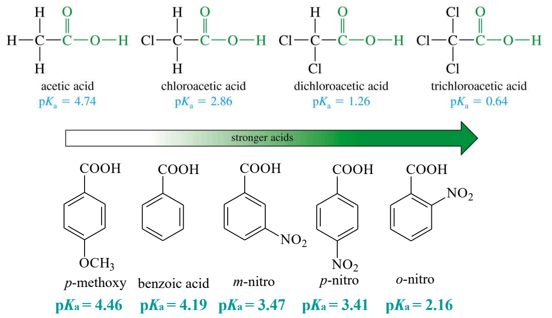
Acidity



Resonance Stabilization



Substituent Effects on Acidity



Substituent Effects on Acidity

- **Electron withdrawing groups** will stabilize the anion, decrease the ΔH, shift the ionization to the right, increasing the Ka, **increasing acid strength**.
- **Electron donating groups** will destabilize the anion, increase the ΔH, shift the ionization in water to the left, decreasing the Ka, **decreasing acid strength**.

$-NH_2$, $-NHR$, $-NR_2$ -OH -OR $-NHCOCH_3$ $-C_6H_5$ -R	electron donating
-H	
-X -CHO, -COR $-SO_3H$ -COOH, -COOR -CN $-NR_3^+$ $-NO_2$	electron withdrawing

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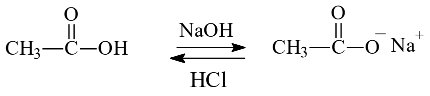
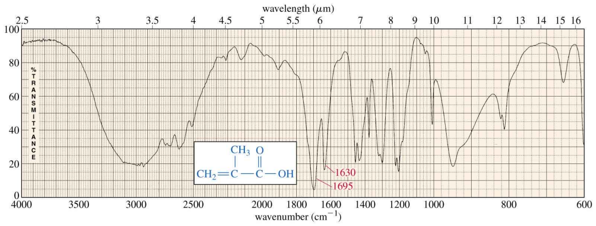
Salts of Carboxylic Acids

- Sodium hydroxide removes a proton to form the salt.
- Adding a strong acid, like HCl, regenerates the carboxylic acid.



$$CH_3-\overset{O}{\overset{\|}{C}}-OH \underset{HCl}{\overset{NaOH}{\rightleftharpoons}} CH_3-\overset{O}{\overset{\|}{C}}-O^{-}\ Na^{+}$$

IR Spectroscopy



UV Spectroscopy

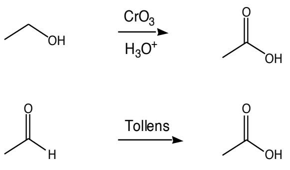
- Saturated carboxylic acids absorb very weakly around 200-215 nm.
- If C=C is conjugated with C=O, molar absorptivity = 10,000 at 200 nm.
- An additional conjugated double bond increases the absorption wavelength to 250 nm.

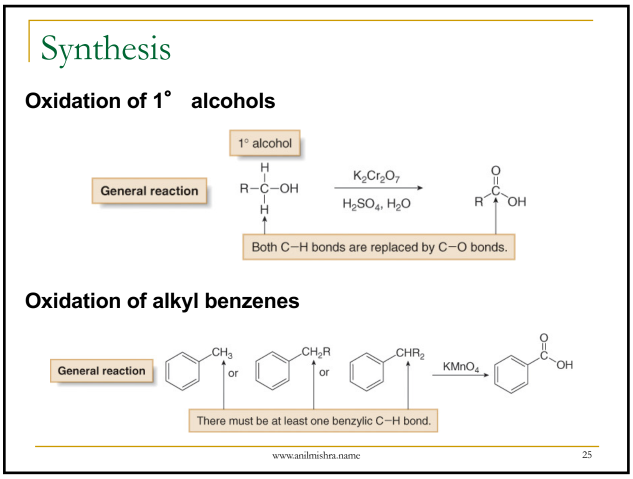
Synthesis

- Oxidation of primary alcohols and aldehydes with chromic acid.
- Cleavage of an alkene with hot KMnO4 produces a carboxylic acid if there is a hydrogen on the double-bonded carbon.
- Alkyl benzene oxidized to benzoic acid by hot KMnO4 or hot chromic acid.

Synthesis

- Carboxylic acids can be prepared by oxidation of primary alcohols or aldehydes
- Primary alcohols form acids when treated with Jones' reagent (CrO_3/H_3O^+), as well most other oxidizing agents
- Aldehydes can be oxidized to carboxylic acids with most oxidizing agents, such as Tollens'reagent ($AgNO_3/NH_3$)
  - alcohols do not react with Tollens



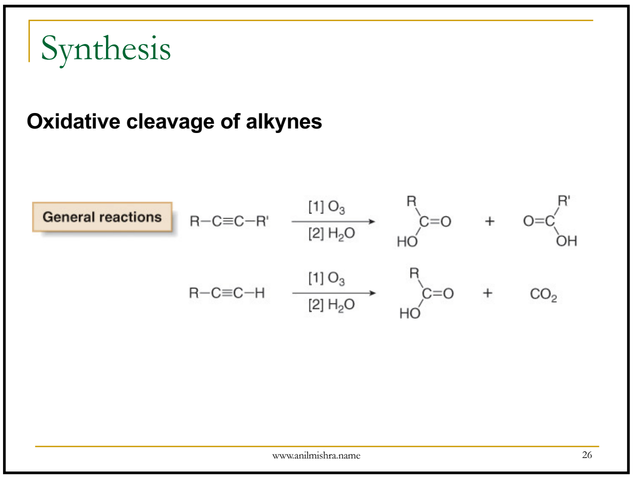


Synthesis

Oxidation of 1° alcohols

Oxidation of alkyl benzenes

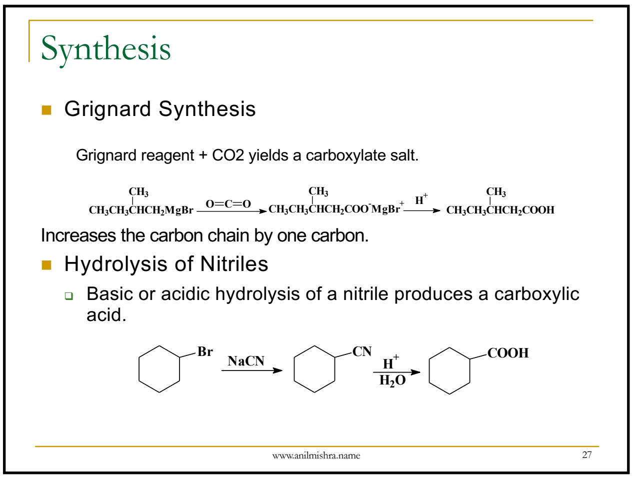
25



Synthesis

Oxidative cleavage of alkynes

26



Synthesis

- Grignard Synthesis

Grignard reagent + CO2 yields a carboxylate salt.

Increases the carbon chain by one carbon.

- Hydrolysis of Nitriles
  - Basic or acidic hydrolysis of a nitrile produces a carboxylic acid.

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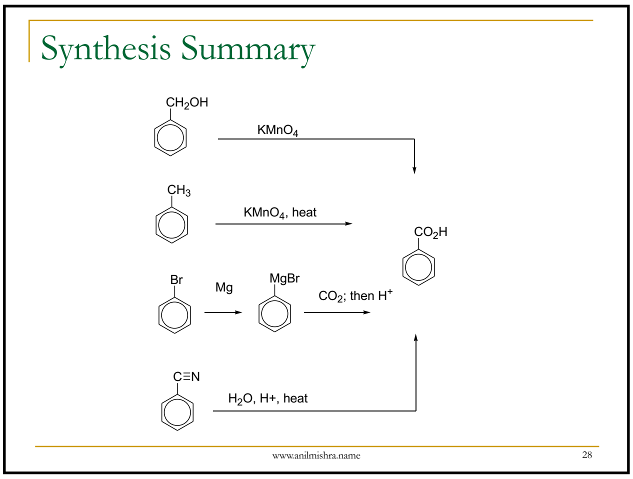

Synthesis Summary

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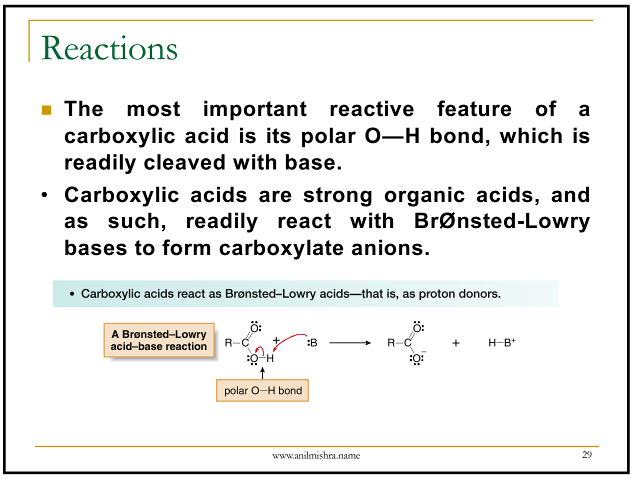

Reactions

- **The most important reactive feature of a carboxylic acid is its polar O—H bond, which is readily cleaved with base.**
- **Carboxylic acids are strong organic acids, and as such, readily react with BrØnsted-Lowry bases to form carboxylate anions.**

- Carboxylic acids react as Brønsted–Lowry acids—that is, as proton donors.

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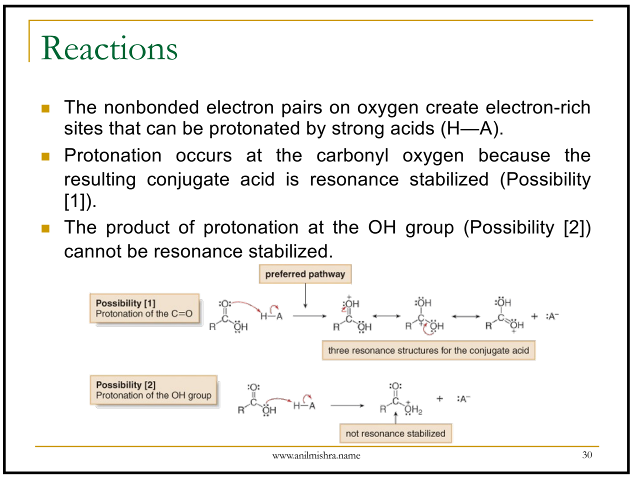

Reactions

- The nonbonded electron pairs on oxygen create electron-rich sites that can be protonated by strong acids (H—A).
- Protonation occurs at the carbonyl oxygen because the resulting conjugate acid is resonance stabilized (Possibility [1]).
- The product of protonation at the OH group (Possibility [2]) cannot be resonance stabilized.

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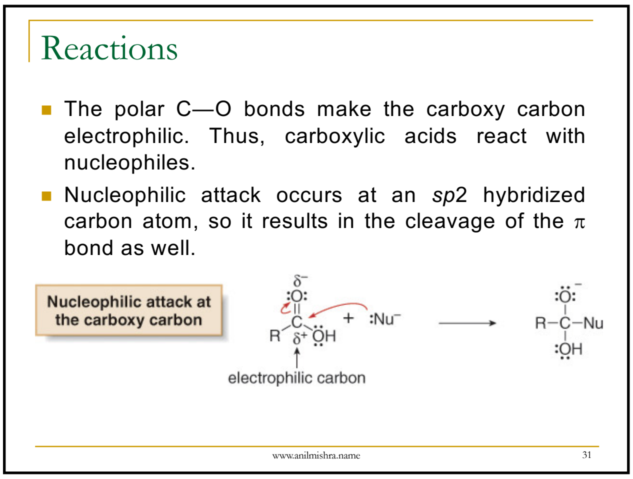

Reactions

- The polar C—O bonds make the carboxy carbon electrophilic. Thus, carboxylic acids react with nucleophiles.
- Nucleophilic attack occurs at an *sp*2 hybridized carbon atom, so it results in the cleavage of the π bond as well.

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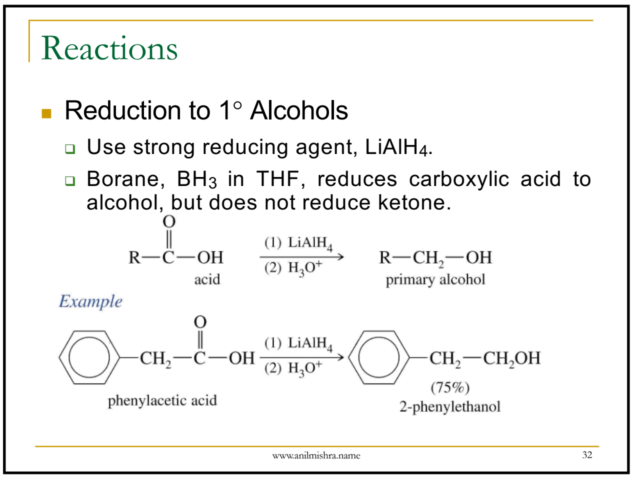


Reactions

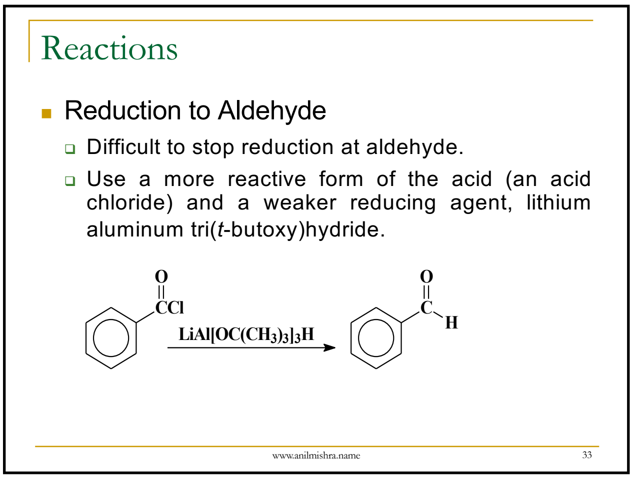
- Reduction to 1° Alcohols
  - Use strong reducing agent, $LiAlH_4$.
  - Borane, BH_3 in THF, reduces carboxylic acid to alcohol, but does not reduce ketone.

$$\underset{\text{acid}}{R-\overset{\overset{\displaystyle O}{\|}}{C}-OH} \xrightarrow[(2)\ H_3O^+]{(1)\ LiAlH_4} \underset{\text{primary alcohol}}{R-CH_2-OH}$$

Example

$$C_6H_5-CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-OH \xrightarrow[(2)\ H_3O^+]{(1)\ LiAlH_4} C_6H_5-CH_2-CH_2OH$$

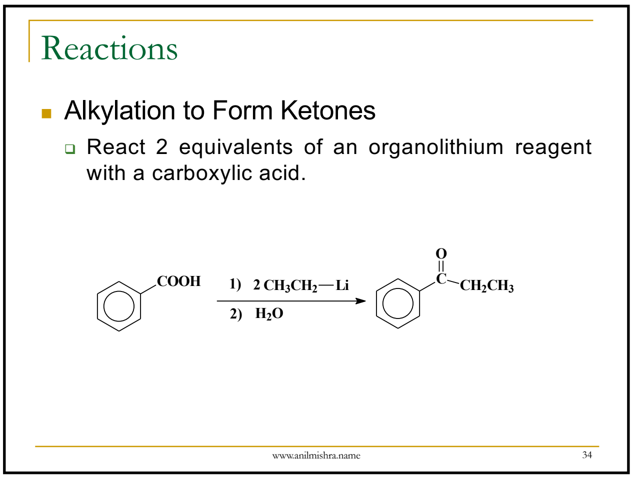
32



Reactions

- Reduction to Aldehyde
  - Difficult to stop reduction at aldehyde.
  - Use a more reactive form of the acid (an acid chloride) and a weaker reducing agent, lithium aluminum tri(*t*-butoxy)hydride.

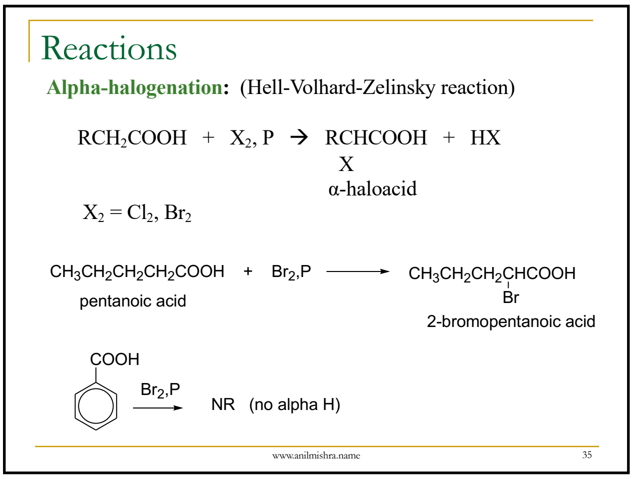
33



Reactions

- Alkylation to Form Ketones
  - React 2 equivalents of an organolithium reagent with a carboxylic acid.

34



Reactions

Alpha-halogenation: (Hell-Volhard-Zelinsky reaction)

$$RCH_2COOH + X_2, P \rightarrow \underset{\text{X}}{RCHCOOH} + HX$$

α-haloacid

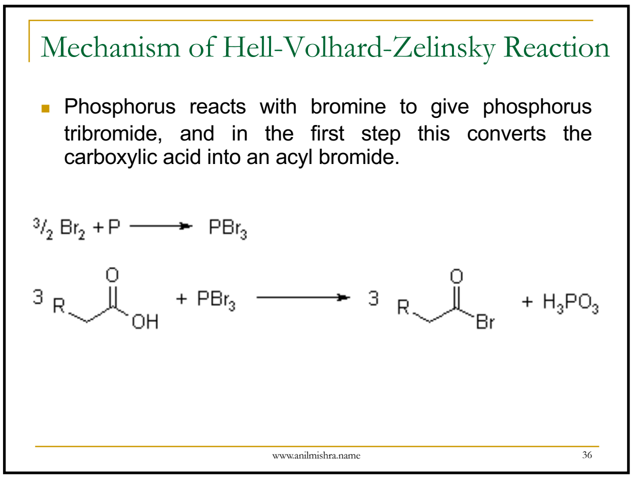
$X_2 = Cl_2, Br_2$

$$CH_3CH_2CH_2CH_2COOH + Br_2,P \longrightarrow CH_3CH_2CH_2\underset{\text{Br}}{C}HCOOH$$

pentanoic acid

2-bromopentanoic acid

35



Mechanism of Hell-Volhard-Zelinsky Reaction

- Phosphorus reacts with bromine to give phosphorus tribromide, and in the first step this converts the carboxylic acid into an acyl bromide.

$$^3/_2\ Br_2 + P \longrightarrow PBr_3$$

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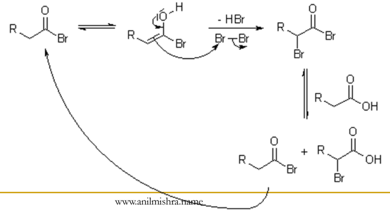
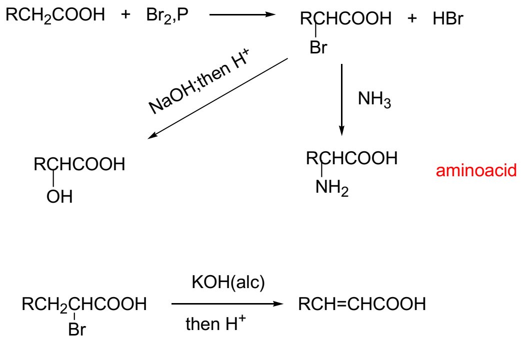
Mechanism of Hell-Volhard-Zelinsky Reaction

- An acyl bromide can readily exist in the enol form, and this tautomer is rapidly brominated at the α-carbon.
- The monobrominated compound is much less nucleophilic, so the reaction stops at this stage.
- This acyl intermediate compound can undergo bromide exchange with unreacted carboxylic acid via the anhydride, which allows the catalytic cycle to continue until the conversion is complete.



Reactions



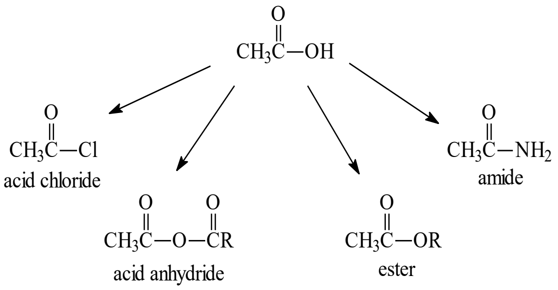
$RCH_2COOH + Br_2,P \longrightarrow \underset{Br}{RCHCOOH} + HBr$

$\underset{Br}{RCHCOOH} \xrightarrow{NaOH;then\ H^+} \underset{OH}{RCHCOOH}$

$\underset{Br}{RCHCOOH} \xrightarrow{NH_3} \underset{NH_2}{RCHCOOH}$ aminoacid

$\underset{Br}{RCH_2CHCOOH} \xrightarrow[\text{then } H^+]{KOH(alc)} RCH{=}CHCOOH$

Carboxylic Acid Derivatives



$CH_3\overset{O}{\overset{\|}{C}}{-}OH$

$CH_3\overset{O}{\overset{\|}{C}}{-}Cl$ acid chloride

$CH_3\overset{O}{\overset{\|}{C}}{-}O{-}\overset{O}{\overset{\|}{C}}R$ acid anhydride

$CH_3\overset{O}{\overset{\|}{C}}{-}OR$ ester

$CH_3\overset{O}{\overset{\|}{C}}{-}NH_2$ amide

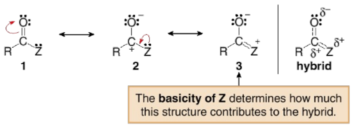
Carboxylic Acid Derivatives

- The group bonded to the acyl carbon determines the class of compound:
  - -OH, carboxylic acid
  - -Cl, acid chloride
  - -OR’, ester
  - -NH_2, amide
- These interconvert via nucleophilic acyl substitution.

Carboxylic Acid Derivatives

Structure and Bonding:

- **Three resonance structures stabilize carboxylic acid derivatives (RCOZ) by delocalizing electron density.**
- **The more resonance structures 2 and 3 contribute to the resonance hybrid, the more stable RCOZ is.**

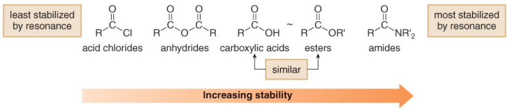


The **basicity of Z** determines how much this structure contributes to the hybrid.

- The more basic Z is, the more it donates its electron pair, and the more resonance structure 3 contributes to the hybrid.

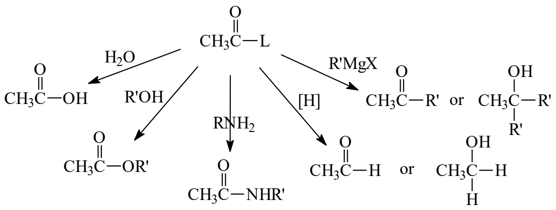
Carboxylic Acid Derivatives

- Derivatives—Nucleophilic Acyl Substitution
  - Structure and Bonding
  - Because the basicity of Z determines the relative stability of the carboxylic acid derivatives, the following stability order results:



  - In summary, as the basicity of Z increases, the stability of RCOZ increases because of added resonance stabilization.

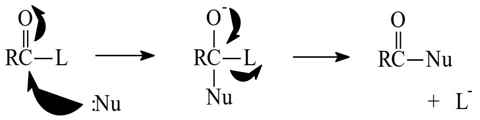
Carboxylic Acid Derivative Synthesis



Carboxylic Acid Derivative Synthesis

- All have a Common Mechanism!
  - **2-step Acyl Substitution:**

    1. Addition to C=O (to create a tetrahedral C)
    2. Elimination of the best L to reform the C=O

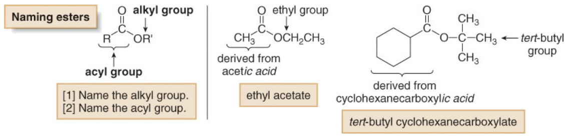


(gem diol-like intermediate; unstable w/r to reformation of the carbonyl group & displacement of the best leaving group)

Ester

Nomenclature

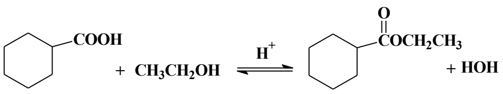
- **Name the R' as an alkyl group. This becomes the first part of the name.**
- **Name the acyl group by changing the *ic acid* ending of the parent carboxylic acid to the suffix *–ate*.**



- **Esters are often written as RCOOR', where the alkyl group (R') is written last. When the ester is named however, the R' group appears first in the name.**

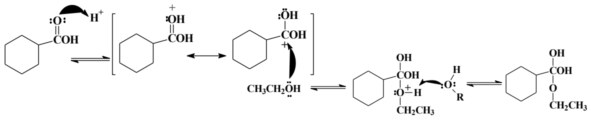
Fischer Esterification

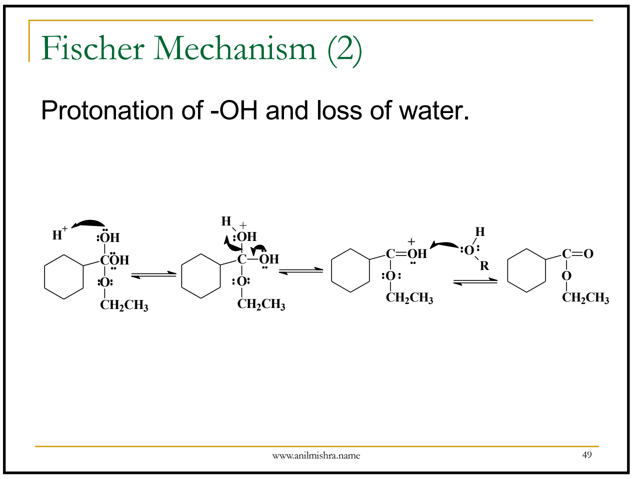
- Acid + alcohol yields ester + water.
- Acid catalyzed for weak nucleophile.
- All steps are reversible.
- Reaction reaches equilibrium.



Fischer Mechanism (1)

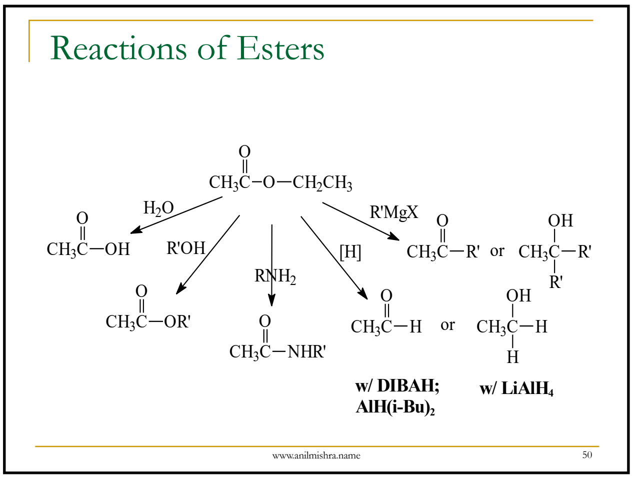
Protonation of carbonyl and attack of alcohol, a weak nucleophile.





Fischer Mechanism (2)

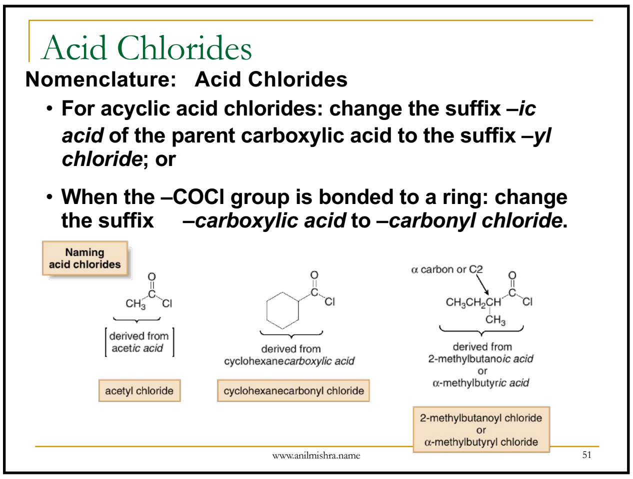
Protonation of -OH and loss of water.



Reactions of Esters

w/ DIBAH; AlH(i-Bu)$_2$

w/ LiAlH$_4$



Acid Chlorides

Nomenclature: Acid Chlorides

- **For acyclic acid chlorides: change the suffix *–ic acid* of the parent carboxylic acid to the suffix *–yl chloride*; or**
- **When the –COCl group is bonded to a ring: change the suffix *–carboxylic acid* to *–carbonyl chloride*.**

Naming acid chlorides

derived from acet*ic acid*

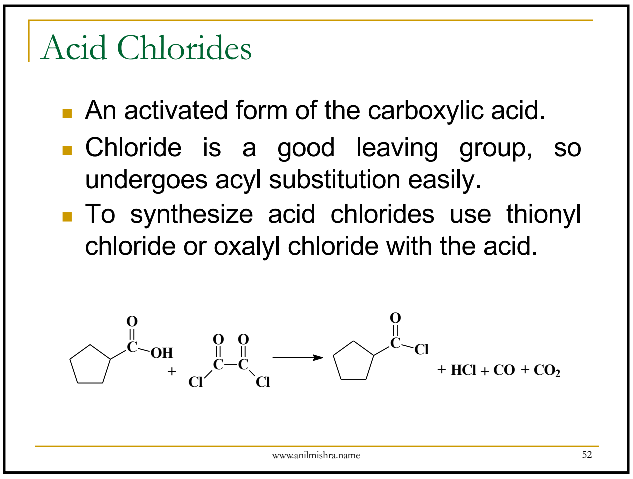
acetyl chloride

derived from cyclohexane*carboxylic acid*

cyclohexanecarbonyl chloride

derived from 2-methylbutano*ic acid* or α-methylbutyr*ic acid*

2-methylbutanoyl chloride or α-methylbutyryl chloride

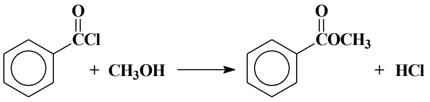


Acid Chlorides

- An activated form of the carboxylic acid.
- Chloride is a good leaving group, so undergoes acyl substitution easily.
- To synthesize acid chlorides use thionyl chloride or oxalyl chloride with the acid.

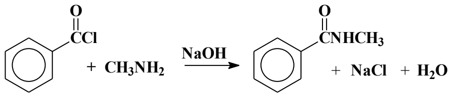
Esters from Acid Chlorides

- Acid chlorides react with alcohols to give esters in good yield.
- Mechanism is nucleophilic addition of the alcohol to the carbonyl as chloride ion leaves, then deprotonation.

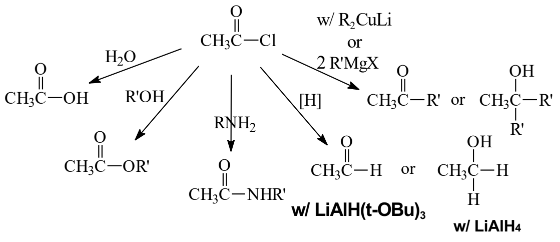


Amides from Acid Chlorides

- Acid chlorides react with ammonia and amines to give amides.
- A base (NaOH or pyridine) is added to remove HCl by-product.



Reactions of Acid Chlorides



Nitrile

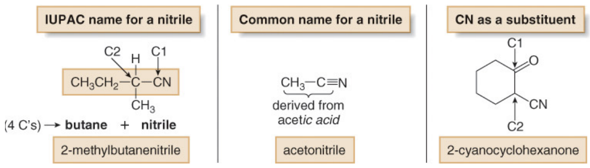
Nomenclature

- In contrast to the carboxylic acid derivatives, nitriles are named as alkane derivatives.
- Find the longest chain that contains the CN and add the word nitrile to the name of parent alkane. Number the chain to put CN at C1, but omit this number from the name.
- Common names of nitriles are derived from the names of the carboxylic acid having the same number of carbon atoms by replacing the *–ic acid* ending of the carboxylic acid with the suffix *–onitrile*.
- When the CN is named as a substituent it is called a cyano group.

Nitrile

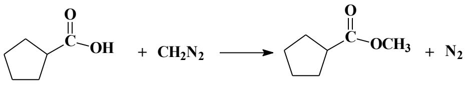
Nomenclature

- **In naming a nitrile, the CN carbon is one carbon atom of the longest chain. CH_3CH_2CN is propanenitrile, not ethanenitrile.**

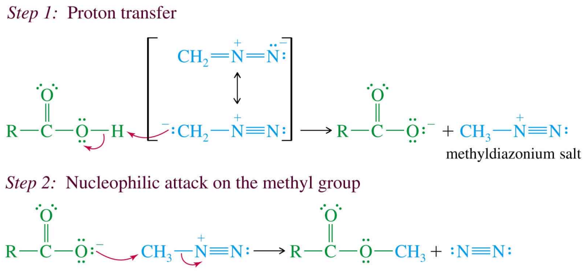


Diazomethane

- CH_2N_2 reacts with carboxylic acids to produce methyl esters quantitatively.
- Very toxic, explosive. Dissolve in ether.



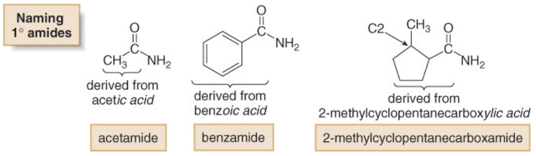
Mechanism for Diazomethane



Amides

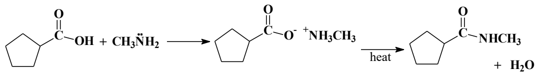
Nomenclature

- **All 1° amides are named by replacing the *-ic acid*, *-oic acid*, or *-ylic acid* ending with the suffix amide.**



Amides from Acids

- Amine (base) removes a proton from the carboxylic acid to form a salt.
- Heating the salt above 100°C drives off steam and forms the amide.



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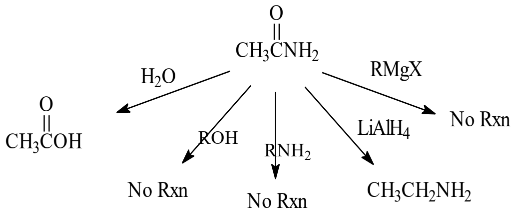
Reactions of Amides (unreactive)



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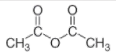
Anhydrides

Nomenclature: Anhydrides

- **Symmetrical anhydrides are named by changing the acid ending of the carboxylic acid to the word *anhydride*.**
- **Mixed anhydrides, which are derived from two different carboxylic acids, are named by alphabetizing the names for both acids and replacing the word *acid* with the word *anhydride*.**

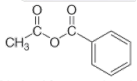
Symmetrical anhydride



[derived from acetic acid]

acetic anhydride

Mixed anhydride



[derived from acetic acid and benzoic acid]

acetic benzoic anhydride

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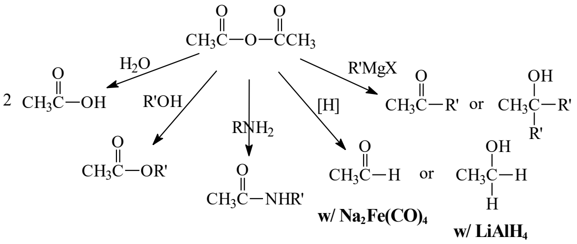
Reactions of Anhydrides



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