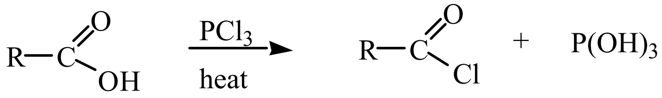
Reactions of Carboxylic acids

Three types of reactions:
1. Replacement of OH group
2. alteration of the carbonyl group
3. reaction at the α carbon

1. Replacement of OH

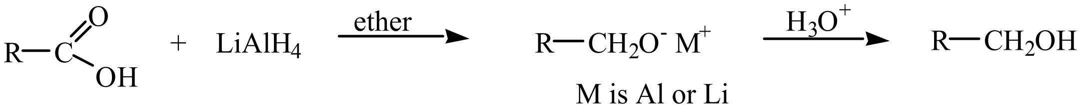
replacement of OH by X using PX_3 or (for Cl) $SOCl_2$

e.g.



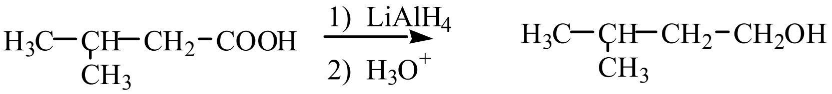
acyl chloride
very reactive

2. Reduction of C=O to CH_2 with $LiAlH_4$ to give a primary alcohol



M is Al or Li

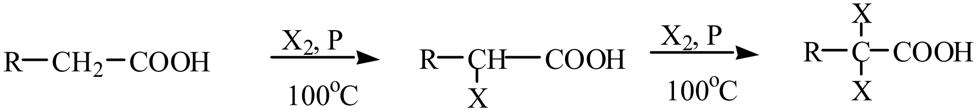
e.g.



$$H_3C-\underset{CH_3}{CH}-CH_2-COOH \xrightarrow[2)\ H_3O^+]{1)\ LiAlH_4} H_3C-\underset{CH_3}{CH}-CH_2-CH_2OH$$

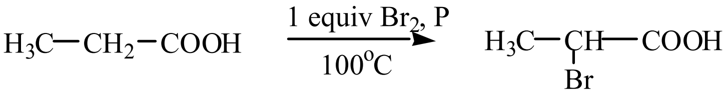
90 - 99% yield

3. Reaction at the α carbon: the Hell-Volhard-Zelinsky reaction.



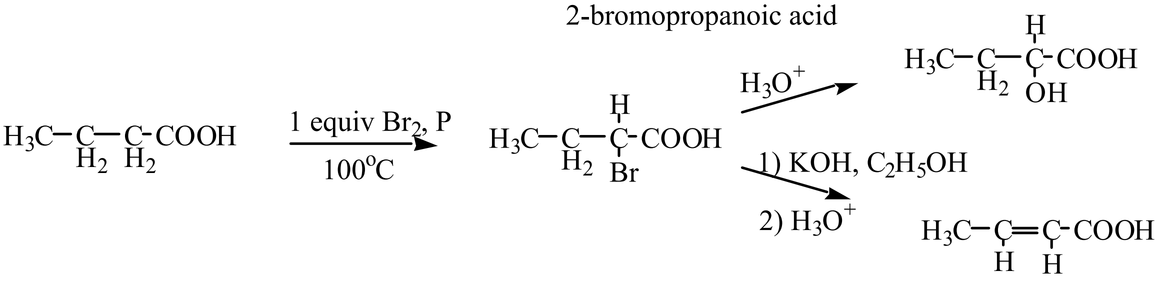
$$R-CH_2-COOH \xrightarrow[100^oC]{X_2,\ P} R-\underset{X}{CH}-COOH \xrightarrow[100^oC]{X_2,\ P} R-\overset{X}{\underset{X}{C}}-COOH$$

e.g.



$$H_3C-CH_2-COOH \xrightarrow[100^oC]{1\ equiv\ Br_2,\ P} H_3C-\underset{Br}{CH}-COOH$$

α–bromopropionic acid
2-bromopropanoic acid



$$H_3C-\underset{H_2}{C}-\underset{H_2}{C}-COOH \xrightarrow[100^oC]{1\ equiv\ Br_2,\ P} H_3C-\underset{H_2}{C}-\overset{H}{\underset{Br}{C}}-COOH \xrightarrow{H_3O^+} H_3C-\underset{H_2}{C}-\overset{H}{\underset{OH}{C}}-COOH$$

$$H_3C-\underset{H_2}{C}-\overset{H}{\underset{Br}{C}}-COOH \xrightarrow[2)\ H_3O^+]{1)\ KOH,\ C_2H_5OH} H_3C-\underset{H}{C}=\underset{H}{C}-COOH$$

2-butenoic acid

This reaction can be used to make α–bromo acids, α–hydroxy acids, and α,β–unsaturated acids

Another example of the Hell-Volhard-Zelinsky reaction:

$$CH_3COOH \xrightarrow[100^{o}C]{\text{excess } Cl_2,\ P} CCl_3COOH$$

trichloroacetic acid

Examples of Dicarboxylic Acids

$HOOC\text{-}COOH$
oxalic aicd
ethanedioic acid

$HOOC\text{-}CH_2\text{-}COOH$
malonic acid
propanedioic acid

$HOOC\text{-}CH_2\text{-}CH_2\text{-}COOH$
succinic acid
butanedioic acid

$HOOC\text{-}CH_2\text{-}CH_2\text{-}CH_2\text{-}COOH$
glutaric acid
pentanedioic acid

$HOOCCH_2CH_2CH_2CH_2COOH$
adipic acid
hexanedioic acid

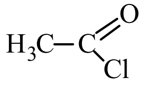
$HOOCCH_2CH_2CH_2CH_2CH_2COOH$
pimelic acid
heptanedioic acid

$HOOCCH_2CH_2CH_2CH_2CH_2CH_2COOH$
sebacic acid
octanedioic acid

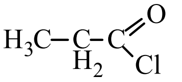
Acyl Chlorides

named by dropping 'ic acid' from the name of the acid and adding 'yl chloride'

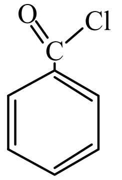
e.g.



acetyl chloride
ethanoyl chloride



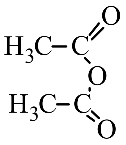
propanoyl chloride



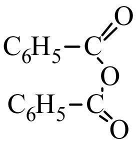
benzoyl chloride

Anhydrides

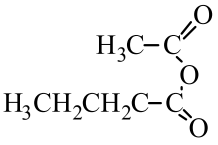
named by dropping the word acid from the parent name and substituting anhydride



acetic anhydride
ethanoic anhydride



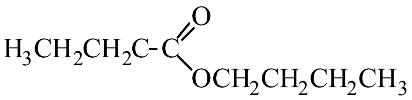
benzoic anhydride



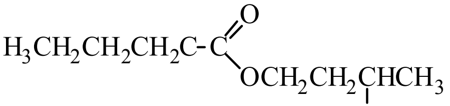
butanoic ethanoic anhydride
acetic butyric anhydride

Esters

Names are derived from the group attached to the oxygen and from the acid. The 'ic acid' is dropped and 'ate' or 'oate' added.



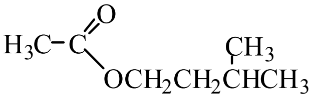
1-butyl butanoate
odor of pineapple



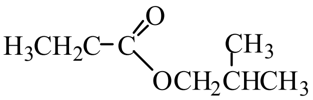
3-methyl-1-butyl butanoate
isopentyl valerate

bad smell

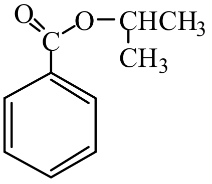
group attached to oxygen is named as the alkyl



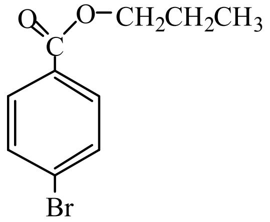
3-methyl-1-butyl ethanoate
isoamyl acetate
odor of bananas



2-methyl-1-propyl propionate
isobutyl propionate
rum odor



isopropyl
benzoate

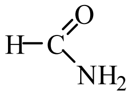


1-propyl 4-bromobenzoate

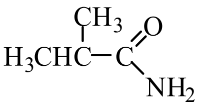
Esters give rise to the characteristic odors and flavors of fruits and vegetables.

Amides

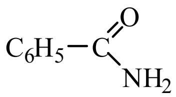
Named by dropping the 'ic or oic acid' and replacing with 'amide'



formamide

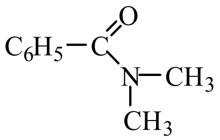


2-methylpropanamide
isobutyramide



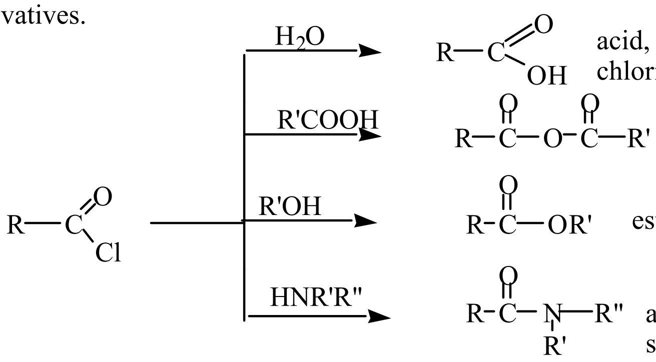
benzamide

The hydrogens on the nitrogen can be substituted:



N,N-dimethylbenzamide

The acid chloride is easy to make (with $SOCl_2$) from the acid, so it is usually used to make the other derivatives.



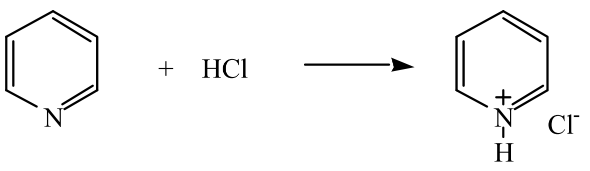
acid, this illustrates the destruction of the acid chloride by water

anhydride

ester

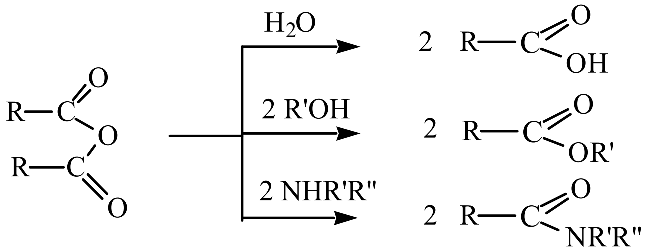
amide, the amine must be primary or secondary

All of these reactions are fast. The side product in all of the reactions is HCl which has to be removed or the reverse reaction can occur. Pyridine can be added to remove the HCl.

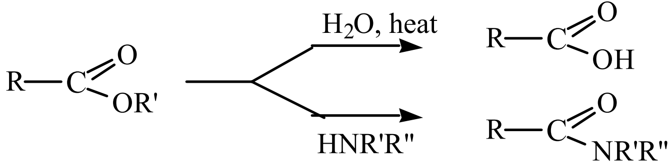


stable salt which precipitates out of solution

Similar reactions can occur with anhydrides, but they are slower than with acyl chlorides

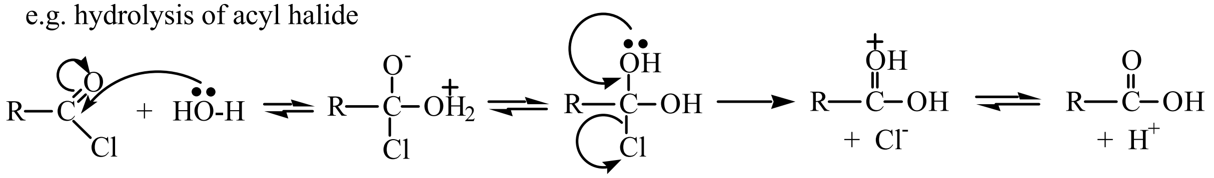


Reactions are even slower with esters

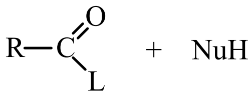


Amides are unreactive and need strong acid or base to hydrolyze them to acids
All of the reactions shown proceed by the same general mechanism:

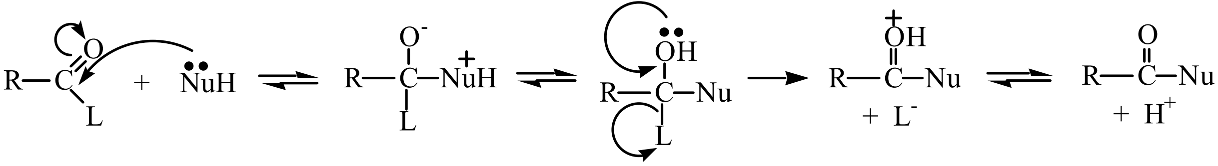
e.g. hydrolysis of acyl halide



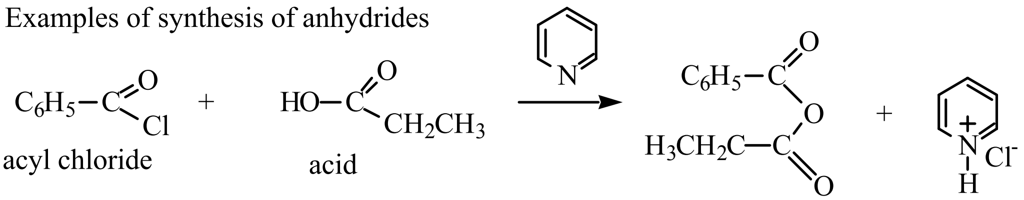
general mechanism



where L is the leaving group, i.e. Cl for acyl chloride, OCOR for anhydride, OR for ester
and Nu is a nucleophilic group, i.e. NR'R", OR, OH

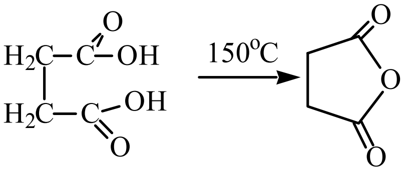


Examples of synthesis of anhydrides


acyl chloride

acid

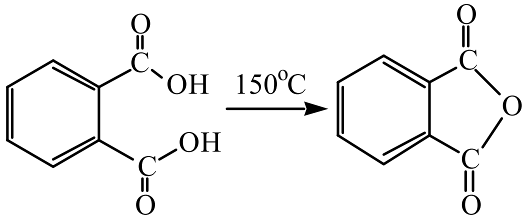
Cyclic anhydrides can be prepared by heating since the groups are held close to one another



succinic acid

succinic anhydride

Water is removed as steam at the temperature
of the reaction so that it does not reverse



phthalic acid

phthalic anhydride