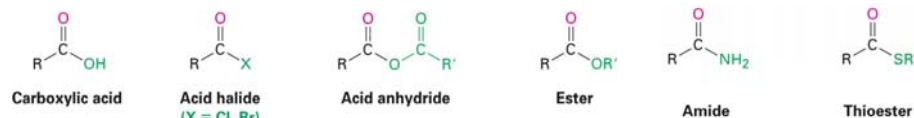


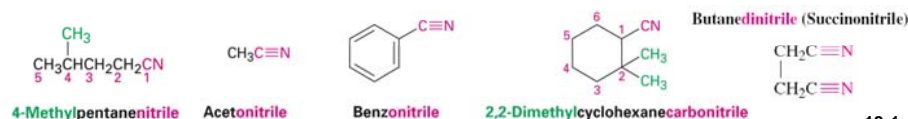
Carboxylic Acid Derivatives: Nucleophilic Acyl Substitution Reactions



Nitriles $R-C\equiv N$ (Nitriles are treated as acid derivatives as they have similar reactivity.)

Compounds containing $-C\equiv N$ functional group are called nitriles:

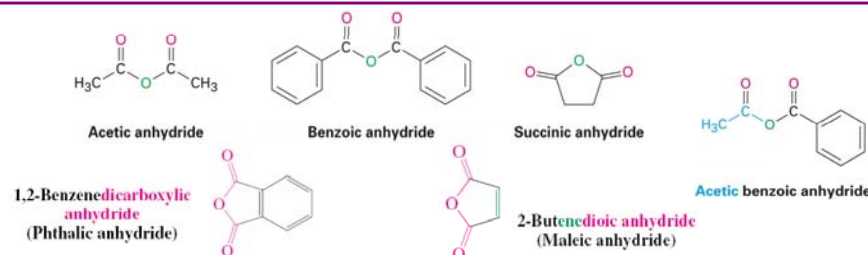
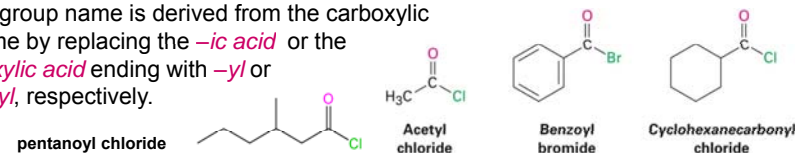
- Simple open-chain nitriles are named by adding *-nitrile* as a suffix to the alkane names, with the nitrile carbon numbered C1;
- Nitriles can also be named as derivatives of carboxylic acids by replacing the *-ic acid* or *-oic acid* ending with *-onitrile*, or by replacing the *-carboxylic acid* ending with *-carbonitriles*;
- The nitrile carbon is attached to C1 carbon.



18-1

Naming Carboxylic Acid Derivatives

Acid halides are named by identifying first the acyl group and then the halide; the acyl group name is derived from the carboxylic acid name by replacing the *-ic acid* or the *-carboxylic acid* ending with *-yl* or *-carbonyl*, respectively.

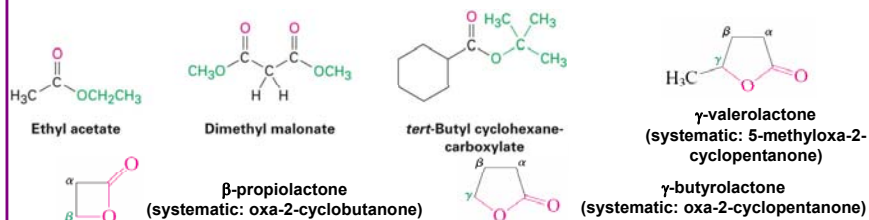


Symmetric anhydrides and **cyclic anhydrides** are named by replacing the word *acid* with *anhydride*; **unsymmetrical anhydrides** are named by citing the two acid alphabetically and then adding *anhydrides*.

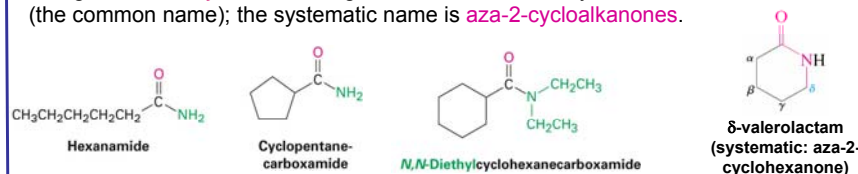
18-2

Naming Carboxylic Acid Derivatives

Esters are named by first identifying the alkyl group attached to the oxygen and then the carboxylic acid, with the *-ic acid* replaced with *-ate*. A cyclic ester is called a **lactone** (the common name); the systematic name is *oxa-2-cycloalkanone*.



Amides are named by replacing the *-ic acid* or *-oic acid* ending with *-amide*, or by replacing the *-carboxylic acid* ending with *-carboxamide*. Cyclic amide are called **lactams** (the common name); the systematic name is *aza-2-cycloalkanones*.

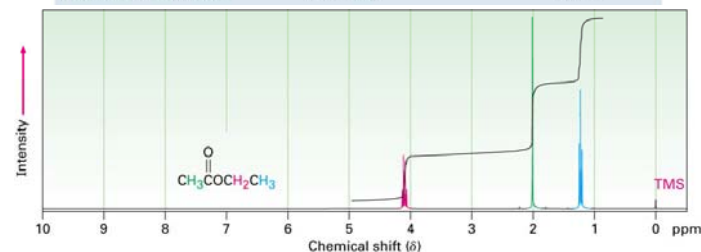


18-3

Spectroscopy of Carboxylic Acid Derivatives

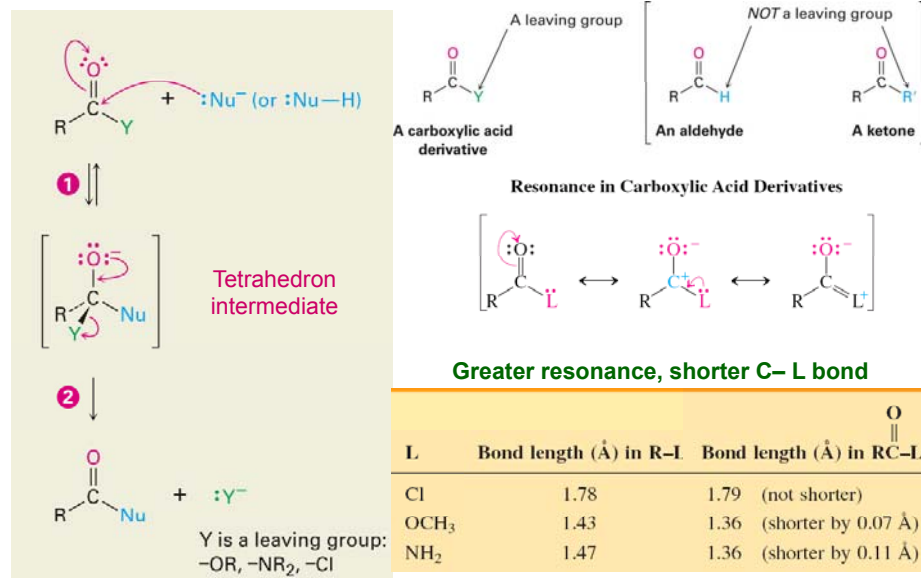
Table 21.3 Infrared Absorptions of Some Carbonyl Compounds

Carbonyl type	Example	Absorption (cm^{-1})
Saturated acid chloride	Acetyl chloride	1810
Aromatic acid chloride	Benzoyl chloride	1770
Saturated acid anhydride	Acetic anhydride	1820, 1760
Saturated ester	Ethyl acetate	1735
Aromatic ester	Ethyl benzoate	1720
Saturated amide	Acetamide	1690
Aromatic amide	Benzamide	1675
N-Substituted amide	N-Methylacetamide	1680
N,N-Disubstituted amide	N,N-Dimethylacetamide	1650
(Saturated aldehyde)	Acetaldehyde	1730
(Saturated ketone)	Acetone	1715
(Saturated carboxylic acid)	Acetic acid	1710



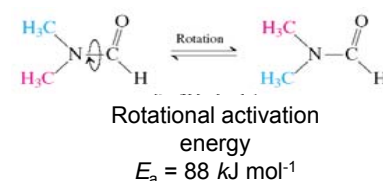
18-4

Nucleophilic Acyl Substitution Reactions



18-5

Factoids of Acid Derivatives

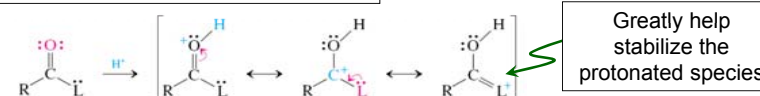


stretching frequency of C=O

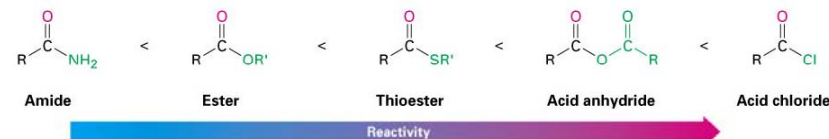
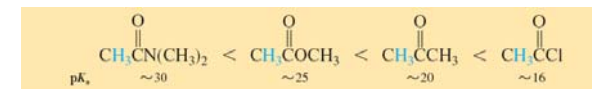
L	$\bar{\nu}_{\text{C=O}}$ (cm ⁻¹)
Cl	1790–1815
O	1740–1790
OCR	1800–1850
OR	1735–1750
NR' ₂	1650–1690

Two bands corresponding to symmetric and asymmetric stretching motions

Acid derivatives are both basic and acidic

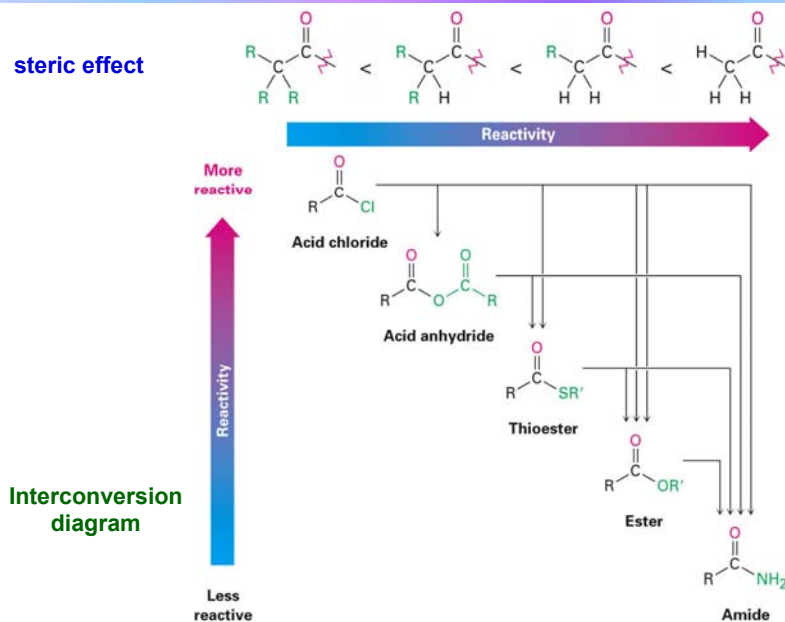


Relative reactivity: electronic effect



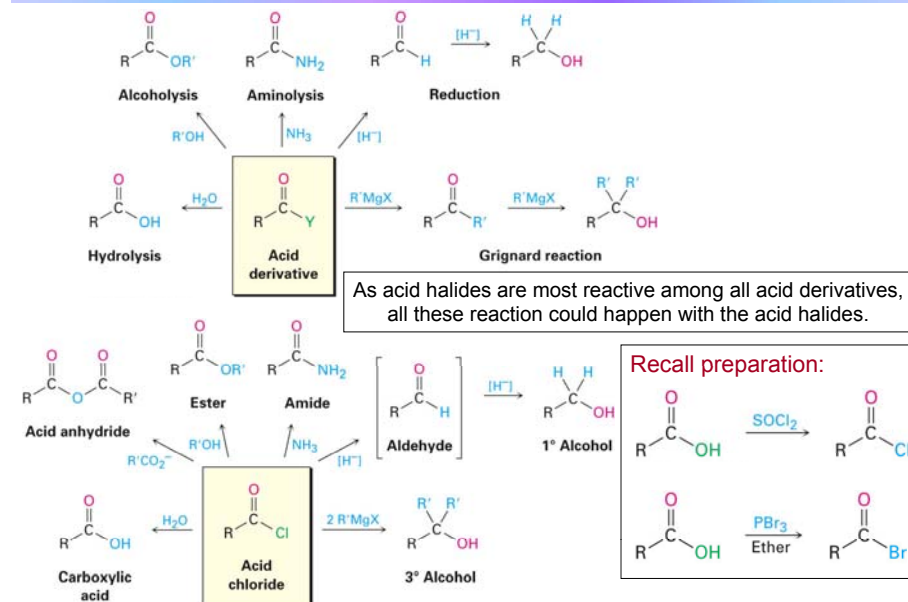
18-6

Relative Reactivity of Carboxylic Acid Derivatives



18-7

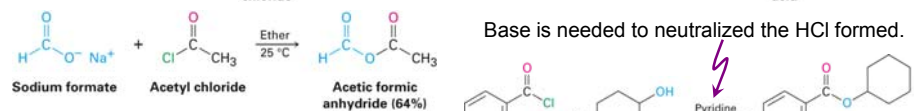
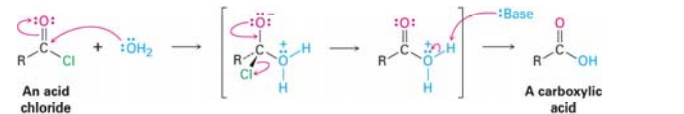
Acyl Substitution Reactions of Acid Halides



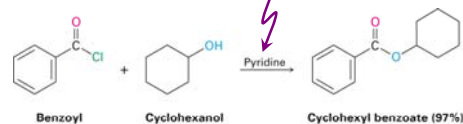
18-8

Acyl Substitution Reactions of Acid Halides

Hydrolysis:

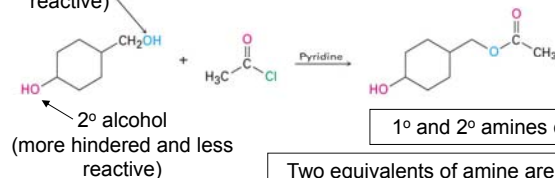


Base is needed to neutralize the HCl formed.



1° alcohol
(less hindered and more reactive)

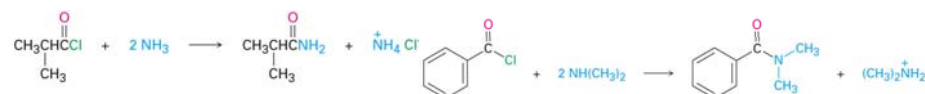
Alcoholysis:



Aminolysis:

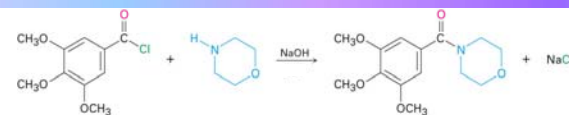
1° and 2° amines can be used, but not 3° amines

Two equivalents of amine are used due to the HCl formation.



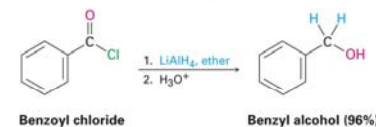
18-9

Reactions of Acid Halides



When the amine is valuable, 1 eq. of NaOH can be added in addition to 1 eq. of the amine.

Reduction: hydride substitution-addition



The modified LAH reacts with acid chloride faster than with the resulting aldehyde.

Modified LAH:



Preparation of reagent

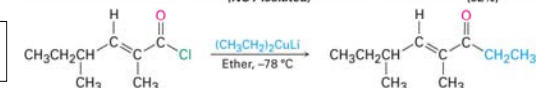


With Grignard Reagent:



Reaction of diorganocopper reagent happens only with acid halides; but not with carboxylic acids, esters, amides, or acid anhydrides.

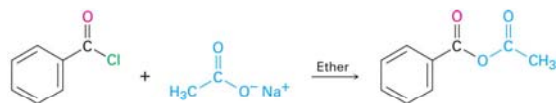
With Gilman Reagent:



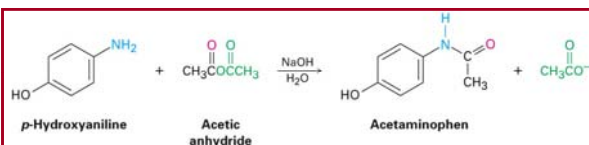
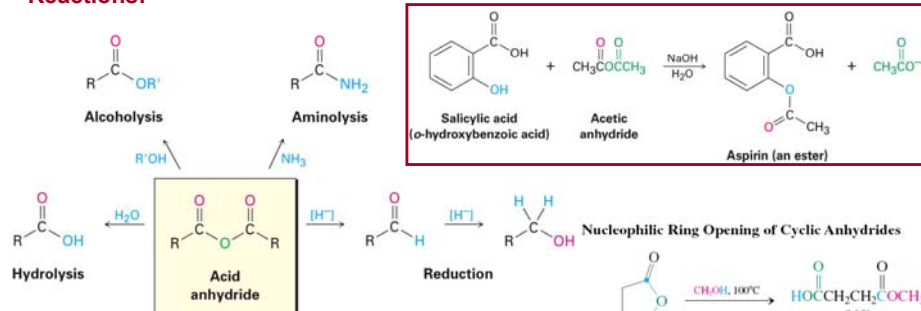
18-10

Chemistry of Acid Anhydrides

Preparation:



Reactions:

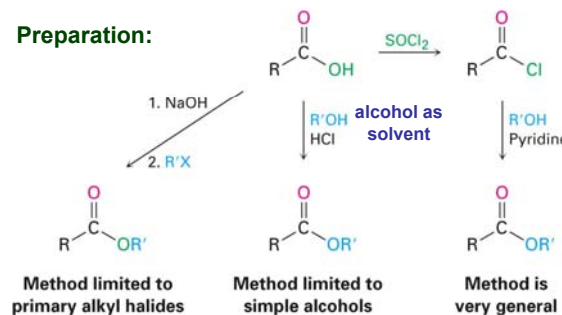


The -NH₂ is more nucleophilic than the -OH group (under basic conditions).

18-11

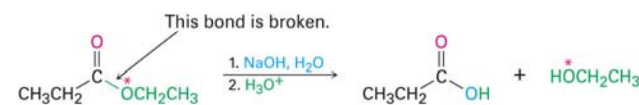
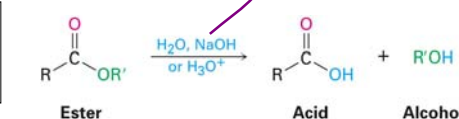
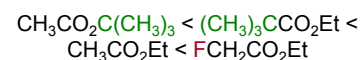
Chemistry of Esters

Preparation:



Ester hydrolysis in basic solution is also called saponification, after the Latin word *sapo*, meaning "soap". Soap is in fact made by boiling animal fat with base to hydrolyze the ester linkage.

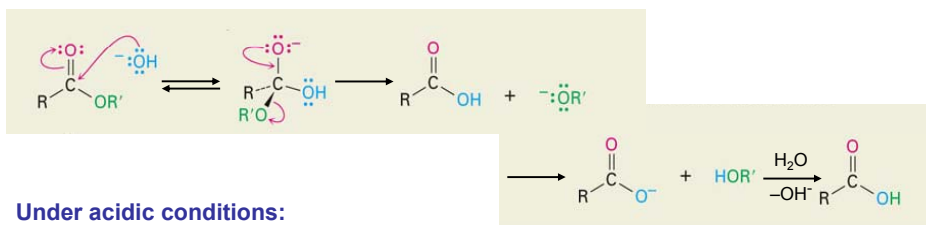
Relative rate of hydrolysis in basic solution:



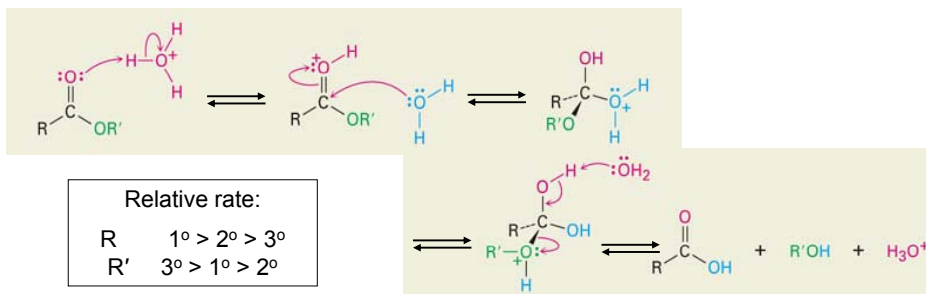
18-12

Mechanisms of Ester Hydrolyses

Under basic conditions:



Under acidic conditions:

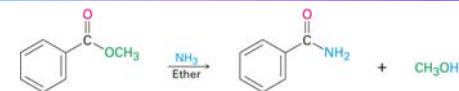


(* Tertiary alcohol goes by a different mechanism)

18-13

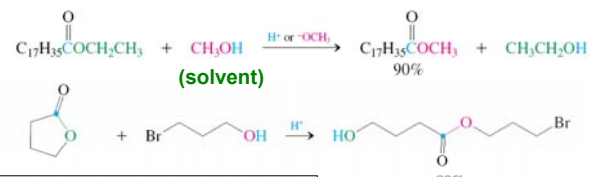
Reactions of Esters

Aminolysis:



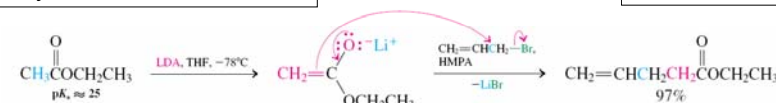
Not commonly used;
amides are more often
made from acid chlorides.

Transesterification:

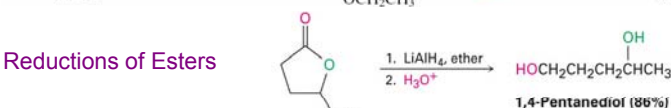


Transesterification is usually an equilibrium process, which can be shifted toward the product either by using the reactant alcohol as a solvent, or removing the product alcohol from the system.

Alkylation of an ester enolate:

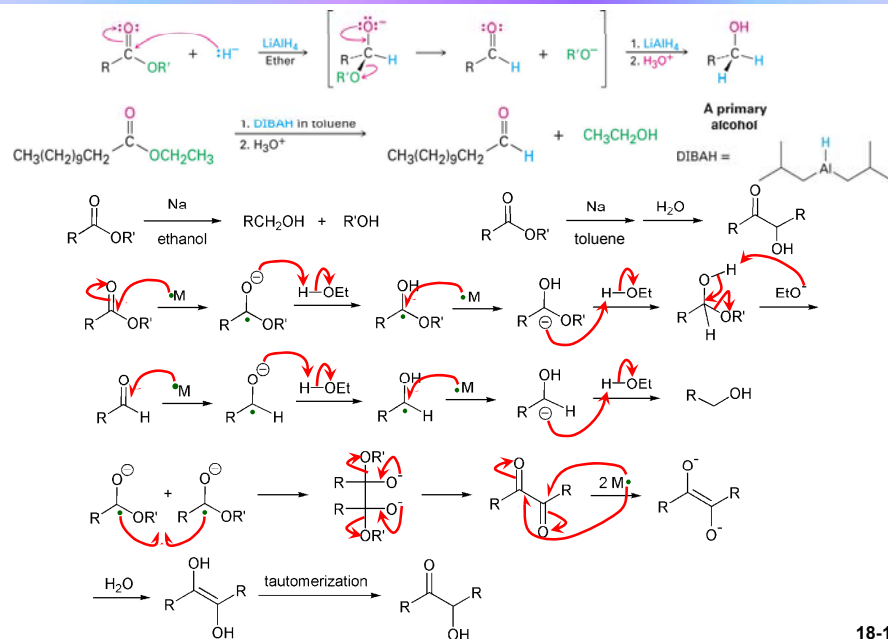


Reductions of Esters



18-14

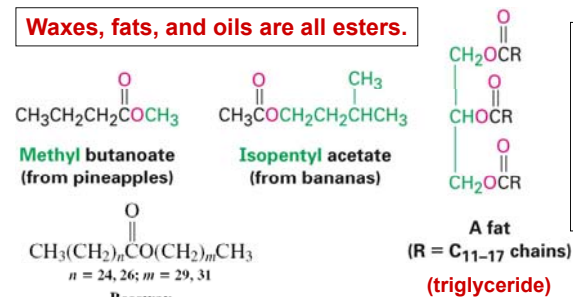
Reductions of Esters



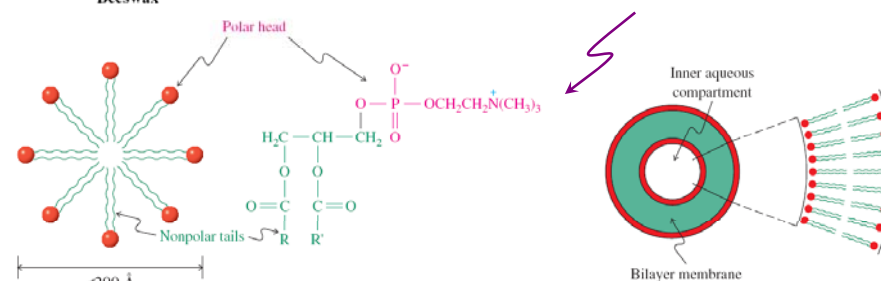
18-15

Esters in Nature

Waxes, fats, and oils are all esters.



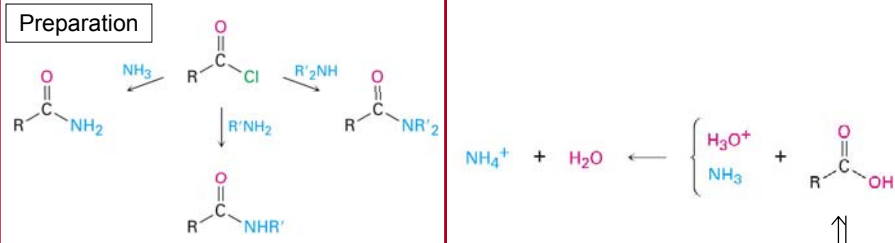
Phospholipids are substituted esters derived from carboxylic acids and phosphoric acids. They are essential components of cell membranes. These molecules are soluble in nonpolar solvent by aggregating into micelles or vesicles (lipid bilayer).



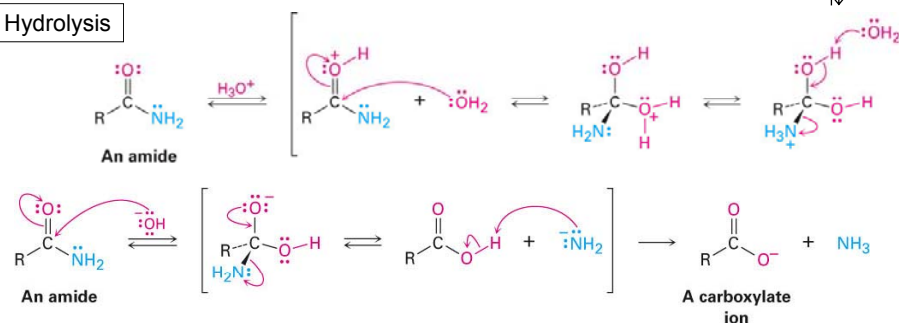
18-16

Preparation and Reactions of Amides

Preparation

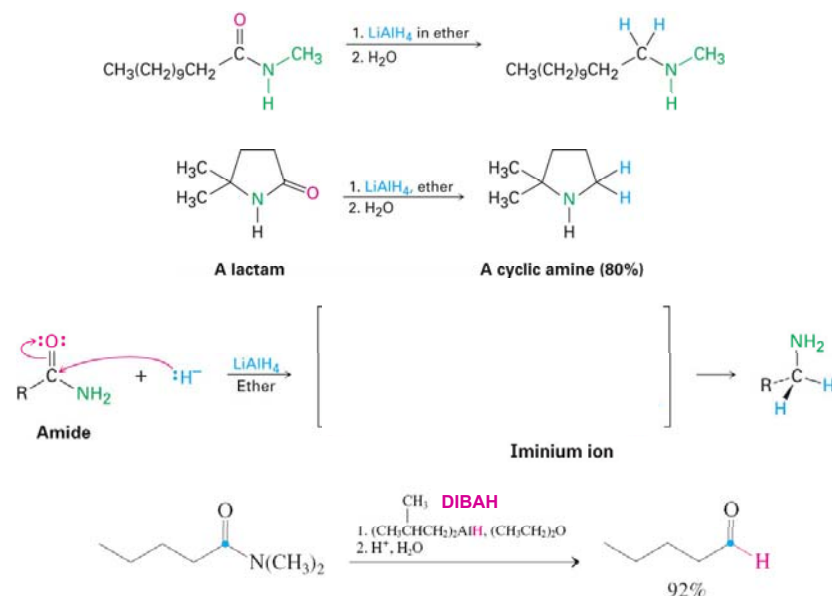


Hydrolysis



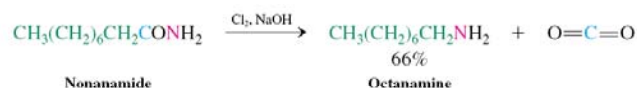
18-17

Reduction of Amides into Amines

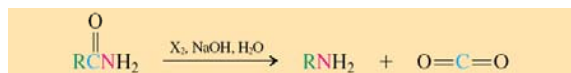


18-18

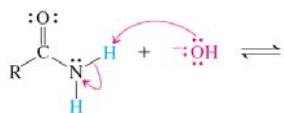
Hofmann Rearrangement



Hofmann Rearrangement

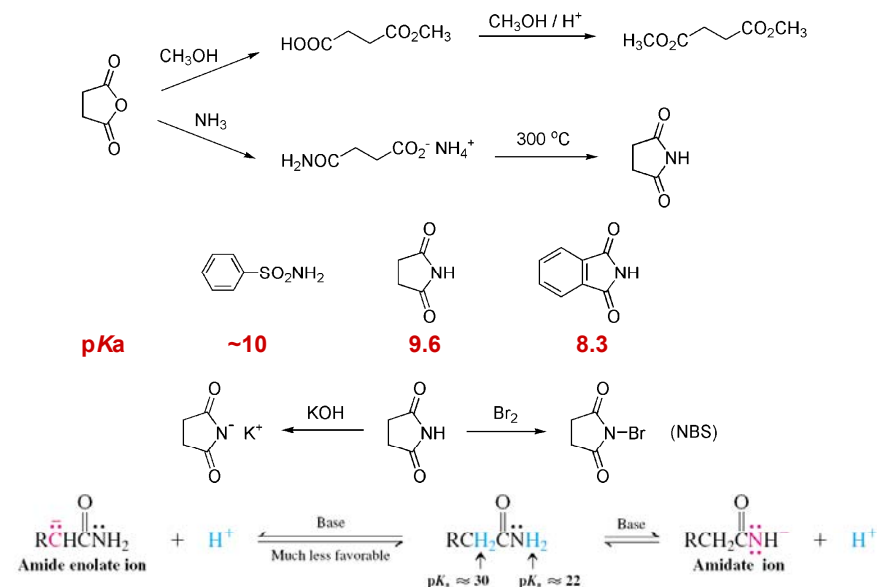


Mechanism:



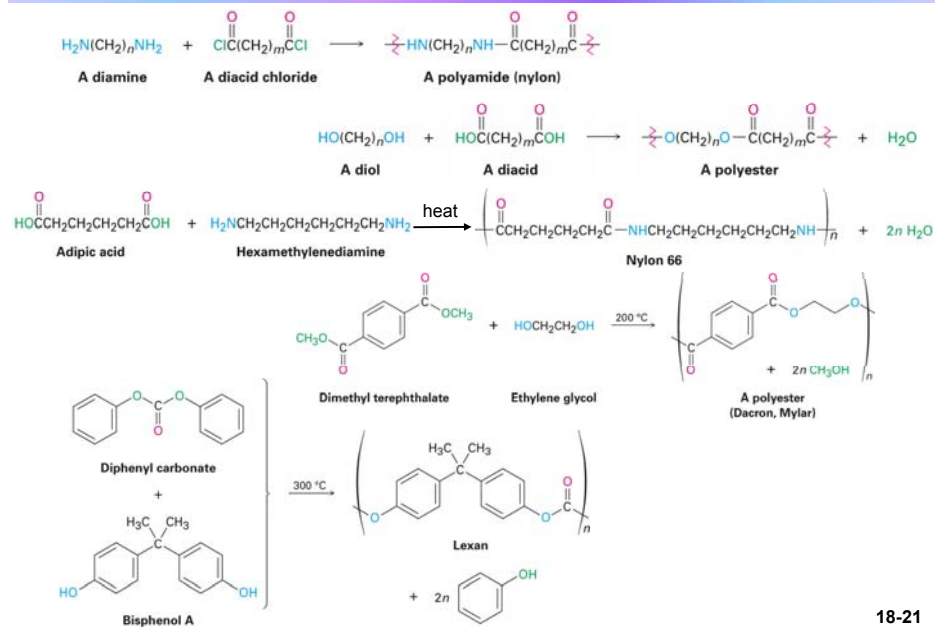
18-19

Preparation and Chemistry of Imides



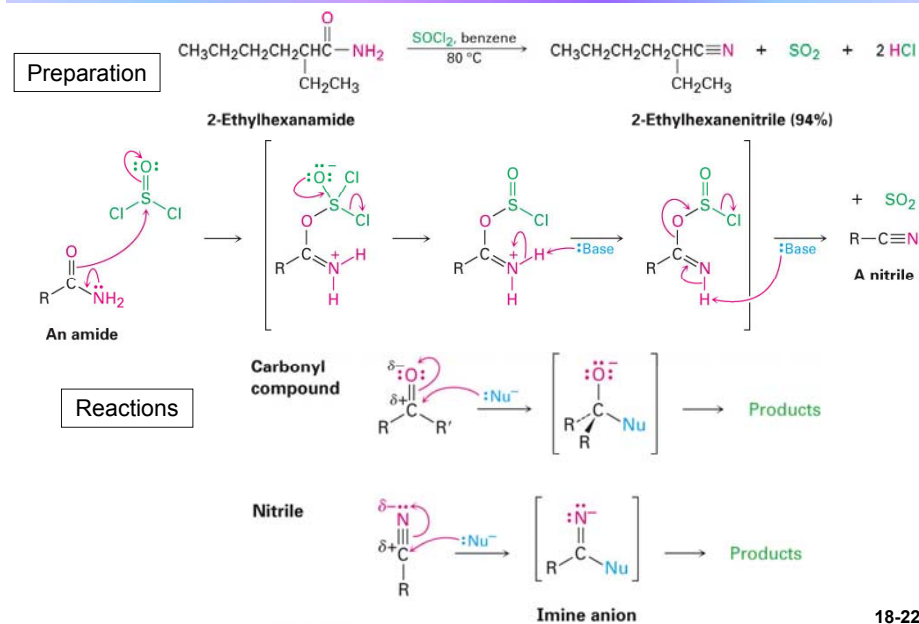
18-20

Preparations of Some Step-Growth Polymers



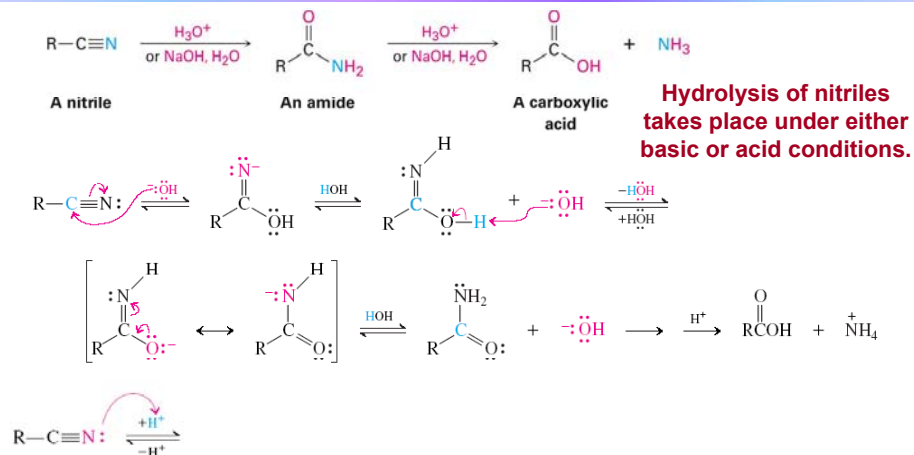
18-21

Nitriles



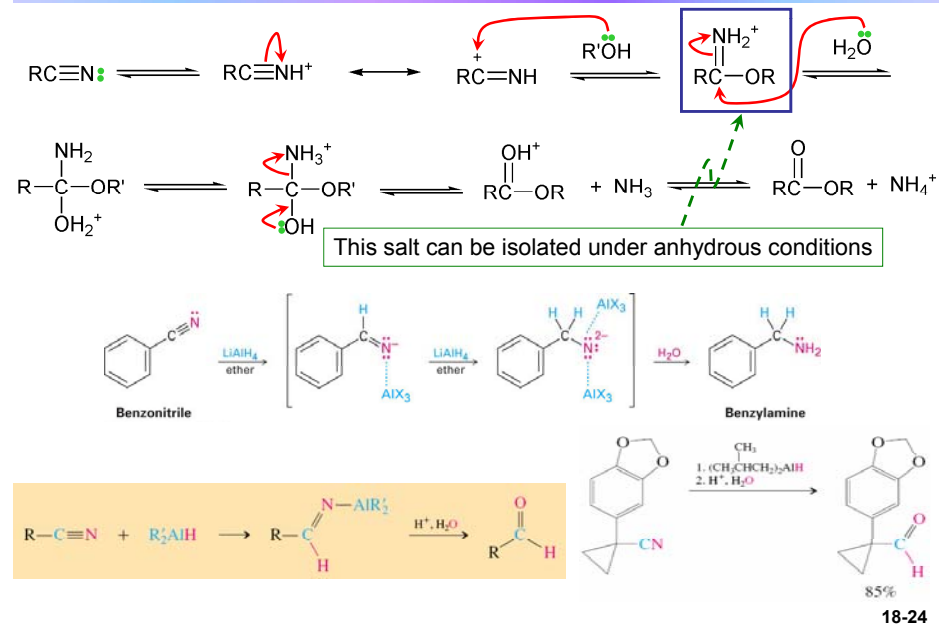
18-22

Hydrolysis of Nitriles



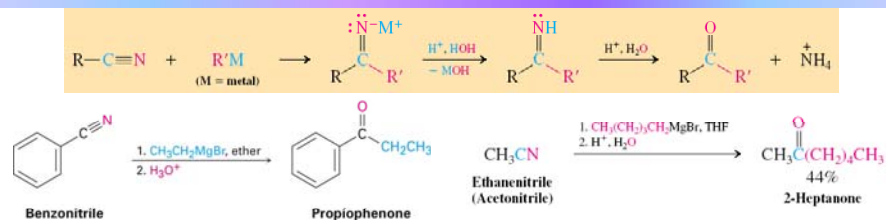
18-23

Alcoholysis and Reduction of Nitriles



18-24

Reactions of Nitriles

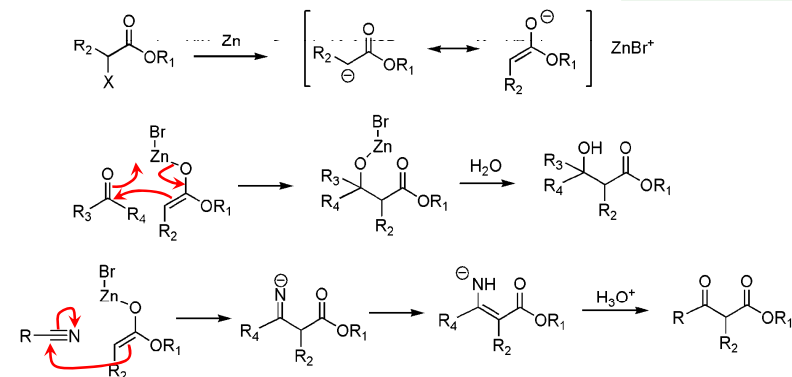
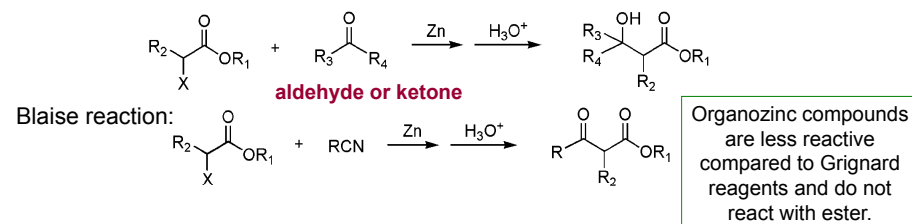


Summary on Reactions of Carbonyl Compounds with Organometallic Reagents and Metal Hydrides

	R'MgX	R'Li	R ₂ 'CuLi	LiAlH ₄	DIBALH (1 eq)	
RCOOH	RCOOMgX	RCOR'	—	RCH ₂ OH	RCHO	RCH ₂ OH (BH ₃)
RCOX	RR ₂ 'COH	RR ₂ 'COH	RCOR'	RCH ₂ OH	RCHO	RCH ₂ OH (NaBH ₄) RCHO [LiAl(OR) ₃ H]
RCHO	RR'CHOH	RR'CHOH	—	RCH ₂ OH	RCH ₂ OH	RCH ₂ OH [NaBH ₄ , LiAl(OR) ₃ H or BH ₃]
RCOR	R ₂ R'COH	R ₂ R'COH	—	R ₂ CHOH	R ₂ CHOH	R ₂ CHOH [NaBH ₄ , LiAl(OR) ₃ H or BH ₃]
RCO ₂ R''	RR ₂ 'COH	RR ₂ 'COH	—	RCH ₂ OH	RCHO	*NaBH ₄ can reduce thiol esters but not esters
RCONH ₂	RCONH ⁻	RCONH ⁻	—	RCH ₂ NH ₂	RCHO	—
RCN	RCOR'	RCOR'	—	RCH ₂ NH ₂	RCHO	—

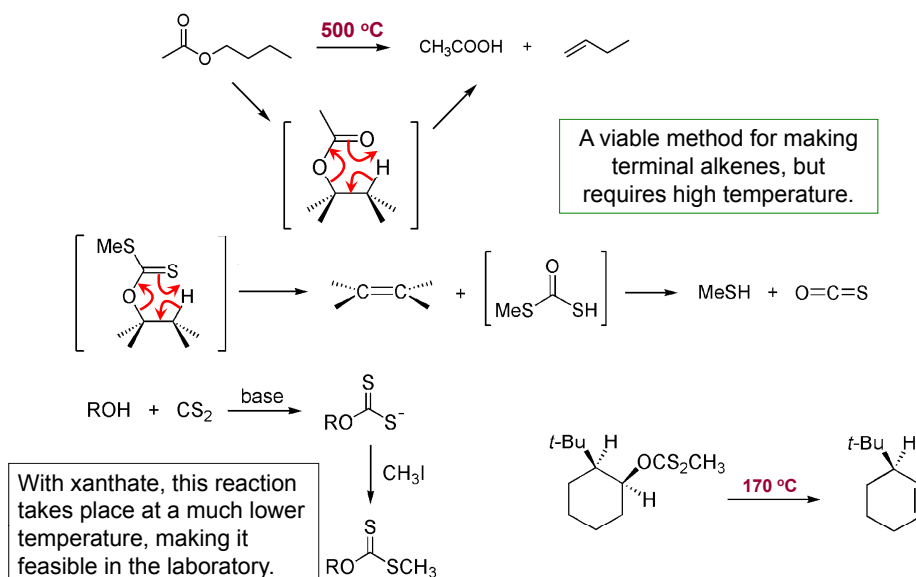
18-25

Reformatsky Reaction



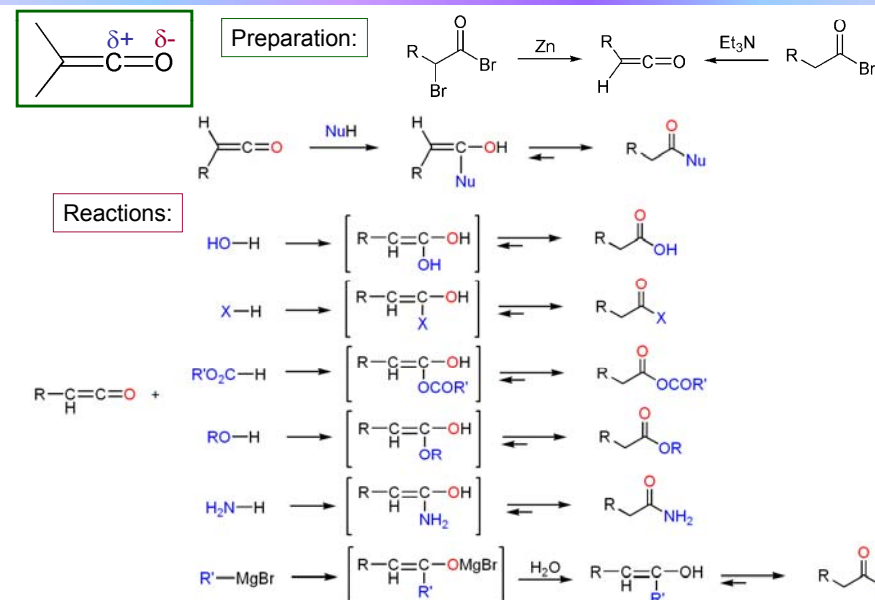
18-26

Chugaev Reaction



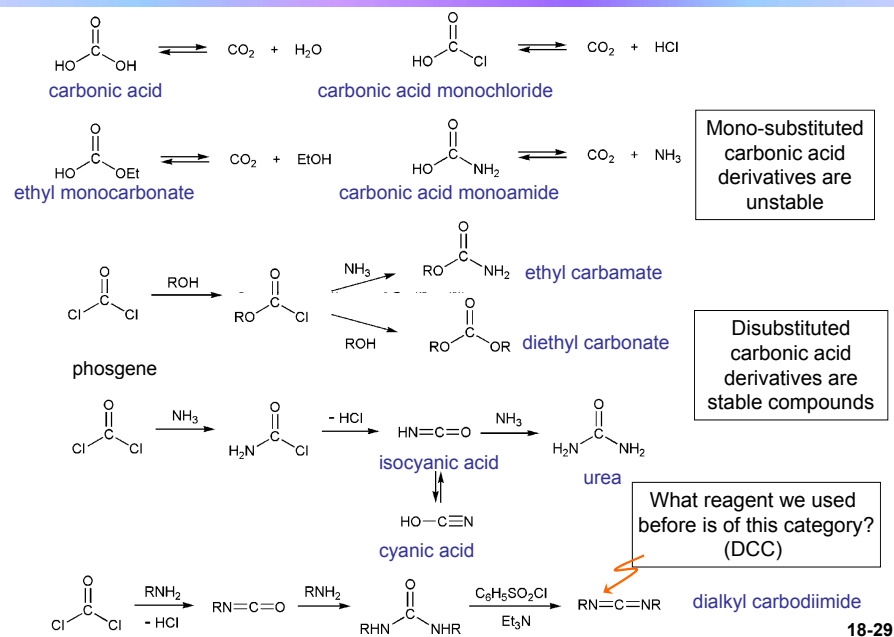
18-27

Ketenes



18-28

Carbonic Acid and Derivatives



Orthoformic Acid and Ester

