

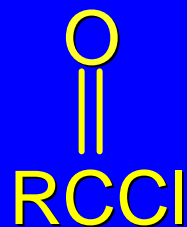
Chapter 20
Carboxylic Acid Derivatives
Nucleophilic Acyl Substitution

The key to this chapter is the next slide.

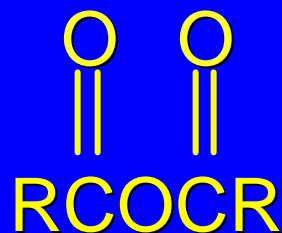
It lists the various carboxylic acids in order of decreasing reactivity toward their fundamental reaction type (nucleophilic acyl substitution).

The other way to read the list is in order of increasing stabilization of the carbonyl group.

*Carboxylic
Acid
Derivatives*



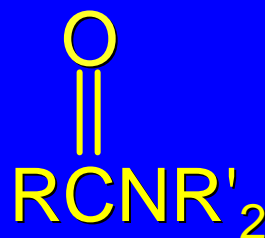
Acyl chloride



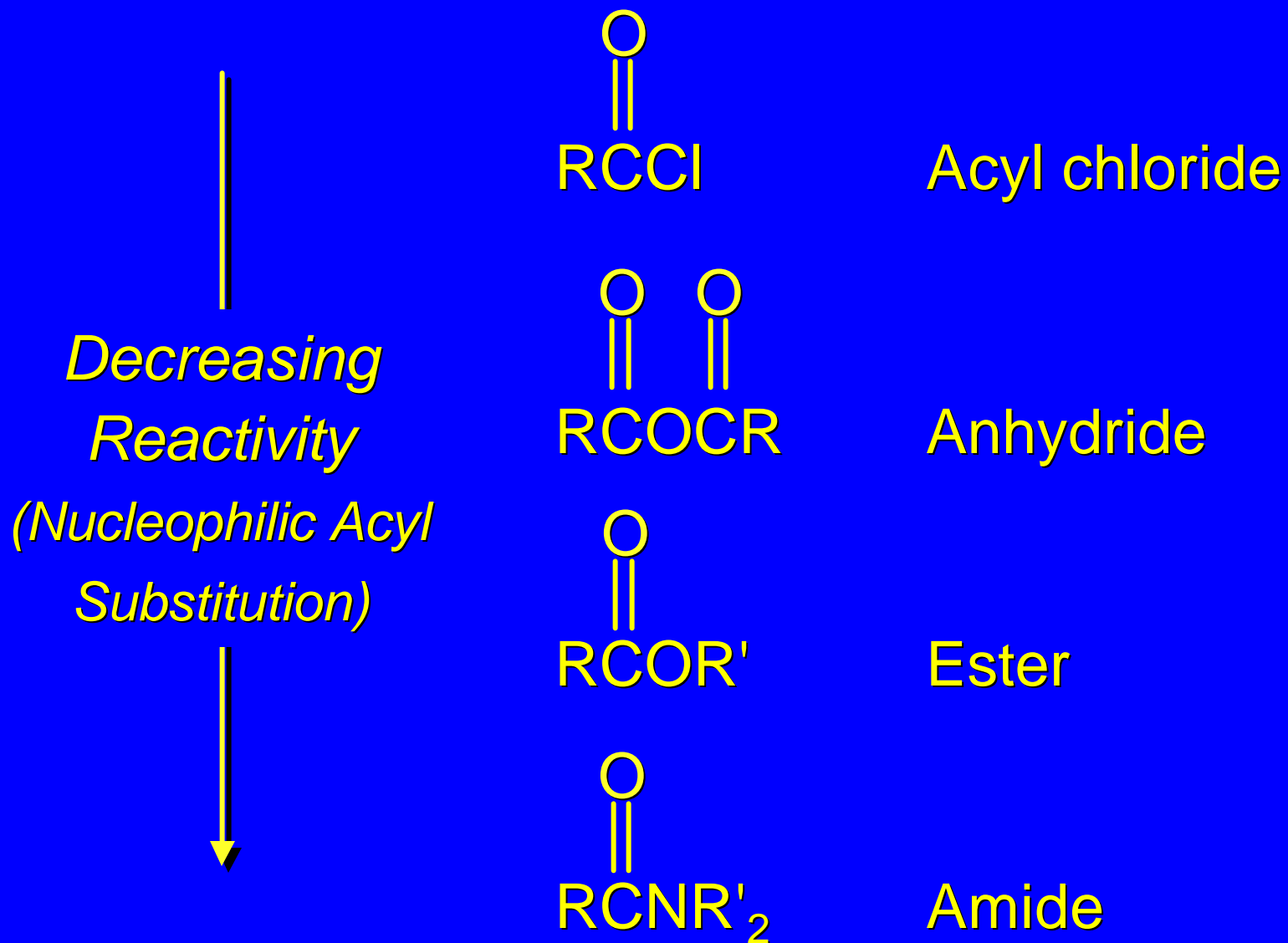
Anhydride



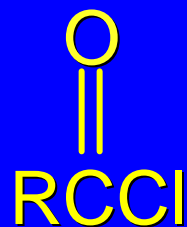
Ester



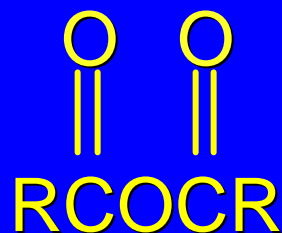
Amide



Increasing
stabilization
of C=O



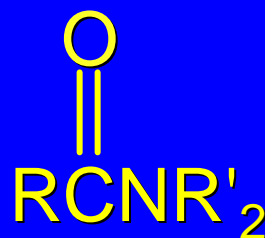
Acyl chloride



Anhydride



Ester

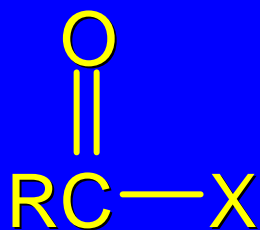


Amide

20.1

Nomenclature of Carboxylic Acid Derivatives

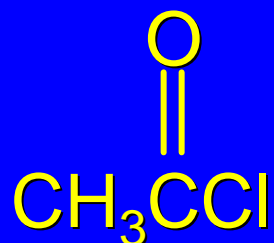
Acyl Halides



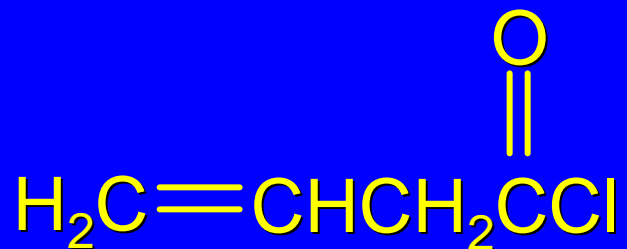
name the acyl group and add the word *chloride*, *fluoride*, *bromide*, or *iodide* as appropriate

acyl chlorides are, by far, the most frequently encountered of the acyl halides

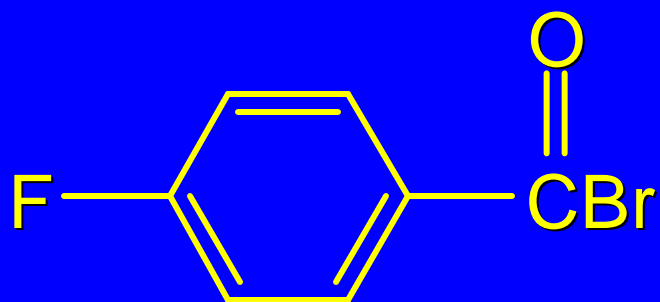
Acyl Halides



acetyl chloride

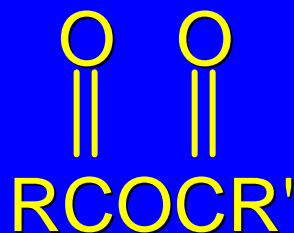


3-butenoyl chloride



p-fluorobenzoyl bromide

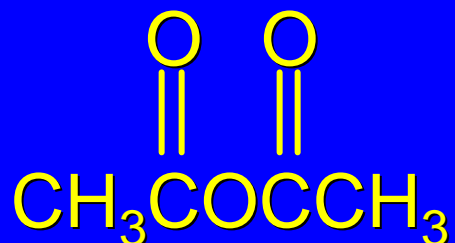
Acid Anhydrides



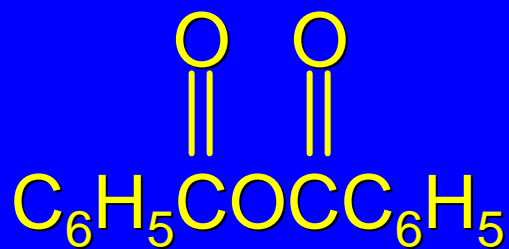
when both acyl groups are the same, name the acid and add the word *anhydride*

when the groups are different, list the names of the corresponding acids in alphabetical order and add the word *anhydride*

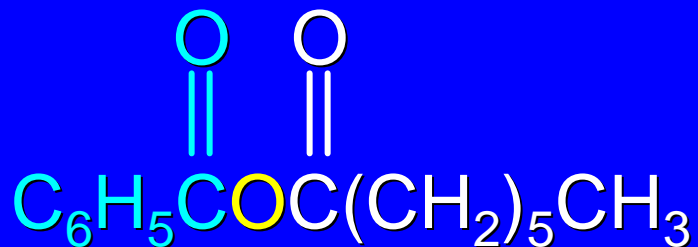
Acid Anhydrides



acetic anhydride

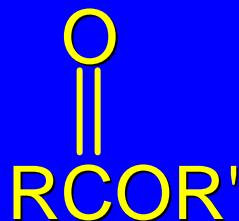


benzoic anhydride



benzoic heptanoic anhydride

Esters

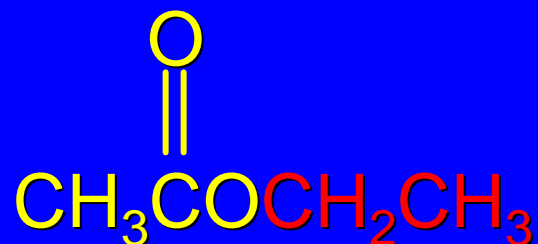


name as *alkyl alkanoates*

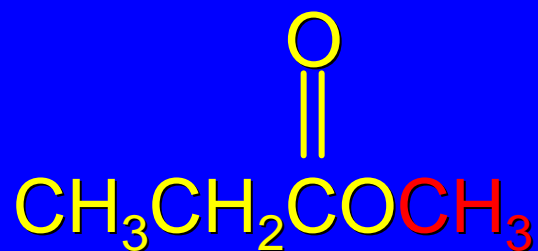
cite the alkyl group attached to oxygen first (R')

name the acyl group second; substitute the suffix
-ate for the *-ic* ending of the corresponding acid

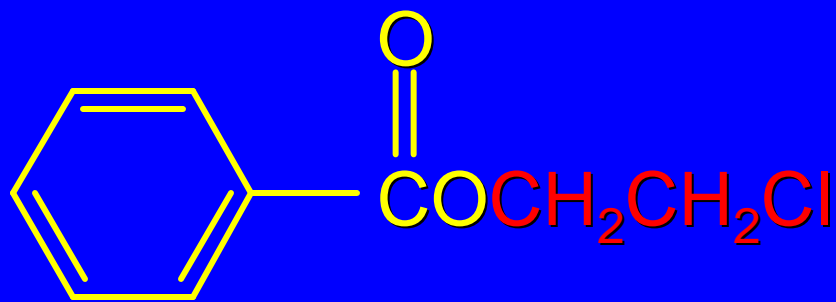
Esters



ethyl acetate

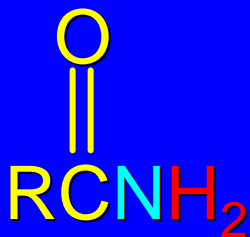


methyl propanoate



2-chloroethyl benzoate

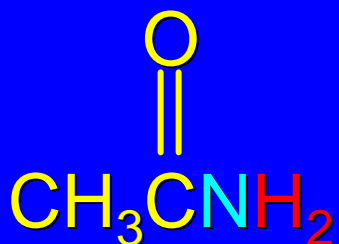
Amides having an NH₂ group



identify the corresponding carboxylic acid

replace the *-ic acid* or *-oic acid* ending by *-amide*.

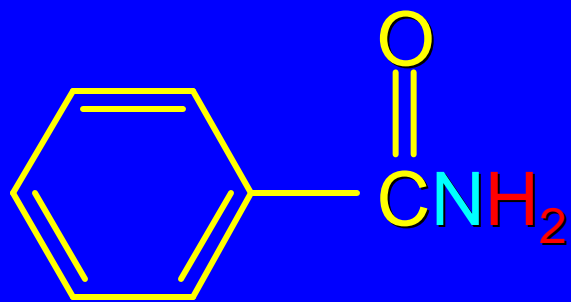
Amides having an NH₂ group



acetamide



3-methylbutanamide



benzamide

Amides having substituents on N

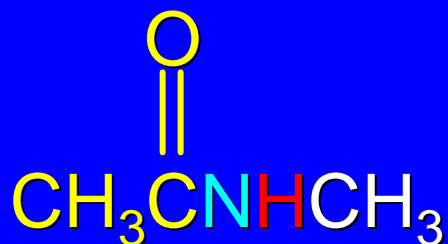


name the amide as before

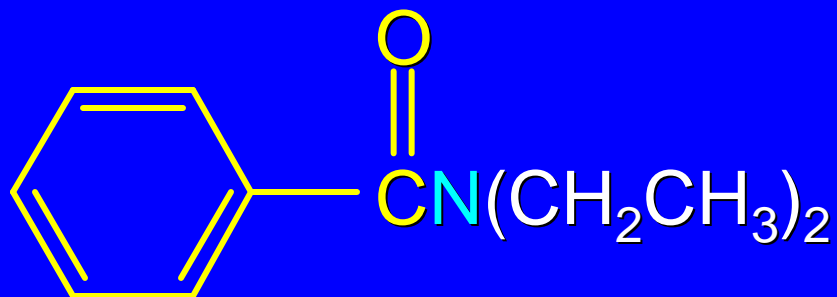
precede the name of the amide with the name of the appropriate group or groups

precede the names of the groups by the letter *N*- (standing for nitrogen and used as a locant)

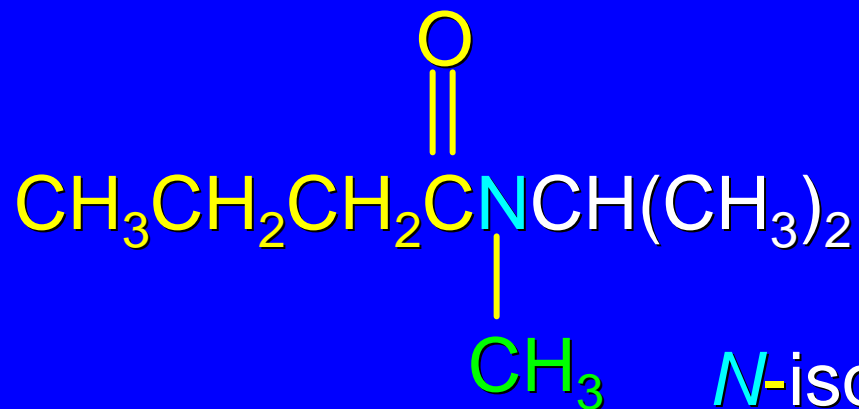
Amides having substituents on N



N-methylacetamide



N,N-diethylbenzamide



N-isopropyl-*N*-methylbutanamide

Nitriles



add the suffix *-nitrile* to the name of the parent hydrocarbon chain (including the triply bonded carbon of CN)

or: replace the *-ic acid* or *-oic acid* name of the corresponding carboxylic acid by *-onitrile*

or: name as an *alkyl cyanide* (functional class name)

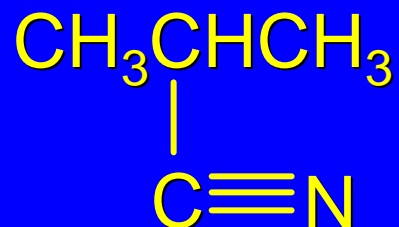
Nitriles



ethanenitrile
or: acetonitrile
or: methyl cyanide



benzonitrile



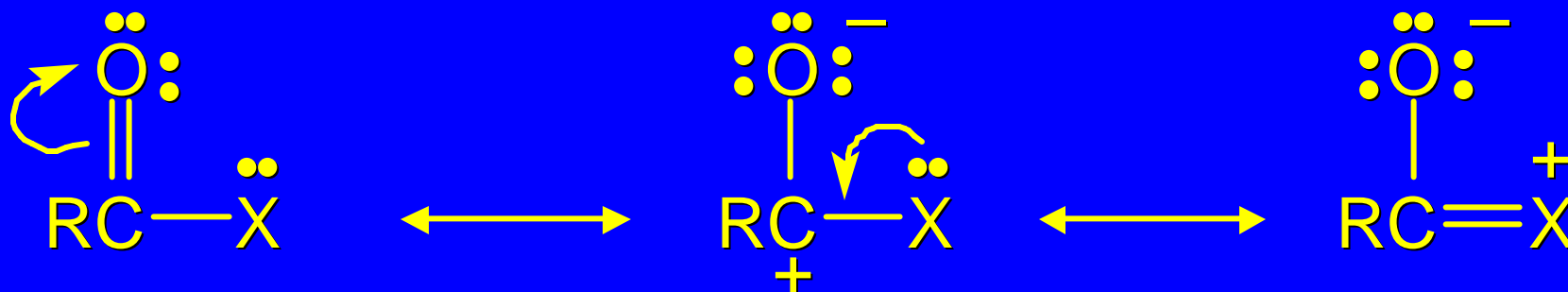
2-methylpropanenitrile
or: isopropyl cyanide

20.2

Structure of Carboxylic Acid Derivatives

Electron Delocalization and the Carbonyl Group

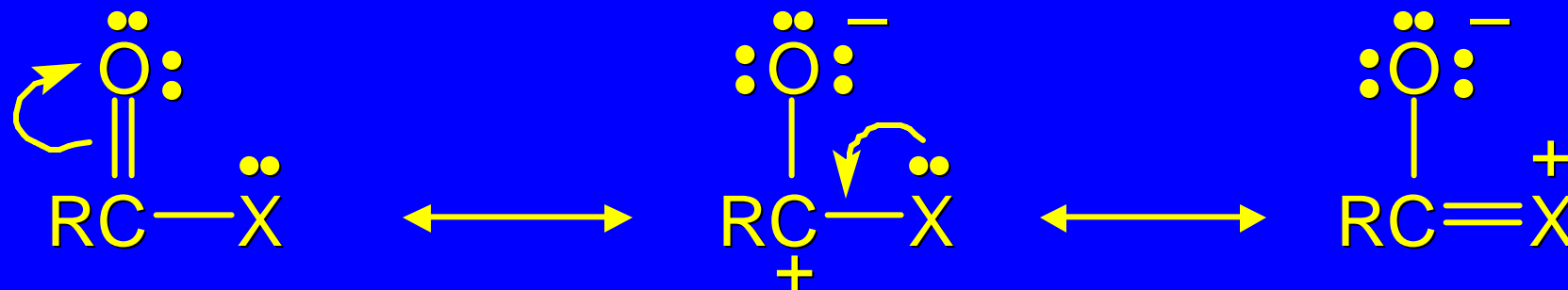
The main structural feature that distinguishes acyl chlorides, anhydrides, esters, and amides is the interaction of the substituent with the carbonyl group. It can be represented in resonance terms as:



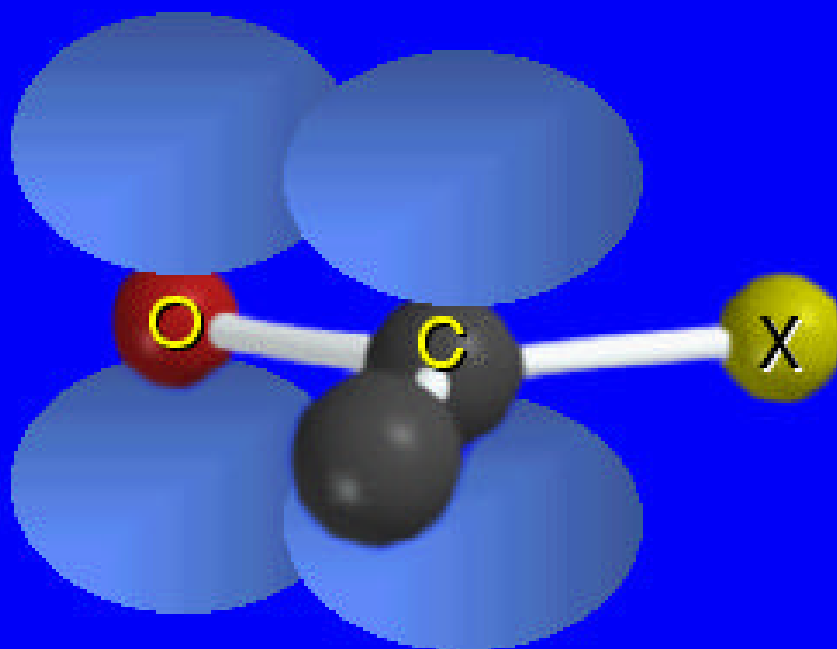
Electron Delocalization and the Carbonyl Group

The extent to which the lone pair on X can be delocalized into C=O depends on:

- 1) the electronegativity of X
- 2) how well the lone pair orbital of X interacts with the *p* orbital of C=O

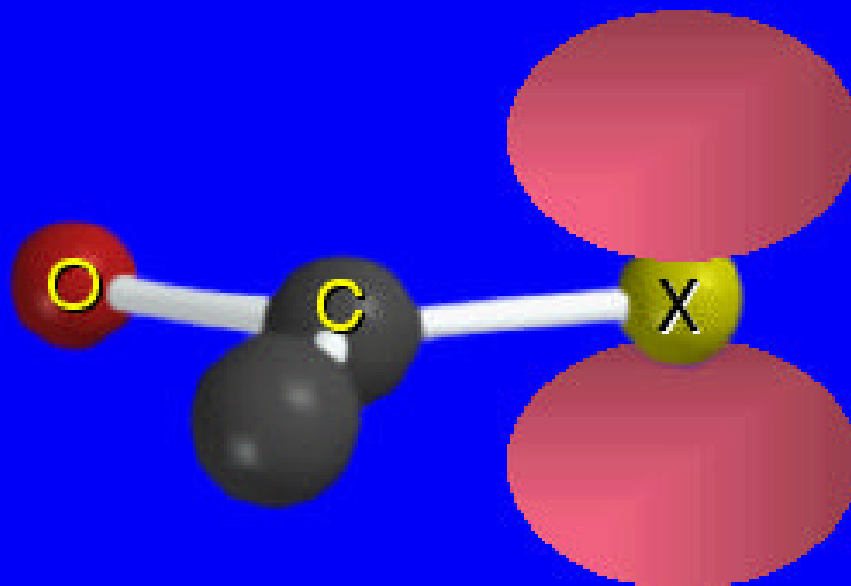


Orbital overlaps in carboxylic acid derivatives



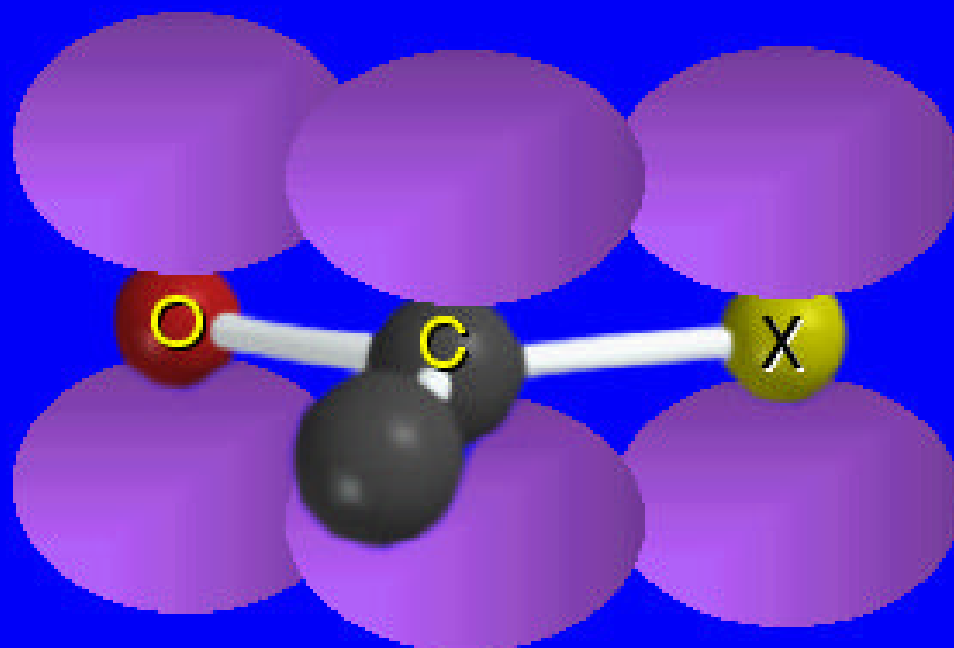
p orbital of carbonyl group

Orbital overlaps in carboxylic acid derivatives



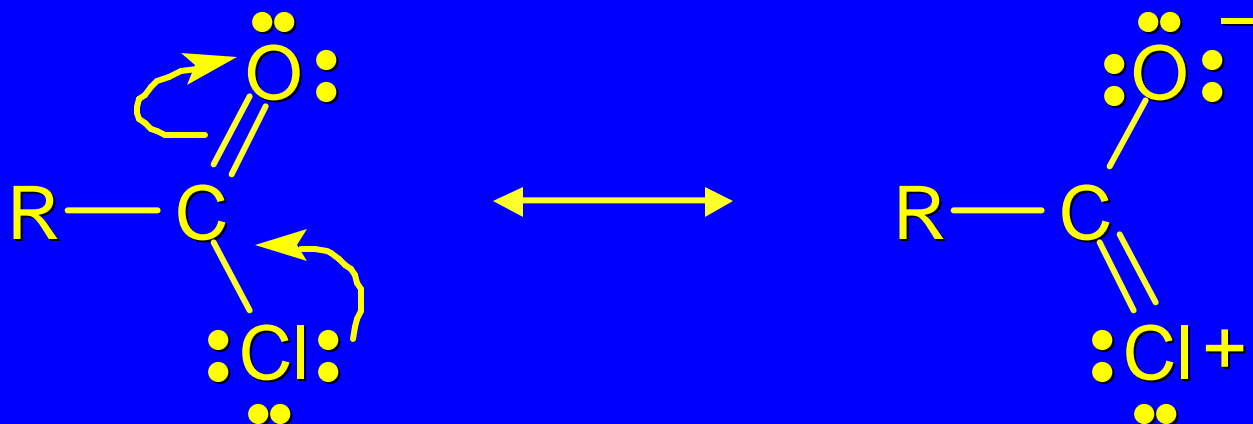
lone pair orbital
of substituent

Orbital overlaps in carboxylic acid derivatives



electron pair of substituent delocalized into
carbonyl *p* orbital

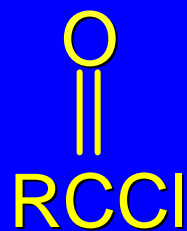
Acyl Chlorides



acyl chlorides have the least stabilized carbonyl group

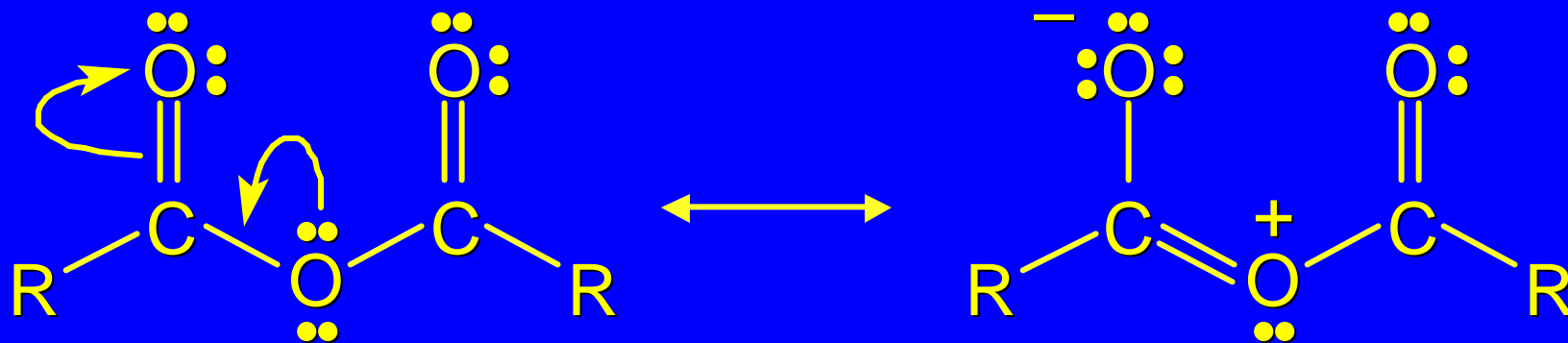
delocalization of lone pair of Cl into C=O group is not effective because C—Cl bond is too long

least stabilized C=O



most stabilized C=O

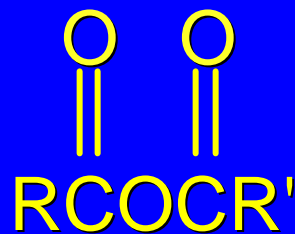
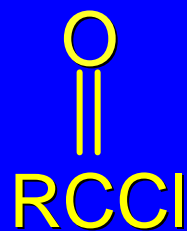
Acid Anhydrides



lone pair donation from oxygen stabilizes the carbonyl group of an acid anhydride

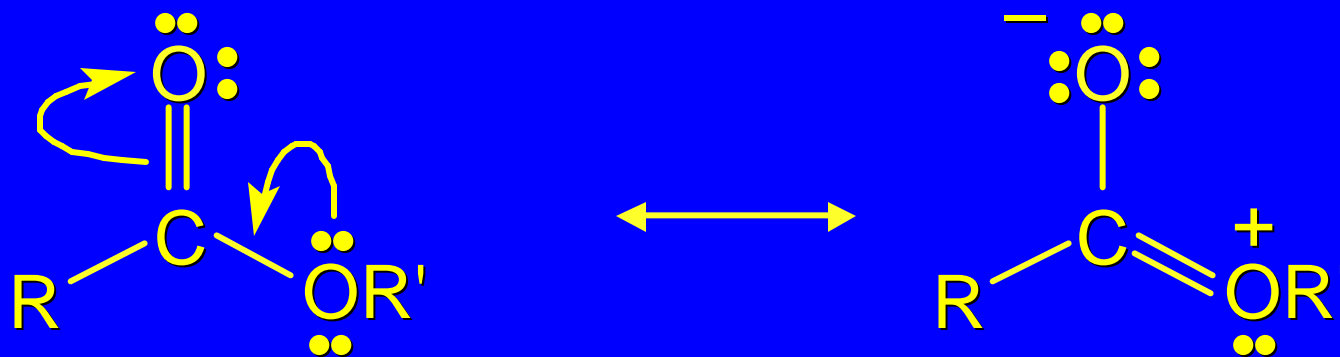
the other carbonyl group is stabilized in a manner by the lone pair

least stabilized C=O



most stabilized C=O

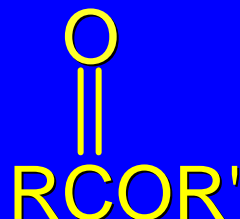
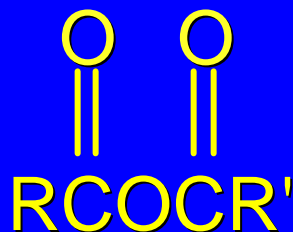
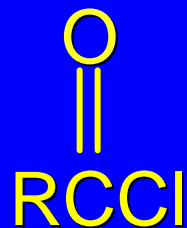
Esters



lone pair donation from oxygen stabilizes the carbonyl group of an ester

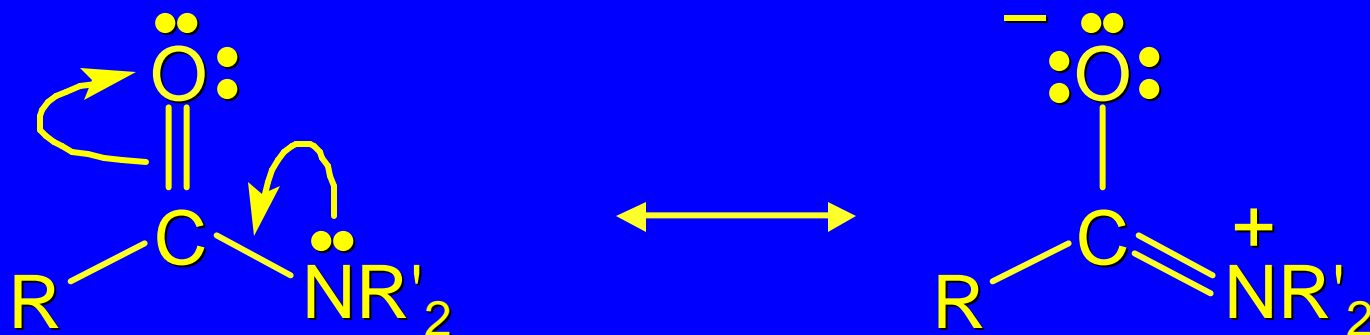
stabilization greater than comparable stabilization of an anhydride

least stabilized C=O



most stabilized C=O

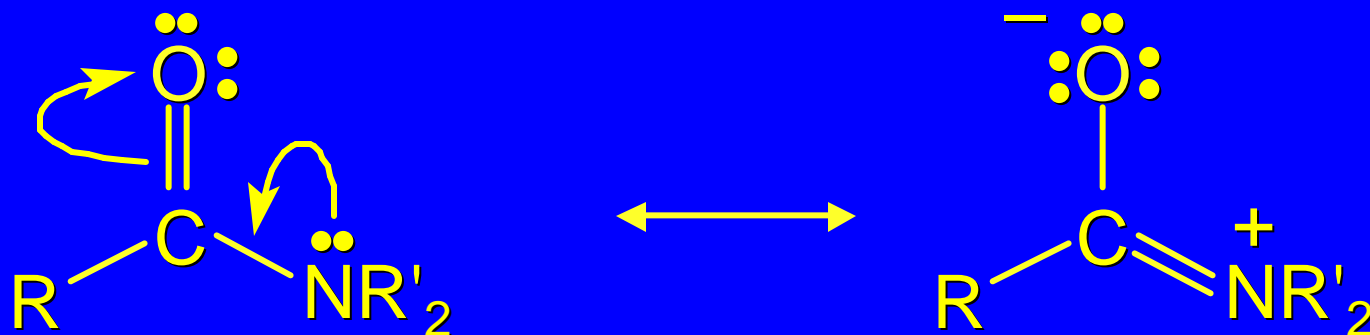
Amides



lone pair donation from nitrogen stabilizes the carbonyl group of an amide

N is less electronegative than O; therefore, amides are stabilized more than esters and anhydrides

Amides

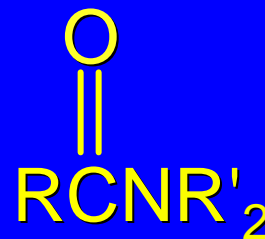
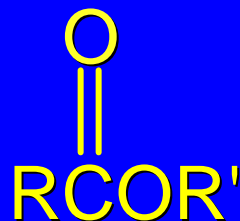
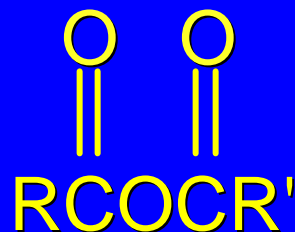
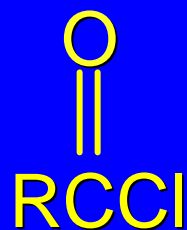


amide resonance imparts significant double-bond character to C—N bond

activation energy for rotation about C—N bond is 75-85 kJ/mol

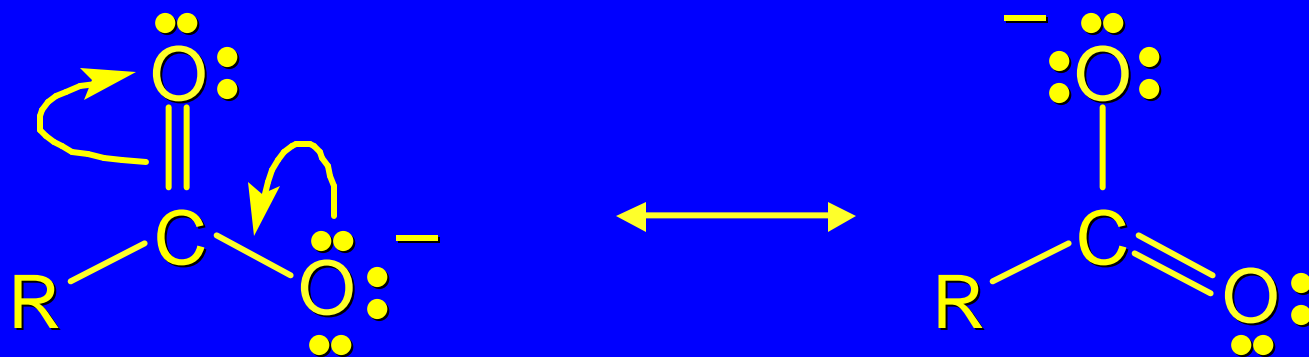
C—N bond distance is 135 pm in amides versus normal single-bond distance of 147 pm in amines

least stabilized C=O



most stabilized C=O

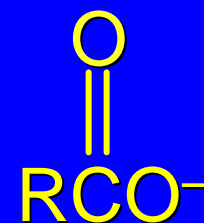
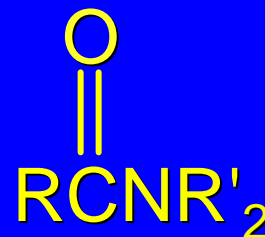
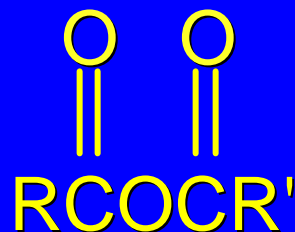
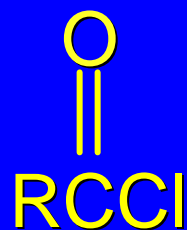
Carboxylate ions



very efficient electron delocalization and dispersal
of negative charge

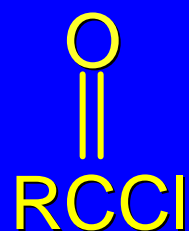
maximum stabilization

least stabilized C=O



most stabilized C=O

Reactivity is related to structure: Table 20.1

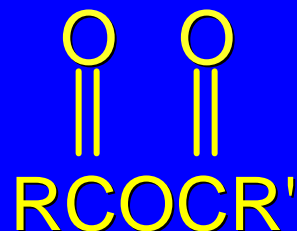


Stabilization

Relative rate
of hydrolysis

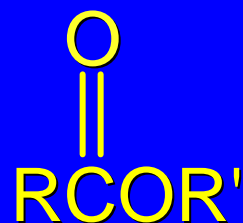
very small

10^{11}



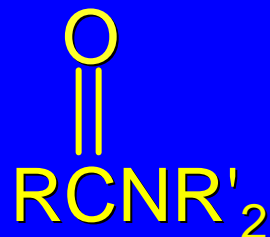
small

10^7



moderate

1.0

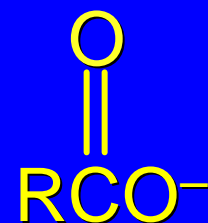
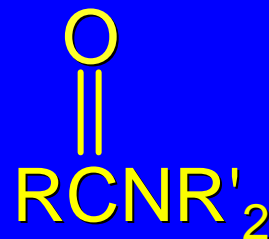
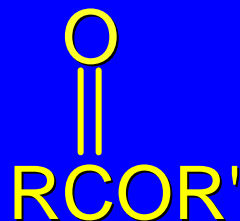
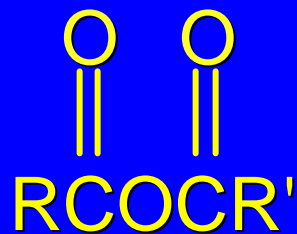
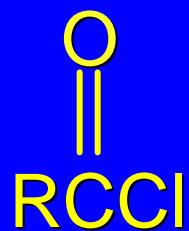


large

$< 10^{-2}$

The more stabilized the carbonyl group, the less reactive it is.

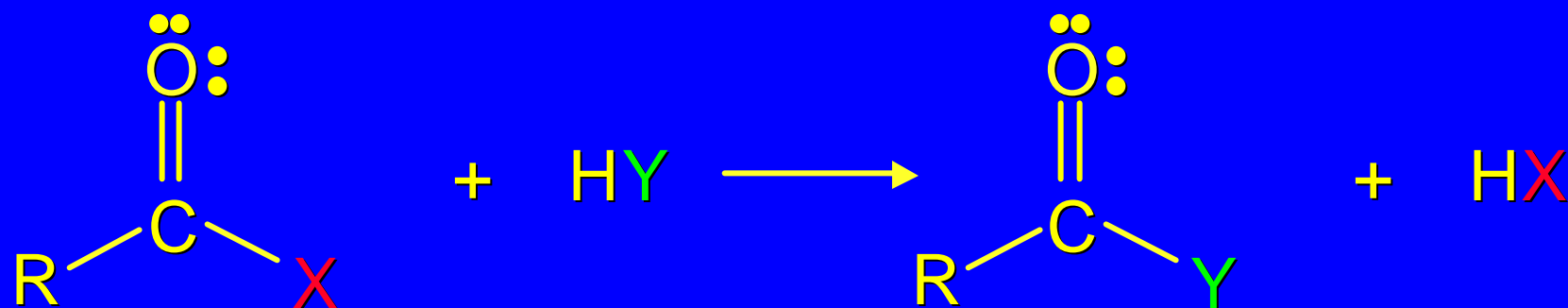
most reactive



least reactive

Nucleophilic Acyl Substitution

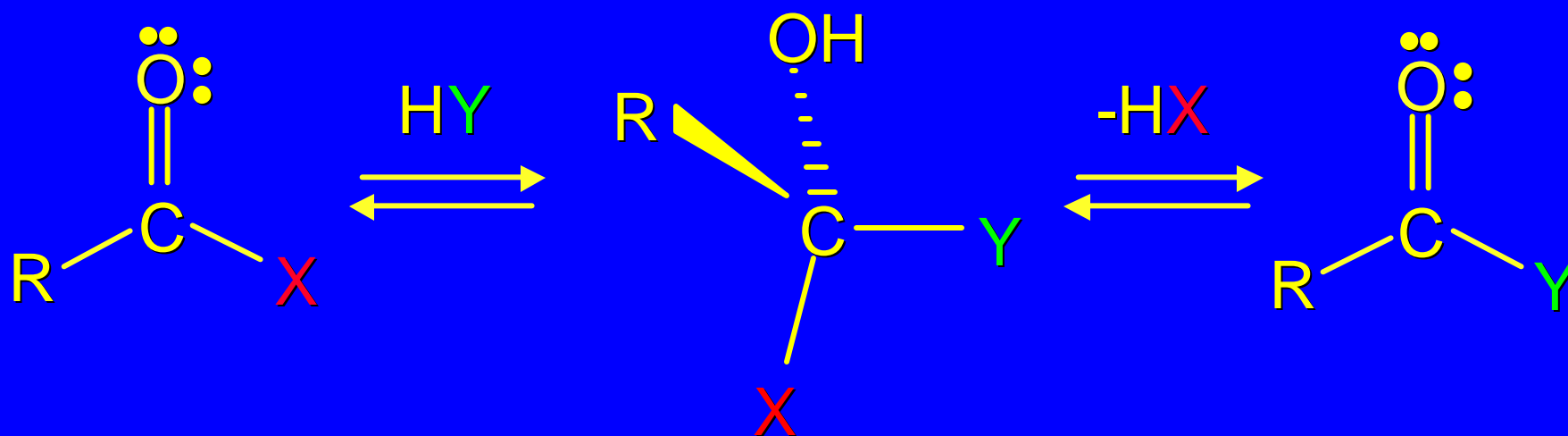
In general:



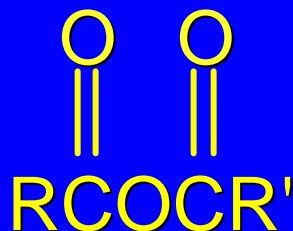
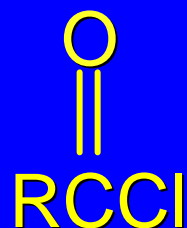
Reaction is feasible when a less stabilized carbonyl is converted to a more stabilized one (more reactive to less reactive).

General Mechanism for Nucleophilic Acyl Substitution

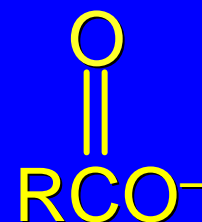
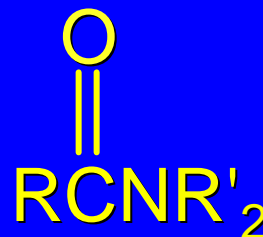
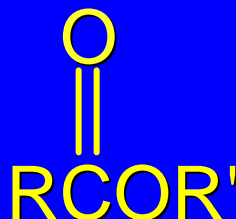
involves formation and dissociation
of a tetrahedral intermediate



most reactive



a carboxylic acid derivative can be converted by nucleophilic acyl substitution to any other type that lies below it in this table



least reactive