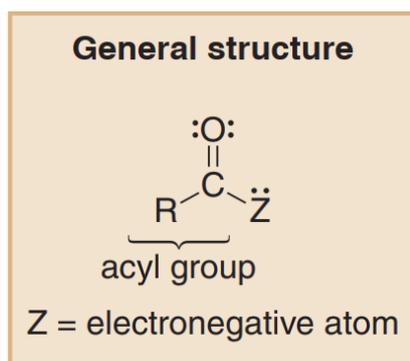


كلية التربية للعلوم الصرفة	الكلية
قسم الكيمياء	القسم
Organic chemistry	المادة باللغة الانجليزية
الكيمياء العضوية	المادة باللغة العربية
المرحلة الثانية	المرحلة الدراسية
د. عمر جمال مهدي العسافي	اسم التدريسي
Carboxylic acid derivatives	عنوان المحاضرة باللغة الانجليزية
مشتقات الحوامض الكربوكسيلية	عنوان المحاضرة باللغة العربية
التاسعة	رقم المحاضرة
<i>Organic Chemistry</i> 6 ^{ed} , William H. Brown, Christopher S. Foote, Brent L. Iverson, Eric V. Anslyn, Bruce M. Novak, 2012	المصادر والمراجع
<i>Organic Chemistry</i> 3 ^{ed} , Janice Gorzynski Smith, 2011	
<i>Organic Chemistry</i> '' by Jonathan Clayden, Nick Greeves, and Stuart Warren	

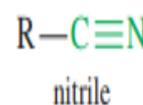
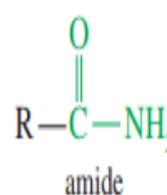
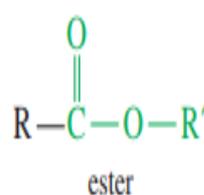
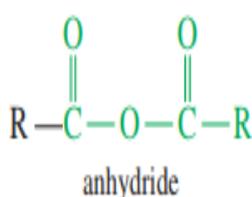
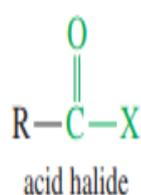


1. Introduction

Carbonyl compounds bonded to an electronegative atom called an acyl group. These include carboxylic acids and their derivatives such as acid chlorides, anhydrides, esters, and amides.



Carboxylic acid derivatives are defined as compounds with functional groups that can be converted to carboxylic acids by a simple acidic or basic hydrolysis.



Condensed structure: RCOX

$(\text{RCO})_2\text{O}$

$\text{RCO}_2\text{R}'$

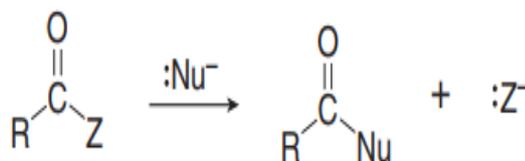
RCONH_2

RCN

All of these compounds contain an acyl group bonded to an electronegative atom Z that can serve as a leaving group. As a result, these compounds undergo nucleophilic acyl substitution.

Recall that aldehydes and ketones do not undergo nucleophilic substitution because they have no leaving group on the carbonyl carbon.

Nucleophilic substitution

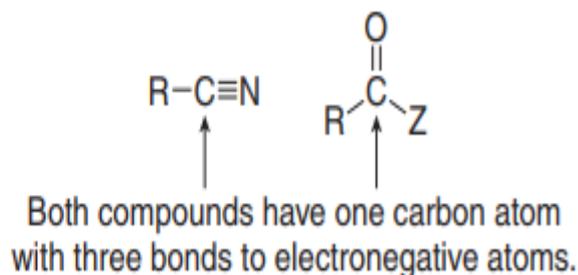
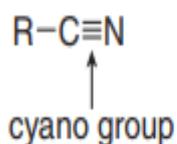


Nu replaces Z.



Nitriles are compounds that contain a cyano group, C N, bonded to an alkyl group. Nitriles have no carbonyl group, so they are structurally distinct from carboxylic acids and their derivatives. The carbon atom of the cyano group, however, has the same oxidation state as the carbonyl carbon of carboxylic acid derivatives, so there are certain parallels in their chemistry.

General structure—Nitriles

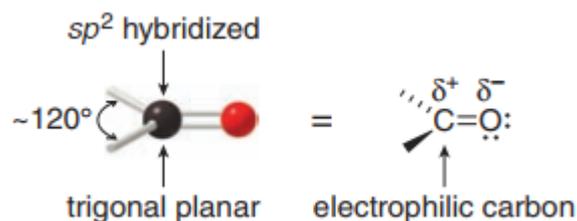


Both compounds have one carbon atom with three bonds to electronegative atoms.

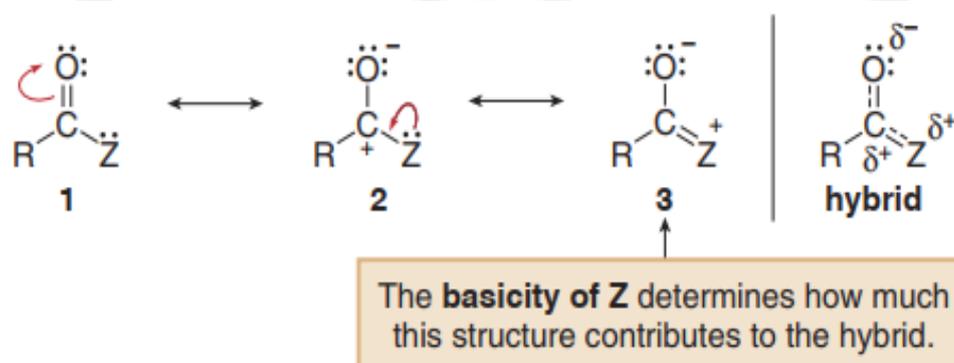
2- Structure and Bonding

The two most important features of any carbonyl group, regardless of the other groups bonded to it, are the following:

- The carbonyl carbon is sp^2 hybridized and trigonal planar, making it relatively uncrowded.
- The electronegative oxygen atom polarizes the carbonyl group, making the carbonyl carbon electrophilic.



Because carboxylic acid derivatives (RCOZ) all contain an atom Z with a nonbonded electron pair, three resonance structures can be drawn for RCOZ, compared to just two for aldehydes and ketones. These three resonance structures stabilize RCOZ by delocalizing electron density. In fact, the more resonance structures 2 and 3 contribute to the resonance hybrid, the more stable RCOZ is.



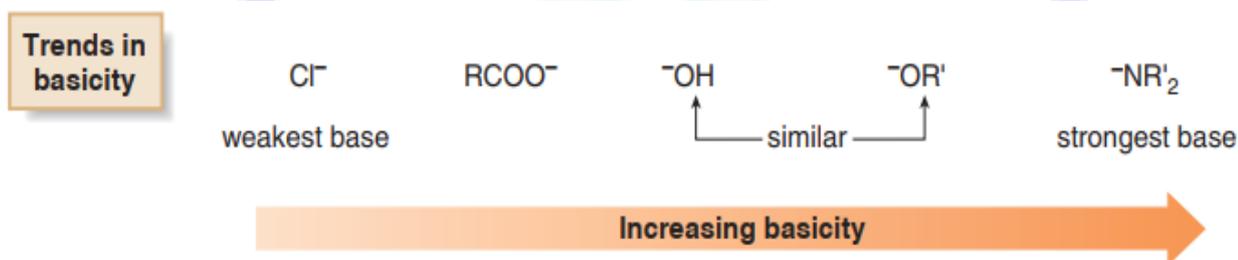
The basicity of Z determines how much this structure contributes to the hybrid.

The more basic Z is, the more it donates its electron pair, and the more resonance structure 3 contributes to the hybrid. order of basicity results:

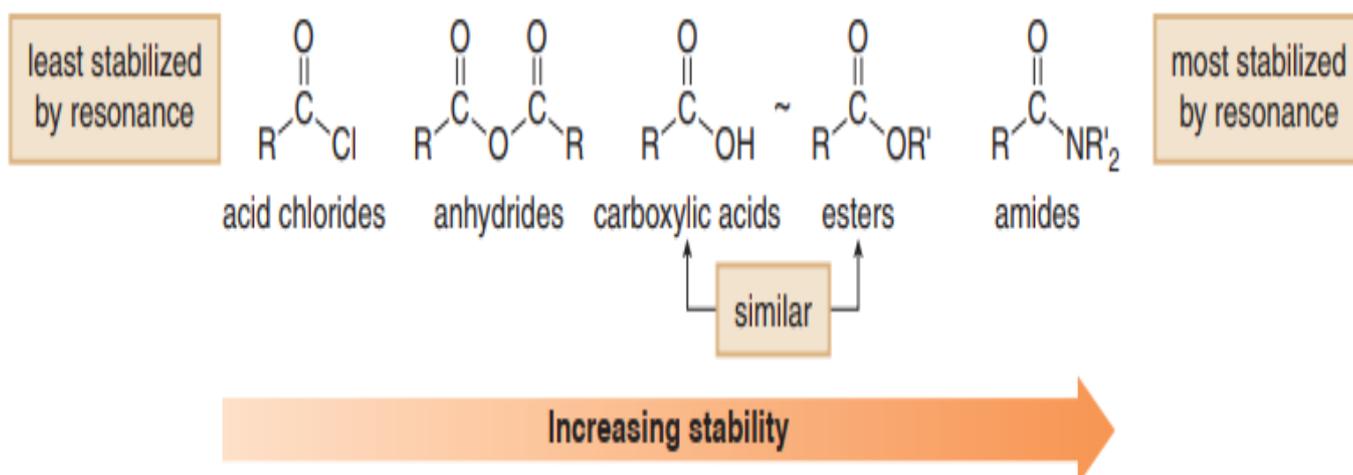
To determine the relative basicity of the leaving group Z, we compare the pKa values of the conjugate acids HZ, given in Table 1. The following order of basicity results:

Table 1 pK_a Values of the Conjugate Acids (HZ) for Common Z Groups of Acyl Compounds (RCOZ)

Structure	Leaving group (Z ⁻)	Conjugate acid (HZ)	pK_a
RCOCl acid chloride	Cl ⁻	HCl	-7
(RCO)₂O anhydride	RCOO ⁻	RCOOH	3-5
RCOOH carboxylic acid	⁻ OH	H ₂ O	15.7
RCOOR' ester	⁻ OR'	R'OH	15.5-18
RCO⁻NR'₂ amide	⁻ NR' ₂	R' ₂ NH	38-40



Because the basicity of Z determines the relative stability of the carboxylic acid derivatives, the following order of stability results:



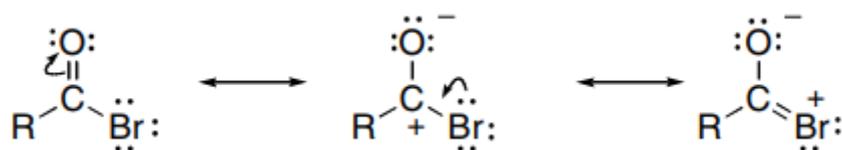
Reactivity	Derivative	Leaving group	Basicity
more reactive ↑	acid chloride $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{Cl}$	Cl^-	less basic ↓
	anhydride $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}$	$-\text{O}-\overset{\text{O}}{\parallel}{\text{C}}-\text{R}$	
	ester $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}-\text{R}'$	$-\text{O}-\text{R}'$	
	amide $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{NH}_2$	$-\text{NH}_2$	
less reactive	carboxylate $\text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}^-$	—	more basic

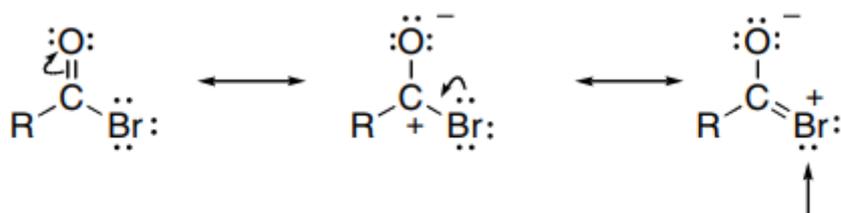
Thus, an acid chloride is the least stable carboxylic acid derivative because Cl^- is the weakest base. An amide is the most stable carboxylic acid derivative because $-\text{NR}'_2$ is the strongest base.

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

Problem Draw the three possible resonance structures for an acid bromide, RCOBr . Then, using the pK_a values in Appendix A, decide if RCOBr is more or less stabilized by resonance than a carboxylic acid (RCOOH).

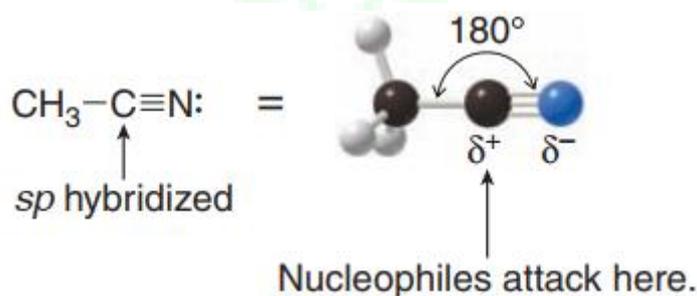
Solution :





The **basicity of Z** determines how much this structure contributes to the hybrid.
 Br^- is less basic than ^-OH , so RCOBr is less stable than RCOOH .

The structure and bonding in nitriles is very different from the carboxylic acid derivatives, and resembles the carbon-carbon triple bond of alkynes.



- The carbon atom of the CN group is sp hybridized, making it linear with a bond angle of 180° .
- The triple bond consists of one σ and two π bonds.

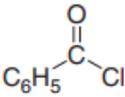
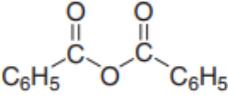
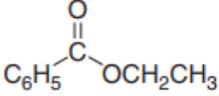
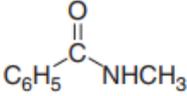
Like the carboxylic acid derivatives, nitriles contain an electrophilic carbon atom, making them susceptible to nucleophilic attack.

3-Nomenclature

The names of carboxylic acid derivatives are formed from the names of the parent carboxylic acids discussed in section previous. Keep in mind that the common names formic acid, acetic acid, and benzoic acid are virtually always used for the parent acid, so these common parent names are used for their derivatives as well.

Table 2 summarizes the most important points about the nomenclature of carboxylic acid derivatives.

Table .2 Summary: Nomenclature of Carboxylic Acid Derivatives and Nitriles

Compound	Name ending	Example	Name
acid chloride	-yl chloride or -carbonyl chloride		benzoyl chloride
anhydride	anhydride		benzoic anhydride
ester	-ate		ethyl benzoate
amide	-amide		<i>N</i> -methylbenzamide
nitrile	-nitrile or -onitrile	$C_6H_5-C\equiv N$	benzonitrile

4- Physical Properties

Because all carbonyl compounds have a polar carbonyl group, they exhibit dipole–dipole interactions. Nitriles also have dipole–dipole interactions because they have a polar CN group.

Because they contain one or two N-H bonds, 1° and 2° amides are capable of intermolecular hydrogen bonding. The N – H bond of one amide intermolecularly hydrogen bonds to the CO of another amide, as shown using two acetamide molecules (CH₃CONH₂).

How these factors affect the physical properties of carboxylic acid derivatives is summarized in Table 3.

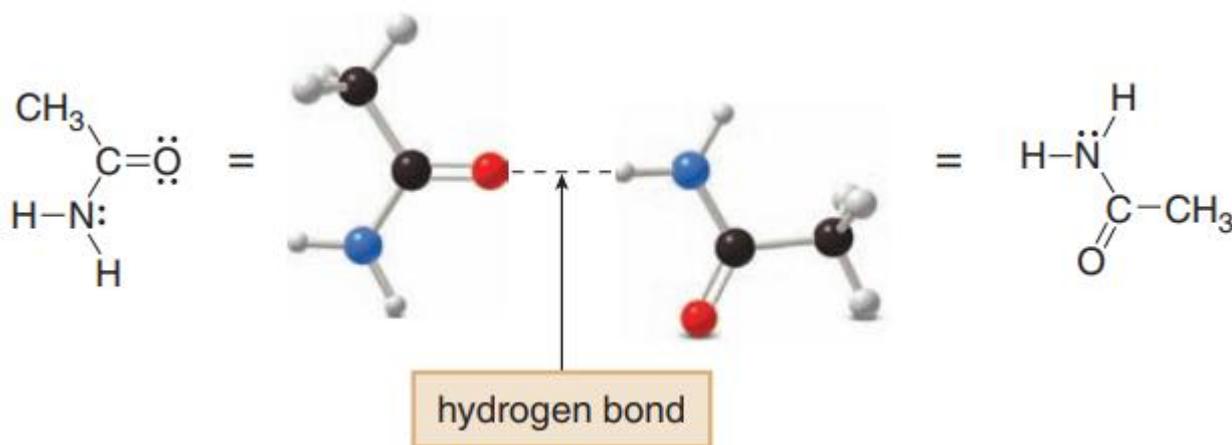
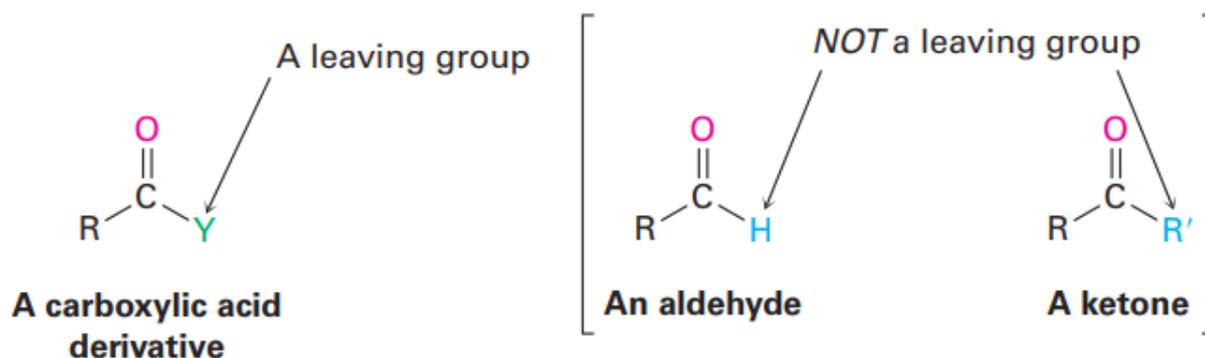


Table .3 Physical Properties of Carboxylic Acid Derivatives

Property	Observation
Boiling point and melting point	<ul style="list-style-type: none"> Primary (1°) and 2° amides have <i>higher</i> boiling points and melting points than compounds of comparable molecular weight. The boiling points and melting points of other carboxylic acid derivatives are similar to those of other polar compounds of comparable size and shape. <div style="text-align: center; margin-top: 10px;"> <p style="text-align: center;"> $\text{CH}_3\text{C}(=\text{O})\text{Cl}$ $\text{CH}_3\text{C}(=\text{O})\text{OCH}_3$ $\text{CH}_3\text{C}(=\text{O})\text{CH}_2\text{CH}_3$ $\text{CH}_3\text{CH}_2\text{C}(=\text{O})\text{NH}_2$ MW = 78.5 MW = 74 MW = 72 MW = 73 bp 52 °C bp 58 °C bp 80 °C bp 213 °C ~ ~ < higher boiling point similar boiling points 1° amide </p> </div>
Solubility	<ul style="list-style-type: none"> Carboxylic acid derivatives are soluble in organic solvents regardless of size. Most carboxylic acid derivatives having ≤ 5 C's are H₂O soluble because they can hydrogen bond with H₂O Carboxylic acid derivatives having > 5 C's are H₂O insoluble because the nonpolar alkyl portion is too large to dissolve in the polar H₂O solvent.

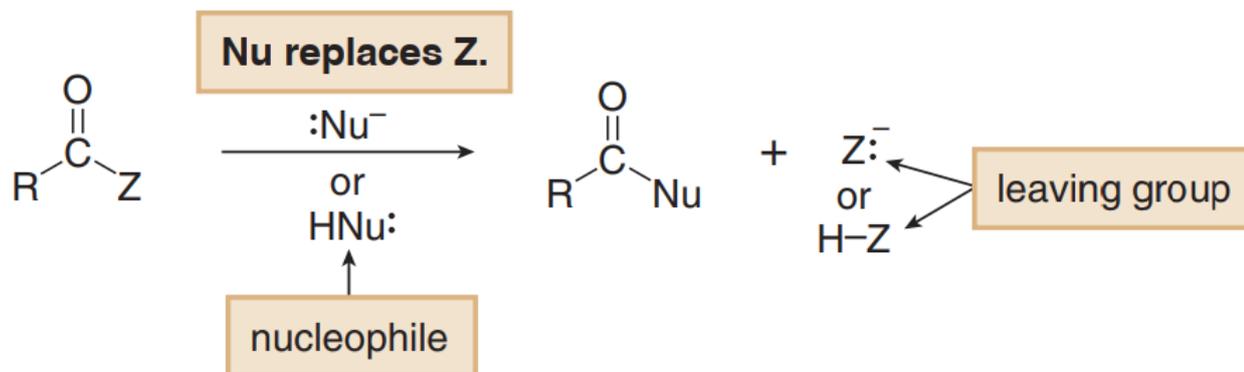
5. Introduction to Nucleophilic Acyl Substitution

The different behavior toward nucleophiles of aldehydes/ketones and carboxylic acid derivatives is a consequence of structure. Carboxylic acid derivatives have an acyl carbon bonded to a group-Y that can leave as a stable anion. As soon as addition of a nucleophile occurs, the group leaves and a new carbonyl compound forms. Aldehydes and ketones have no such leaving group, however, and therefore don't undergo substitution.



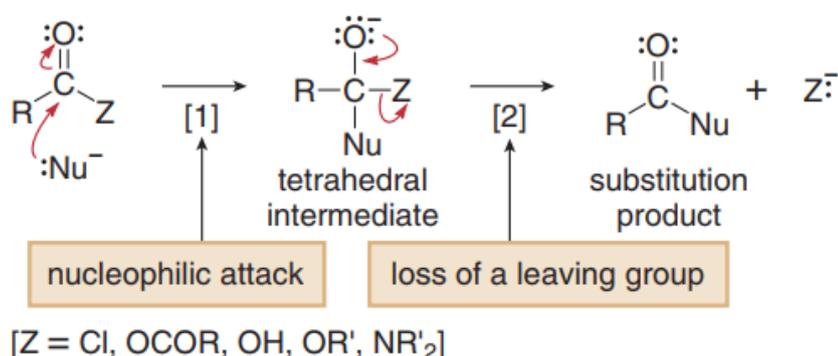
This is a general reaction that occurs with both negatively charged nucleophiles (Nu^-) and neutral nucleophiles ($\text{HNu}:$).

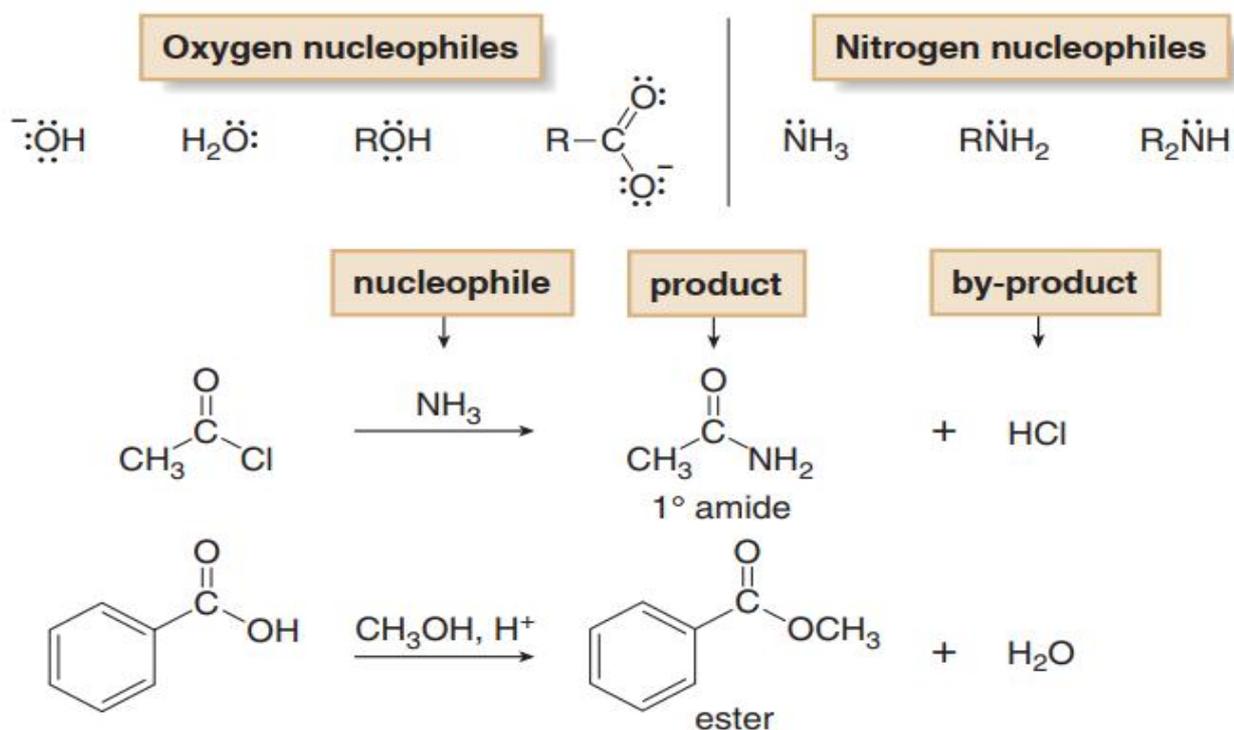
Nucleophilic substitution



- Carboxylic acid derivatives (RCOZ) react with nucleophiles because they contain an electrophilic, unhindered carbonyl carbon.
- Substitution occurs, not addition, because carboxylic acid derivatives (RCOZ) have a leaving group Z on the carbonyl carbon.

Mechanism General Mechanism—Nucleophilic Acyl Substitution





Each reaction results in the replacement of the leaving group by the nucleophile, regardless of the identity of or charge on the nucleophile. To draw any nucleophilic acyl substitution product:

- **Find the sp^2 hybridized carbon with the leaving group.**
- **Identify the nucleophile.**
- **Substitute the nucleophile for the leaving group.** With a neutral nucleophile a proton must be lost to obtain a neutral substitution product.

Problem: Draw the products of each reaction.

