

# PART 5

# Carbonyl Compounds

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Chapter

15. RCOOH and derivatives

16. RCHO and RCOR'

17. Rxn at alpha-C of C=O

# Chapter 15

## Carboxylic Acids and Derivatives

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carbonyl comp'ds

nucleophilic addition-elimination

# Carbonyl compounds

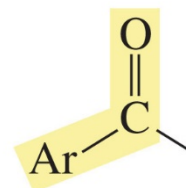
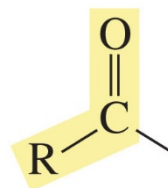
Ch 15 #3

□ compounds containing **carbonyl group** [C=O]

■ **acyl group** ~ RC=O or ArC=O



a carbonyl group



acyl groups

alkyl  
aryl  
acyl  
aroyl  
acetyl [R = Me]  
benzoyl [Ar = Ph]  
phenyl, benzyl

□ Remember 4 families (of functional groups)?

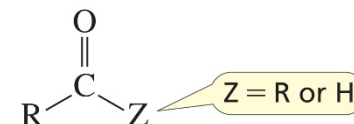
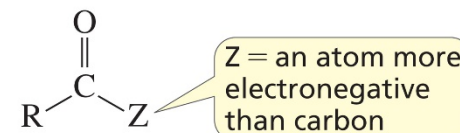
■ Group I ~ C=C, C≡C ~ addition

■ Group II ~ R-Z (X, OH, OR, NH<sub>2</sub>...) ~ S<sub>N</sub>, E

■ **Group III ~ carbonyls**

■ Group IV ~ aromatics, heterocyclics

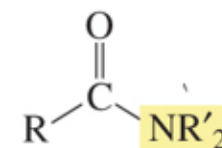
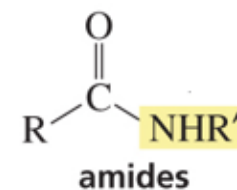
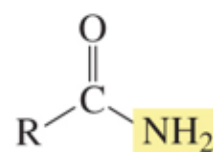
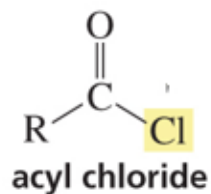
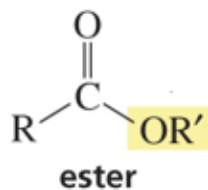
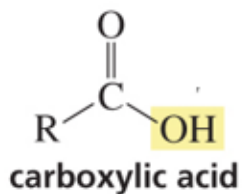
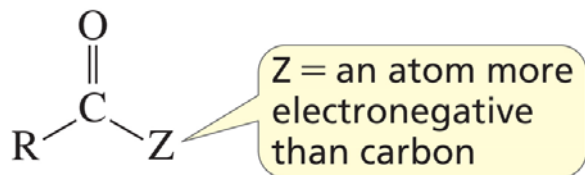
Group III



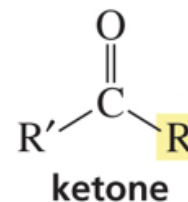
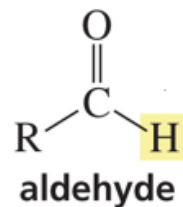
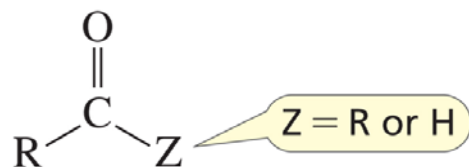
# 2 classes of C=O compounds

Ch 15 #4

- with Z that **can be** replaced by Nu: **Chapt 15**



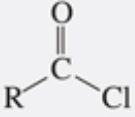
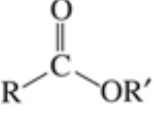
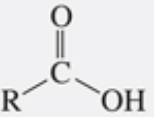
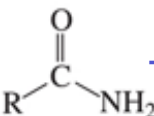
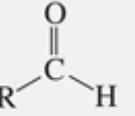
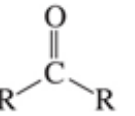
- with Z that **cannot be** replaced **Chapt 16**



# Z as leaving group

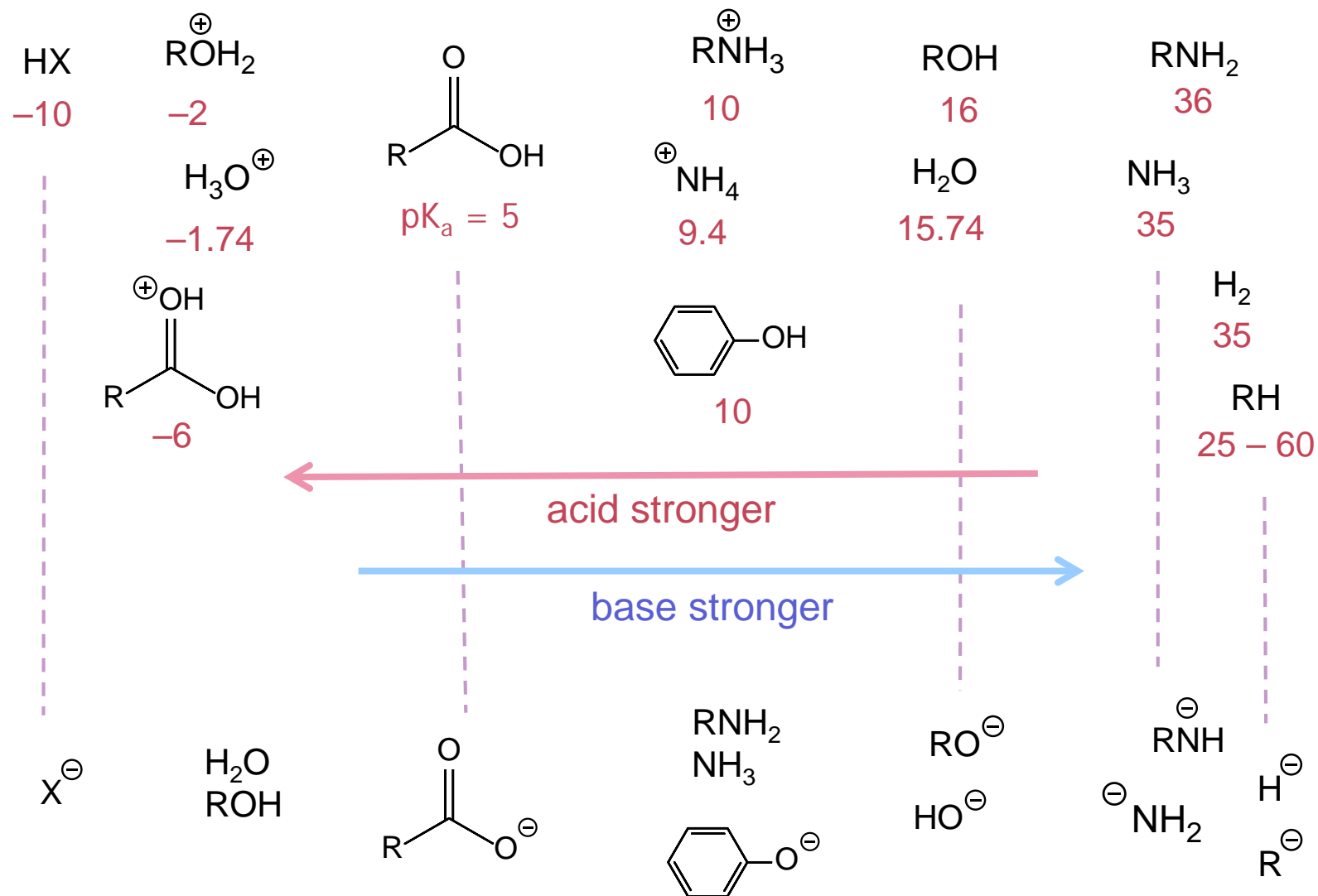
Ch 15 #5

- weaker base leaves more easily

Carbonyl compound	Leaving group	Conjugate acid of the leaving group	pK <sub>a</sub>
<b>Carboxylic Acids and Carboxylic Acid Derivatives</b>			
	Cl <sup>-</sup>	HCl	-7
	<sup>-</sup> OR'	R'OH	~15-16
	<sup>-</sup> OH	H <sub>2</sub> O	15.7
 <sup>-</sup> +NH <sub>3</sub>	<sup>-</sup> NH <sub>2</sub> NH <sub>3</sub>	NH <sub>3</sub> <sup>+</sup> NH <sub>4</sub>	9.4 36*
<b>Aldehydes and Ketones</b>			
	H <sup>-</sup>	H <sub>2</sub>	35
	R <sup>-</sup>	RH	> 60

# Acidity/basicity

Ch 15 #6



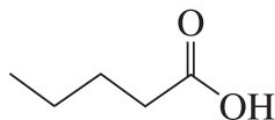
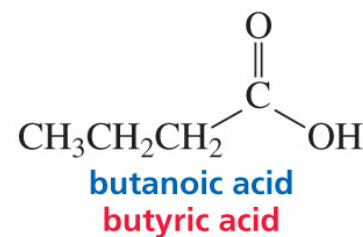
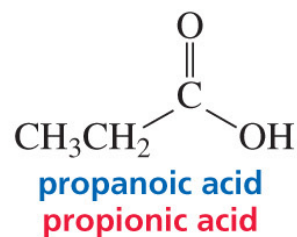
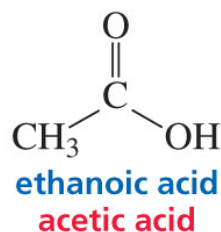
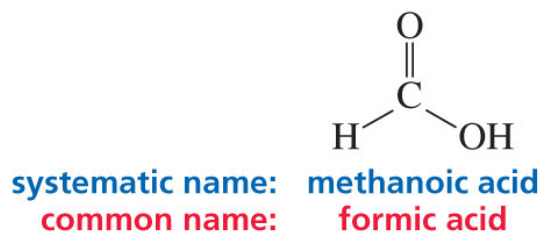
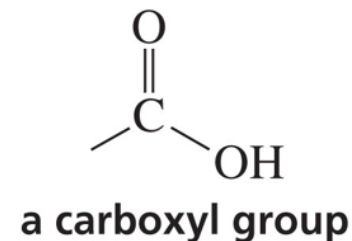
# Nomenclature: RCOOH

Ch 15 #7

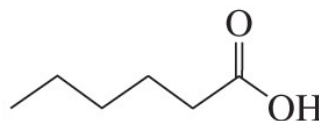
## □ carboxylic acid



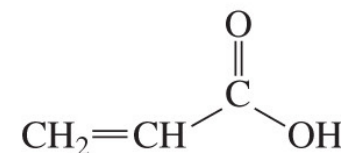
■ alkane  $\rightarrow$  **alkanoic acid**  
**--ic acid**



**pentanoic acid**  
**valeric acid**

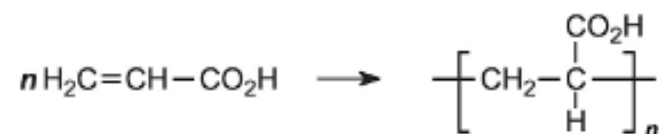


**hexanoic acid**  
**caproic acid**

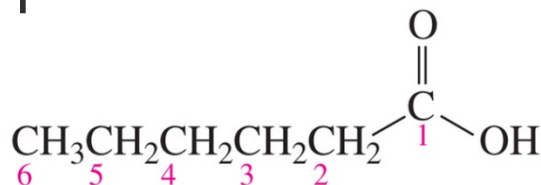


**propenoic acid**  
**acrylic acid**

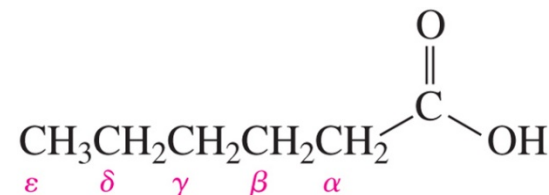
acet = 2 C's including carbonyl C  
valer = 5 C's, capro = 6 C's



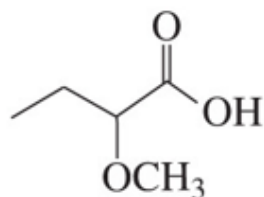
▣ substituted RCOOH



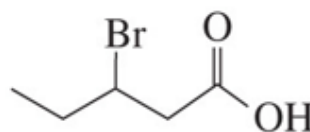
systematic nomenclature



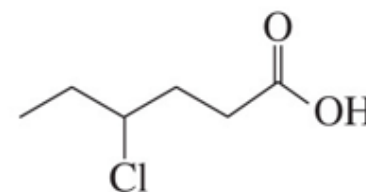
common nomenclature



**2-methoxybutanoic acid**  
 **$\alpha$ -methoxybutyric acid**

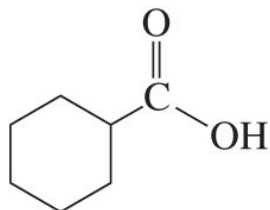


**3-bromopentanoic acid**  
 **$\beta$ -bromovaleric acid**

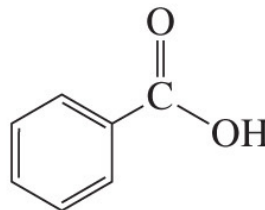


**4-chlorohexanoic acid**  
 **$\gamma$ -chlorocaproic acid**

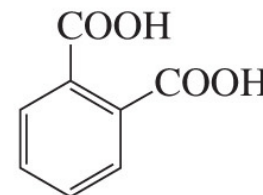
■ cyclic ~ ring+carboxylic acid



**cyclohexanecarboxylic acid**



**benzenecarboxylic acid**  
**benzoic acid**



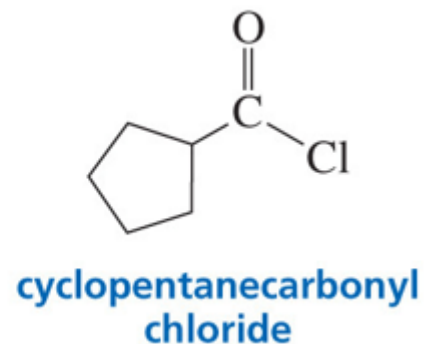
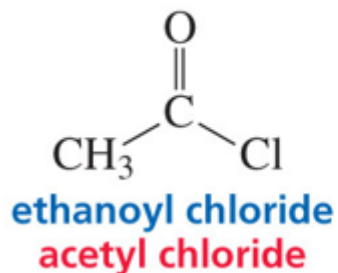
**1,2-benzenedicarboxylic acid**



# Nomenclature: RCOX

Ch 15 #9

- acyl halide [acid halide]
  - alkane → alkanoyl halide
  - cyclic ~ ring+carbonyl halide

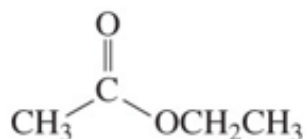
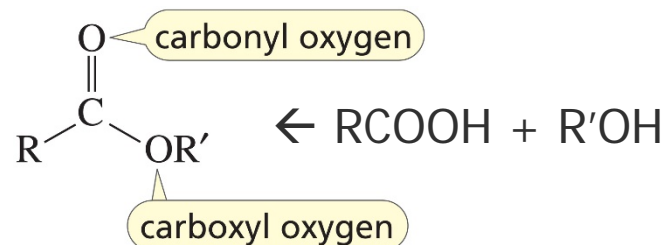


# Nomenclature: esters

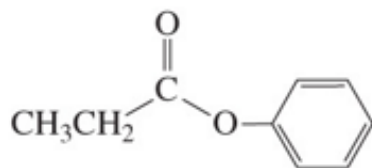
Ch 15 #10

## □ RCOOR'

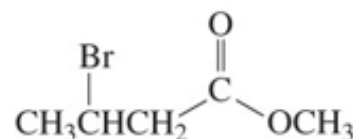
- R' alkanoate    --ate
- cyclic ~ R' ring+carboxylate



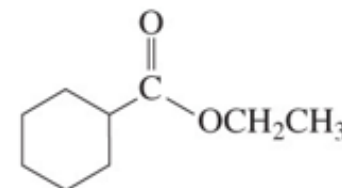
ethyl ethanoate  
ethyl acetate



phenyl propanoate  
phenyl propionate



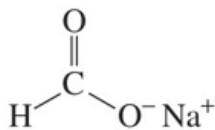
methyl 3-bromobutanoate  
methyl  $\beta$ -bromobutyrate



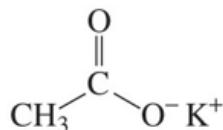
ethyl cyclohexanecarboxylate

## □ salt RCOO<sup>-</sup> M<sup>+</sup>

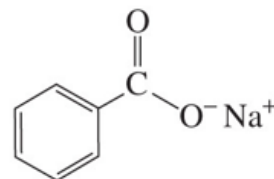
- cation alkanoate



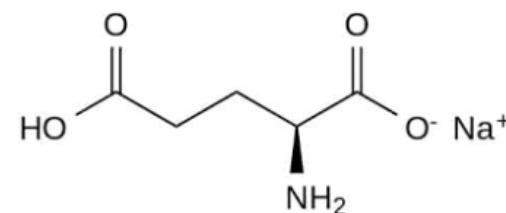
sodium methanoate  
sodium formate



potassium ethanoate  
potassium acetate



sodium benzenecarboxylate  
sodium benzoate

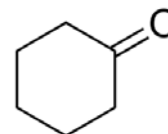


NH<sub>2</sub>

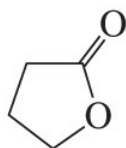
□ **lactone** = cyclic ester

■ 2-oxacycloalkanone

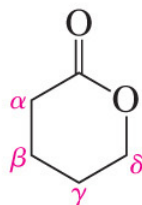
■ --olactone



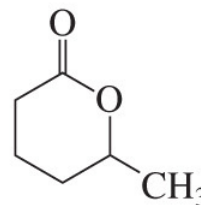
cyclohexanone



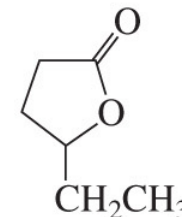
2-oxocyclopentanone  
**γ-butyrolactone**  
a γ-lactone



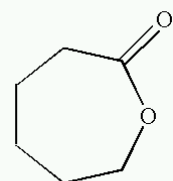
2-oxocyclohexanone  
**δ-valerolactone**  
a δ-lactone



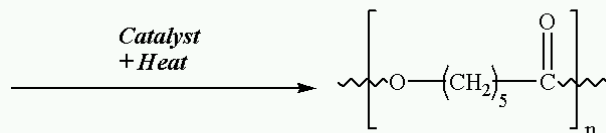
3-methyl-2-oxocyclohexanone  
**δ-caprolactone**  
a δ-lactone



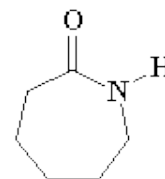
3-ethyl-2-oxocyclopentanone  
**γ-caprolactone**  
a γ-lactone



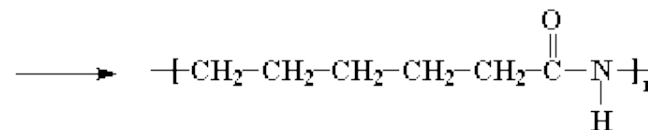
ε-Caprolactone



PolyCaprolactone



ε-caprolactam



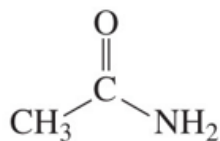
nylon 6

# Nomenclature: amides

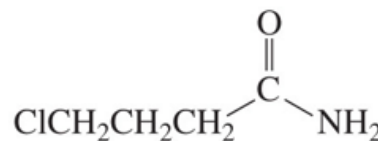
Ch 15 #12

## □ RCONH<sub>2</sub>

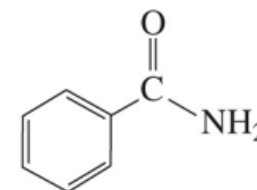
### ■ alkanamide



ethanamide  
acetamide

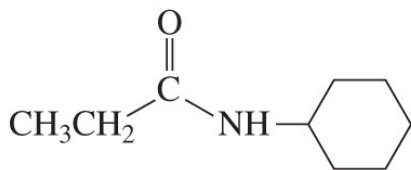


4-chlorobutanamide  
γ-chlorobutyramide

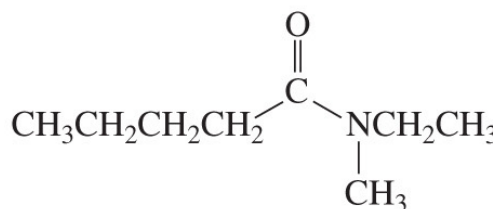


benzenecarboxamide  
benzamide

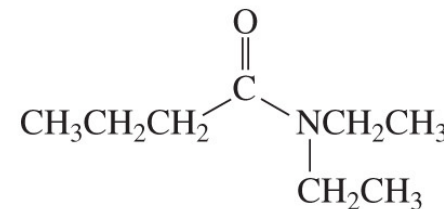
## □ RCONHR', RCONR'<sub>2</sub> ~ N-substituted ~ N-R'alkanamide



N-cyclohexylpropanamide



N-ethyl-N-methylpentanamide

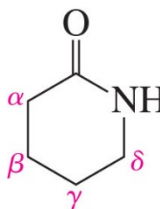


N,N-diethylbutanamide

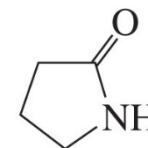
## □ lactam = cyclic amide

### ■ 2-azacycloalkanone

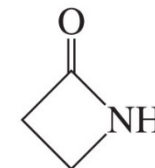
### ■ --olactam



2-azacyclohexanone  
δ-valerolactam  
a δ-lactam



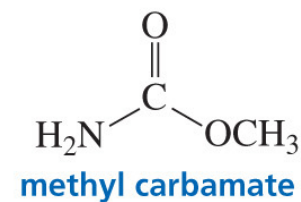
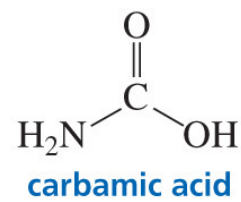
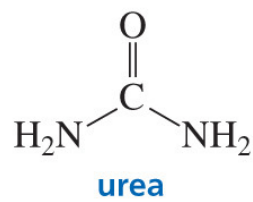
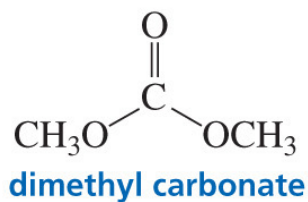
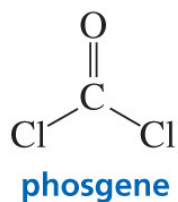
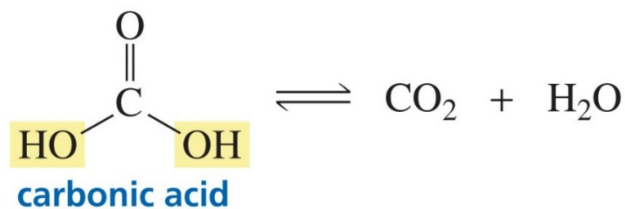
2-azacyclopentanone  
γ-butyrolactam  
a γ-lactam



2-azacyclobutanone  
β-propiolactam  
a β-lactam

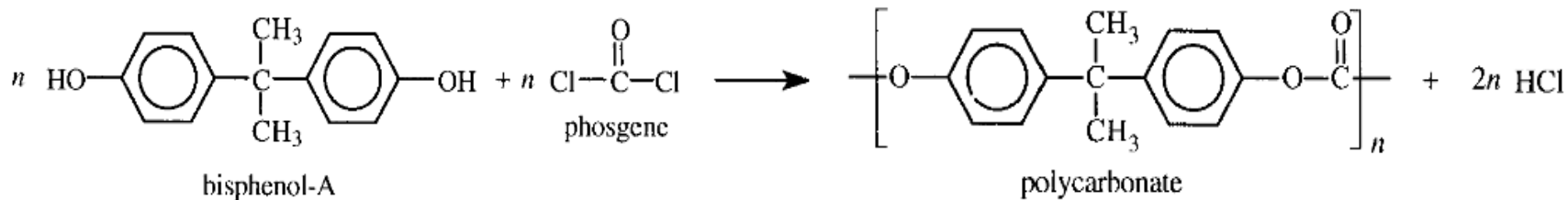
# Nomenclature: carbonic acid

Ch 15 #13



carbonate  
= ester of carbonic acid

carbamate  
= ester of carbamic acid

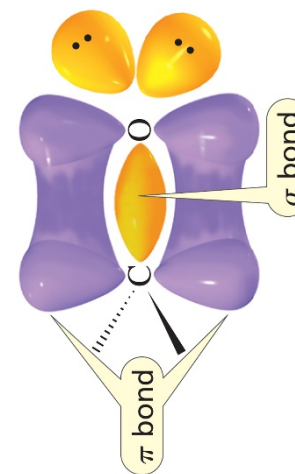
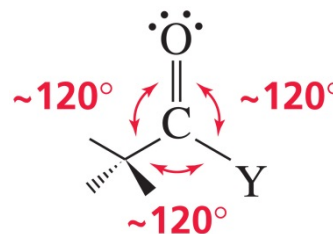


# Structure

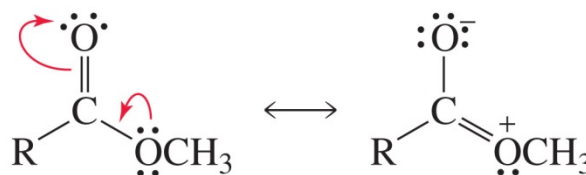
Ch 15 #14

## □ geometry

- carbonyl C and O ~  $sp^2$



## □ resonance



stronger resonance. why?

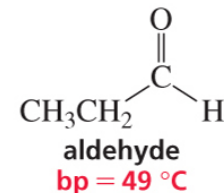
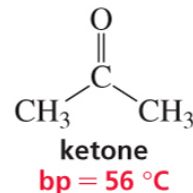
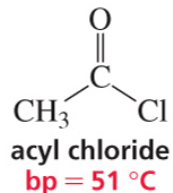
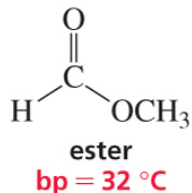
- $RC(O)X$ ? weak resonance. why?

# Physical properties

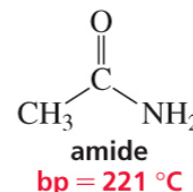
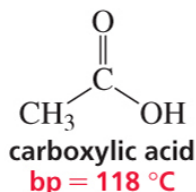
Ch 15 #15

## □ bp

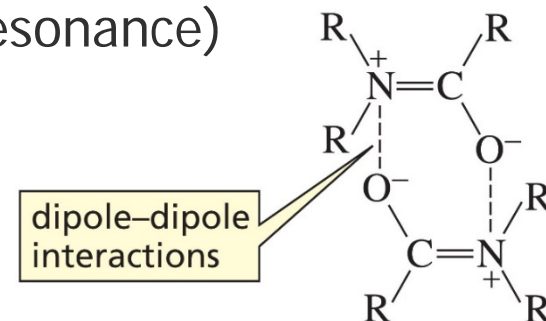
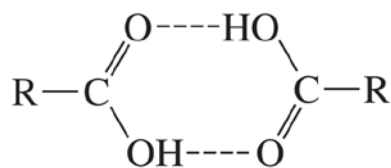
$\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$   
alcohol  
bp = 97.4 °C



$\text{CH}_3\text{CH}_2\text{OCH}_3$   
ether  
bp = 10.8 °C



- alcohol >  $\text{RC(O)Z}$  > ether > RH
  - HB, dipole-dipole interaction
- alcohol <  $\text{RCOOH}$  < amide
  - double HB, dipole-dipole interaction (in resonance)



## □ solubility

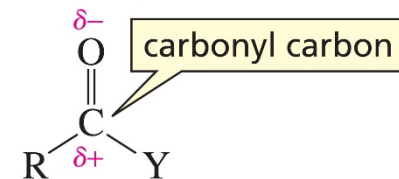
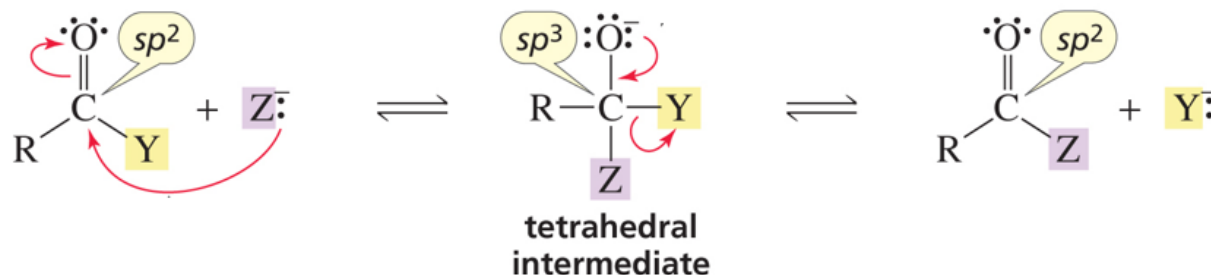
- Carbonyls with less than 4 C's are water-soluble.
  - like ROH, ether §3.10
- Carbonyls are soluble in ether, RX, ArH.
  - not in RH
- Esters and N,N-disub'd amides can be solvents.
  - polar
  - aprotic [no active H (like NH<sub>2</sub> or OH)] §9.2 p438



# How to react

Ch 15 #17

## □ nucleophilic addition–elimination reaction



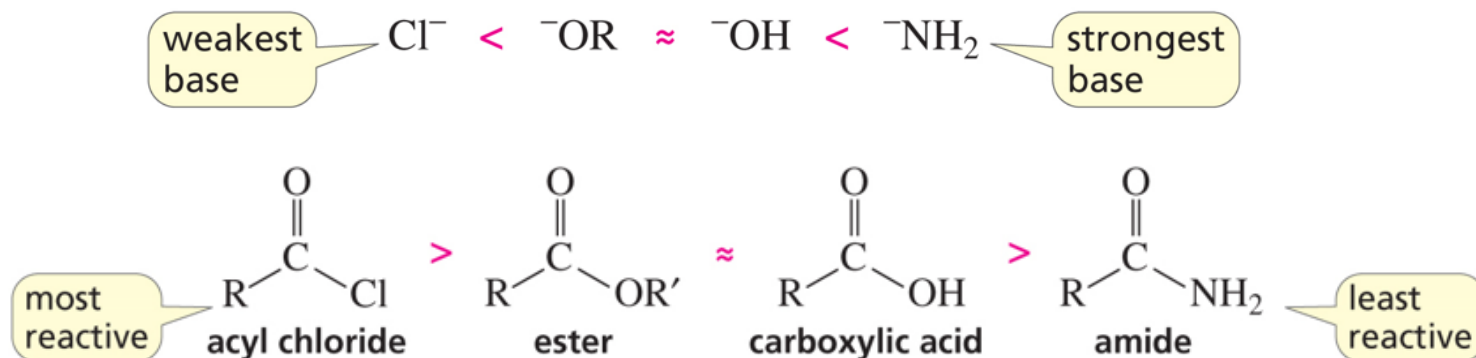
- addition of Nu: Z, followed by elimination of leaving group Y
  - intermediate not stable  $\leftarrow$  C-O<sup>-</sup> and 2 L's
  - Better L [weaker B:] leaves. Y or Z.
- also called
  - nucleophilic acyl substitution (of Y on acyl by Z)
  - acyl transfer (from Y to Z)
- difference from S<sub>N</sub>2 or S<sub>N</sub>1?
  - Nu: approaches  $\rightarrow$   $\pi$  bond breaks [weakest]  $\rightarrow$  add'n-elim'n  
C-L weakest in S<sub>N</sub>

Generally speaking, a comp'd having  $sp^3$  C bonded to two EN atoms is unstable. p730 & p804

# Relative reactivities

Ch 15 #18

- reactivity (of substrate) and basicity (of leaving group)



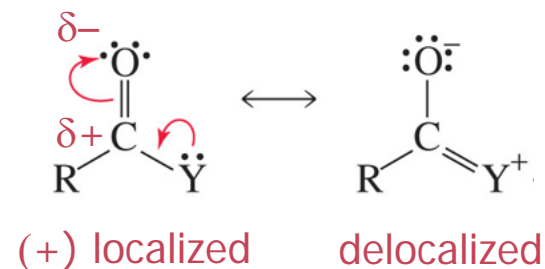
- in the 1st step [addition]

- Weaker B: makes C more e-philic.

← smaller contribution from 2nd form

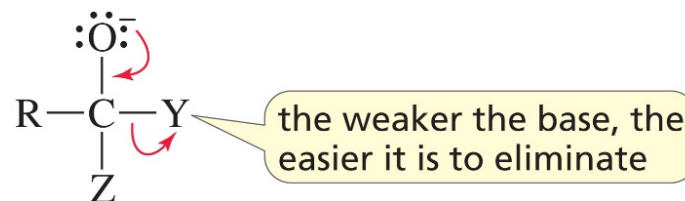
← delocalization of (+) ~  $\text{Cl} < \text{O} < \text{N}$

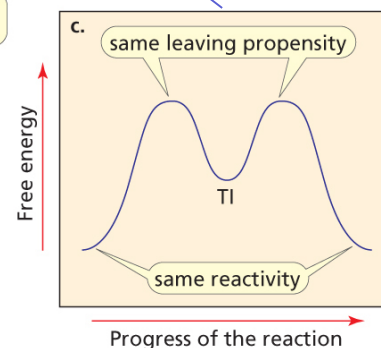
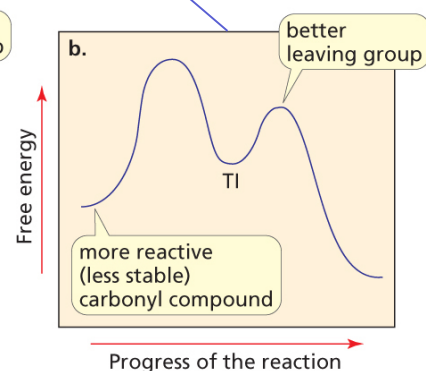
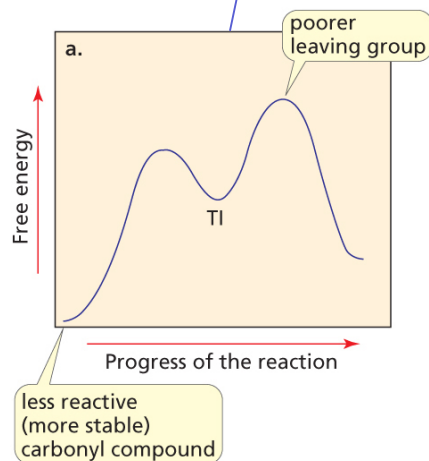
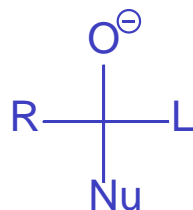
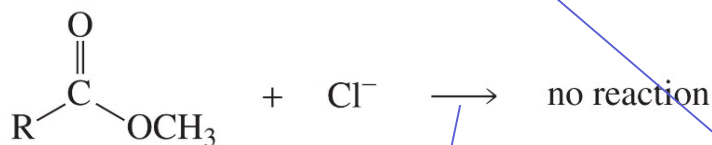
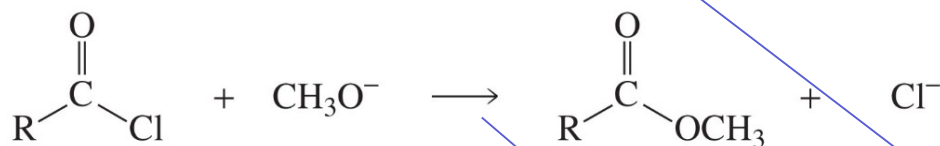
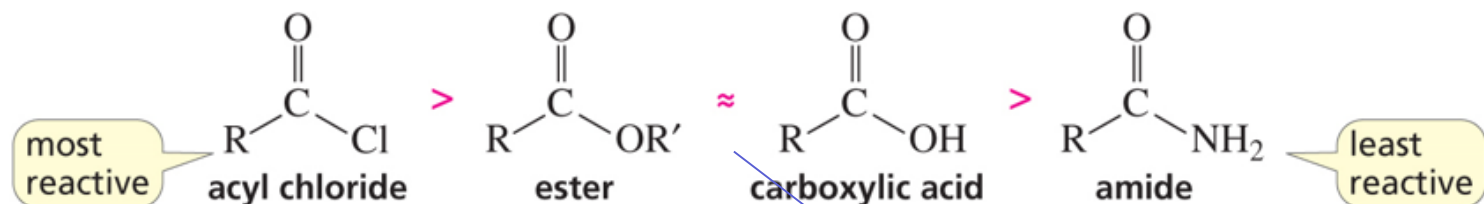
← EN (+ size for Cl)



- in the 2nd step [elimination]

- Weaker B: leaves better.





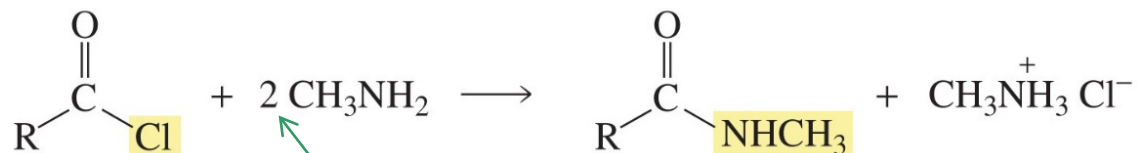
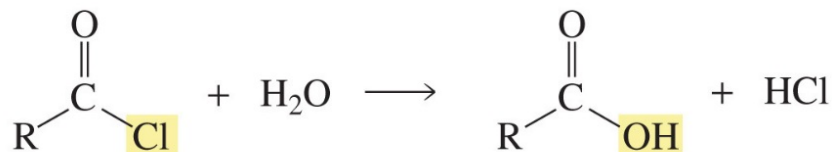
Nu: stronger B:  
1st step RDS

1/1 mixture

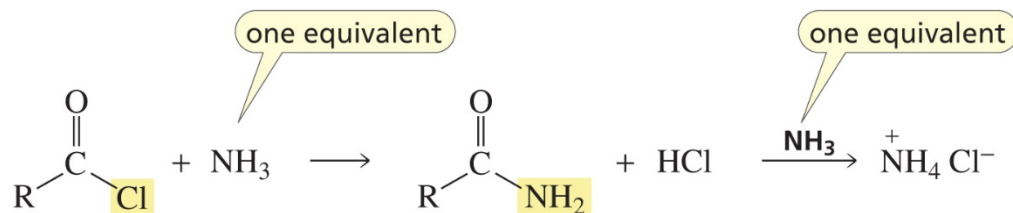
# Rxn of RCOCl

Ch 15 #20

- to ester, acid, or amide



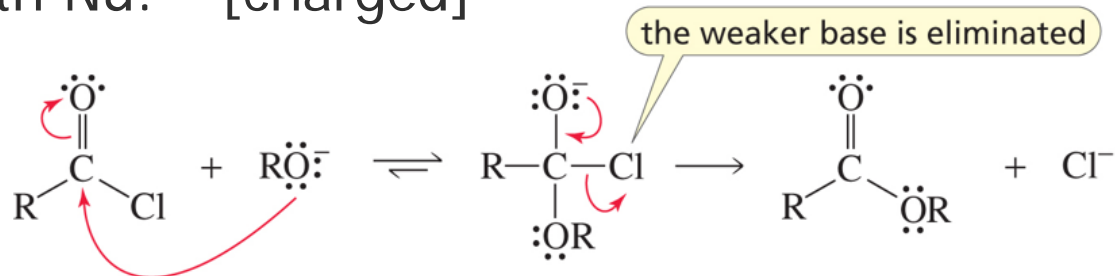
- For amides, 2 equivalents of amine or ammonia are required.



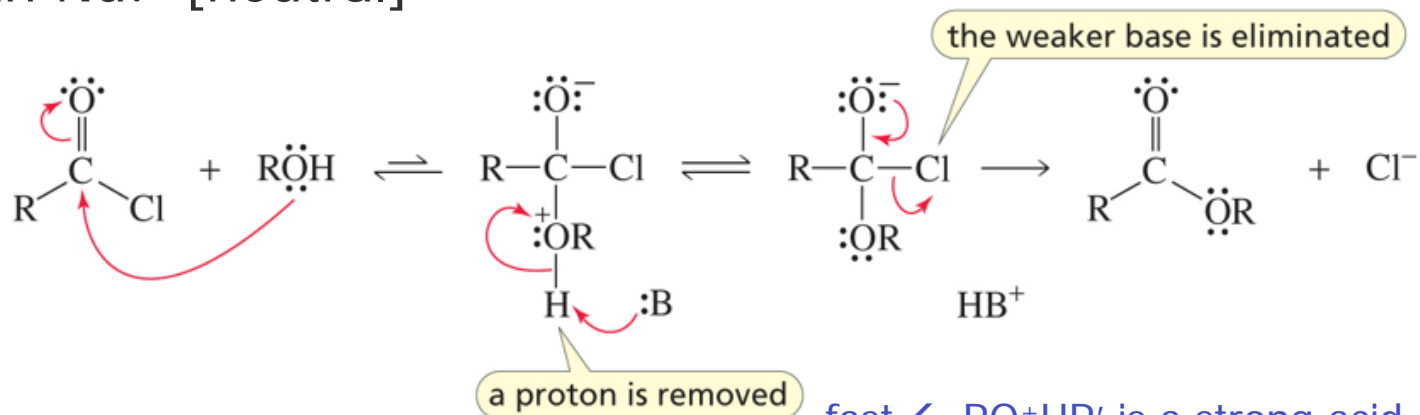
In the 2nd mechanism,  
:NH<sub>3</sub> is used as the B:  
← stronger B: than Cl<sup>-</sup>

## □ mechanism

### ■ with Nu:<sup>-</sup> [charged]



### ■ with Nu: [neutral]

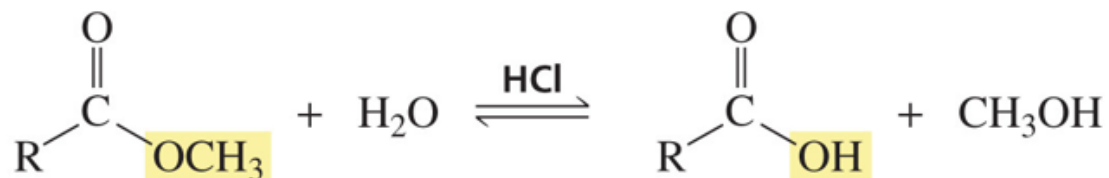


fast ← RO<sup>+</sup>HR' is a strong acid. pK<sub>a</sub>?

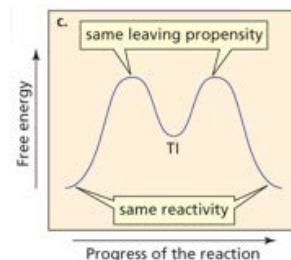
# Rxn of RCOOR'

Ch 15 #22

- hydrolysis to RCOOH + R'OH

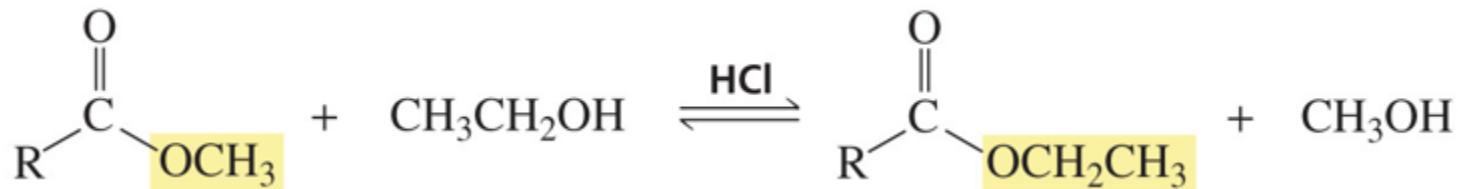


- very slow ← poor Nu: H<sub>2</sub>O, poor L [strong B:] -OR
- need acid or base catalyst



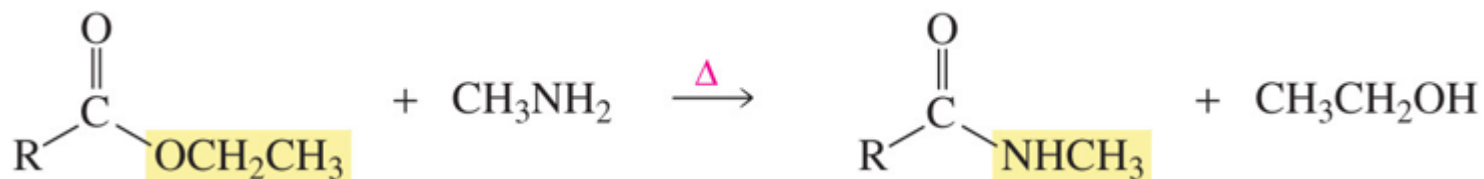
- transesterification to (new) RCOOR'' + R'OH

- alcoholysis, ester exchange



- also slow and need catalyst

□ aminolysis to amide + R'OH



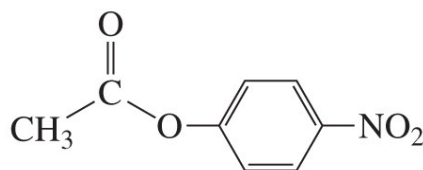
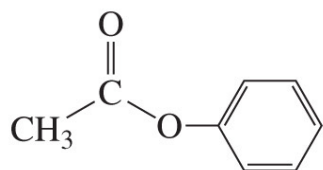
- not that slow ← amine a better Nu: ~ N: better than O:
  - cannot be acid-catalyzed, anyway ~  $\text{RNH}_3^+$
  - use heat if necessary
- need only 1 equiv of amine or ammonia
  - $-\text{OR}$ , a stronger B: than amine, react with  $\text{H}^+$ .  
<cf> 2 equiv for  $\text{RCOCl}$ , why?

➤ Problem 19a.

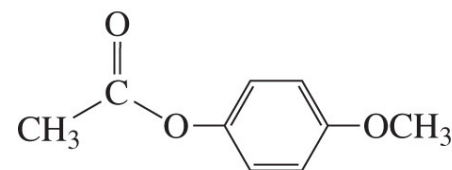
which more reactive (in nu-philic acyl substit'n),  
methyl acetate or phenyl acetate?

➤  $\text{CH}_3\text{O}^-$  vs  $\text{PhO}^-$  as L  $\leftarrow$   $\text{pK}_a$  of MeOH vs phenol

➤ Problem 18. relative reactivity? not a good question



-I and -M



-I < +M

§8.10 p379

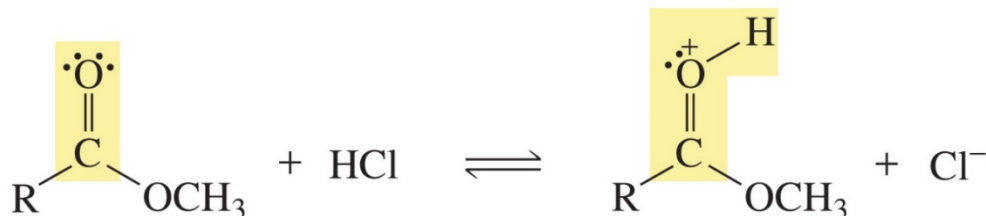


# Acid-catalyzed hydrolysis of ester

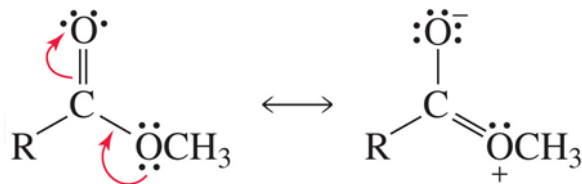
Ch 15 #25

- In acidic solution, all the comp'ds [reactants, intermediates, and products] are neutral or positive.
- In basic condition, no positive comp'd is present.

□ acid-catalysis = protonation

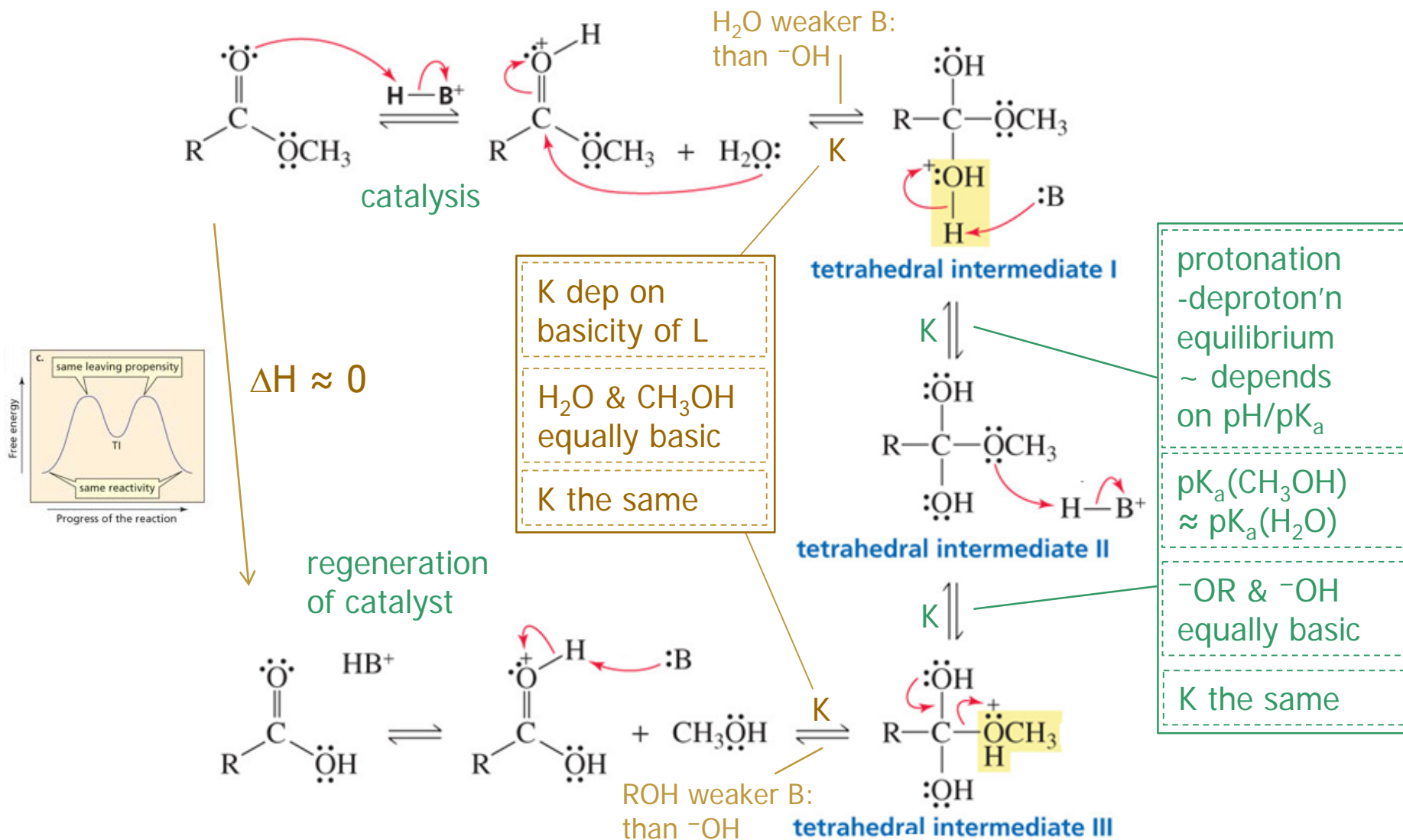


□ where? atom with highest e density



■ inductive and resonance

## mechanism



□ to force the equili forward

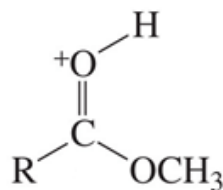
- use xs water



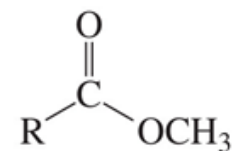
- remove product [alcohol] (at high T)

□ role of acid catalyst

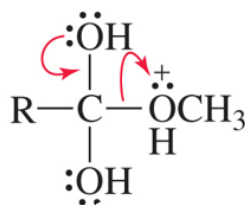
- make O more EW →  
make C more e-philic  
(in the 1st step)



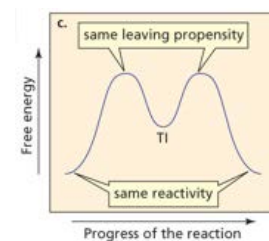
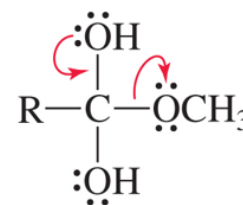
VS



- make L less basic  
(in the 2nd step)



VS

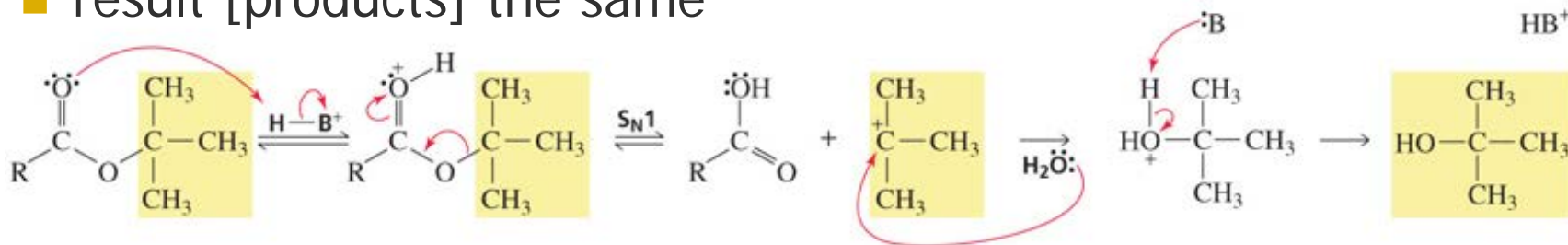


□ mechanism for ester with 3° alkyl

- S<sub>N</sub>1 rather than addition-elimination

← stable C<sup>+</sup> + weak Nu:

- result [products] the same

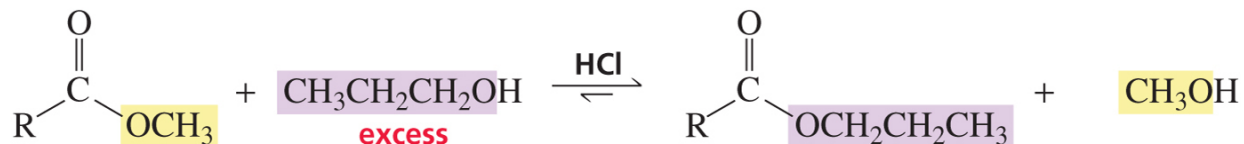


□ transesterification

- mechanism (exactly) the same to that of hydrolysis

- except for the Nu: (ROH) ~ alcoholysis

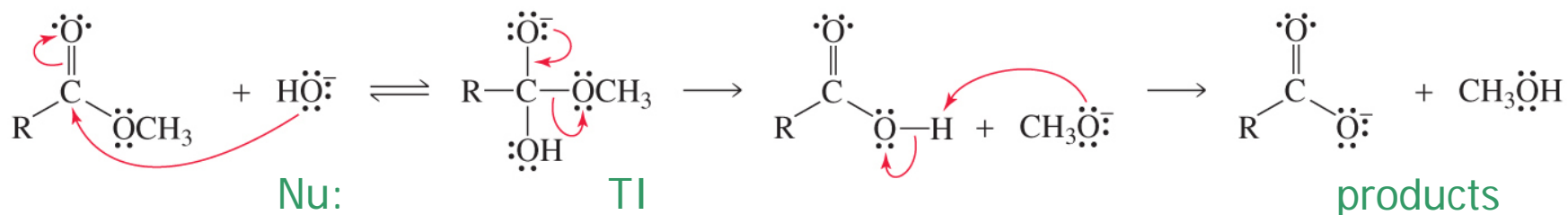
- for higher yield



# Hydroxide-ion-promoted hydrolysis

Ch 15 #29

## mechanism



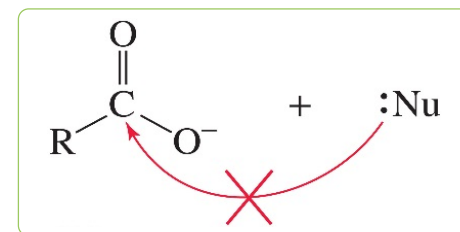
Products are not ROOH + RO<sup>-</sup>, but RCOO<sup>-</sup> + ROH.

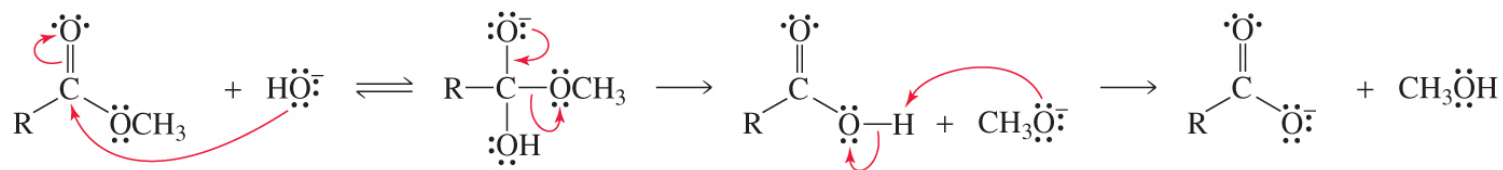
- RO<sup>-</sup> is stronger B: than RCOO<sup>-</sup>, and protonated first.

- A-B rxn moves to weaker A and B.

irreversible (unlike acid-catal'd)

- Nu: not react with (-) species [RCOO<sup>-</sup>]





## □ role of $\text{OH}^-$

■ better Nu: than  $\text{H}_2\text{O}$

□ to form TI better

■  $\text{MeO}^-$  easier from  $(-)$  TI

□ thru lower-energy TS



TS from neutral TI  
with  $\delta^+$  on O

□ why ' $\text{OH}^-$ -promoted' not ' $-$ -catalyzed'?

□ Can  $\text{OH}^-$  promote transesterification?

■ No. Use conj B: (of ROH) instead.

