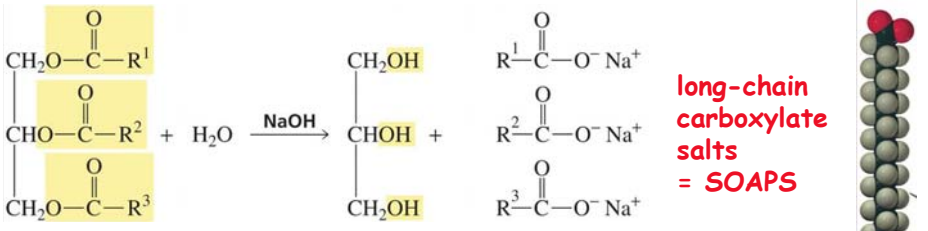
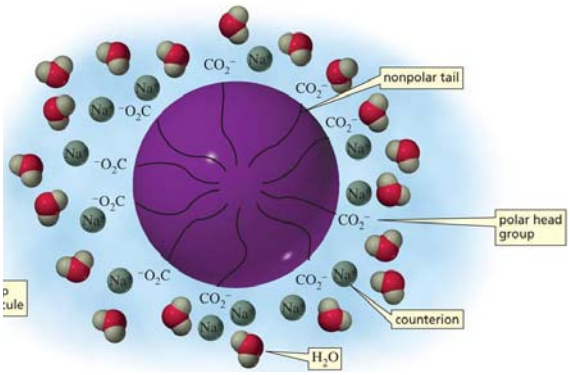
SAPONIFICATION = basic hydrolysis of fatty acid esters



A triglyceride
= fat or oil

glycerol

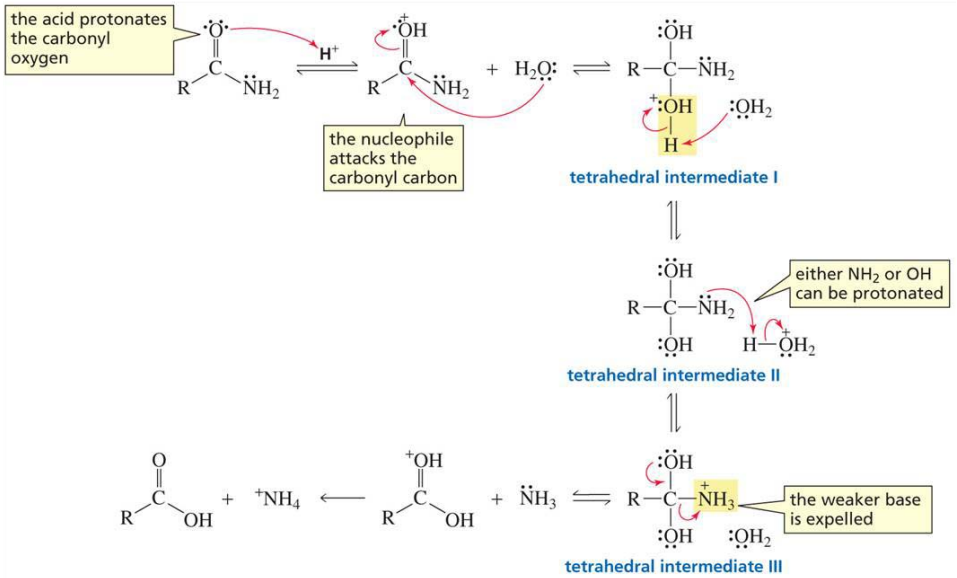
long-chain carboxylate salts = SOAPS



16.14 - for interest only

Make sure you have worked through this yourselves…

Acid-catalyzed hydrolysis of amides (16.17…)



(2)

CHEM 222 section 01

LECTURE #23 Tues., Nov.20, 2007

Lecture topics & readings

Today's class

- continue rxns of carbonyl compounds (Ch.16-18)

Before next class

- PRACTICE Ch.16-17 problems
- PRACTICE mechanisms involving N-nucleophiles

Next class

- continue rxns of carbonyl compounds (Ch.17-18)

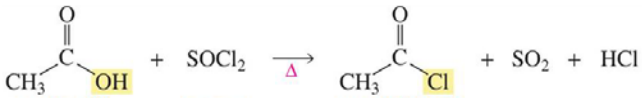
LAB EXAM: Thurs. Nov.22 – 1st 40 minutes of class (+ lecture)

16.21 Activation of carboxylic acids: *to make esters, amides…*

- RCOOH = readily available starting materials - in lab & in nature
- BUT: **must be activated to make LG better…**

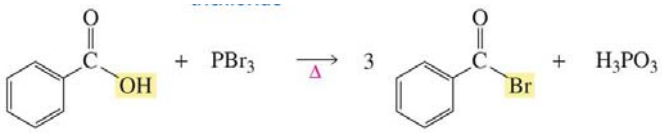
Typical lab activation: convert to acid halide (most reactive derivative)

$SOCl_2$ via LG = $-O\overset{O}{\overset{\|}{S}}Cl$



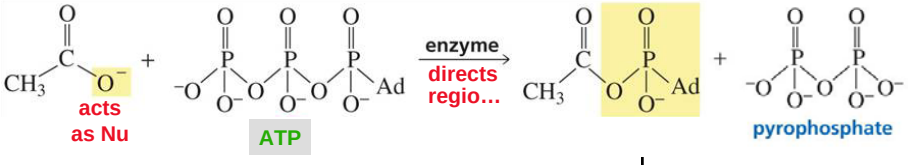
Mechanism:

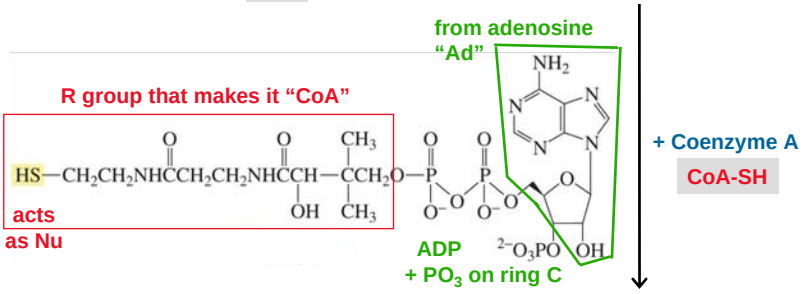
PCl_3 or PBr_3 via LG = $-OPX_2$



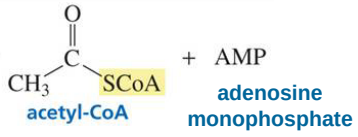
Nature's way: phosphate esters & thioesters (16.22 - for interest only…)

A phosphoester

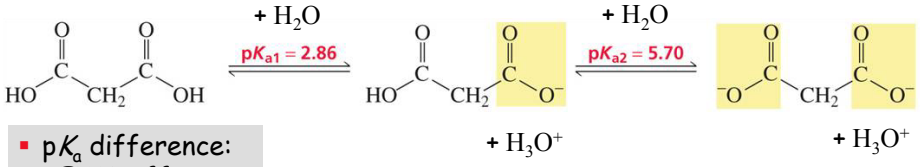




R-CoA = a thioester: (LG = -SCoA)
- most common activated RCOOH in cells
- used to make esters & amides for:
  neutrotransmittors, gene activation…

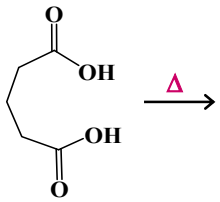


16.23 Dicarboxylic acids: 1st H+ easier to remove…



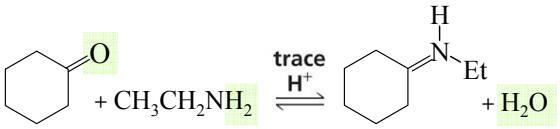
- pK_a difference: EWG effects & resonance…

What could this dicarboxylic acid do to itself?



(6)
- HOW: intramolecular Nu attack ⇨ dehydration…
- WHY: via 6-membered ring ‡ *(other molecules: 5-memb. ring…)*
- WHEN: heating *OR* dehydrating agent *OR* acid halide / anhydride

17.8 Rxns of aldehydes & ketones with NITROGEN-Nu's



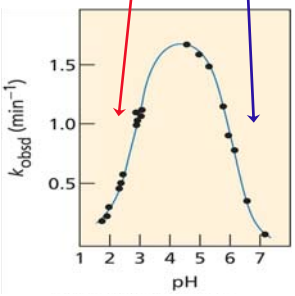
Fully reversible reaction

Rxn: addition/elimination
(& quite sensitive to pH)

Mechanism:

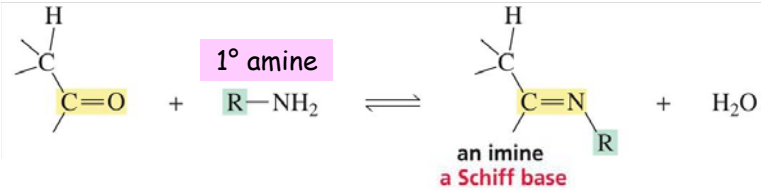
$-{}^+OH_2 \rightarrow -OH$
not LG...

$RNH_2 \rightarrow R\text{-}NH_3^+$
not Nu



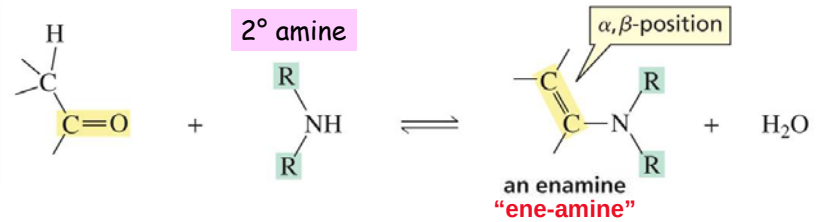
(7) ***What if we'd used a 2° amine?***

Pay attention to mechanism to understand imine *vs.* enamine



1. Nu attack by AMINE
2. H⁺n of Td int. ⇨ carbinolamine int. (neutral)
3. H⁺ transfer ⇨ to make LG = H_2O
4. H⁺ loss to eliminate H_2O

↖ **MOST ACIDIC SITE ATTACKED BY BASE:** NH if possible...
β-elimination if not !



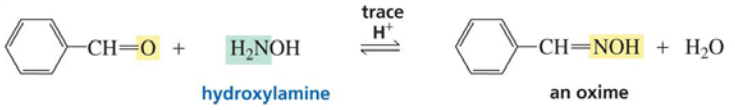
(8)

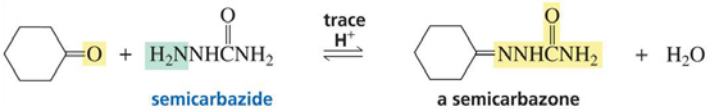
Why should we care about imines / enamines?

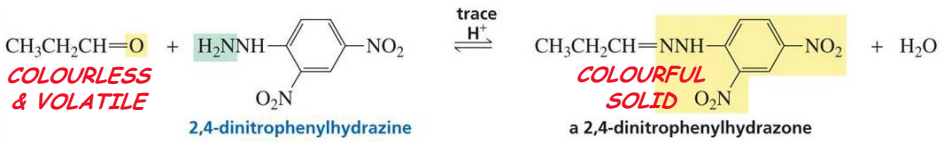
0. Biology: *DNA contains A,G,C,T but RNA has U instead of T… (27.9)*

1. Imine derivatives: non-spectroscopic method of identifying carbonyls

- Solid compounds: easy to measure m.p. (compare to known samples…)
- Inexpensive…

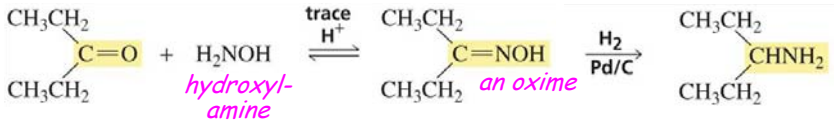




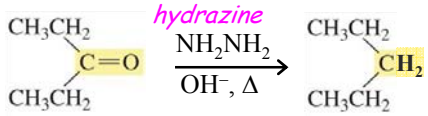


2. Synthetic uses of imines/enamines:

a) ROUTE TO AMINES: carbonyl + ammonia, then reduce imine



b) WOLFF-KISHNER REDUCTION: to deoxygenate a carbonyl cmpd

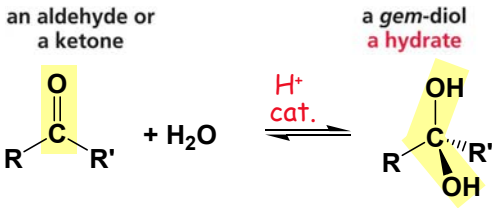


Mechanism:

1. *Imine formation (hydrazone…)*
2. *Successive de-H⁺n by OH⁻ & H⁺n by H_2O*
3. *Loss of N_2(g) DRIVES EQM FWD*

17.9-10 Rxns of aldehydes & ketones with OXYGEN-Nu's
Water & alcohols

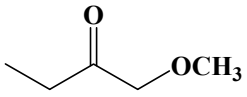
Which is more stable?
= which dominates at eqm?

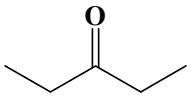


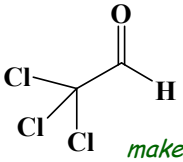
Stabilized by:
R = alkyl groups
(electronic effect)

Destabilized by:
R = alkyl groups
(steric effect)

Which compound will form the most hydrate in aqueous solution?







makes "chloral hydrate"

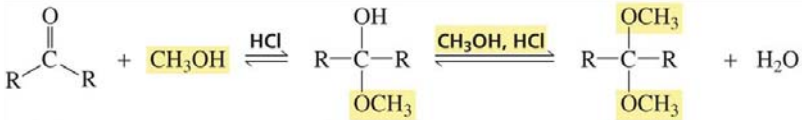
(11)

Acid-catalyzed acetal / ketal formation

ALDEHYDE
KETONE

hemiacetal
hemiketal

acetal
ketal



Mechanism: same as hydrate formation

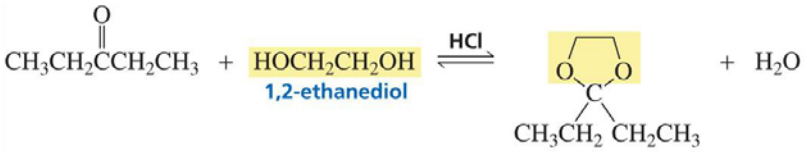
(12) **NOTE: drive rxn in preferred rxn using Le Châtelier's principle…**

17.11-12 Protection of functional groups

Protecting carbonyl groups: as acetals/ketals

Strategy:

1. Protect: ROH (or diol) + acid catalyst -- **DRIVE FWD: REMOVE H_2O**
2. Perform C=O incompatible chemistry
3. Deprotect: warm, aqueous acid -- **DRIVE BACK: EXCESS H_2O**



Acid catalysts:

- HCl
- p-TsOH (organic soluble)

Using protecting groups in synthesis

Protecting alcohols: as silyl ethers (deprotect via aqueous acid)

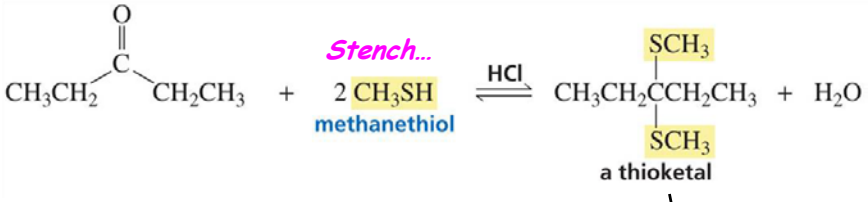
Protecting carboxylic acids: as esters (deprotect via hydrolysis)

Protecting amines: as amides (deprotect via acid-cat. hydrolysis)

Thiols: for protecting carbonyls, or for decarbonylation…

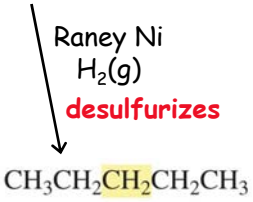
Strategy: as a protecting group

1. Protect: RSH (or dithiol) + acid catalyst -- **DRIVE FWD: REMOVE H_2O**
2. Perform C=O incompatible chemistry
3. Deprotect: warm, aqueous acid -- **DRIVE BACK: EXCESS H_2O**



Strategy: to remove O from C=O group

1. "Protect": RSH (or dithiol) + acid catalyst
2. Desulfurize with Raney Ni



3rd way to deoxygenate a compound:

1. Clemmensen reduction
2. Wolff-Kishner reduction
3. Thioketal desulfurization