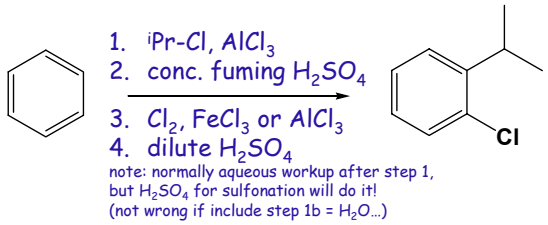
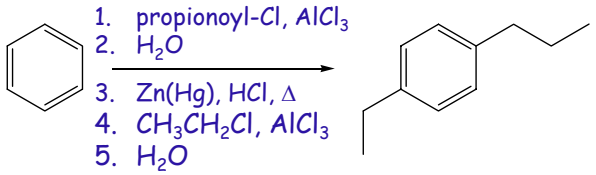
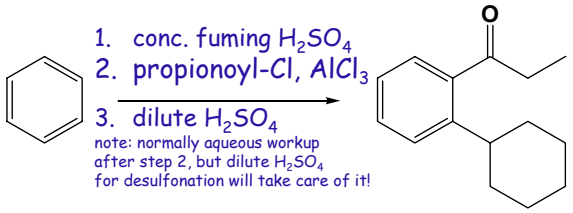
Provide a rxn sequence to make these as the major products…

Answers:



note: normally aqueous workup after step 1, but H_2SO_4 for sulfonation will do it! (not wrong if include step 1b = H_2O…)





note: normally aqueous workup after step 2, but dilute H_2SO_4 for desulfonation will take care of it!

CHEM 222 section 01

LECTURE #22 Thurs., Nov.15, 2007

Lecture topics & readings

Today's class

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

Before next class

- xxxxxxxxxxxxxxx

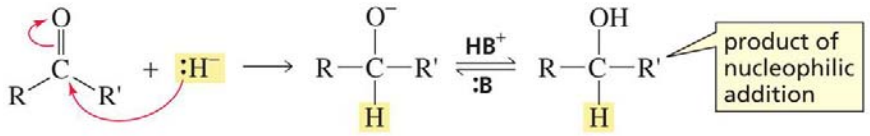
Next class

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

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

Rxns with H-nucleophiles: reduction to ROH (17.6, 19.1)

Class II - aldehydes & ketones: H^- addition



Hydride-transfer reagents:

- Sodium borohydride: $NaBH_4$ *weaker*
- Lithium aluminum hydride: $LiAlH_4$ *stronger*
  (LAH)

} **Violently reactive to H_2O !**

Which reagent?

- *$NaBH_4$ not reactive enough to donate H^- to esters, RCOOH, amides (less reactive than aldehydes / ketones)*

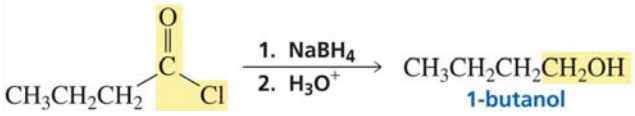
Procedure:

- use anhydrous, aprotic solvent
- 1st step: add hydride reagent to carbonyl compound solution
- 2nd step: aqueous acidic workup (carefully: Lewis acid byproduct)

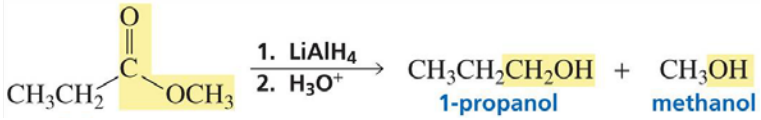
(3)

Class I: H^- addition + elimination of LG ← less nucleophilic than H^-

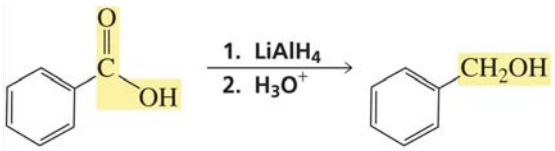
Acid halides (anhydrides)



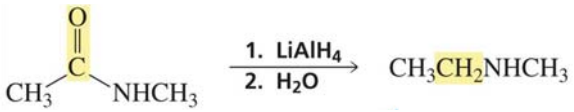
Esters



Carboxylic acids



Amides



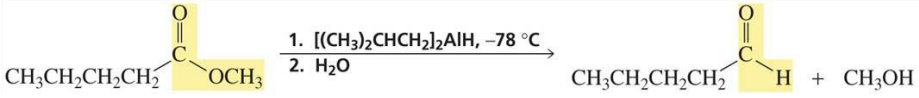
Acidic workup would yield ammonium salt

Mechanisms similar – see 17.6 for differences

H^- reduction of class I carbonyl proceeds via 2 successive Nu additions

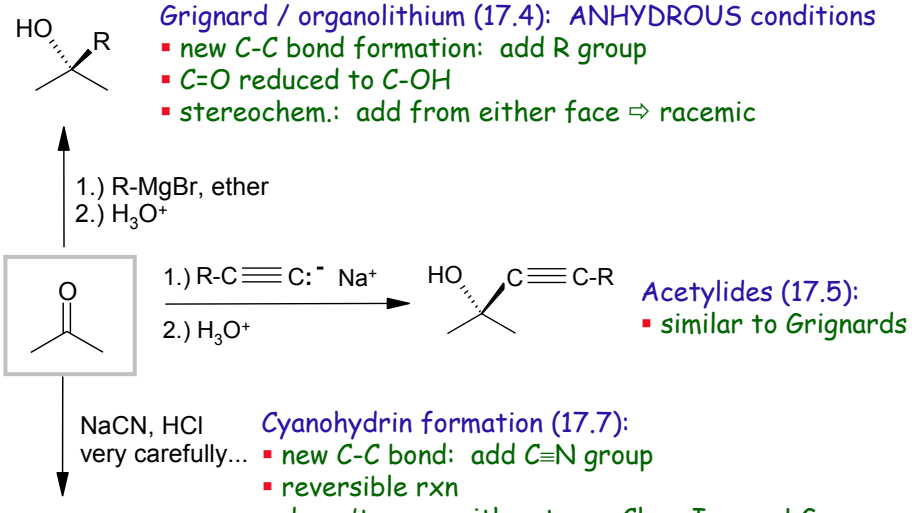
Mechanism for ester reduction (…& acid halides & anhydrides):

Reagent that stops at aldehyde intermediate: "DIBALH"



For RCOOH & amides: acidic H's present ⇨ changes mechanism… (not via aldehyde) check it out on your own

Rxns with C-nucleophiles: some seen already (17.4, 5, 7)



Grignard / organolithium (17.4): ANHYDROUS conditions
- new C-C bond formation: add R group
- C=O reduced to C-OH
- stereochem.: add from either face ⇨ racemic

Acetylides (17.5):
- similar to Grignards

Cyanohydrin formation (17.7):
- new C-C bond: add C≡N group
- reversible rxn
- doesn't occur with esters: Class I, poor LG…
- useful route to other groups:
  - reduce C≡N to **1° NH_2** (use H_2/Pt/C)
  - hydrolyze C≡N **to COOH** (see 16.19)…

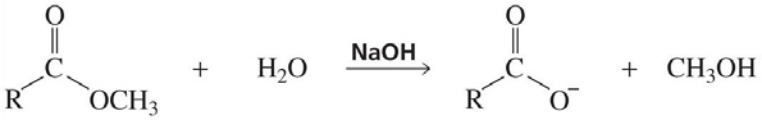
Overview: Carbonyl compounds react with NUCLEOPHILES

Class of Nu	Act like…	Reagents	Result when add to C=O ADDITION +/- ELIMINATION
C-Nu	C^-	RMgX, RLi $RC{\equiv}C{:}^-\ Na^+$ $N{\equiv}C{:}^-\ Na^+$ *+ more exotic ones later…*	Reduction + framework extension: alcohol + new C-C bond alcohol + new C-C bond (to C≡CR…) alcohol + new C-C bond (to C≡N…)
H-Nu	H^-	$NaBH_4$ *(milder)* $LiAlH_4$ *(stronger)*	Reduction: R-OH forms + Class I cmpds also lose their LG…
O-Nu		H_2O, ROH…	Next topic… 1st Class I compounds, then Class II
N-Nu		NH_3, amines…	

Rxns of esters with O & N nucleophiles: *if Nu ≥ LG….*
⇨ ADDITION+ELIMINATION

(16.10,12) Basic conditions, Nu = OH^-, or OR^-…: like acyl halides…

Hydrolysis: yieldS carboxylate (& ROH)



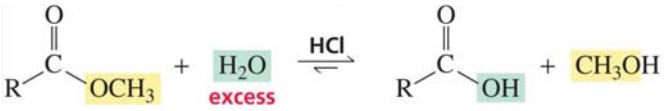
+ acidic workup ⇨ RCOOH

Mechanism:
1. Nu attack by OH^-
2. Td collapse
(3.) H^+ transfer to RO^-

Transesterification: (switch to different alkoxy group on ester)

(16.10-11) Acidic conditions, Nu = H_2O, or HOR…: *protonated ester*
⇨ ADDITION+ELIMINATION

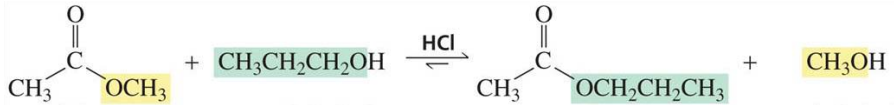
Acid-catalyzed Hydrolysis: yields RCOOH & ROH…



To drive eqm fwd:
1. excess H_2O
2. remove product as forms…

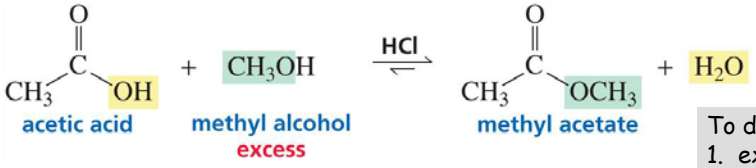
Mechanism:
1. *protonate ester*
2. *Nu attack*
3. *H^+ transfers*
4. *Td collapse*

Transesterification: via similar acid-catalyzed mechanism



Rxns of RCOOH with O & N nucleophiles: *going the other way…*
⇨ ADDITION+ELIMINATION

Push the equilibrium the other direction: *Fischer esterification*

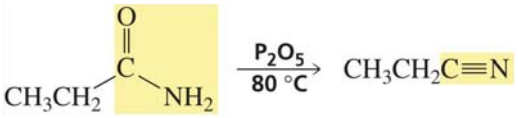


To drive eqm fwd:
1. excess ROH
2. remove H_2O as forms…

Can make ammonium carboxylate salts too: if Nu = amine

(16.16-17) Rxns of amides with O & N Nus: *less reactive…*

1st, USEFUL SYNTHETIC RXN - Can dehydrate amides to yield nitriles:

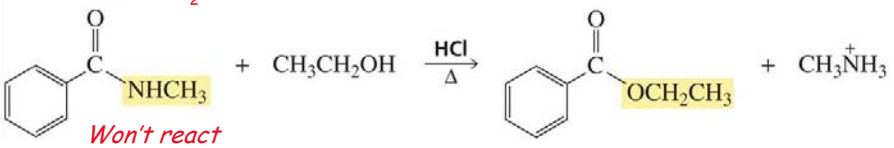


Dehydrating agents:
1. P_2O_5
2. $POCl_3$
3. $SOCl_2$

More "biologically relevant": acid-catalyzed hydrolysis (or alcoholysis)

Acidic conditions, Nu = H_2O or HOR…: ***addition + elimination…***

Stable in base conditions:
$^-NR_2$ > ^-OR ≥ ^-OH

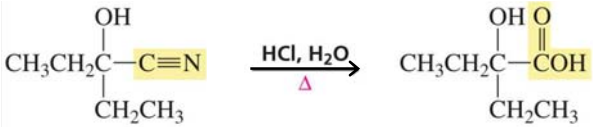


Won't react unless C=O protonated

(11) *Work through the mechanism on your own: 16.17.*

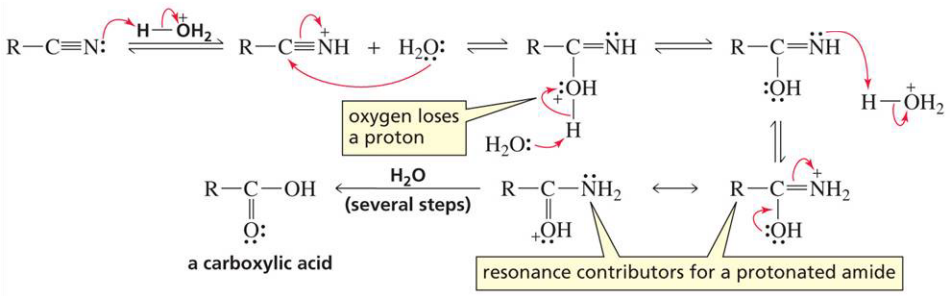
Hydrolysis of a nitrile yields a carboxylic acid (16.19)

(occurs in either acidic or basic conditions…)



an α-hydroxy acid

General mechanism of acid-catalyzed hydrolysis of a nitrile:



(12) *Don't memorize this one – just follow through the logic.*