Acid Derivatives II

Details of

- Esters
- Amides
- Reduction & Grignard Rxns

Spectroscopy

Ref 18: (5 – 8)

Prob 18: 11, 12a, 14, 24 (except f, g, p, 8th ed.)
(except f, 9th ed.)

25, 28, 29, 30a,b, 35,36

Adv Rdg 17: 1 - 3

Ester Prep.

3 methods

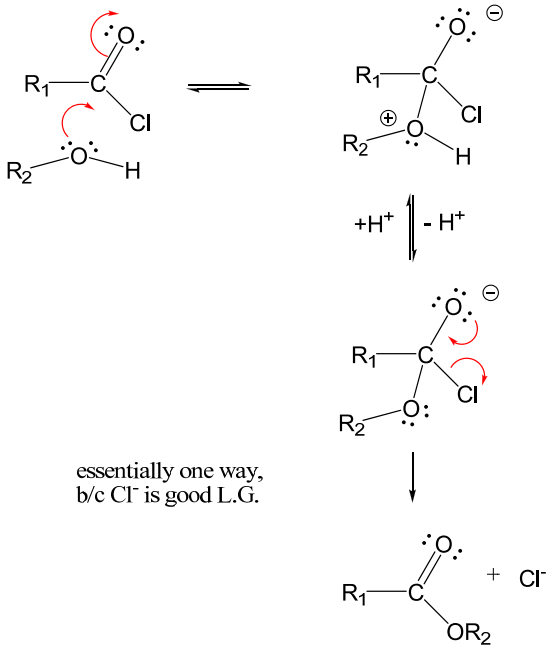
1.) rxn w/ acid chlorides

2.) "Fischer Esterification"

3.) S_N2 rxn

Also: "Inorganic Esters"

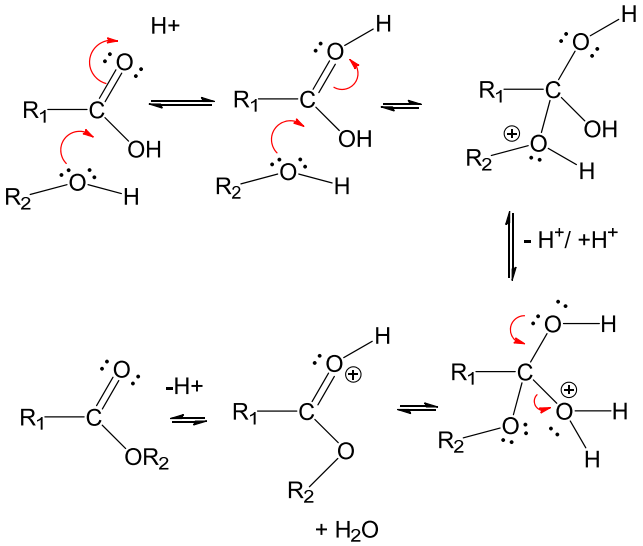
1.) Rxn w/ Acid Chlorides



2.) "Fischer" Esterification

R_1CO_2H; R_2OH; strong acid (e.g. H_2SO_4); T ↑

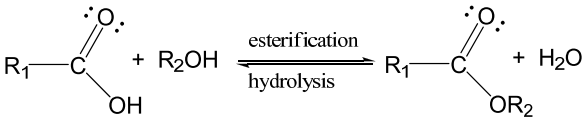
Mech.



"Fischer" ...

rxn totally reversible

HMWK: write mech for hydrolysis (reverse) rxn



Equilibrium postion affected
acc. to Le Chatelier Principle

- remove H_2O → favors ester
- add xs R_2OH → favors ester
- add xs H_2O → favors acid / alcohol mix.

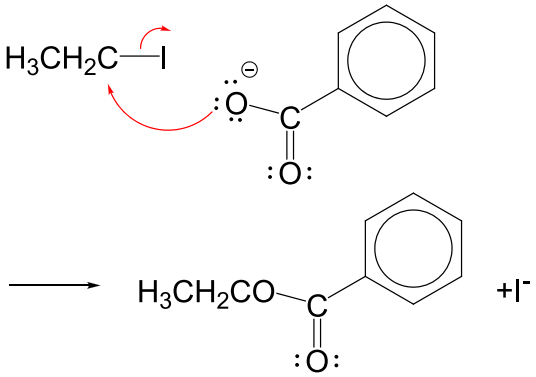
3.) Ester by S_N2

recall from CHEM 261:

1° (2°) halide, tosylate .... + carboxylate anion

→ ester

Ex.



works well w/ 1° alcohol (2 °, ±)

"Inorganic Esters"

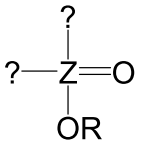
(from inorganic acid + alcohol)

important:

as "activated intermediates"

presence in DNA ...

General Structure



"acyl type arrangement"

where Z = S, P, Cr, N, Mn, Os ....

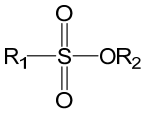
and groups at ? may or may not be present

inorganic ..

Survey

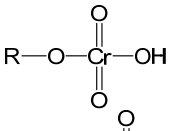
(*we encountered quite a few of them already)*

sulfonates; (tosylates)



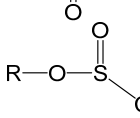
good as L.G.'s in S_N2

chromates



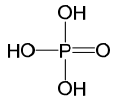
seen in oxidation of alcohols to aldehydes

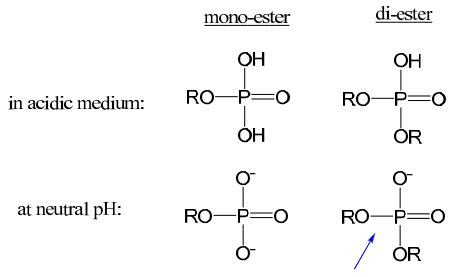
chlorosulfites



seen in prep. of acyl- and alkyl chlorides

mono- and di-esters of phosphoric acid, H_3PO_4,





Rxns of Esters

1.) Hydrolysis

a.) acidic

b.) basic

2.) Hydride Reduction → 1° ROH

3.) Organometallic Rxns → 3° ROH

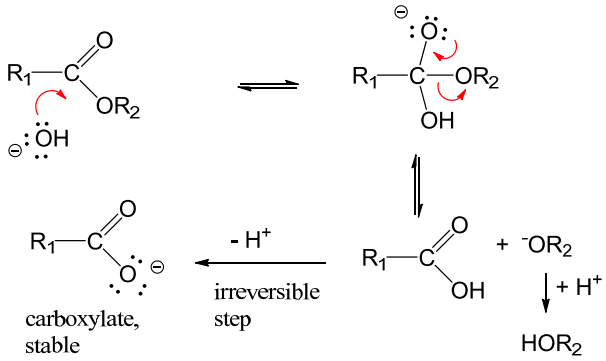
later

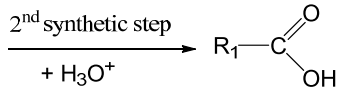
1.) Hydrolysis

a.) acidic = reverse of Fischer esterification, seen before, do as HMWK

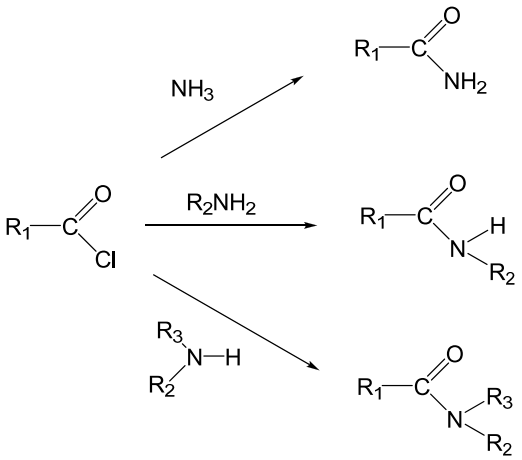
1.) Hydolysis

b.) basic = "saponification"



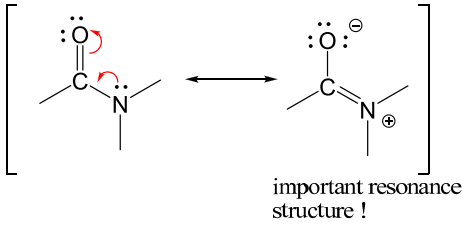


Prep of Amides



- mech. analogous to prep. of esters from acyl chlorides
- do as HMWK

Structure of Amides



- C–N has substantial double bond character
- N essentially sp^2 hybridized
- rotation around C–N bond restricted (similar to C=C bond)
- cis, trans isomers observable; e.g., by NMR

structure ...

• "trans isomer" more predominant

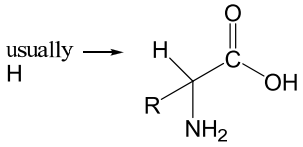
(more stable, b/c less steric strain)

"trans" "cis"

• important for 3D structure of proteins

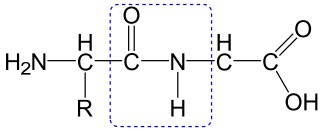
Intro to Protein Chem.

• made from α amino acids



• connected by amide (="peptide" linkage)

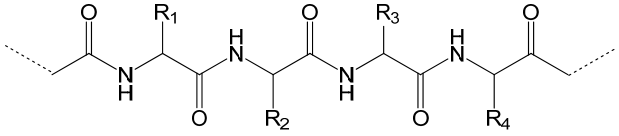
"di-peptide":



"peptide linkage"

protein = multi-peptide

protein ...



• R_1, R_2, R_3, ... can be:

– H

– CH_3

– CH_2OH

– CH_2CO_2H

– $(CH_2)_4 – NH_2$, etc.

≈ 20 amino acids exist (biologically)

• # of peptide links in proteins can be large:

20 ..... ∞

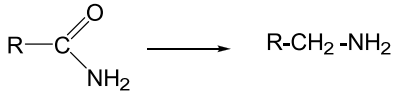
Rxn of Amides

1.) Hydrolysis

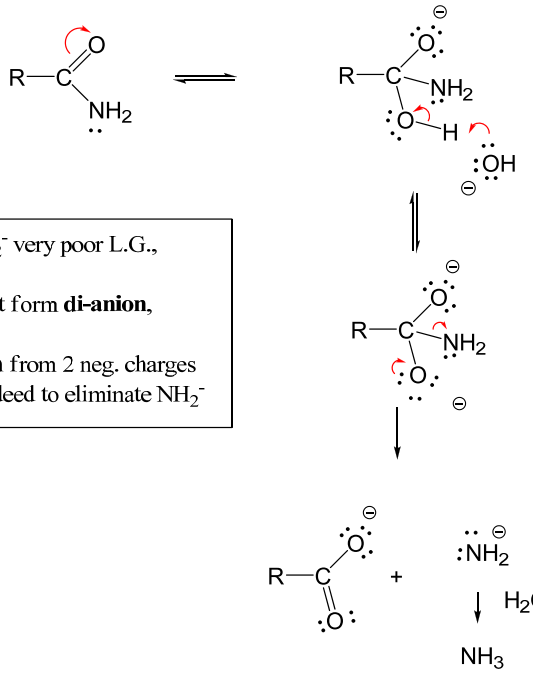
a.) in acid; analogous to ester;
do as HMWK

b.) in base (follows)

2.) Hydride Reduction



Hydrolysis in Base



NH_2^- very poor L.G.,

must form **di-anion**,

push from 2 neg. charges needeed to eliminate NH_2^-

"Reduction of Acid Derivatives"

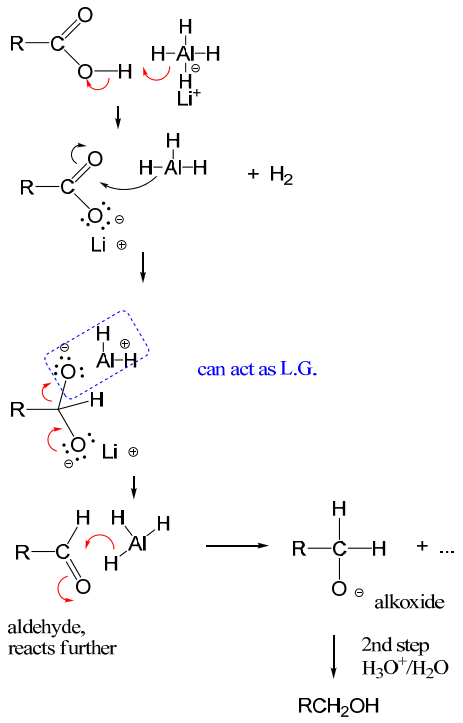
Summary

substrate	$LiAlH_4$	RLi / RMgX
acid	1° ROH *	ketone *
ester	1° ROH *	3° ROH *
amide	amine *	**X**
(nitrile	amine	ketone)

* mech. will be presented (& must be known)

Acids + $LiAlH_4$ → Alcohols

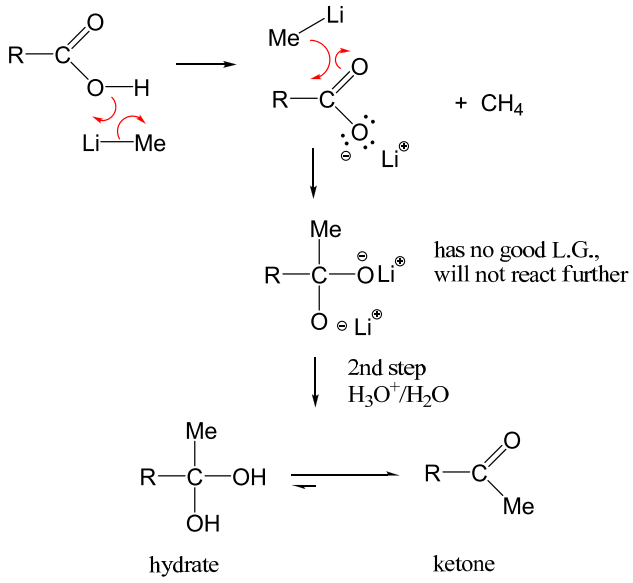
Mech.



Acids + O/M → Ketones

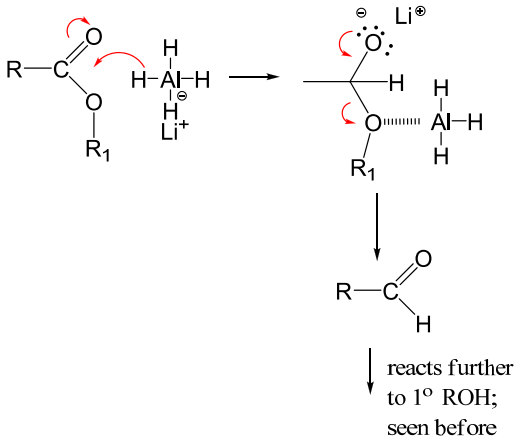
(O/M = organometallics, e.g. Me-Li)

Example Mech.



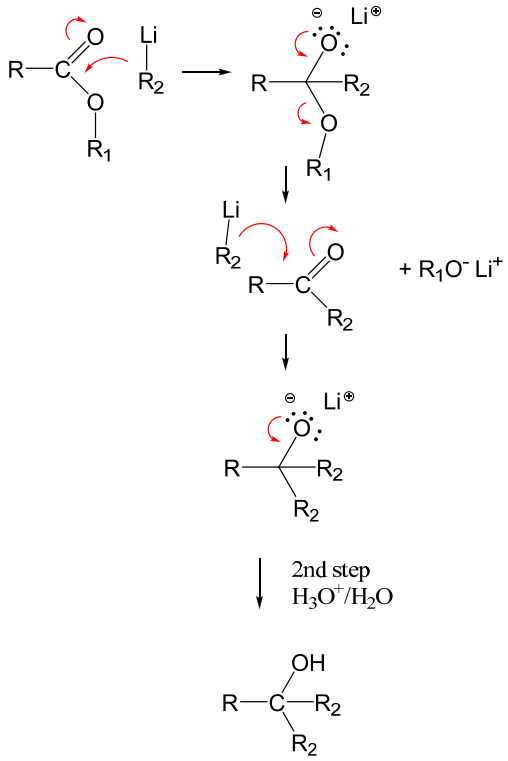
Esters + $LiAlH_4$ → Alcohols

Mech.



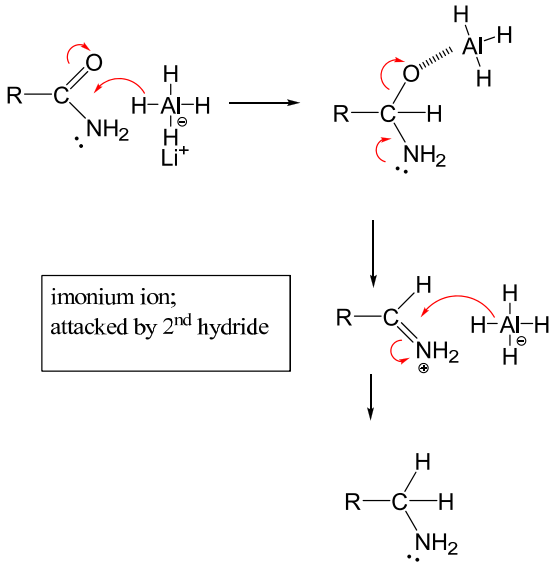
Esters + O/M → 3° Alcohol

Mech.



Amides + $LiAlH_4$ → Amines

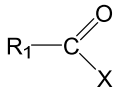
Mech.



Spectroscopy

IR

trends parallel those of reactivity



if X is e^- withdrawing ,

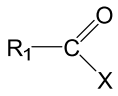
C=O • has more double bond character,

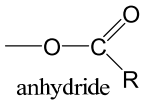
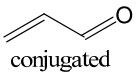
• stronger (stiffer) bond

• ν, $\tilde{\nu}$ larger

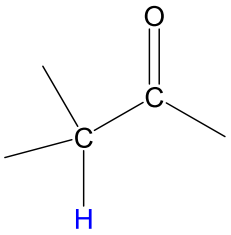
acc. to Hooke's Law: $\tilde{\nu} = \sqrt{\frac{k}{\mu}}$

where k = force const. (old hat)

IR Trends for 

X	$\tilde{\nu}$ (cm^{-1})	
– Cl	1815	EWG
 anhydride	1815,1765	EWG
– OR (ester)	1745	EWG
– H (aldehyde)	1730	ref.
– R (ketone)	1715	EDG
 conjugated	1685	EDG
– NH_2 (amide)	1685	EDG

NMR



δ of α H:

~ 2.5 ppm (+/- 0.5 ppm)