# 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

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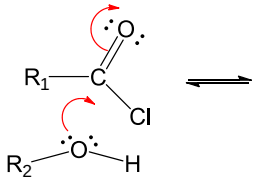
Also: "Inorganic Esters"



# 1.) Rxn w/ Acid Chlorides



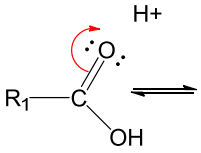

essentially one way,
b/c $Cl^-$ is good L.G.



# 2.) "Fischer" Esterification

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

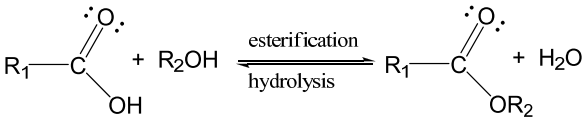
Mech.



"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.



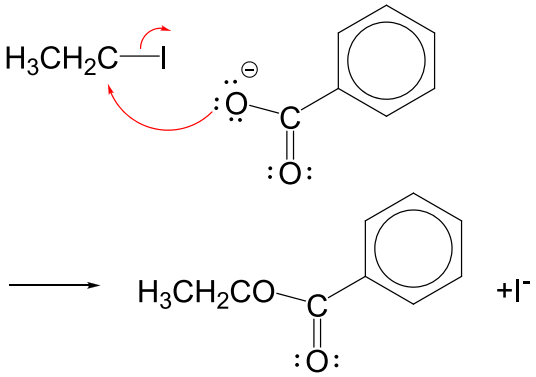
# 3.) Ester by $S_N2$

recall from CHEM 261:

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

→ ester

Ex.




works well w/ 1° alcohol (2 °, ±)



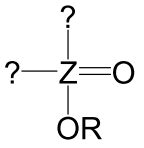
# "Inorganic Esters"

(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

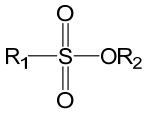


inorganic ..

Survey

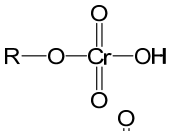
(*we encountered quite a few of them already)*

sulfonates; (tosylates)



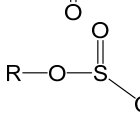

good as L.G.'s in $S_N2$

chromates



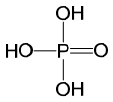

seen in oxidation of alcohols to aldehydes

chlorosulfites




seen in prep. of acyl- and alkyl chlorides

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




in acidic medium:

at neutral pH:

# Rxns of Esters

1.) Hydrolysis

a.) acidic

b.) basic

2.) Hydride Reduction → 1° ROH

3.) Organometallic Rxns → 3° ROH

later

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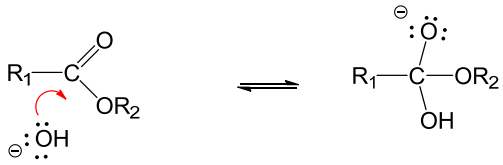
1.) Hydrolysis

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



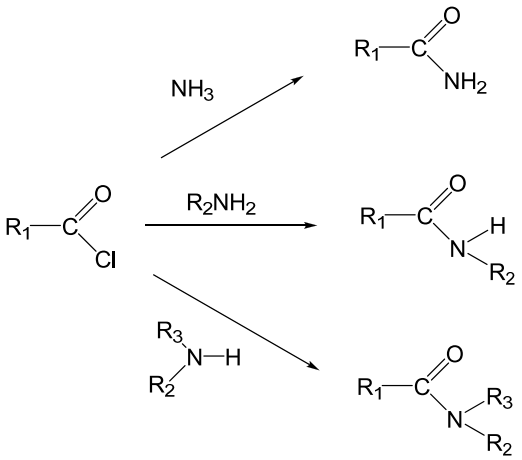
1.) Hydrolysis

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)

• important for 3D structure of proteins



# Intro to Protein Chem.

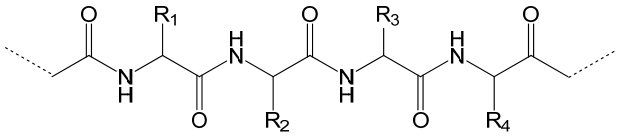
• made from α amino acids

• connected by amide (= "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 ..... ∞



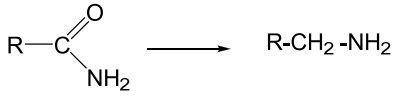
# Rxn of Amides

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 needed to eliminate $NH_2^-$



# "Reduction of Acid Derivatives" Summary

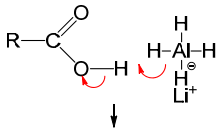
| substrate | $LiAlH_4$ | RLi / RMgX |
|---|---|---|
| acid | 1° ROH * | ketone * |
| ester | 1° ROH * | 3° ROH * |
| amide | amine * | **X** |
| (nitrile | amine | ketone) |

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



# Acids + $LiAlH_4$ → Alcohols

Mech.





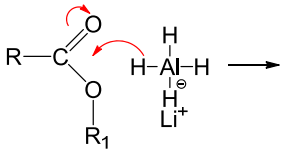

# Acids + O/M → Ketones

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

Example Mech.

# Esters + $LiAlH_4$ → Alcohols

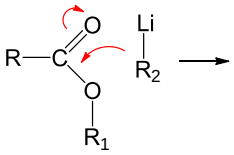
Mech.





# Esters + O/M → 3° Alcohol

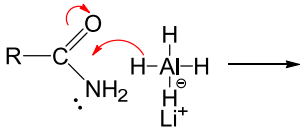
Mech.





# Amides + $LiAlH_4$ → Amines

Mech.



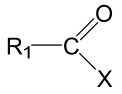
imonium ion;
attacked by 2nd hydride



# Spectroscopy

## IR

trends parallel those of reactivity



if X is $e^-$ withdrawing ,

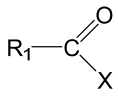
C=O • has more double bond character,

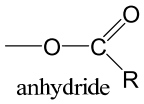
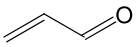
• stronger ( stiffer) bond

• ν, $\tilde{\nu}$ larger

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

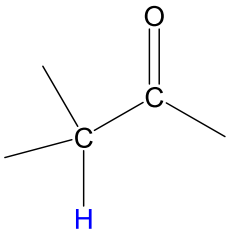
*where k = force const. (old hat)*

# IR Trends for 

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



# NMR



δ of α H:

~ 2.5 ppm (+/- 0.5 ppm)