

CH 310 N

T TH 2-3:30

LECTURE 15

Textbook Assignment: Chapter 18

Homework (for credit): POW 7 posted

Today's Topics: Derivatives of Carboxylic Acids

Notice & Announcements:

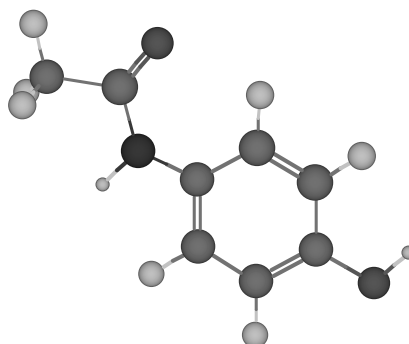
Exam II: Monday 10/19 7-9 PM

Last Name A-L: WEL 1.308

Last Name M-Z: WEL 2.224

ORGANIC LECTURE SERIES

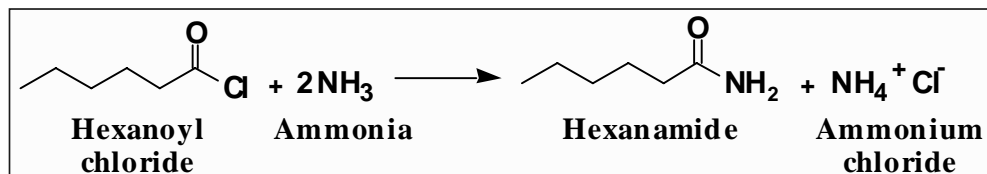
*Functional
Derivatives of
Carboxylic Acids*



Reaction with Ammonia

Acid halides react with ammonia, 1° amines, and 2° amines to form amides

– 2 moles of the amine are required per mole of acid chloride

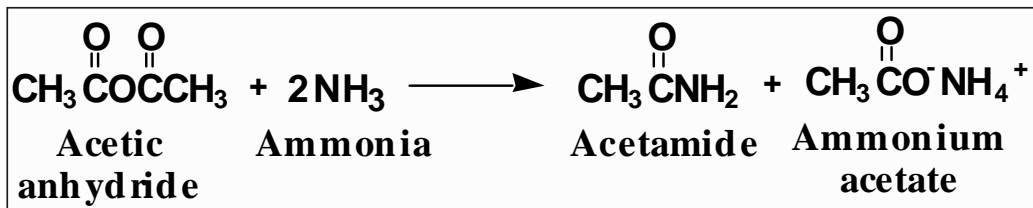


3

Reaction with Ammonia

Acid anhydrides react with ammonia, and 1° and 2° amines to form amides

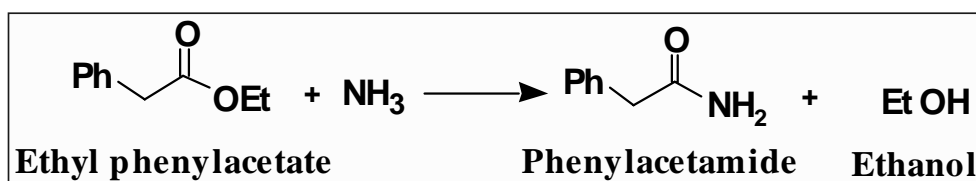
– 2 moles of ammonia or amine are required



4

Reaction with Ammonia

- Esters react with ammonia, and 1° and 2° amines to form amides
 - esters are less reactive than either acid halides or acid anhydrides

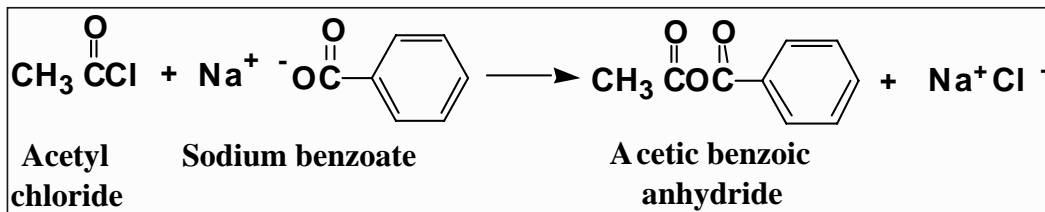


- Amides do not react with ammonia, or 1° or 2° amines

5

Acid Chlorides with Salts

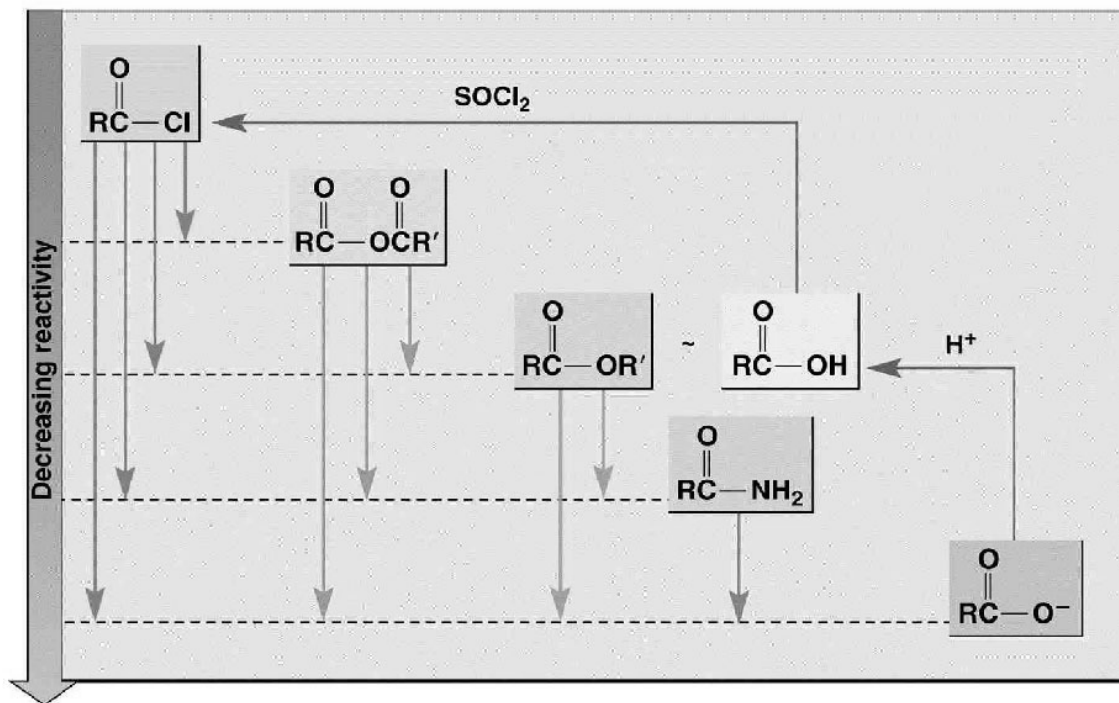
- Acid chlorides react with salts of carboxylic acids to give anhydrides
- most commonly used are sodium or potassium salts



This is a method to prepare mixed acid anhydrides

6

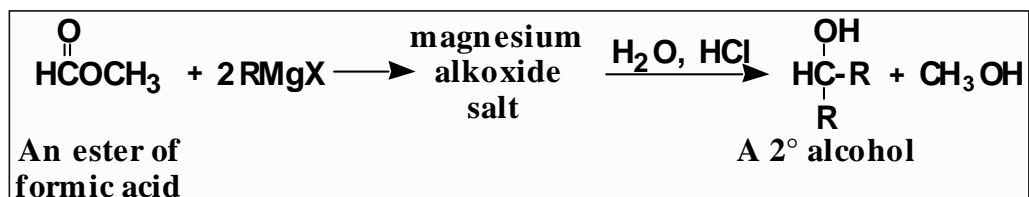
Interconversions



7

Reactions with Grignard Reagents

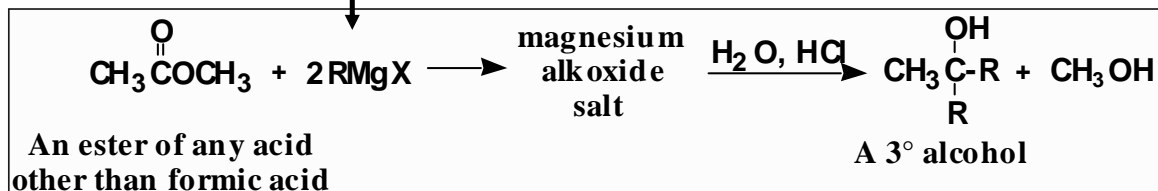
–treating a formic ester with 2 moles of Grignard reagent followed by hydrolysis in aqueous acid gives a 2° alcohol



8

Reactions with Grignard Reagents

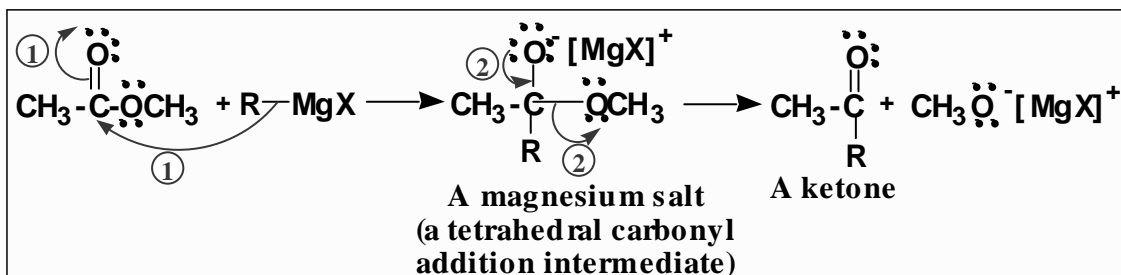
- treating other esters with 2 equivalents of Grignard reagent followed by hydrolysis in aqueous acid gives a 3° alcohol



9

Reactions with Grignard Reagents

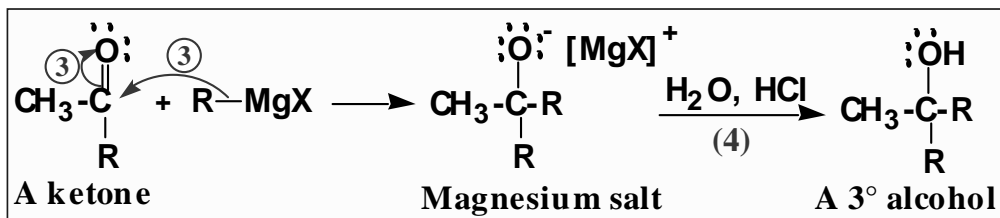
1. addition of 1 mole of RMgX to the carbonyl carbon gives a TCAI
2. collapse of the TCAI gives a ketone (an aldehyde from a formic ester)



10

Reactions with Grignard Reagents

3. reaction of the ketone with a 2nd mole of RMgX gives a second TCAI
4. treatment with aqueous acid gives the alcohol

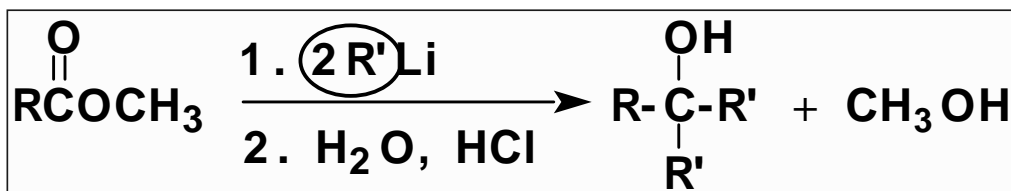


11

Reactions with Organolithium

Organolithium compounds are even more powerful nucleophiles than Grignard reagents

- they react with esters to give the same types of 2° and 3° alcohols as do Grignard reagents
- and often in higher yields

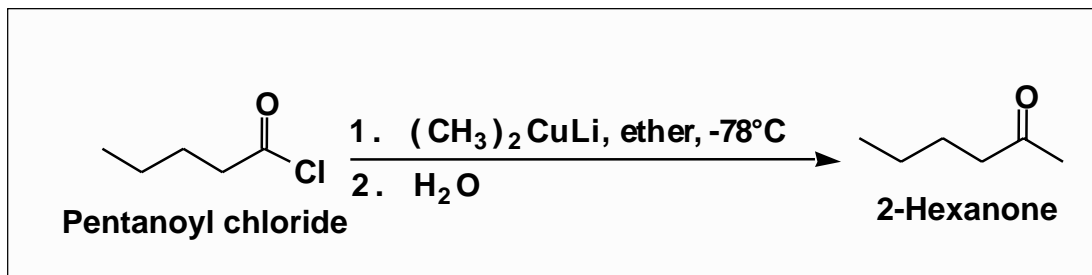


12

Reactions with Organocuprate Reagents

Acid chlorides at -78°C react with Gilman reagents to give ketones

- under these conditions, the TCAI is stable, and it is not until acid hydrolysis that the ketone is liberated



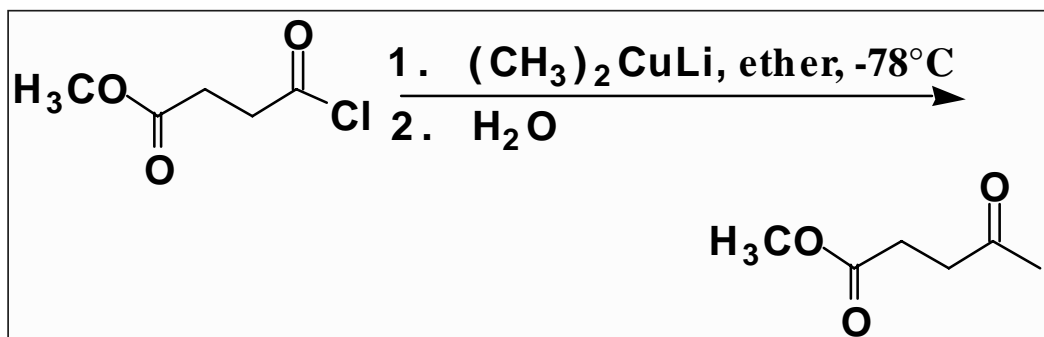
This is analogous to Gilman coupling with alkyl halides.

Experimental note: -78°C is dry ice & acetone or IPA

13

Reactions with Organocuprate Reagents

- Gilman reagents react only with acid chlorides
- they do not react with acid anhydrides, esters, amides, or nitriles under the conditions described

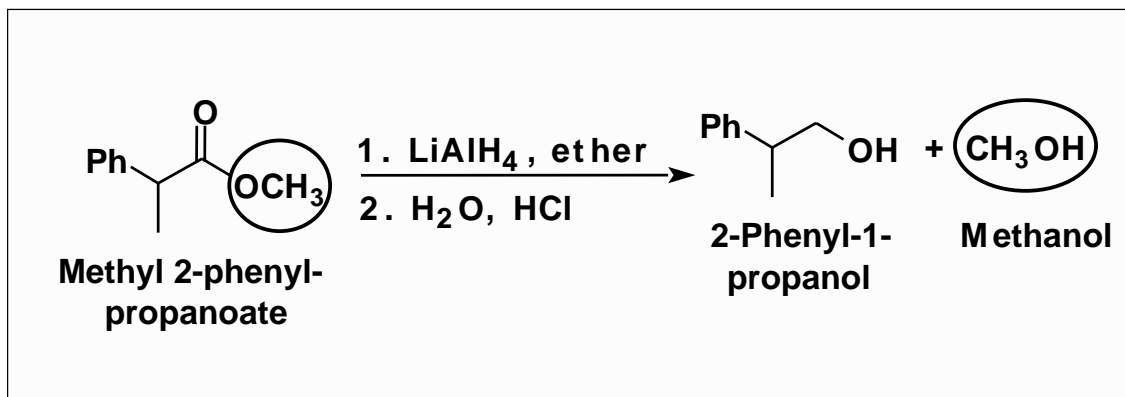


14

Reduction - Esters by LiAlH_4

Most reductions of carbonyl compounds now use hydride reducing agents

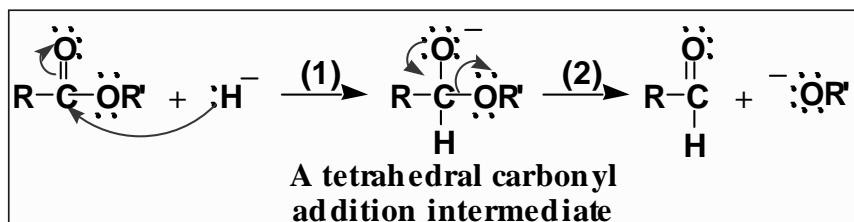
- esters are reduced by LiAlH_4 to two alcohols
- the alcohol derived from the carbonyl group is primary



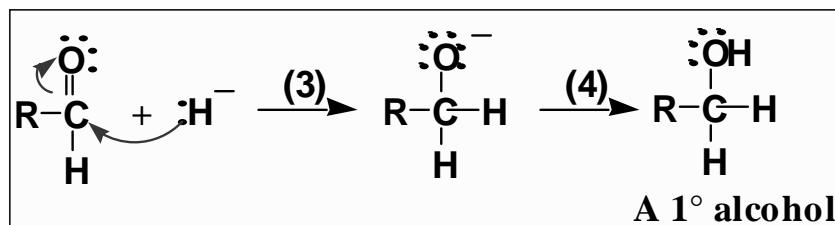
15

Reduction - Esters by LiAlH_4

- Reduction occurs in three steps plus workup
 - Steps 1 and 2 reduce the ester to an aldehyde



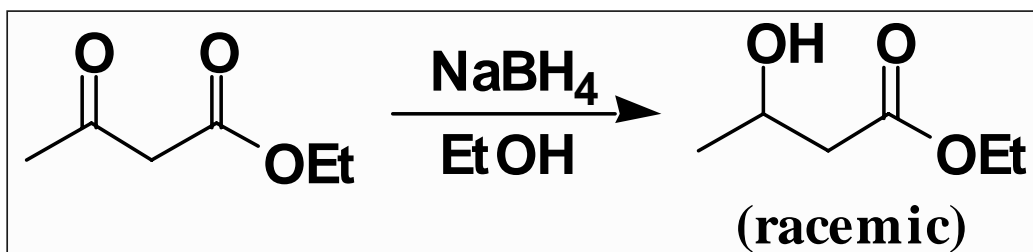
- Step 3 reduction of the aldehyde followed by work up gives a 1° alcohol



16

Reduction - Esters & NaBH₄

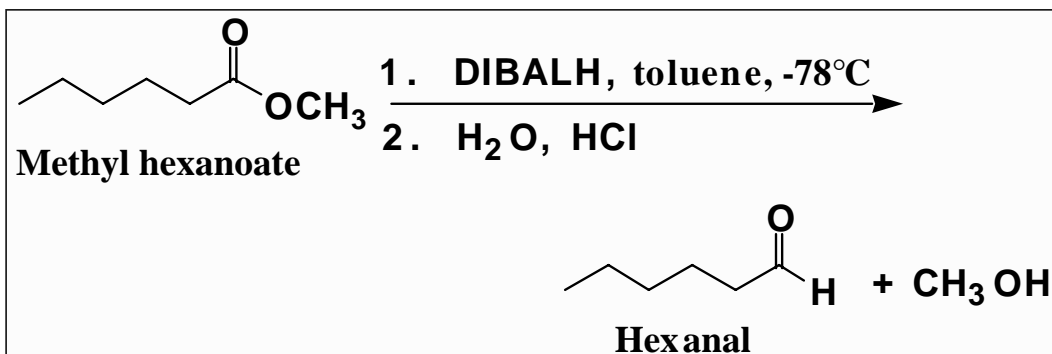
- NaBH₄ does not normally reduce esters, but it does reduce aldehydes and ketones
- Selective reduction is often possible by the proper choice of reducing agents and experimental conditions



17

Reduction - Esters by DIBALH

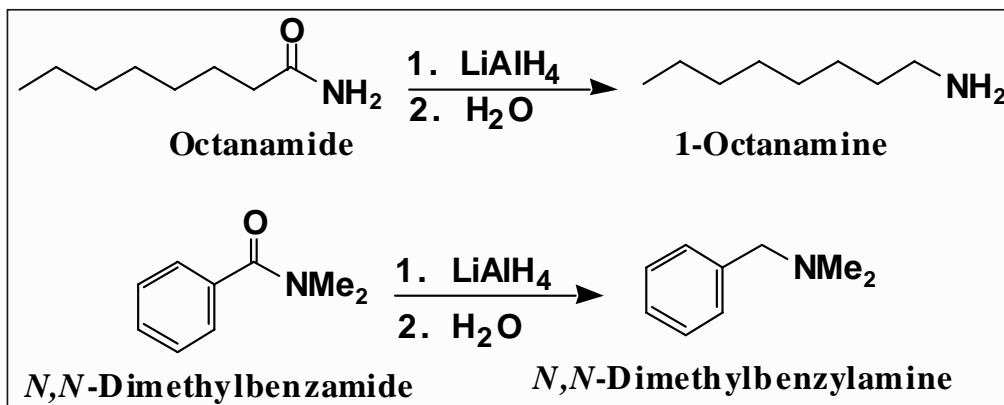
- Diisobutylaluminum hydride (**DIBALH**) at -78°C selectively reduces an ester to an aldehyde
 - at -78°C, the TCAI does not collapse and it is not until hydrolysis in aqueous acid that the carbonyl group of the aldehyde is liberated



18

Reduction - Amides by LiAlH_4

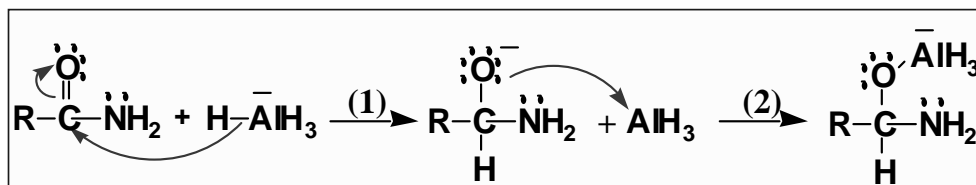
- LiAlH_4 reduction of an amide gives a 1° , 2° , or 3° amine, depending on the degree of substitution of the amide



19

Reduction - Amides by LiAlH_4

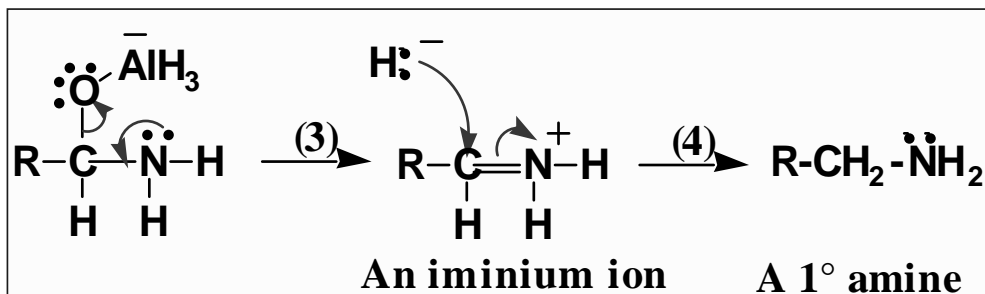
- The mechanism is divided into 4 steps
 - Step 1: transfer of a hydride ion to the carbonyl carbon
 - Step 2: a Lewis acid-base reaction and formation of an oxygen-aluminum bond



20

Reduction - Amides by LiAlH_4

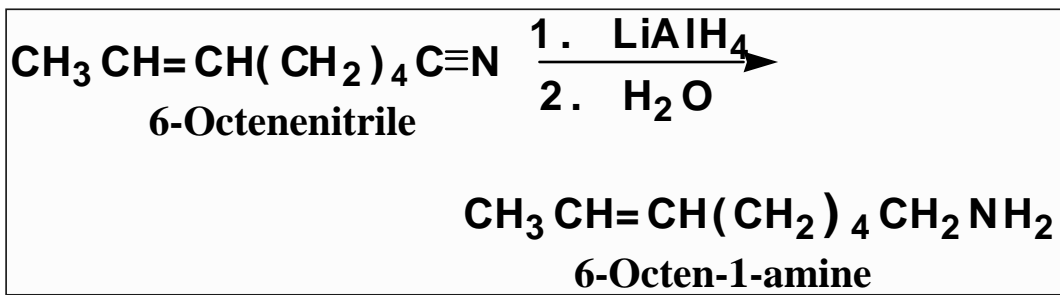
- Step 3: redistribution of electrons and ejection of H_3AlO^- gives an iminium ion
- Step 4: transfer of a second hydride ion to the iminium ion completes the reduction to the amine



21

Reduction - Nitriles by LiAlH_4

- The cyano group of a nitrile is reduced by LiAlH_4 to a 1° amine



22

**STOP HERE
FOR EXAM
MATERIAL**