CH 318 N LECTURE 16

Textbook Assignment: Chapter 19

Homework (for credit): POW 8 posted

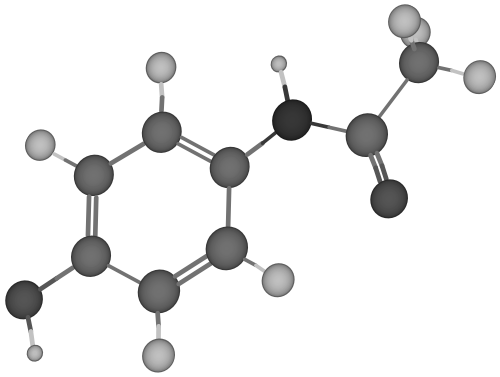
Today's Topics: Enolates

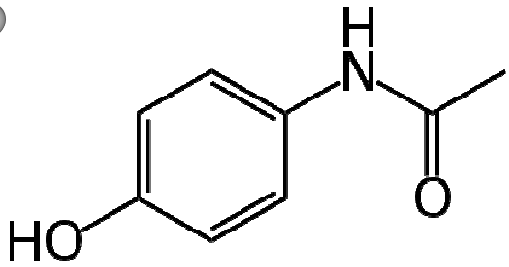
Notice & Announcements:

Exam II: Tuesday 10/20-

Wel 2.122 7-9 PM

Functional Derivatives of Carboxylic Acids

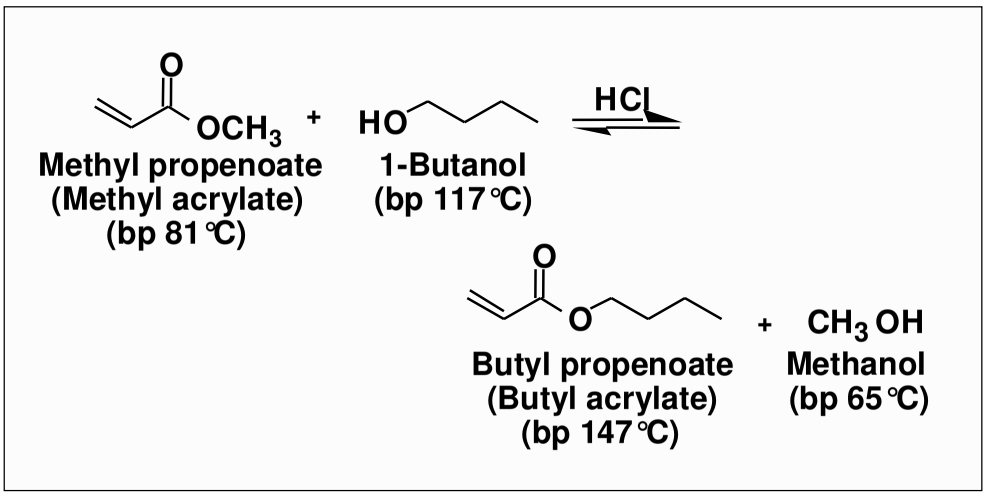




acetaminophen

Reaction with Alcohols

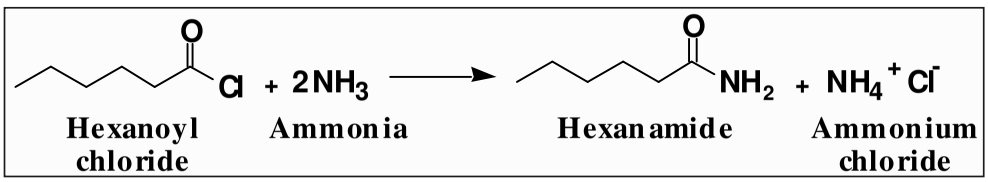
- Esters react with alcohols in the presence of an acid catalyst in an equilibrium reaction called **transesterification**



Reaction with Ammonia

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

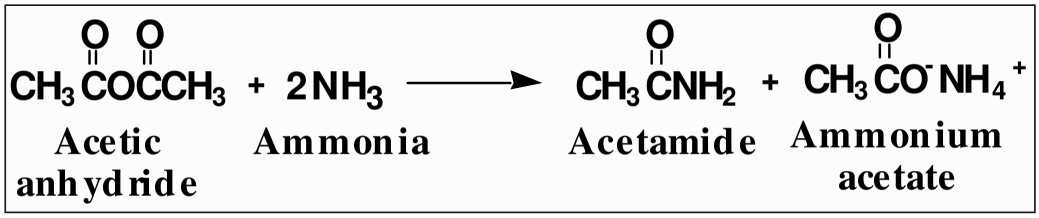
- 2 moles of the amine are required per mole of acid chloride



Reaction with Ammonia

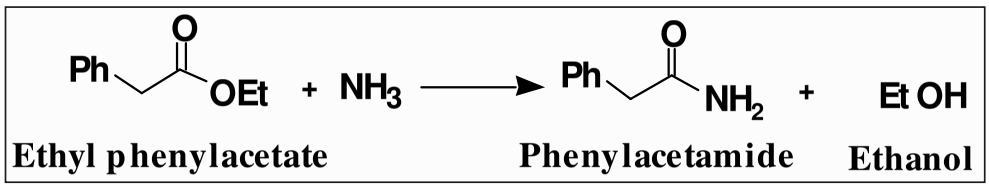
Acid anhydrides react with ammonia, and 1° and 2° amines to form amides

- 2 moles of ammonia or amine are required



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

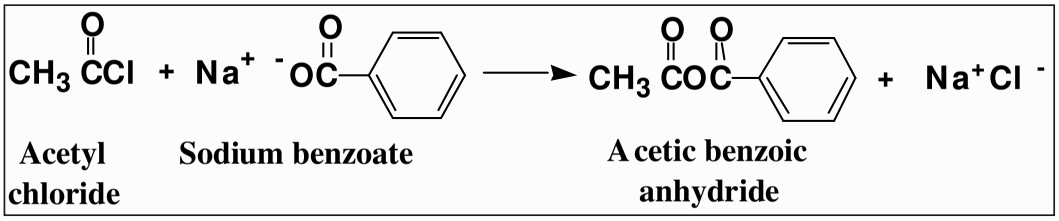


- Amides do not react with ammonia, or 1° or 2° amines

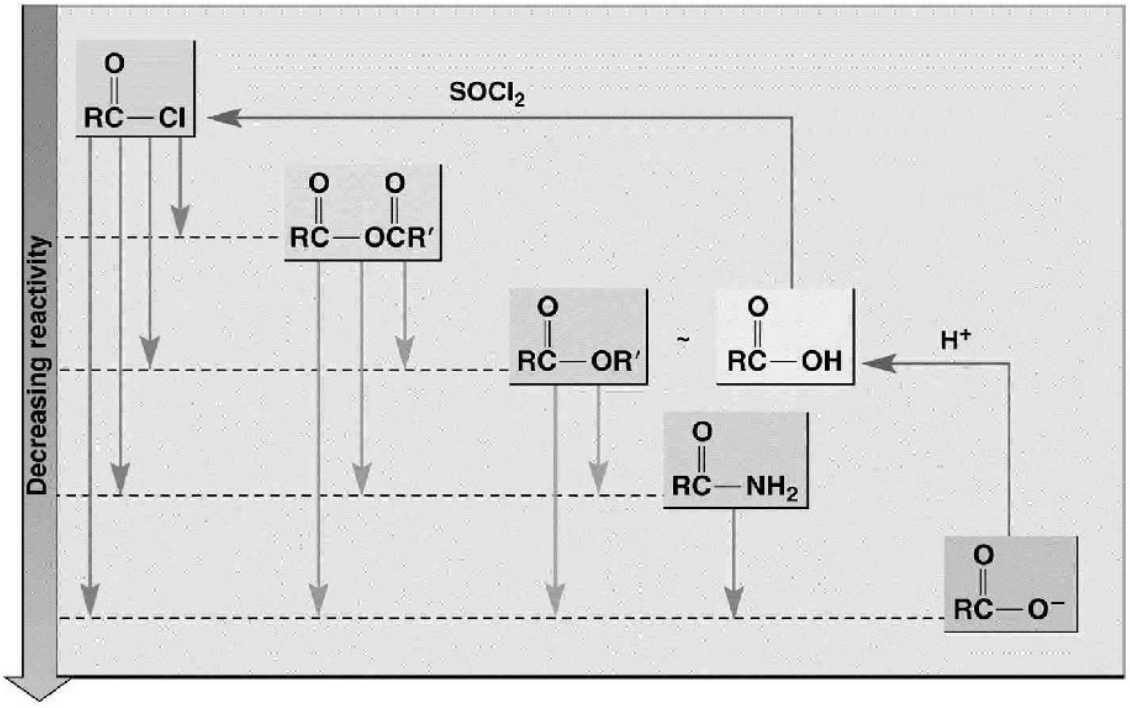
Acid Chlorides with Salts

Acid chlorides react with salts of carboxylic acids to give anhydrides

- most commonly used are sodium or potassium salts

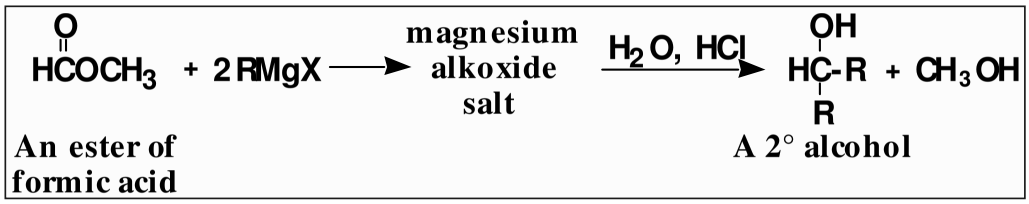


Interconversions



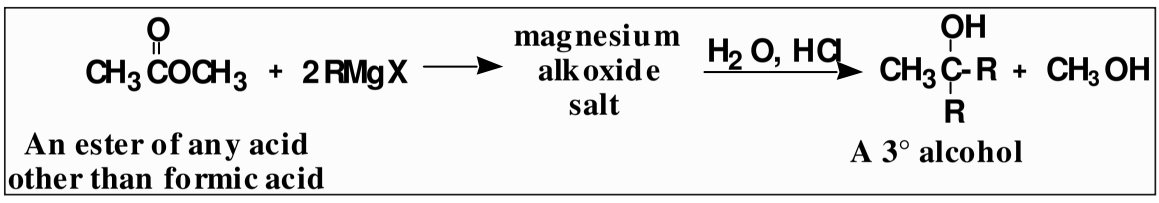
Reactions with Grignard Reagents

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



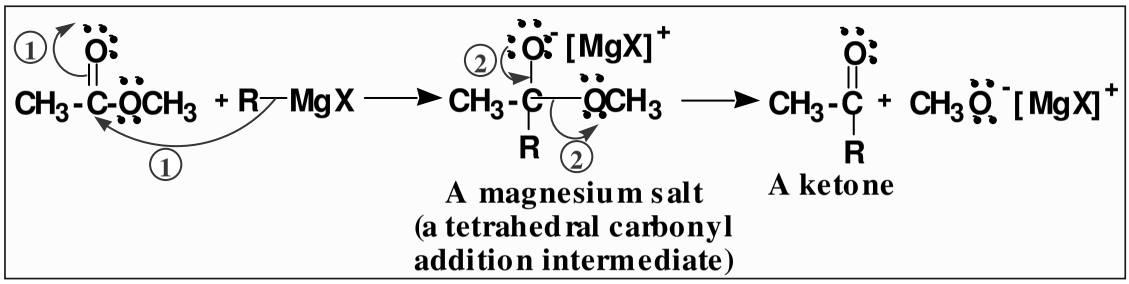
Reactions with Grignard Reagents

– treating other esters with a Grignard reagent followed by hydrolysis in aqueous acid gives a 3° alcohol



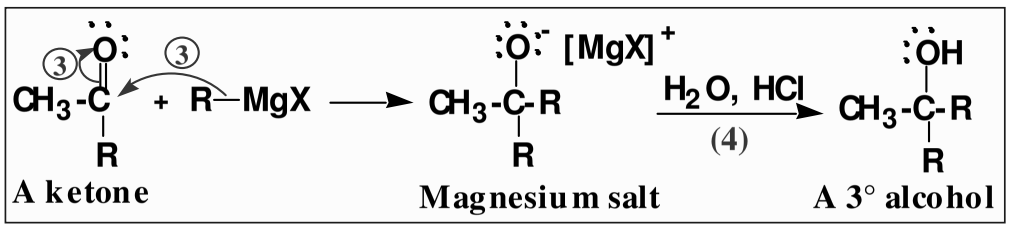
Reactions with Grignard Reagents

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)



Reactions with Grignard Reagents

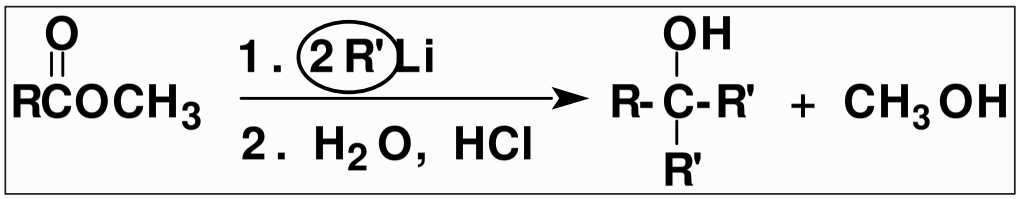
3. reaction of the ketone with a 2nd mole of RMgX gives a second TCAI
4. treatment with aqueous acid gives the alcohol



Reactions with Organolithium

Organolithium compounds are even more powerful nucleophiles than Grignard reagents

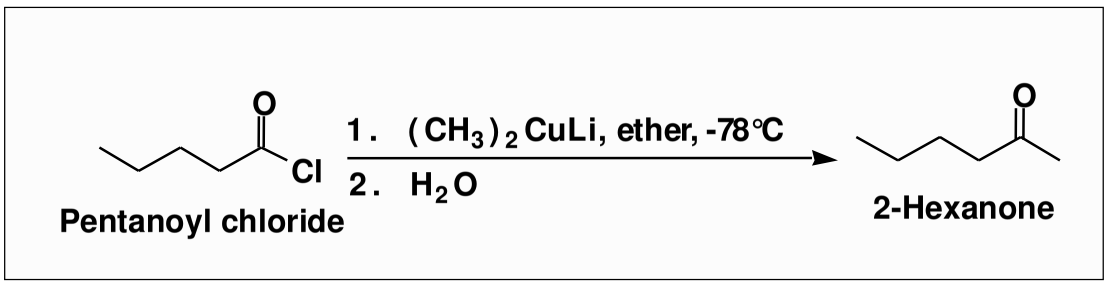
- they react with esters to give the same types of 2° and 3° alcohols as do Grignard reagents
- and often in higher yields



Reactions with Organocuprate Reagents

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

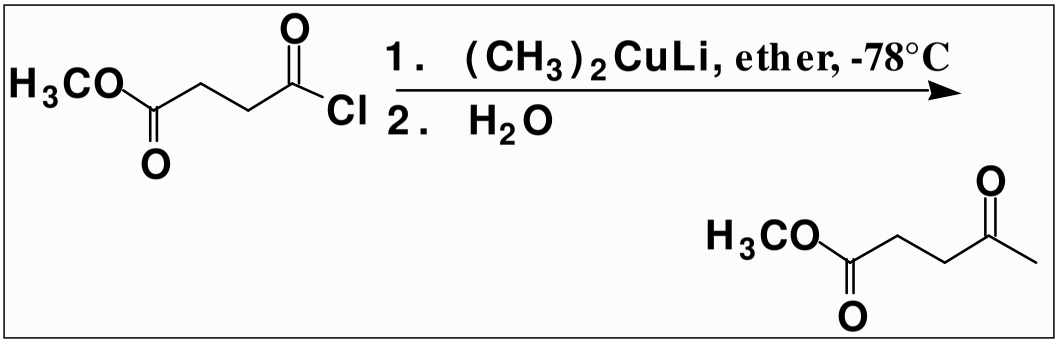
- under these conditions, the TCAI is stable, and it is not until acid hydrolysis that the ketone is liberated



This is analgous to Gilman coupling with alkyl halides.

Reactions with Organocuprate Reagents

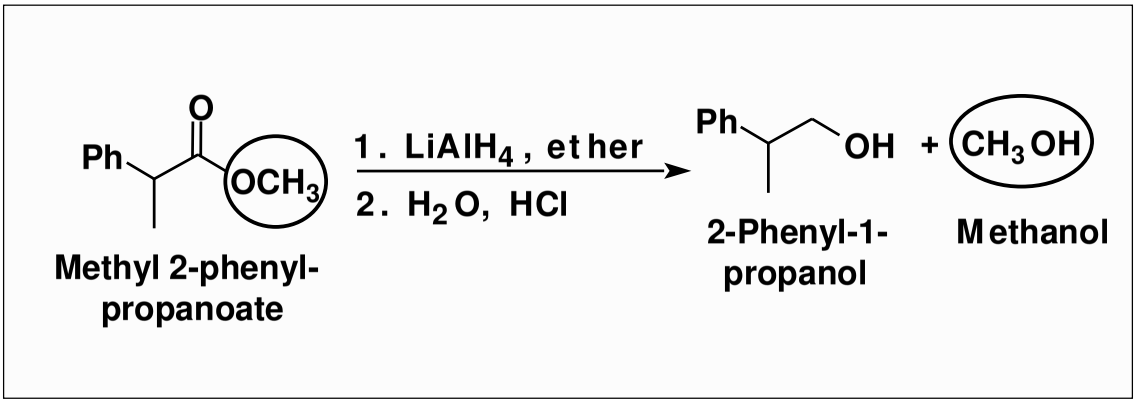
- Gilman reagents react only with acid chlorides
- they do not react with acid anhydrides, esters, amides, or nitriles under these conditions



Reduction - Esters by $LiAlH_4$

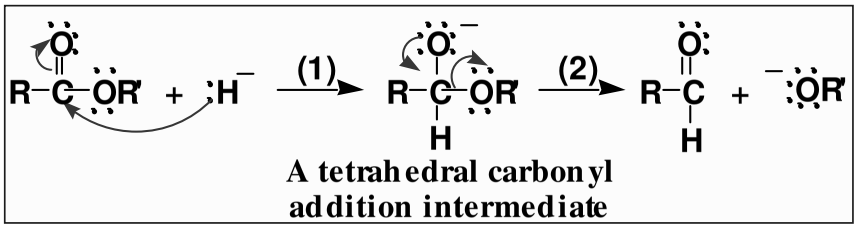
Most reductions of carbonyl compounds now use hydride reducing agents

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

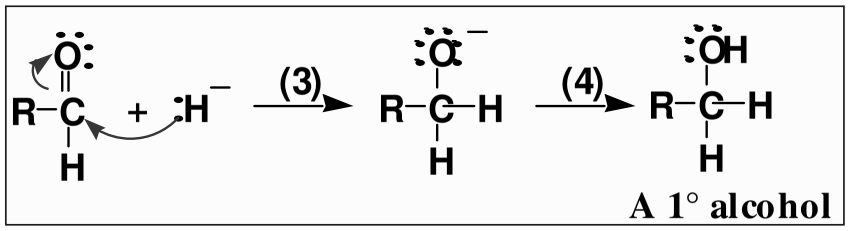


Reduction - Esters by $LiAlH_4$

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

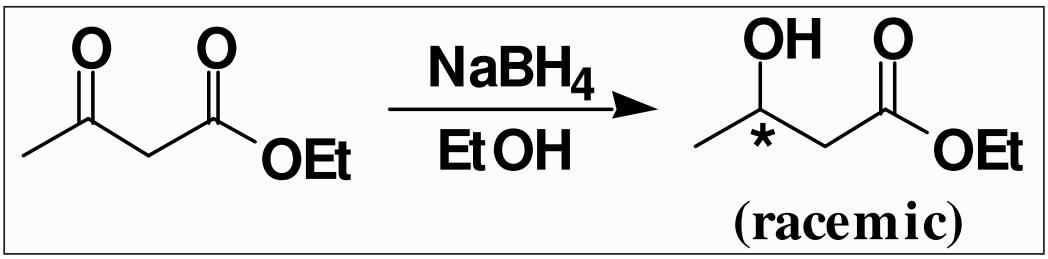


  - Step 3 reduction of the aldehyde followed by work up gives a 1° alcohol



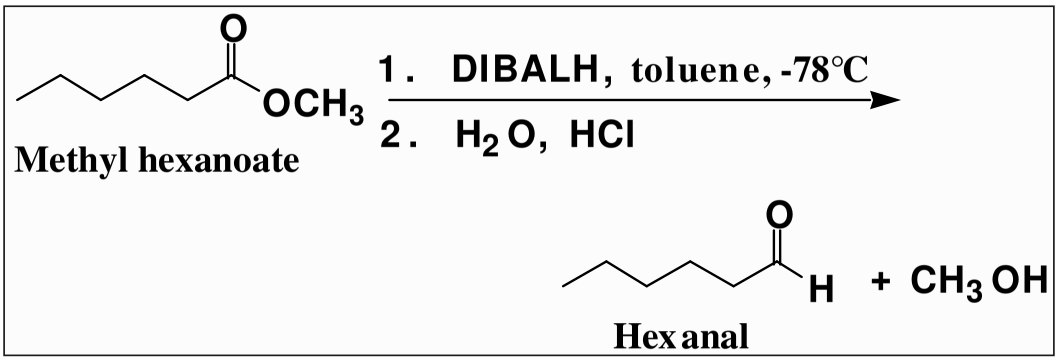
Reduction - Esters & $NaBH_4$

- $NaBH_4$ 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



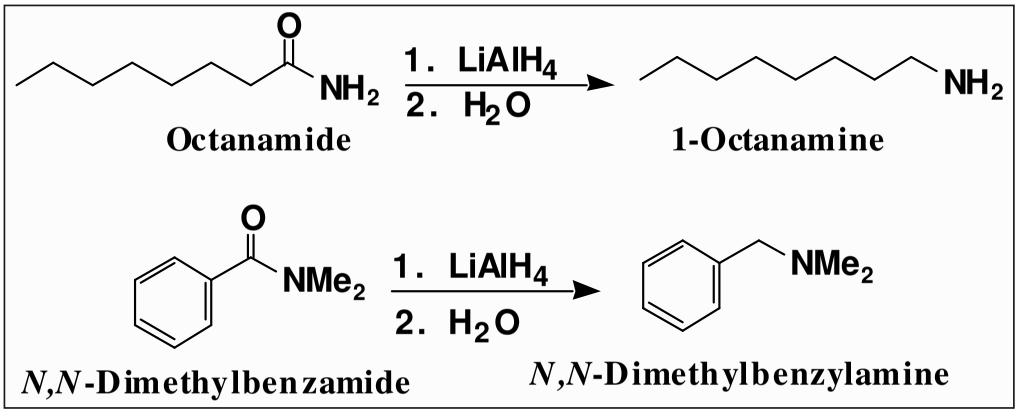
Reduction - Esters by DIBAlH

- 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



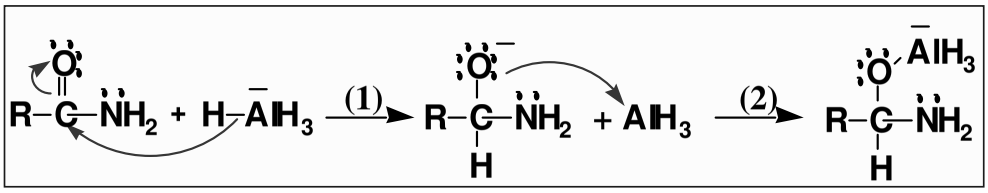
Reduction - Amides by $LiAlH_4$

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



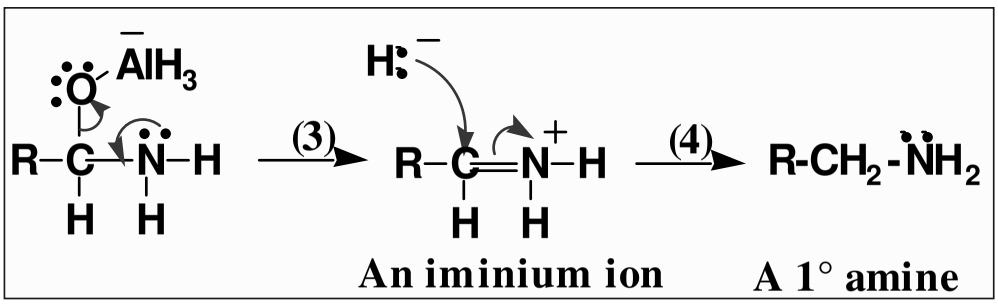
Reduction - Amides by LiAlH4

- 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



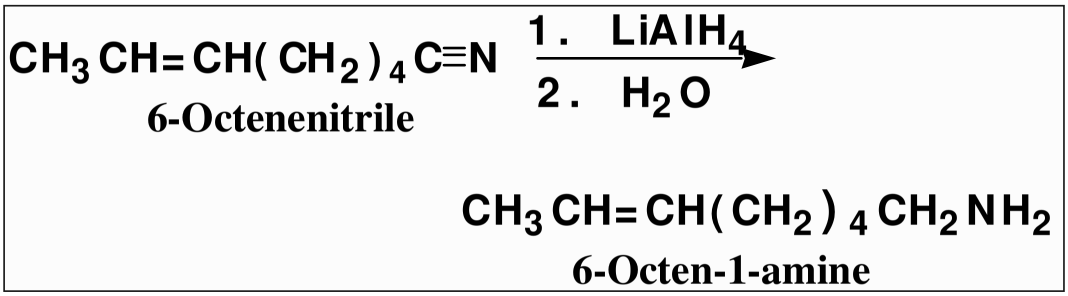
Reduction - Amides by $LiAlH_4$

- 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



Reduction - Nitriles by $LiAlH_4$

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



Exam 2:

Chapters 16-18