UF | UNIVERSITY of FLORIDA

Pre-Health Post-Baccalaureate Program
Study Guide and Practice Problems

Course: CHM 2211

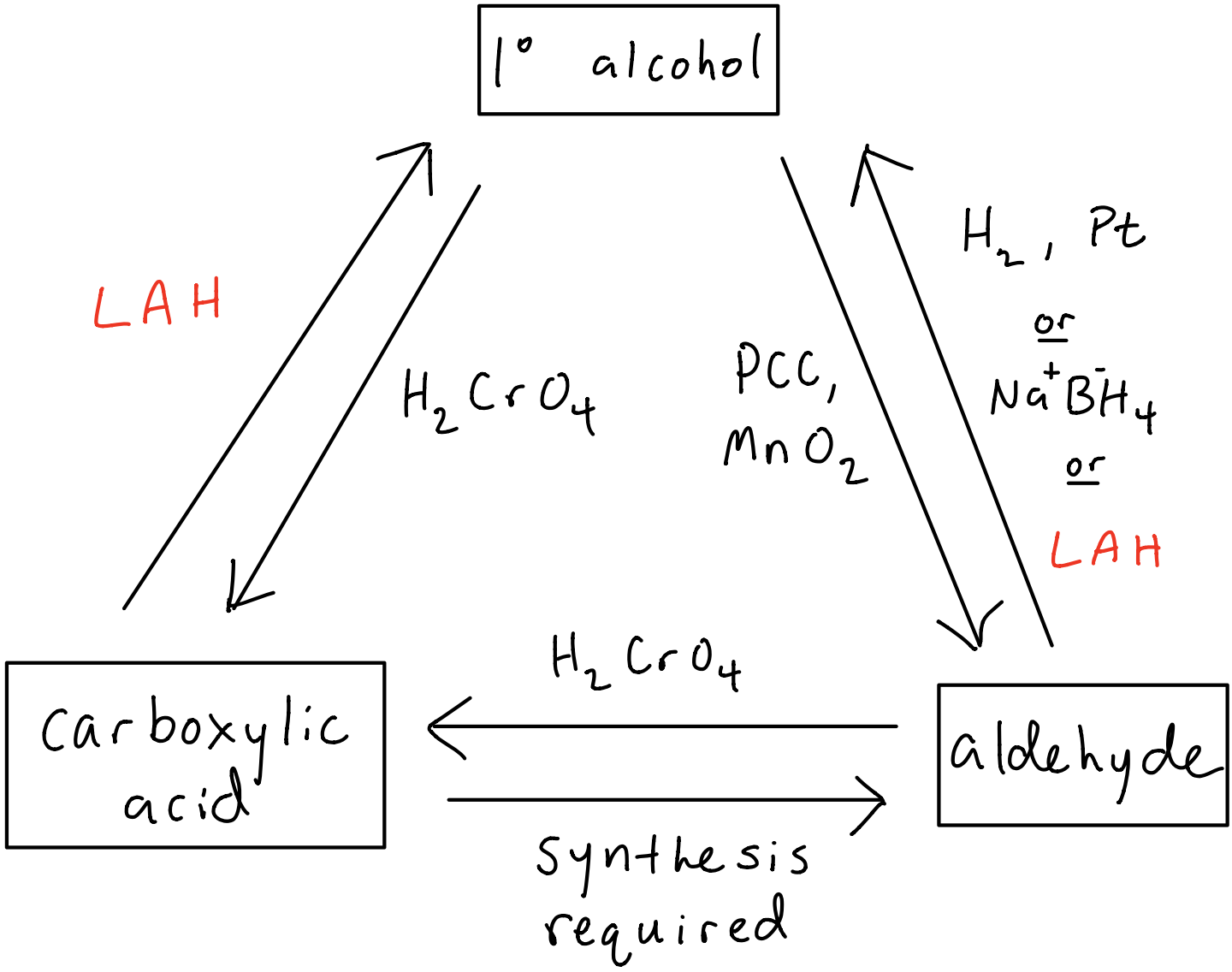
Textbook Chapter: Week 10 LTPs

Topics Covered: LAH and Redox
Grignard Reagent

Created by Isaac Loy

"Closing the Last Loop" with LAH

- We have been working with carboxylic acids for a while now, but we still don't have a way of reducing a carboxylic acid to a primary alcohol.
- With the introduction of Lithium Aluminum Hydride ($LiAlH_4$ or simply LAH), however, we can.
- LAH is first a very strong base, and secondly a very strong nucleophile (don't forget your rules! proton transfer is #1... if there is an available proton, you can be sure that LAH will pluck it off).
- LAH, as Dr. J says, is a "hydride delivery system" via acyl substitution.
- Let's look at our completed loop:



- Note the aldehyde to 1° alcohol pathway: if a species can be reduced by H_2, Pt or $Na^+BH_4^-$, it can also be reduced by the stronger reducing agent, LAH.

Reactions Involving LAH

– For each reaction below, determine how many equivalents of LAH are required (a mechanism might help...).

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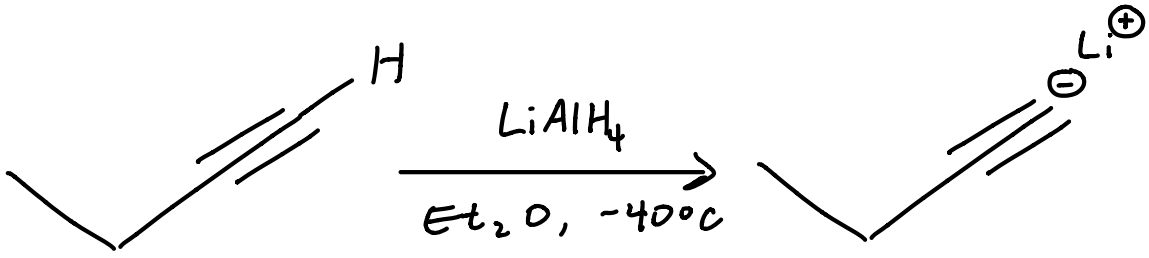
① Simple deprotonation of acidic protons

EX



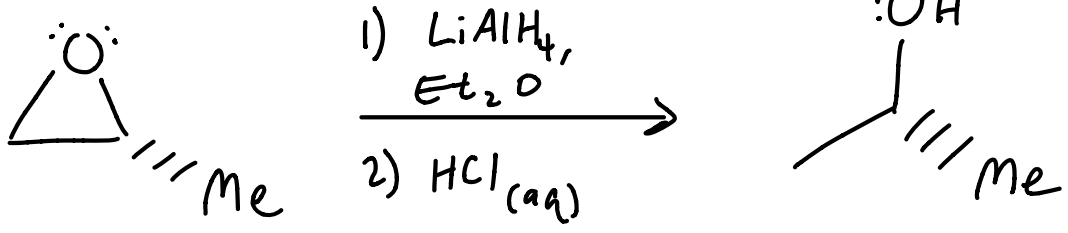
② S_N2 Dehalogenation

EX

$$H_3C-Br \xrightarrow[Et_2O,\ 0^\circ]{LiAlH_4} CH_4$$

③ Epoxide Ring Opening

EX



④ Reduction of aldehydes

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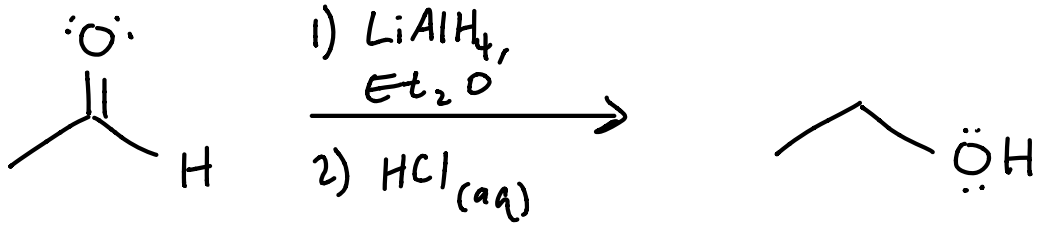

⑤ Reduction of ketones

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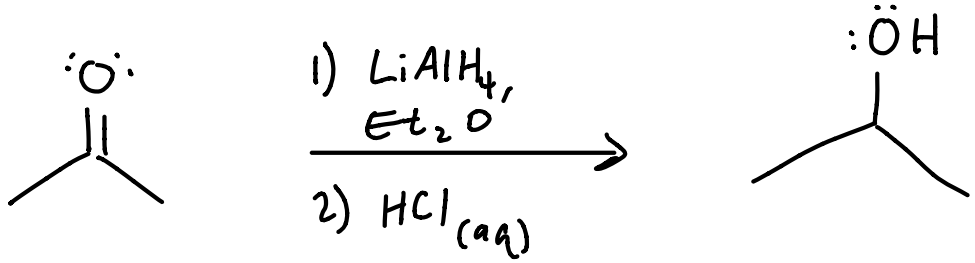

⑥ Reduction of carboxylic acids

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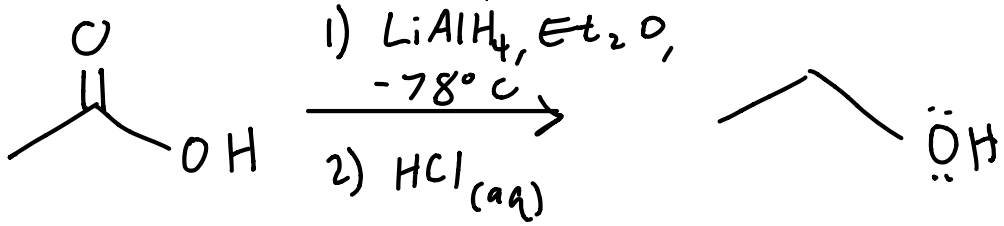
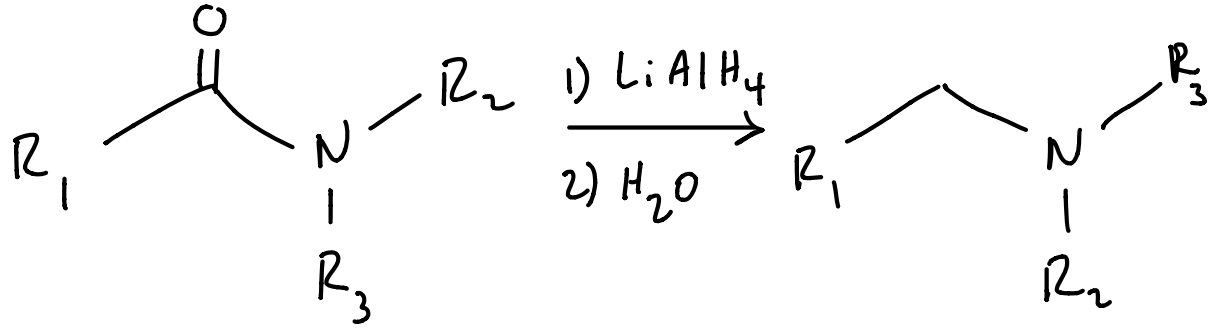


⑦ Reduction of amines

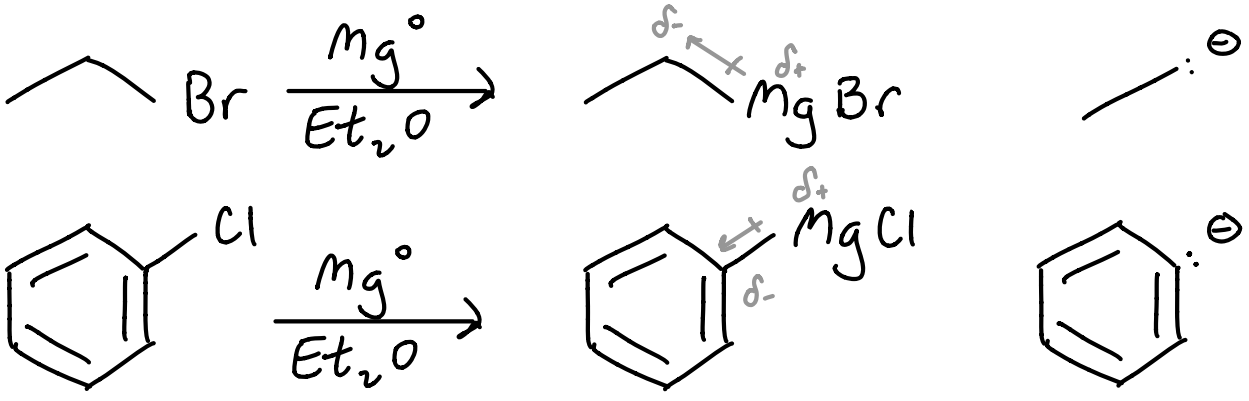
EX



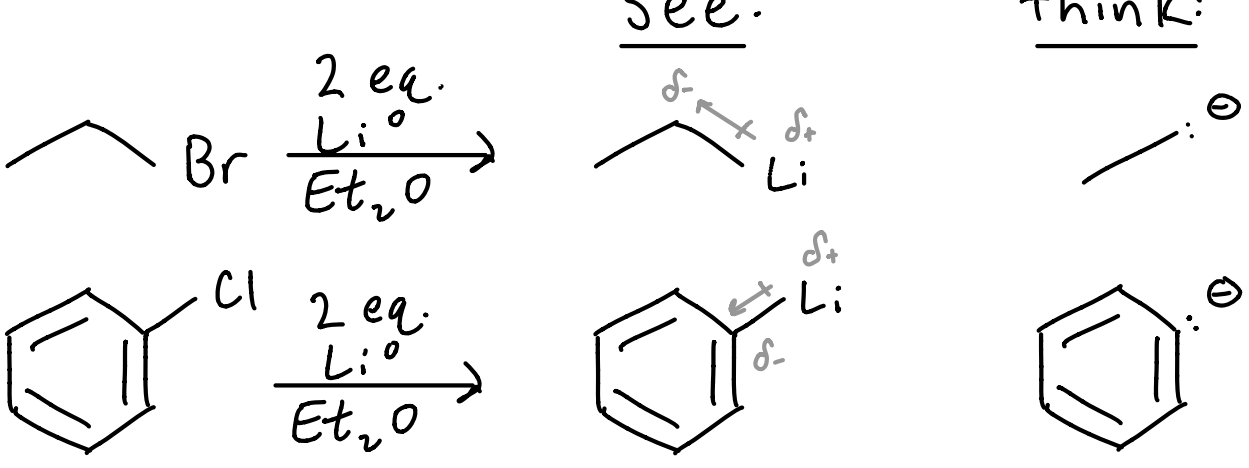
The Grignard Reagent

- The Grignard Reagent is our newest carbon nucleophile and an easy way of making bonds.
- We form the Grignard reagent one of two ways:

① Organomagnesium route:



② Organolithium route:



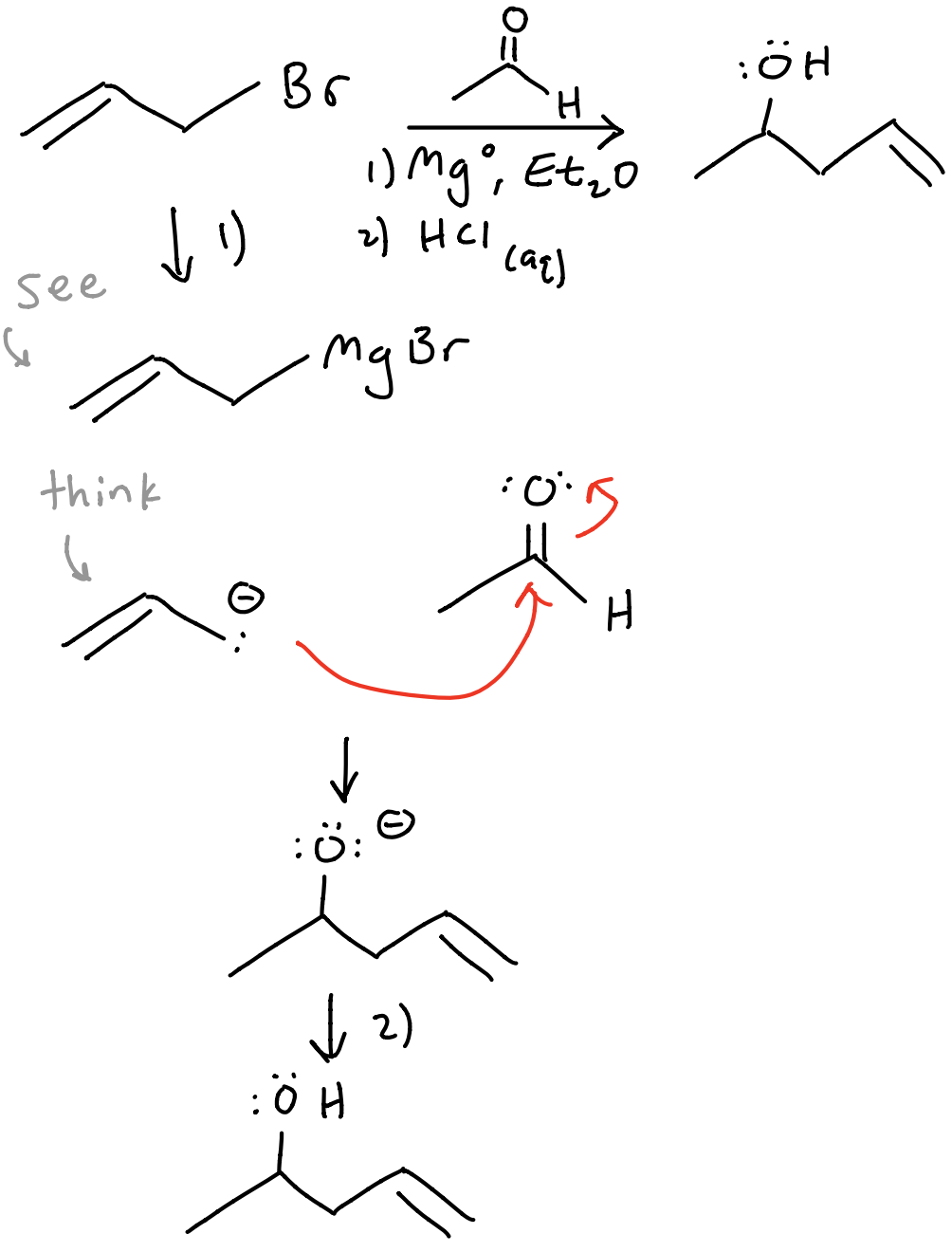
- Warning:

  DO NOT use with protic solvents

  DO NOT use with alkyl halides

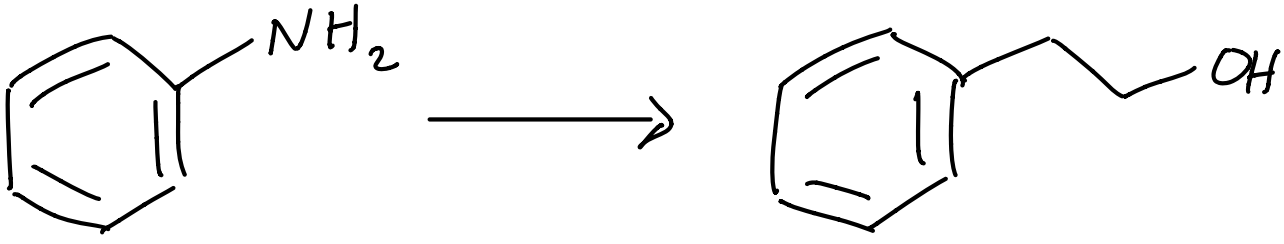
- Let's see it in action

Ex



Problems

① Propose a synthesis using the Grignard conditions for the following overall reaction:



(2) ΔS and ΔH for the Diels-Alder reaction are:

a) Both negative

b) Both positive

c) Posative, negative

d) Negative, positive

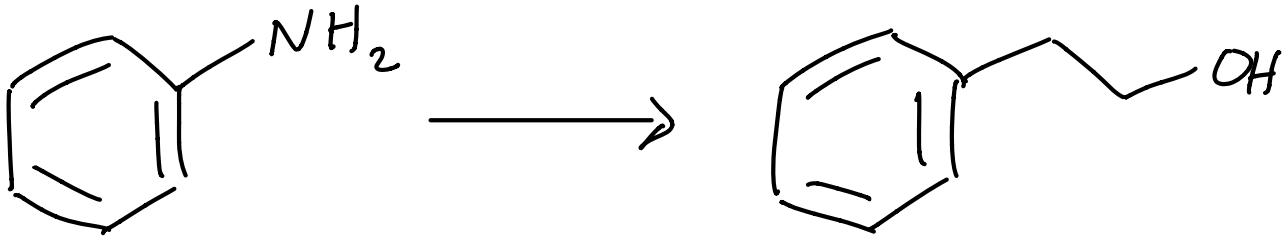
③ Identify any mistakes in the following sentence and make the appropriate corrections:

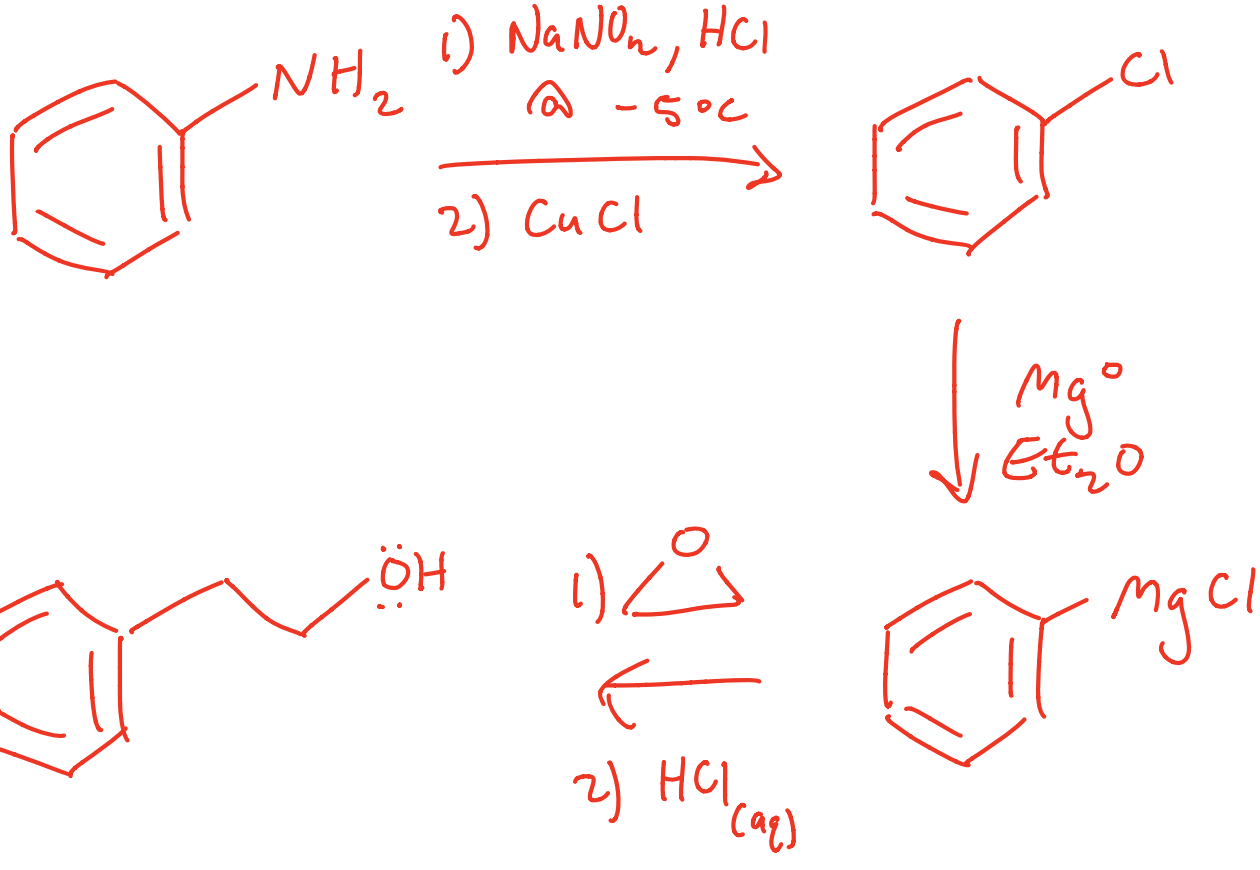
NaH is a better base and nucleophile than $NaBH_4$.

④ Provide a mechanism that describes why hydrogen gas forms as a byproduct in the full reduction of a carboxylic acid.

Solutions

① Propose a synthesis using the Grignard conditions for the following overall reaction:





(2) ΔS and ΔH for the Diels-Alder reaction are:

a) Both negative

b) Both positive

c) Posative, negative

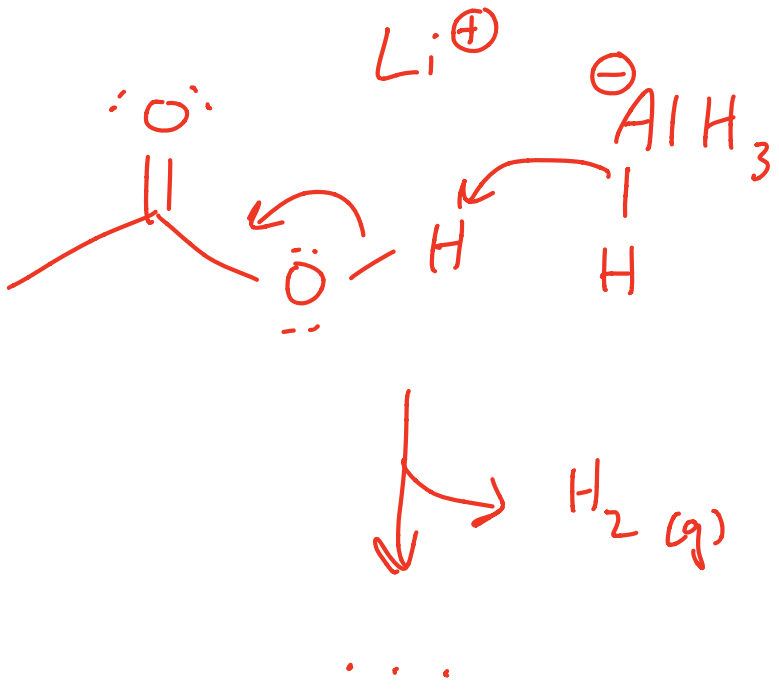
d) Negative, positive

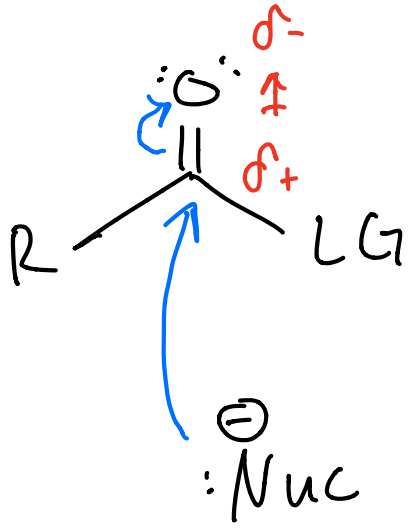
(3) Identify any mistakes in the following sentence and make the appropriate corrections:

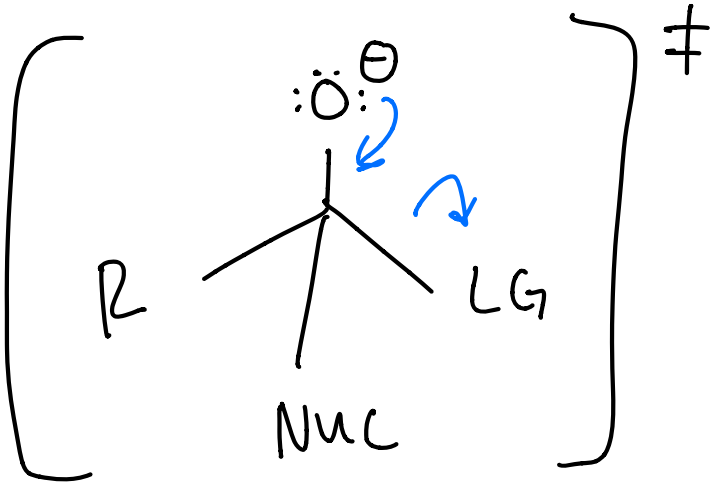
NaH is a better base and nucleophile than $NaBH_4$.

NaH is a better base, but it is non-nucleophilic.

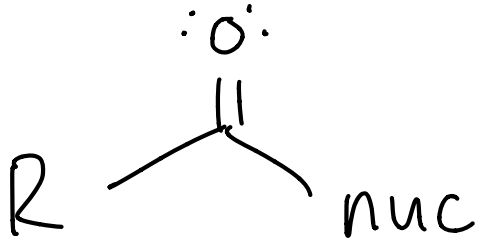
④ Provide a mechanism that describes why hydrogen gas forms as a byproduct in the full reduction of a carboxylic acid.







tet. intermediate



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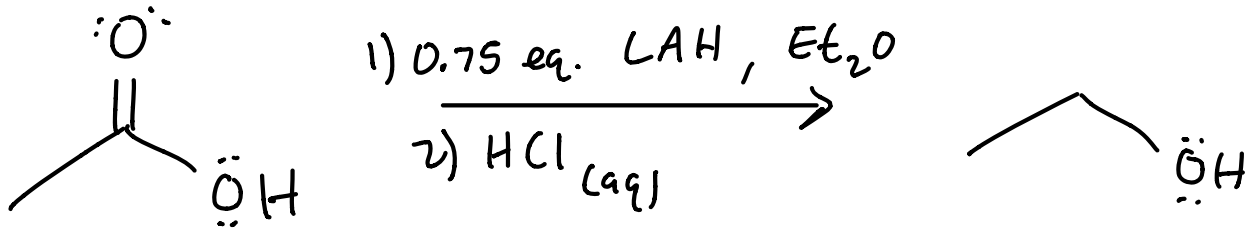
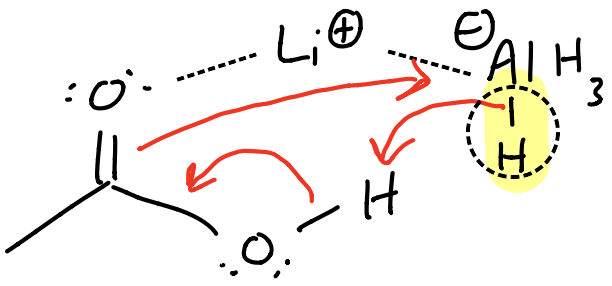
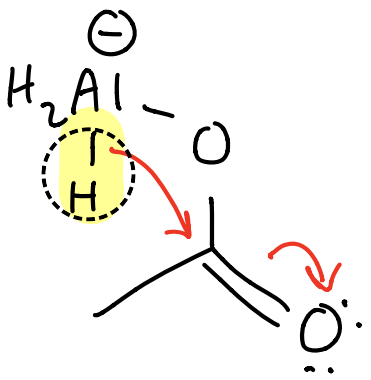
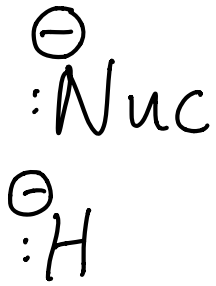
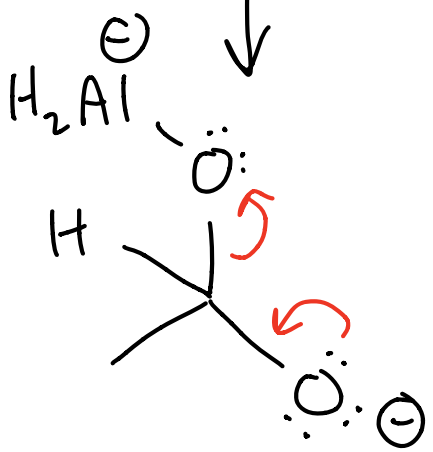


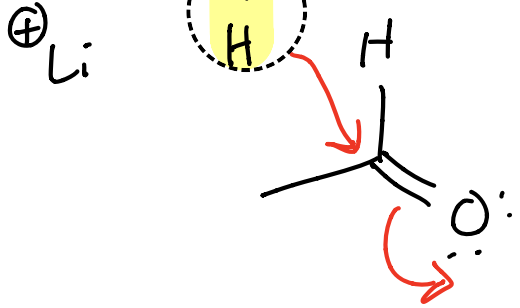


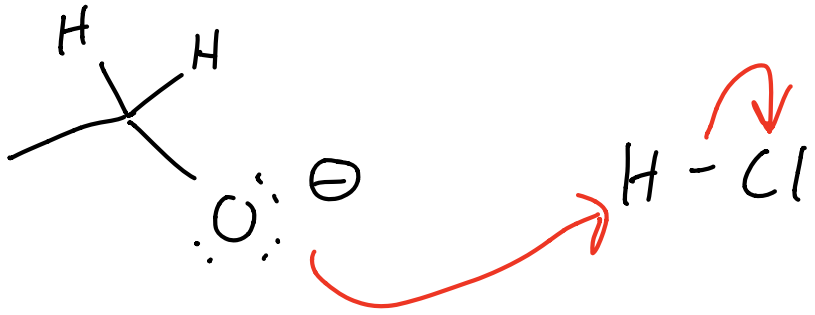
H_2 leaves

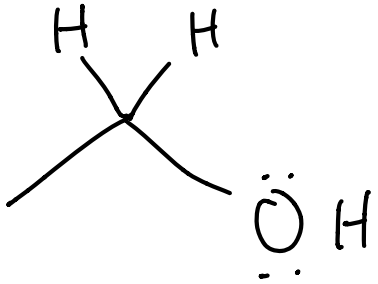


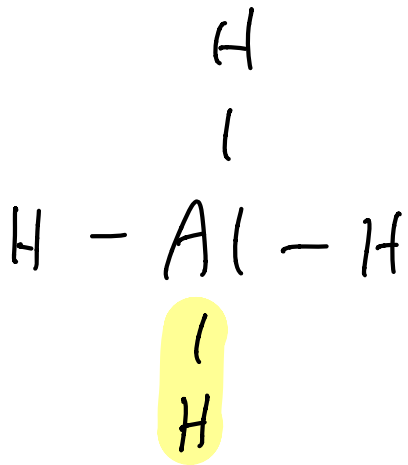








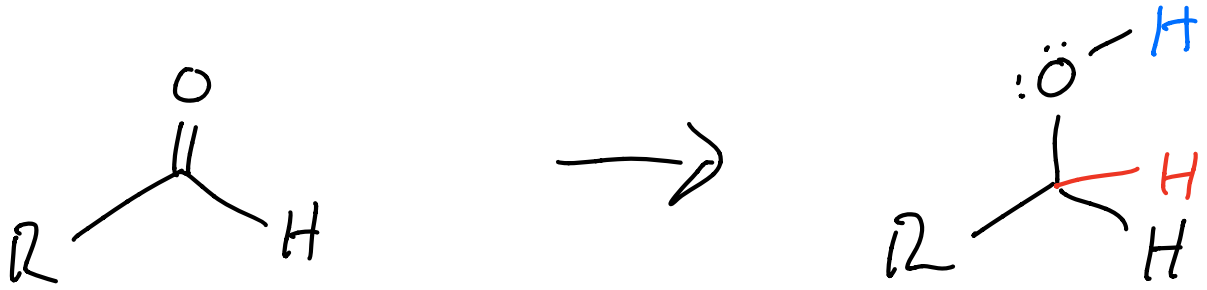




$Li^{\oplus}\,Al^{\ominus}H_4$

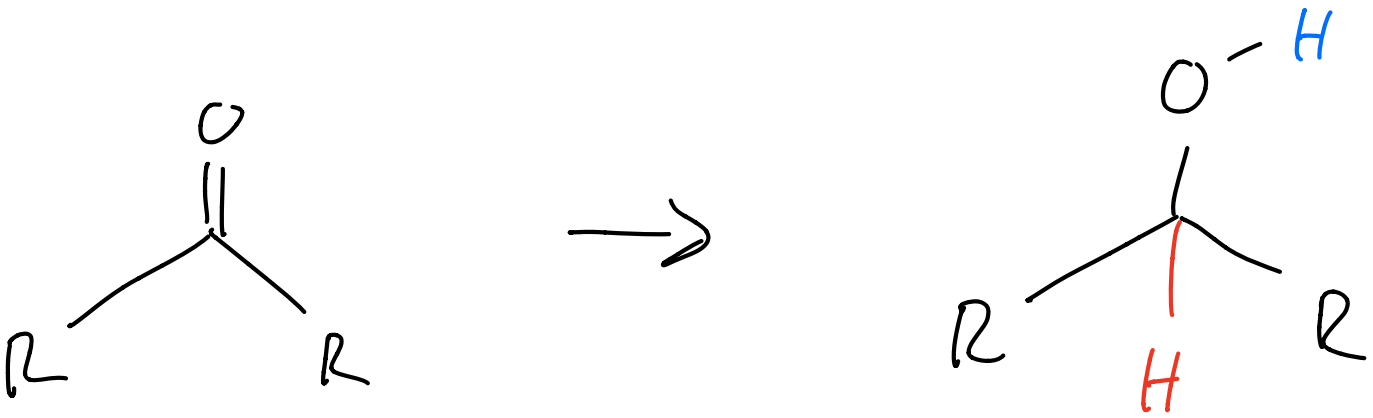
1 hydride

4 possible hydrides



Workup

From LAH



"Reductive Amination"
(reducing amides)

1° amide → 1° amine

1 eq

2° amide → 2° amine

0.75 eq

3° amide → 3° amine

0.50 eq

C.A. → 1° alcohol

0.75 eq

Aldehyde → 1° alcohol

0.25 eq

Ketone → 2° alcohol

0.25 eq