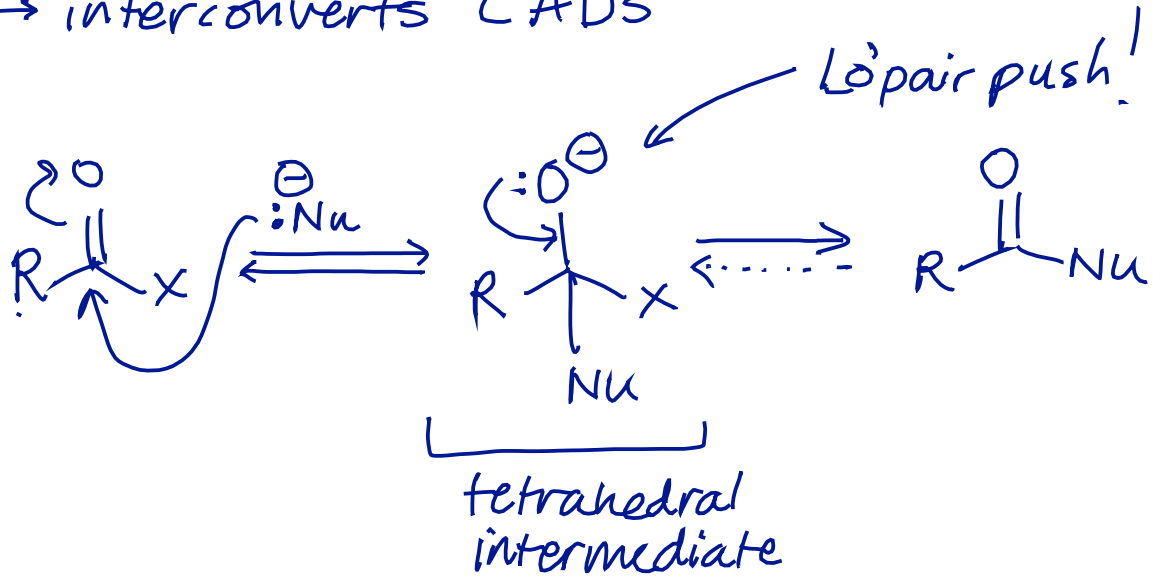
Recap:

- Nucleophilic Acyl Substitution
  → interconverts CADs



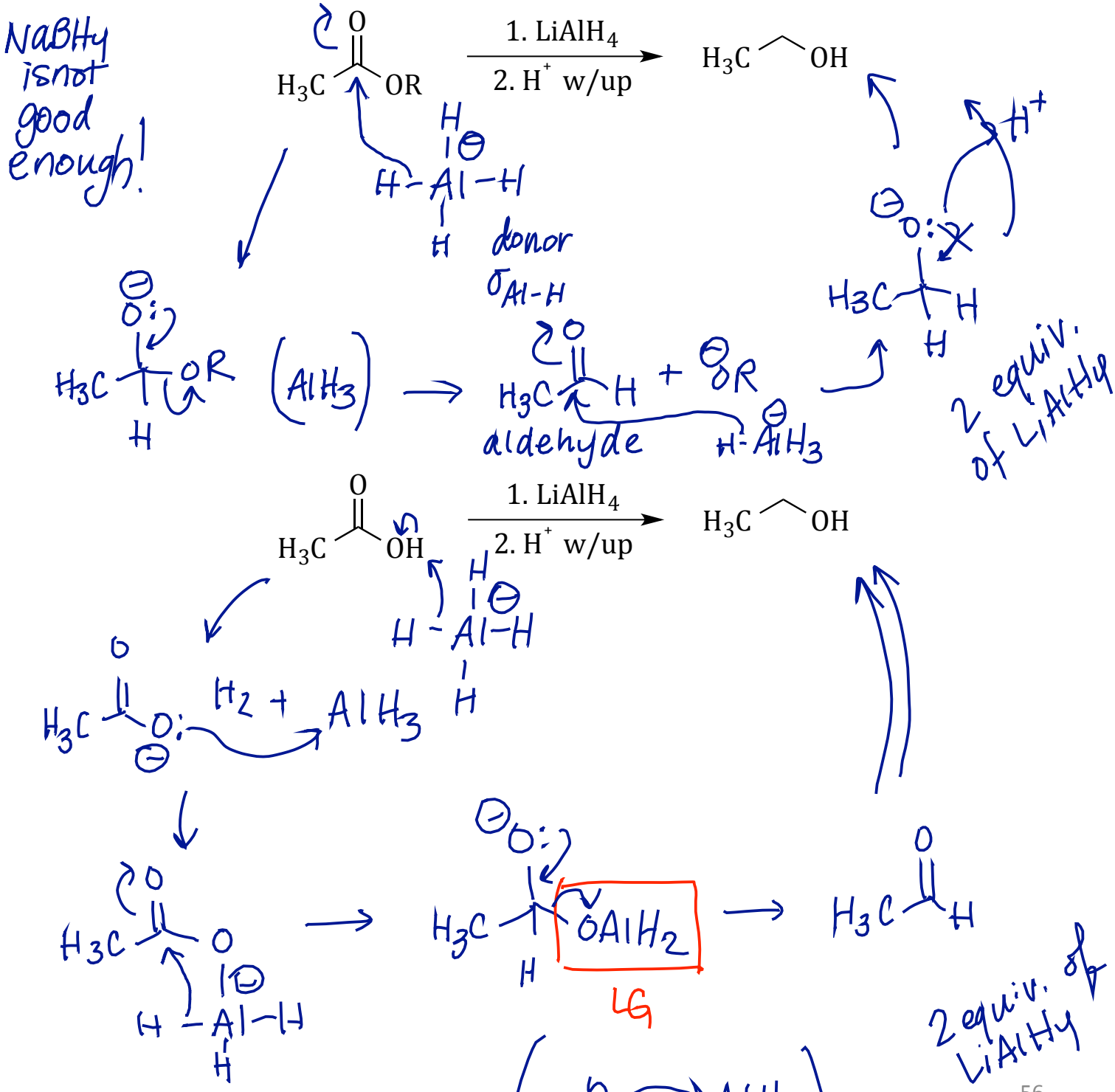
General Rxns for this week:

- EAS
- NAS/S_NAr — 2 mechanisms
- Nuc Addn to Ketones/Aldehydes
- Nuc Acyl Substitution
- Ox/Red in carbonyl compounds (more today!)

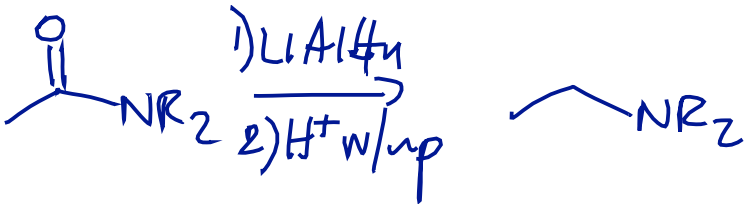
NOT (COMPLETELY) COMPREHENSIVE!

Irreversible Addition to CADs:
Reduction of Esters & Acids with $LiAlH_4$

Provide complete curved-arrow mechanisms for the following reactions:

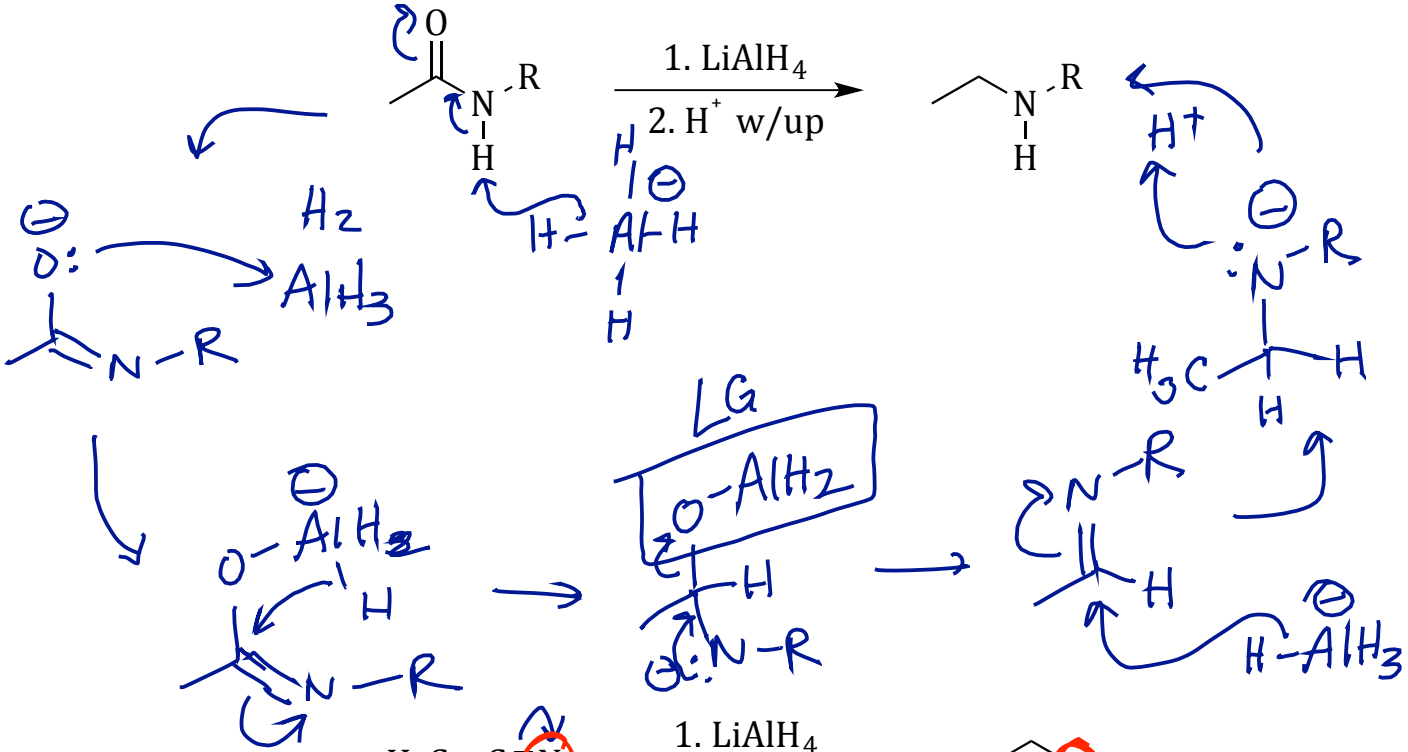


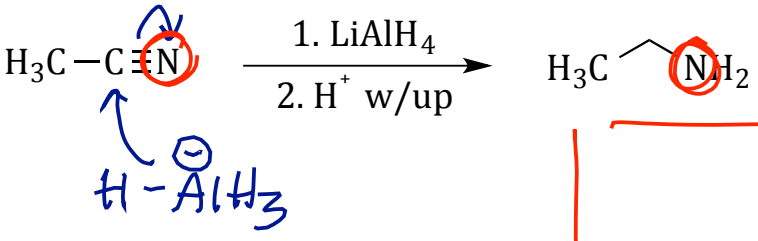
Reading: Sections 20.10, 21.8

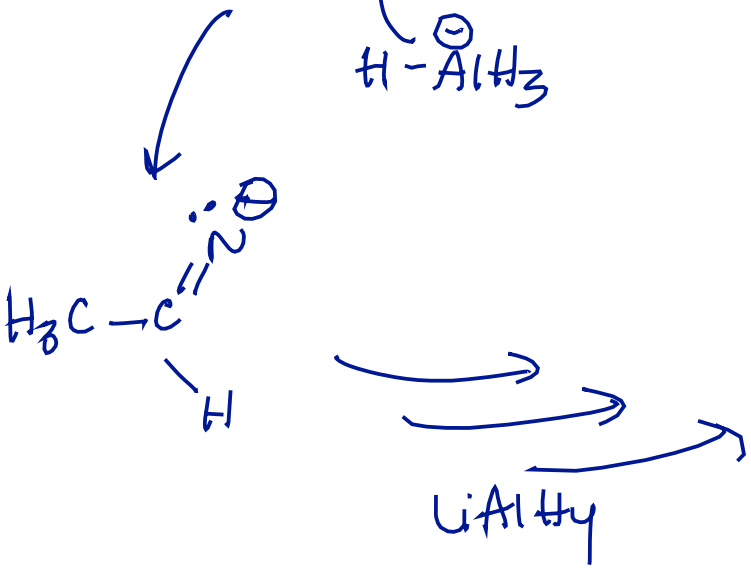


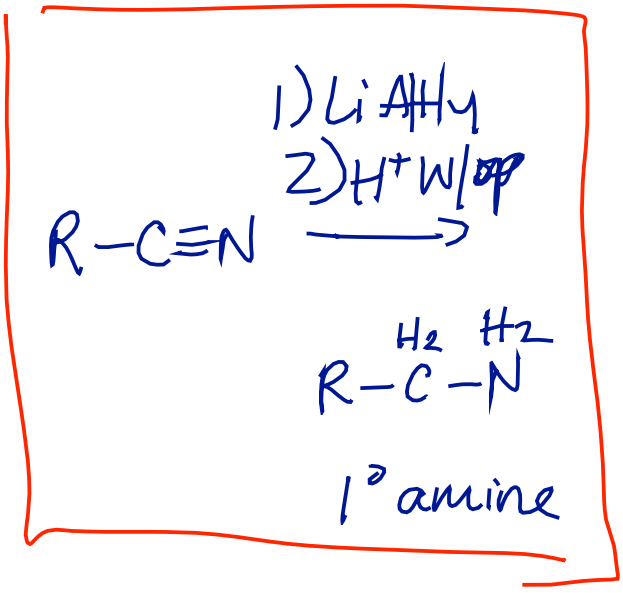
Irreversible Addition to CADs:
Reduction Amides and Nitriles with $LiAlH_4$

Provide complete curved-arrow mechanisms for the following reactions:





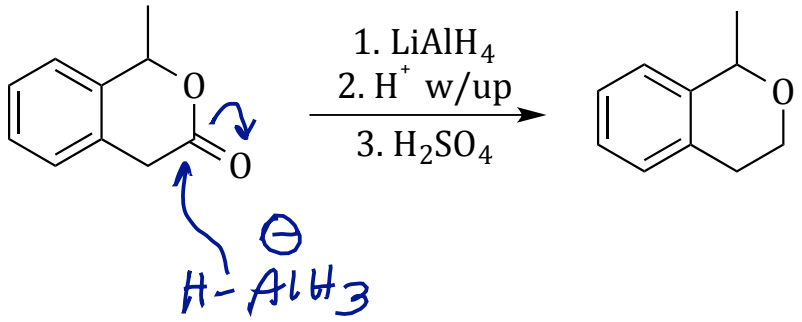




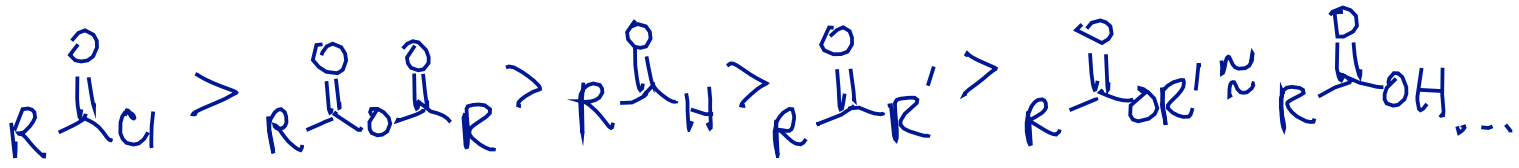
Reading: Section 21.8

Test Yourself Now!

Provide a complete curved-arrow mechanism for the following reaction:



Reactivity: of Carbonyl Cpds (towards Nucleophiles)



Reading: Section 21.8

C–Metal = organometallic

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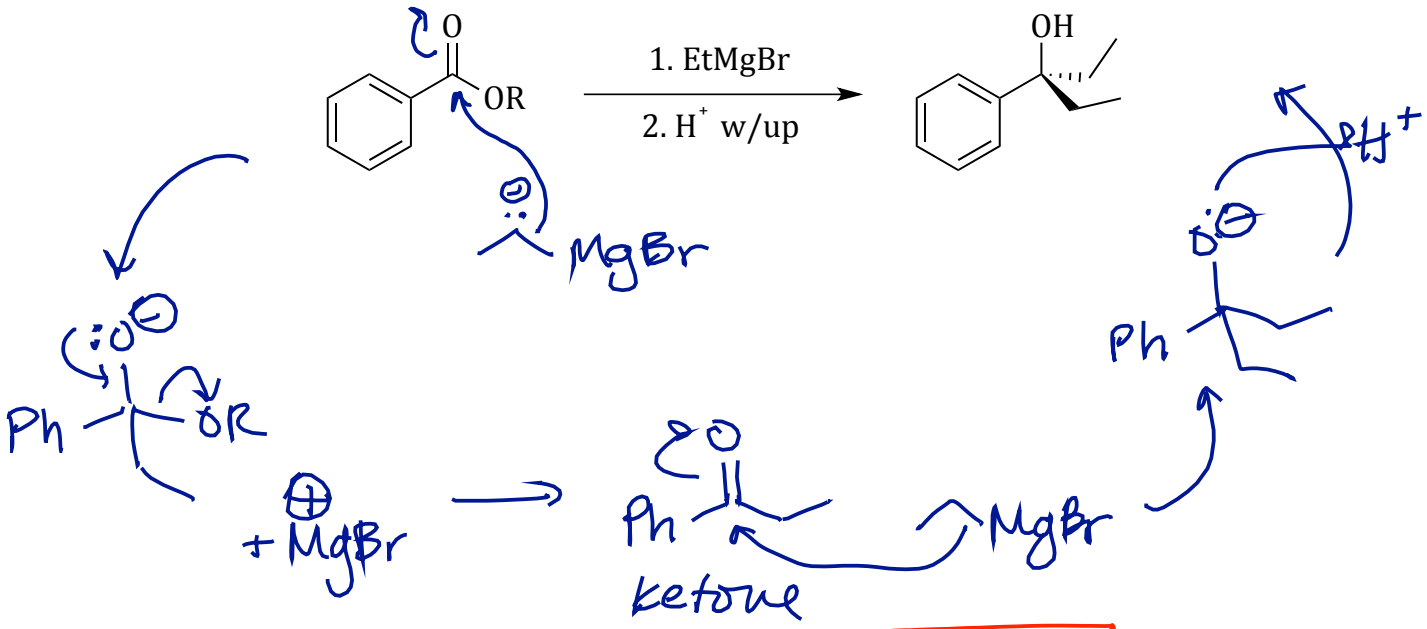
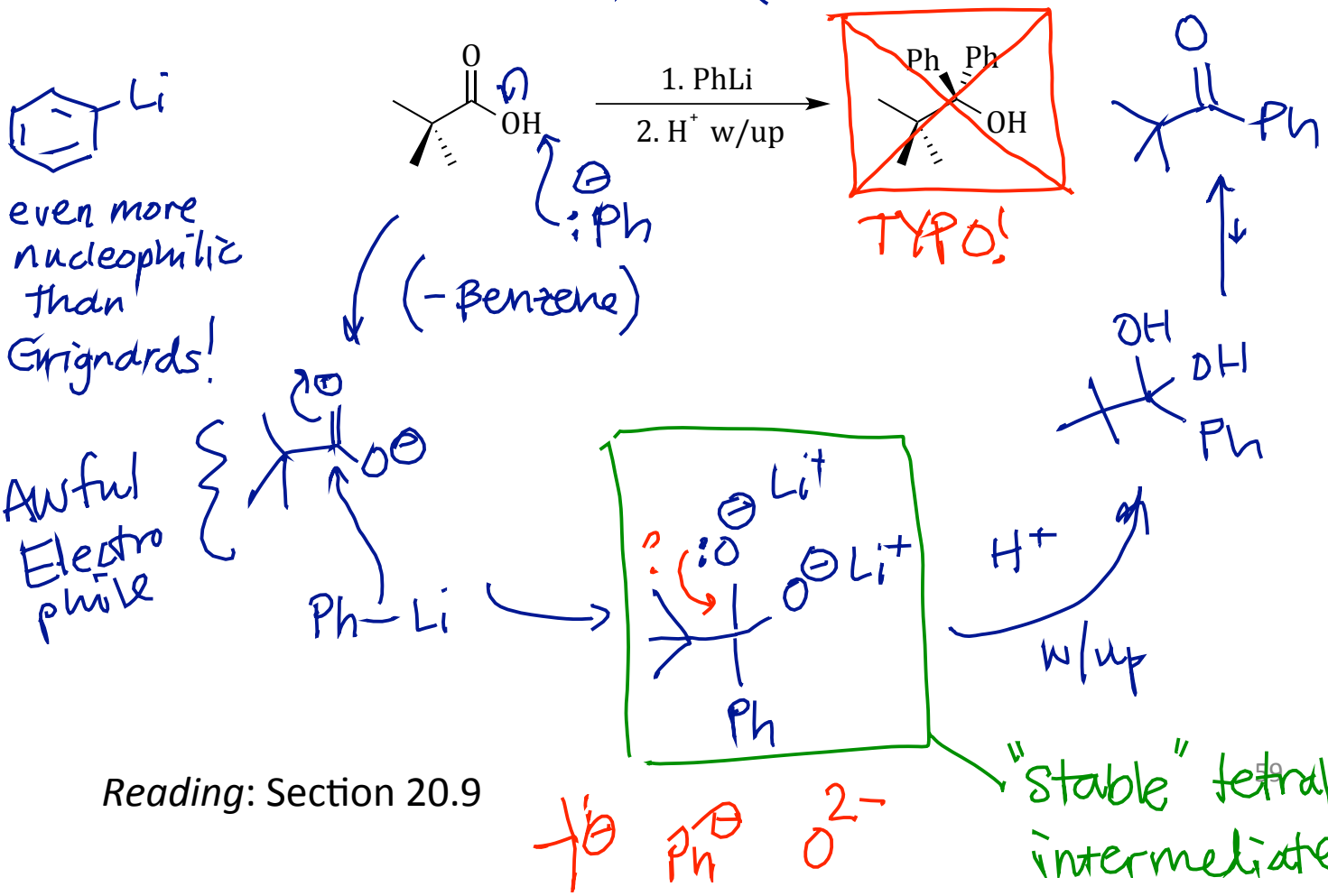
Irreversible Addition to CADs:
Organometallic Reagents

Provide complete curved-arrow mechanisms for the following reactions:

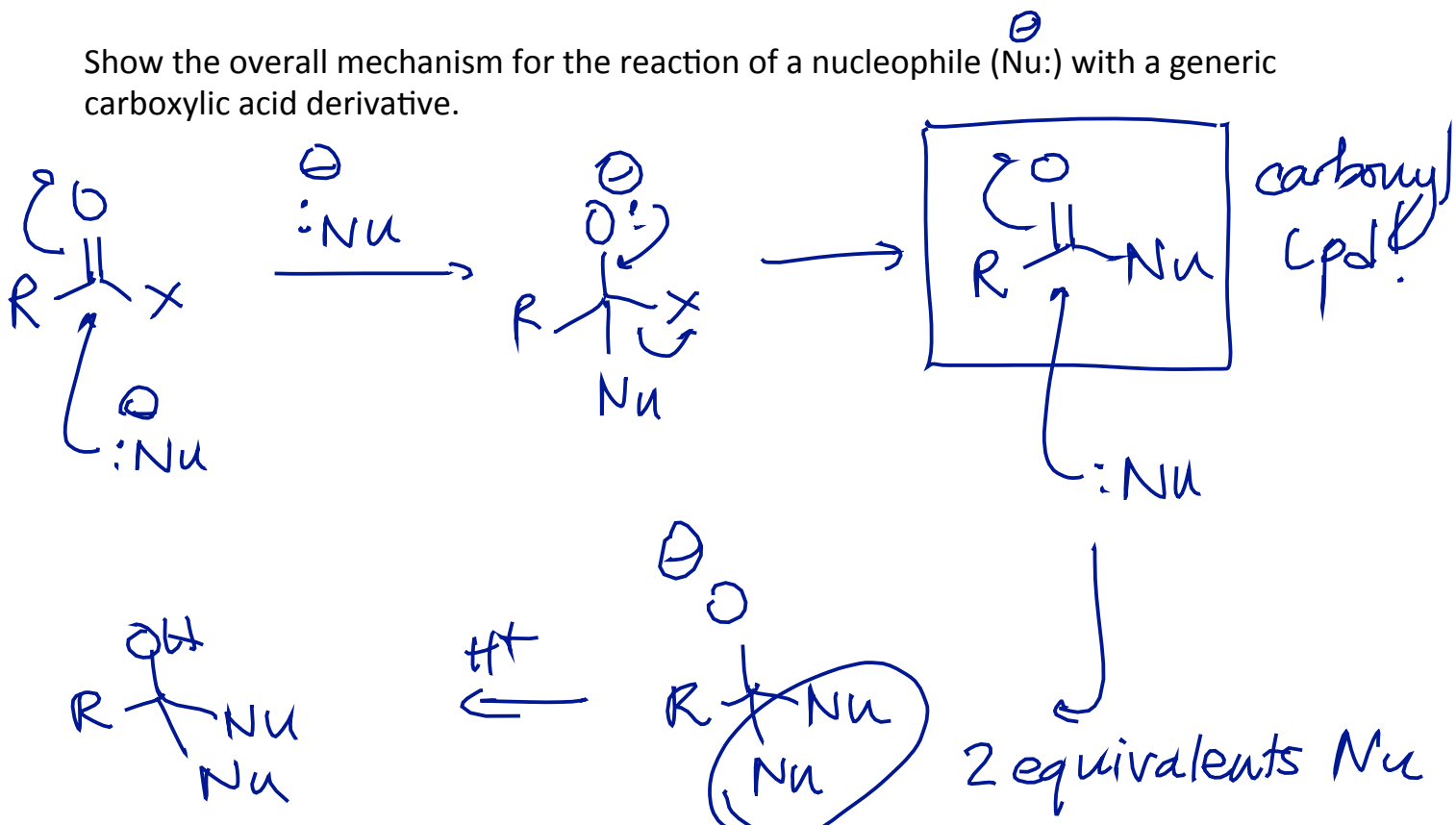




Reading: Section 20.9

How Can We Add Only One Equivalent?

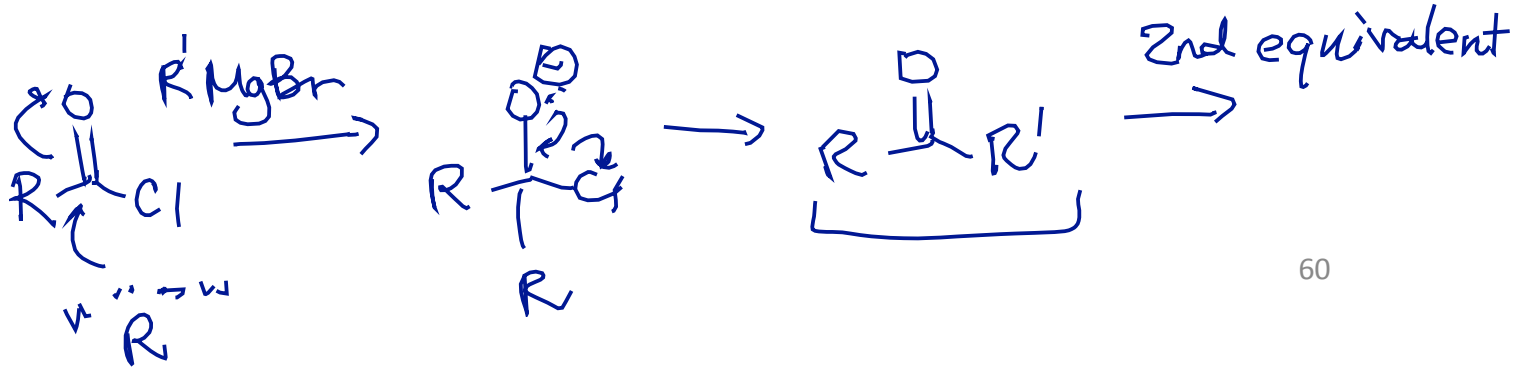
Show the overall mechanism for the reaction of a nucleophile (Nu:) with a generic carboxylic acid derivative.



What are two strategies for making sure that **only one equivalent** of the nucleophile is added?

1) Stabilize tetrahedral intermediate (prevent LPP)

2) Take advantage of relative reactivity



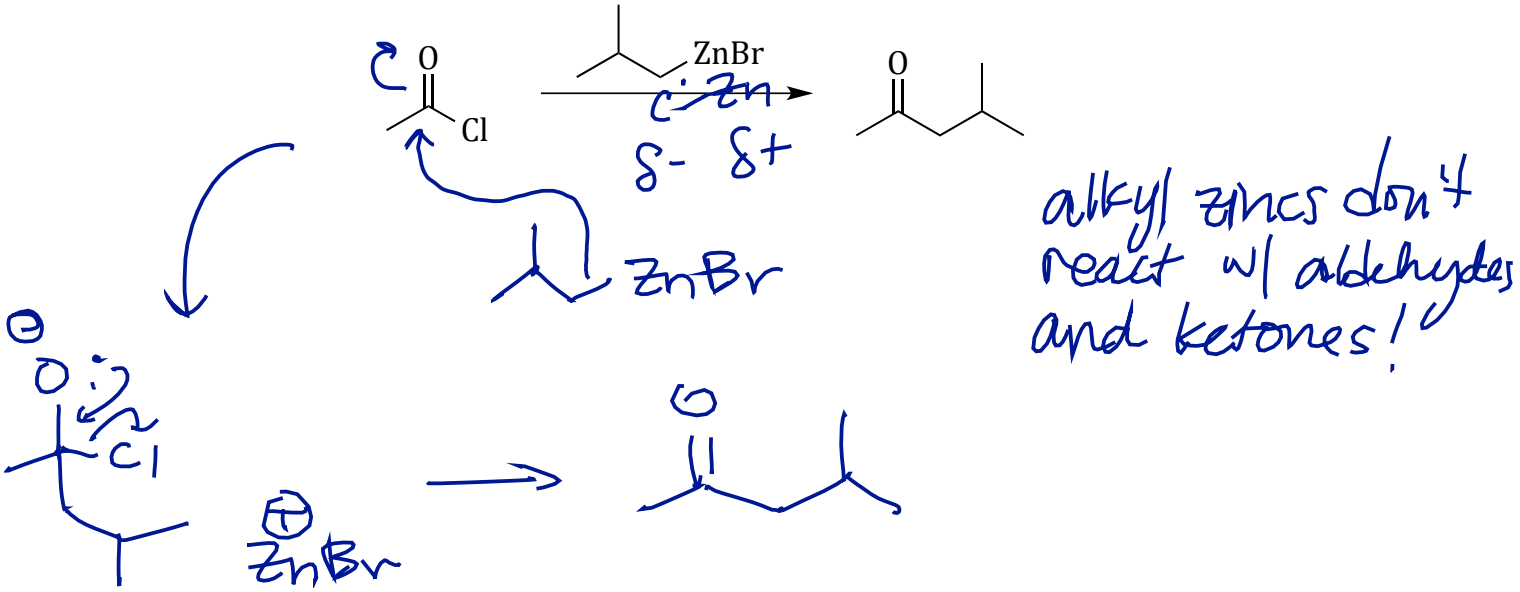
R-Zn-Br "alkyl zinc bromides"

 R-Mg-Br Grignard Zn is fluffy :)

Method 1:

Take Advantage of Relative Reactivity

Provide a complete curved-arrow mechanism for the following reaction:



Why is no work-up step required for this reaction?

product is neutral!

Are there *other* carbon nucleophiles that can be used for this reaction?

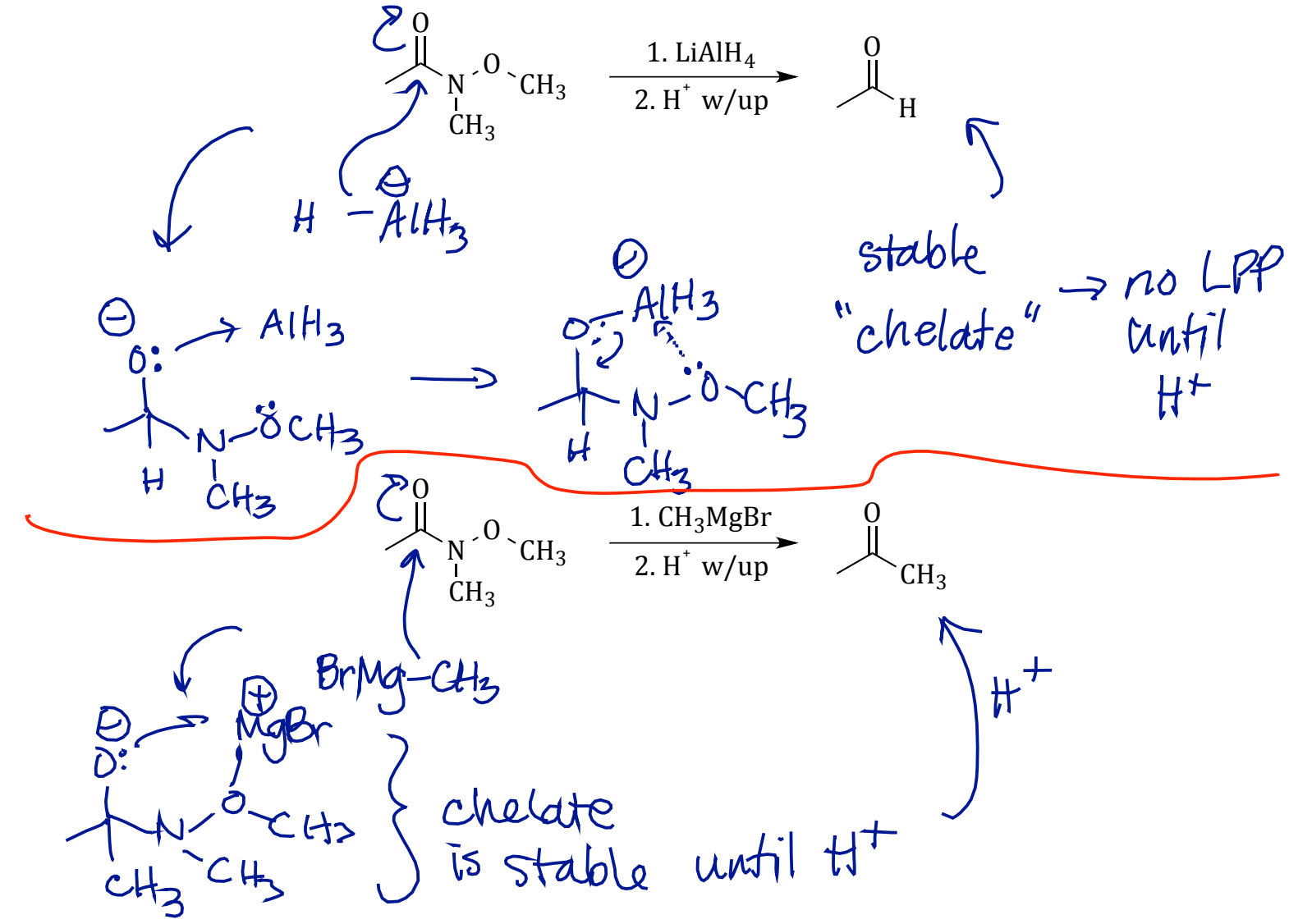
Yes, but not yet.... (R_2CuLi)

Reading: Section 21.10

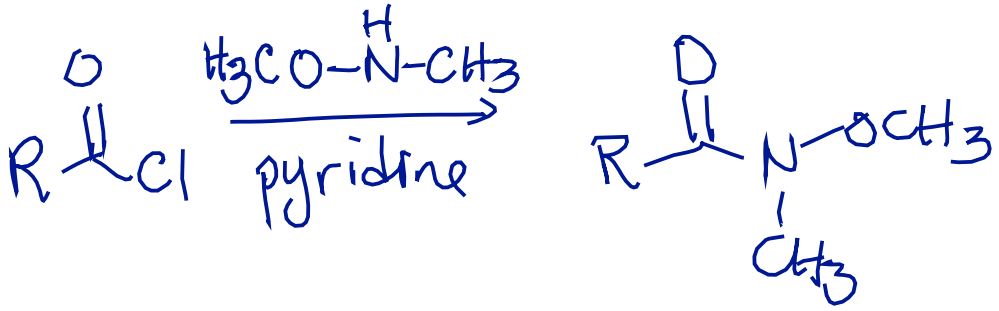
At best, box problem

Method 2: Form a Stable Tetrahedral Intermediate (Weinreb Amides)

Provide complete curved-arrow mechanisms for the following reactions:



How can we prepare these **Weinreb Amides**?



DIBAL-H "diisobutyl aluminum hydride"

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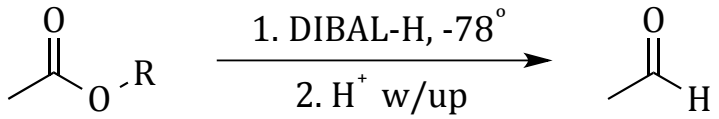
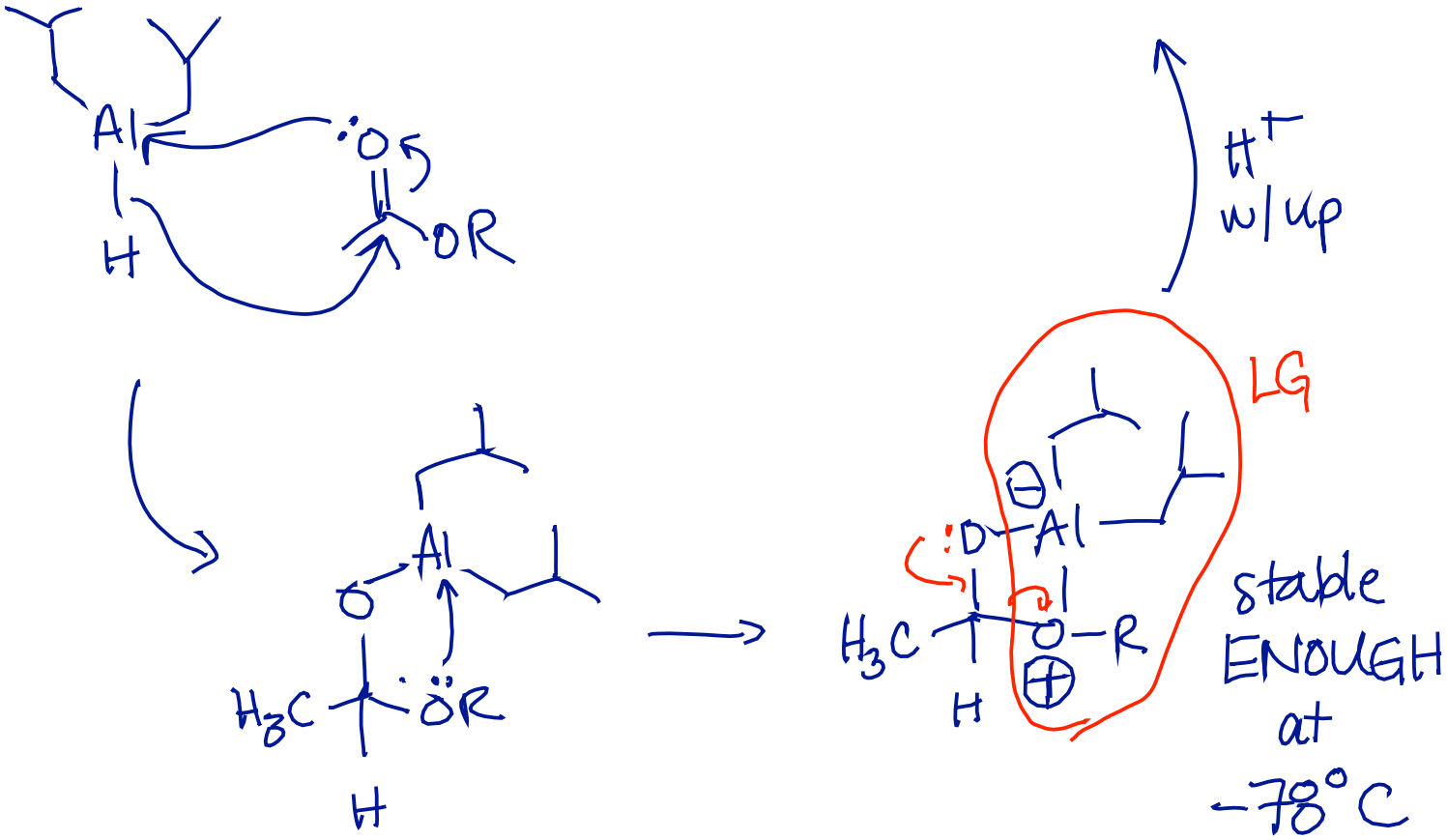
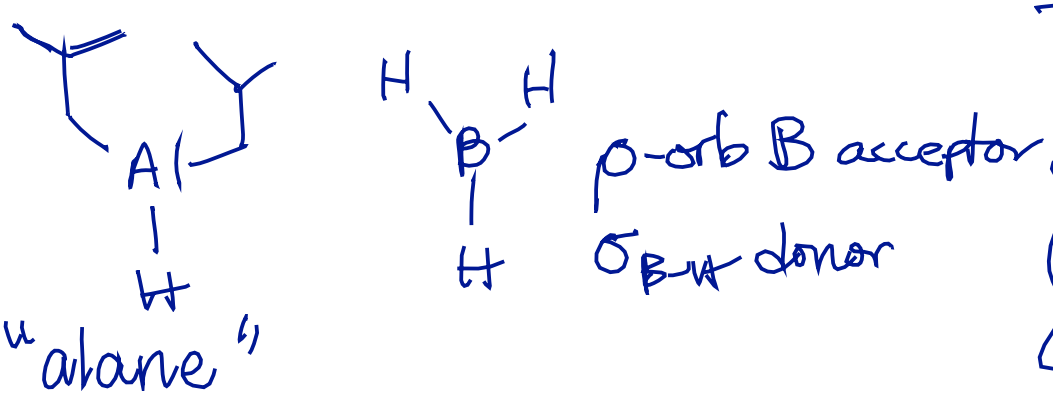
Method 2: Form a Stable Tetrahedral Intermediate (DIBAL-H)

Here's another reaction that produces a stable tetrahedral intermediate. Provide a complete curved-arrow mechanism.





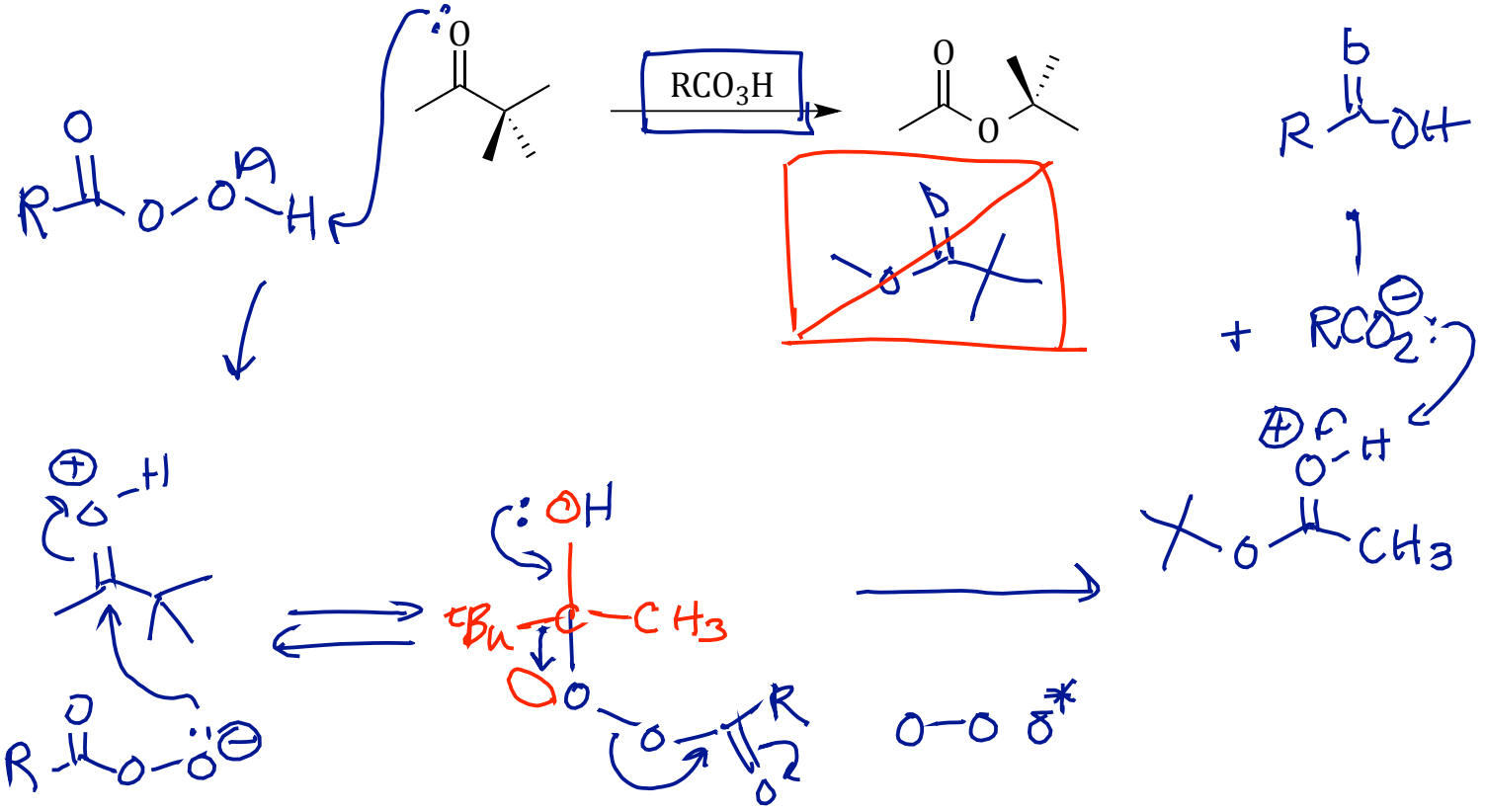


Reduction: LiAlH4, Grignards, Alanes

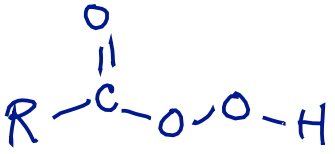
Oxidation of ketones (aldehydes)

Going Backward: Oxidizing Ketones
The Baeyer-Villiger Reaction

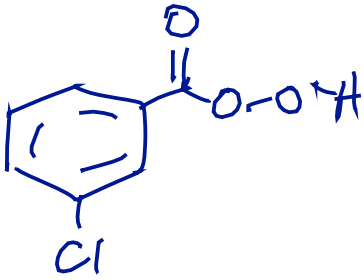
Provide a complete curved-arrow mechanism for the following reaction:



Have you seen the reagent "RCO_3H" before?



"peracid" :. mCPBA

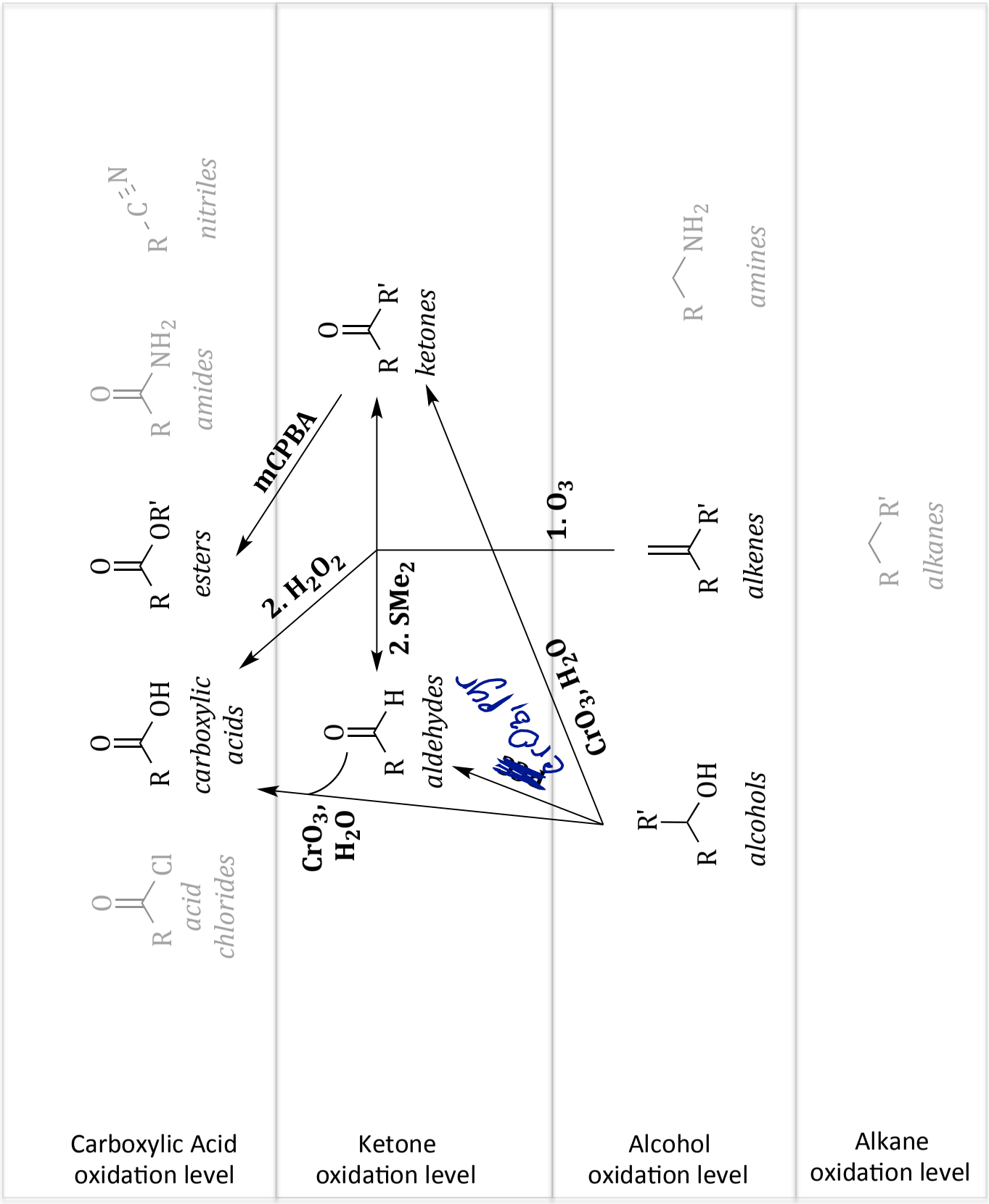


Which of the ketone's R groups will migrate in this reaction?

migratory aptitude follows carbocation stability patterns:

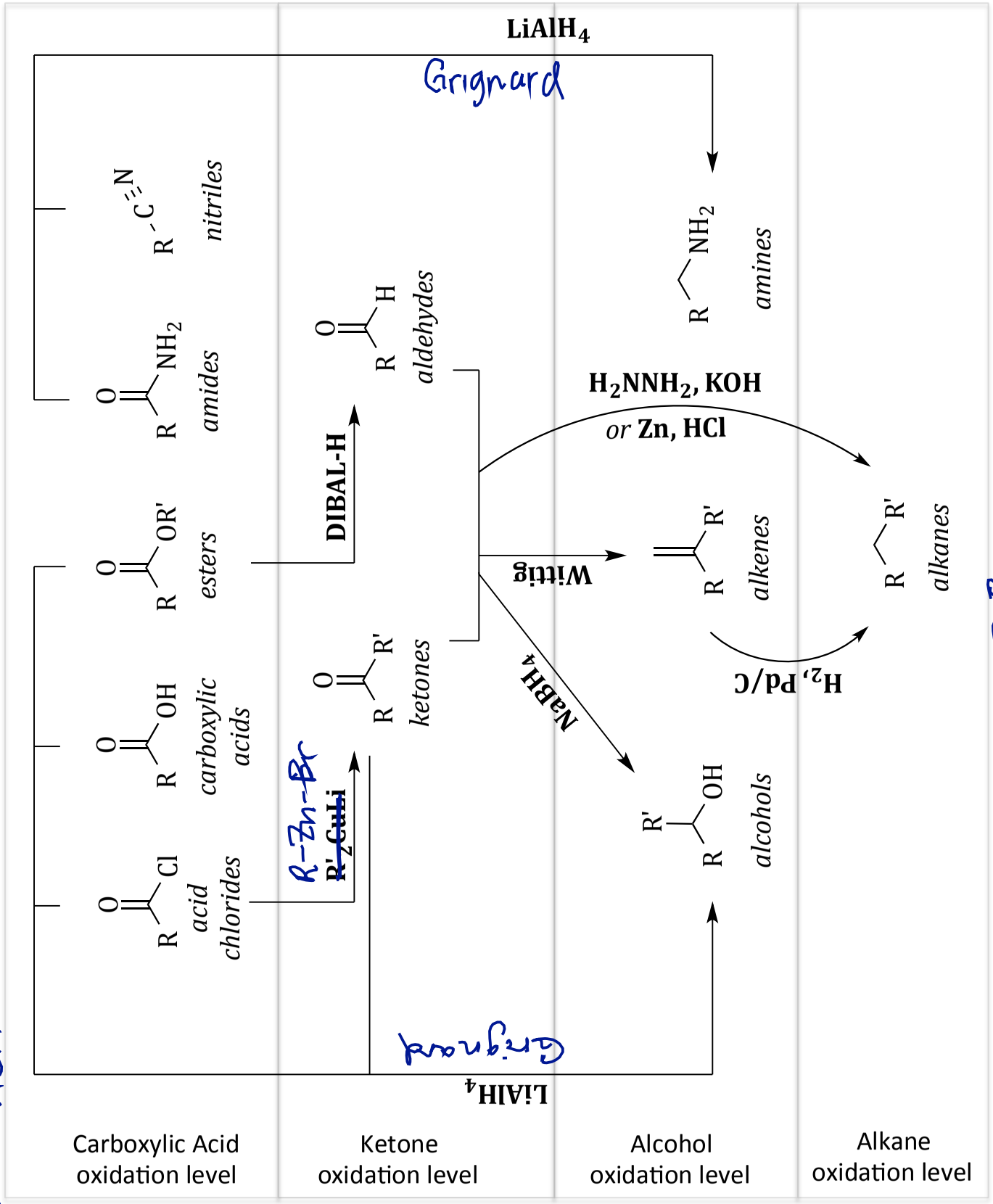
$3^\circ > 2^\circ > Ph > 1^\circ > Me$

Putting It Together: Oxidative Carbonyl Chemistry



KNOW OXIDIZING AGENTS: CrO_3, O_3, mCPBA

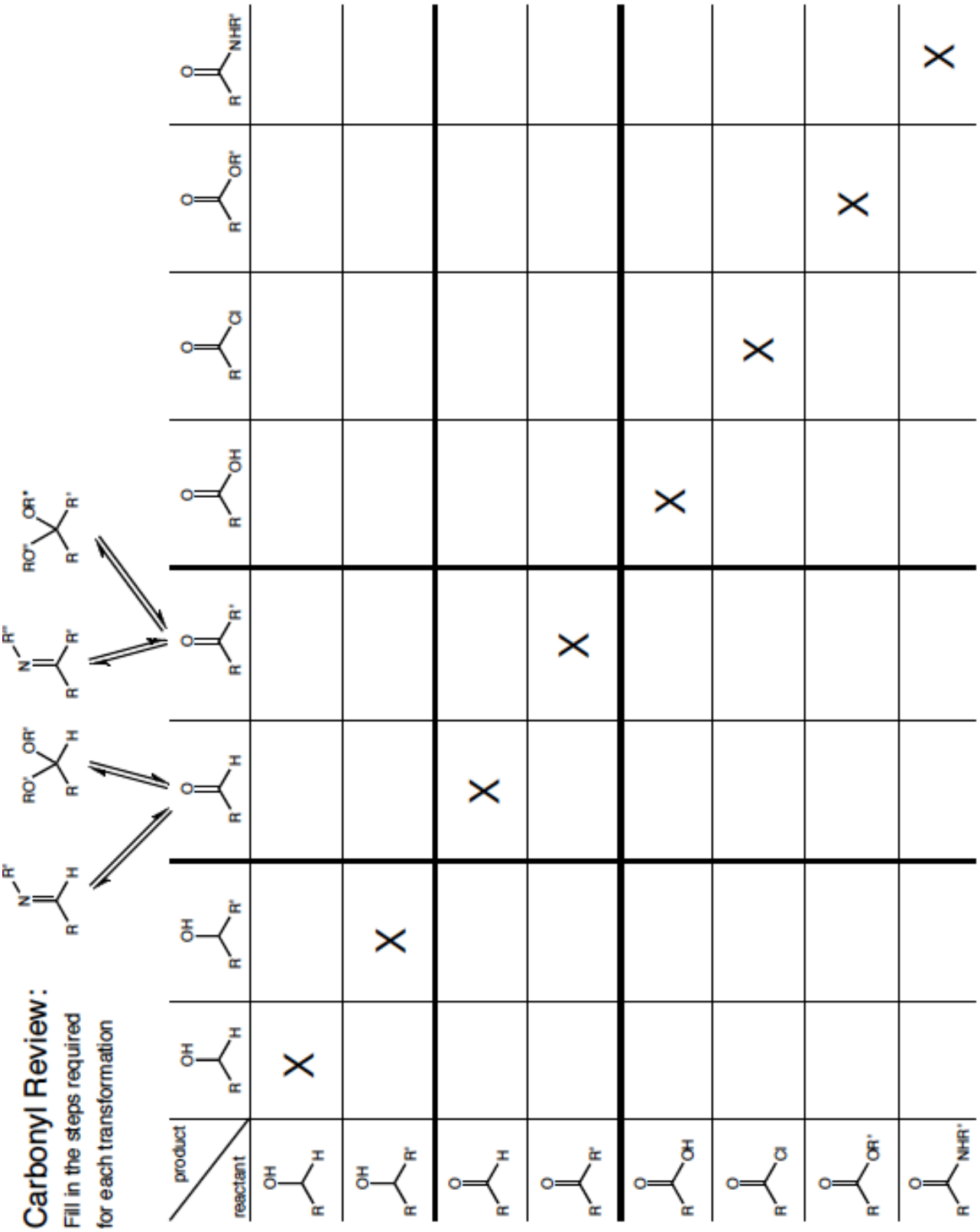
Putting It Together: Reductive Carbonyl Chemistry



2 oxidation levels: LiAlH4, Grignards, RLi
1 oxidation levels: RZnBr

Making R-ZnBr : R-Br $\xrightarrow[(Et_2O)]{Zn^0}$ R-Zn-Br

Putting It Together: The Grid of Carbonyl Love



1) ID FGs 2) # carbons 3) Make list on bonds made and broken

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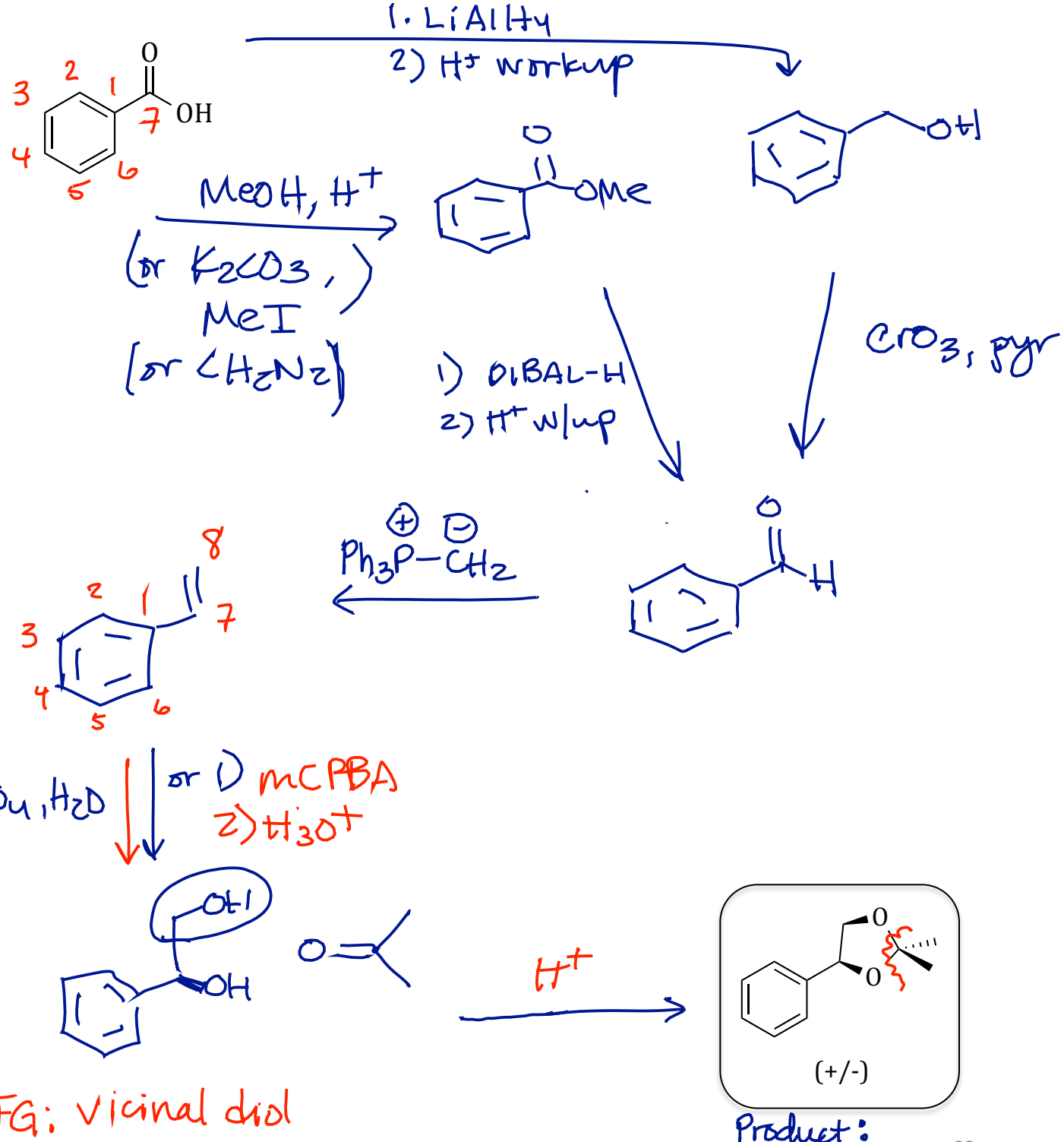
Provide a multi-step synthesis of the desired product from the indicated starting material. You may use any organic or inorganic reagents, but all of the carbons in the starting material must end up in the product. The best answer will require six or fewer steps.

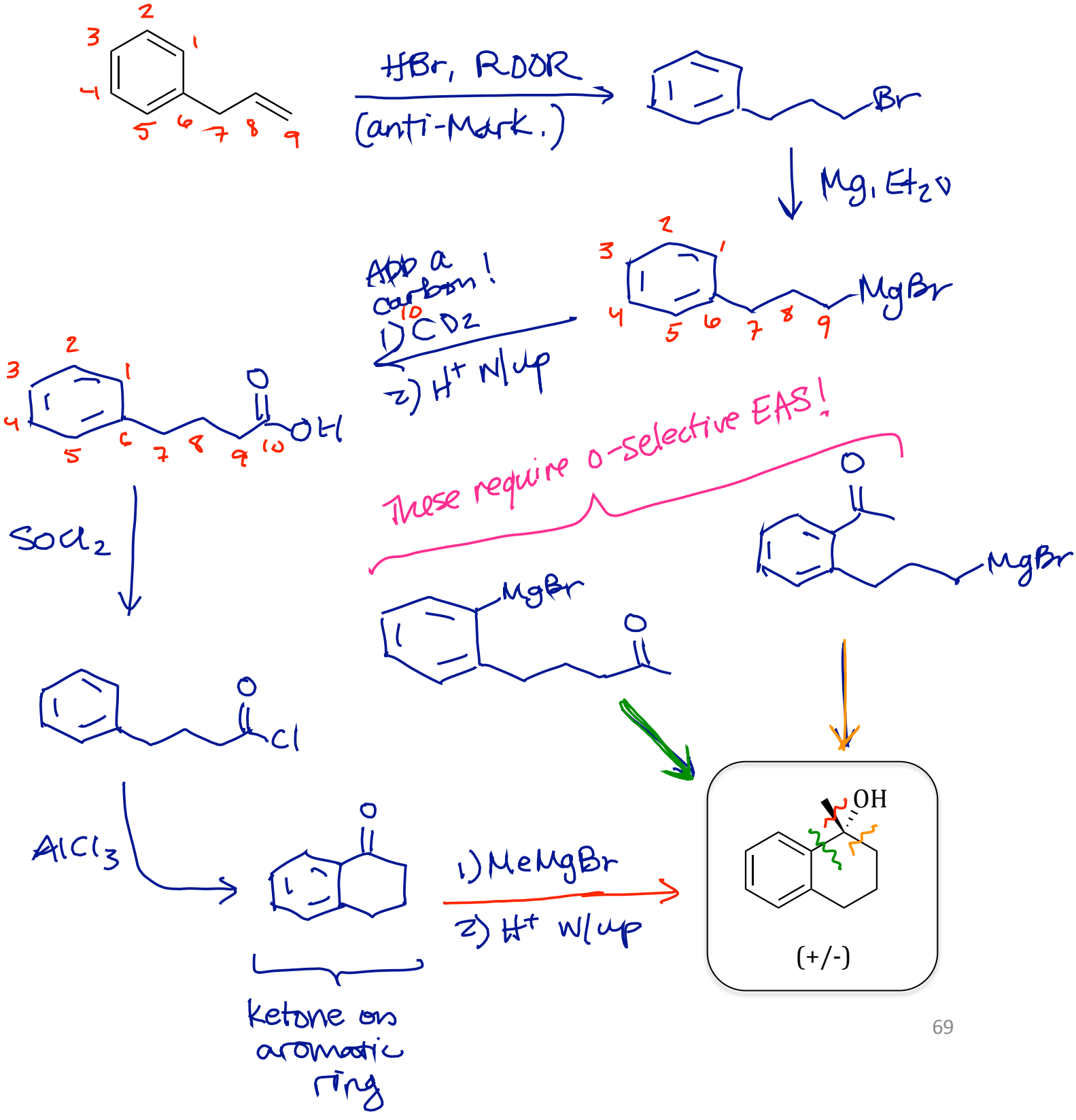


FG: vicinal diol

OsO4/H2O } syn

epoxides w/ H3O+ } anti

Provide a multi-step synthesis of the desired product from the indicated starting material. You may use any organic or inorganic reagents, but all of the carbons in the starting material must end up in the product. The best answer will require eight or fewer steps.



Provide a multi-step synthesis of the desired product from the indicated starting material. You may use any organic or inorganic reagents that add *two or fewer* carbon atoms. The best answer will require four or fewer steps.