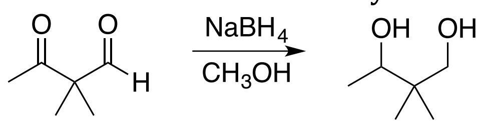
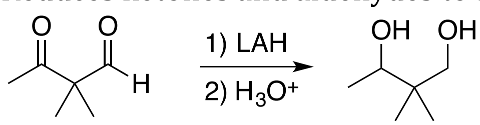
Reaction Summary
Synthetic Transformation of Carbonyl Compounds

Reduction

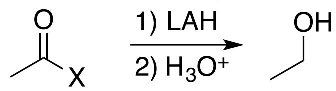
- Sodium borohydride in methanol ($NaBH_4$, CH_3OH)
  - Reduces ketones and aldehydes to secondary and primary alcohols, respectively.



- Lithium aluminum hydride (LAH): Conditions = 1. $LiAlH_4$, 2. H_3O^+
  - LAH is the strongest of the reducing agents that we have discussed.
  - Reduces ketones and aldehydes to secondary and primary alcohols, respectively.

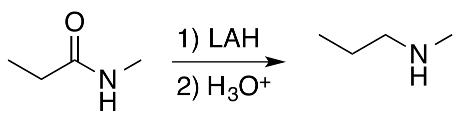


  - Reduces carboxylic acids, esters and acid chlorides to primary alcohols.

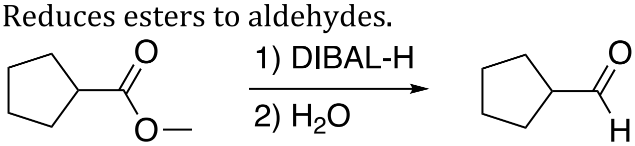


X = OH, OR, Cl, Br

  - Reduces amides to amines.



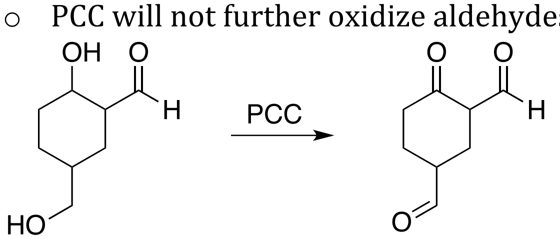
- Diisobutylaluminum hydride (DIBAL-H): Conditions = 1. DIBAL-H, 2. H_2O
  - Reduces esters to aldehydes.



  - Carboxylic acids and amides are unreactive to DIBAL-H.
  - Will reduce aldehydes and ketones to alcohols, but generally not used for this purpose.

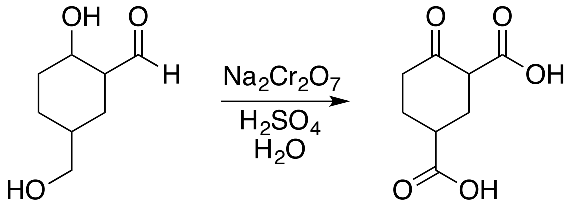
Oxidation

- Tertiary alcohols and carboxylic acids cannot be further oxidized.
- PCC Oxidation
  - Primary alcohols will be oxidized to aldehydes
  - Secondary alcohols will be oxidized to ketones
  - PCC will not further oxidize aldehydes



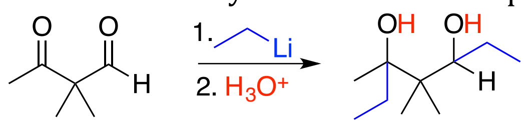
  - Dess-Martin Periodinane is an alternative to PCC that does esspentially the same thing (it is a mild oxidizing agent)

- $M_2Cr_2O_7$, H_2SO_4, H_2O (M = Na or K)] “Active agent = H_2CrO_4” and C_rO_3/H^+ (Jones)
    - Primary alcohols will be oxidized to carboxylic acids
    - Secondary alcohols will be oxidized to ketones
    - Aldehydes will be oxidized to carboxylic acids

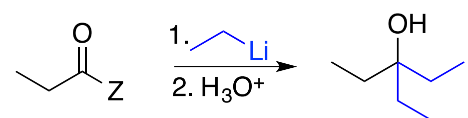


<u>Addition of Organometallic Reagents to Carbonyl Compounds</u>

- Reactivity: R-Li > R-MgX > R_2CuLi
- Organometallic reagents act as nucleophiles and bases. They are incompatible with protic solvents such as alcohols and water because a fast acid/base reaction results.
  (i.e. R-Li + H-O-H → R-H + LiOH)
- Organolithium Reagents (R-Li)
    - Preparation: R-X + 2 Li → R-Li + LiX
    - React with aldehydes and ketones to provide 2° and 3° alcohols, respectively.

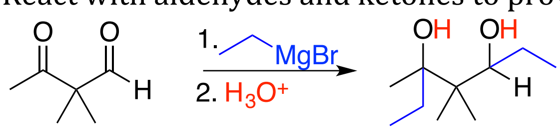


    - Two equivalents of R-Li will react with an ester or acid chloride to provide a 3° alcohol.

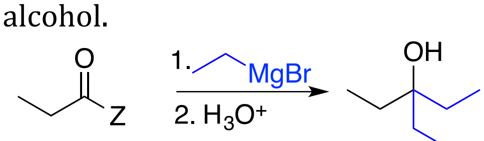


Z = OR, Cl

- Grignard Reagents (R-MgX)
    - Preparation: R-X + Mg → R-MgX
    - React with aldehydes and ketones to provide 2° and 3° alcohols, respectively.

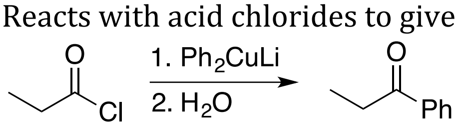


    - Two equivalents of R-MgX will react with an ester or acid chloride to provide a 3° alcohol.

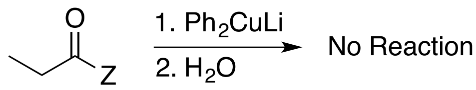


Z = OR, Cl

- Organocuprate Reagents (Gilman Reagents)
    - Preparation: 2 R-Li + CuI → R_2CuLi + LiI
    - Reacts with acid chlorides to give ketones

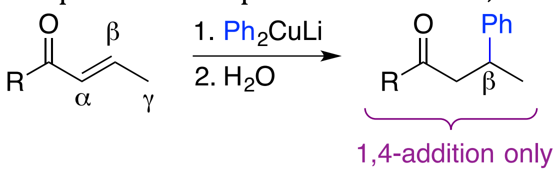


- Organocuprate Reagents (continued)
    - Does not react with carboxylic acids, esters, amides, aldehydes, or ketones (with the exception of α,β-unsaturated aldehydes and ketones).

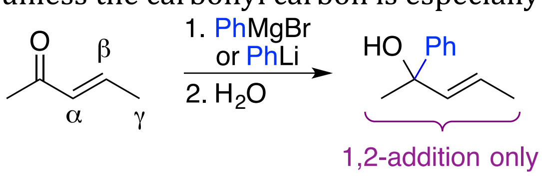


$Z = CH_3$, H, OH, OR, NR_2

    - Reacts with α,β-unsaturated aldehydes and ketones to give β-substituted carbonyl compounds. This process is called 1,4-addition or conjugate addition.



    - Organolithium and Grignard reagents generally do not react via 1,4-addition unless the carbonyl carbon is especially hindered.



Protecting Groups

- Used to "protect" an alcohol from reacting with a strong nucleophile such as a hydride reagent, Grignard reagent, or organolithium species.
- The most common protecting group is an organosilicone species.
- Three steps:
    - A. Protect the alcohol (reaction of alcohol with R_3SiCl).
    - B. Perform desired reaction
    - C. Deprotect the alcohol (remove the Si group by reaction with F^-).