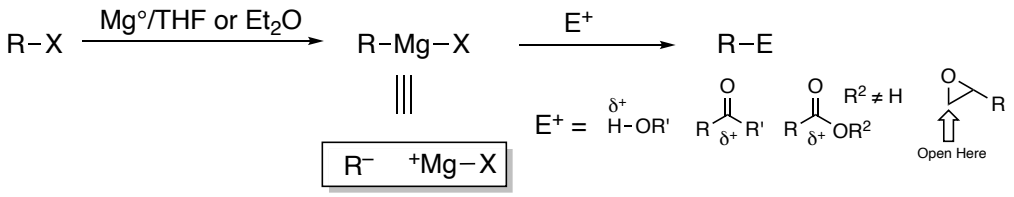
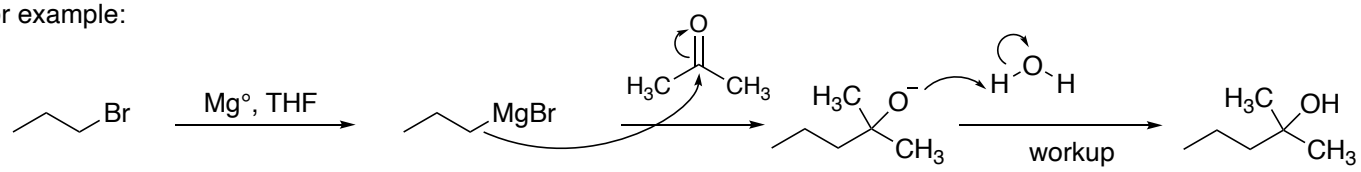
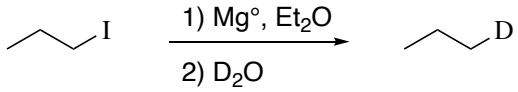


For example:

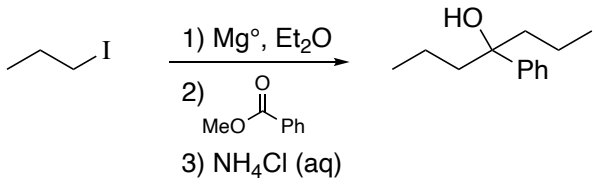
A.



B.



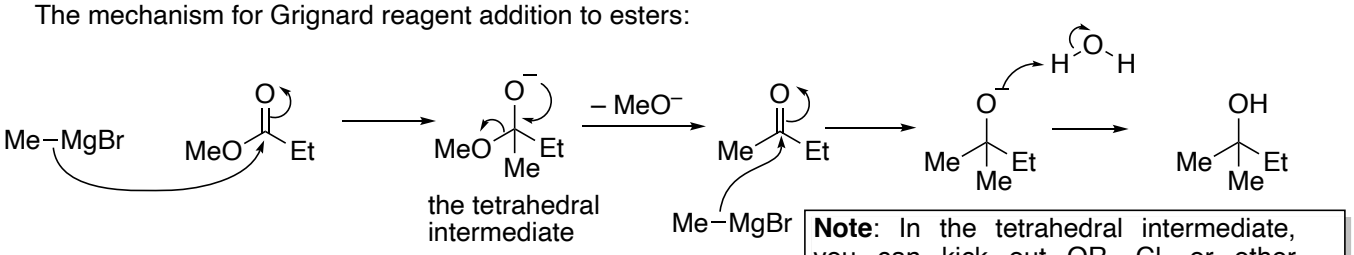
C.



Note 1: NH_4Cl is a weak acid used to quench the alkoxide

Note 2: When using esters assume excess Grignard reagent is used

The mechanism for Grignard reagent addition to esters:

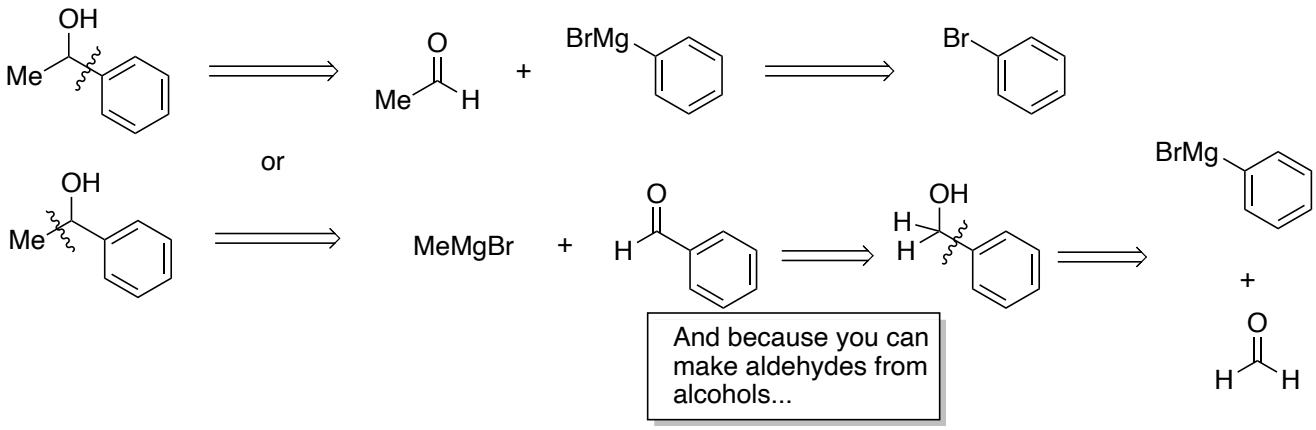


Note: Grignard reagents add to aldehydes faster than to ketones Grignard reagents add to ketones much faster then to esters

Note: In the tetrahedral intermediate, you can kick out OR, Cl, or other common leaving group. You cannot have an alkyl (R) group or hydrogen as the leaving group

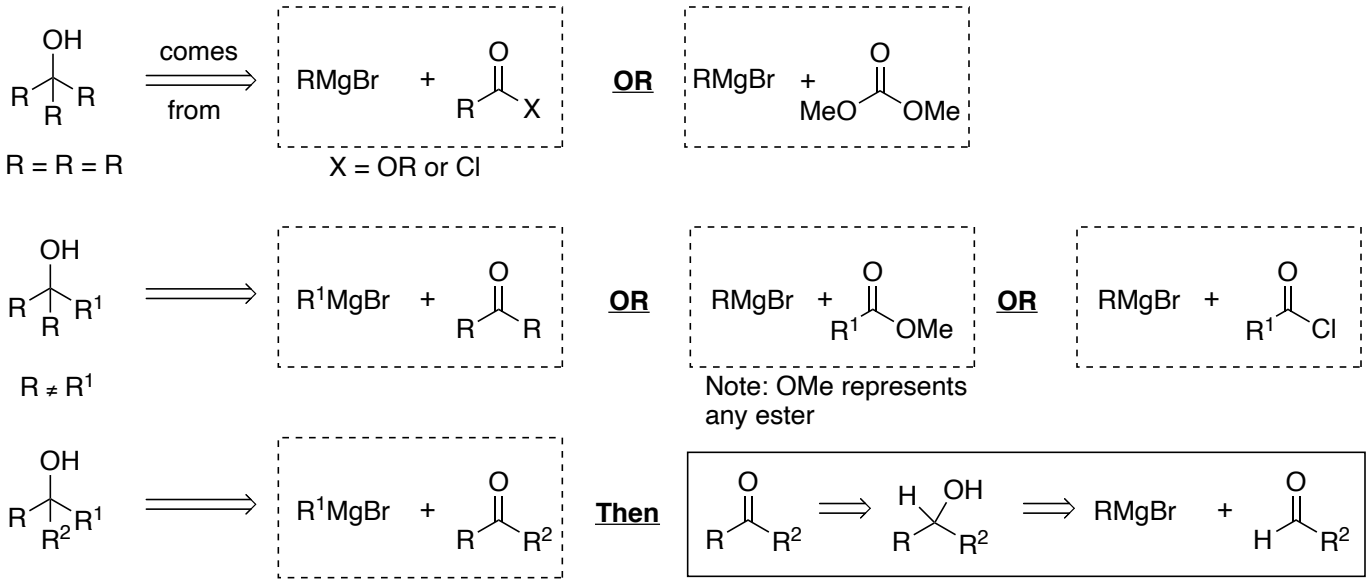
Using Grignard reagents to synthesize alcohols:

Nearly all carbon-carbon bonds at an alcohol functional group could be prepared using Grignard technologies.

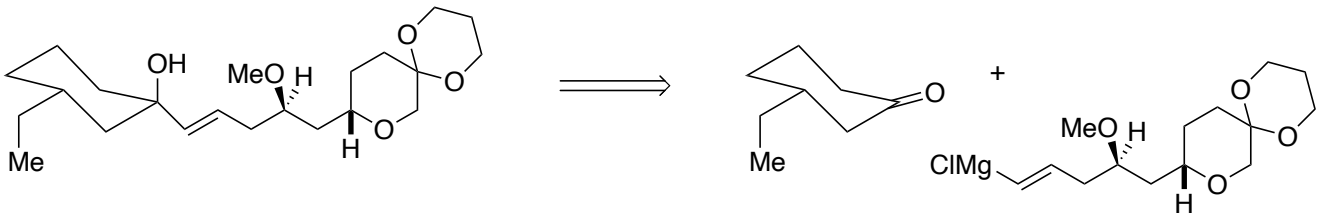


Grignard reagents & Reducing reagents 2/1/2021

Retrosynthetic analysis tips:



For Example:



Three last notes on Grignard reagents:

1) Grignard reagents are nucleophiles that add to the specific types of electrophiles shown in this handout (ie. that are not generally used for S_N2 reactions on alkyl halides).

2) Alkyl Na, Li, and K reagents (i.e. $H_3CC{\equiv}CNa$) react very similarly to Grignard reagents.

3) An R^- addition to a carbonyl is a reduction just like a hydride H^- delivered from BH_4^-

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H_2

Reducing Reagents

Na, Li, or K : Used to reduce alkynes to *trans*-alkenes

BH_3 : Adds to alkenes and alkynes (reducing them)
With the CBS Catalyst, reduces ketones to alcohols, enantioselectively
Selectively reduces carboxylic acids to alcohols (Does react with esters)

$NaBH_4$: Reduces aldehydes, acid chlorides, and ketones to the corresponding alcohol (reduces esters very slowly)

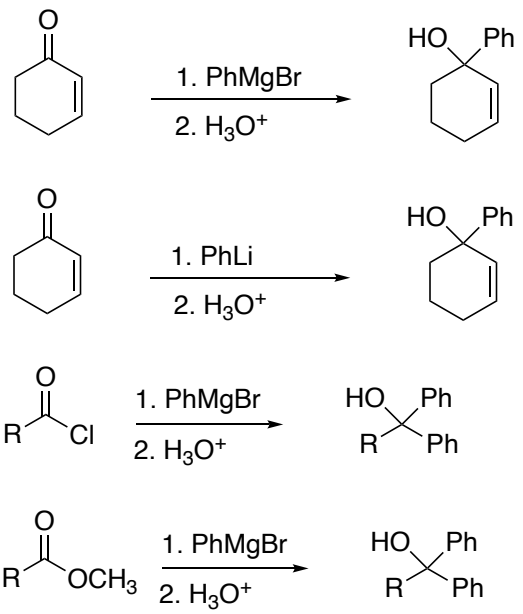
$LiBH_4$: Reduces esters, ketones, acid chlorides, and aldehydes to the corresponding alcohol

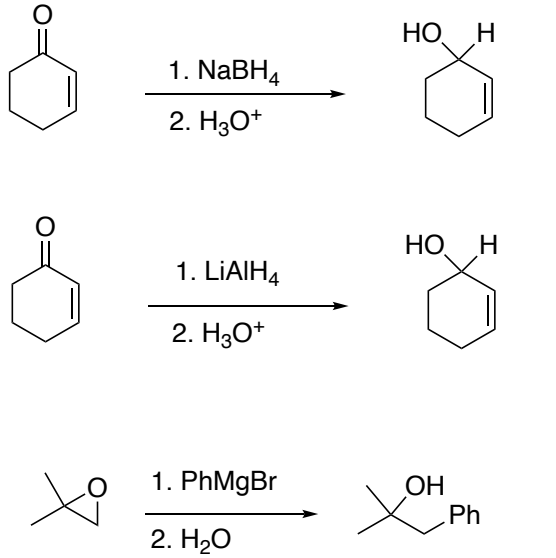
$LiAlH([OC(CH_3)_3]_3$: Used to reduce acid chlorides and esters (at –78 °C) to aldehydes (stops at the aldehyde!)
Reduces ketones, acid chlorides,and aldehydes to the corresponding alcohol

i-Bu_2AlH (DIBAL): Used to reduce esters and acid chlorides (at –78 °C) to aldehydes (stops at the aldehyde!)
Reduces ketones, acid chlorides,and aldehydes to the corresponding alcohol

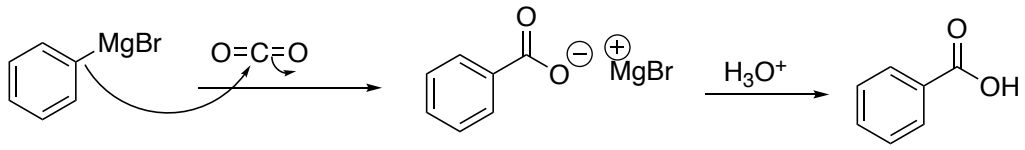
$LiAlH_4$: (LAH) Very powerful reducing agent also reduces carboxylic acids
Reduces ketones, acid chlorides,and aldehydes to the corresponding alcohol
Reduces amides to the corresponding amine

Nucleophilic Additions





RLi and R_2CuLi will also open epoxides



Hydroxyl Protecting Groups