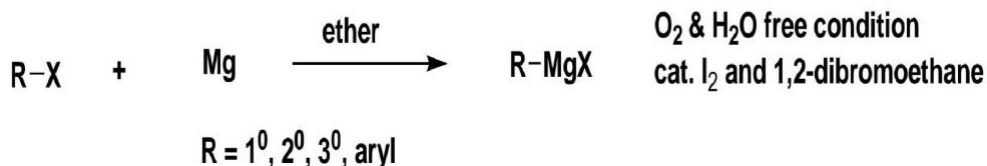
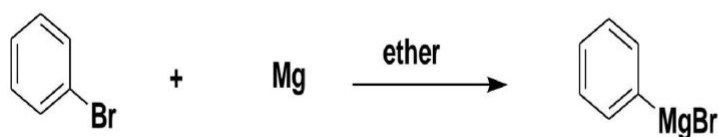
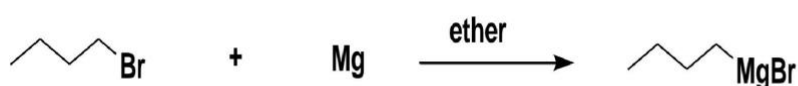


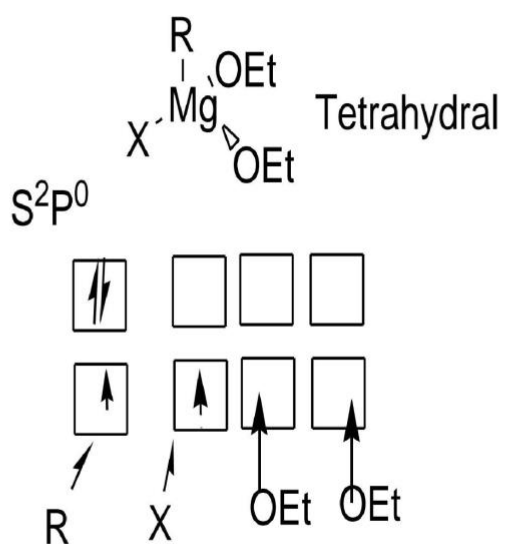
Organometallic compounds

- Compounds that contain metal-carbon bonds, R-M: R= alkyl, aryl gr ; M= Mg, Li, Na, Cu, Zn etc.
- Provide nucleophilic carbon atom, utilize for new C-C bond formation
- Can be treated as $R-M = R^-M^+$
- reagent can be formulated as $RMgX$ or R_2Mg .
- Grignard

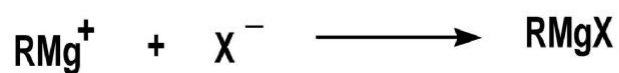
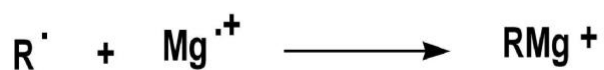
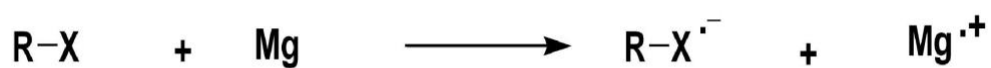
Laboratory preparation of Grignard reagent



Structure



Mechanism:



Reactivity

Reactivity

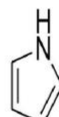


Low bond energy toward iodide

Alkyl halide > Vinyl or aryl halides

Reactive Groups

Acidic Protons: CO_2H , OH , SH , NH_2 , $CONHR$

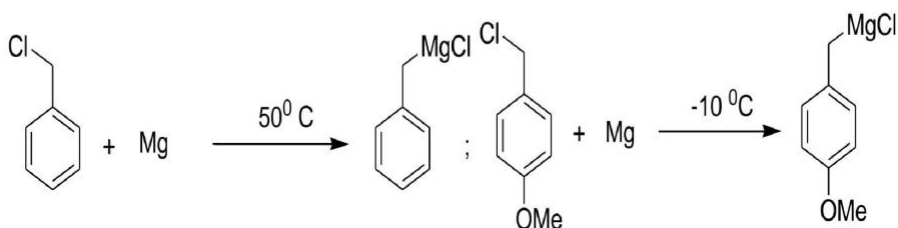
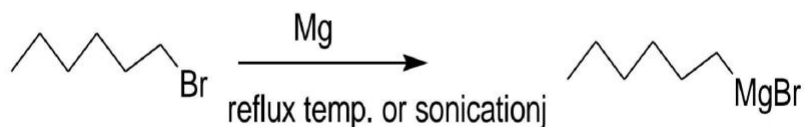
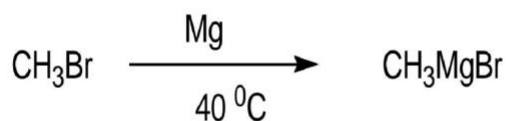
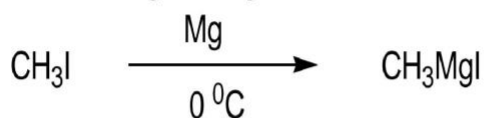


GWE — EWG

Reactive functional group: aldehyde, ketone, ester, amides, halides, nitrile

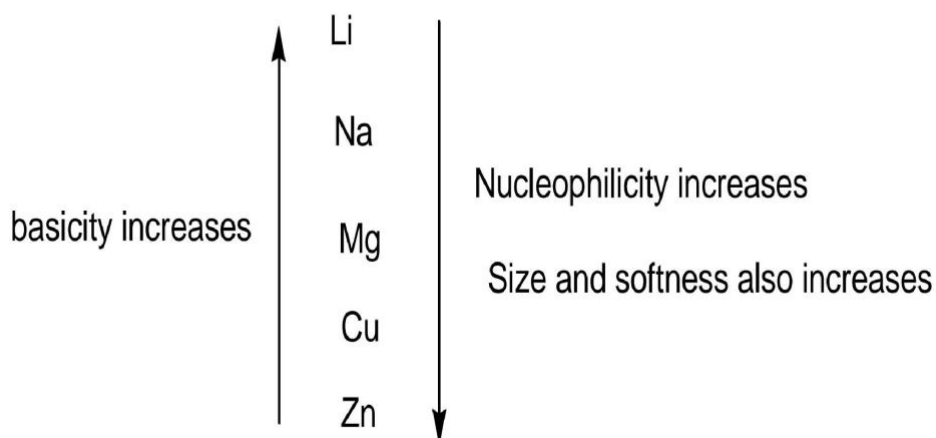
Acidic
hydrogen >> aldehyde > keto > ester > nitrile > amide

Temperature dependent Grignard preparation

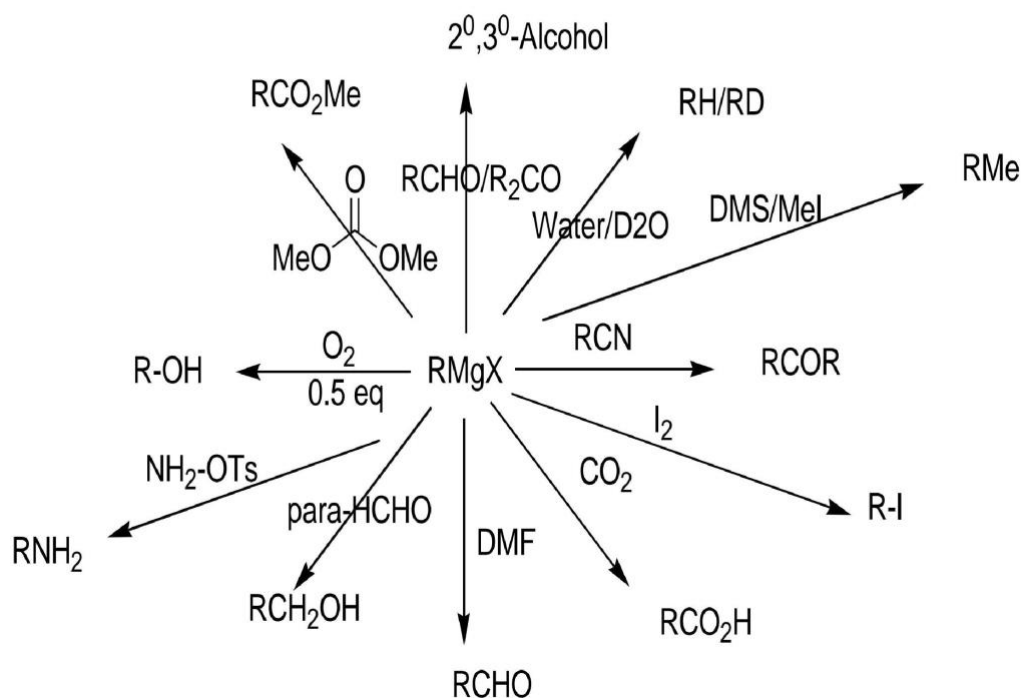


Basicity vs Nucleophilicity

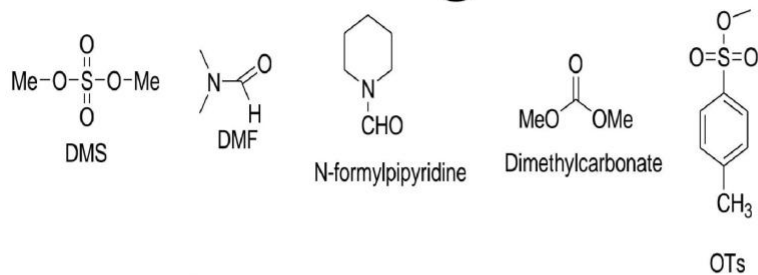
Basicity vs Nucleophilicity of organometallic reagent



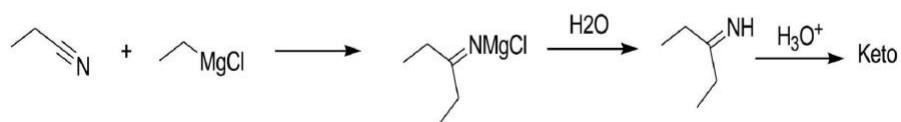
Common Reactions



Usefull reagents

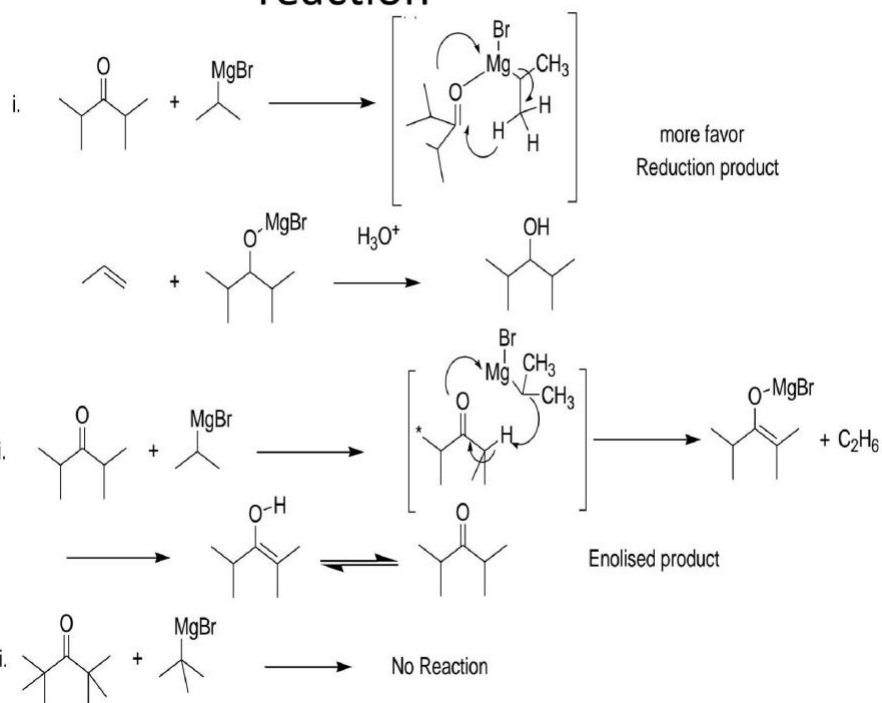


triethyl orthoformate/ triethoxymethane: protected ethylformate



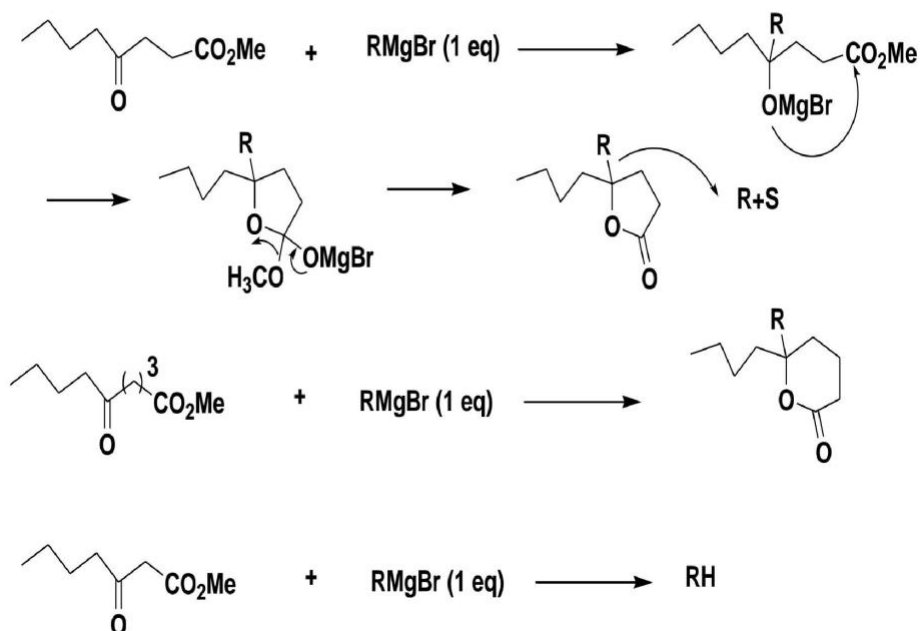
Secondary amine preparation

Abnormal behaviour/side reaction

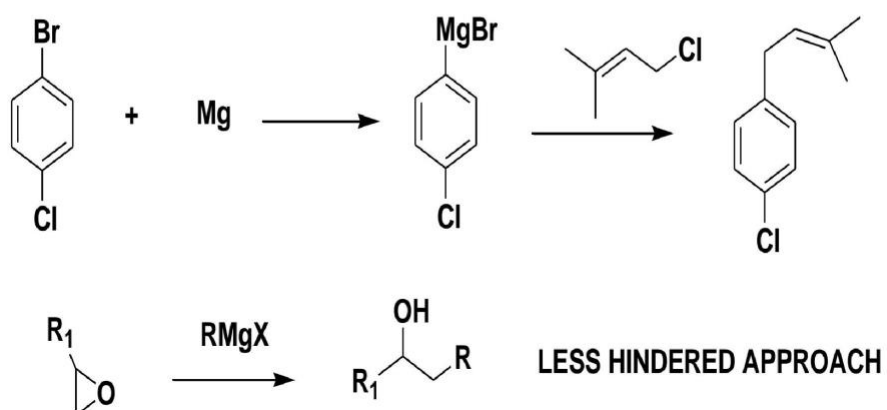


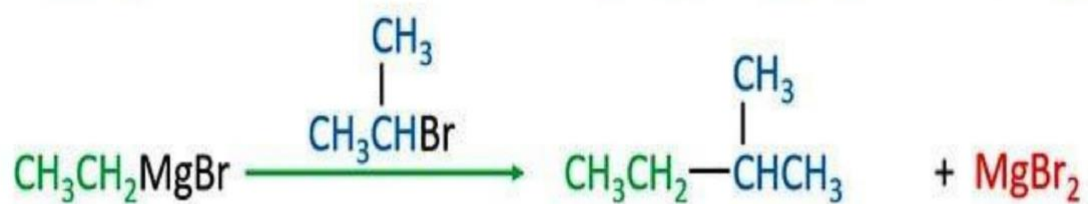
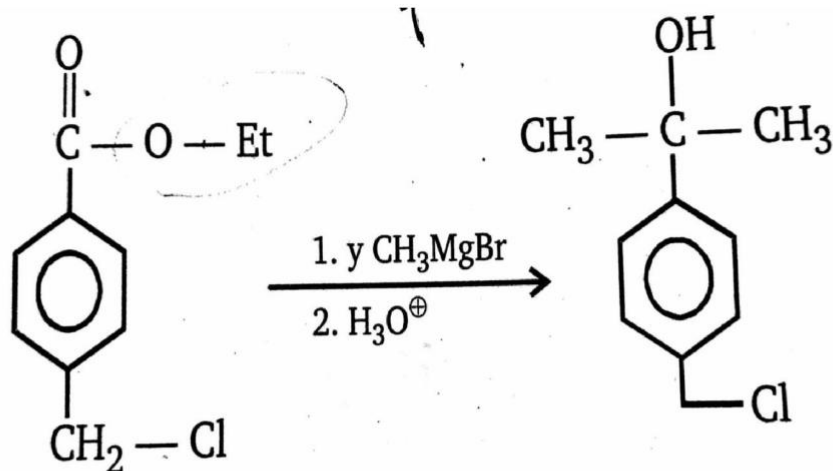
Q. Between i and ii which one favor? explain.

Intramolecular reaction

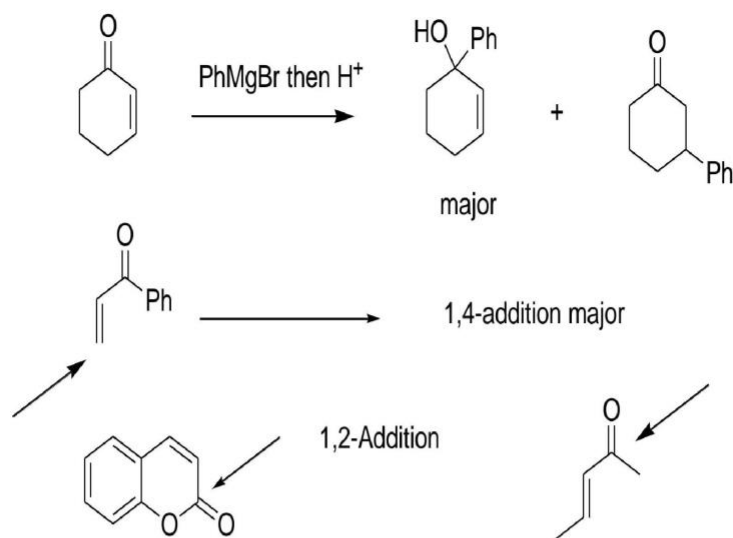


$\text{S}_{\text{N}}2$ -type reaction



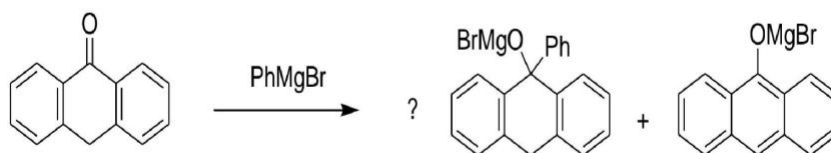


1,2-vs1,4-addition



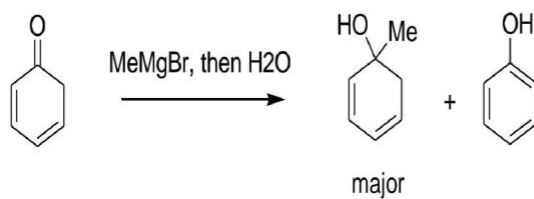
Hindered group at 2-position allow to addition at 4-position

Temperature control reaction

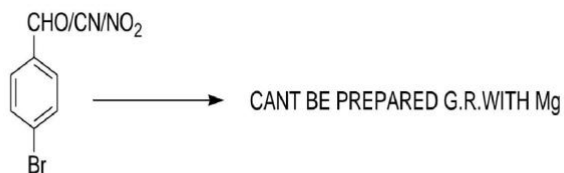


At low temperature → high yield

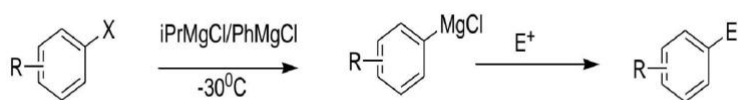
room temperature → high yield



Sensitive Grignard reagent preparation

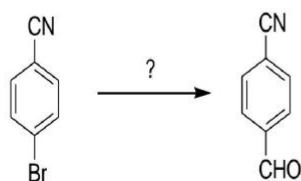


Halogen-Magnesium exchange reaction

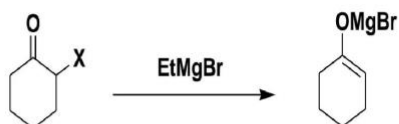


R = CN, NO₂, CO₂Et

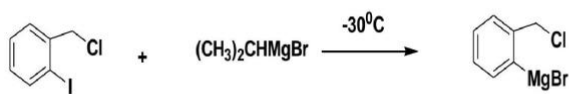
X = Br, I



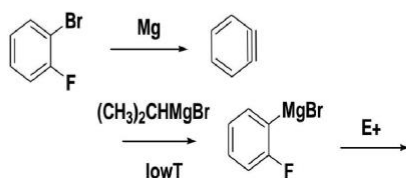
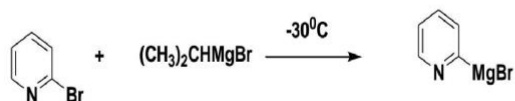
Magnesium enolate formation



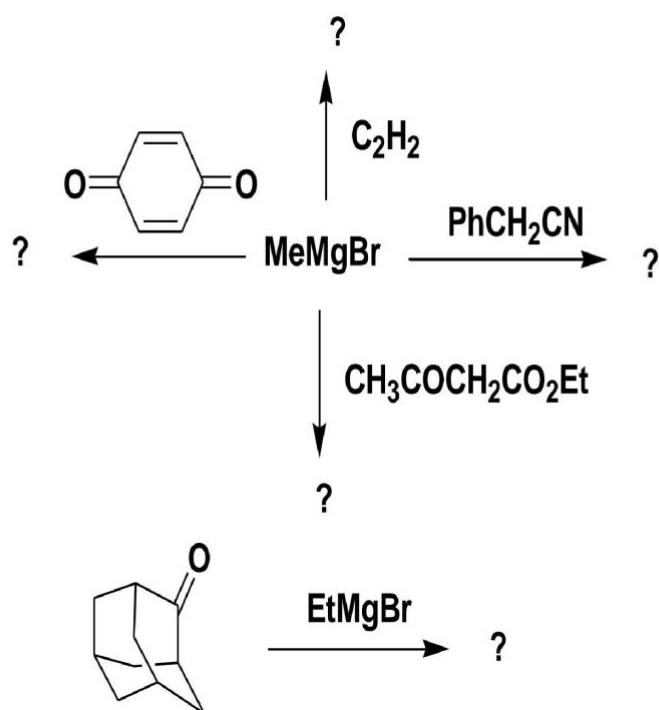
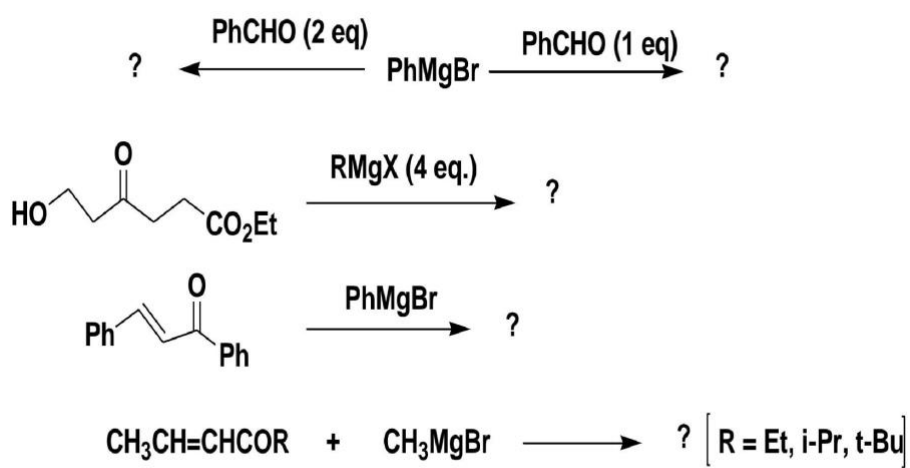
X = Br/I/Cl



Competition between aryl iodide and benzyl chloride if use Mg metal

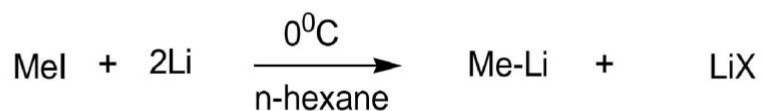
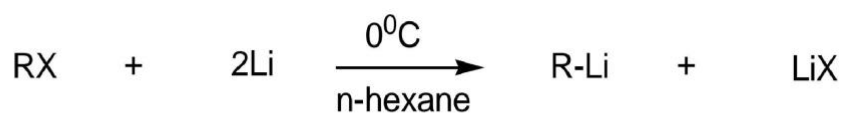


Problem



Organolithium compounds

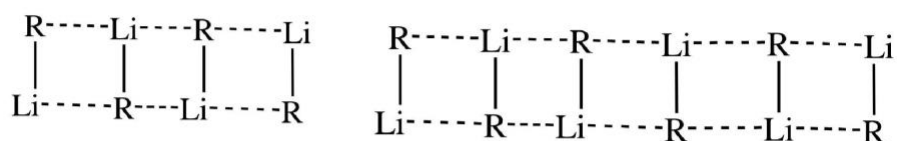
Laboratory preparation of Li reagent



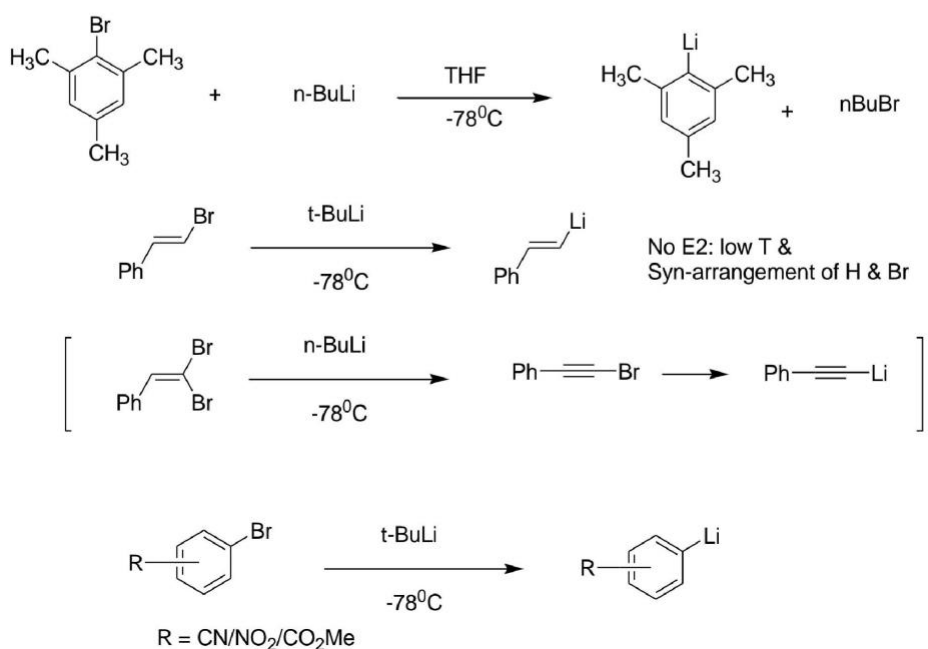
hydrocarbon solvent: hexamers

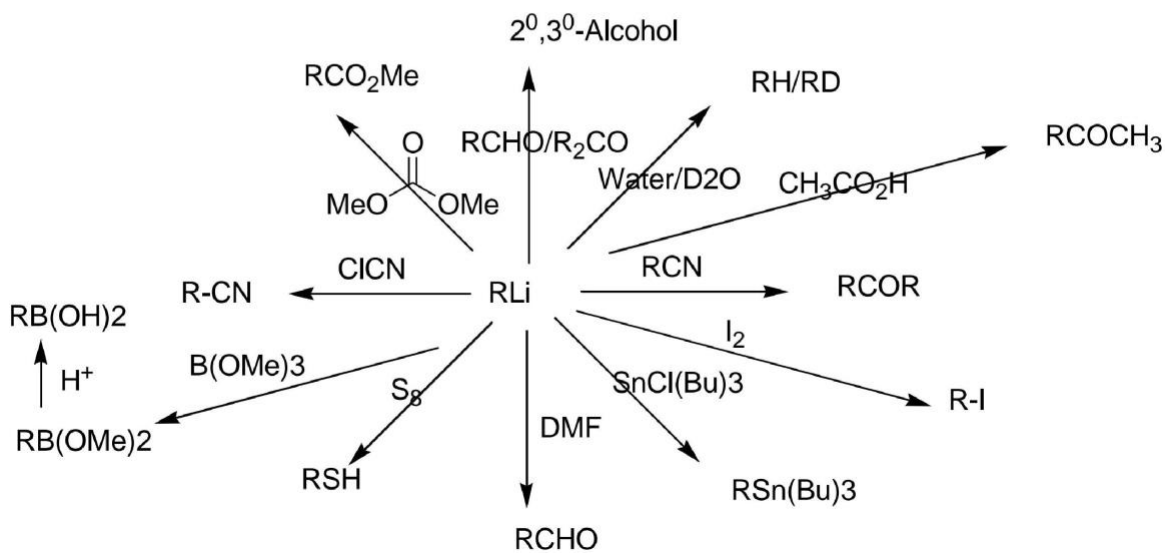
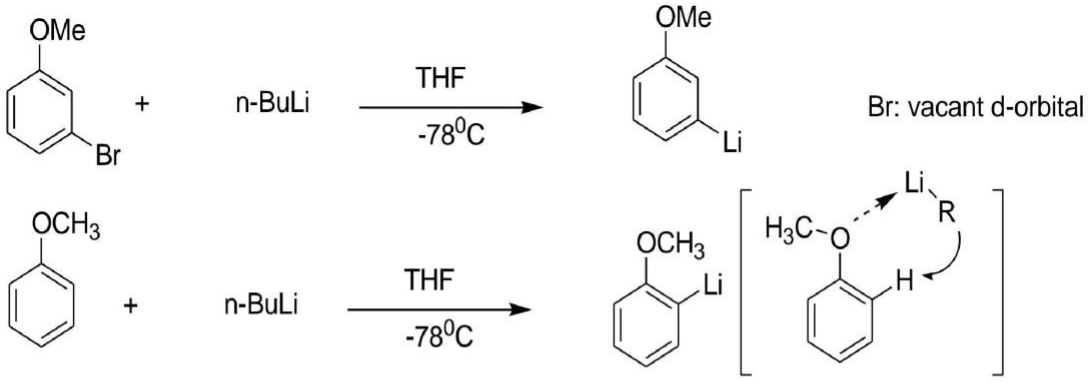
in ether : tetramers

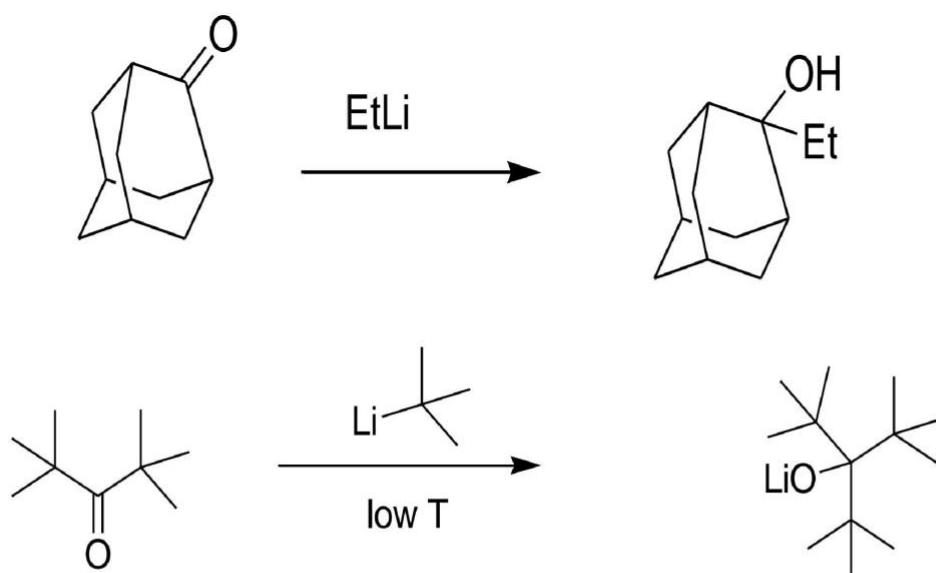
chelating solvent: monomer
TMEDA, HMPA



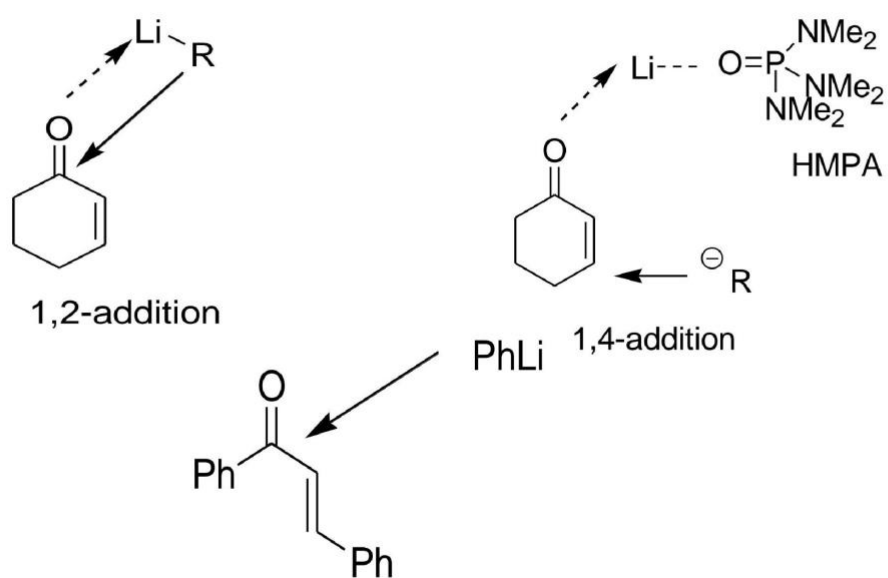
Halogen-Metal exchange or metallation or Lithiation





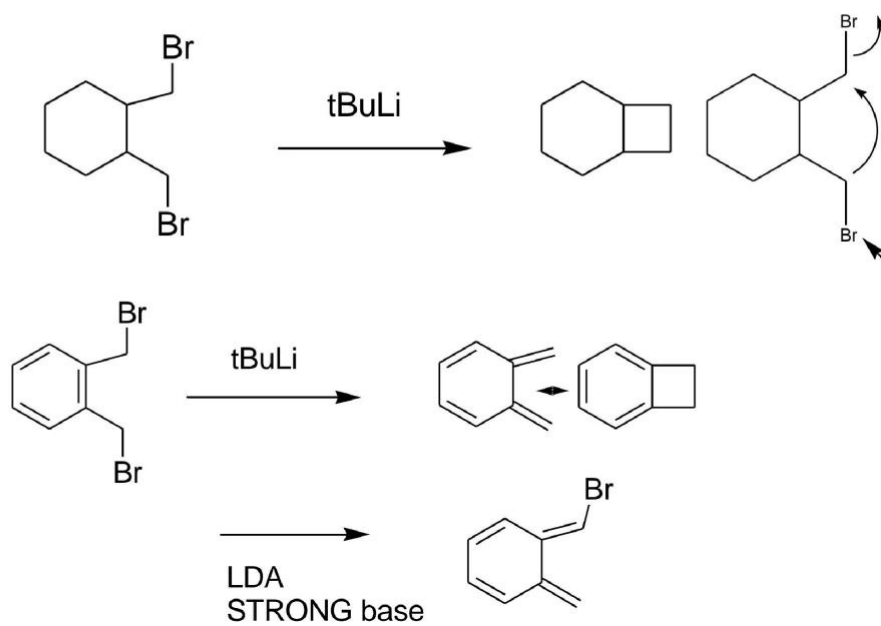
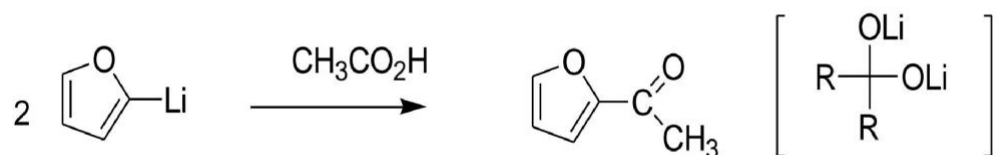
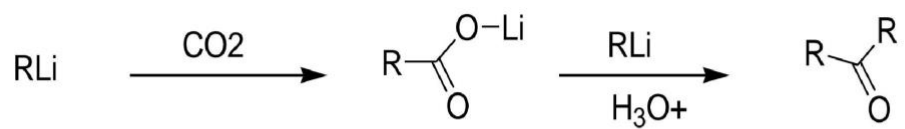


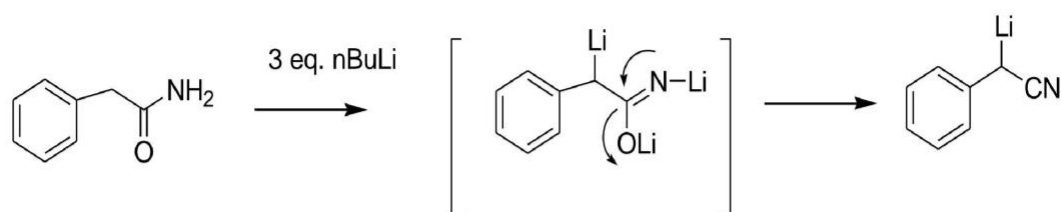
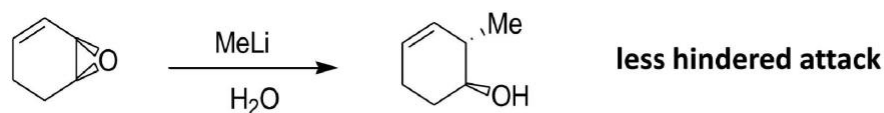
1,2-addition vs 1,4-addition



Highly reactive RLi usually react 1,2-addition but addition of HMPA favor 1,4-addition

Synthesis of ketone from carboxylic acid





Amide to nitrile

Copper reagent

Use of organocopper reagents offers a very efficient method for coupling of two different carbon moieties. Since copper is less electropositive than lithium and magnesium, the C-Cu bond is less polarized than the C-Li and C-Mg bonds.

Organocopper complexes (RCu)

Lower-order cuprates (R_2CuLi , also known as [Gilman reagents](#))

Lower-order cyanocuprates (RCu(CN)Li)

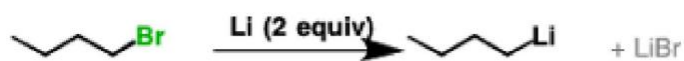
Higher-order cyanocuprates ($\text{R}_2\text{Cu(CN)Li}_2$)

The organocopper reagents are more selective and can be acylated with acid chlorides without concomitant attack on ketones, alkyl halides, and esters

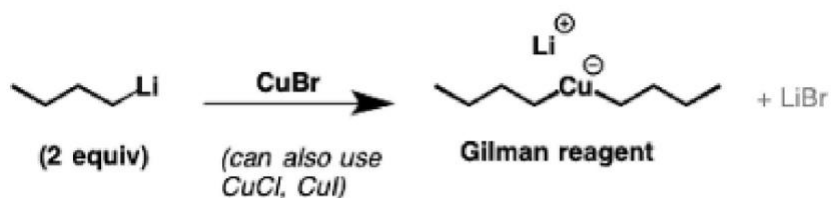
Relative reactivity: $\text{RCOCl} > \text{RCHO} > \text{tosylates, iodides} > \text{epoxides} > \text{bromides} > \text{ketones} > \text{esters} > \text{nitriles}$

Preparation

Step 1: formation of organolithium



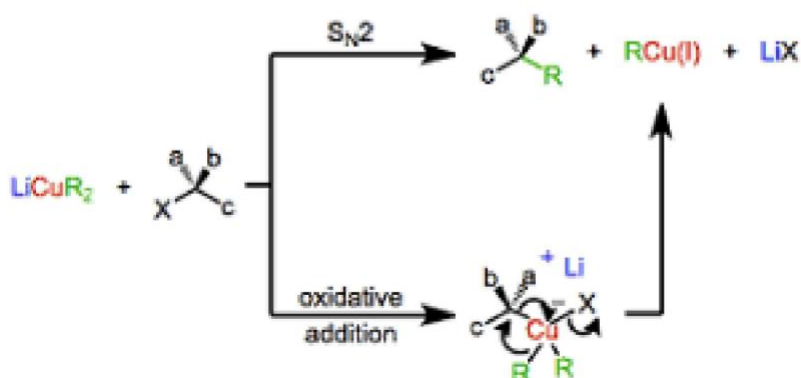
Step 2: formation of organocuprate (Gilman reagent)



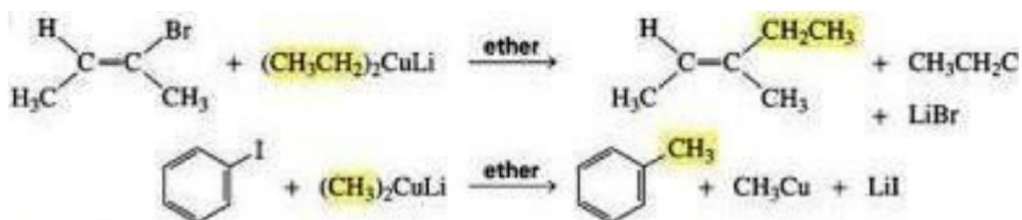
An alternative way of writing the same thing...



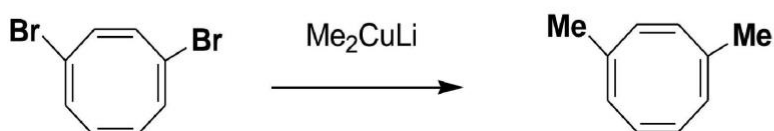
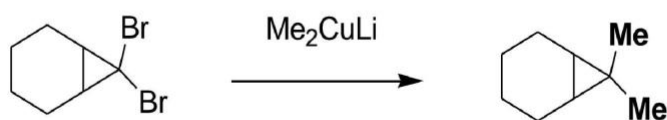
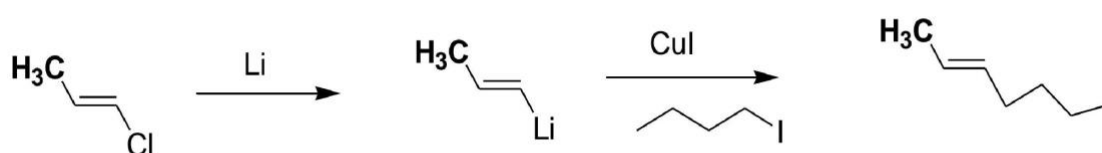
SN2 & SN2' type reaction



Same side attack of Nu to LG



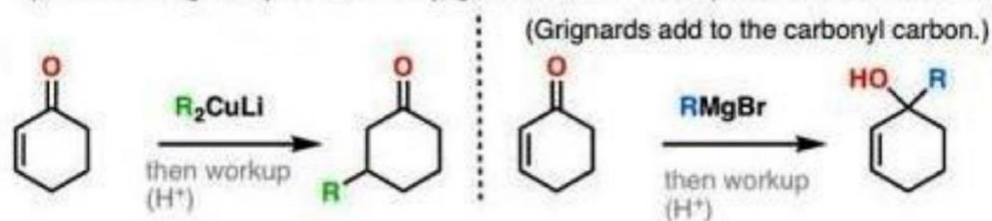
- When a Gilman reagent reacts with an alkyl halide (except F⁻) one of the alkyl groups replaces the halide
- Alkyl groups can substitute halogens attached to alkene or aromatic C with Gilman reagent; impossible with S_N1 or S_N2 reaction
- Mechanism unknown, probably radical



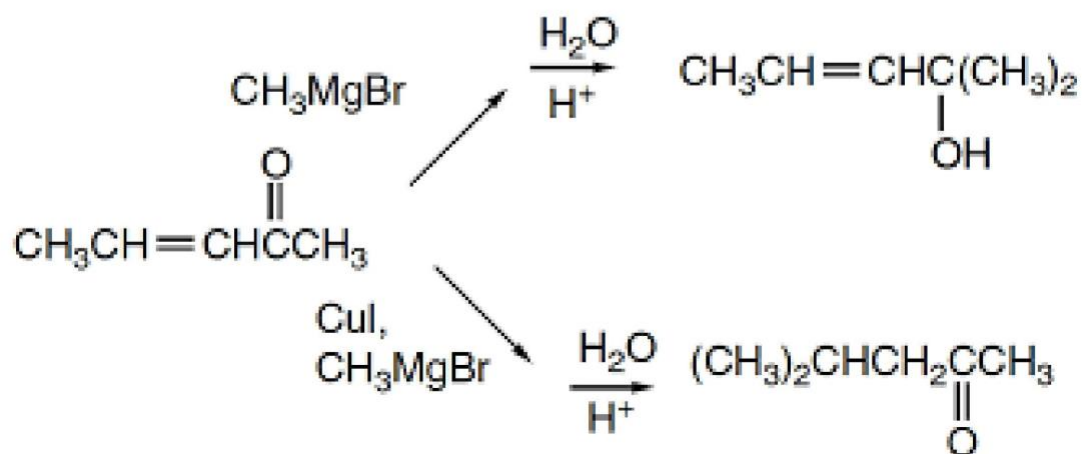
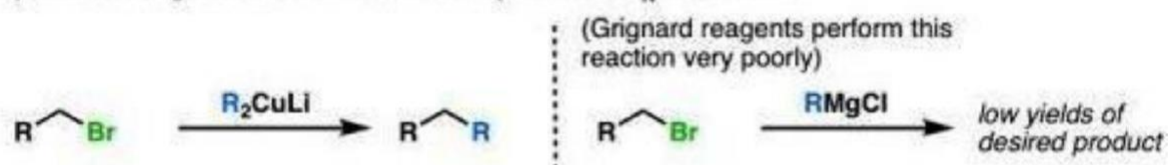
Only 1,4-addition

Summary: Gilman reagents (organocuprates) contrast with Grignard (and organolithium reagents) in two important ways:

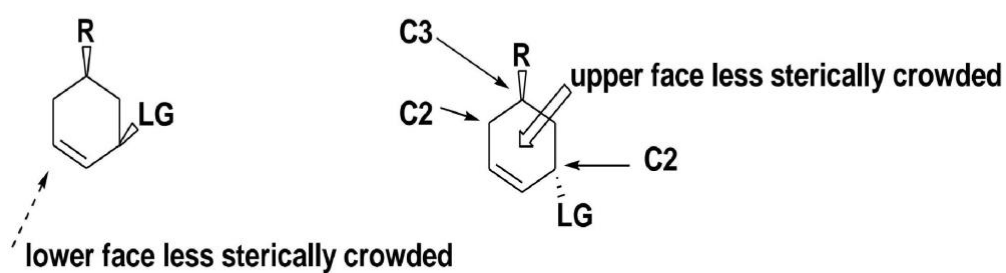
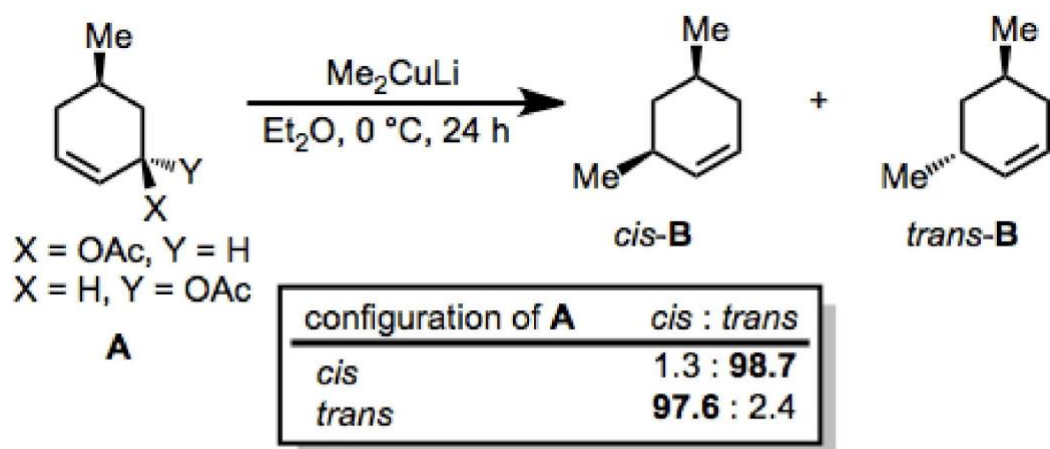
1) Gilman reagents perform "conjugate addition" to α, β unsaturated ketones



2) Gilman reagents are effective nucleophiles for S_N2 reactions

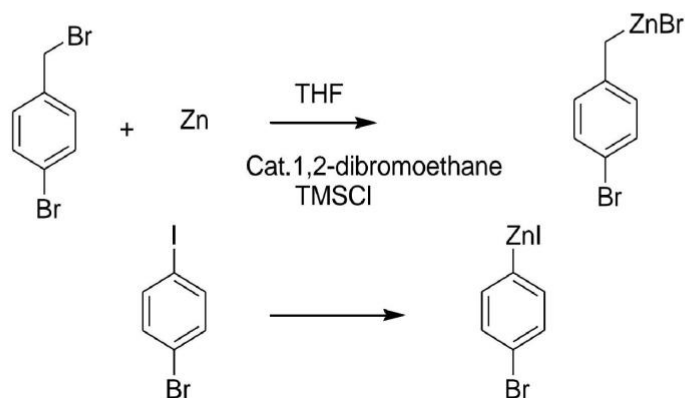
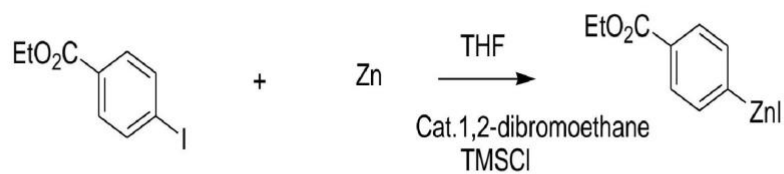
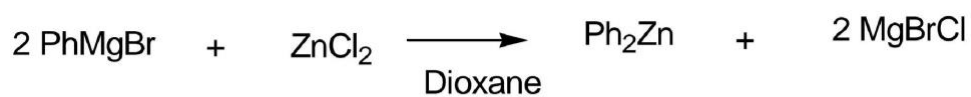






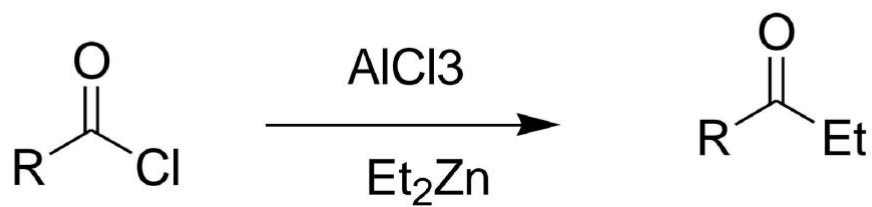
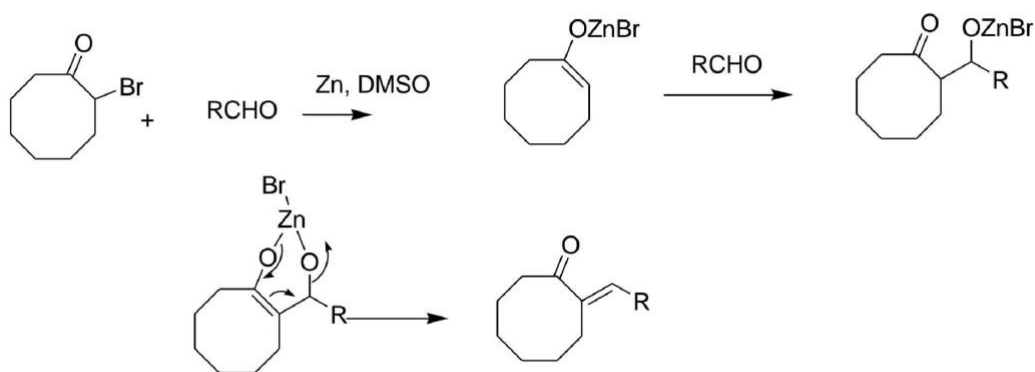
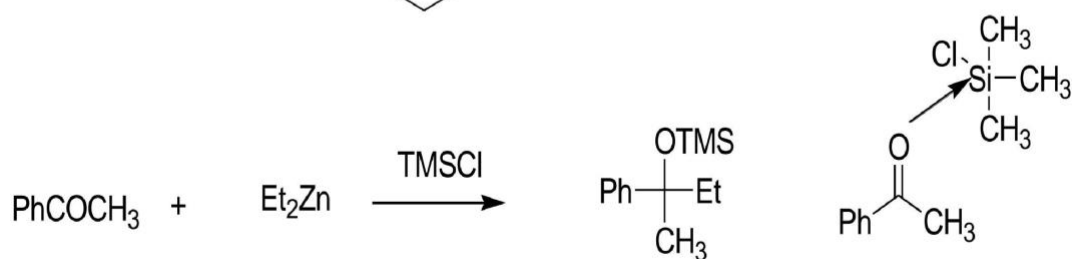
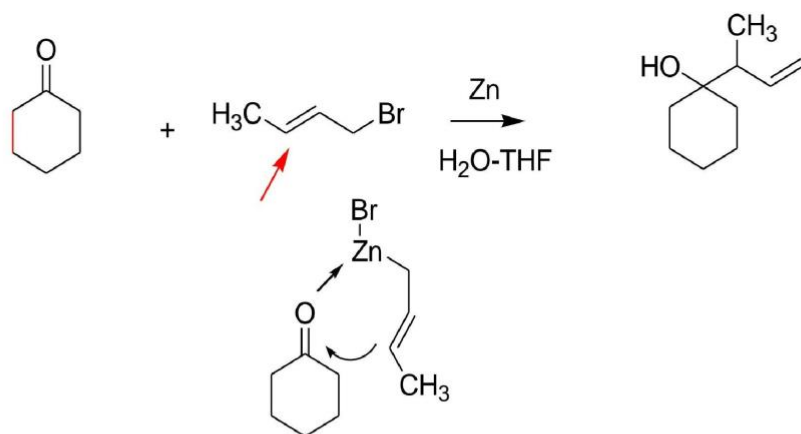
Organo zinc reagent

Preparation

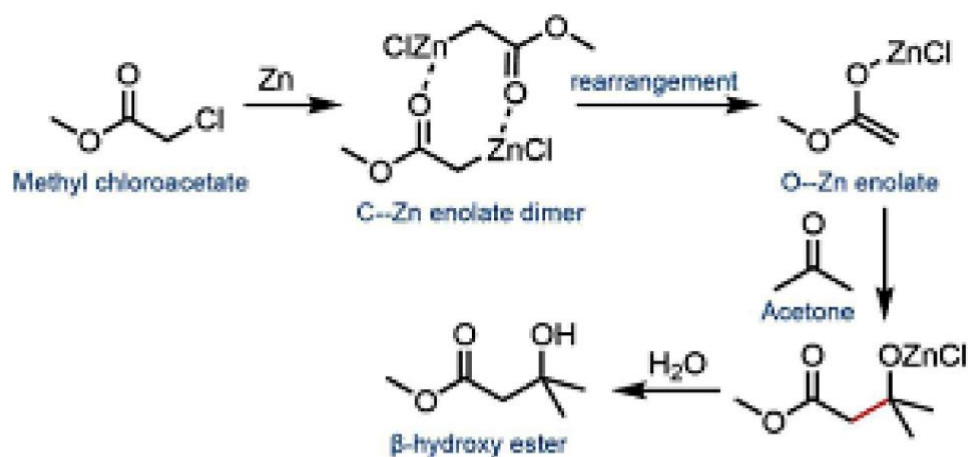


Reaction

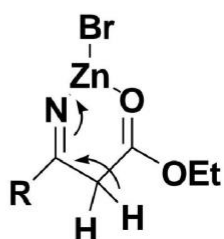
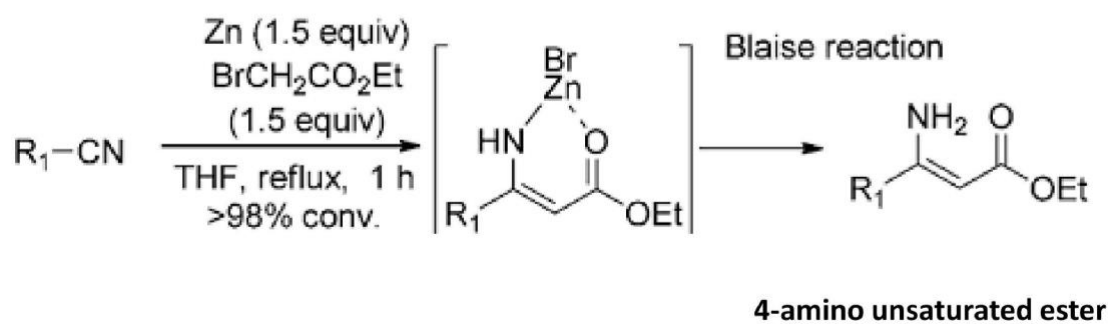




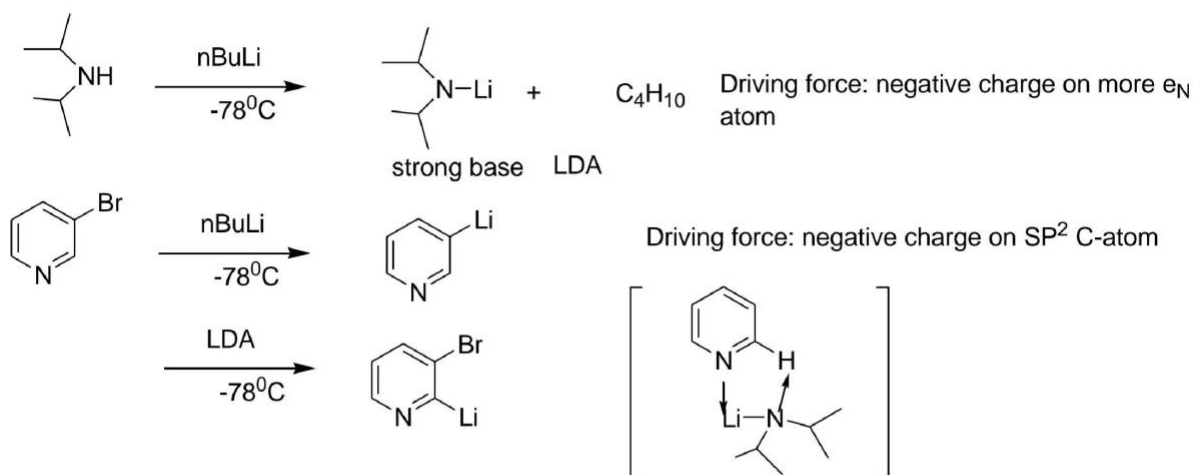
Reformatsky reaction



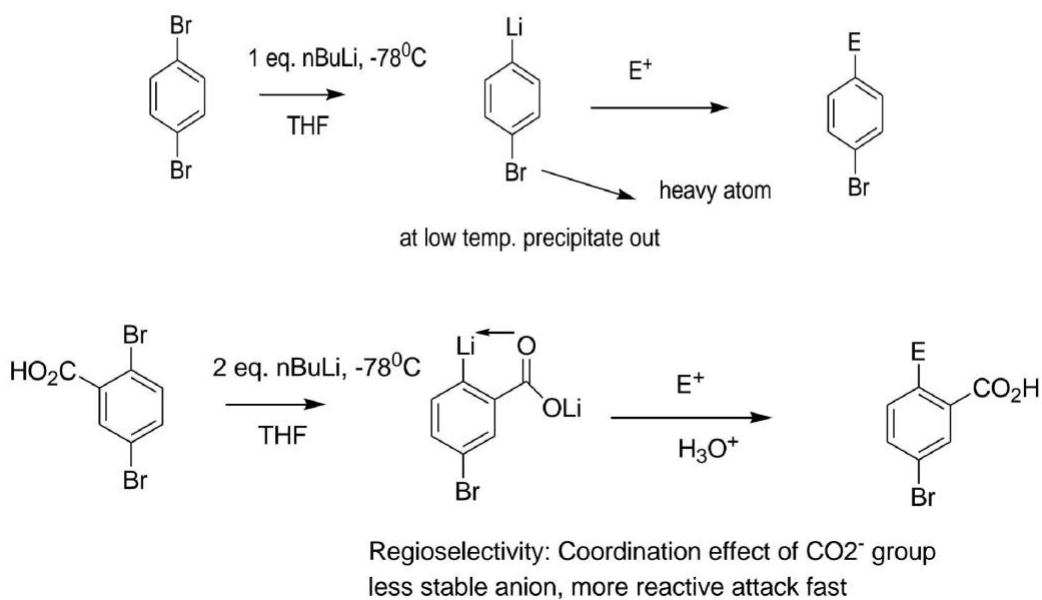
Blaise reaction



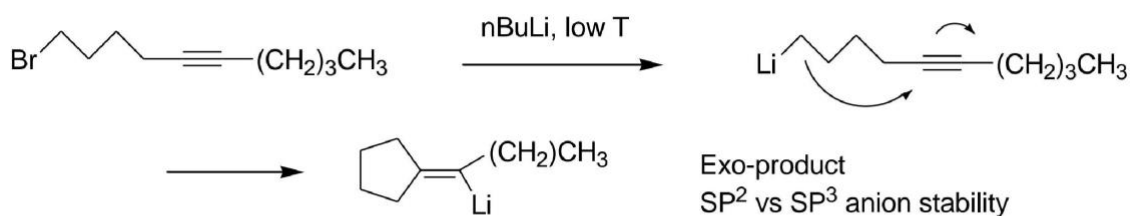
LDA preparation & use



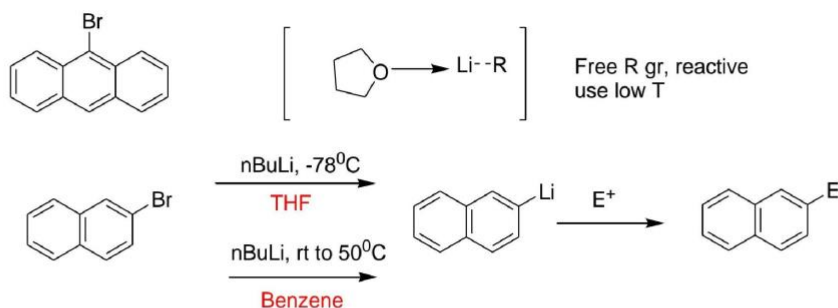
Selective mono-lithiation at low temperature in presence of heavy atom



Alkynyl lithium reagents undergo exo-cyclisation to cycloalkylidene isomer

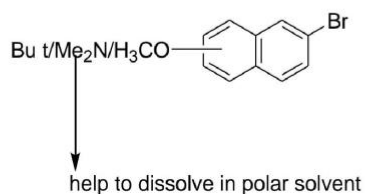


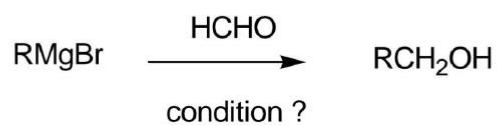
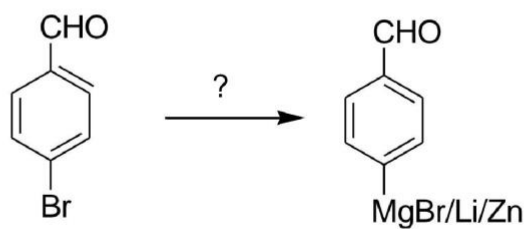
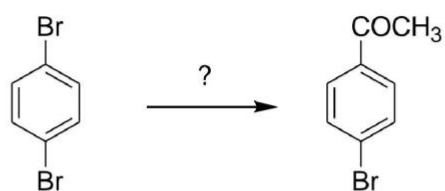
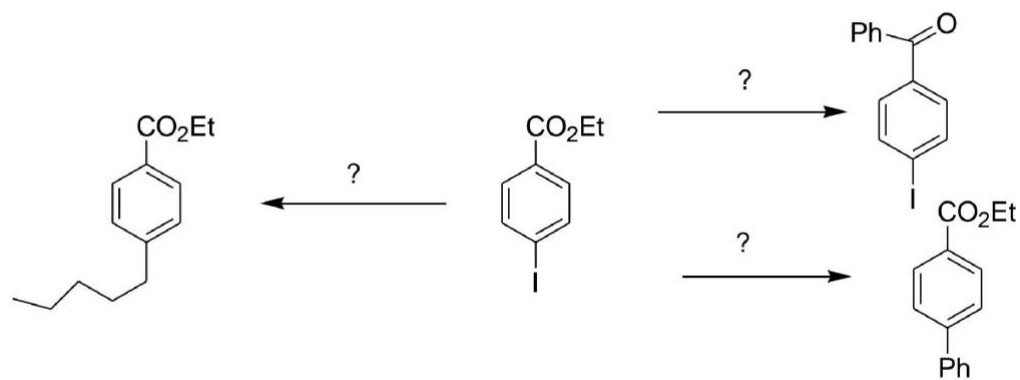
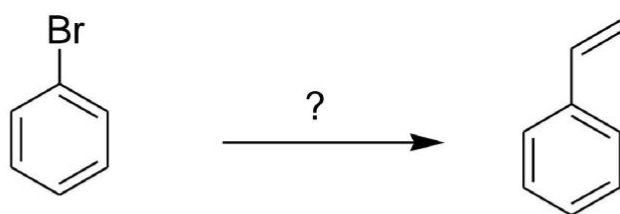
Solvent dependent lithiation at different temperature

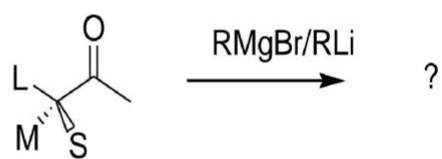
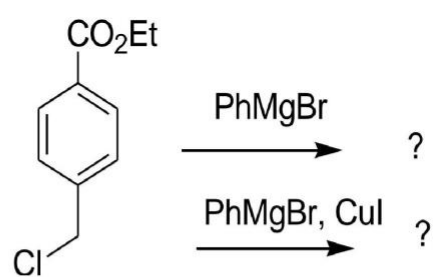


At low T, for simple hydrocarbon halide with no functional gr, highly insoluble in THF but in benzene it is soluble at rt or higher T

Coordinating solvent like THF required low T
BUT non coordinating solvent benzene, can be done in high T

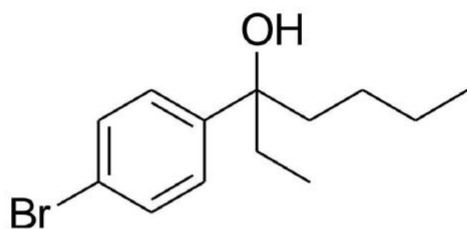






L = Large gr or coordinating gr

Prepare using suitable Grignard reagent.



Prepare from iodobenzene

