

Organometallic Compounds

Organometallic Compounds

- **Organometallic compound:** a compound that contains a carbon-metal bond
- In this chapter, we focus on organometallic compounds of Mg, Li, and Cu
 - these classes illustrate the usefulness of organometallics in modern synthetic organic chemistry
 - they illustrate how the use of organometallics can bring about transformations that cannot be accomplished in any other way

Organometallic Reagents

The Key Concepts:

Make a carbon negatively charged/polarized so it is nucleophilic. Reaction with electrophilic carbons can make carbon-carbon bonds.

This is a *Big Deal!*

Grignard Reagents



Victor Grignard

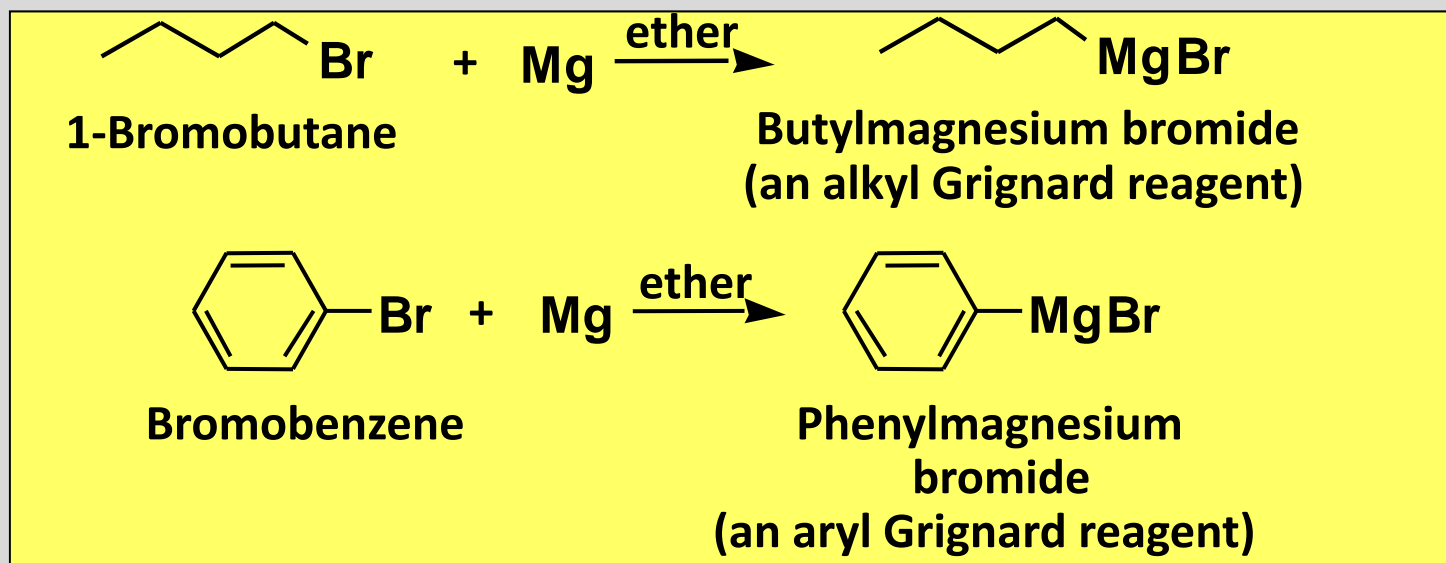
- Discovered by Victor Grignard in 1900
 - Key factors are ethereal solvent and water-free conditions
- **Awarded Nobel Prize in 1912**



Grignard, Victor , 1871–1935, French chemist. He shared the 1912 Nobel Prize in Chemistry for his work in organic synthesis based on his discovery (1900) of the **Grignard Reagent**. He taught at the Univ. of Nancy (1909–19) and at the Univ. of Lyons (from 1919 until the end of his career).

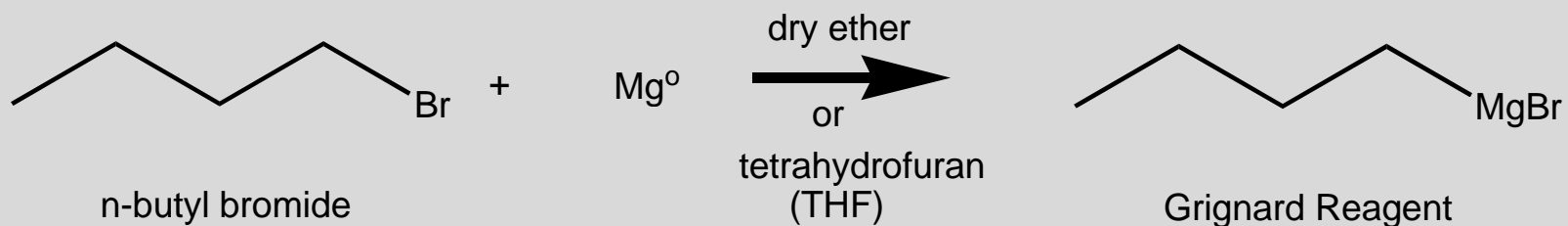
Grignard Reagents

- **Grignard reagent:** an organomagnesium compound
 - prepared by addition of an alkyl, aryl, or alkenyl (vinylic) halide to Mg metal in diethyl ether or THF

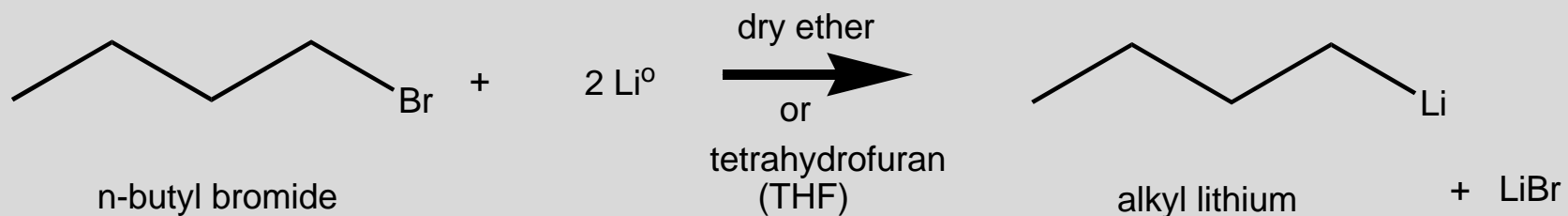


An Alternative to Grignard Reagents are Alkyl Lithiums

Both are prepared from alkyl, vinyl, and aryl halides under anhydrous conditions



recall: THF = 

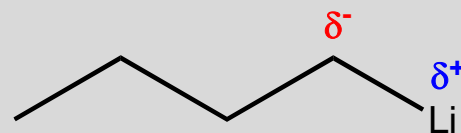


Grignard and Organolithium Reagents

- Given the difference in electronegativity between carbon and magnesium (lithium), the C-Mg (C-Li) bond is polar covalent, with $C^{\delta-}$ and $Mg^{\delta+}$ ($Li^{\delta+}$)
 - Grignard and organolithium reagents behave like carbanions
- Carbanion: an anion in which carbon has an unshared pair of electrons and bears a negative charge



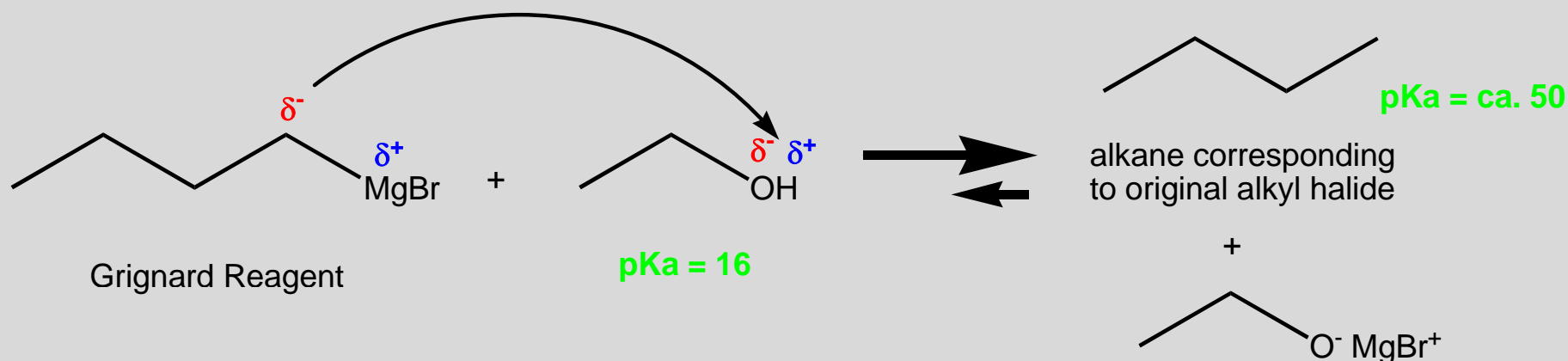
Grignard Reagent



alkyl lithium

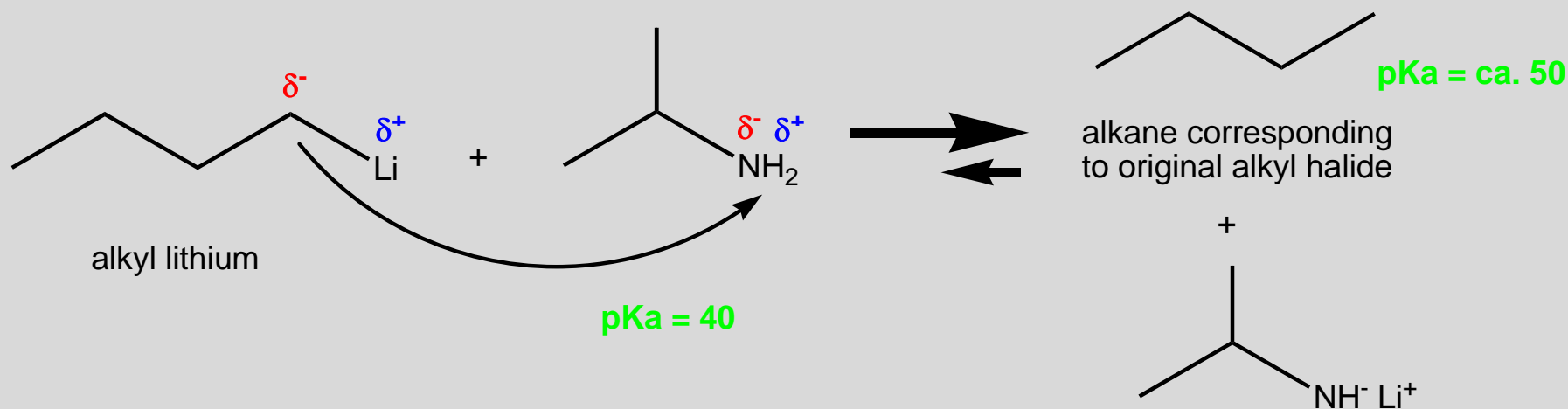
Grignard and Organolithium Reagents

- Carbanion: an anion in which carbon has an unshared pair of electrons and bears a negative charge
 - Carbanions are strong bases--they are easily quenched by even very weak acids (water, alcohols, amines, amides, carboxylic acids, even terminal alkynes). A limitation to utility!



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Limitations

- Can't make Grignards with acidic or electro-philic functional groups present in the molecule:

-

R_2NH pK_a 38-40

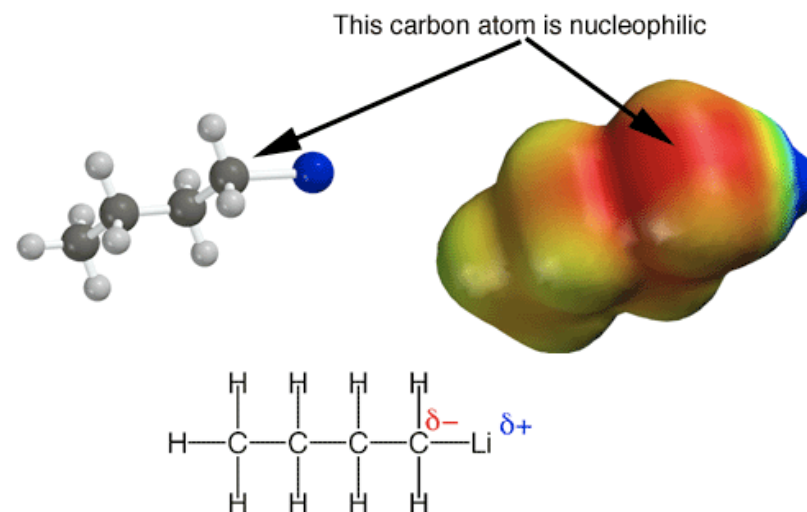
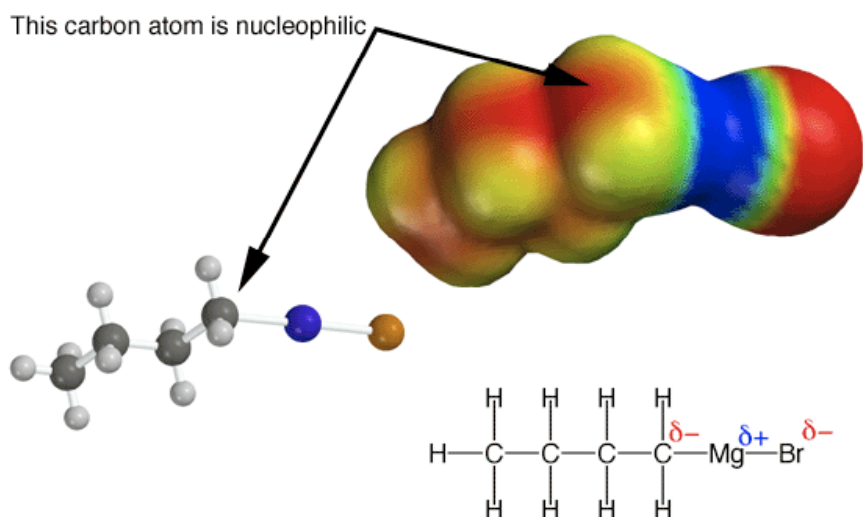
Terminal Alkynes pK_a 25

ROH pK_a 16-18

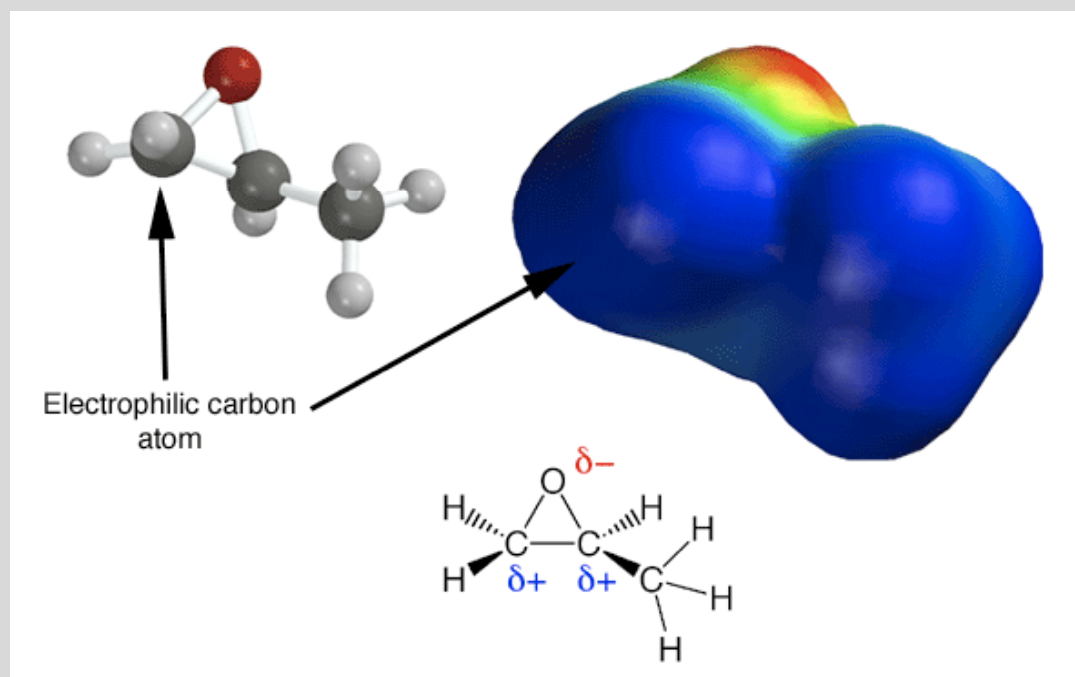
Carbonyls & Nitros pK_a 11-27

Grignard and Organolithium Reagents

- Carbanion: an anion in which carbon has an unshared pair of electrons and bears a negative charge
 - Carbanions are also great nucleophiles. This is the reason for their great utility!



- Key Point: Grignard and Organolithium Reagents
 - Great nucleophiles that add efficiently to electrophilic carbons, such as epoxides and carbonyl group of aldehydes, ketones and esters. However, their basicity can be a limitation!
 - Epoxides illustrate how many common organic functional groups contain electrophilic carbons



Grignard and Organolithium Reagents

- Carbanions (nucleophiles) can react with electrophilic carbon centers in favorable cases. The net result is a carbon-carbon bond--a big deal!
- Grignards and organolithium reagents react with many oxygen-containing electrophiles, but not with alkyl halides.
- We'll illustrate this with epoxides.
- Recall, acidic protons will “kill” our reagents and/or won't allow them to be generated in the first place

Grignard reagents react productively with:

formaldehyde to give primary alcohols

aldehydes to give secondary alcohols

ketones to give tertiary alcohols

esters to give tertiary alcohols

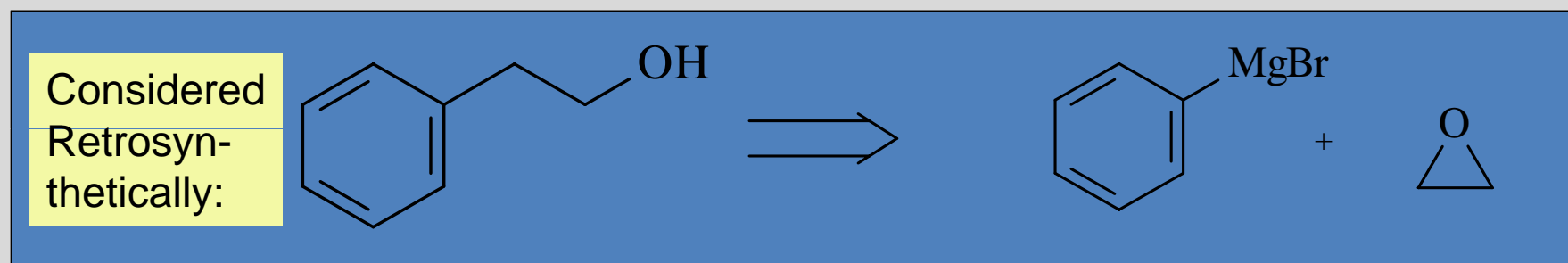
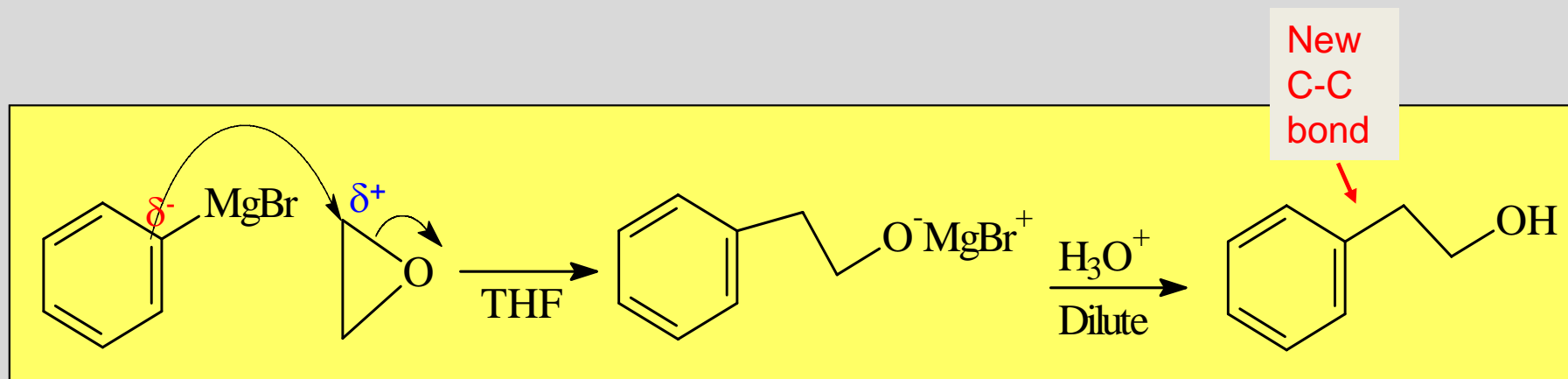
CO₂ to give acids

epoxides to give primary alcohols

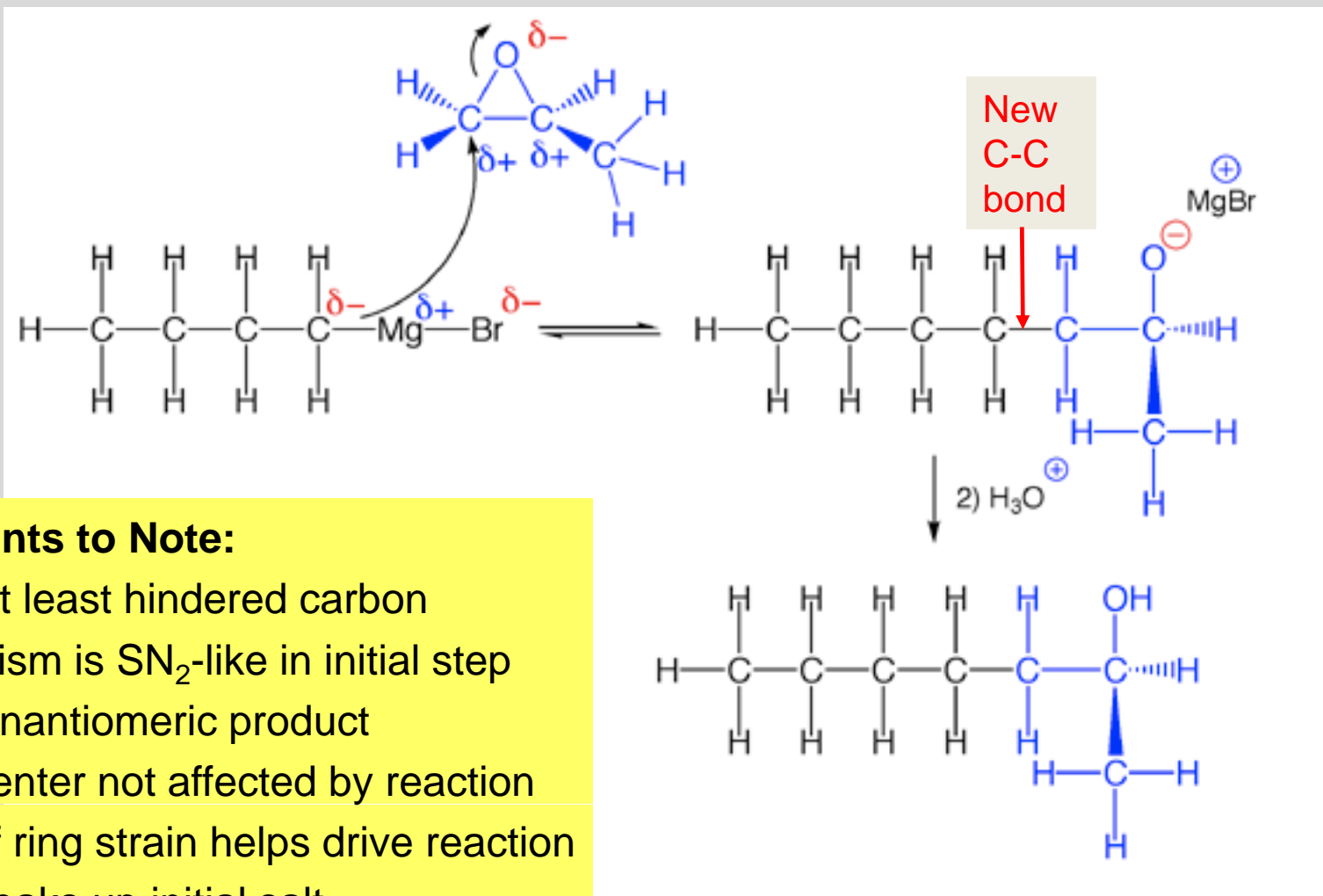


The one we are
choosing for the sake
of initial illustration

Epoxides: The Example We Want to Stress



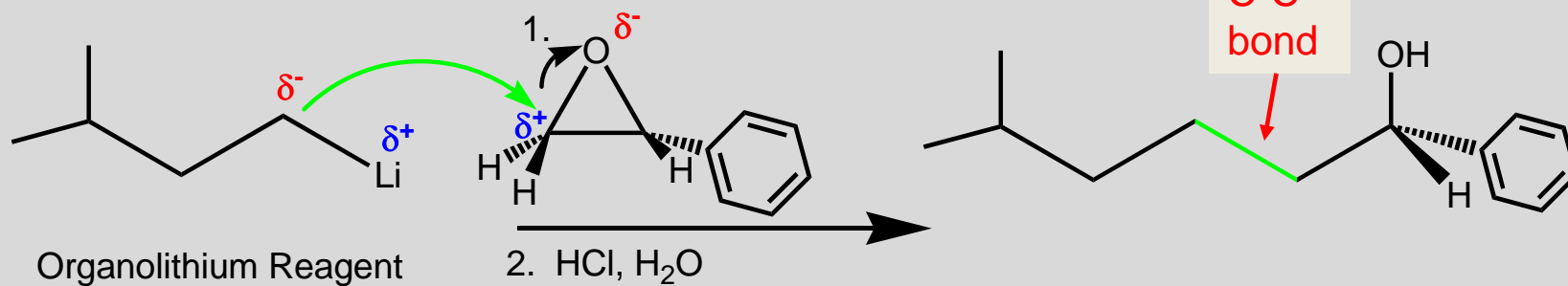
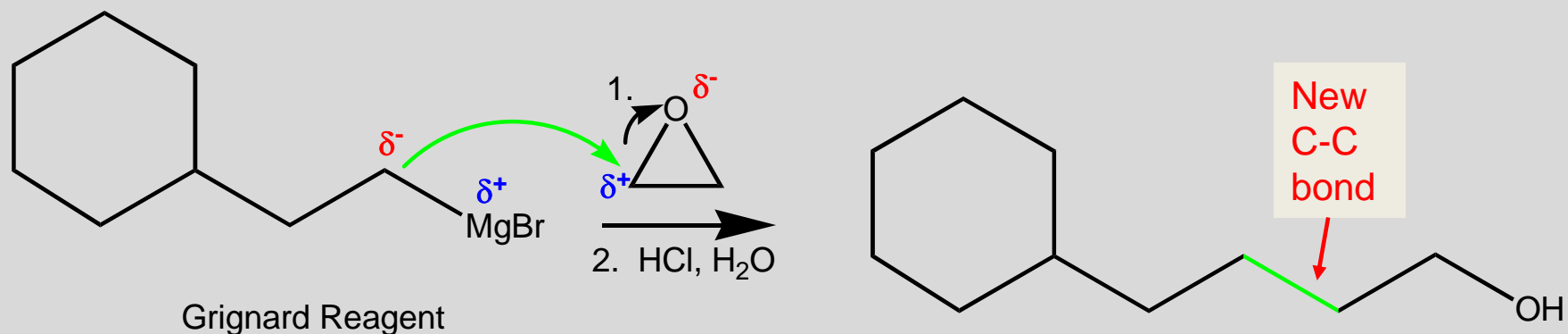
Detailed Mechanism Highlighting Retention of Stereochemistry



Key Points to Note:

- Attack at least hindered carbon
- Mechanism is $\text{S}_{\text{N}}2$ -like in initial step
- Single enantiomeric product
- Chiral center not affected by reaction
- Relief of ring strain helps drive reaction
- H_3O^+ breaks up initial salt

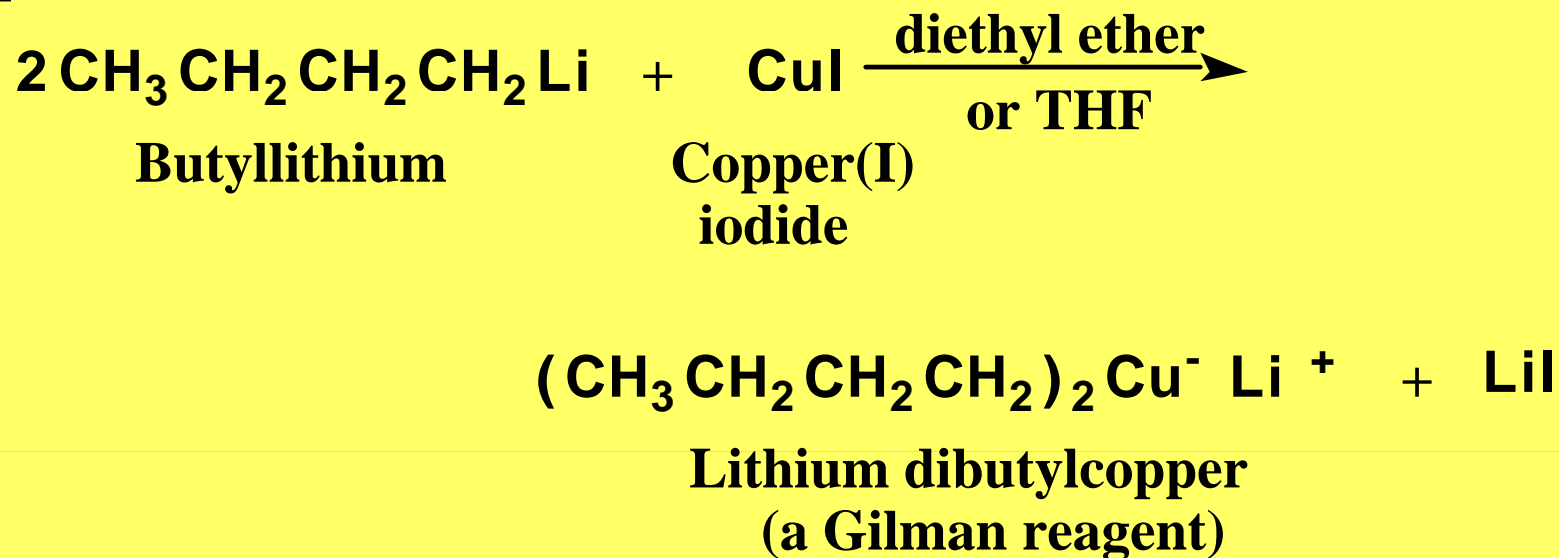
Two More Examples of Additions to Epoxides



Note: Stereochemistry at epoxide retained in product

Gilman Reagents

- Lithium diorganocopper reagents, known more commonly as **Gilman reagents**
 - prepared by treating an alkyl, aryl, or alkenyl lithium compound with Cu(I) iodide

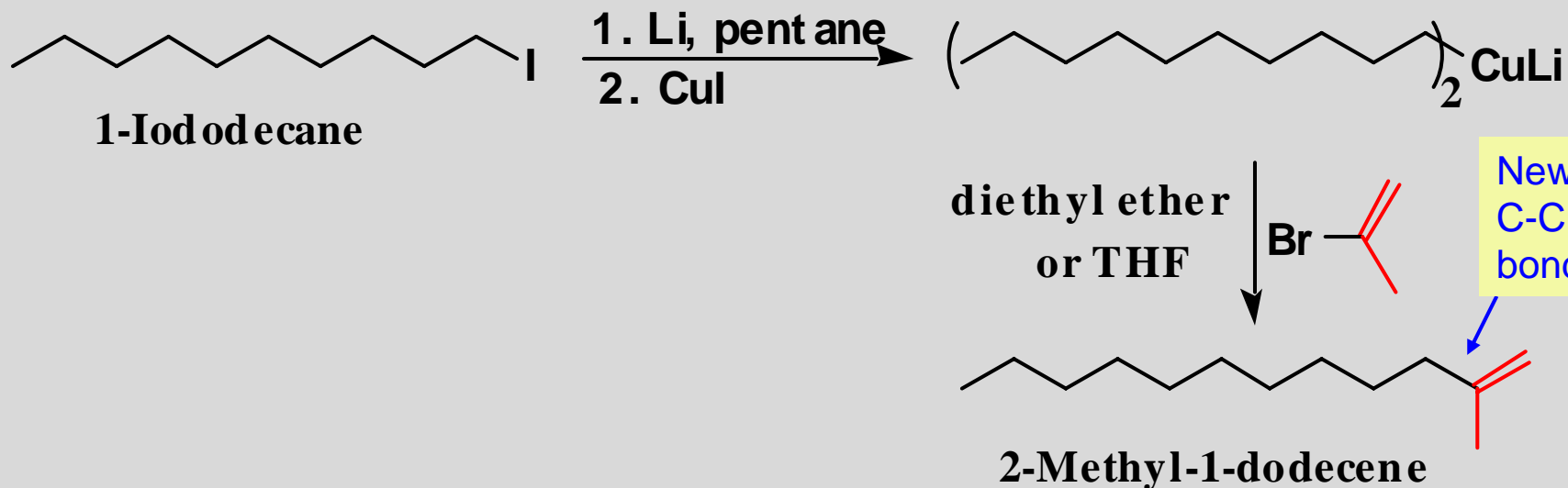


Gilman Reagents

- Coupling with organohalogen compounds
 - form new carbon-carbon bonds by coupling with alkyl and alkenyl chlorides, bromides, and iodides. (Note that this doesn't work with Grignard or organolithium reagents. THEY ARE TOO BASIC AND DO E2 ELIMINATIONS.)

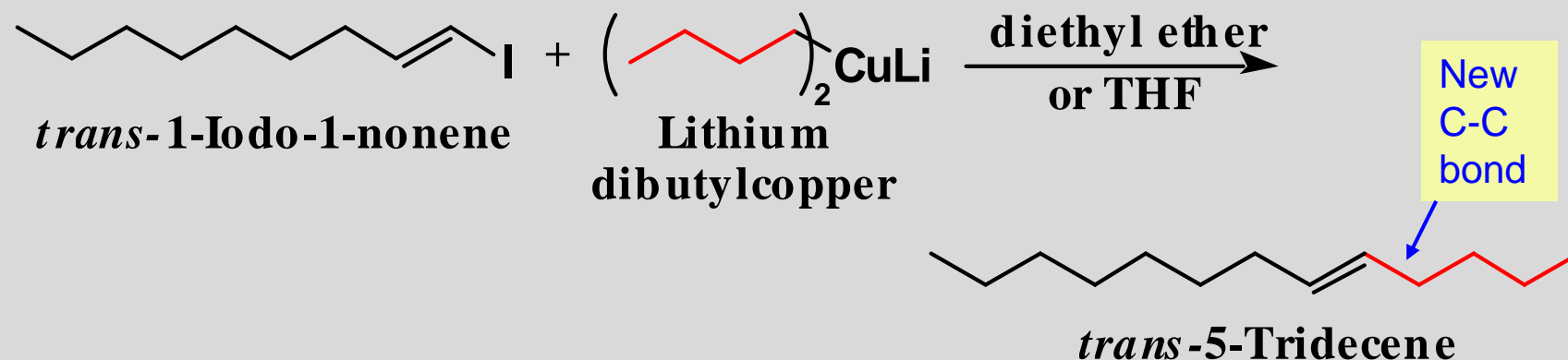


• Example



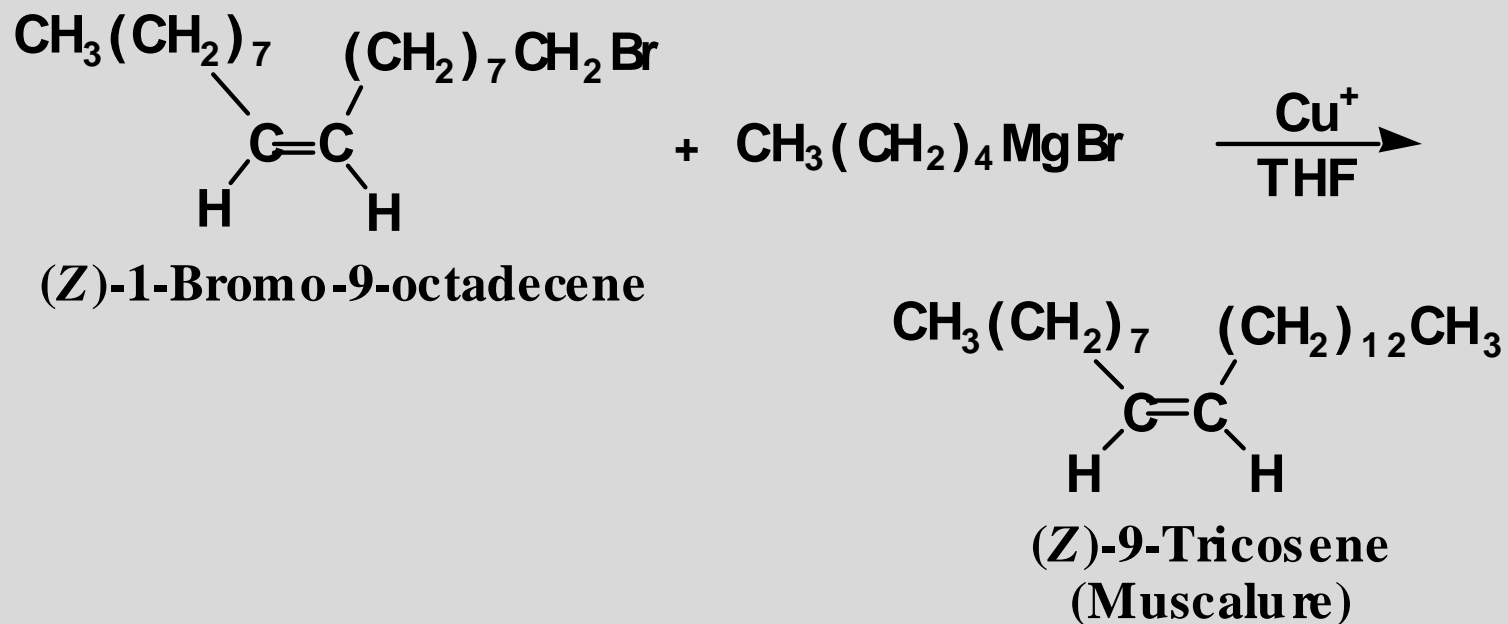
Gilman Reagents

- coupling with a vinylic halide is stereospecific; the configuration of the carbon-carbon double bond is retained



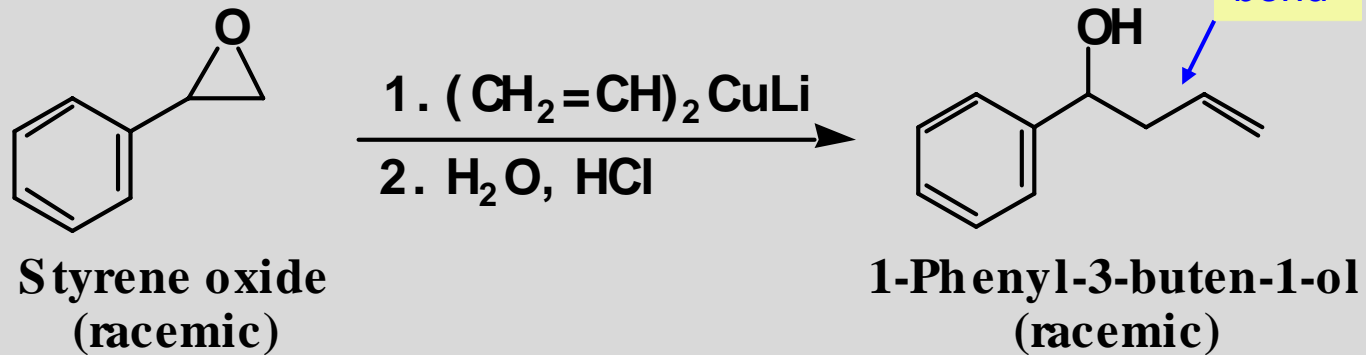
Gilman Reagents

- A variation on the preparation of a Gilman reagent is to use a Grignard reagent with a catalytic amount of a copper(I) salt



Gilman Reagents

- Reaction with epoxides
 - regioselective ring opening (**attack at least hindered carbon**)



Interim Summary of Introduction to Organometallic Reagents...

Organolithium reagents and Grignard reagents are very basic but also great nucleophiles. They react with epoxides at the less hindered site to give a two-carbon chain extended alcohol. They do not couple with alkyl-, aryl-, or vinyl halides.

Gilman reagents react with epoxides as do organolithium reagents and Grignard reagents. However, they also add to alkyl-, aryl-, and vinyl halides to make new C-C bonds.

Feeling Lost?

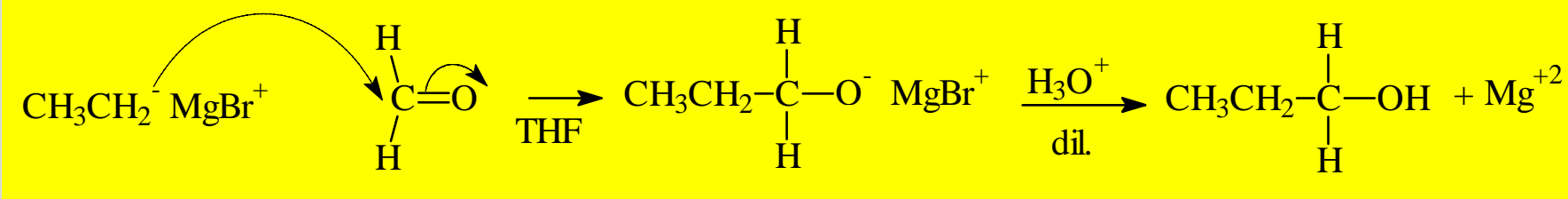


Fortunately, Dr. Iverson will be back on Monday!

Meanwhile....

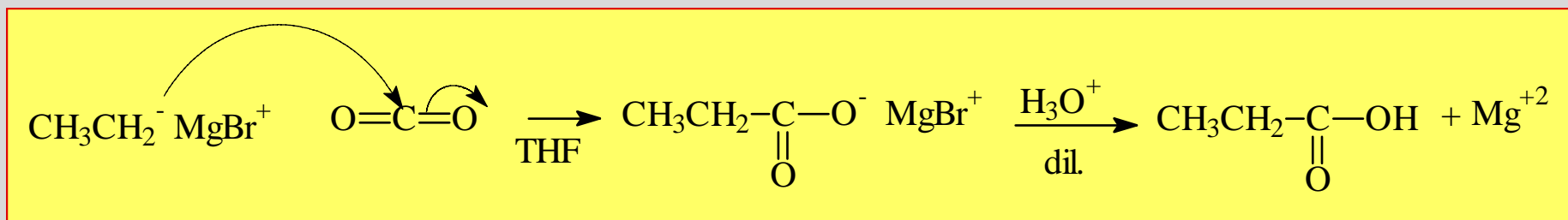
Back to Grignard Reagents...

- Addition of a Grignard reagent to formaldehyde followed by H_3O^+ gives a 1° alcohol



- This sequence (mechanism) is general and important!

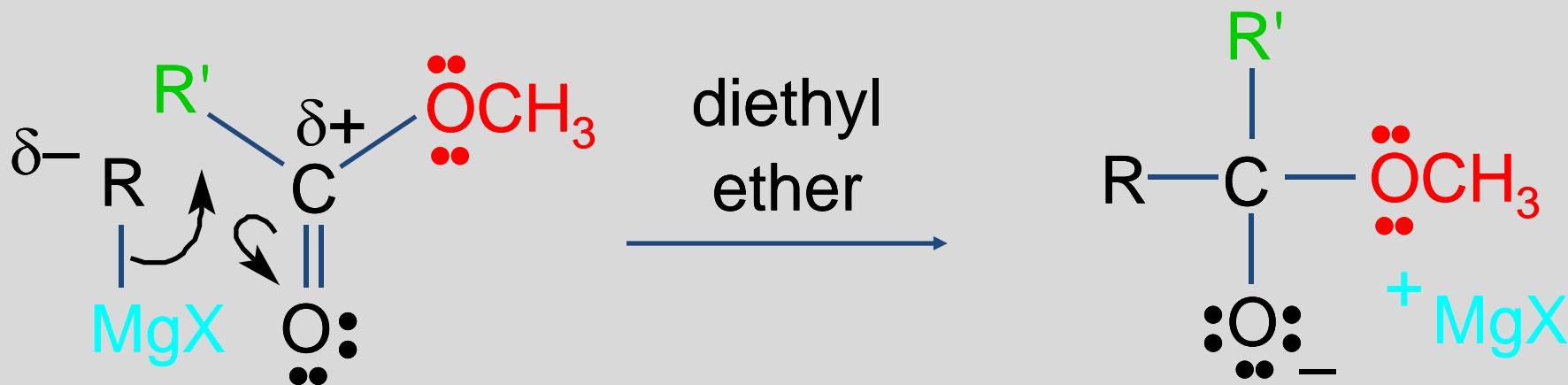
Grignard Reactions



These are valuable and important reactions...

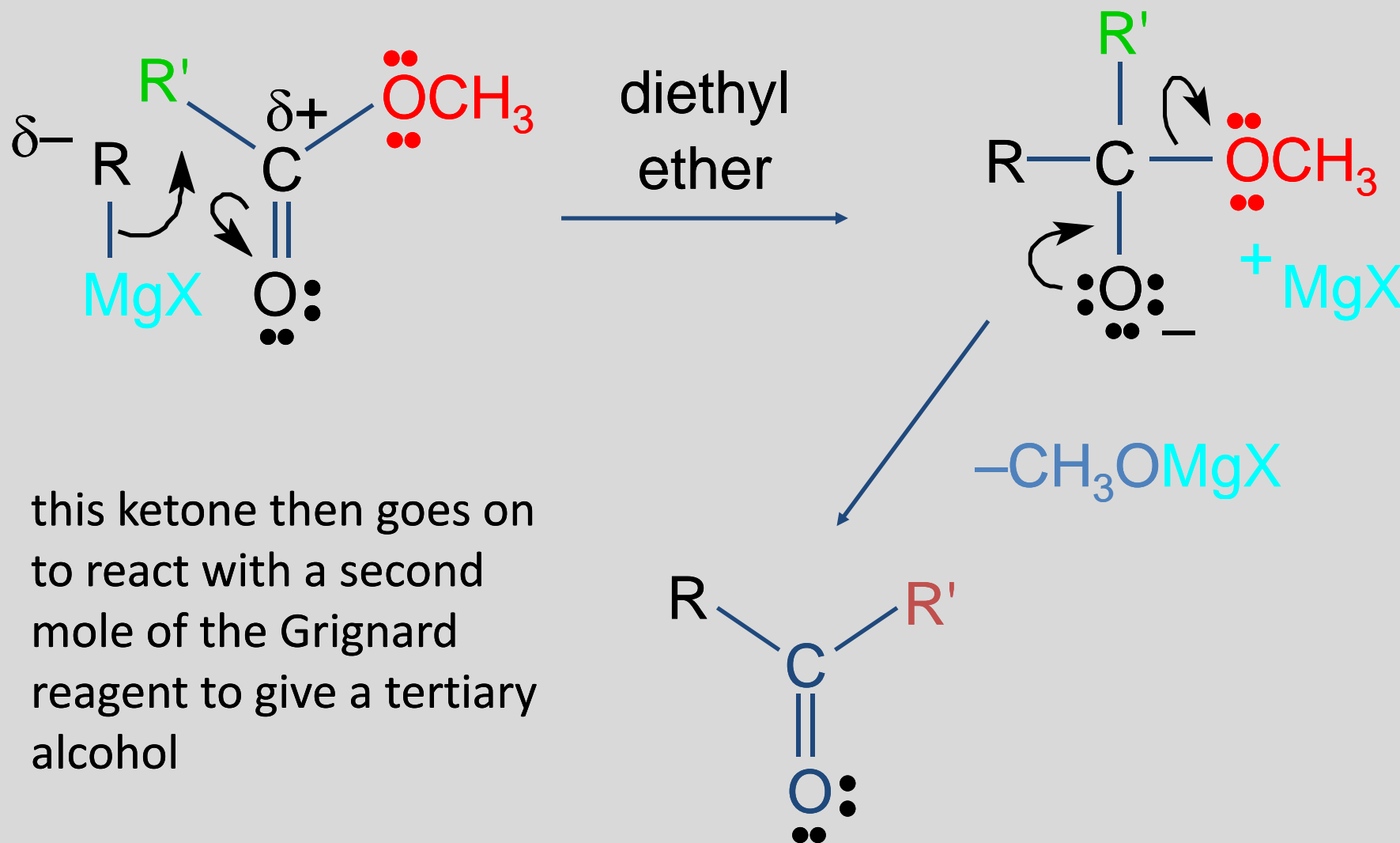
Please add to your card stock!

Grignard reagents react with esters



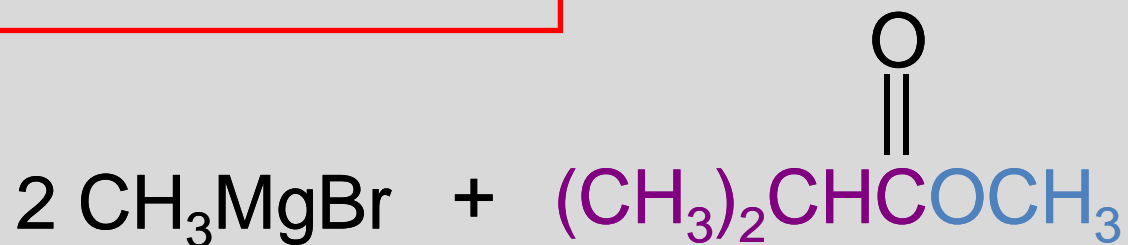
but species formed is unstable and dissociates under the reaction conditions to form a ketone

Grignard reagents react with esters



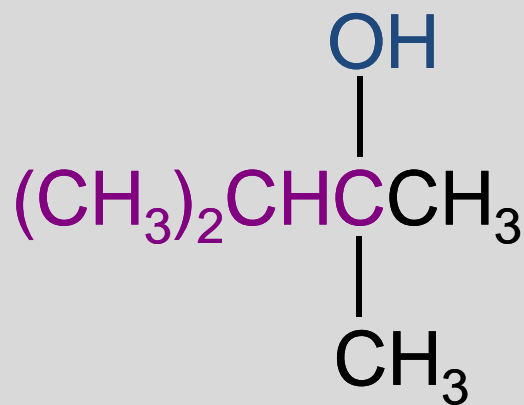
this ketone then goes on to react with a second mole of the Grignard reagent to give a tertiary alcohol

Example



1. diethyl ether

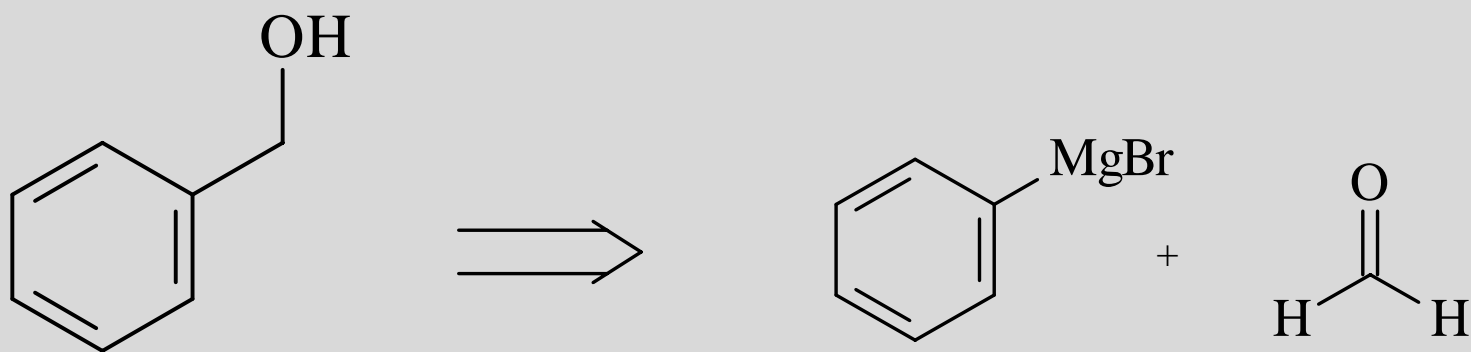
2. H_3O^+



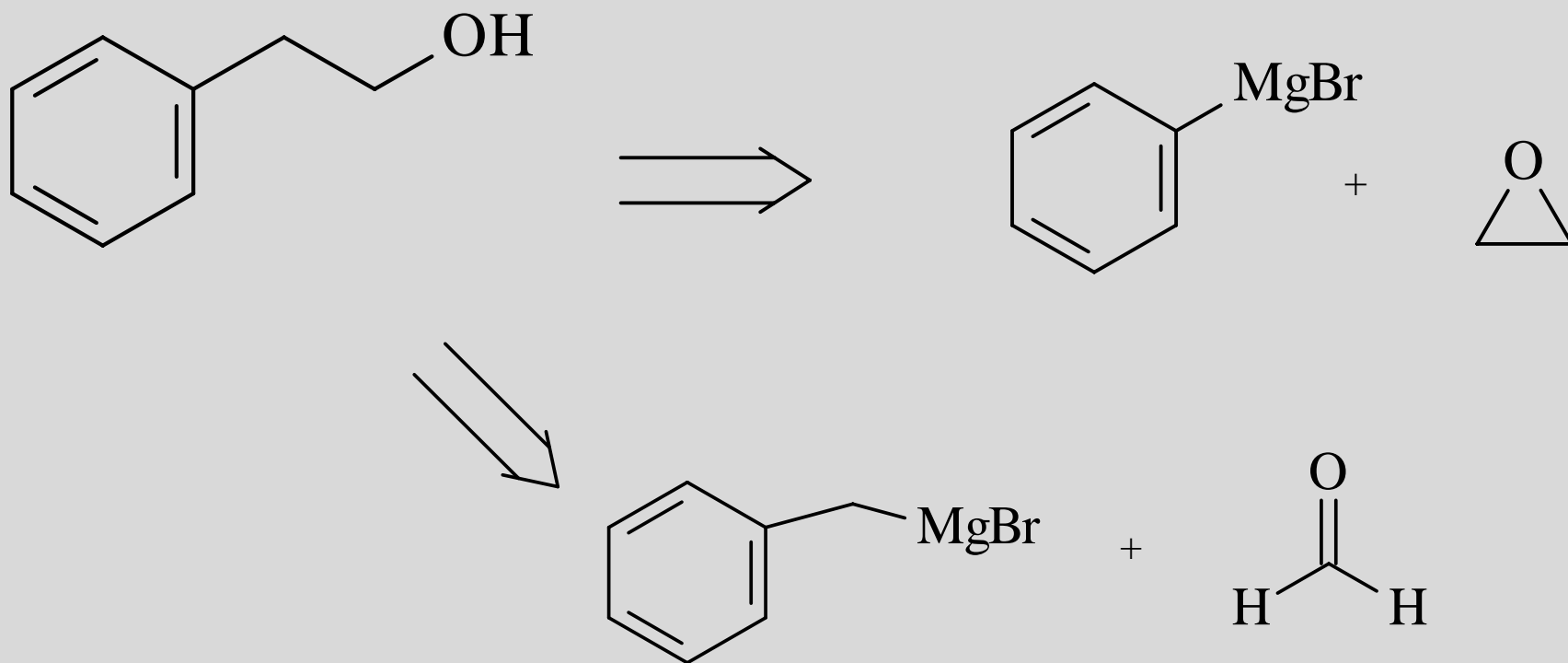
(73%)

Two of the groups attached to the tertiary carbon come from the Grignard reagent

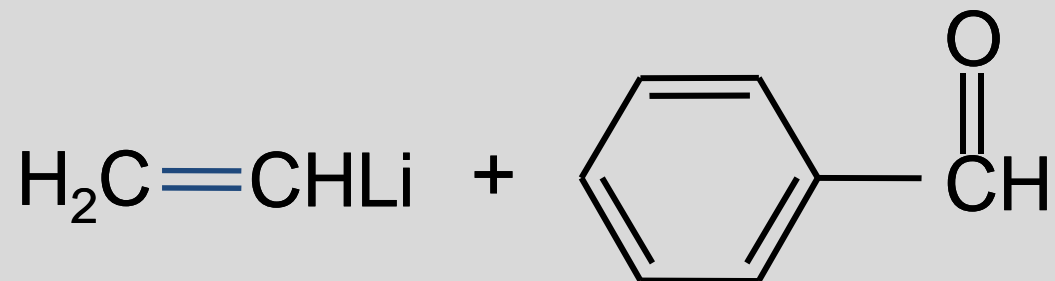
Practice



Practice

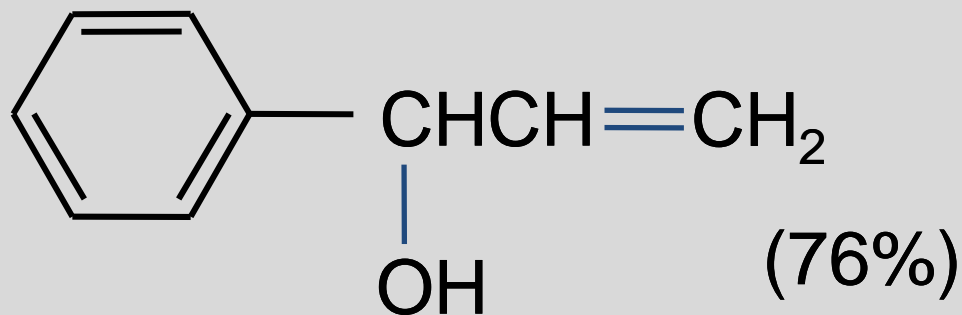


The Same Chemistry is seen With Organolithium Reagents



1. diethyl ether

2. H_3O^+



Practice

