

Organometallic Compounds

(Chapter 15)

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Organometallic compound

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

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Organometallic reagents have 2 general types of reactions:

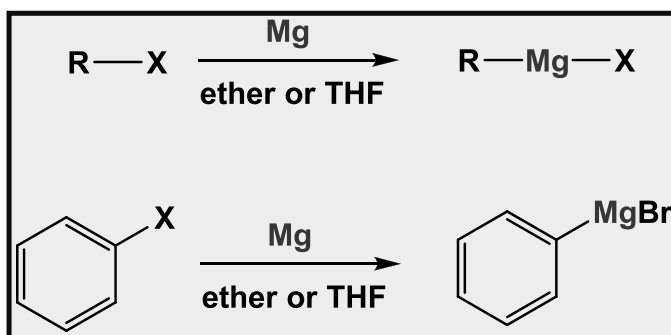
1. As Strong bases (Bronsted-Lowry)
2. As nucleophilic reagents.

Regard the alkyl group as "R-"

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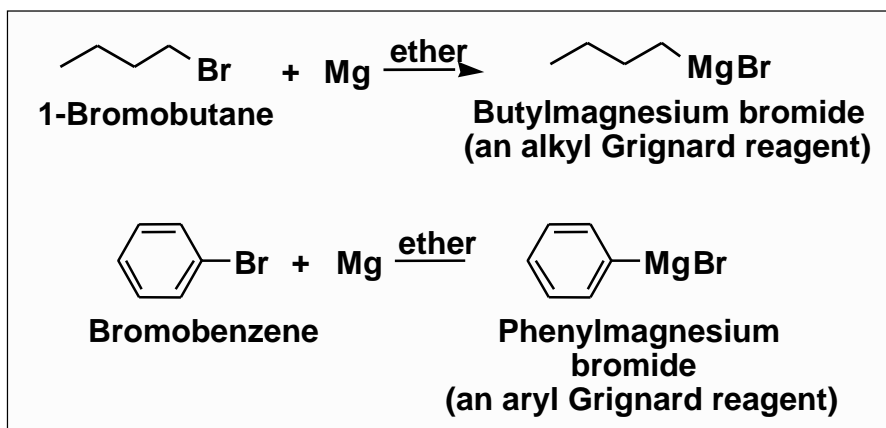
Grignard Reagents

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



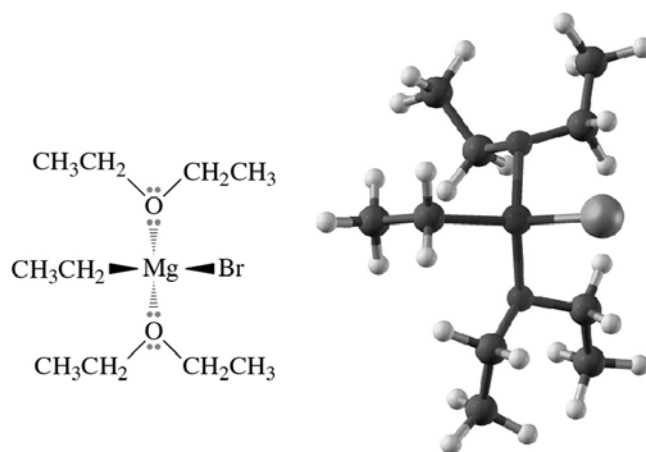
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Preparation of Grignard reagents:



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- Grignard reagents dissolve as coordination compounds solvated by ether – ethylmagnesium bromide, EtMgBr



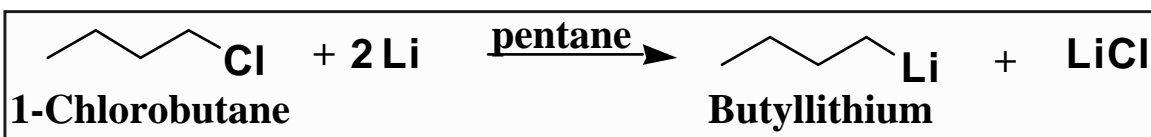
Ethylmagnesium bromide dietherate

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Organolithium reagents

- **Organolithium reagents**

- prepared by reaction of an alkyl, aryl, or alkenyl halide with lithium metal



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The carbon-metal bonds in RMgX and RLi are polar covalent

C-M Bond	Difference in Electronegativity	Percent Ionic character*
C-Li	2.5 - 1.0 = 1.5	60
C-Mg	2.5 - 1.2 = 1.3	52
C-Al	2.5 - 1.5 = 1.0	40
C-Zn	2.5 - 1.6 = 0.9	36
C-Sn	2.5 - 1.8 = 0.7	28
C-Cu	2.5 - 1.9 = 0.6	24
C-Hg	2.5 - 1.9 = 0.6	24

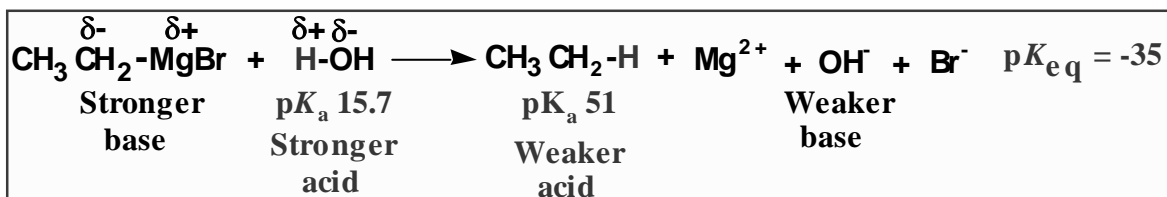
Increasing Ionic Character

Stronger Nucleophile

$$\text{*Percent ionic character} = \frac{E_C - E_M}{E_C} \times 100$$

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- Reaction with proton donors:
 - RMgX and RLi are strong bases



– they react readily with these proton acids

R_2NH	$\text{RC}\equiv\text{CH}$	ROH	HOH	ArOH	RSH	RCOOH
pK_a 38-40	pK_a 25	pK_a 16-18	pK_a 15.7	pK_a 9-10	pK_a 8-9	pK_a 4-5
1° and 2° Amines	Terminal alkynes	Alcohols	Water	Phenols	Thiols	Carboxylic acids

This is often an undesired side reaction-to be avoided!!

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Organometallic reagents have 2 general types of reactions:

1. As Strong bases (Bronsted-Lowry)
2. As nucleophilic reagents:



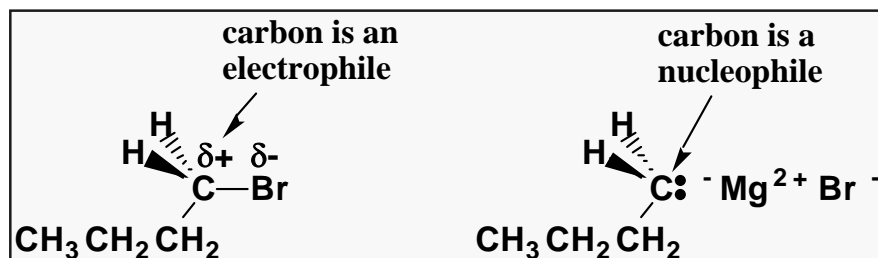
Regard the alkyl group as "R⁻"

Organometallic reagents

ORGANIC LECTURE SERIES

- **RMgX and RLi are valuable in synthesis as nucleophiles**

- the carbon bearing the halogen is transformed from an electrophile to a nucleophile

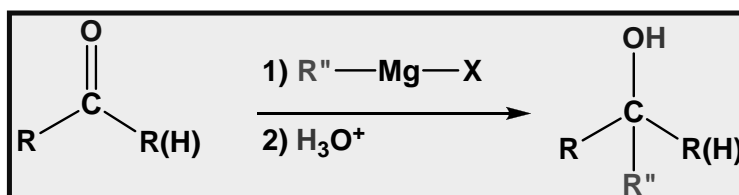
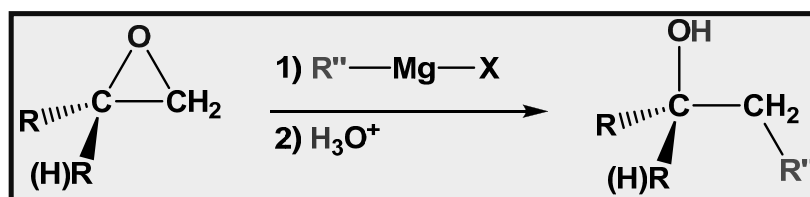


- their most valuable use is addition to the electrophilic carbon of C=O groups of aldehydes, ketones, carboxylic esters, and acid chlorides to form a new carbon-carbon bonds

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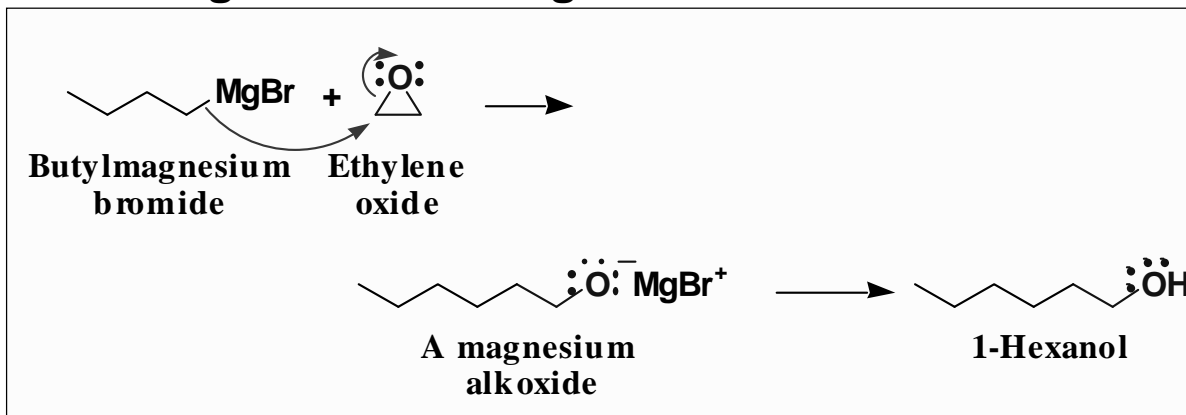
General Reactions of Grignard Reagents

ORGANIC LECTURE SERIES



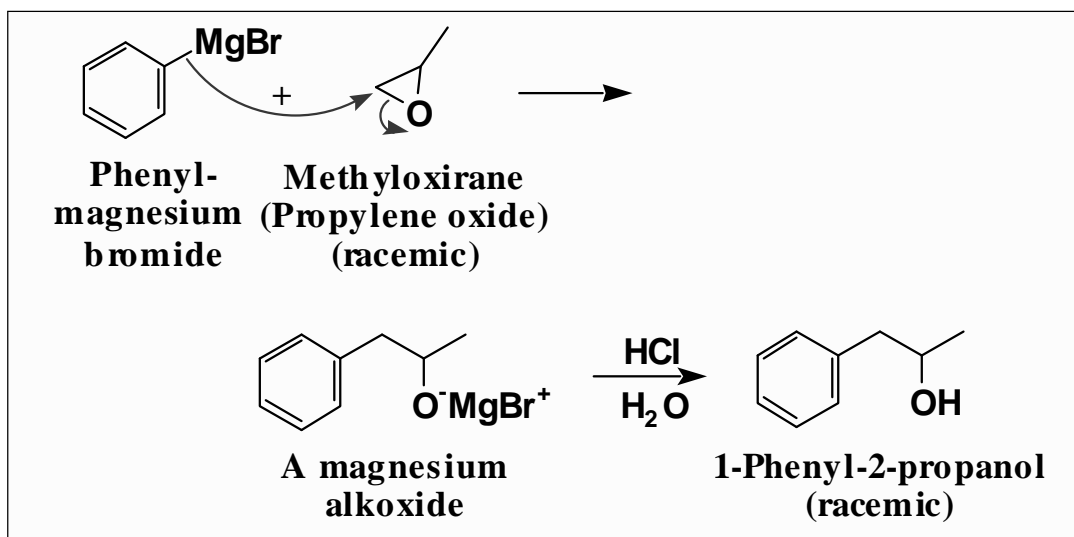
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- Reaction with oxiranes (epoxides)
 - reaction of RMgX or RLi with an oxirane followed by protonation gives a **primary alcohol with a carbon chain two carbons longer than the original chain**



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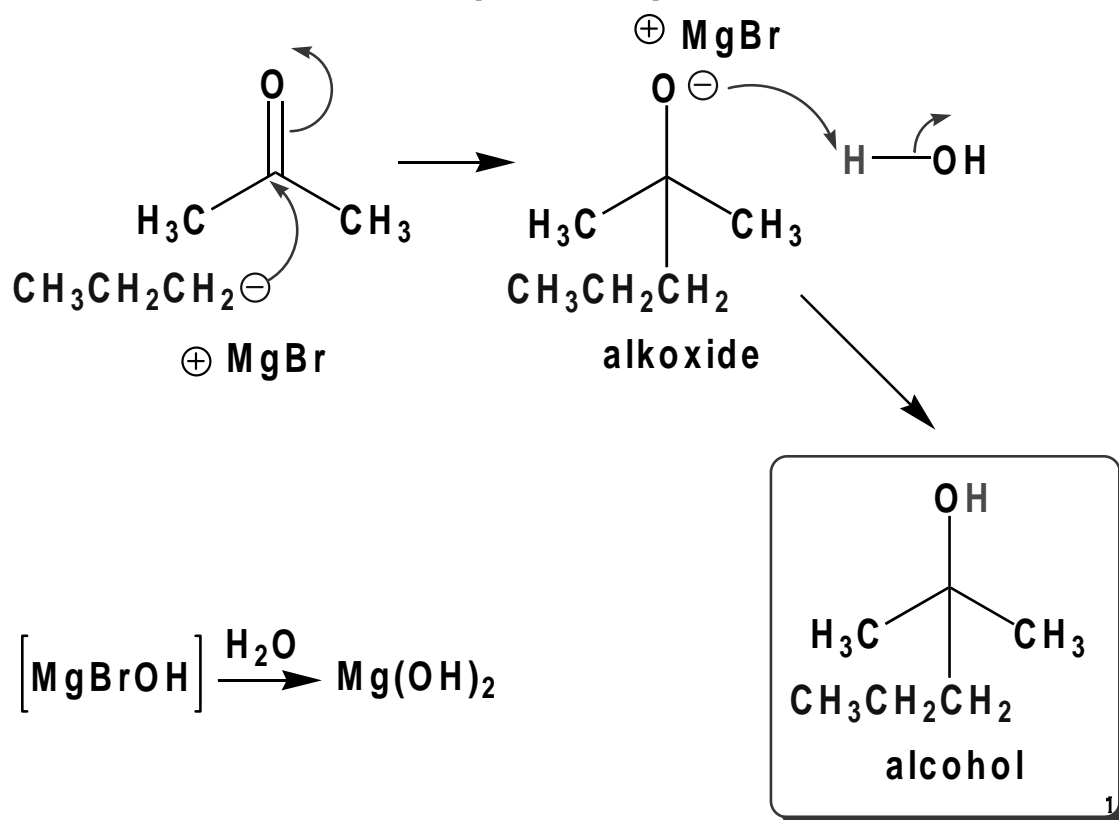
- Reaction with oxiranes (epoxides)
 - the major product corresponds to S_N2 attack of RMgX or RLi on less hindered carbon of the epoxide



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A Simple Example:

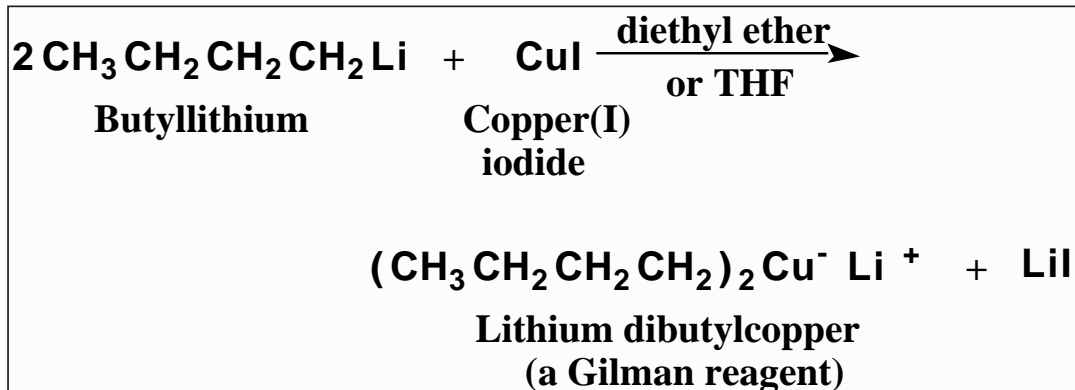
ORGANIC LECTURE SERIES



Gilman reagents

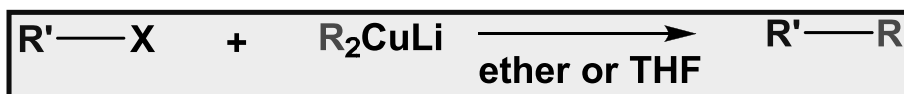
ORGANIC LECTURE SERIES

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



Coupling within organohalogen compounds

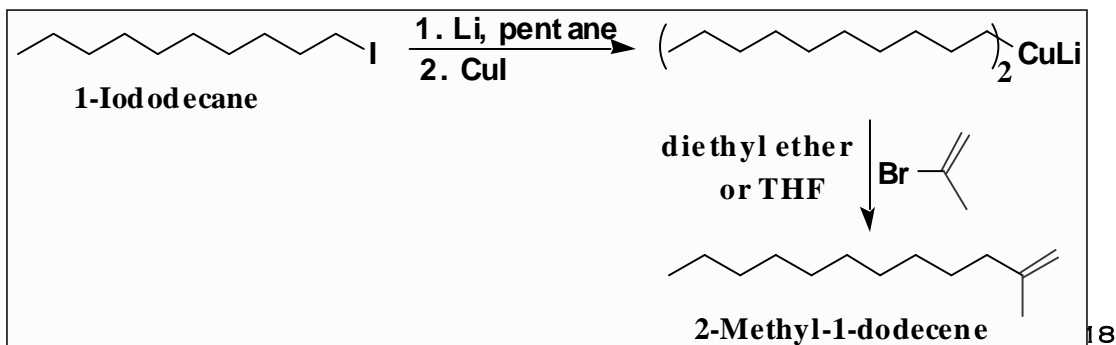
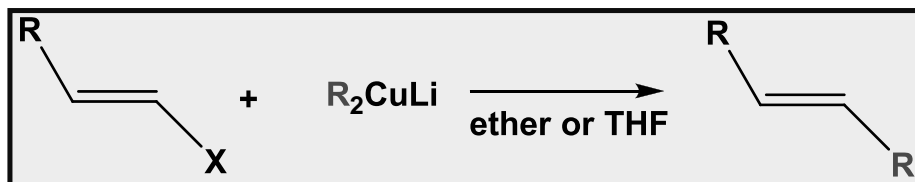
- form new carbon-carbon bonds by coupling with alkyl chlorides, bromides, and iodides



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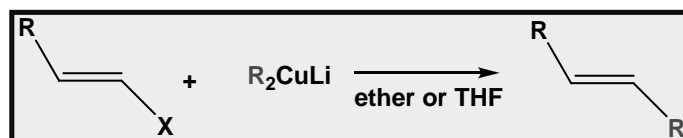
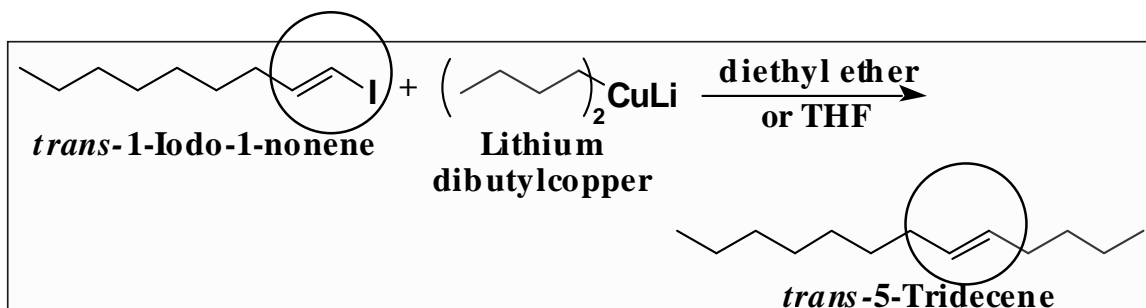
Coupling within organohalogen compounds

- form new carbon-carbon bonds by coupling with alkenyl chlorides, bromides, and iodides



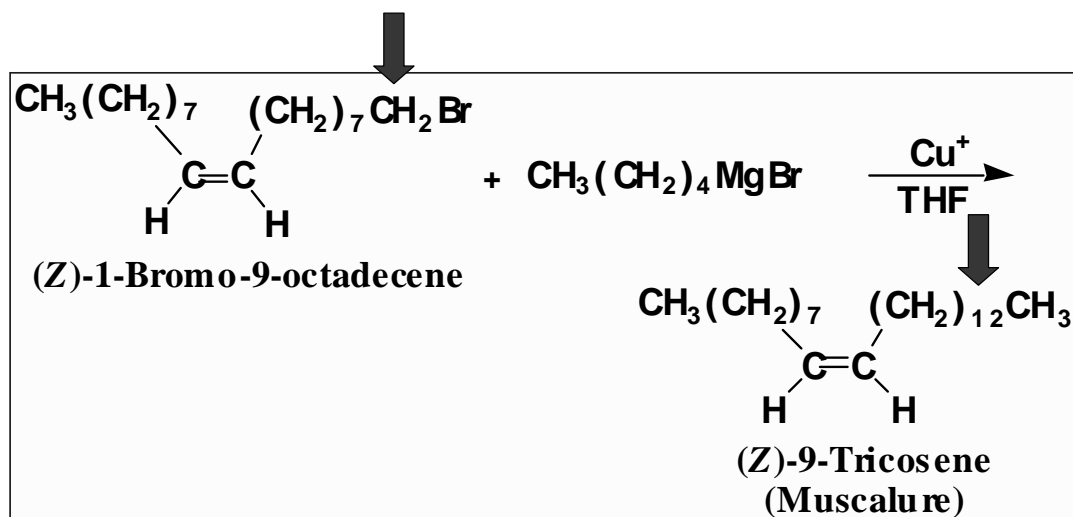
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coupling with a vinylic halide is stereospecific: the configuration of the carbon-carbon double bond is retained



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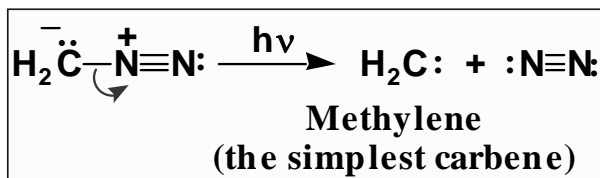
- A variation on the preparation of a Gilman reagent is to use a Grignard reagent with a catalytic amount of a copper(I) salt



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Carbenes & Carbenoids

- **Carbene**, R_2C : a neutral molecule in which a carbon atom is surrounded by only six valence electrons
- Methylene, the simplest carbene
 - prepared by photolysis or thermolysis of diazomethane



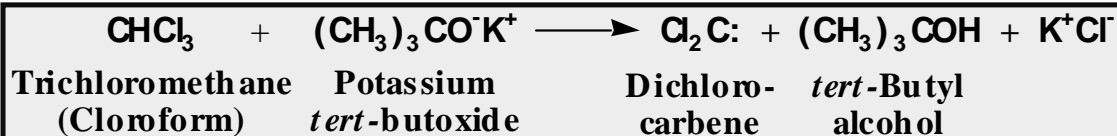
- methylene prepared in this manner is so nonselective that it is of little synthetic use

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Carbenes & Carbenoids

Dichlorocarbene

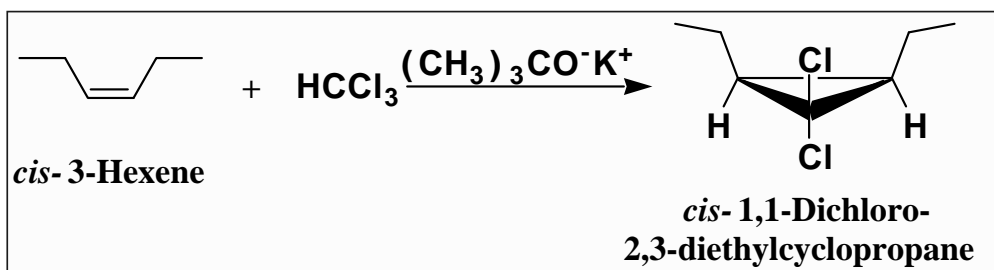
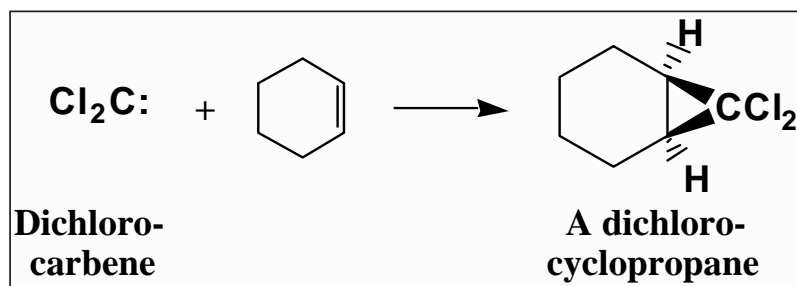
- prepared by treating chloroform with potassium *tert*-butoxide



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Dichlorocarbene

reacts with alkenes to give dichlorocyclopropanes



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• Simmons-Smith reaction

- a way to add **methylene** to an alkene to form a cyclopropane
- generation of the Simmons-Smith reagent



Diiodo-
methane Zinc-copper
 couple

Iodomethylzinc iodide
(Simmons-Smith reagent)

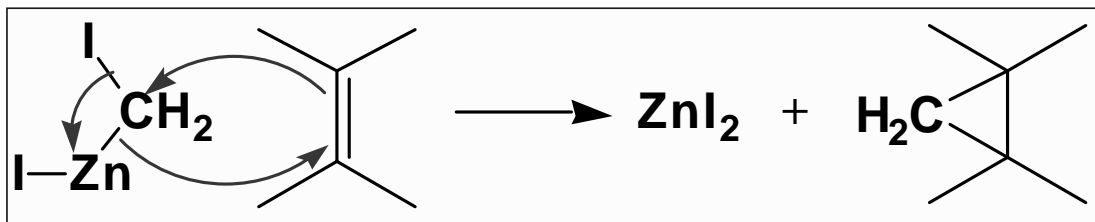
- this organozinc compound reacts with a wide variety of **alkenes to give cyclopropanes**

(prepared by: Zn dust; CuCl & heat)

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Simmons-Smith reaction:

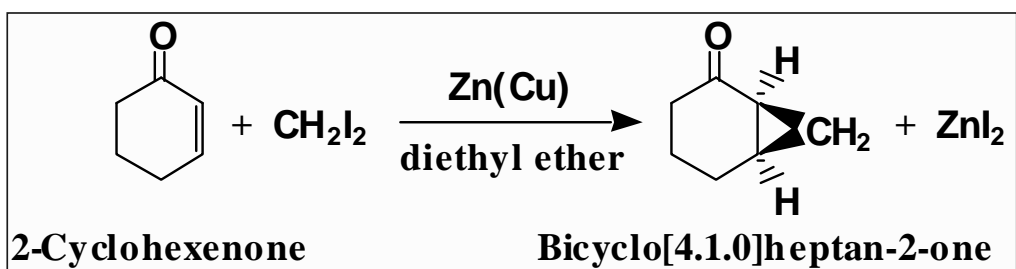
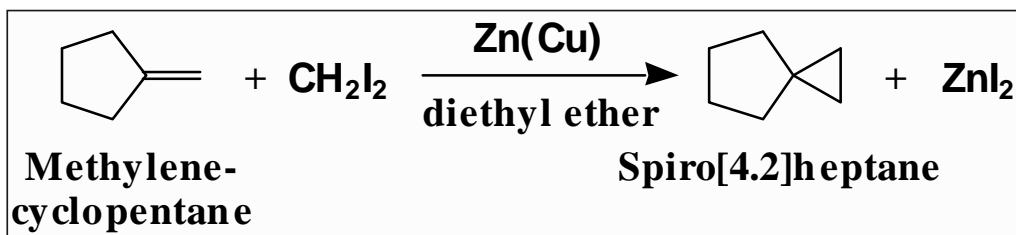
the organozinc compound reacts with an alkene by a concerted mechanism*



***concerted mechanism**-one in which there is simultaneous bond breaking and bond formation.

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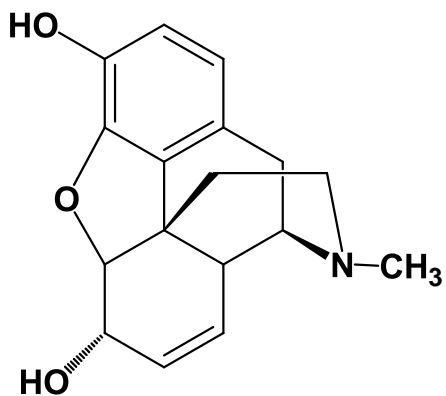
Uses of the Simmons-Smith reagent:



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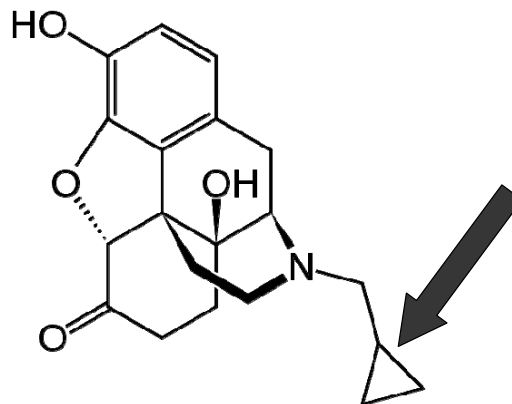
Example of a drug which has a cyclopropane moiety:

Morphine



- Sedation
- Analgesia
- Euphoria
- Constipation (GI)
- Respiratory depression
- Addiction liability

Naltrexone



opioid receptor antagonist used primarily in the management of alcohol dependence and opioid dependence.