

Organic Chemistry Workshop Spring 2021

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The workshop will discuss resonance, acidity, nucleophilic substitution, elimination, additions (alkenes/alkynes), organolithium and organomagnesium compounds as bases and nucleophiles.

- **Day 1** (1pm – 5pm on January 12th): Resonance, acidity, nucleophilic substitution, elimination

- **Day 2** (1pm – 5pm on January 13th): Additions (alkenes/alkynes), organolithium and organomagnesium compounds as bases and nucleophiles

A) Octet rule

Hydrogen has only a first shell and thus only one 1 orbital → **hydrogen forms one bond!**

Covalent bond → two electrons shared between two atoms.

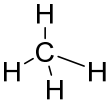



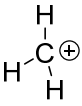



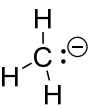



Carbon is a second shell atom → there are four orbitals in the second shell (one s and three p orbitals) → **a maximum of 8 electrons is allowed**

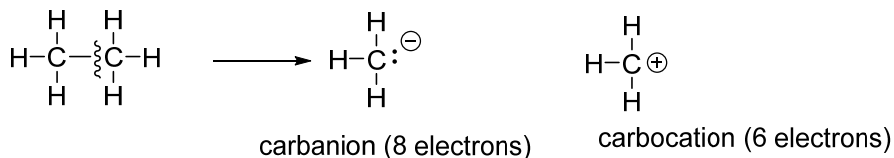
All second shell atoms can form a maximum of four bonds attached to that atom → 2 electrons involved in each bond to give a total of 8 electrons.

The observation of a maximum of four bonds to second-row atoms was demonstrated by G.N. Lewis in 1916.

SECOND ROW ATOMS WILL BE MOST STABLE WITH EIGHT ELECTRONS IN THE OUTER SHELL.

Formal Charges

4 valence electrons	5 valence electrons	6 valence electrons	7 valence electrons
IV	V	VI	VII
C Si Ge Sn Pb	N P As Sb Bi	O S Se Te Po	F Cl Br I
			
4 bonds (formal charge=0)	3 bonds+ 1 lone pair (formal charge=0)	2 bonds+ 2 lone pairs (formal charge=0)	1 bonds+ 3 lone pairs (formal charge=0)
			
3 bonds, no lone pair (formal charge=+1)	4 bonds and no lone pair (formal charge=+1)	3 bonds+ 1 lone pair (formal charge=+1)	2 bonds+ 2 lone pairs (formal charge=+1)
			
3 bonds+ 1 lone pair (formal charge=-1)	2 bonds + 2 lone pairs (formal charge=-1)	1 bond + 3 lone pairs (formal charge=-1)	no bonds+ 4 lone pairs (formal charge=-1)

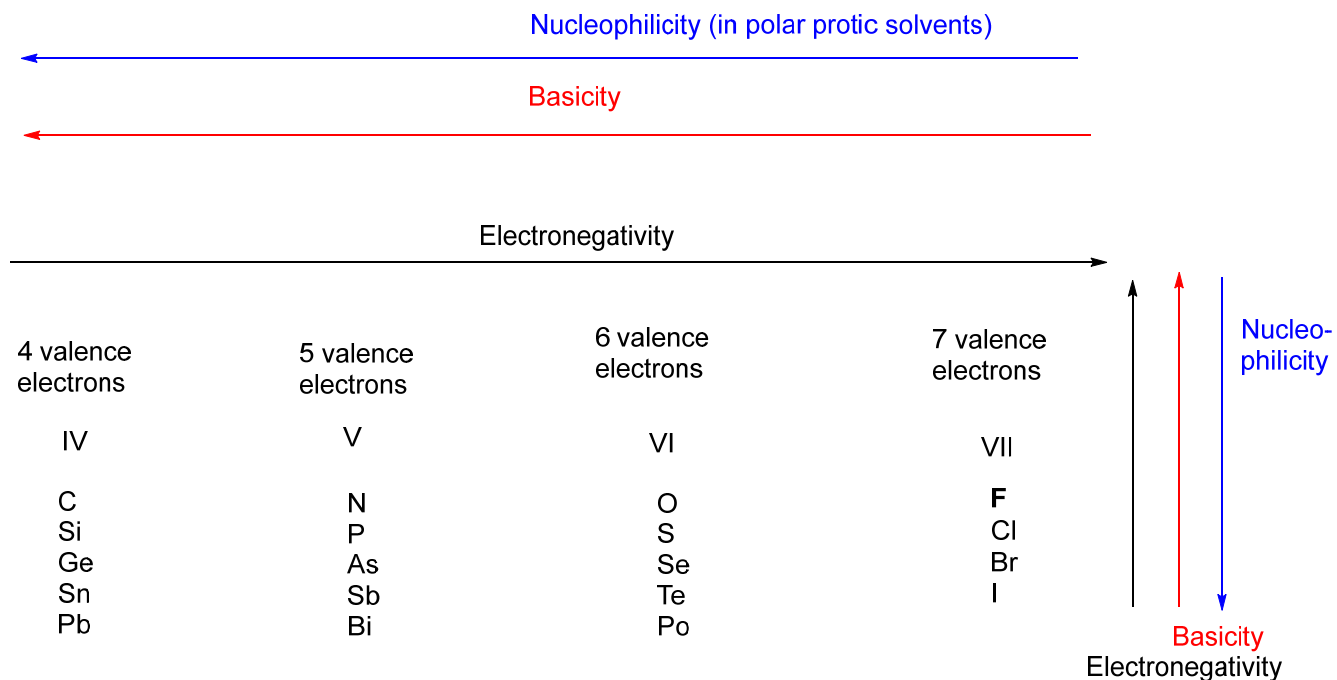


Bond breaks in such a way that one carbon takes both electrons from the bond and the other carbon takes no electrons

B) Electronegativity and Bond Polarity

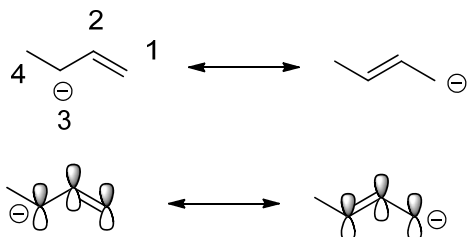
Electrons are shared in covalent bonds. By sharing electrons, each atom can have a filled outer shell to satisfy the octet rule. However, two electrons may not be shared equally in a bond. The electrons can be closer to one atom than the other on-time average. When a bond is between identical atoms, the electrons will be shared equally. When the bond is between two different atoms, the electrons will not be shared equally. The property of atoms attracting electrons is called **ELECTRONEGATIVITY**. When two different atoms are bonded, the more electronegative of the two atoms will attract more electrons on-time average.

Basicity trends are important when ranking by acidity!



Fluorine is the most electronegative atom!

C) Hybridization = number of sigma bonds + number of lone pairs



Exception: Carbon 3 hybridization is sp^2 and not sp^3 . The definition above applied as would give you sp^3 hybridization for carbon 3. If you write a resonance structure, you will get the correct answer: sp^2 hybridization for carbon 3. The following statement can help you to determine the hybridization of carbon 3 quickly. "If an atom (X) has one or more lone pairs of electrons and it is bonded to an sp^2 hybridized atom, then the hybridization of the atom (X) is also sp^2 . This **is not a rule**, and it is only given to you to help you to determine hybridization without writing the resonance structure. However, **the correct answer comes from the resonance structure**.

Atomic Orbitals:	s	p	d	f
	1	3	5	7

no of atomic orbitals = no of hybrid orbitals (if we combine 4 atomic orbitals, we generate 4 hybrid orbitals)

sp^3 hybridization \rightarrow 1s atomic orbital + 3 p atomic orbitals \rightarrow 4 sp^3 hybrid orbitals

sp^2 hybridization \rightarrow 1s atomic orbital + 2 p atomic orbitals \rightarrow 3 sp^2 hybrid orbitals + 1 unhybridized p orbital

sp hybridization \rightarrow 1s atomic orbital + 1p atomic orbital \rightarrow 2 sp hybrid orbitals + 2 unhybridized p orbitals

Sigma (σ) bond \rightarrow single bond \rightarrow forms from sp^3 , sp^2 , sp , and p orbitals

Pi (π) bond \rightarrow multiple bond \rightarrow forms by side to side overlap of p orbitals (cannot form from sp^3 , sp^2 , or sp orbitals)

Double bond = one sigma bond + one pi bond

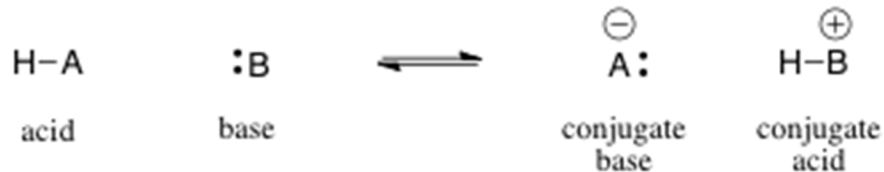
Triple bond = one sigma bond + 2 pi bonds

D) Key Points for Writing Resonance Structures

- 1) Write the Lewis structure of the analyzed compound
- 2) Only electrons move. Atoms do not move.
- 3) Only π (pi) electrons and lone pairs move. Pi electrons are electrons in pi bonds. Pi bonds are formed by the side-to-side overlap of unhybridized p orbitals.
- 4) Sigma bonds (single bonds) never move.
- 5) The total number of electrons in the overall structure does not change.

ONLY ELECTRONS IN P ORBITALS RESONATE!!!!

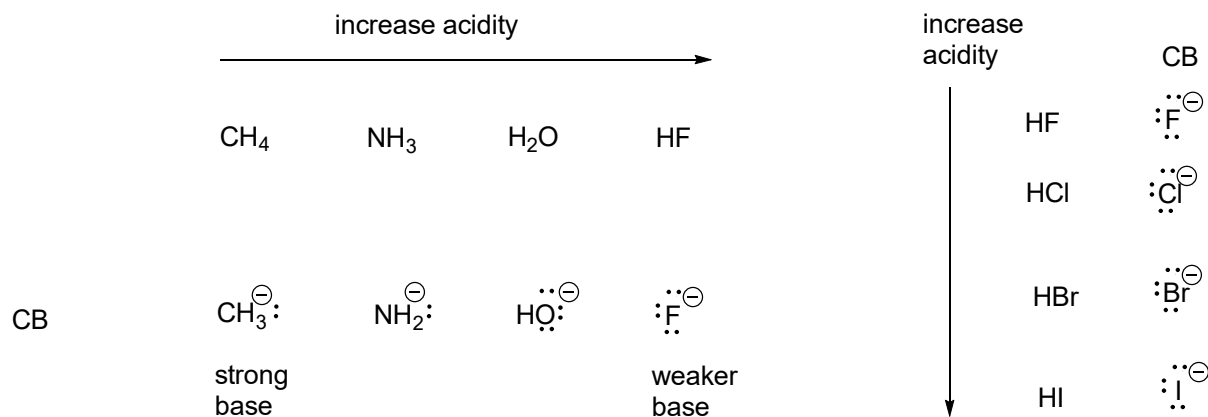
E) Acidity (Factors that Affect Acidity)



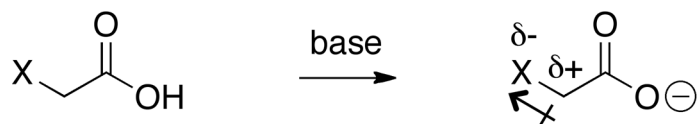
Strong Acid → Weak Conjugate Base

Weak Acid → Strong Conjugate Base

1) **Atom Effects:** The acidity of H-A increases from left to right across the row and increases down a column of the periodic table.

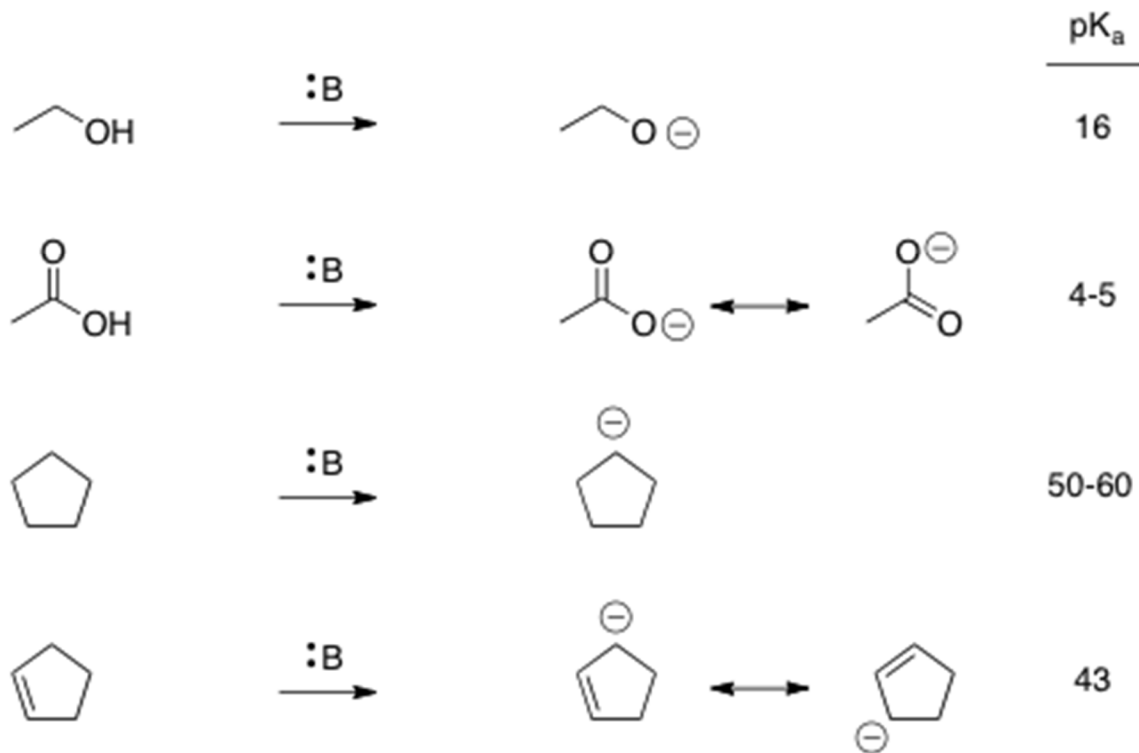


2) **Inductive Effects:** The acidity of H-A increases with the presence of an electron-withdrawing group in A

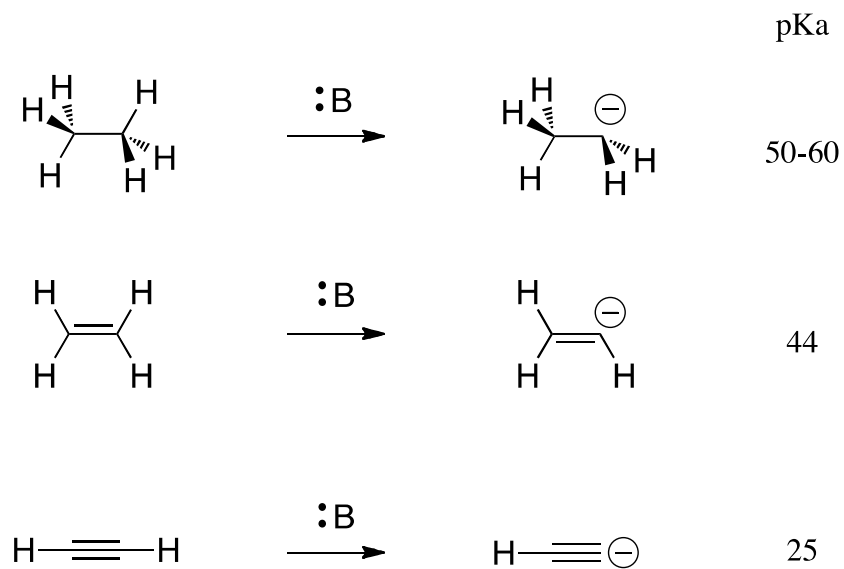


X	pK _a
H	4.8
Cl	2.9
F	2.6

3) **Resonance Effects:** The acidity of H-A increases when the conjugated base is resonance stabilized



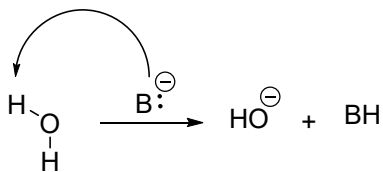
4) **Hybridization Effects:** The acidity of H-A increases as the percentage of s character increase



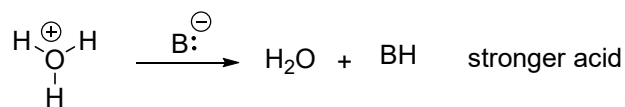
sp³ carbanion conjugate base has ~25% s character
sp² carbanion conjugate base has ~33% s character
sp carbanion conjugate base has ~50% s character

Explanation: s orbitals are closer to nucleus than p orbitals → an electron in s orbital experiences a stronger nuclear attraction than an electron in p orbital → higher s character indicate higher electronegativity → placing the negative charge on the sp hybridized carbon (from deprotonation of alkyne) is a more stable base (less basic)

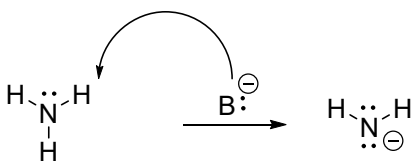
5) Charge also matters for acidity



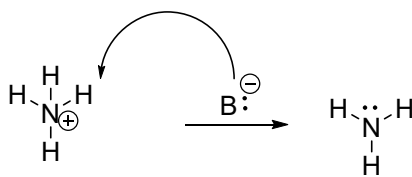
pka = 14



pka = - 1.7



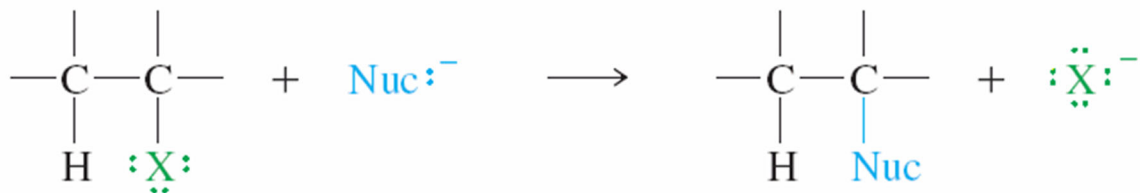
pka=38



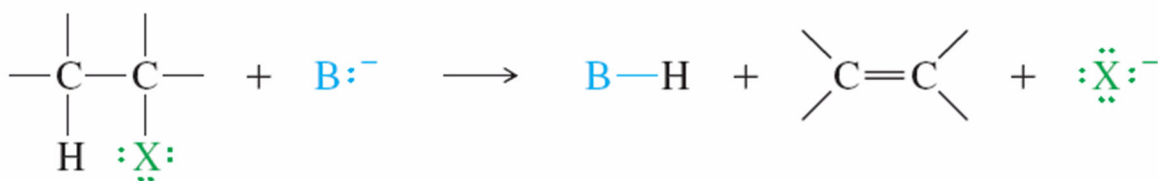
pka=9.2

F) Nucleophilic Substitution and Elimination Reactions

Nucleophilic Substitution (SN2 or SN1)



Elimination (E2 or E1)



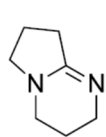
Substrate and Nucleophile

Type of Alkyl Halide	Poor NUC (e.g. EtOH)	Good NUC. Weak base (e.g. CH ₃ SNa)	Good NUC, strong, Unhindered base (e.g. CH ₃ ONa)	Good NUC, strong, hindered base (e.g. (CH ₃) ₃ CONa)
methyl	No reaction	S _N 2	S _N 2	S _N 2
1°				
unhindered	No reaction	S _N 2	S _N 2	E2
branched	No reaction	S _N 2	E2	E2
2°	Slow S _N 1, E1	S _N 2	S _N 2 or E2	E2
3°	S _N 1, E1	S _N 1, E1	E2	E2

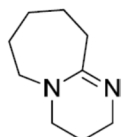
Particularities of SN and E reactions

mechanism	stereochemistry	rate	rearrangements
S_N2	Inversion	$k[\text{substrate}][\text{NUC}]$	never
S_N1	Racemic, sometimes inversion preference	$k[\text{substrate}]$	Often, if possible
E2	Anti-coplanar Zaitsev rule	$k[\text{substrate}][\text{base}]$	never
E1	Zaitsev rule	$k[\text{substrate}]$	Often, if possible

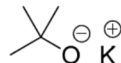
Bulky bases favor E2



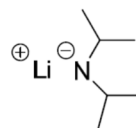
DBN



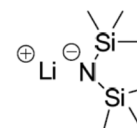
DBU



KOt-Bu

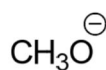
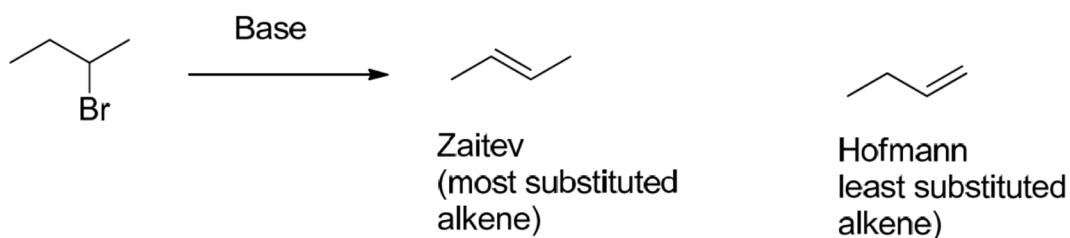


LDA

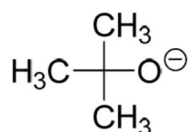


LHMDS

The use of bulky bases for E2 reactions favors the Hofmann product



81% Zaitsev product + 19% Hofmann product



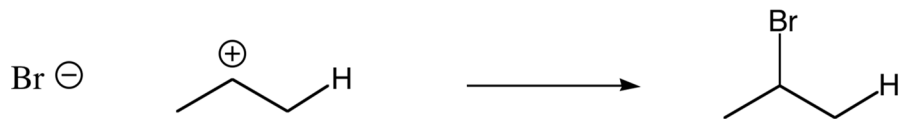
47% Zaitsev product + 53% Hofmann product

G) Additions to alkenes and alkynes

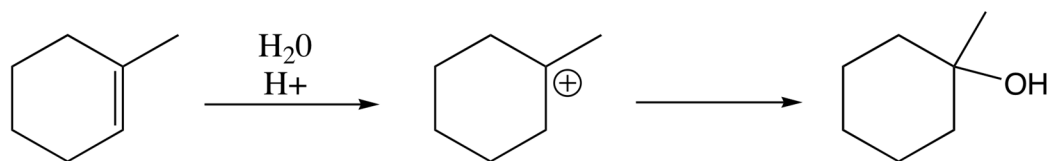
Alkenes

Pi electrons of the alkenes will react as nucleophiles to attack various electrophiles

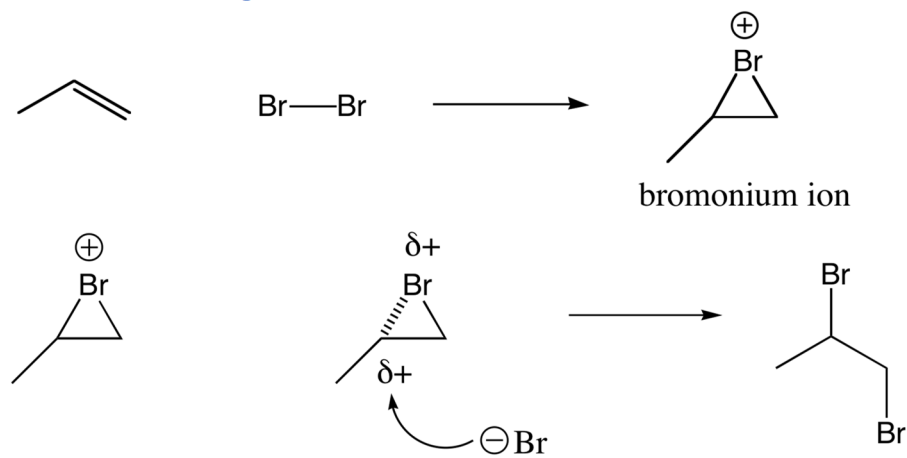
Addition of HX



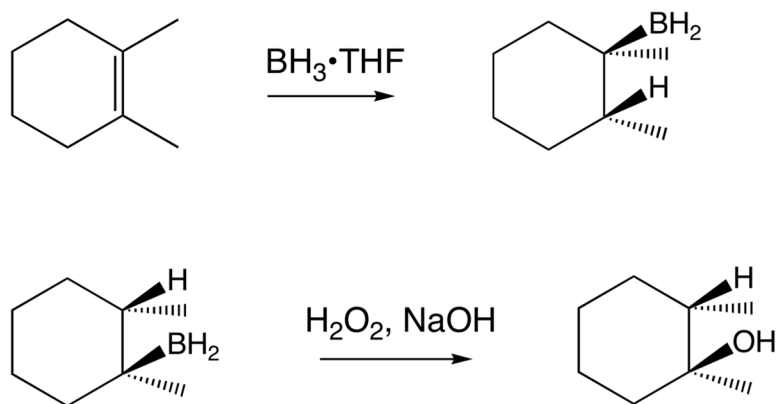
Addition of Water



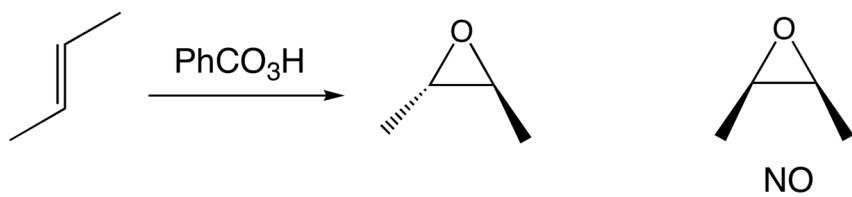
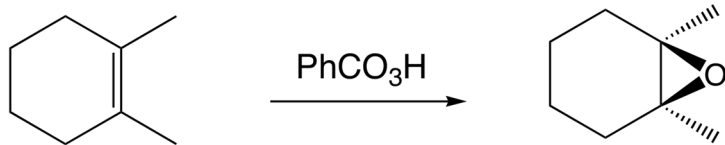
Addition of Halogens



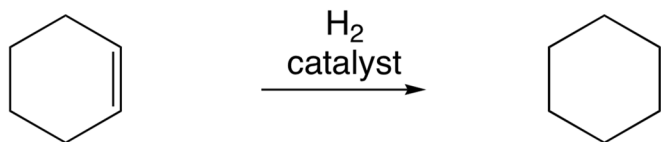
Hydroboration-Oxidation (anti-Markovnikov product)



Epoxydation



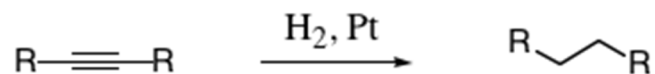
Hydrogenation (uses Pt, Pd, or Ni catalyst (syn addition))



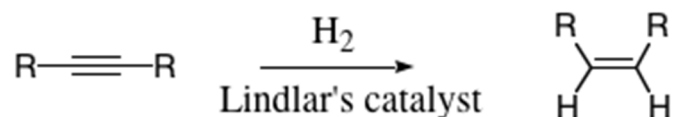
Alkynes

Pi electrons of the alkynes will react as nucleophiles to attack various electrophiles

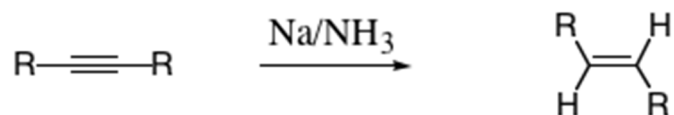
Hydrogenation (cannot stop at alkene)



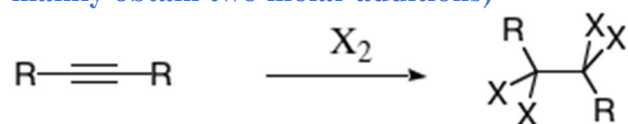
Hydrogenation with a poisoned catalyst (will give cis alkene)



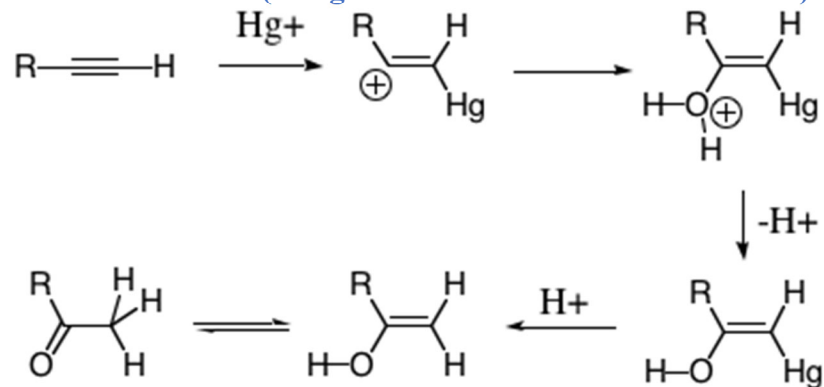
Reduction with Na/NH₃ to give trans alkene



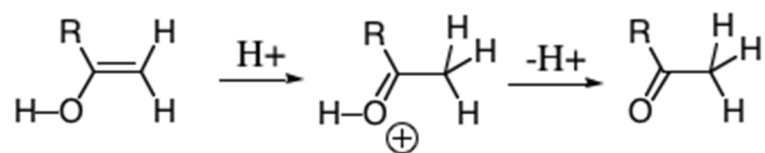
Addition of halogens (it is very difficult to stop at only one addition of halogen to an alkyne, mainly obtain two molar additions)



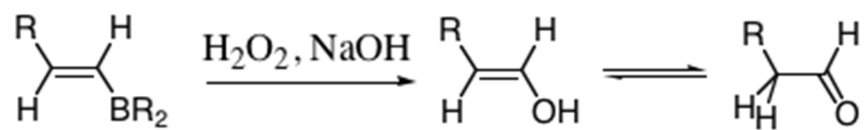
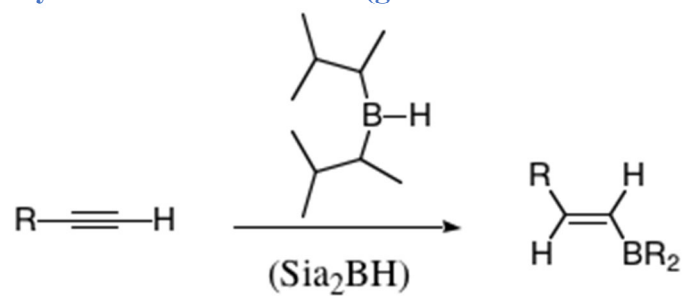
Addition of water (will give enol → keto-enol tautomerism)



Keto-Enol Tautomerism

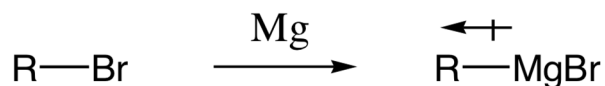


Hydroboration-oxidation (gives enol which tautomerizes to keto form)



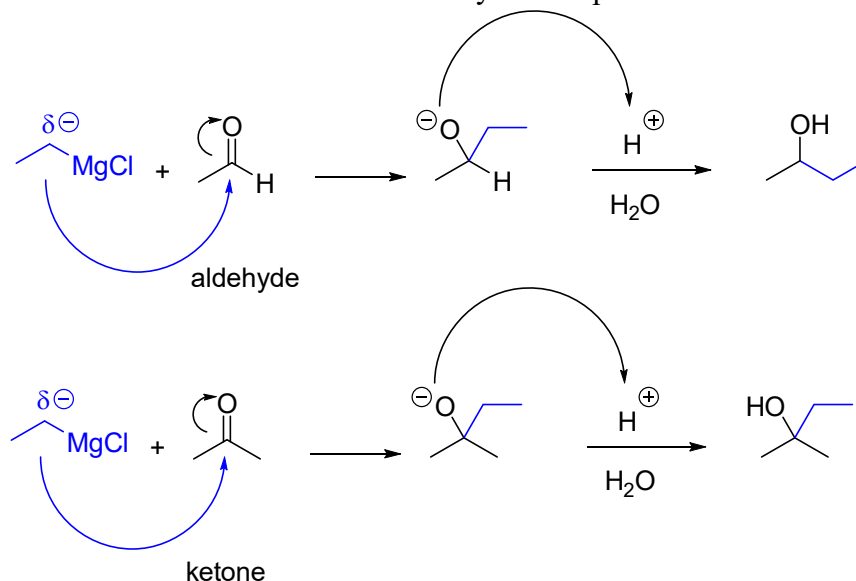
H) Organomagnesium compounds (Grignard reagents) and organolithium compounds

Grignard reagents are synthesized by reacting halides with magnesium in diethyl ether or tetrahydrofuran as solvent. **Grignard reagents are strong bases and strong nucleophiles.**

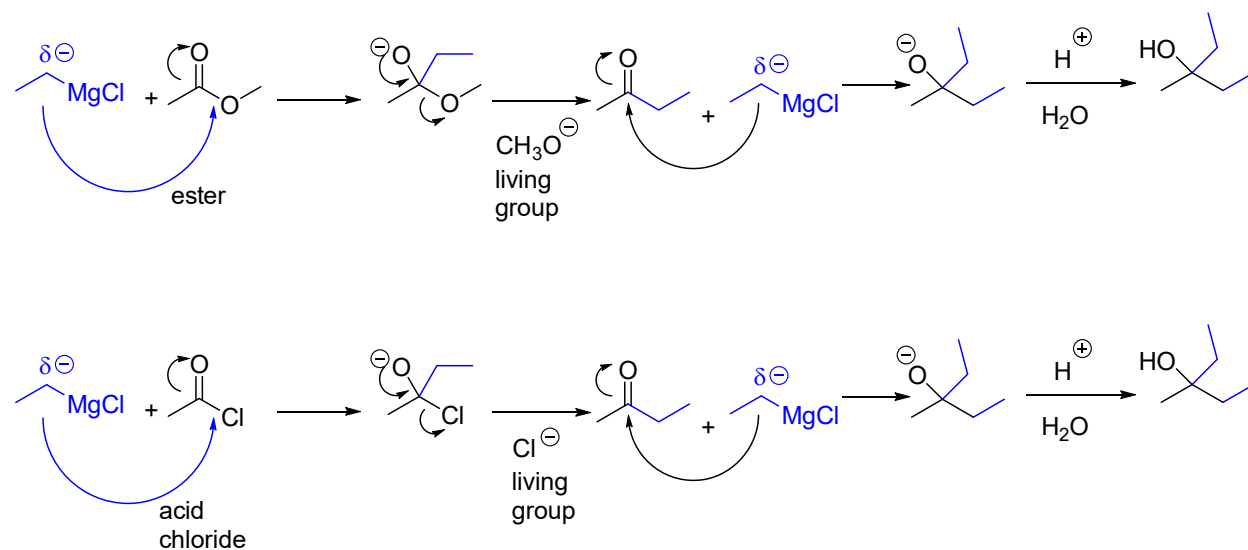


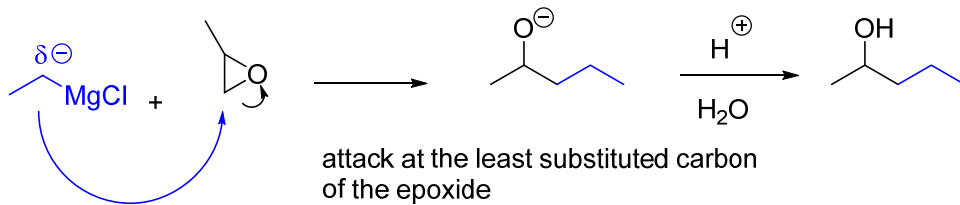
Grignard reagents react with aldehydes, ketones, acid chlorides, esters, nitriles, and epoxides. In these reactions the Grignard reagent is acting as a nucleophile to attack an electrophilic carbon (from carbonyl, ester, acid chloride, nitrile, or epoxide)

For **aldehydes** and **ketones** react once and follow by work-up with acidic water.



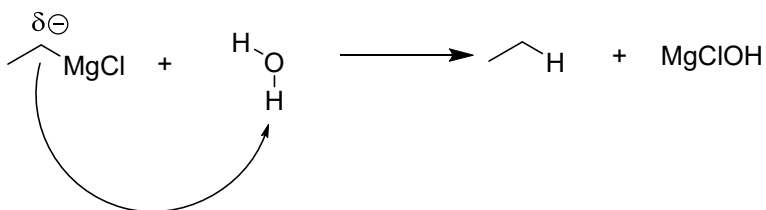
For **esters** and **acid chlorides** react twice; after the first step regenerate the carbonyl and then react one more time.



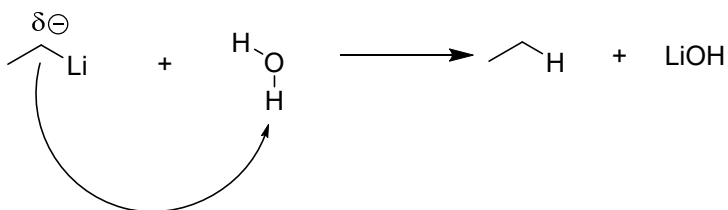


Organolithium compounds react the same way as Grignard reagents aldehydes, ketones, acid chlorides, esters, and epoxides.

Grignard reagents and organolithium compounds are not tolerant to water, alcohol, amines.



Grignard reagent reacts as a base to abstract a proton from water



Organolithium reagent reacts as a base to abstract a proton from water