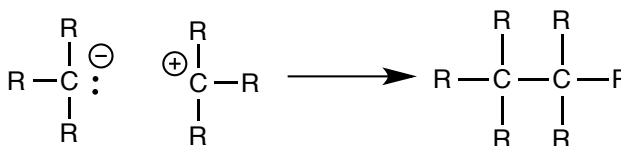
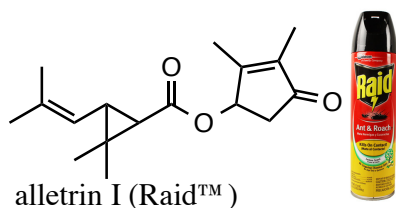


Organometallic Reagents

[Chapter 3 Section 3.4; <http://ochem.jsd.claremont.edu/tutorials.htm#>]

Making C-C bonds

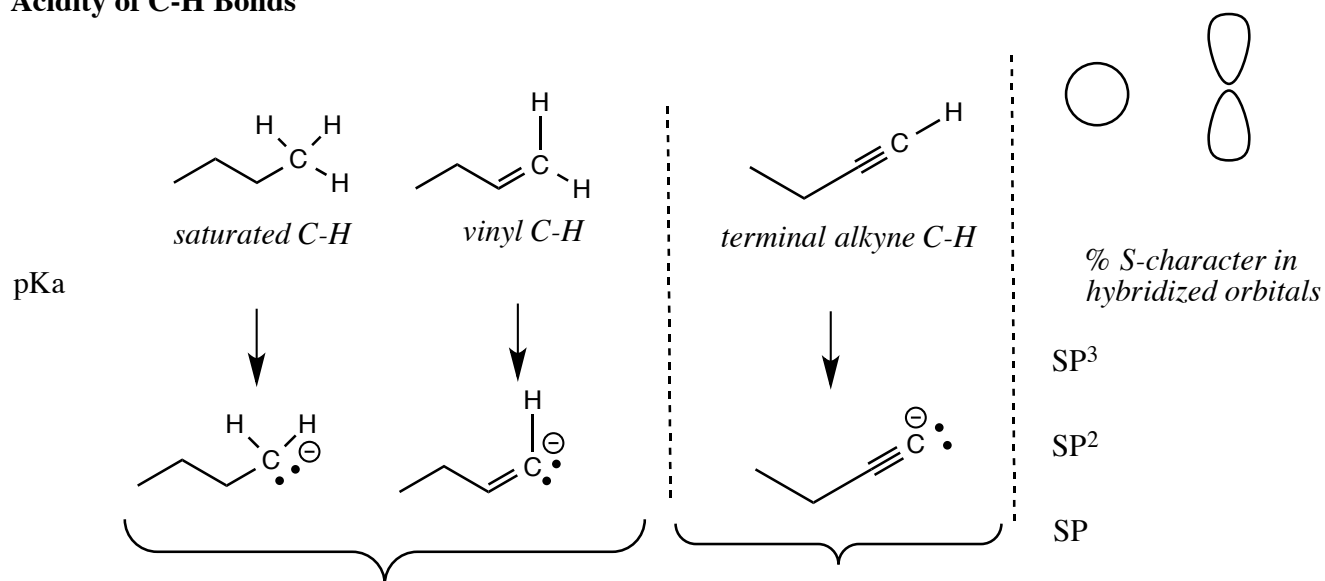


- creating C-C bonds allows forming larger organic molecules from smaller molecules
- a nucleophilic source of carbon and an electrophilic source of carbon are required
- negatively charged carbon is an excellent nucleophile since C has low electronegativity
- electrophilic sources of carbon are readily available in the form of alkyl halides and tosylates



- nucleophilic sources of carbon, however, are often more difficult to generate

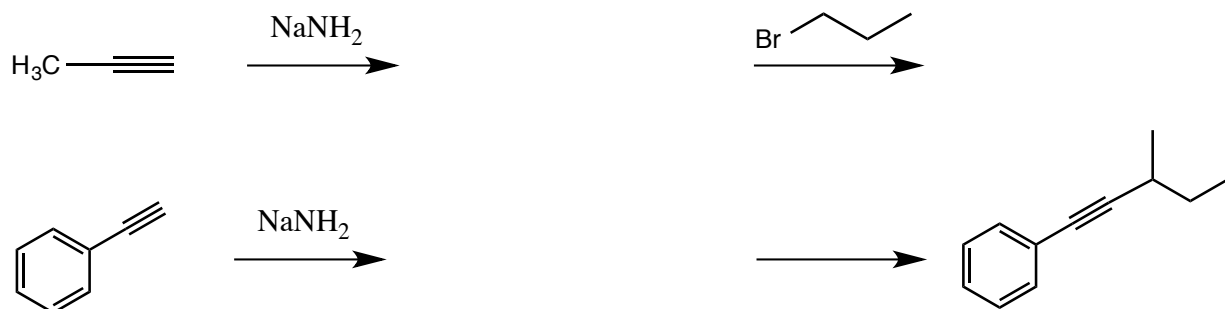
Acidity of C-H Bonds



- negatively charged electrons want to be as close to a positive charge as possible
- positive charge on an atom is at the nucleus
- the S orbital is closer to the nucleus on average than a P-orbital
- greater amount of S-character means the negative charge is, on average, closer to the nucleus, and therefore more stable
- as always, greater stability translates into greater ease of formation = more acidic
- hybridization affects acidity: SP-hybridized carbons are more acidic than SP² > SP³
- NOTE that only terminal alkynes have this unusual acidity because they have an H directly attached to the SP hybridized carbon. Internal alkynes $\text{R}-\text{C}\equiv\text{C}-\text{R}$ are not particularly acidic.

Problems: 1,2

Generating Carbon Nucleophiles by Deprotonation of Terminal Alkynes



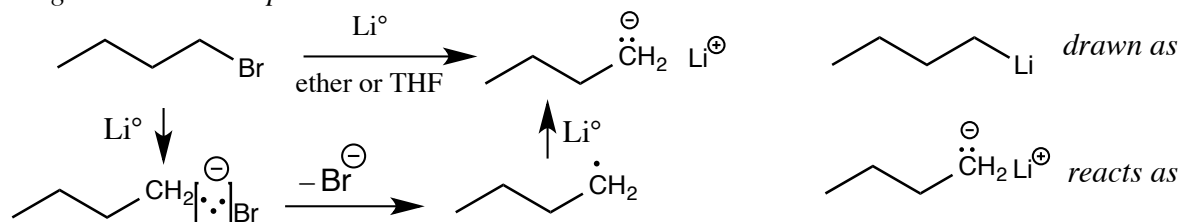
- carbon-carbon bond formation can be accomplished using deprotonated terminal alkynes as the carbon nucleophile
- the terminal alkyne **MUST** first be deprotonated in order to render the carbon nucleophilic (i.e., in order for it to gain a lone pair and negative charge)
- typical deprotonation conditions: NaNH_2 in NH_3 as solvent; NaH in Et_2O or THF as solvent

Generating Carbon Nucleophiles via Organometallic Compounds

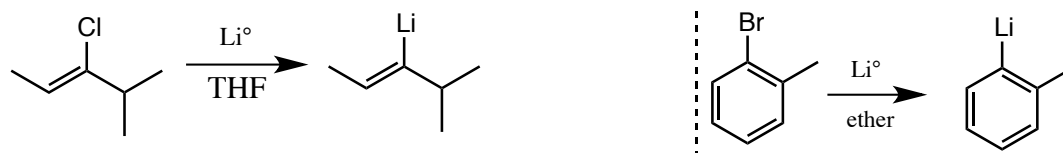


- as stated above, SP^3 and SP^2 hybridized carbons **CANNOT** be directly deprotonated to form the negatively charged nucleophilic carbon atoms since no bases are strong enough to remove these protons directly

A. Organolithium Compounds

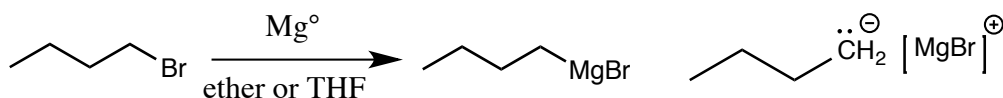


- organolithium compounds are formed via reaction of Lithium metal with alkyl halides
- alkyl chlorides, bromides and iodides are acceptable (alkyl fluorides are not reactive)
- the Li forms a bond to the carbon to which the halogen is initially attached (i.e., no rearrangements)
- the C-Li bond is almost a covalent bond and is usually drawn as a covalent bond, but **it reacts as if it is ionic in nature** and should be viewed that way



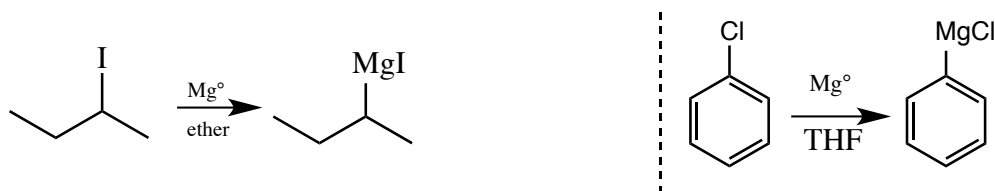
- SP^2 hybridized carbons (i.e., vinyl and aromatic halides) react similarly to SP^3 hybridized carbons

B. Grignard Reagents



Victor Grignard
1871-1935

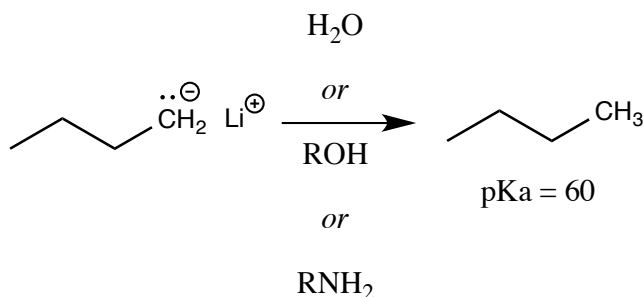
- Grignard reagents (organomagnesium compounds) are synthesized analogously to the organolithiums, via addition of magnesium metal to an alkyl halide
- the counterion, MgX^+ , is more complicated than the Li^+ , but serves the same purpose: it acts as a spectator ion only
- the reactions of Grignard reagents and organolithiums are essentially identical, and selection of one or the other for a reaction is based primarily out of practical considerations



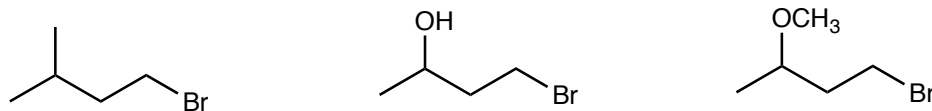
- for both alkyllithiums and Grignard reagents, no rearrangements are ever observed: where ever the halogen is on the starting alkyl halide, that is where the metal bond is formed
- tosylates do NOT react to form alkyllithiums or Grignards

Problems: 6

Basicity of organometallic reagents [Caution!]



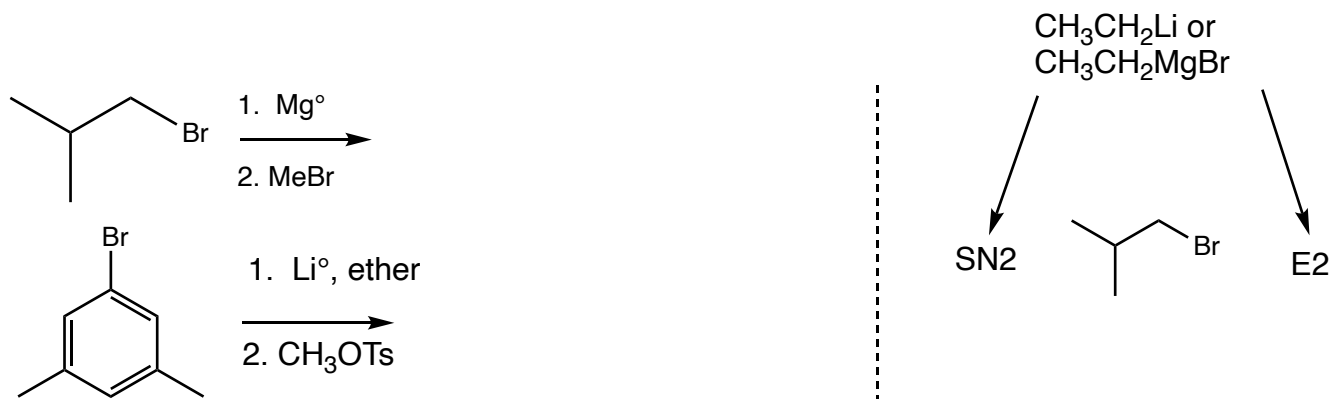
- organolithiums are exceptionally strong bases! contact with water **MUST** be avoided
- they are incompatible with any molecule containing OH or NH bonds since these types of hydrogens are very acidic in relation to the organolithiums
- therefore organolithiums can only be made from starting organohalides that do NOT contain groups that are acidic



- anhydrous ethers are typically used as solvents since they are unreactive towards strong bases and are polar enough to dissolve the organolithiums

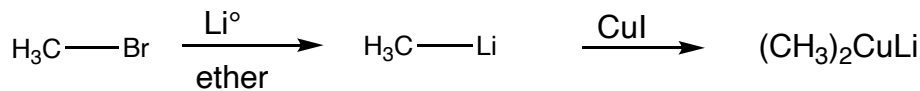
Organometallics Acting as Nucleophiles versus Bases

- Both Grignard reagents and organolithiums are potent nucleophiles
- they both react well via the S_N2 reaction with the very reactive S_N2 substrates methyl halides and tosylates
- however, since they are very strong bases, the major mode of reaction with other alkyl halides and tosylates is via elimination ($E2$ reaction)



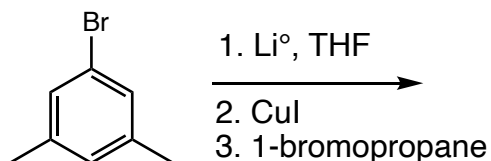
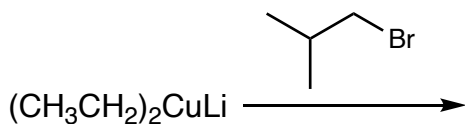
- the inability of Grignards and alkyllithiums to act as nucleophiles towards most alkyl halides and tosylates is a major limitation on their usefulness

Organocuprates (Gilman Reagents)

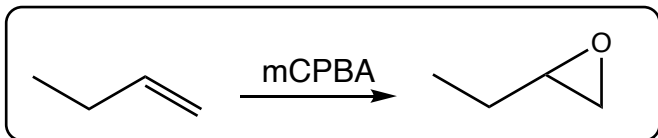


- an alkyllithium
- strong base
- DOES NOT engage in S_N2 reactions with alkyl halides (or tosylates) other than methyl

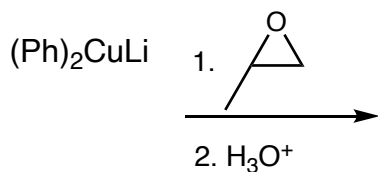
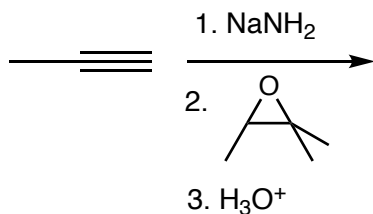
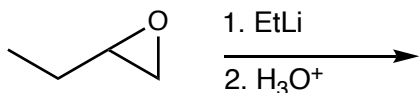
- an organocuprate
- weak base
- WILL engage in S_N2 reactions with alkyl halides (and tosylates) other than methyl



Reaction of Organometallic Reagents with Epoxides (yet another source of electrophilic carbon!)




- epoxides are generally formed via epoxidation of alkenes
- mCPBA
- epoxides provide another source of electrophilic carbon that is reactive with all of the carbon nucleophiles we have discussed

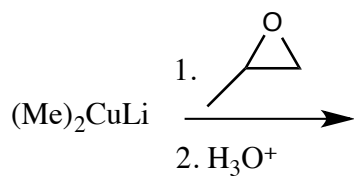
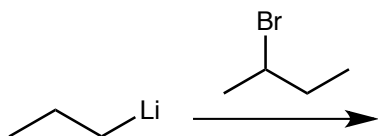
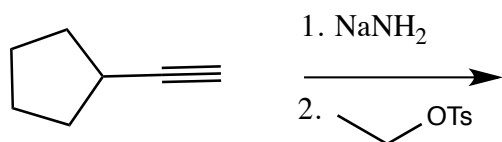
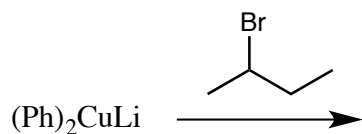
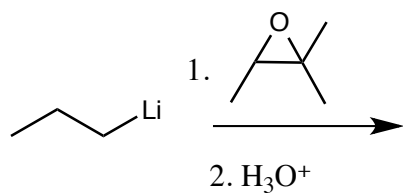


- all of the organometallic compounds attack the least substituted carbon atom of the epoxide ring

Summary of Carbon Nucleophile Reactivity

	R-X or R-OTs	
$R-C\equiv C:^{\ominus}$	yes	yes
$R-Li$ or $R-MgBr$	<i>methyl substrates only!!!</i>	yes
$(R)_2CuLi$	yes	yes

Examples



Essential Concepts

1. Understand the basic concept behind making C–C bonds
2. Know why deprotonation to generate carbon nucleophiles is generally not a good strategy with the exception of terminal alkynes
3. Know the relative pKa's of CH bonds
4. Know how to generate carbon nucleophiles from terminal alkynes, and via organolithium, Grignard and organocuprate reagents.
5. Know which types of electrophiles can be matched with the various carbon nucleophiles and be able to draw products resulting from these reactions.