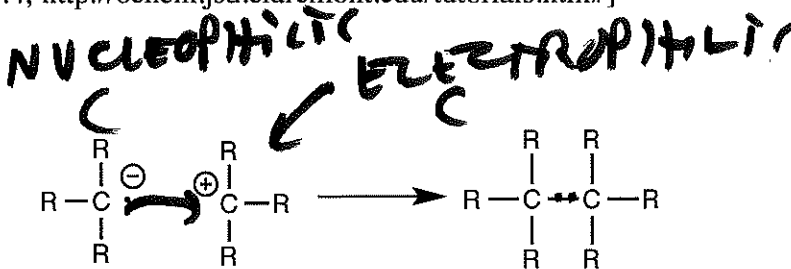
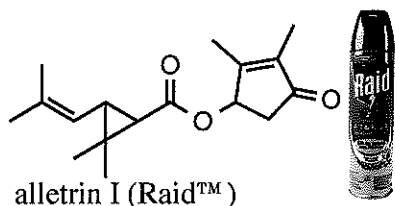


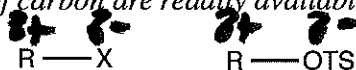
# Organometallic Reagents

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

## Making C-C bonds

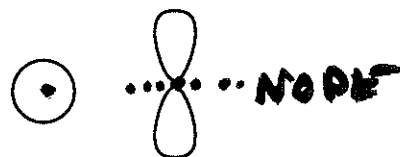
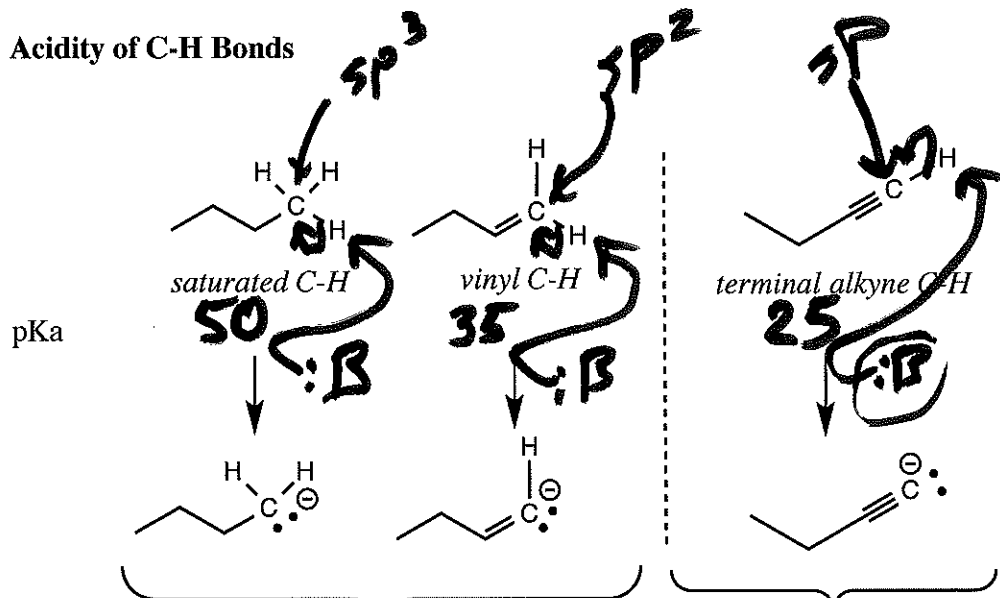


- creating C-C bonds allows forming larger organic molecules from smaller molecules
- a nucleophilic source of carbon and an electrophilic source of carbon are required
- negatively charged carbon is an excellent nucleophile since C has low electronegativity
- electrophilic sources of carbon are readily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

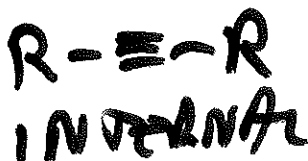


% S-character in hybridized orbitals

SP <sup>3</sup>	75% P	25% S
SP <sup>2</sup>	66% P	33% S
SP	50% P	50% S

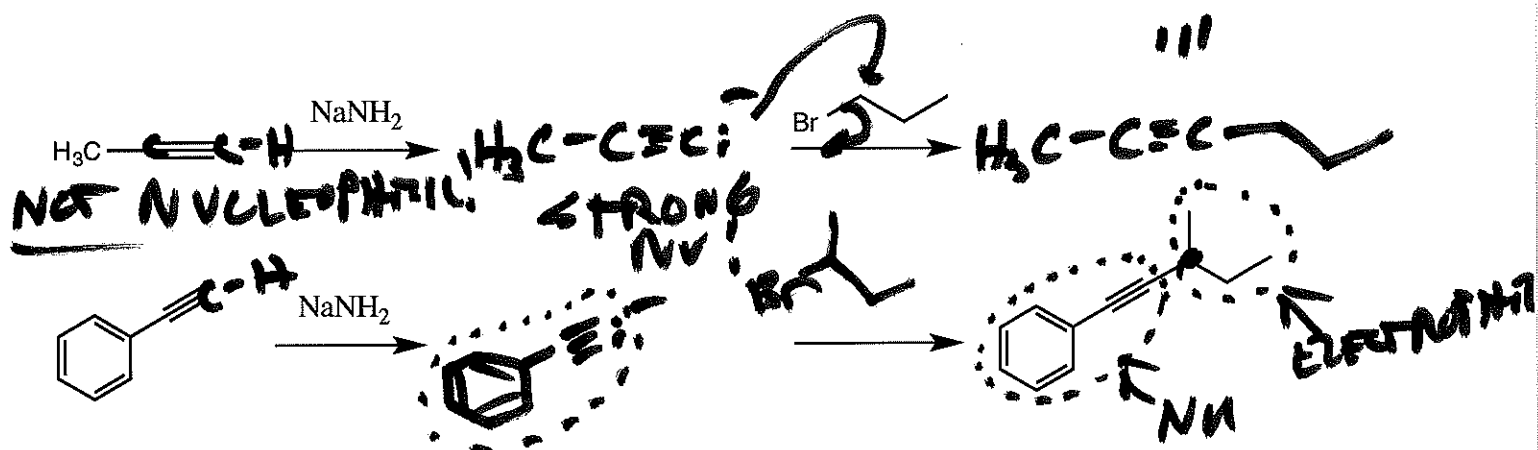
**CANNOT DEPROTONATE** **CAN DEPROTONATE**

- 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 SP<sup>2</sup> > SP<sup>3</sup>
- 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



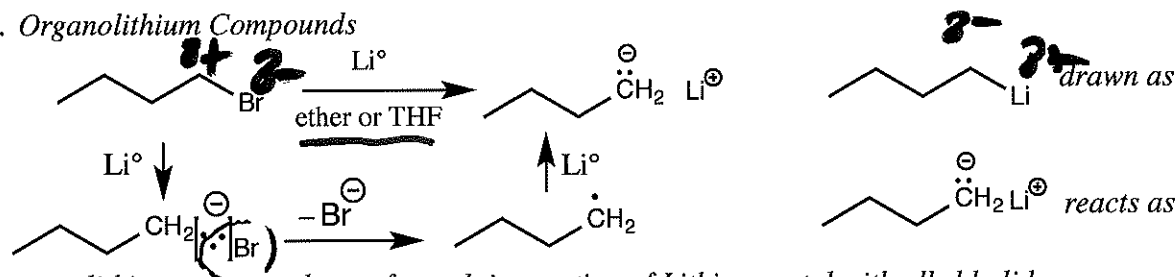
- carbon-carbon bond formation can be accomplished using deprotonated terminal alkynes as the carbon nucleophile
- the terminal alkyne **MUST** first be deprotonated in order to render the carbon nucleophilic (i.e., in order for it to gain a lone pair and negative charge)
- typical deprotonation conditions:  $\text{NaNH}_2$  in  $\text{NH}_3$  as solvent;  $\text{NaH}$  in  $\text{Et}_2\text{O}$  or  $\text{THF}$  as solvent

## Generating Carbon Nucleophiles via Organometallic Compounds

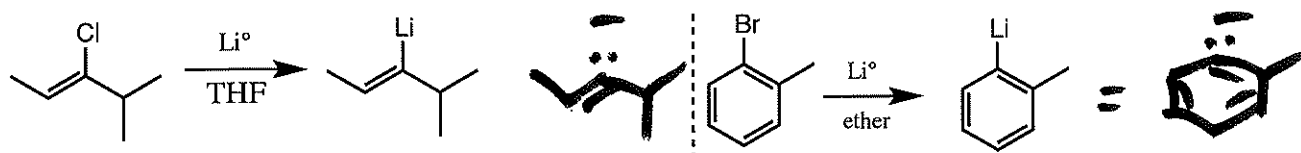


- as stated above,  $\text{SP}^3$  and  $\text{SP}^2$  hybridized carbons **CANNOT** be directly deprotonated to form the negatively charged nucleophilic carbon atoms since no bases are strong enough to remove these protons directly

### A. Organolithium Compounds

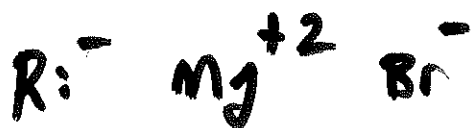


- organolithium compounds are formed via reaction of Lithium metal with alkyl halides
- alkyl chlorides, bromides and iodides are acceptable (alkyl fluorides are not reactive)
- the  $\text{Li}$  forms a bond to the carbon to which the halogen is initially attached (i.e., no rearrangements)
- the  $\text{C}-\text{Li}$  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

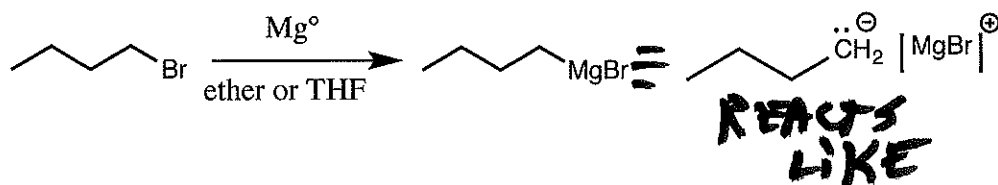


- $\text{SP}^2$  hybridized carbons (i.e., vinyl and aromatic halides) react similarly to  $\text{SP}^3$  hybridized carbons





## B. Grignard Reagents



**Victor Grignard**  
1871-1935

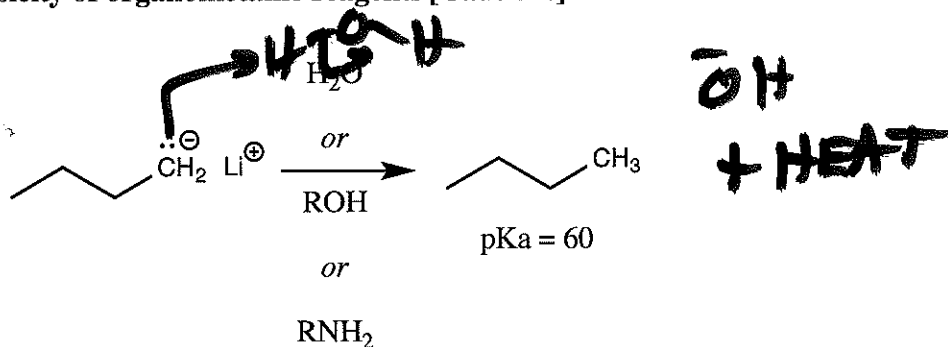
- Grignard reagents (organomagnesium compounds) are synthesized analogously to the organolithiums, via addition of magnesium metal to an alkyl halide
- the counterion,  $\text{MgX}^+$ , is more complicated than the  $\text{Li}^+$ , but serves the same purpose: it acts as a spectator ion only
- the reactions 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



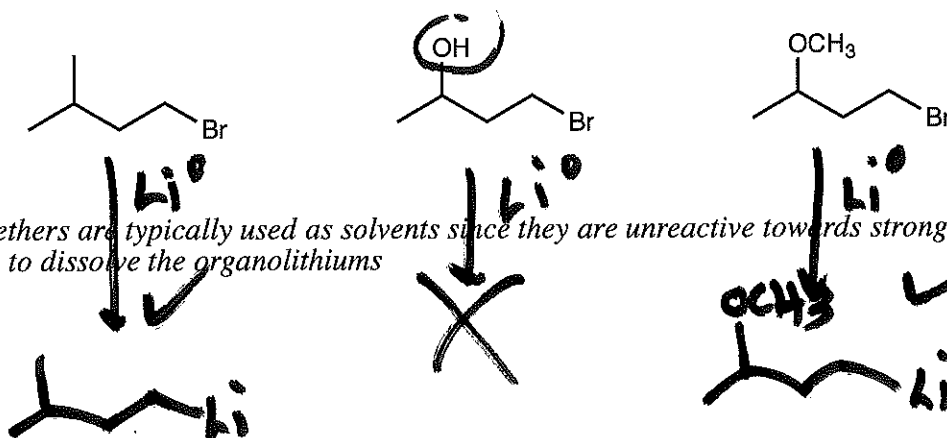
- for both alkyllithiums and Grignard reagents, no rearrangements are ever observed: where ever the halogen is on the starting alkyl halide, that is where the metal bond is formed
- tosylates do NOT react to form alkyllithiums or Grignards

Problems: 6

## Basicity of organometallic reagents [Caution!]



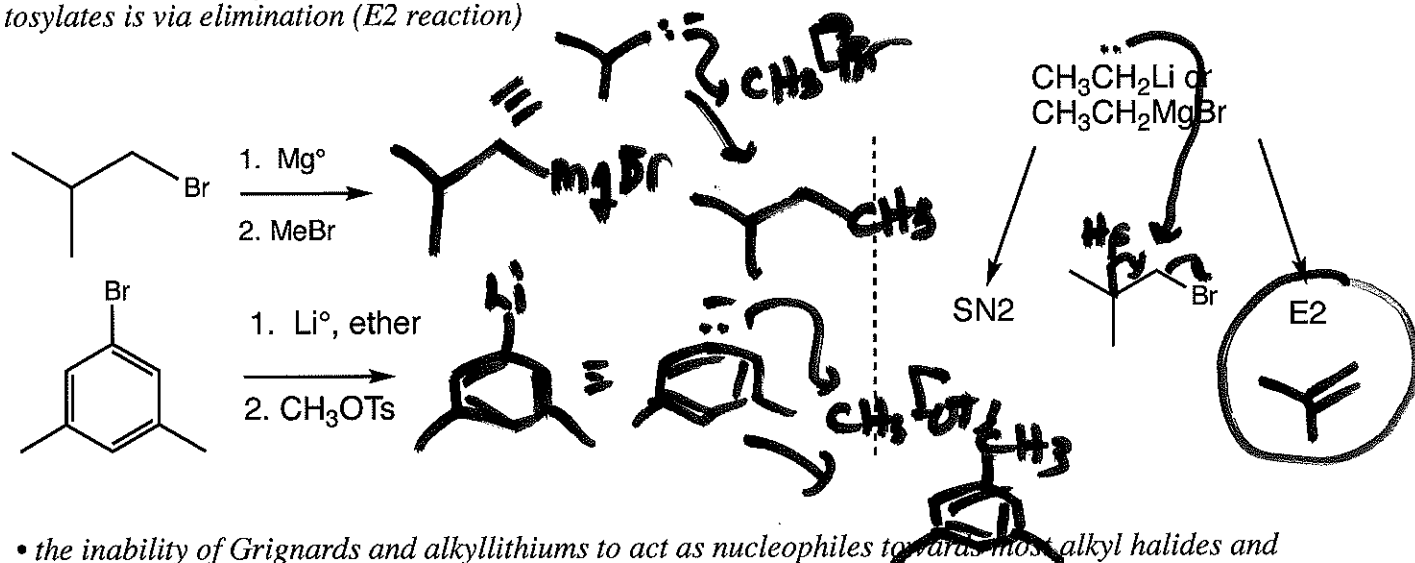
- organolithiums are exceptionally strong bases! contact with water **MUST** be avoided
- they are incompatible with any molecule containing OH or NH bonds since these types of hydrogens are very acidic in relation to the organolithiums
- therefore organolithiums can only be made from starting organohalides 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

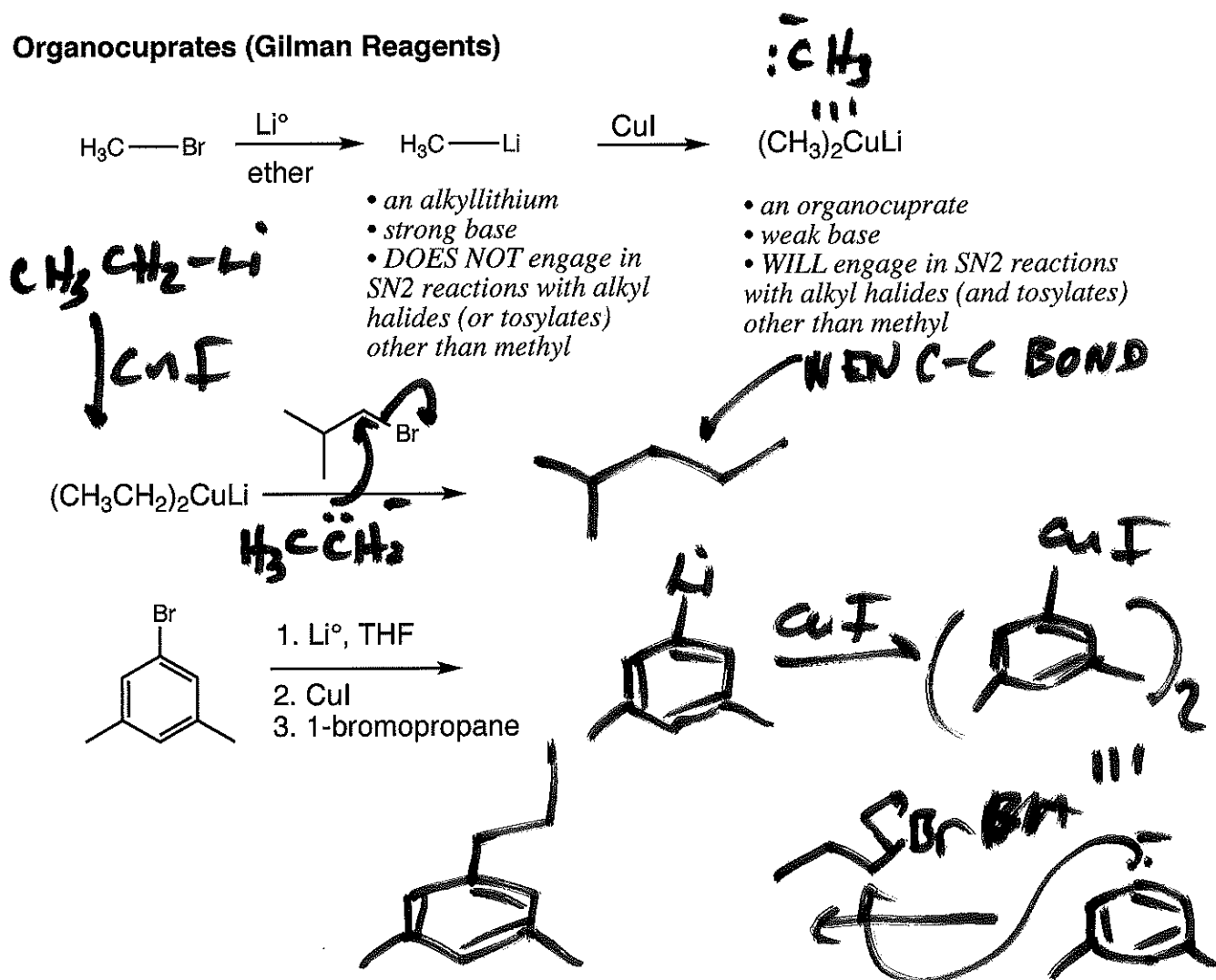
## Organometallics Acting as Nucleophiles versus Bases

- 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)

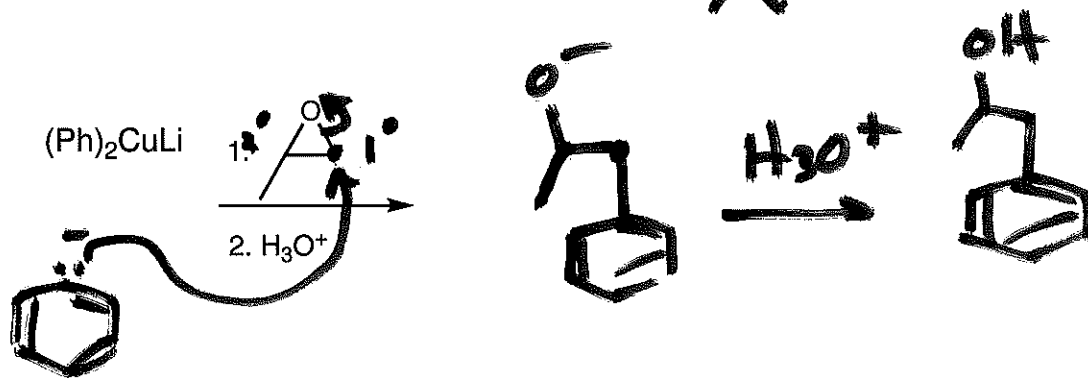
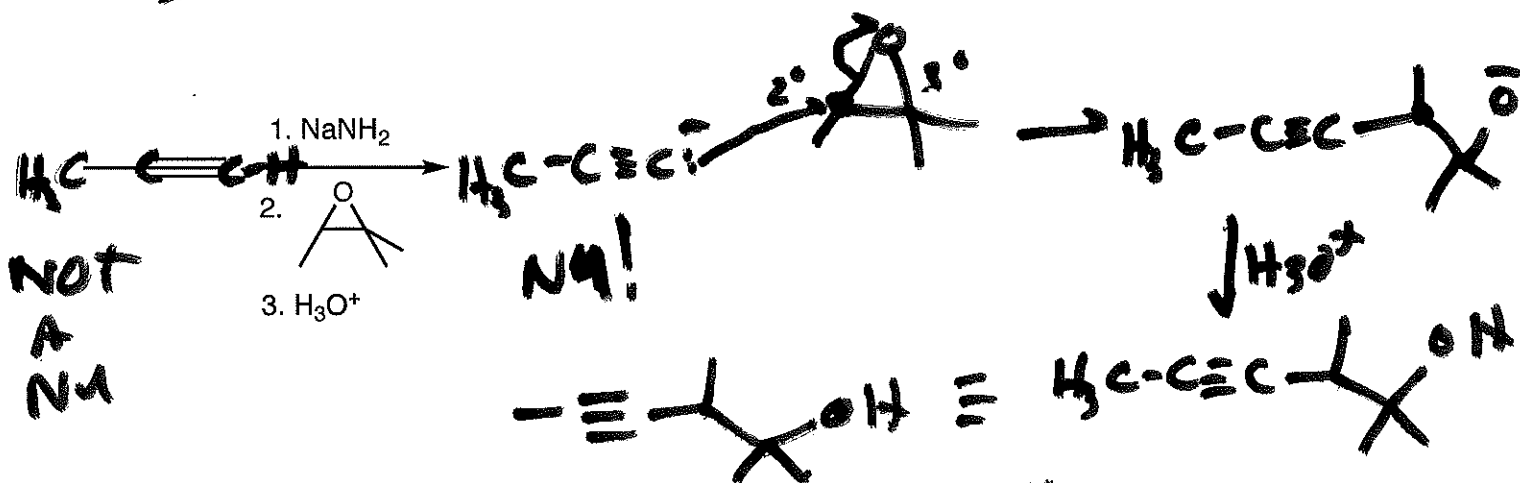
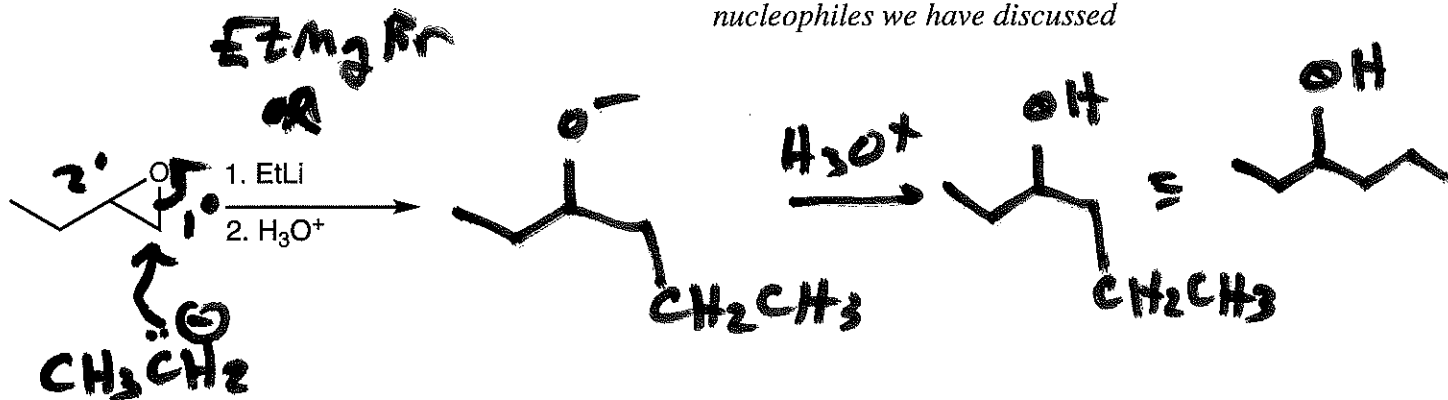




Reaction of Organometallic Reagents with Epoxides (yet another source of electrophilic carbon!)



- 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

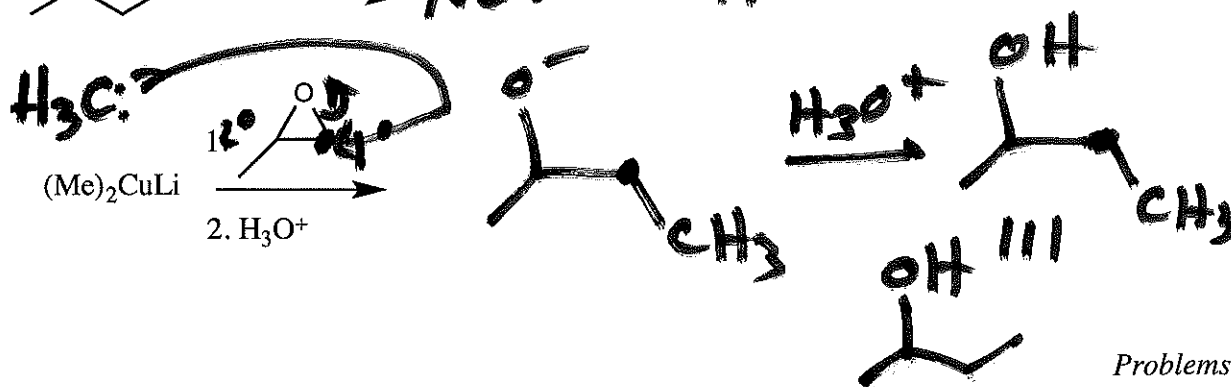
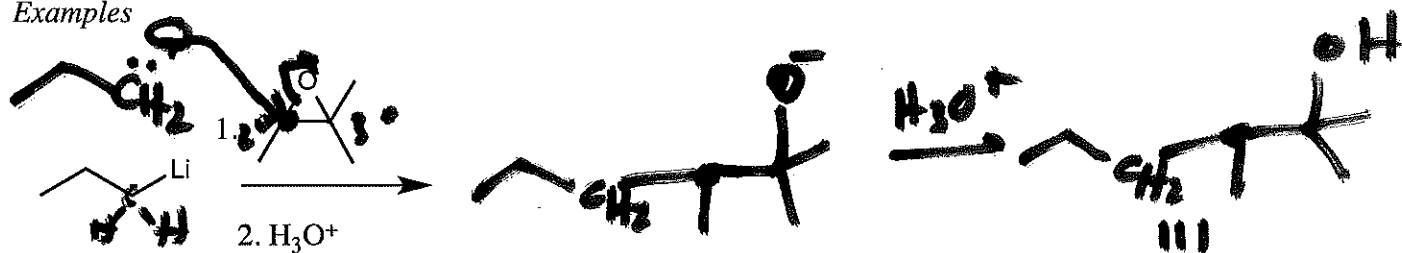


• all of the organometallic compounds attack the least substituted carbon atom of the epoxide ring

## 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



Problems: 3-7