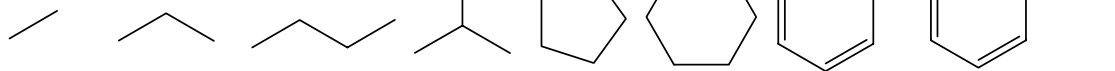
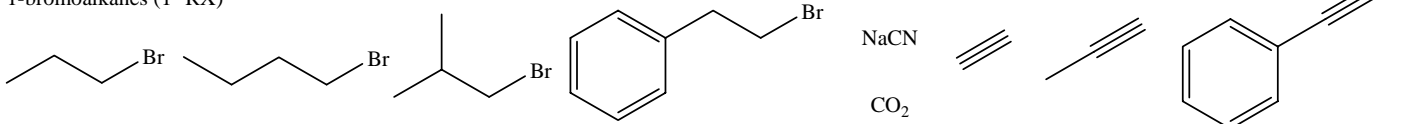


Available chemicals from the catalog. (pages 1 & 2)Allowed sources of carbon *before* alkenes and alkynes are covered.

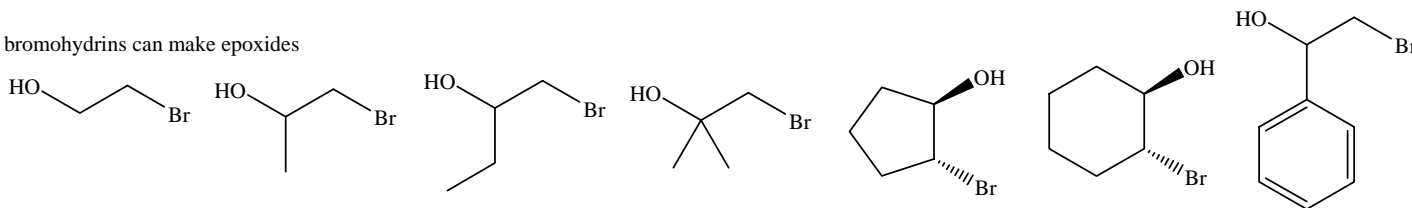
hydrocarbons

CH<sub>4</sub>

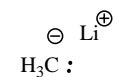
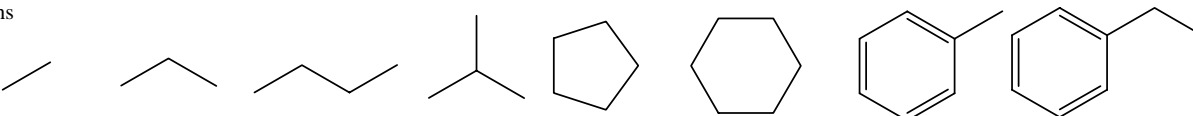
1-bromoalkanes (1° RX)



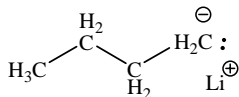
bromohydrins can make epoxides

Allowed sources of carbon *after* alkenes and alkynes are covered.

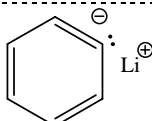
hydrocarbons

CH<sub>4</sub>

methyl lithium



n-butyl lithium

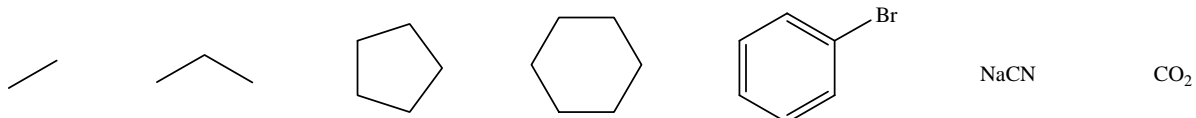


phenyl lithium

NaCN

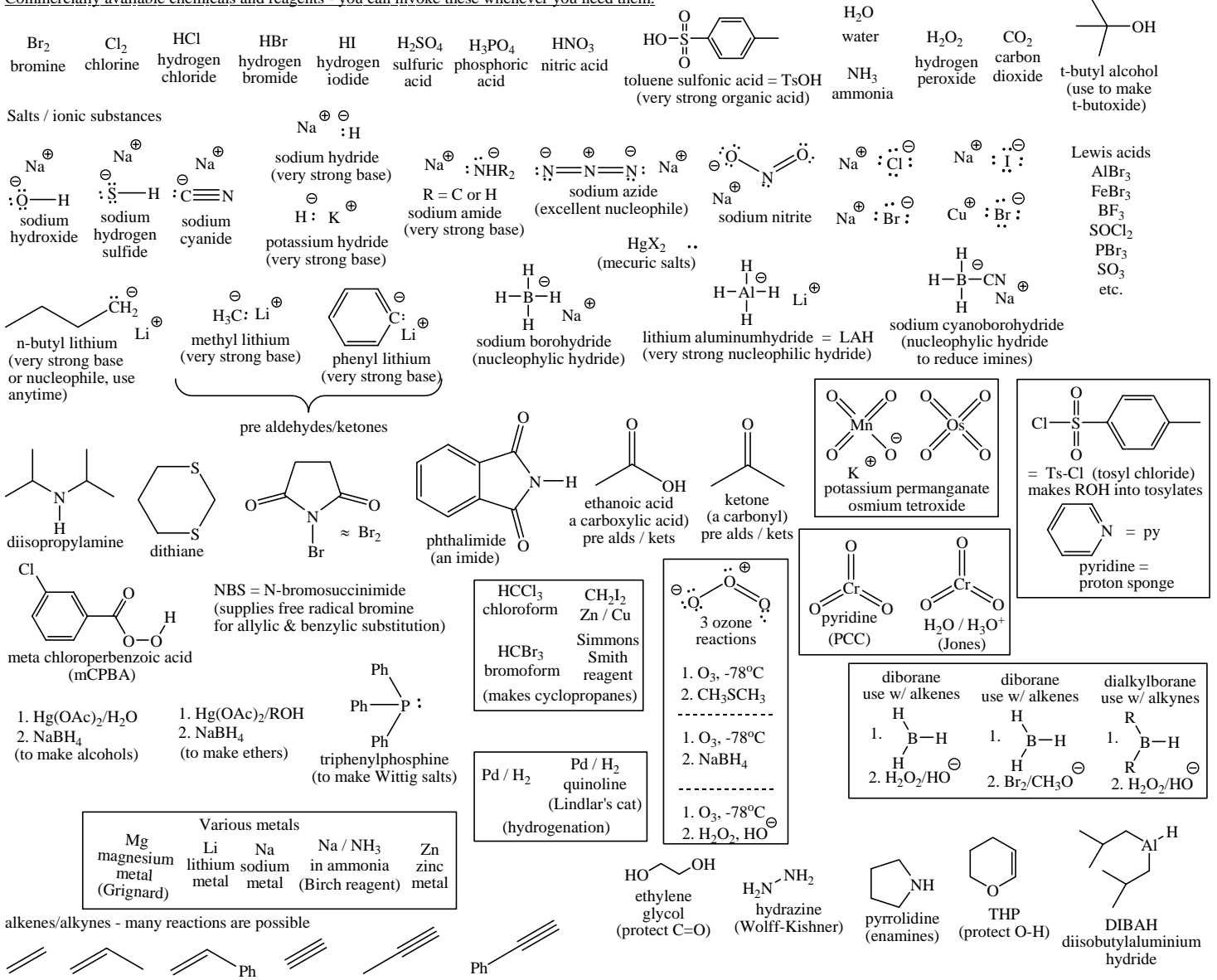
CO<sub>2</sub>Allowed sources of carbon *after* aldehydes and ketones are covered.

hydrocarbons

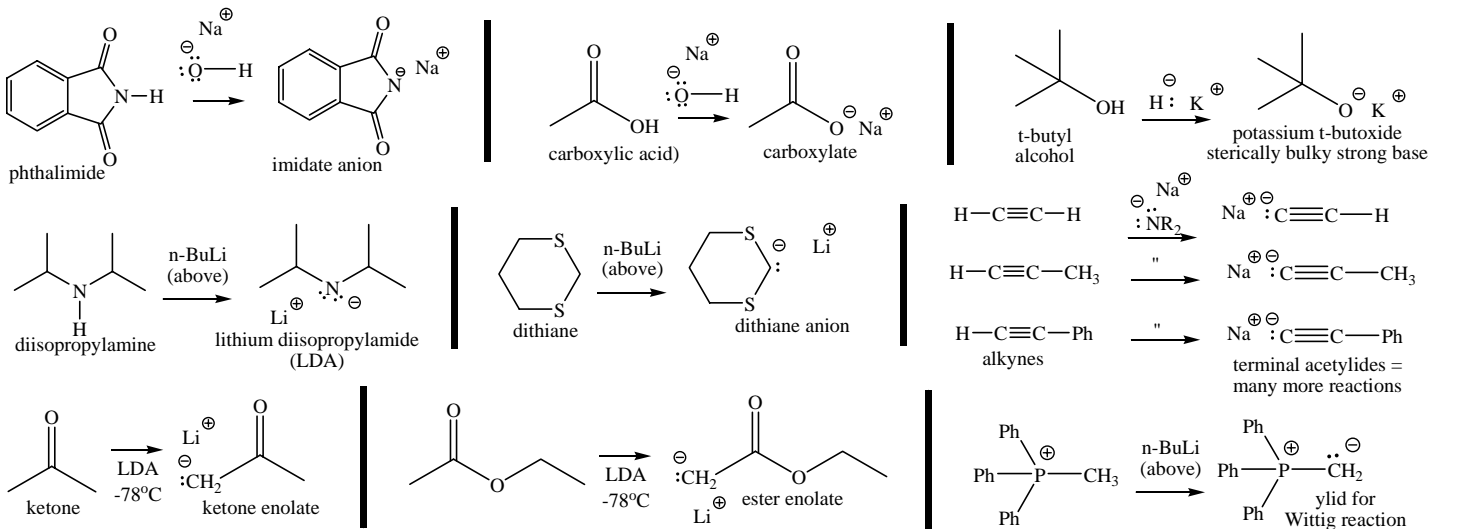
CH<sub>4</sub>

You can use any of the typical “first year” reagents of organic chemistry (most are listed on the next page). If you know how to correctly use other reagents that are not listed, you can use those too. Some of the reagents that are at the bottom of the next page you will have to make, as indicated.

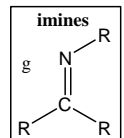
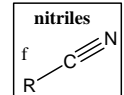
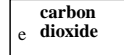
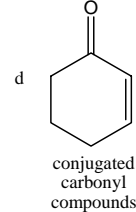
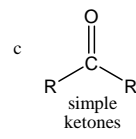
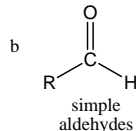
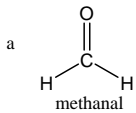
Commercially available chemicals and reagents - you can invoke these whenever you need them.



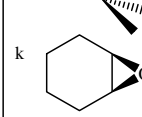
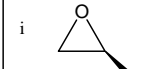
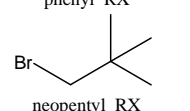
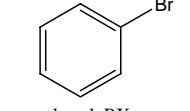
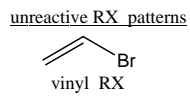
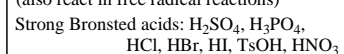
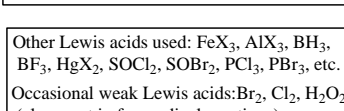
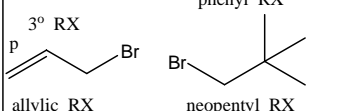
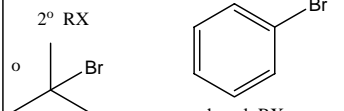
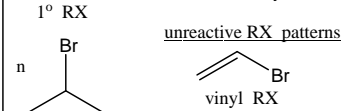
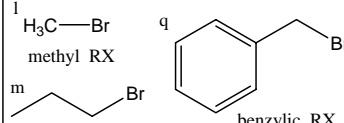
Make these from above reagents - examples are provided in the pages that follow.



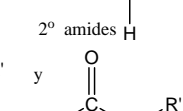
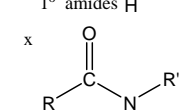
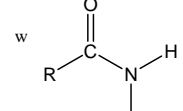
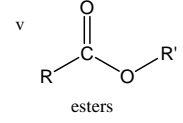
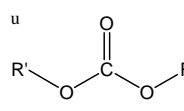
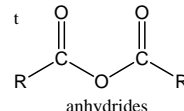
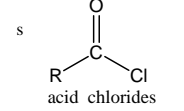
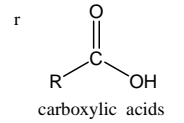
## Electrophiles (Lewis acids)

aldehydes and ketones,  
carbonyl addition reactions

## epoxide derivatives

RX derivatives  
S<sub>N</sub>2/E2 and S<sub>N</sub>1/E1

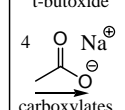
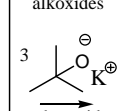
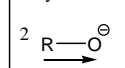
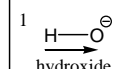
Other Lewis acids used: FeX<sub>3</sub>, AlX<sub>3</sub>, BH<sub>3</sub>, BF<sub>3</sub>, HgX<sub>2</sub>, SOCl<sub>2</sub>, SOBr<sub>2</sub>, PCl<sub>3</sub>, PBr<sub>3</sub>, etc.  
Occasional weak Lewis acids: Br<sub>2</sub>, Cl<sub>2</sub>, H<sub>2</sub>O<sub>2</sub> (also react in free radical reactions)  
Strong Bronsted acids: H<sub>2</sub>SO<sub>4</sub>, H<sub>3</sub>PO<sub>4</sub>, HCl, HBr, HI, TsOH, HNO<sub>3</sub>

carboxylic acids and derivatives,  
carbonyl substitution reactions

Some of these become even more reactive when protonated or complexed with a strong Lewis acid, like BF<sub>3</sub>.

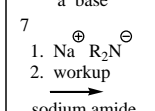
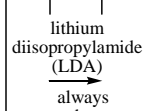
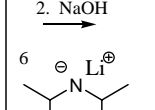
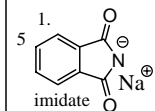
## Nucleophiles (Bases)

## oxygen nucleophiles and/or bases

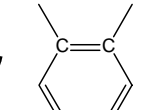
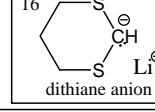
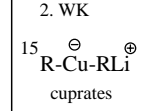
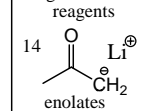
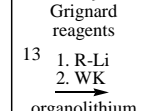
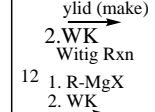
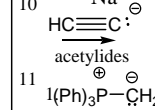
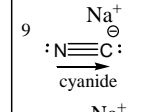


Occasional weak Lewis bases: R-Cl, R-Br, R-I, Br<sub>2</sub>, Cl<sub>2</sub>; sometimes with strong Lewis acids like: FeX<sub>3</sub>, AlX<sub>3</sub>, Ag(NO<sub>3</sub>), etc.

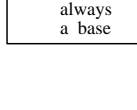
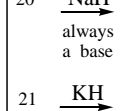
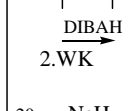
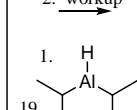
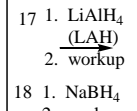
## nitrogen nucleophiles and/or bases



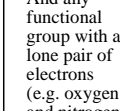
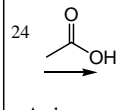
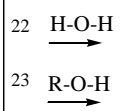
## carbanion nucleophiles and/or bases



## hydride nucleophiles and/or bases

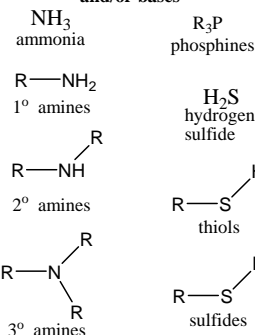


## weak nucleophiles and/or bases

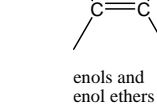
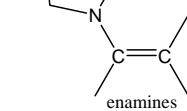
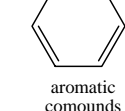
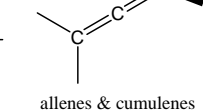
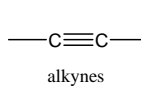
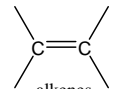


And any functional group with a lone pair of electrons (e.g. oxygen and nitrogen)

## miscellaneous neutral nucleophiles and/or bases



## neutral carbon nucleophiles



Every mechanism so far, except free radical substitution of alkanes, involves two electron transfers with each arrow.

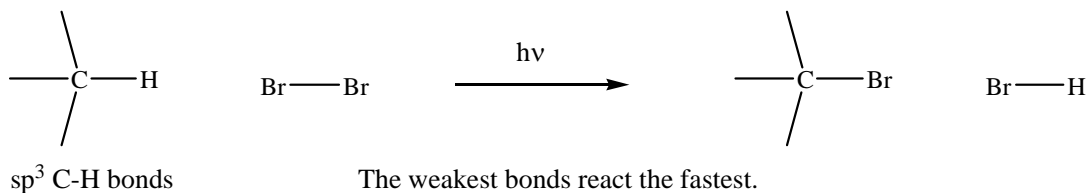
**Electrophiles** = electron loving = any electron pair acceptor = Lewis acid, (often an acidic proton)

**Nucleophiles** = nucleus/positive loving = any electron pair donor = Lewis base, (often donated to an acidic proton)

**Problems** - In the following reactions each step has been written without the formal charge or lone pairs of electrons and curved arrows. Assume each atom follows the normal octet rule, except hydrogen (duet rule). Supply the lone pairs, formal charge and the curved arrows to show how the electrons move for each step of the reaction mechanism. Identify any obvious nucleophiles and electrophiles in each of the steps of the reactions below (on the left side of each reaction arrow). Let me know when you find errors.

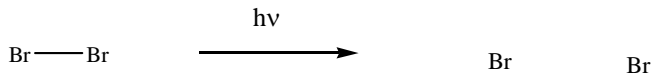
Mechanisms for the following reactions include 1. free radical halogenation, 2. acid/base chemistry, 3.  $S_N2$  reactions, 4.  $E2$  reactions, 5.  $S_N1$  reactions, 6.  $E1$  reactions, 7. acyl substitutions, 8. acyl additions and 9. addition reactions to alkenes and alkynes. Other mechanisms will be presented as we proceed through the course.

1. Overall Reaction (shows just the essentials): Make R-Br from R-H (free radical substitution at  $sp^3$  C-H)

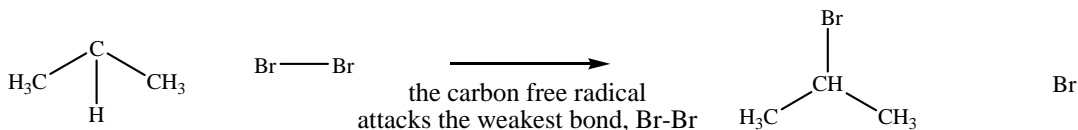
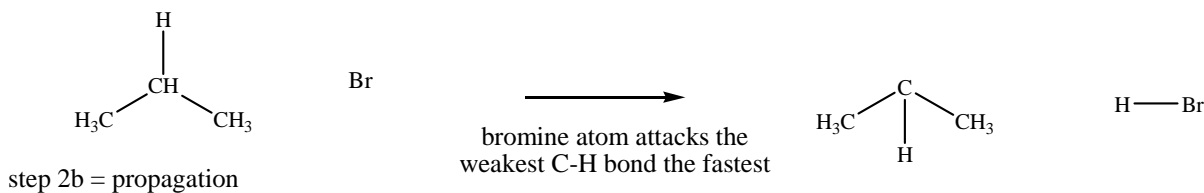


**Mechanism** - fill in all necessary details (lone pairs, formal charge, curved arrows, resonance structures = best plus one other)

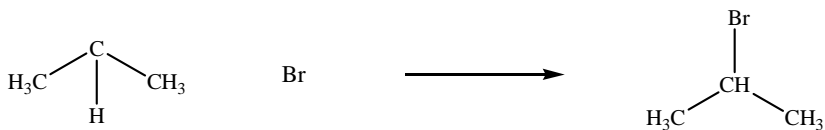
step 1 = initiation - the halogen bond is the weakest bond and most reactive to cleavage by  $h\nu$ .



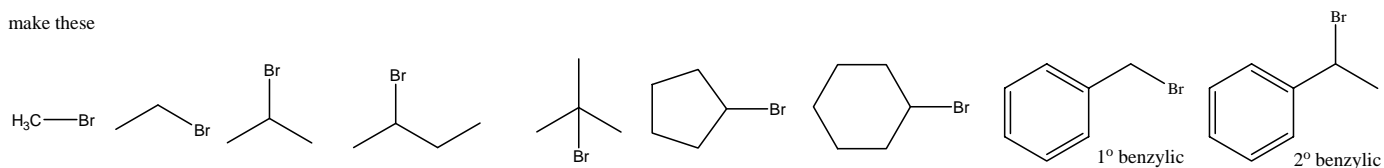
-----  
step 2a = propagation - these steps happen 100's to 1000's of times per initiation



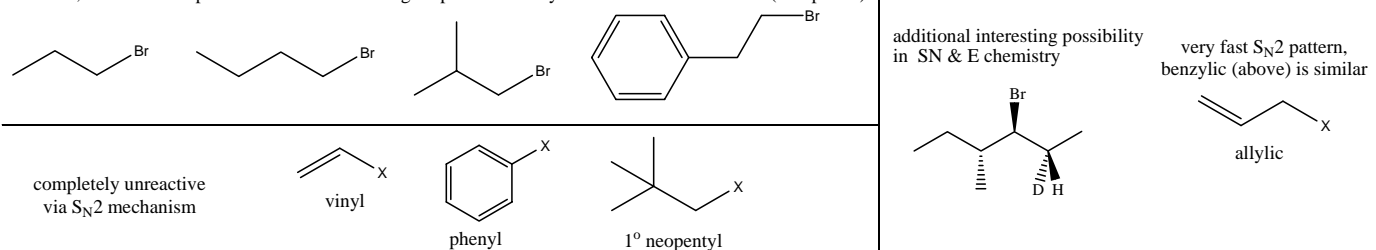
-----  
step 3 = termination - two free radicals encounter on another, pure release of energy, rare event



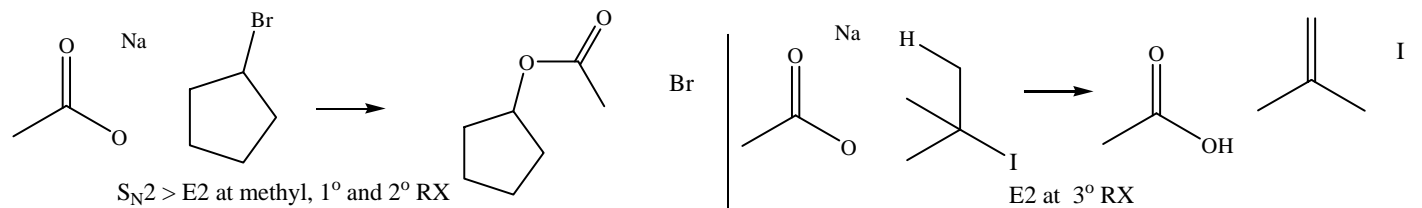
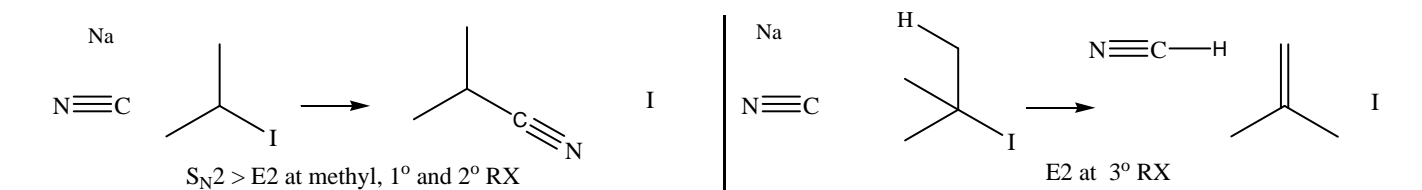
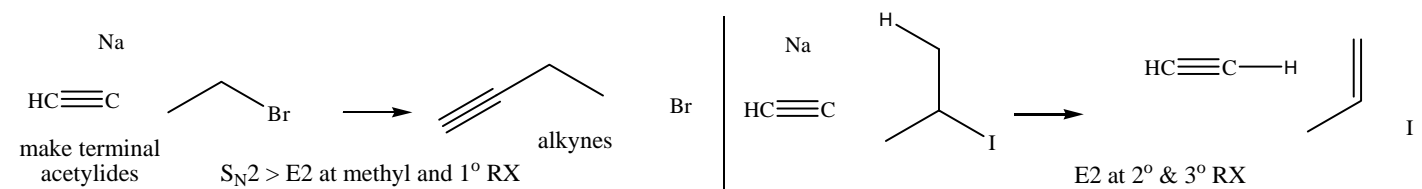
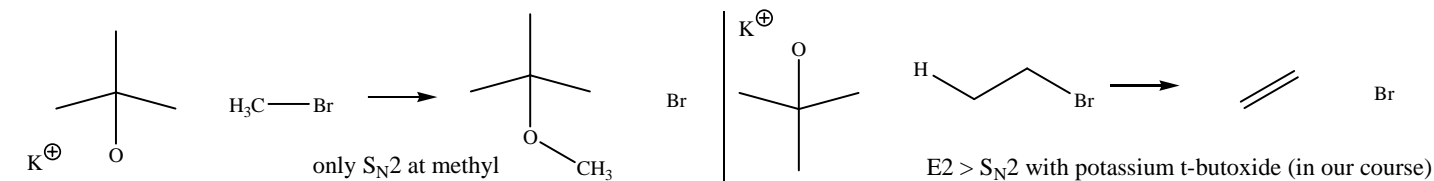
make these



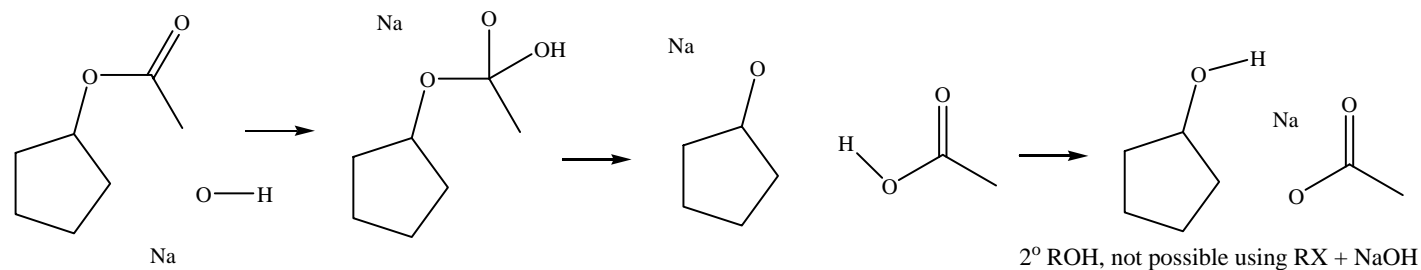
For now, these RX compounds are available through topic 11. Later you will have to make them (in topic 12).

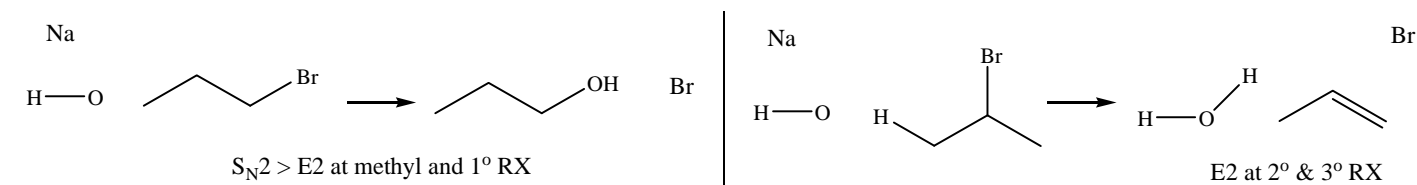


2.  $S_N2$  reactions with R-X patterns (above): methyl, 1°, 2° (sometimes), allylic and benzylic are very good for  $S_N2$ , (R-X = RCl, RBr, RI, ROTs), E2 is the competition. You add all necessary mechanistic details (lone pairs, charge, curved arrows). If no reaction or a different reaction occurs, indicate this. Shown below are syntheses of alcohols, esters, ethers, nitriles, alkynes, thiols, thioethers and amines. Alkenes and alkynes can be made using E2 reactions. That's 10 different functional groups, and we left out ketone and ester enolates, dithianes and cuprate chemistry.

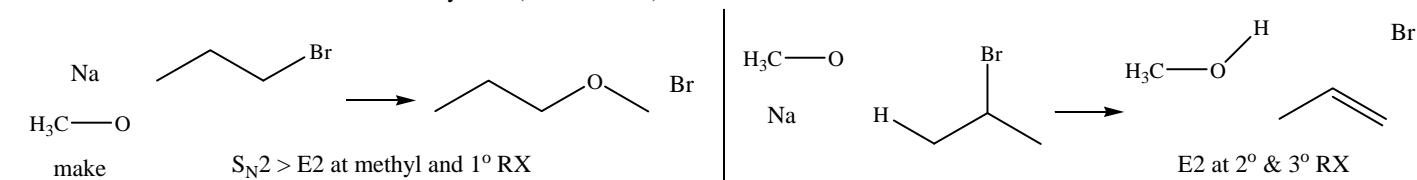


acyl substitution - further reaction with NaOH at ester can be used to make secondary alcohols = base hydrolysis (see imides below)

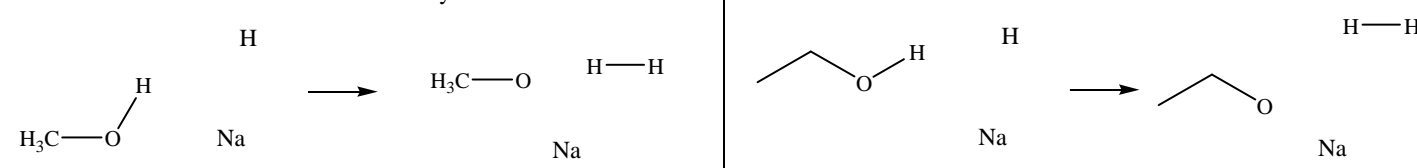




alkoxides are similar to hydroxide, except the  $S_N2$  products are ethers instead of alcohols (potassium t-butoxide is our big exception = E2) make alkoxides from alcohols and sodium hydride (in our course)



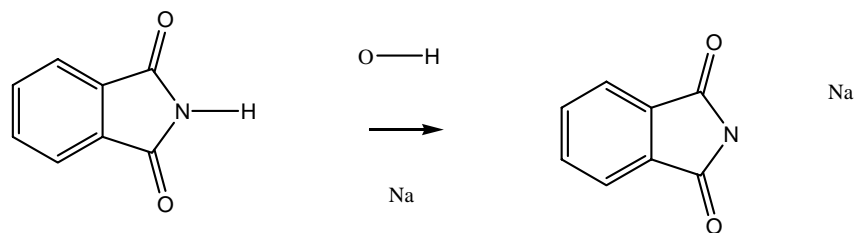
make alkoxides from alcohols and sodium hydride



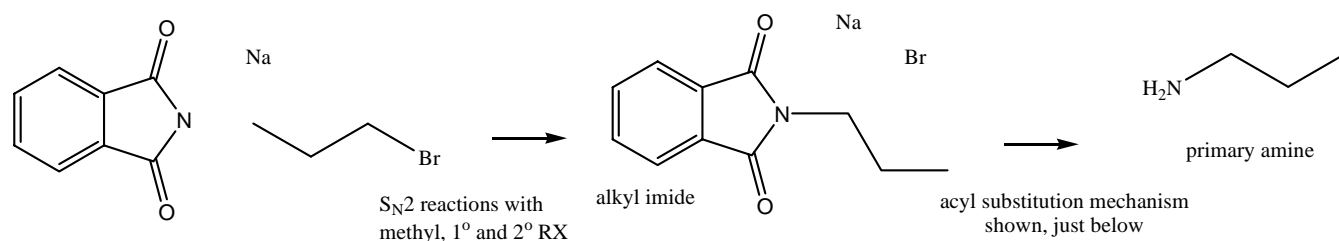
Using  $S_N2$  reaction to make primary ( $1^\circ$ ) amines

a. Gabriel amine synthesis

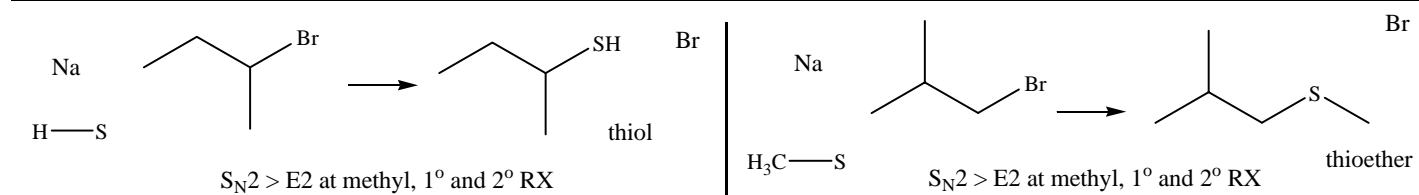
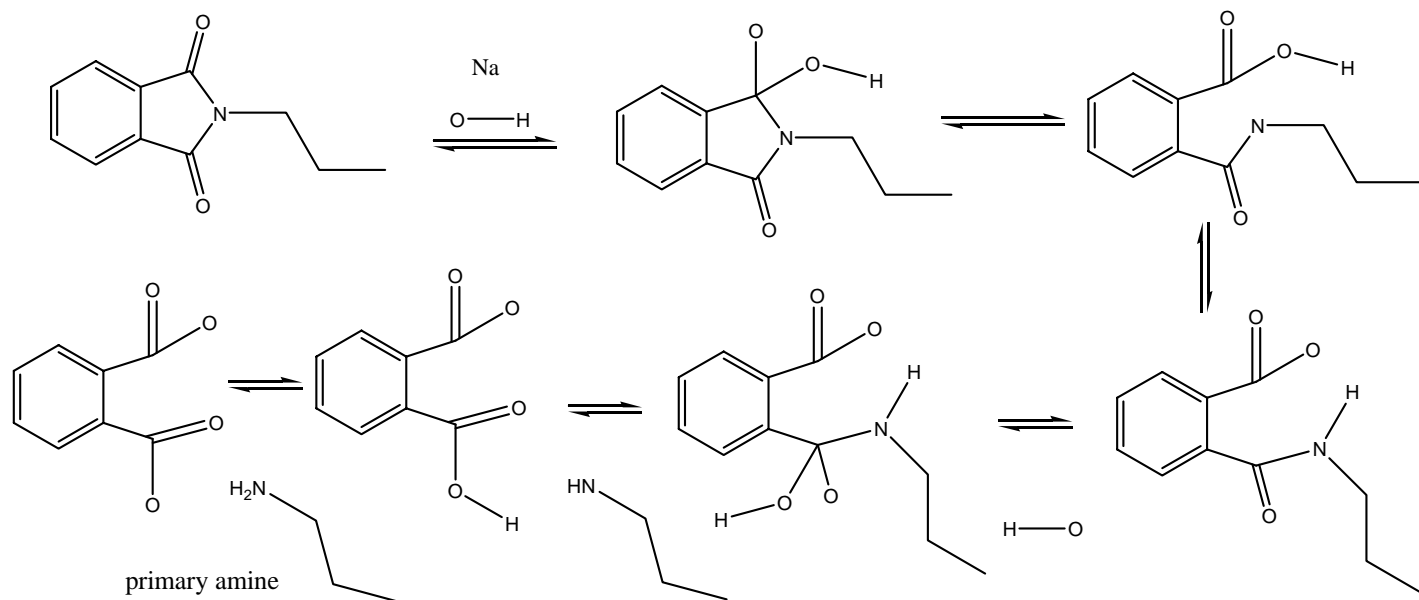
make imidate nucleophile - acid/base chemistry



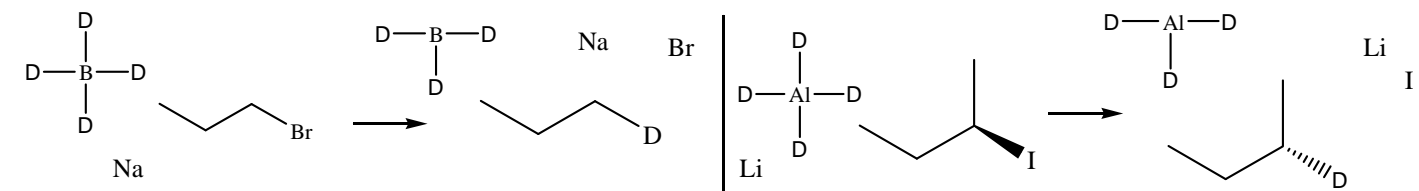
$S_N2$  reaction of imidate anion at methyl,  $1^\circ$  and  $2^\circ$  RX



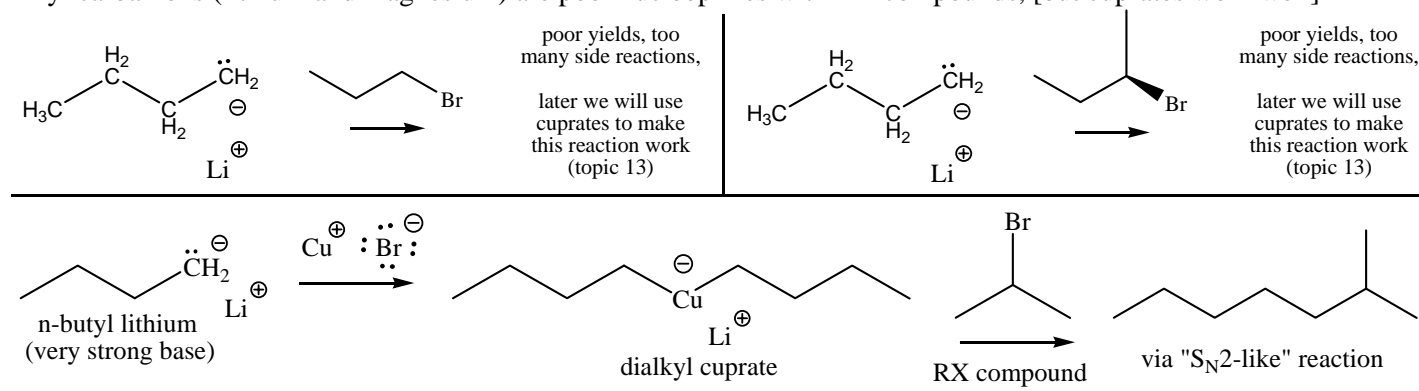
acyl substitution - further reaction with NaOH at imide (2x), base hydrolysis (similar to esters, but twice)



Nucleophilic hydride = sodium borohydride ( $\text{NaBH}_4$ ) and lithium aluminum hydride ( $\text{LiAlH}_4 = \text{LAH}$ ), [deuterium is used below to show reaction site] –  $S_N2$  reaction at Me, 1° and 2° RX.

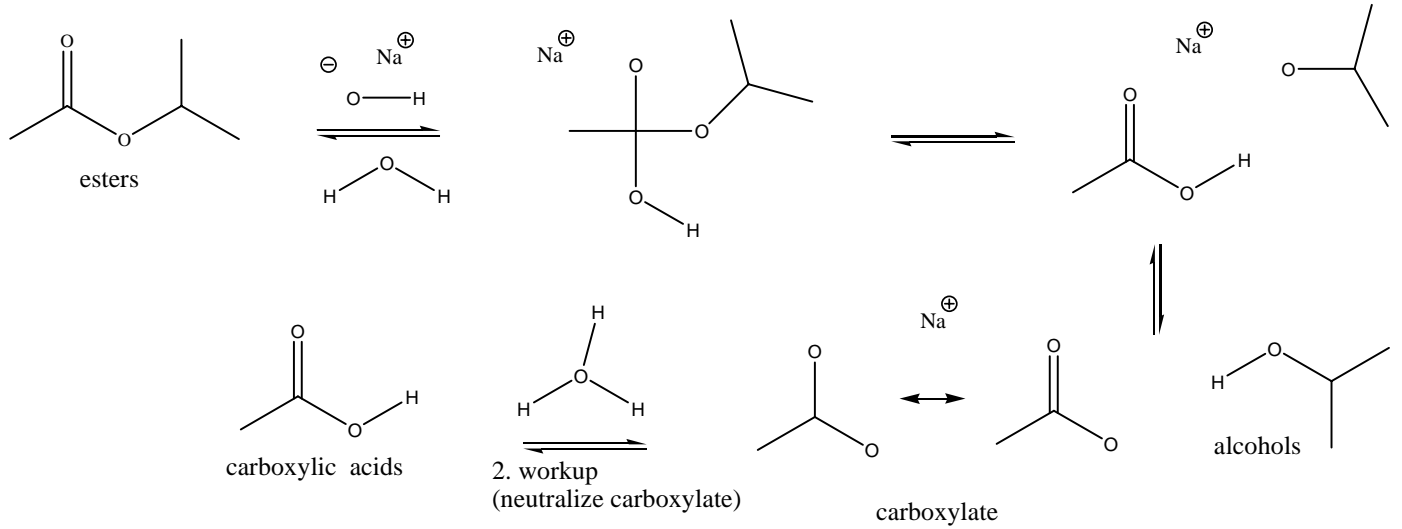


Alkyl carbanions (lithium and magnesium) are poor nucleophiles with RX compounds, [but cuprates work well]



extra reaction – also on p. 4 and similar to imide hydrolysis, just above

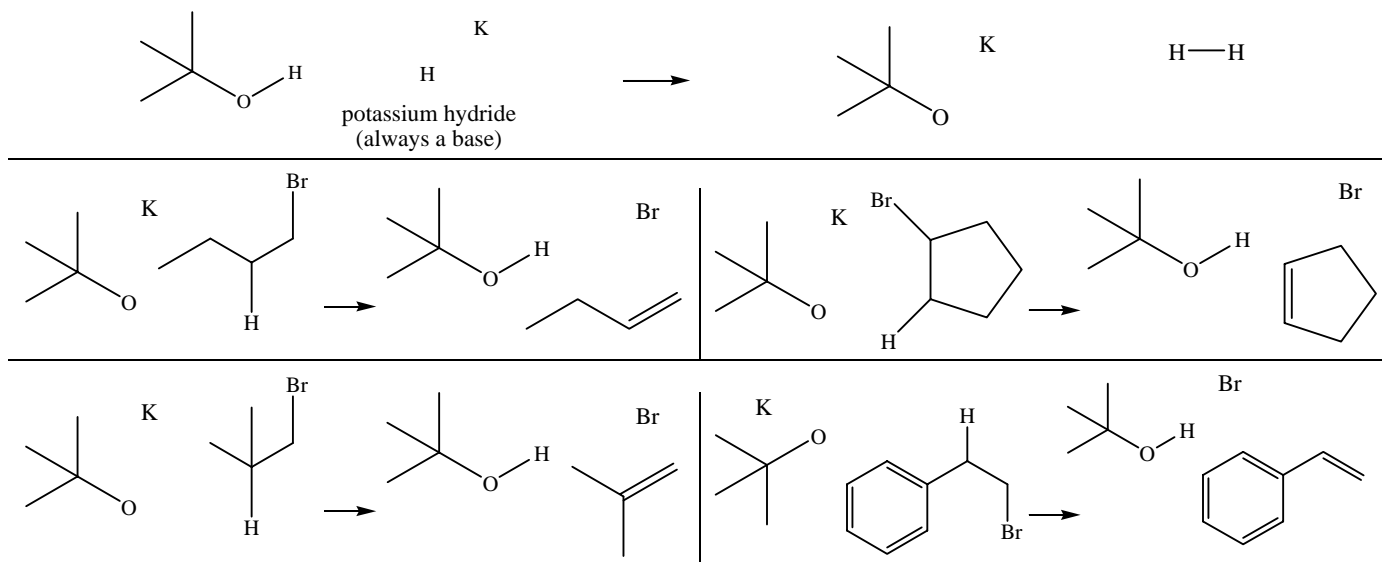
base hydrolysis of ester to form alcohol, including acid neutralization of the carboxylate to recover the carboxylic acid (if desired)



3. E2 reactions with R-X patterns, usually with potassium t-butoxide as the base (to make alkenes) and  $\text{NaNR}_2$  as the base with dibromoalkanes (to make alkynes).  $\text{S}_{\text{N}}2$  is very weak competition. Remember,  $\text{C}_{\beta}\text{-H}$  and  $\text{C}_{\alpha}\text{-X}$  should be “anti”.

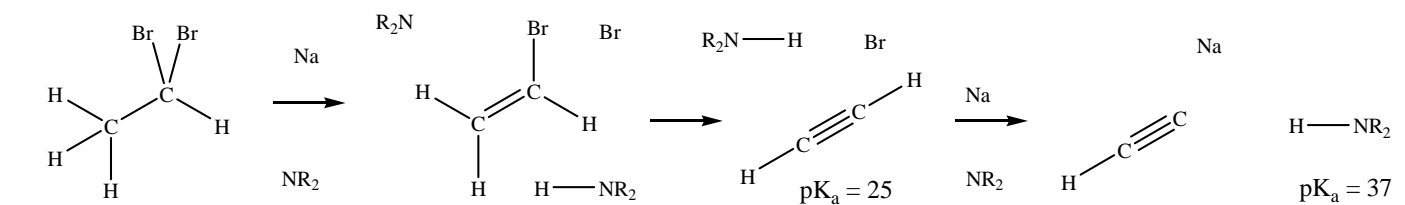
a. potassium t-butoxide with  $1^\circ$ ,  $2^\circ$  and  $3^\circ$  RX compounds to make alkenes (in our course)

make potassium t-butoxide using t-butyl alcohol and potassium hydride (in our course)

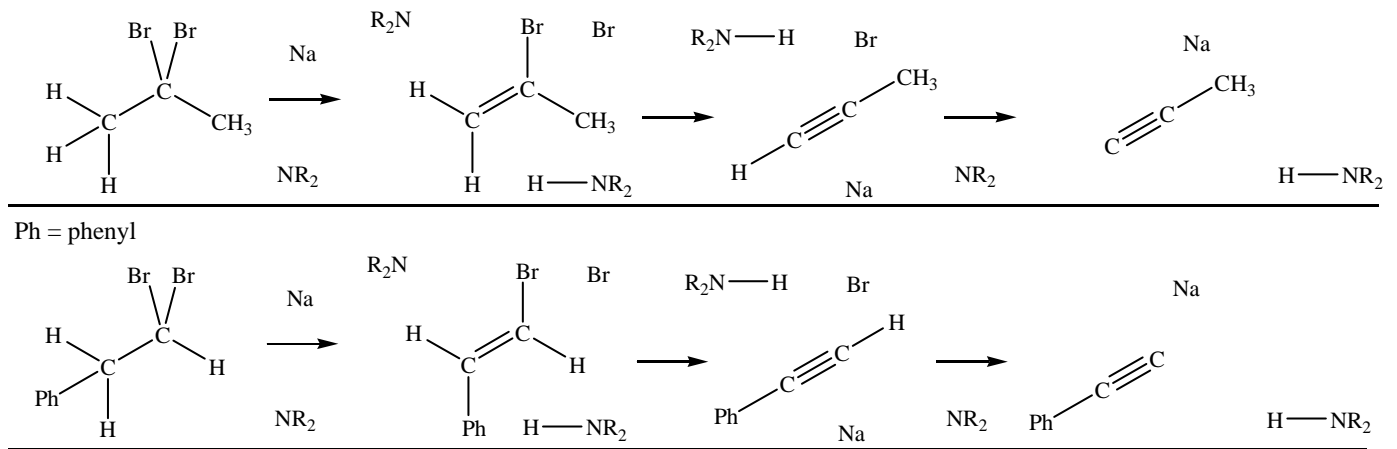


b. sodium amide with dialkyl  $\text{RX}_2$  compounds to make alkynes (in our course).

make the alkyne (two E2 reactions and terminal sp C-H ( $\text{pK}_{\text{a}} = 25$ ) is lost to the amide anion (conj. acid,  $\text{NH}_3$ ,  $\text{pK}_{\text{a}} = 37$ ))







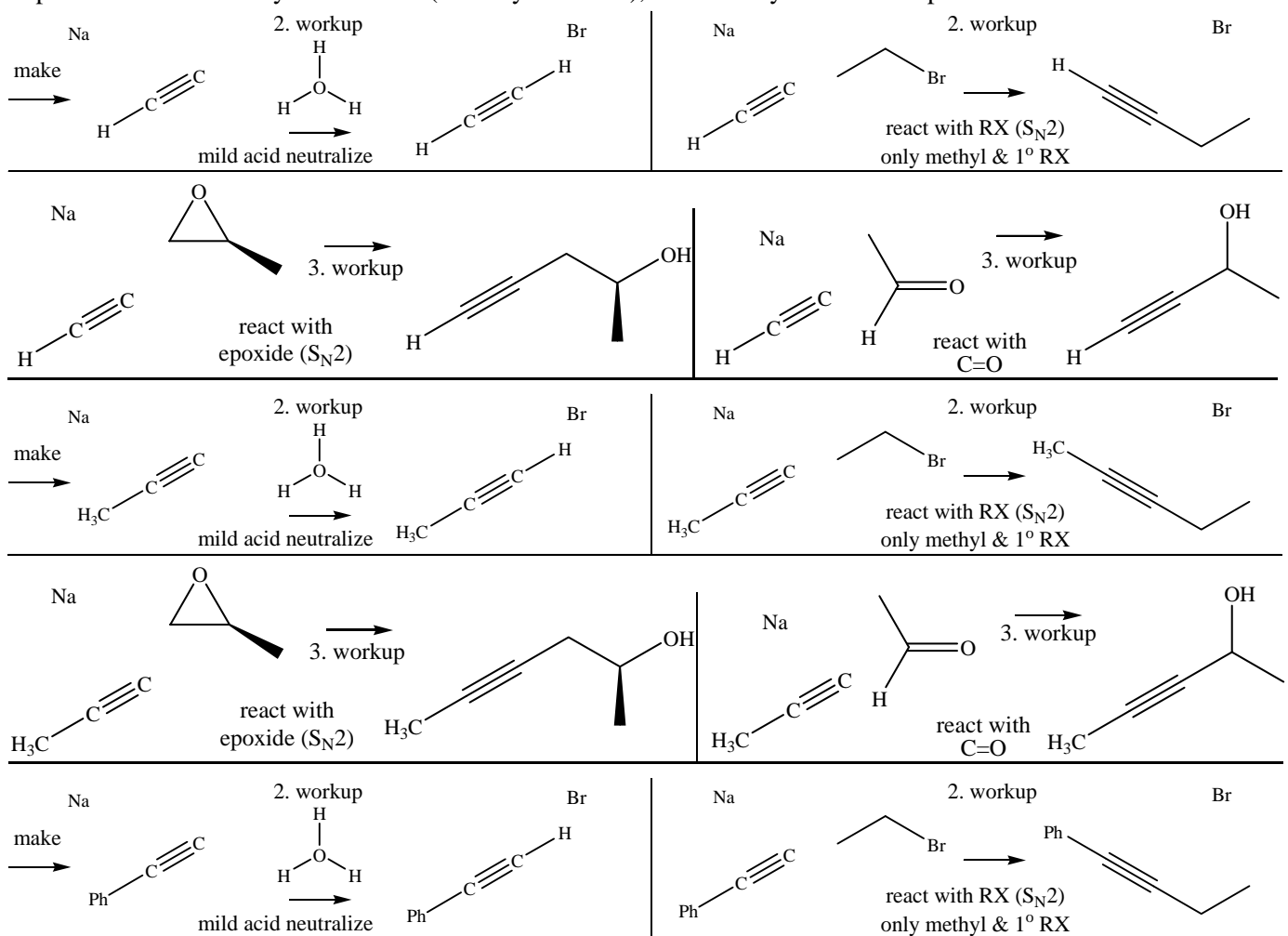
Four workup reactions with terminal acetylides available in our course (Step 2).

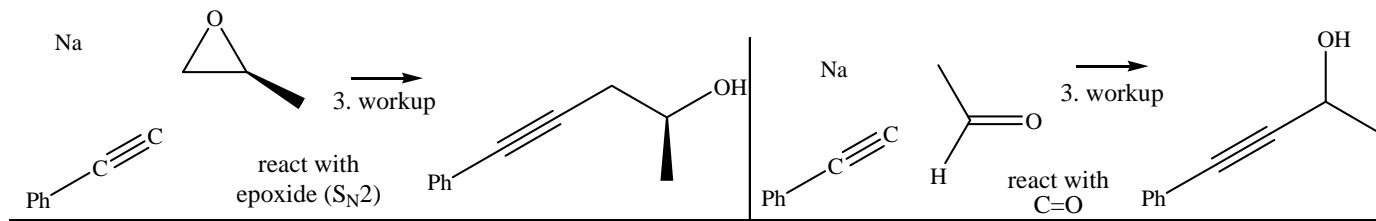
Step 2 = Neutralize with mild acid to get a terminal alkyne, or

Step 2 = react with methyl or 1° RX ( $S_N2$ ), or

Step 2 = react with epoxide (best  $S_N2$  site reacts fastest) followed by mild acid to protonate the alkoxide, or

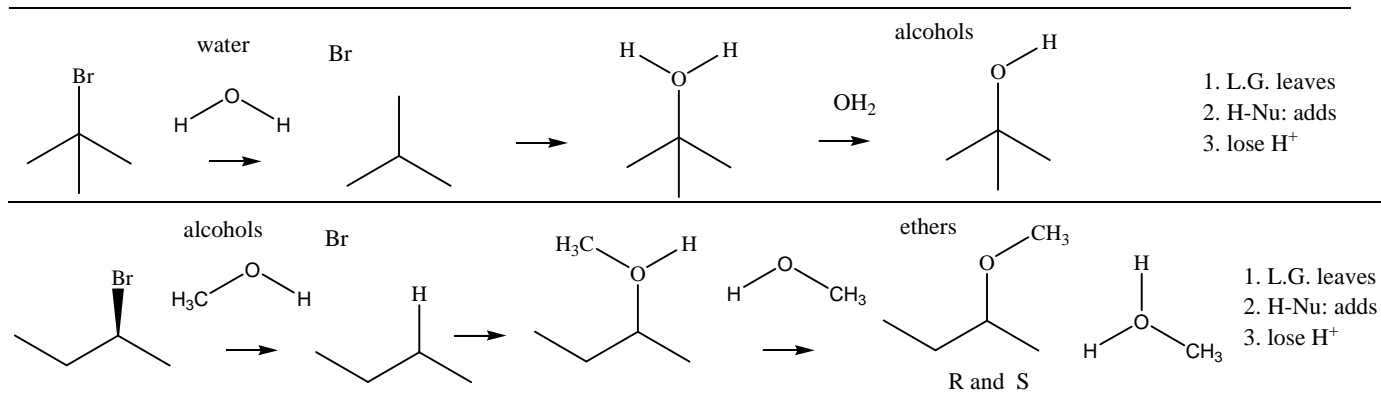
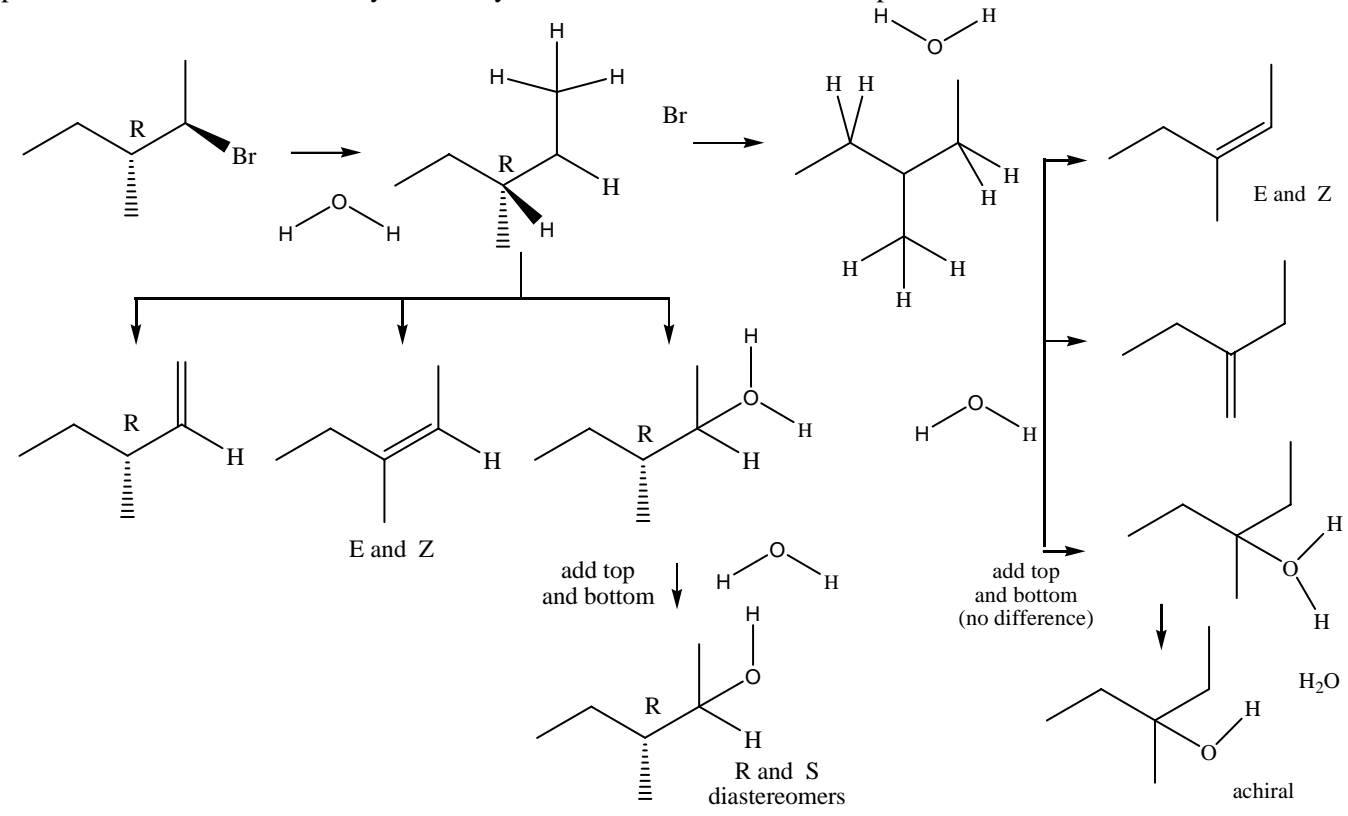
Step 2 = react with aldehyde or ketone (carbonyl addition), followed by mild acid to protonate the alkoxide.

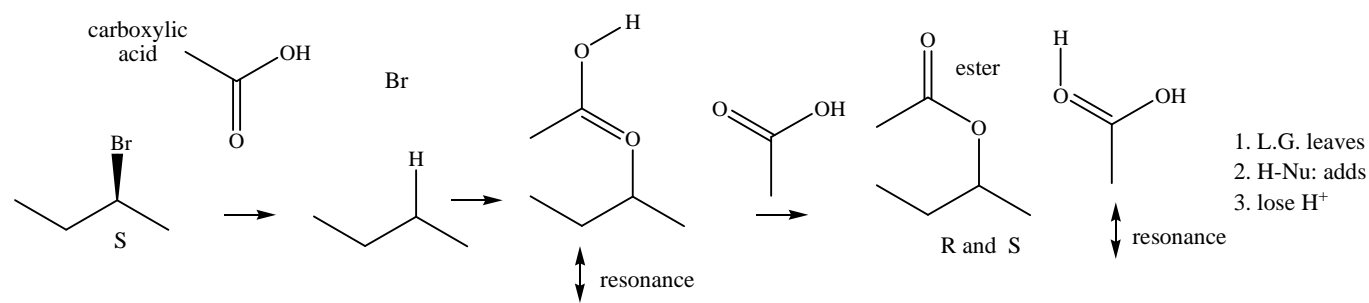




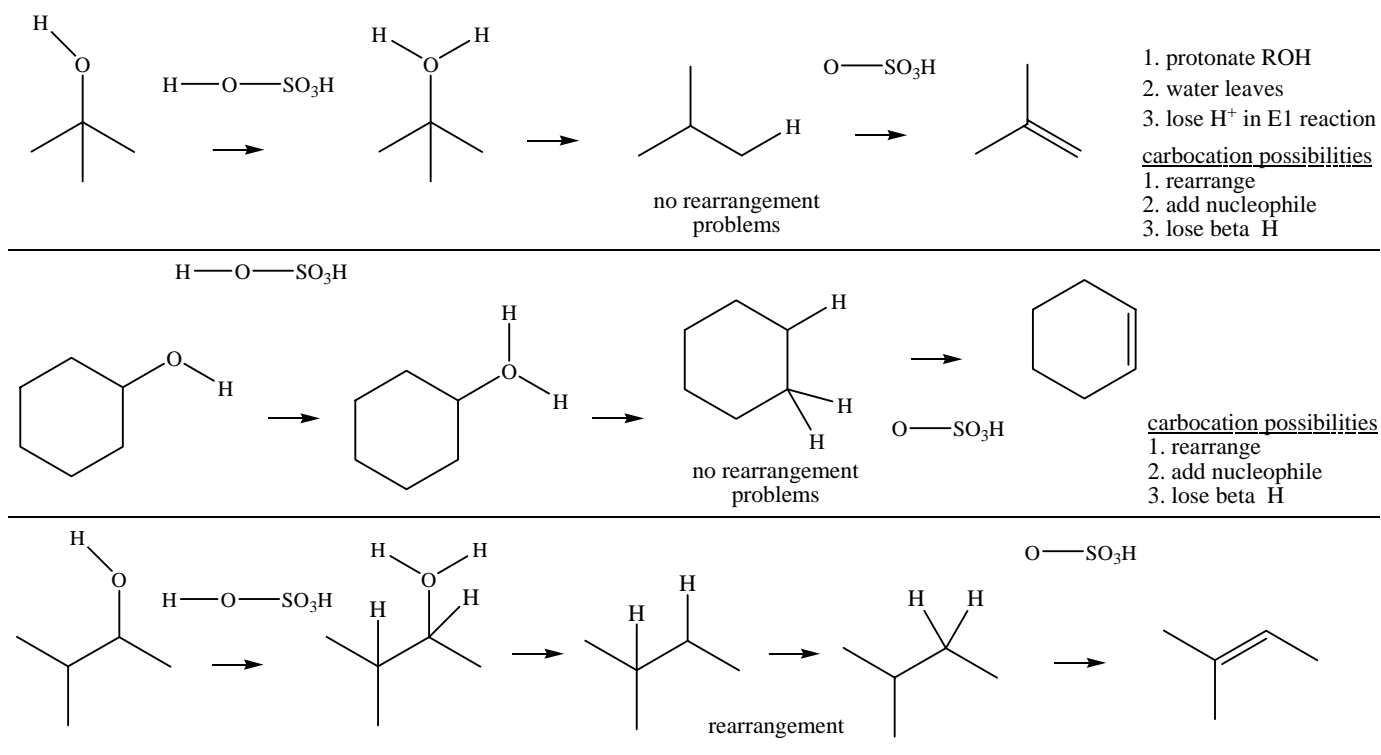
4. Examples of useful  $S_N1$  reactions –  $S_N1$  and E1 reactions require  $2^\circ$ ,  $3^\circ$ , allylic or benzylic RX so that an energetically stable carbocation can form. Useful reactions should not have rearrangement possibilities.

$S_N1$  and E1 possibilities (1. rearrangement, 2. add nucleophile, 3. lose beta proton). This example shows all three possibilities and would not be synthetically useful. Our three weak nucleophiles are  $H_2O$ , ROH and  $RCO_2H$



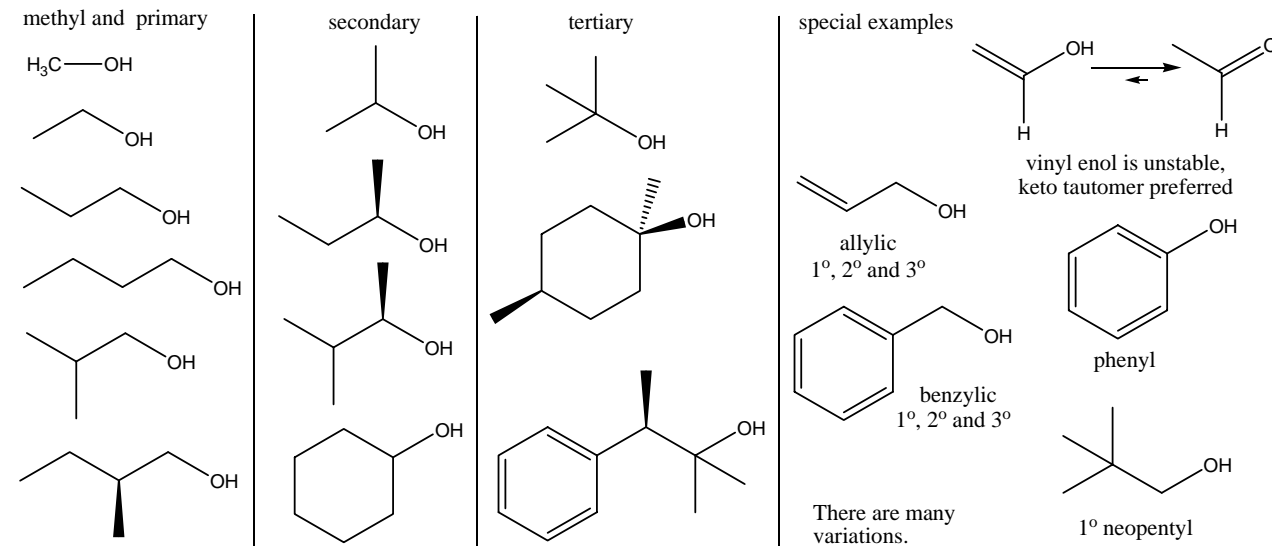


5. Examples of useful E1 reactions – The only example in our course is  $H_2SO_4/\Delta$  conditions with alcohols. We propose that 1°, 2° and 3° alcohols all work. The less stable the carbocation, the higher the temperature required. This E1 reaction works because the alkene is distilled away from the reaction mixture, continually shifting the equilibrium in the E1 direction until the starting material is used up. A diabolical trick on the  $S_N1$  reaction, the usual winner. Rearrangements are possible, with the most stable carbocation usually being the major alkene product

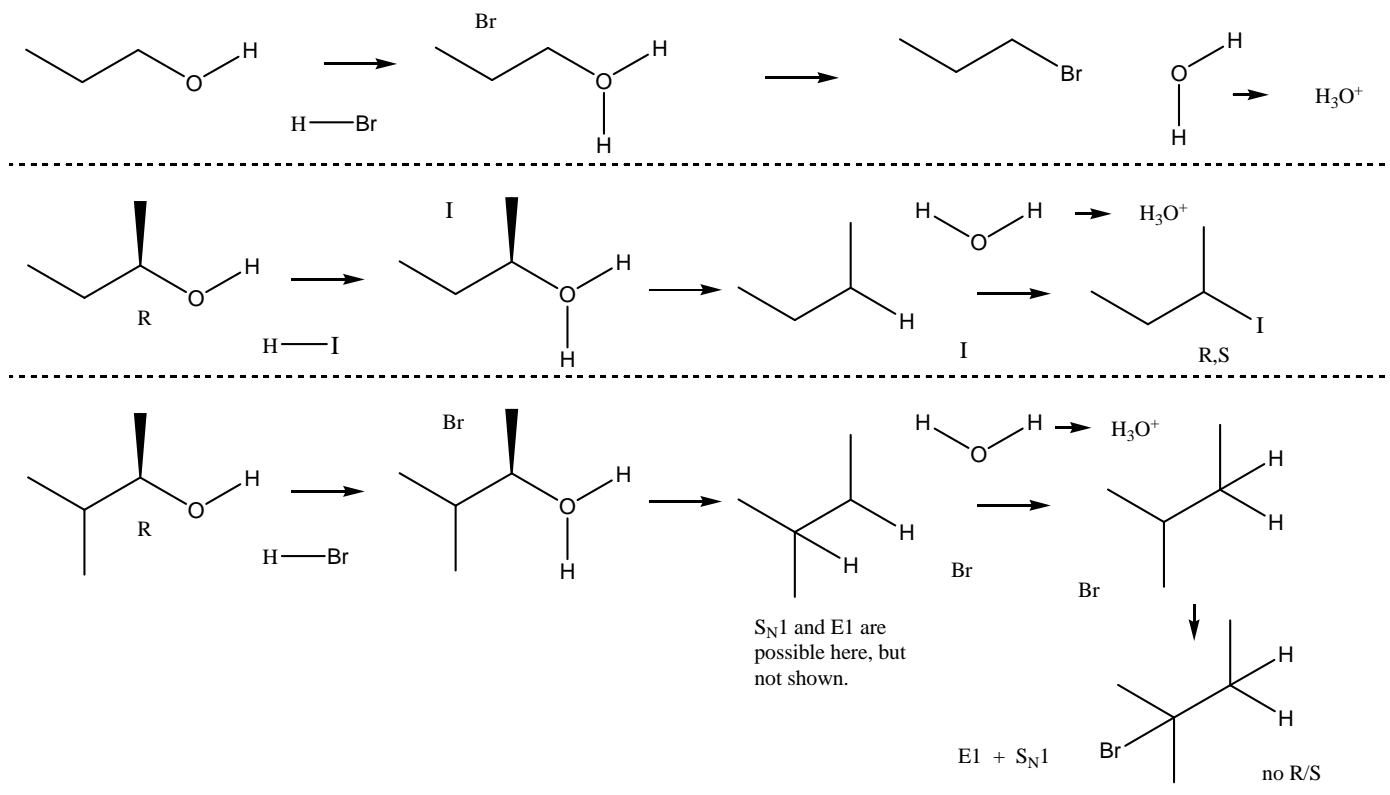


6. **Alcohol Reactions** ( $S_N$  and E reactions) (oxidation reactions with  $\text{CrO}_3$ , with water  $\rightarrow$  acids and ketones and without water  $\rightarrow$  aldehydes and ketones) (1. tosylate synthesis 2.  $S_N2$  with  $\text{NaBr} \rightarrow \text{RBr}$ ) ( $\text{SOCl}_2$ ,  $\text{SOBr}_2$ ,  $\text{PCl}_3/\text{PBr}_3 \rightarrow \text{RX}$  compounds from alcohols, can also make acid halides) (formation of alkoxides with  $\text{NaH}$  which can form ethers and esters –  $S_N2$  above and acyl substitution with acid chlorides)

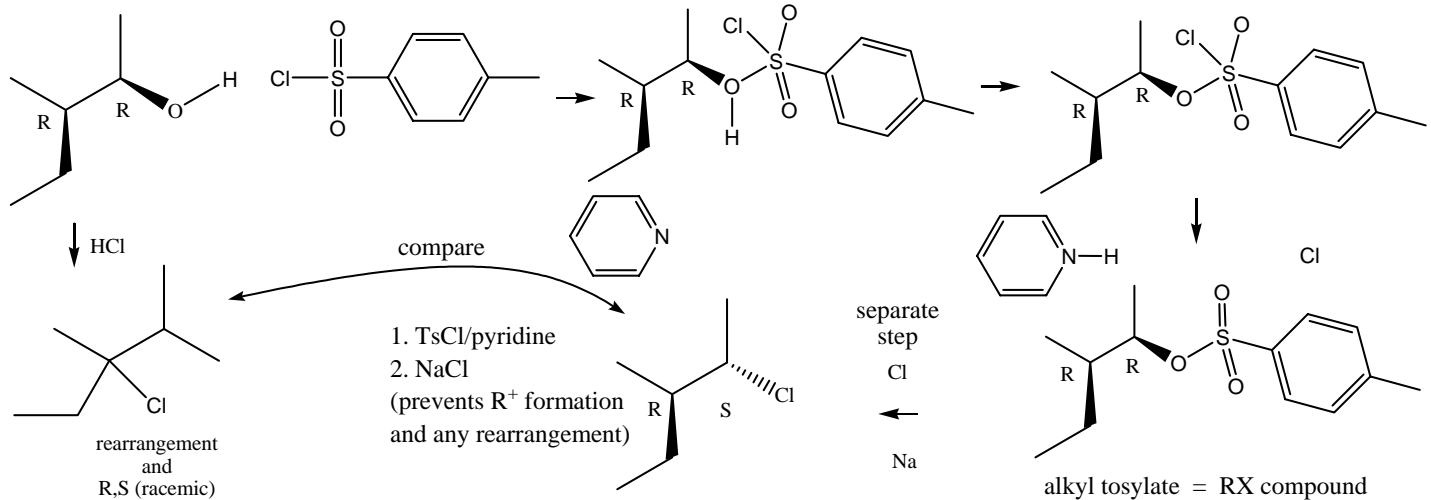
Examples of important patterns to know in our course (plus a few others).



- a.  $\text{HX} + \text{ROH}$  ( $S_N2$  at methyl and primary  $\text{ROH}$  and  $S_N1$  at secondary, tertiary, allylic and benzylic  $\text{ROH}$  in our course,  $\text{HX} = \text{HCl}, \text{HBr}, \text{HI}$ )

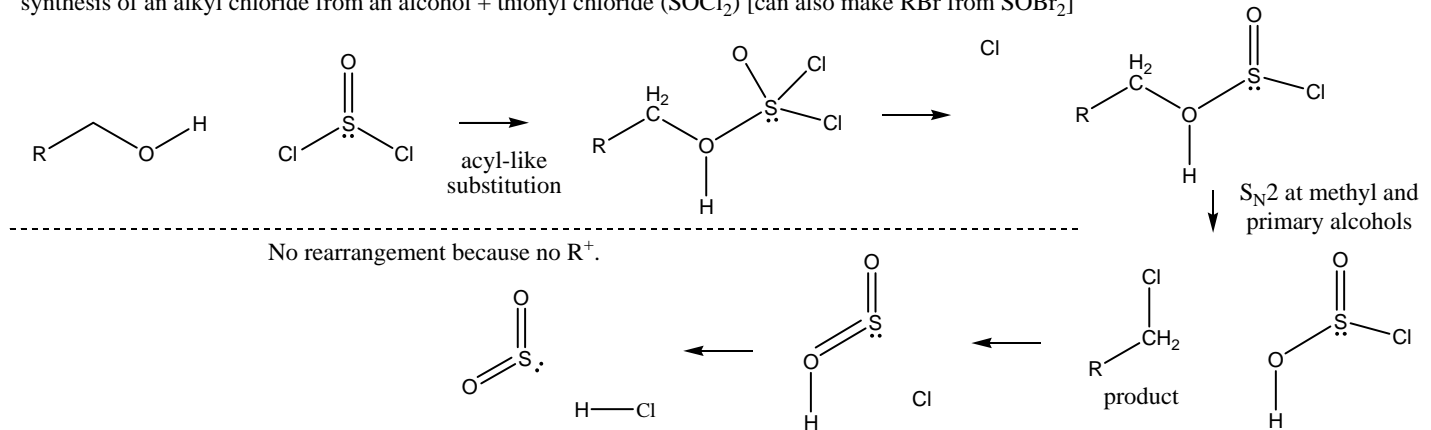


b. Formation of tosylates from ROH + TsCl (toluenesulfonyl chloride = tosyl chloride),  $S_N/E$  chemistry is possible



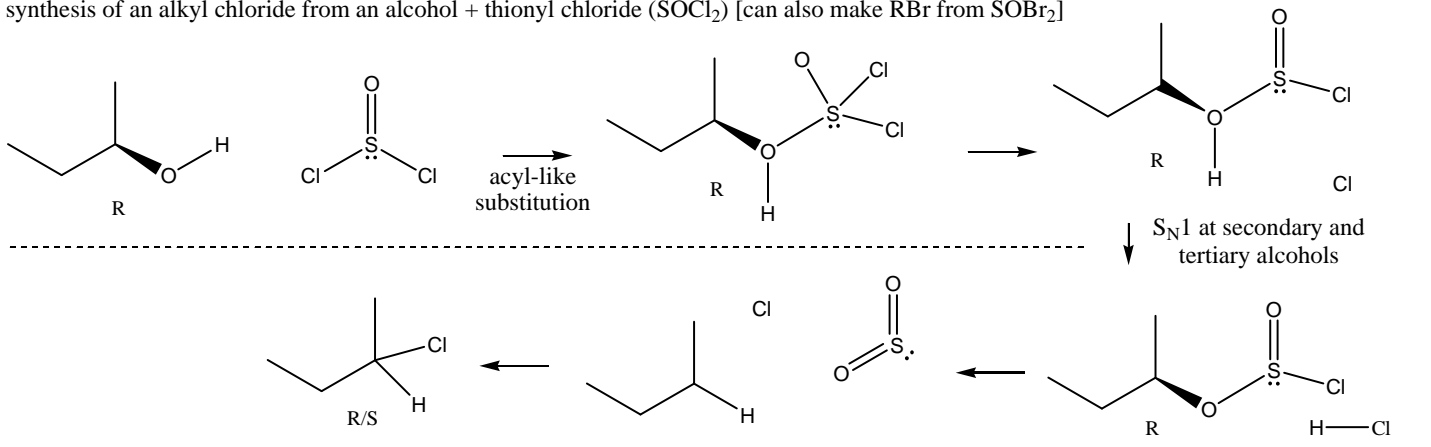
c. Thionyl chloride with methyl,  $1^\circ$  ROH = acyl-like substitution at  $SOCl_2$ , then  $S_N2$  at methyl and primary RX.

synthesis of an alkyl chloride from an alcohol + thionyl chloride ( $SOCl_2$ ) [can also make RBr from  $SOBr_2$ ]

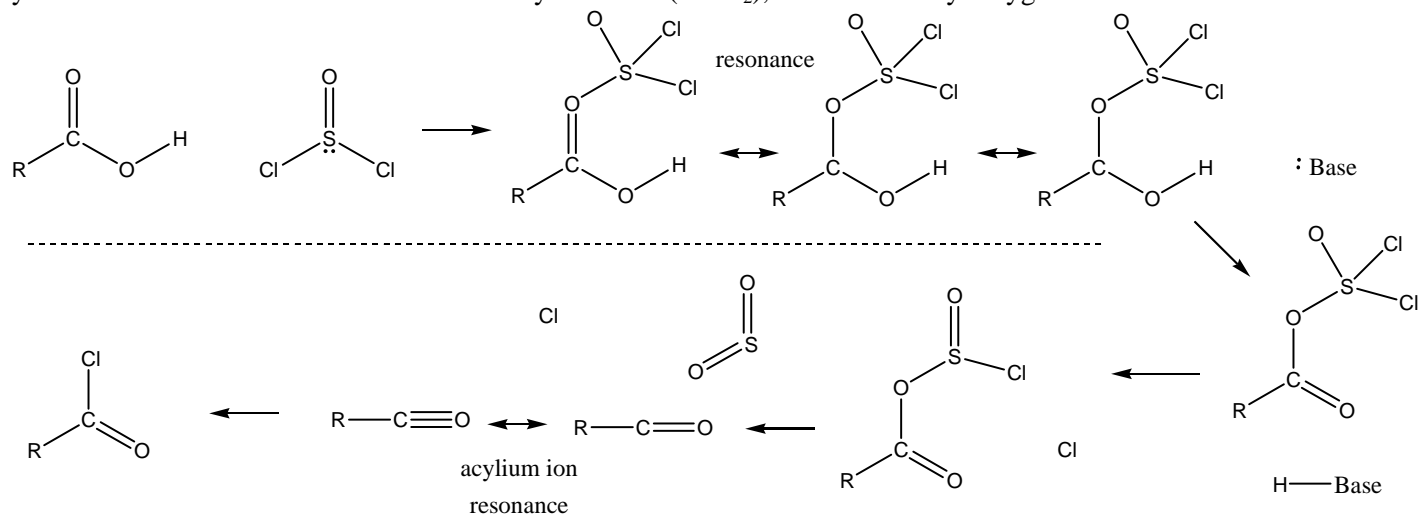


Thionyl chloride with  $2^\circ$  and  $3^\circ$  ROH = acyl substitution, then  $S_N1$  (there are various ways you can write this mechanism)

synthesis of an alkyl chloride from an alcohol + thionyl chloride ( $SOCl_2$ ) [can also make RBr from  $SOBr_2$ ]

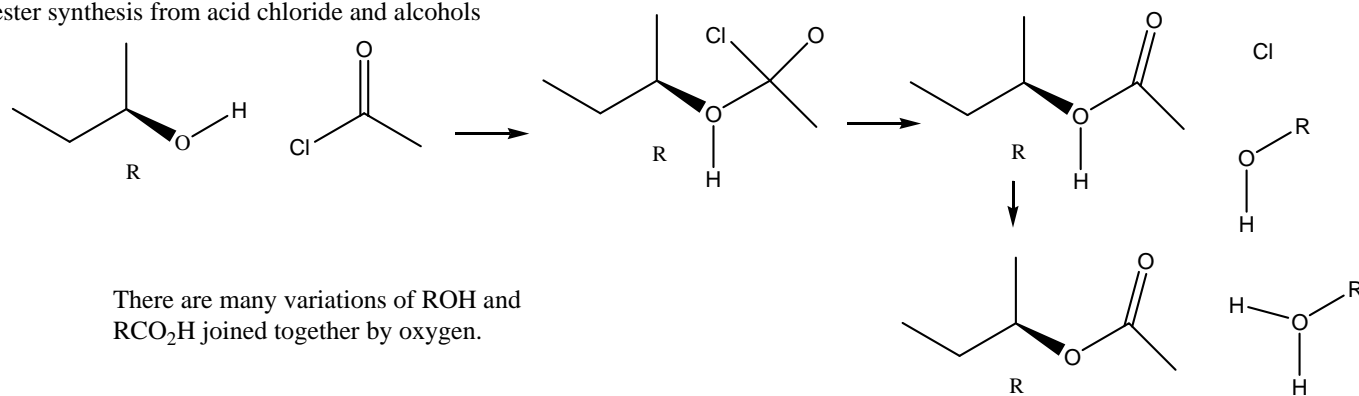


Synthesis of acid chlorides from acids + thionyl chloride ( $\text{SOCl}_2$ ), use the carbonyl oxygen over the OH.

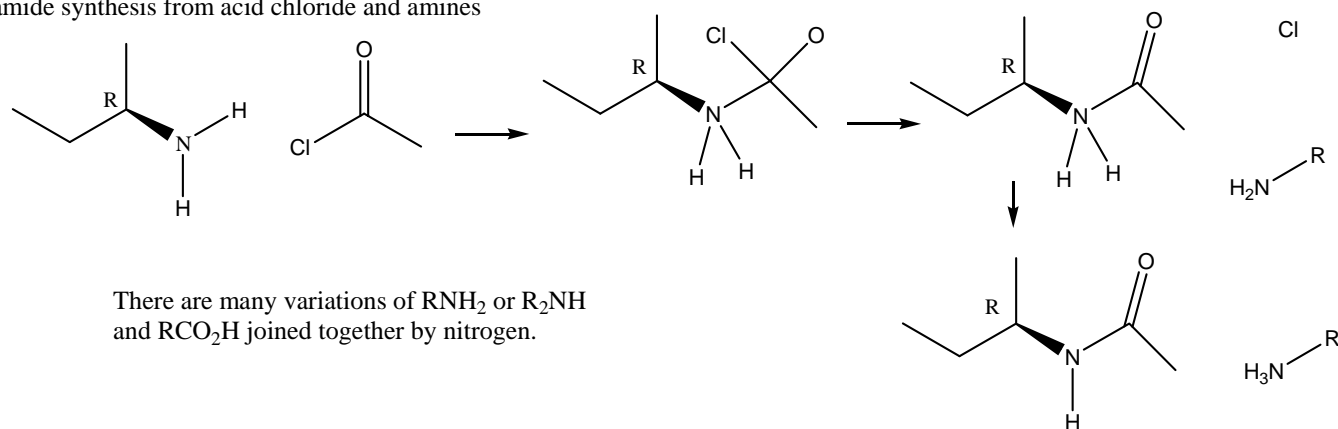


d. Formation of esters from  $\text{ROH} + \text{acid chlorides}$  and amides from  $\text{RNH}_2$  or  $\text{R}_2\text{NH} + \text{acid chlorides}$

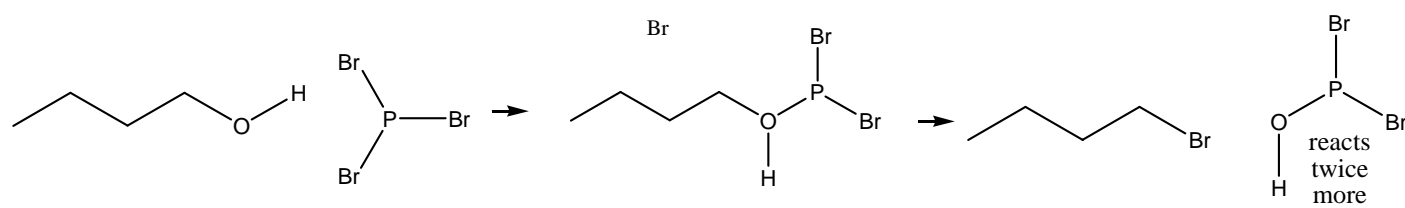
ester synthesis from acid chloride and alcohols



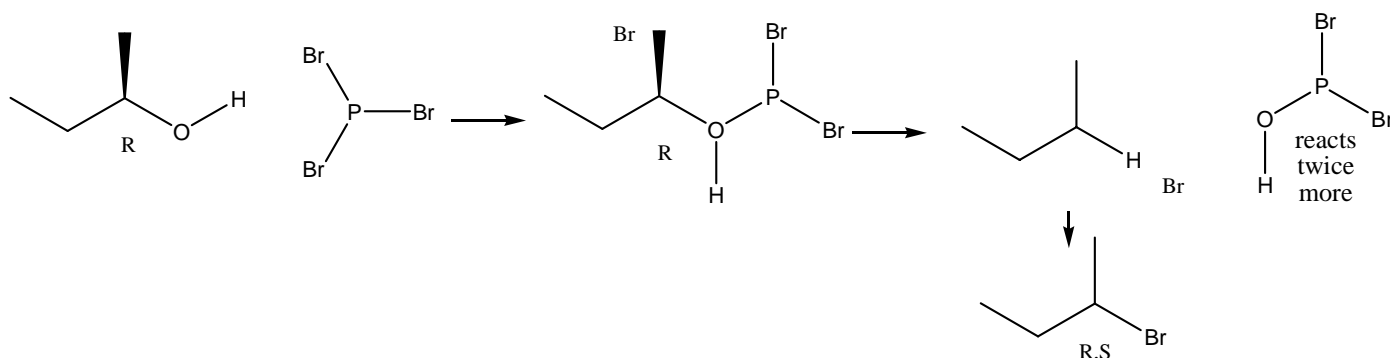
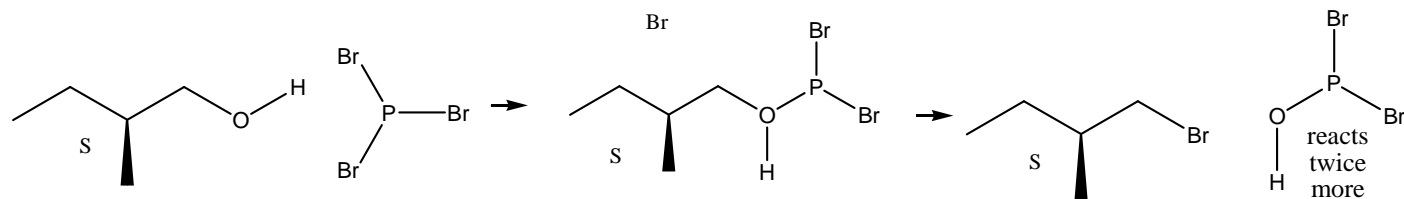
amide synthesis from acid chloride and amines



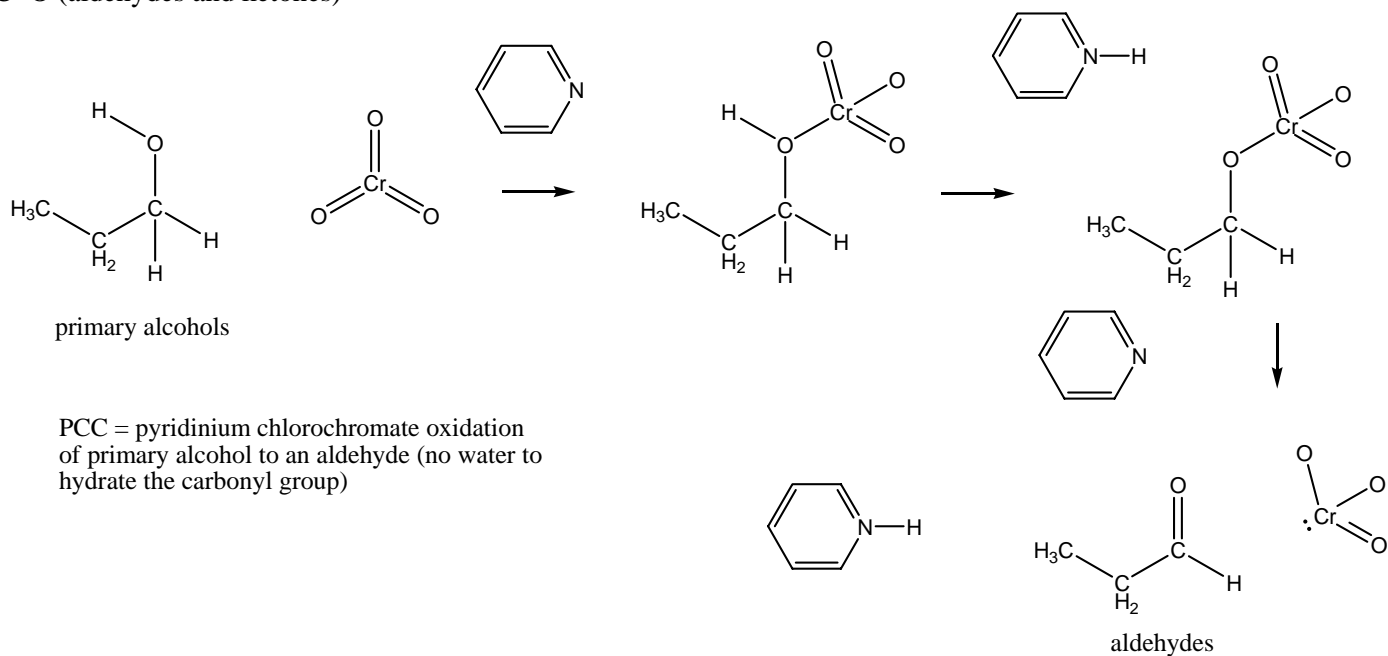
e. Phosphorous tribromide ( $\text{PBr}_3$ ) =  $\text{S}_{\text{N}}2$  at  $\text{PBr}_3$ , then  $\text{S}_{\text{N}}2$  (at methyl and primary  $\text{ROH}$ )



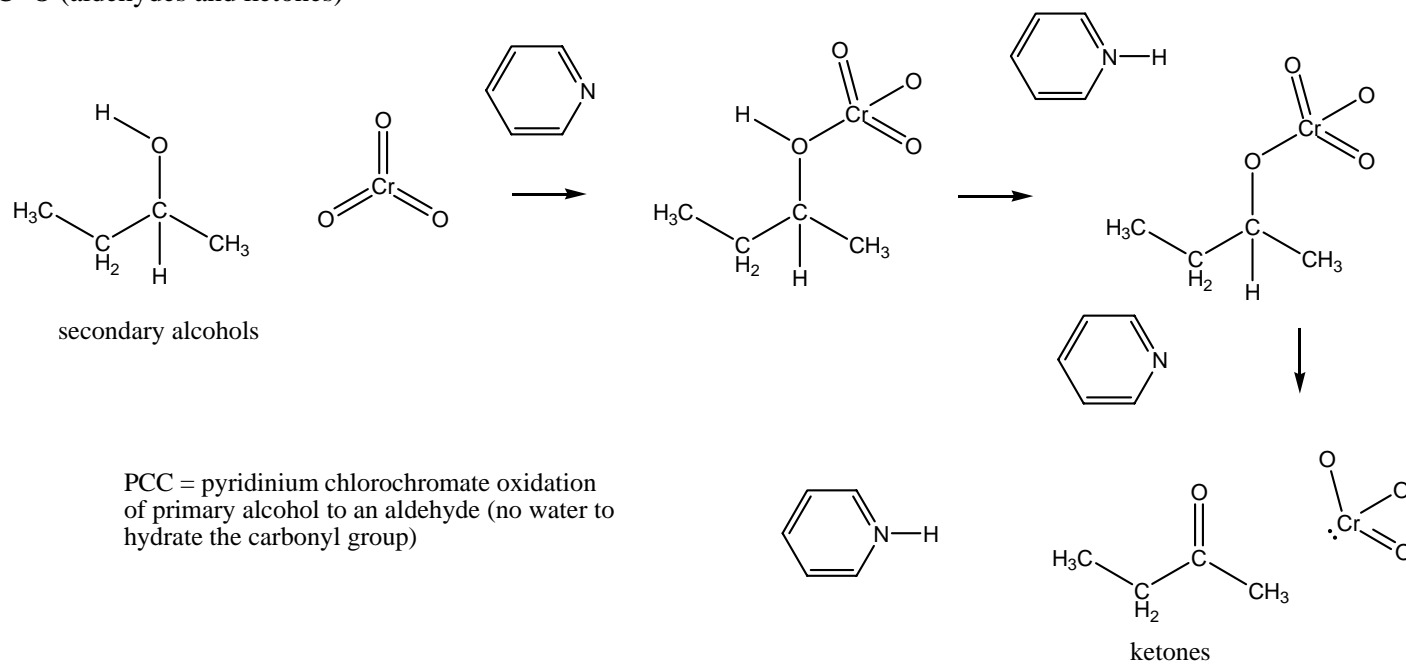
Phosphorous tribromide ( $\text{PBr}_3$ ) =  $\text{S}_{\text{N}}2$ , then  $\text{S}_{\text{N}}1$  (at secondary, tertiary, allylic and benzylic ROH)



f.  $\text{CrO}_3$  oxidations of alcohols (methyl,  $1^\circ$  and  $2^\circ$  ROH) without water = PCC,  $\text{Cr}=\text{O}$  addition, acid/base and  $\text{E}2$  to form  $\text{C}=\text{O}$  (aldehydes and ketones)

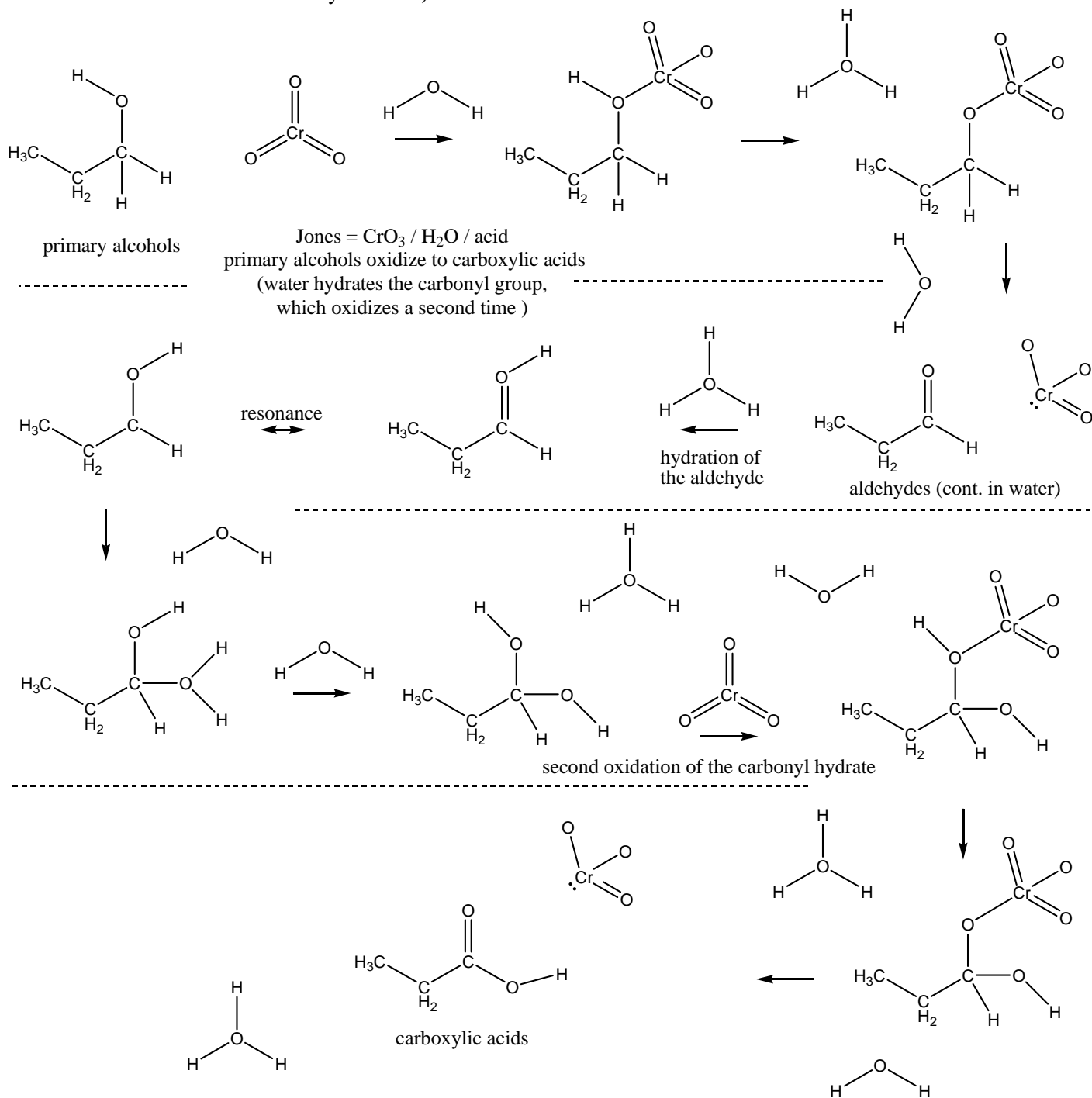


$\text{CrO}_3$  oxidations of alcohols (methyl,  $1^\circ$  and  $2^\circ$  ROH) without water = PCC, Cr=O addition, acid/base and E2 to form C=O (aldehydes and ketones)

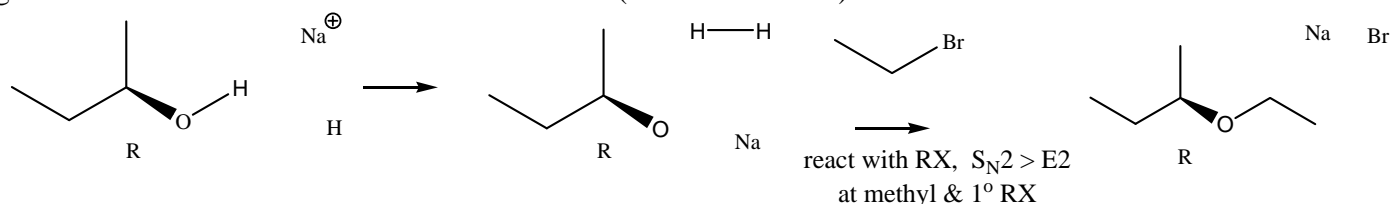


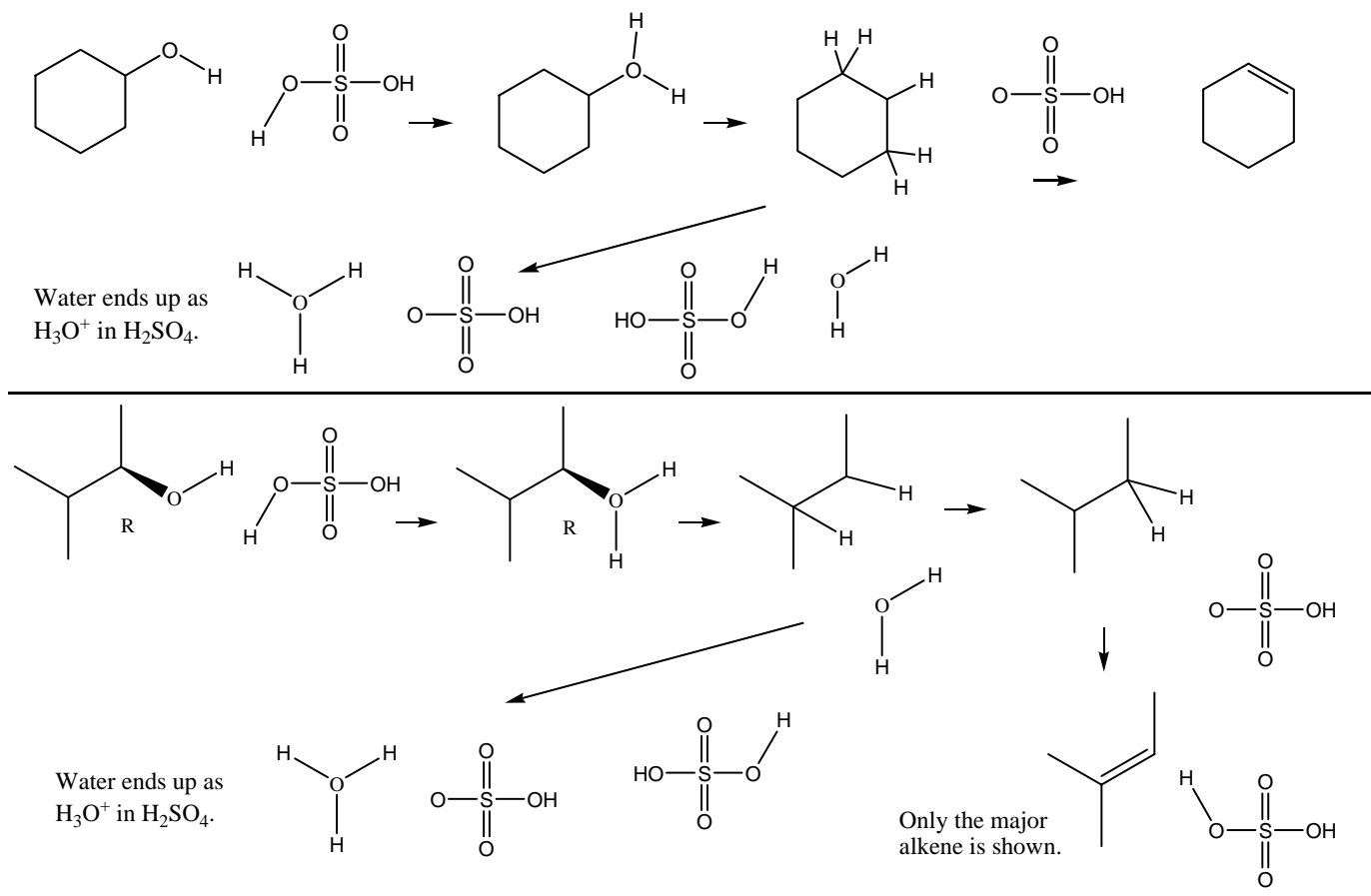


CrO<sub>3</sub> oxidations of alcohols (methyl, 1° and 2° ROH) with water = Jones reagent, Cr=O addition by alcohol, acid/base and E2 to form C=O, then hydration of C=O and repeat reactions when 1° alcohol (forms carboxylic acids from primary alcohols and ketones from secondary alcohols)



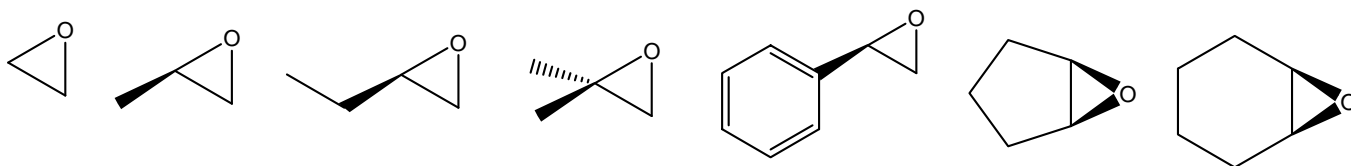
g. Formation of alkoxide from ROH + NaH or KH (acid/base reaction)



h. Dehydration to alkene (E1) from ROH + H<sub>2</sub>SO<sub>4</sub>/Δ (possibility of rearrangements)

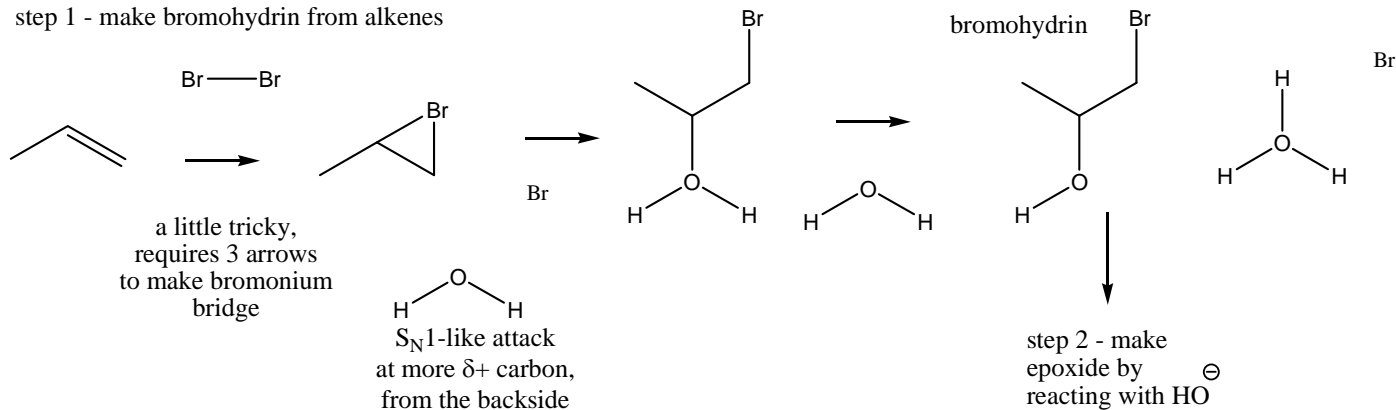
**Epoxide reactions**

a. Examples of important patterns to know from our starting materials.

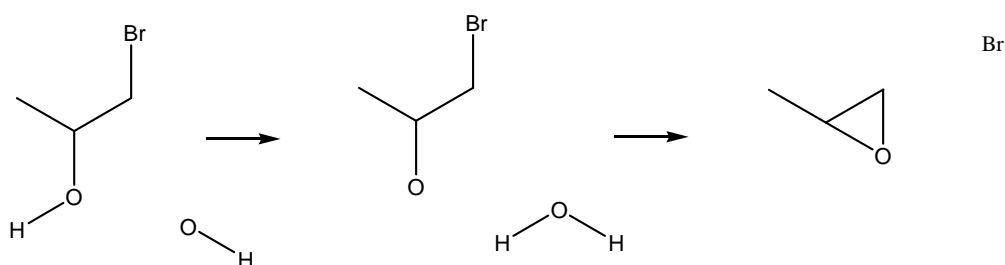


We can make epoxides from alkenes using 1.  $\text{Br}_2/\text{H}_2\text{O}$ , 2.  $\text{NaOH}$ . (Later we'll make epoxides using mCPBA too.)

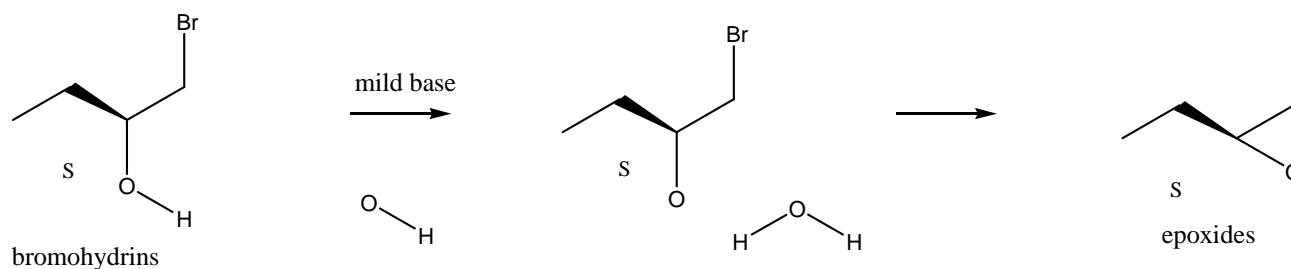
step 1 - make bromohydrin from alkenes



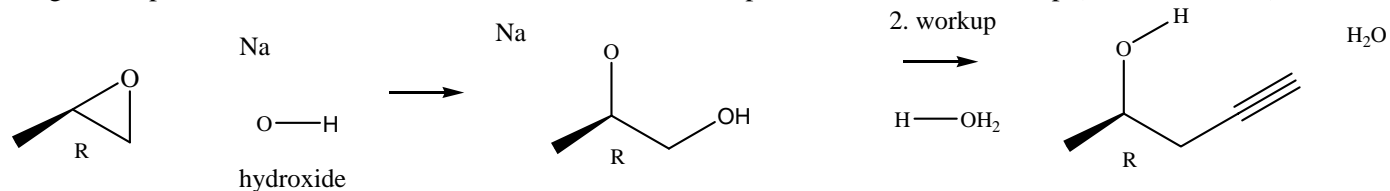
step 2 - make epoxide by reacting with  $\text{HO}^-$

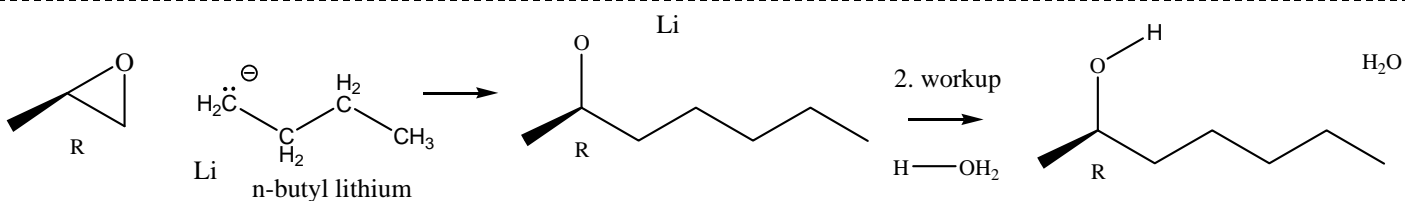
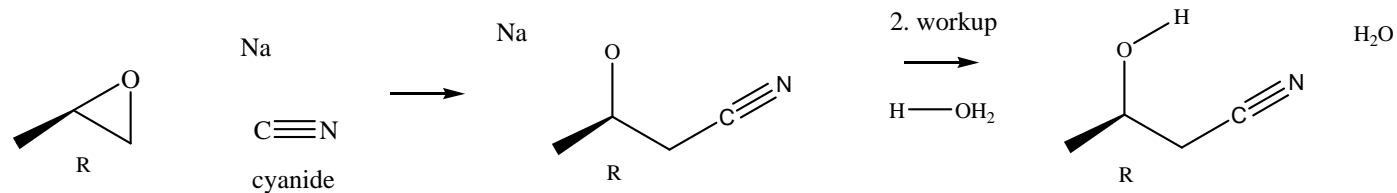
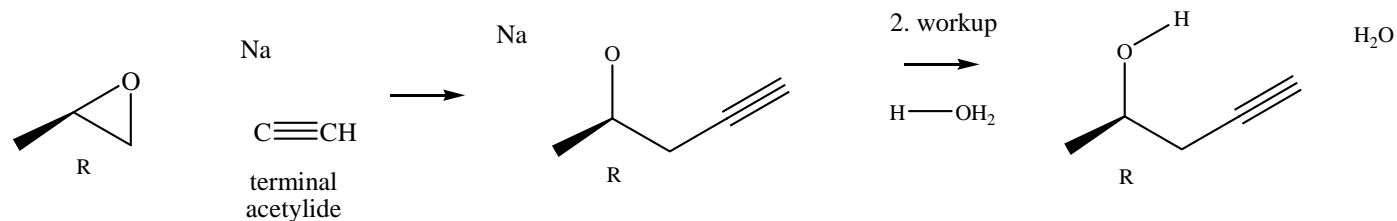
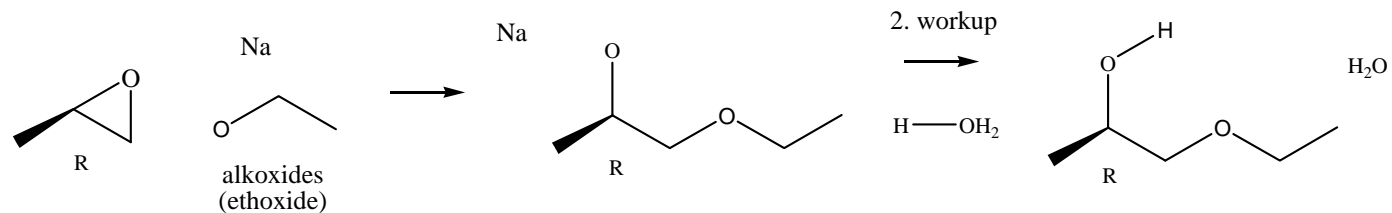


epoxide synthesis from bromohydrin

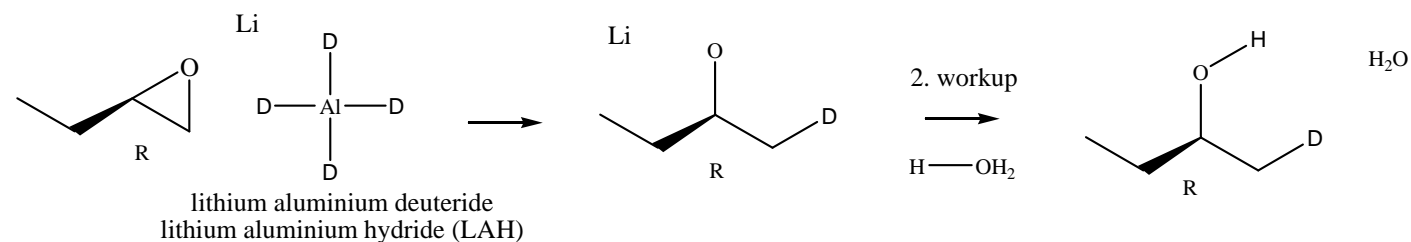
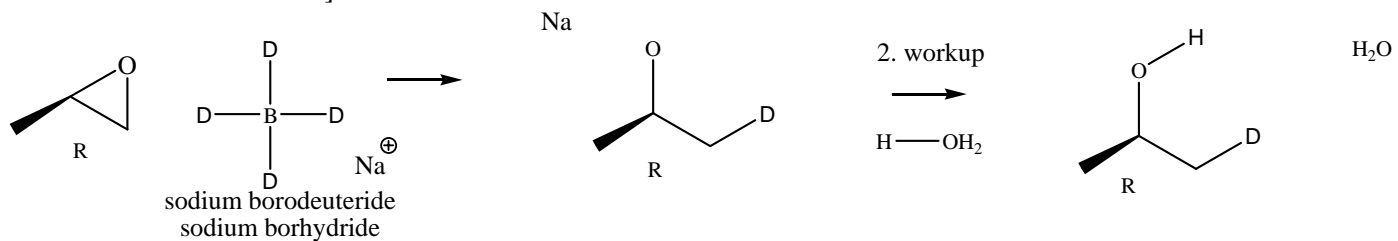


Strong nucleophile conditions -  $\text{S}_{\text{N}}2$  like attack at less hindered epoxide carbon, and workup (overall addition)

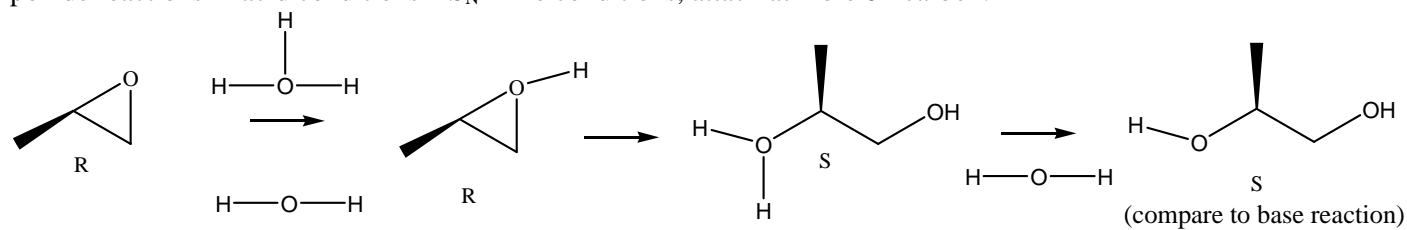


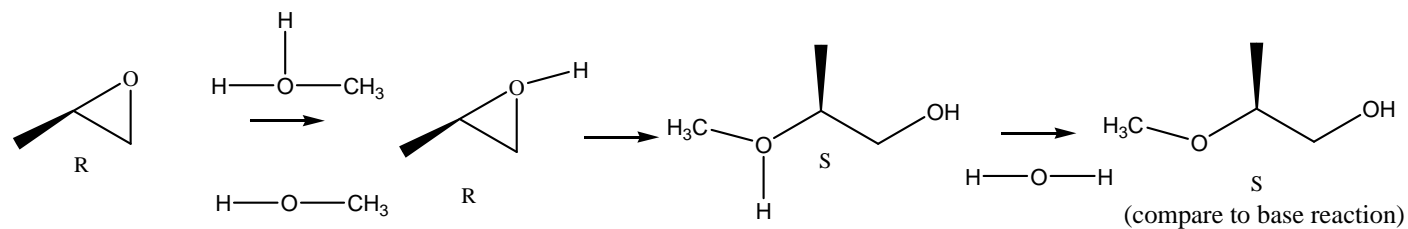


Nucleophilic hydride = sodium borohydride (NaBH<sub>4</sub>) and lithium aluminum hydride (LiAlH<sub>4</sub> = LAH), [deuterium is used below to show reaction site]

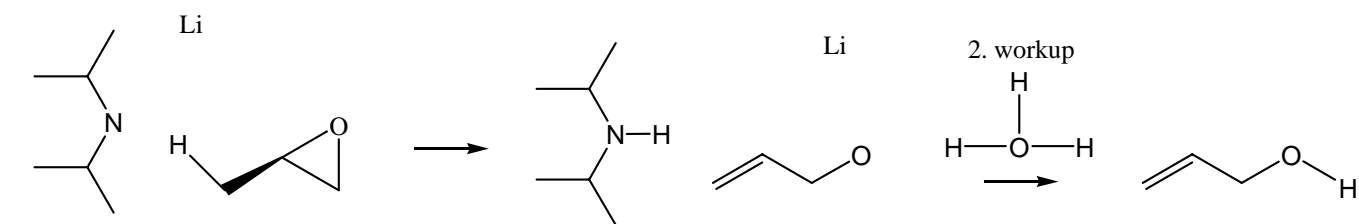


Epoxide reactions in acid conditions – S<sub>N</sub>1-like conditions, attack at more δ<sup>+</sup> carbon.

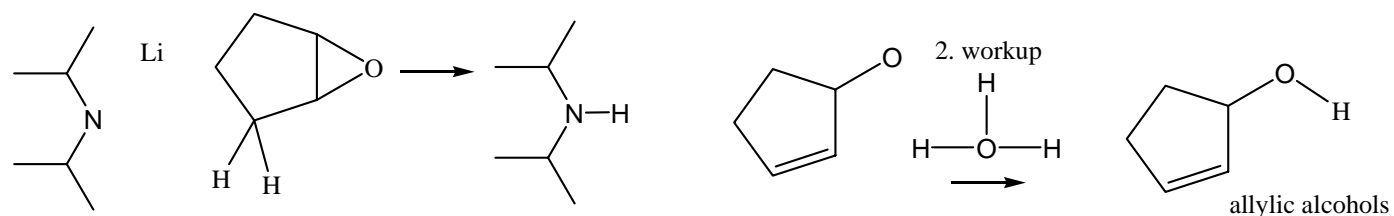




Our only E2 reaction for epoxides. Uses very basic, sterically bulky LDA (always a base).

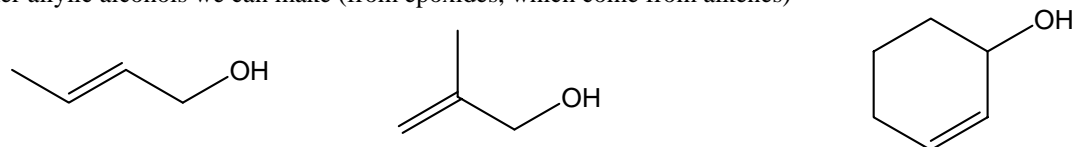


LDA = lithium diisopropylamine (always a base)



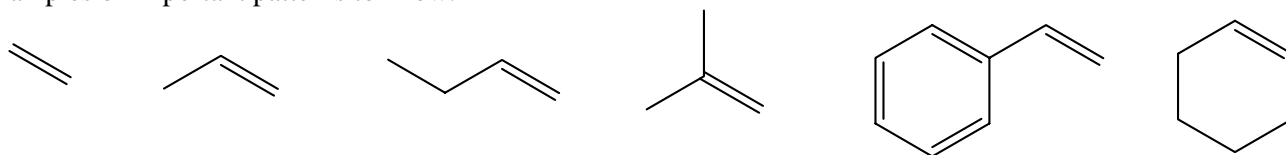
allylic alcohols

other allylic alcohols we can make (from epoxides, which come from alkenes)

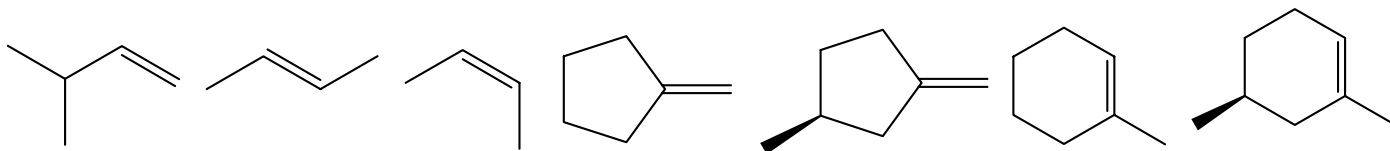


**Alkene and Alkyne reactions**

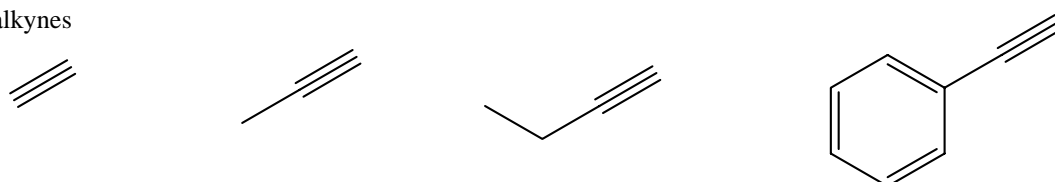
Examples of important patterns to know.



other patterns showing regioselectivity and stereoselectivity



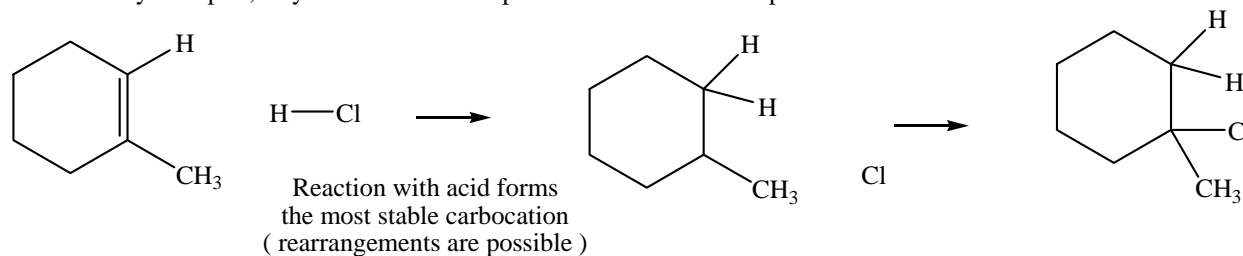
alkynes



We can make alkenes from RX (E2 reactions) and ROH ( $\text{H}_2\text{SO}_4/\Delta$ ), and alkynes from  $\text{RX}_2$  ( $\text{NaNR}_2$ ), for now.

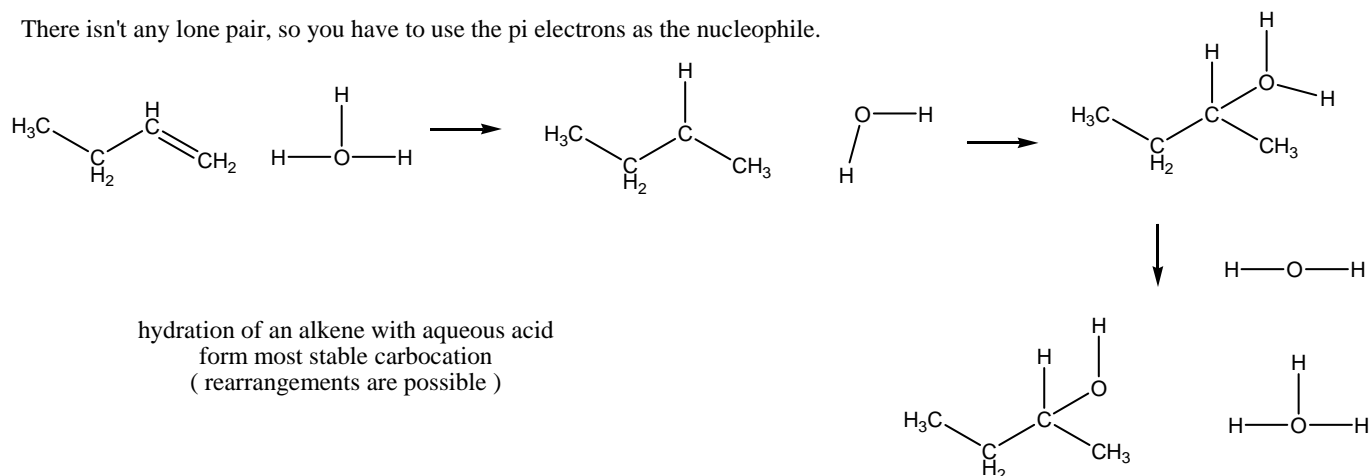
a. C=C addition reaction with H-Cl (H-Br and H-I are similar), Markovnikov addition forms most stable carbocation

There isn't any lone pair, so you have to use the pi electrons as the nucleophile.



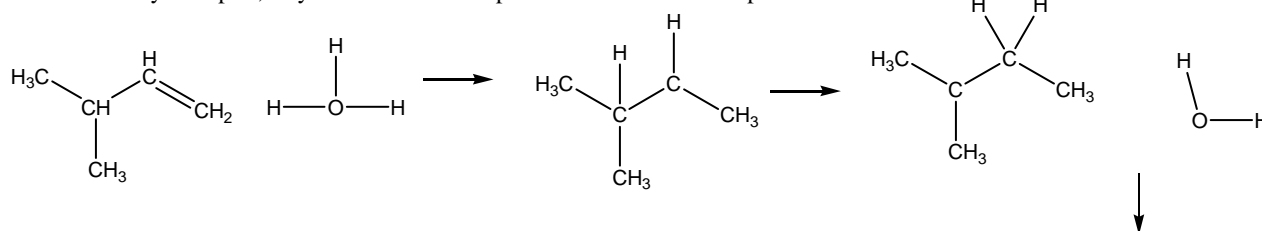
b. C=C aqueous acid hydration reaction, goes via top/bottom addition (hydration of an alkene)

There isn't any lone pair, so you have to use the pi electrons as the nucleophile.

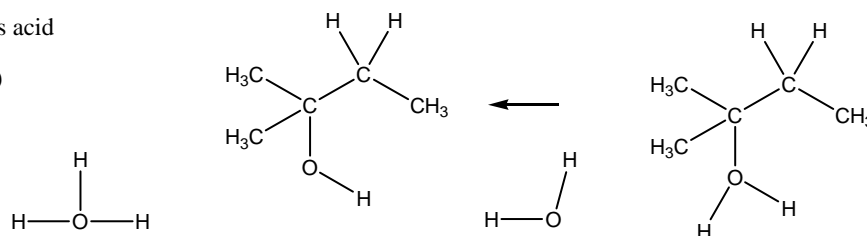


## C=C addition reaction (hydration of an alkene), with rearrangement

There isn't any lone pair, so you have to use the pi electrons as the nucleophile.

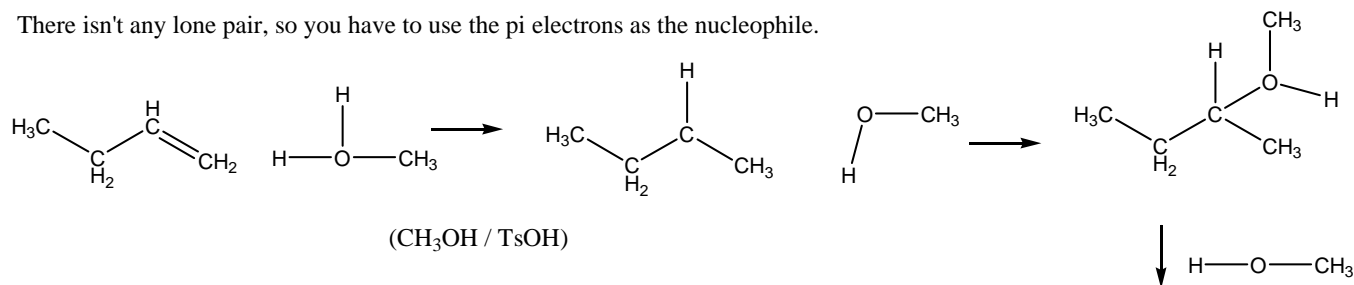


hydration of an alkene with aqueous acid  
form most stable carbocation  
(rearrangements are possible)

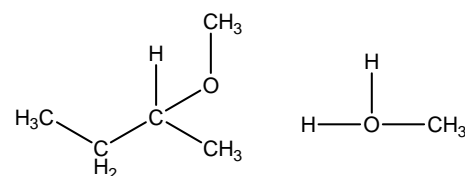


## c. C=C addition reaction (ether synthesis from an alkene by addition of alcohols)

There isn't any lone pair, so you have to use the pi electrons as the nucleophile.

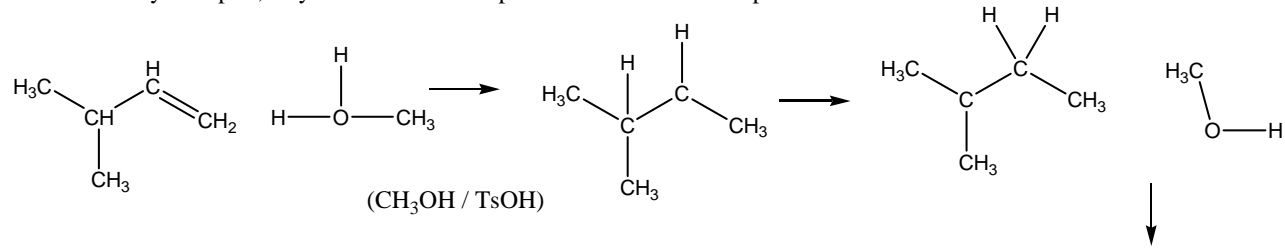


hydration of an alkene with aqueous acid  
form most stable carbocation  
(rearrangements are possible)

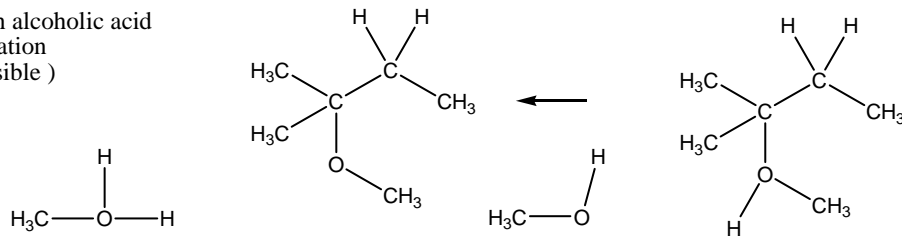


## d. C=C addition reaction (ether synthesis from an alkene by addition of alcohols), with rearrangement

There isn't any lone pair, so you have to use the pi electrons as the nucleophile.



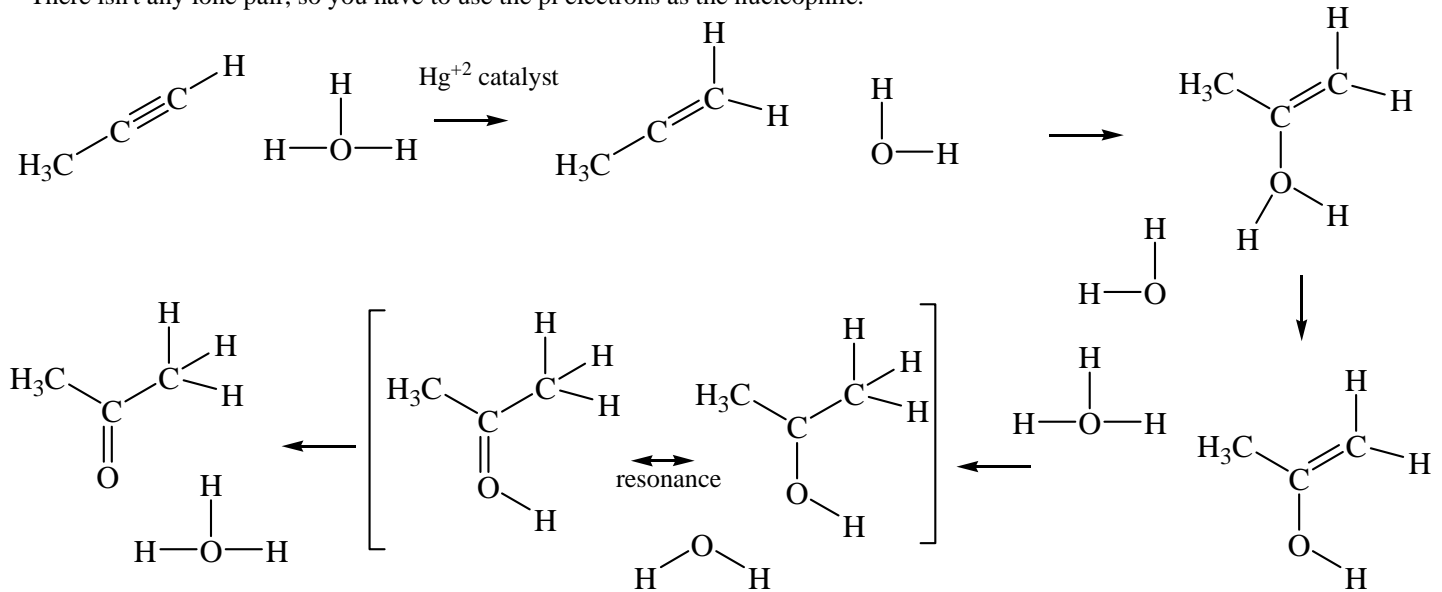
ether synthesis from an alkene with alcoholic acid  
form most stable carbocation  
(rearrangements are possible)



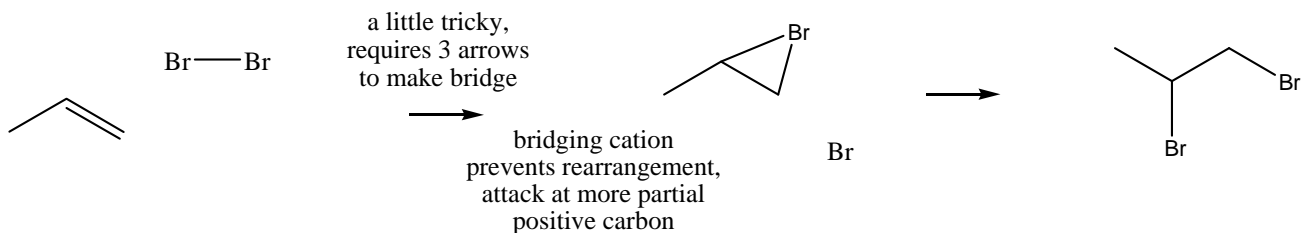
## e. Mercuration, reduction – minimizes rearrangements

f. Hydration of alkynes (Markovnikov addition forms most stable carbocation), enol intermediate tautomerizes to keto tautomer. (The  $\text{Hg}^{+2}$  has been left out of the mechanism to simplify the mechanism.)

There isn't any lone pair, so you have to use the pi electrons as the nucleophile.

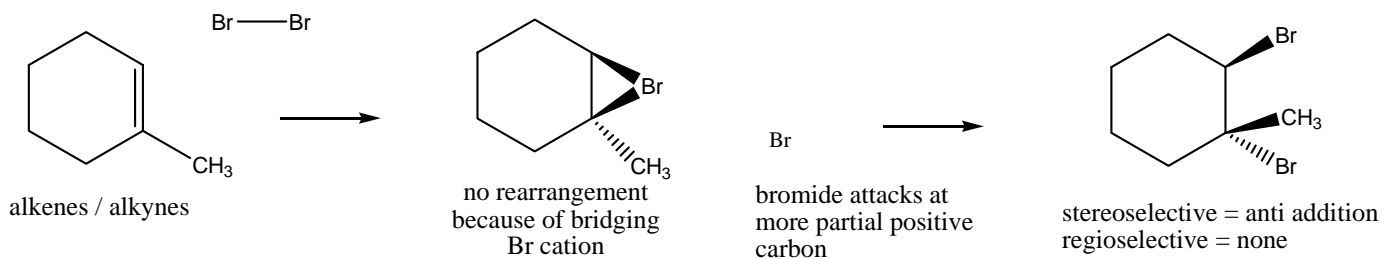


## g. Bromination of alkenes, goes via anti addition

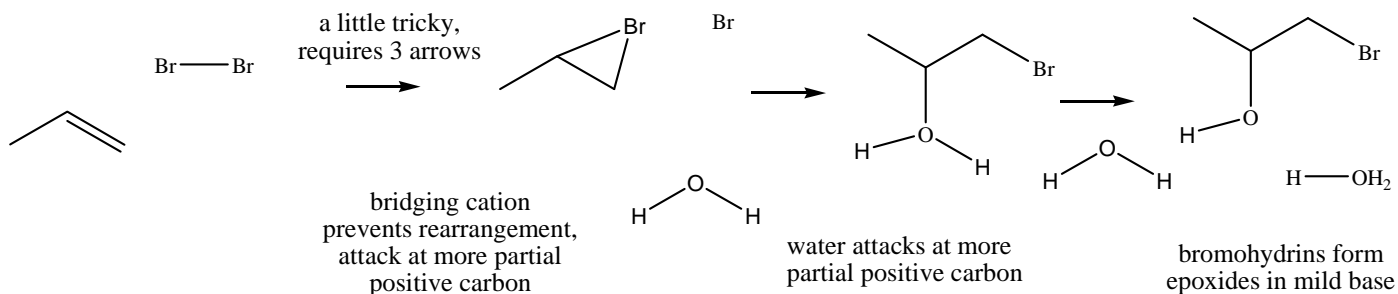




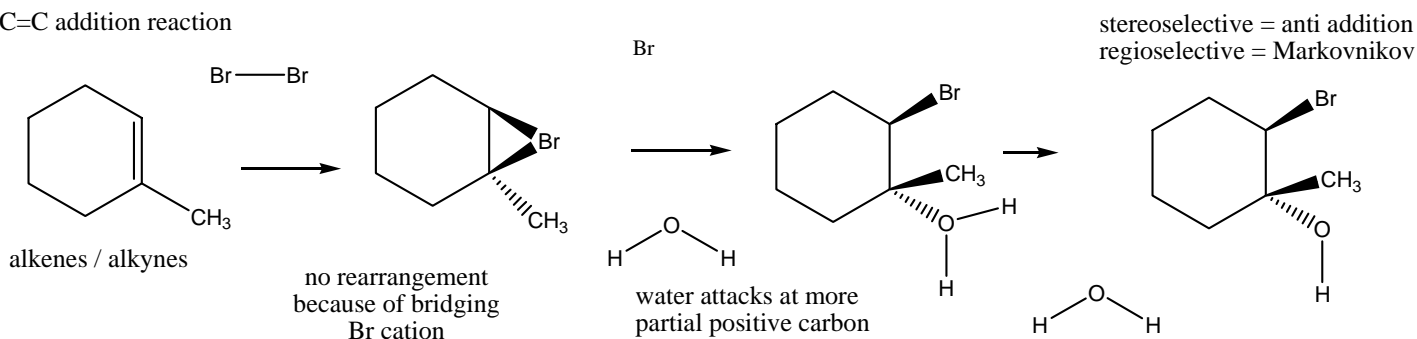
## C=C addition reaction



## h. Bromhydrin formation from alkenes, goes via anti addition



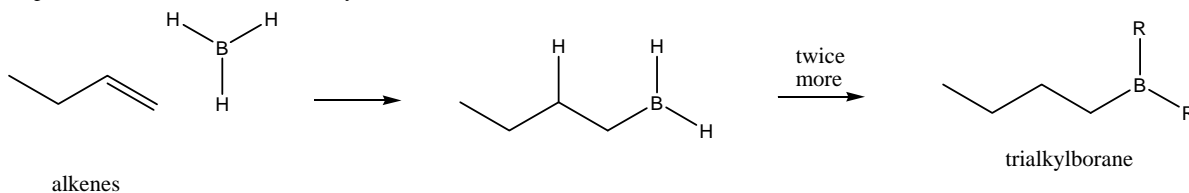
## C=C addition reaction



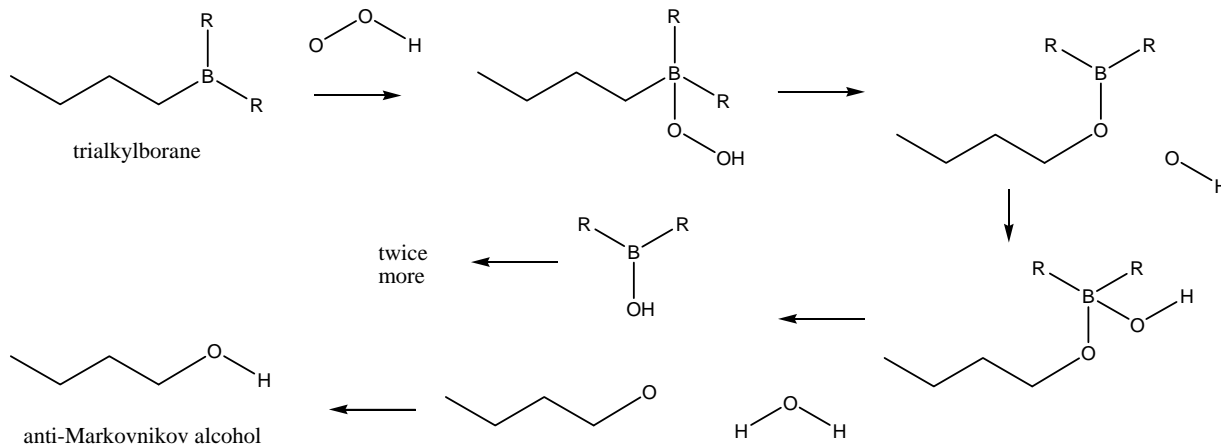
## i. Hydroboration of alkenes = anti-Markovnikov addition (opposite regioselectivity to normal hydration conditions)

anti-Markovnikov addition to C=C (hydration makes alcohols), two steps: 1.  $\text{BH}_3$  2.  $\text{H}_2\text{O}_2/\text{HO}^\ominus$ 

step 1 = concerted addition to C=C by borane



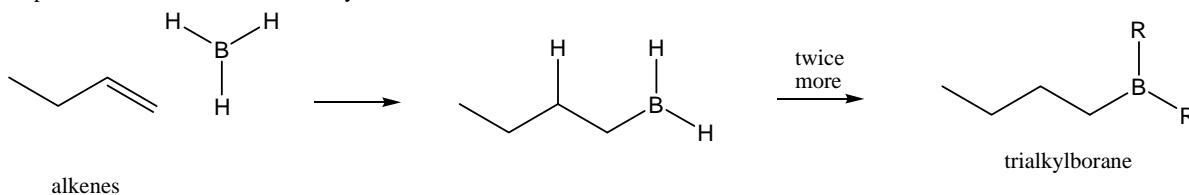
step 2 = oxidation by hydrogen peroxide and rearrangement to anti-Markovnikov alcohol



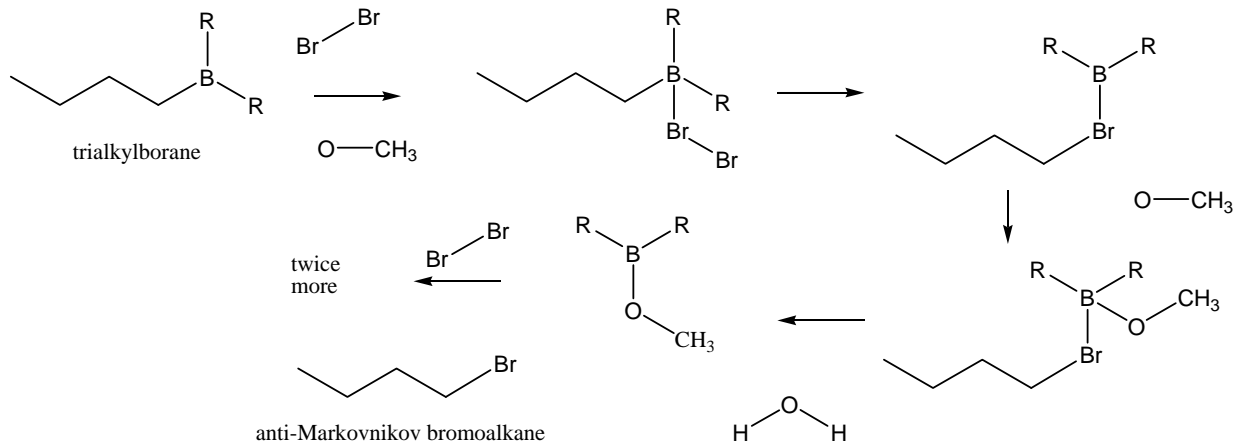
## j. bromination “anti” – looks very similar to hydration reaction, just above

anti-Markovnikov addition to C=C (bromination makes R-Br), two steps: 1.  $\text{BH}_3$  2.  $\text{Br}_2/\text{CH}_3\text{O}^\ominus$ 

step 1 = concerted addition to C=C by borane



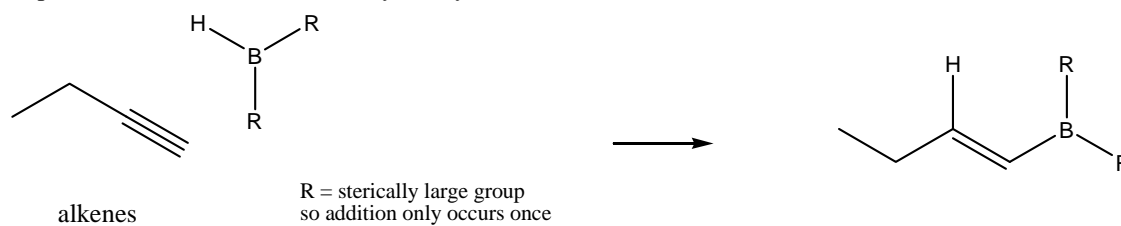
step 2 = oxidation by bromine and rearrangement to anti-Markovnikov R-Br



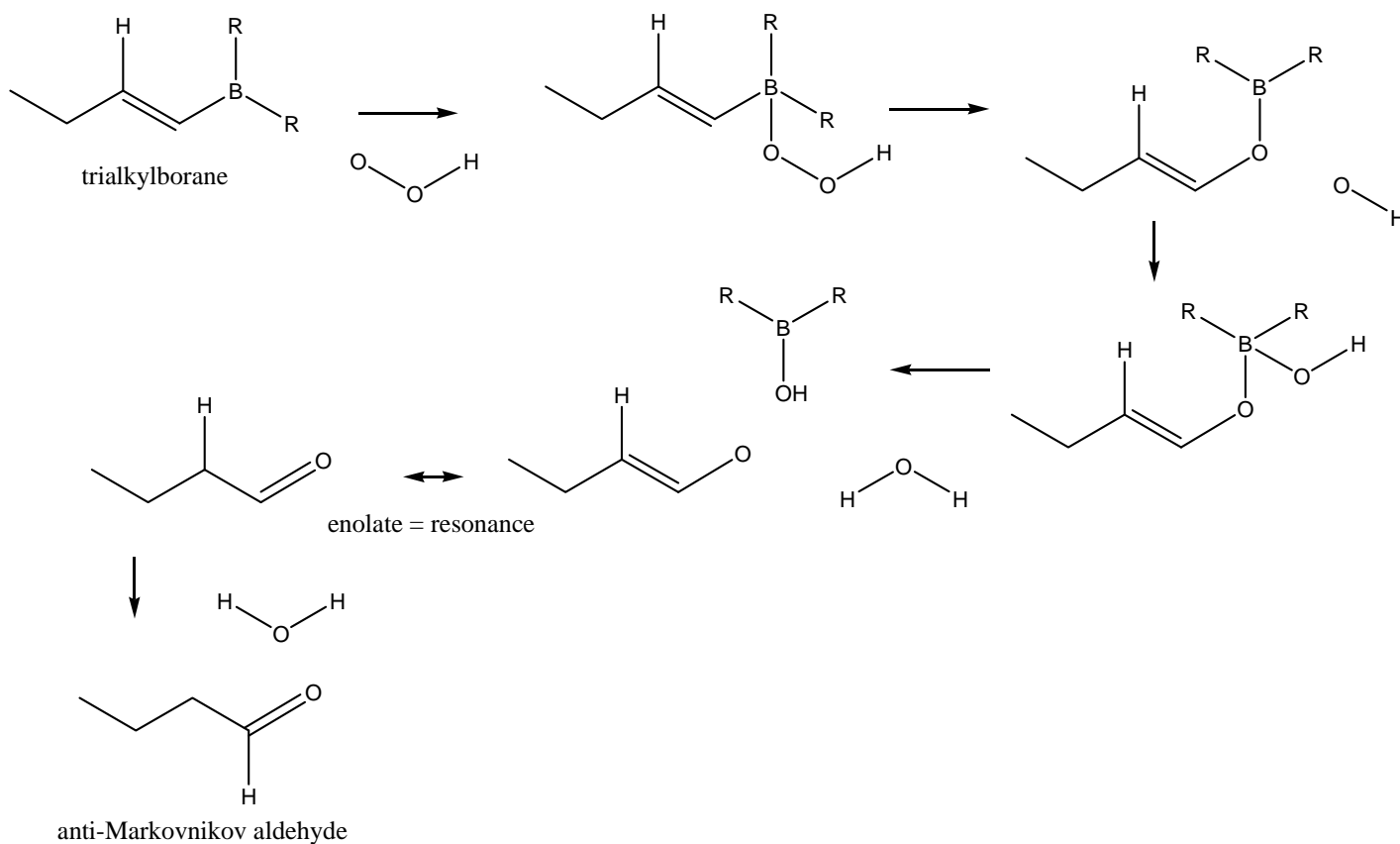
## k. Hydroboration of alkynes = anti-Markovnikov addition (opposite regioselectivity to normal conditions)

anti-Markovnikov addition to CC (hydration makes aldehydes), two steps: 1  $R_2BH$  2.  $H_2O_2/HO^\ominus$

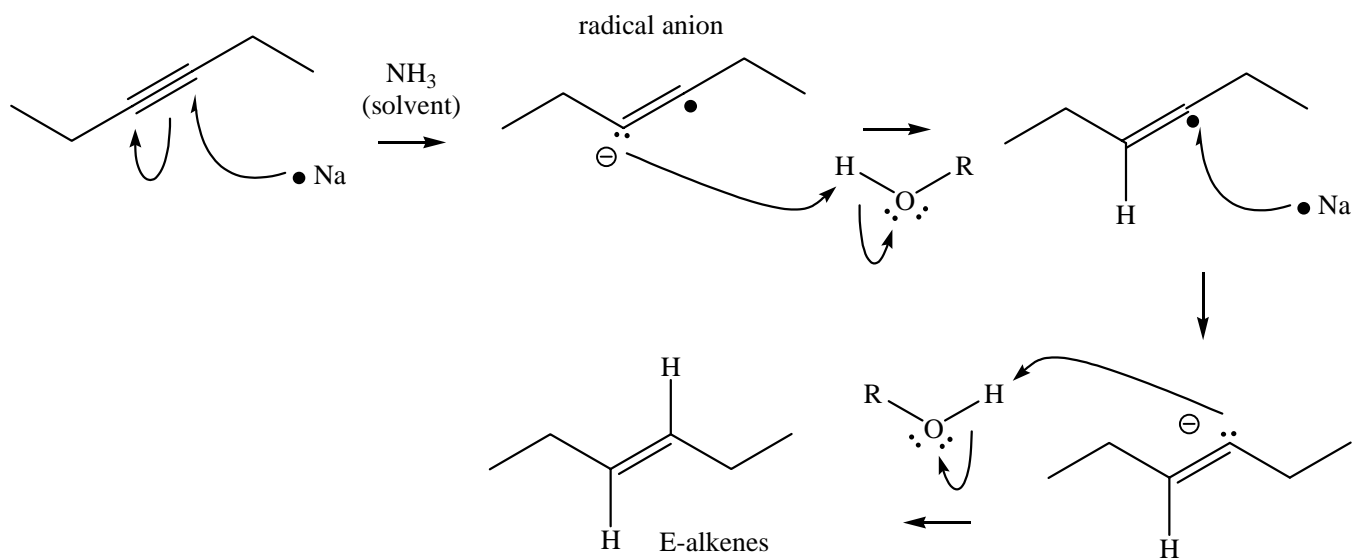
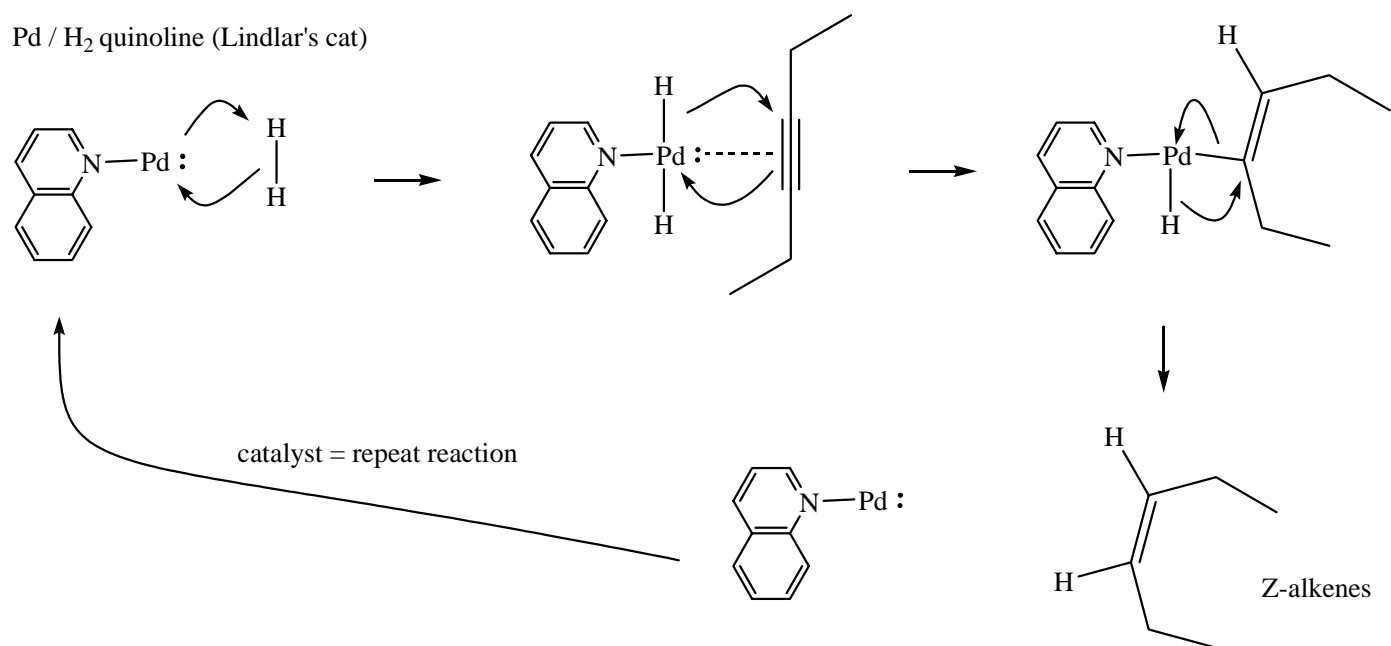
step 1 = concerted addition to CC by dialkylborane



step 2 = oxidation by hydrogen peroxide and rearrangement to anti-Markovnikov aldehyde

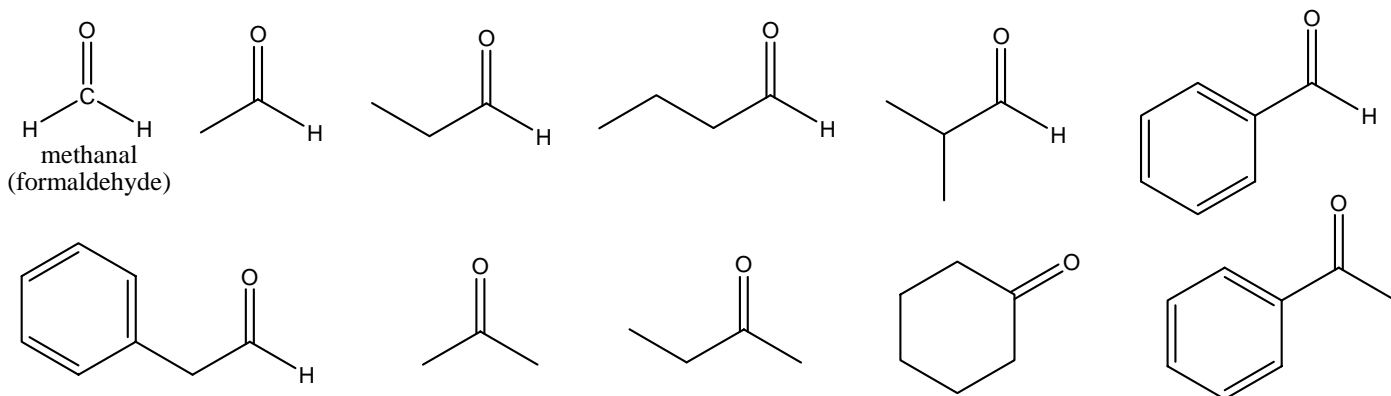


## Reduction of alkynes (Z and E alkenes)

Birch conditions (Na / NH<sub>3</sub>)Pd / H<sub>2</sub> quinoline (Lindlar's cat)

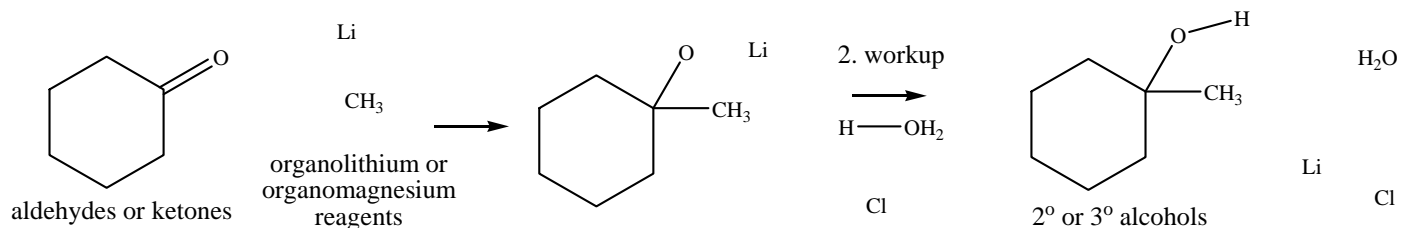
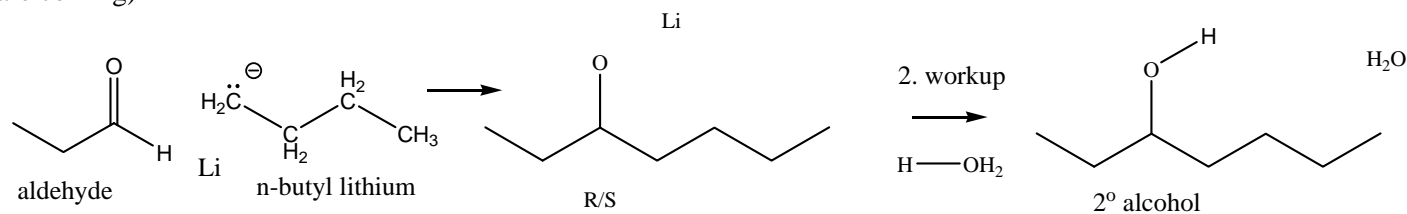
**Aldehyde and Ketone reactions**

Examples of important patterns to know from our starting materials.

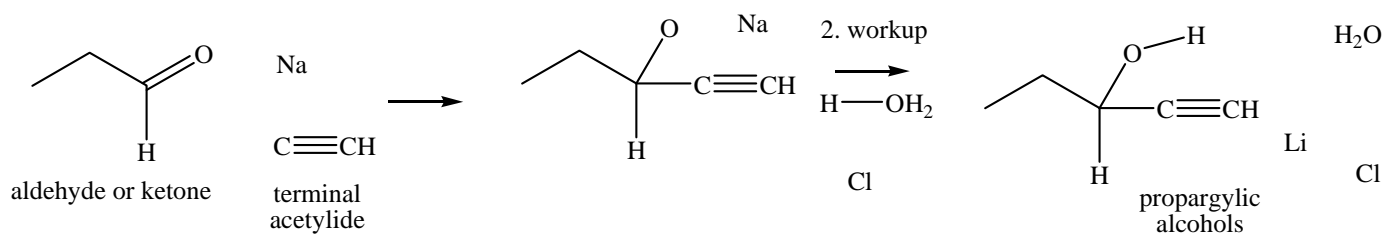


We can make aldehydes and ketones from alcohols and alkynes (for now).

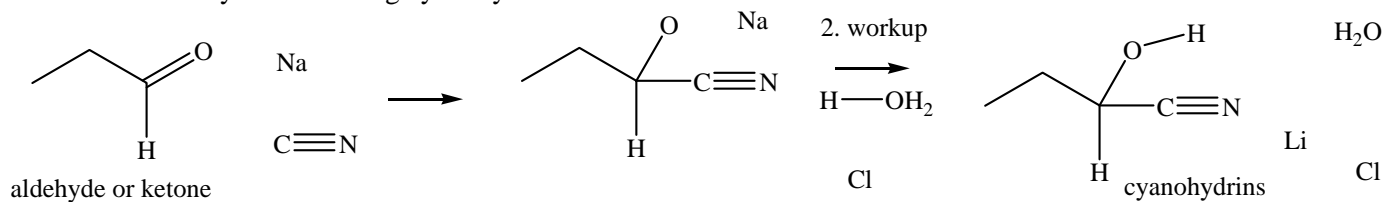
a. C=O addition with organolithium reagent, and workup (use n-butyl lithium, methyl lithium or phenyl lithium, others are coming)



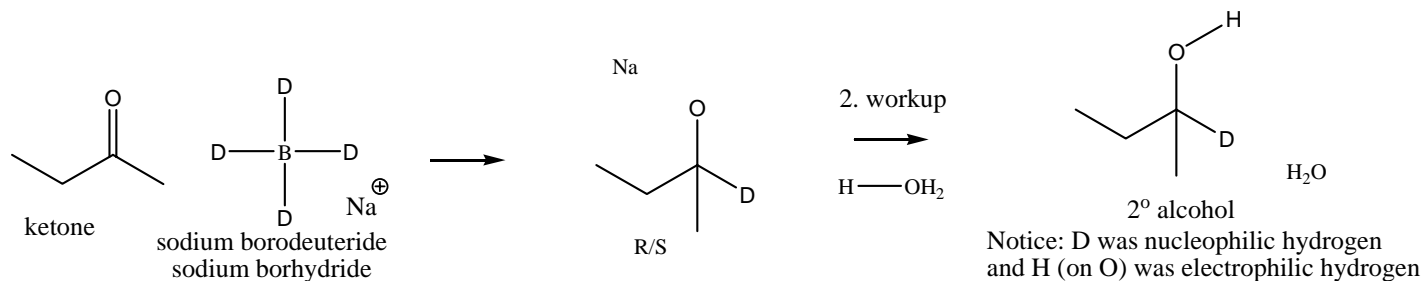
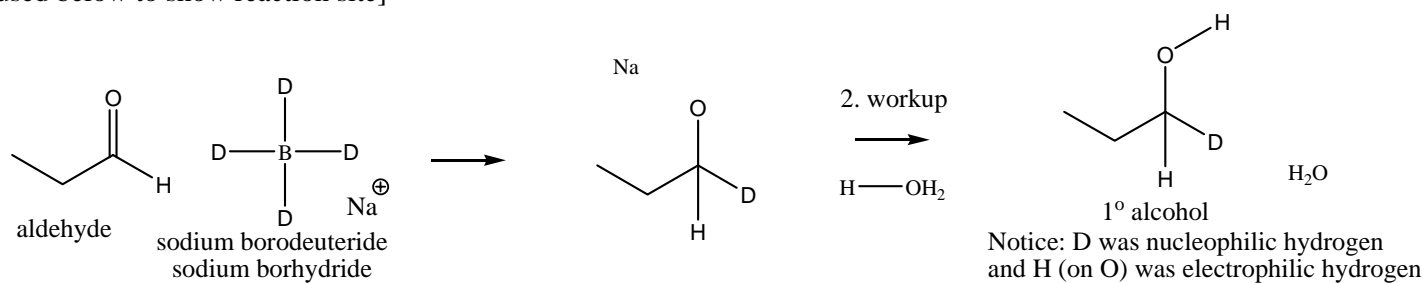
b. C=O addition with terminal acetylides to form propargylic alcohols or with cyanide to form cyanohydrins



C=O addition with cyanide forming cyanohydrin

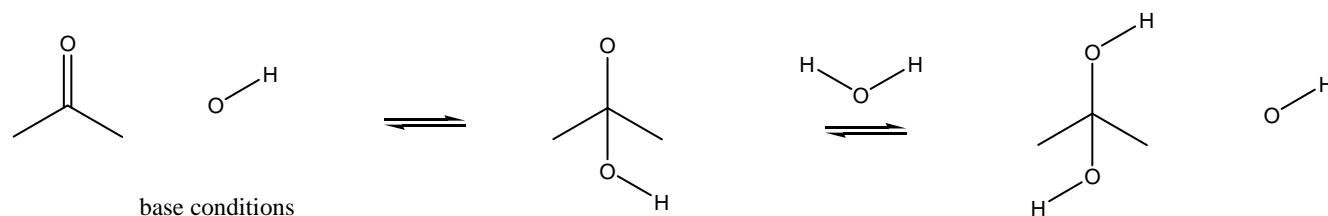
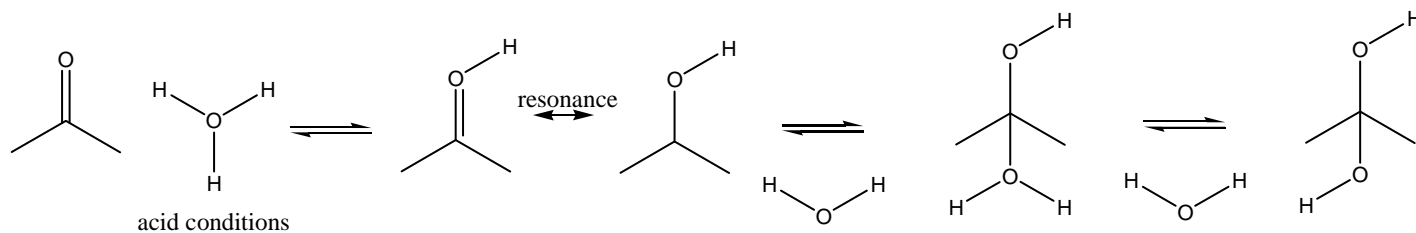


c. Nucleophilic hydride = sodium borohydride ( $\text{NaBH}_4$ ) and lithium aluminum hydride ( $\text{LiAlH}_4 = \text{LAH}$ ), [deuterium is used below to show reaction site]



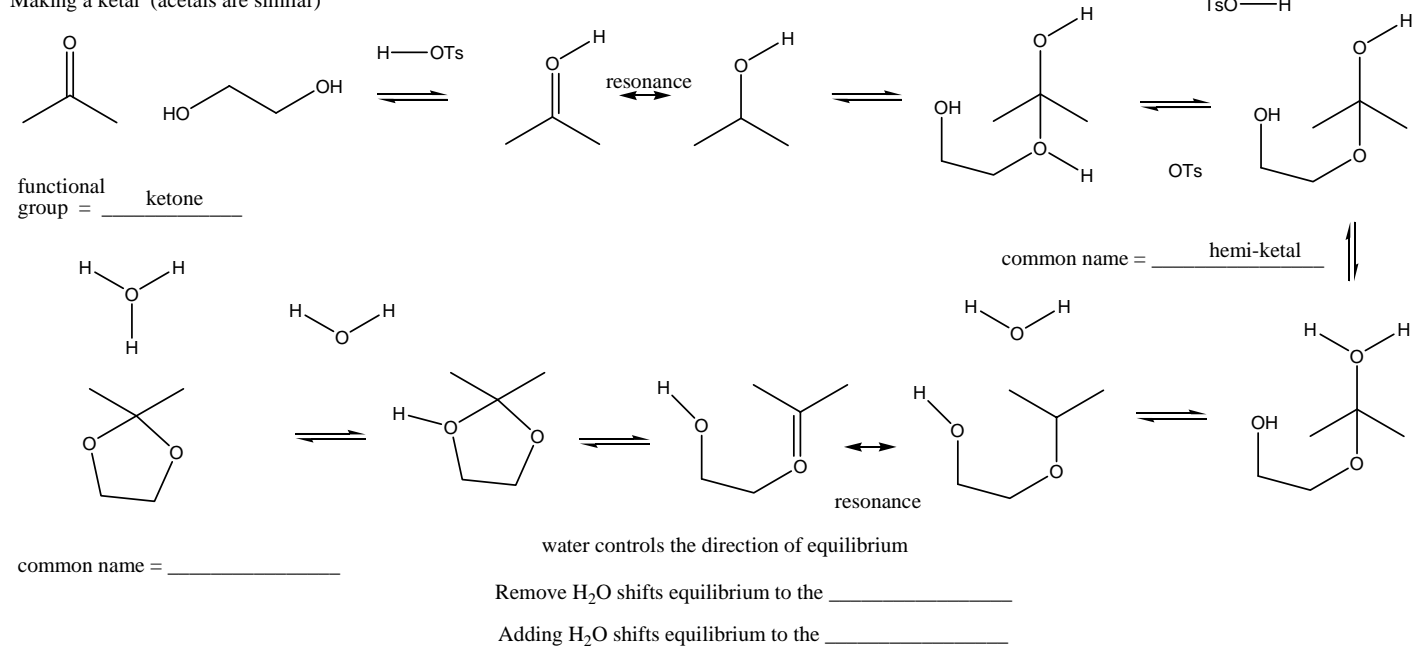
d. Hydration of  $\text{C}=\text{O}$  in acid or base conditions (also tautomerization conditions, competing reactions)

Hydration of  $\text{C}=\text{O}$  is similar to making acetals and ketals and hydrolysis of esters



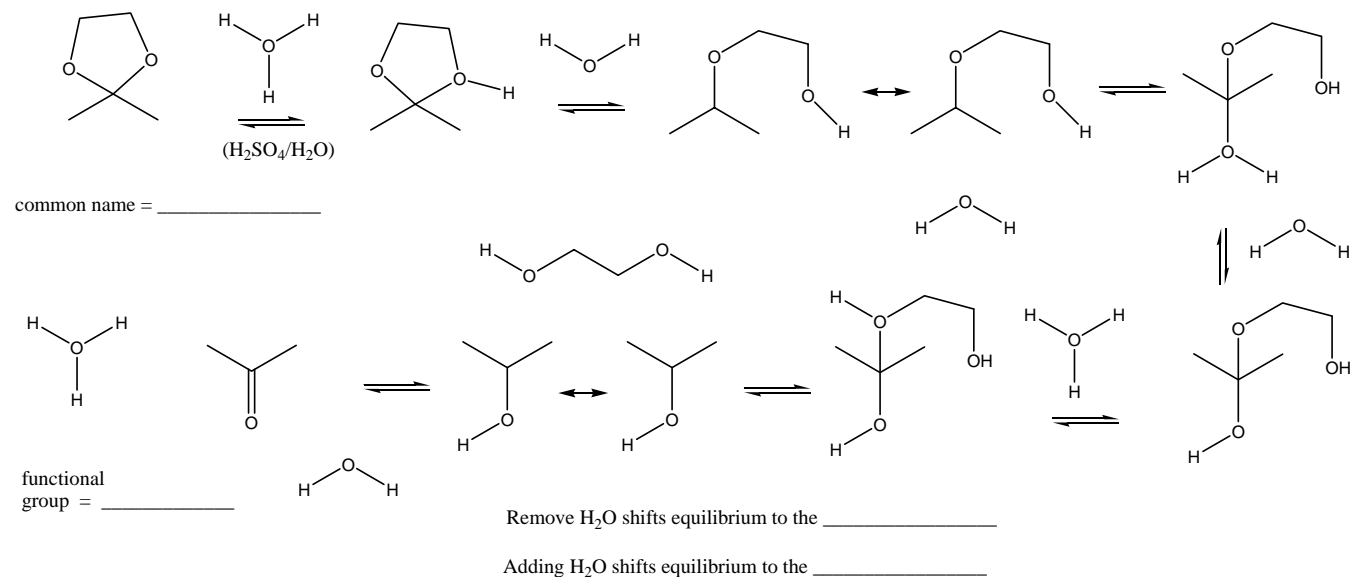
e. Ketone to hemi-ketal to ketal and aldehyde to hemi-acetal to acetal (protects C=O as ether during other reactions conditions)

Making a ketal (acetals are similar)



Deprotection of ketal (acetal) to regenerate ketone or aldehyde, S<sub>N</sub>1 reaction, then E1 reaction to form C=O (deprotection of a ketone or aldehyde)

1 Hydrolysis of a ketal back to a ketone and ethylene glycol (acetals are similar and go back to aldehydes and ethylene glycol)



Still to do

Primary amines  $\rightarrow$  imines  $\rightarrow$  reduced to amines with sodium cyanoborohydride (can form 1°, 2°, 3° amines)

Secondary amines + C=O  $\rightarrow$  enamines  $\rightarrow$  react with electrophiles + hydrolyze  $\rightarrow$  ketones with new bonds

THP protection of alcohols & deprotection

Wittig reactions (ylid + C=O)  $\rightarrow$  Z alkenes (no rearrangements)

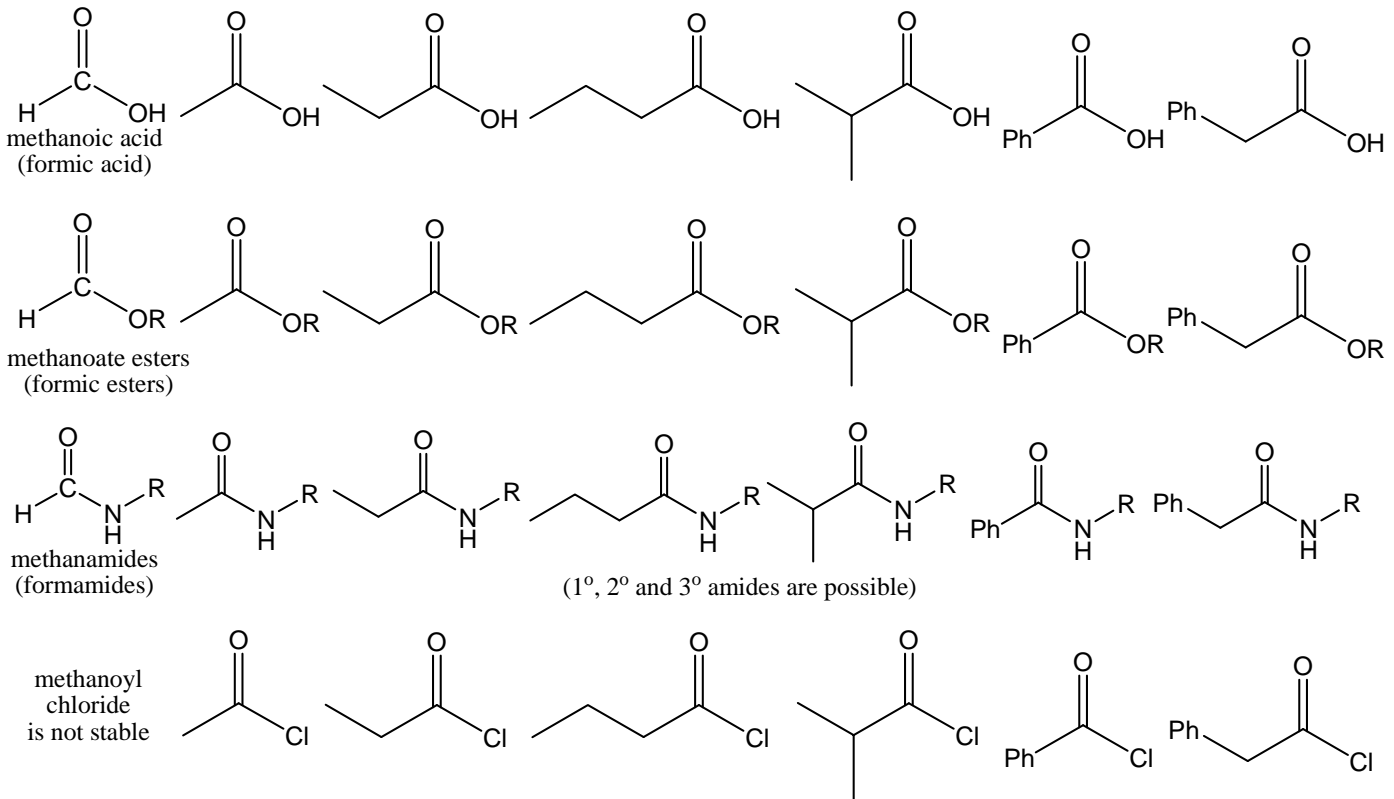
Cuprate reactions (couple with RX, with acid chlorides  $\rightarrow$  ketones, with  $\alpha,\beta$ -unsaturated C=O  $\rightarrow$  conjugate addition)

DIBAH reactions (with nitriles, acid chlorides, esters  $\rightarrow$  aldehydes)



**Carboxylic acids and derivatives – reactions**

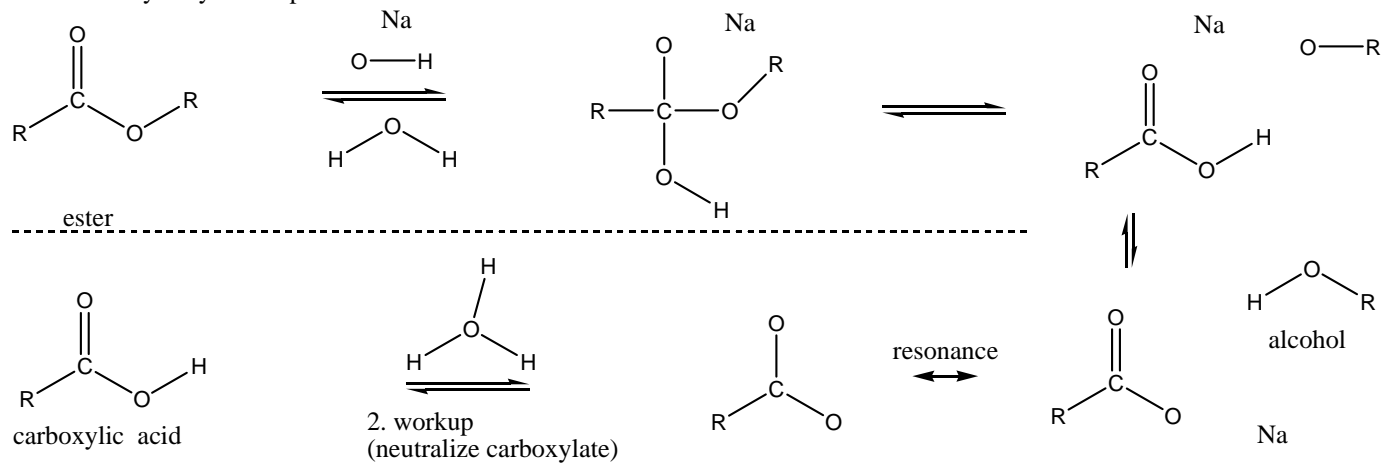
Examples of important patterns to know from our starting materials.



We can make carboxylic acids from 1° alcohols, aldehydes and nitriles (for now).

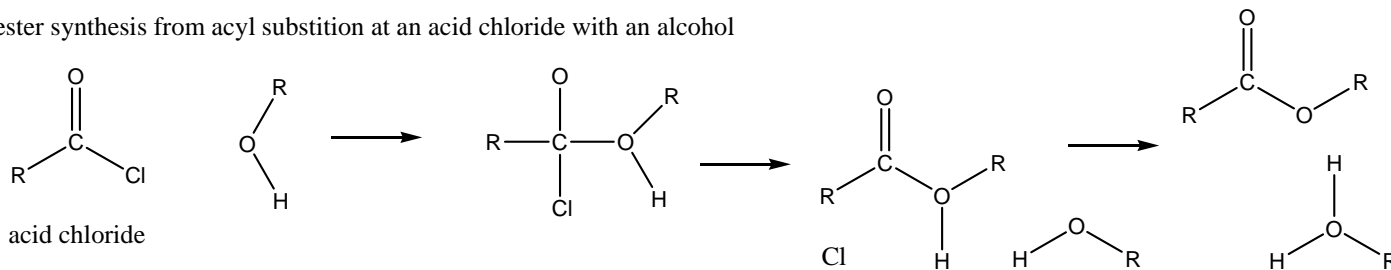
a. Base hydrolysis of esters

ester base hydrolysis = saponification



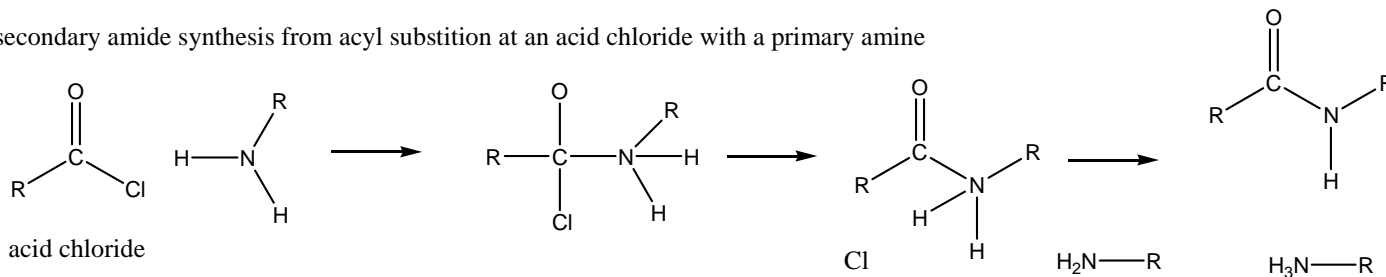
b. acid chloride + ROH = esters (notice two different R groups joined together by an oxygen)

ester synthesis from acyl substitution at an acid chloride with an alcohol



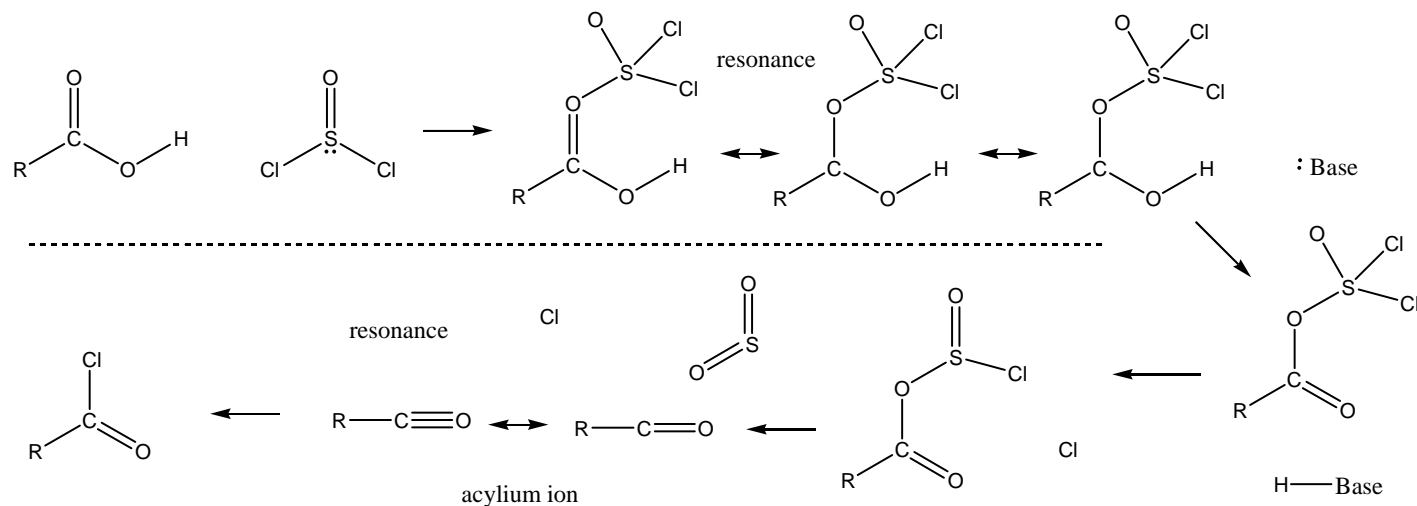
c. acid chloride + RNH<sub>2</sub> = 2° amides (notice two different R groups joined together by a nitrogen)

secondary amide synthesis from acyl substitution at an acid chloride with a primary amine

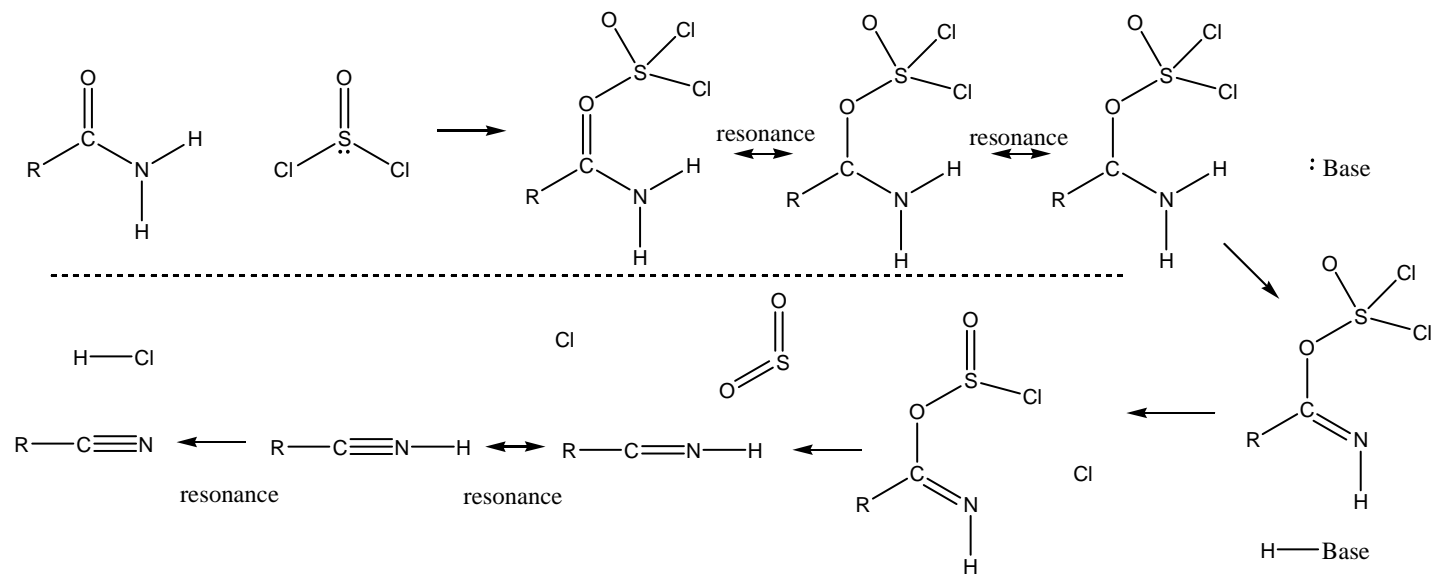


d. Synthesis of acid chlorides, acyl substitution, twice

synthesis of an acid chloride from an acid + thionyl chloride (SOCl<sub>2</sub>)



## e. acyl substitution, then two elimination reactions

synthesis of a nitrile from an 1° amide + thionyl chloride (SOCl<sub>2</sub>)

## f. addition reaction (hydration) to imidate, tautomers to amide, acyl substitution to carboxylic acid

HCl / H<sub>2</sub>O hydrolysis of a nitrile to an amide (in H<sub>2</sub>SO<sub>4</sub> / H<sub>2</sub>O hydrolysis continues on to a carboxylic acid)