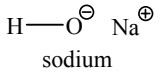
What kind of mechanisms are possible? What is the major mechanism occuring? Write in ALL mechanism details (lone pairs, formal charge, curved arrows, etc.). Redraw your structure each time you show a different reaction with the RX structure.

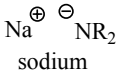
Mechanism choices at this point in organic chemistry: S_N2,E2,S_N1, E1,acid/base reaction, free radical substitution, no reaction

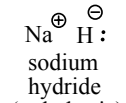
Nuclephile/Bases (and other reagents) to choose from include:

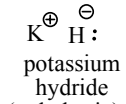
purchase / given - you can invoke these whenever you need them

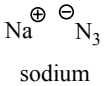
Br_2 hν

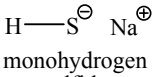

sodium hydroxide

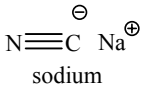

sodium amide

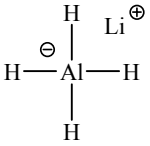

sodium hydride (only basic)

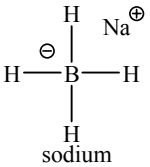

potassium hydride (only basic)

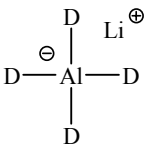

sodium azide

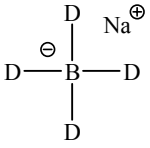

monohydrogen sulfide

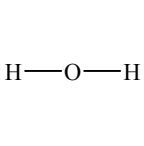

sodium cyanide

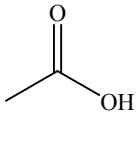

lithium aluminium hydride (nucleophilic)

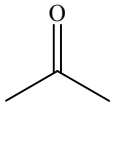

sodium borohydride (nucleophilic)


lithium aluminium hydride (nucleophilic)

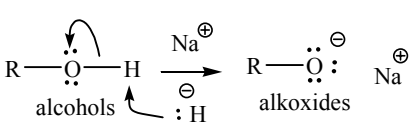

sodium borohydride (nucleophilic)

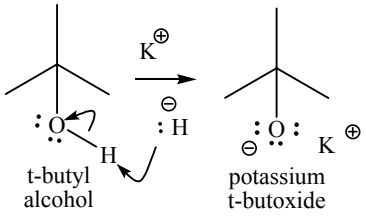

water

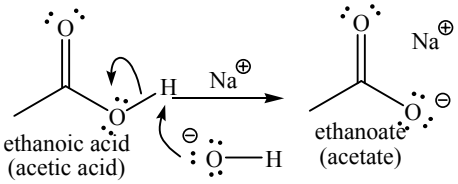

ethanoic acid

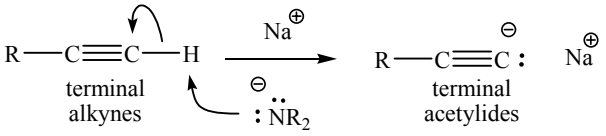

propanone (acetone)

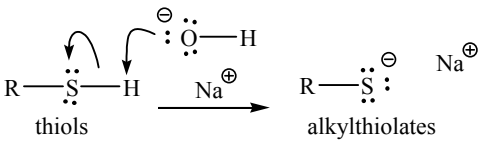
you have to make these using acid/base reactions


alcohols → alkoxides

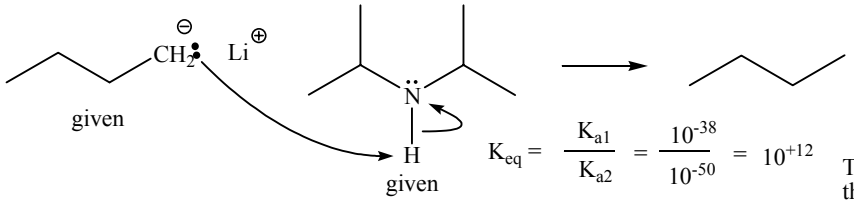

t-butyl alcohol → potassium t-butoxide

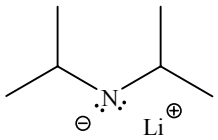

ethanoic acid (acetic acid) → ethanoate (acetate)


terminal alkynes → terminal acetylides


thiols → alkylthiolates

Synthesis of lithium diisopropyl amide, LDA, used to remove C_α-H proton of carbonyl groups. (acid / base reaction)

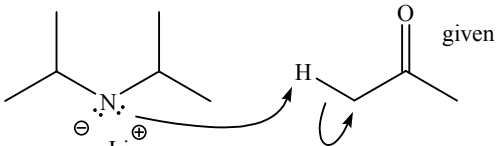




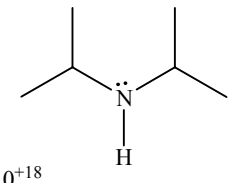
LDA = lithium diisopropyl amide

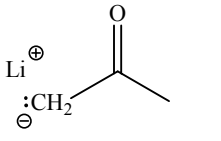
Think - sterically bulky, very basic that goes after weakly acidic protons.

Make enolate (ketones and esters)

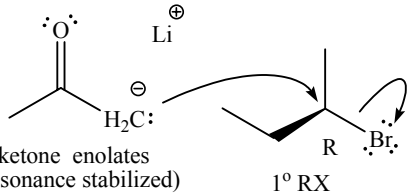


$K_{eq} = \frac{K_{a1}}{K_{a2}} = \frac{10^{-20}}{10^{-38}} = 10^{+18}$

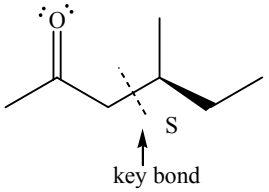



ketone enolates (resonance stabilized)

React ketone enolate with RX compounds (methyl, 1° and 2° RX)

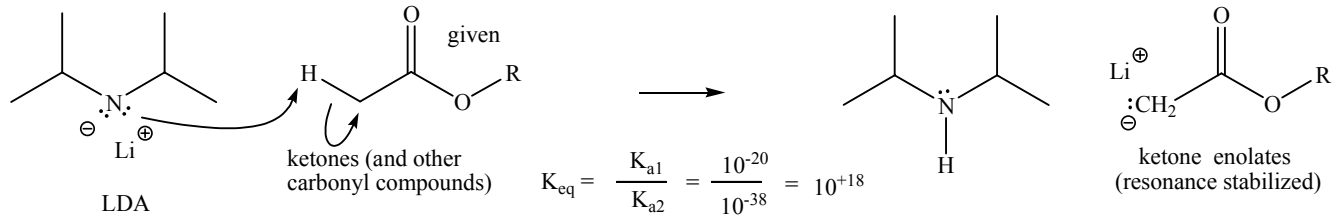


S_N2 reactions →

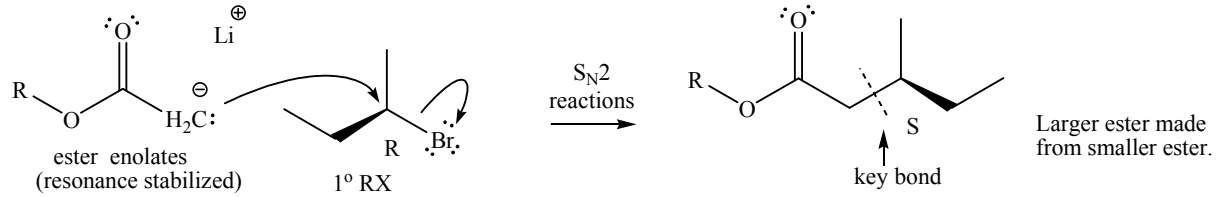


Larger ketone made from smaller ketone.

Make enolate (esters)



React ester enolate with RX compounds (methyl, 1° and 2° RX)



S_N and E reactions

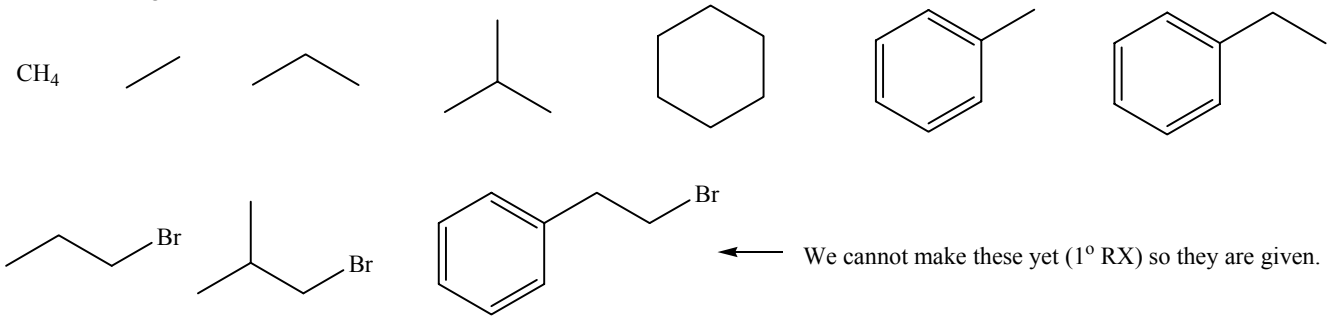
S_N2 reactions = substitution nucleophilic bimolecular
Rate = $k_{SN2}[RX][Nu:^{\ominus}]$ bimolecular kinetics, both RX and $Nu:^{\ominus}$ participate in the slow step of the reaction; $k_{SN2} = Ax10^{\frac{-Ea(SN2)}{2.3xRxT}}$

E2 reactions = elimination bimolecular
Rate = $k_{E2}[RX][B:^{\ominus}]$ bimolecular kinetics, both RX and $B:^{\ominus}$ participate in the slow step of the reaction; $k_{E2} = Ax10^{\frac{-Ea(E2)}{2.3xRxT}}$

S_N1 reactions = substitution nucleophilic unimolecular
Rate = $k_{SN1}[RX]$ unimolecular kinetics, only RX participates in the slow step of the reaction; $k_{SN1} = Ax10^{\frac{-Ea(SN1)}{2.3xRxT}}$

E1 reactions = elimination unimolecular
Rate = $k_{E1}[RX]$ unimolecular kinetics, only RX participates in the slow step of the reaction; $k_{E1} = Ax10^{\frac{-Ea(E1)}{2.3xRxT}}$

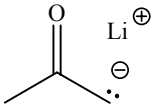
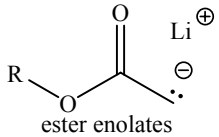
Allowed starting structures - main sources of carbon



← We cannot make these yet (1° RX) so they are given.

These structures represent your starting points to synthesize target molecules below. You will need to propose a step-by-step synthesis for each target molecule from the given structures above. Every step needs to show a reaction arrow with the appropriate reagent(s) above each arrow and the major product of each step. The product of each step becomes the starting material for the next step until you reach the target structure. As new reagents are introduced this list will expand and as new reactions are learned the necessary hydrocarbons will contract.

R-X patterns - typical reaction patterns in our course (bold = atypical result)

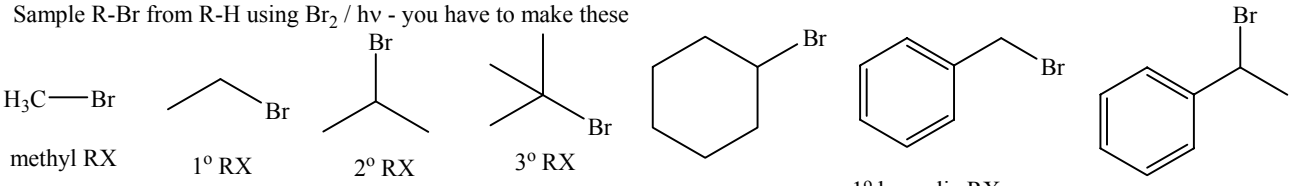
Reagents	methyl RX	1° RX primary	2° RX secondary	3° RX tertiary	1° neopentyl RX	allylic RX	benzylic RX
$Na^{\oplus}\ ^{\ominus}OH$	only S_N2	S_N2 > E2	**E2 > S_N2**	only E2	no reaction	very fast S_N2	very fast S_N2
$Na^{\oplus}\ ^{\ominus}OR$	only S_N2	S_N2 > E2	**E2 > S_N2**	only E2	no reaction	very fast S_N2	very fast S_N2
$Na^{\oplus}\ ^{\ominus}O_2CR$	only S_N2	S_N2 > E2	S_N2 > E2	only E2	no reaction	very fast S_N2	very fast S_N2
$K^{\oplus}\ ^{\ominus}O\text{-}C(CH_3)_3$ t-butoxide	only S_N2	**E2 > S_N2**	**only E2**	only E2	no reaction	very fast S_N2	very fast S_N2
$Na^{\oplus}\ ^{\ominus}C{\equiv}N$	only S_N2	S_N2 > E2	S_N2 > E2	only E2	no reaction	very fast S_N2	very fast S_N2
$Na^{\oplus}\ ^{\ominus}C{\equiv}C{-}R$	only S_N2	S_N2 > E2	**E2 > S_N2**	only E2	no reaction	very fast S_N2	very fast S_N2
$Na^{\oplus}\ ^{\ominus}N_3$	only S_N2	S_N2 > E2	S_N2 > E2	only E2	no reaction	very fast S_N2	very fast S_N2
$Na^{\oplus}\ ^{\ominus}SH$	only S_N2	S_N2 > E2	S_N2 > E2	only E2	no reaction	very fast S_N2	very fast S_N2
$Na^{\oplus}\ ^{\ominus}SR$	only S_N2	S_N2 > E2	S_N2 > E2	only E2	no reaction	very fast S_N2	very fast S_N2
$Na^{\oplus}\ H{-}^{\ominus}BH_3$	only S_N2	S_N2 > E2	S_N2 > E2	only E2	no reaction	very fast S_N2	very fast S_N2
$Na^{\oplus}\ D{-}^{\ominus}BD_3$	only S_N2	S_N2 > E2	S_N2 > E2	only E2	no reaction	very fast S_N2	very fast S_N2
$Li^{\oplus}\ H{-}^{\ominus}AlH_3$	only S_N2	S_N2 > E2	S_N2 > E2	only E2	no reaction	very fast S_N2	very fast S_N2
$Li^{\oplus}\ D{-}^{\ominus}AlD_3$	only S_N2	S_N2 > E2	S_N2 > E2	only E2	no reaction	very fast S_N2	very fast S_N2
 ketone enolates	only S_N2	S_N2 > E2	S_N2 > E2	only E2	no reaction	very fast S_N2	very fast S_N2
 ester enolates	only S_N2	S_N2 > E2	S_N2 > E2	only E2	no reaction	very fast S_N2	very fast S_N2

The following are synthetic approaches to *some* target molecules using S_N and E reactions. They are presented as examples of how you might approach synthesis problems (these and others like them). You need to not only look at structures that I included below but think about other possibilities using all of the structures available to you. I do not list every possibility, but you need to be able to consider every possibility. The best strategy is to work backwards from the target molecule one step at a time to an allowed starting structure (called retrosynthetic analysis). That way you are only thinking about "one" backward step at a time, instead of an "unknown" number of steps forward from a starting structure. This is the way I presented the approaches below. You should also know the mechanism for every reaction below. I can write these pages until I am blue in the face, but they can't help you learn, unless you do the work of trying them out. My job is to give you an opportunity to learn, and your job is to take advantage of that opportunity. These schemes were made quickly, so be on the lookout for mistakes. (I hope not too many.)

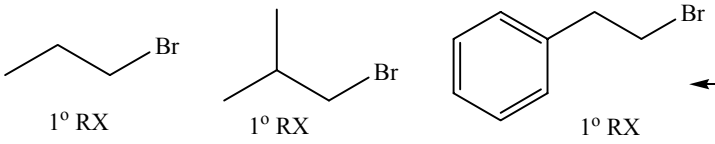
1. Free radical substitution at sp^3 C-H

Free radical substitution mechanism: 1. initiation 2a and 2b. propagation 3. termination. ΔH of each step is controlled by relative bond energies (R-H + Br_2 + light)

Sample R-Br from R-H using Br_2 / hν - you have to make these

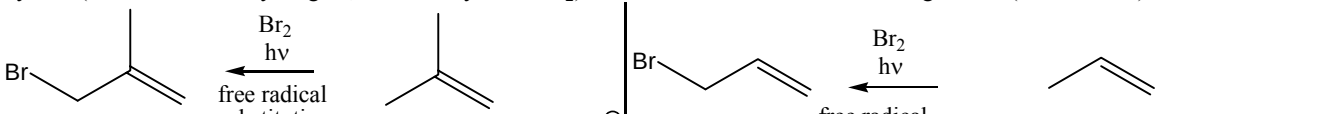


methyl RX; 1° RX; 2° RX; 3° RX; 2° RX; 1° benzylic RX; 2° benzylic RX

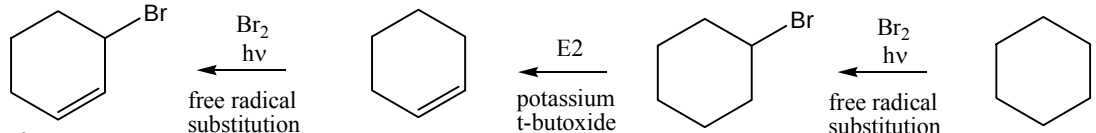


1° RX; 1° RX; 1° RX ← We cannot make these yet (1° RX) so they are given.

allylic - (NBS is more likely reagent, but we only know Br_2). You will need to make the starting alkene (E2 reactions)



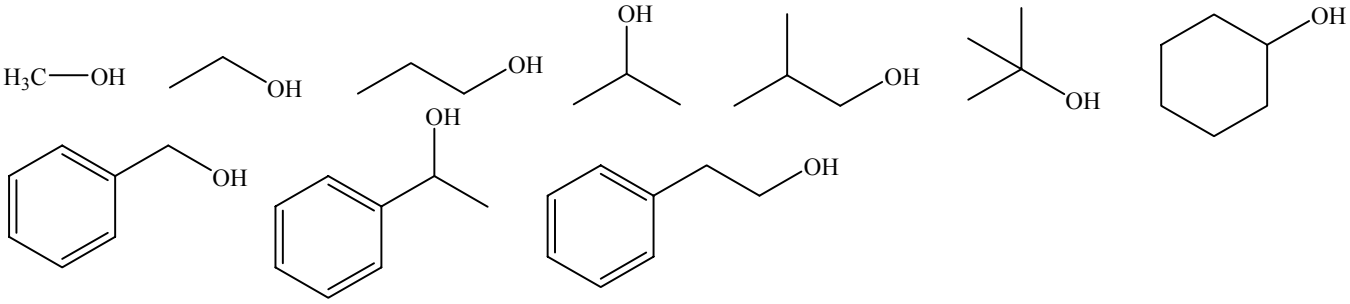
1° allylic RX; 1° allylic RX



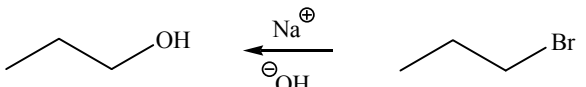
2° allylic RX

2. alcohol synthesis

Sample alcohols - S_N2 reactions using (R-X + $HO^{\ominus}$) or S_N1 reactions using (R-X + H_2O)

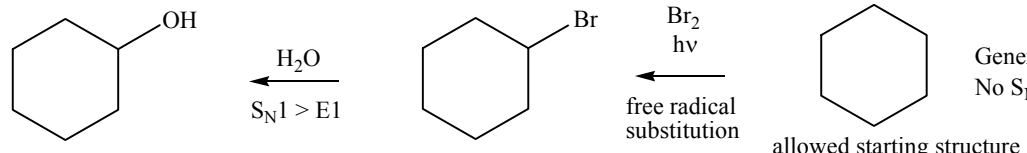


alcohols - various approaches, S_N2 at methyl and primary RX using NaOH and S_N1 at secondary and tertiary RX using H_2O



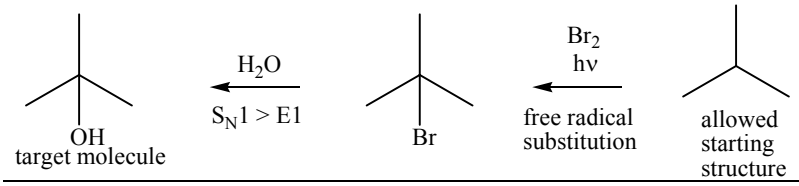
target molecule; S_N2 > E2; allowed starting structure

Hydroxide and alkoxides are OK nucleophiles at methyl and 1° RX, but E2 > S_N2 at 2° RX and only E2 at 3° RX.



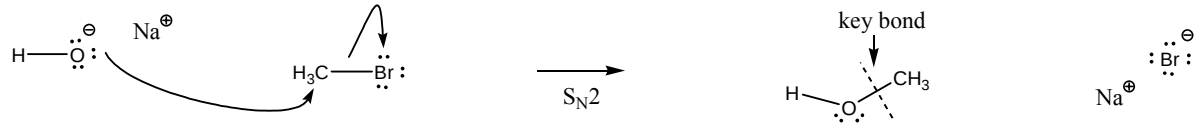
target molecule; S_N1 > E1; free radical substitution; allowed starting structure

Generally, S_N1 > E1 at 2° and 3° RX. No S_N1/E1 at methyl and 1° RX.



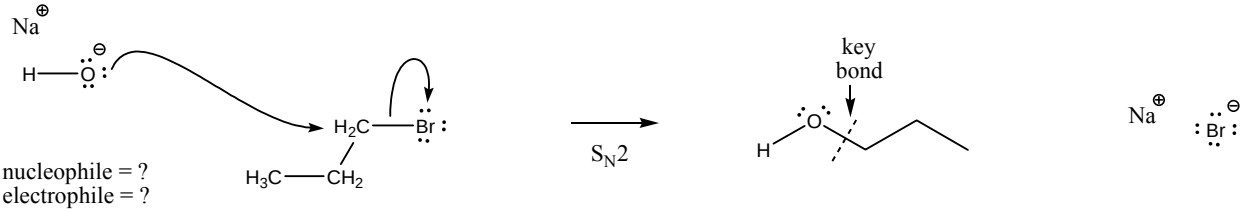
Generally, S_N1 > E1 at 2° and 3° RX.
No S_N1/E1 at methyl and 1° RX.

aqueous hydroxide → introduces a new alcohol functional group (R-OH)



nucleophile = ?
electrophile = ?

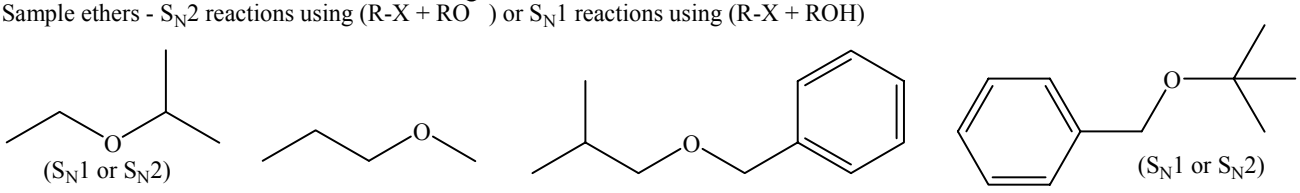
nucleophile = ?
electrophile = ?



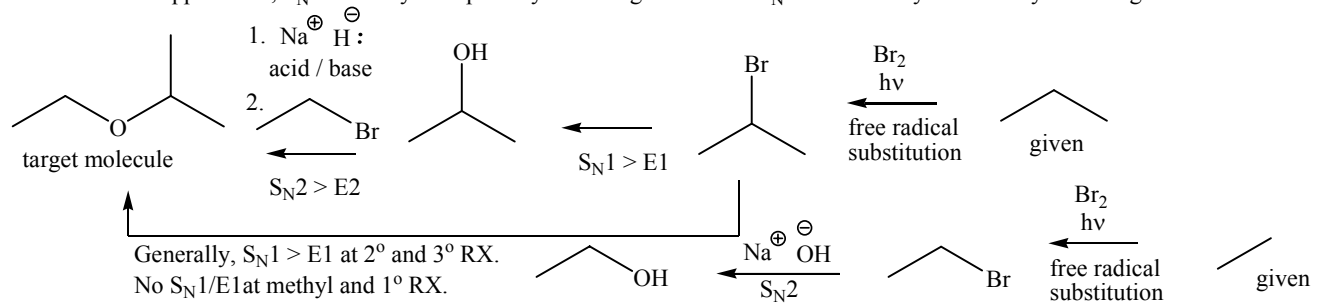
nucleophile = ?
electrophile = ?

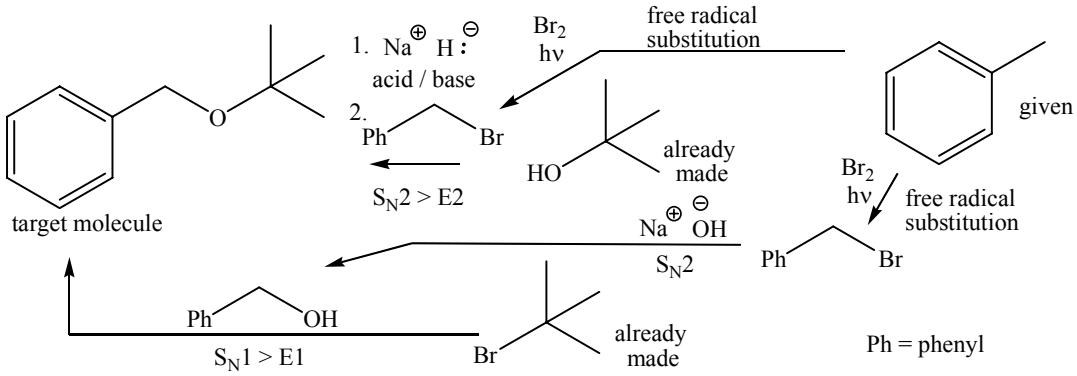
3. ether synthesis

Sample ethers - S_N2 reactions using (R-X + $RO^{\ominus}$) or S_N1 reactions using (R-X + ROH)

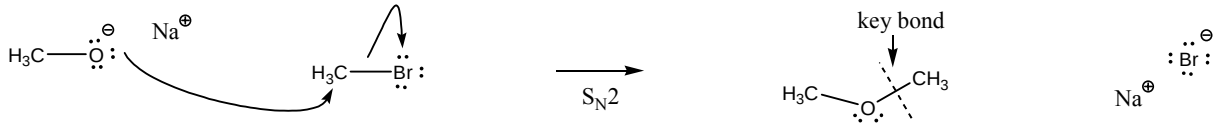


ethers - various approaches, S_N2 at methyl and primary RX using NaOR and S_N1 at secondary and tertiary RX using ROH

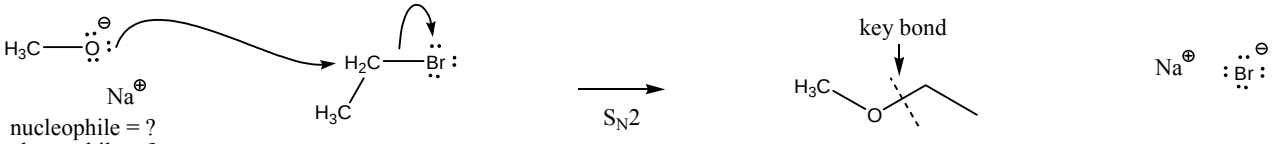




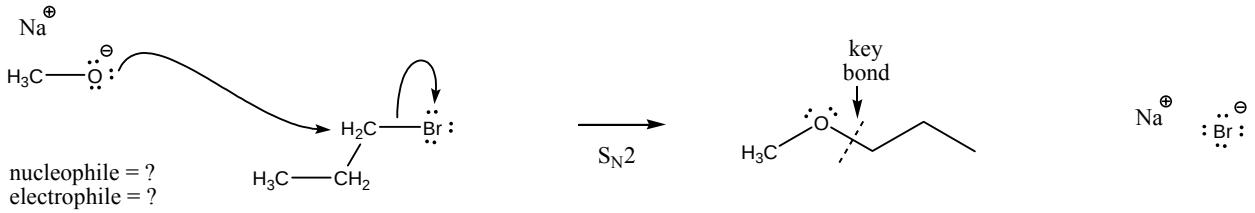
alkoxide → introduces a new ether group (R-OR')



nucleophile = ?
electrophile = ?



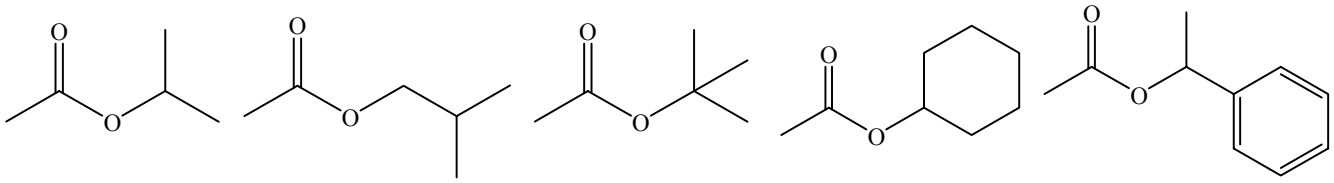
nucleophile = ?
electrophile = ?



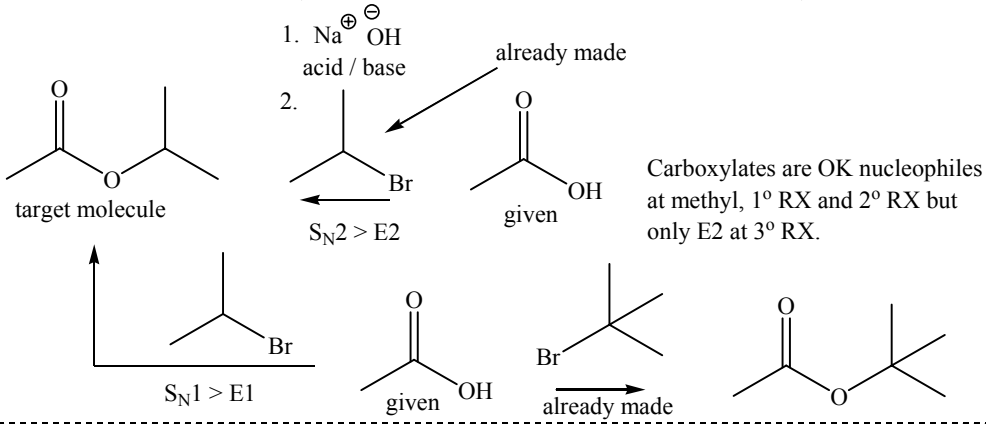
nucleophile = ?
electrophile = ?

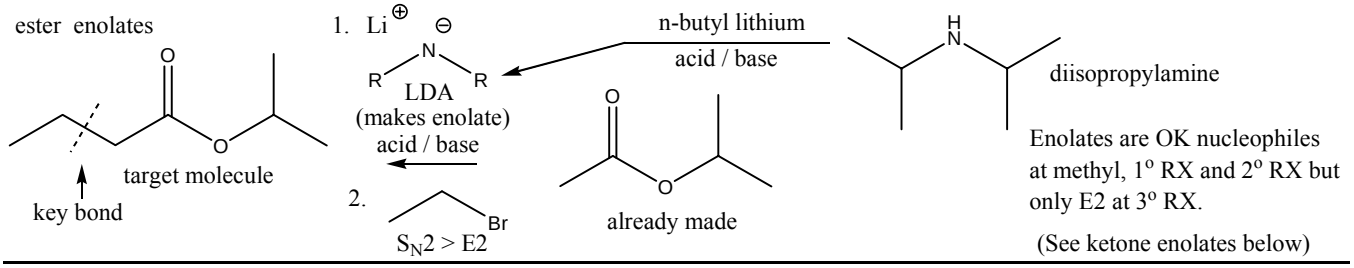
4. ester synthesis (and one ketone example using enolates)

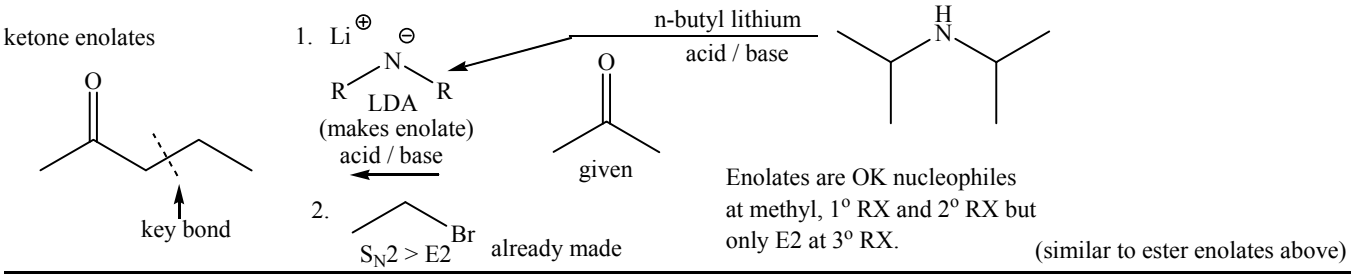
Sample esters - S_N2 reactions using (R-X + $RCO_2^{\ominus}$) or S_N1 reactions using (R-X + RCO_2H)



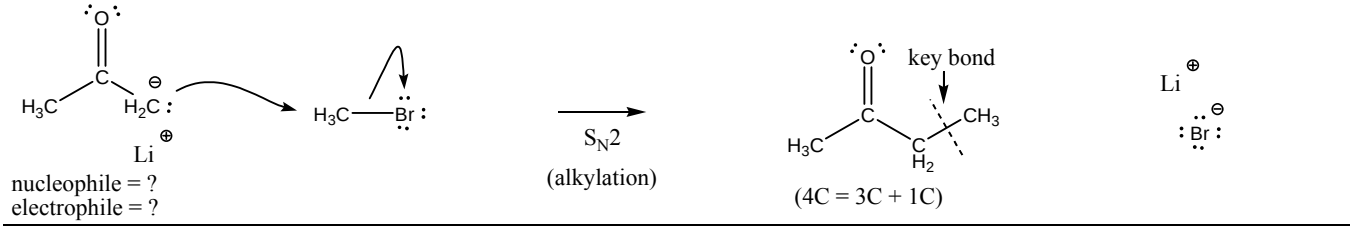
esters - various approaches, S_N2 at methyl and primary RX using RCO_2Na and S_N1 at secondary and tertiary RX using RCO_2H

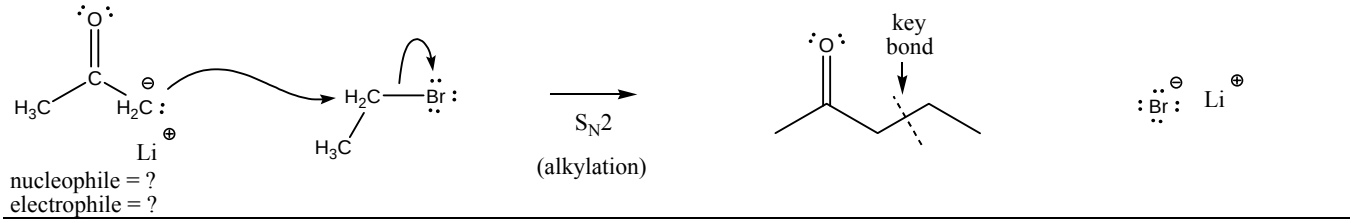


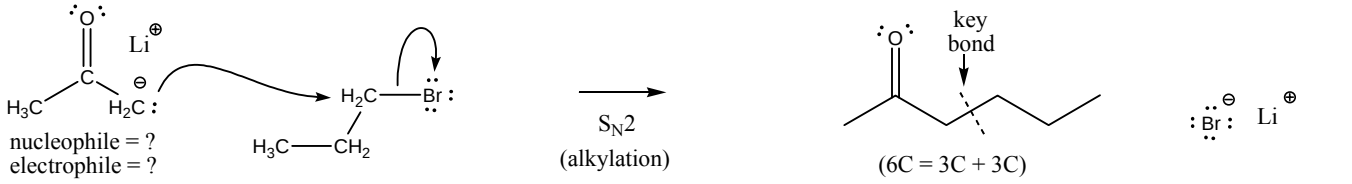




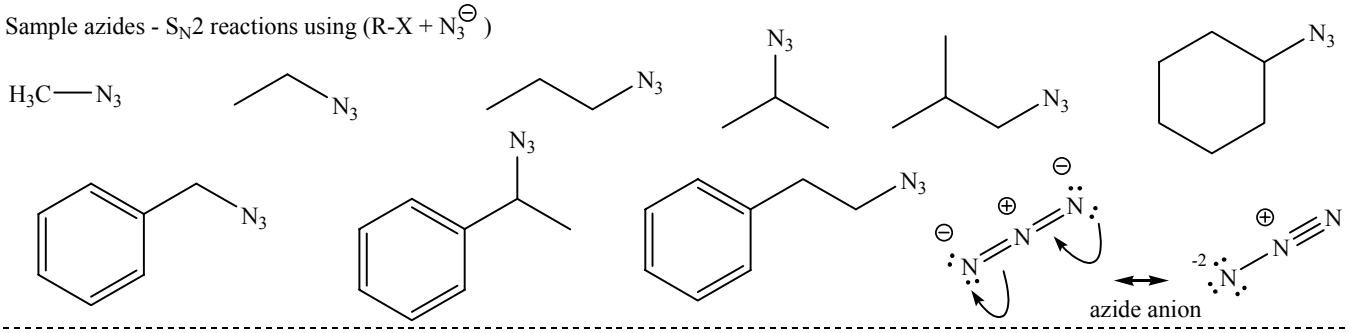
ketone enolates (good nucleophiles at epoxides, carbonyls and CH_3X, 1°RX and 2°RX) → bigger ketones

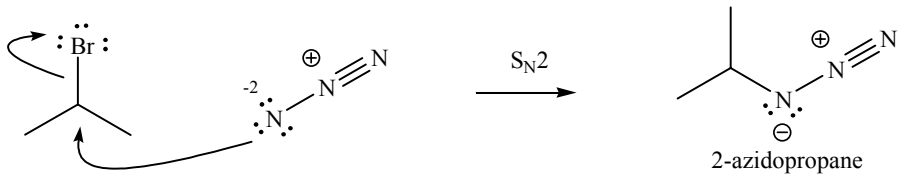






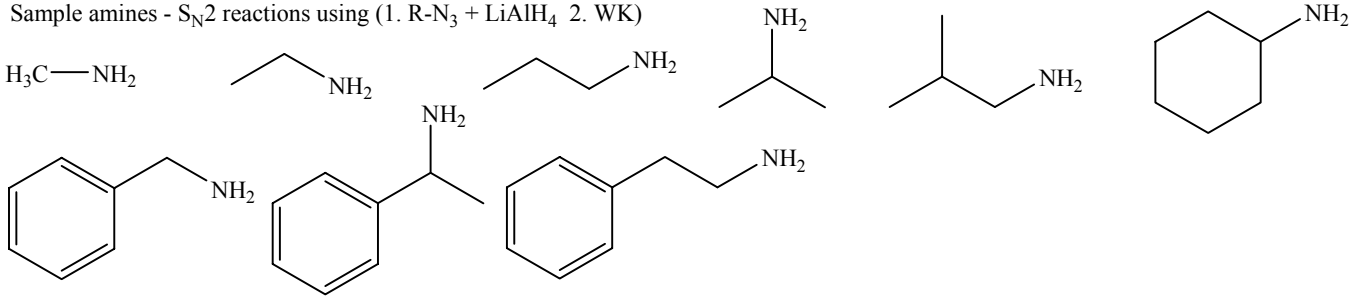
5. azide synthesis (these can be made into primary amines via 1. $LiAlH_4$ 2. workup)

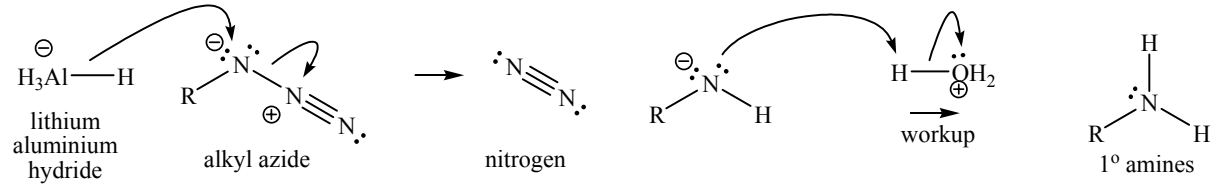




6. amine synthesis (at this point primary amines are made from azido compounds via 1. $LiAlH_4$ 2. workup)

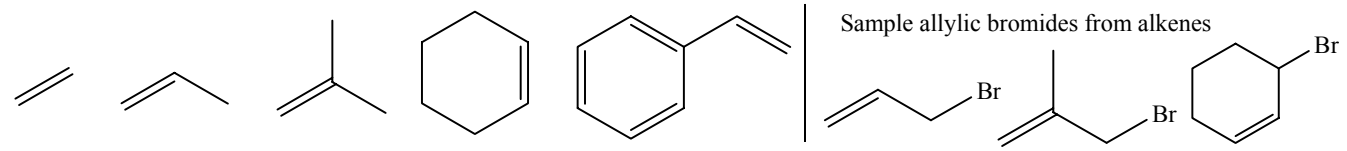
Sample amines - S_N2 reactions using (1. R-N_3 + $LiAlH_4$ 2. WK)





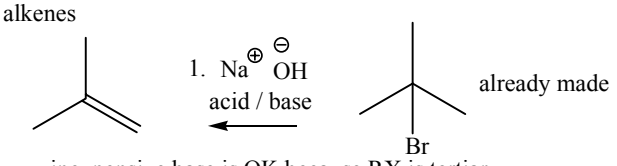
7. alkene synthesis (via E2 reactions, one time)

Sample alkenes using E2 reactions: R-X + t-butoxide; alkenes can make allylic R-X compounds



Sample allylic bromides from alkenes

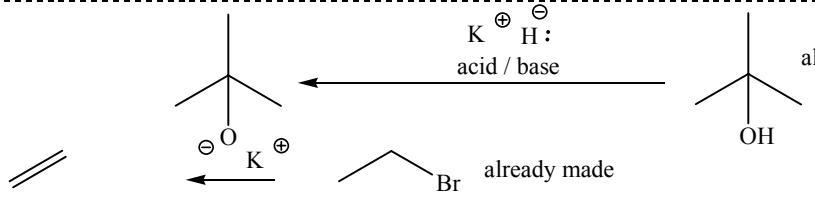
alkenes



inexpensive base is OK because RX is tertiary

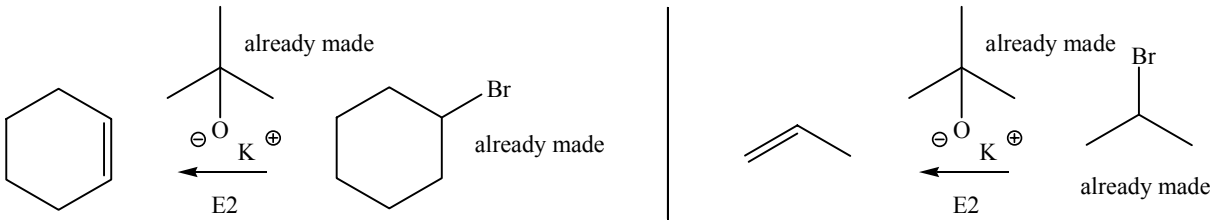
Use steric bulk and/or extreme basicity to drive E2 > S_N2.

relative alkene stabilities = tetrasub. > trisub. > trans-disub > cis-disub ≈ gem-disub > monosub > unsub.



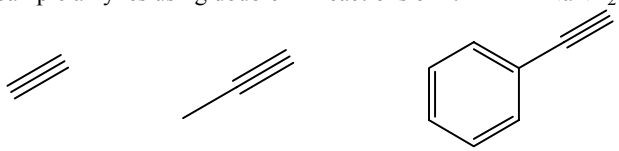
Use steric bulk and/or extreme basicity to drive E2 > S_N2.

E2 > S_N2 (need strong, bulky base to favor E2 at 1° RX)



8. alkyne synthesis (via E2 reactions, two times)

Sample alkynes using double E2 reactions of 1. RBr2 + $NaNR_2$ 2. workup



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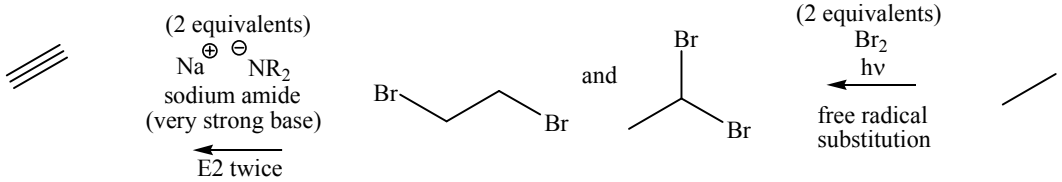
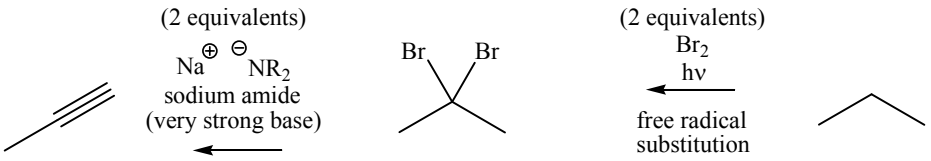
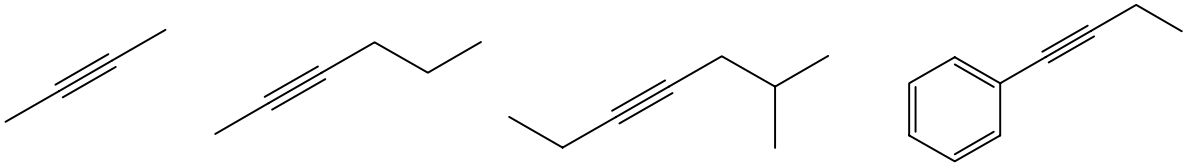
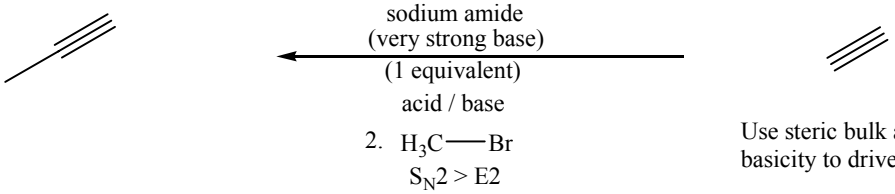
alkynes (use two leaving groups)



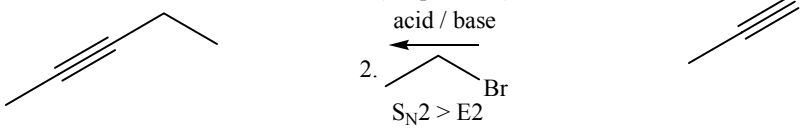


Sample alkynes using S_N2 reactions of 1. terminal alkyne + $NaNR_2$ 2. methyl or primary R-X (twice with ethyne)



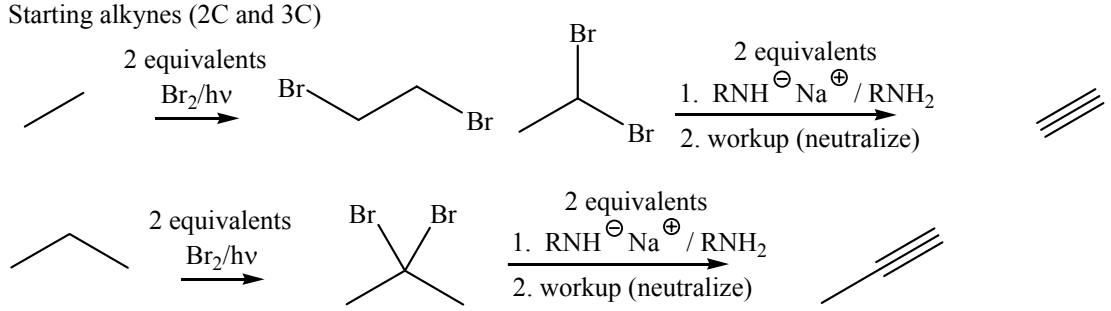


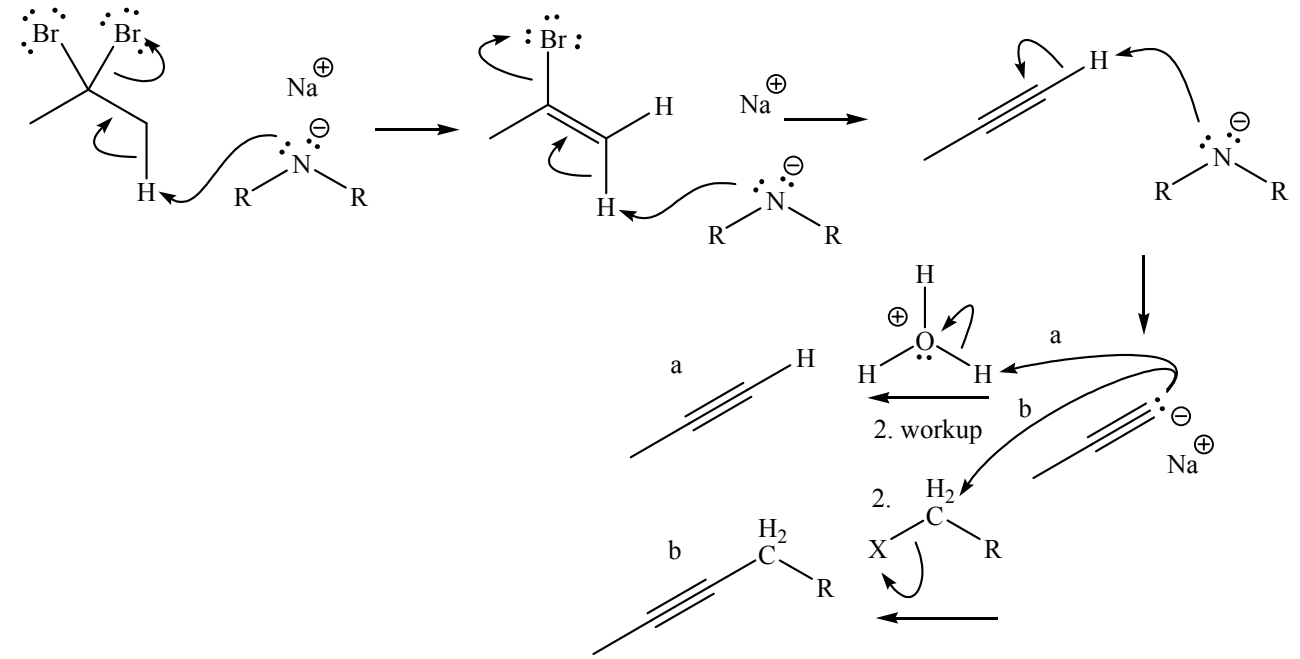
Use steric bulk and/or extreme basicity to drive E2 > S_N2.

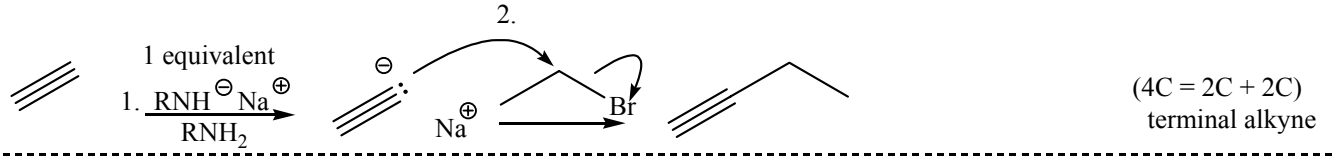


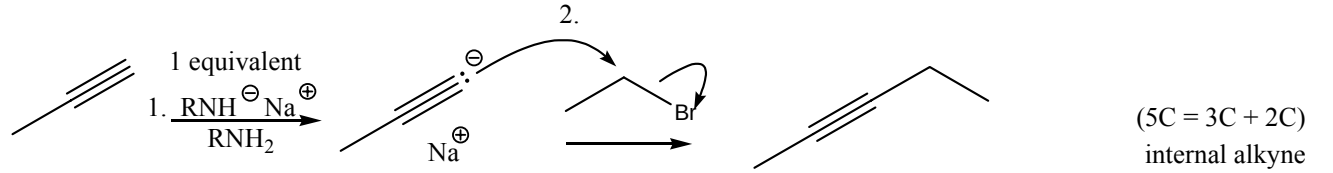
Terminal acetylides are OK nucleophiles at methyl and 1° RX, but E2 > S_N2 at 2° RX and only E2 at 3° RX.

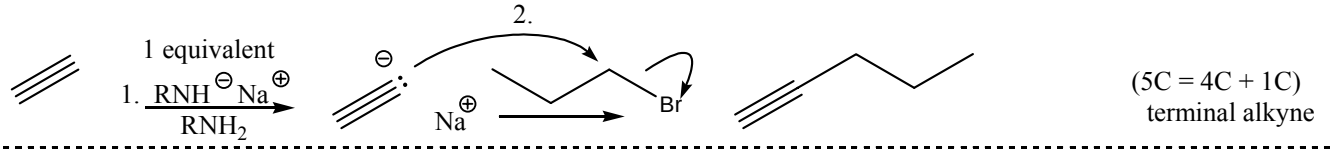
Starting alkynes (2C and 3C)

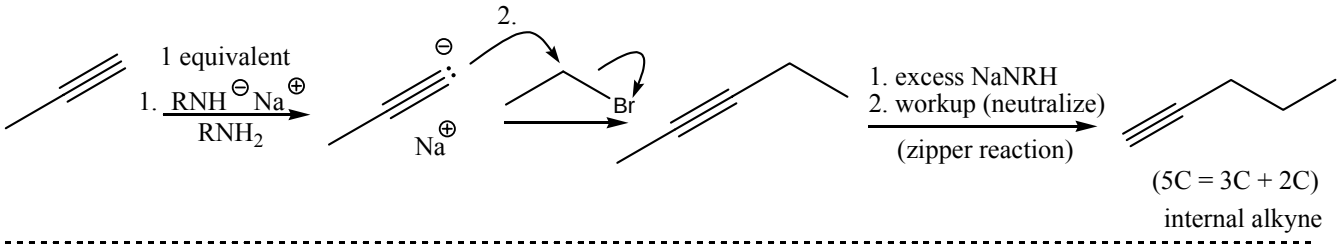


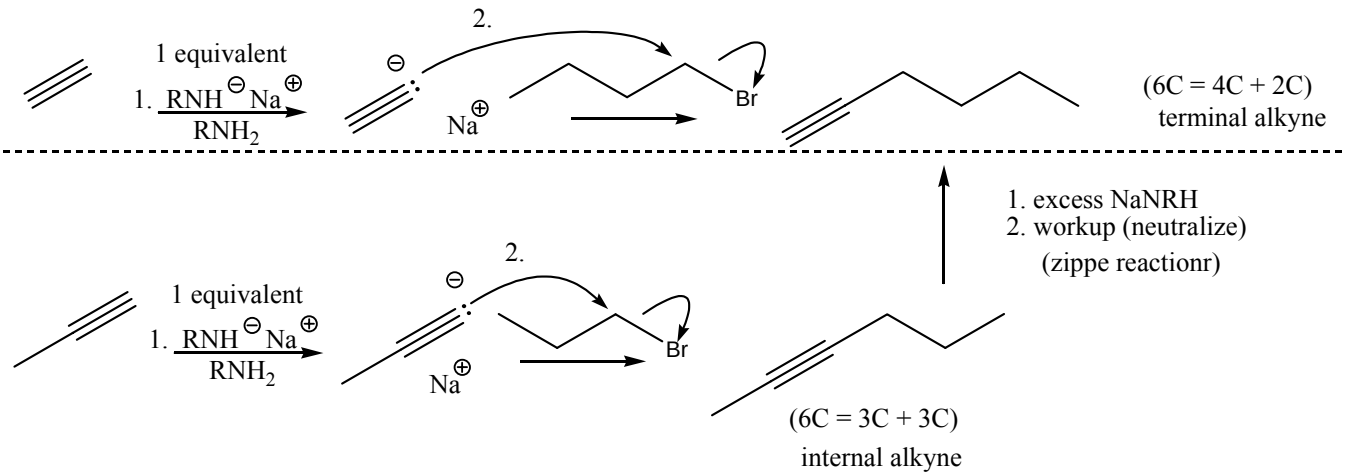




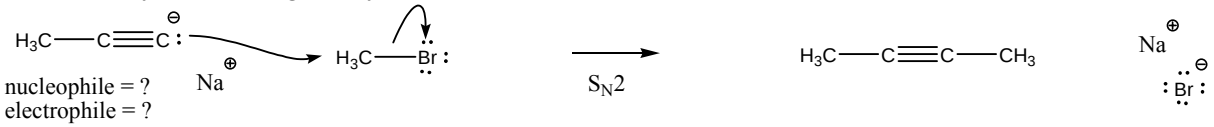


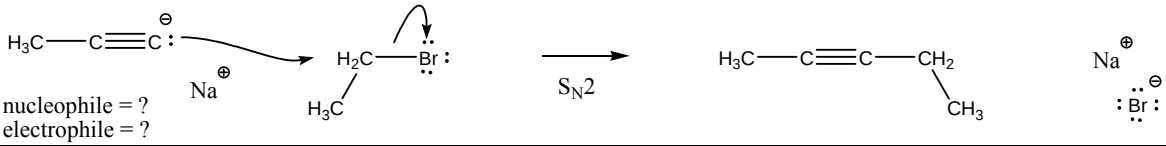


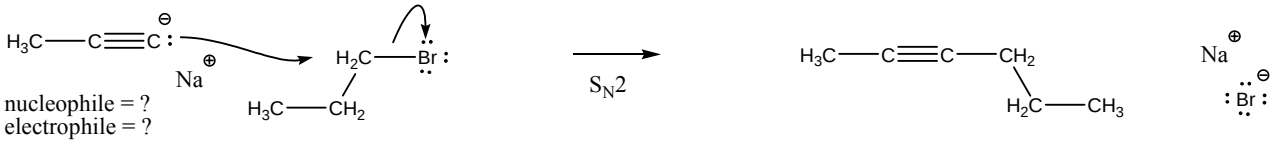




terminal acetylides → larger alkynes

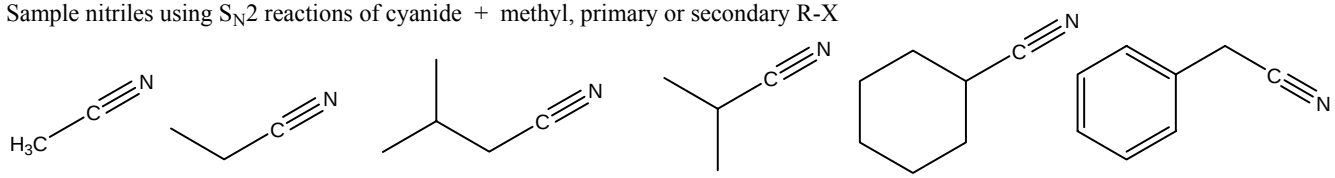


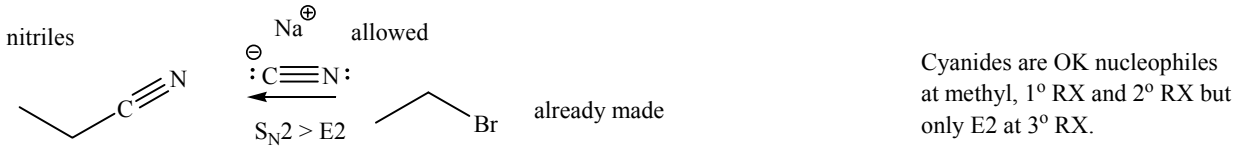


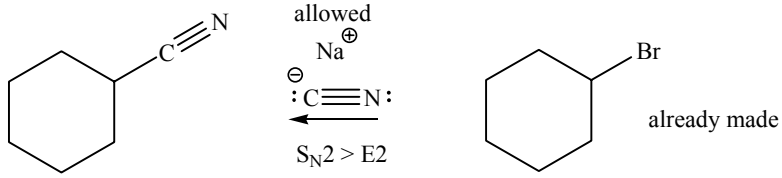


9. nitrile synthesis (via S_N2 reaction)

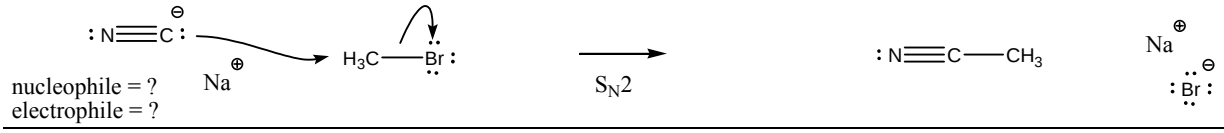
Sample nitriles using S_N2 reactions of cyanide + methyl, primary or secondary R-X

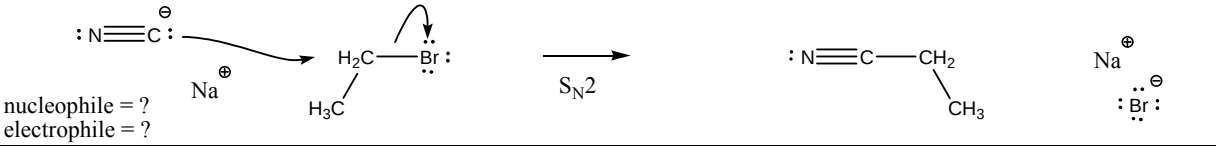


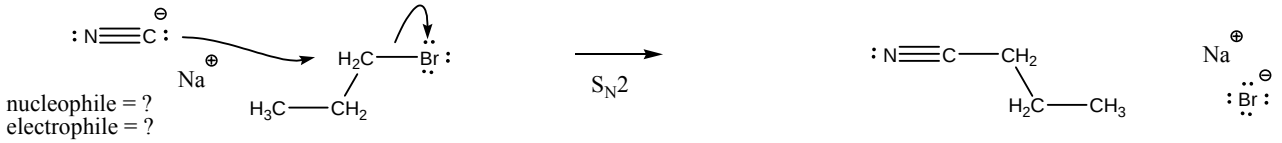




cyanide → nitriles

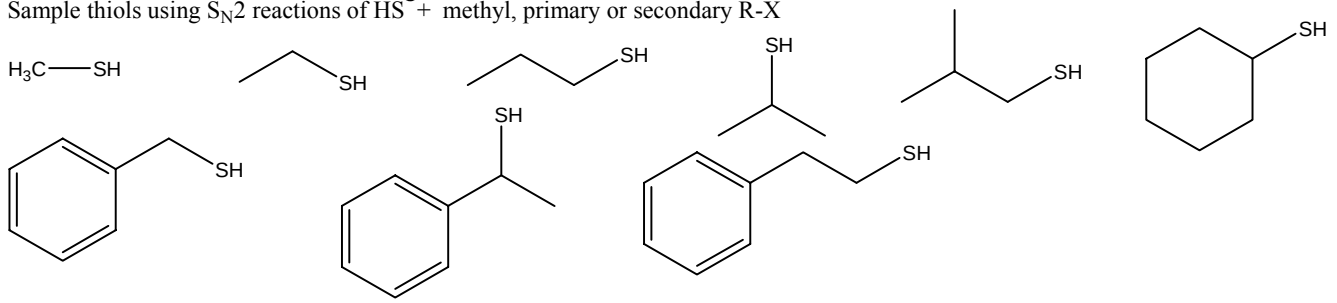




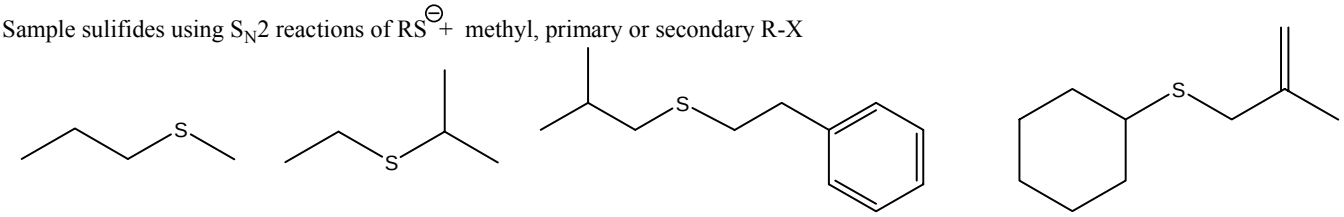


10. thiols and sulfides synthesis (via S_N2 reaction)

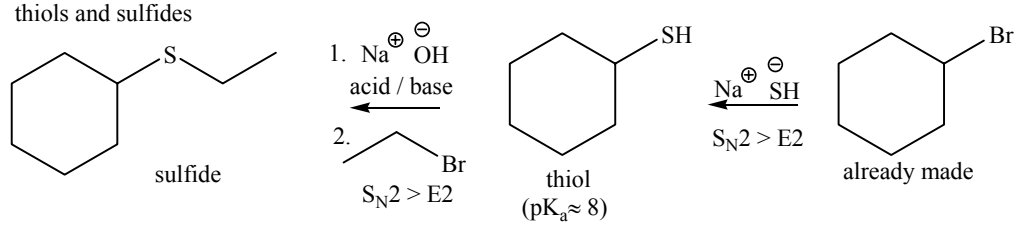
Sample thiols using S_N2 reactions of $HS^{\ominus}$ + methyl, primary or secondary R-X



Sample sulifides using S_N2 reactions of $RS^{\ominus}$ + methyl, primary or secondary R-X



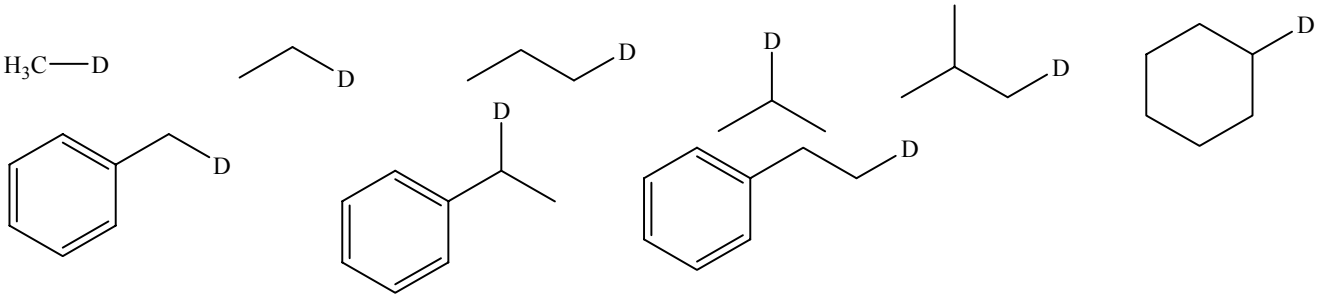
thiols and sulfides

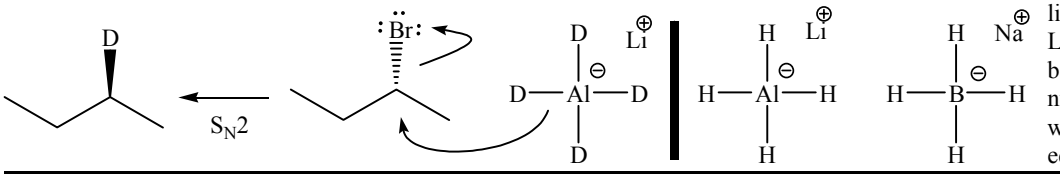


Sulfides are OK nucleophiles at methyl, 1° RX and 2° RX but only E2 at 3° RX.

11. introducing hydride or deuteride into organic molecules (via S_N2 reaction)

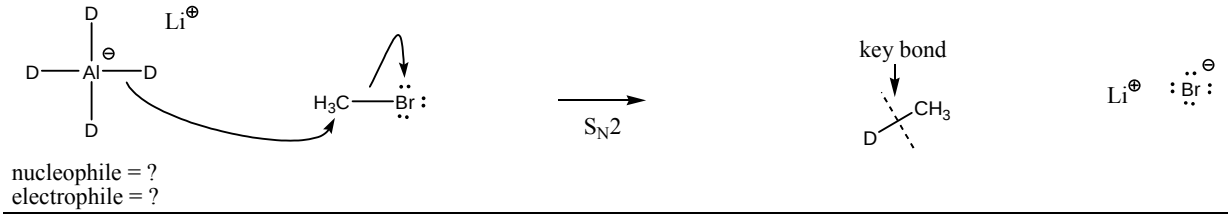
Sample deuterium added using S_N2 reactions of $LiAlD_4$ or $NaBD_4$ + methyl, primary or secondary R-X



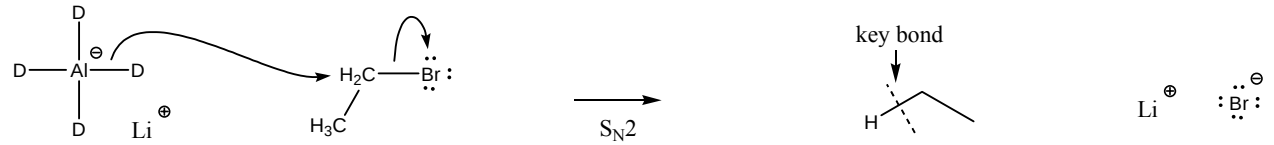


lithium aluminium hydride = LAH = (Li AlH_4) and sodium borohydride ($NaBH_4$) are both nucleophilic hydride. For now we will consider them to be equivalent reagents.

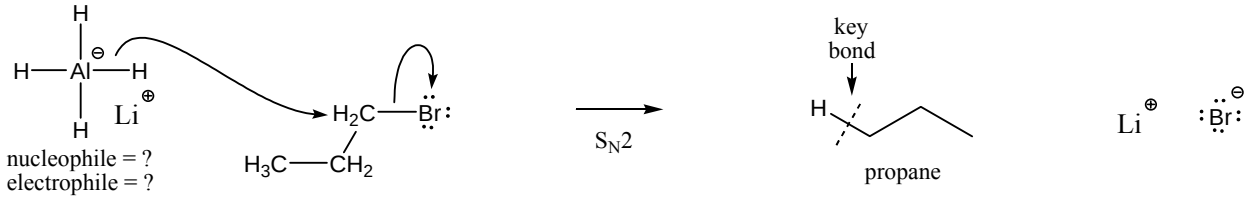
lithium aluminium hydride ($LiAlH_4$) and sodium borohydride ($NaBH_4$) = nucleophilic hydride
(using "deuteride" shows where the "hydrogen" goes)



nucleophile = ?
electrophile = ?



nucleophile = ?
electrophile = ?



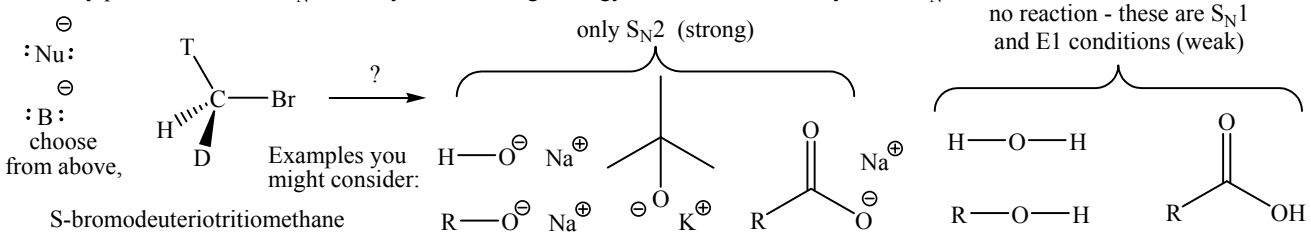
nucleophile = ?
electrophile = ?

Mechanisms Worksheet

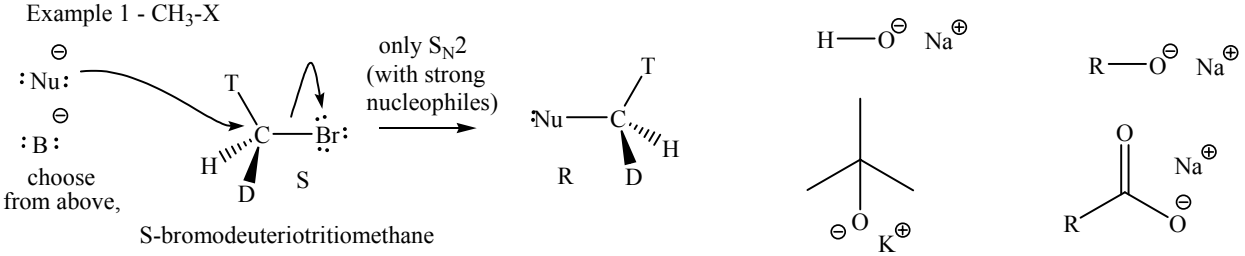
You need to be able to write your own mechanism from starting structures. I suggest you should practice using the nucleophiles from the list with the various RX compounds listed above. Writing mechanisms for each possibility would give you more than enough practice to learn the mechanism. Common mistakes include lone pairs, formal charge, curved arrows, correct Lewis structures, correct products predicted. This stuff takes practice – AND – correcting your mistakes. I have set up the following worksheet to give you templates to fill in so that you can use them multiple times by copying the basic framework and then filling in the details. If you don't practice, you will be taking 314 again – and you don't want to do that. DO THE WORK!

S_N2 then E2 examples first, followed by S_N1 and E1 reactions

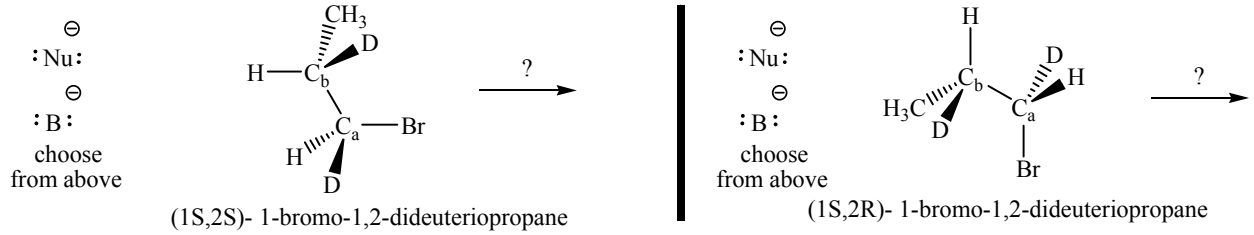
Example 1 - CH_3-X (deuterium - D, and tritium = T are isotopes of hydrogen that can be distinguished from H)
The only possible choice is S_N2. Methyl R^+ is too high energy for solution chemistry, so no S_N1/R1.



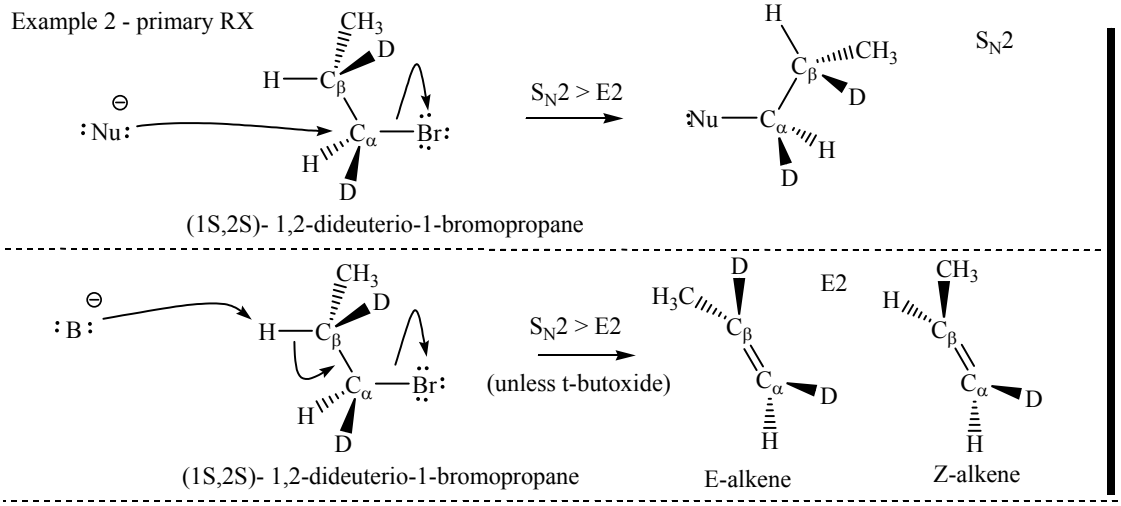
Example 1 - CH_3-X



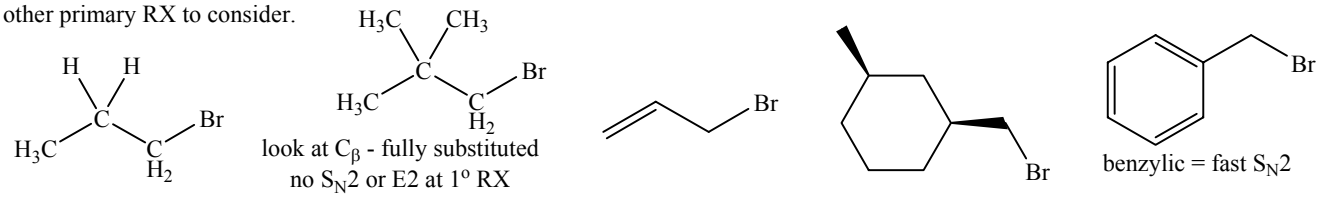
Example 2 - primary RX (deuterium is an isotope of hydrogen that can be distinguished from H)



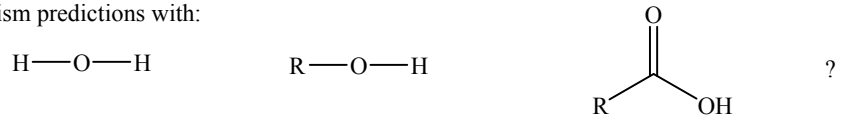
Example 2 - primary RX



other primary RX to consider.

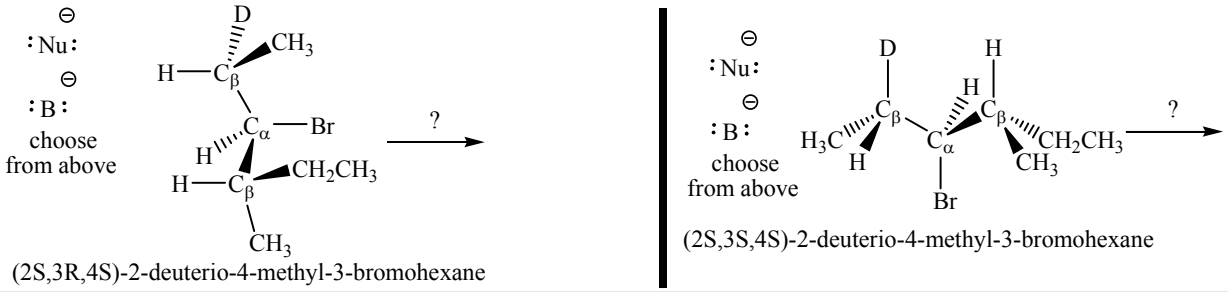


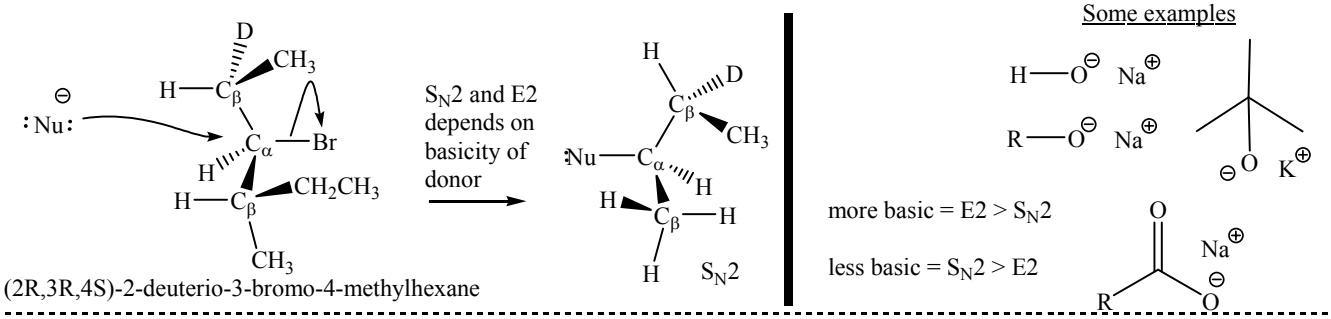
Mechanism predictions with:

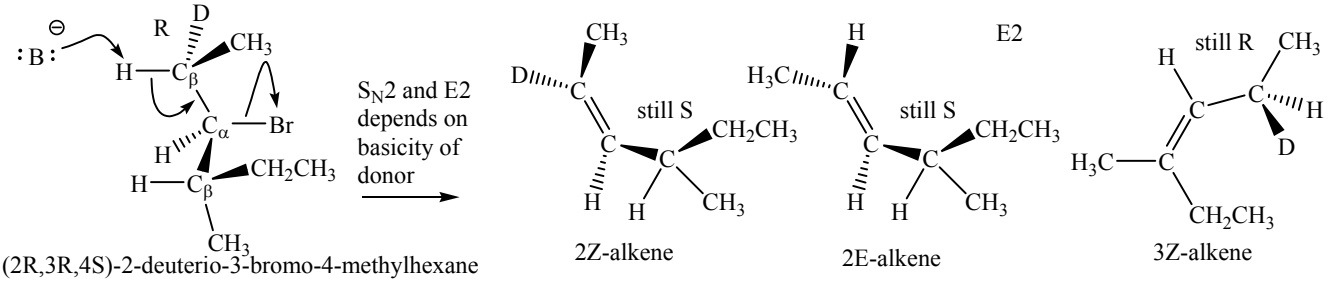


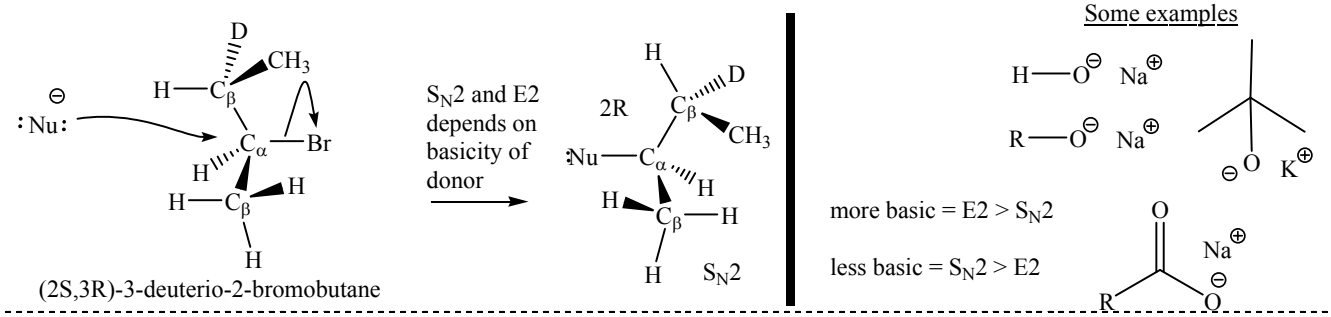
No S_N1/E1 is possible at primary RX in solution chemistry. The primary R^+ is too high in energy.

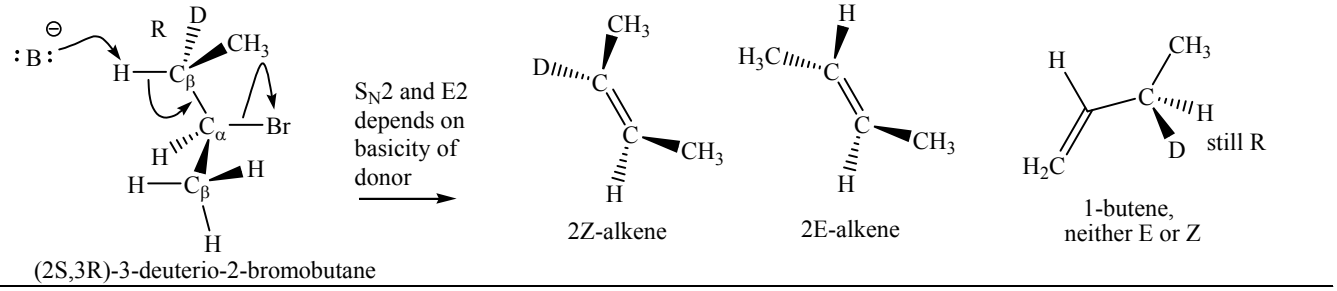
Example 3 - secondary RX (deuterium is an isotope of hydrogen that can be distinguished from H)



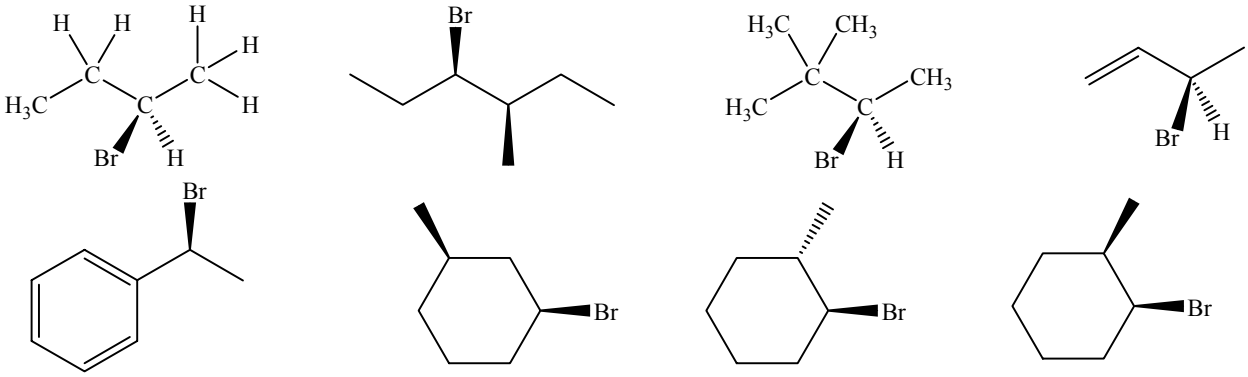




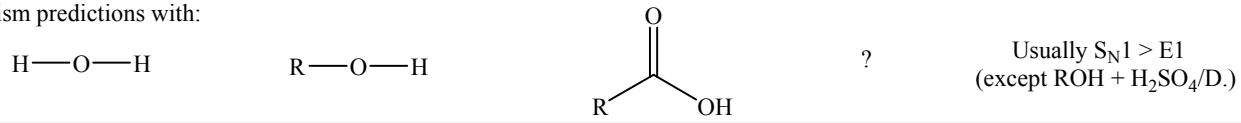




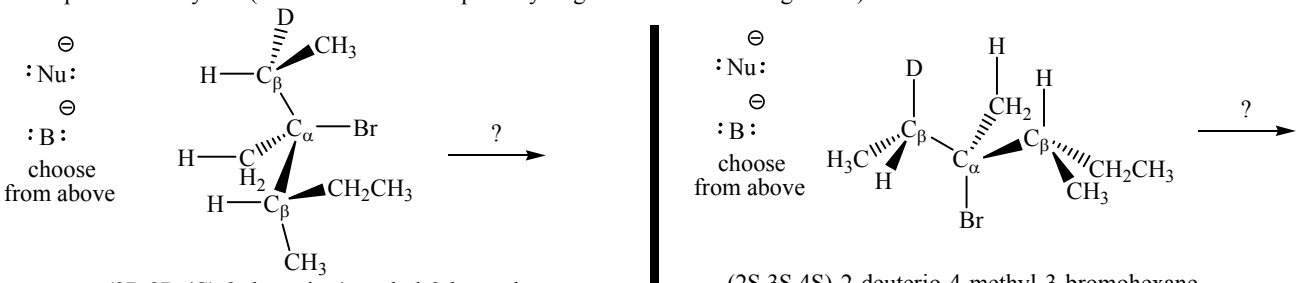
other secondary RX to consider.

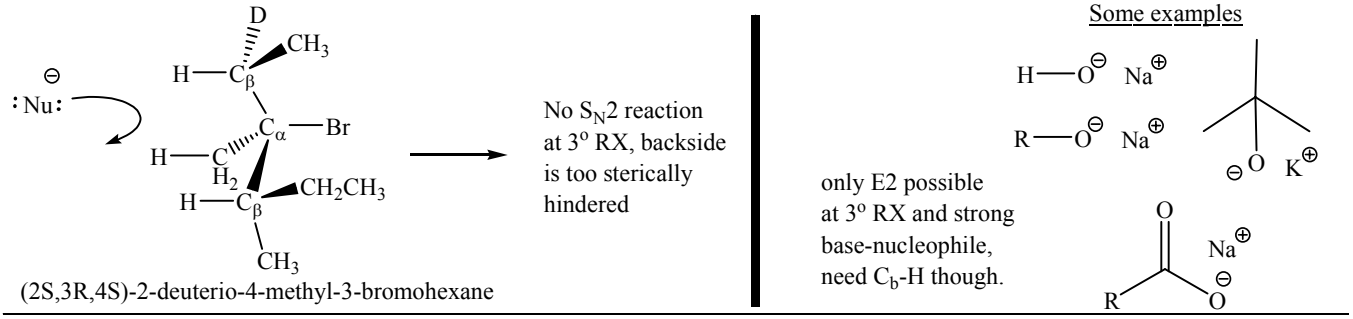


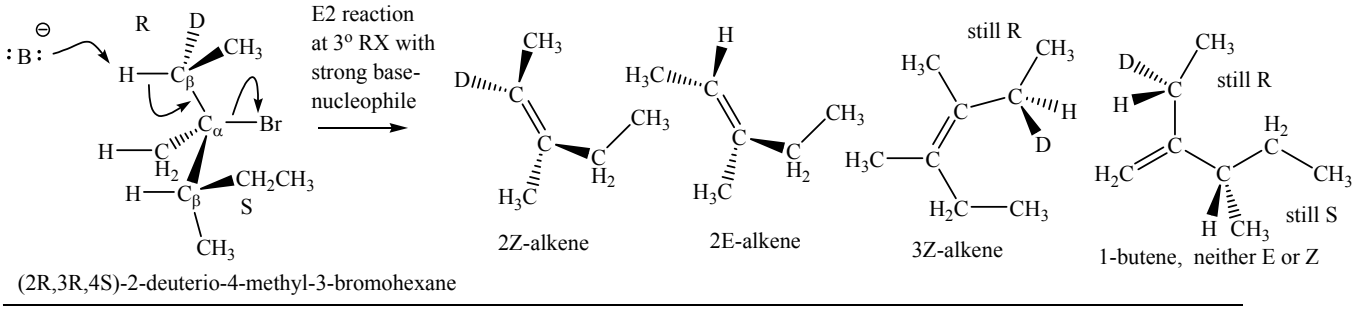
Mechanism predictions with:



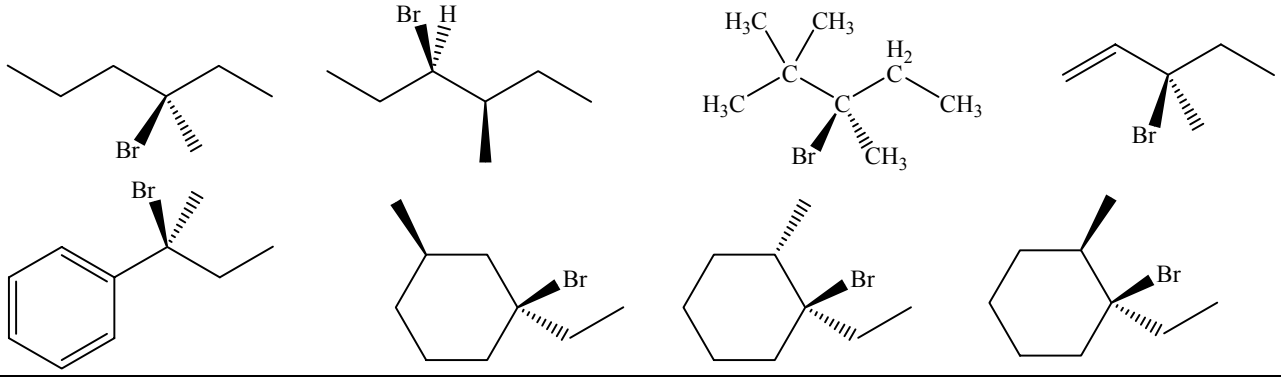
Example 4 - tertiary RX (deuterium is an isotope of hydrogen that can be distinguished)



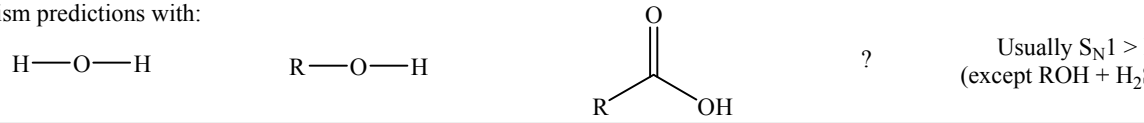




other tertiary RX to consider.

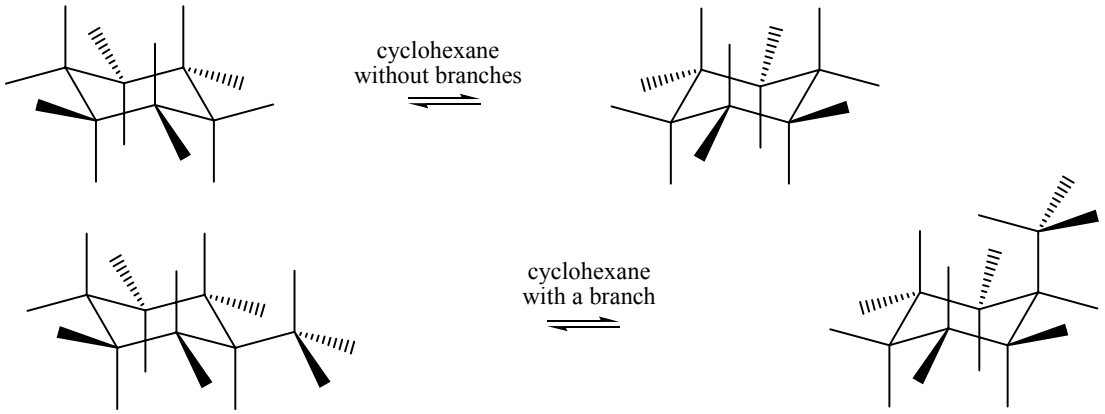


Mechanism predictions with:

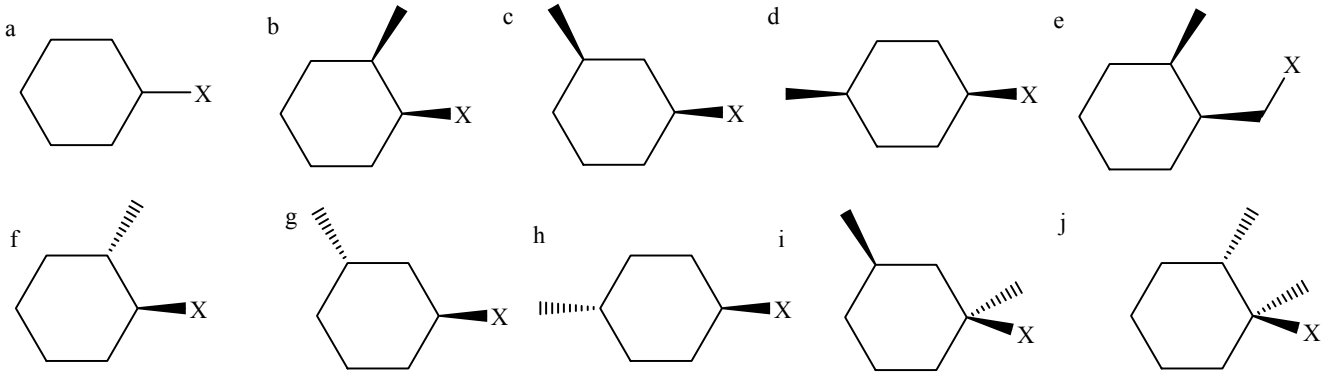


Usually S_N1 > E1
(except ROH + H_2SO_4/D.)

Example 5 - cyclohexane structures to consider (X must be axial to react by S_N2 and E2) (X can be axial or equatorial to react by S_N1 and E1). Essential details can be filled in on the following templates.

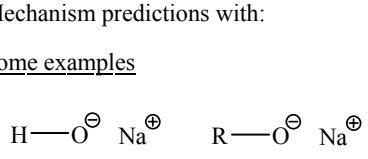


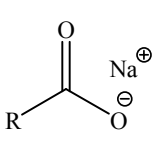
Many substitution patterns are possible.



Mechanism predictions with:

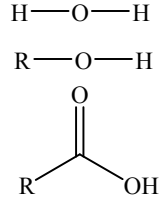
Some examples





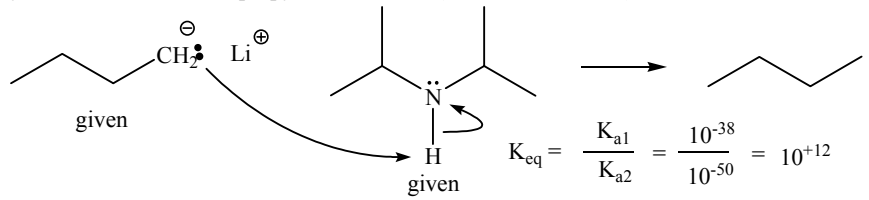
strong nucleophile/bases + other anions shown above

weak
nucleophiles

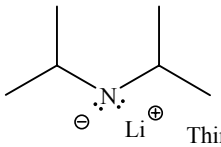


S_N chemistry with enolates (mechanisms)

Synthesis of lithium diisopropyl amide, LDA. (acid / base reaction)

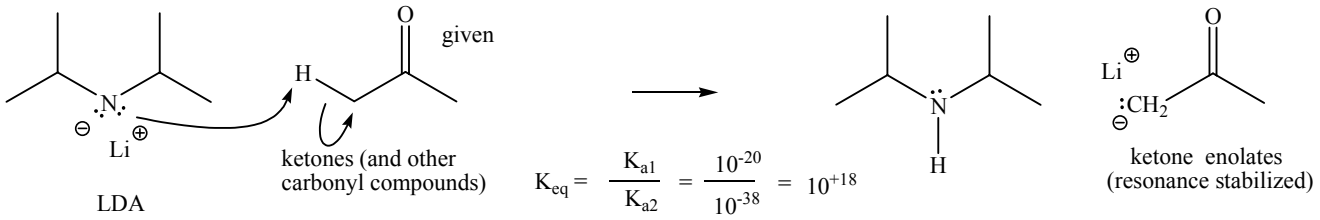


LDA = lithium diisopropyl amide

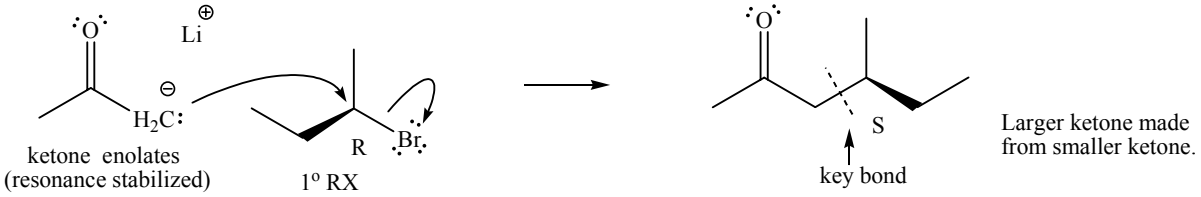


Think - sterically bulky, very basic that goes after weakly acidic protons.

Make enolate (ketones and esters)

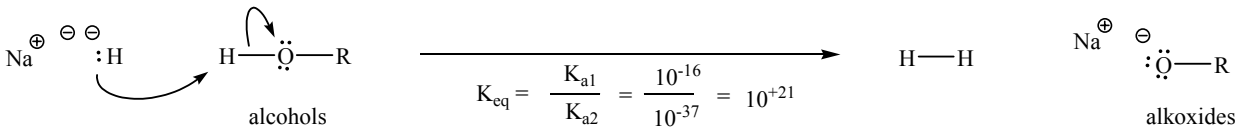


React enolate with RX compounds (methyl, 1° and 2° RX)

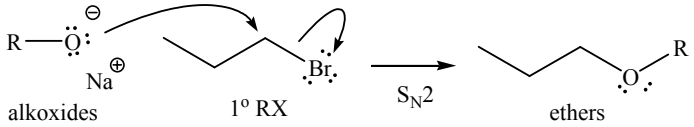


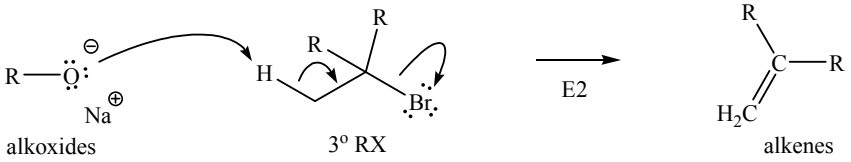
Larger ketone made from smaller ketone.

Synthesis of alkoxide nucleophiles with sodium hydride. (acid / base reaction)

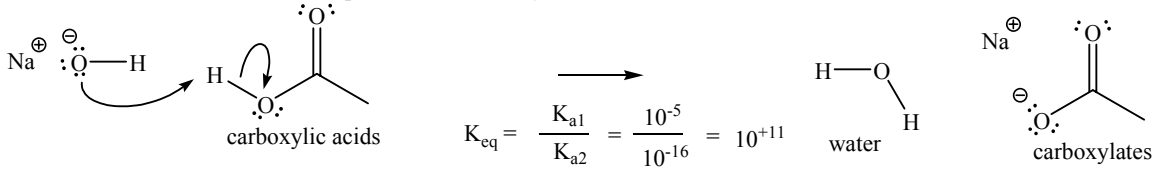


React alkoxides with RX compounds (methyl and 1° S_N2 favored, 2° and 3° RX E2 favored)

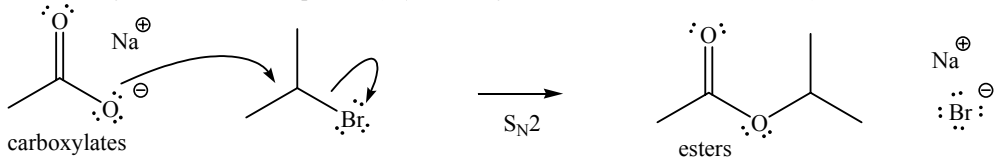


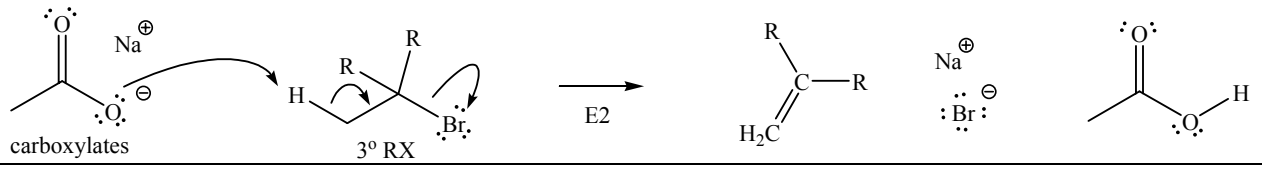


Synthesis of ethanoate (acetate) nucleophile with sodium hydroxide. (acid / base reaction)

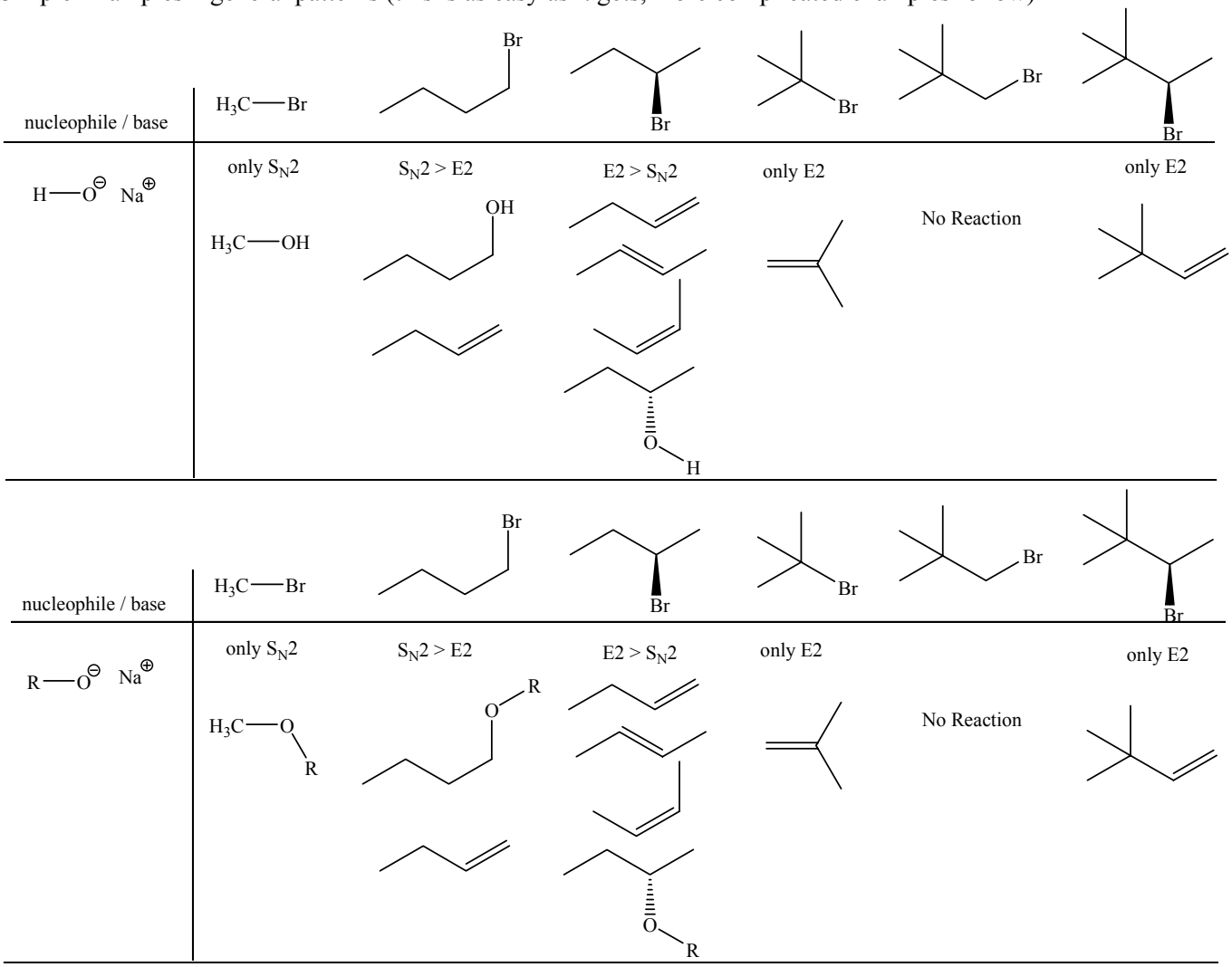


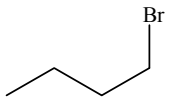
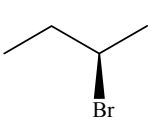
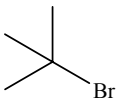
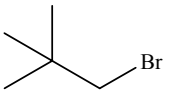
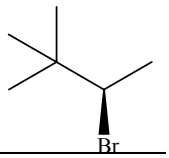
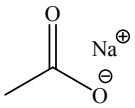
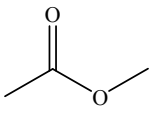
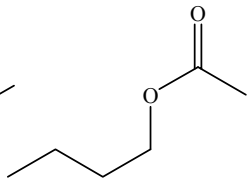
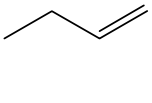
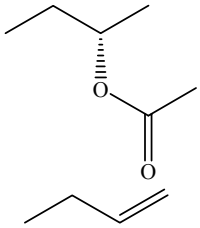
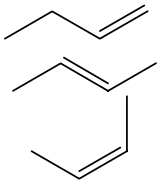
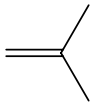
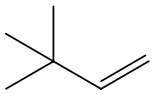
React carboxylates with RX compounds (S_N2 at methyl, 1° and 2° RX and E2 at 3° RX)

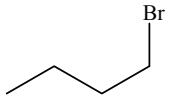
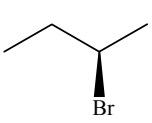
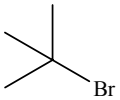
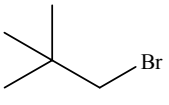
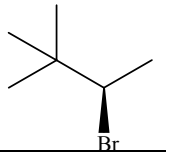
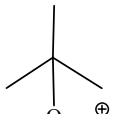
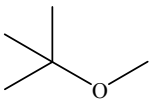
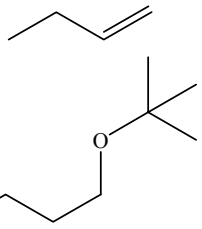
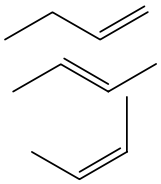
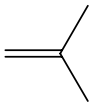
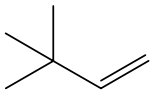


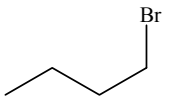
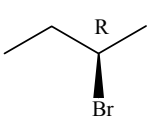
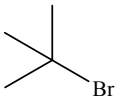
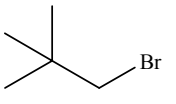
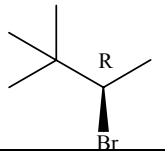
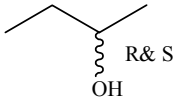
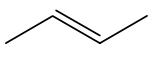
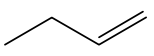
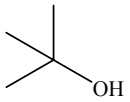
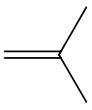
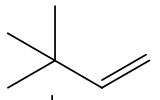
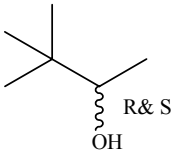
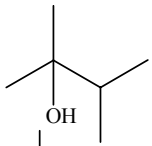
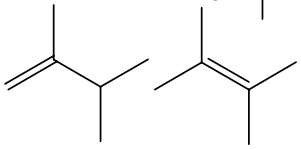


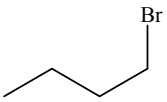
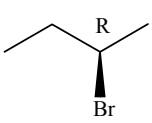
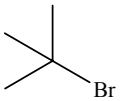
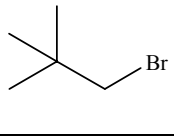
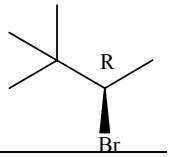
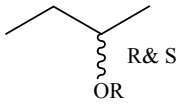
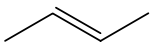
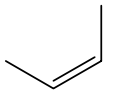
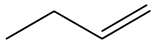
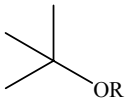
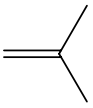
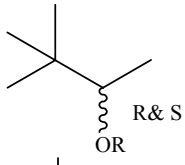
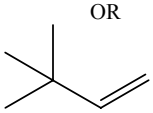
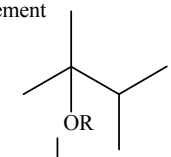
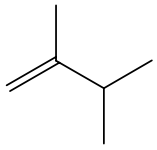
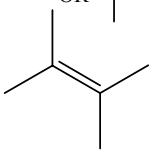
Simple Examples – general patterns (this is as easy as it gets, more complicated examples follow)

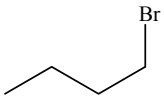
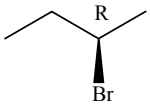
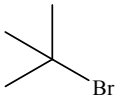
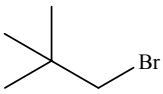
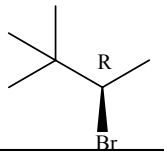
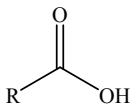
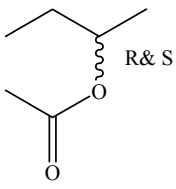
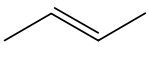
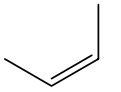
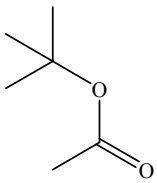
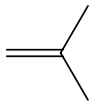
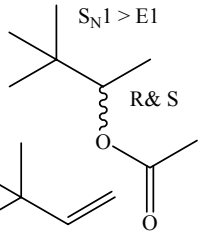
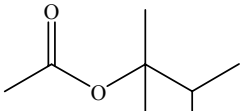
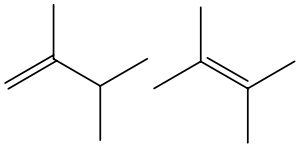


nucleophile / base	$H_3C—Br$					
	only S_N2 	$S_N2 > E2$  	$S_N2 > E2$  	only E2 	No Reaction	only E2 

nucleophile / base	$H_3C—Br$					
	only S_N2 	$E2 > S_N2$ 	only E2 	only E2 	No Reaction	only E2 

nucleophile / base	$H_3C—Br$					
$H—O—H$	No Reaction	No Reaction	$S_N1 > E1$   	$S_N1 > E1$  	No Reaction	$S_N1 > E1$   with rearrangement  

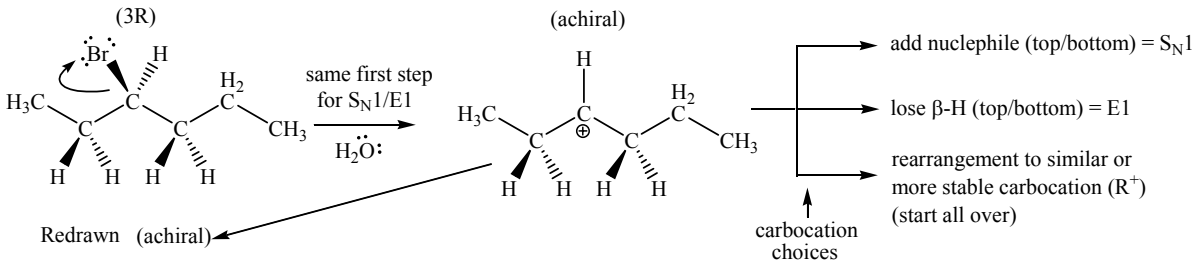
nucleophile / base	$H_3C—Br$					
R—O—H	No Reaction	No Reaction	$S_N1 > E1$    	$S_N1 > E1$  	No Reaction   with rearrangement   	$S_N1 > E1$

nucleophile / base	$H_3C—Br$					
	No Reaction	No Reaction	$S_N1 > E1$    	$S_N1 > E1$  	No Reaction  with rearrangement  	$S_N1 > E1$

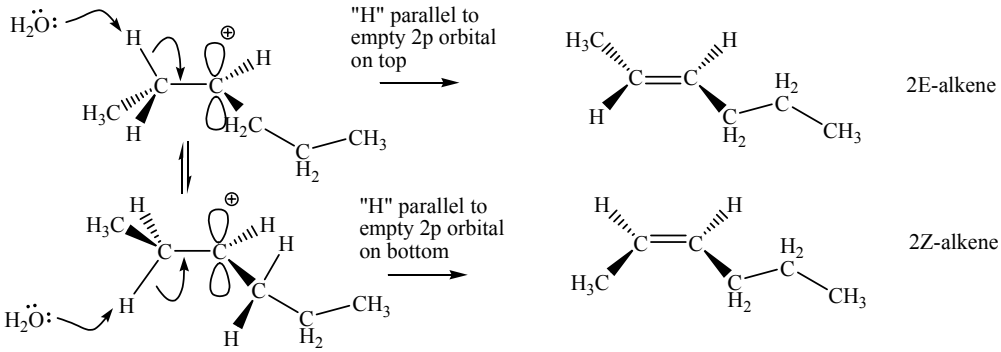
S_N1 / E1 possibilities –extra complications at C_β positions, 2° RX, rearrangements NOT considered (H_2O,ROH,RCO_2H)

Examples of weak nucleophile/bases in our course

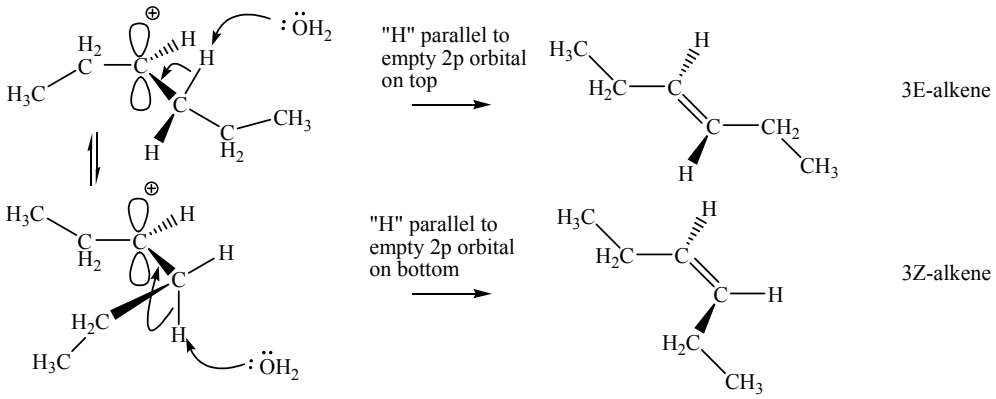
a water b alcohols c carboxylic acids



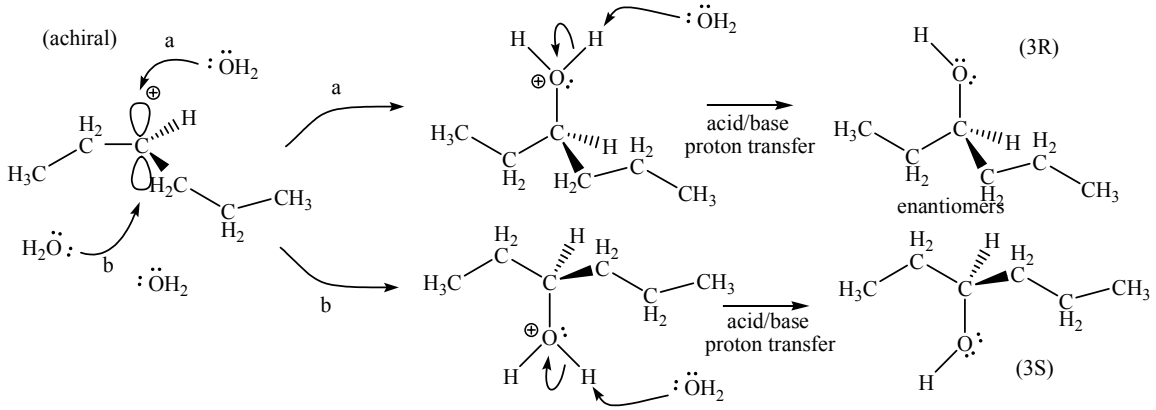
E1 product from left C_β carbon atom



E1 product from right C_β carbon atom

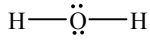


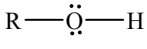
S_N1 product (a. add from top and b. add from bottom)

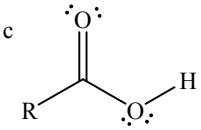


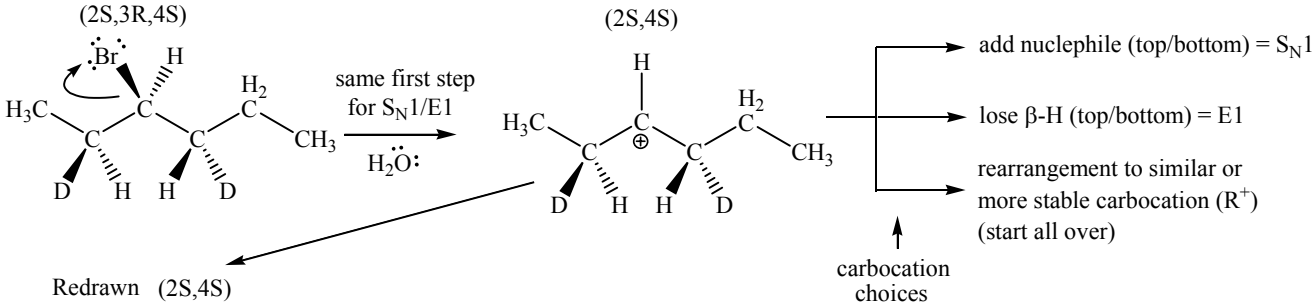
S_N1 / E1 possibilities –extra complications at C_β positions, 2° RX, rearrangements NOT considered, with deuterium (makes it a little harder)

Examples of weak nucleophile/bases

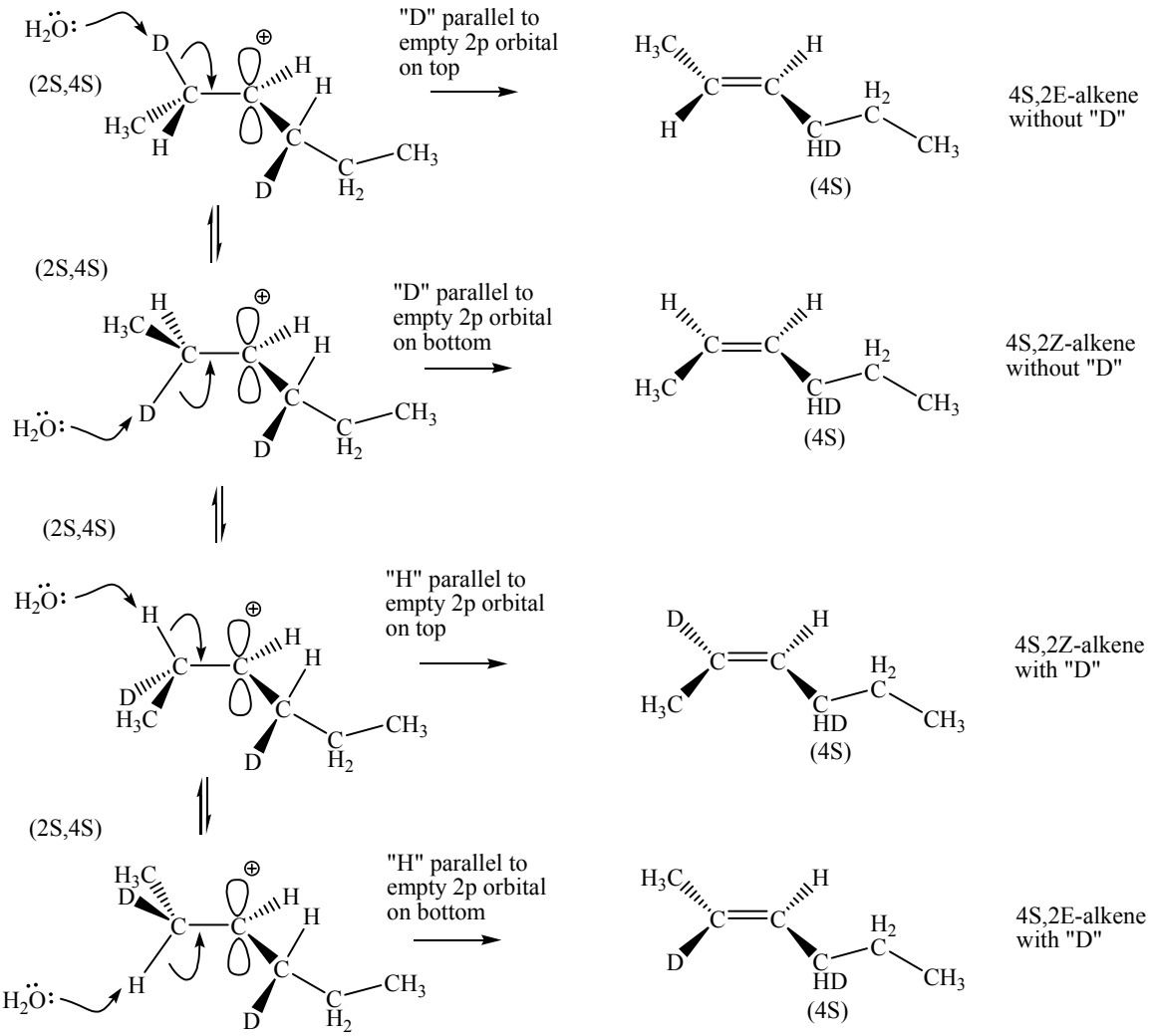
a  water

b  alcohols

c  carboxylic acids

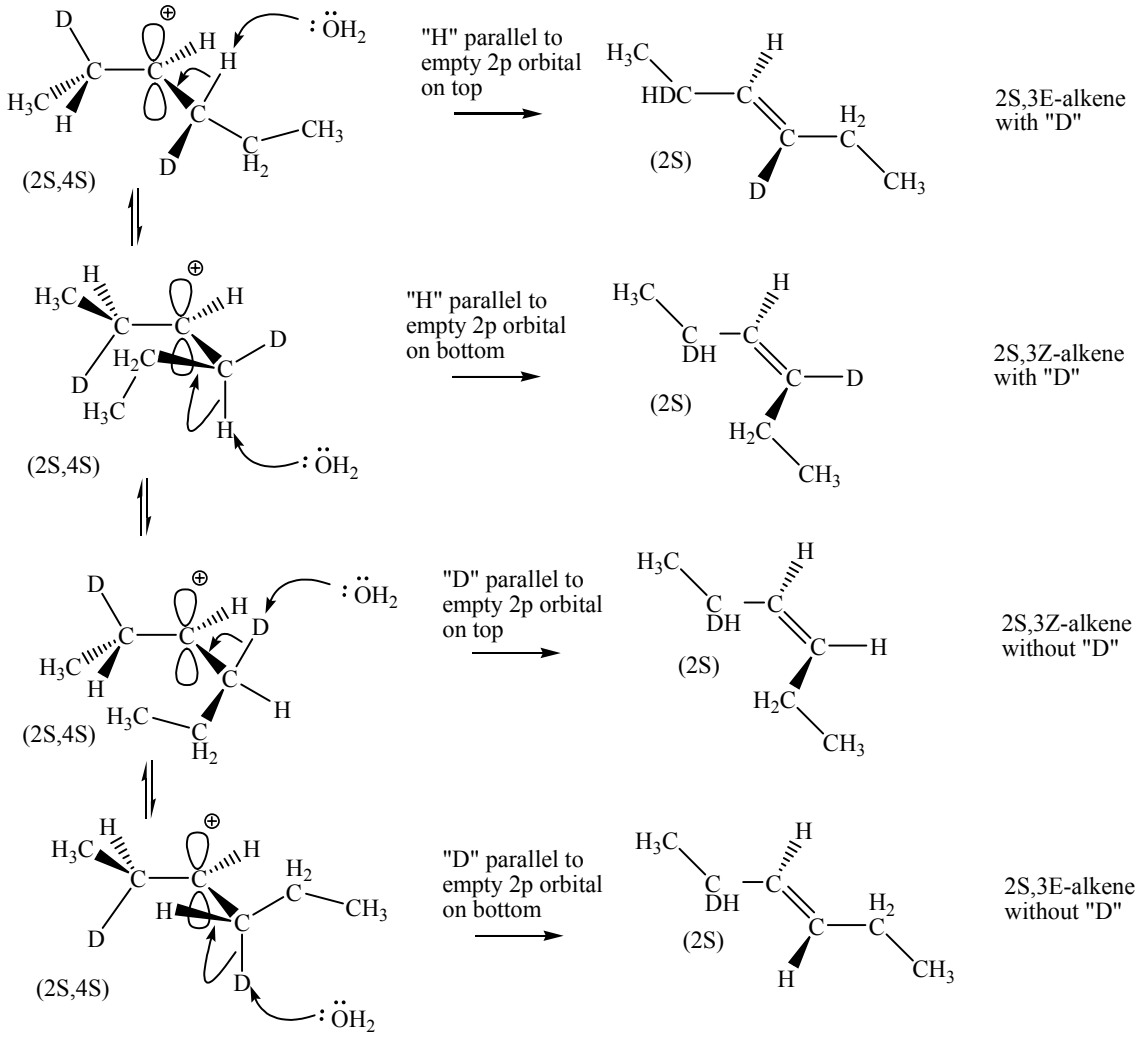


E1 product from left C_β carbon atom

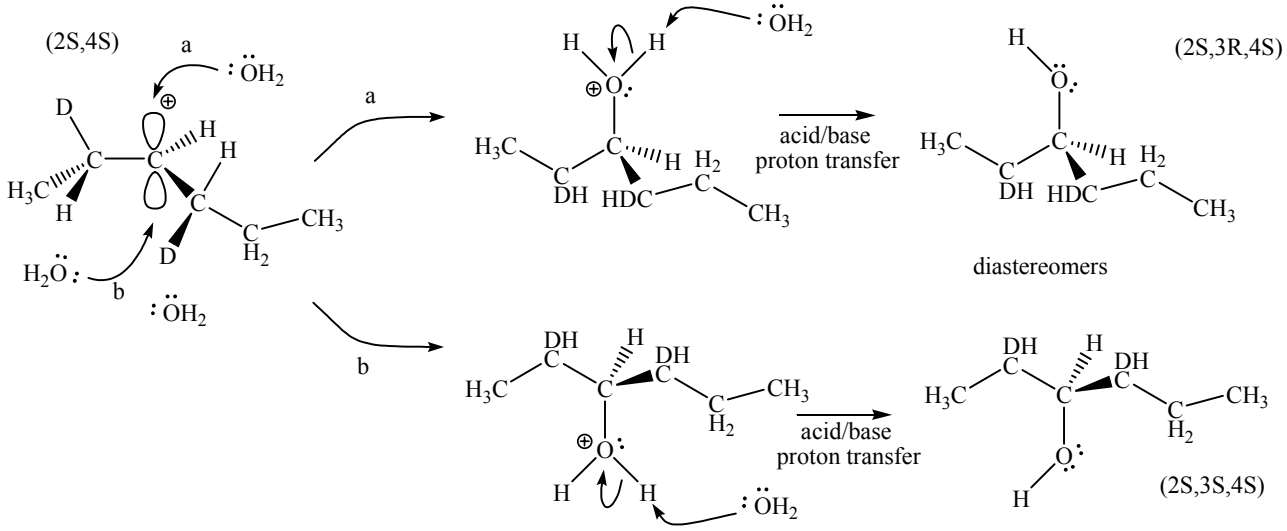


Redrawn from above (2S,4S)

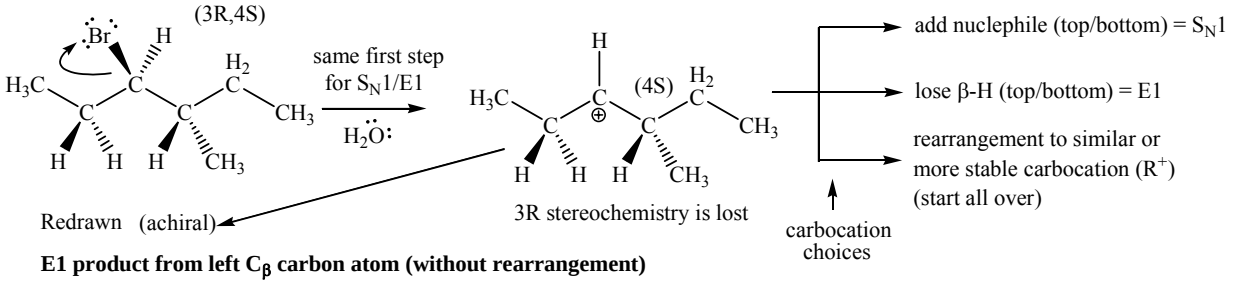
E1 product from right C_β carbon atom



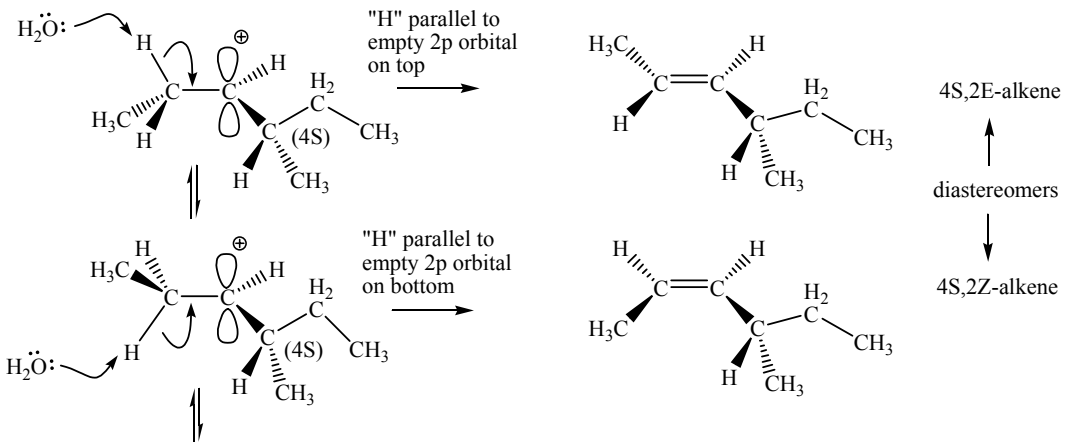
S_N1 product (a. add from top and b. add from bottom)



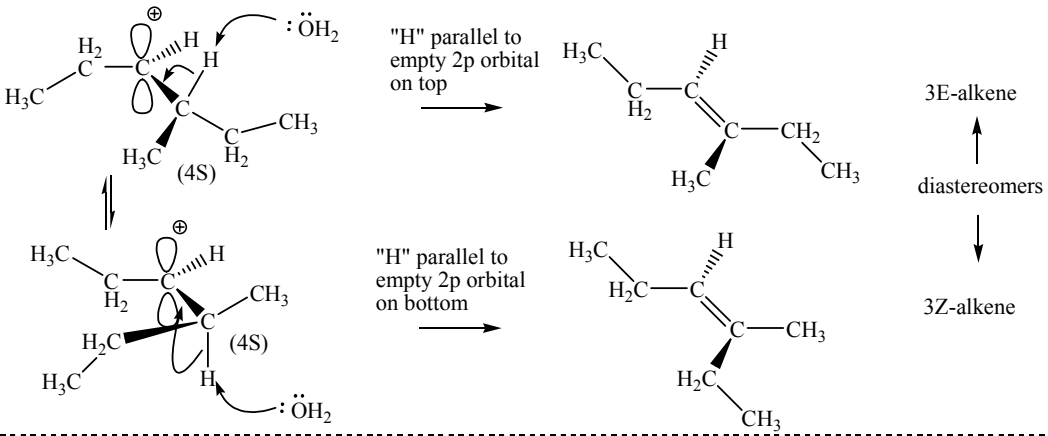
S_N1 / E1 possibilities –extra complications at C_β positions of 2° RX, rearrangement to more stable 3° R^+ considered



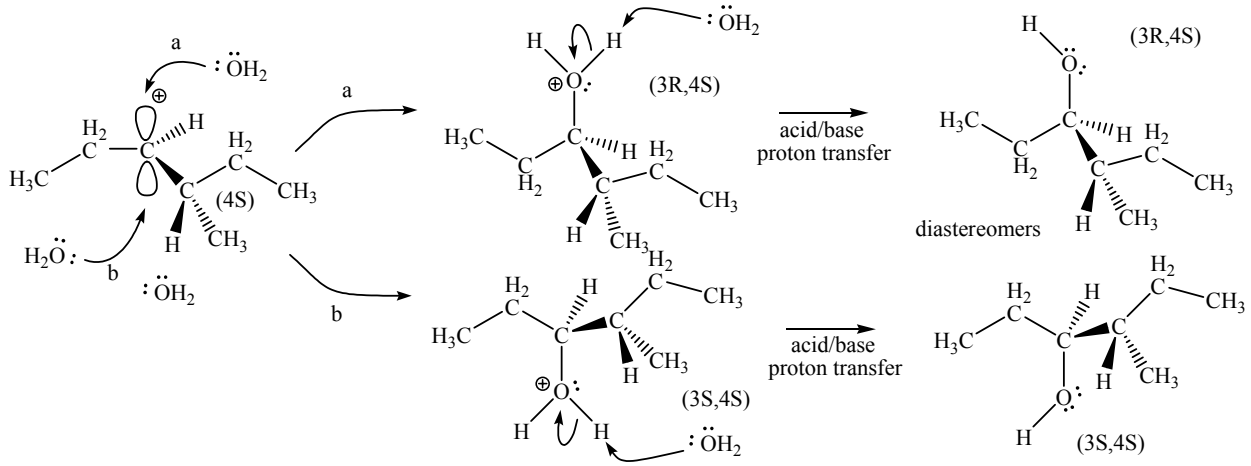
E1 product from left C_β carbon atom (without rearrangement)



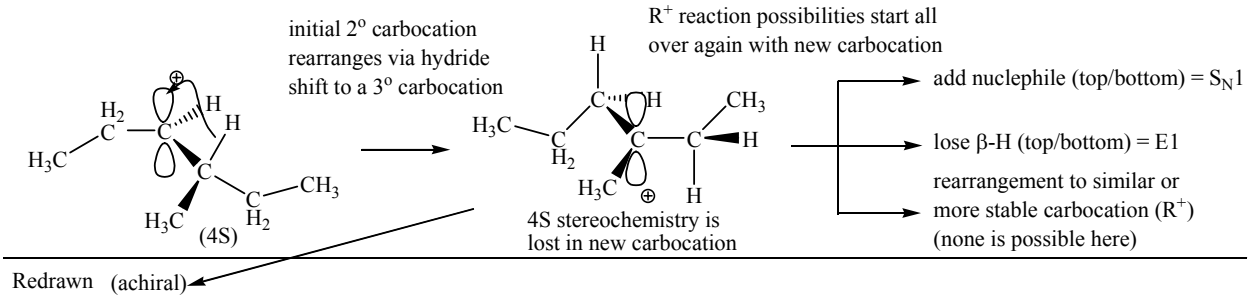
E1 product from right C_β carbon atom (without rearrangement)



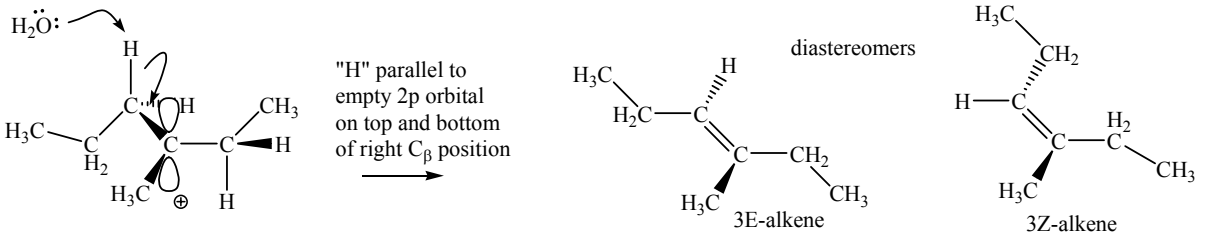
S_N1 product (a. add from top and b. add from bottom), (without rearrangement)



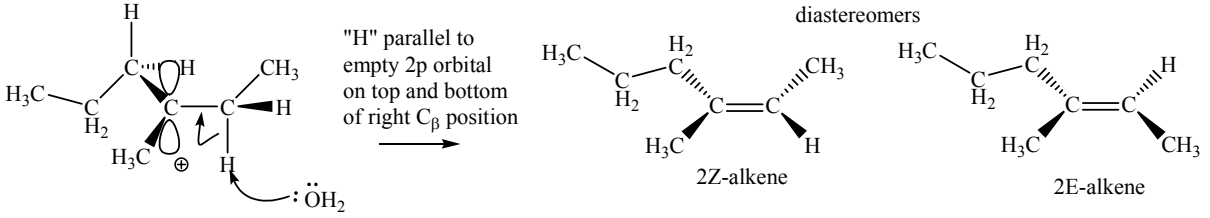
After rearrangement to 3° carbocation (R^+) – We will skip rearrangements in Chem 314



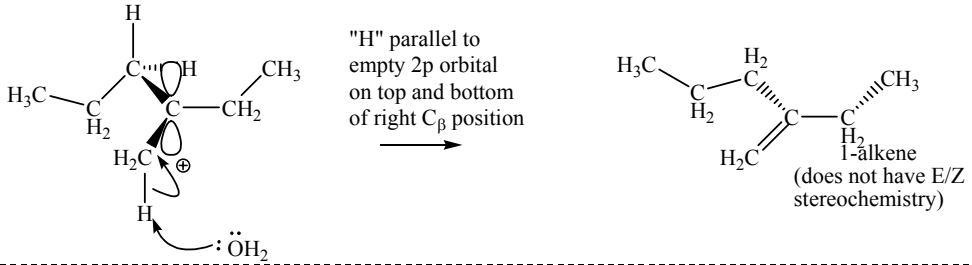
E1 products from left C_β carbon atom (top and bottom, after rearrangement)



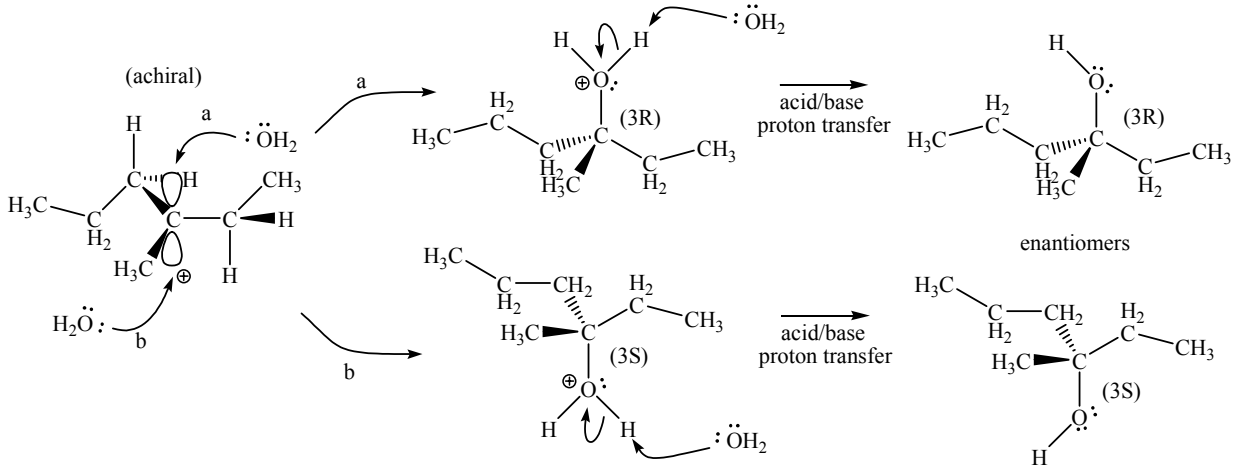
E1 product from right C_β carbon atom (top and bottom, after rearrangement)



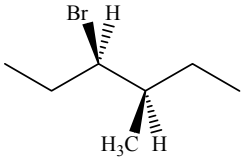
E1 product from methyl C_β carbon atom (top and bottom, after rearrangement, only one product from the methyl)



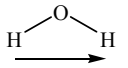
S_N1 product (a. add from top and b. add from bottom), (after rearrangement)



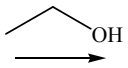
Homework problems: The number of each type of product (SN1, E1, SN2, E2) is listed after a reaction arrow for each starting structure (assuming I analyzed the possibilities accurately in my head, while sitting at the computer). See if you can generate those products using a valid mechanism for each one.



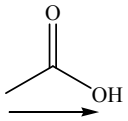
a. initial carbocation
b. after rearrangement



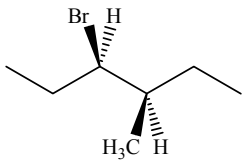
	S_N1	E1
a.	2	4
b.	2	5

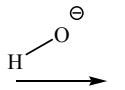


	S_N1	E1
a.	2	4
b.	2	5

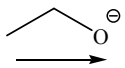


	S_N1	E1
a.	2	4
b.	2	5

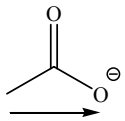




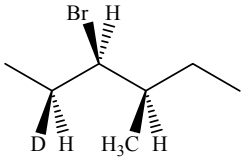
S_N2	E2
1	3



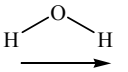
S_N2	E2
1	3



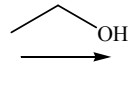
S_N2	E2
1	3



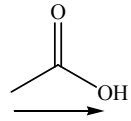
a. initial carbocation
b. after rearrangement



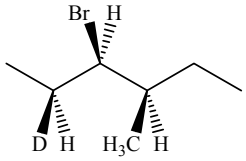
	S_N1	E1
a.	2	6
b.	2	5

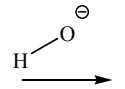


	S_N1	E1
a.	2	6
b.	2	5

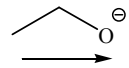


	S_N1	E1
a.	2	6
b.	2	5

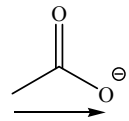




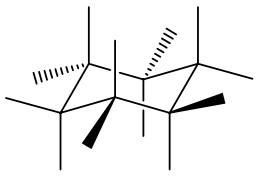
S_N2	E2
1	3



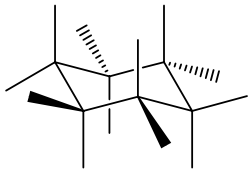
S_N2	E2
1	3



S_N2	E2
1	3



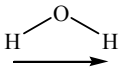
chair 1



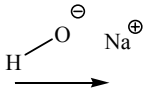
chair 2

Only consider carbocation rearrangements that immediately go to a more stable carbocation (not equally stable carbocations = too many possibilities)

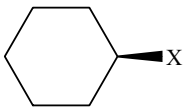
condition 1



condition 2

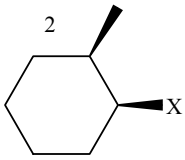


1



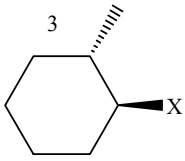
S_N1	E1	S_N2	E2
1	1	1	1

2



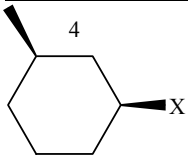
S_N1	E1	S_N2	E2
a. 2	2	1	2
b. 1	2		

3



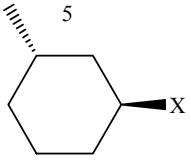
S_N1	E1	S_N2	E2
a. 2	2	0	1
b. 1	2		

4



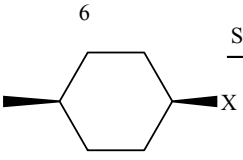
S_N1	E1	S_N2	E2
2	2	1	2

5



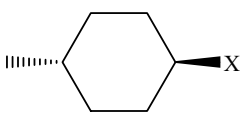
S_N1	E1	S_N2	E2
2	2	1	2

6



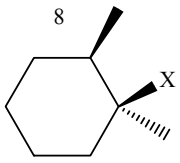
S_N1	E1	S_N2	E2
2	2	1	2

7



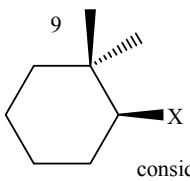
S_N1	E1	S_N2	E2
2	2	1	2

8



S_N1	E1	S_N2	E2
2	3	0	3

9

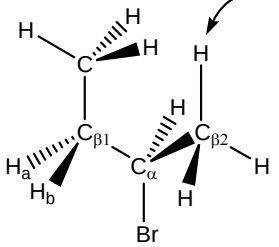


S_N1	E1	S_N2	E2
a. 2	1	0	1
b. 4	5		
c. 1	2		
d. 1	2		

consider any 3° R^+ possibility and consider stereoisomers

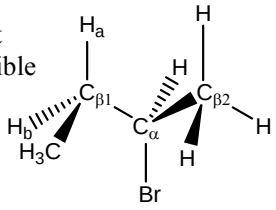
When methyl on $C_\beta 1$ is anti to C-Br, no S_N2 is possible and no E2 is possible from $C_\beta 1$.

Rotation of C_α-$C_{\beta 1}$ brings H_a or H_b anti to C-Br, which allows S_N2 and two different E2 possibilities: H_a (Z) and H_b (E). Since $C_{\beta 2}$ is a simple methyl, there is no $C_{\beta 2}$ substituent to inhibit either of these reactions.



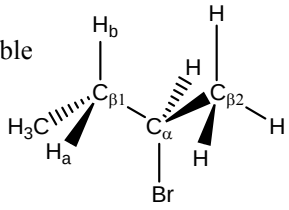
No S_N2 possible and no E2 from $C_{\beta 1}$, but E2 from $C_{\beta 2}$ (1-butene) is possible.

full rotation at C_α-C_β is possible in chain



S_N2 possible
E2 from $C_{\beta 1}$ (2Z- butene)
E2 from $C_{\beta 2}$ (1-butene)

full rotation at C_α-C_β is possible in chain



S_N2 possible
E2 from $C_{\beta 1}$ (2E- butene)
E2 from $C_{\beta 2}$ (1-butene)

alkene stabilities ⇒ tetrasubstituted > trisubstituted > trans-disubstituted > gem-disubstituted ≈ cis-disubstituted > monosubstituted

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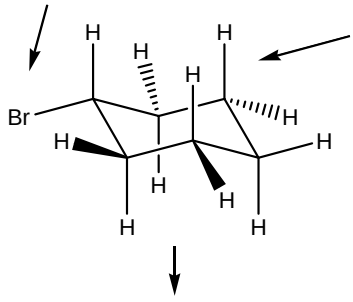
Use these ideas to understand cyclohexane reactivity.

equatorial leaving group



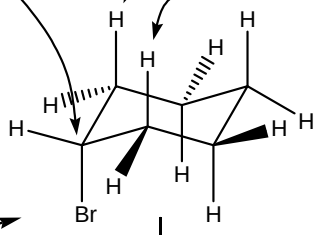
No S_N2 or E2 when "X" is in equatorial position.

No S_N2 is possible (1,3 diaxial positions block approach of nucleophile), and no E2 is possible because ring carbons are anti.

⇌ only partial rotation is possible in ring

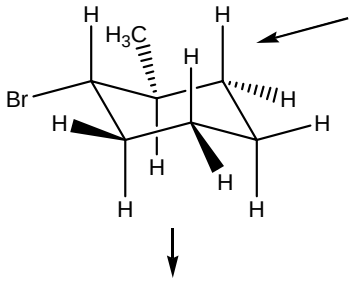
S_N2 possible if C_α is not tertiary and there is no anti C_β "R" group.

E2 possible with anti C_β-H.



axial leaving group

Both S_N2 and E2 are possible in this conformation with leaving group in axial position.



No S_N2 or E2 when "X" is in equatorial position.

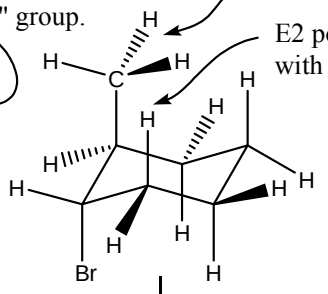
No S_N2 is possible (1,3 diaxial positions block approach of nucleophile), and no E2 is possible because ring carbons are anti.

⇌ only partial rotation is possible in ring

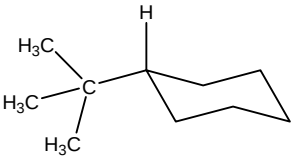
No S_N2 possible if there is an anti C_β "R" group.

No E2 possible, no anti C_β-H.

E2 possible with anti C_β-H.



Only E2 is possible in this conformation. Leaving group is in axial position.

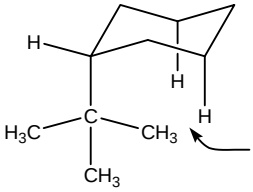


t-butyl substituent locks in chair conformation with equatorial t-butyl

Cyclohexane structures have two chair conformations possible.

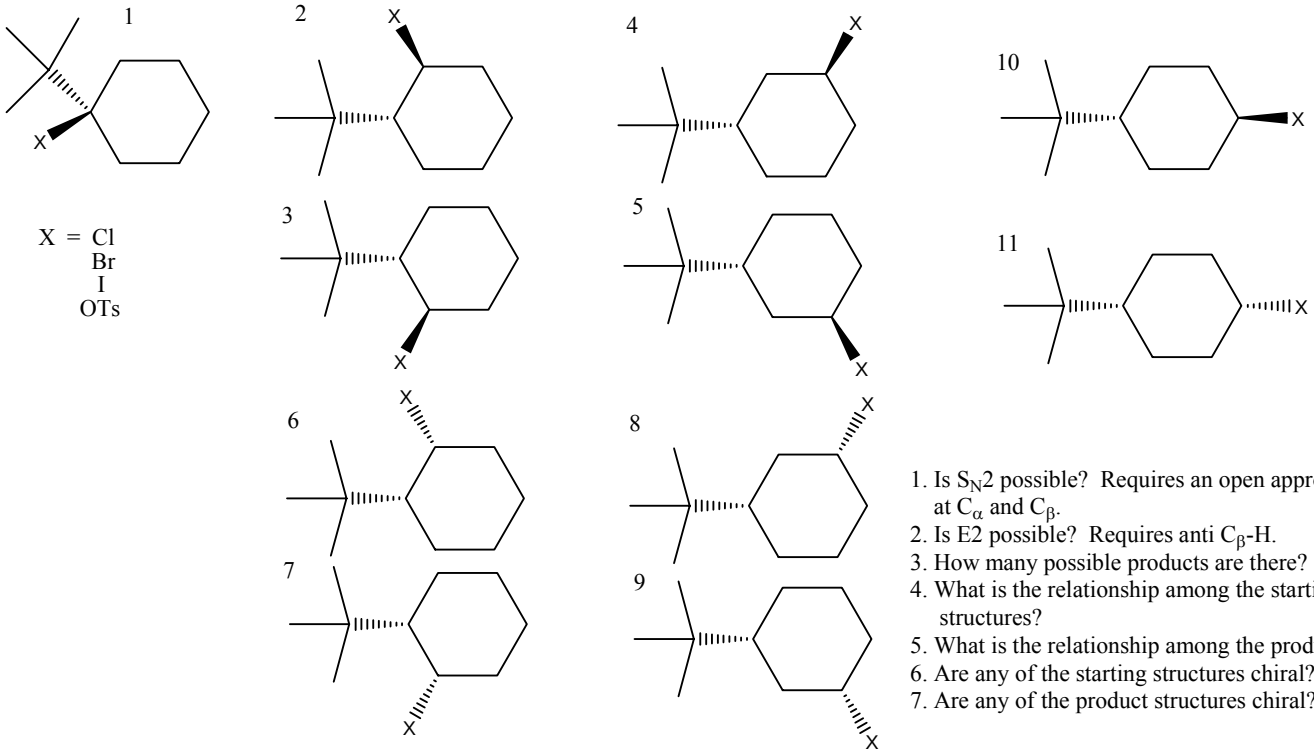
$\rightleftharpoons$

$K_{eq} \approx \frac{1}{9{,}999}$



severe steric repulsion

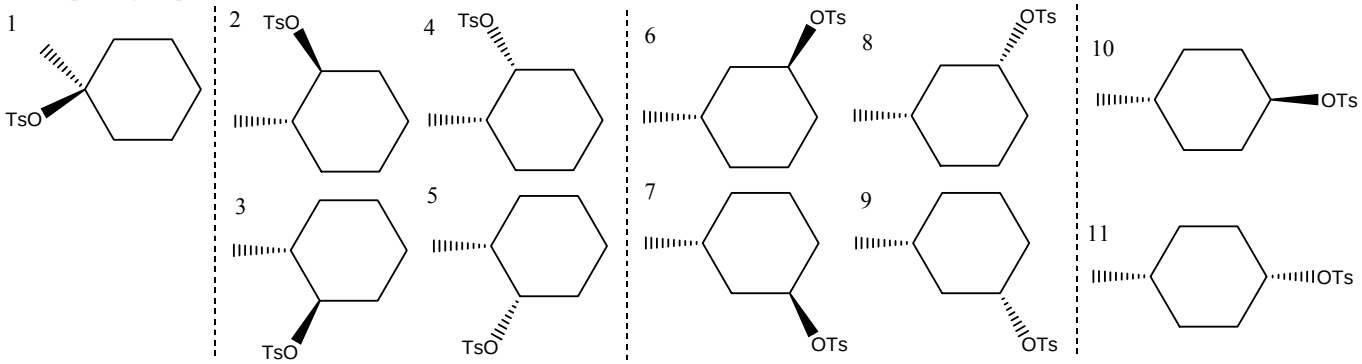
Examples - group A



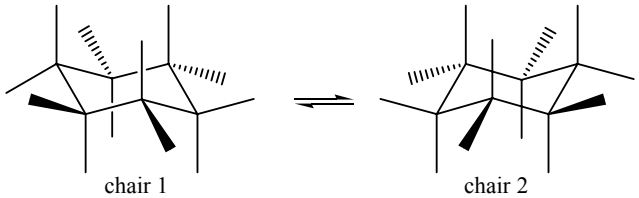
X = Cl
Br
I
OTs

1. Is S_N2 possible? Requires an open approach at C_α and C_β.
2. Is E2 possible? Requires anti C_β-H.
3. How many possible products are there?
4. What is the relationship among the starting structures?
5. What is the relationship among the products?
6. Are any of the starting structures chiral?
7. Are any of the product structures chiral?

Examples - group B



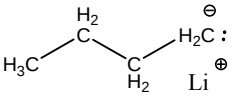
1. Which conformation is reactive?
2. Is S_N2 possible? Requires an open approach at C_α and C_β.
3. Is E2 possible? Requires anti C_β-H.
4. How many possible products are there?
5. What is the relationship among the starting structures?
6. What is the relationship among the products?
7. Are any of the starting structures chiral?
8. Are any of the product structures chiral?



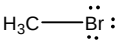
chair 1 $\rightleftharpoons$ chair 2

strong base/nucleophile conditions (E^+ = electrophile, Nu: = nucleophile)

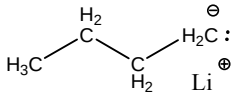
n-butyl lithium (powerful nucleophile at epoxides and carbonyls (C=O), and the "most powerful base" at other times)



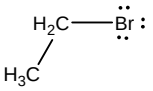
nucleophile = ?
electrophile = ?



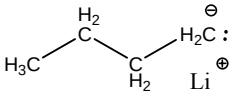
Should be S_N2, but does not work well. Too many side reactions.



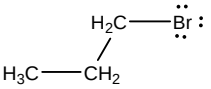
nucleophile = ?
electrophile = ?



Should be S_N2, but does not work well. Too many side reactions.



nucleophile = ?
electrophile = ?



Should be S_N2, but does not work well. Too many side reactions.
