Chem 2010
Midterm #2
Fall, 2018
Beauchamp

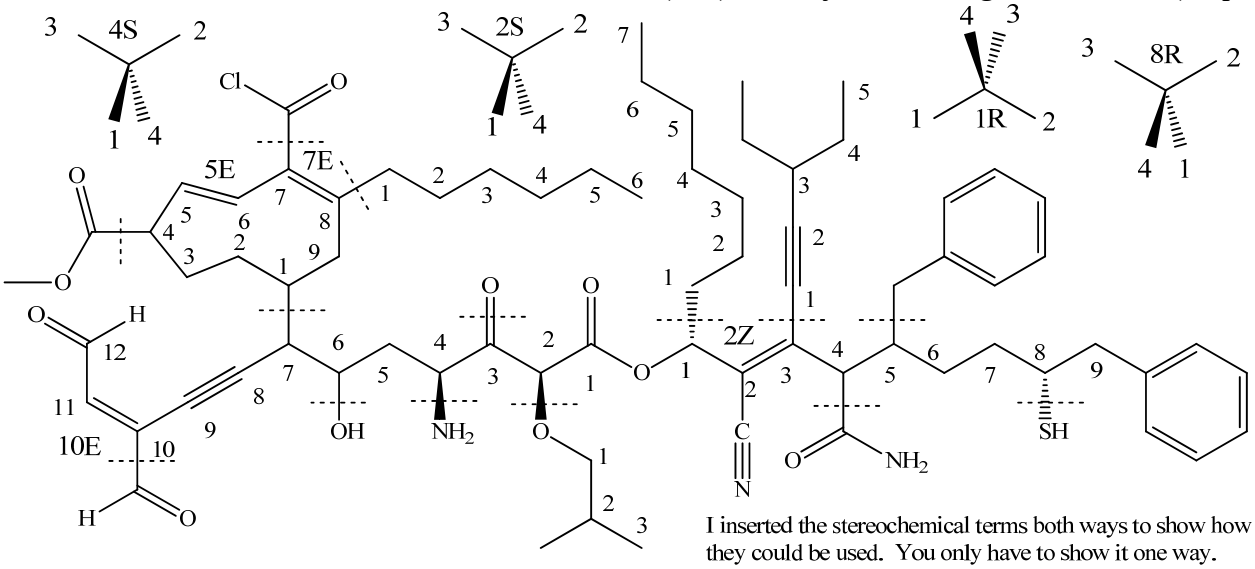
Name _____**KEY**_____
(Print your name legibly)

Problem	Points	Credit
1. Nomenclature (one structure)	30	
2. Explain relative stabilities based on logic arguments of organic chemistry	20	
3. Chair conformations or Chain conformations or Stereochemistry or 2D/3D structures, hybridization	25	
4 Acid/base equations, draw mechanism details, estimate K_{eq}, explain answer	24	
5. S_N and E mechanisms, including stereochemical details	40	
6. Predict products (20)	30	
7.Propose short syntheses (2)	30	
8. Carbocation rearrangement	15	
9. Free Radicals, Predict products provide mechanism	30	
Total	244	

This is a long exam. It has been designed so that no one question will make or break you. The best strategy is to work steadily, starting with those problems you understand best. Make sure you show all of your work. Draw in any lone pairs of electrons, formal charge and curved arrows to show electron movement in mechanism and explanation problems. If resonance is part of an answer, draw the best resonance structure, plus at least one additional resonance structure to show that resonance is present. Only write answers in the space available. Do your best to show me what you know in the time available.

Your mission in life is not merely to survive, but to thrive; and to do so with some passion, some compassion, some humor and some style. Maya Angelou

1. Provide an acceptable name for the following structure. Indicate the absolute configuration of any chiral centers shown in three dimensional form (R/S) and any E/Z stereogenic centers. (30 pts)



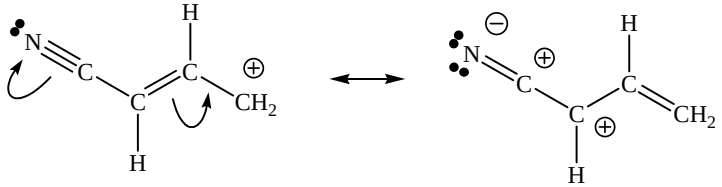
I inserted the stereochemical terms both ways to show how they could be used. You only have to show it one way.

(1R,2Z,8R)-1R-heptyl-2-cyano-3-(3-ethylpent-1-ynyl)-4-amido-5-benzyl-8R-mercapto-9-phenylnon-2Z-enyl

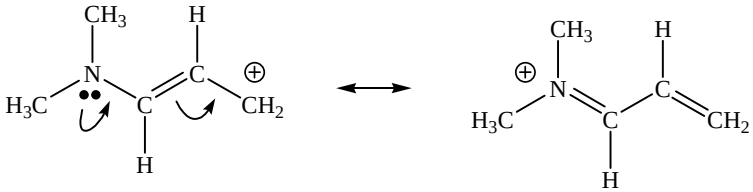
(2S,4S,10E)-2S-(2-methylpropoxy)-3,12-dioxo-4S-amino-6-hydroxy-7-(4-methoxycarbonyl-7-chlorocarbonyl-

8-hexylcyclonona-5E,7E-dienyl)-10-formyldodec-10E-en-8-ynoate

2. a. What is the most stable cation? Explain your reasoning, using structures, if necessary. Include curved arrows, formal charge and lone pairs. Hint: Consider the resonance of a C≡N group and a lone pair of electrons. (10 pts)

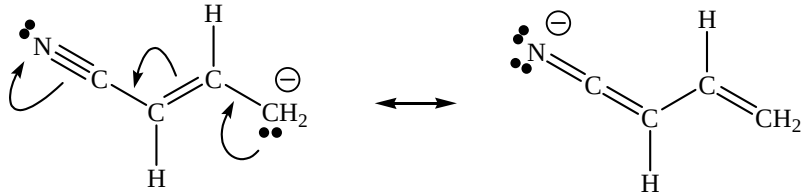


The first example is very destatilizing. Two types of resonance are shown, the resonance of a nitrile group and the resonance of an allyl carbocation. This places 2 cation sites next to one another which would be highly repulsive and destabilizing.

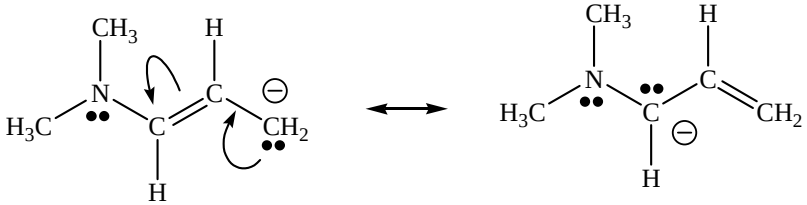


The second example is very stabilizing. The nitrogen lone pair can share its electron density with the carbocation site, making an additional bond and completing the octet of the carbocation carbon. This is very good resonance.

b. What is the most stable anion? Explain your reasoning, using structures, if necessary. Include lone pairs, formal charge and lone pairs. Hint: Consider the resonance of a C≡N group and a lone pair of electrons. (10 pts)



The first example is more stable because resonance puts the negatve charge on more electronegative nitrogen.



The second example is less stable because anion resonance puts the negatve charge next to another lone pair of electrons which destabilizes it due to greater electron/electron repulsion. The negative charge cannot be pushed onto the nitrogen atom because it is sp^3 and has full octets.

3. a. Use Newman projections of the C3→C4 bond of 4-phenyl-2-methylhexane to show the lowest energy and highest energy conformations and calculate the relative energies**. Show the most stable conformation first**. Calculate a $K_{equilibrium}$ between the least stable and most stable conformations. Assume R = 2 cal/(mol-K) and T = 300 K. (20 pts)

Approximate Eclipsing Energy Values (kcal/mole)
Some were estimated by me.

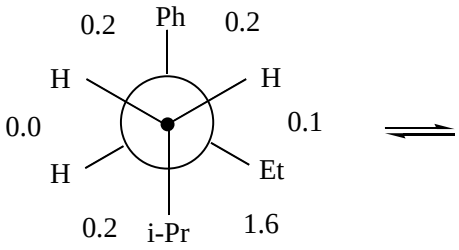
	H	Me	Et	i-Pr	t-Bu	Ph	Br
H	1.0	1.4	1.5	1.6	3.0	1.7	1.6
Me	1.4	2.5	2.7	3.0	8.5	3.3	2.8
Et	1.5	2.7	3.3	4.0	10.0	3.8	3.1
i-Pr	1.6	3.0	4.0	7.8	13.0	8.1	3.6
t-Bu	3.0	8.5	10.0	13.0	23.0	13.5	9.1
Ph	1.7	3.3	3.8	8.1	13.5	8.3	4.2
Br	1.6	2.8	3.1	3.6	9.1	4.2	3.0

Approximate Gauche Energy Values (kcal/mole)
Some were estimated by me.

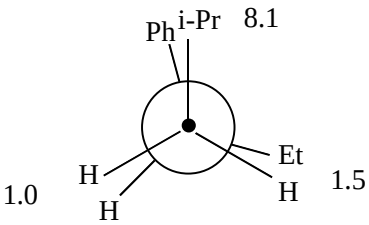
	H	Me	Et	i-Pr	t-Bu	Ph	Br
H	0	0	0.1	0.2	0.5	0.2	0.1
Me	0	0.8	0.9	1.1	2.7	1.4	1.0
Et	0.1	0.9	1.1	1.6	3.0	1.7	1.2
i-Pr	0.2	1.1	1.6	2.4	3.5	2.1	1.6
t-Bu	0.5	2.7	3.0	3.5	7.2	3.9	3.3
Ph	0.2	1.4	1.7	2.1	3.9	2.7	1.9
Br	0.1	1.0	1.2	1.6	3.3	1.9	1.1

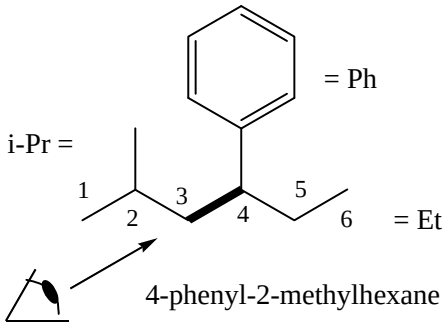
$K_{eq} = 10^{\frac{-\Delta H}{2.3RT}}$

most stable Newman Conformation



least stable Newman conformation





4-phenyl-2-methylhexane

0.2
0.1
1.6
0.2
0.0
0.2
2.3

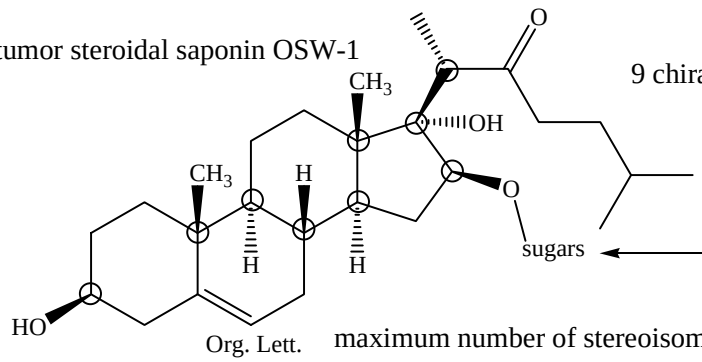
Δ = 10.6 - 2.3 = 8.3 kcal/mole

8.1
1.5
1.0
10.6

$K_{eq} = 10^{\frac{-8,300}{1400}} = 10^{-5.9} = 1.3 \times 10^{-6} \approx 1 / 800,000$

b. Derivatives of the antitumor steroidal saponin were recently prepared. The are highly potent and selective anticancer compounds. They inhibit Na^{+}/Ca^{+2} exchange leading to higher Ca^{+2} in the cytosol and mitochrondria causing cell death (apotosis) (Org. Lett. ASAP, 2014). Circle all chiral centers and any other stereogenic features in the partial structure below, and calculate the maximum number of stereoisomers possible. (5 pts)

antitumor steroidal saponin OSW-1



9 chiral centers

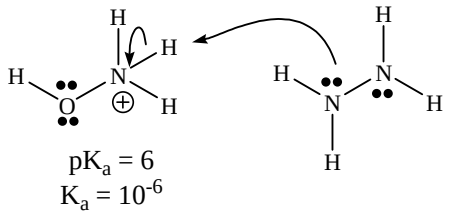
There are even more chiral centers in the sugar(s) here, but are not shown.

Org. Lett.

maximum number of stereoisomers = 2^9 possible stereoisomers = 512

4. The reactant acids and bases are given in two acid/base equations below. Also given with each equation are two pK_a values. Complete each acid/base equation including any formal charge, lone pairs and curved arrows to show how the reactants react. Use the pK_a values to calculate a K_{eq} for each reaction. Provide a very brief explanation for which side is favored. (24 pts)

a.

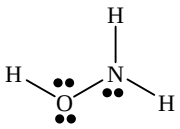


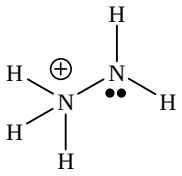
$pK_a = 6$
$K_a = 10^{-6}$

This is the stronger acid because of the inductive withdrawal of the oxygen atom. This nitrogen is less willing to donate its electrons and is therefore a weaker base, which makes its conjugate acid the stronger acid.

pK_a values = 6 and 8

equilibrium favors the right side



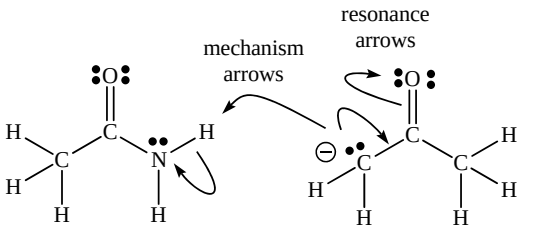


$pK_a = 8$
$K_a = 10^{-8}$

This is the weaker acid because of the inductive withdrawal of nitrogen is less than oxygen. This nitrogen is more willing to share its electrons and is therefore a stronger base, which makes its conjugate acid the weaker acid.

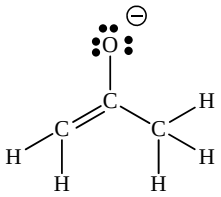
$$K_{eq} = \frac{K_a\,(HONH_3^+)}{K_a\,(H_2NNH_3^+)} = \frac{10^{-6}}{10^{-8}} = 10^{+2}$$

b.



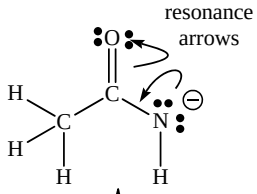
$pK_a = 15$
$K_a = 10^{-15}$

resonance A

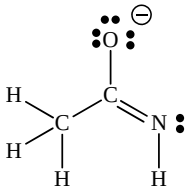


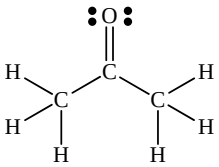
pK_a values = 15 and 20

equilibrium favors the right side



resonance B





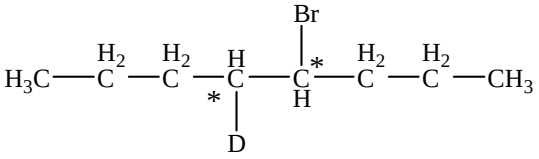
$pK_a = 20$
$K_a = 10^{-20}$

$$K_{eq} = \frac{K_a\,(A)}{K_a\,(B)} = \frac{10^{-15}}{10^{-20}} = 10^{+5}$$

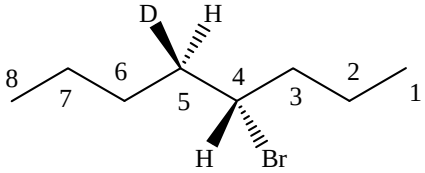
Resonance in the amide anion is much better than the ketone anion resonance because the more electronegative nitrogen atom (than carbon atom) helps the oxygen atom to carry the negative charge. Since the amide conjugate base is much more stable, its acid is much stronger than the ketone acid and the equilibrium will lie far to the right. Acid/base equilibria always lie to the side opposite of the stonger acid and stronger base (right in this reaction).

5. Use 4S-bromo-5R-deuteriooctane to provide a simple, arrow-pushing mechanism for each of the following reaction conditions (show curved arrows, lone pairs & formal charge). Fill in the necessary details to clearly indicate any stereochemical features and/or conformational requirements. If reactants are not drawn in the proper orientation to show how the reaction must proceed, then redraw them in a more informative way that shows this. **Do not** consider carbocation rearrangement possibilities. (40 pts)

a. Draw a 2D structure and then a 3D structure of the reacting molecule. A 3D structure will be provided for the cost of the points of this part. (3 pts)

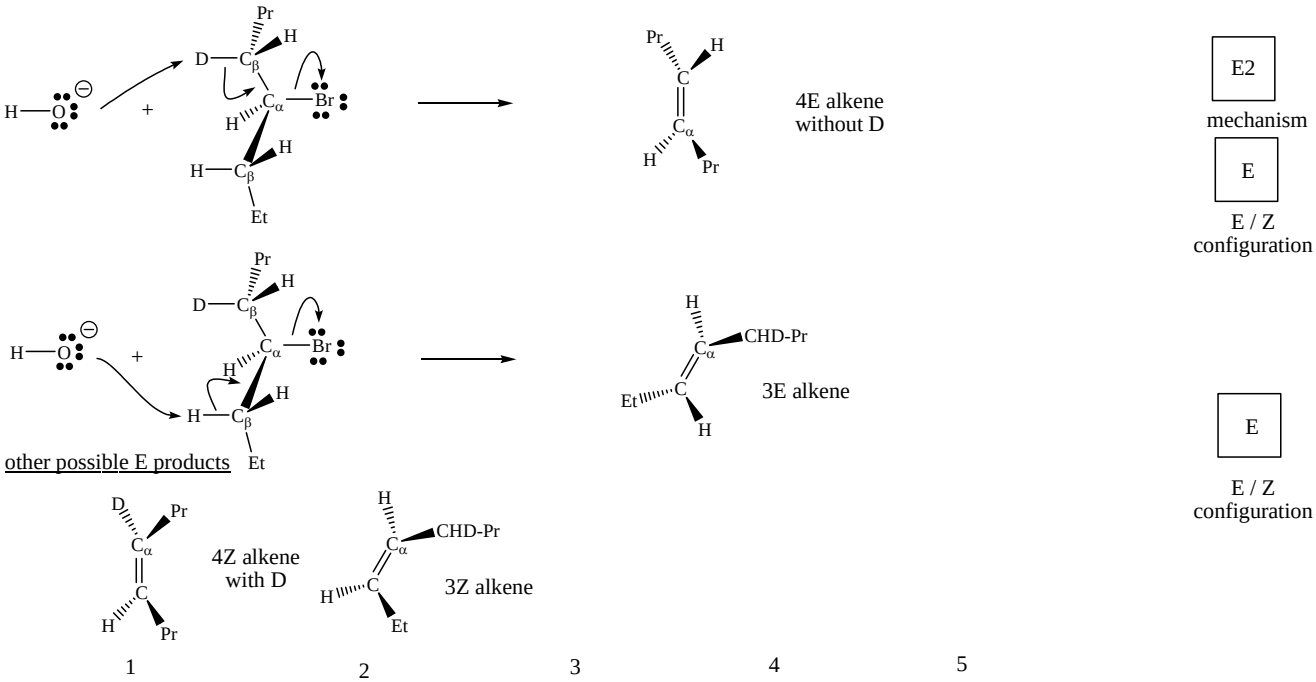


2D structure
* = chiral center

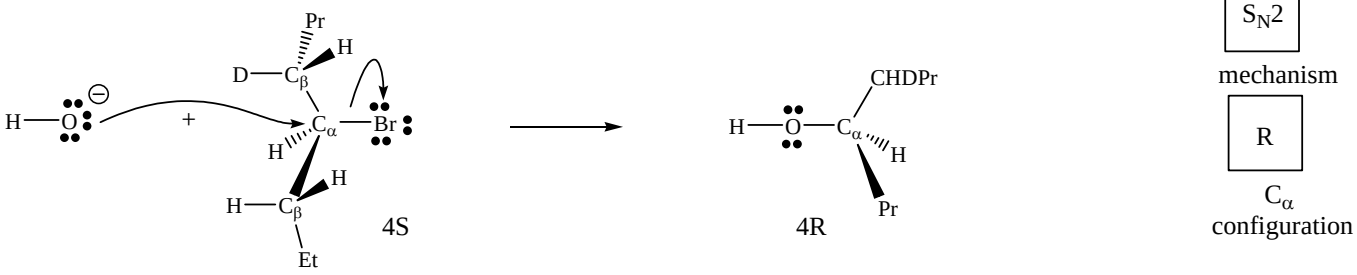


3D structure of (4S,5R)-5-deuterio-4-bromooctane

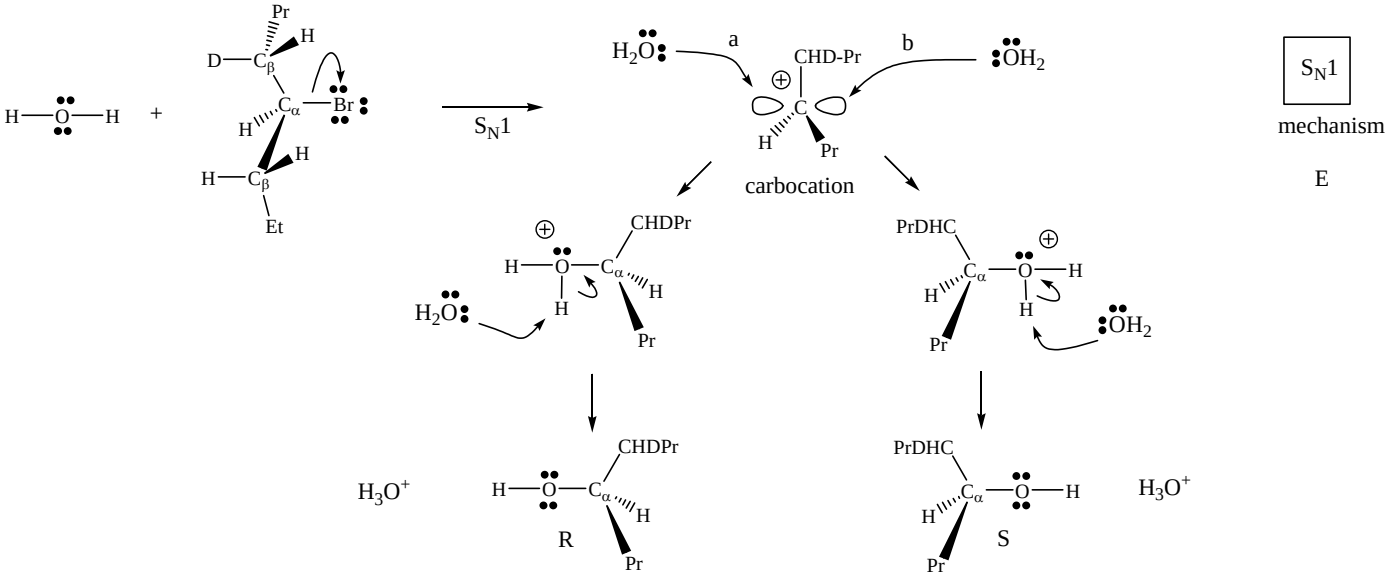
b. Show a mechanism for each C_β position and simply draw all other possible E reaction products (what kind?). Indicate if E, Z or neither. You can abbreviate common branch names if they are not part of your mechanism There may or may not be fewer products than there are numbers. (10 pts)



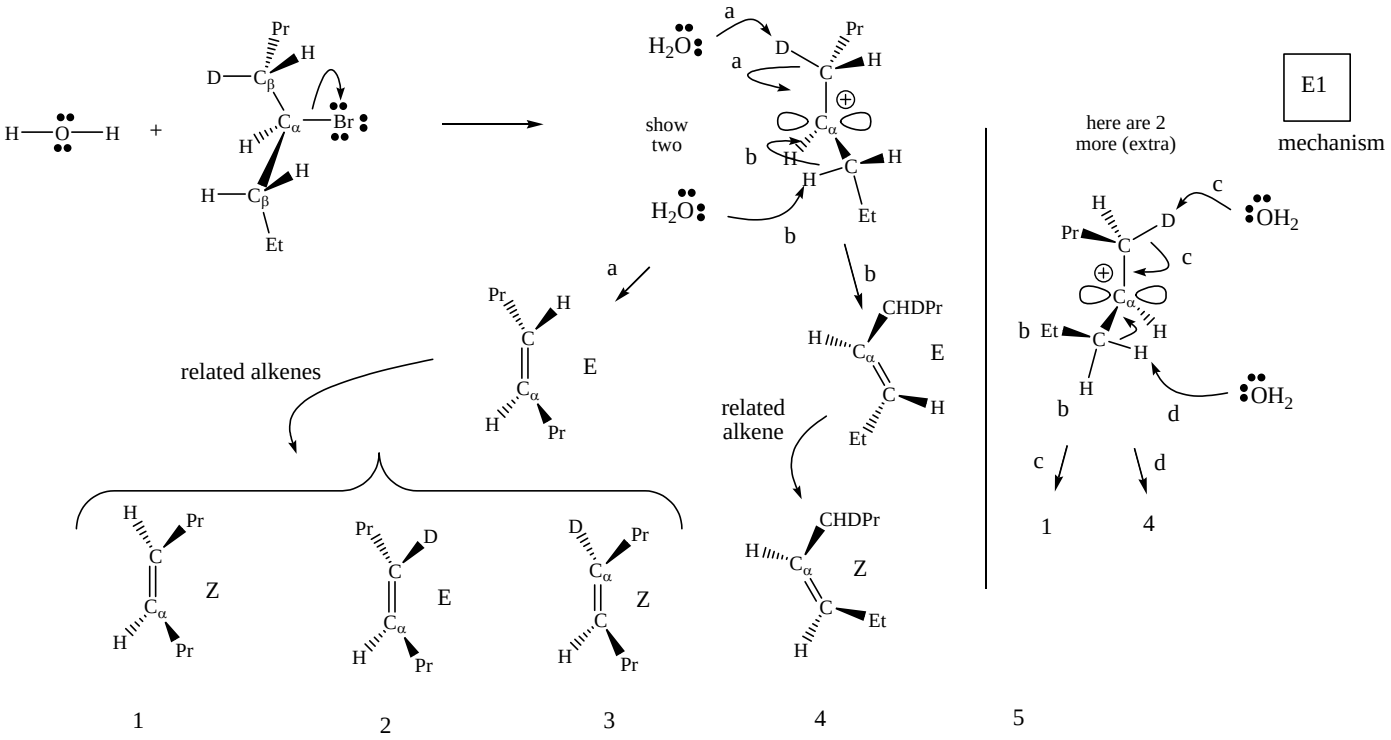
c. Show the S_N reaction (what kind?), indicate the absolute configuration(s) of the C_α center in the product. (6 pts)



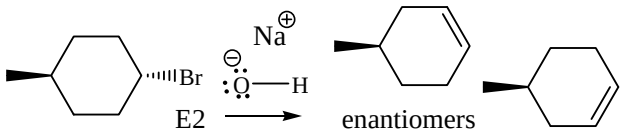
d. Show all steps of the S_N reaction (what kind?). You can use one intermediate to show all possible S_N possibilities. Indicate the absolute configuration(s) of the C_α center in the product. You can abbreviate common branch names if they are not part of your mechanism (9 pts)

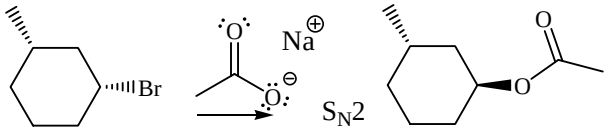


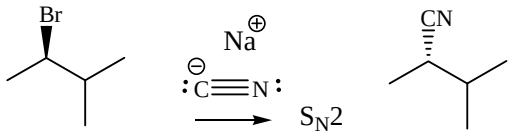
e. Show a mechanism for two E products and simply draw all other possible E reaction products (you can use the same intermediate for your two mechanisms). Indicate if E, Z or neither. There may or may not be fewer products than numbers. (12 pts)

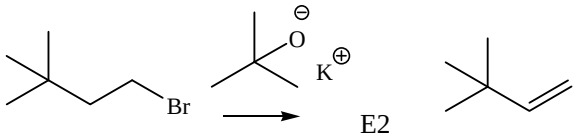


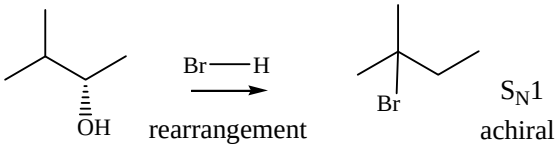
6. Write in the major product and type of reaction for each set of conditions below. Arrow pushing is not required (1.5 each, 30 pts)

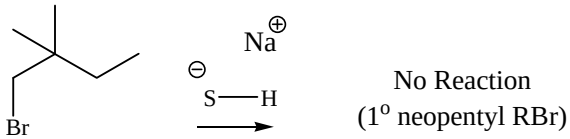
a 

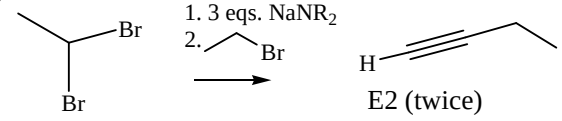
b 

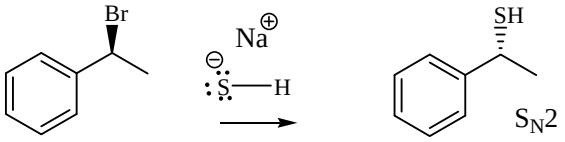
c 

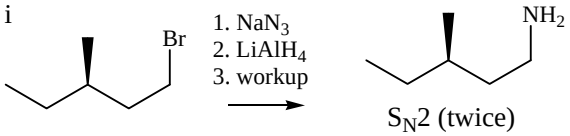
d 

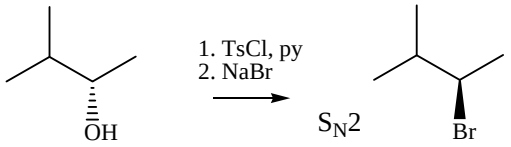
e 

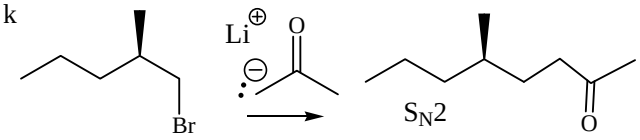
f 

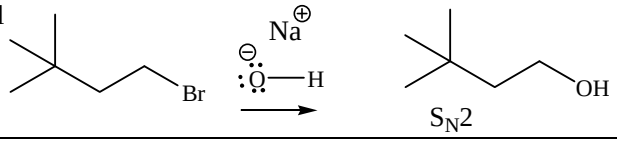
g 

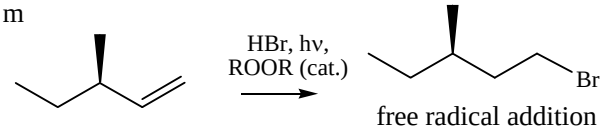
h 

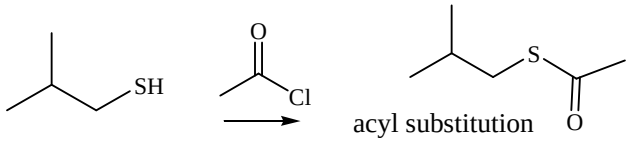
i 

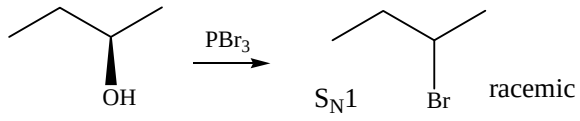
j 

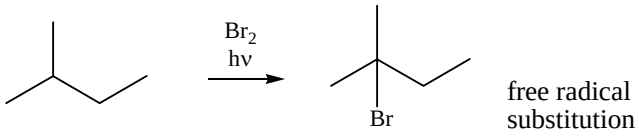
k 

l 

m 

n 

o 

p 

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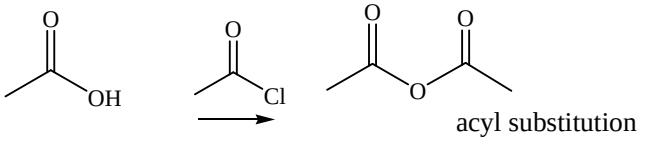
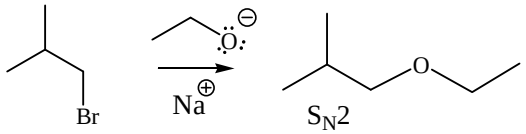
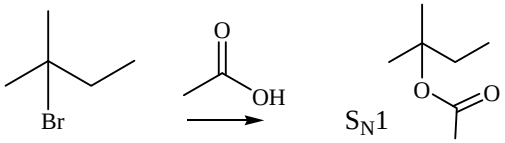
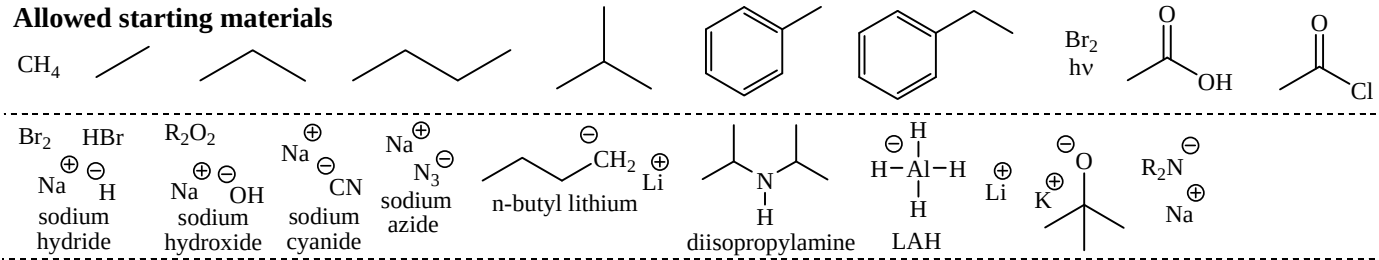
r 

s 

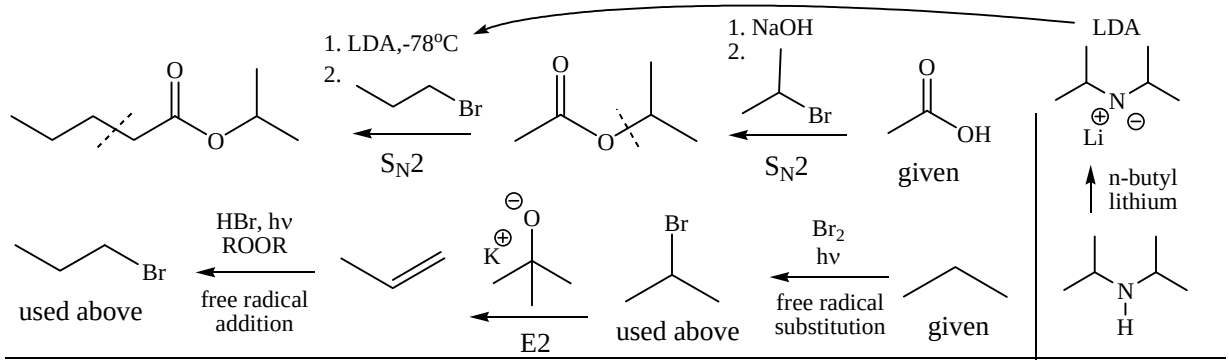
t 

7. Propose a reasonable synthetic sequence to make the given target molecules using the given starting materials. Show each step with an arrow and the necessary reagents to accomplish the indicated transformation. If you make a molecule in one part you can use it in any other part. (30 pts)

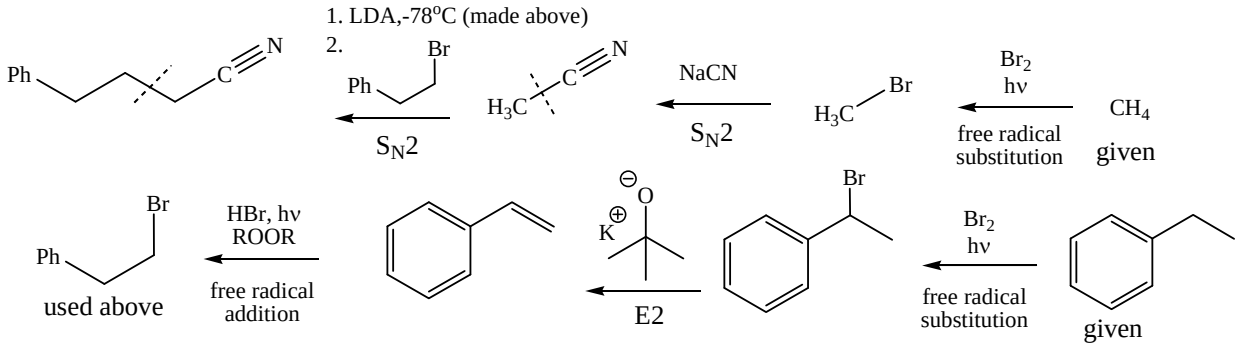
Allowed starting materials



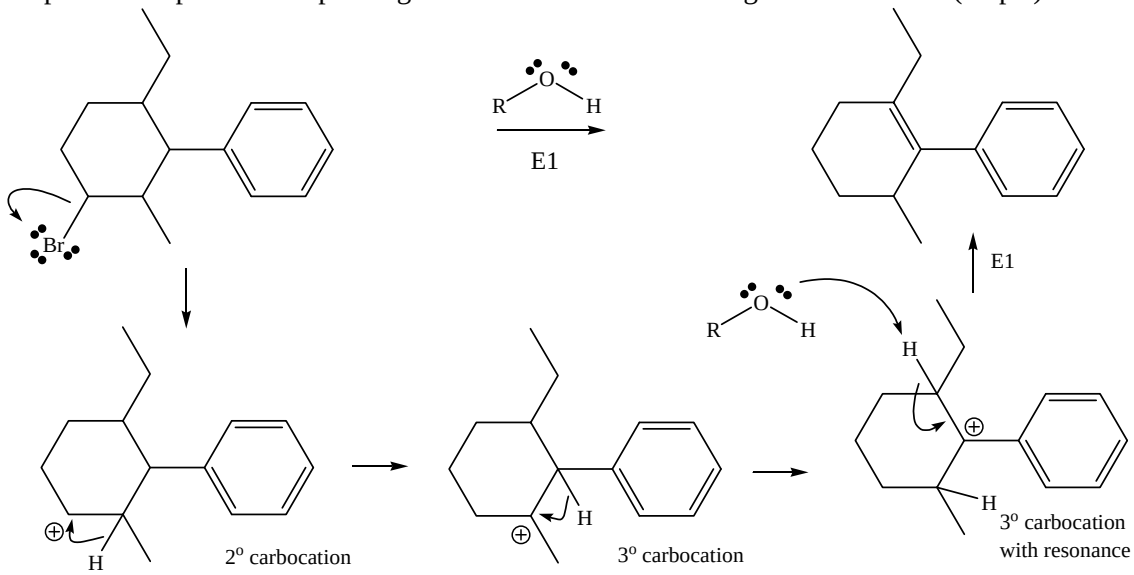
a.



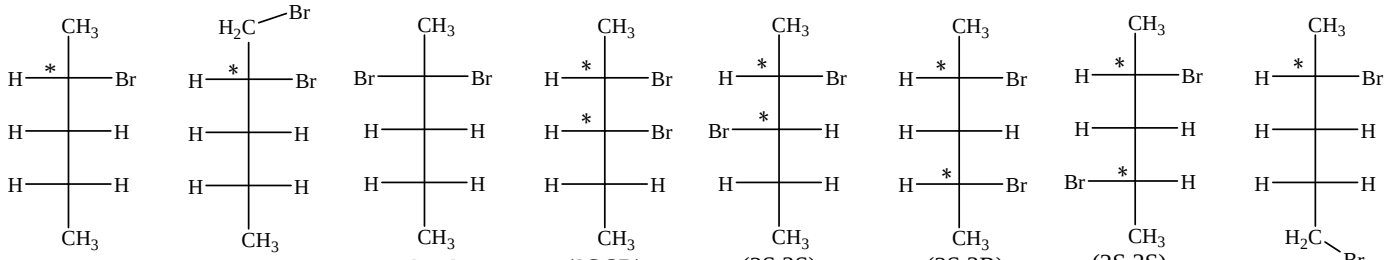
b.



8. Propose a complete arrow-pushing mechanism for the following transformation. (15 pts)



a. How many different types of sp^3 hydrogen atoms are present in 2S-bromopentane? Show all possible products when 2S-bromopentane is brominated with $Br_2/h\nu$? Use Fischer projections. Put a dot by any chiral centers. If stereoisomers form, specify what type of isomerism is present (enantiomers, diastereomers, meso compounds, achiral, etc.). Indicate the approximate relative amounts of each product formed if the relative rates of reaction of a bromine atom with an sp^3 C-H bond are: primary = 1, secondary = 80, tertiary = 1600 and bromine substituted carbon = 2000. (21 pts)



relative amounts = (# H)(rel. reactivity)

A = (3)(1) = 3

C = D = E = F = (1)(80) = 80 each

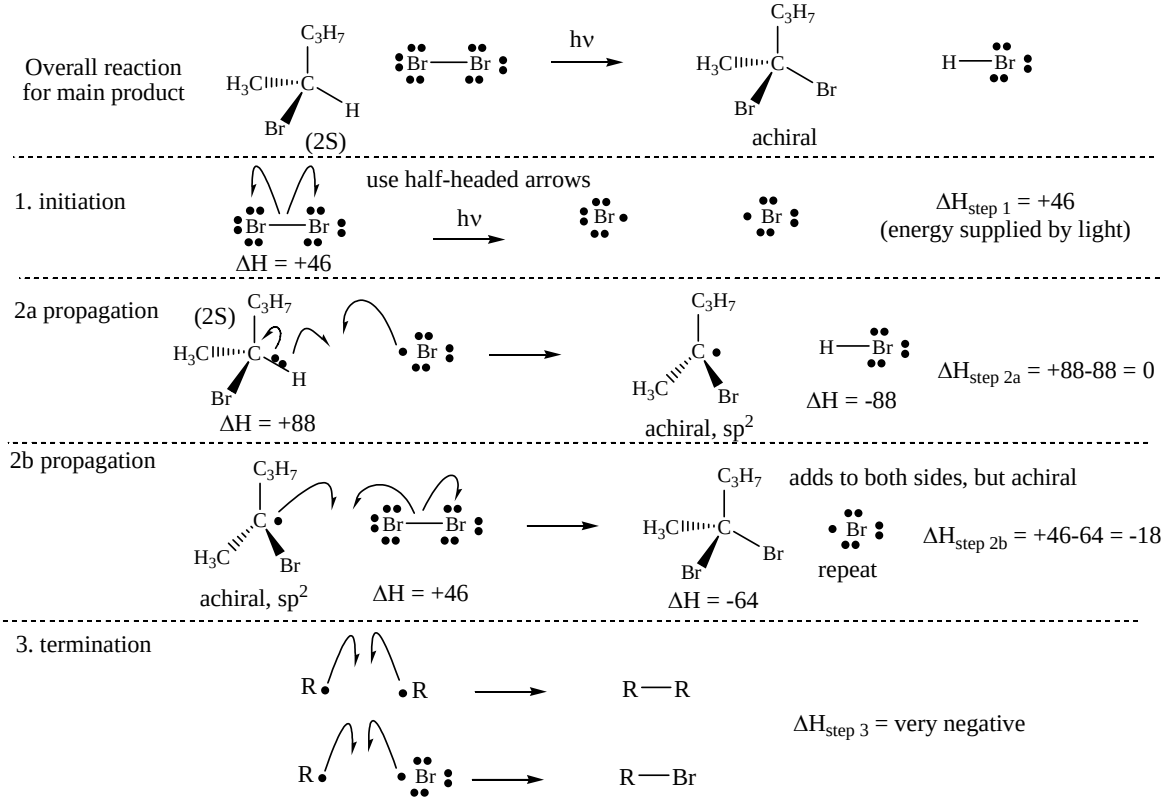
G = (3)(1) = 3

B = (1)(2000) = 2000 = main product

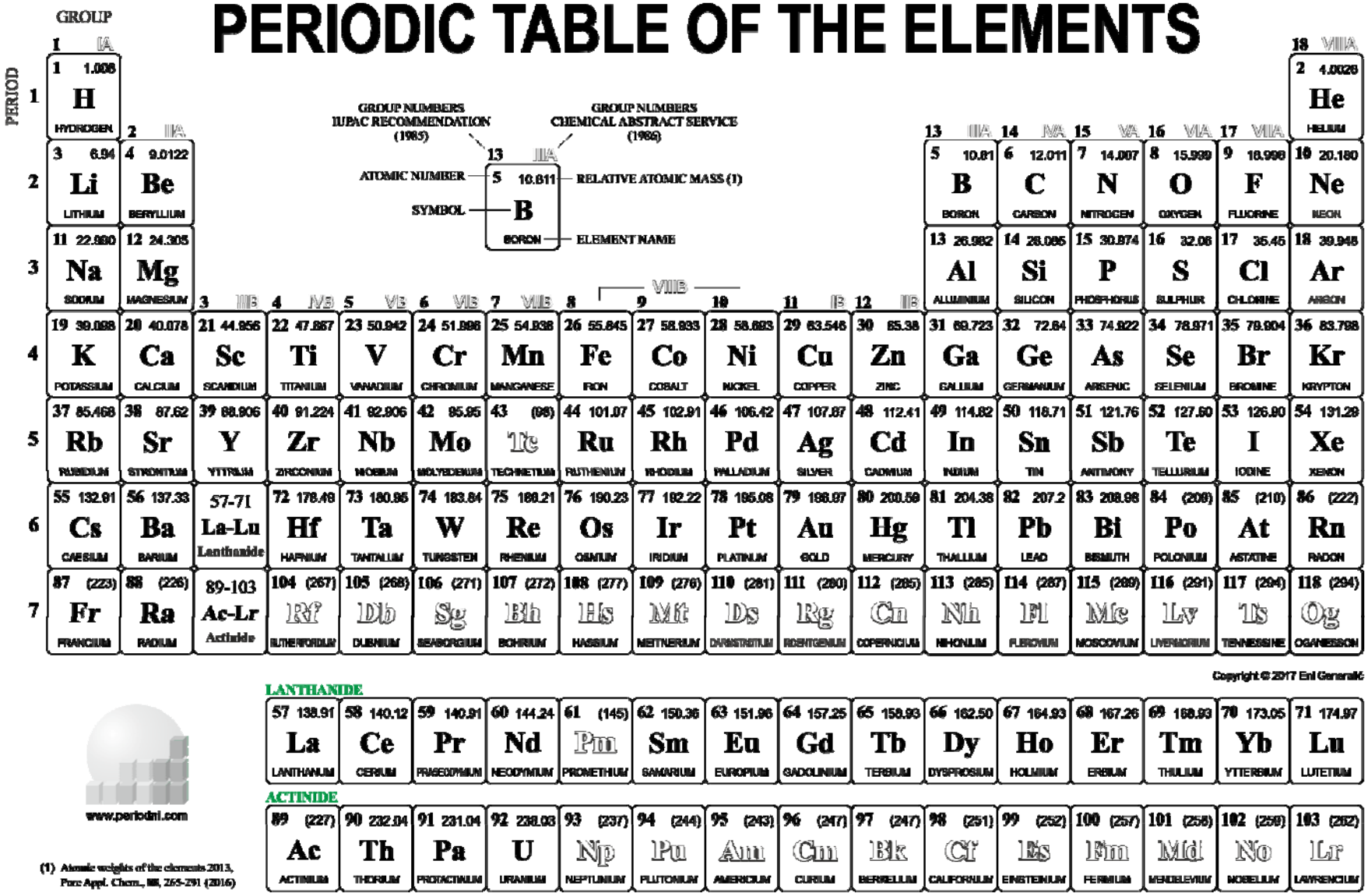
enantiomers = none
diastereomers = (C,D (E,F)
meso = (E)

b. Provide a complete arrow pushing mechanism to explain formation of the major product from the above reaction (show proper curved arrow conventions, lone pairs as two dots and single electrons as one dot). Clearly label each distinct part of the reaction mechanism. Calculate an overall ΔH for each step of your mechanism using the given bond energies. (15 pts)

Br—Br	46
H—Br	88
CH_3-H	105
1° C-H	98
2° C-H	95
3° C-H	92
C_αBr-H	88
CH_3-Br	70
1° C-Br	68
2° C-Br	67
3° C-Br	66
C_αBr-Br	64



It is in your moments of decision that your destiny is shaped. Tony Robbins


PERIODIC TABLE OF THE ELEMENTS
GROUP
PERIOD
GROUP NUMBERS IUPAC RECOMMENDATION (1985)
GROUP NUMBERS CHEMICAL ABSTRACT SERVICE (1986)
ATOMIC NUMBER
SYMBOL
RELATIVE ATOMIC MASS (1)
ELEMENT NAME
VIIB
LANTHANIDE
ACTINIDE
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(1) Atomic weights of the elements 2013, Pure Appl. Chem., 88, 265-291 (2016)