

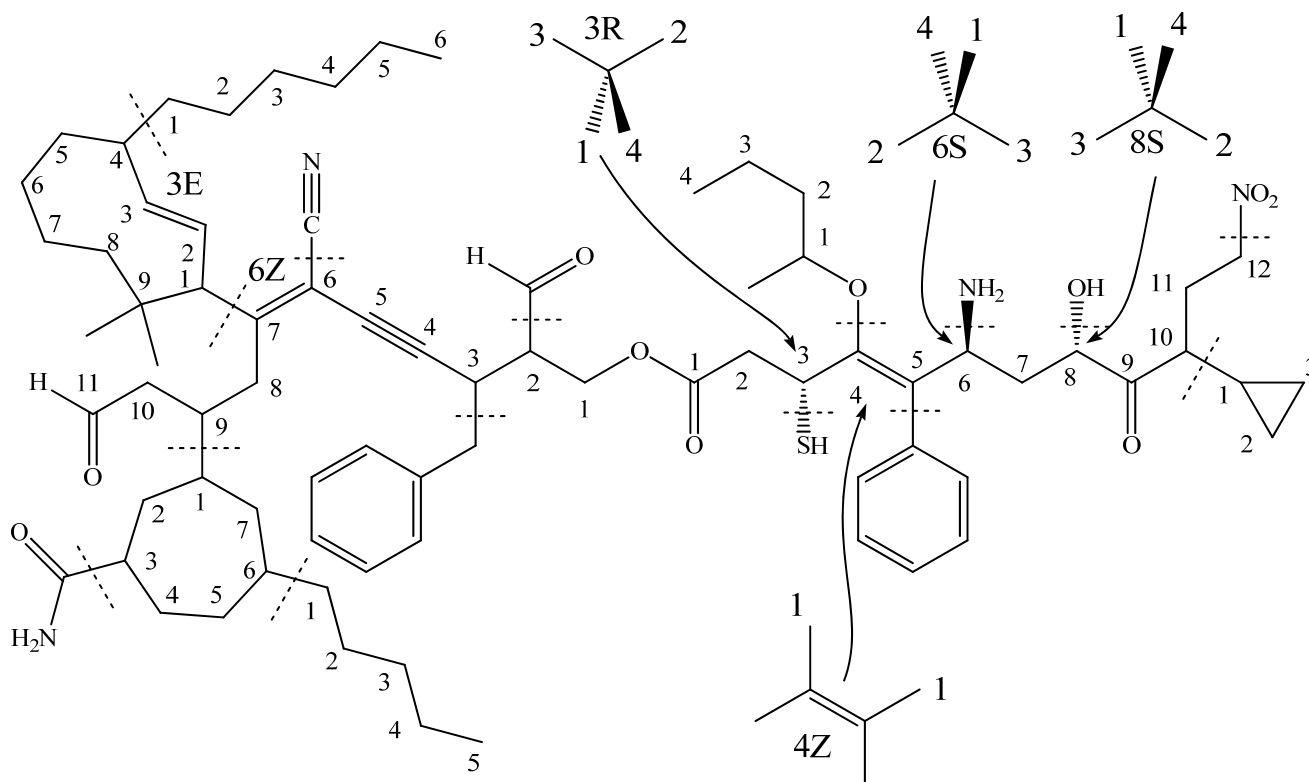
Problems	Points	Credit
1. Functional Group Nomenclature (1 large structure)	30	
2. Lewis Structures, Resonance, Formal Charge	18	
3. Cyclohexane Conformations, 2 substituents, Newman Projections, Relative Energies	30	
4. Newman Projections, Conformational Energies, K_{eq} Calculation	30	
5. Stereochemical Analysis	30	
6. 2D Resonance Structures, 3D Structure, Hybridization, Angles, Shapes	30	
7. Dipole Moments and Inductive versus Resonance Effects	15	
8. Quantitative Acid/Base Equation, Identify Conjugate Acid and Base and Calculate $K_{equilibrium}$, Supply Curved Arrows.	15	
9. Acid / Base Chemistry, Explanation, Curved Arrows, Formal Charge, Qualitative Equilibrium (7)	35	
10. S_N/E 3D Mechanisms, with all of the details, Templates Provided	43	
11. Various Reactions, predict the products (20 reactions)	30	
12. Fill in all mechanistic details, curved arrows, lone pairs, formal charge,	15	
13. S_N/E Mechanism, Carbocation Reactions	15	
14. Free Radical Substitution Problem – Predict Possible Products, How Much, Stereochemistry and Provide a Mechanism For Major Product	30	
Total	361	

Premidterm material = 183
Postmidterm material = 193

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 where appropriate. Do your best to show me what you know in the time available.

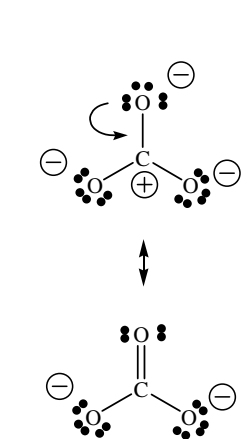
"Change your thoughts and you change your world." – Norman Vincent Peale

1. Provide an acceptable name for the following molecule. Only specify R and S where shown as 3D. (30 pts)

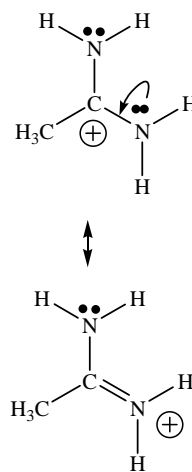
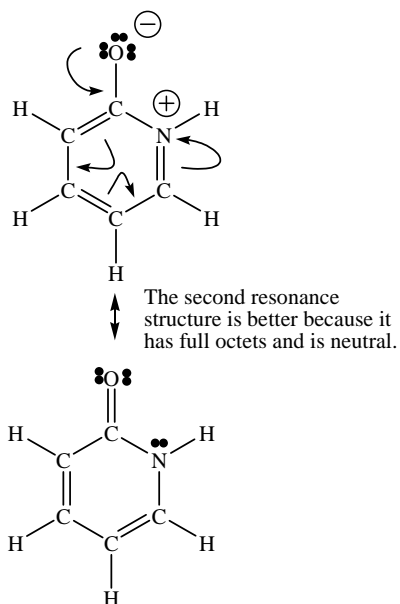


2-formyl-3-benzyl-6-cyano-7-(4-hexyl-9,9-dimethylcyclo-non-2E-enyl)-9-(3-amido-6-pentylcycloheptyl)-11-oxoundec-6Z-en-4-ynyl 3R-mercapto-4-(1-methylbutoxy)-5-phenyl-6S-amino-8S-hydroxy-9-oxo-10-cyclopropyl-12-nitrododec-4Z-enoate

2. Indicate all formal charges present in the following structures. Assume all electrons are shown as lines or dots. If other reasonable resonance structures are possible, draw the best other resonance structure using the proper arrow conventions. Indicate which resonance structure is better or if they are equivalent. (18 pts)

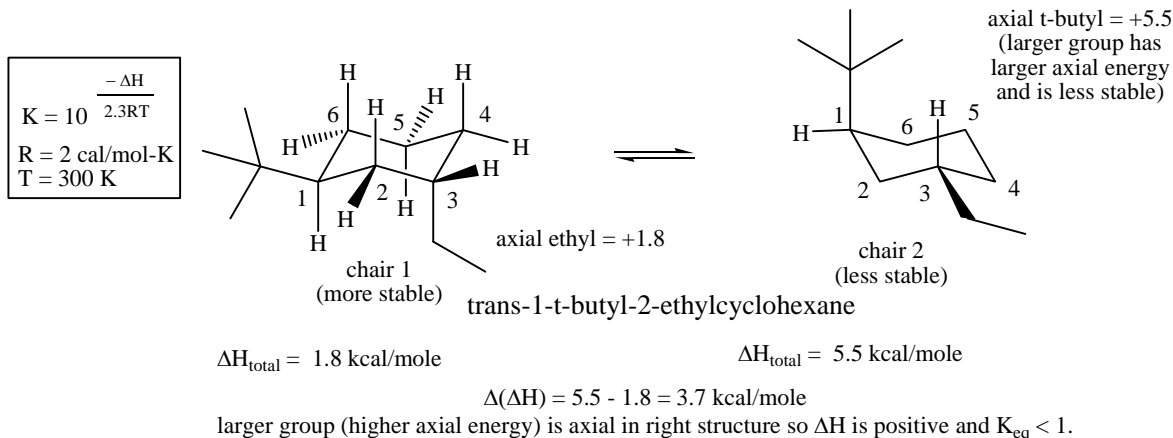


The second resonance structure is better because it has an extra bond and has full octets and there is less charge. There are 2 other equivalent resonance structures.

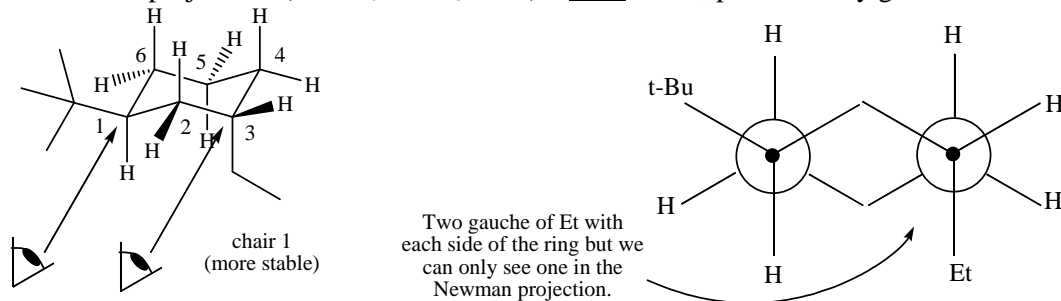


The second resonance structure is better because it has an extra bond and full octets. There is an equivalent resonance structure with + on the other nitrogen.

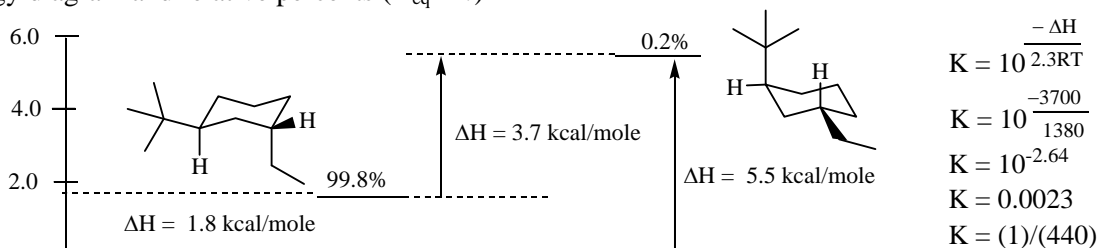
3. Draw all possible chair conformations of trans-1-t-butyl-3-ethylcyclohexane. Make the left most ring carbon C1 and number towards the front. Show all axial and equatorial groups in the first chair. Which conformation is more stable? Provide a reason for your answer. Draw a Newman projections of the most stable conformation using the C₁→C₆ and C₃→C₄ bonds to sight along. Point out any gauche interactions shown in your Newman projection. If the axial energy of a t-butyl group is 5.5 kcal/mole and the axial energy of an ethyl group is 1.8 kcal/mole and a t-butyl/ethyl gauche interaction is 3.0 kcal/mole, what is the ratio of the two conformations at equilibrium? Show your work. Sketch an energy diagram that shows how the energy changes (lower to higher) with the conformational changes and estimate the ratio of the two conformations at equilibrium. (30 pts)



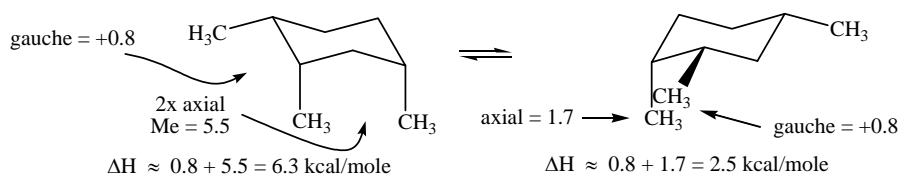
- b. Newman projection (C₁→C₆ and C₃→C₄) – most stable, point out any gauche interactions with the substituent(s)



- c. Energy diagram and relative percents ($K_{\text{eq}} = ?$)



- d. Calculate an approximate ΔH difference between the two conformations. Use that value to estimate a K_{eq} . (Assume $R = 2 \text{ cal/mol-K}$ and $T = 300 \text{ K}$.) Use energy values provided in the box. Show your work.



The energy table is not shown here.

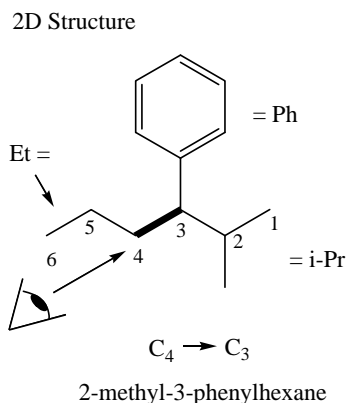
$$\Delta(\Delta H) = 2.5 - 6.3 = -3.8 \text{ kcal/mole}$$

$$K = 10^{\frac{-(-3800)}{1380}} = 10^{+2.75} = 570 / 1$$

4. Use a Newman projection of the C₄→C₃ bond of 2-methyl-3-phenylhexane to **show the most stable conformation first**. Rotate through all of the eclipsed and staggered conformations. Using the energy values provided in the table below, calculate the relative energies of the different conformations. Plot the changes in energy in the graph diagram provided. Calculate a ratio of least stable to most stable based on ΔH values. Hint: Draw a 2D structure first and “bold” the bond viewed in your Newman projection, then decide your line of sight. (25 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



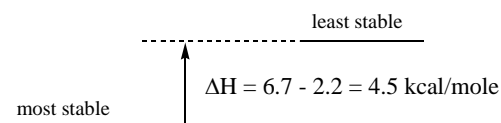
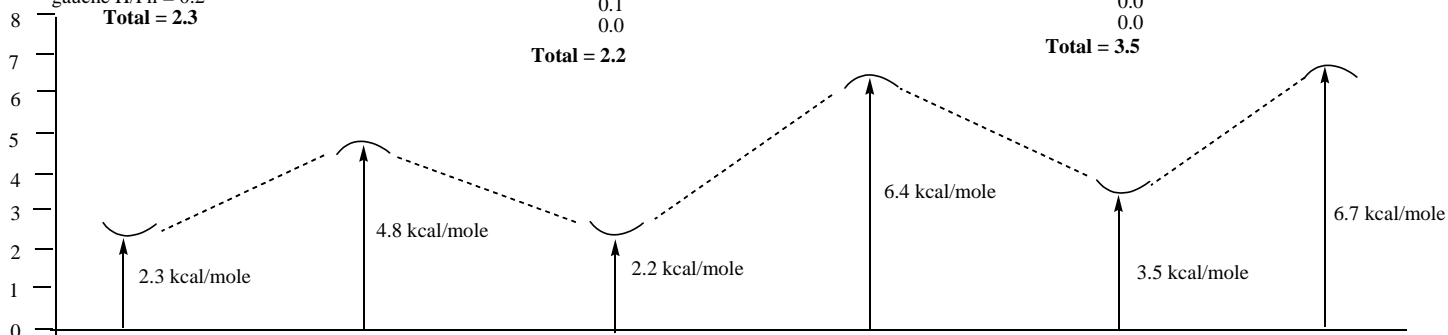
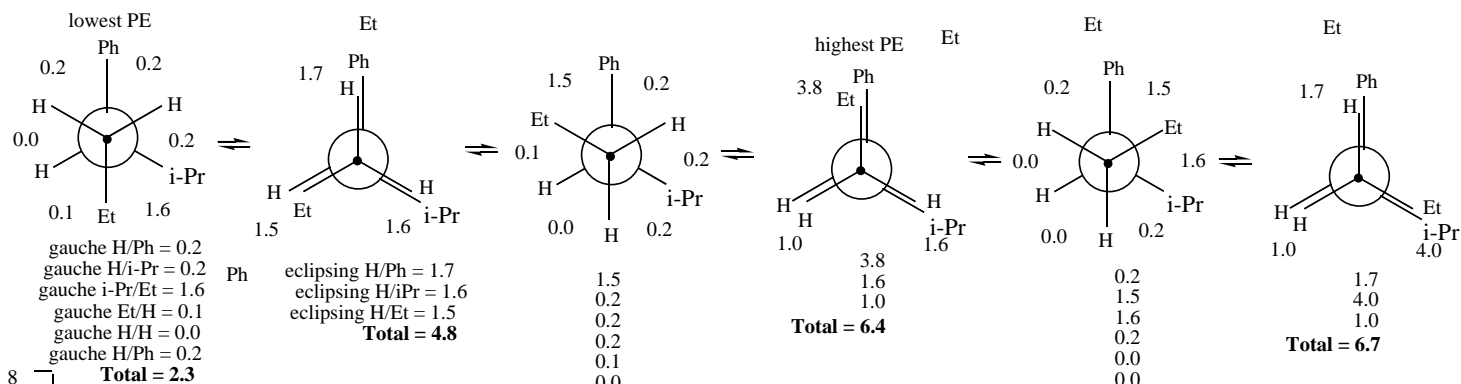
$$\Delta G \approx \Delta H$$

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

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	1.5	1.3
i-Pr	0.2	1.1	1.6	2.0	4.1	2.1	1.6
t-Bu	0.5	2.7	3.0	4.1	8.2	3.9	3.3
Ph	0.2	1.4	1.5	2.1	3.9	2.3	1.9
Br	0.1	1.0	1.3	1.6	3.3	1.9	1.1

Newman projections:

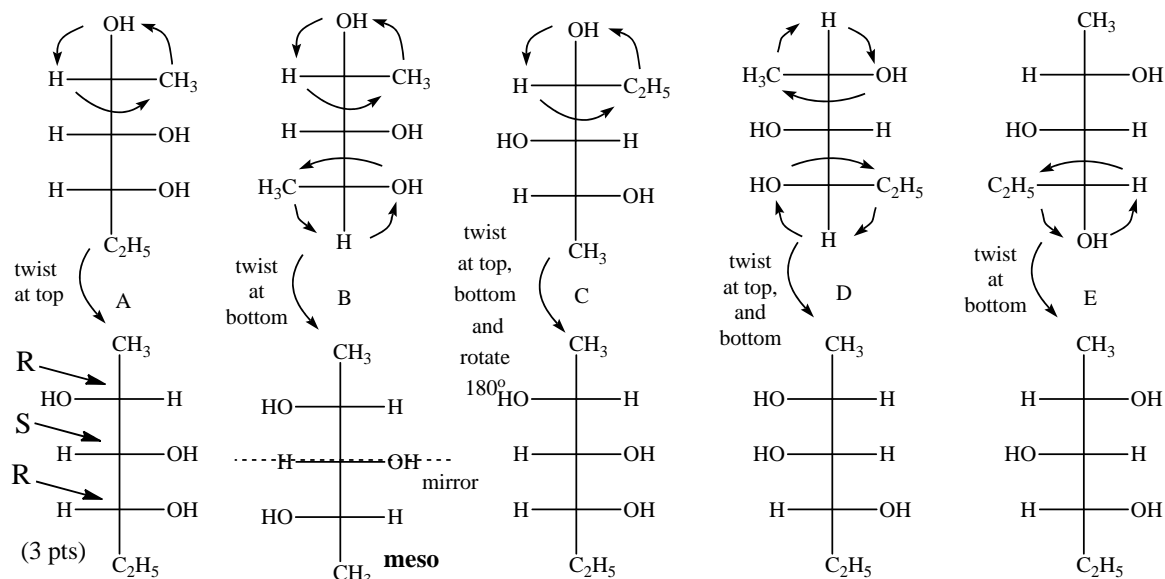


$$\Delta(\Delta H) = 6.7 - 2.2 = 4.5 \text{ kcal/mole}$$

$$K_{eq} = 10^{\frac{-4500}{1380}}$$

$$K_{eq} = 10^{-3.62} = 0.00055 = 1 / 1800 = (\text{least}) / (\text{most})$$

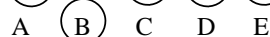
5. Use the following set of Fischer projections to answer each of the questions below by circling the appropriate letter(s) or letter combination(s). Hint: Redraw the Fischer projections with the longest carbon chain in the vertical direction and having similar atoms in the top and bottom portion. Classify all chiral centers in the first structure as R or S absolute configuration. (25 pts)



a. Which are optically active?



b. Which are meso?



(17 pts)

c. Which is not an isomer with the others?



d. Which pairs are enantiomers?



e. Which pairs are identical?



f. Which pairs are diastereomers?



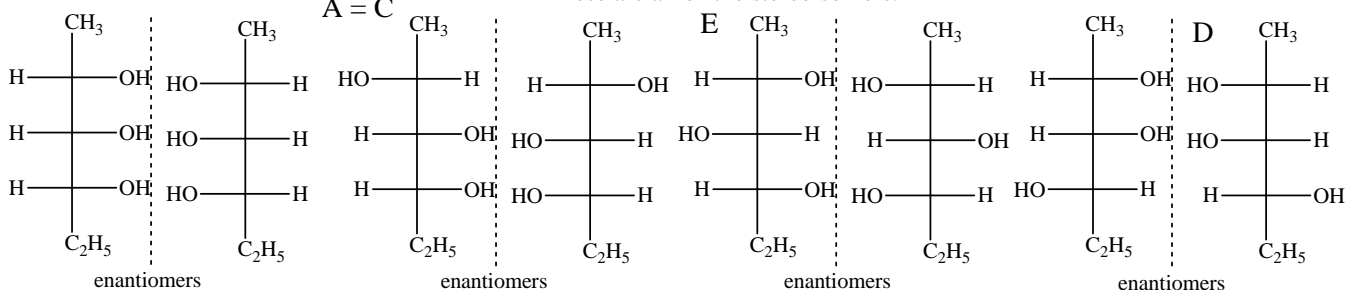
g. Which pairs, when mixed in equal amounts will not rotate plane polarized light?



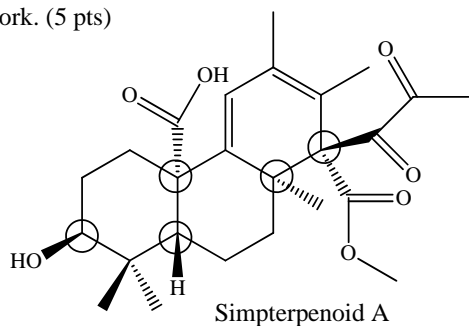
h. Draw any stereoisomers of hexan-2,3,4-triol as Fischer projections, which are not shown above.

If there are none, indicate this. (5 pts)

These are all of the stereoisomers.



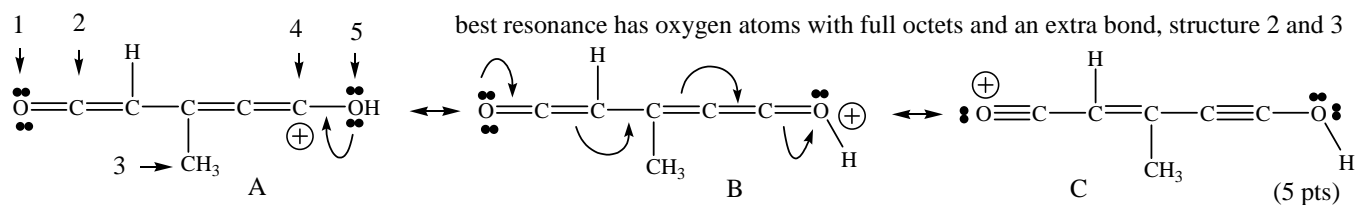
i. In the most recent Organic Letters, 2018, 20, 1465-8, a new natural product was isolated, Simpterpenoid A, from a fungal source in the south China Sea. Circle all of the chiral centers. How many stereoisomers are possible? Show work. (5 pts)



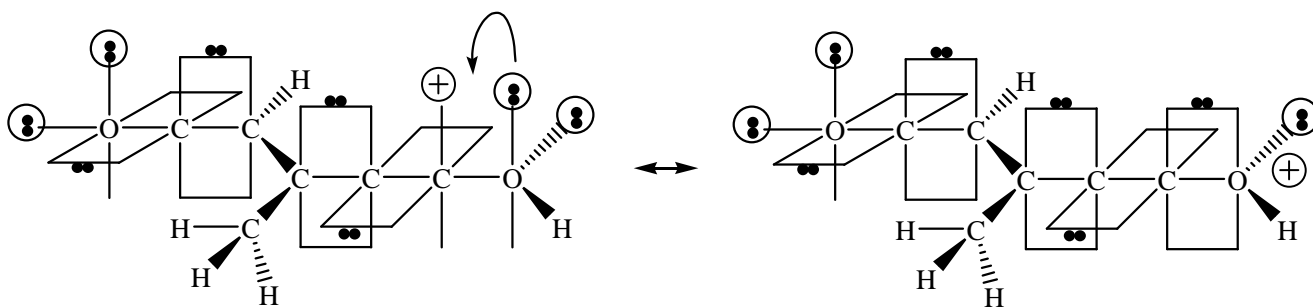
There are 5 chiral centers.

Maximum stereoisomers = $2^5 = 32$

6. Draw two additional “better” 2D resonance structures of the given structure. Assume all nonhydrogen atoms have full octets except for + carbon. Add in any necessary lone pairs and use proper curved arrows. Which structure(s) is(are) best and why? Draw a 3D structure for the given resonance structure. Show bonds in front of the page as wedges, bonds in back of the page as dashed lines and bonds in the page as simple lines. Show orbitals for pi bonds and lone pairs along with their electrons. Identify the hybridization, bond angles and descriptive shape for all numbered atoms in the given structure. (30 pts)



(15 pts)

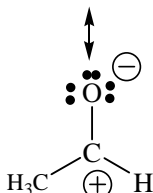
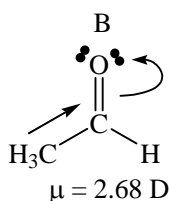
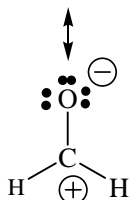
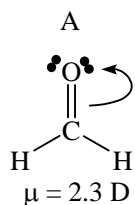


The best resonance has positive on either oxygen because there is an extra bond and full octets. Those are NOT the first structure. The second resonance structure is also shown here.

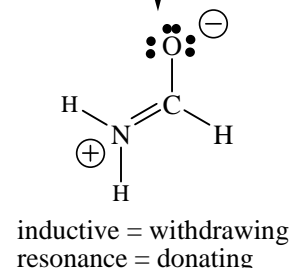
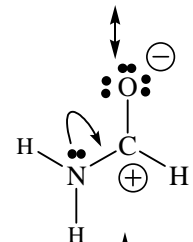
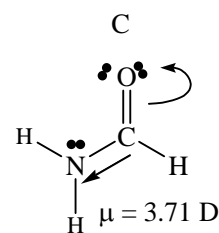
Use the given (first) Lewis structure to answer this part.

Atom	Shape	Hybridization	Bond Angles	# sigma bonds	# pi bonds	# lone pairs
1	linear	sp	180	1	1	2
2	linear	sp	180	2	2	0
3	tetrahedral	sp ³	109	4	0	0
4	linear	sp	180	2	1	0
5	trigonal planar	sp ²	120	2	0	2

7. Explain what the following dipole moments suggest about inductive effects and resonance effects. You will need to draw additional structures to help your explanation. (15 pts)

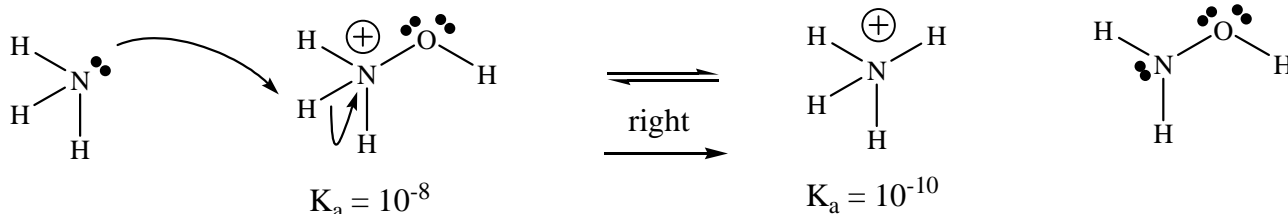


inductive = donating
no resonance effect



B (ethanal) is more polar than A (methanal), so the methyl (an R group) must be inductively donating compared to hydrogen, which allows oxygen to steal away even more electron density. Nitrogen is more electronegative than carbon and is inductively withdrawing, which should make the amide (C) less polar than methanal (A). However, nitrogen can use its lone pair to resonance donate to $\delta+$ of carbon (3rd resonance structure), which should make the molecule even more polar. Resonance must be more powerful than the inductive effect with methanamide (formamide) because polarity went way up (methanamide, C, has a much larger dipole moment than methanal, A).

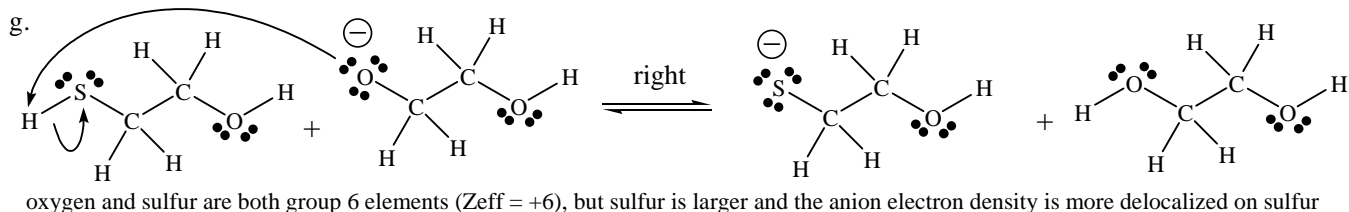
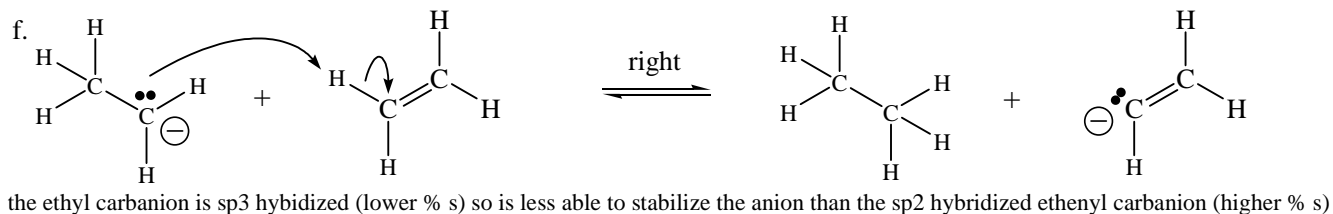
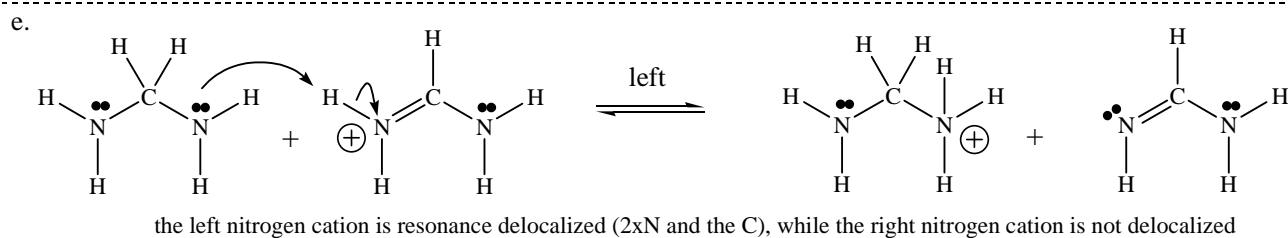
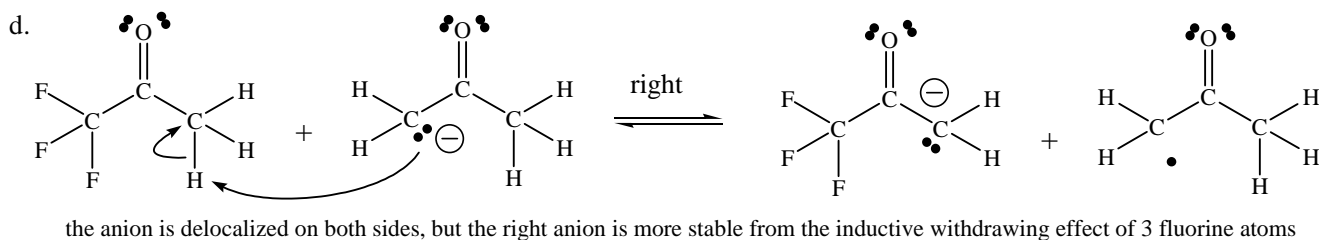
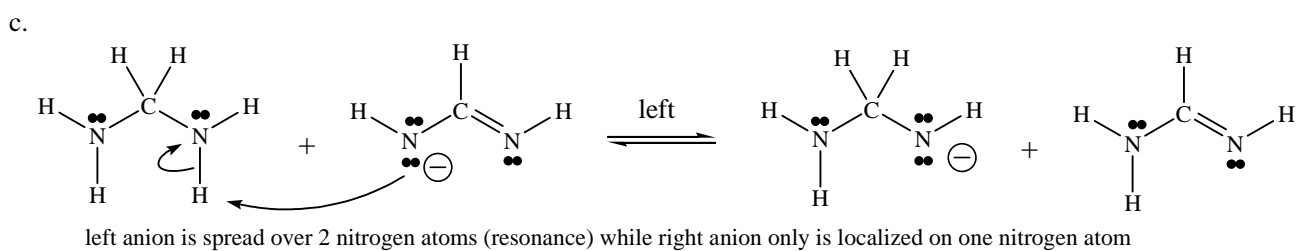
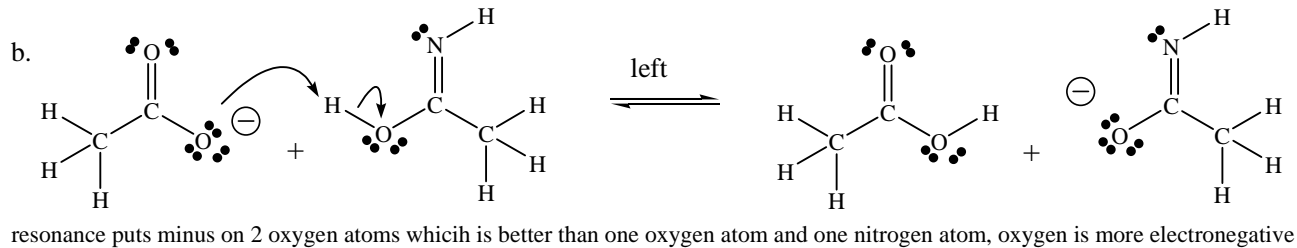
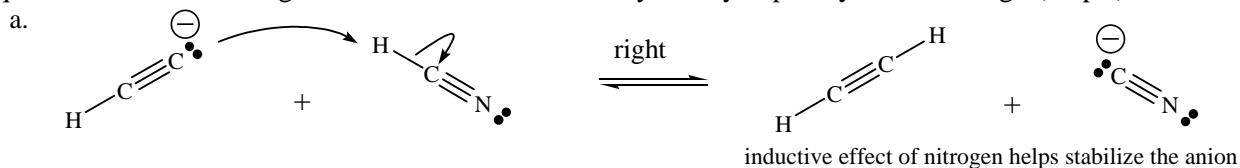
8. Only the reactant acid and base are drawn below. Decide which is which and draw a mechanism to show formation of the conjugate base and acid. The two acids have pK_a 's of 10 and 8 (K_a values are 10^{-10} and 10^{-8}). Match the K_a values with the proper acid, write a $K_{\text{equilibrium}}$ expression and calculate a quantitative $K_{\text{equilibrium}}$ value for the reaction. Show your work. Provide an explanation for your value of $K_{\text{equilibrium}}$. (15 pts)



The inductive withdrawing effect of the oxygen makes the left acid more acidic. Its conjugate base (hydroxyl amine) is less basic. Ammonia is more basic and the ammonium ion is less acidic. The equilibrium shifts away from the stronger acid and stronger base (and towards the weaker acid and weaker base). The equilibrium should favor the right side, and it does (100 / 1).

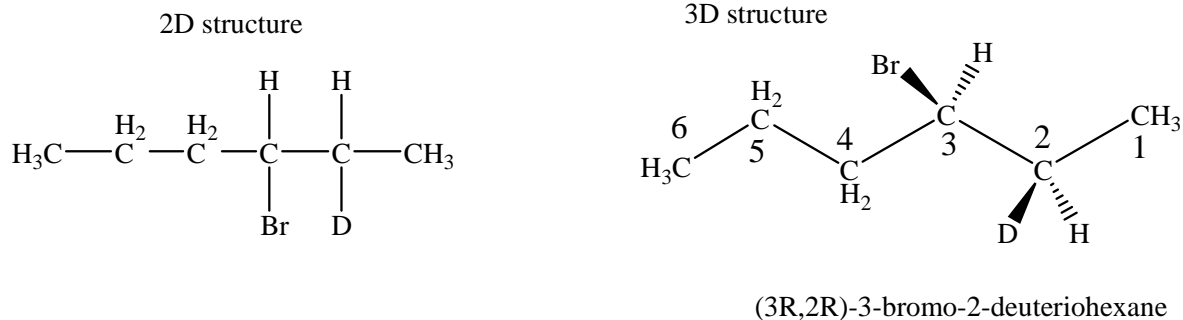
$$K_{\text{equilibrium}} = \frac{[\text{NH}_4^+][\text{H}_2\text{NOH}]}{[\text{NH}_3][\text{H}_3\text{NOH}^+]} = \frac{K_a = 10^{-8}}{K_a = 10^{-10}} = 100 / 1$$

9. Using arrow-pushing mechanisms, write the expected products from the following reactions and indicate whether the equilibrium lies to the "right" or to the "left". Also, very briefly explain your reasoning. (35 pts)

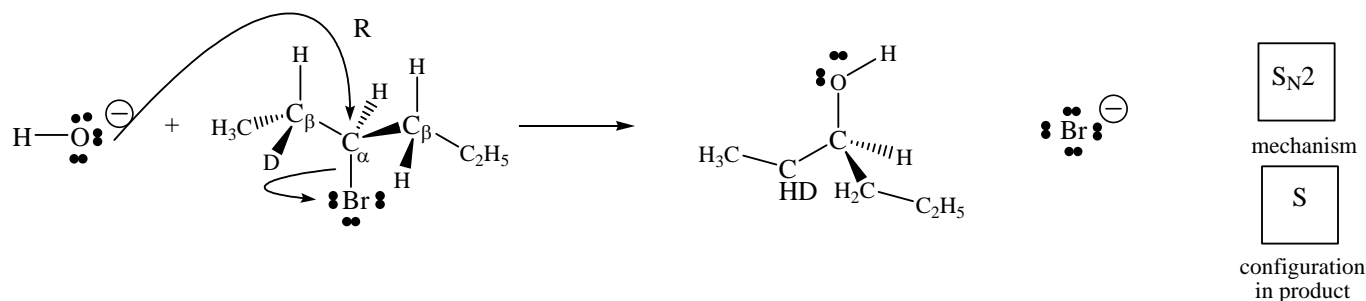


10. Use (2R,3R)-3-bromo-2-deuteriohexane to provide a simple, arrow-pushing mechanism for each of the following reaction conditions (show curved arrows, lone pairs & formal charge). Fill in the necessary details to clearly indicate any stereochemical features and/or conformational requirements. If reactants 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. You can abbreviate (simplify) parts of the molecule that are not part of a reaction. (43 pts)

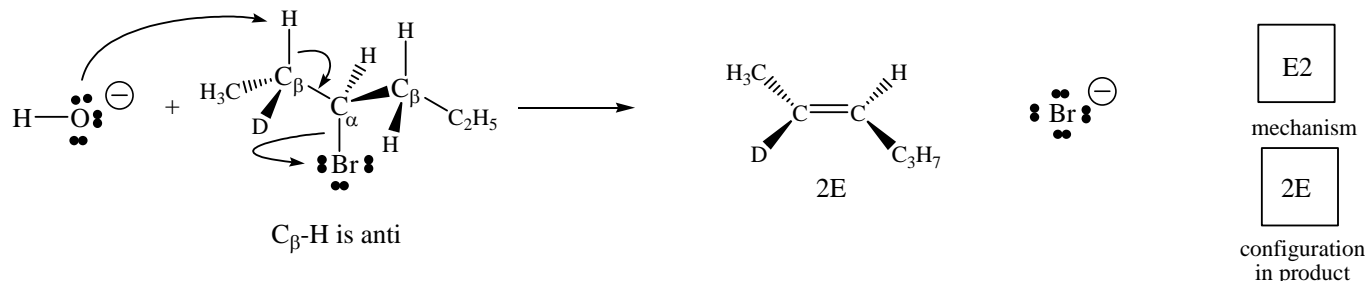
a. Draw a 2D structure and then a 3D structure of the reacting molecule. A 3D structure will be provided for the cost of the points of this part. (3 pts)

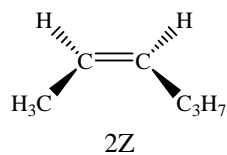
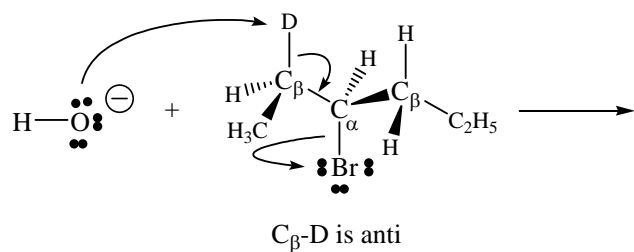


b. Show the S_N reaction (what kind?), indicate the absolute configuration(s) of the C_α center in the product. (7 pts)



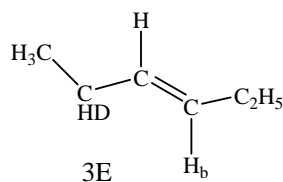
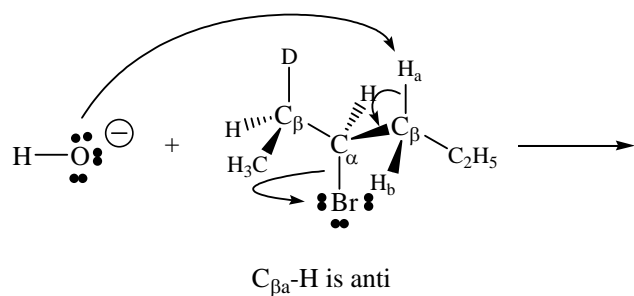
c. Show all possible E reaction products (what kind?). Indicate if E, Z or neither. (13 pts)





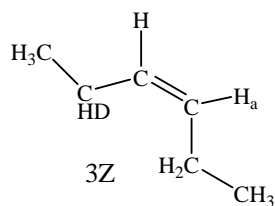
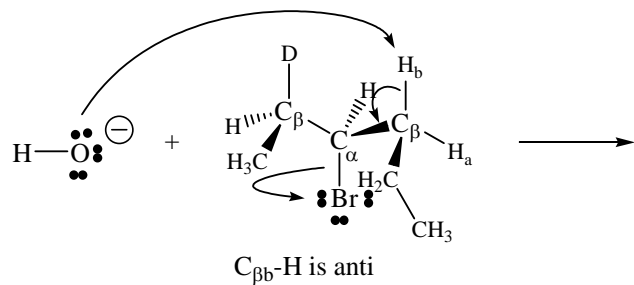
E2
mechanism

2Z
configuration
in product



E2
mechanism

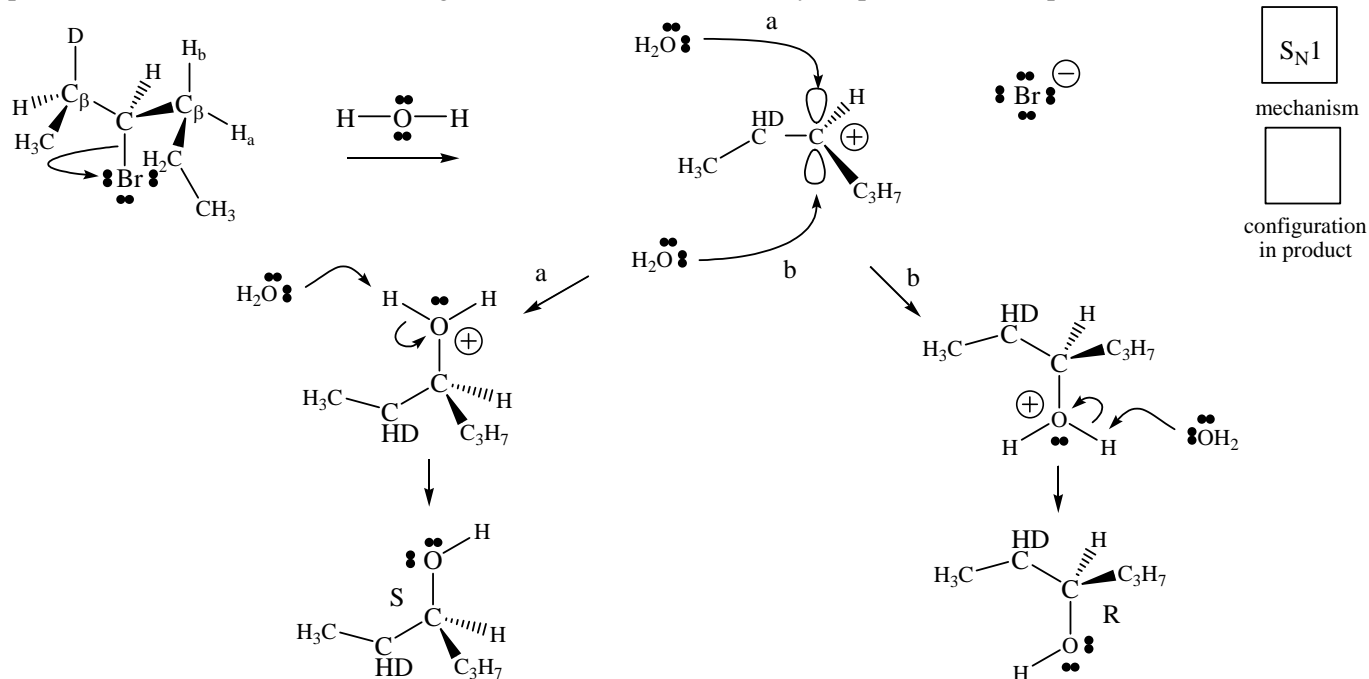
3E
configuration
in product



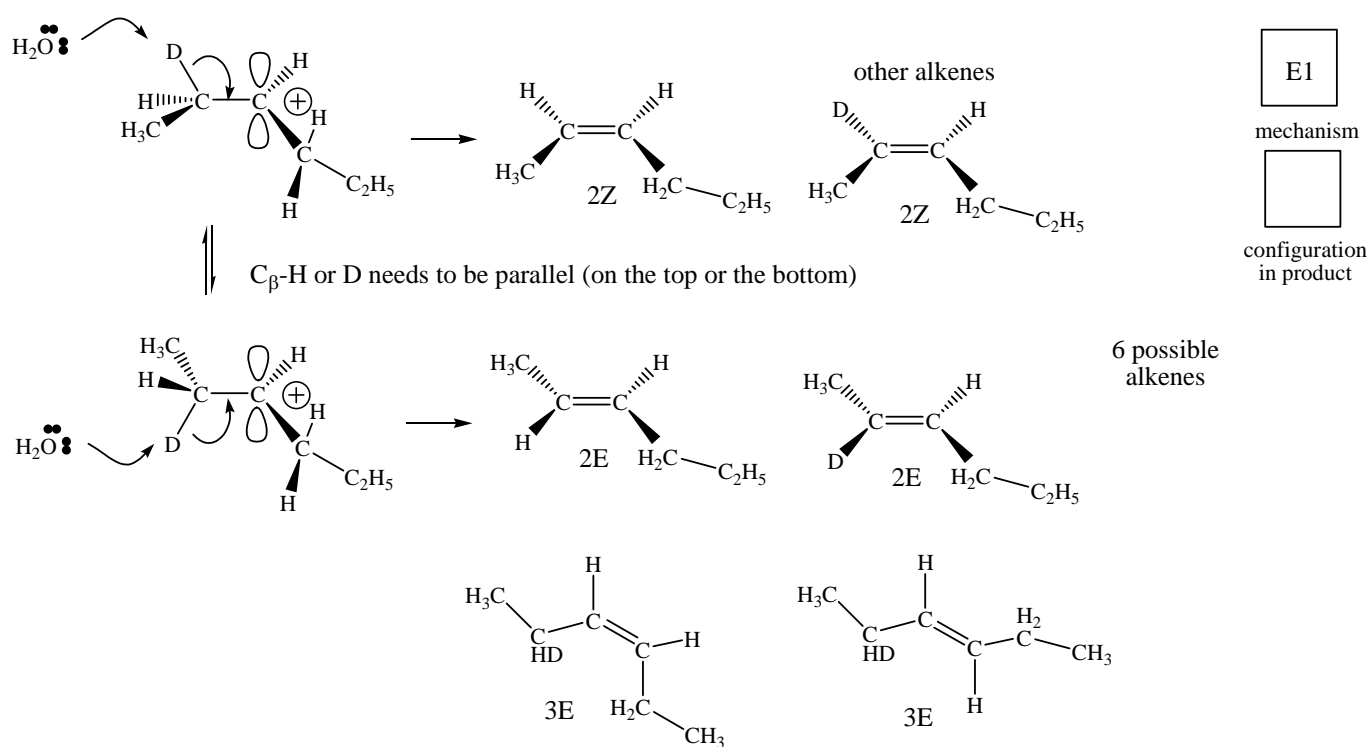
E2
mechanism

3Z
configuration
in product

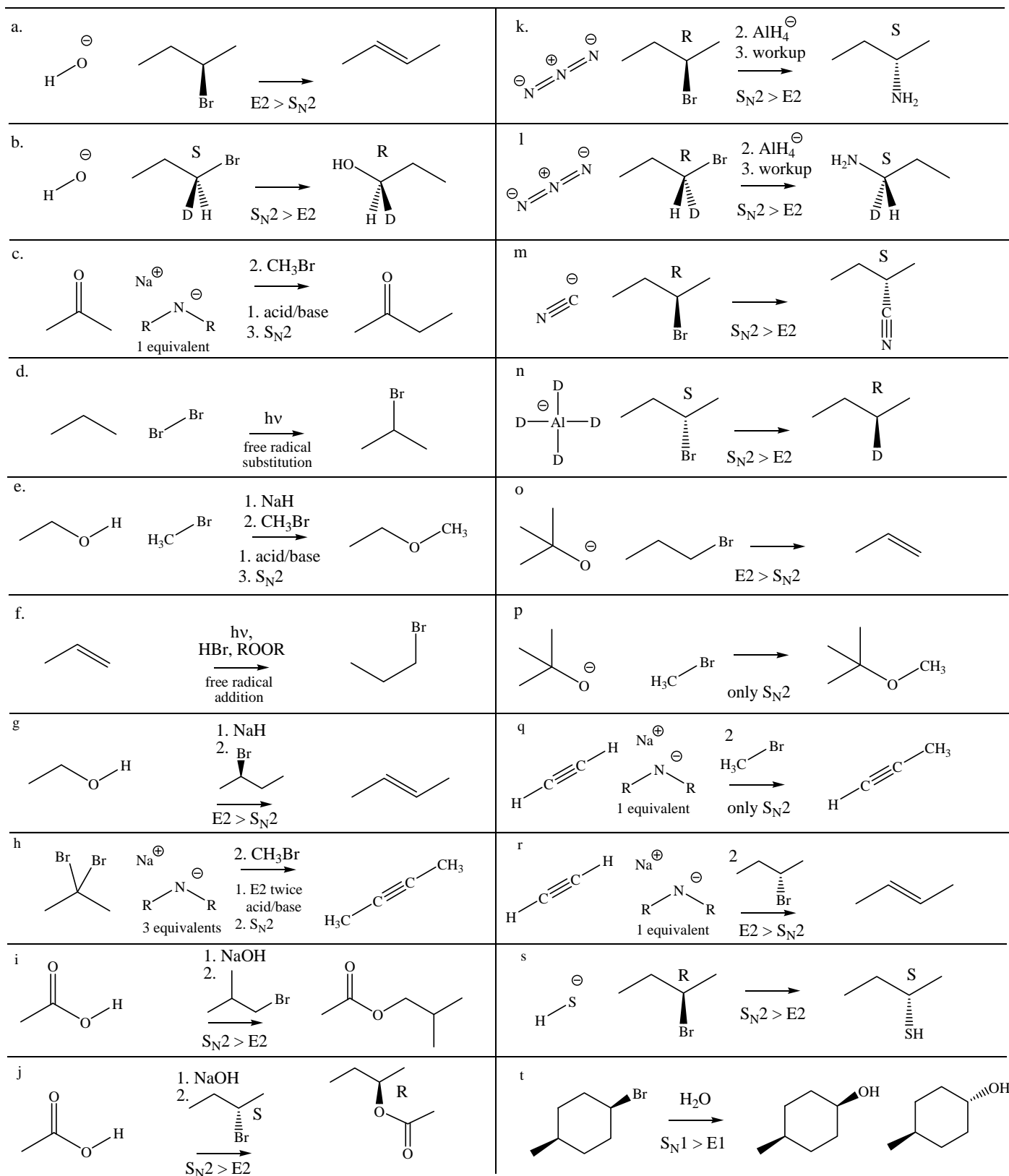
d. Show the S_N reaction (what kind?). You can use one intermediate to show all possible mechanistic S_N possibilities. Indicate absolute configuration(s) of the C_α center in your product(s). (10 pts)



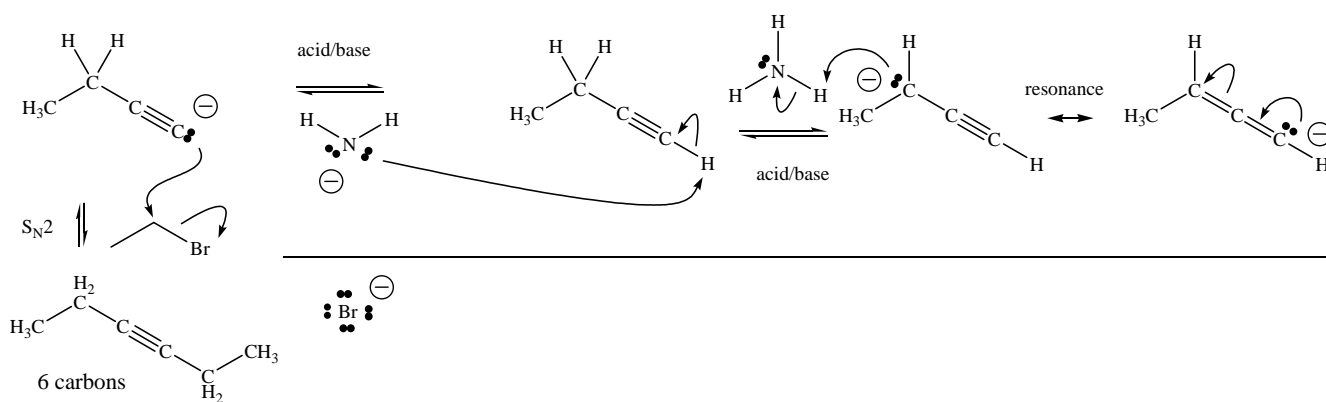
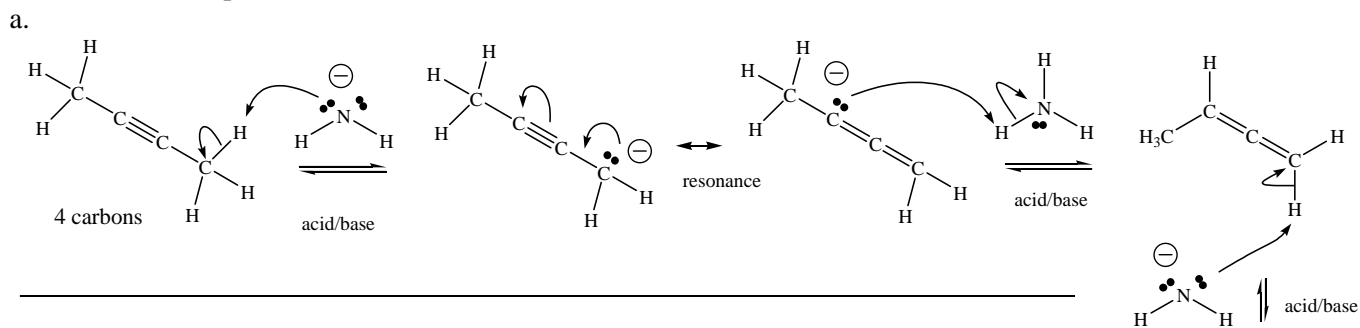
e. Redraw the intermediate used in 8d above to show all possible E reaction products. Indicate if E, Z or neither. If multiple products are formed between two atoms, you can show a single mechanism and just draw the additional possible products. (10 pts)



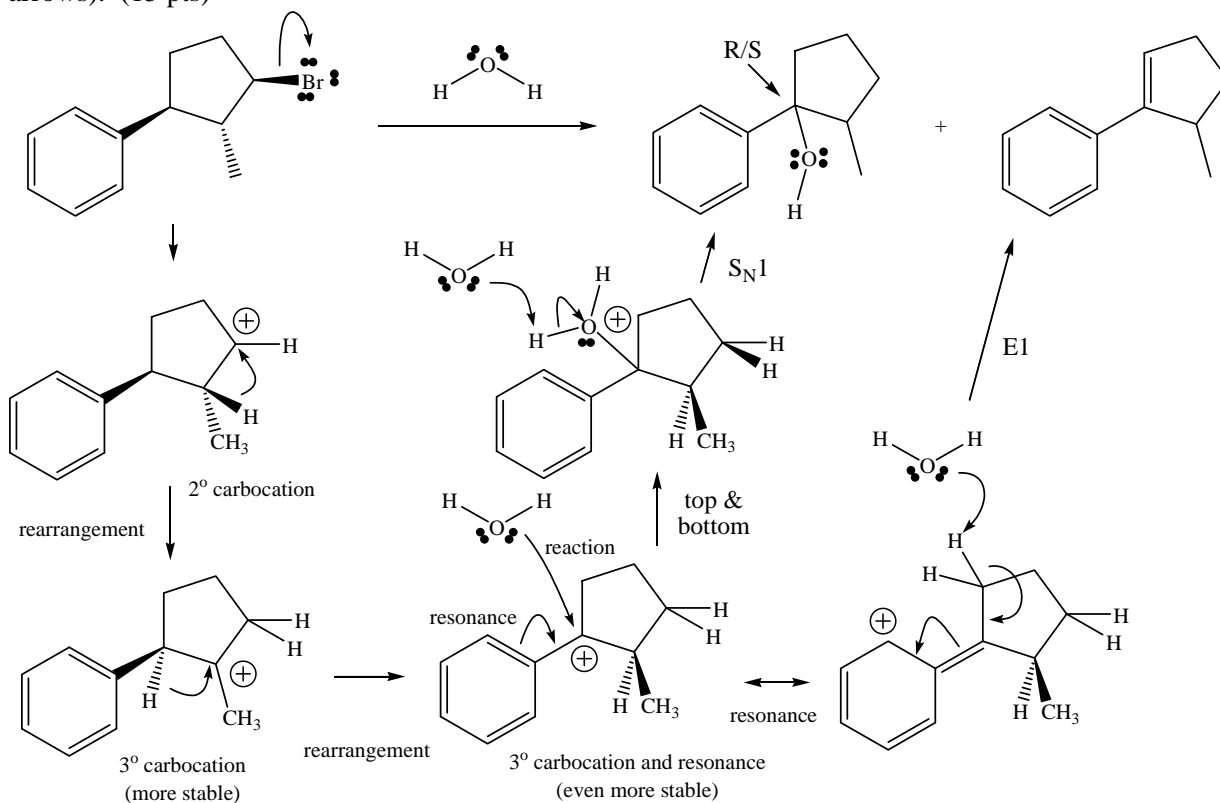
11. Indicate the **major** product in the following reactions. Indicate stereochemistry if part of the reaction. Do NOT show mechanisms. (WK = workup = neutralize conditions) (30 pts)



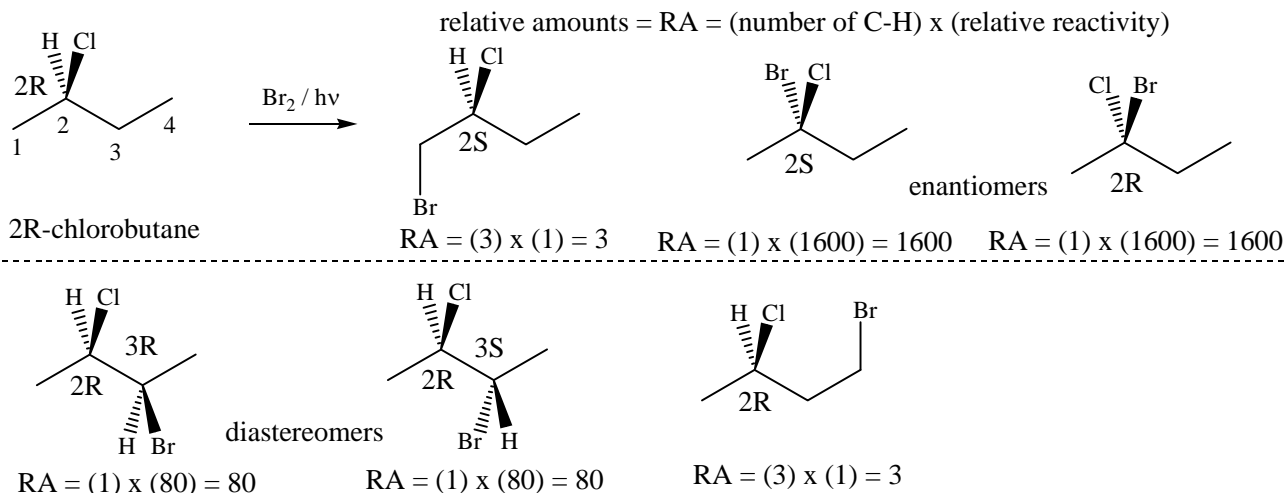
12. Provide all missing arrow-pushing mechanistic details (curved arrows, lone pairs and formal charge) to explain the following transformation. Assume all nonhydrogen atoms have full octets unless a positive charge is written by a carbon atom. (15 pts)



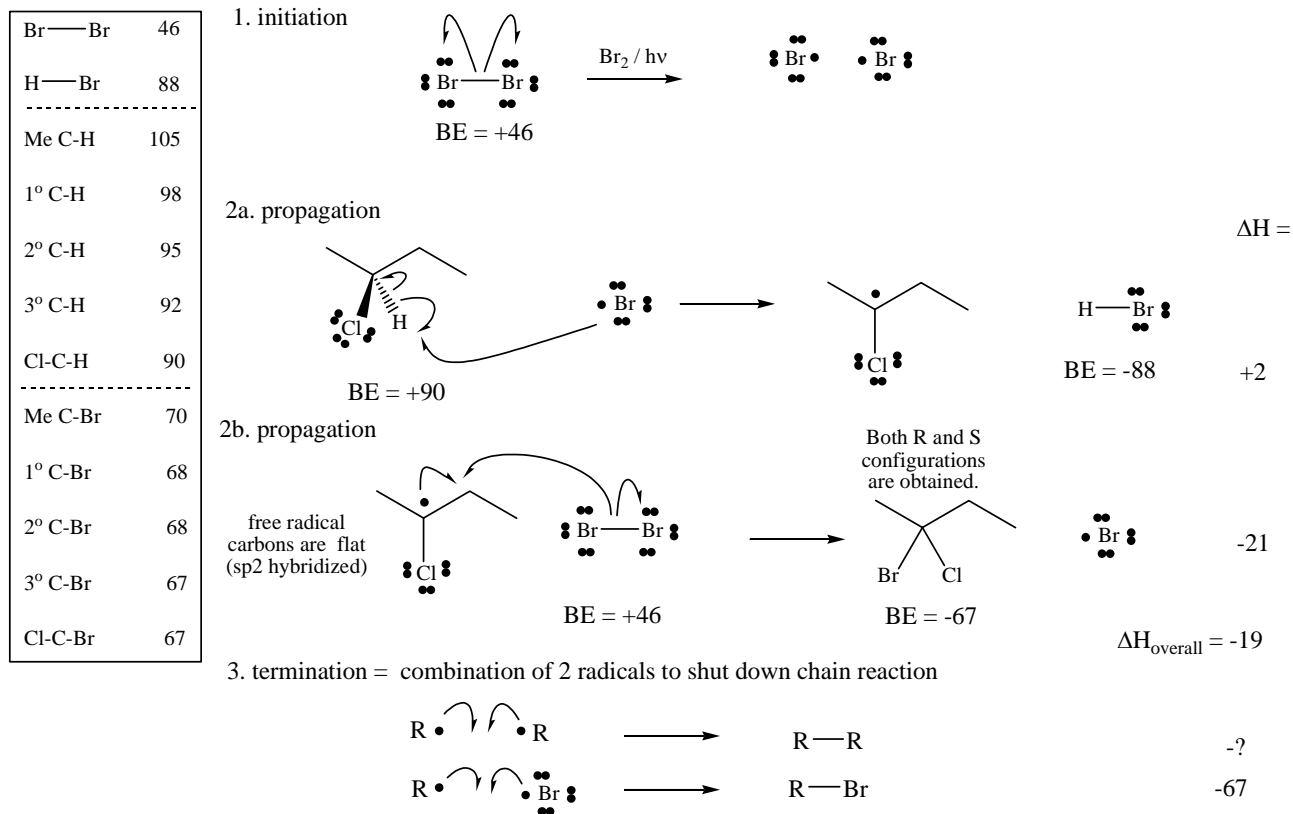
13. Provide a complete arrow-pushing mechanism for the following transformations (lone pairs, formal charge and curved arrows). (15 pts)



14. a. Show all possible products when 2R-chlorobutane is brominated with Br₂/hν? Indicate the approximate relative amounts of each product formed if the relative rates of reaction of a bromine atom with an sp³ C-H bond are: primary = 1, secondary = 80, tertiary = 1600 and C-H on a carbon with chlorine = 2000. Identify any stereoisomers as enantiomers, diastereomers or meso structures. Specify the absolute configuration of any chiral centers. (10 pts)



- b. Provide a complete arrow pushing mechanism to explain formation of the major product from the above reaction (show proper curved arrows, 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. To make a bond is positive energy and to make a bond is negative bond energy. (15 pts)



Talent is God given. Be humble. Fame is man-given. Be grateful. Conceit is self-given. Be careful...
John R. Wooden