

Elimination Reactions

Reading from Brown and Foote

- Chapter 9: Sections 9.5–9.8

Optional Reading

- Klein, Chapter 10

Suggested Text Exercises from Brown and Foote

- Chapter 9: 6-8, 37-46, 48, and 49

Lecture Supplement

- Elimination Reactions

Concept Focus Questions

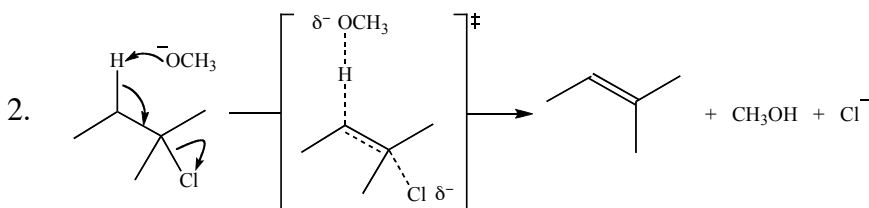
1. Provide precise yet concise definitions for the following terms
(a) β -Hydrogen (h) Elimination reaction (o) Tetrasubstituted alkene
(b) Anti-periplanar (i) Hofmann's rule (p) Trisubstituted alkene
(c) Cis alkene (j) Internal alkene (q) Thermodynamic control
(d) Disubstituted alkene (k) Kinetic control (r) Trans alkene
(e) *E* alkene (l) Monosubstituted alkene (s) Vinyl hydrogen
(f) E1 mechanism (m) Syn-periplanar (t) *Z* alkene
(g) E2 mechanism (n) Terminal alkene (u) Zaitsev's rule
2. Give an example of an E2 reaction, including a curved-arrow mechanism and the transition states for each step of the mechanism.
3. Briefly explain the E2 transition state geometry requirement.
4. What structural and reactivity factors are necessary for an E2 reaction to occur?
5. Give an example of an E1 reaction, including a curved-arrow mechanism and the transition states for each step of the mechanism.
6. What structural and reactivity factors are necessary for an E1 reaction to occur?
7. What is the rate-determining step of the E1 mechanism? Briefly explain your choice.
8. Why is acid necessary to eliminate water from an alcohol to form an alkene?
9. Why can skeletal rearrangement occur in an E1 reaction but not an E2 reaction? Give an example of an E1 reaction (with mechanism) in which rearrangement occurs.
10. If multiple alkene products are possible in an elimination reaction, which alkene is the major product? What factor(s) control this?

11. When deciding if an elimination reaction proceeds via the E2 or E1 mechanism, why is the E2 mechanism considered before the E1 mechanism?

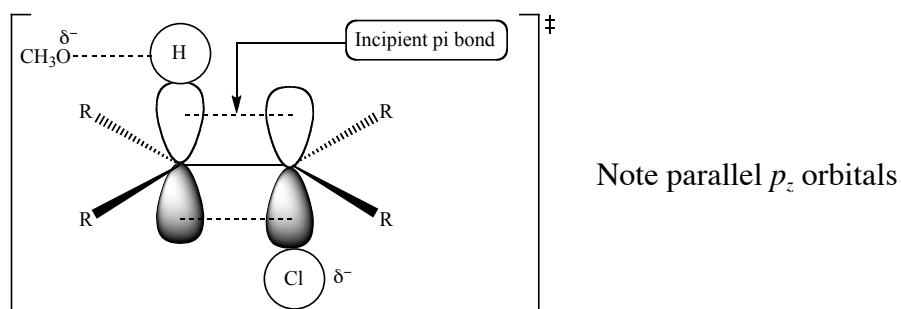
Concept Focus Questions Solutions

1. Illustrated definitions can be found at the Illustrated Glossary of Organic Chemistry available at the course web site
- (a) β -Hydrogen: A hydrogen attached to a β -carbon. In an elimination reaction, this is a hydrogen atom attached to the carbon atom that is attached to the carbon atom bonded to the leaving group (H_{β} -C-C-LG).
 - (b) Anti-periplanar: Two bonds or groups with a 180° dihedral angle (i.e., lying in the same plane but pointing in opposite directions).
 - (c) Cis alkene: An alkene in which the substituents lie on the same face of the molecule (i.e., point in the same direction).
 - (d) Disubstituted alkene: An alkene in which two vinyl hydrogens have been replaced by another atom or group.
 - (e) E alkene: Describes a double bond in which the two groups of highest Cahn-Ingold-Prelog priority lie on opposite sides.
 - (f) E1 mechanism: An elimination mechanism in which the carbon/leaving group scission step and the carbocation deprotonation step do not occur simultaneously. Always has a carbocation intermediate.
 - (g) E2 mechanism: An elimination mechanism in which the carbon/leaving group scission step and the carbocation deprotonation step occur simultaneously. Never has a carbocation intermediate.
 - (h) Elimination reaction: A reaction in which a molecule loses atoms or groups of atoms, usually from adjacent atoms, often resulting in a new pi bond.
 - (i) Hofmann's rule: An elimination reaction occurs to give the less substituted alkene(s) as the major product.
 - (j) Internal alkene: An alkene in which both ends of the carbon-carbon double bond are directly bonded to at least one other carbon.
 - (k) Kinetic control: A reaction in which the product ratio is determined by the rate at which the individual products are produced.
 - (l) Monosubstituted alkene: An alkene in which one vinyl hydrogen has been replaced by another atom or group.

- (m) Syn-periplanar: Two bonds or groups with a 0° dihedral angle (i.e., lying in the same plane and pointing in the same direction).
- (n) Terminal alkene: An alkene in which one end of the double bond is not directly bonded to any other carbons except the other end of the double bond.
- (o) Tetrasubstituted alkene: An alkene in which all vinyl hydrogens have been replaced by another atom or group.
- (p) Trisubstituted alkene: An alkene in which three vinyl hydrogens have been replaced by another atom or group.
- (q) Thermodynamic control: A reaction in which the product ratio is determined by the relative stability of the individual reaction products.
- (r) Trans alkene: An alkene in which the substituents lie on the opposite face of the molecule (i.e., point in the opposite direction).
- (s) Vinyl hydrogen: A hydrogen atom bonded to the sp^2 carbon of an alkene.
- (t) Z alkene: Describes a double bond in which the two groups of highest Cahn-Ingold-Prelog priority lie on the same side.
- (u) Zaitsev's rule: An elimination reaction occurs to give the most substituted alkene(s) as the major product.

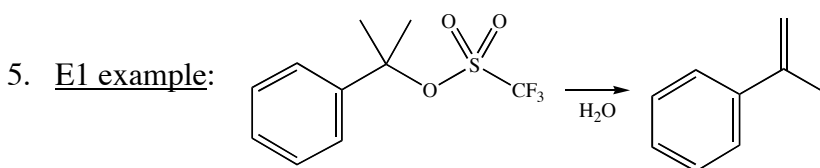


3. The energy of the E2 transition state is lower if the carbon-leaving group and carbon-hydrogen bonds are parallel.

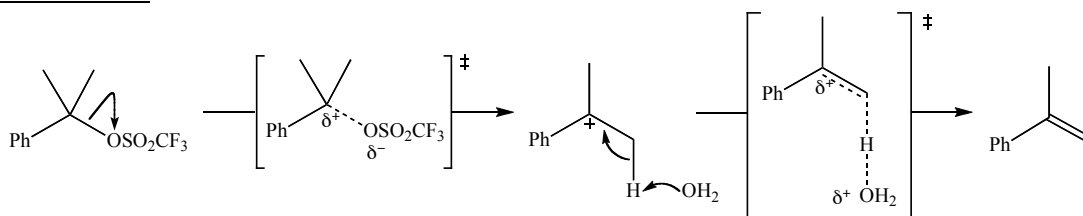


This arrangement is termed **anti-periplanar**, and is preferred over a syn-periplanar arrangement to minimize steric and torsional strain. As the bonds are breaking, the carbons are changing from sp^3 to sp^2 hybridization and lobes of p orbitals are beginning to replace the bonds. If the incipient p orbitals are parallel, they can immediately begin to form the new pi bond. The energy from the incipient pi bond helps replace the bonding energy lost from the carbon-leaving group and carbon-hydrogen bonds, thus stabilizing the transition state.

4. There are three fundamental requirements for the E2 reaction: a moderate or better leaving group, a strong base, and a hydrogen atom that is β and periplanar to the leaving group (the H-C-C-LG arrangement if a C=C bond is formed). The first two factors interact. With a better leaving group a weaker base can be used. With a stronger base, a poorer leaving group can be eliminated.



Mechanism:



Some students include a strong base (such as HO^- or CH_3O^-) in an E1 mechanism. If these species are not part of the given reactants, or they are not generated in any reasonable concentration as part of the reaction, then they are not present in the reaction, and cannot be part of the mechanism.

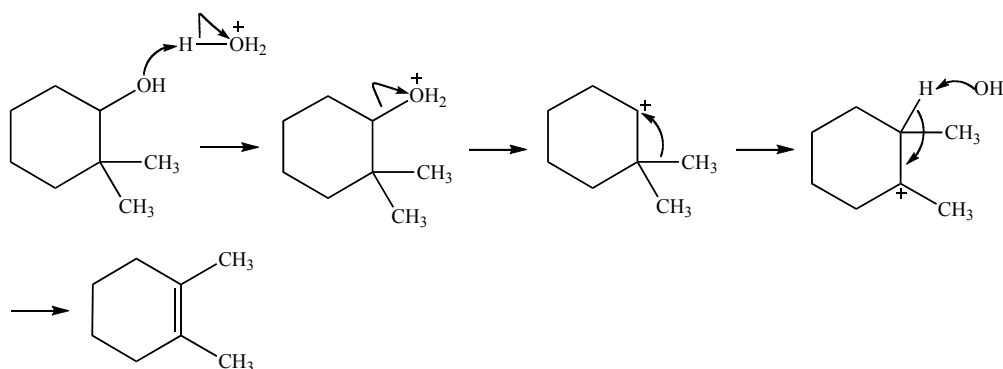
6. There are three fundamental requirements for the E1 reaction: a moderate or better leaving group, a stable carbocation, and a polar solvent. These three factors interact. For example, when a good leaving group and highly polar solvent are present, a less stable carbocation can be formed.

A β -hydrogen that is periplanar to the leaving group is not a requirement because carbocation deprotonation is not the rate-determining step. In addition, the leaving group has already departed before the hydrogen is removed so the periplanar requirement is moot.

7. Every E1 mechanism includes these two steps: ionization of the carbon-leaving group bond to form a carbocation and deprotonation of the carbocation to form a pi bond. (There may be other steps as well, such as protonation of an OH group. These extra steps are not considered in this question because they are not present in every E1

reaction.) Formation of a carbocation is energetically expensive because a bond is lost and no new bond is formed. In the deprotonation step, one sigma and one pi bond are gained while one sigma bond is lost, for a net bonding energy increase. Recall that activation energy controls rate and that to a reasonable approximation, activation energy is controlled by bond energy changes. Therefore, the more energetically expensive step (ionization) is slower.

- Acid is necessary to transform a poor leaving group (HO^-) into a better (but still moderate) leaving group (water). Hydroxide ion is a poor leaving group due to the small atomic radius of oxygen, and the oxygen atom gains a charge as it departs. Water is a better leaving group because the positive charge on oxygen is neutralized when it departs.
- Rearrangement requires a carbocation intermediate. Because carbocations are not formed in the E2 mechanism, there can be no rearrangement.



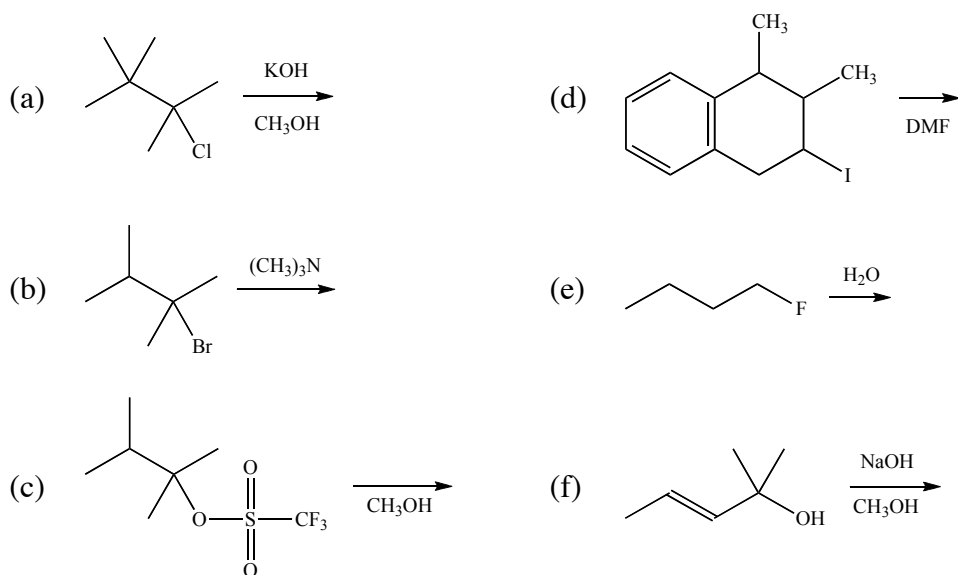
- E2: When the base is sterically hindered or the leaving group is NR_3 , SR_2 , or F^- , the least substituted alkene is favored (Hofmann orientation). Otherwise the most highly substituted alkene is favored (Zaitsev orientation).

E1: The most stable alkene is favored.

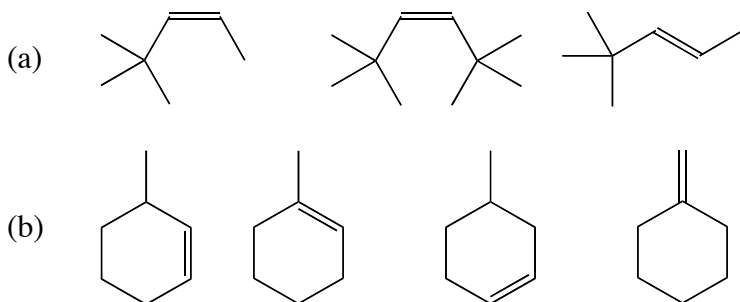
- The E2 mechanism avoids the energetically expensive carbocation formation step of E1. Thus we consider E2 before E1. However, there may be cases where E2 is not disallowed, but E1 is faster because the reaction conditions and reactants favor E1 over E2.

OWLS Problems

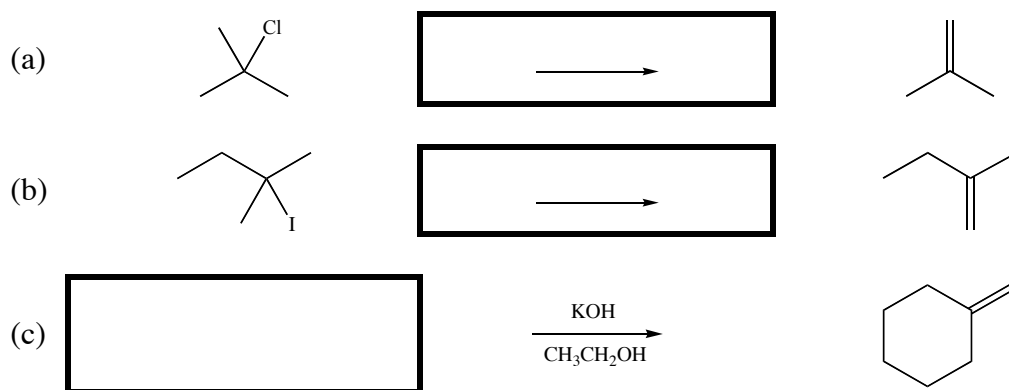
- Suggest products and mechanisms for these *elimination* reactions. Explain how you choose between E2 and E1. If more than one organic product is possible, select the major product and explain your choice. If no elimination occurs write “no elimination” and explain why.



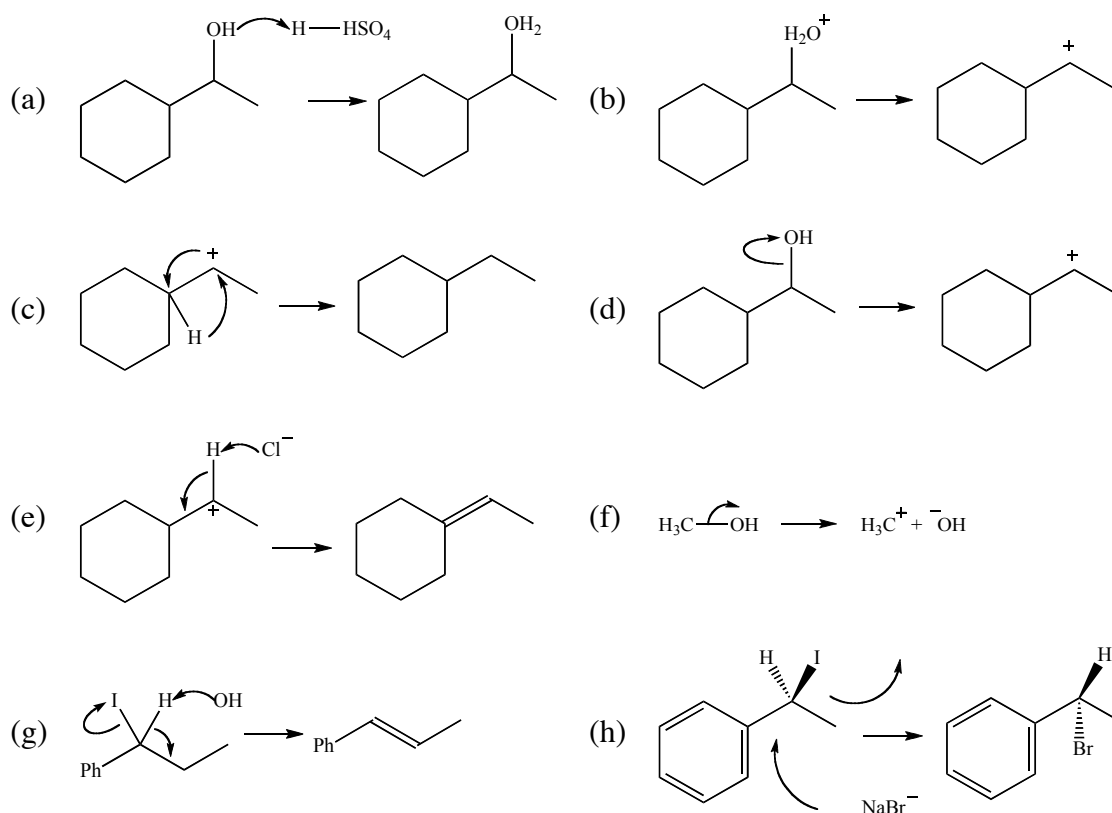
- Which carbocation fates might be observed in an E2 reaction mechanism? Provide examples.
- Which carbocation fates might be observed in an E1 reaction mechanism? Provide examples.
- Explain why the most stable reaction product is usually the major reaction product as well.
- A mechanism or structural effect that has both orbital (electronic) and geometric (stereochemical) factors is called a stereoelectronic effect. Using both words and diagrams together, briefly discuss the stereoelectronic effects that influence the E2 reaction transition state geometry.
- Select the most stable and least stable alkene in each set. Label your choices as *cis/trans* and *E/Z*, as appropriate.

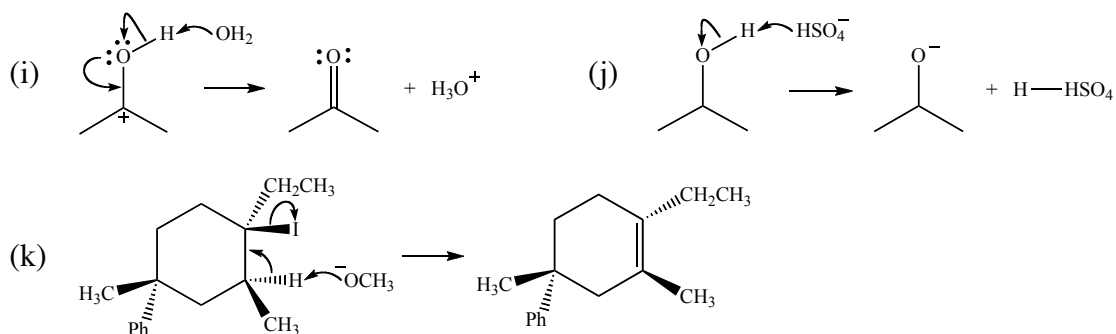


- Complete the following reactions by writing the missing starting materials or reactants in each box. Make sure the reaction gives **mostly elimination**, and not substitution products.



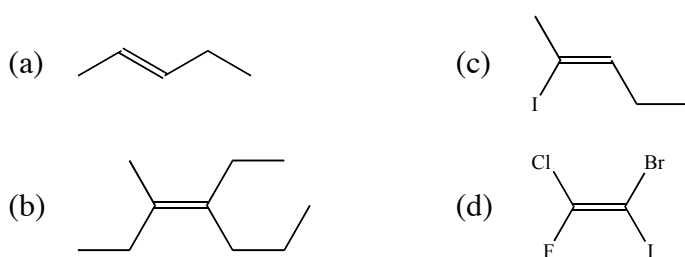
8. Mechanisms are the language of organic reactions. Lewis structures, formal charges and curved arrows are the grammar and punctuation. Not only must grammar and punctuation be used properly and precisely for the meaning of the words to be clear, they can also enrich the sentence beyond the simple implications of the naked words. Here is a chance for you to practice your organic chemistry language skills. The following mechanism steps were drawn from student answers on a midterm. Each contains one or more errors. Identify each error, briefly explain why it is wrong, and write the corrected mechanism step.





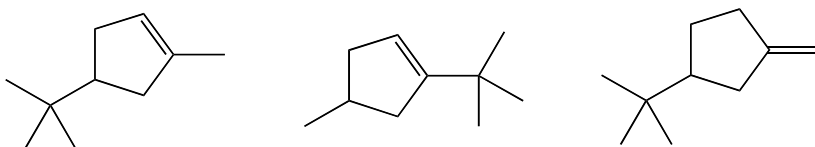
Practice Problems

1. Label each alkene as cis or trans, as well as *E* or *Z*.

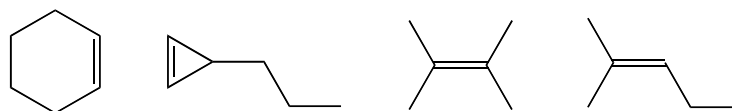


2. (a) Draw an alkene of molecular formula C_4H_8 that is both cis and *Z*.
 (b) By changing just one atom, redraw your part (a) molecule so that it is now cis and *E*.

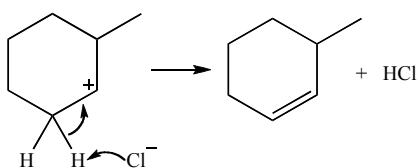
3. Select the most stable alkene:



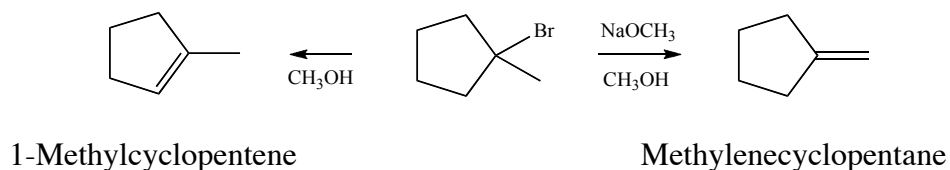
4. Select the most stable and least stable molecule:



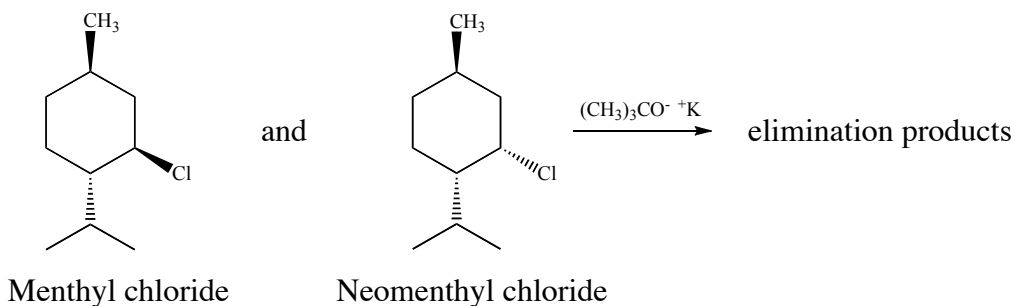
5. Does the carbocation mechanism step shown below proceed as written (i.e., nothing else is more likely to occur) or not (i.e., something else is more likely to occur)? Briefly explain your answer.



6. For elimination reactions (and many other reactions we will encounter later) it is important to be able to quickly categorize an acid or base as strong, moderate or weak. For example, H_2SO_4 ($\text{p}K_a -9$) and H_3O^+ ($\text{p}K_a -1.8$) are strong acids. Their conjugate bases, HOSO_3^- and H_2O , are weak bases. HO^- and CH_3O^- are strong bases. (Review your Chem 14C notes if necessary in order to understand the relationship between molecular structure and acid/base strength.)
- (a) Categorize each of the following acids as strong, moderate, or weak: CH_3OH_2^+ , H_2O , CH_3OH , and NH_3 .
- (b) Categorize each of the following bases as strong, moderate, or weak: $\text{CH}_3\text{CH}_2\text{O}^-$, $(\text{CH}_3)_3\text{CO}^-$, NH_3 , I^- , and F^- .
7. State Zaitsev's Rule. Write an E2 reaction including mechanism that clearly illustrates Zaitsev's Rule.
8. Unlike E2 reactions, E1 reactions always give the more stable alkene product, regardless of the leaving group. Explain why.
9. For the elimination reaction shown below:

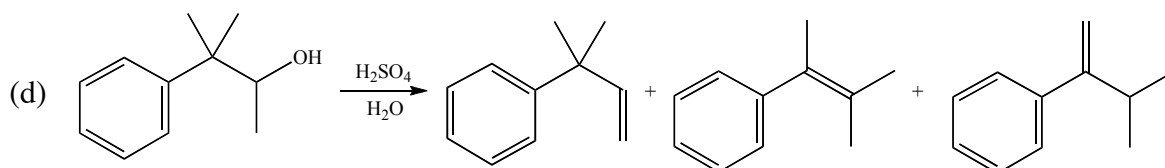
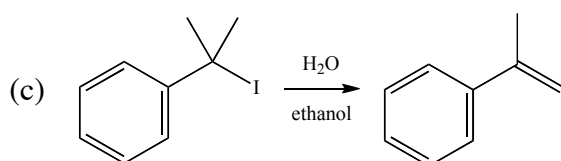
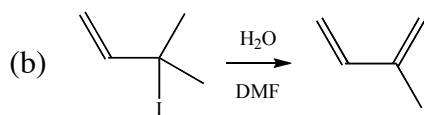
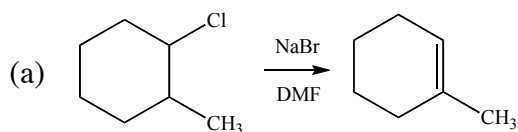


10. Examination of the elimination reactions of menthyl and neomenthyl chlorides was important in establishing the mechanism of ionic substitution and elimination reactions. Give the E2 products formed in the following reactions, along with a brief explanation.



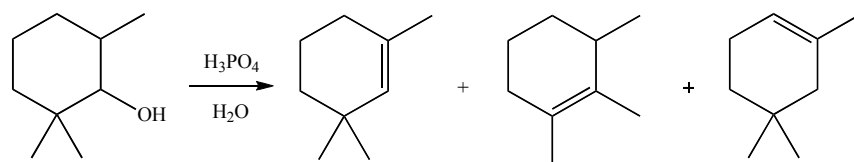
11. Give the major alkene products that result when menthyl and neomenthyl chlorides are subjected to E1 elimination (water, heat).

12. Provide mechanisms. Briefly explain your choice (E2 versus E1).

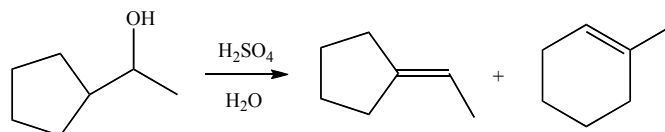


13. Very briefly explain why the reaction of question 12(d) does not occur in the absence of a strong acid such as H_2SO_4 or H_3PO_4 .

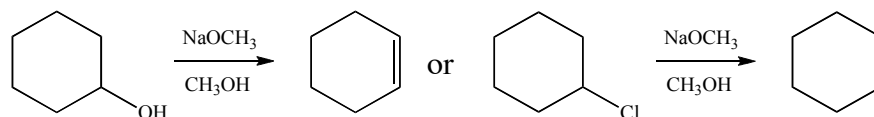
14. Provide a mechanism.



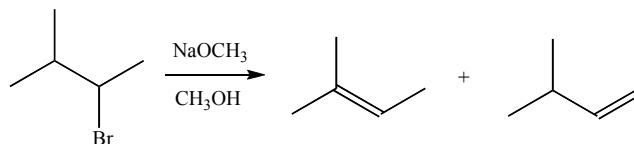
15. Provide a mechanism. Label the rate-determining step with "rds."



16. Which reaction is faster? Write a very similar reaction that occurs by the same mechanism but is obviously faster.

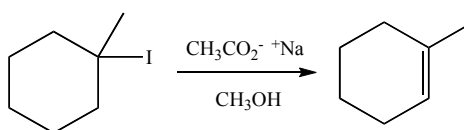


17. For the reaction shown below: (a) write the transition state for the slowest step in the E2 mechanism, and (b) determine the more likely mechanism (E2 or E1).



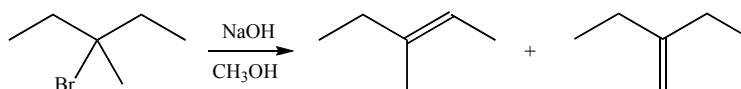
18. For the reaction shown below:

- Write an E1 mechanism.
- Write an E2 mechanism.
- What is the more likely mechanism? Briefly explain.



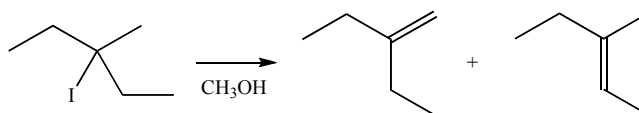
19. For the reaction shown below:

- Select the major product.
- Write the mechanism for the major product of this reaction.
- Very briefly explain your choice for the reaction mechanism.



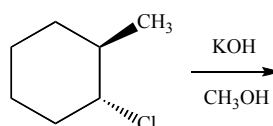
20. For the reaction shown below:

- Select the major product.
- Write the mechanism for the major product of this reaction.
- Very briefly explain your choice for the reaction mechanism.

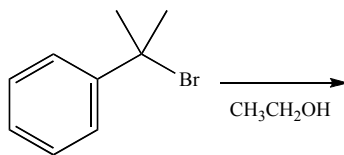


21. For the reaction shown below:

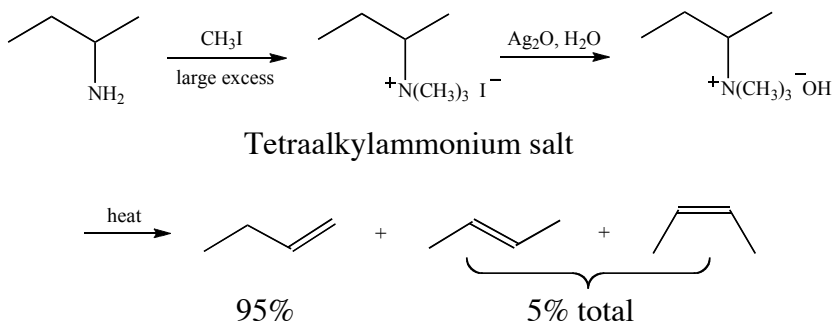
- Write the major product of this reaction.
- Provide a curved arrow mechanism, including all transition states, showing how this major product is formed.
- Very briefly explain your choice of mechanism for this reaction.



22. For the reaction shown below:
- Write all the products of this reaction.
 - Provide a mechanism that clearly shows how all of your products are formed.
 - Briefly explain why you eliminated other ionic substitution and elimination mechanisms in part (a).

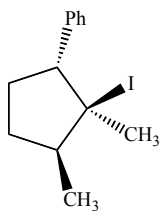


23. The Hofmann degradation of an amine consists of three steps: Conversion of the amine to a tetraalkylammonium salt (R_4N^+), changing of the ammonium salt anion to hydroxide, and finally E2 elimination. The elimination step gives the less substituted alkene as the major product. Consider the Hofmann degradation shown below.



Explain, from the viewpoint of torsional and steric strain, why E2 elimination of the tetraalkylammonium salt gives the less substituted alkene as the major product. Hint: Use models and Newman projections.

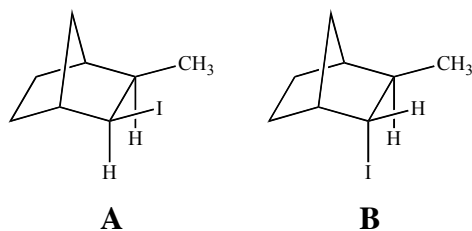
24. Consider the E2 reaction of the molecule shown below with NaOCH_3 in CH_3OH .



- Write all three possible E2 reaction products.
- Does the location of the phenyl group enhance or decrease the amount of each of these three products?
- Does the alignment (anti-periplanar versus syn-periplanar) of the carbon- β -hydrogen and carbon-leaving groups bonds enhance or decrease the amount of each of these three products?

- (d) Select the major product of the reaction. Carefully consider all assumptions that you make.
- (e) What would you use in place of NaOCH₃ to favor formation of the product with the least number of vinylic hydrogens?

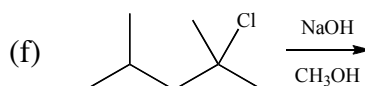
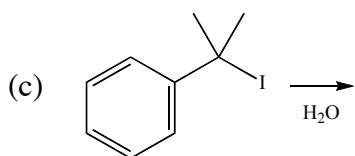
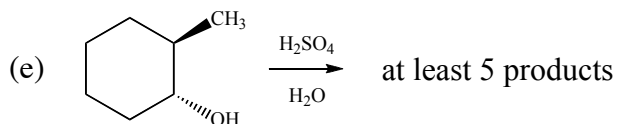
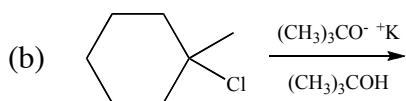
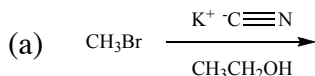
25. Alkyl iodides **A** and **B** were both subjected to E2 elimination by treatment with KOC(CH₃)₃. One alkyl iodide gave an alkene of molecular formula C₈H₁₂, while the other failed to react. Write the structure of the alkene product that was formed, and explain why the other alkyl iodide failed to give an elimination product. Hint: Explore alkyl iodides **A** and **B** with models.



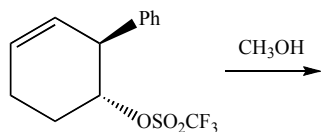
26. An important Chemistry 30A skill that you will need to develop is the ability to determine the most probable mechanism for a reaction, even when the products are not given. The mechanism choice is based on a series of logical decisions, as well as gut instinct (which you will develop by doing lots of problems). A flowchart is a convenient way to lay out the sequence of the logical choices. Make such a flowchart for the four reaction mechanisms we have studied so far, assuming the reaction product is known. (You might want to create a flowchart when the product is not known as well.)

We will add to this flowchart throughout the course, so keep it handy.

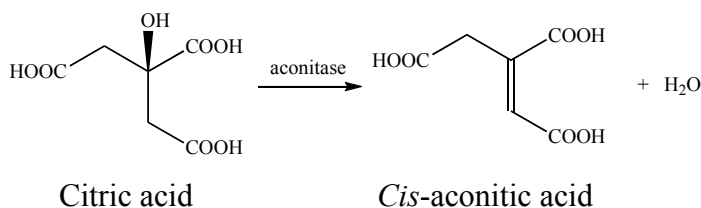
27. The following reactions may occur by the E2, S_N2, E1, or S_N1 mechanisms. Predict the major product(s) in each case. If no reaction occurs, write NR. Provide a brief explanation for your mechanism choices.



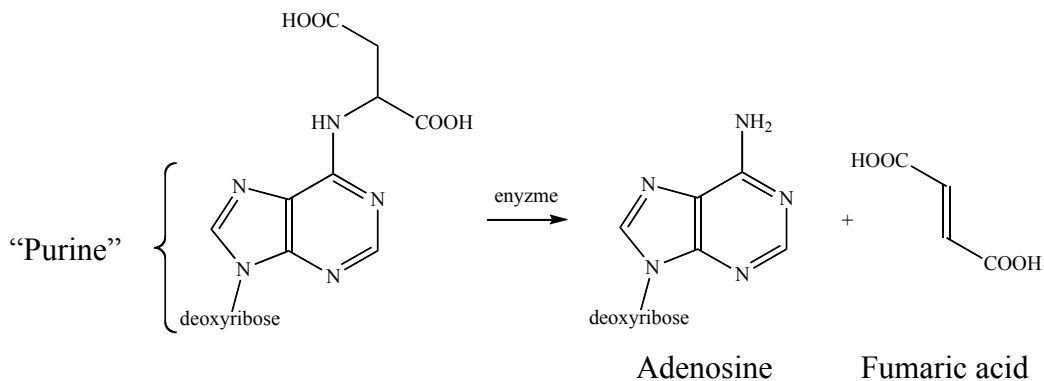
28. For the reaction shown below,
- What feature(s) of the reactants favor each of the following mechanisms: E2, S_N2, E1, and S_N1?
 - The reaction produces four major S_N1 products and two major E1 products. Write the products, along with the mechanisms for their formation.



29. Consider the dehydration of citric acid by the enzyme aconitase:



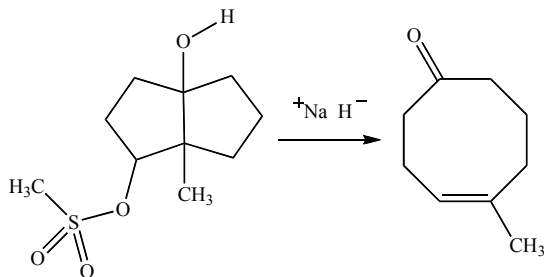
- What is the most probable mechanism for this reaction?
 - Briefly explain your mechanism choice. Clearly state any assumptions you make about the structure of aconitase.
 - Draw a curved arrow mechanism for the dehydration of citrate by aconitase.
30. Consider the biosynthesis of adenosine, a nucleoside building block of nucleic acids. The final step in adenosine biosynthesis is an elimination reaction.



- What is the mechanism of this reaction?
- Briefly explain your mechanism choice. You may make any assumptions that you want as long as they are logical and are clearly stated.
- Provide the detailed and complete curved arrow mechanism for this elimination reaction. You may use "purine" as an abbreviation for the fused aromatic ring system with the four nitrogen atoms.

31. As your knowledge and understanding of organic reactions increases so should your ability to work out mechanisms for reactions that have odd quirks, or for reactions you have never seen before.

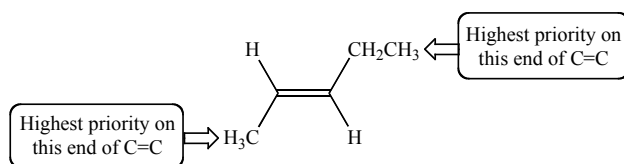
- (a) The reaction of NaI with $\text{ICH}_2\text{CH}_2\text{Cl}$ in acetone produces I_2 , $\text{H}_2\text{C}=\text{CH}_2$, and NaCl. The observed rate law is $\text{rate} = k [\text{NaI}] [\text{ICH}_2\text{CH}_2\text{Cl}]$. Write a mechanism that is consistent with these facts.
- (b) Suggest a mechanism for the following reaction. $\text{Na}^+ \text{H}^-$ (sodium hydride) is a strong base. The mechanism does not involve any carbocations.



32. Why are E1 and $\text{S}_{\text{N}}1$ reactions faster in the Arctic and Antarctic than at the equator? (Hint: This is a joke, so think like Dr H!)

Practice Problems Solutions

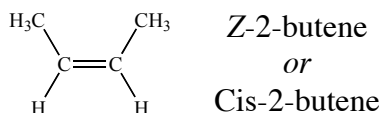
1. (a) This is a trans-alkene because the carbon chains are on opposite faces of the carbon-carbon double bond. This is an *E*-alkene because the highest priority group on each of the sp^2 carbons (methyl and ethyl) is on opposite faces of the double bond.



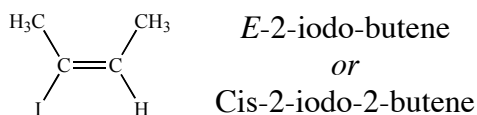
- (b) This alkene cannot be labeled as cis or trans because the double bond has four carbon groups. This is a *Z*-alkene because the highest priority groups on each sp^2 carbon (ethyl on the left and propyl on the right) are on the same face of the double bond.
- (c) This is a trans-alkene because the carbon groups are on opposite faces of the double bond. This is a *Z*-alkene because the highest priority groups on each sp^2 carbon (iodine and ethyl) are on the same face of the alkene. *Not all trans alkenes are E-alkenes, and not all cis alkenes and Z-alkenes.*
- (d) This alkene cannot be labeled as cis or trans because there are no carbon groups attached to the alkene. This is an *E*-alkene because the highest priority groups on each sp^2 carbon (Cl and I) are on opposite faces of the double bond.

Note that among these structures we cannot always label the alkene as *cis* or *trans*, but we can always use *E* or *Z*. This is why the *E/Z* system is preferred over the *cis/trans* system.

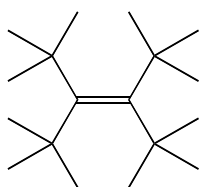
2. (a) Only one answer is possible: *Z*-2-butene. This alkene is *cis* because the methyl groups are on the same side of the double bond. This alkene is *Z* because the highest priority group on each sp^2 carbon (i.e., the methyl groups) lie on the same side of the double bond.



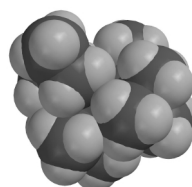
- (b) The methyl groups must remain as they are in order to preserve the *cis* configuration. *E* configuration requires that the two highest priority groups be on opposite side of the double bond. Therefore we must transmute a vinyl hydrogen atom into an atom of higher priority. Luckily, any atom has a higher Cahn-Ingold-Prelog priority than hydrogen.



3. The left and middle alkenes are both internal and trisubstituted. The alkene on the right is terminal and disubstituted, and therefore the least stable of the three. We saw in lecture that large substituents can destabilize an alkene due to severe van der Waals eclipsing interactions. Recall the case of tetra-*tert*-butylethylene, discussed in lecture.

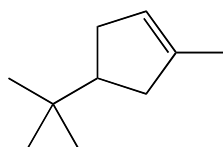


Tetra-*tert*-butylethylene

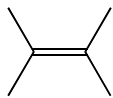


A space-filling model of tetra-*tert*-butylethylene, showing severe torsional and steric strain among the four *tert*-butyl groups.

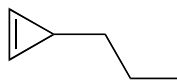
In this problem, the left alkene has a methyl group eclipsing with the alkene hydrogen whereas the middle alkene has a much larger *tert*-butyl group eclipsing with the alkene hydrogen. The most stable alkene is shown below.



4. The most stable alkene is 2,3-dimethyl-2-butene (tetrasubstituted). The least stable alkene is 2-propylcyclopropene (disubstituted with ring strain).



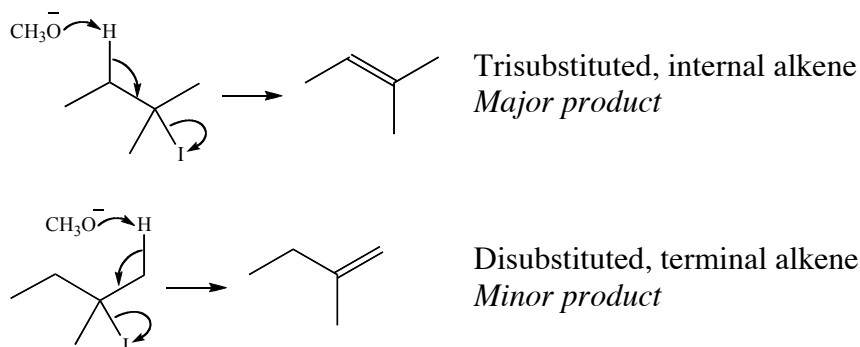
2,3-Dimethyl-2-butene



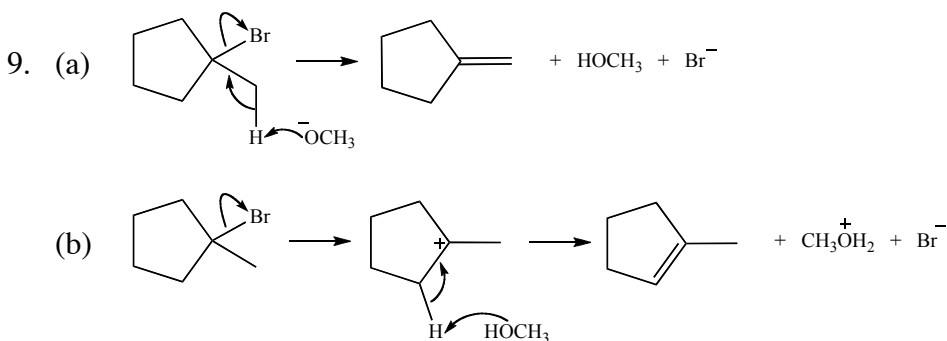
2-Propylcyclopropene

2-Propylcyclopropene is a disubstituted alkene because each of the alkene carbons is bonded to a carbon. It does not matter that both alkene carbons are bonded to the same carbon, because substitution influences alkene stability by the number of bonds, and not the number of carbons.

5. This mechanism step does not occur as written. This mechanism step is another one of the three carbocation fates: lose a proton to form a pi bond. In this case proton loss leads to a disubstituted alkene whereas loss of a different proton leads to a trisubstituted alkene. A trisubstituted alkene is more stable than an isomeric disubstituted alkene isomer, so this proton loss is unlikely to occur.
6. (a) CH_3OH_2^+ is a strong acid, similar to H_3O^+ .
 H_2O is a weak acid.
 CH_3OH is a weak acid, similar to H_2O .
 NH_3 is a very weak acid.
- (b) $\text{CH}_3\text{CH}_2\text{O}^-$ is a strong base, similar to HO^- and CH_3O^- .
 $(\text{CH}_3)_3\text{CO}^-$ is a strong base, similar to HO^- , CH_3O^- , and $\text{CH}_3\text{CH}_2\text{O}^-$.
 NH_3 is a moderate base.
 I^- is a very poor base due to large atomic radius and high polarizability.
 F^- is a moderate base due to small atomic radius and low polarizability.
7. In a β -elimination reaction, the most highly substituted alkene is the major product. The E2 example must have a strong base, moderate or better leaving group, and β -hydrogen. The mechanism is a single step. To clearly illustrate Zaitsev's Rule, there must be at least two possible alkene products with different levels of substitution, and the most highly substituted must be the major product.

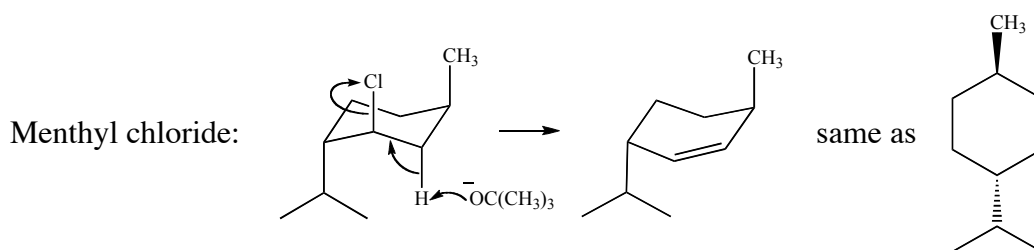


8. In an E2 reaction, the nature of the leaving group can influence which alkene product is major because the leaving group is departing in the same mechanism step in which the alkene is formed. In an E1 reaction, the leaving group has departed before the alkene is formed, so the leaving group has little if any influence on which alkene product is major.

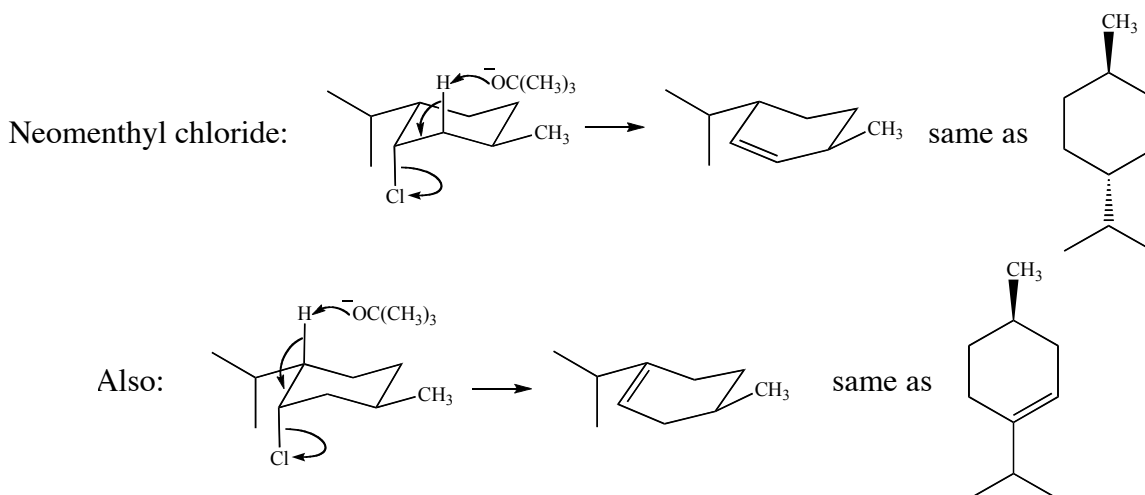


Carbocations are very strongly driven to lose a proton (they have very low pK_a) that just about any species in the reaction with an electron pair is sufficient to deprotonate them. In this case the carbocation can be deprotonated by CH_3OH (as shown) or by Br^- . CH_3OH is the reaction solvent and therefore present in much higher concentration than Br^- . Thus the carbocation is more likely to encounter (and thus be deprotonated by) CH_3OH than by Br^- . The mechanism shows this.

10. Recall that an E2 reaction requires the C–H bond and C–Cl bond to be anti to each other. (Review the E2 transition state discussion in the Elimination Reactions Lecture Supplement.) Recall also that cyclohexane rings prefer a chair conformation. Thus, we must see if there are any chair conformations that have an anti periplanar arrangement of the C–H and C–Cl bonds. Explore a model of cyclohexane to convince yourself that this can only occur when the C–Cl and C–H bonds are both axial.

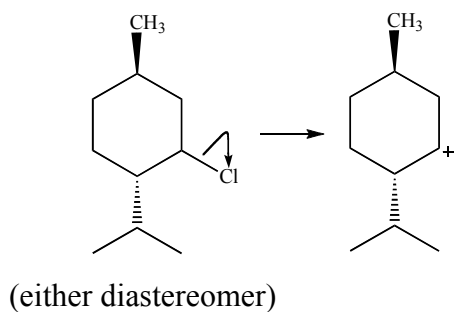


Thus, we see only one alkene product from this reaction because there is only one hydrogen atom that is anti-periplanar to the leaving group. The more stable trisubstituted alkene cannot form because the C–H bond next to the isopropyl group cannot become anti-periplanar to the C–Cl bond.

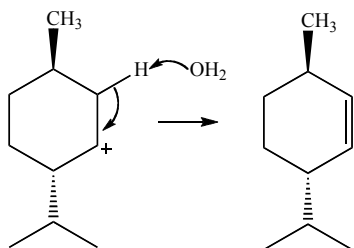


Thus, we expect to see two alkene products from this E2 reaction. But which is the major one? Because the base is sterically hindered, Hofmann elimination dominates (i.e., the least substituted alkene is the major product).

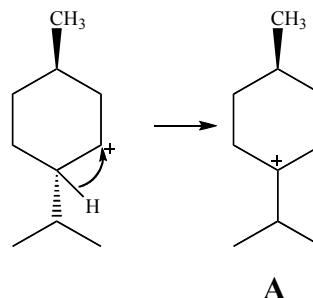
11. E1 elimination proceeds via a carbocation. Once the carbocation is formed, think about the three carbocation fates. Since we are considering only elimination and not substitution in this case, we need only think about lose a proton to make a pi bond and rearrange; we can ignore capture a nucleophile.



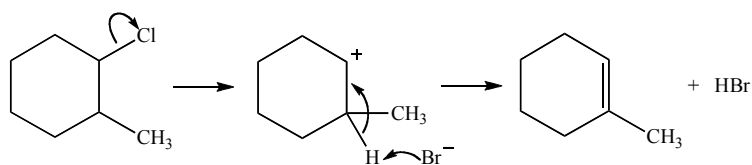
Lose a proton to form a pi bond:



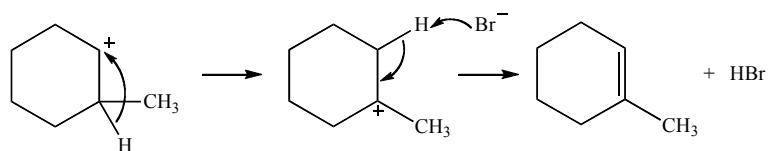
Rearrange (2° to 3° in this case):



We must now consider the three fates of this new tertiary carbocation **A**. Once again, we ignore capture a nucleophile. A more stable carbocation (2° with resonance or 3°



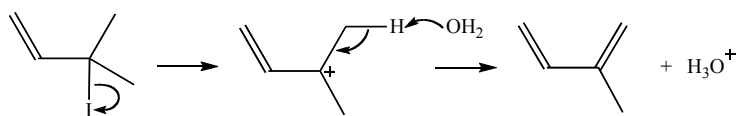
Carbocation rearrangement is possible, but its presence is invisible because it leads to the same major product:



(b) When considering elimination reaction mechanisms, we consider E2 before E1. The absence of strong base indicates this cannot be an E2 reaction. The E1 requirements are:

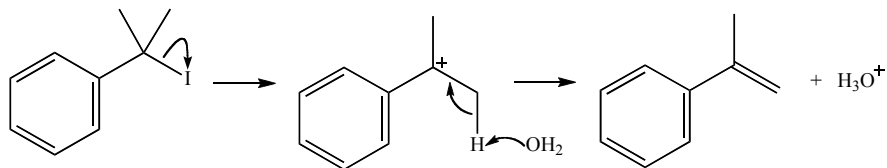
- Moderate or better leaving group (iodide ion is among the best);
- Stable carbocation (the carbocation intermediate is 3° with resonance); and
- Polar solvent (the solvent is a mixture of water ($\epsilon = 80$) and DMF ($\epsilon = 37$), so its ϵ is somewhere between the two. The exact value of ϵ depends upon the water: DMF ratio).

The reaction therefore occurs by the E1 mechanism.



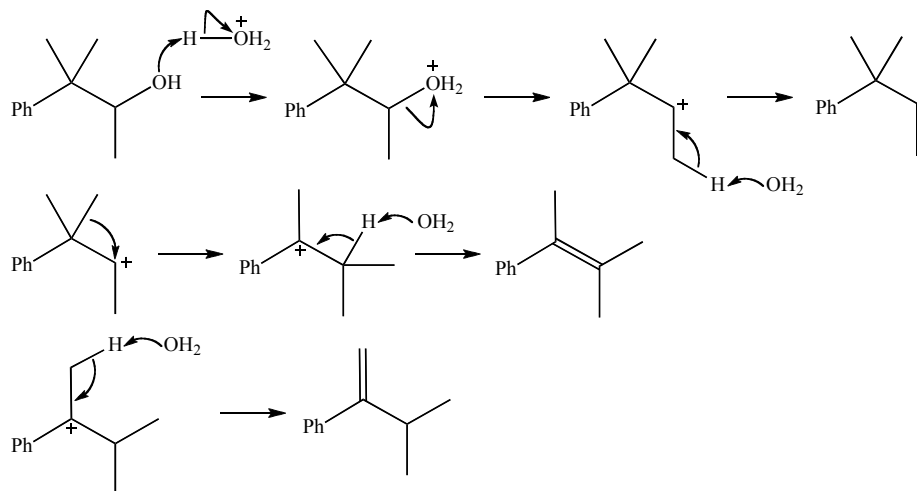
Any base that was present at the start of the reaction or generated during the reaction can be used for the deprotonation step. Carbocations are very reactive, so even weak bases (iodide ion, water, or even DMF) can perform the deprotonation that produces a full octet on carbon.

(c) This is an E1 reaction, because there is no strong base present.

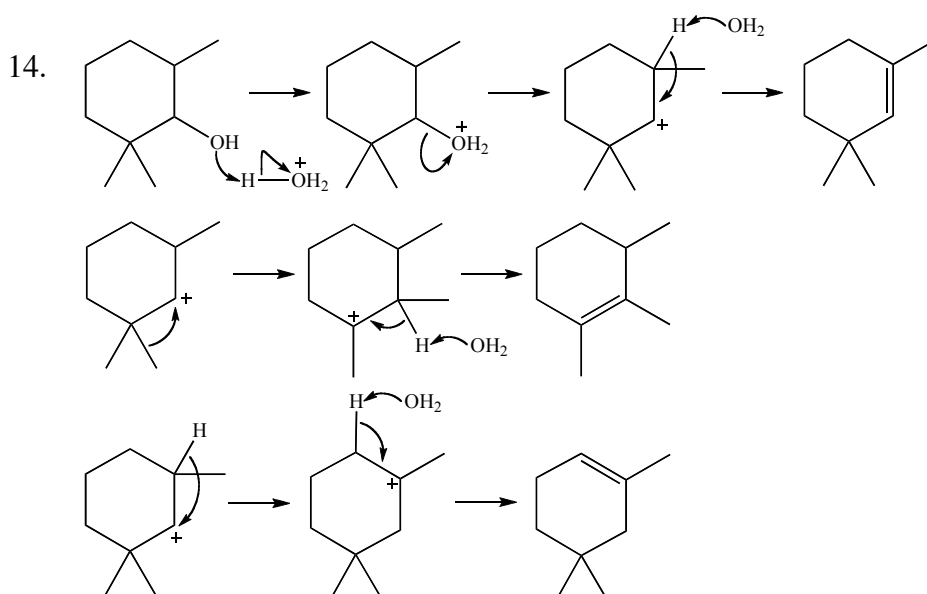


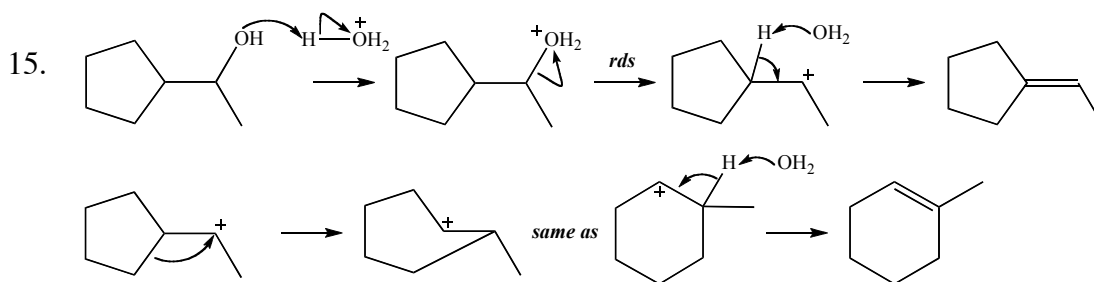
(d) The mechanism cannot be E2 because no strong base is present.

In water, H_2SO_4 ($\text{p}K_a$ -9) is completely ionized to form H_3O^+ ($\text{p}K_a$ -1.78). Only in instances in which there is no water, or in which the number of moles of water is less than the number of moles of H_2SO_4 are there any non-ionized H_2SO_4 in solution. Thus, in aqueous H_2SO_4 , the material that protonates the alcohol is H_3O^+ , not H_2SO_4 .



13. The reaction involves elimination of water from an alcohol to form an alkene. In the absence of acid, the leaving group is hydroxide ion. This is a very poor leaving group (due to the small atomic radius of oxygen, and the change from neutral to negative charge) and in conjunction with the energetically expensive process of carbocation formation, does not allow the reaction to proceed. Protonation of the alcohol by acid converts the leaving group into water. Water is a moderate leaving group because the charge of the oxygen atom changes from positive to neutral when it leaves. That water is a better leaving group than hydroxide ion helps to overcome the difficulty in forming the carbocation, so the reaction can proceed.

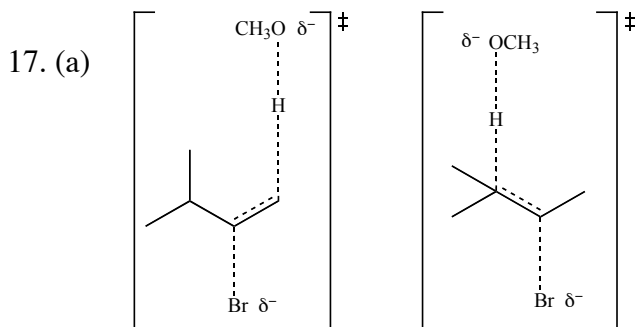
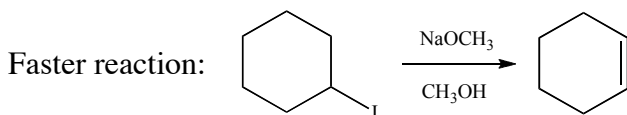




16. These are obviously elimination reactions. When analyzing elimination mechanisms, we consider E2 before E1. The E2 requirements are:

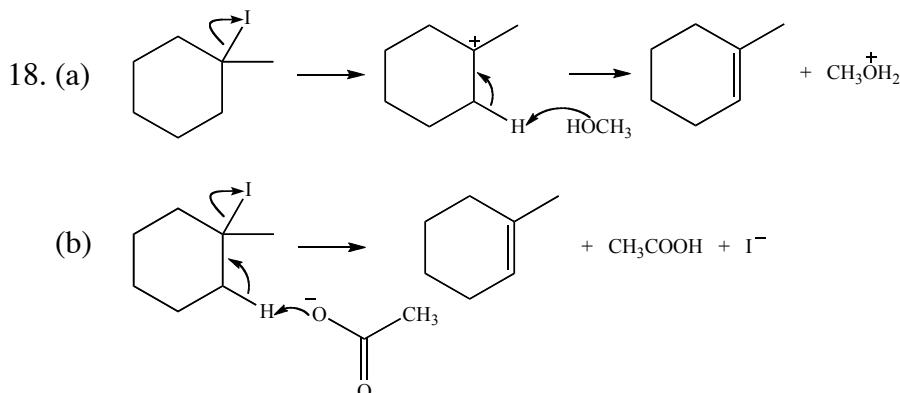
- Moderate or better leaving group (HO^- is very poor; Cl^- is moderate),
- Good base (CH_3O^- is a strong base), and
- H-C-C-LG arrangement (present).

Thus we predict that cyclohexyl chloride reaction can occur by the E2 mechanism and cyclohexanol reaction cannot. The cyclohexanol reaction cannot occur by the E1 mechanism under these conditions because hydroxide ion is a poor leaving group. Thus the cyclohexyl chloride reaction is faster because the cyclohexanol reaction cannot occur at all under the given reaction conditions, regardless of mechanism. We can accelerate this E2 reaction by using a better leaving group (illustrated below).



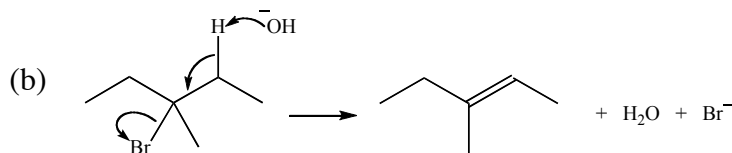
(b) The E1 reaction mechanism involves the energetically expensive step of carbocation formation. E2 avoids this step, and so is energetically cheaper. Thus, if other reaction conditions allow, an elimination reaction usually proceeds by the E2 mechanism in preference to the E1 mechanism. (Under conditions where both are allowed both mechanisms may operate simultaneously). For an elimination to proceed via the E2 mechanism, there are three requirements: strong base (methoxide ion is present), moderate or better leaving group (Br^-), and the leaving group

must be beta to the hydrogen being removed (H-C-C-LG arrangement). All of these requirements are met, so the E2 mechanism predominates in this case.



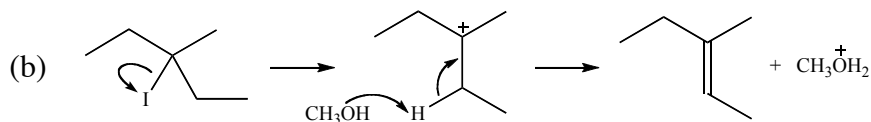
(c) An E2 elimination requires a moderate or better leaving group (iodide ion), H-C-C-LG arrangement, and a good base. Acetate ion is a modest base, but iodide is an excellent leaving group. Therefore, the reaction can occur by the E2 mechanism. The E1 mechanism requires a moderate or better leaving group (iodide ion), polar solvent (methanol), and stable carbocation (tertiary). These requirements are met, so the reaction can occur by the E1 mechanism. Given a choice, we predict the reaction occurs by the E2 mechanism because this avoids the energetically expensive step of carbocation formation. However, E2 is slowed in this case because acetate is a modest base. Thus, the reaction might occur by either mechanism.

19. (a) The first alkene is more substituted and is therefore the major product.



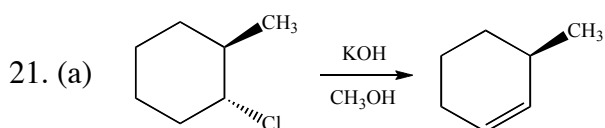
(c) This is an elimination reaction. The common elimination mechanisms are E2 and E1. We consider E2 before E1, because E2 is less energetically expensive (no carbocation formation). E2 requires a strong base (HO⁻), a moderate or better leaving group (Br⁻), and H-C-C-LG arrangement. These are all present, so the reaction proceeds via the E2 mechanism.

20. (a) The more substituted alkene (the alkene on the right) is the major product.

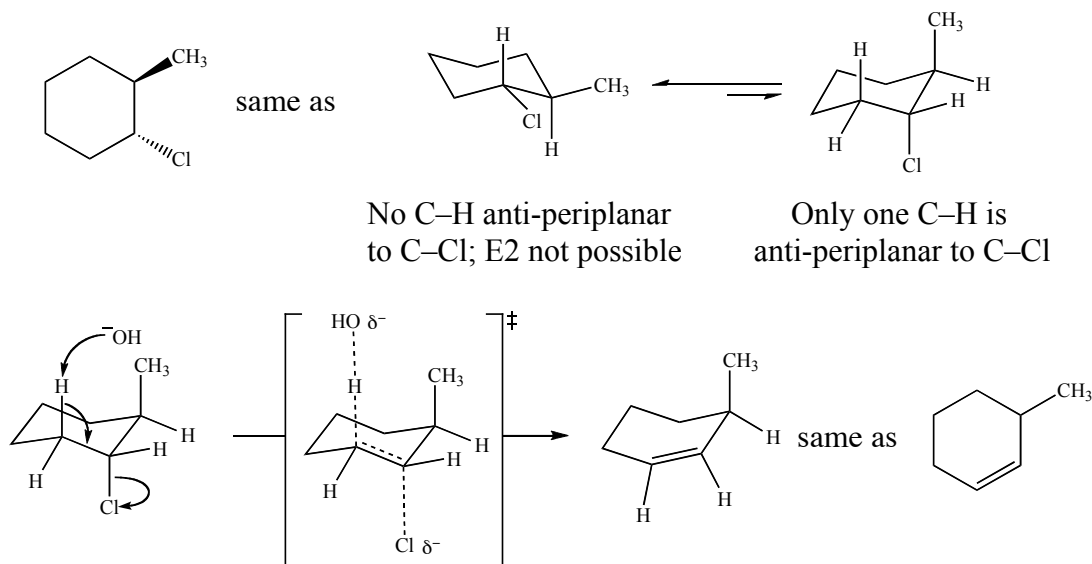


The carbocation can also be deprotonated by iodide ion, but it is less prevalent than CH_3OH (the solvent). The carbocation most likely encounters a molecule of methanol before an iodide ion.

- (c) The reaction mechanism cannot be $\text{S}_{\text{N}}1$ or $\text{S}_{\text{N}}2$ because this is an elimination, not a substitution, reaction. When deciding between E2 and E1, we examine E2 first, because it is less energetically demanding (no carbocation is formed). E2 requires a strong base, moderate or better leaving group, and H-C-C-LG arrangement. There is no strong base present, so E2 is ruled out. (CH_3OH is a weak base; CH_3O^- is a strong base, but is not present). E1 requires moderate or better leaving group, stable carbocation, and polar solvent, all of which are present in this case.

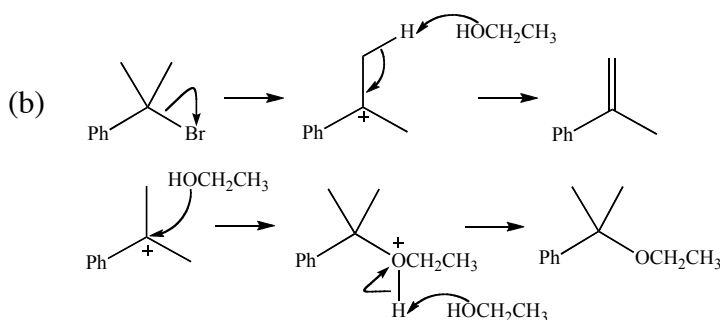
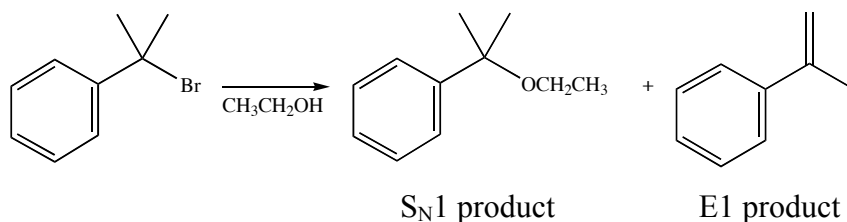


- (b) In an E2 reaction, the C-H and C-LG bonds being broken must be periplanar. In a cyclohexane ring, this can only be achieved when both bonds are axial. The C-H next to the methyl cannot be axial at the same time as the C-Cl bond thus the trisubstituted alkene (1-methylcyclohexene) cannot form in this case.



- (c) This is an elimination reaction so the mechanism choices are E2 and E1. We consider E2 before E1 because E2 avoids the energetically expensive step of carbocation formation. E2 requires strong base (HO^- is strong), H-C-C-LG (present), and moderate or better leaving group (Cl^- is a moderate leaving group). The E2 requirements are satisfied so we predict the E2 mechanism dominates.

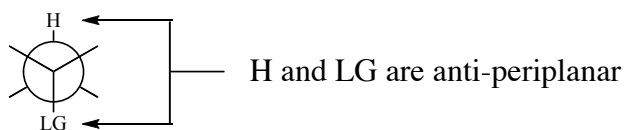
22. (a) Mechanism analysis suggests this to be an E1/S_N1 reaction.



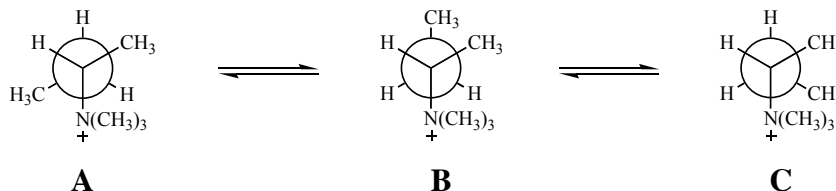
(c) S_N2: Ethanol (CH₃CH₂OH) is a poor nucleophile. Bromide is not a good enough leaving group to overcome this poor nucleophilicity, so S_N2 is ruled out. More obviously, the carbon bearing the leaving group is 3°!

E2: Ethanol is a poor base. Bromide is not a good enough leaving group to overcome this poor basicity, so E2 is eliminated (if you will pardon the pun).

23. Recall that E2 elimination requires a periplanar alignment (dihedral angle of 0° or 180°) for the C–H and C–LG bonds that are being broken. A Newman projection viewed along the carbon-carbon bond bearing both the hydrogen removed and the leaving group looks like this gauche conformation:

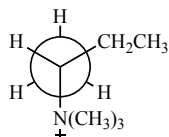


Any C_{sp3}–C_{sp3} bond has just three gauche conformations like this. Here are the three staggered conformations along the C2–C3 bond of 2-butanamine that might lead to 2-butene.

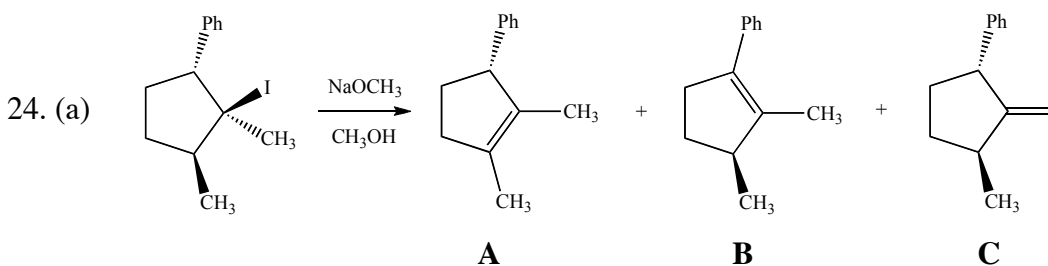


The $\text{N}(\text{CH}_3)_3$ group is larger than a methyl group, so conformation **B** has less torsional strain than conformations **A** and **C**. The molecule spends most of its time in conformation **B**, and only rarely is found in conformations **A** or **C**. Conformation **B** does not lead to elimination because there are no β -hydrogen atoms that are periplanar to the leaving group. Therefore elimination to form 2-butene is slow because the molecule does not spend much time in a conformation that can lead to this product.

All three of staggered conformations of the C1–C2 bond of 2-butanamine look alike.



All of these conformations have a β -hydrogen that is periplanar to the leaving group, so regardless of conformation elimination to form 1-butene can happen anytime the base approaches. Formation of 1-butene is therefore the major reaction pathway.



(b) Conjugation of the alkene with the phenyl group favors enhances the amount of **B** produced, but not the amounts of **A** or **C**.

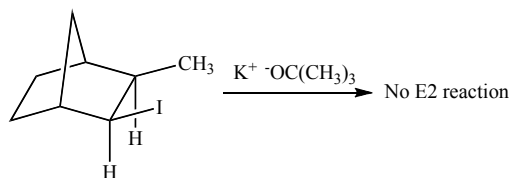
(c) Alkenes **A** and **C** result from an anti-periplanar alignment of the carbon-leaving group and carbon- β -hydrogen bonds. Formation of alkene **B** requires a syn-periplanar arrangement of these bonds. An anti-periplanar alignment has less torsional strain than a syn-periplanar alignment, so the bond alignment favors **A** and **C** and disfavors **B**.

(d) Product **A** is not conjugated, but it comes from an anti-periplanar transition state (less torsional strain). Product **B** is conjugated but comes from a syn-periplanar transition state (more torsional strain). Therefore our prediction of major product depends on which factor we assume has a greater amount of influence. If torsional strain carries more weight than conjugation, then product **A** is major. If conjugation carries more weight than torsional strain, then product **B** is major.

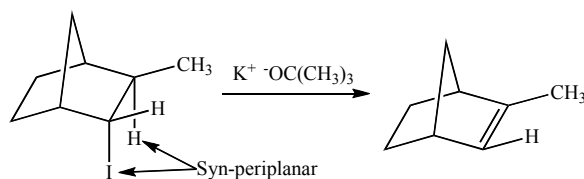
Product **C** is formed in the least amount because it is a terminal, disubstituted, and nonconjugated alkene.

(e) The product with the most number of vinylic hydrogens (hydrogens attached to the alkene carbons) is **C**. This is the major product under Hofmann conditions, so it will be major when the base highly hindered, such as $\text{K}^+ \text{OC}(\text{CH}_3)_3$.

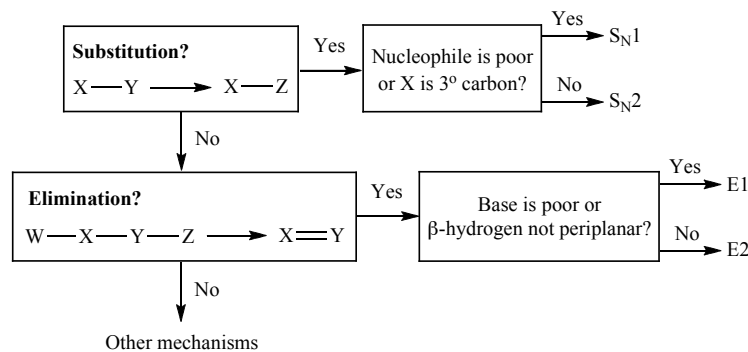
25. The leaving group of alkyl iodide **A** is not periplanar to any β -hydrogen, so E2 elimination is not possible. Therefore alkyl iodide **A** does not react.



In alkyl iodide **B**, the β -hydrogen next to the methyl group is syn-periplanar to the leaving group, so E2 is possible:



26. The flowchart format shown here is just one of many possible formats.



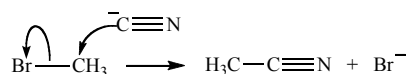
27. Recall that we consider the substitution/elimination mechanism possibilities in the order listed below. In each case, the requirements for that mechanism to occur are noted. If one of the requirements is not met, then the reaction cannot occur by that mechanism. *The flowchart developed in the previous question may be useful here!*

- E2: strong base; $\text{H}-\text{C}-\text{C}-\text{LG}$; moderate or better leaving group.
- $\text{S}_{\text{N}}2$: good nucleophile; moderate or better leaving group; carbon undergoing substitution not 3° . An aprotic solvent is better than a protic solvent, but a protic solvent does not necessarily prevent $\text{S}_{\text{N}}2$. Moderate solvent polarity is best ($\epsilon \sim 20$ to 40), when the reaction involves a negatively charged nucleophile and neutral electrophile. (Other charge combinations may call for high solvent polarity.)

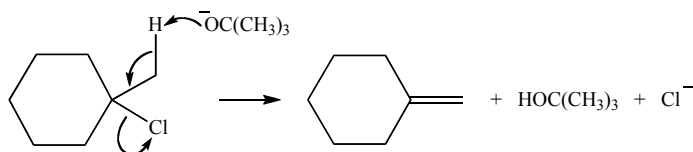
- E1/S_N1: stable carbocation; moderate or better leaving group; polar solvent

(a) E2: lacks the H-C-C-LG arrangement.

S_N2: has good nucleophile (cyanide ion), has little steric hindrance (CH₃), and a moderate leaving group (Br⁻). The solvent is protic and has modest polarity (ε = 28), which is acceptable for an S_N2 reaction with Br⁻. Therefore this is an S_N2 reaction.



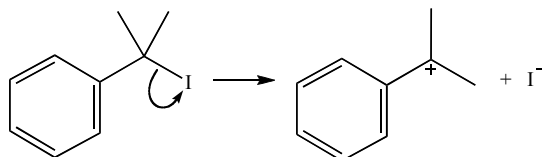
(b) E2: strong base (*tert*-butoxide); moderate or better leaving group (Cl); H-C-C-LG arrangement present. (Hydrogen bonding by a protic solvent reduces basicity in the same way it reduces nucleophilicity, but RO⁻ in ROH retains enough basicity for the E2 mechanism.) Therefore this is an E2 elimination. *Tert*-butoxide is a large base, so the Hofmann elimination product (less substituted alkene) is favored.



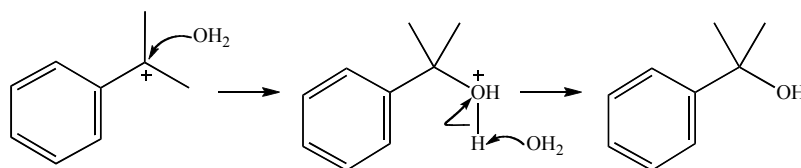
(c) E2: no strong base.

S_N2: no good nucleophile.

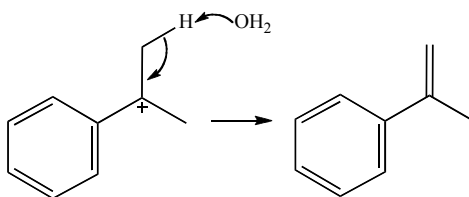
E1/S_N1: The carbocation is easily formed (3° with resonance), moderate or better leaving group (I), and polar solvent (water). Thus, the reaction proceeds via the E1/S_N1 mechanisms.



Remember the three carbocation fates! This carbocation cannot rearrange to become more stable. Iodide capture returns it to starting material. So we need to consider water capture.



Or losing a proton to form a pi bond:



(d) E2: no strong base.

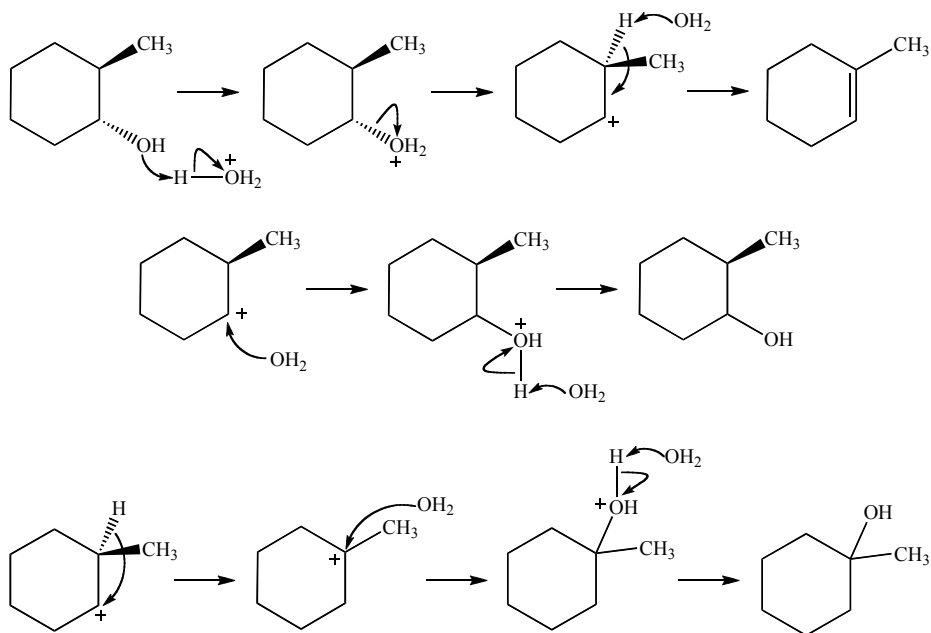
S_N2: no moderate or better leaving group.

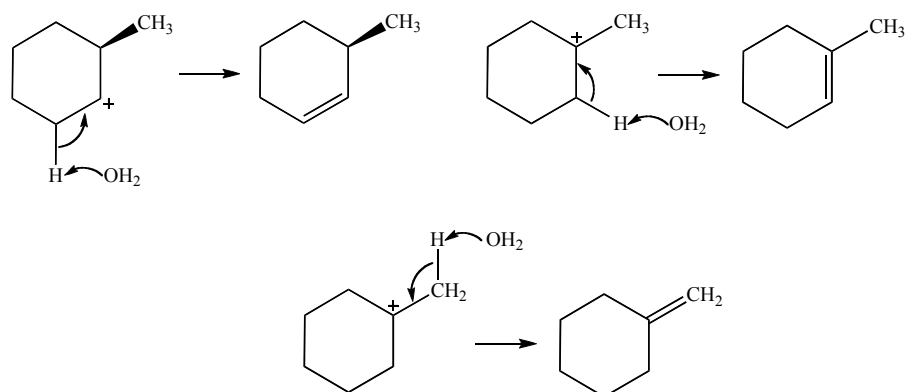
E1/S_N1: the methyl carbocation is too unstable to form. None of these three mechanisms can operate, so this is a case of no reaction.

(e) E2: No strong base.

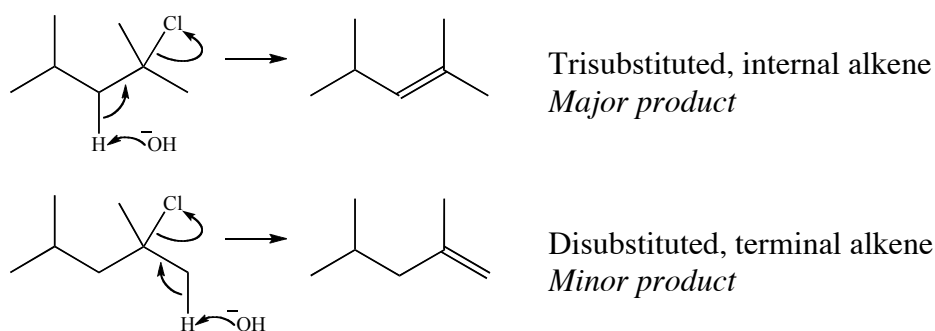
S_N2: no strong nucleophile.

E1/S_N1: protonation of the OH affords water (a moderate leaving group), loss of which leads to a secondary carbocation. Water is a polar solvent. So we conclude E1/S_N1 to be reasonable in this case. Because S_N1 and E1 compete, we cannot easily predict the major product. Recall, however, the among the E1 products, the more highly substituted alkene is more stable and therefore is produced in a greater amount than other alkenes.





- (f) E2: Strong base (HO^-), H-C-C-LG (present), and moderate or better leaving group (Cl is moderate). The E2 requirements are met, so we predict E2 is the major mechanism.

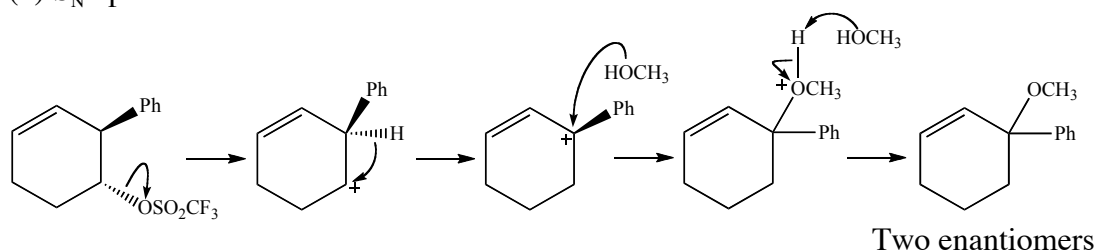


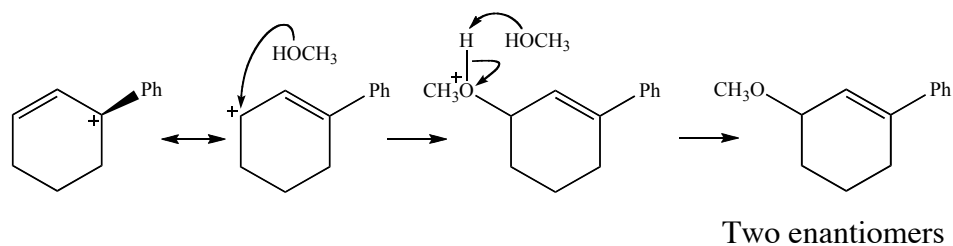
28. (a) E2: Good leaving group and periplanar β -hydrogen.

S_N2: Good leaving group attached to a carbon that is not tertiary.

E1 and S_N1: Good leaving group, polar solvent, and resonance-stabilized secondary carbocation intermediate. (A tertiary carbocation with resonance stabilization is also an intermediate, but because this carbocation is not formed in the rate-determining step, its presence does not have a significant impact on the reaction rate.) *These mechanisms have the same rate-determining step, so the reactant features that favor their operation are also the same.*

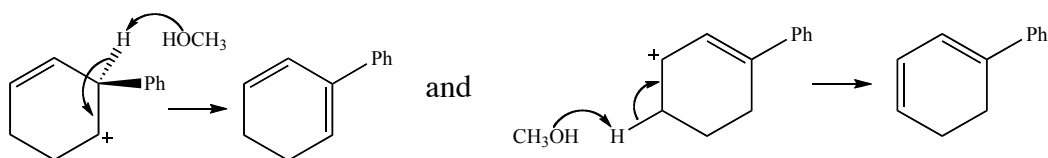
- (b) S_N1 products:



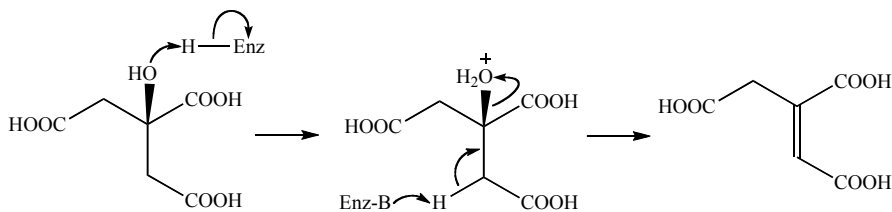


The carbocation rearrangement ($2^\circ \rightarrow 3^\circ$ with resonance) is very highly favored, so the 2° carbocation may not survive long enough to capture methanol.

E1 products:

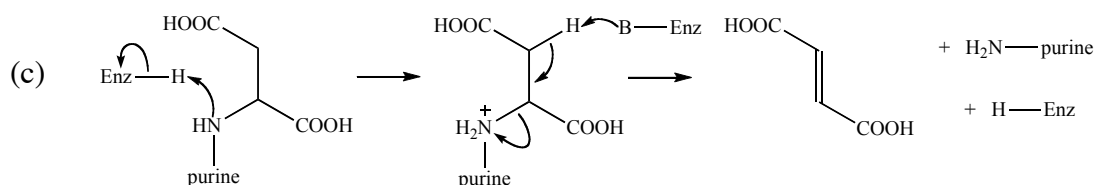


29. (a) The more probable mechanism is E2. (The answer to this question depends upon your assumptions.)
- (b) Given a choice between E1 and E2, an elimination reaction generally proceeds via the E2 mechanism because this avoids the energetically expensive step of carbocation formation. Thus, we can make some reasonable assumptions that allow the E2 mechanism to proceed. E2 requires:
- Moderate or better leaving group: Hydroxide is a poor leaving group, but protonation by aconitase converts hydroxide to water, a much better leaving group.
 - Strong base: No strong base is present. However, we might assume the enzyme assists its departure, probably by hydrogen bonding.
 - H-C-C-LG arrangement: This is present in citrate.
- (c) H-enz = acidic group in the enzyme active site. B-enz = basic group in the enzyme active site.

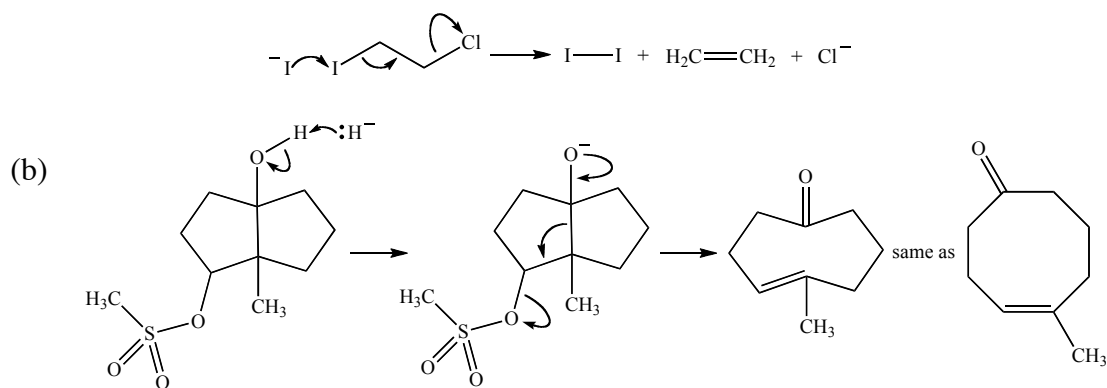


30. (a) This more probable mechanism for this elimination reaction is E2.

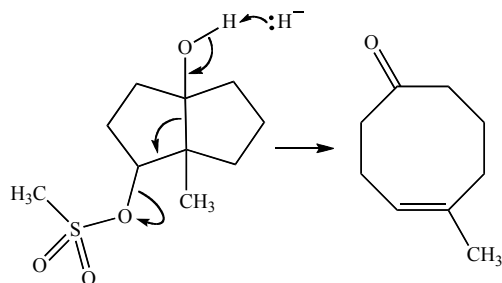
(b) E2 is generally less energetically expensive than E1. In addition, E1 involves carbocations, which may lead to undesirable side reactions such as capture of a nucleophile. Therefore we might reasonably assume that biological processes tend to favor E2 processes over E1 processes if possible. What assumptions do we need to make in order for this to be an E2 reaction? E2 requires a good base (assume the enzyme provides this, perhaps in the form of an amine), a moderate or better leaving group (the adenosine nitrogen that lies outside the ring may be protonated first) and a β -hydrogen (present).



31. (a) The rate expression includes both reactants, suggesting that the rate-determining step also includes both of these reactants. The most reasonable mechanism that gives the observed products and fits the rate law is:



A concerted mechanism in which the OH is deprotonated simultaneously with the fragmentation is also acceptable:



32. Because a more "polar" environment assists the ionization of the leaving group. Ha ha! (And yes, there are no polar bears in the Antarctic. And yes, there may soon be no polar bears in the Arctic, either.)