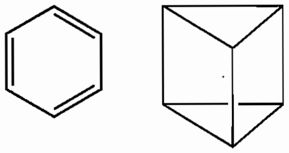
14

Aromaticity

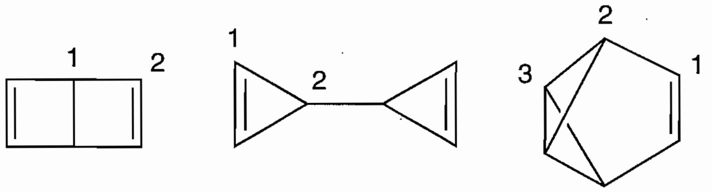
This chapter consists almost entirely of an exploration of the structural implications of the stabilizing effects of aromaticity. Reactivity does creep in, but only in a small way, as an introduction to the elaborate substitution reactions of Chapter 15. The following problems allow you to explore resonance and molecular orbital theory in order to find examples of molecules that possess the stabilizing quality called aromaticity. You will also get plenty of practice in drawing strange molecules of quite remarkable and varied structures. In addition, you will have a chance to work a bit on reactions. You will see the classic aromatic substitution process, as well as reactions that destroy the usually robust aromatic ring and reactions at the position adjacent to an aromatic ring, the "benzyl" position.

Problem 14.1 Cyclohexatriene and Ladenburg benzene each shows only a single ^{13}C NMR signal for its six equivalent carbons.

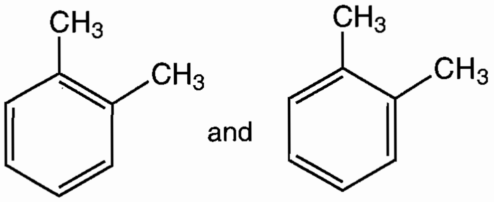


All carbons are
equivalent in each
of these molecules

Dewar benzene and bicyclopropenyl each have two different carbons, and benzvalene has three.



Problem 14.2 A Kekulé representation predicts two isomers of any 1,2-disubstituted benzene. In one, the two substituents, here methyl groups, are on the same double bond; in the other, they are on different double bonds.



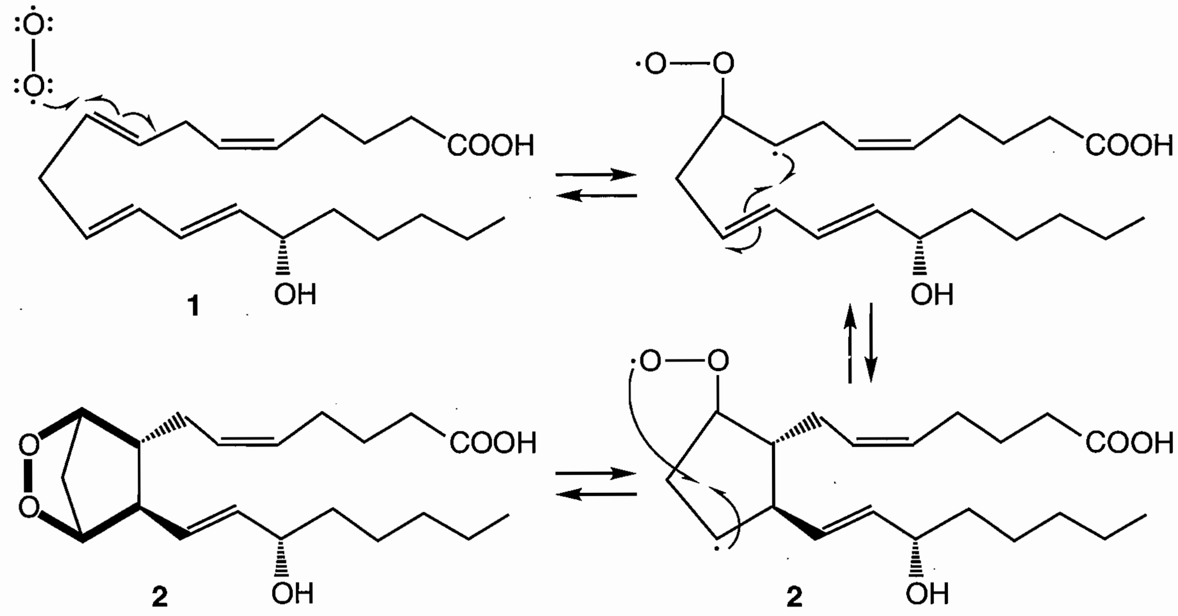
As there is only one real molecule, this poses severe problems for a 1,3,5-cyclohexatriene picture of benzene.

Problem 13.68 No, the LUMO density is about the same size on the two carbons that share the positive charge.

Problem 13.69 The product of the 1,4-addition is lower in energy because it has a more substituted double bond than the 1,2-addition product. The 1,4-addition product is not always the most stable. When we start with *trans*-1,3-pentadiene, the 1,4-addition and 1,2-addition products are both *trans*-4-bromo-2-pentene.

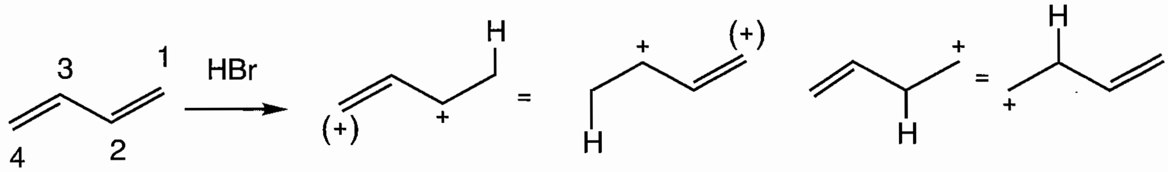
Problem 13.70 The nucleophile is the HOMO and it is located on the diene. The electrophile is the LUMO and it is located on the alkene (the dienophile). The diene is the nucleophile because the π electrons are more available from the HOMO of the conjugated system, particularly with the electron-donating group on the diene. The dienophile is the electrophile because the π orbitals that are empty are lower in energy. The carbonyl on the alkene is an electron-withdrawing group, which lowers the energy level of the empty orbital.

Problem 13.66 *(continued)*



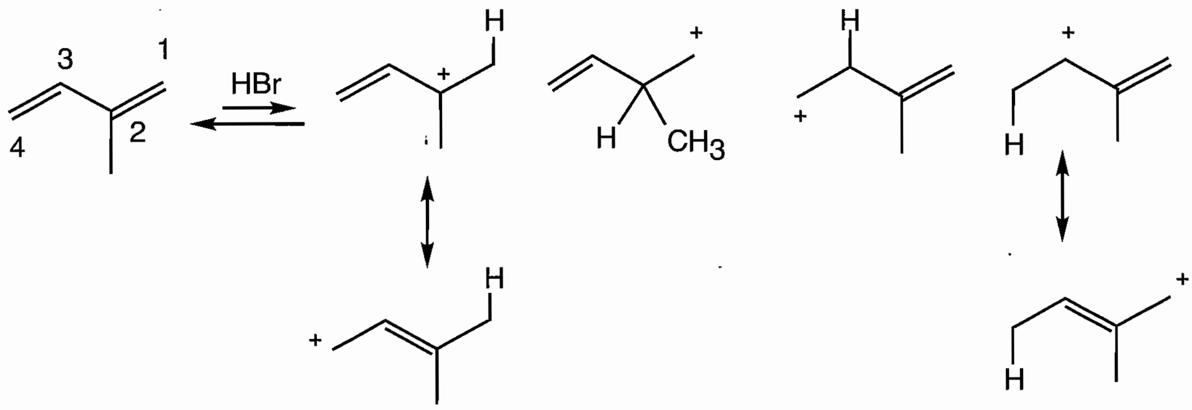
Problem 13.67

Protonation at: carbon 1 carbon 4 carbon 2 carbon 3



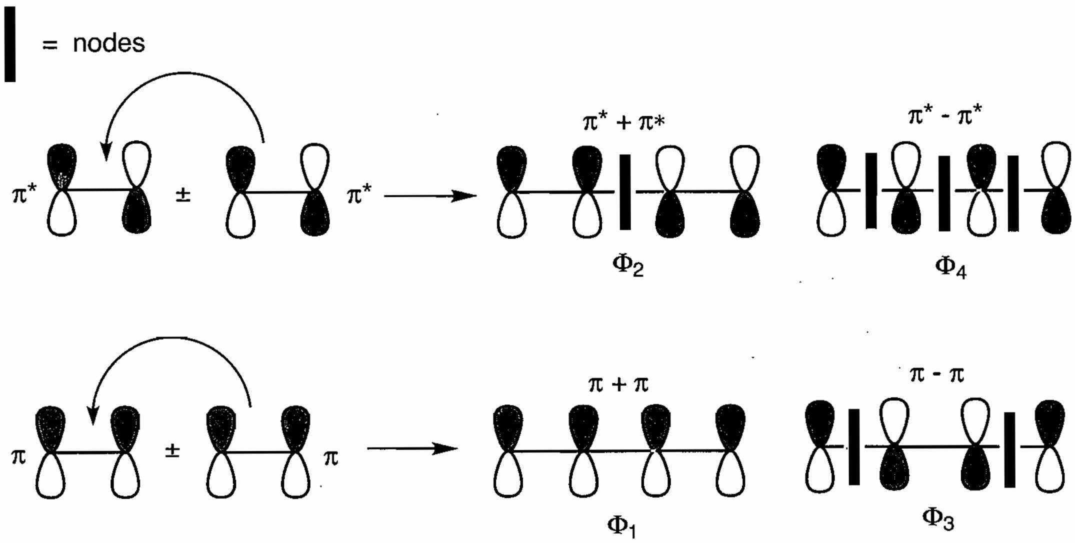
resonance stabilized—more stable

Protonation at: carbon 1 carbon 2 carbon 3 carbon 4

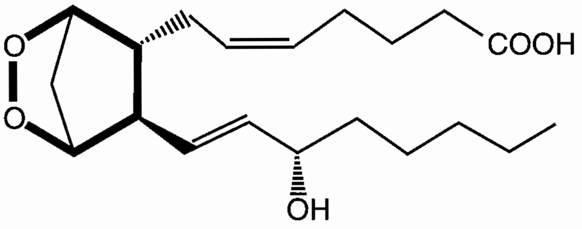


This one is the most stable.
Note the tertiary carbocation

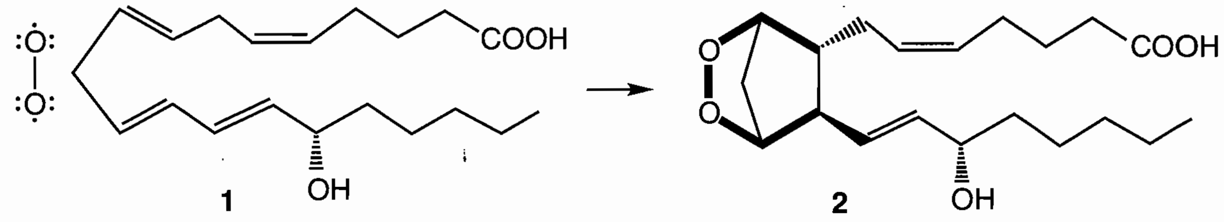
Problem 13.65 It is only necessary to interact the orbitals closest in energy: π ± π and π* ± π* in this case. The same four molecular orbitals result as in the procedure outlined in Figure 13.16, but they are not formed in the same order. The following figure shows the orbitals along with the nodes used to order them in energy.



Problem 13.66 The six-membered ring is shown in bold.



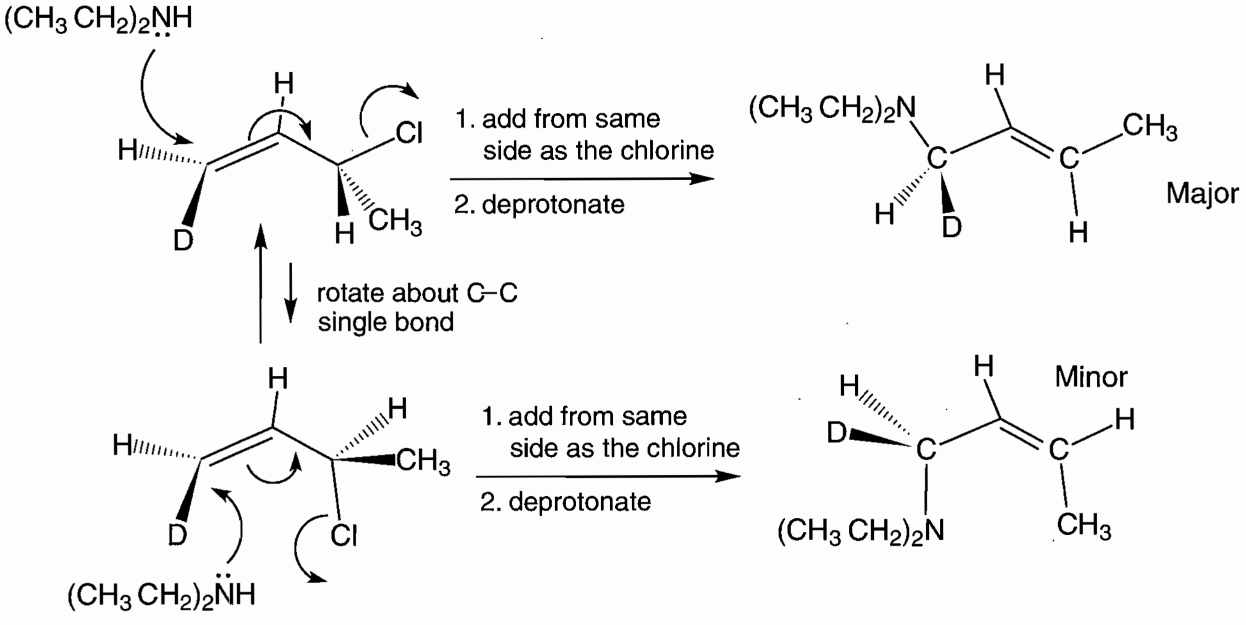
Oxygen must be reacting with compound **1** to give **2**.



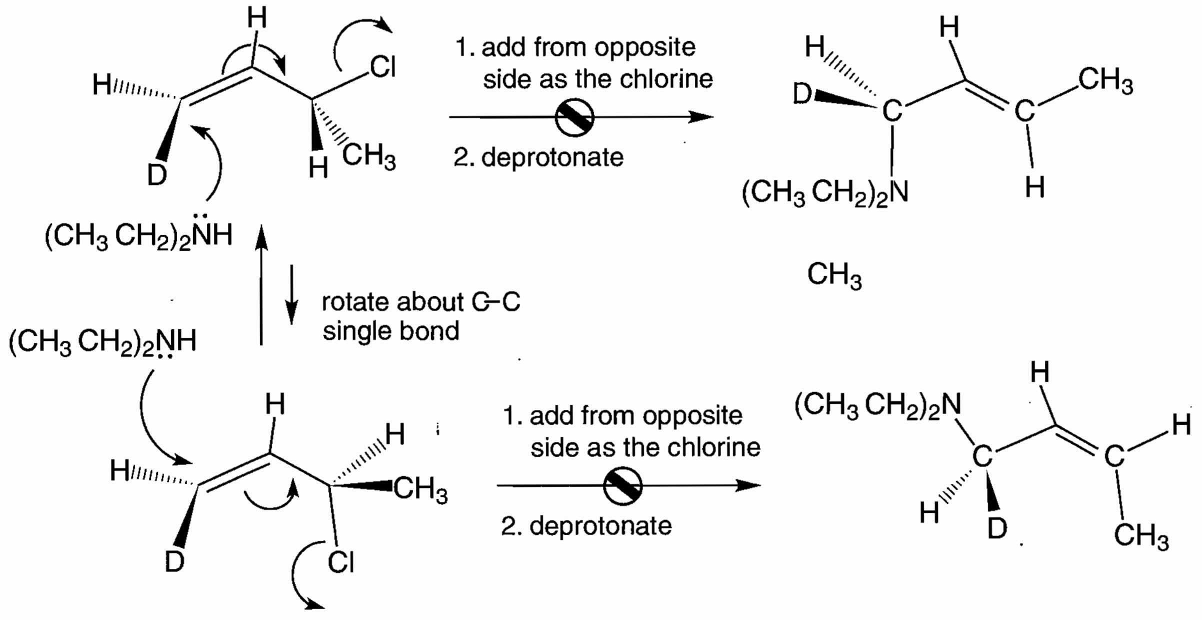
However, there are two reasons the reaction is not likely to be a simple Diels–Alder-related cycloaddition. First, oxygen is a triplet molecule, with two unpaired electrons. It cannot form **2** directly. Recall our discussion of singlet and triplet carbenes in Chapter 11 (p. 506ff). Second, a concerted cycloaddition would not give the observed trans stereochemistry of **2**. The mechanism probably involves a stepwise process as shown in the figure. Note that there must be an inversion of spin somewhere in the mechanism, and that steric factors will lead to trans stereochemistry in the ring closure step.

(continued)

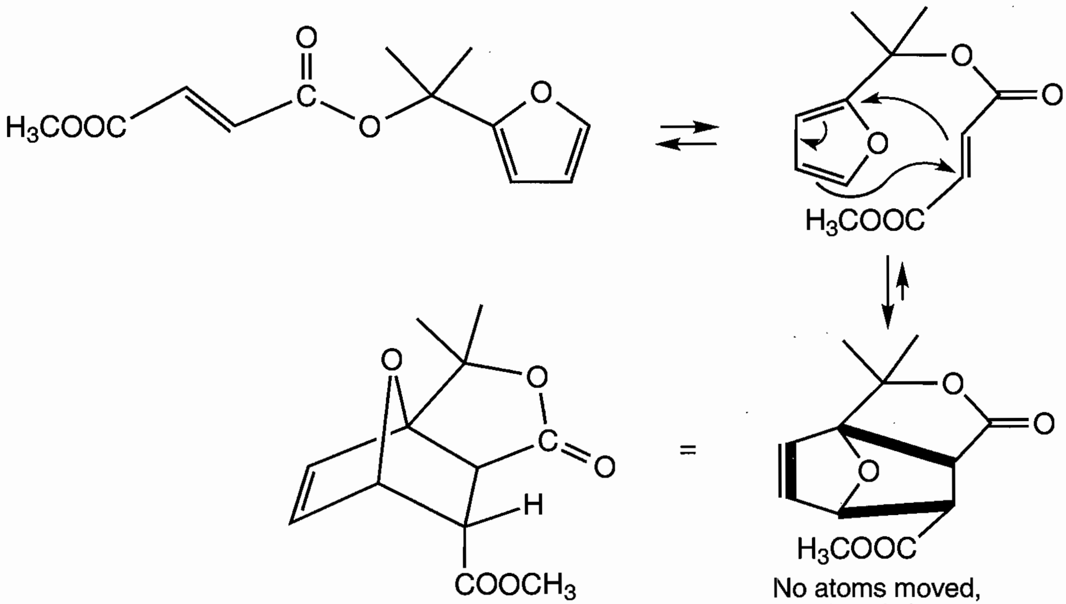
Problem 13.64 The data in the problem show that addition of the nucleophile is from the same side as the chlorine. The two products result from the presence of two rotational isomers of the starting material. In each case, diethylamine adds from the same side as chlorine.



If addition had been from the opposite side, different products would have been observed.

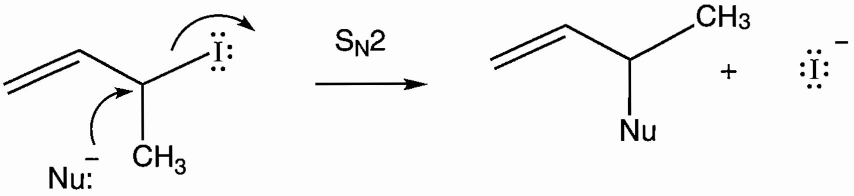


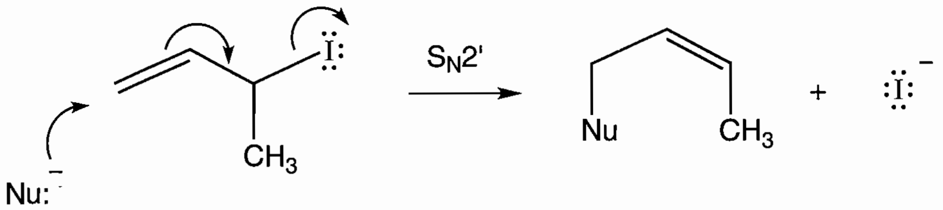
(d) This final transformation is also an example of the intramolecular Diels–Alder reaction, with the furan ring acting as the diene. Once again, it is necessary to draw the molecule in an arrangement that shows the proximity of the diene and dienophile. The product of the Diels–Alder reaction is first drawn without moving any atoms, then relaxed to a more realistic picture. This technique is very useful.



No atoms moved,
new bonds in boldface

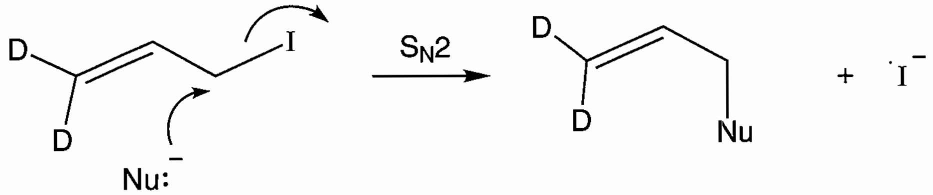
Problem 13.62 We need a label, and almost any will do. A methyl group would work. For example,

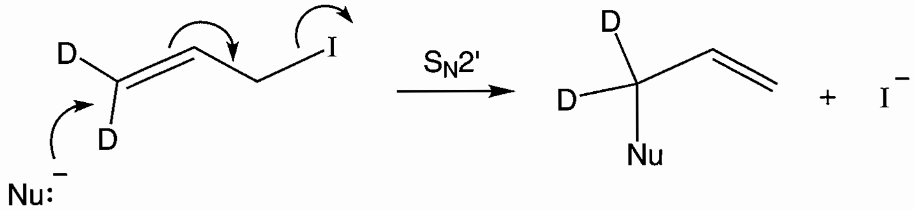




Now the two products are not the same, and we can tell which reaction is operative.

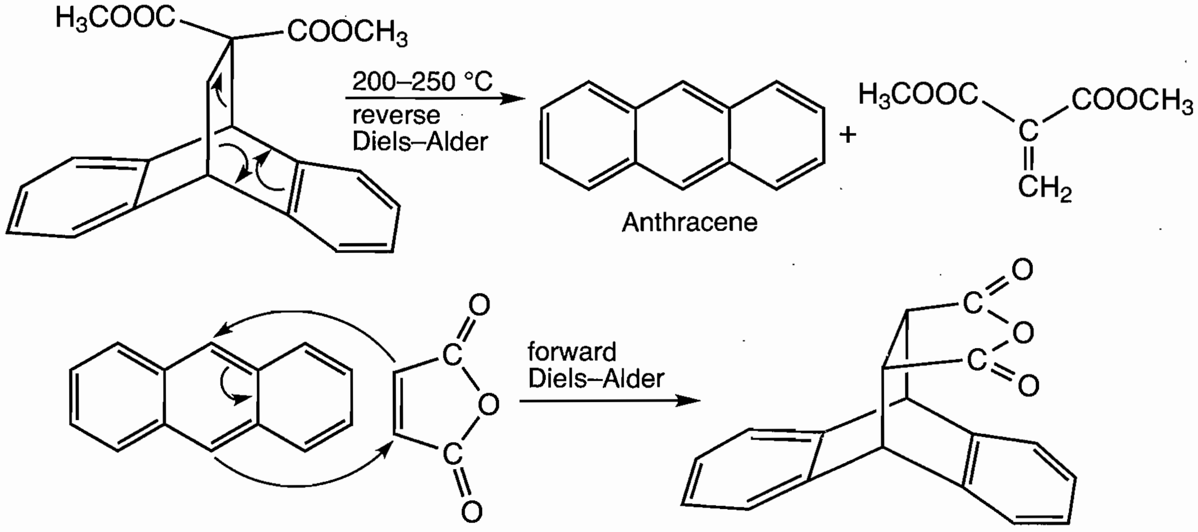
Problem 13.63 An easy one for a change. Any of a large number of possible labeling experiments will work. Here is one suggestion.



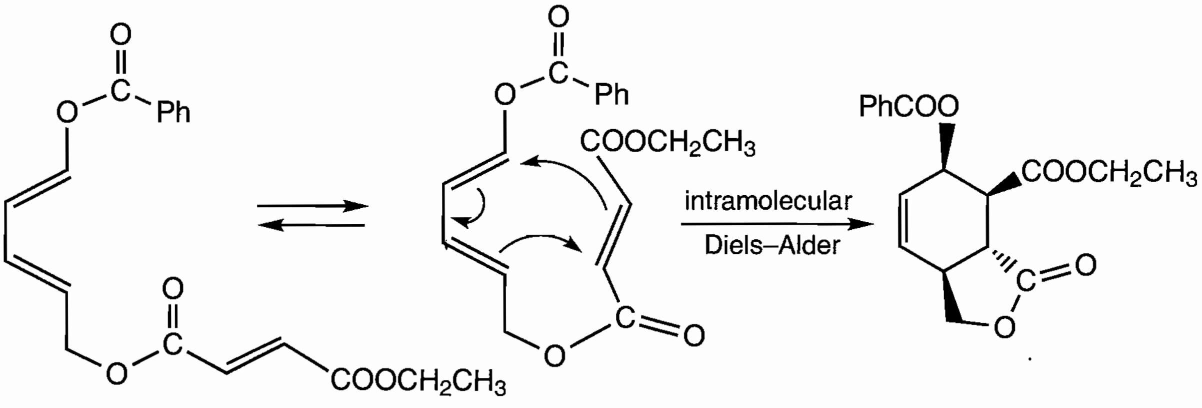


Problem 13.61 *(continued)*

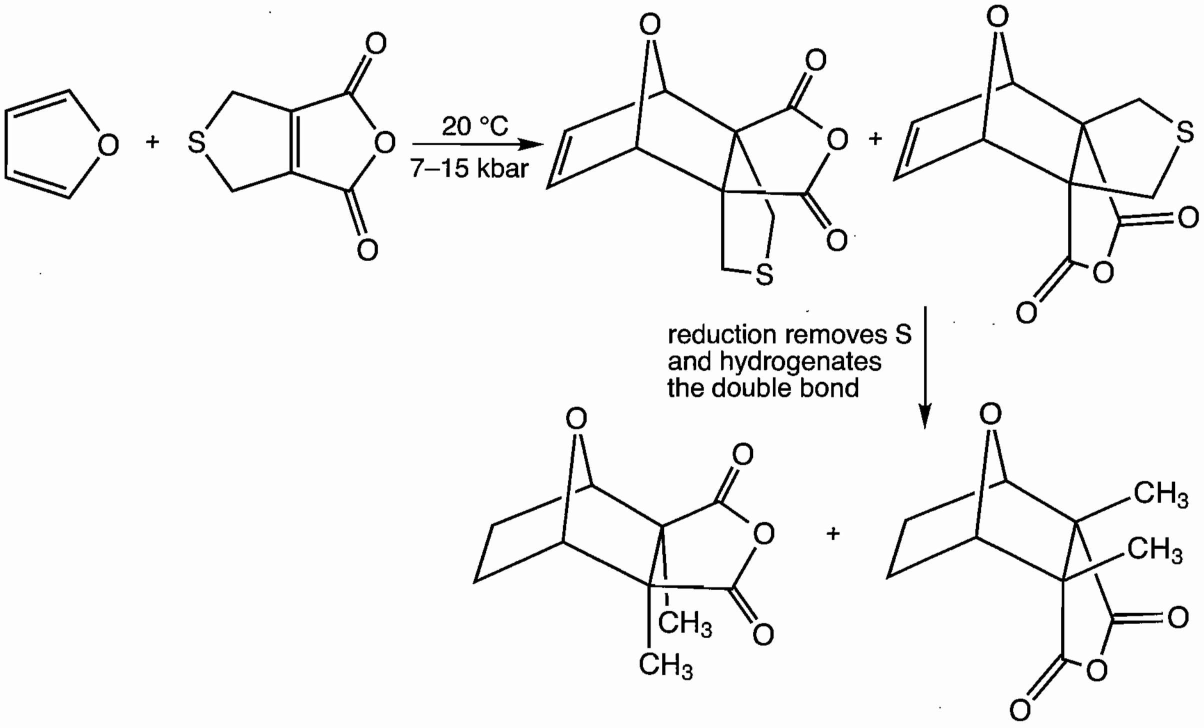
(b) This part also involves a reverse Diels–Alder reaction. In this case, the anthracene formed by the reverse reaction is captured in a "forward" Diels–Alder by maleic anhydride. A good clue here is the structure of the second product. Ask yourself how it can arise from starting material, and the reverse Diels–Alder reaction should appear. Alternatively, work backward. Ask what compounds can react to give the final adduct. The answer is maleic anhydride and anthracene. Again the need to make anthracene from starting material should suggest a reverse Diels–Alder reaction.



(c) Here we have an intramolecular Diels–Alder reaction. These reactions are notoriously hard to see, especially at the beginning. The reaction is certainly easier to see if the starting material is drawn in a "suggestive" way (as it almost never is in problems!). *Aside:* Notice that the one-step nature of the Diels–Alder reactions allows us to fix the stereochemistry at four different atoms (the termini where the new σ bonds are made) in this reaction. That's quite a synthetic advantage.

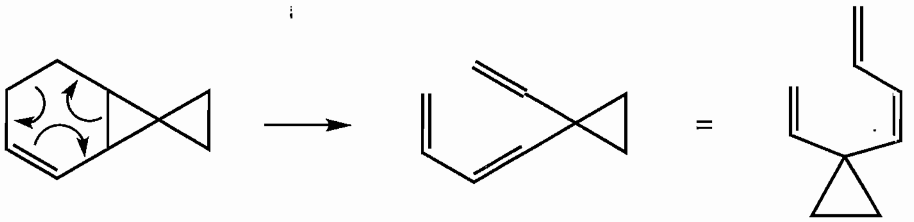


Reactions such as the Diels–Alder reaction, which proceed with a net decrease in volume (two molecules are made into one), can be accelerated under high pressure. This Diels–Alder reaction fails even at pressures up to 40 kbar. However, this synthetic problem was finally solved by William Dauben and his co-workers at Berkeley. Dauben's group used a dienophile with fewer steric problems, along with high pressure. This is *not* a route you were expected to think up! If you came up with the reasonable ideas shown earlier, you did just fine.



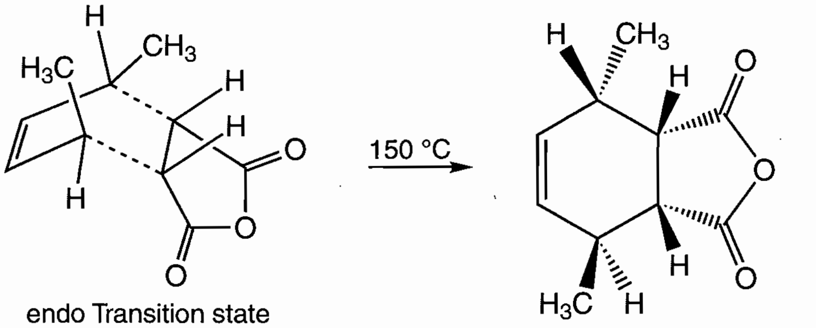
The desired exo compound could be crystallized from the mixture and isolated in 51%–63% yield.

Problem 13.61 (a) This is a simple reverse Diels–Alder reaction brilliantly camouflaged by the molecular architecture. The lesson here is that every time you see a cyclohexene, THINK REVERSE DIELS–ALDER! *All* cyclohexenes are conceptually related to a 1,3-diene and a dienophile. The thermodynamic driving force for this reaction is the strain relief in opening one three-membered ring. In the answer, the product is first drawn without moving any atoms, then "relaxed" to the real structure.



(continued)

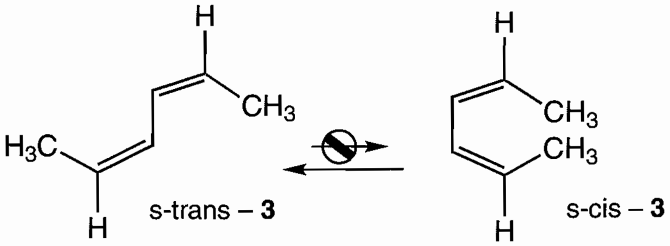
Problem 13.59 *(continued)*



endo Transition state

Product from endo transition state is formed

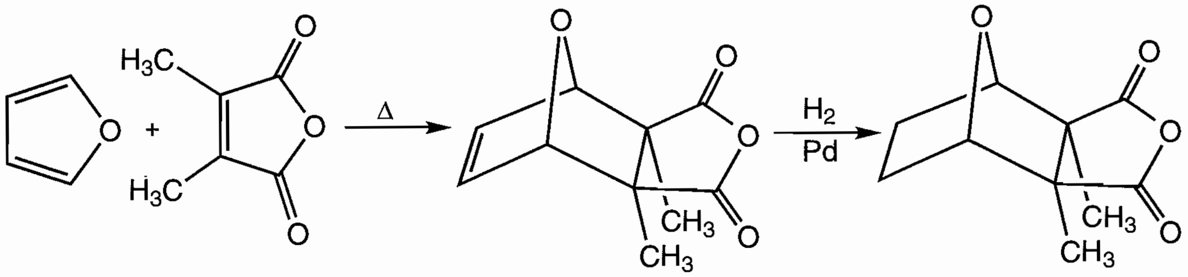
In **3**, both methyl groups must be "inside." We predict that this arrangement is too destabilizing and that no significant amount of Diels–Alder product would be formed at 150 °C. Though this diene was not examined by Alder, there is ample evidence from other examples that this notion is correct.



s-trans – **3**

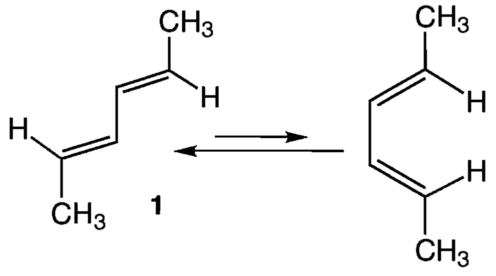
s-cis – **3**

Problem 13.60 If you proposed a Diels–Alder reaction of furan with dimethylmaleic anhydride, followed by catalytic hydrogenation of the carbon–carbon double bond, you'd be in very good company. This route was proposed as early as 1928.

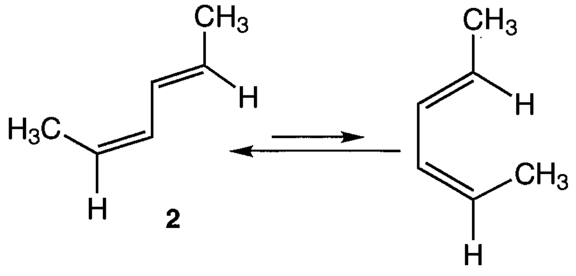


Unfortunately, the required Diels–Alder reaction was not successful. Dimethylmaleic anhydride is a poor dienophile, presumably because of steric destabilization introduced by the two methyl groups. In addition, cycloadducts of furan are prone to undergo retro Diels–Alder reactions, and it may be that product is formed but is not thermodynamically stable relative to starting material.

Problem 13.59 All Diels–Alder reactions require an s-cis diene. The first thing to do in solving this problem is to draw the s-cis forms of the diene in each case.

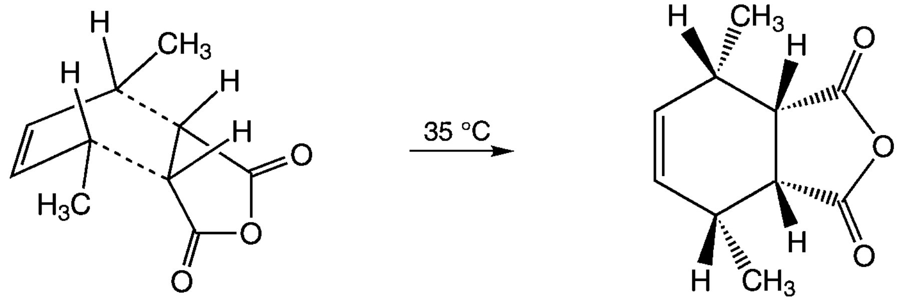


s-trans s-cis



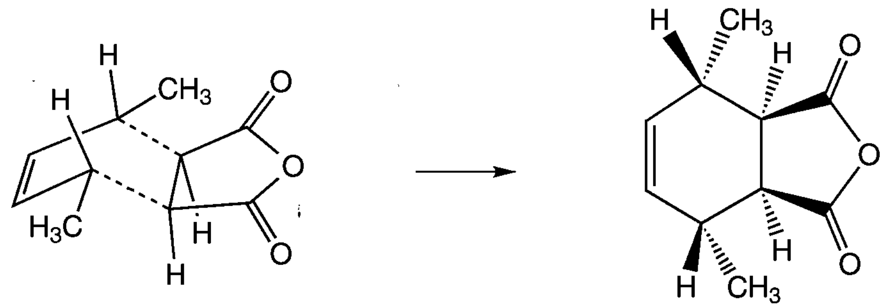
s-trans s-cis

In **2**, a relatively large methyl group must be "inside," and this is surely destabilizing. So, at 35 °C there are no significant amounts of the required s-cis diene for **2**. Reaction of maleic anhydride takes place with the s-cis form of **1** to give product. Even this reaction is more complicated than it might seem at first. The stereochemical relationships of the substituents on the diene must be preserved in this one-step reaction, so the methyl groups must be cis in the product. However, addition can take place through either an endo or exo transition state to give endo or exo product. As usual (Chapter 13, p. 622), the endo transition state is lower in energy than the exo transition state, and the endo product is formed as the major product.



endo Transition state

Product from endo transition state is the major product



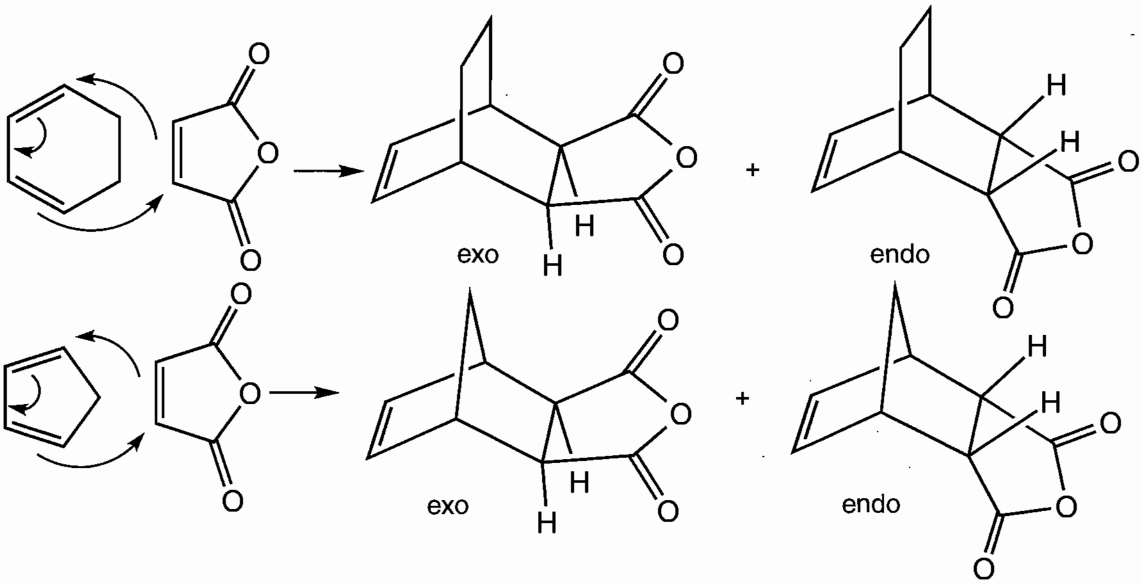
exo Transition state

Product from exo transition state is a minor product

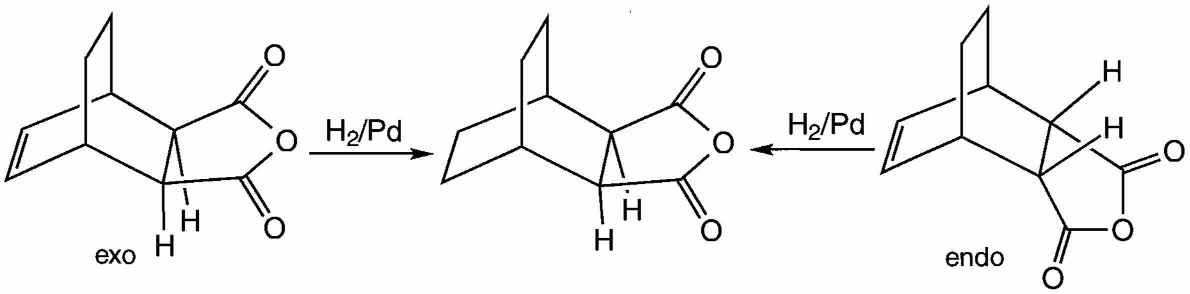
For **2**, higher temperature is required to form significant amounts of the s-cis form. When reaction occurs, once again the stereochemical relationship of the methyl groups in the s-cis conformation of the diene will be preserved in the adducts. In this case, they must be trans. As the methyl groups are trans, with one "up" and the other "down," there is only one product possible. The exo and endo transition states lead to the same product in this case.

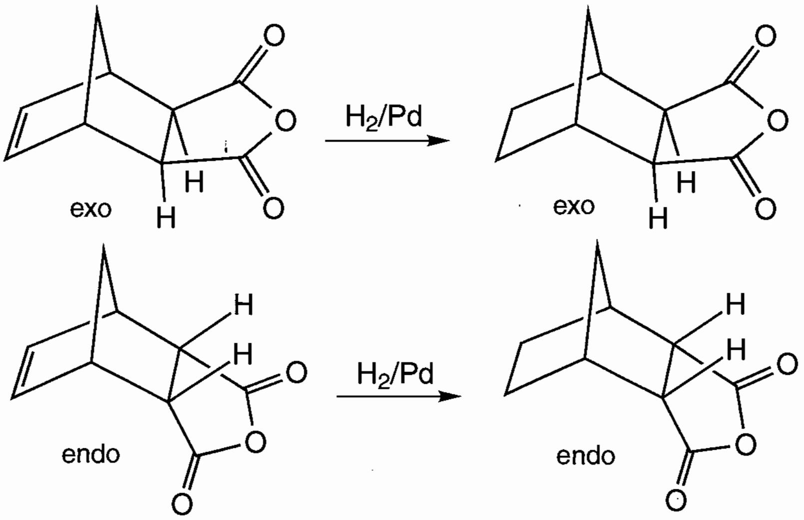
(continued)

Problem 13.58 Work through what the products must be and you will see how it comes out. In each case, there are two Diels–Alder products possible: one endo and one exo.

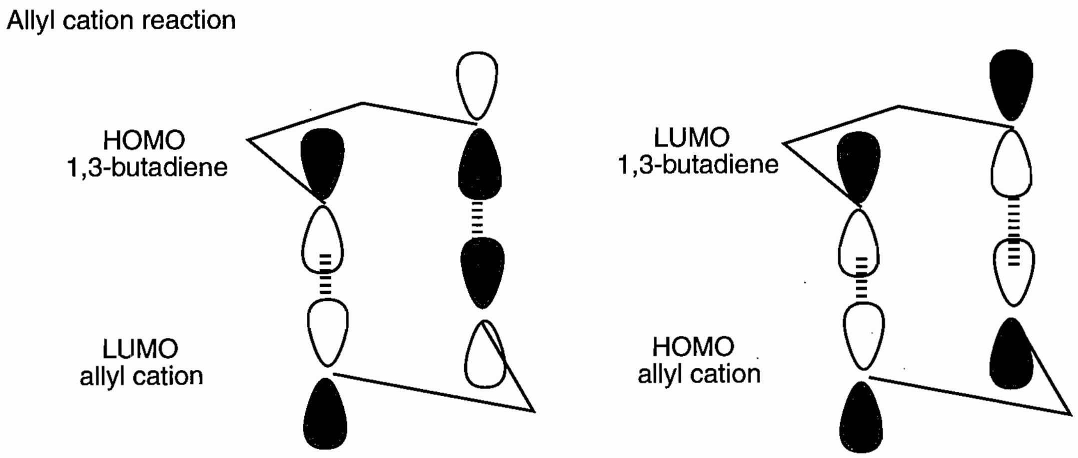


However, when the products are hydrogenated, each of the adducts from 1,3-cyclohexadiene gives the same product. If the drawing does not make this obvious to you, be sure to make models and convince yourself that the "two" hydrogenated compounds are really the same thing. The hydrogenated adducts from reaction of 1,3-cyclopentadiene are still different.



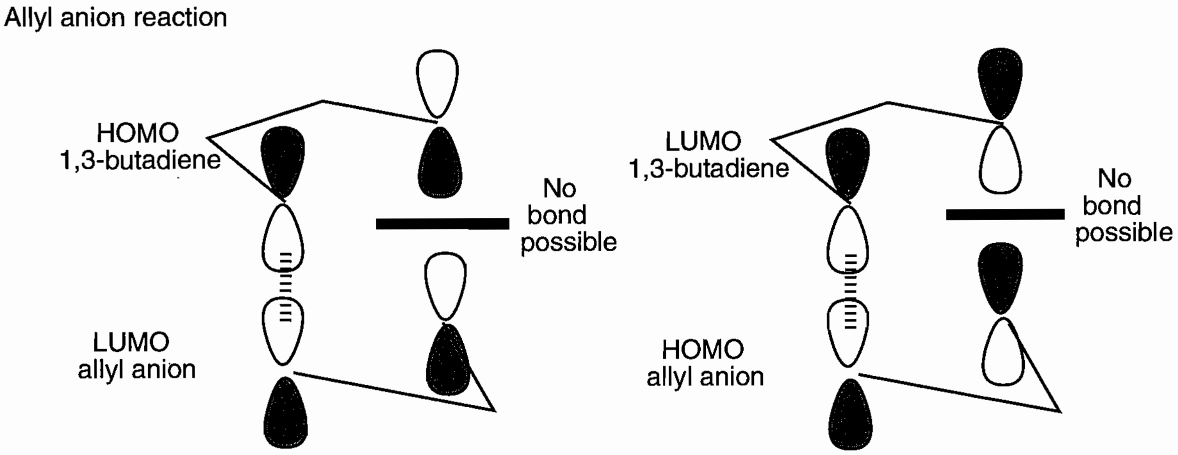


For the reaction to be successful, there must be bonding interactions at the points of formation of both new bonds. Here are the HOMO–LUMO interactions for the reaction of the allyl cation with 1,3-butadiene, showing only the points at which new bonds are made.



In each case, both new interactions are bonding. The new bonds can be made.

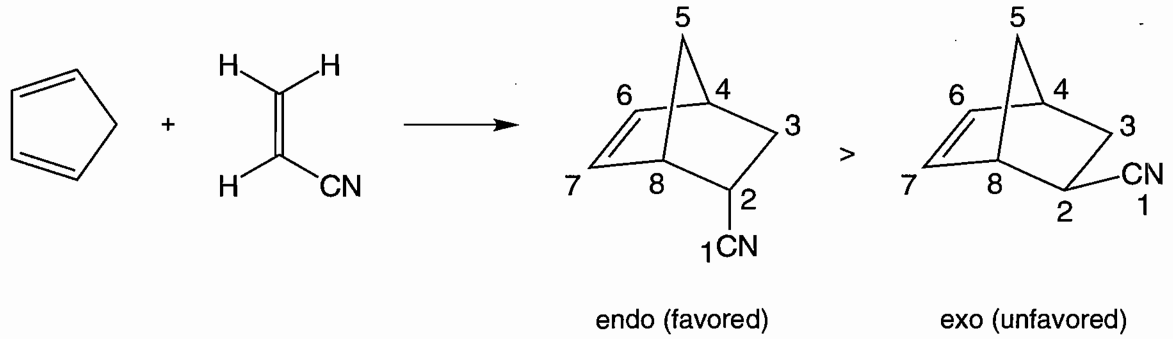
The situation turns out quite otherwise in cycloadditions of the allyl anion. The two HOMO–LUMO interactions are shown below.



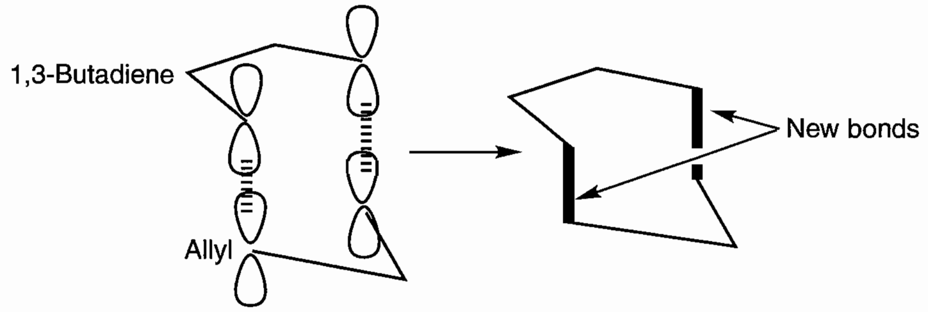
It is not possible to make two bonds in either HOMO–LUMO interaction. The reaction of the allyl anion fails.

Problem 13.56 *(continued)*

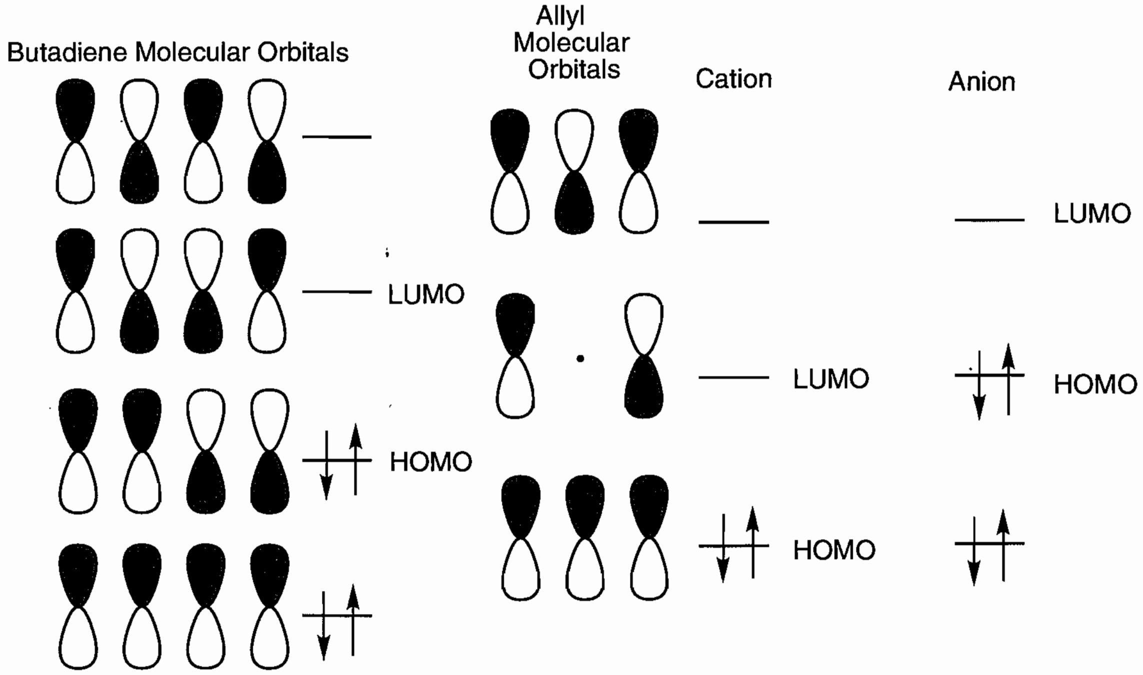
There is a similar problem in part (c). First draw the two products, the endo and exo isomers. The endo adduct will be favored kinetically, but ^{13}C NMR spectroscopy will not be able to distinguish the favored endo product from the unfavored exo, as each has eight different carbon atoms.



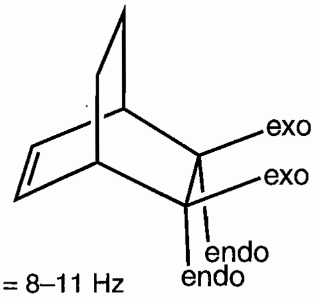
Problem 13.57 First of all, draw an arrow formalism for the reaction of an allyl species with 1,3-butadiene. *Remember*: The two participants in the reaction approach each other in parallel planes. There is no attempt in this schematic to show the orbital phases; this is a mapping exercise only.



In each reaction there are two HOMO–LUMO interactions possible, HOMO (diene)–LUMO (dienophile) and HOMO (dienophile)–LUMO (diene). Look at both interactions in each case. For the participants in the reactions, 1,3-butadiene, the allyl cation, and the allyl anion, the molecular orbitals are

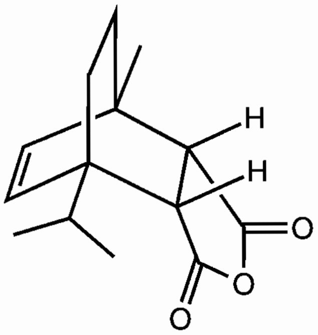


Typical values for cis ($J_{exo,exo}$ and $J_{endo,endo}$; $\phi \sim 0°$) and trans ($J_{exo,endo}$; $\phi \sim 120°$) vicinal coupling constants for bicyclo[2.2.2]octenes are shown.



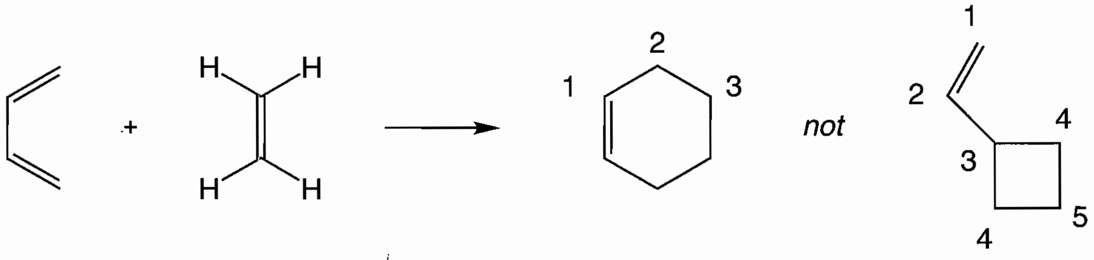
J_{cis} = 8–11 Hz
J_{trans} = 2.5–6 Hz

Although it is not possible to deduce the exo versus endo stereochemistry of cycloadduct **C** from the available spectral data, **C** has endo stereochemistry. The actual stereochemistry has been determined by using more complex spectral techniques, by chemical transformations, and by independent synthesis of the exo isomer.

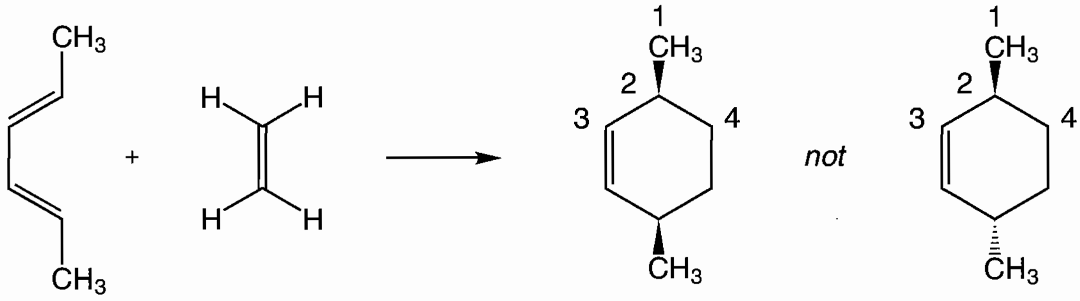


endo-**C**

Problem 13.56 In part (a), the Diels–Alder reaction will lead to cyclohexene, not the vinylcyclobutane (p. 618). ^{13}C NMR spectroscopy could easily distinguish the two possibilities, as cyclohexene has only three different carbons and vinylcyclobutane has five.



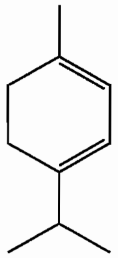
In part (b), the cis product will be formed, *not* the trans, as the Diels–Alder reaction occurs in a single step. However, ^{13}C NMR spectroscopy will be ineffective in distinguishing the two possibilities, as they each have four different carbons.



(continued)

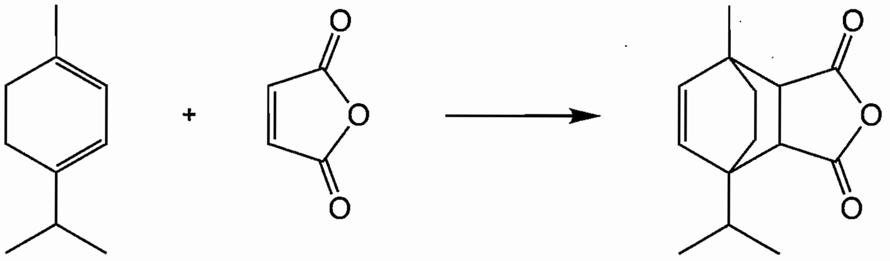
Problem 13.55 *(continued)*

However, a more complicated dehydration of **A** could afford the conjugated diene, α-terpinene. You should be able to write a mechanism for this dehydration.



α-Terpinene

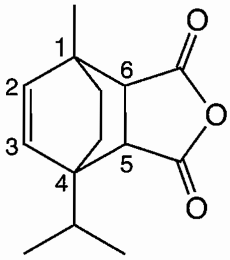
Clearly, α-terpinene and maleic anhydride could undergo a Diels–Alder reaction to give a 1:1 cycloadduct, and this could be compound **C**. Let's see if the rest of the spectral data are consistent with this proposal.



C

The two carbonyl stretches at 1840 cm^{-1} and 1780 cm^{-1} in the IR spectrum of **C** are consistent with the presence of a cyclic anhydride.

The NMR spectral data are also consonant with the proposed structure for **C**. The chemical shift assignments are summarized. Note that the isopropyl methyl groups are diastereotopic, as required by the intrinsic asymmetry of the proposed structure. Also note that the 6 degrees of unsaturation for compound **C** are three rings, 1 C=C and 2 C=O bonds.



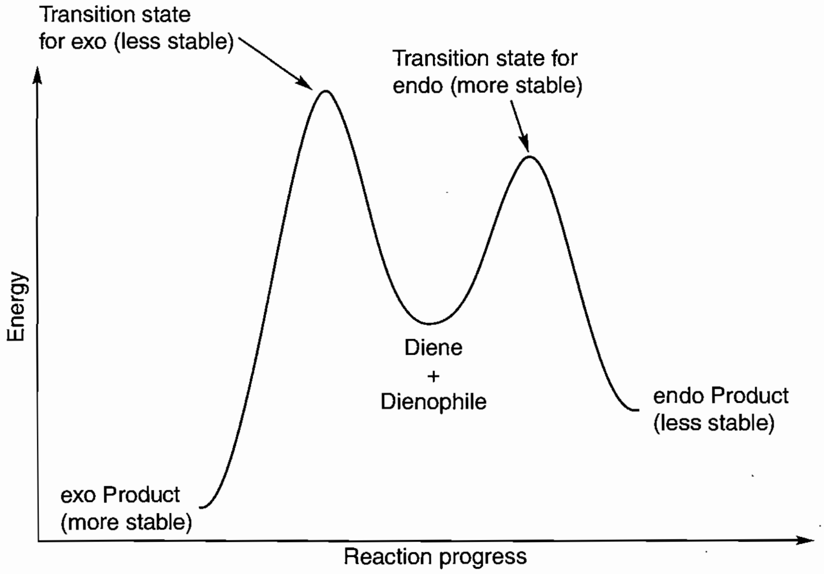
C

δ	
0.98	$(C\underline{H}_3)_2CH$
1.08	
1.36	Bridge CH_2's
1.46	C(1) CH_3
2.60	$(CH_3)_2C\underline{H}$
2.80	H(5) and H(6)
3.20	
6.01	H(2) and H(3)
6.10	

Two questions still remain concerning the stereochemistry of cycloadduct **C**.

(1) Are H(5) and H(6) cis or trans to each other?
(2) Is the cycloadduct endo or exo?

One of these questions can be answered with the available spectral data, whereas the other cannot. As you might expect from what you already know about the Diels–Alder reaction, the cis stereochemistry present in maleic anhydride is preserved in the cycloadduct; that is, H(5) and H(6) have a cis relationship. This assignment is supported by the magnitude of their coupling constant (J = 9 Hz). From the Karplus curve, it is known that vicinal coupling constants are dependent on the dihedral angle (ϕ) between the vicinal protons—with large coupling constants for dihedral angles of 0° and 180° and smaller coupling constants for dihedral angles approaching 90°.



At high temperature, all barriers are passable, and the major product will be the more stable exo adduct. At low temperature, the reaction is less reversible, and the major product will be determined by the relative energies of the transition states, which typically favor the endo product in the Diels–Alder reaction.

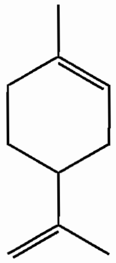
Problem 13.55 First, we will determine the molecular formulas of compounds **B** and **C**. Compound **B** is a dehydration product of α-terpineol (**A**) (i.e., $C_{10}H_{18}O - H_2O = C_{10}H_{16}$). If compound **B** reacts with maleic anhydride to give a 1:1 adduct, compound **C** has a molecular formula of $(C_{10}H_{16} + C_4H_2O_3) = C_{14}H_{18}O_3$. The molecular weight for this formula is 234 g/mol. Thus, our surmise that compound **C** is a 1:1 adduct of **B** and maleic anhydride is consistent with the mass spectrum of **C**. This proposal is also supported by the presence of 18 hydrogens in the ^1H NMR spectrum of **C**.

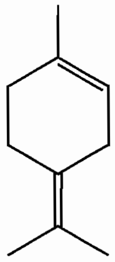
Now we need to work out the number of degrees of unsaturation in **C**.

$$\Omega = [2(14) + 2 - 18]/2 = 6$$

So far in these problems, 6 degrees of unsaturation has generally suggested the possibility of a benzene ring, thus accounting for 4 degrees of unsaturation. Could this problem be an exception to this expectation? There seems no easy way to get an aromatic compound in this reaction.

As was already noted, compound **C** is a 1:1 adduct of **B** and maleic anhydride. Futhermore, **B** is a dehydration product of α-terpineol (**A**). It is worth speculating at this point about the structure of compound **B**. Simple dehydration of compound **A** could afford dienes **D** and **E**; perhaps one of these is compound **B**. This possibility seems unlikely, as neither **D** nor **E** is a conjugated diene, and therefore, neither can react in Diels–Alder fashion with maleic anhydride.

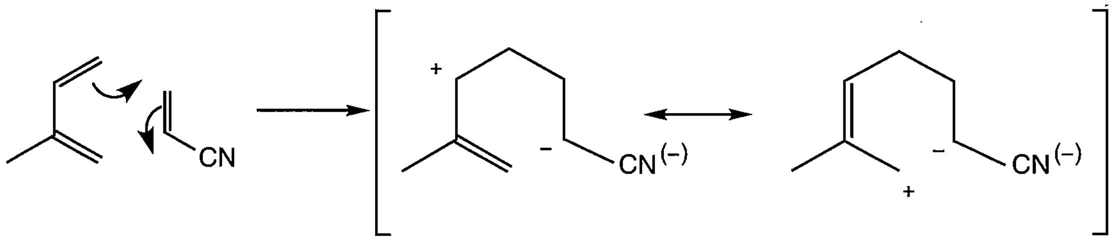

D


E

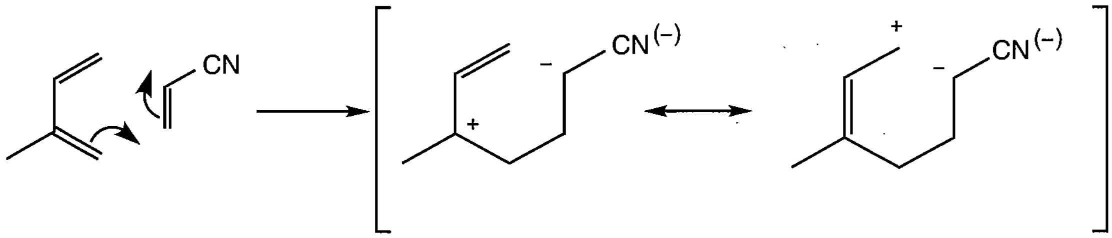
(continued)

Problem 13.53 A polar, stepwise mechanism would surely put the minus charge near the CN (so it will be stabilized by resonance), leaving the plus charge on carbon, where it, too, is resonance stabilized. There are two ways to do this:

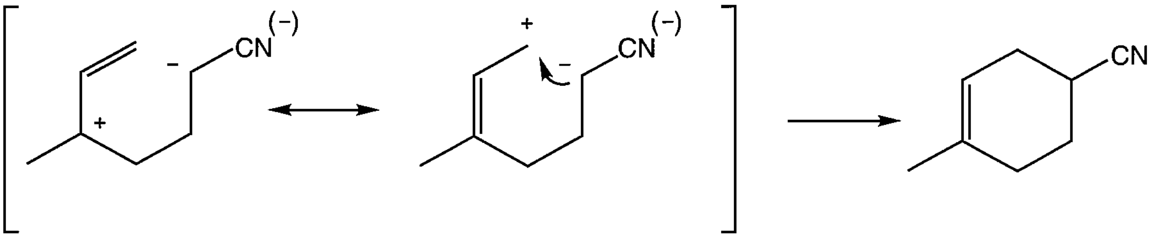
A



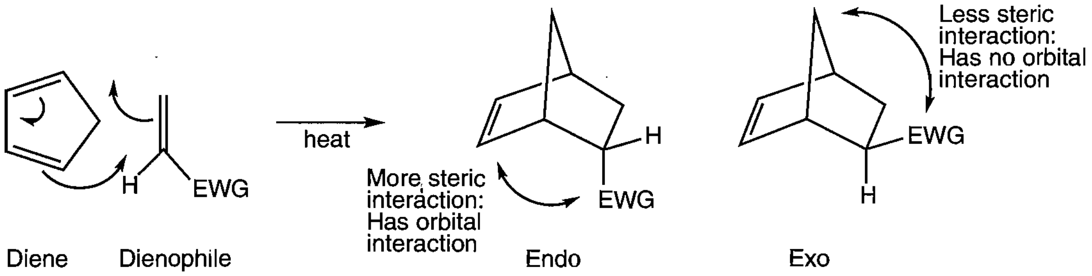
B



Path **B** will be favored because the carbocation has a resonance form in which the positive charge is borne on a tertiary carbon. Closure would give the product shown.

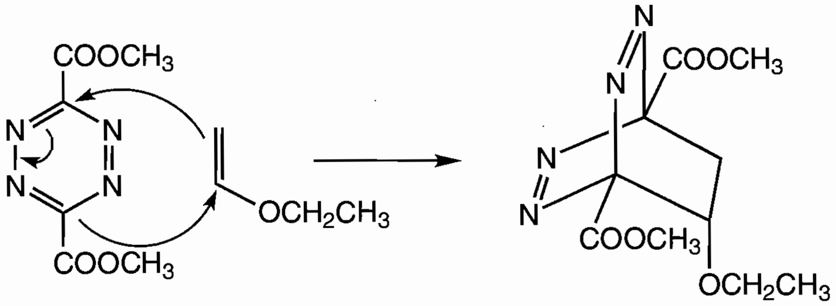


Problem 13.54 This problem is a classic case of thermodynamic versus kinetic control, quite similar to the situation encountered in Section 13.10 (Fig. 13.35, p. 609) for the addition of chlorine to 1,3-butadiene. Consider the general reaction shown here.

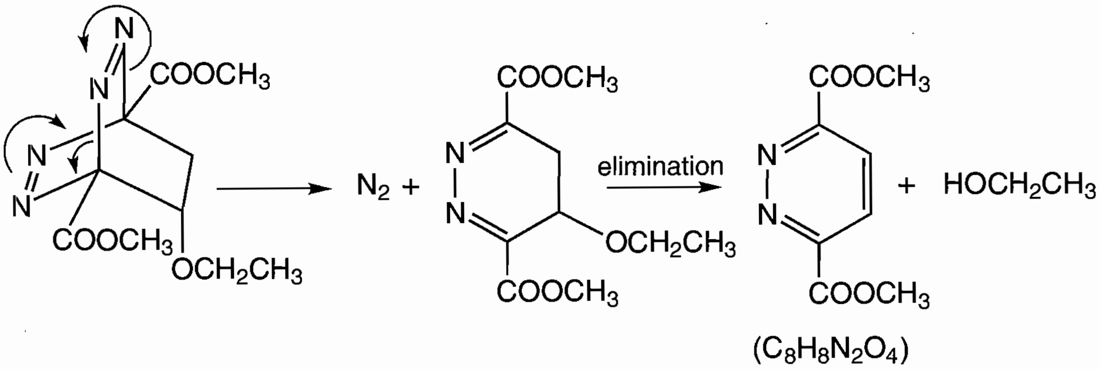


The exo compound is more stable than the endo compound because the EWG (electron-withdrawing group) points toward the smaller bridge, not toward the larger bridge. This is a steric issue. However, the transition state leading to the less stable endo product benefits from (1) molecular orbital interaction between the EWG and the developing alkene and/or (2) a solvent exclusion as the dienophile approaches the diene (p. 622).

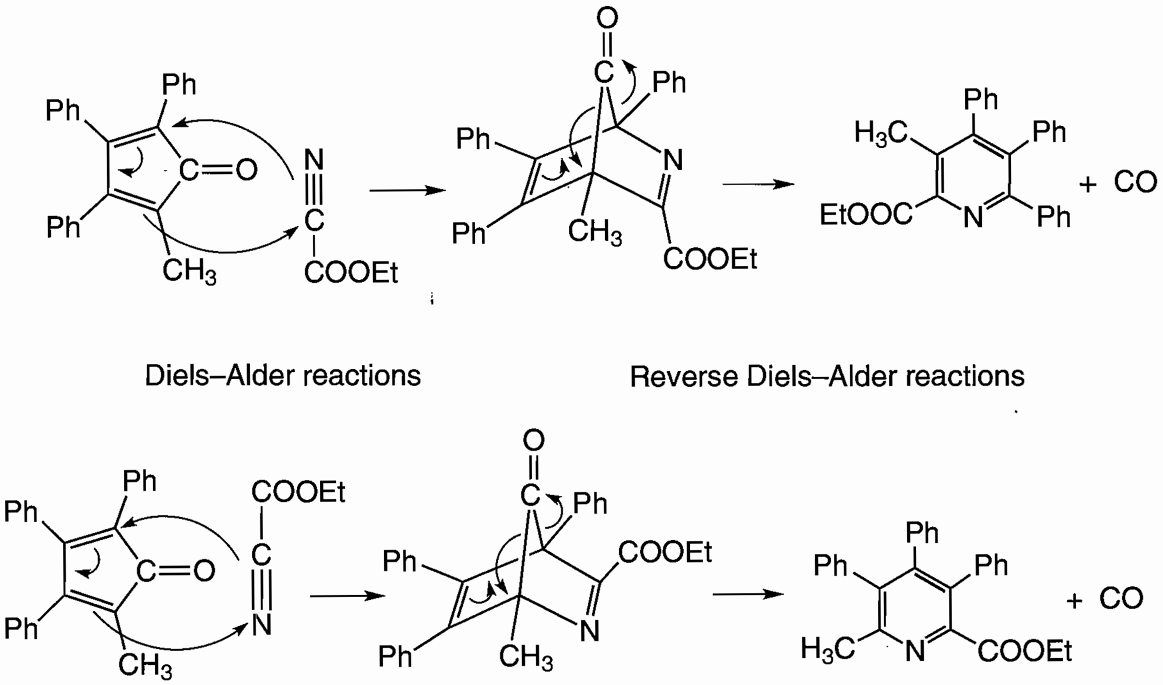
(g) In this example, we first have to realize that a "1,3-diene" is present. True, it contains two nitrogen atoms, but it remains a 1,3-diene nonetheless. Otherwise the first reaction is quite simple.



Now, as in part (d), a small molecule is lost, this time N_2. Elimination of another molecule, ethyl alcohol, also occurs to give the final product.

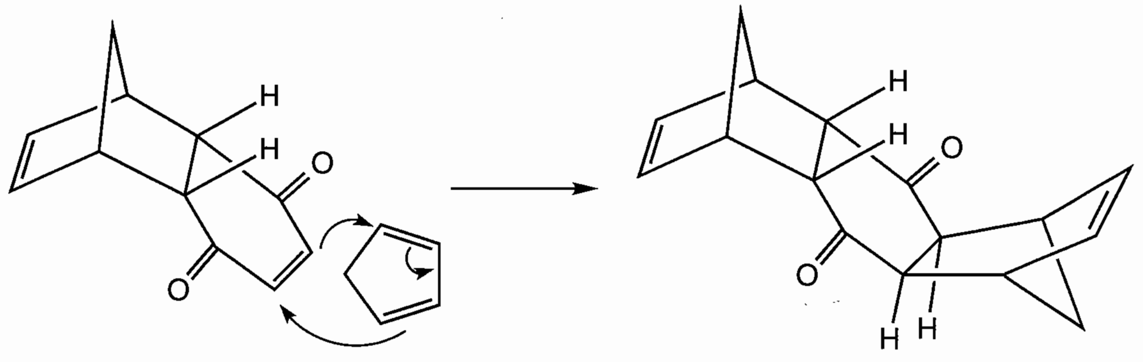


Problem 13.52 This reaction involves a Diels–Alder cycloaddition with the nitrile acting as dienophile. In this case, two initial cycloadducts are possible because both the nitrile and the diene are unsymmetrical. Loss of carbon monoxide from the primary adducts gives the two observed pyridines.

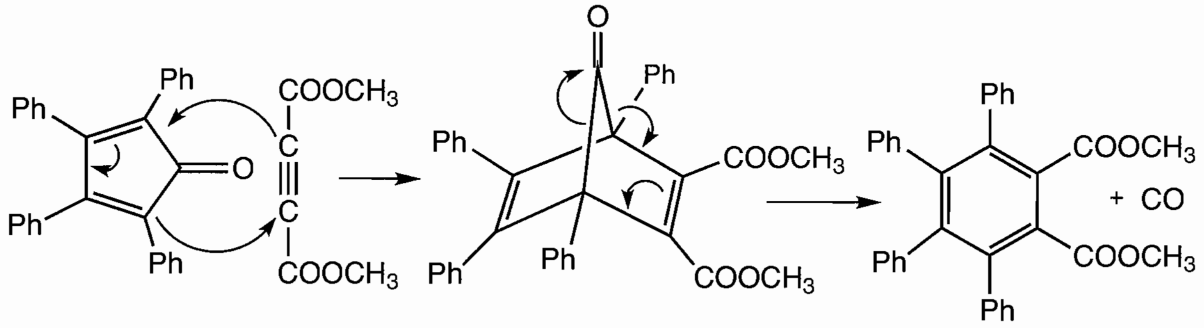


Problem 13.51 *(continued)*

You may have noticed that the product of this Diels–Alder reaction still has a double bond with two attached carbonyl groups. This carbon–carbon double bond is also a quite reactive dienophile. When this reaction is run in the presence of two equivalents of 1,3-cyclopentadiene, a 2:1 adduct is readily formed. The second addition occurs from the more available face of the enone.

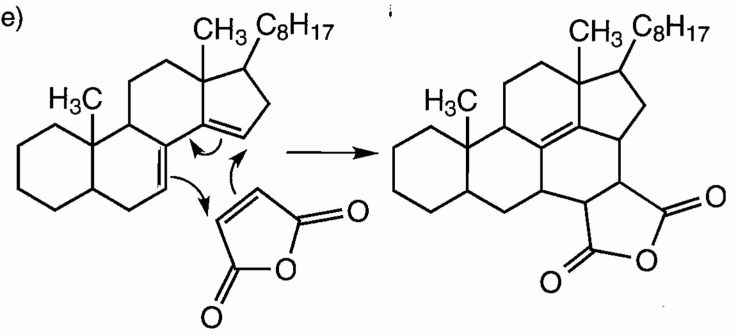


(d) This reaction illustrates another useful variation of the Diels–Alder reaction in which the primary adduct loses a small molecule such as carbon monoxide, carbon dioxide, or nitrogen. In this problem, the loss of carbon monoxide is indicated by the molecular formula. In problems such as these, watch for losses such as this one. The formula will usually tell you, but if it is not given, you must be alert for the possibility, as it is often encountered both in the real world and the world of examination problems.

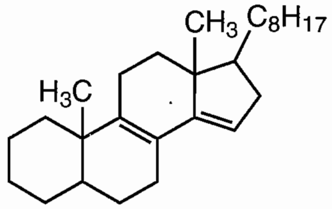


(e and f) The Diels–Alder reaction has been used to deduce the position of double bonds in steroids. In example part (e), the diene is locked into an s-cis arrangement, and the Diels–Alder reaction occurs. In part (f), the diene is s-trans, and the Diels–Alder reaction is not possible. Be sure you see why.

(e)

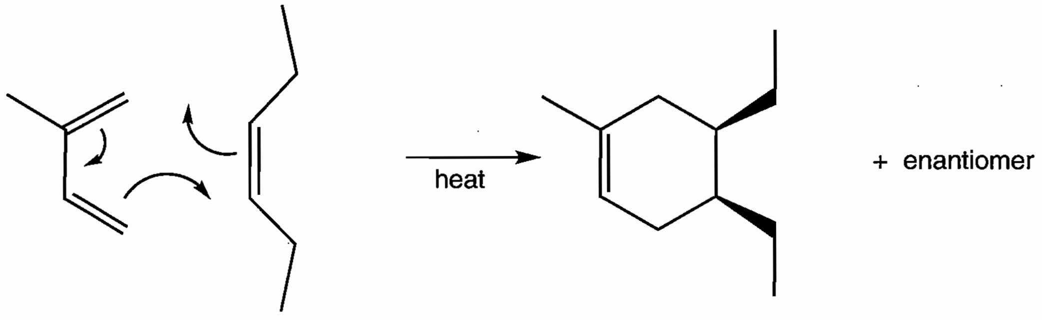


(f)



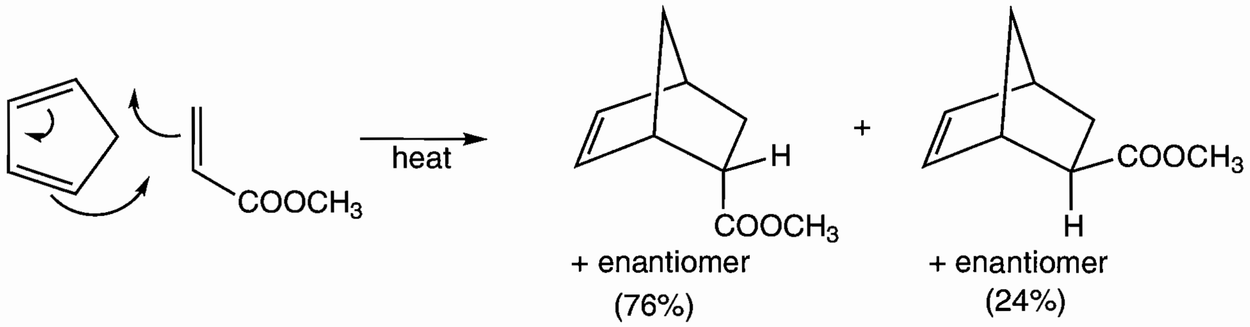
No reaction with maleic anhydride

(d)

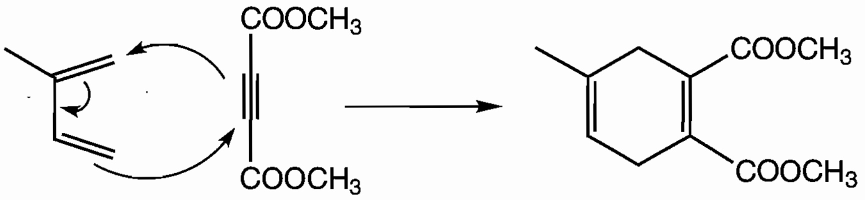


Problem 13.51 This problem was designed to illustrate the scope and variety of compounds available from the Diels–Alder reaction.

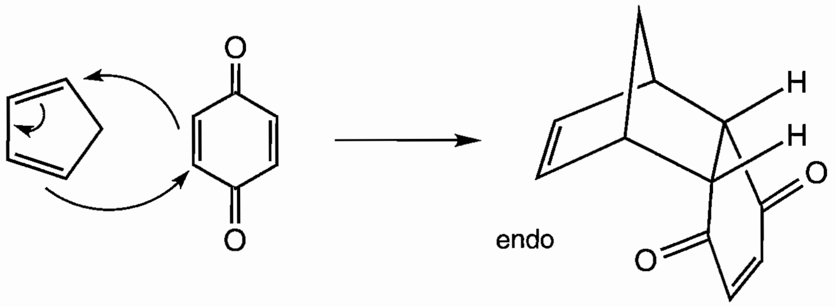
(a) In this reaction, a 76:24 mixture of endo and exo products is obtained. Be sure you see how these two products arise from a relatively more stable endo transition state and a relatively less stable exo transition state. In doubt? See Figure 13.57 (p. 622).



(b) The only unusual thing about this variation of the Diels–Alder reaction is the use of an alkyne as a dienophile rather than the more usual alkene. The product is a 1,4-cyclohexadiene rather than a cyclohexene. Note that only one π bond of the alkyne is involved in this Diels–Alder reaction.



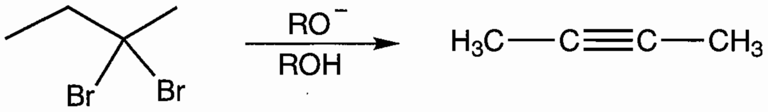
(c) In this variation, both the diene and the dienophile are cyclic compounds. The first complication is to decide whether the reaction will pass over an endo or exo transition state. In fact, the major cycloadduct has the endo stereochemistry, and this reaction is normal in that respect.



(continued)

Problem 13.48 *(continued)*

Now a pair of E2 reactions will give mostly 2-butyne. There are other possible products, 1-butyne and 1,2-butadiene, but they should be less favored.



Problem 13.49 Here is the target:

$$(CH_3)_3C-C\equiv C-CH_2CH_2CH_2CH_3$$

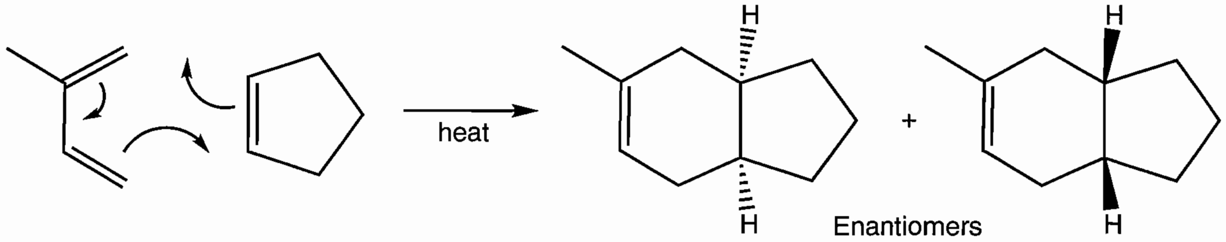
We are going to use an acetylide to do an S_N2 displacement. Because we can't do an S_N2 displacement at a tertiary carbon, there is only one way to do this reaction.

$$(CH_3)_3C-C\equiv C-H \xrightarrow[\text{2. } CH_3CH_2CH_2CH_2Br]{\text{1. } NaNH_2} (CH_3)_3C-C\equiv C-CH_2CH_2CH_2CH_3$$

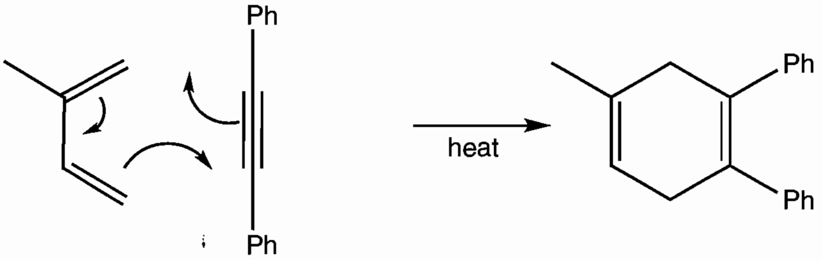
C_6H_{10}

Problem 13.50

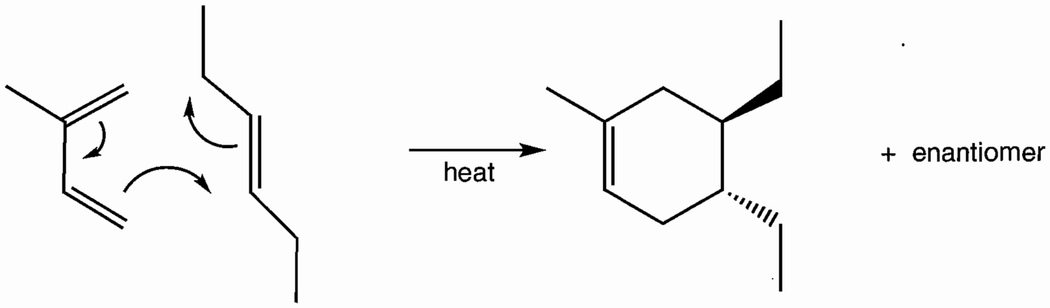
(a)



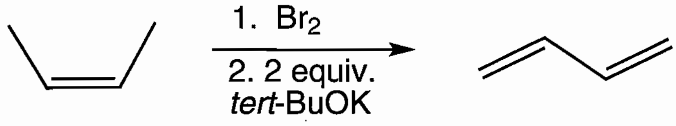
(b)



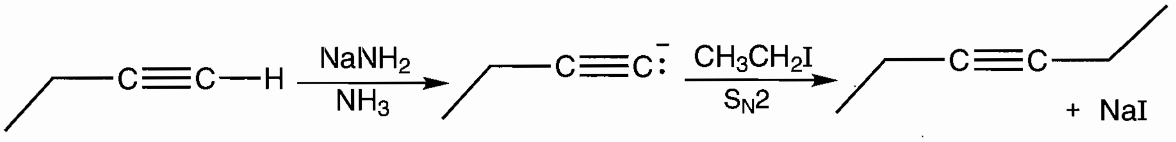
(c)



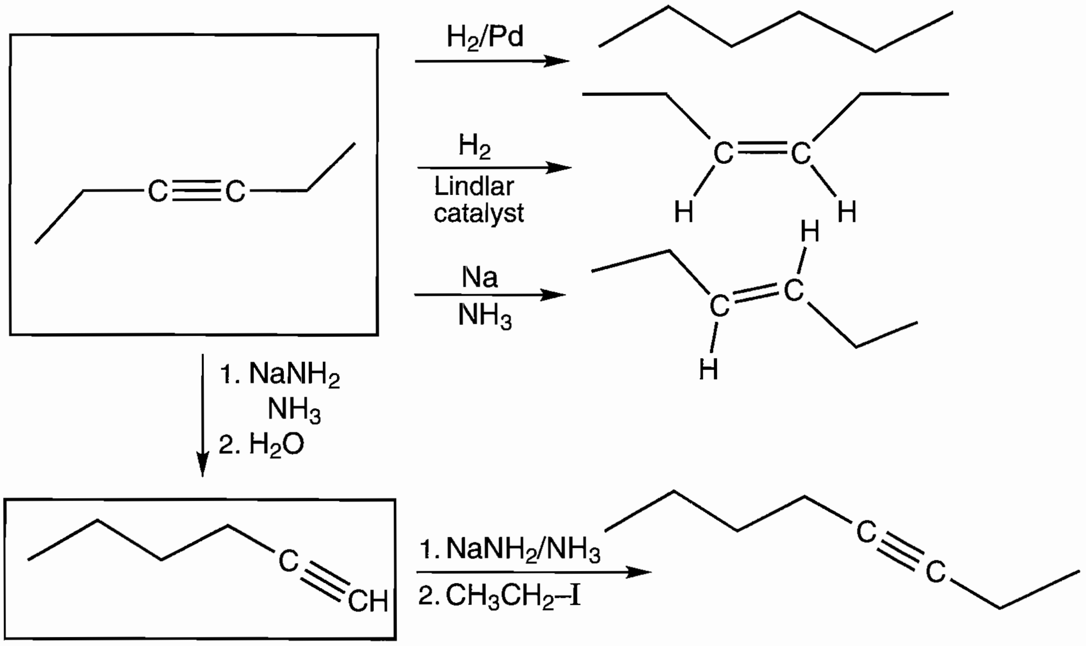
So, all we need to do is to convert *cis*-2-butene into 1,3-butadiene. Here's how to do it.



Problem 13.47 This synthesis problem should be relatively easy. The only real difficulty might be that it is a cascade problem; you have to be able to make one of the products in order to get the others. In this case, the critical compound is 3-hexyne. It comes from formation of the acetylide from 1-butyne followed by an S_N2 reaction on ethyl iodide.



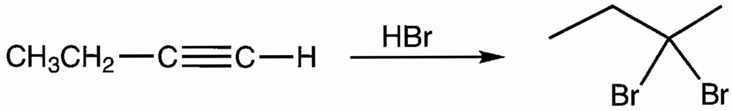
Once 3-hexyne is made, the others all follow in straightforward fashion.



Problem 13.48 Converting 2-butyne into 1-butyne involves a "zipper" reaction.

$$H_3C{-}C{\equiv}C{-}CH_3 \xrightarrow[2.\ H_2O]{1.\ NaNH_2,\ NH_3} CH_3CH_2{-}C{\equiv}C{-}H$$

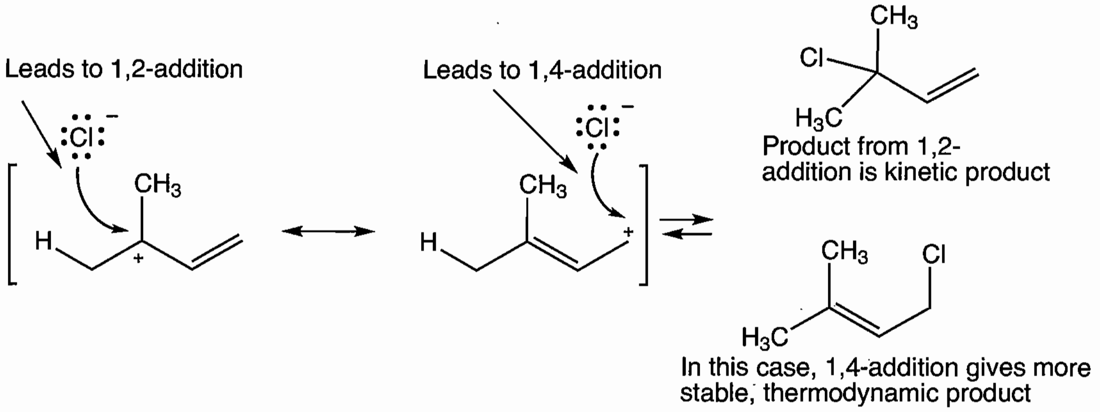
As the problem suggests, going the other way poses more problems. Here is one suggestion. First, add two molecules of HBr in polar, Markovnikov fashion to give 2,2-dibromobutane.



(continued)

Problem 13.44 *(continued)*

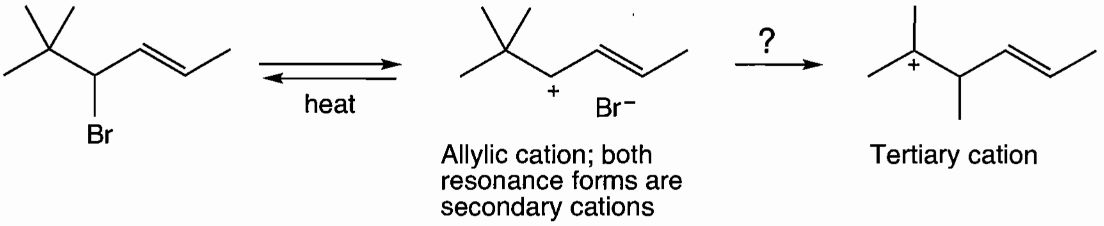
Addition of chloride at the relatively nearby position sharing the positive charge leads to the product of 1,2-addition (kinetic control). Addition at the relatively remote position sharing the positive charge gives the more stable, but kinetically disfavored, product of 1,4-addition (thermodynamic control).



Product from 1,2-addition is kinetic product

In this case, 1,4-addition gives more stable, thermodynamic product

Problem 13.45 This question asks if the allylic cation shown below is likely to undergo an alkyl shift to give the tertiary cation.



Allylic cation; both resonance forms are secondary cations

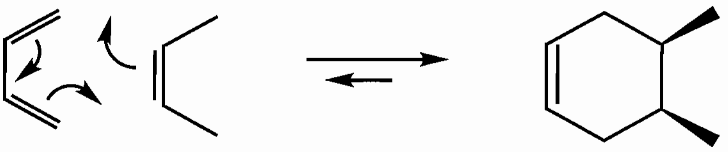
A

Tertiary cation

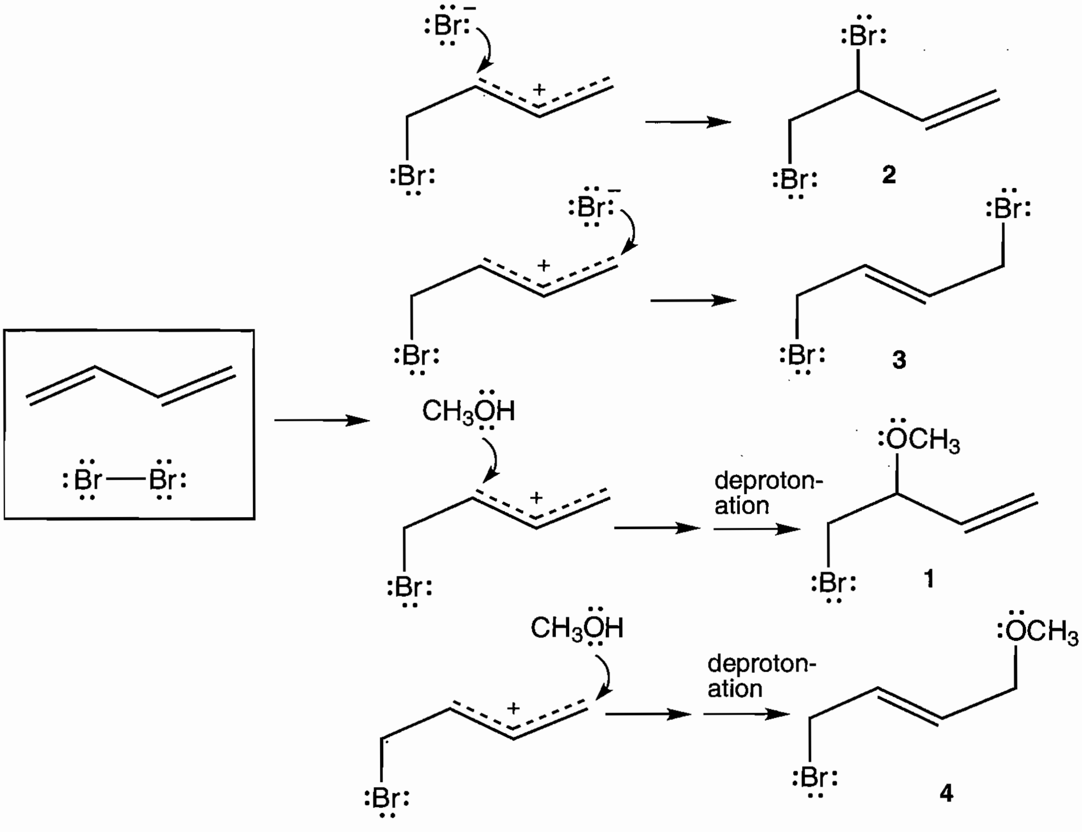
B

To answer this question, we need to compare **A** (an allylic cation that is secondary in both resonance forms) to **B** (a tertiary cation). Whichever is more stable will be the intermediate involved in S_N1 or E1 chemistry of this allylic bromide. We can get a good idea about the stability of these cations by comparing the rate of formation of similar cations listed in Table 13.2. However, the table does not list an allylic cation that is a combination of two secondary cations. Fortunately, we have the allylic cation that is tertiary and primary, which would be a close comparison. Formation of the tertiary cation has a relative rate of 3×10^4, and an allylic cation that is tertiary and primary has a relative rate of about 5×10^6 (taking the average of the two tertiary/primary entries). It is about 100 times faster to make the allylic cation. We can conclude that the intermediate **A** is more stable and that an alkyl shift is not likely.

Problem 13.46 "All" cyclohexenes come from the Diels–Alder reaction, so we need to do the following reaction:

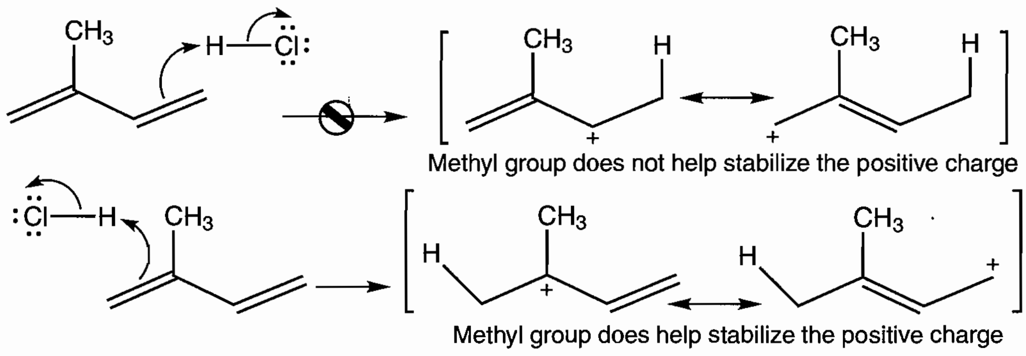


Alternatively, the intermediate could be seen as a resonance-stabilized allylic carbocation. Addition of the two nucleophiles, bromide and methyl alcohol, leads to the observed four products.



It is not possible to distinguish between these two possibilities without further experiments. It is worth noting that the ratios of the two types of 1,2- and 1,4-addition products are appreciably different; structure **2**/structure **3** = 2.2, structure **1**/structure **4** = 15. This result must be ascribed to the greater nucleophilicity of bromide ion relative to that of methyl alcohol.

Problem 13.44 As with 1,3-butadiene, the kinetic (more easily) formed product will be that from 1,2-addition. Under thermodynamic conditions, the more stable 1,4-adduct prevails. The problem is that there are two possible 1,2-addition products. The issue can be decided by examining the two possible allyl cations formed by protonation at the different ends of the 1,3-diene.



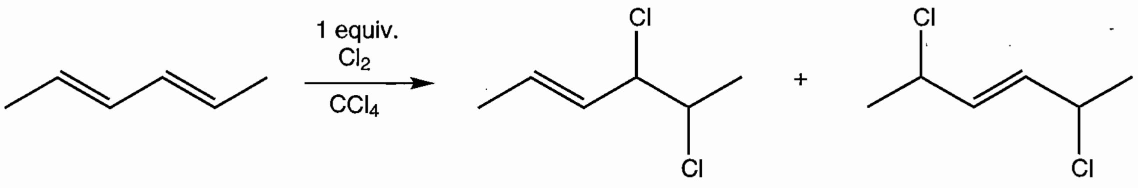
Methyl group does not help stabilize the positive charge

Methyl group does help stabilize the positive charge

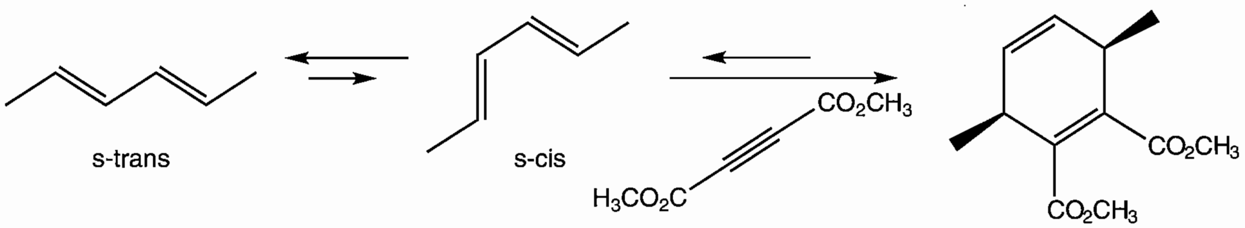
(continued)

Problem 13.42 *(continued)*

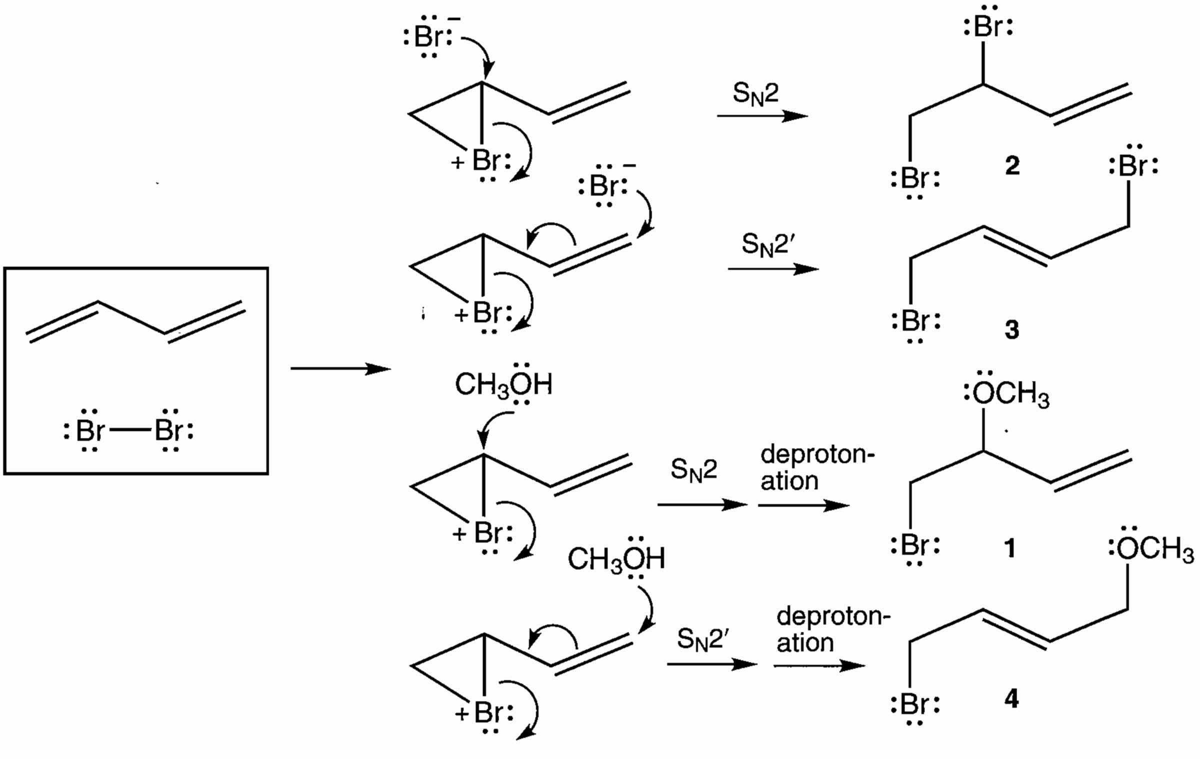
(c) Reaction of a diene with one equivalent of the electrophilic Cl_2 (or Br_2) gives both 1,2- and 1,4-addition products. Adding more Cl_2 (or Br_2) gives the tetrachloride.



(d) The Diels–Alder reaction requires the diene to be in the s-cis conformation. For (*E*,*E*)-2,4-hexadiene, this conformation is available in low concentrations. The cycloaddition with the dienophile (the alkyne in this example) in a concerted process that requires heat. It is a reversible reaction, but the more stable product is the Diels–Alder adduct. Notice that the diene stereochemistry (methyl groups pointing in the same direction—both out) is retained in the cyclohexene product (methyl groups pointing in the same direction—both up or both down).

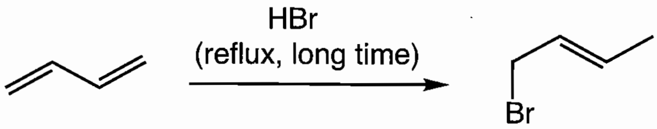


Problem 13.43 Compounds **2** and **3** are the 1,2- and 1,4-addition products of 1,3-butadiene and bromine. Compounds **1** and **4** involve addition of one bromine atom and the methoxy group of methyl alcohol. In principle, two mechanisms can be written for these additions, depending on how the intermediate cation is envisioned. If a bromonium ion is involved, direct S_N2 additions of the bromide ion or methyl alcohol to the bromonium ion give the 1,2-addition products **2** and **1**. The 1,4-addition products **3** and **4** could be formed by what is called an S_N2' reaction with bromide ion or methyl alcohol acting as nucleophile. (See Problems 13.62–13.64.)

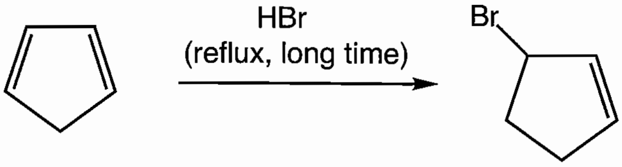


Problem 13.41 In part (a), the 1,4-addition product is more stable than the 1,2-addition product. In part (c), the (*Z*) double bond from 1,2-addition is less stable than the (*E*) double bond from 1,4-addition. The reactions of (b) and (d) will have no product selectivity because the 1,2- and 1,4-addition products have the same level of substitution. In (e), the trisubstituted double bond makes 1,2-addition dominate.

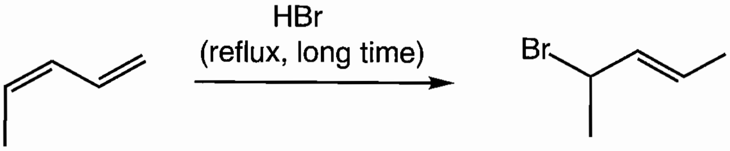
(a)



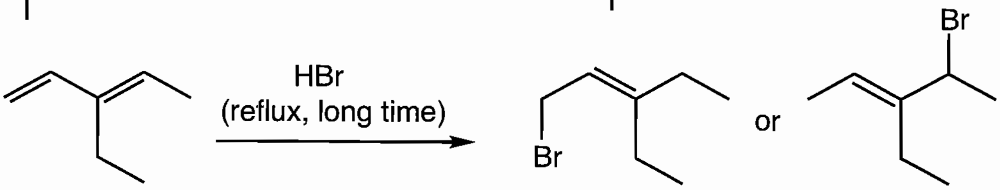
(b)



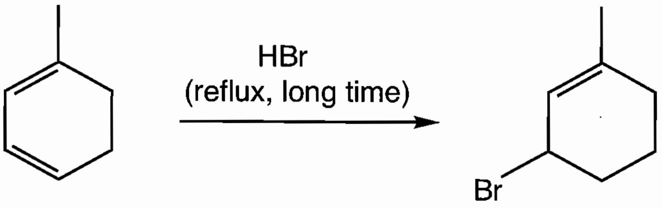
(c)



(d)

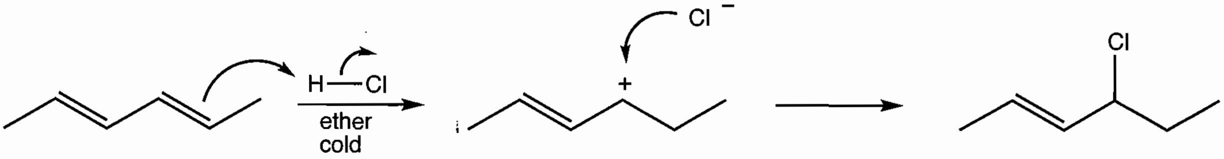


(e)

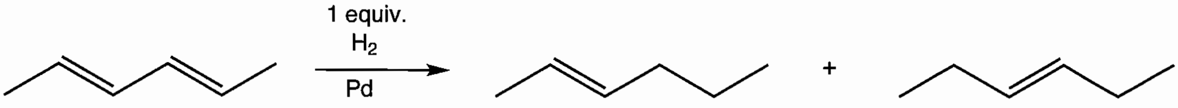


Problem 13.42

(a) A diene reacts with the electrophilic H—Cl to give a resonance-stabilized allylic cation. With the cold conditions, the kinetic product will predominate. The kinetic product results from 1,2-addition.

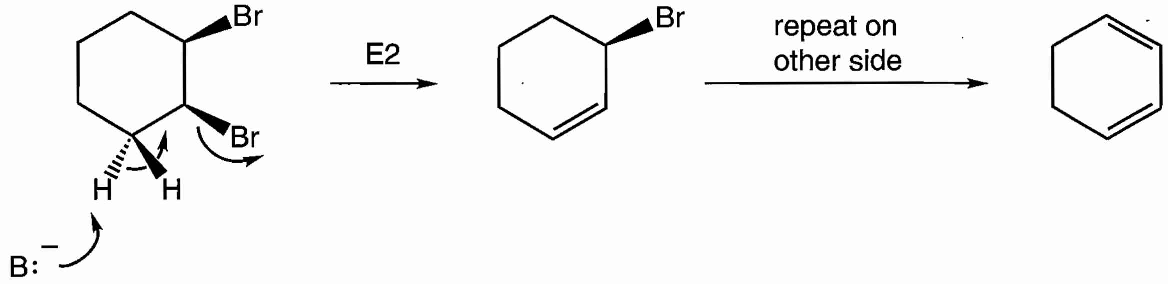


(b) Hydrogenation (with one equivalent of H_2) of a conjugated diene can result in hydrogen adding across one of the double bonds or adding to the end atoms of the conjugated system.

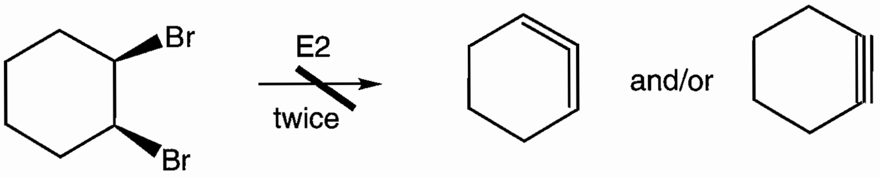


(continued)

Problem 13.39 There is an easy "double E2" elimination to give 1,3-cyclohexadiene, which is certain to be the major product.

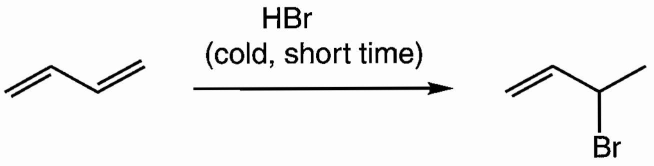


There really is no other reasonable process. In principle, you could eliminate HBr two times to give either 1,2-cyclohexadiene or cyclohexyne, but both of these products have hideous angle strain (note the *sp*-hybridized carbon that "wants" to be linear).

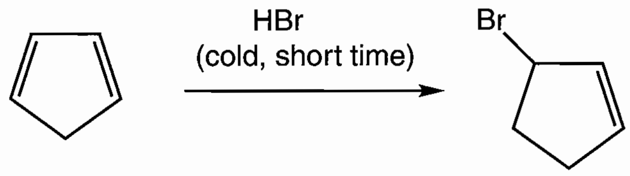


Problem 13.40 In each case, the conditions of kinetic control will make 1,2-addition the favored process. In all the following reactions, the initial protonation forms the most stable possible cation.

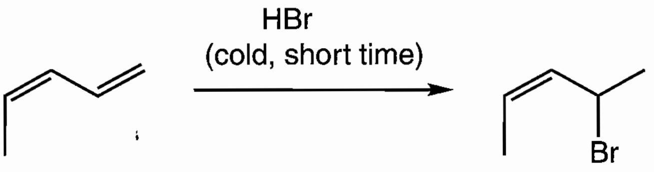
(a)



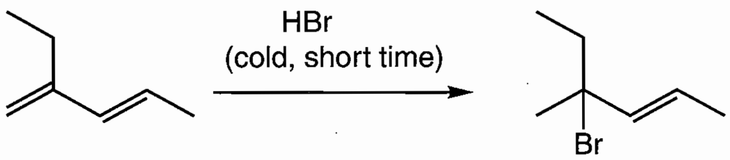
(b)



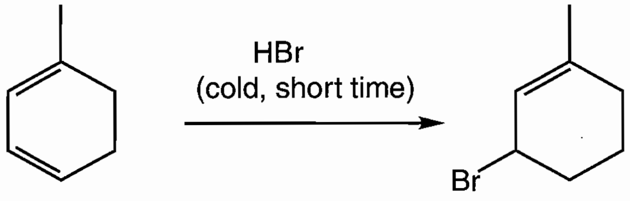
(c)



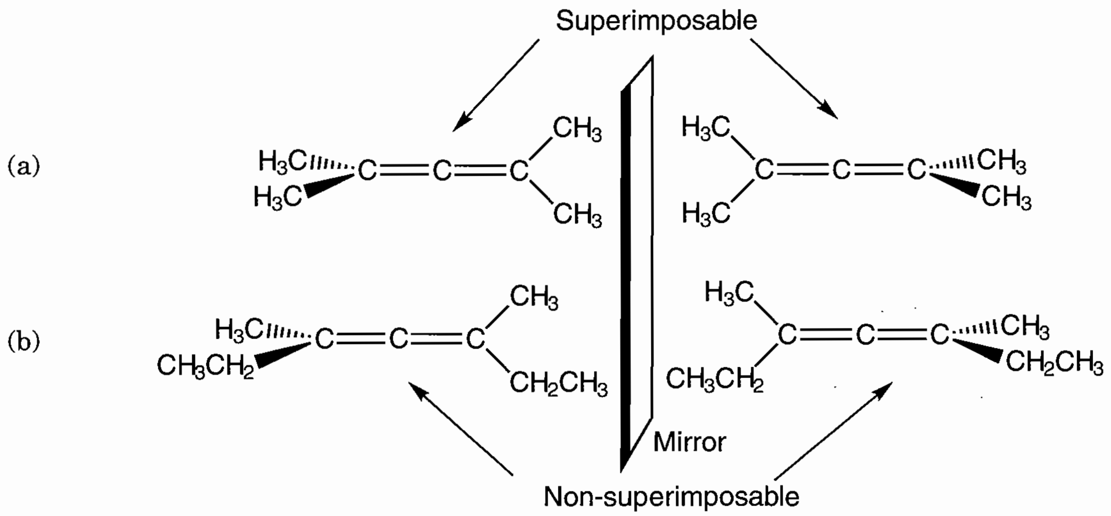
(d)

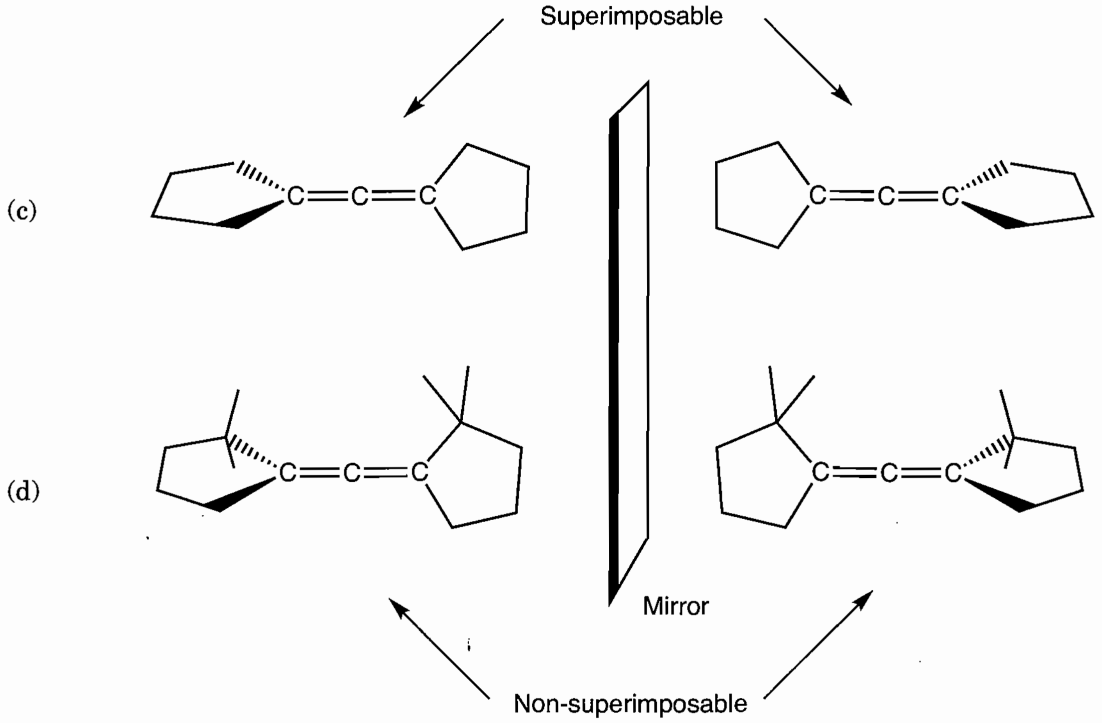


(e)

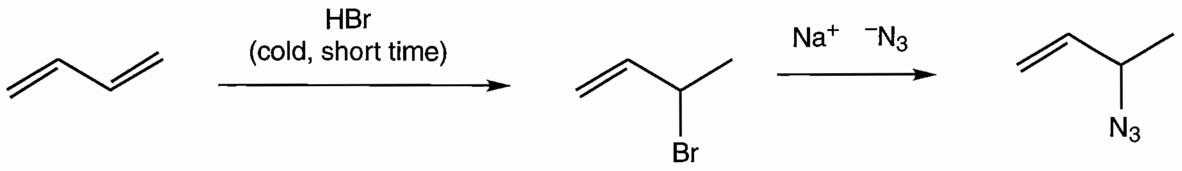


Problem 13.37 In each of the pairs, it is the second, right-hand compound that is chiral. In the following figure, to see that the two compounds of the upper pair are identical (superimposable), and the lower pair is non-superimposable, rotate 90° along a longitudinal axis. By all means make models! This one is not easy to see.



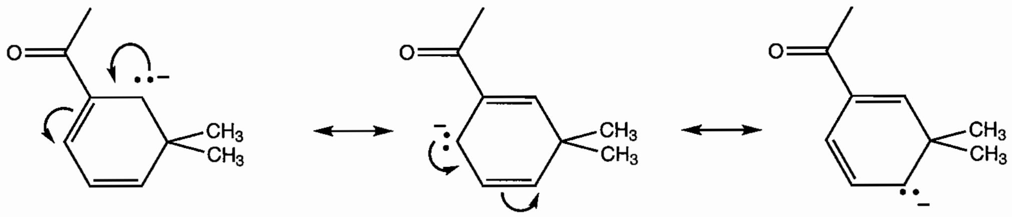


Problem 13.38 Azide is a great nucleophile, so a reasonable plan is to displace a good leaving group with it. The trick is to be sure that addition to 1,3-butadiene puts that leaving group in the right position. We need to do a 1,2-addition, not a 1,4-addition, and therefore we must use gentle conditions that ensure kinetic control.

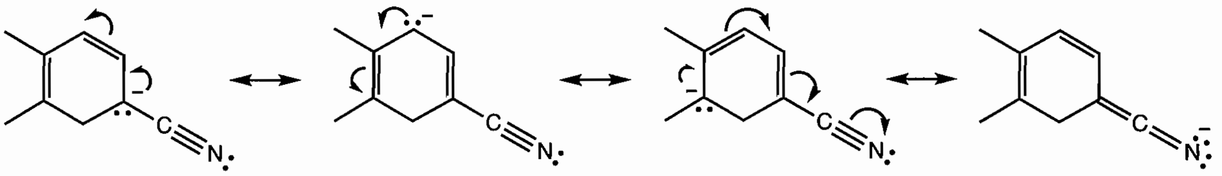


Additional Problem Answers

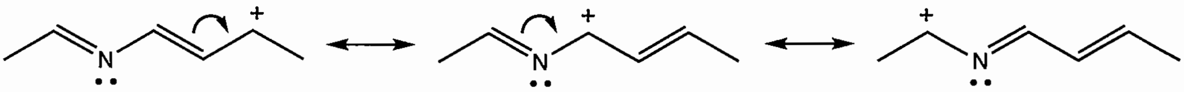
Problem 13.36 In the first ion, there are only three atoms that share the negative charge. The resonance structures are shown. The carbonyl group is not involved in resonance stabilization of the anion.



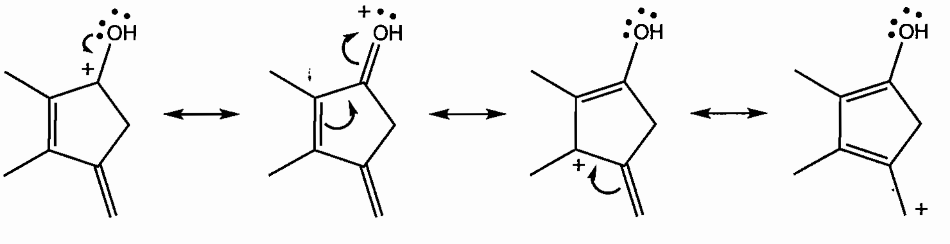
In the cyano-substituted cyclohexadienyl anion, the negative charge is located on an atom that does allow for delocalization out of the ring onto the more electronegative nitrogen.



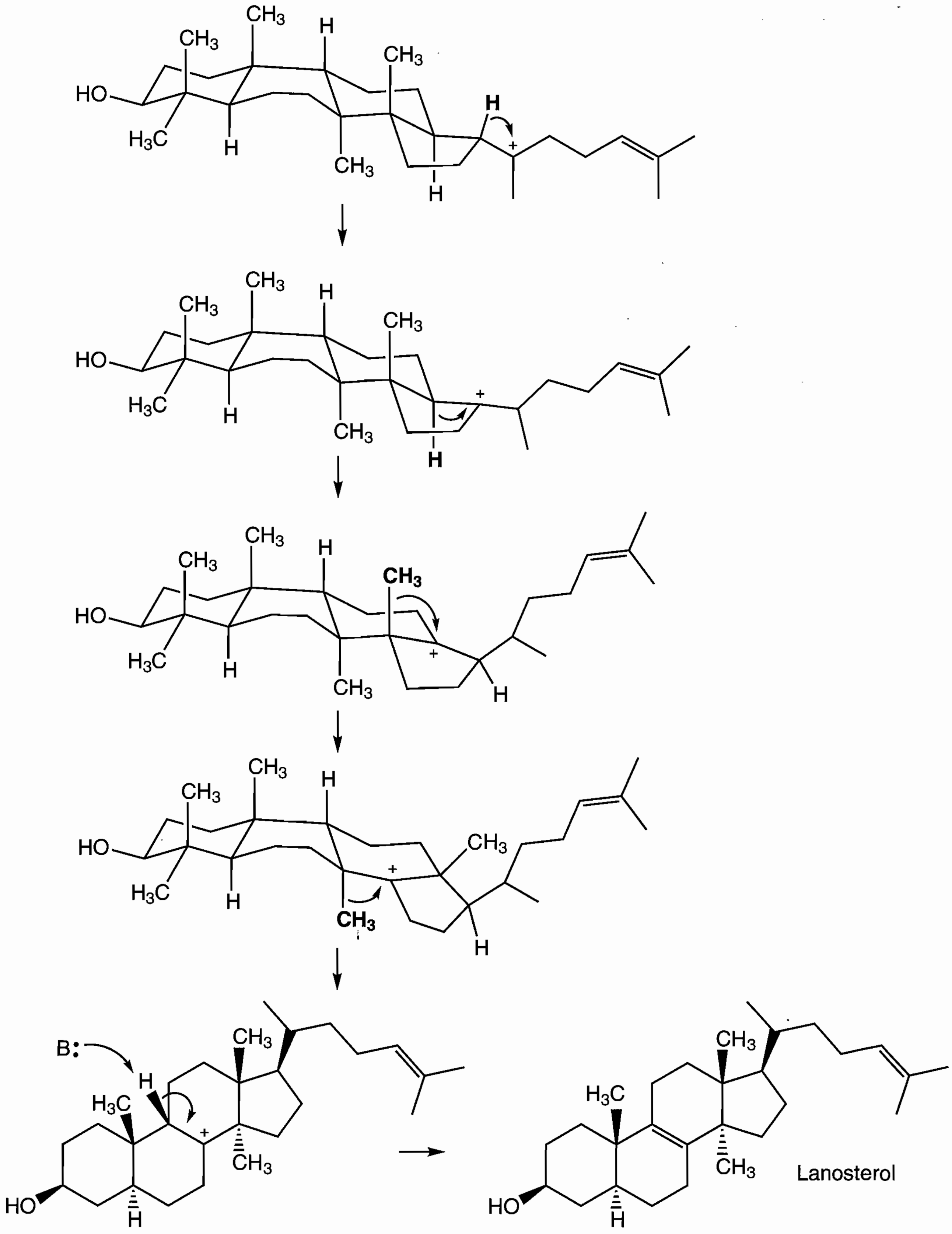
In the straight-chain ion, there are only three resonance structures if the nitrogen is sp^2 hybridized. They are shown here. The lone pair of the nitrogen is not able to delocalize into the p orbital of the π system because it is perpendicular to the dienyl system.



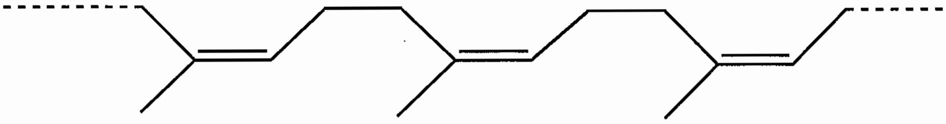
The last ion is the cyclopentenyl cation. It has four resonance structures.



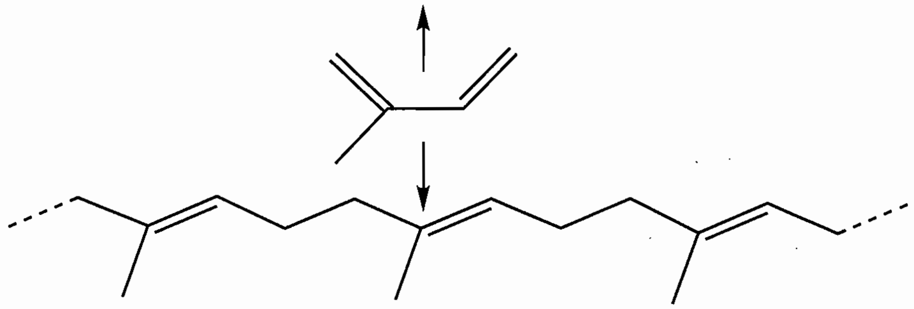
Problem 13.35 Each rearrangement step is tertiary carbocation to tertiary carbocation.



Problem 13.31 In the rubber molecule shown on page 625, all the double bonds are (*Z*). There is another form with all the double bonds (*E*), which is called gutta percha. Of course, there could also be all sorts of polymers with some double bonds (*E*) and others (*Z*). These molecules may be reasonable answers to the problem as set, but they do not occur in nature.

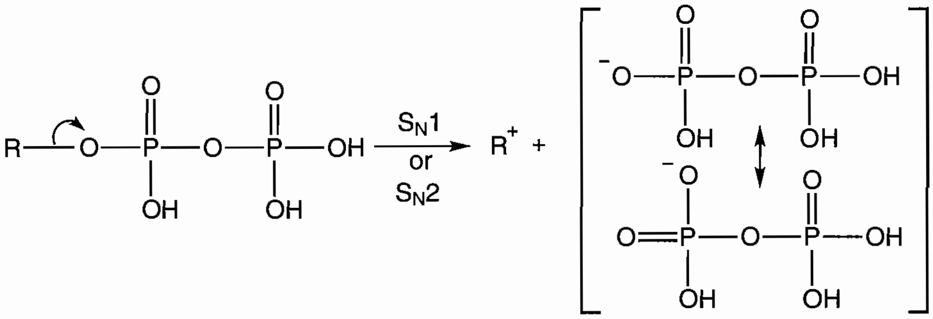


Polyisoprene, one form of natural rubber with all double bonds (*Z*)

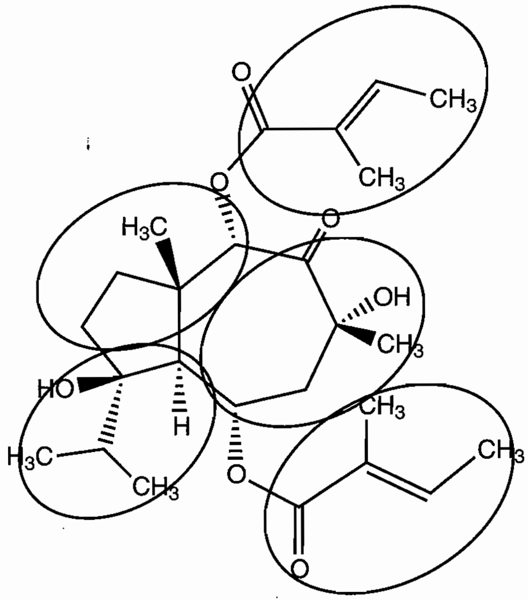


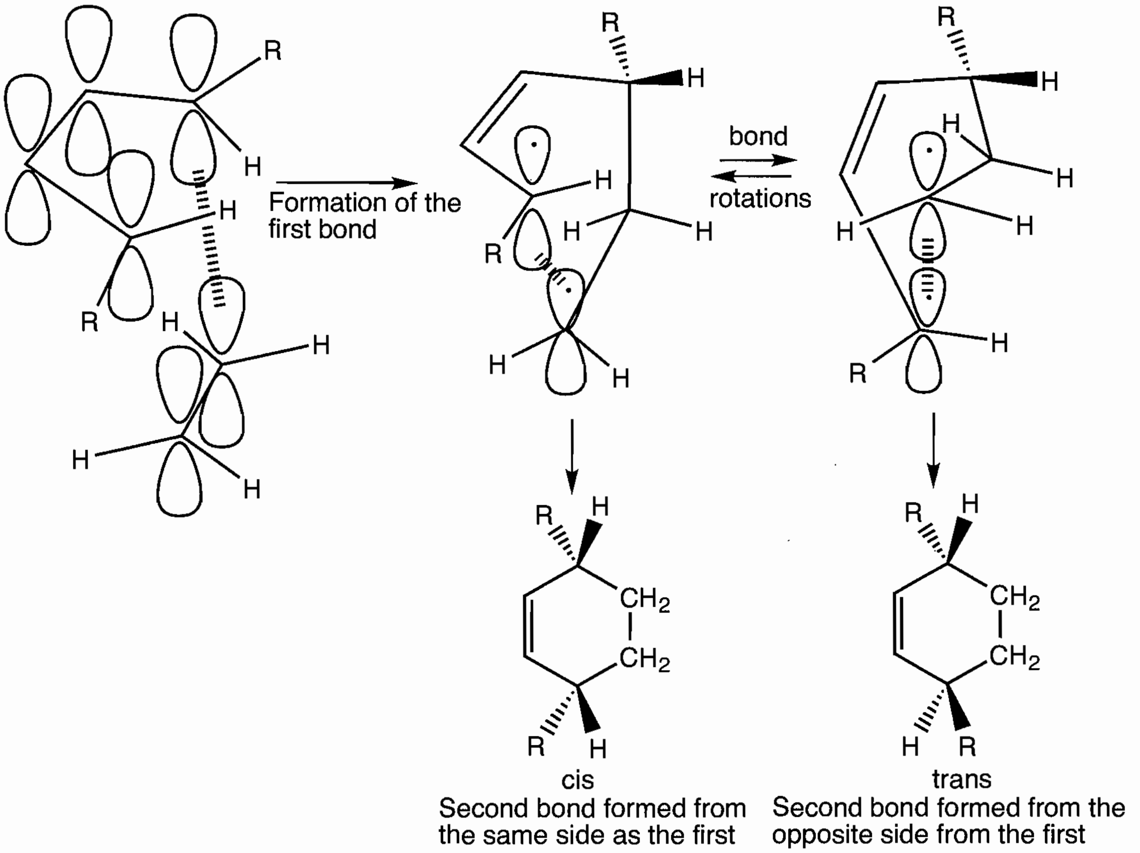
Polyisoprene with all double bonds (*E*), gutta percha

Problem 13.32 Loss of the diphosphate ion, shown here as an S_N1 reaction, leads to a resonance-stabilized diphosphate anion. The resonance stabilization of the anion makes diphosphate a good leaving group.



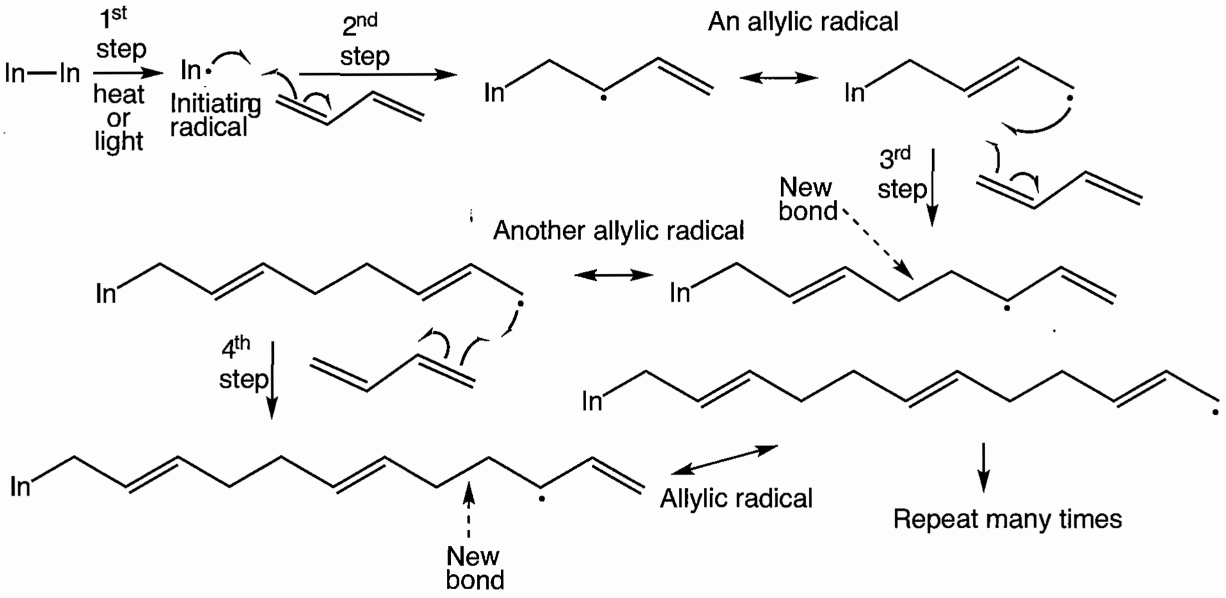
Problem 13.34 There are five isoprene units in laserpitin. The oxygens aren't part of the carbon framework. Each circled group has five carbons that are ultimately derived from isoprene.



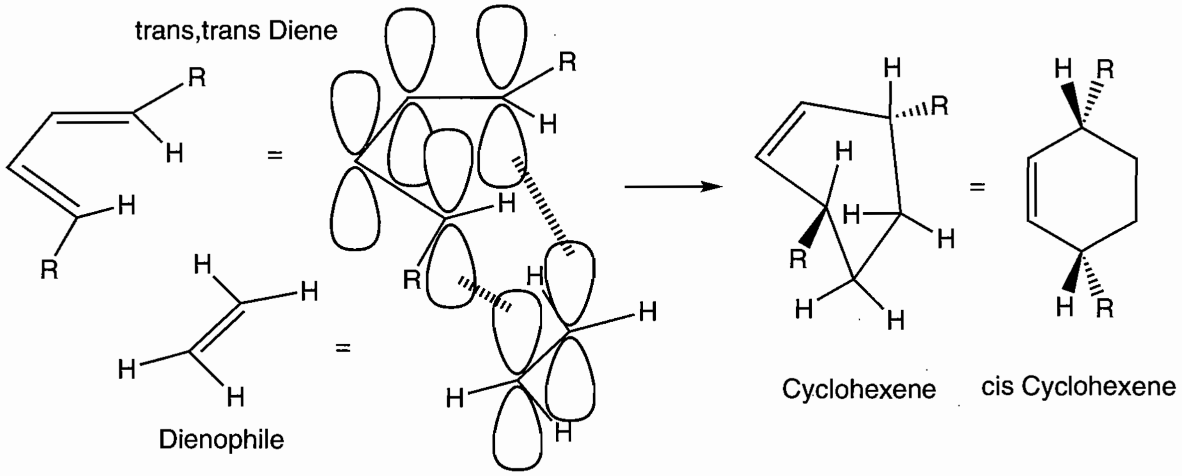


Once again, the experimental results show that the Diels–Alder reaction is concerted; the two new bonds are formed at the same time, and there is no intermediate (Fig. 13.53, p. 620).

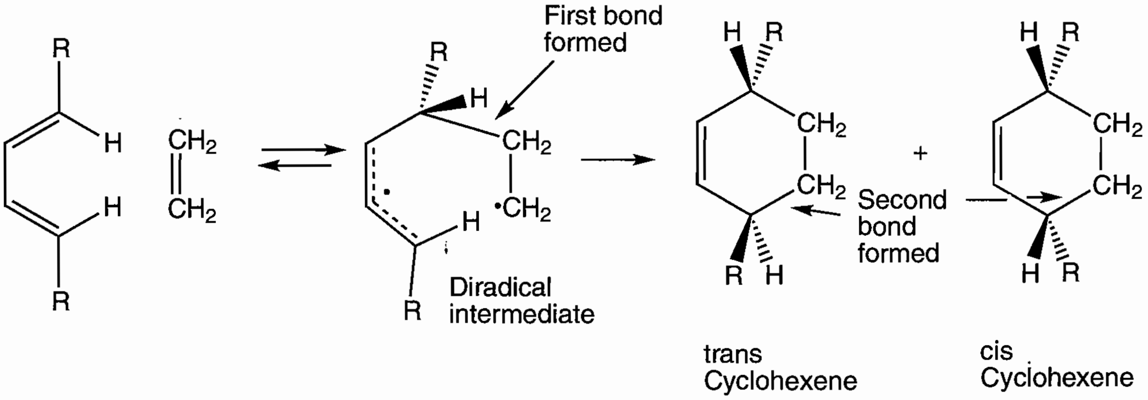
Problem 13.30 An initiating radical (In•) is formed in the first step. It adds to a butadiene to form a resonance-stabilized allylic radical in the second step. This allylic radical then adds to another butadiene to form a new allylic radical. This process is repeated many times to form the polymer.



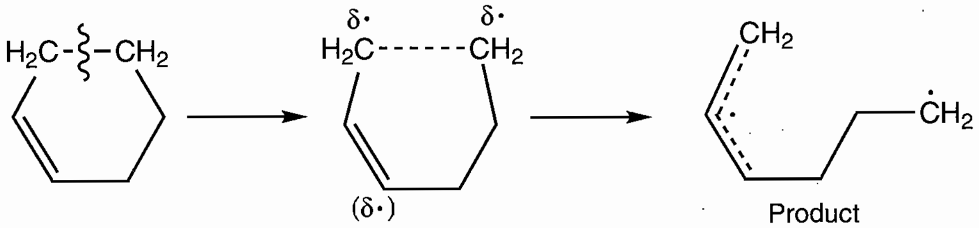
Problem 13.27 A one-step addition to the trans,trans diene must give a single product, the one shown in the problem figure in which the R groups are cis to each other.



This product is exactly what is seen experimentally, so the one-step, concerted mechanism is in accord with experiment. Let's now see if the two-step process works out. If one bond is made before the other, there must be an intermediate diradical in which the second bond can be formed from the same or opposite side as the first. Two different stereoisomers will result. That there should be two isomers depending on the direction of the second bond formation is relatively easy to understand; what's hard to see is just how the groups on the diene appear in the cyclohexene product. Follow the diagram, but do look at models as well.



In cyclohexene, one of the developing radicals is a resonance-stabilized allyl radical, and it is more stable than the simple localized radicals formed in carbon–carbon bond breaking in cyclohexane. Accordingly, the product diradical, and the transition state leading to it, are more stable than those in the cyclohexane reaction. The energy required to break the σ bond in cyclohexene is lower, and this is reflected in the bond dissociation energy quoted in the problem (80 kcal/mol).

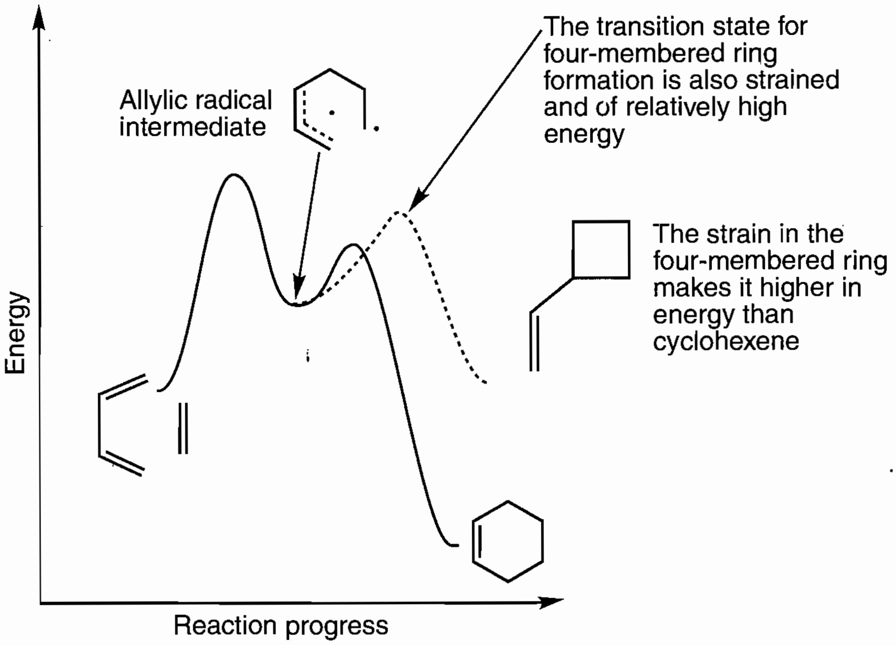


Cyclohexene

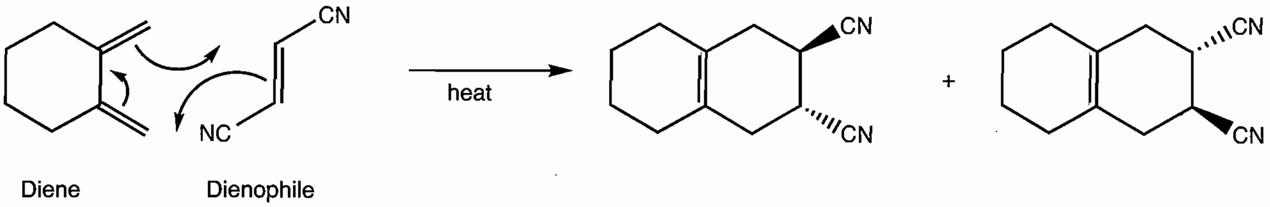
Transition state
[radicals are developing on two carbons (δ •); one end is delocalized]

Product
(a diradical in which one end is resonance stabilized)

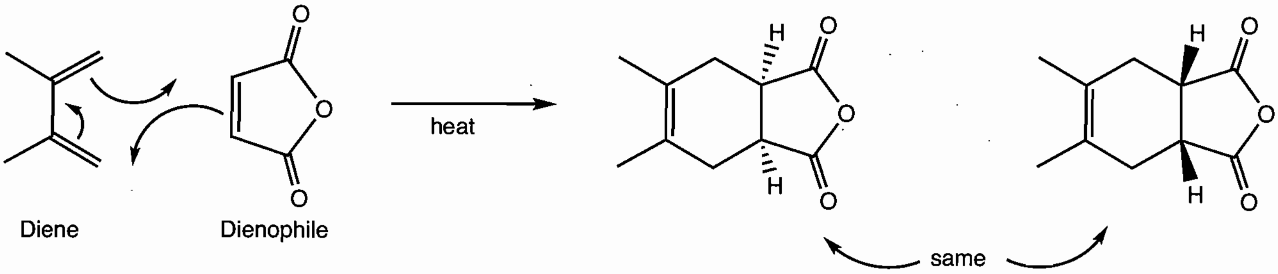
Problem 13.26 Vinylcyclobutane lies higher in energy than cyclohexene, largely because of the strain energy in the molecule. In the transition state for formation of vinylcyclobutane (see dashed lines), some of this strain will be present. Accordingly, it, too, lies relatively high in energy.



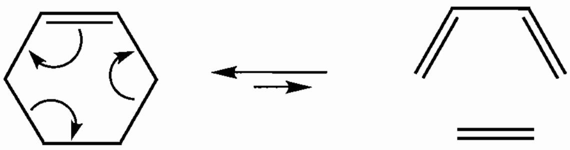
Problem 13.22 *(continued)*



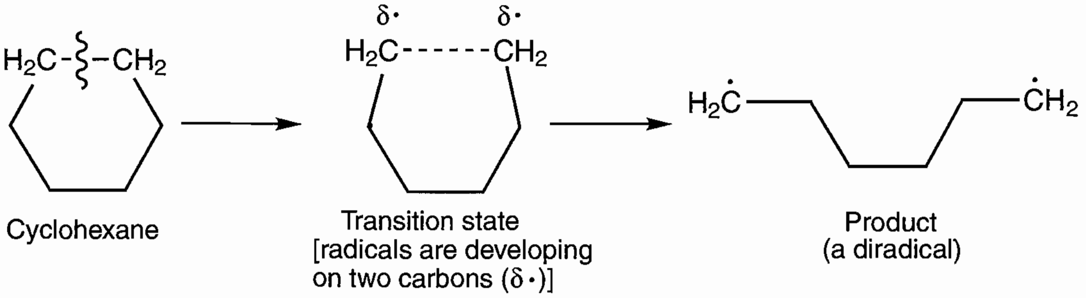
(d) Only one dienophile can be used to make this bicyclic product. We cannot use the (*E*) dienophile because we can't have a five-membered ring containing a trans double bond. This reaction gives a single product.

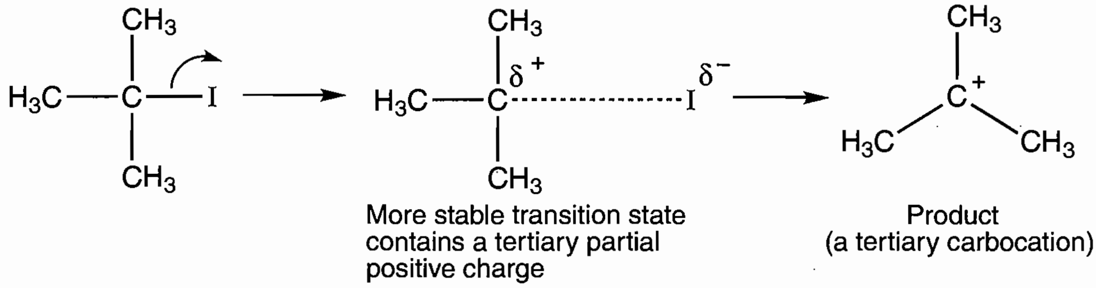


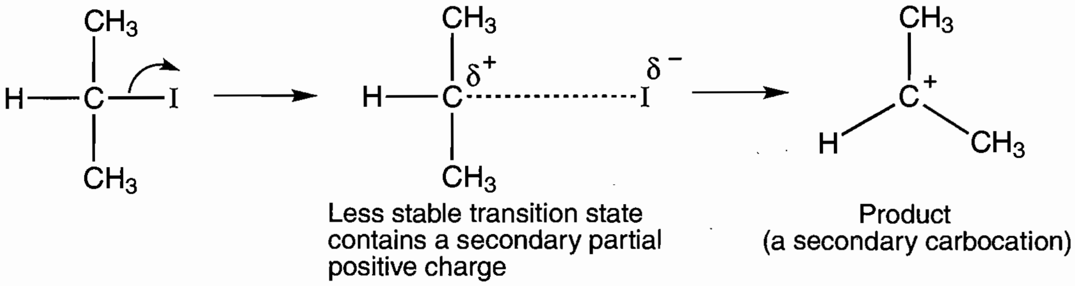
Problem 13.23 Nothing to it.



Problem 13.24 In the transition state for bond breaking, the bond is stretching, and radical centers are developing on the bonded carbons (δ•). This process is illustrated for carbon–carbon bond breaking in cyclohexane, a reasonable model for ethane.

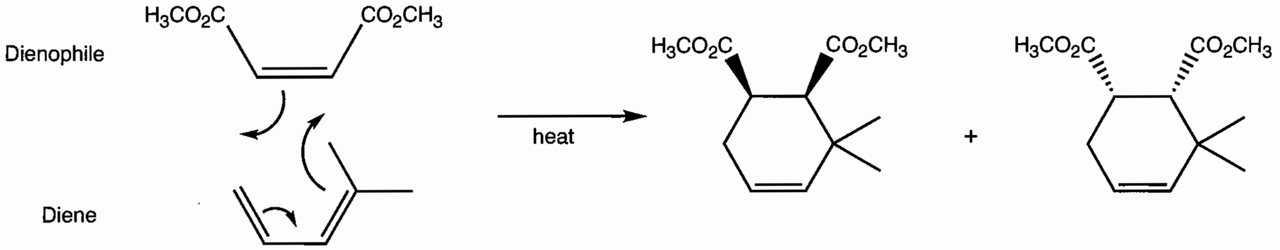




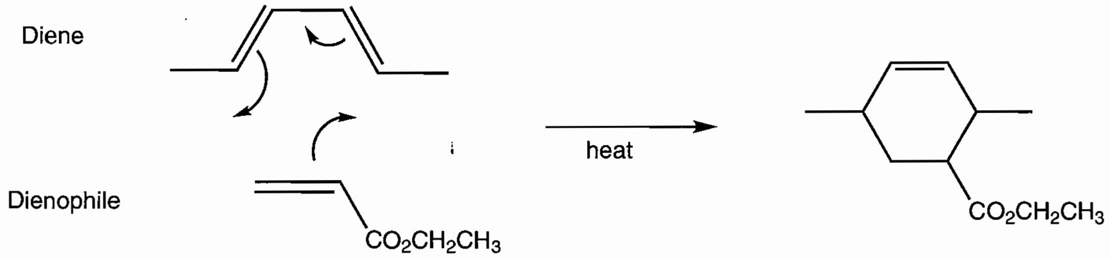


Problem 13.22

(a) Because the stereochemistry of the esters on the ring is not specified, we could use either the (*E*) or the (*Z*) starting dienophile. The answer that is shown uses the (*Z*) dienophile, which gives the cis product (both enantiomers). If we start with the (*E*) dienophile, we would obtain the trans product (both enantiomers).



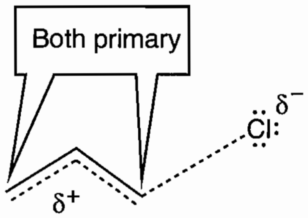
(b) This reaction will give a mixture of stereoisomers.



(c) The best Diels–Alder reaction for making this product uses dicyanoethylene, which is a great dienophile. The stereochemistry of the product is not specified. The (*E*) dieneophile is used this time to show the trans substitution (both enantiomers) in the product. If we used the (*Z*) dienophile, then we would obtain the cis isomer (which is achiral).

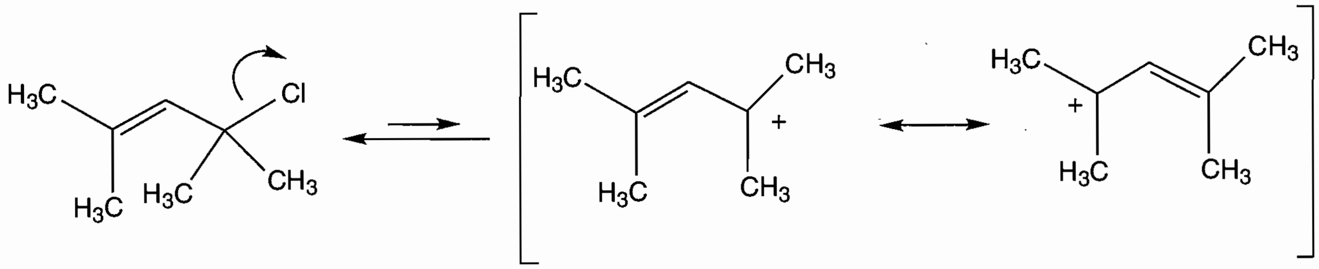
(continued)

Problem 13.20 *(continued)*

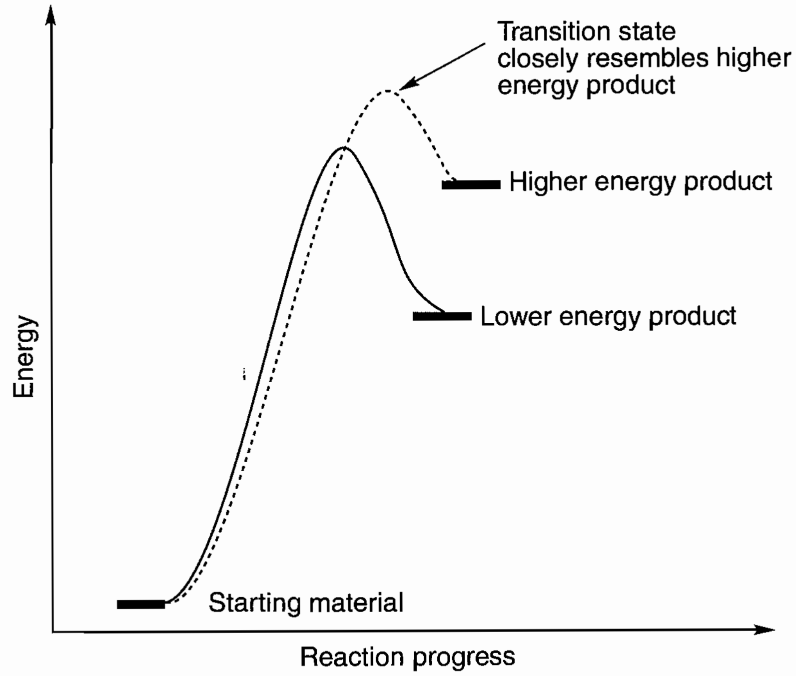


In this transition state, the positive charge is shared between two primary positions; this is the less stable transition state

There are, of course, many possible molecules that would ionize faster. Perhaps the simplest modification would be to add two methyl groups as shown. Now the resonance-stabilized cation is tertiary at both ends.

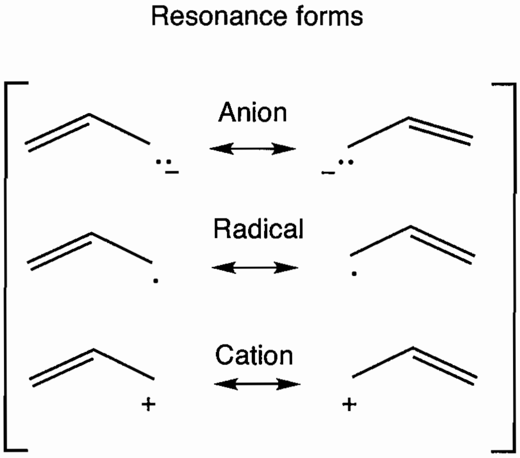


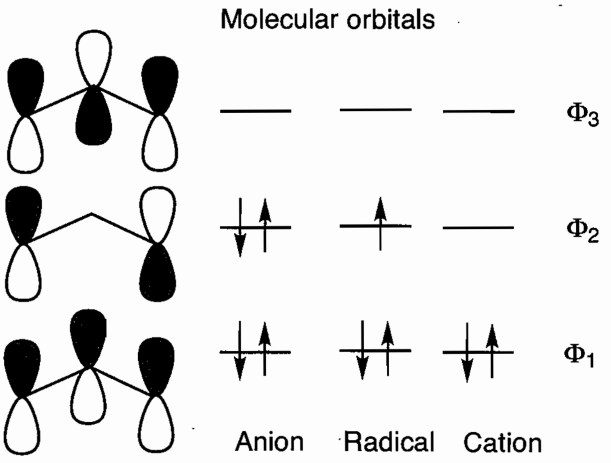
Problem 13.21 The problem is to explain why there should be a connection between the stability of the products (thermodynamics) and the energies of the transition states leading to the products (kinetics). Why should thermodynamics and kinetics be related? Ionization is surely an endo-thermic process, and, as noted by the Hammond postulate, the more endothermic the reaction, the more the transition state will look like the product. Accordingly, the thermodynamic stability of the allyl cation formed is related to the ease of formation, a kinetic property.



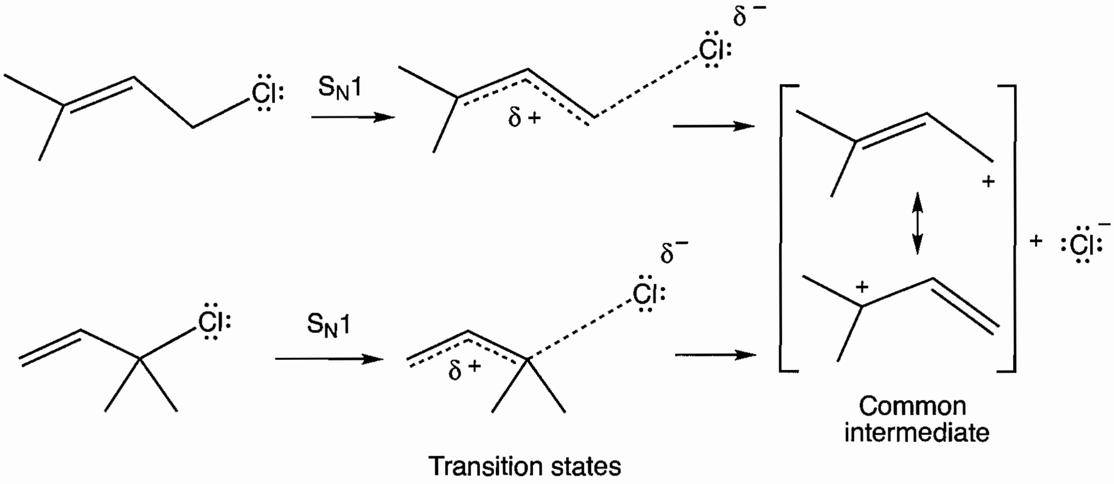
There is another way to put it. The transition states for ionizations to give carbocations will contain partially developed positive charges. A partially developed tertiary positive charge will be more stable than a partially developed secondary positive charge, and this difference will be reflected in the relative energies of the transition states.

Problem 13.19 There are two π electrons in the allyl cation, three π electrons in the allyl radical, and four π electrons in the allyl anion. The resonance picture shows the individual electronic descriptions contributing to the real, delocalized structures.

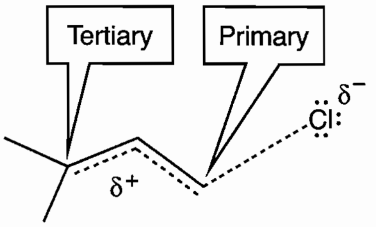




Problem 13.20 The two compounds ionize to the same carbocation intermediate. Although the two transition states are different, the ion will be partially developed in the transition state, and the rates of chloride loss will be quite similar.



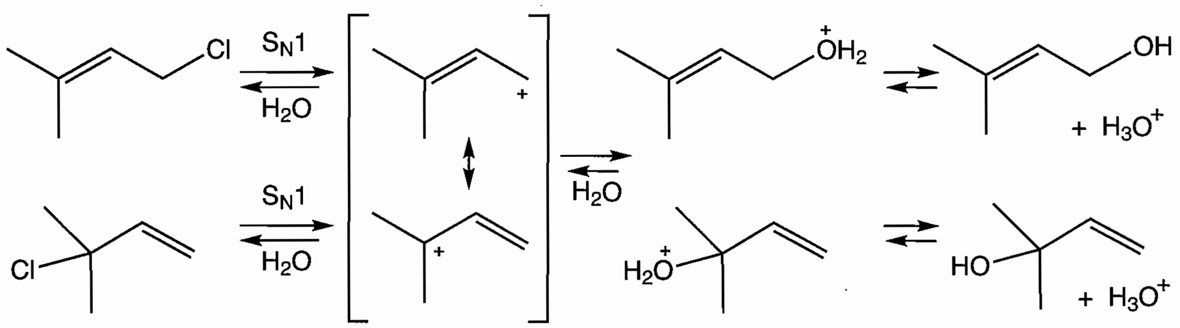
Both compounds ionize faster than the others in Table 13.2 because of the tertiary δ^+ in the transition state. A tertiary partial positive charge is more stable than a secondary or primary partial positive charge. For example,



In this transition state, the positive charge is shared between a tertiary and primary position; this is the more stable transition state

(continued)

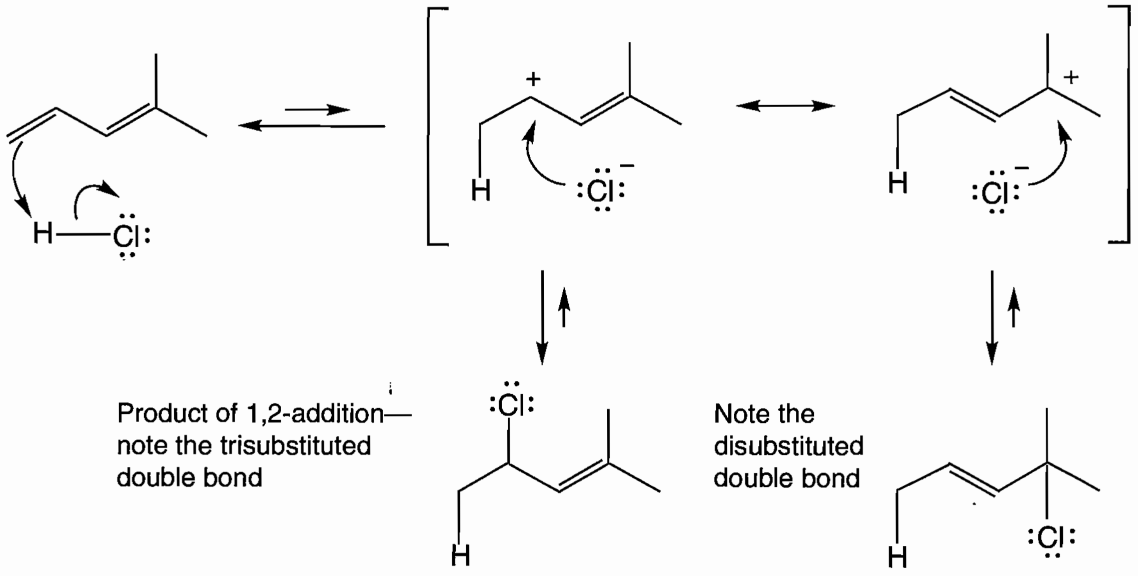
Problem 13.15 The same resonance-stabilized carbocation is formed on S_N1 solvolysis of both chlorides. The positive charge is shared by two carbons. The nucleophile, water, can add to each of these carbons to give, after proton loss, two alcohols. As the same carbocation intermediate is formed from each chloride, the two alcohols must be produced in the same ratio.



One, resonance-stabilized cation

Addition of water at the two positions sharing the positive charge leads to two oxonium ions and, after deprotonation, the two alcohols

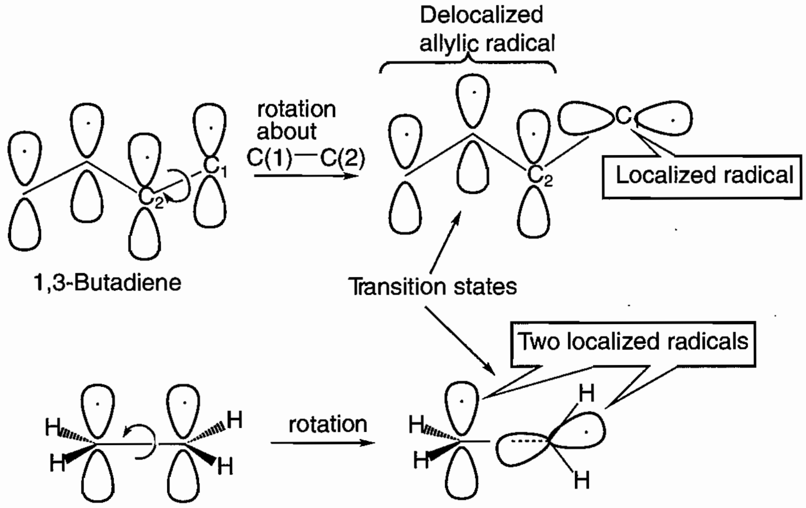
Problem 13.18 The initial protonation gives the resonance-stabilized cation shown. The kinetic product will be the one that results from 1,2-addition for the reasons summarized in Figure 13.38, p. 611. Given the broad hint in the problem, you surely won't pick the product of 1,4-addition as the thermodynamic product. In this case, the kinetic and thermodynamic products are the same. The question is why. Compare the products formed in 1,2- and 1,4-additions. The product of 1,2-addition contains a trisubstituted double bond, whereas the product of 1,4-addition has only a less stable disubstituted double bond.



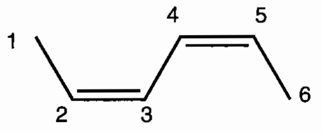
Product of 1,2-addition—note the trisubstituted double bond

Note the disubstituted double bond

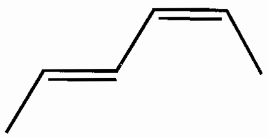
Problem 13.13 The transition state for rotation about one of the "double" bonds in a 1,3-butadiene contains a localized radical and a delocalized allylic radical. It is this delocalization of the allylic radical in the transition state that makes this rotation more favorable than the related motion in a simple ethylene. In an alkene, two localized radicals appear in the transition state for rotation about a carbon–carbon bond.



Problem 13.14 Based on the information from Problem 13.13, the rotation around the C(2)—C(3) bond of the (*Z*,*Z*)-2,4-hexadiene conjugated system should be about 52 kcal/mol (217 kJ/mol). We might expect the energy to be somewhat less than 52 kcal/mol as there is more destabilizing steric interaction with the C(1) methyl than is present in the 1,3-butadiene, the data for which are given in Problem 13.13. It is easier to isomerize when the starting (*Z*) isomer is higher in energy (less stable).



(*Z*,*Z*)-2,4-Hexadiene



(*E*,*Z*)-2,4-Hexadiene

If we want the *K* value to be 5:95 (which is 0.053), and ΔG is 52 kcal/mol, we can use the *R* value of 1.98×10^{-3} kcal/mol•kelvin and the formula $\Delta G = -RT \ln K$.

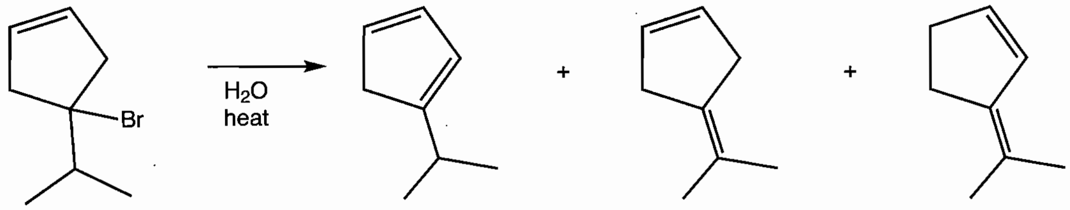
The math goes like this:

$52\ \text{kcal/mol} \div 1.98 \times 10^{-3}\ \text{kcal/mol}\cdot\text{kelvin} = -T \ln 0.053$
$26{,}300\ \text{kelvin} = -T(-2.94)$
$8{,}940\ \text{kelvin} = T$
$8{,}670\ °\text{C} = T$

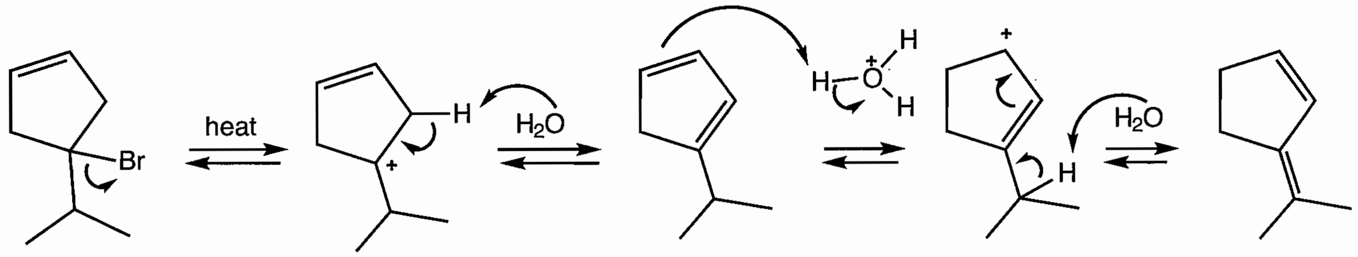
Therefore, a very high temperature would be required to have a ratio of 95:5 for the *E*:*Z* isomers. However, at 150 °C, the equilibrium for the *E*/*Z* isomerization is about 10^{-27}:1!

Problem 13.10 *(continued)*

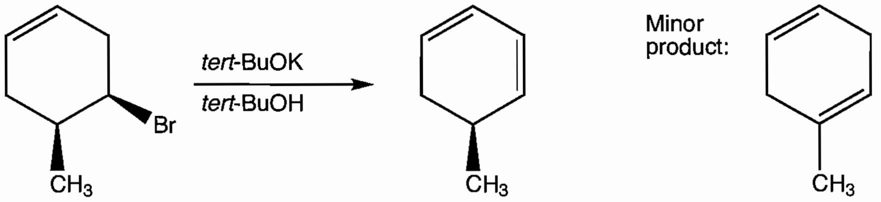
(b) An E1 reaction is reversible. With time the most stable diene, which is the conjugated diene with the most substitution in this example, will be formed. The mechanism for its formation is shown.



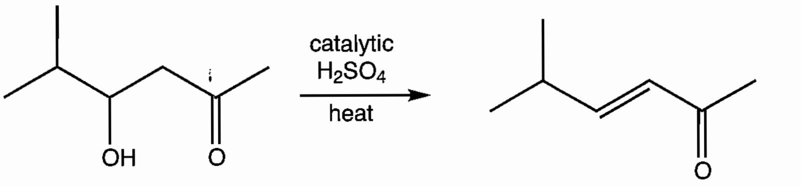
Most stable product



(c) This reaction is an E2 process that requires a β anti-periplanar hydrogen. There are two such hydrogens available, but the allylic hydrogen will be more acidic and more accessible (it is a secondary hydrogen and the other one is tertiary). In addition, the conjugated diene is thermodynamically more stable than the unconjugated diene.



(d) This E1 reaction will favor the conjugated system. The product is called an enone.



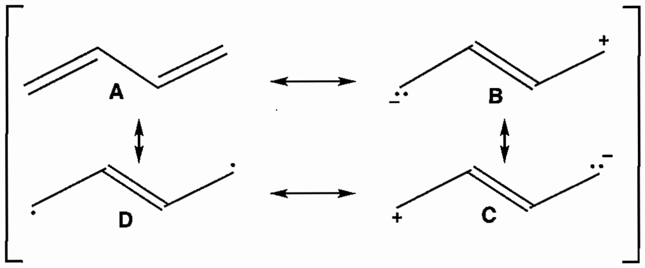
Problem 13.12 The equation to use is $\Delta G = -2.3RT \log K$.

So, $-2.5 = -1.364 \log K$ [at 25 °C, $2.3RT = 1.364$ kcal/mol (Footnote 2, Chapter 7, p. 276)]

$\log K = 1.83$

$K = 68$, and there is only 1.4% of the s-cis compound present at equilibrium.

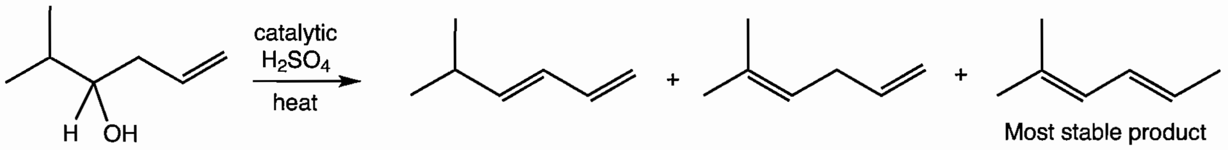
Problem 13.9



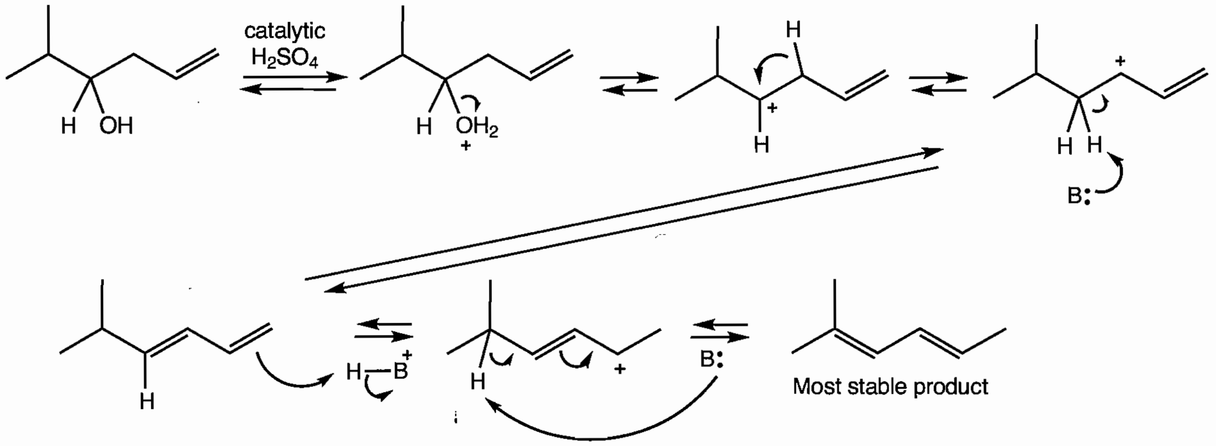
Forms **B**, **C**, and **D** all have one fewer bond than form **A**. In addition, forms **B** and **C** have separated charges. Only **A** has a filled octet for each carbon. Form **A** is by far the major contributing structure.

Problem 13.10

(a) This reaction will be complicated by the reversible nature of alcohol dehydration. The most stable product is the result of two hydride shifts. It is the most stable because it has the most substituted conjugated diene.

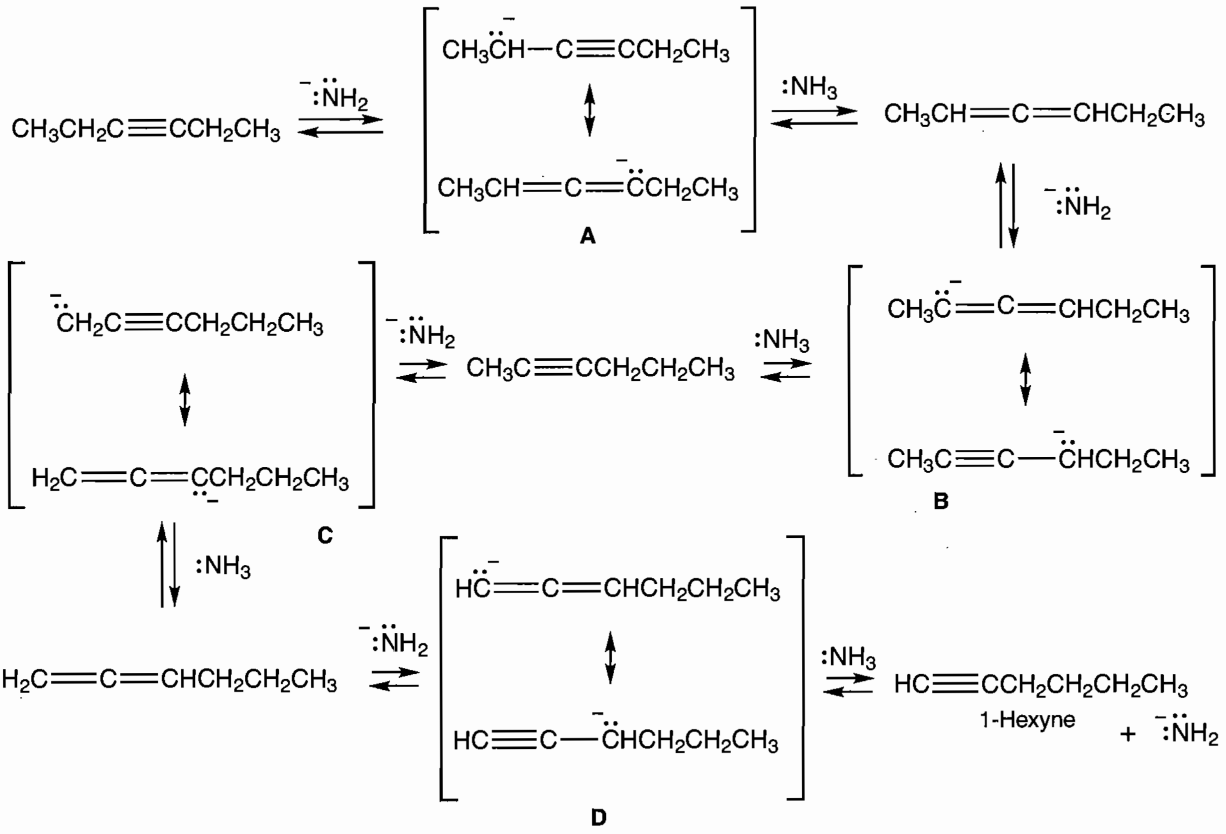


The mechanism for the formation of the most stable product is shown here.



(continued)

Problem 13.6 *(continued)*

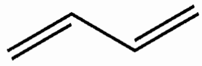


Now the terminal acetylene can lose its acetylenic hydrogen to generate an acetylide, and the reaction stops at this critical point. The 1-alkyne is a *much* stronger acid than any of the other species in equilibrium. Removal of the acetylenic proton is greatly favored thermodynamically. When the solution is quenched through addition of water, the acetylide protonates to produce 1-hexyne under conditions (neutral) to which it is stable.

$$HC{\equiv}CCH_2CH_2CH_2CH_3 \xrightleftharpoons[:NH_3]{^-:\ddot{N}H_2} {}^-C{\equiv}CCH_2CH_2CH_2CH_3$$

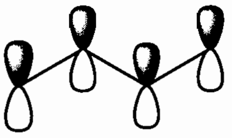
$$\bar{:}C{\equiv}CCH_2CH_2CH_2CH_3 \xrightleftharpoons{H_2O} HC{\equiv}CCH_2CH_2CH_2CH_3$$

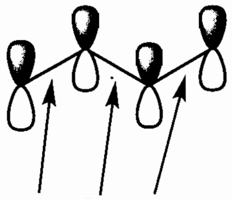
Problem 13.8 Each carbon in 1,3-butadiene is sp^2 hybridized. Therefore, each C—C bond is made by mixing an sp^2 orbital from one carbon with the sp^2 orbital of the adjacent carbon.



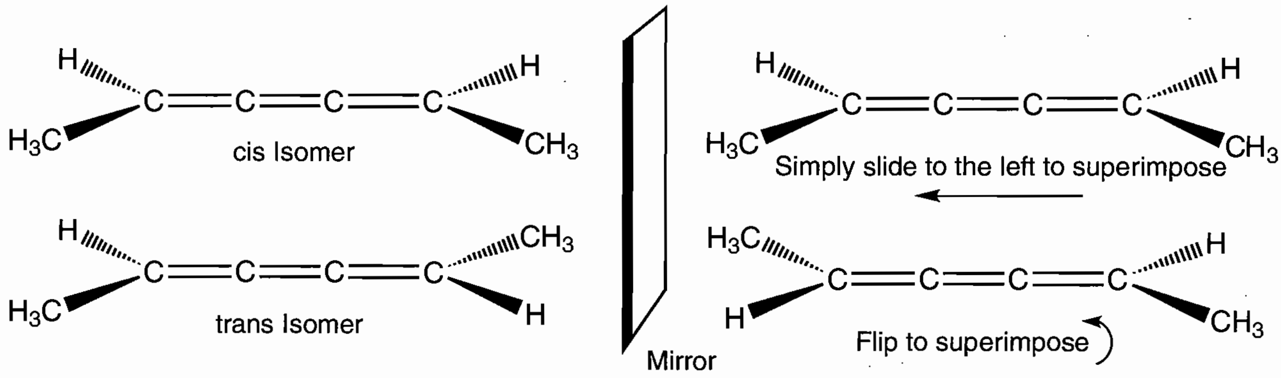
1,3-Butadiene

Showing the *p* orbitals for the π bonds

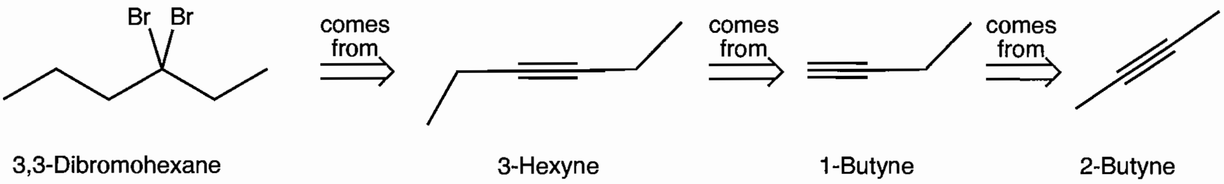




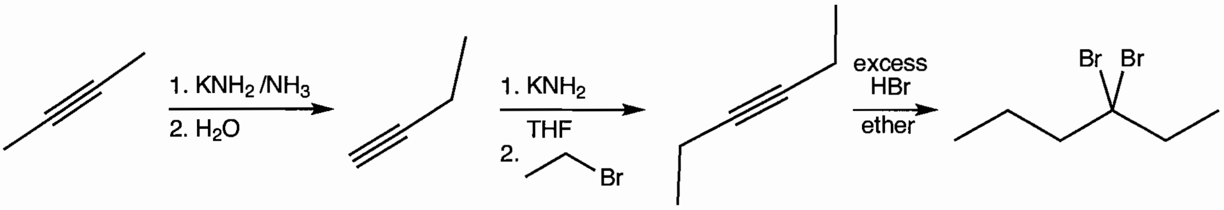
These flat molecules are all achiral, just like ethylene. Their mirror images are always superimposable on the originals.



Problem 13.5 The 3,3-dibromohexane can come from 3-hexyne. We know that an alkyne reacts with excess HBr to give the geminal dibromide (p. 520). 3-Hexyne can come from alkylation of 1-butyne with ethyl iodide. The 1-butyne can come from 2-butyne by the process shown in Figure 13.7.



The forward reactions are shown. Because the 3-hexyne is symmetrical, treatment with excess HBr gives only one product.

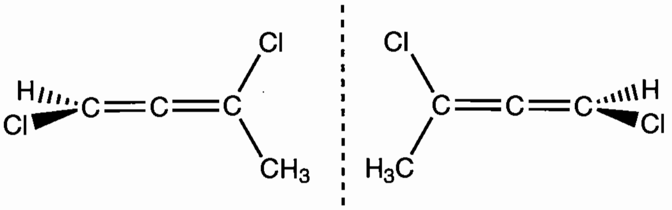


Problem 13.6 This is just a two-stage version of the mechanism outlined in Figures 13.7–13.13. Strong base removes a proton from the carbon adjacent to the triple bond to give resonance-stabilized anion **A**. Reprotonation can occur in two places, one of which gives an intermediate allene. The allene is also acidic, and strong base can remove a proton to produce a second resonance-stabilized anion, **B**. Reprotonation, followed by a third removal of a proton, gives **C**, which protonates to give a second allene. One more cycle of deprotonation to anion **D**, followed by reprotonation, generates 1-hexyne.

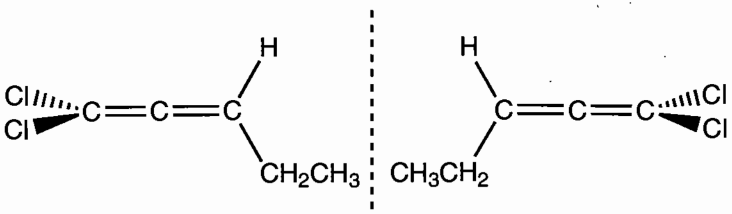
(continued)

Problem 13.2 *(continued)*

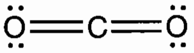
(c) 1,3-Dichloro-1,2-butadiene is chiral. The mirror image is non-superimposable on the original structure. There is no plane of symmetry.



(d) 1,1-Dichloro-1,2-pentadiene is achiral. The mirror image is superimposable on the original structure. There is a plane of symmetry, which is the plane of the paper.

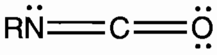


Problem 13.3 All these molecules are related to allenes.



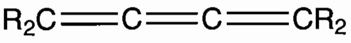
$\ddot{\underset{\cdot\cdot}{O}}=C=\ddot{\underset{\cdot\cdot}{O}}$

Carbon dioxide



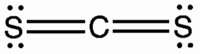
$R\ddot{N}=C=\ddot{\underset{\cdot\cdot}{O}}$

Isocyanates



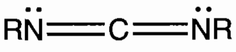
$R_2C=C=C=CR_2$

Cumulenes
(butatrienes)



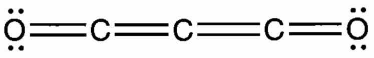
$\ddot{\underset{\cdot\cdot}{S}}=C=\ddot{\underset{\cdot\cdot}{S}}$

Carbon disulfide



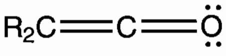
$R\ddot{N}=C=\ddot{N}R$

Carbodiimides



$\ddot{\underset{\cdot\cdot}{O}}=C=C=C=\ddot{\underset{\cdot\cdot}{O}}$

Carbon suboxide

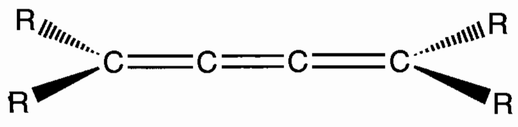


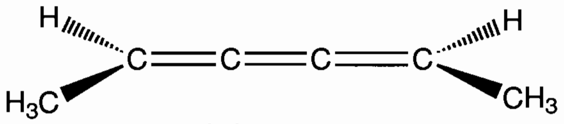
$R_2C=C=\ddot{\underset{\cdot\cdot}{O}}$

Ketenes

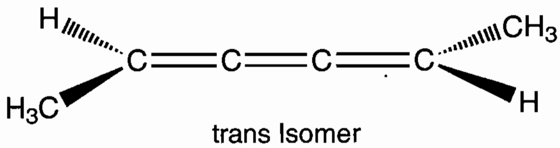
Problem 13.4 Just as in ethylene (but not in allene), the end groups of this molecule are coplanar. Therefore, there can be cis and trans stereoisomers.

In this molecule, the R–C–R groups are coplanar





cis Isomer



trans Isomer

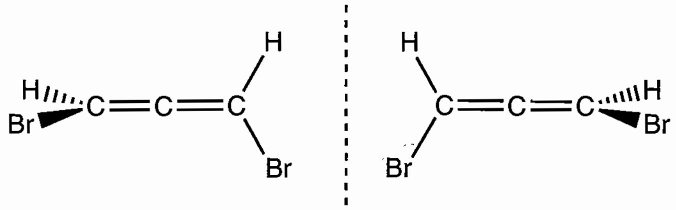
13

Dienes and the Allyl System: 2*p* Orbitals in Conjugation

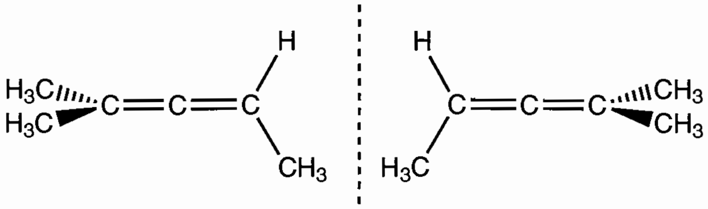
This chapter opens a three-chapter sequence in which we will explore the consequences of overlap of more than two 2*p* orbitals, "conjugation." There are both structural and chemical consequences, and the following problems deal with both areas. Two exceptionally important reactions emerge: the formation of allyl cations through protonation of 1,3-dienes and the Diels–Alder reaction. The former opens up synthetic possibilities and leads to a discussion of thermodynamic and kinetic control of reactions. The latter is arguably the most important synthetic reaction in the chemist's arsenal and leads in a single step to all manner of complex compounds containing six-membered rings. The following problems give lots of practice in both areas.

Problem 13.2

(a) 1,3-Dibromopropadiene is chiral. The mirror image is non-superimposable on the original structure. Notice that there is no plane of symmetry in this molecule.

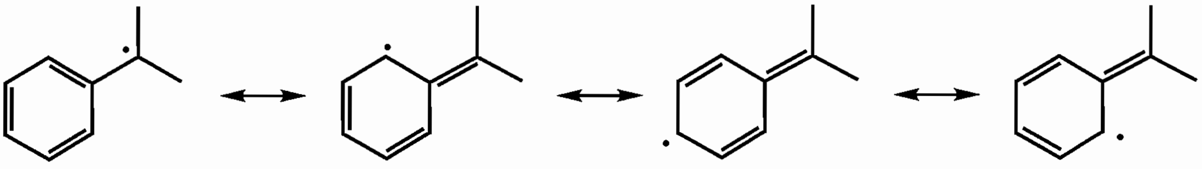


(b) 2-Methyl-2,3-pentadiene is achiral. The mirror image is superimposable on the original structure. The plane of the paper is a plane of symmetry for this molecule.

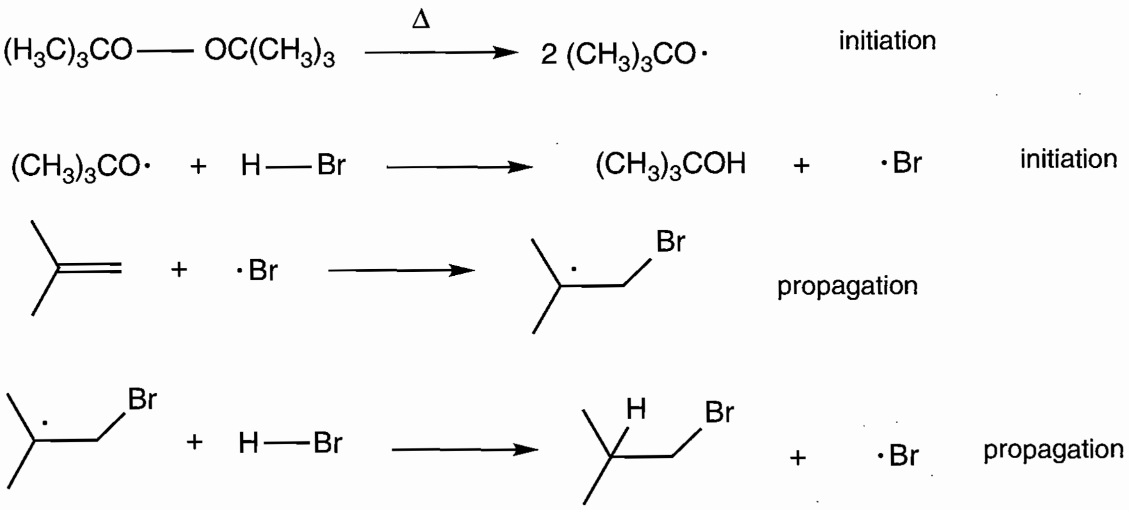


(continued)

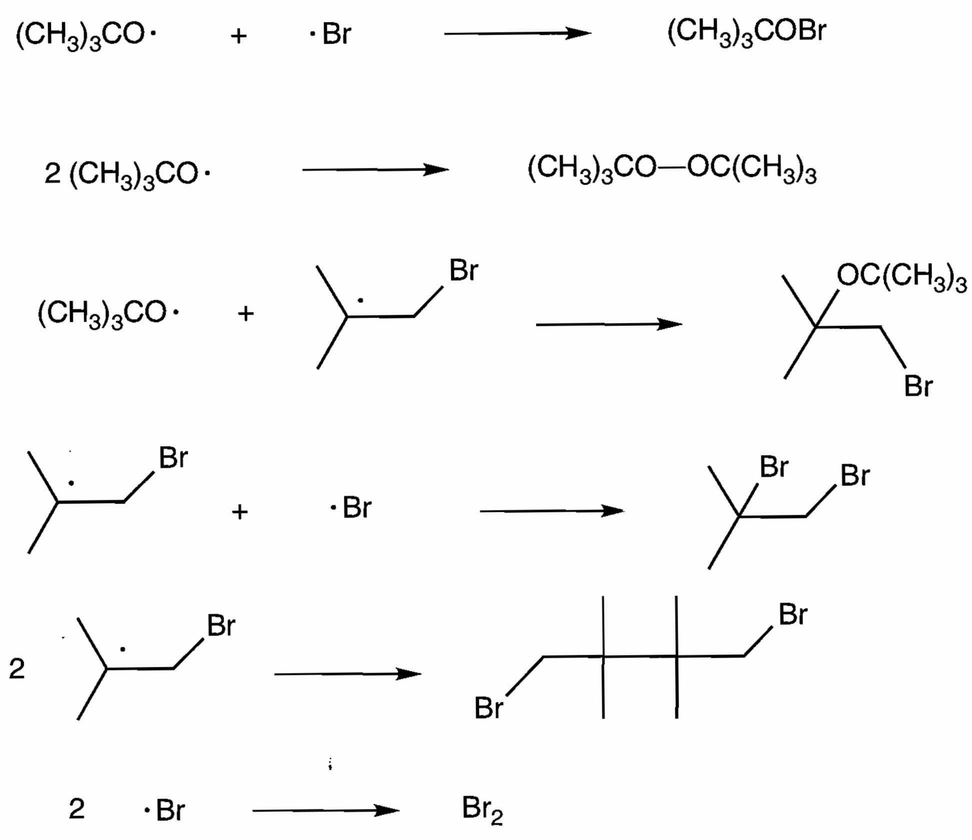
Problem 12.66 Oxygen is a diradical. It is able to abstract a hydrogen atom from the benzylic position. No, the benzylic hydrogen is not particularly acidic (pK_a of about 41) and oxygen is not a strong base. In this case, the hybridization of the radical carbon is sp^2, and it is not likely to change because sp^2 hybridization maximizes overlap with the π electrons of the aromatic ring. The carbon must be sp^2 in order to delocalize the radical density into the adjacent π system (see the structures in the figure). Notice that each resonance structure requires that the benzylic carbon be sp^2 hybridized.



Problem 12.63

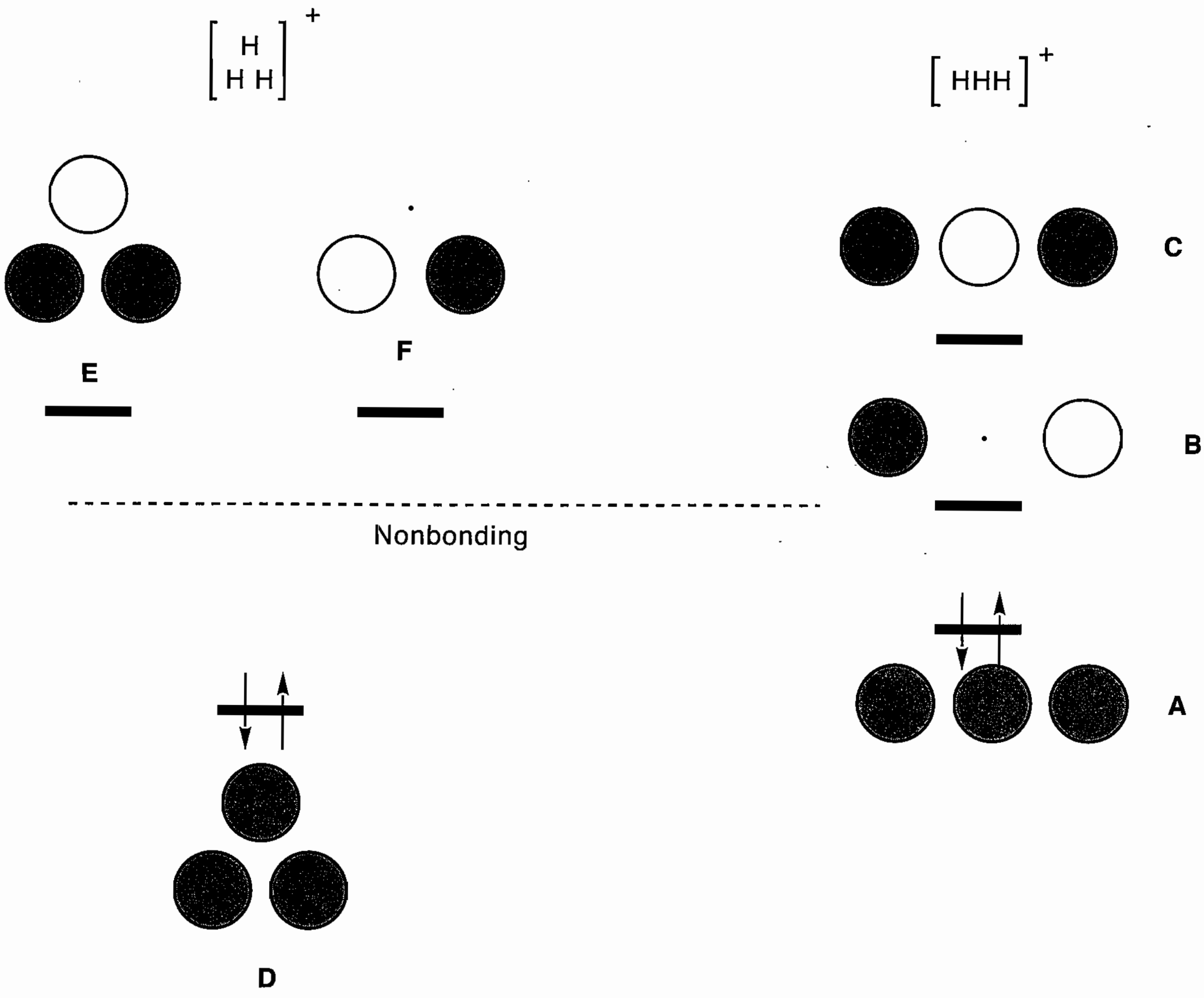


Problem 12.64

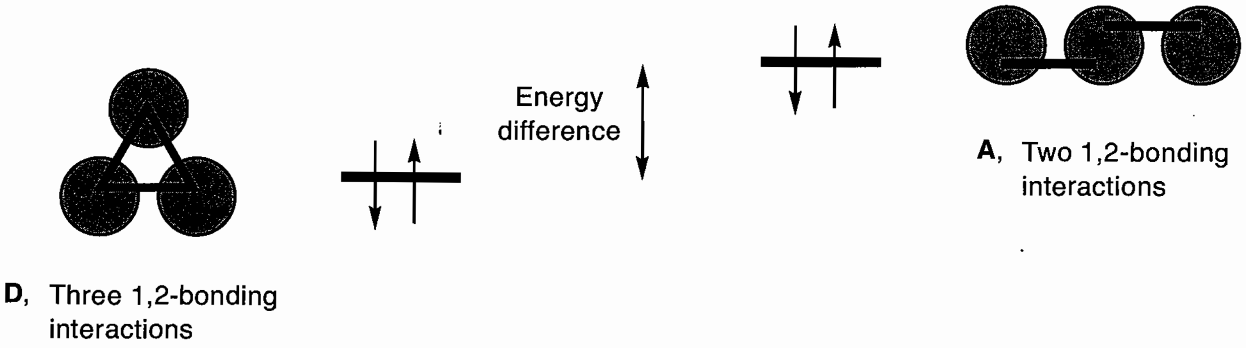


Problem 12.65 The central carbon is sp^2 hybridized in the animation. The sp^2 hybridization maximizes overlap with the sigma bonds on the adjacent carbons, in other words, hyperconjugation. The SOMO track shows the orbital mixing with the sigma bonds on the methyl groups. We have learned that the radical carbon is probably a rapidly inverting pyramid, somewhere between sp^2 and sp^3 hybridization.

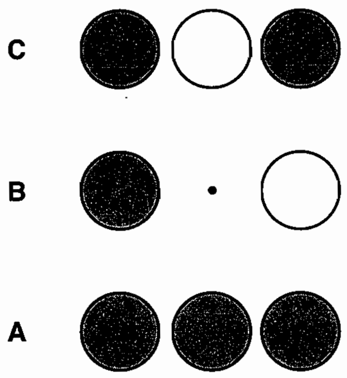
Problem 12.62 *(continued)*



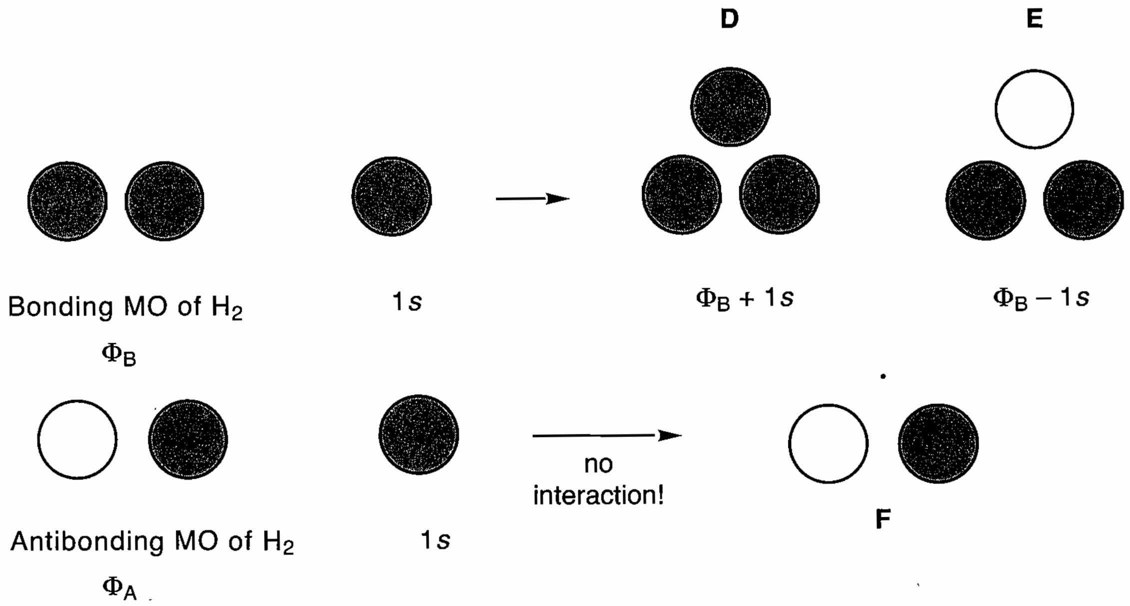
So, the critical question is, which is lower in energy, **D** or **A**? Only **D** and **A** are occupied by electrons, so it is only their energies that matter. As the diagram shows, **D** is lower in energy, and H_3^+ will be triangular. Why? Look at all the 1,2-bonding interactions in **D**. There are three in **D**, but only two in **A**.



Problem 12.62 We'll start by borrowing the molecular orbitals (MOs) for HHH from Problem 1.64 (p. 50).

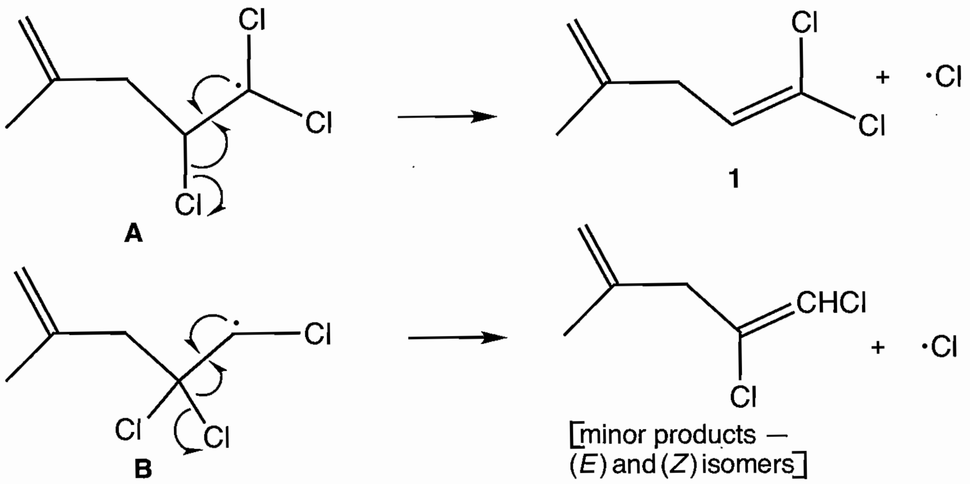


Here are the molecular orbitals for cyclic H_3. We'll build them just as we made the molecular orbitals on p. 50.



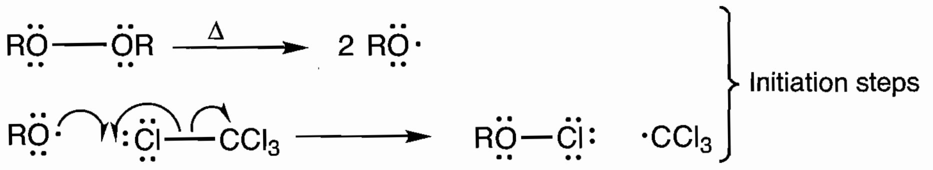
(continued)

Problem 12.60 *(continued)*

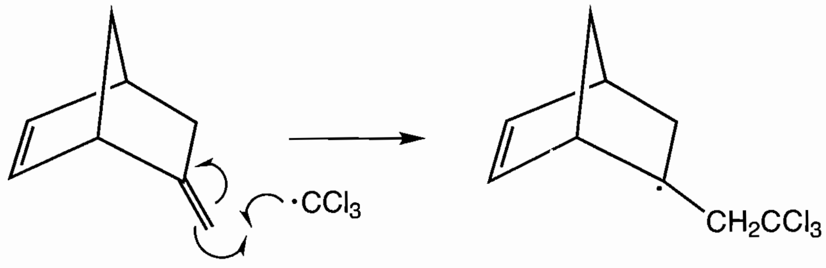


[minor products — (*E*) and (*Z*) isomers]

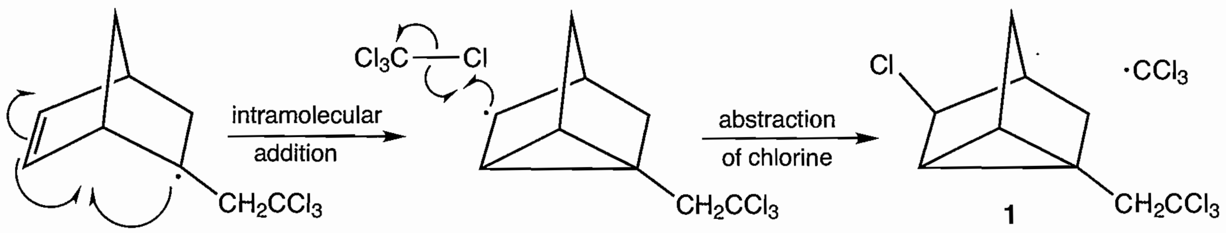
Problem 12.61 The initiation steps are easy.



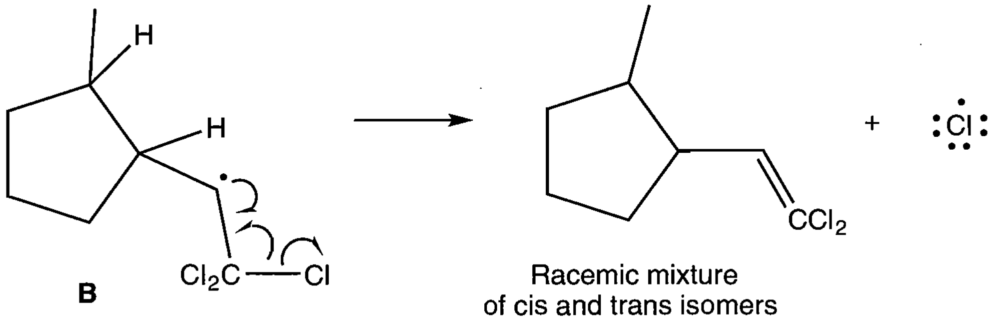
Addition of the trichloromethyl radical to the exocyclic double bond accomplishes one goal, the formation of a CH_2CCl_3 group.



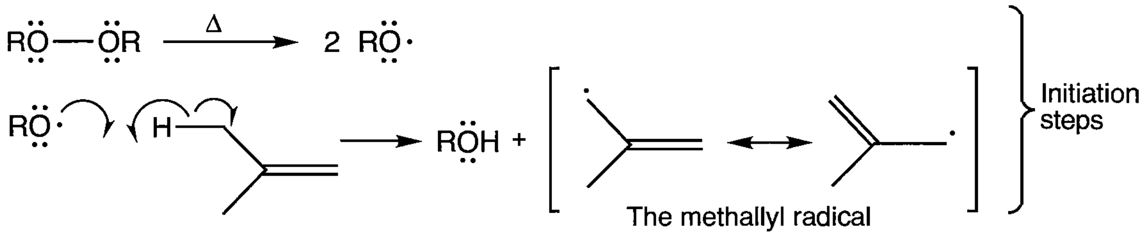
A second goal, the construction of the three-membered ring, is attained through an intramolecular addition reaction. The reaction is completed by abstraction of a chlorine atom from CCl_4 to give **1** and a chain-carrying trichloromethyl radical.



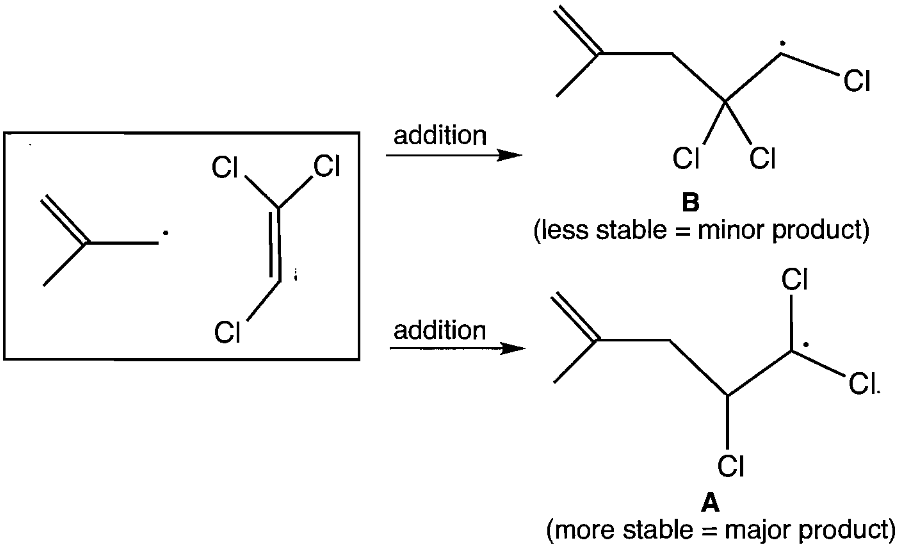
Loss of a chlorine atom finishes the mechanism.



Problem 12.60 This is another free radical chain reaction. An alkoxy radical formed in the first initiation step abstracts a hydrogen atom from isobutene to generate a resonance-stabilized methallyl radical.



The methallyl radical adds to trichloroethylene to give either radical **A** or **B**. Formation of **A** will be preferred both because it is more stable than **B** (resonance stabilization by two chlorines instead of one) and on the grounds that approach of the methallyl radical to the end of trichloroethylene bearing only one large chlorine will be preferred as a result of steric congestion.



Loss of a chlorine atom from **A**, the predominant radical intermediate, leads to **1**, the major product of the reaction. The minor products come from chlorine loss from the less favored radical intermediate **B**.

(continued)

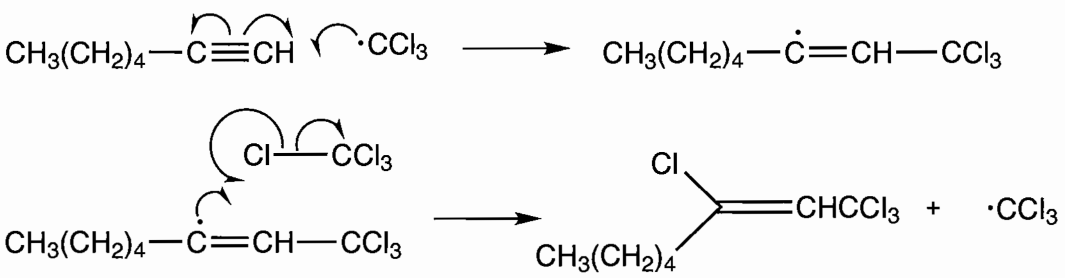
Problem 12.58 *(continued)*

In several of these reactions, the benzyl radical, $\mathrm{Ph\dot{C}H_2}$, appears. If it dimerizes, the final product, $\mathrm{PhCH_2CH_2Ph}$, is formed.

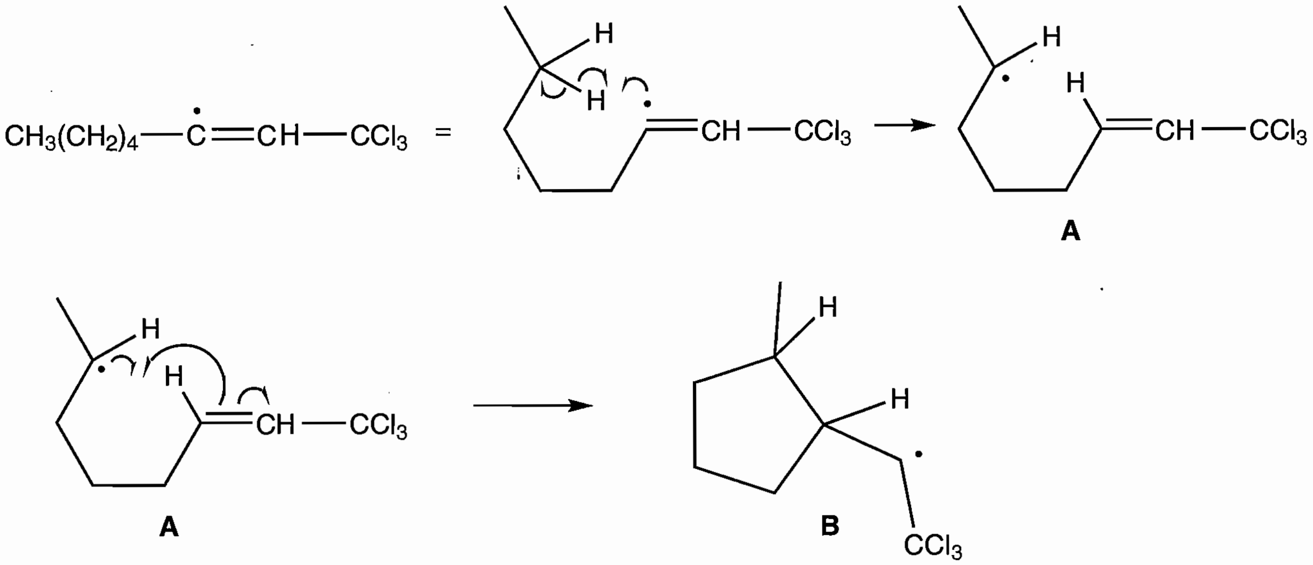
$$2\ \mathrm{Ph\dot{C}H_2} \longrightarrow \mathrm{PhCH_2CH_2Ph}$$

Problem 12.59 The acyclic product comes from a straightforward radical chain addition reaction. Note that in the last step, the chain-carrying trichloromethyl radical is regenerated.

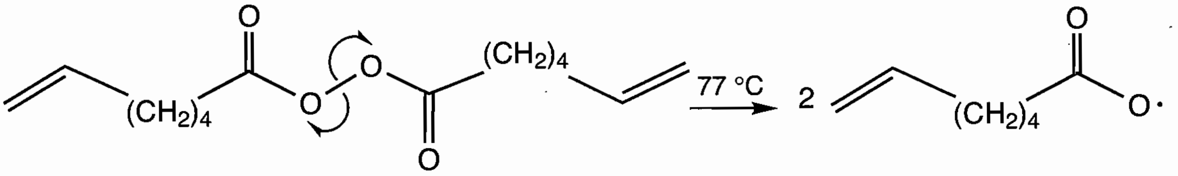
$$\left.\begin{array}{l} \mathrm{R\ddot{\underset{\cdot\cdot}{O}}{-}\ddot{\underset{\cdot\cdot}{O}}R} \xrightarrow{\Delta} 2\ \mathrm{R\ddot{\underset{\cdot\cdot}{O}}\cdot} \\ \mathrm{R\ddot{\underset{\cdot\cdot}{O}}\cdot} + \mathrm{CCl_4} \longrightarrow \mathrm{ROCl}\ \ \cdot\mathrm{CCl_3} \end{array}\right\}\text{Initiation steps}$$



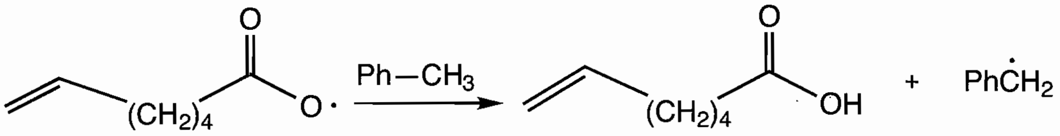
The cyclic product is more difficult. What do we have to do? The two major things that must be accomplished in this reaction are formation of a five-membered ring and loss of a chlorine atom. Formation of the cyclic product starts with an intramolecular hydrogen abstraction to give **A**. Radical **A** then undergoes an intramolecular addition to produce **B**. This reaction completes one major goal: the formation of the five-membered ring.



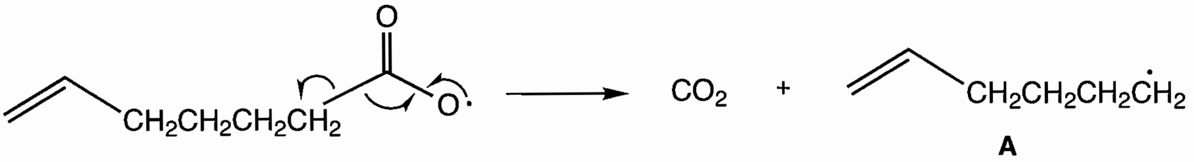
Problem 12.58 Decomposition of the peroxide occurs by breaking the weak oxygen–oxygen bond to give a pair of carboxy radicals:



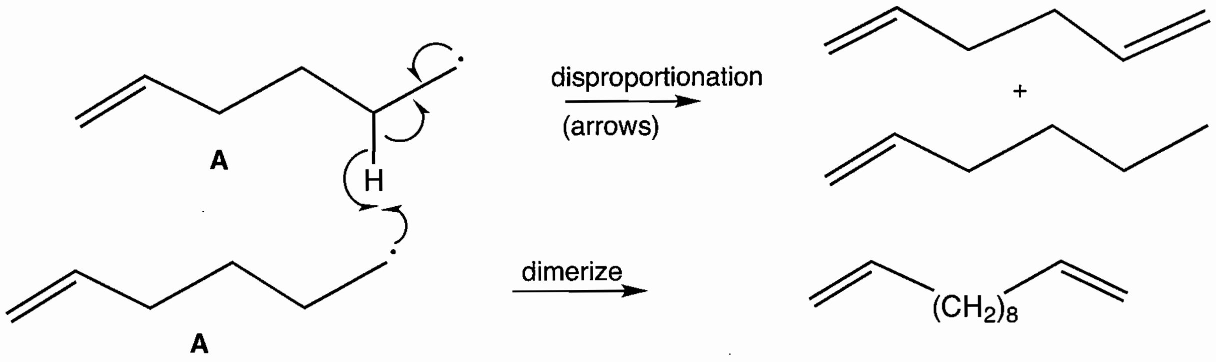
One product comes from simple abstraction of hydrogen from toluene ($PhCH_3$) by this radical.



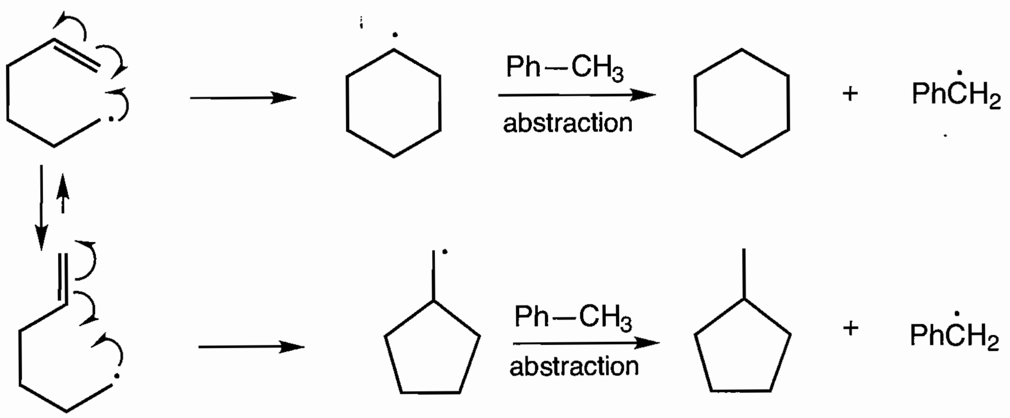
The carboxy radical can also lose carbon dioxide to give radical **A**, the source of most of the other products.



Disproportionation of **A** produces 1-hexene and 1,5-hexadiene, and dimerization of **A** gives the C_{12} product.

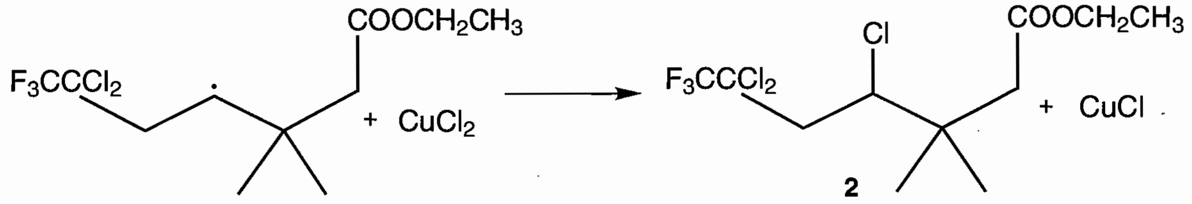


The radical **A** can also undergo an intramolecular cyclization. In fact, this can occur in two ways to give either a five- or six-membered ring. Abstraction of hydrogen yields the cycloalkanes.



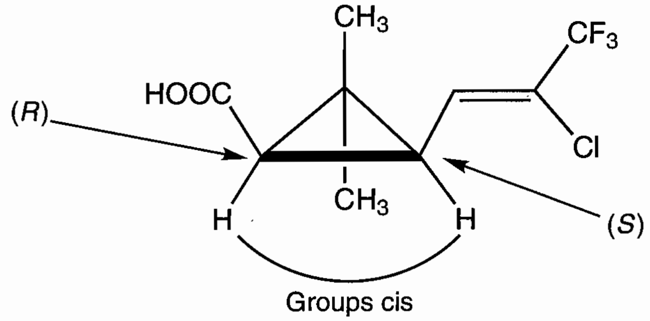
(continued)

Problem 12.56 *(continued)*

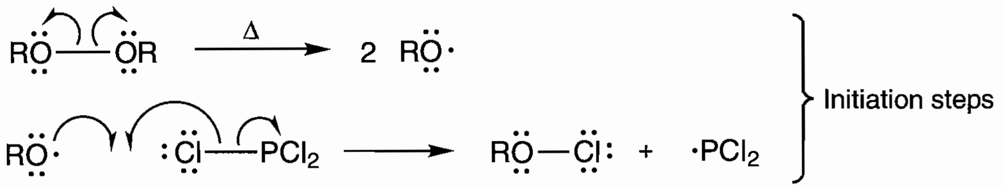


(b) Three steps need to occur in the conversion of **2** into **1**: (1) cyclopropane formation, (2) loss of hydrogen chloride, and (3) hydrolysis of the ester to the carboxylic acid.

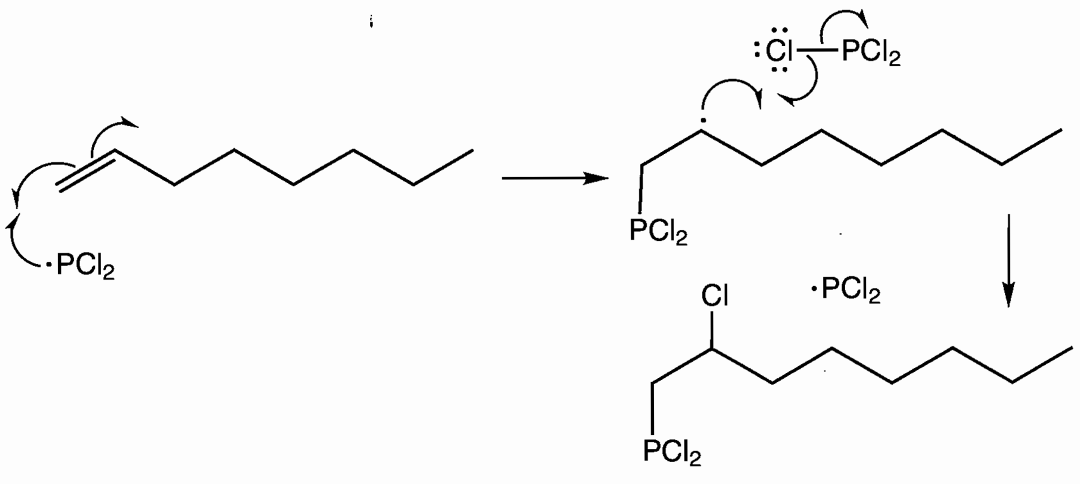
(c) There are four possible stereoisomers of carboxylic acid **1**. There is a pair of enantiomeric cis isomers and a pair of enantiomeric trans isomers. The cis (1*R*,3*S*) isomer is shown below:



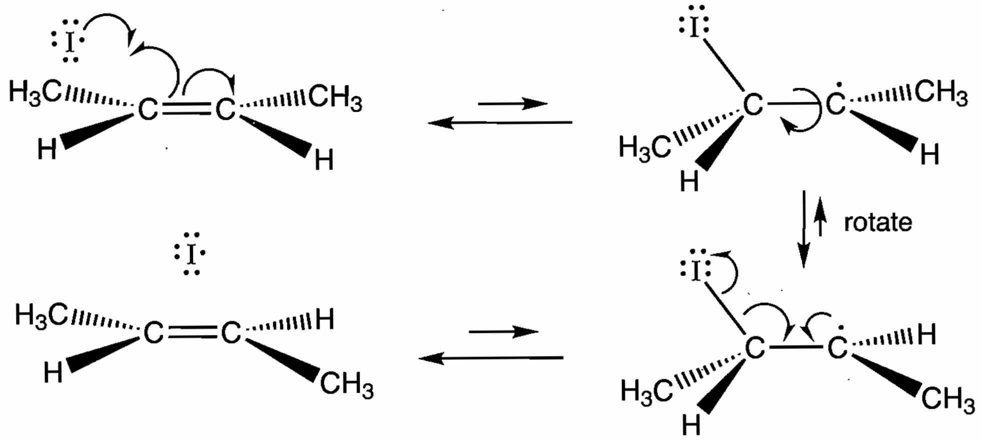
Problem 12.57 This reaction is a standard radical chain process. In the initiation steps, the weak oxygen–oxygen bond breaks to give a pair of alkoxy radicals. Abstraction of a chlorine atom from PCl_3 gives a dichlorophosphorous radical, $\cdot PCl_2$.



The propagation steps include addition of $\cdot PCl_2$ to 1-octene and abstraction of a chlorine atom from PCl_3. These reactions form a molecule of product and regenerate the chain-carrying radical, $\cdot PCl_2$. Note the regiochemistry of the reaction. The $\cdot PCl_2$ radical adds so as to generate the more stable secondary radical.

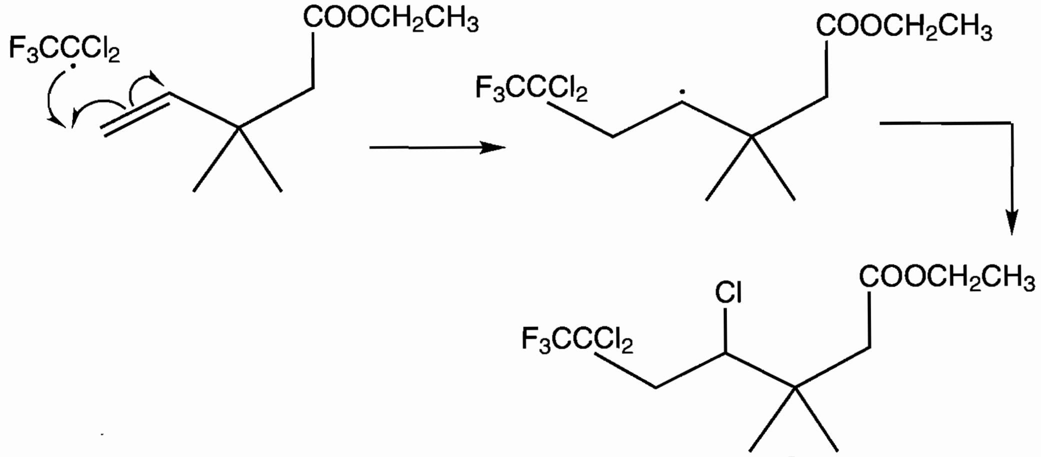


Problem 12.55 The initial addition of an iodine atom to *cis*-2-butene is endothermic and reversible. Addition leads to a radical in which rotation about a carbon–carbon single bond is fast. Reversal of the addition leads to both *cis*- and *trans*-2-butene.



Problem 12.56

(a) Somehow, the radical $F_3CCl_2C^{\bullet}$ must be formed, as the only reasonable mechanism for formation of **2** involves addition of this radical to the alkene, followed by chlorine abstraction.



2

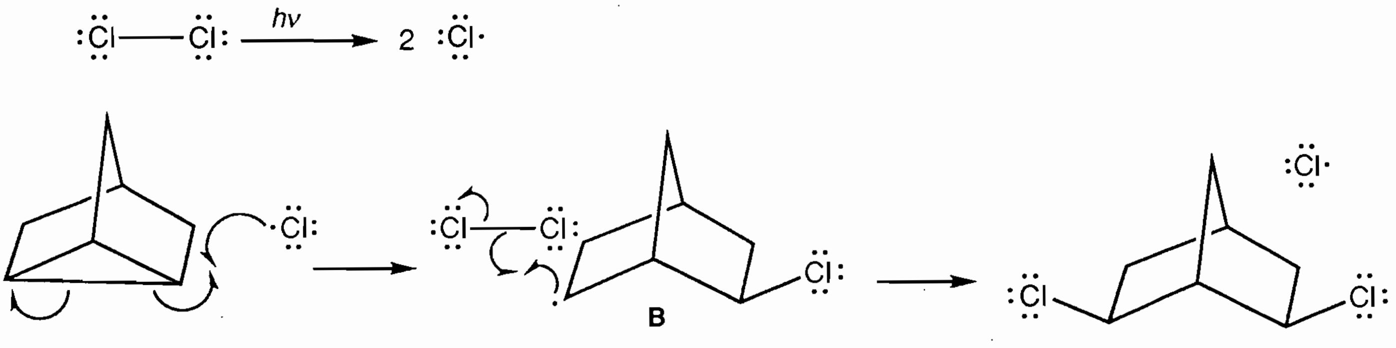
The problems now are to find a suitable source of $F_3CCl_2C^{\bullet}$ and the chlorine atom. An examination of Table 7.2 (p. 277) reveals that carbon–chlorine bonds are weaker than carbon–fluorine bonds. Accordingly, one mechanism that has been proposed is a Cu-catalyzed redox-transfer chain mechanism. This initiation step involves abstraction of a chlorine atom from the polyhalide by CuCl.

$$Cu^{I}Cl \quad + \quad F_3CCCl_3 \longrightarrow Cu^{II}Cl_2 \quad + \quad F_3C\dot{C}Cl_2$$

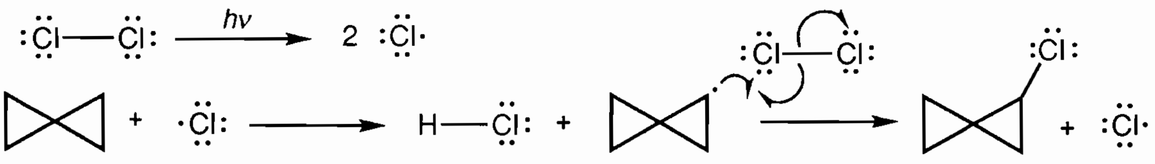
$Cu^{II}Cl_2$ is presumably a more reactive chlorine donor than the polyhalide. Abstraction of chlorine from $Cu^{II}Cl_2$ gives **2** and $Cu^{I}Cl$. The $Cu^{I}Cl$ is then recycled to begin the process anew.

(continued)

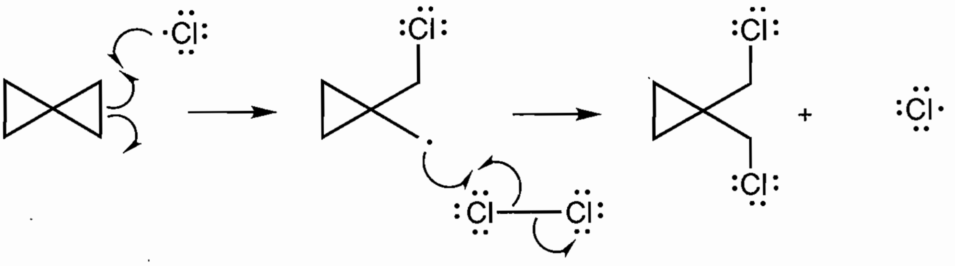
Problem 12.53 The key to this problem is the recognition that the strained three-membered ring will react with a chlorine atom much as will a double bond. An addition reaction gives the radical **B** that then abstracts a chlorine atom from Cl_2. This reaction makes a product molecule and generates a new chlorine atom to carry the chain.



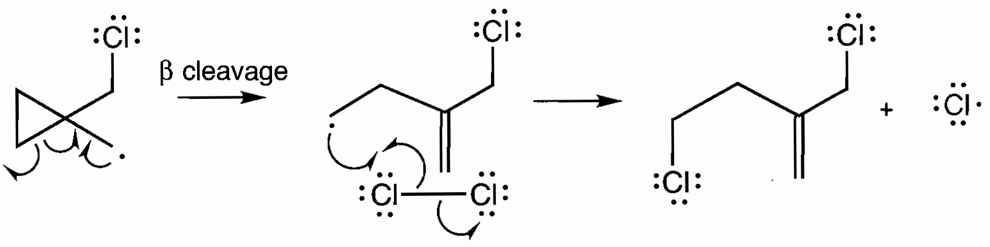
Problem 12.54 Chlorospiropentane is formed by a straightforward photochlorination chain reaction.



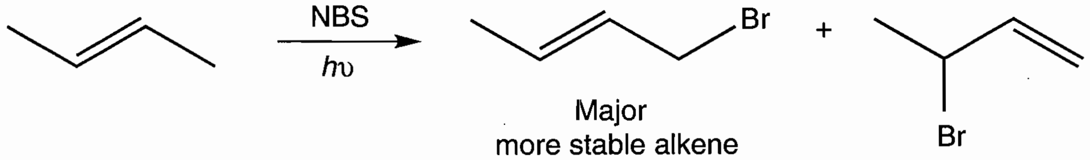
The strained three-membered ring can also be opened by a chlorine atom (see Problem 12.53). Abstraction of a chlorine atom from chlorine leads to one product and a new chlorine atom.



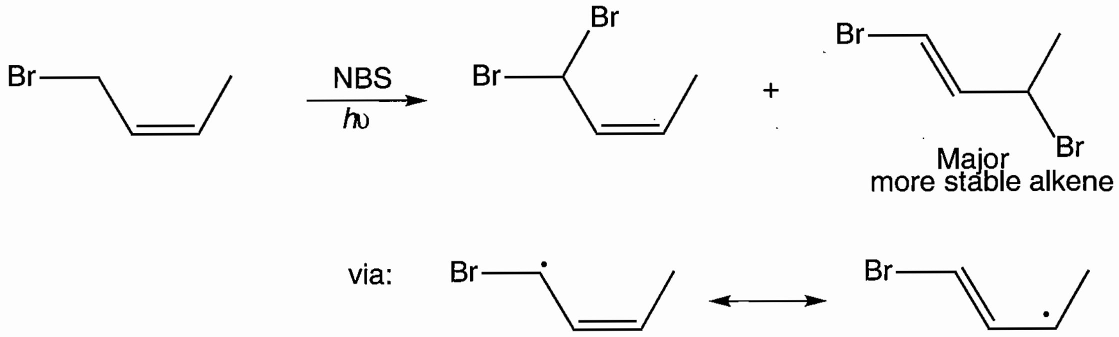
The final product is by far the hardest to rationalize. It comes from opening of the second three-membered ring (a β cleavage), followed by chlorine abstraction.



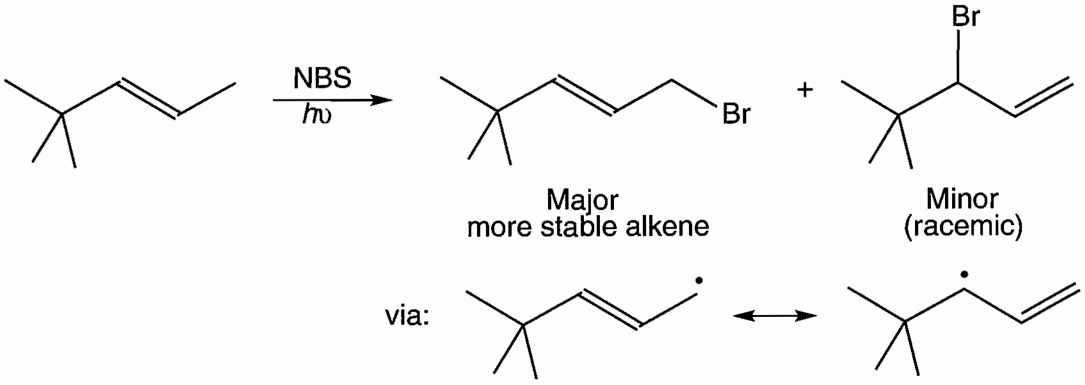
(b) Two allylic bromination products possible.



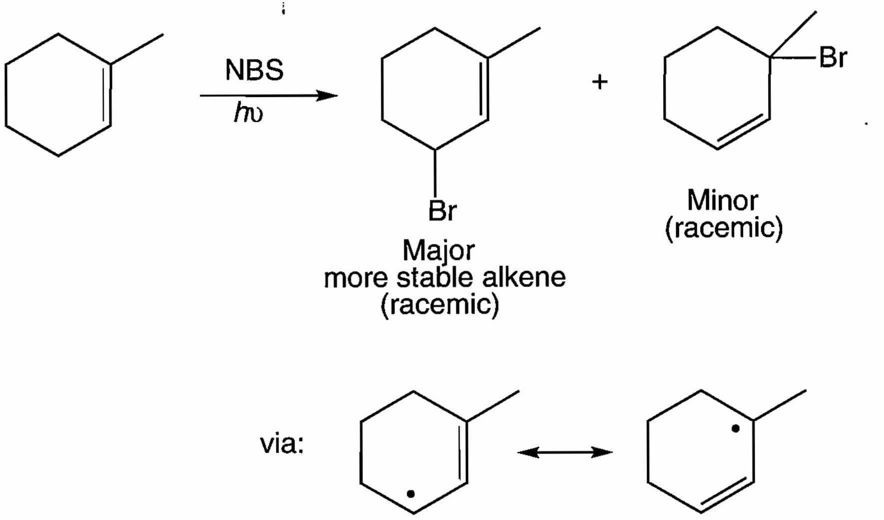
(c) The allylic hydrogen that would be abstracted is the one that leads to the bromine-stabilized allylic radical. That species has two resonance structures, and each carbon sharing the radical would react with bromine to give the dibromides shown. The 1,3-dibromide is stabilized by resonance and is more stable than the 1,1-dibromide product. The transition state leading to the 1,3-dibromide will be lower and, as a result, the 1,3-dibromide will be the major product.



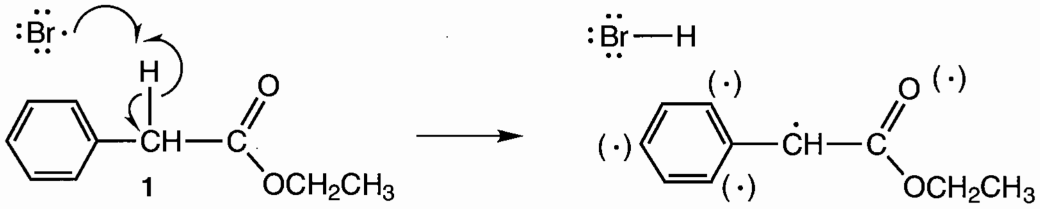
(d) There is only one allylic radical intermediate that can be formed in this reaction. Bromination can occur at either carbon of the allylic radical. The more substituted alkene is the more stable.



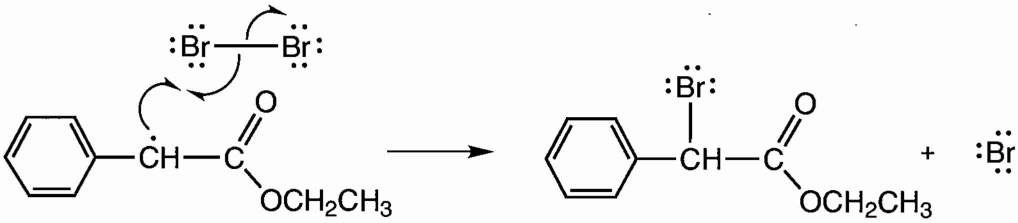
(e) There are several allylic radicals that could be formed in this reaction. The most stable intermediate is the allylic radical that is secondary and tertiary. Two products can arise from that intermediate. The more stable product is the more substituted alkene.



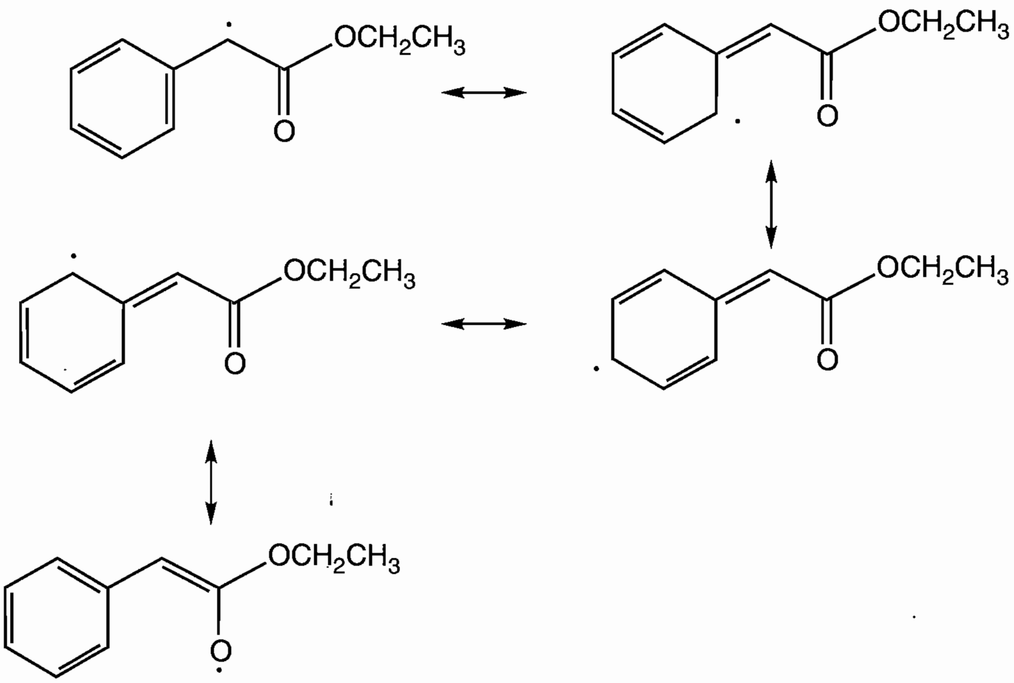
Problem 12.50 Decomposition of NBS generates a bromine atom. The bromine atom then abstracts a hydrogen atom from the methylene group adjacent to both the ring and the carbonyl group. This radical is resonance stabilized. The positions sharing the free electron are indicated by (•).



The hydrogen bromide then reacts with NBS to form the low steady-state concentration of bromine necessary to carry the reaction as shown on p. 577. Bromine reacts with the newly formed radical to give the brominated product and regenerate a chain-carrying bromine atom.

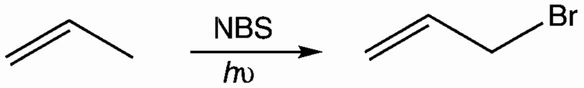


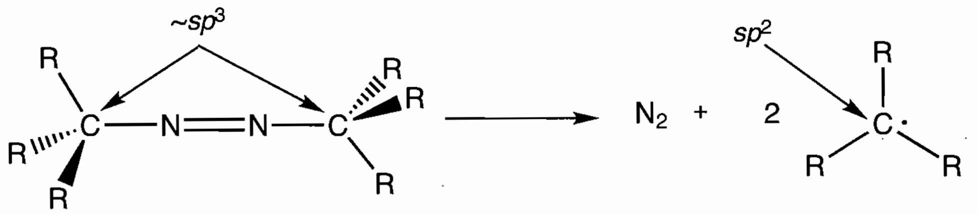
Problem 12.51



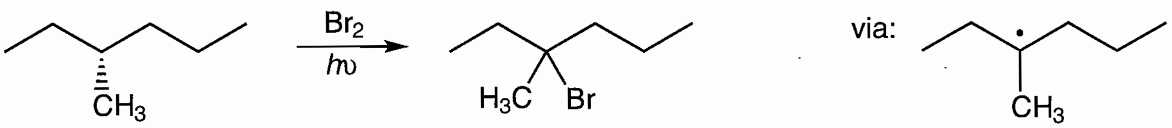
Problem 12.52

(a) Only one allylic bromination product possible.



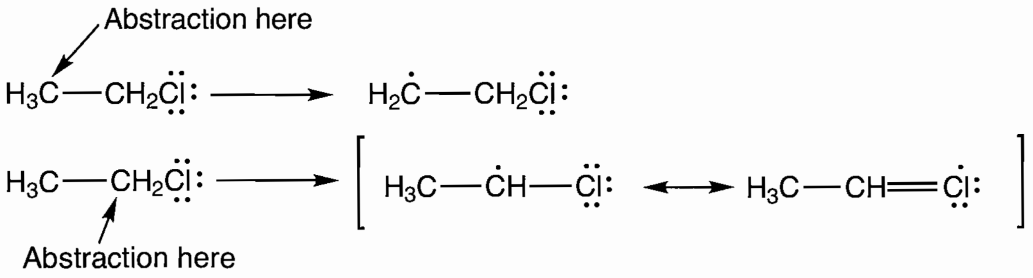


Problem 12.48 The major product for the bromination of (*R*)-3-methylhexane is 3-bromo-3-methylhexane. This product is chiral. It will be formed as a racemic mixture because the radical intermediate will lose its stereochemical purity. The radical easily goes from sp^3 to sp^2. Once it becomes planar it has no preference for returning to the (*R*) configuration or becoming the (*S*) enantiomer. Reaction of the radical with Br_2 will occur from either face of the tertiary radical to give the racemic mixture.

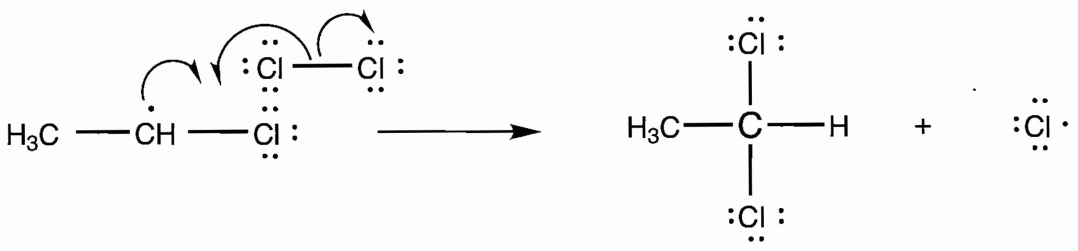


(*R*)-3-Methylhexane 3-Bromo-3-methylhexane

Problem 12.49 There are only two possibilities for hydrogen atom abstraction from ethyl chloride. A simple primary radical would be produced from abstraction of a methyl hydrogen, whereas a resonance-stabilized radical appears when a hydrogen atom is removed from the carbon already attached to one chlorine.

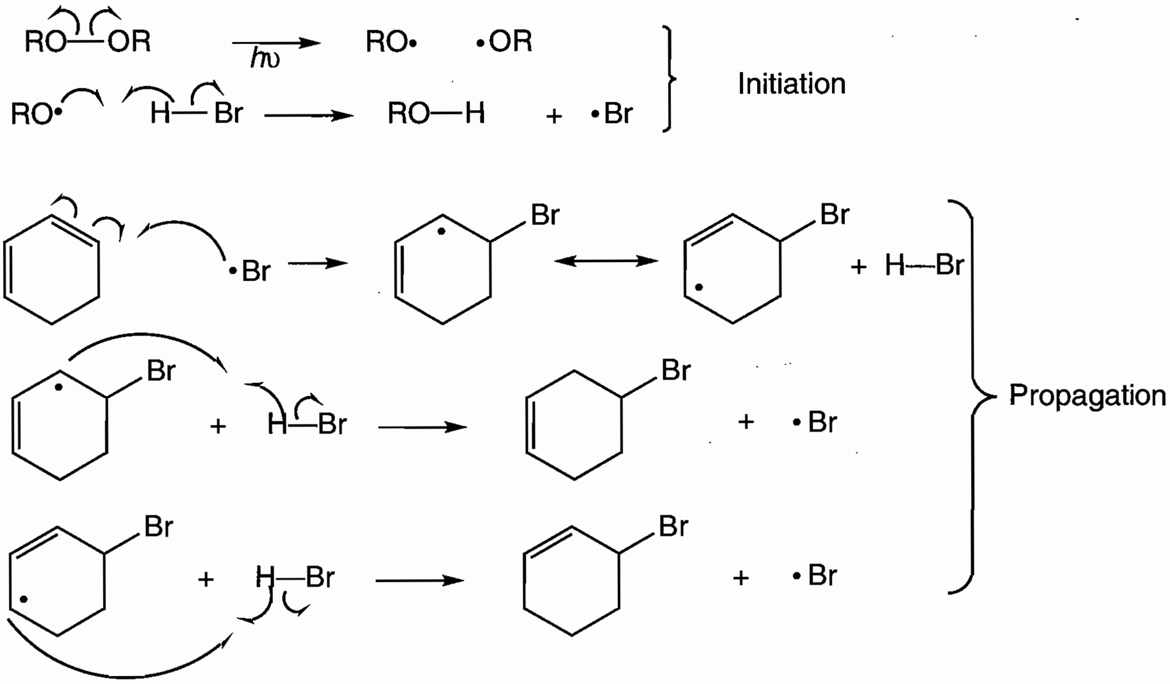


The more stable radical will be formed preferentially and will abstract a chlorine atom to yield a geminal dichloroethane, 1,1-dichloroethane, not the vicinal dichloride, 1,2-dichloroethane.



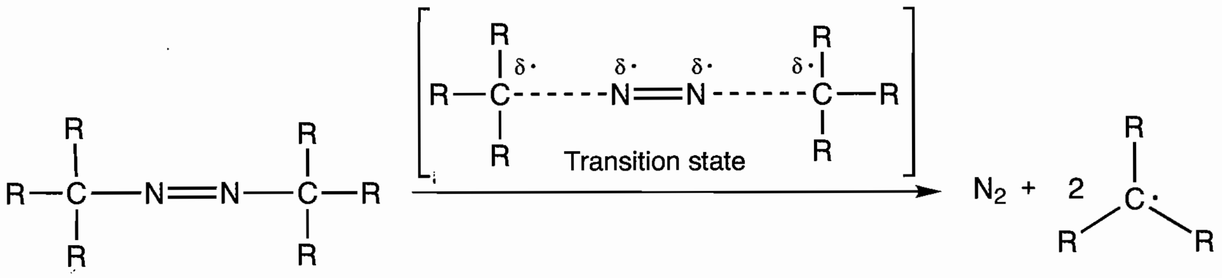
Problem 12.45 *(continued)*

The mechanism for the reaction is shown here:



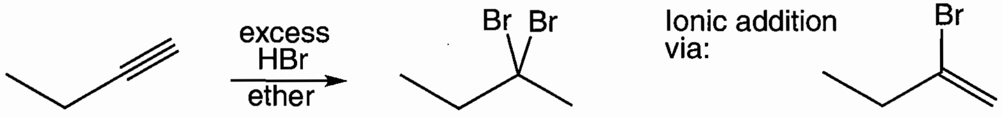
Problem 12.46 The less stable methyl radical recombines faster than the more substituted, more stable, and thus longer lived isopropyl radical. The more bulky isopropyl radical has more difficulty in recombining than does the smaller methyl radical.

Problem 12.47 This problem is similar to Problem 12.46, although the steric argument is a little more subtle. First, one might argue that formation of the more substituted, more stable radicals should be faster than formation of the less substituted, less stable radicals. That idea would be right, as the transition state for radical formation will have partially formed radicals and will benefit energetically from substitution.

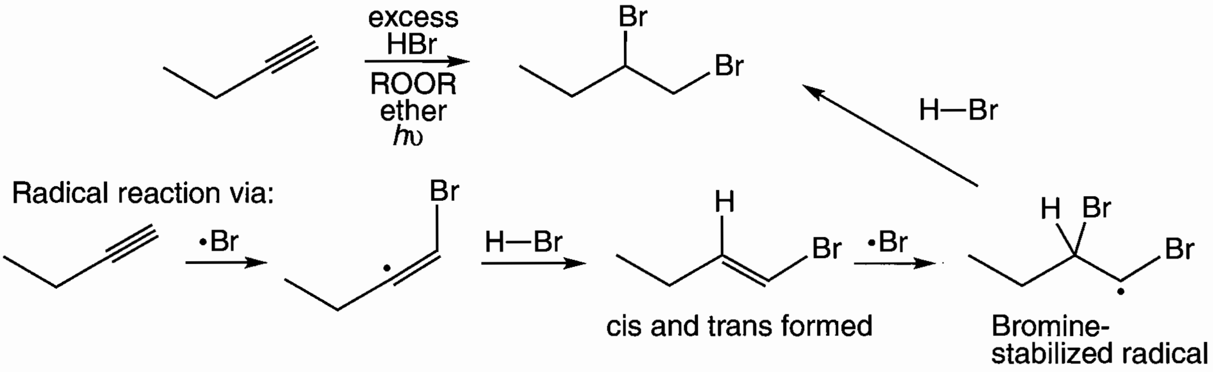


But this analysis ignores an even more subtle steric argument. There will be an energy incentive for the larger R groups to go from sp^3 to sp^2 hybridization as the azo compound is transformed into nitrogen and a pair of radicals. The R–C–R angle will change from about 109° to about 120°. The more relatively large methyl groups, the stronger this effect, and the faster the rate of radical formation.

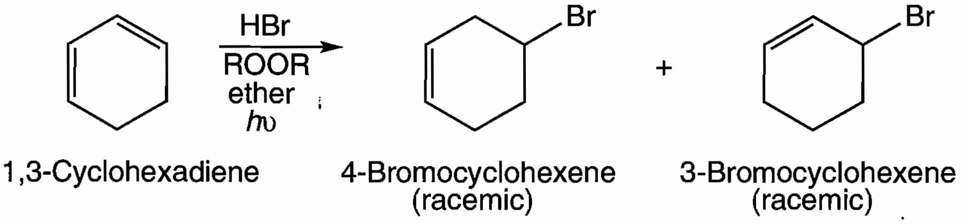
(g) The alkyne reacts with HBr forming 2-bromo-1-butene. A second addition occurs via the bromine-stabilized carbocation. The product is the achiral geminal dibromide.



(h) This reaction is a radical process that gives the vicinal dibromide. The bromine radical formed from the initiation steps adds to the alkyne to give the most stable vinyl radical intermediate. The vinyl radical will abstract hydrogen from H—Br. The newly formed alkene (cis and trans) will react with another bromine radical to give a radical on the carbon bonded to bromine, which allows resonance stabilization. The last step will be the carbon radical abstracting a hydrogen from H—Br. The final product would be a racemic mixture.



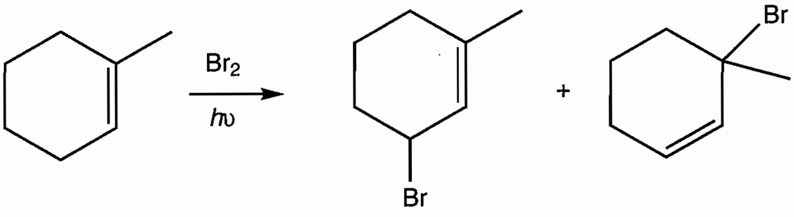
Problem 12.45 The two products formed in this reaction will be 4-bromocyclohexene and 3-bromocyclohexene.



(continued)

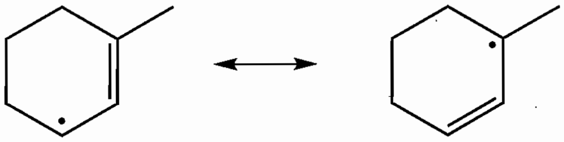
Problem 12.44 *(continued)*

(d) The most stable radical intermediate is the allylic radical that is both secondary and tertiary. So 3-bromo-1-methylcyclohexene and 3-bromo-3-methylcyclohexene would be the major products.

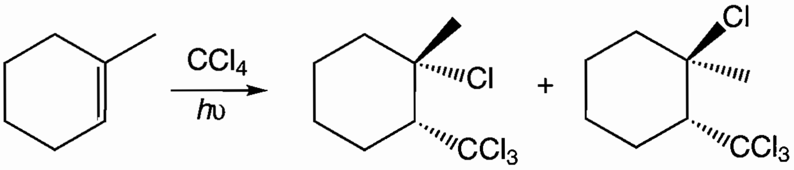


Racemic Racemic

Radical reaction via:



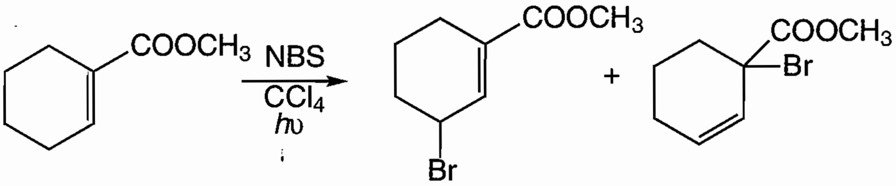
(e)



Radical reaction; both cis and trans isomers will be formed

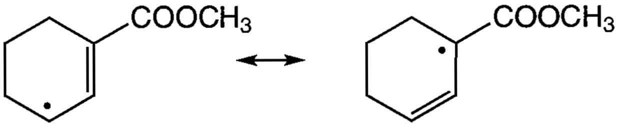
Racemic Racemic

(f) First we need to decide which radical intermediate is most likely involved. The radical formed at C(3) of the cyclohexene ring is fully conjugated and is more stable than any other. There are two bromide products that could be formed from that radical intermediate. The more stable product retains the conjugation of the double bond with the ester carbonyl group.

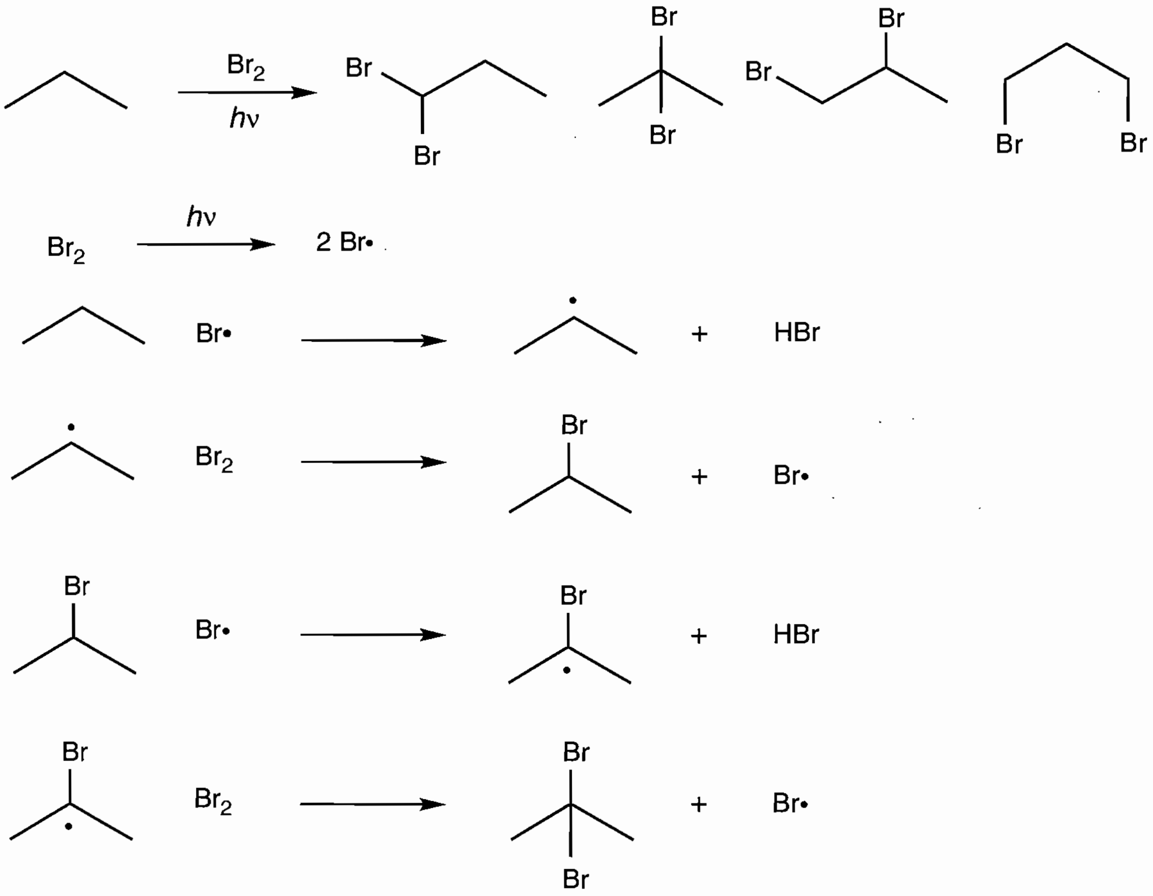


More stable (racemic) Racemic

Radical reaction via:

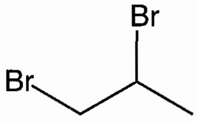


Problem 12.42



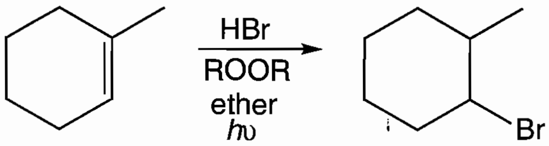
Problem 12.43

Only this one is chiral and it will be formed as a racemic mixture



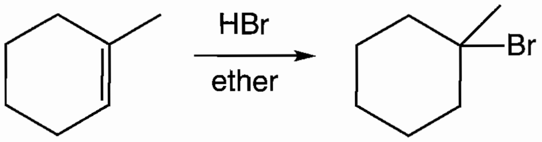
Problem 12.44

(a)



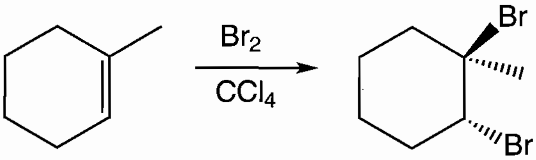
Radical reaction; a racemic mixture of both cis and trans isomers will be formed

(b)



Ionic addition of HBr (Markovnikov addition)

(c)

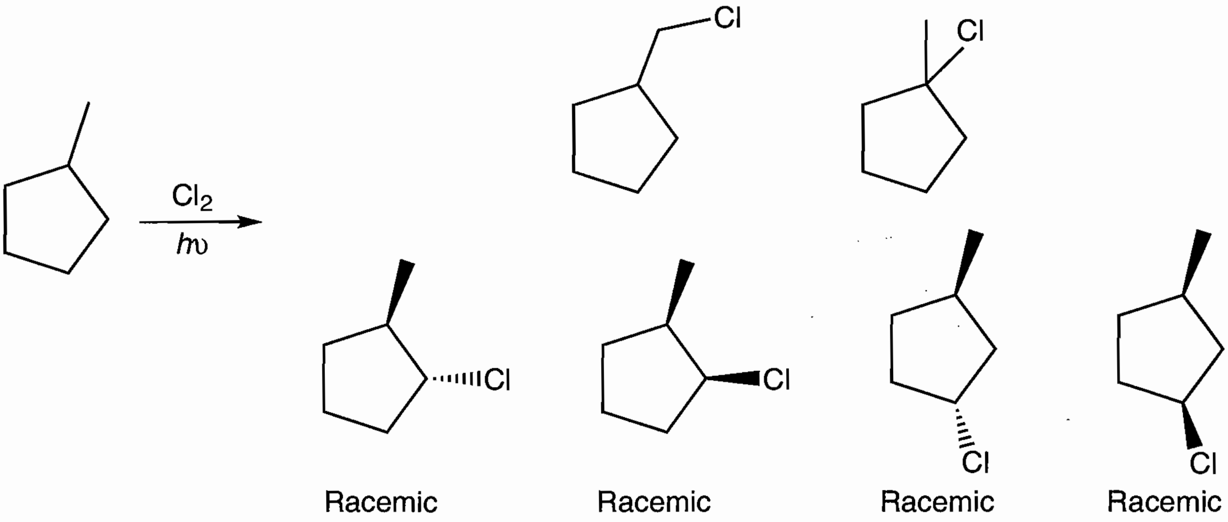


Anti addition of Br_2 via bromonium ion; racemic mixture formed

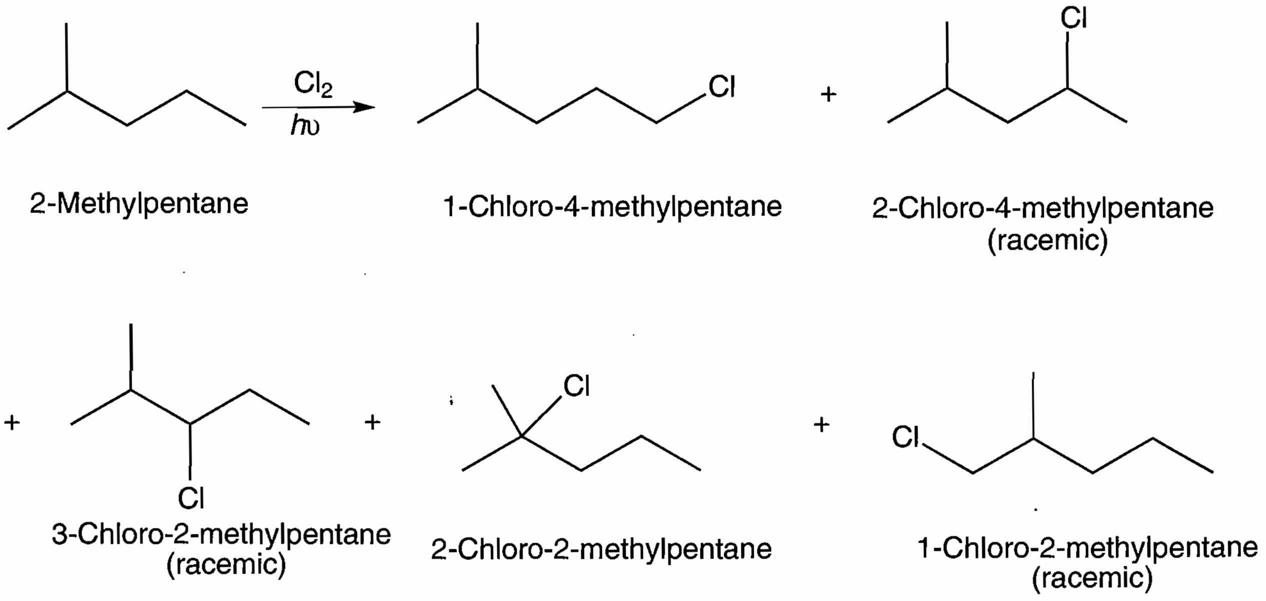
(continued)

Problem 12.41 *(continued)*

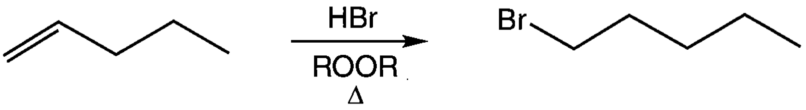
(c) There are only four different carbons in methylcyclopentane. Chlorination at these different carbons gives (chloromethyl)cyclopentane, 1-chloro-1-methylcyclopentane, 1-chloro-2-methylcyclopentane, and 1-chloro-3-methylcyclopentane. But the disubstituted ring compounds (1-chloro-2-methylcyclopentane and 1-chloro-3-methylcyclopentane) can be formed as cis or trans isomers. The 1,2- and 1,3-disubstituted cyclopentanes will be formed as racemic mixtures.

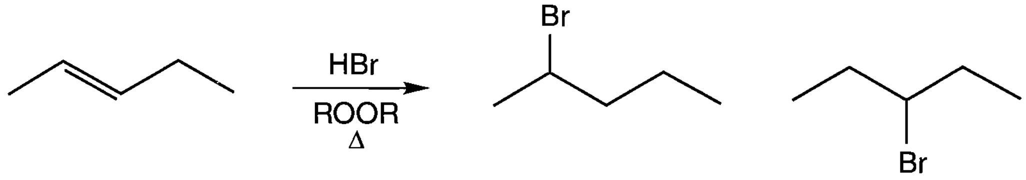


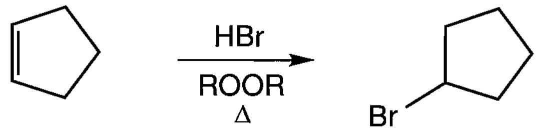
(d) There are five monochlorides that can be formed in this reaction. The three that are chiral would be formed as racemic mixtures.

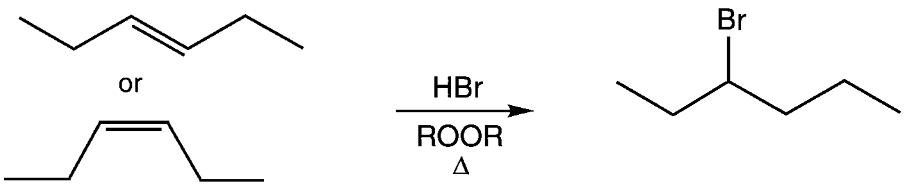


Problem 12.40

(a)


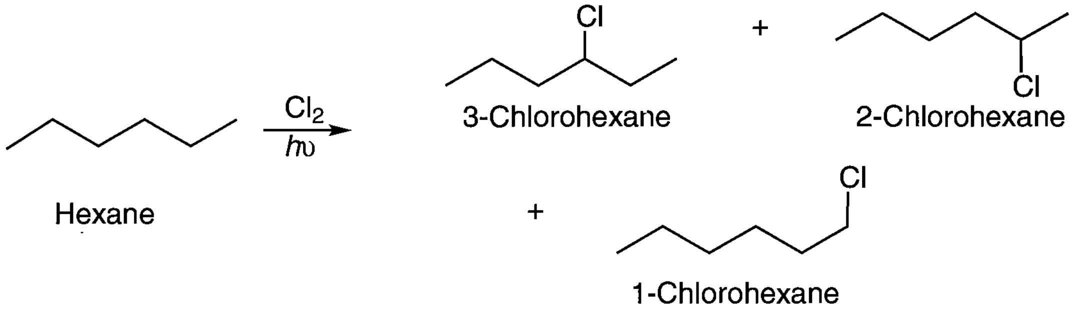
(b)


(c)


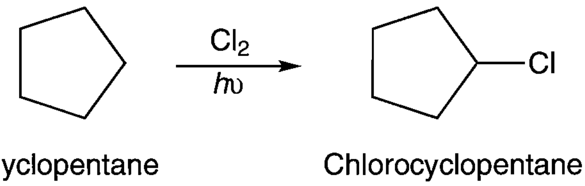
(d, e)


Problem 12.41

(a) There are three possible monochlorides that can be formed in this reaction.



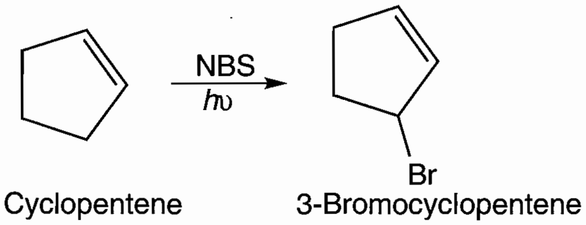
(b) Cyclopentane will give only one monochloride in this reaction. All carbons of cyclopentane are identical.



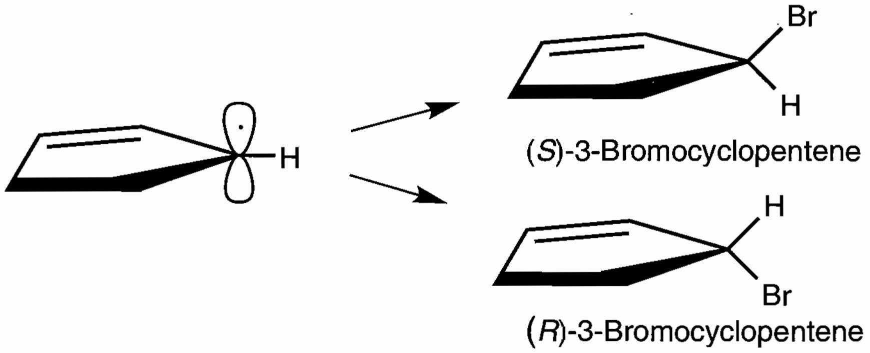
(continued)

Additional Problem Answers

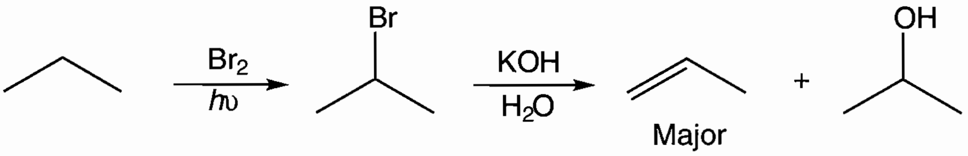
Problem 12.36 The allylic bromination of cyclopentene gives 3-bromocyclopentene. This molecule is chiral. Carbon 3 is a stereogenic carbon.



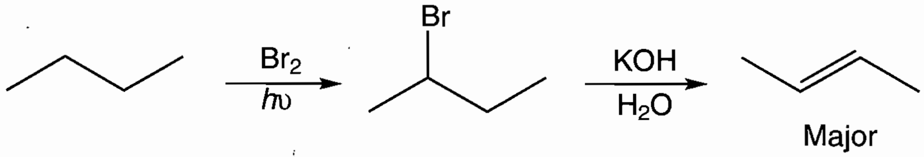
The starting material is achiral, so we know that we will form a racemic mixture of 3-bromocyclopentene. The bromine will add to the flat allylic radical intermediate on either the top face, as shown, forming the (*S*) enantiomer, or on the bottom face, forming the (*R*) enantiomer.



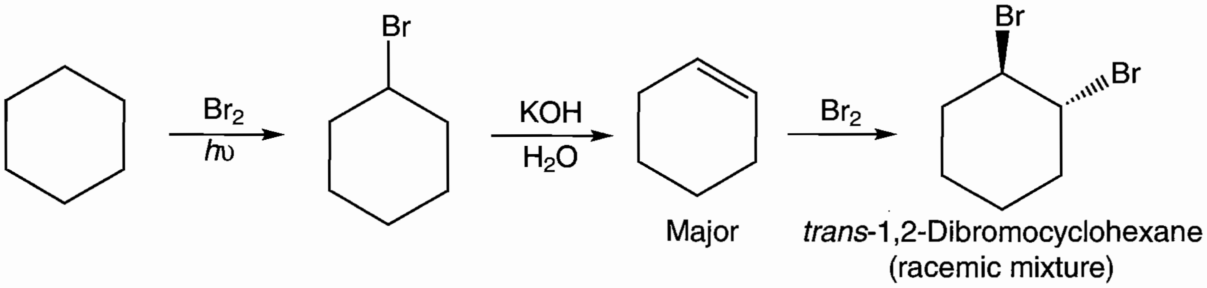
Problem 12.37

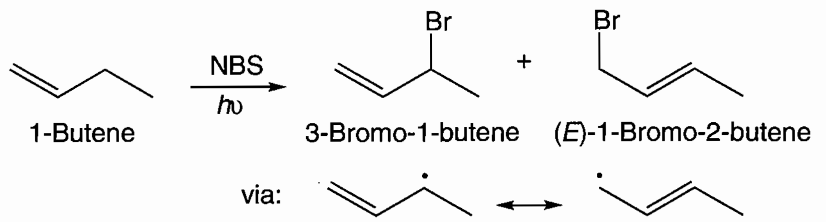


Problem 12.38

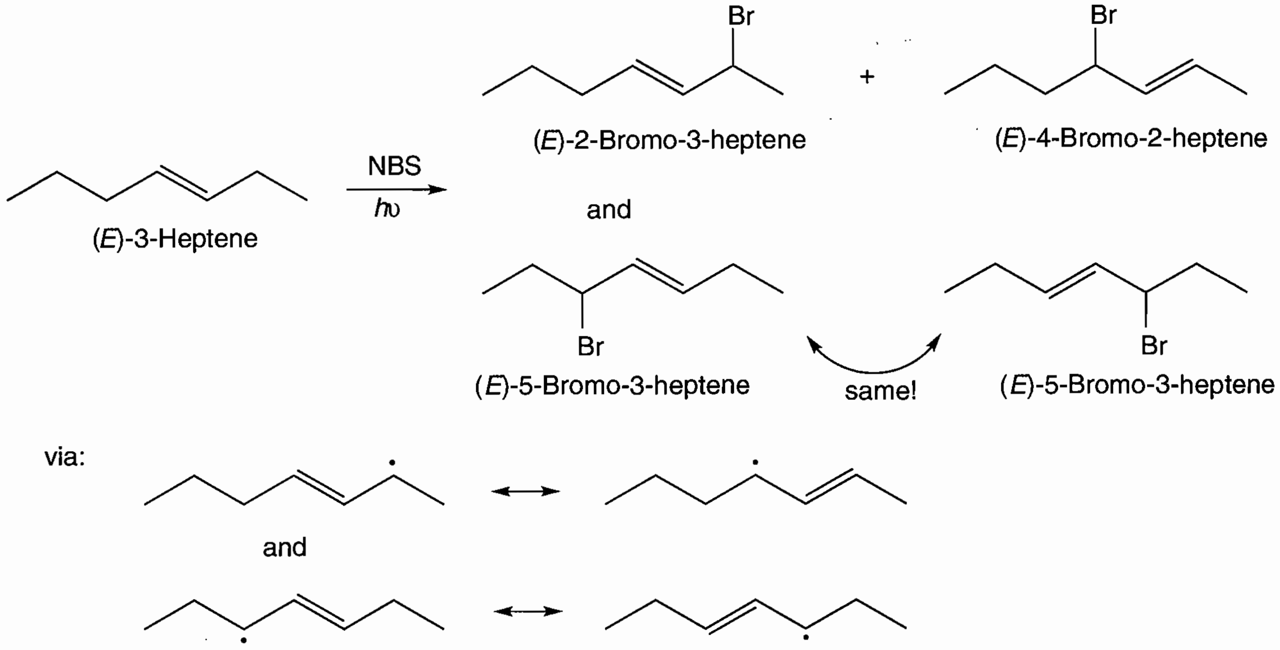


Problem 12.39

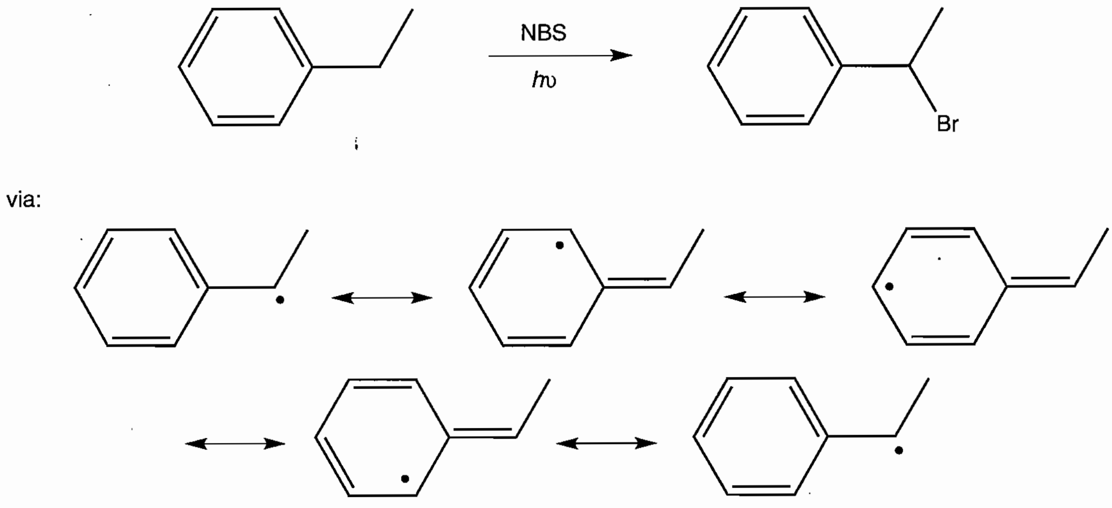




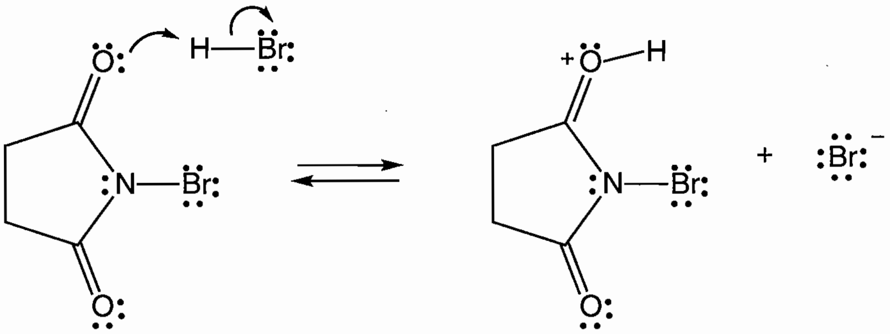
(c) Allylic bromination of (*E*)-3-heptene gives three products. The initial radical can be formed on C(2) or C(5) of the 3-heptene. Both of these initial radicals are resonance stabilized and that means in principle that there can be four products. The reason that there are only three is that the resonance structure for the radical on C(5) is symmetrical. Capture at either end of the allylic radical gives (*E*)-5-bromo-3-heptene.



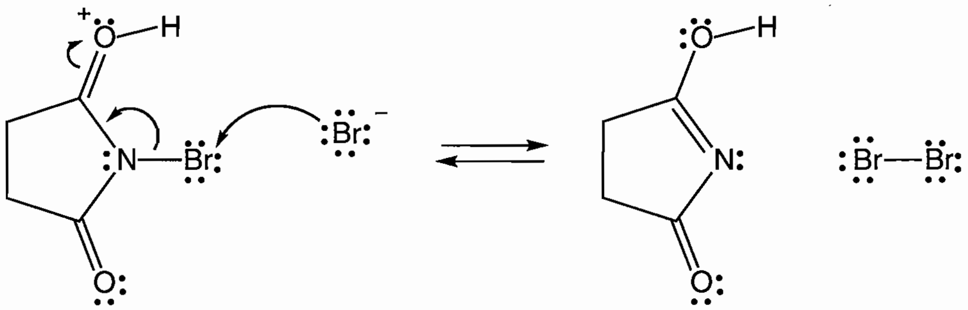
(d) This reaction is an example of bromination at the benzylic position. It is a very clean reaction. Only one product is formed. The radical intermediate certainly has resonance stabilization, but the only reactive sight is the benzylic position because it is the only product that maintains the aromatic ring. We will discuss the amazing stability of the aromatic ring in Chapter 14.



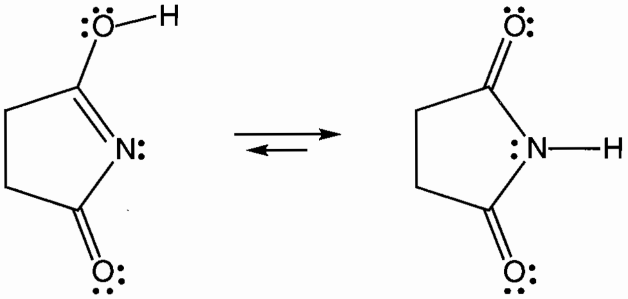
Problem 12.32 The carbonyl oxygen is a base and can be protonated by hydrogen bromide.



Now bromide can form Br_2 by attacking the protonated NBS at bromine:

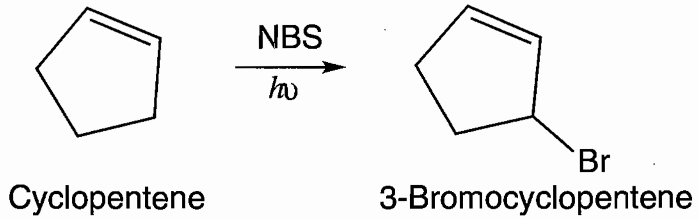


Succinimide itself is produced by a series of proton transfers. Can you write a mechanism for this reaction? (See Section 11.8, p. 523.)



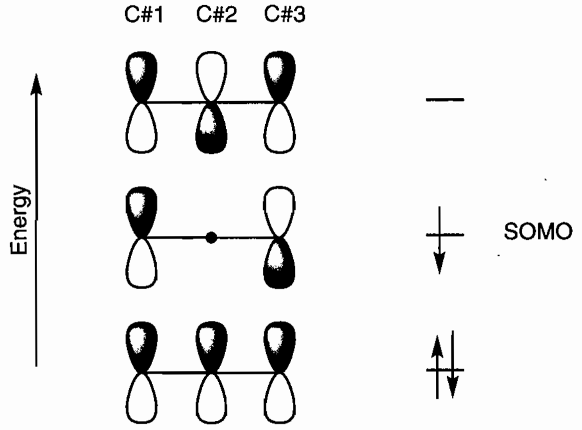
Problem 12.33

(a) The allylic bromination of cyclopentene gives only the racemic 3-bromocyclopentene.

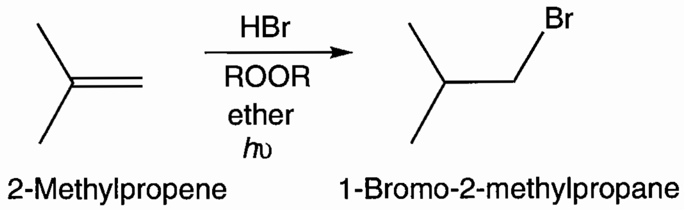


(b) Allylic bromination of 1-butene will give racemic 3-bromo-1-butene and the isomer (*E*)-1-bromo-2-butene because the intermediate allylic radical has a resonance structure that can also add bromine.

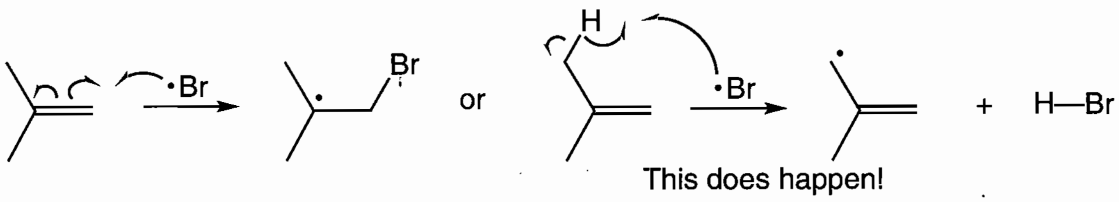
The molecular orbital (MO) analysis gives us the same answer, of course. It is just another (and probably more accurate) way to analyze the reaction. Allyl is a three *p*-orbital system. The molecular orbitals obtained from mixing the three *p* orbitals can be represented as shown in the following diagram. See p. 447 in the text for a discussion of the allyl orbitals. There are three π electrons in the allyl radical. The orbital that will be used by the allyl radical to make a bond with bromine is the SOMO (singly occupied molecular orbital). It should be clear that the orbital density for the SOMO will be localized on carbons number 1 and number 3. This is where the radical will begin to form a new bond to the Br_2 in the propagation step.



Problem 12.31 Aha! This is a great question. If you have been wondering about this issue, then you are on top of the subject. First, let's review the HBr/ROOR/h*ν* reaction. The reaction of 2-methylpropene, for example, gives 1-bromo-2-methylpropane.

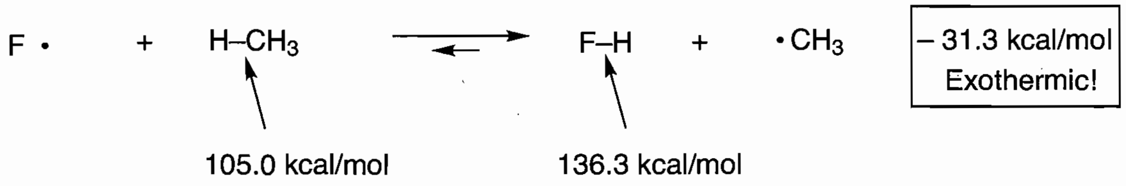


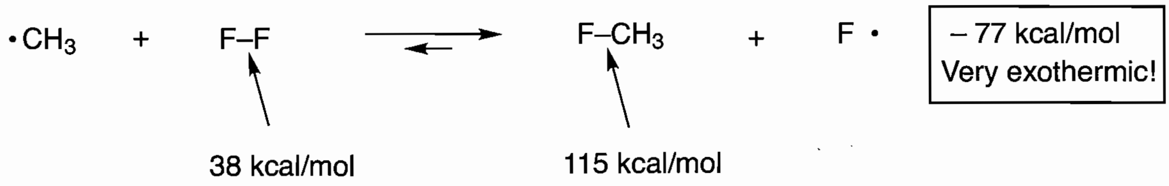
We know that the bromine radical adds to the alkene in the first propagation step of this reaction so that the tertiary radical intermediate is formed. Rather than add to the alkene, why not abstract an allylic hydrogen to give the very stable allyl radical? The answer is that, in fact, allylic hydrogen abstraction is almost always favored and it does happen.

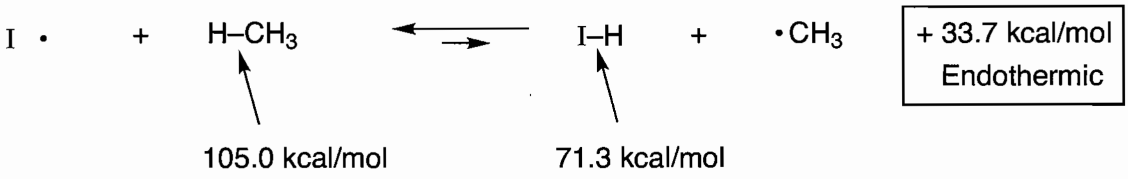


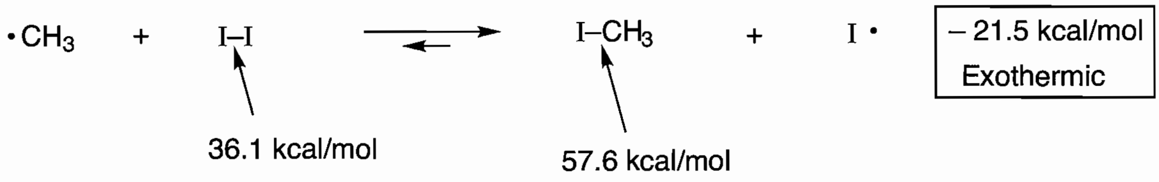
The difference is that in the HBr reaction, the allylic radical can only abstract an H from H—Br, which just reforms the starting material. Only in Br_2 can the allylic position react to give the allylic bromide product.

Problem 12.29

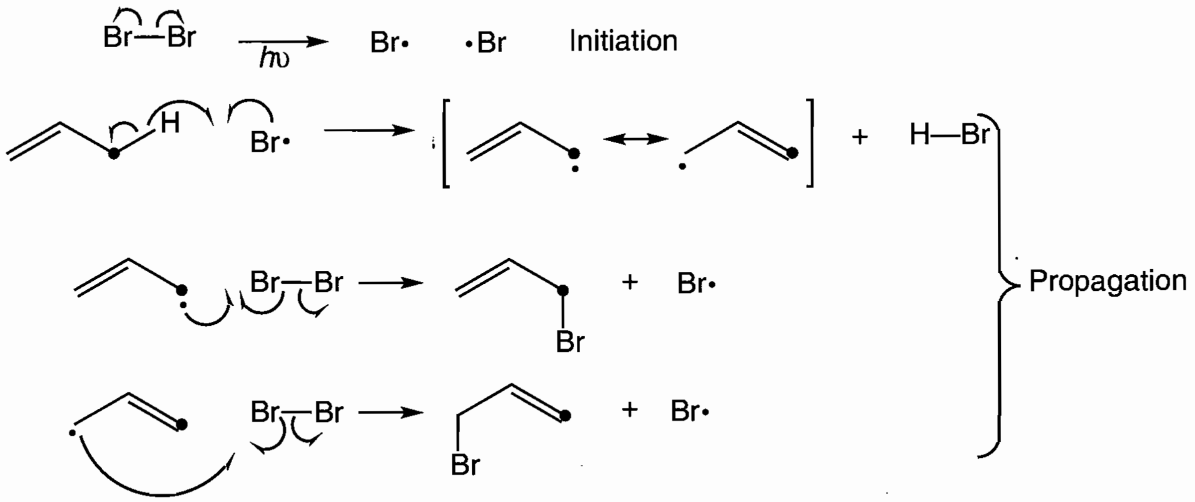




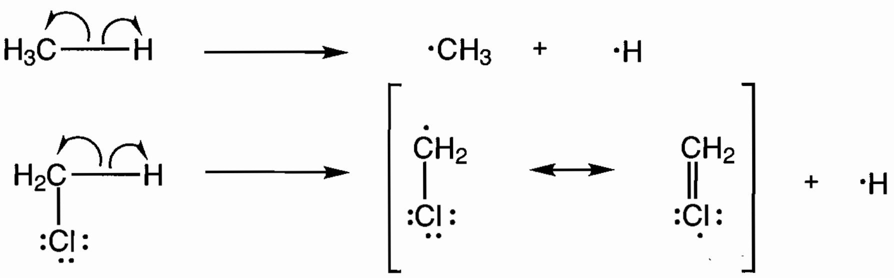




Problem 12.30 The mechanism for photohalogenation of labeled propene involves an unsymmetrical allyl radical. Reaction of the allyl radical with Br_2 gives two products. Both products are 3-bromopropene, but they differ in the location of the ^{13}C label. One has the ^{13}C on carbon 3 and the other has it on carbon 1.

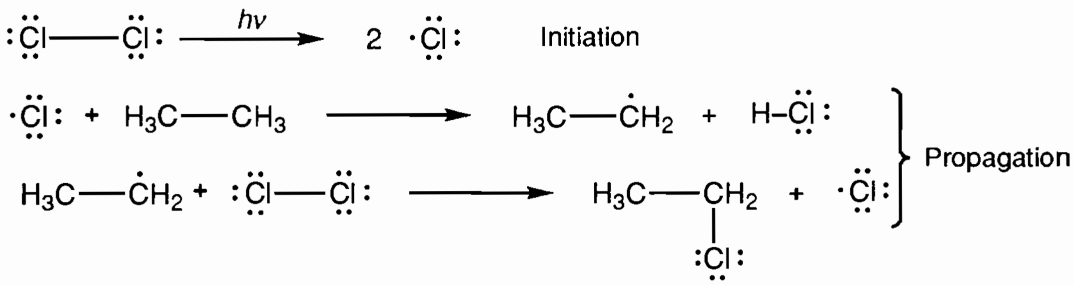


Problem 12.26 When the carbon–hydrogen bond in methane breaks, a methyl radical and a hydrogen atom are produced. Methyl chloride gives a hydrogen atom and a chloromethyl radical, which is stabilized by resonance and, therefore, more stable than the unstabilized methyl radical. Accordingly, the bond is easier to break. Are you getting the idea that one of the generic answers to questions in organic chemistry is, It's resonance stabilized and therefore more stable? Well, you're right.



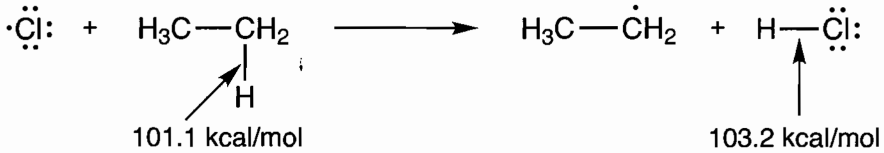
Resonance stabilized – more stable – easier to form

Problem 12.27

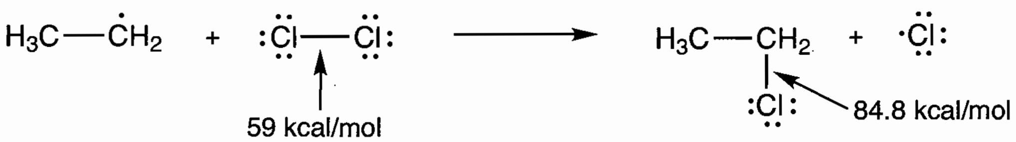


There are many possible termination steps.

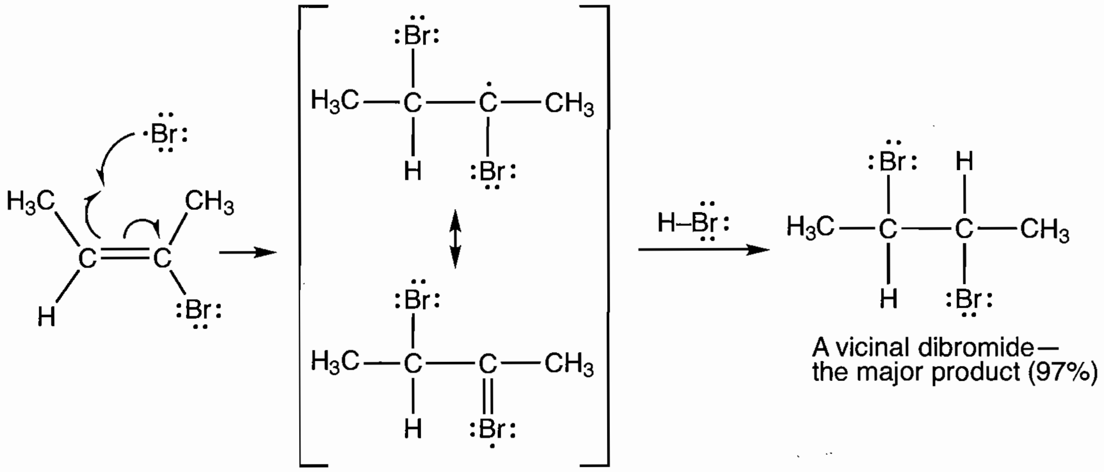
Problem 12.28 The first step is exothermic by 2.1 kcal/mol (103.2 – 101.1 = 2.1). The hydrogen–chlorine bond is stronger than the carbon–hydrogen bond in ethane.



The second propagation step is also exothermic, this time by 25.8 kcal/mol (84.8 – 59 = 25.8).



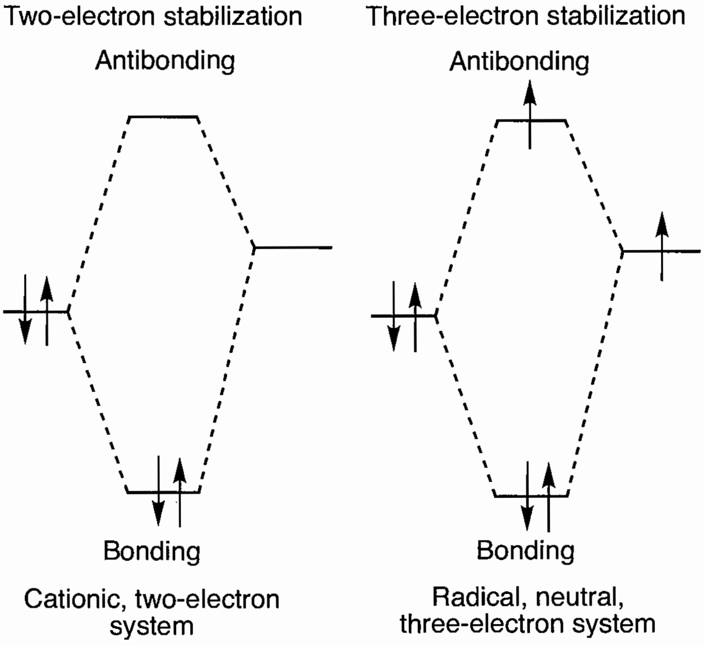
Problem 12.24 *(continued)*



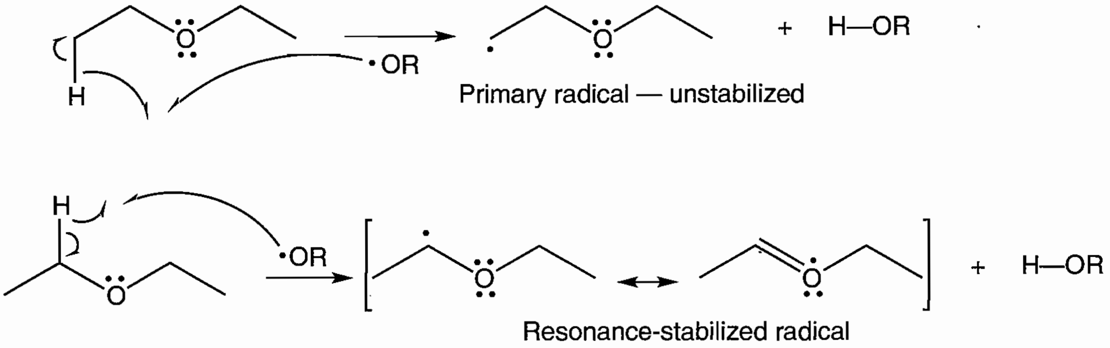
More stable radical is formed much more easily

A vicinal dibromide—the major product (97%)

This resonance stabilization is special, however. In this three-electron system, two electrons are well stabilized in a low-energy bonding molecular orbital, but one electron must occupy an antibonding molecular orbital. This system is stabilized overall, but the situation is not as straightforward as many two-electron cases.



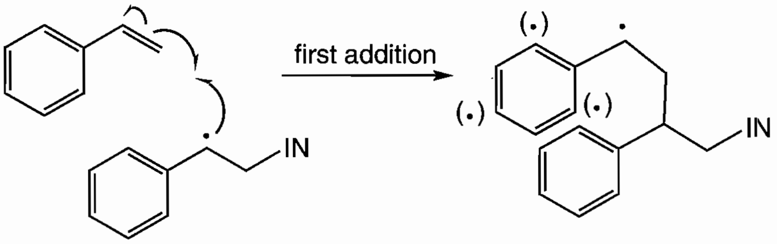
Problem 12.25 Abstraction of the methyl hydrogen leads to an unstabilized primary radical, whereas abstraction from the methylene position leads to a resonance-stabilized radical. This resonance stabilization is a three-electron π system.



Primary radical — unstabilized

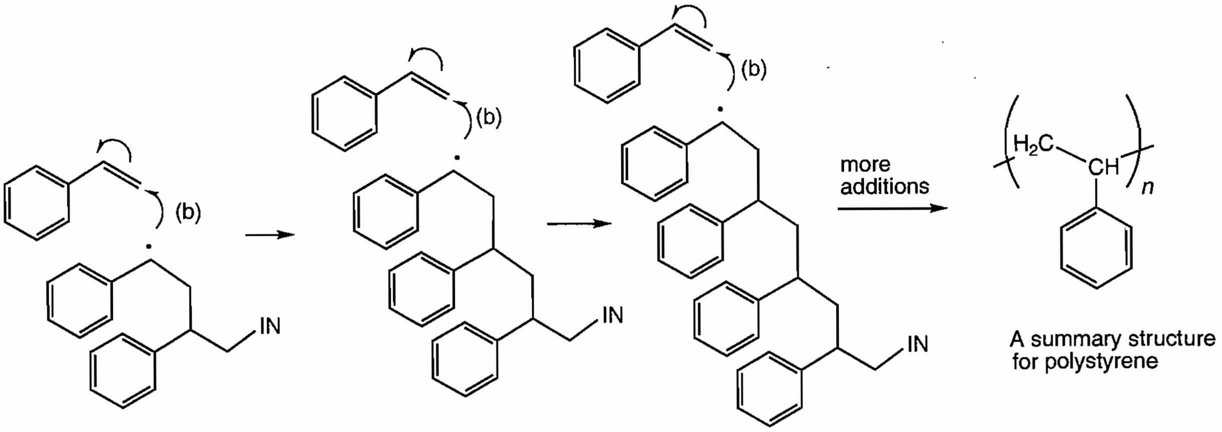
Resonance-stabilized radical

Now, this new radical can add to styrene as the initiator radical did. The same two choices exist: addition along (a) or (b). Again, and for the same reasons, (b) is favored because it gives the resonance-stabilized intermediate.



A resonance-stabilized radical with the positions sharing the single electron shown by (•)

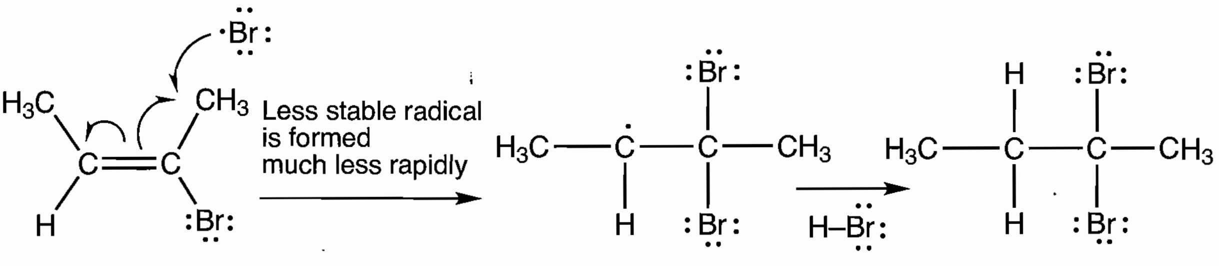
Repeated additions in the (b) sense lead to the polymer



A summary structure for polystyrene

Problem 10.13 shows the polymerization of styrene under acid-catalyzed conditions. The pathway is the same, except the intermediates are cations rather than radicals. Cationic polymerization is more sensitive to traces of water and other impurities than radical polymerization. Radical polymerization is typically the process that industry uses to make polystyrene.

Problem 12.24 Addition of a radical to the vinyl halide can lead to either of two new radicals. In the more stable radical, the free electron is adjacent to a halogen and is resonance stabilized. The other possible radical is not resonance stabilized and is less stable.

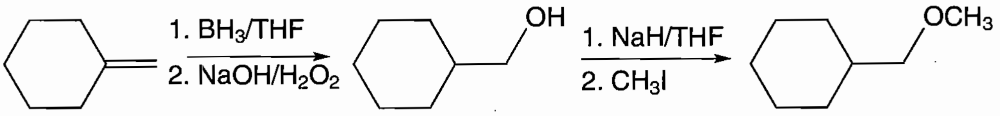


Geminal dibromide—
a very minor product (< 3%)

(continued)

Problem 12.20 *(continued)*

(d) Another way to make the ether with no E2 complications:



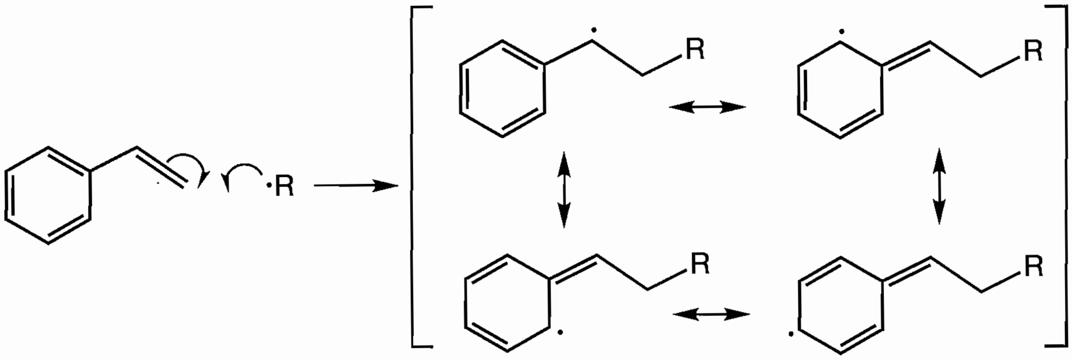
Problem 12.21 Many exist. The destruction of any chain-carrying radical will terminate the chain reaction. Here are three examples.

$$\cdot CCl_3 + \cdot CCl_3 \longrightarrow Cl_3C{-}CCl_3$$

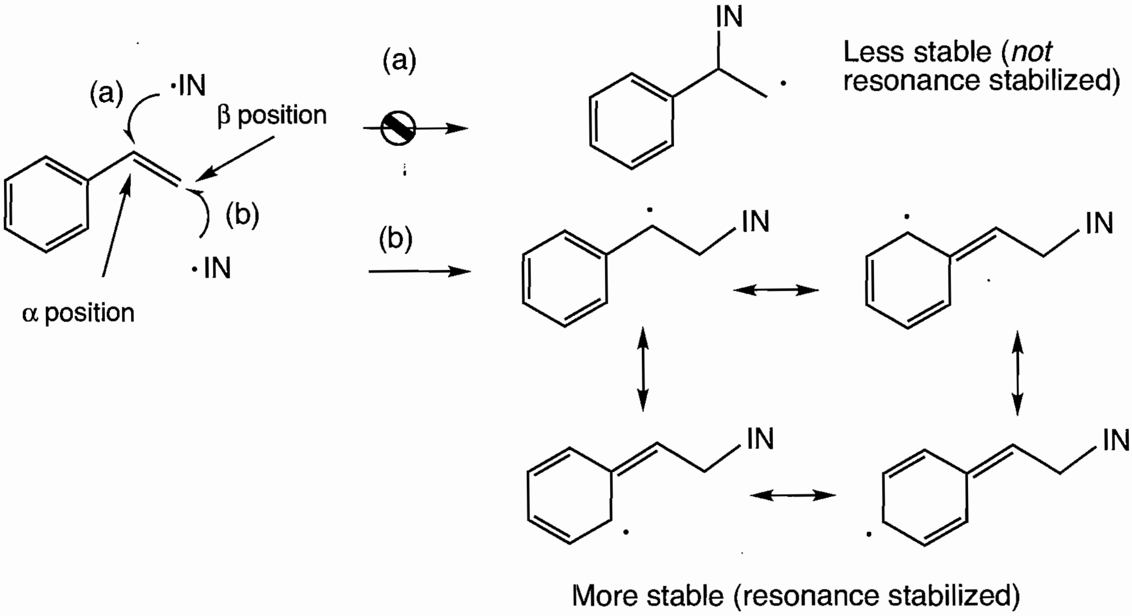
$$\cdot CCl_3 + \cdot CH_2CH_2CCl_3 \longrightarrow Cl_3C{-}CH_2CH_2CCl_3$$

$$\cdot CH_2CH_2CCl_3 + \cdot CH_2CH_2CCl_3 \longrightarrow Cl_3CCH_2CH_2{-}CH_2CH_2CCl_3$$

Problem 12.22 Addition of a radical to styrene gives an exceptionally well resonance stabilized and hence relatively stable radical.

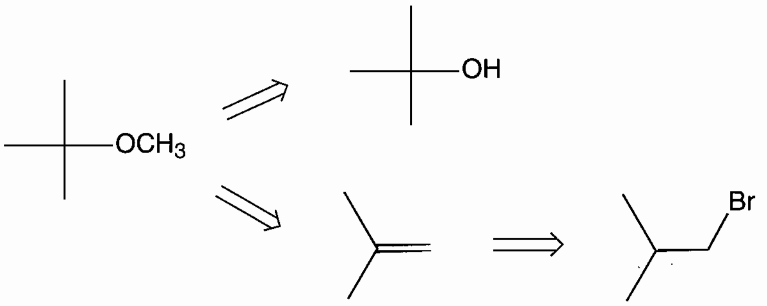


Problem 12.23 An initiator radical (IN•) can add to styrene to give two possible intermediate radicals. Resonance stabilization makes the radical formed from addition at the β position much more stable than that produced from addition at the α position.

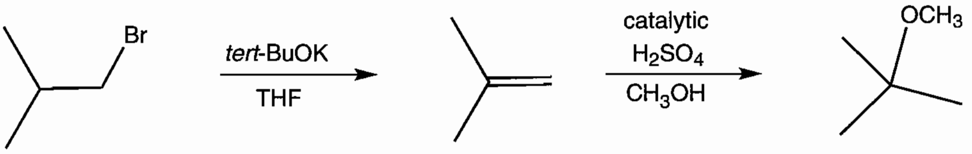


Problem 12.20

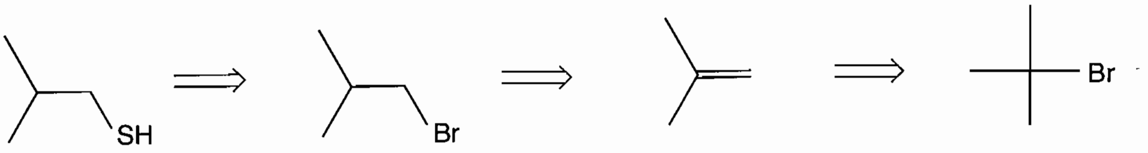
(a) Use a retrosynthesis to analyze this question. What do you need to make the desired ether? It could come from *tert*-butyl alcohol (using NaH and CH_3I). Or it could come from 2-methylpropene (using catalytic acid and CH_3OH). The alkene can come from the 1-bromo-2-methylpropane starting material.



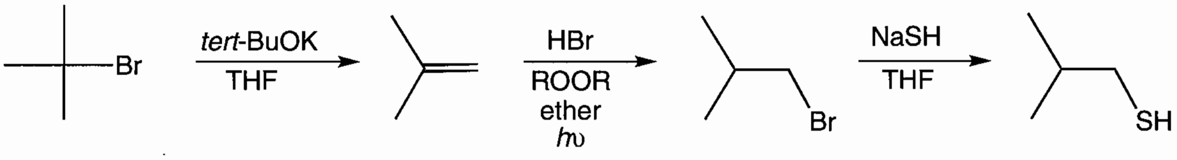
The forward solution is the following:



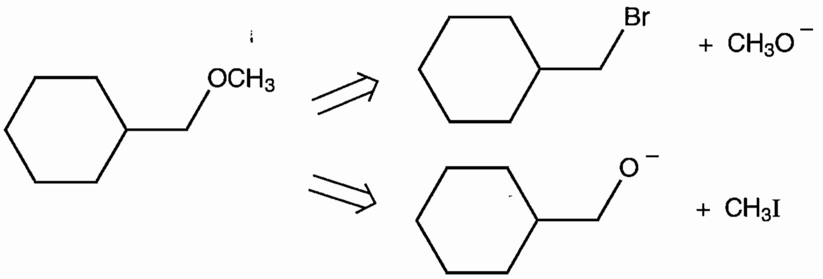
(b) The 2-methyl-1-propanethiol could come from 1-bromo-2-methylpropane via an S_N2 reaction with NaSH. We can make the primary bromide from 2-methylpropene, and the alkene can come from the *tert*-butyl bromide.



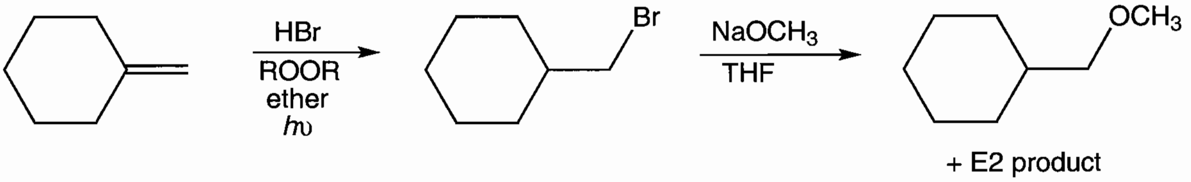
The forward solution is:



(c) The methoxy ether can be formed by an S_N2 reaction on a primary bromide, or it could come from an alkoxide reacting with methyl iodide.



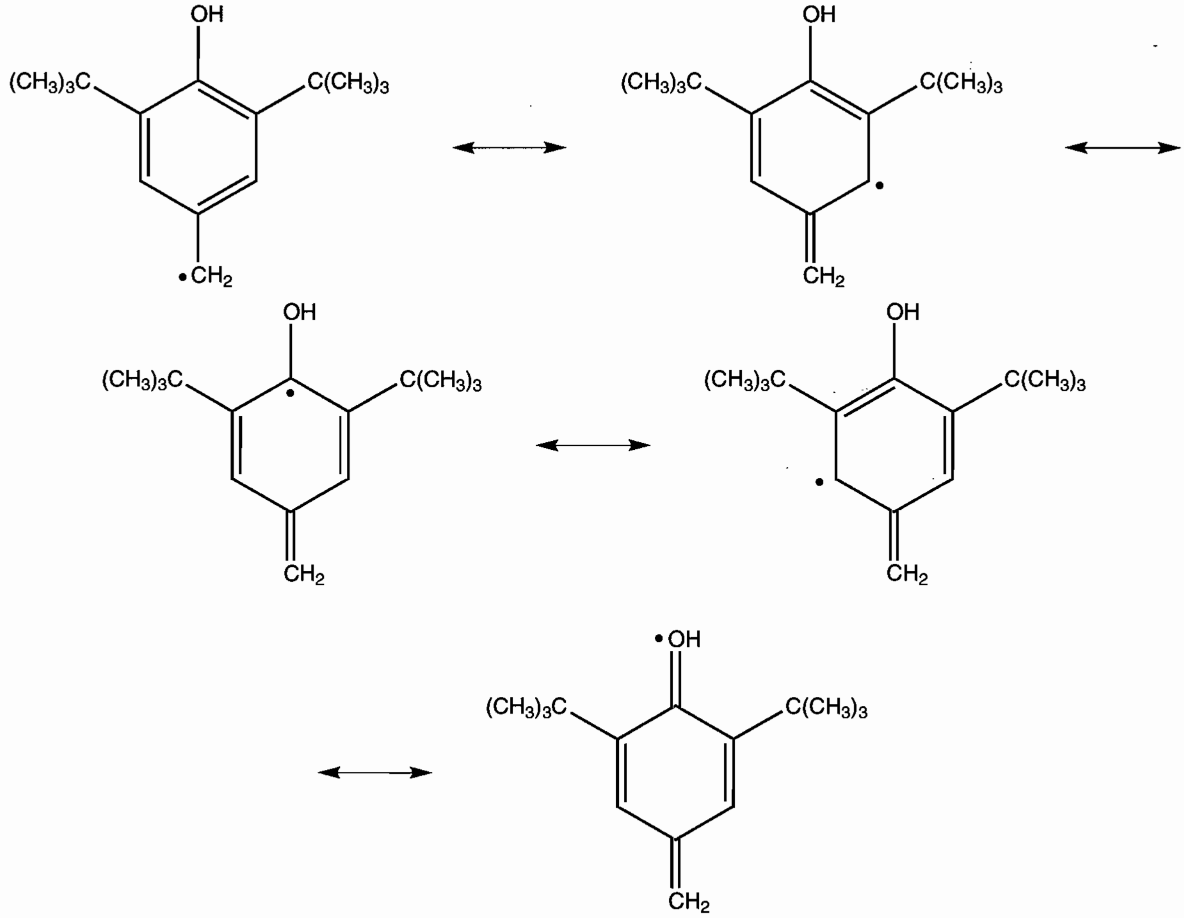
One way to make the ether:



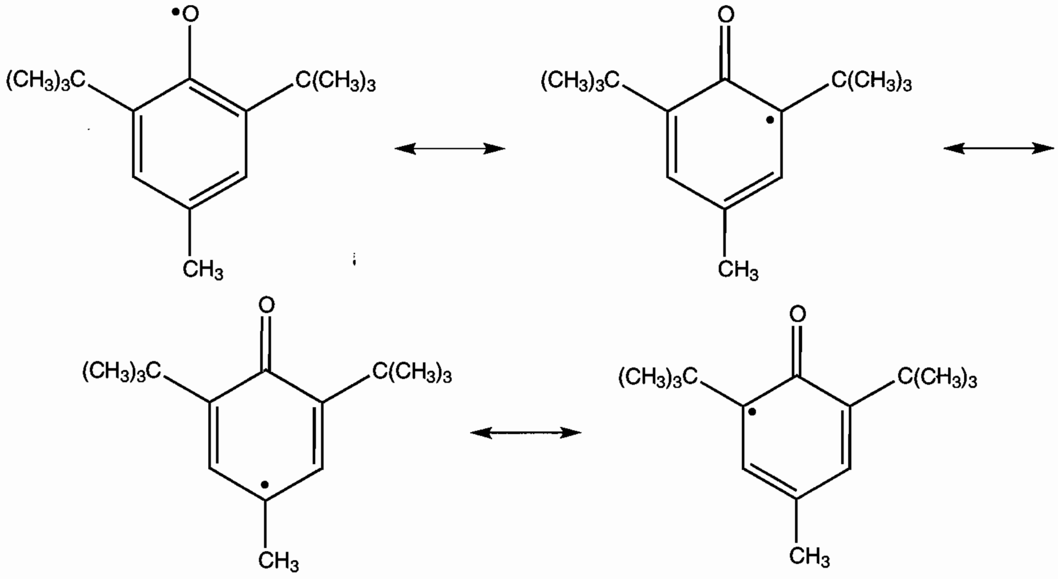
(continued)

Problem 12.19 *(continued)*

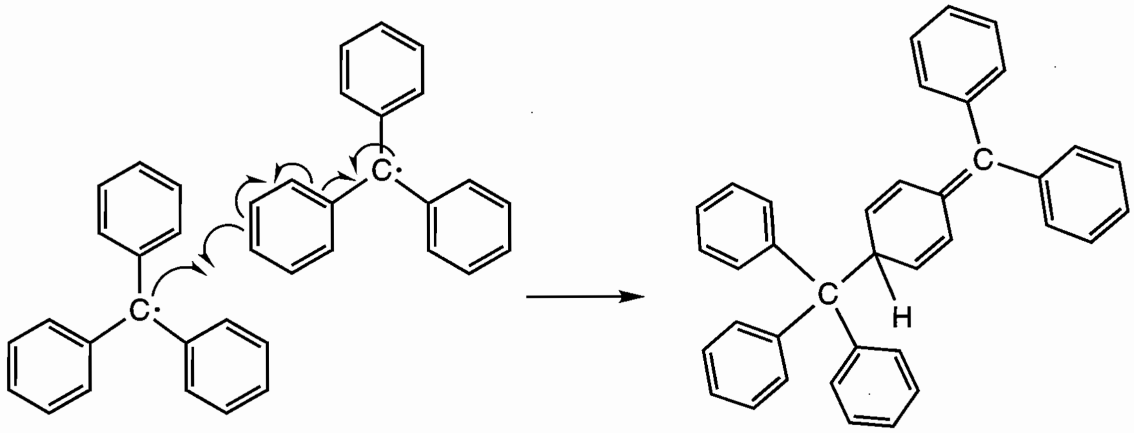
The benzylic radical has several resonance structures that would help stabilize such an intermediate.



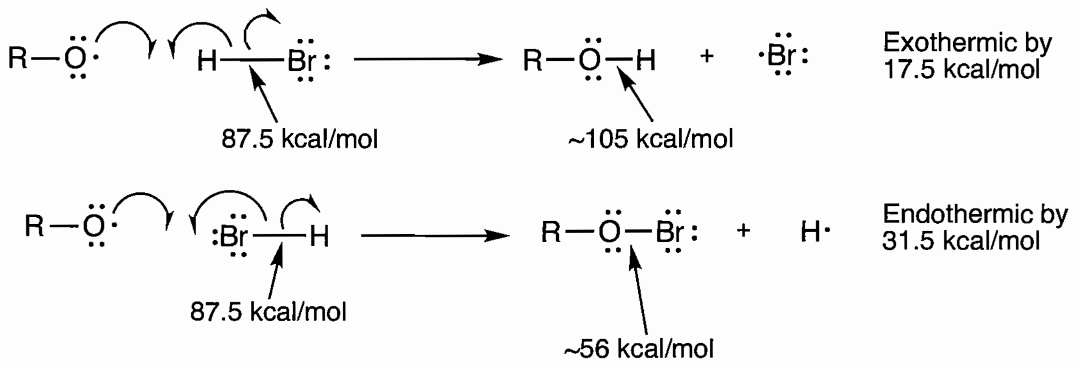
However, the phenoxy radical allows for more substituted radicals in the resonance structures. In addition, the phenoxy radical avoids the steric interaction between the O—H hydrogen and the bulky *tert*-butyl groups. It turns out that the phenoxy radical is more stable.



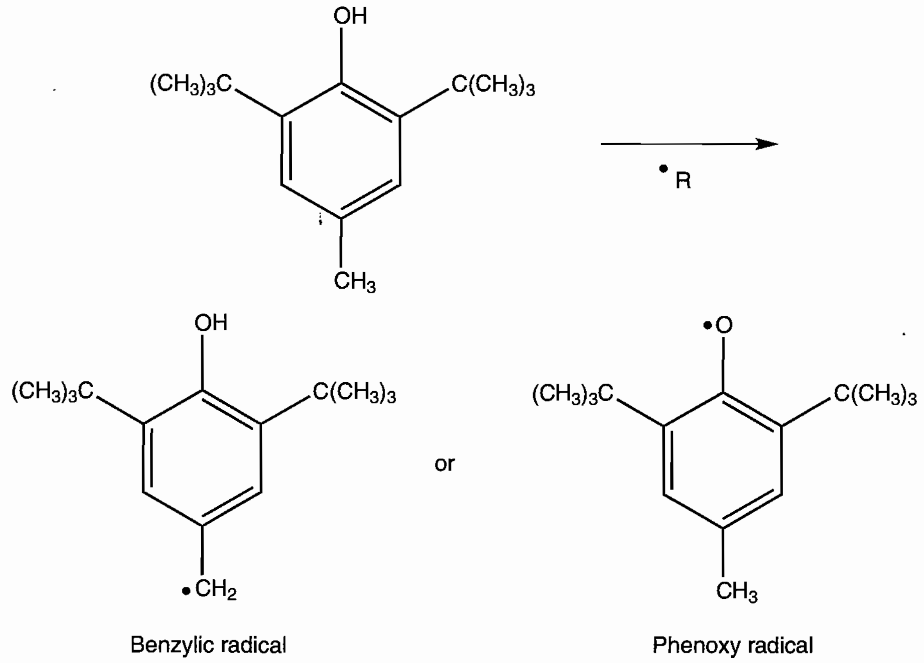
Approach to an "outside" position is not so hindered, and the arrow formalism shows the formation of the real dimer.



Problem 12.18 The bond formed by abstraction of an H atom is an O—H bond, with an approximate bond energy of 105 kcal/mol (Table 7.2, p. 277). Abstraction of Br would lead to an O—Br bond, which is much weaker, about 56 kcal/mol. Formation of the O—H bond is exothermic, whereas formation of the O—Br bond is endothermic.



Problem 12.19 One possible reaction between BHT and a radical is hydrogen abstraction from the benzylic position to form a benzylic radical. An alternative hydrogen abstraction pathway would involve abstraction of the O—H hydrogen, resulting in formation of the phenoxy radical.



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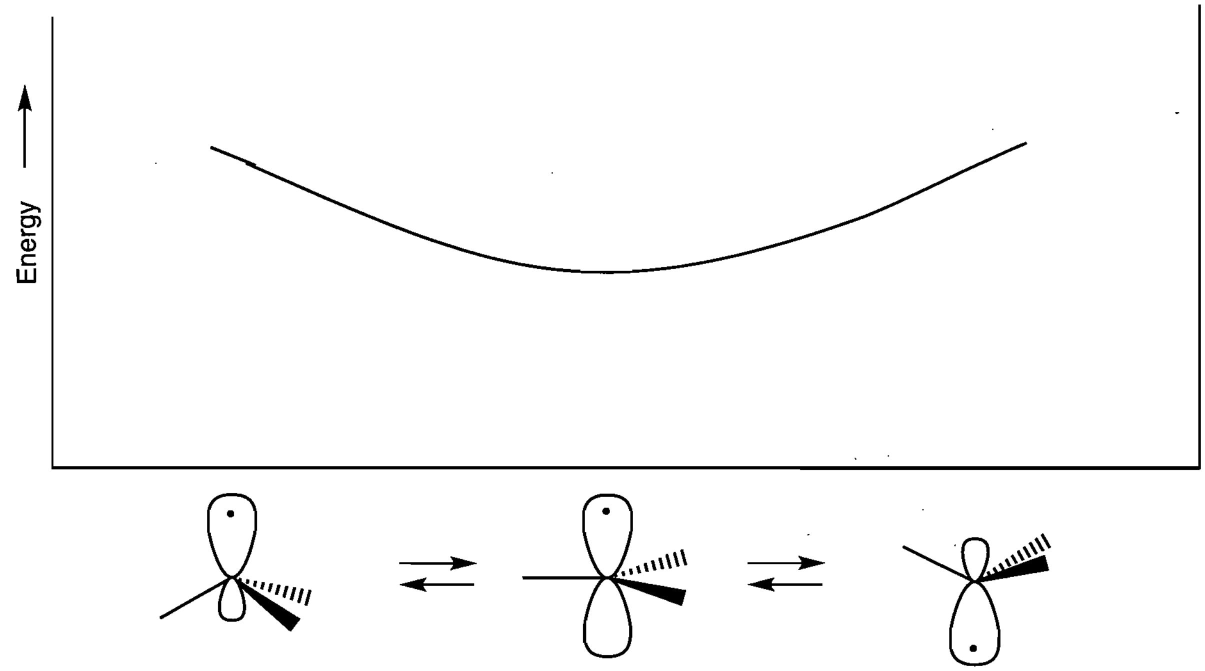
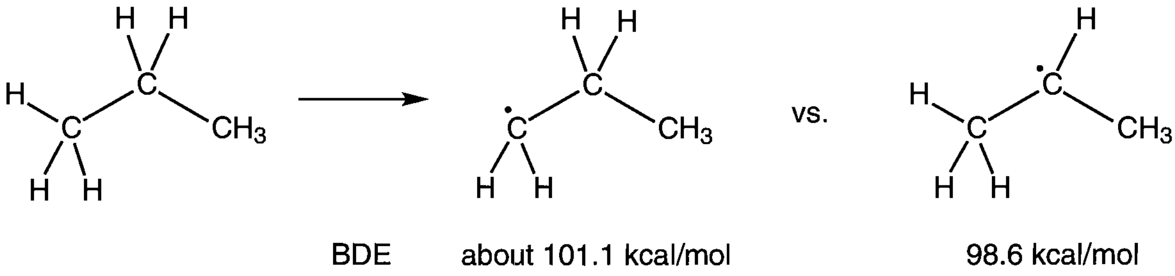
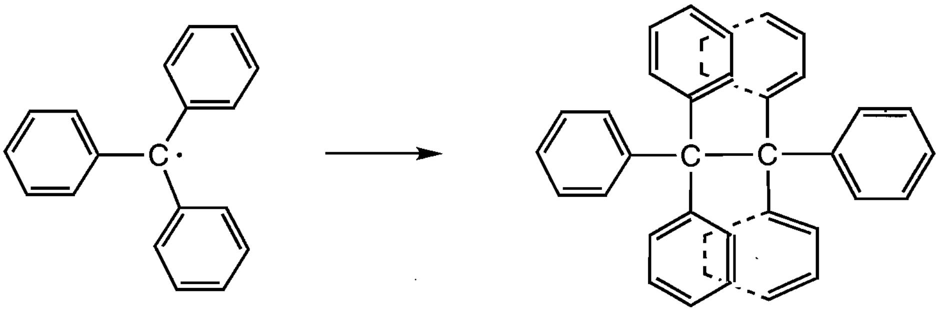
Problem 12.15 *(continued)*



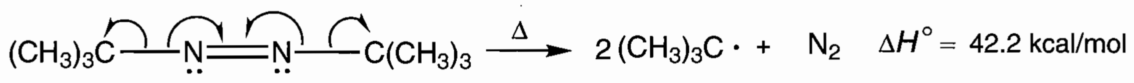
Problem 12.16 Table 12.1 shows the BDE for breaking the C—H bond of propane to give the secondary radical. That value is 98.6 kcal/mol. The closest entry in Table 12.1 for making the primary radical of propane is the value of 101.1 kcal/mol for the ethyl radical. If breaking the primary C—H bond requires about 2.5 kcal/mol more energy than breaking the secondary C—H bond, then we can estimate that the secondary C—H bond is about 2.5 kcal/mol weaker.

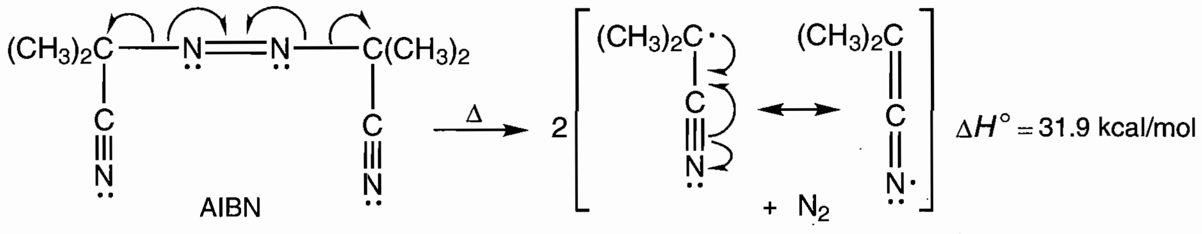


Problem 12.17 The "obvious," "just push 'em together" dimer suffers from severe steric problems. The large groups attached to the central carbons bump into each other.

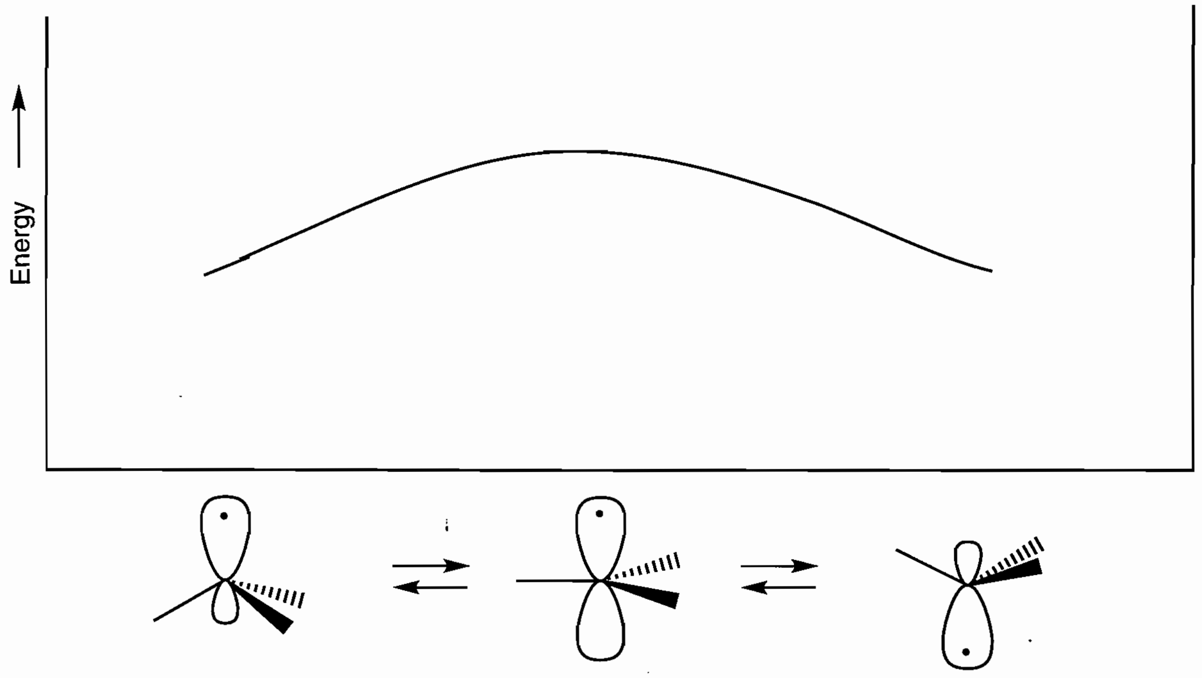


Problem 12.14 Azobisisobutyronitrile (AIBN) decomposes to give two resonance-stabilized radicals, whereas simple azo compounds do not. This stabilization of the products by resonance makes it easier to break the bonds in the starting materials.





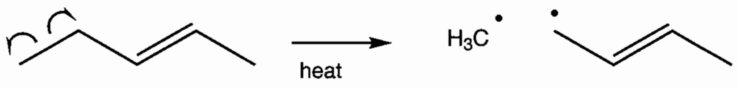
Problem 12.15 The interconversion between the sp^3-hybridized radicals must go though the sp^2 hybrid. The energy diagram shown here is correct if sp^3 is the more stable hybridization for the radical. For allyl and benzyl radicals that can be involved in resonance, the sp^2 form is more stable than the pyramidal sp^3 hybridized atom, as shown on the next page.



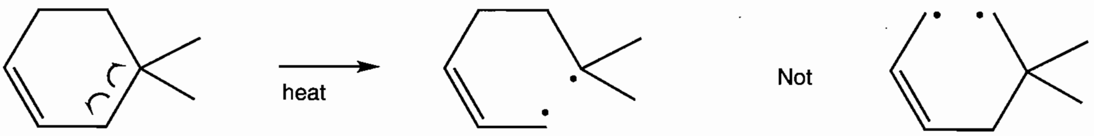
(continued)

Problem 12.12

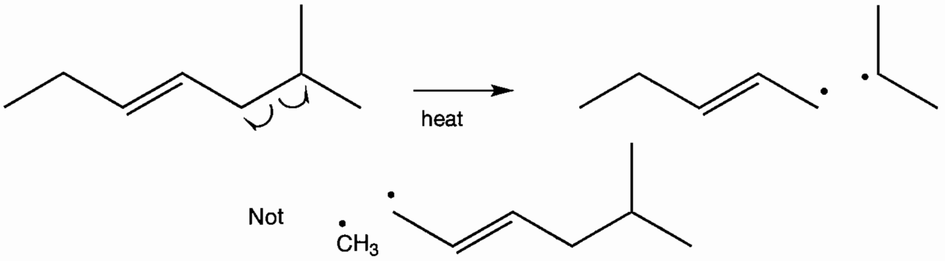
(a) The most likely C—C bond cleavage would be the one between C(4) and C(5) of 2-pentene. Cleavage of that bond would give the resonance-stabilized allylic radical and a methyl radical.



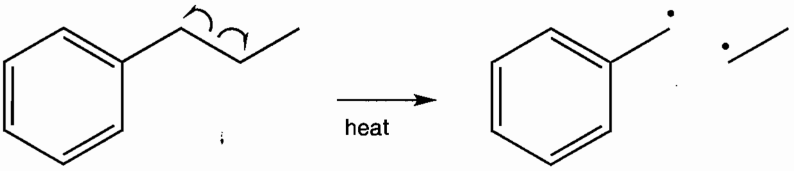
(b) Cleavage between C(3) and C(4) of 4,4-dimethylcyclohexene would form the allyl radical and a tertiary carbon radical. These are the most stable radical intermediates that can be formed by breaking one of the C—C bonds. Cleavage at the other allylic position would give an allylic radical and primary carbon radical.



(c) Thermolysis of 6-methyl-3-heptene would give the most stable radicals by cleavage of the C(5)—C(6) bond. That generates an allylic radical and a secondary radical. Cleavage at the other allylic position would give an allylic radical and the less stable methyl radical.

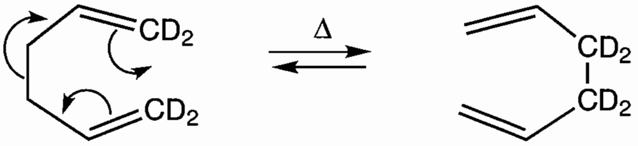


(d) Cleavage of the C(1)—C(2) bond in 1-phenylpropane gives the very stable benzyl radical and the ethyl radical.

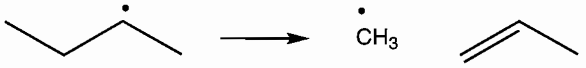


Benzyl radical

Product 12.13 The arrow formalism for this reaction is easy, although little else about this reaction is. The arrows run from the breaking bonds to the new (forming) bonds. We will meet this molecule and this reaction again in exquisite detail in Section 23.6.



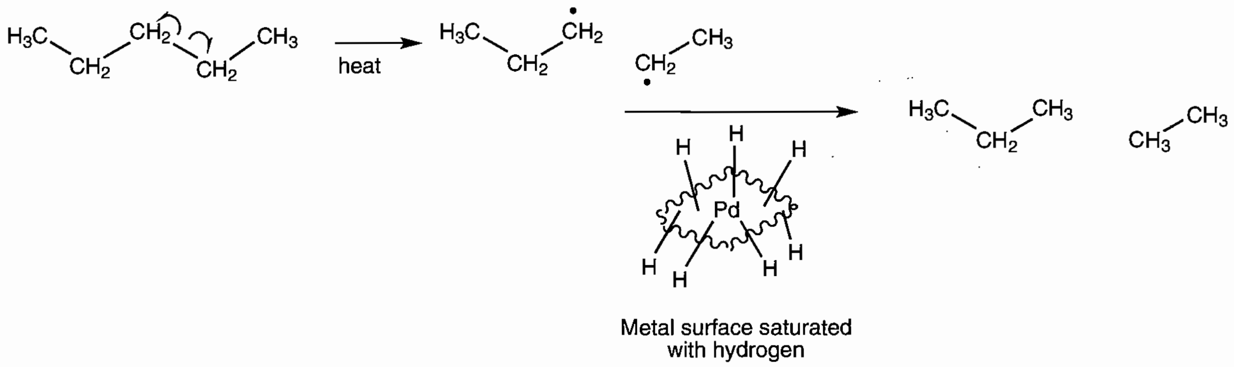
1,1,6,6-Tetradeuterio-1,5-hexadiene 3,3,4,4-Tetradeuterio-1,5-hexadiene



Bond strengths:	favored by 23 kcal/mol	
Radical stability:		favored by 6.4 kcal/mol
Entropy:		favored at higher temp

It must be the entropy factor that favors the β-cleavage reaction.

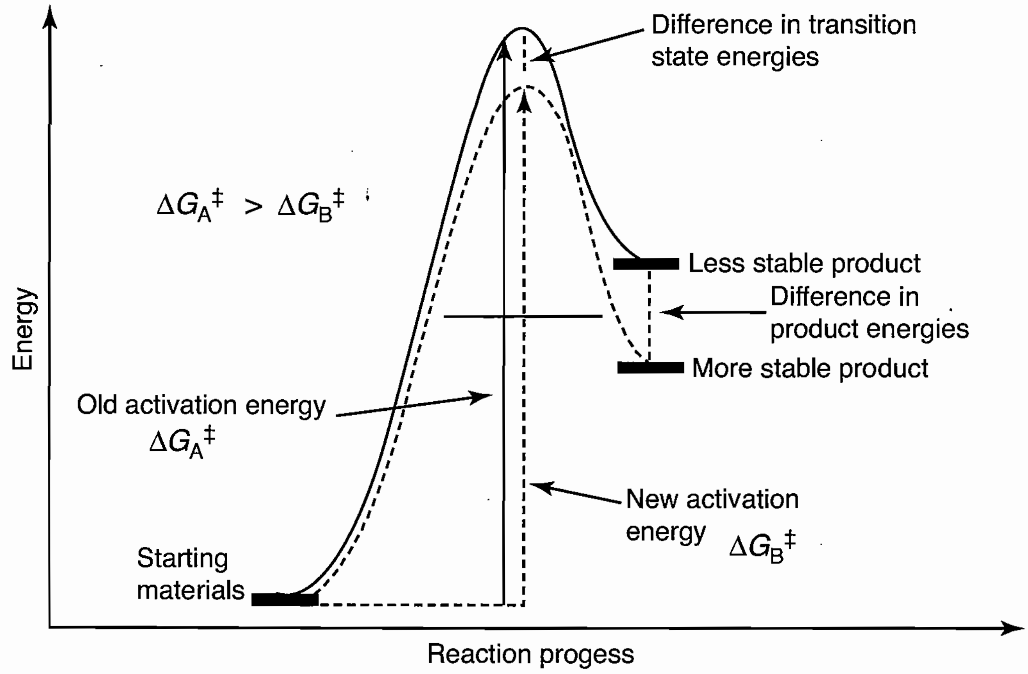
Problem 12.8 The metal catalyst provides a surface from which the carbon radicals can abstract hydrogen atoms. Carbon radicals gain hydrogen atoms to become alkanes.



Problem 12.10 There are, of course, numerous possibilities, and the text will go on to discuss a number of them. The stability of radicals increases with substitution, so one might imagine that the bond dissociation energy of carbon–carbon bonds would decrease as substitution increases. One answer to this problem is as simple as "propane!"

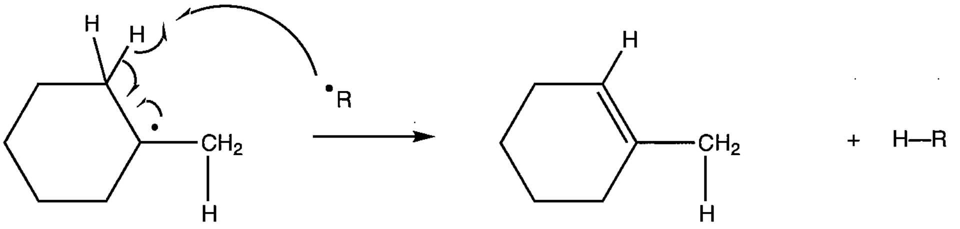
	BDE (kcal/mol)
$H_3C{-}\wr{-}CH_3 \longrightarrow 2 \quad \cdot CH_3$	90.1
$H_3C{-}\wr{-}CH_2CH_3 \longrightarrow \cdot CH_3 + \cdot CH_2CH_3$	89.0

Problem 12.11 Lowering of the product energy is accompanied by a lowering of the energy of the transition state leading to product and, therefore, of the activation energy for the reaction.

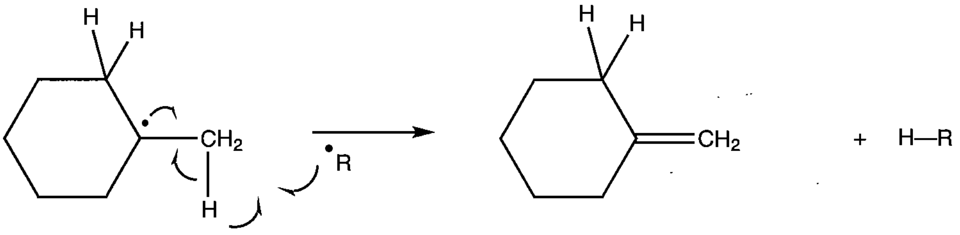


Problem 12.6 *(continued)*

(b) Disproportionation of this radical will give 1-methylcyclohexene and methylenecyclohexane.

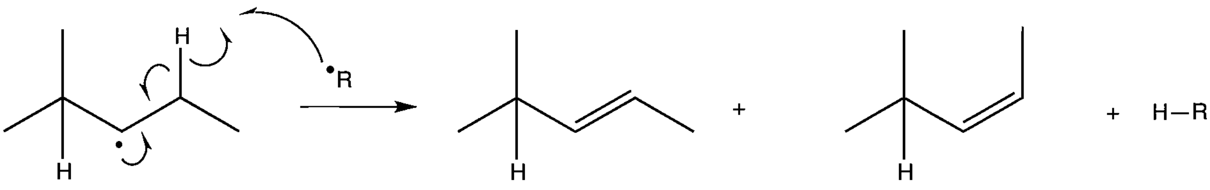


1-Methylcyclohexene

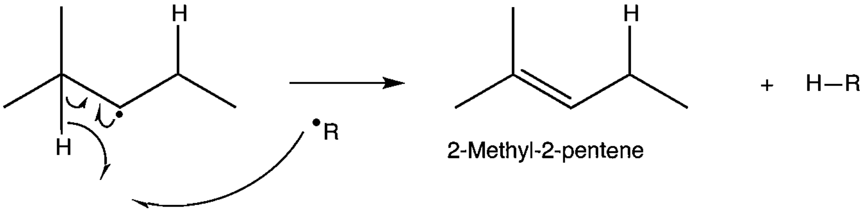


Methylenecyclohexane

(c) This radical will give (*E*) and (*Z*) 4-methyl-2-pentene and 2-methyl-2-pentene.

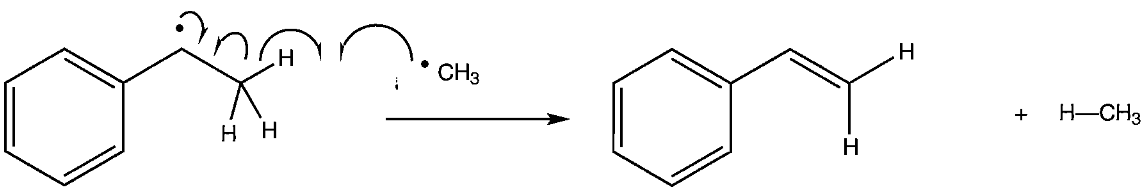


(*E*)-4-Methyl-2-pentene (*Z*)-4-Methyl-2-pentene



2-Methyl-2-pentene

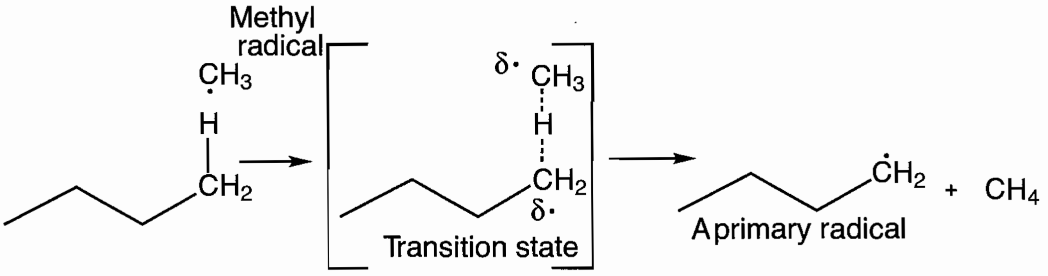
(d) This benzyl radical will undergo disproportionation to give styrene.

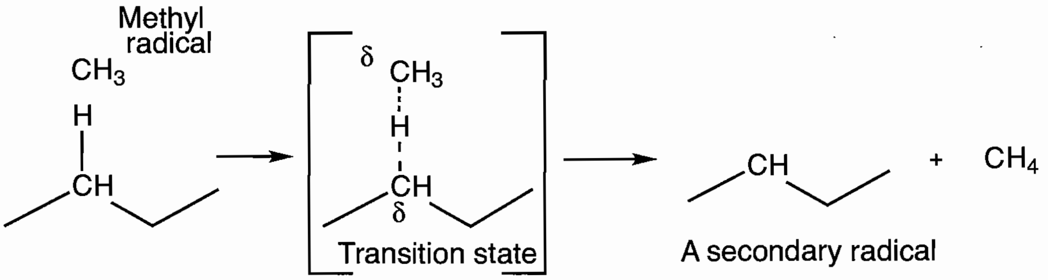


Phenylethene
(styrene)

Problem 12.7 In a β-cleavage reaction, one molecule cleaves into two, causing an increase in entropy. Recall that $\Delta G° = \Delta H° - T\Delta S°$, which means that the entropy factor will become more important as the temperature increases. We see from Table 7.2 that the BDE associated with formation of a secondary radical is 98.6 kcal/mol, and the BDE for formation of the methyl radical is 105 kcal/mol, which means that the products are about 6.4 kcal/mol more stable based on just the stability of the radical intermediates. We do break a σ bond and form a π bond in this β cleavage. In Table 7.2, we see that breaking the C—C bond costs 89 kcal/mol and forming the π bond gains 66 kcal/mol, which means the starting material is 23 kcal/mol more stable based on the bonds broken and formed.

Problem 12.5 In the transition state for abstraction of hydrogen from butane by a methyl radical, the carbon–hydrogen bond of butane is partially broken and the methyl–hydrogen bond is partially made.

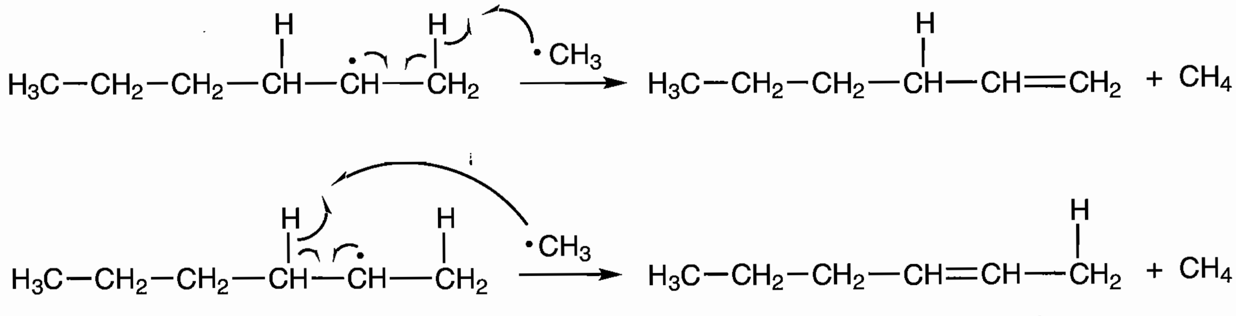




Each of these two reactions is somewhat exothermic, as the carbon–hydrogen bond in methane is stronger than either carbon–hydrogen bond in butane. Accordingly, in each transition state the hydrogen atom is slightly less than halfway transferred (the transition state is slightly "starting material-like"). Recall the Hammond postulate. Do you see why in the transition state for breaking of a secondary carbon–hydrogen bond the hydrogen is slightly less transferred than in the transition state for breaking a primary carbon–hydrogen bond?

Problem 12.6

(a) Disproportionation of this radical will give 1-hexene and the (*E*) and (*Z*) isomers of 2-hexene.

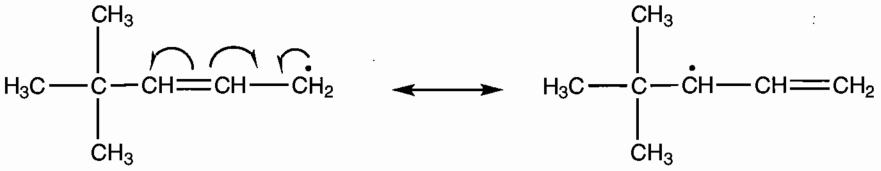


(*E*) and (*Z*) isomers formed

(continued)

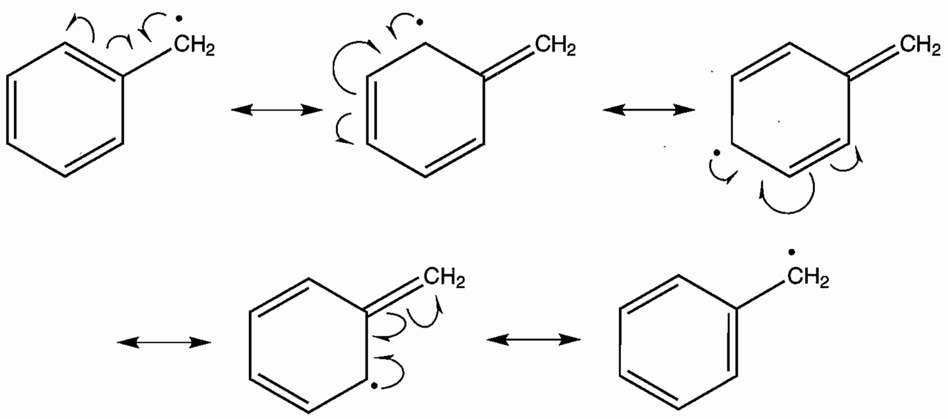
Problem 12.2

(a)

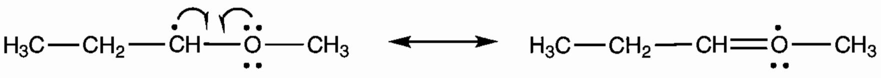


$$\mathrm{H_3C{-}\underset{CH_3}{\overset{CH_3}{C}}{-}CH{=}CH{-}\dot{C}H_2} \longleftrightarrow \mathrm{H_3C{-}\underset{CH_3}{\overset{CH_3}{C}}{-}\dot{C}H{-}CH{=}CH_2}$$

(b) This radical is called a benzyl radical. It is a particularly stable radical.

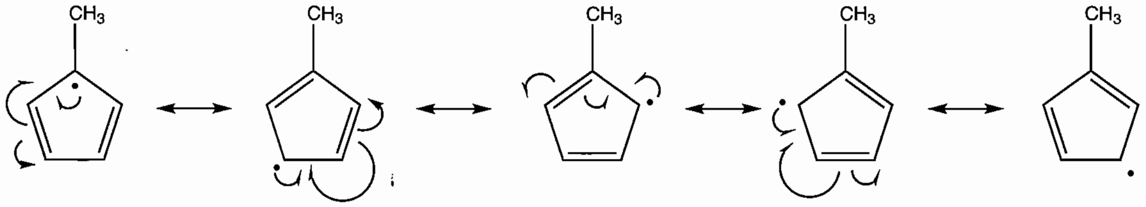


(c) The carbon radical will be in a *p* orbital in order to delocalize with one of the lone pairs of the oxygen. The resonance structure we draw for that mixing has nine electrons around the oxygen. It is a π bond with three electrons (two electrons in the π bonding orbital and one electron in the π antibonding orbital).



$$\mathrm{H_3C{-}CH_2{-}\dot{C}H{-}\underset{\cdot\cdot}{\ddot{O}}{-}CH_3} \longleftrightarrow \mathrm{H_3C{-}CH_2{-}CH{=}\underset{\cdot\cdot}{\dot{O}}{-}CH_3}$$

(d) Notice that all five carbons share the radical.



Problem 12.4 The carbon–carbon bond is weaker (90.1 kcal/mol) than the carbon–hydrogen bond (101.1 kcal/mol) and therefore is easier to break.

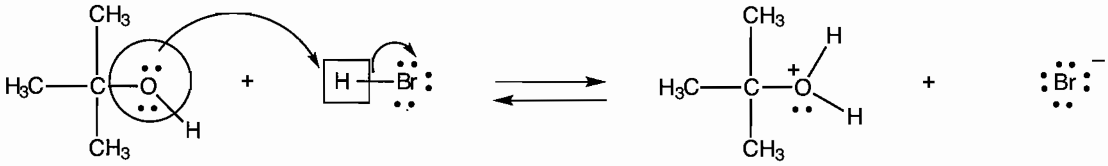
12

Radical Reactions

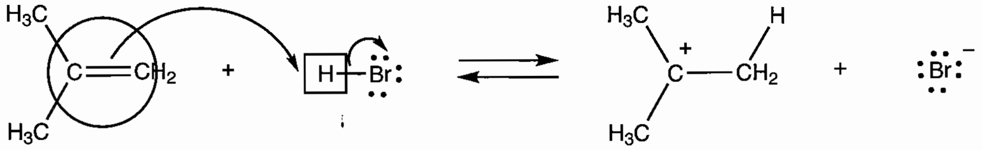
Radical reactions provide new opportunities and new difficulties. Radical reactions allow you to reverse the regiochemistry of addition of hydrogen bromide to alkenes, for example, or to introduce functionality at the position adjacent to a double bond. The following problems allow you to practice such things. Many more radical reactions are known than are discussed in this chapter, and these problems allow you to find a few. Radical chemistry, though different from the polar chemistry we have emphasized so far, nonetheless can be understood through an analysis of structure and orbitals. Keep in mind that chain processes abound in radical chemistry. In such reactions, a chain-carrying radical is produced in one of the propagation steps. In a sense, this is analogous to the regeneration of a catalyst at the end of a polar reaction. There are clues to the presence of a radical reaction: The presence of peroxides or *N*-bromosuccinimide (NBS) is one clue, for example.

Problem 12.1

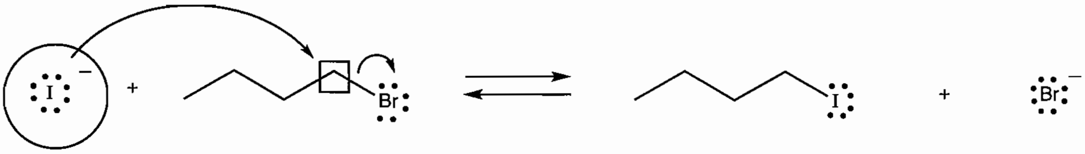
(a) The nucleophile is the oxygen of the alcohol, specifically one of the lone pairs of electrons. The electrophile is the acidic hydrogen of HBr, specifically the antibond of the H—Br sigma bond.



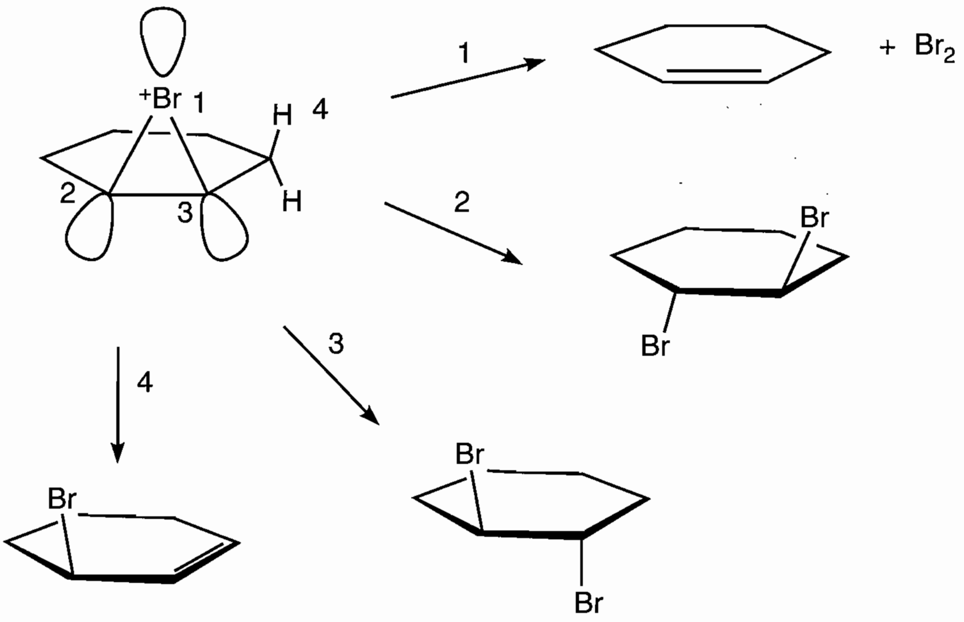
(b) The nucleophile is the π bond of the alkene. The electrophile is the acidic hydrogen of HBr, specifically the antibond of the H—Br sigma bond.



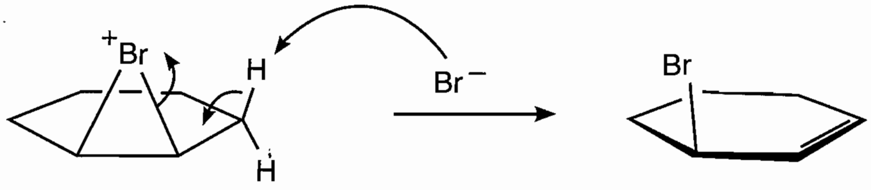
(c) The nucleophile is the iodide ion, specifically one of the lone pairs of electrons of the iodide. The electrophile is the carbon bonded to the Br, specifically the antibonding orbital of the C—Br bond.



Problem 11.73 The LUMO density for the bromonium ion in this reaction is located on the bromine of the bromonium ion (labeled 1 on structure in the figure), on the left-side carbon of the three-membered ring (labeled 2), on the right-side carbon of the three-membered ring (labeled 3), and on the hydrogen that is on the adjacent carbon to the three-membered ring (labeled 4). The reaction of bromide with the LUMO at position 1 is just the reverse reaction of the formation of the bromonium ion. Reaction at the LUMO on either of the carbons (labeled 2 or 3) gives the enantiomeric trans dibromides shown. Reaction at the LUMO on the hydrogen labeled 4 gives 3-bromocyclohexene.

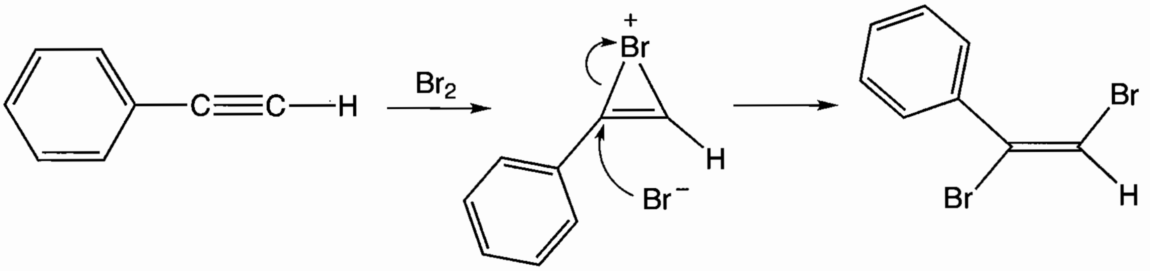


The mechanism for the reaction with the hydrogen labeled 4 is shown.



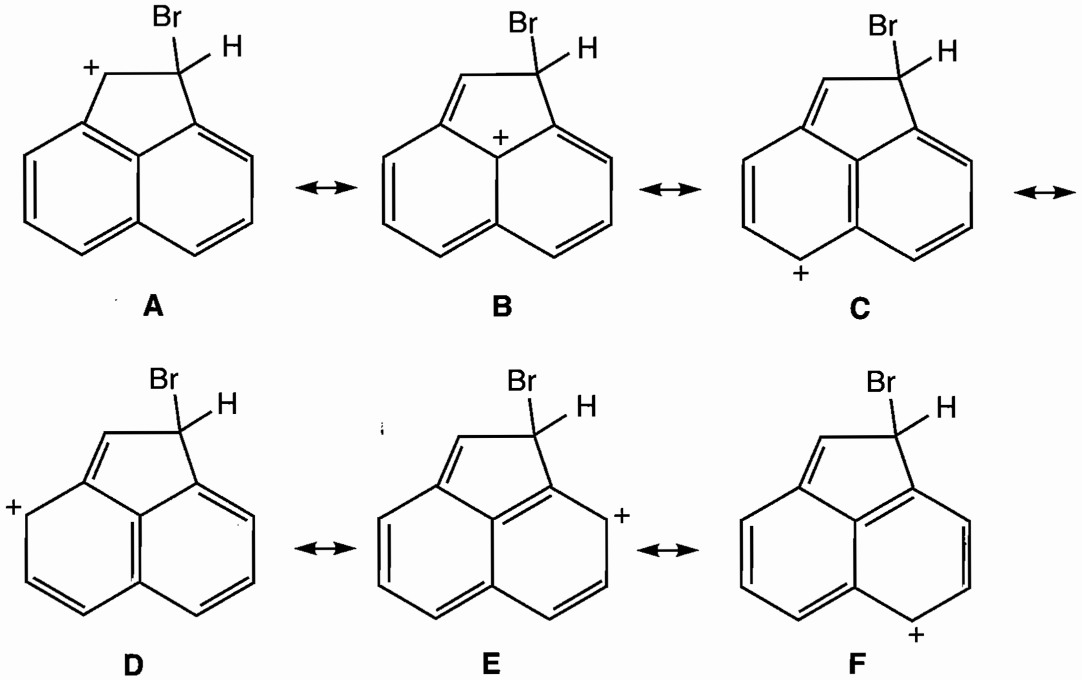
Problem 11.74 Yes, the energy diagram for this reaction is consistent with a concerted reaction. There are no intermediates in the diagram. In Table 7.2 (p. 277), we can see that the alkene π bond and the O—O bond are worth 117 kcal/mol (66 + 51 kcal/mol). The epoxide has two C—O bonds at 92 kcal/mol each. Even with the strain of the three-membered ring (27 kcal/mol), the reaction with hydrogen peroxide should be favored. In practice, hydrogen peroxide works better with electron-poor alkenes such as the enones we will see in Chapter 19.

If a cyclic bromonium ion had been the intermediate, only the trans dibromide could have formed. Because both cis and trans diastereomers are formed, the open cation must be involved.

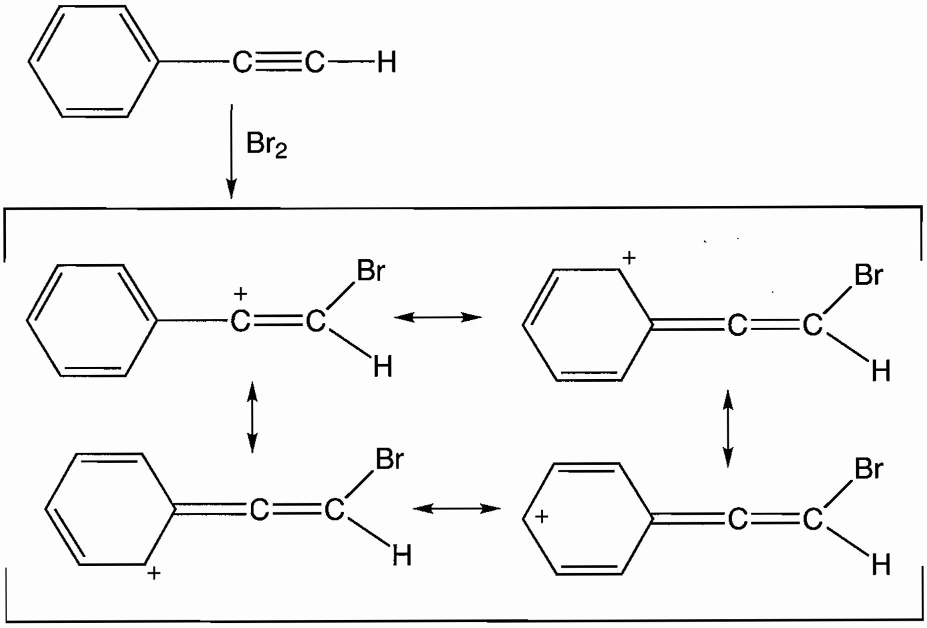


Problem 11.72 The intermediate carbocation is relatively stable. Notice that the energy of the intermediate is relatively close to that of the starting material.

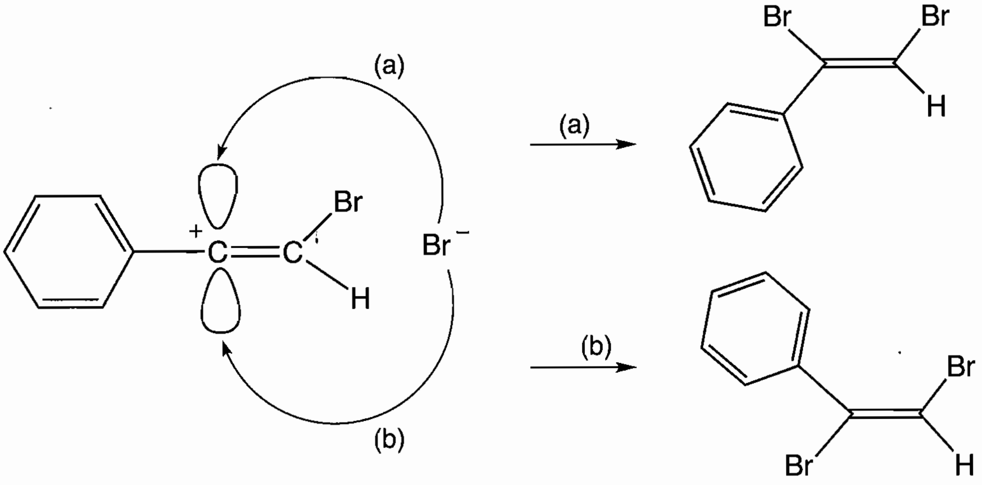
Resonance structures (**A**–**F**) are shown here. Based on the LUMO representation, it appears that structures **C** and **D** contribute most. Perhaps structure **F** contributes least. It is clear that the structures **B**, **E**, and **F** contribute less than do **A**, **C**, and **D**. Notice that **A**, **C**, and **D** maintain three double bonds in one six-membered ring (aromaticity). Structures **B**, **E**, and **F** do not have any aromatic rings. This lack is a likely reason for the higher weighting factor of **A**, **C**, and **D**.



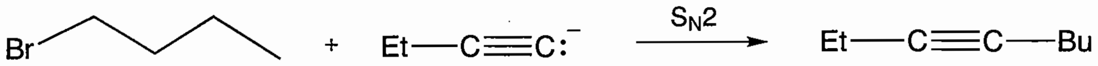
Problem 11.71 In addition reactions of bromine, there is always a competition between formation of a cyclic bromonium ion and an open carbocation. Anything that will favor one over the other may tip the balance in favor of that mechanism. In this case, formation of an open ion is favored by resonance stabilization.



Now, addition of the bromide ion can be to either lobe of the empty 2*p* orbital, thus giving both stereoisomers.



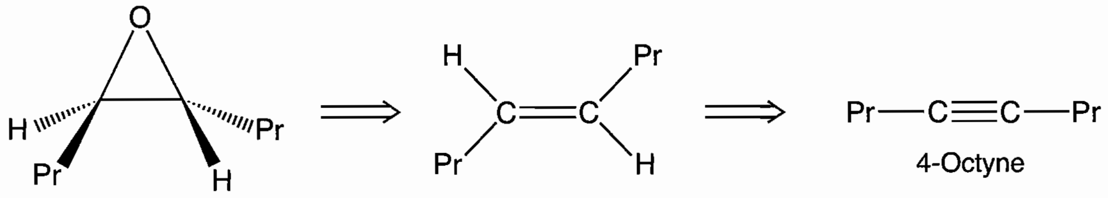
3-Octyne can be prepared by alkylation of the acetylide of 1-butyne with bromobutane, a molecule we made in (a).



The acetylide comes from the corresponding acetylene:

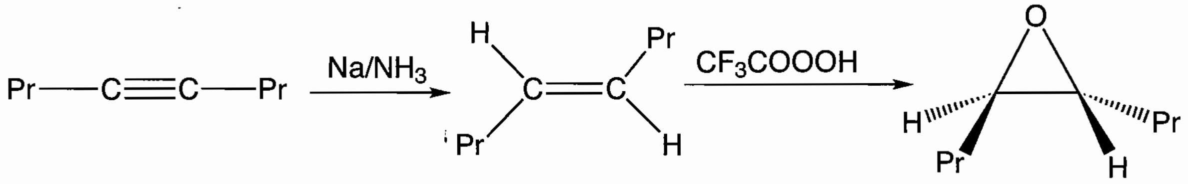
$$\text{Et—C}\equiv\text{CH} \xrightarrow{\text{NaNH}_2/\text{NH}_3} \text{Et—C}\equiv\text{C}:^- \quad \text{Na}^+$$

(d) The trans epoxide must come from epoxidation of a trans alkene. In turn, the trans alkene comes from a stereospecific reduction of an alkyne, in this case, 4-octyne.

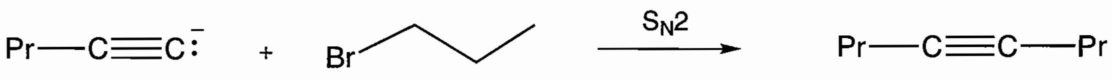


Pr = propyl, $CH_2CH_2CH_3$

or

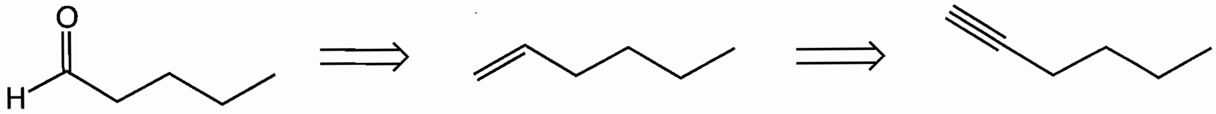


4-Octyne can be made from the acetylide of 1-pentyne and propyl bromide. Both reagents were made in (b).

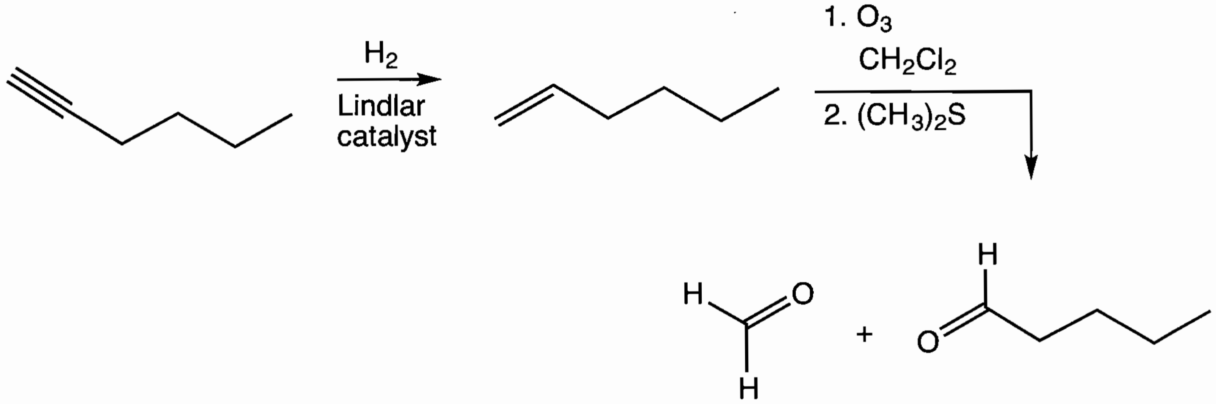


Problem 11.70 *(continued)*

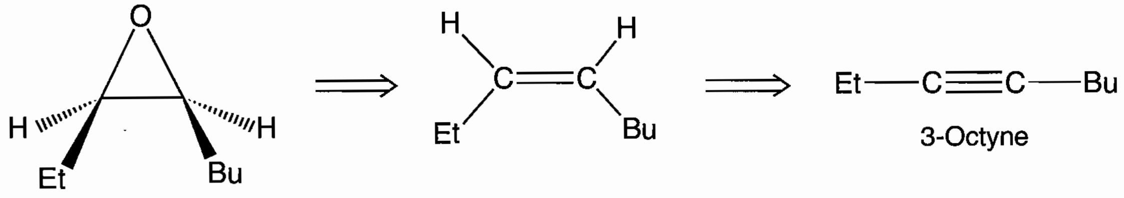
There are other possibilities. For example, we could use the 1-hexyne we made in part (a). The retrosynthetic analysis looks like this:



In other words,

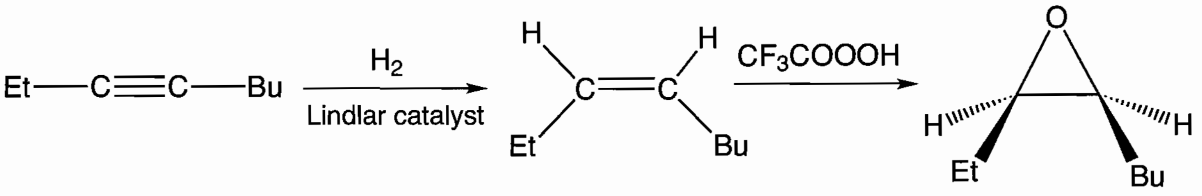


(c) Retrosynthetic analysis suggests that our target epoxide should be available from 3-octyne.

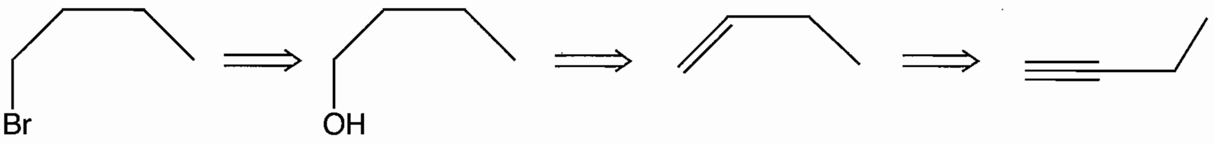


Bu = butyl, $CH_2CH_2CH_2CH_3$
Et = ethyl, CH_2CH_3

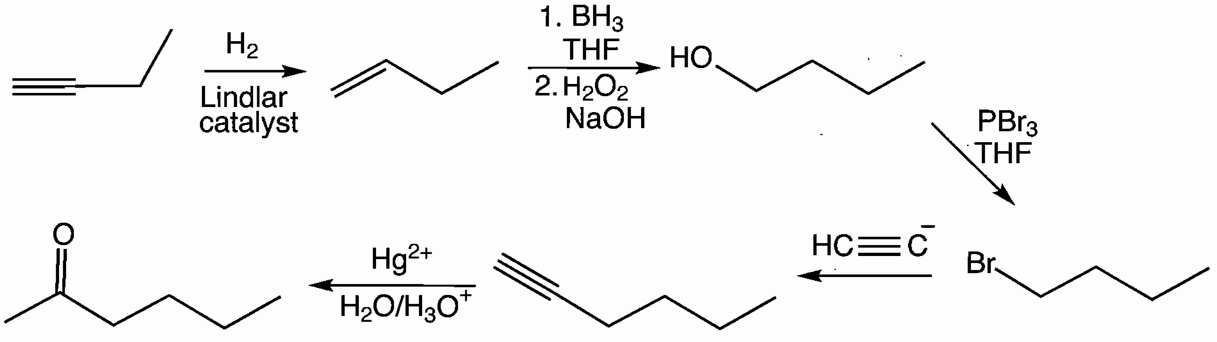
In conventional terms,



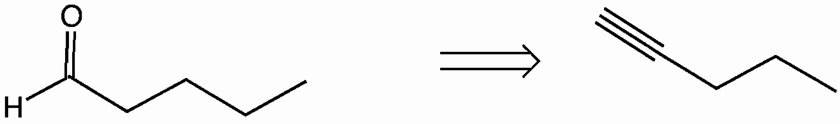
We still need to make bromobutane, however, because this material isn't an allowed starting material. We might reduce 1-butyne to 1-butene, hydroborate, and then form the bromide.



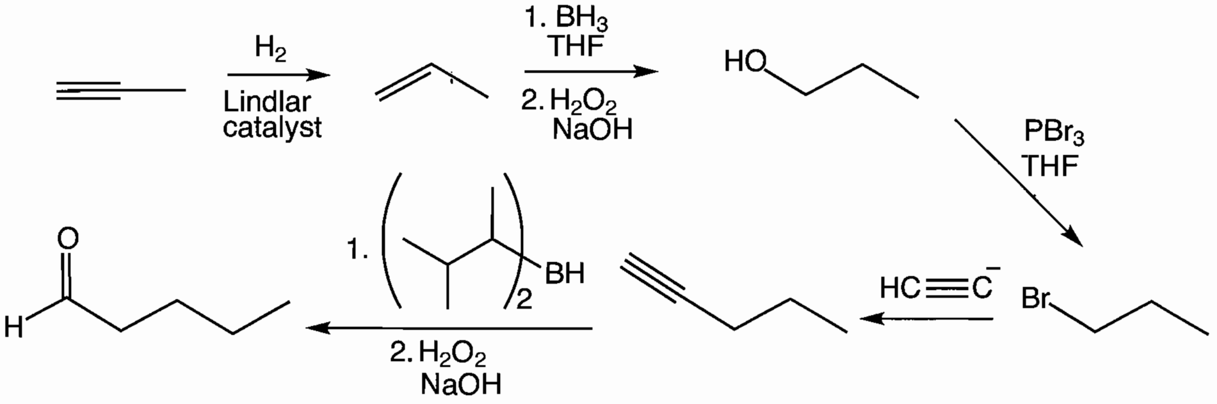
So the synthesis would look like this:



(b) The target molecule, pentanal, should be available from 1-pentyne through a hydroboration-oxidation sequence with diisoamylborane, $HB[CHCH_3CH(CH_3)_2]_2$. 1-Pentyne can be made through a sequence similar to that used for 1-hexyne in (a).



Here is the synthesis:



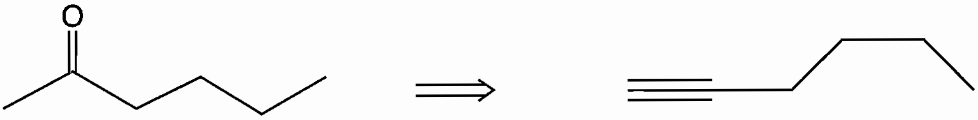
(continued)

Problem 11.70 In all synthesis problems, it is imperative that you work backward. This is called "retrosynthetic analysis" by those who do it for a living, and *every* successful synthetic chemist analyzes problems this way. There is even a special, "retrosynthetic" arrow that points to the immediate precursors to the target. Thus,

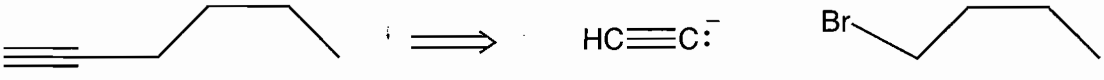
$$\text{Target} \underset{\text{(retrosynthetic arrow)}}{\Longrightarrow} \text{Precursor molecules}$$

Who are we to disagree? We won't. In practice, the rather fancy term "retrosynthetic analysis" simply means, "search for the *immediate* precursor for the target molecule." *Do not* attempt to see all the way back to the ultimate starting material. At this point, when we have relatively few synthetic methods in our arsenal, it may be possible to do synthetic problems "forward." But this practice is bad technique, and it is best to do these problems the right way.

(a) In this case, we can see that the target, 2-hexanone, could be made from the mercury-catalyzed hydration of 1-hexyne. (2-Hexyne would also give some 2-hexanone, but this route would not be practical. Why?)



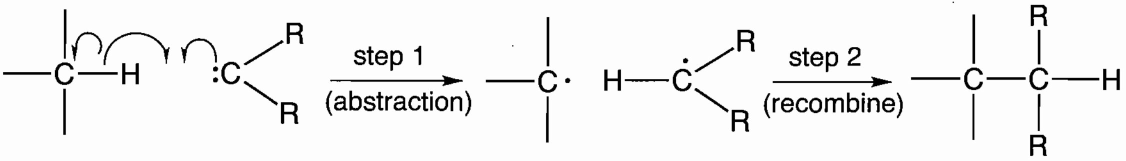
However, 1-hexyne has two more carbons than our allowable starting materials, so we need a synthesis of this molecule. The problem has been reduced to finding a synthesis for 1-hexyne. Here is a suggestion: An S_N2 reaction between an acetylide anion and bromobutane would do the trick.



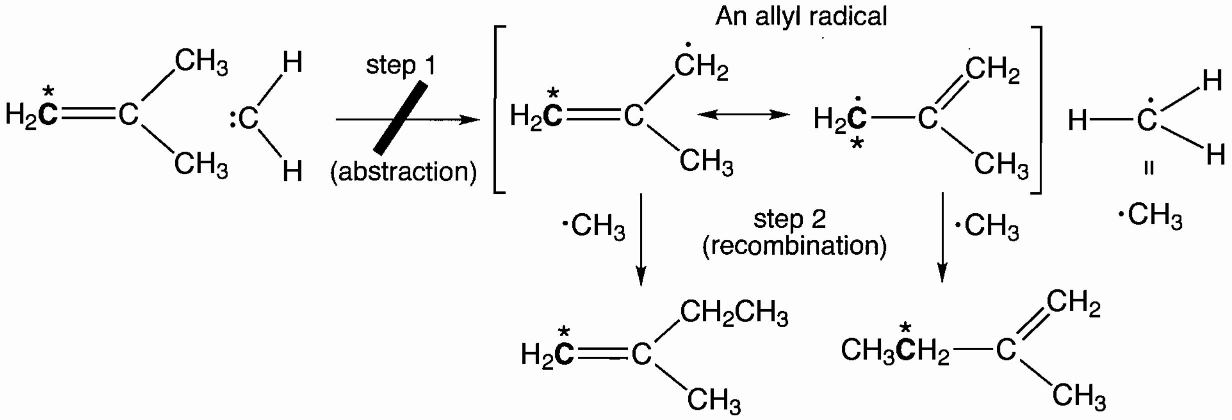
The acetylide can be formed from the reaction of a large excess of acetylene, an allowed starting material, and sodium amide (the excess acetylene reduces the formation of the diacetylide).

$$HC{\equiv}C:^{-} \Longrightarrow HC{\equiv}CH + NaNH_2/NH_3$$

A two-step mechanism must involve hydrogen abstraction followed by recombination:

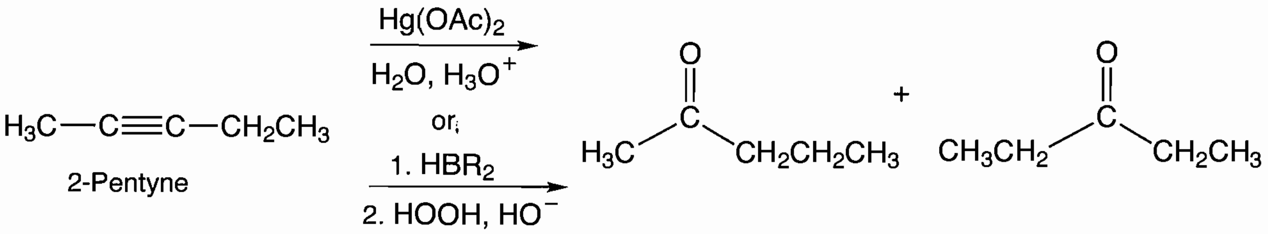


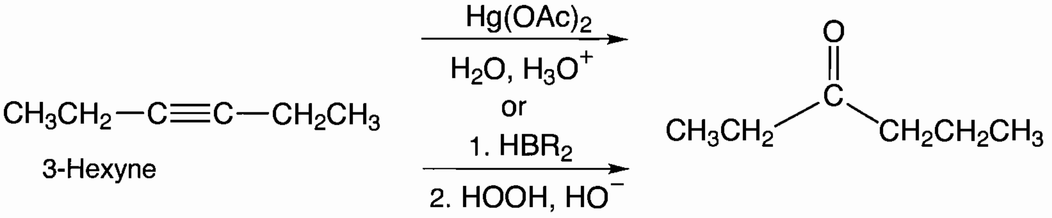
(b) The Doering and Prinzbach experiment shows that the insertion reaction must occur in one step. A two-step process would generate a resonance-stabilized intermediate allyl radical, and the position of the label would be scrambled. As this does not happen, the reaction must be one step.



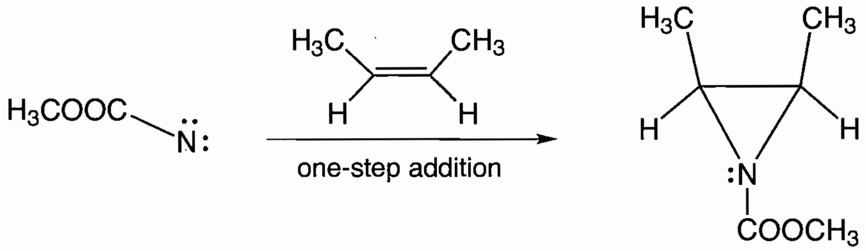
These are the same alkene, but the labeled carbon is in a different position

Problem 11.69 Both hydroboration/oxidation and mercury-catalyzed hydration of 2-pentyne must give a mixture of two ketones, 2-pentanone and 3-pentanone. Neither process is a useful preparative method. By contrast, either procedure applied to the symmetrical alkyne 3-hexyne would give the same product, 3-hexanone. Either would be a reasonable preparative method.





Problem 11.67 Retention of stereochemistry means that aziridine formation must take place in a single step.



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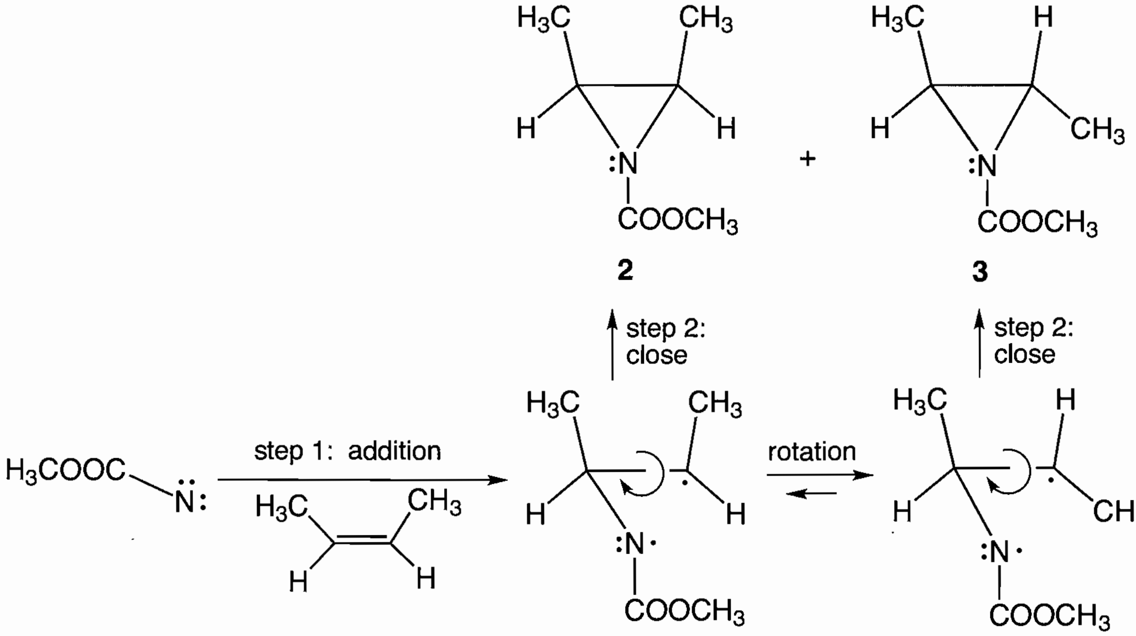
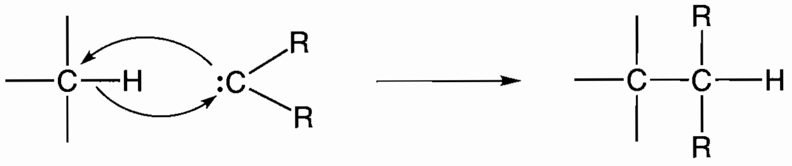
A two-step addition would give both **2** and the stereoisomeric **3**. As only **2** is formed, the reaction must occur in a single step. In turn, that implies a singlet, all-paired electron structure for the nitrene reacting species.



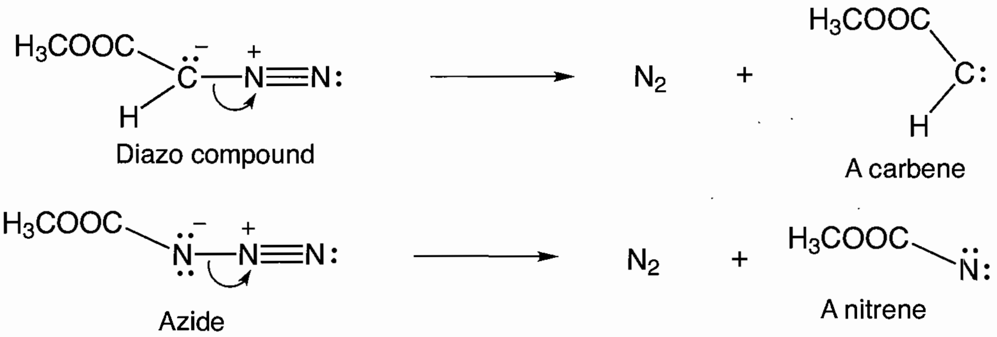
Problem 11.68

(a) In a one-step reaction, there can be no intermediate; the product must be formed directly. There really isn't much to draw in this case.

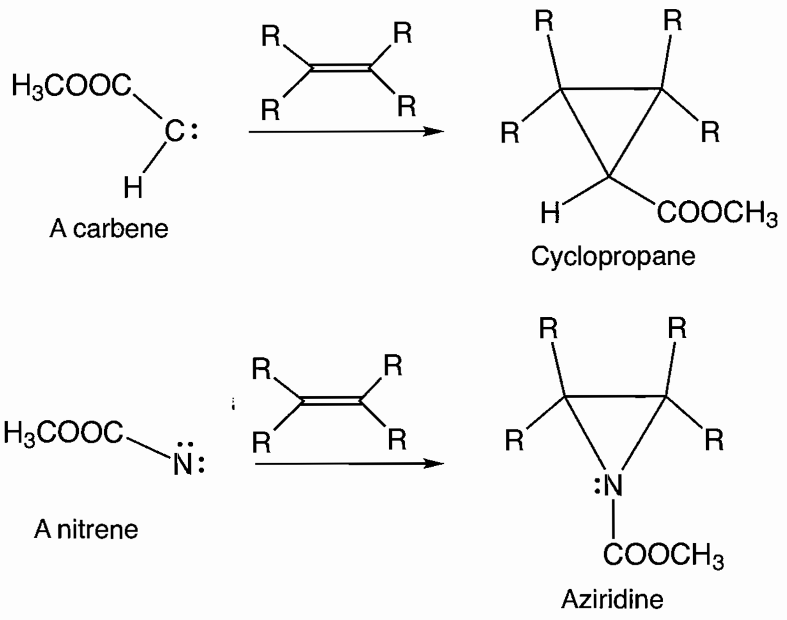


So the formation of **3** becomes diagnostic for the nature of the mechanism of aziridine formation. A one-step mechanism cannot form **3**; a two-step mechanism must form **3**.

Problem 11.66 Azides behave much like diazo compounds. Just as diazo compounds can lose nitrogen to give a carbene (divalent carbon), so azides can lose nitrogen to give "nitrenes" (monovalent nitrogen).



Carbenes add to alkenes to give cyclopropanes. Nitrenes behave in similar fashion, forming the three-membered rings called aziridines.



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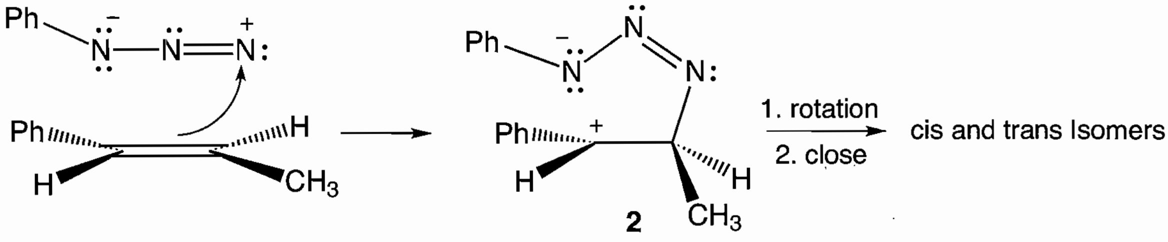
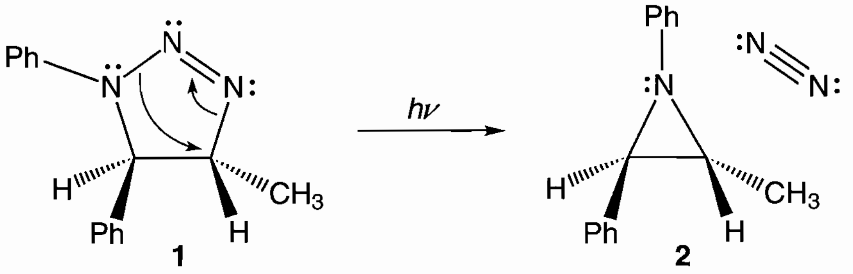
Problem 11.64 *(continued)*

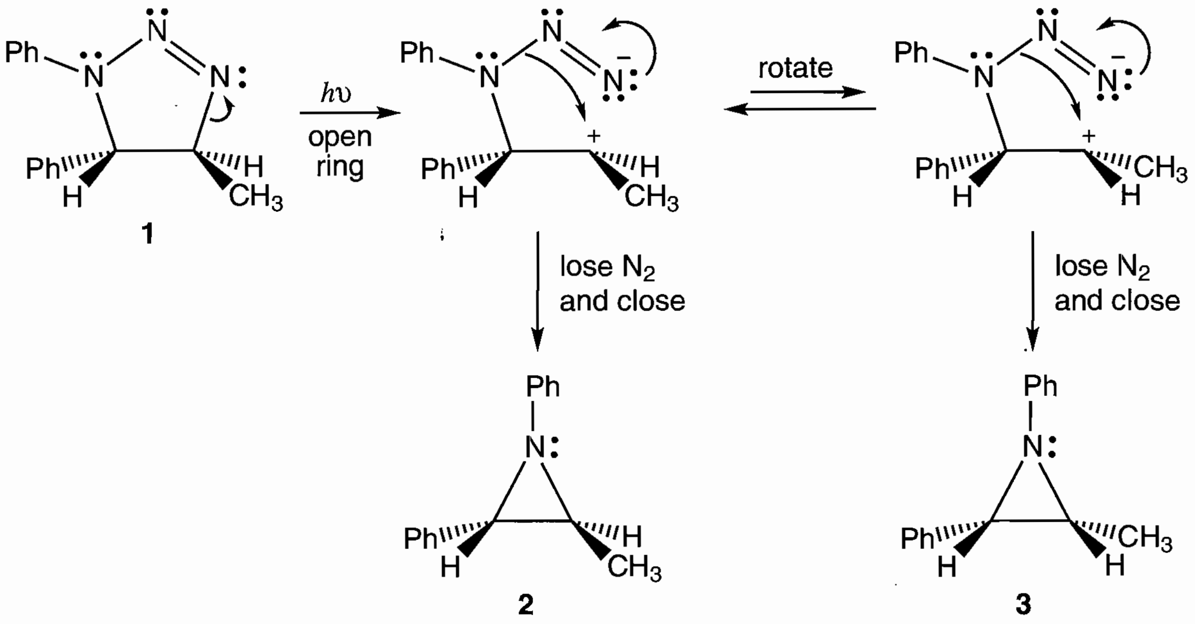
The formation of the single stereoisomer **1** with retention of stereochemistry (the trans alkene gives a trans five-membered ring) means that the mechanism of formation of **1** must involve no free carbocation (**2**, for example) capable of rotation that would scramble the stereochemistry originally present in the alkene. The more electrophilic nitrogen of the azide is the terminal nitrogen, and it probably starts to bond to the C(2) carbon first, which would explain why there is only one regioisomer in this reaction. The ring closing process must occur at essentially the same time, since there is no free carbocation.



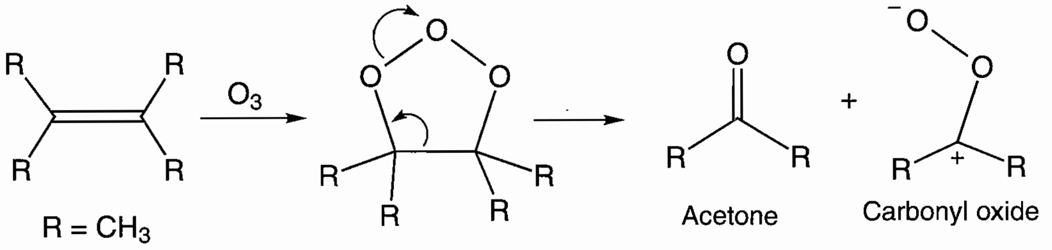
Problem 11.65 In the concerted mechanism, nitrogen is lost in a single step to give aziridine **2**. The trans stereochemistry present in **1** will be preserved in **2**.



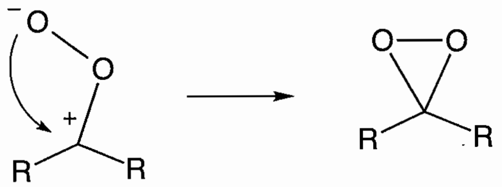
There are many possible two-step (nonconcerted) mechanisms. All must go through an intermediate in which the stereochemical relationships originally present in the alkene and triazoline **1** can be lost. Both **2** and the stereoisomeric **3** will be formed. Here is one possibility.



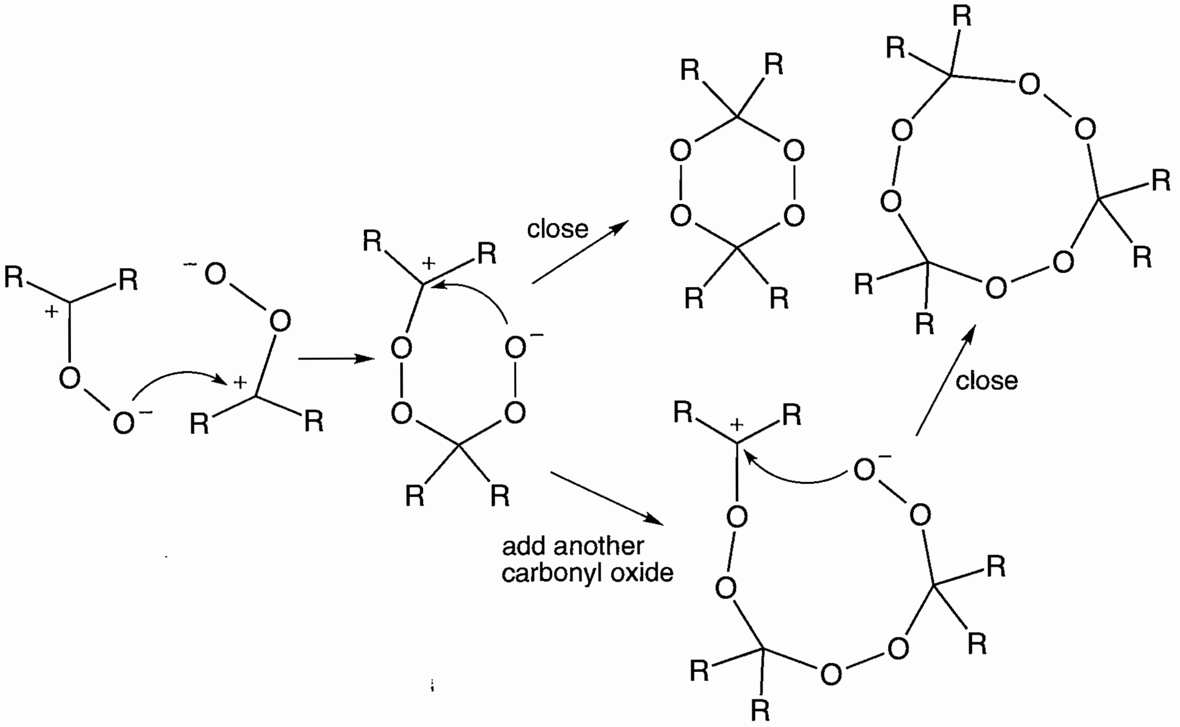
Problem 11.63 First, form the primary ozonide and allow it to break down to give the carbonyl oxide and, in this case, acetone.



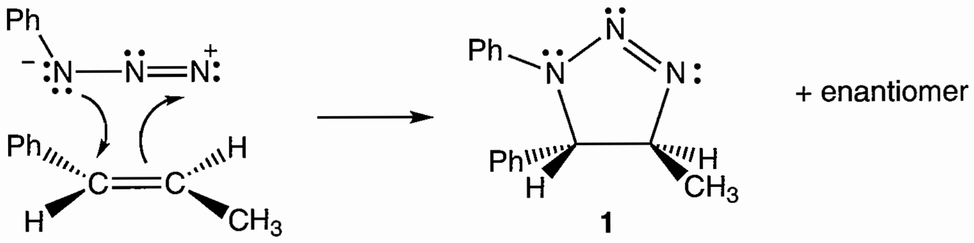
If the carbonyl oxide diffuses away from the acetone, it can collapse to the dioxirane.



Alternatively, it might be captured by another carbonyl oxide molecule, which eventually leads to the six- and nine-membered rings.

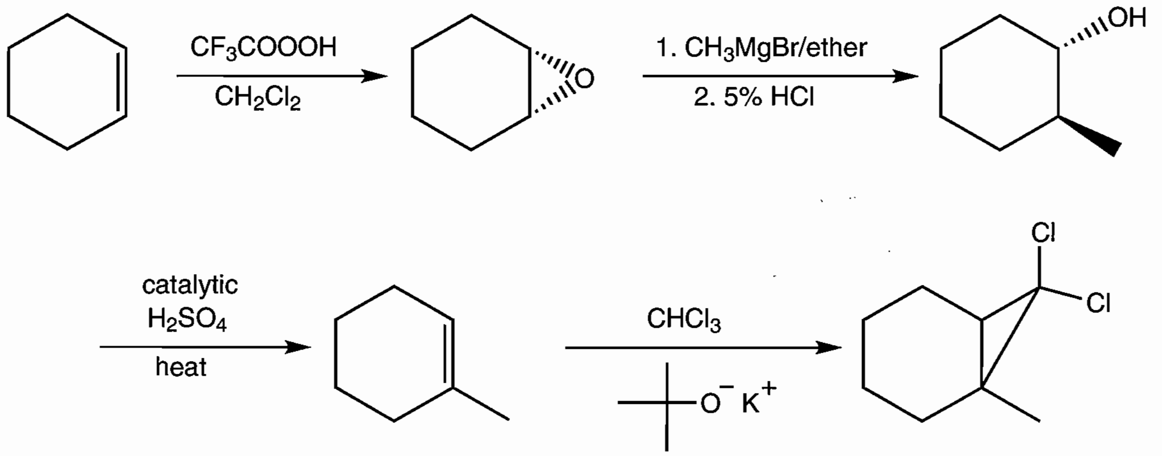


Problem 11.64 The arrow formalism is easy. In principle, but not actually, the compound with the Ph and CH_3 cis might have been formed.

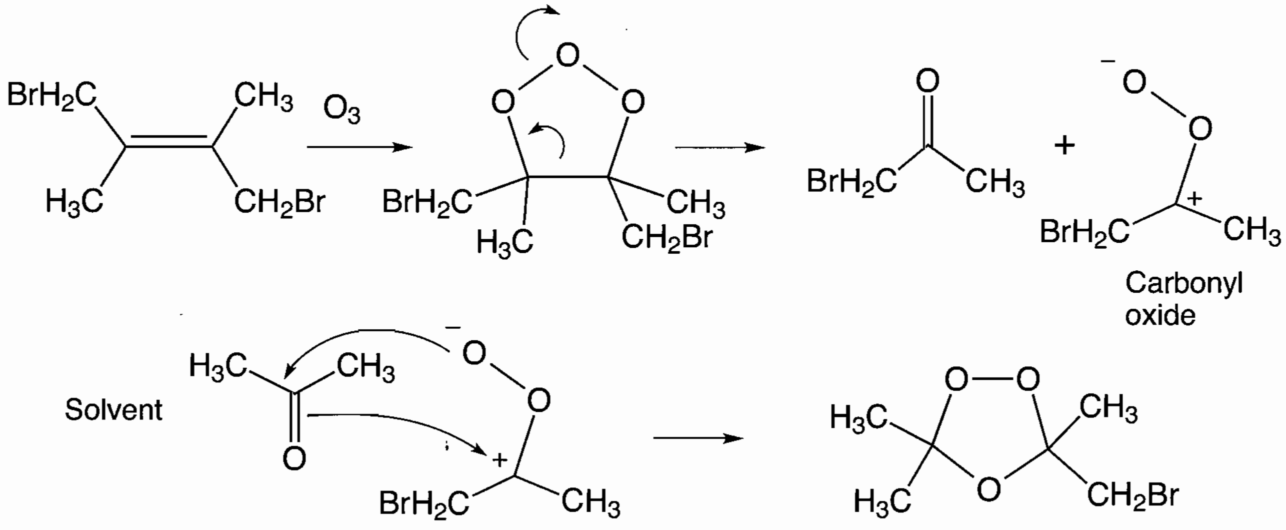


(continued)

Problem 11.61 The third step in this reaction sequence uses an acid-catalyzed dehydration to go from the alcohol to the alkene. This reaction gives the most substituted alkene as the product. It is the desired alkene. You might have been tempted to use an E2 reaction to make the alkene. But you would need to convert the OH group into a leaving group first. If you make it a tosylate (OTs), for example, then the E2 reaction would not give the desired product. The only available anti-periplanar β hydrogen results in formation of the less substituted alkene.

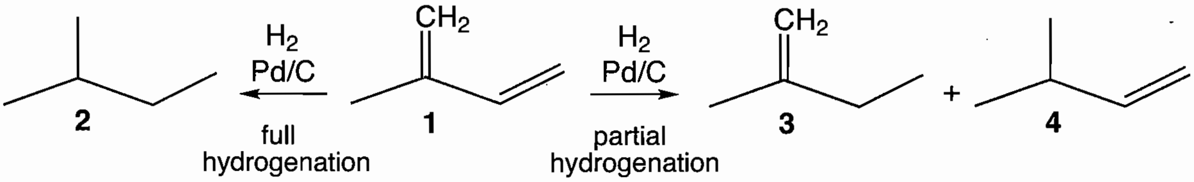


Problem 11.62 Once formed, the carbonyl oxide can be captured by *any* carbonyl group present. If acetone is present as solvent, it will have a great advantage in the capture process over the carbonyl group produced from the original alkene.

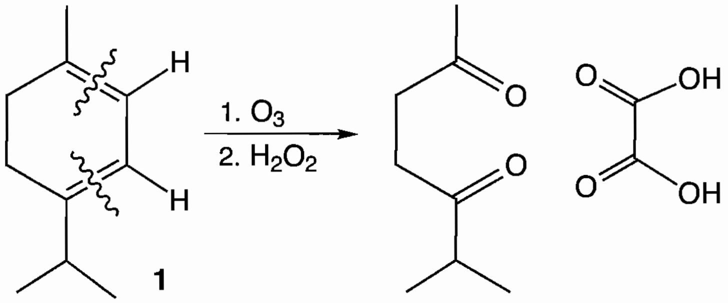


2

Given that **3** and **4** are formed by partial hydrogenation of **1**, we now know **1**. Full hydrogenation of **1** gives **2**.

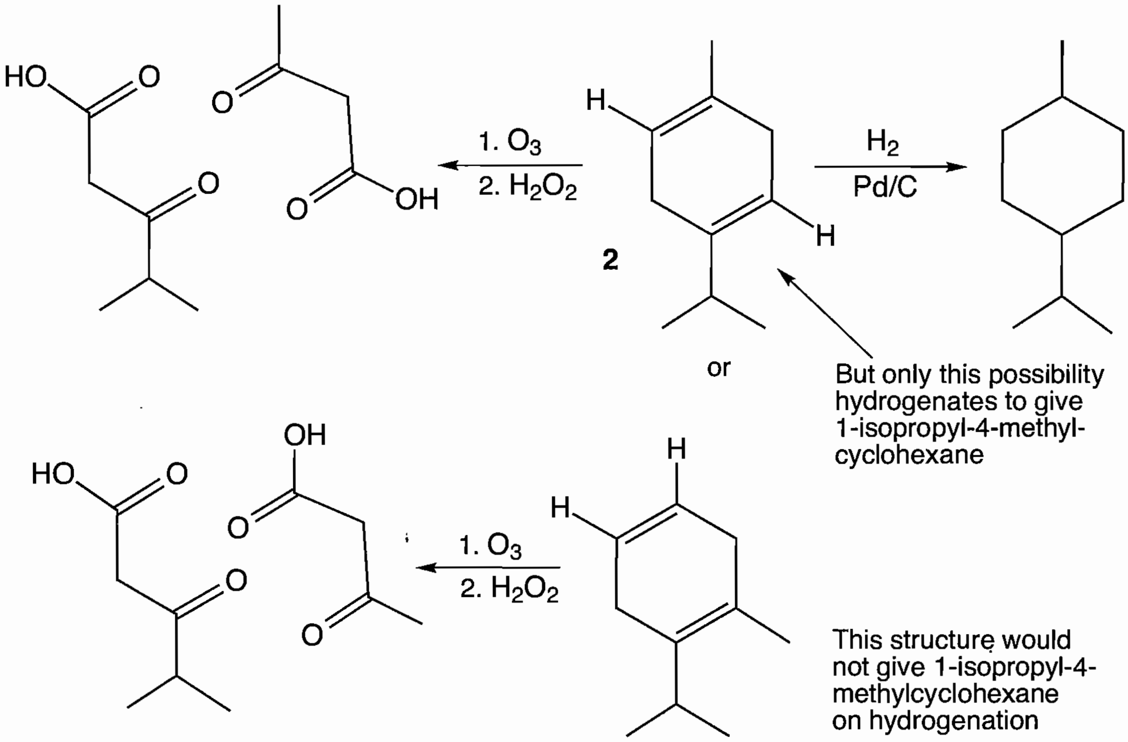


Problem 11.60 For α-terpinene (**1**), there is only one way to put the pieces formed on ozonolysis back together. (*Remember:* With an oxidative workup, carboxylic acids, not aldehydes, are formed.)



These structures allow us to piece together the structure of α-terpinene **1**

For γ-terpinene (**2**), there are two ways to put the pieces back together. However, only one of the possible cyclohexadienes would yield 1-isopropyl-4-methylcyclohexane on hydrogenation.

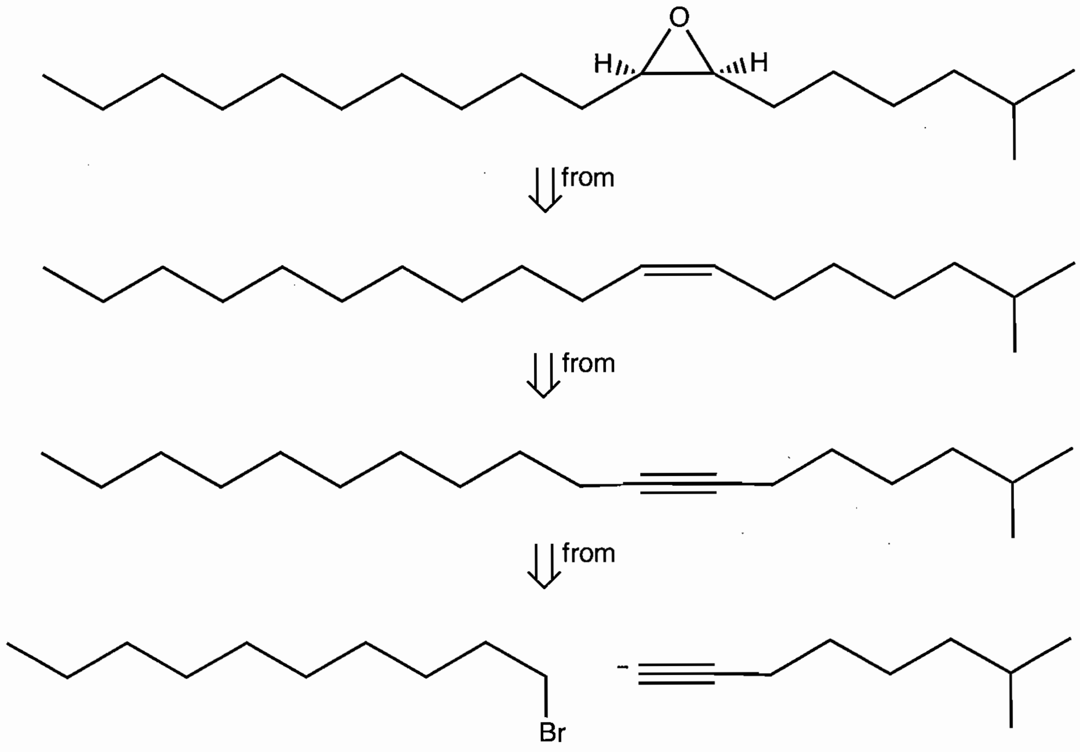


But only this possibility hydrogenates to give 1-isopropyl-4-methylcyclohexane

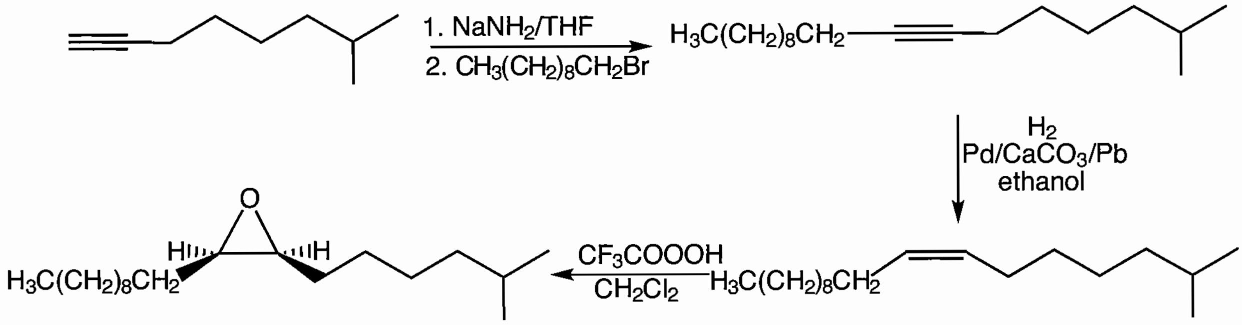
This structure would not give 1-isopropyl-4-methylcyclohexane on hydrogenation

Either set of structures allows us to piece together a possible structure for γ-terpinene

Problem 11.58 *(continued)*

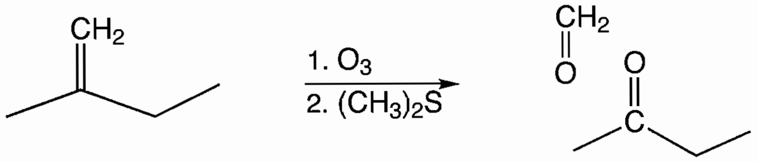


Now we know the path forward. We can deprotonate the 7-methyl-1-octyne, alkylate it with 1-bromodecane, hydrogenate with poisoned Pd, and then epoxidize with a peroxy acid.



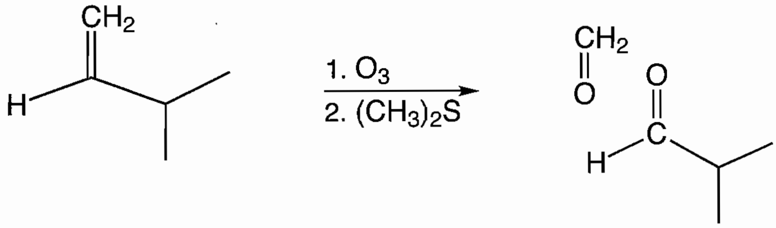
Problem 11.59 The ozonolysis data let us piece together the structures of **3** and **4**. Ozonolysis results in the conversion of a carbon–carbon double bond into a pair of carbon–oxygen double bonds. Accordingly, the structures of the products tell us the structures of **3** and **4**.

3

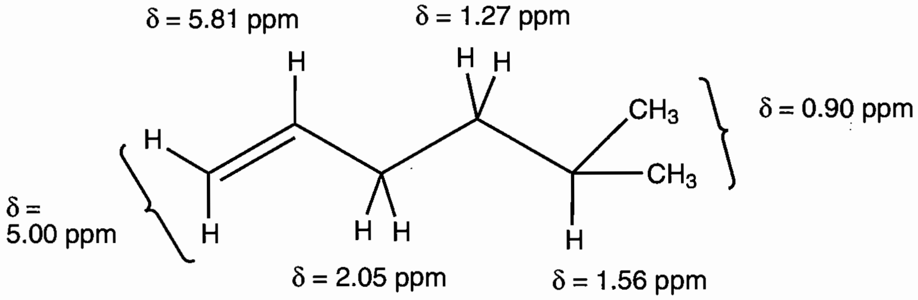


Formation of these two compounds implies the structure of **3**

4



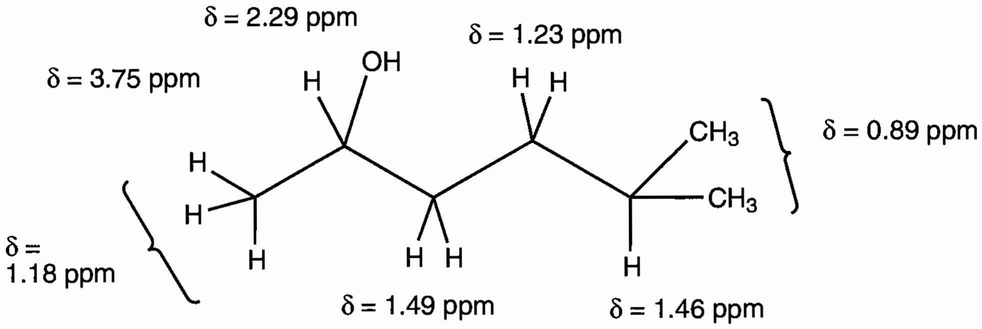
Formation of these two compounds implies the structure of **4**



A

Now we can determine the structure of **B**, because we know that an alkene gives an alcohol when it reacts with catalytic H_2SO_4 and H_2O. Compound **B** must be 5-methyl-2-hexanol. We can see if the NMR spectral data match this structure. The signal for the OH hydrogen should shift when D_2O is added to the sample. Therefore it is the signal at δ 2.29 ppm. The C(2) hydrogen should be strongly deshielded by the oxygen, and we predict its signal to be at δ 3.8 ppm. It must be the 1H signal at δ 3.75 ppm. It should be a sextet because it is adjacent to the C(1) methyl and the C(3) methylene—it "sees" five hydrogens. We would not expect this signal to be a clean sextet, because the five hydrogens are not equivalent. The C(3) hydrogens are diastereotopic, which should add to the complexity of this spectrum.

The signal at δ 1.49 ppm must be a CH_2 once removed from the electronegative oxygen, and the signal at δ 1.18 ppm must be a CH_3 also slightly deshielded by the oxygen. The coupling for the signal at δ 1.49 ppm must be complex due to the hydrogens being diastereotopic (nonequivalent). That makes it difficult to predict the rest of the molecule, but we know there is an isopropyl group because of the 6H doublet at δ 0.89 ppm. That allows us to assign the remaining signals as shown.

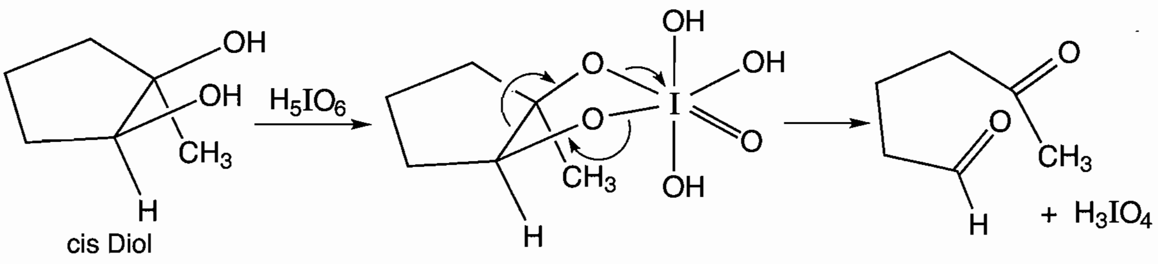


B

Problem 11.58 The epoxide of disparlure must be obtained from epoxidation of the cis-substituted alkene. We know that we can obtain the cis alkene from the corresponding alkyne. Alkynes can be alkylated by S_N2 reactions between the acetylide and primary halides. The structures are shown here:

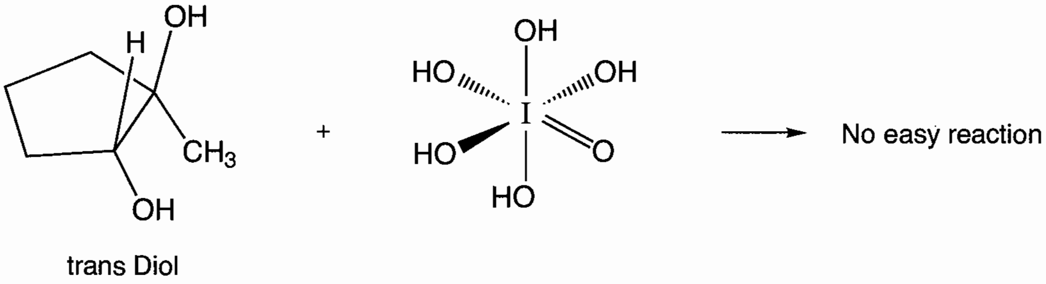
(continued)

Problem 11.56 In this intramolecular version of the periodate cleavage reaction, both new carbonyl groups appear in the same molecule.

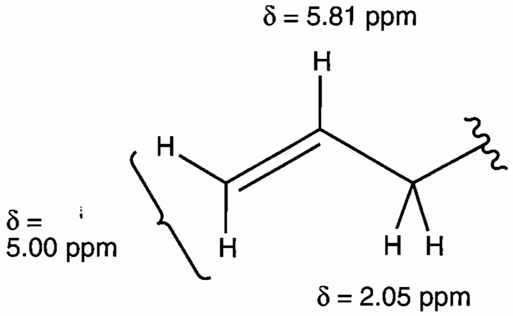


Ozonolysis of 1-methylcyclopentene with a reductive workup [$(CH_3)_2S$ or H_2/Pd] would lead to the same product.

In the trans diol, the two hydroxy groups are too far apart to form the cyclic intermediate easily. Reaction of trans diols with periodate is slow at best.

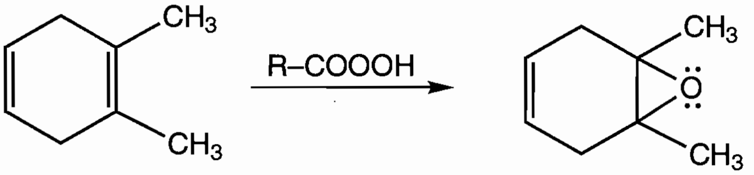


Problem 11.57 Compound **A** (C_7H_{14}) has 1 degree of unsaturation. We know that it will react with catalytic H_2SO_4 and H_2O, so it must be an alkene rather than a ring, which would not react with acid and water. We can see from the NMR spectral data for **A** that there are three vinyl hydrogens. The are no other groups in the molecule that can shift hydrogens downfield to the δ ~5 ppm region. So we know that compound **A** is a terminal alkene. There are two hydrogens at δ 2.05 ppm, which is the chemical shift expected for allylic hydrogens. So far we have this structure for **A**:



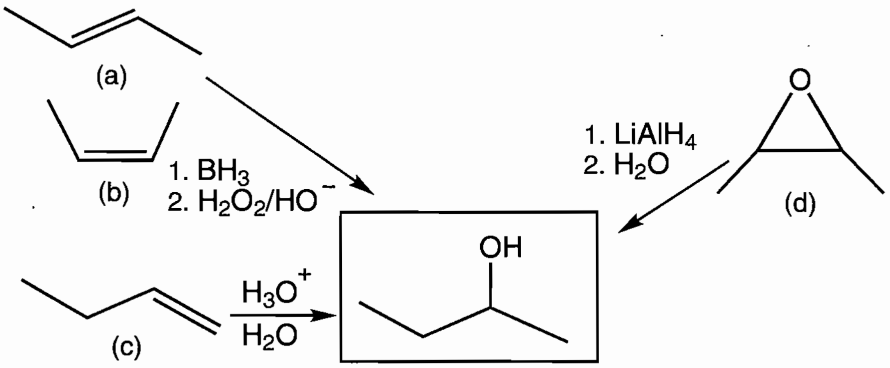
We know that the signal at δ 2.05 ppm is a quartet. That means it must be adjacent to three hydrogens. Because the allylic hydrogens will be coupled by the one vinyl hydrogen at δ 5.81 ppm, there must be a CH_2 on the other side. That CH_2 on the other side must be the signal at δ 1.27 ppm because it is a 2H signal. The signal at δ 1.27 ppm is also a quartet, so it must be adjacent to a CH in addition to the hydrogens at δ 2.05 ppm. The CH signal is at δ 1.56 and it is a nonet. It must be coupled by a total of eight hydrogens. It must be adjacent to the two methyl groups (6 H) that are at δ 0.90 ppm. Therefore, **A** must be 5-methyl-1-hexene.

Problem 11.53 The more substituted an alkene, the better a nucleophile it is. So, it is the tetrasubstituted double bond that is the more reactive site in this diene.



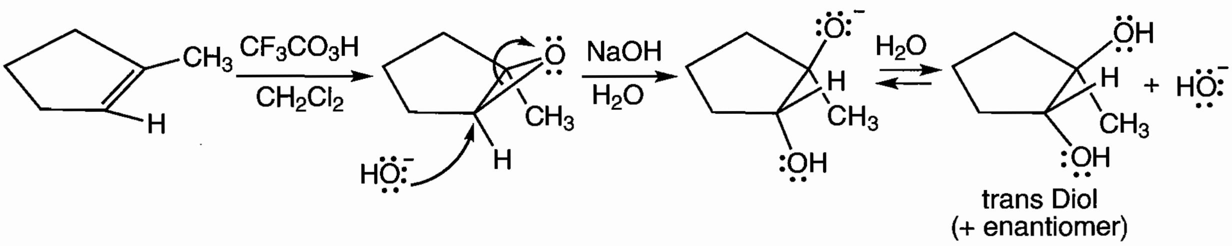
But wait! There is another effect we haven't considered. Is not the tetrasubstituted double bond more hindered sterically? Yes it is, and the steric difficulties should slow the reaction. So, there are two factors working in opposite directions. It is the electronic effect that dominates in this case. A good answer to this question mentions both effects.

Problem 11.54 The alcohol is 2-butanol, and here are the transformations:

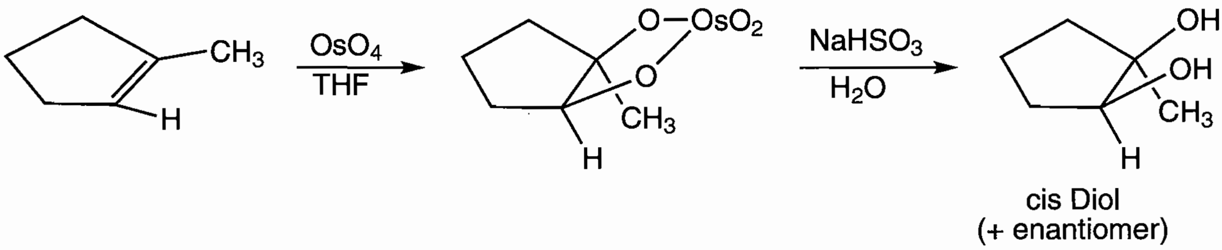


Problem 11.55

(a) Epoxidation is followed by S_N2 opening of the three-membered ring from the rear with hydroxide acting as nucleophile. Notice that in this reaction, the epoxide is opened from the sterically less-encumbered side to give a trans diol.

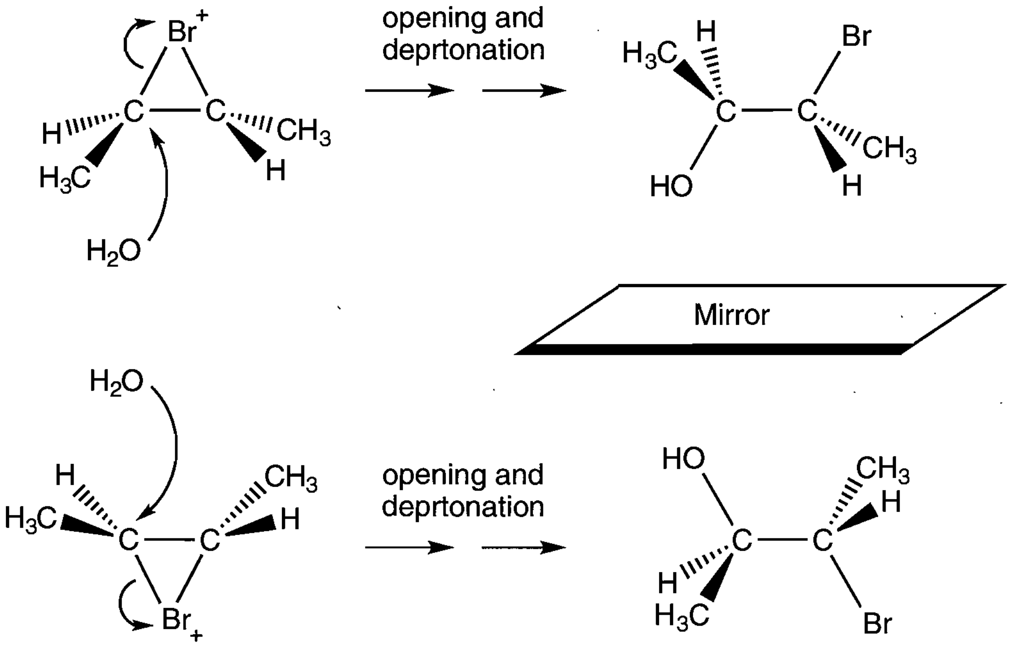


(b) Osmium tetroxide (usually in THF) reacts with an alkene via syn addition to make a five-membered ring intermediate that gives a cis diol after hydrolysis.



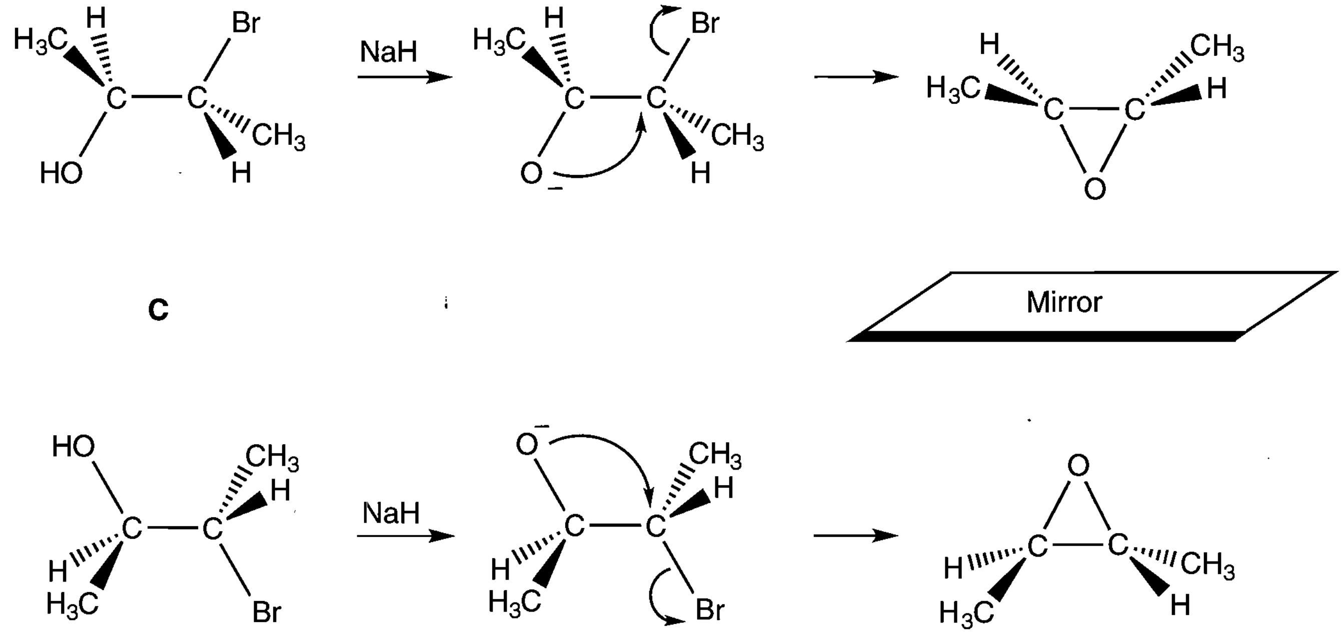
Problem 11.52 *(continued)*

Opening of these bromonium ions with water leads to compound **C**, which is a pair of enantiomeric bromohydrins.



The product **C** is a pair of enantiomers—the mixture is racemic

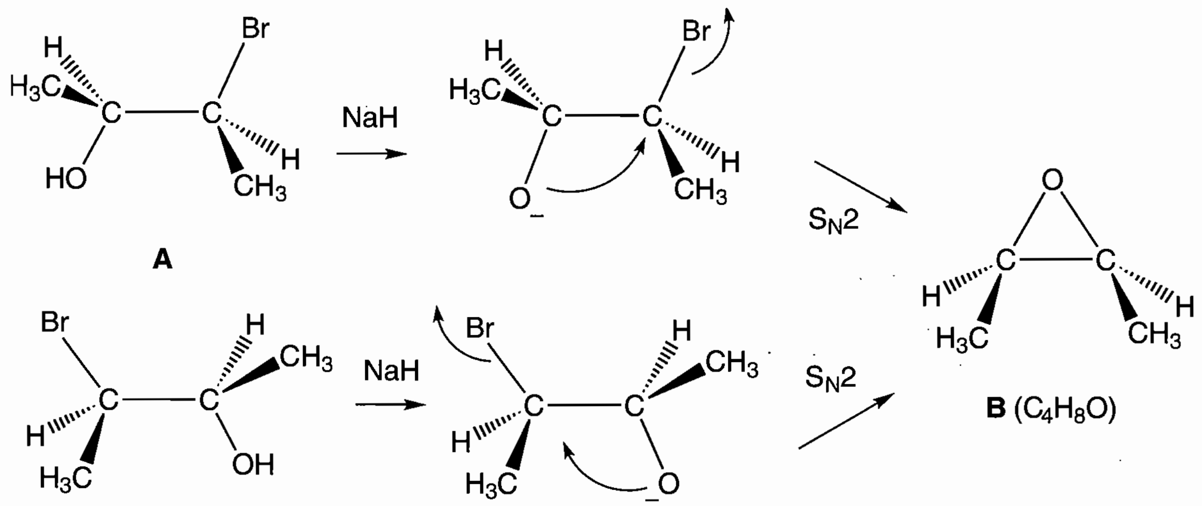
Treatment of **C** with NaH results in intramolecular S_N2 displacement of bromide to give the epoxide **D** as a racemic mixture. The epoxide has two equivalent methyl groups that will be coupled to the hydrogen on the epoxide ring giving rise to a doublet at δ 1.30 ppm. The hydrogens in compound **D** on the ring are equivalent. They will not couple with each other. The chemical shift for these hydrogens will be upfield from the otherwise predicted value (δ ~3.8 ppm) because they are on a three-membered ring. They give rise to the quartet at δ 2.70 ppm.



C

D (C_4H_8O), a racemic mixture of enantiomeric epoxides

Treatment of **A** with NaH forms the alkoxides, and intramolecular S_N2 displacement gives the same meso epoxide, **B**, in each case.

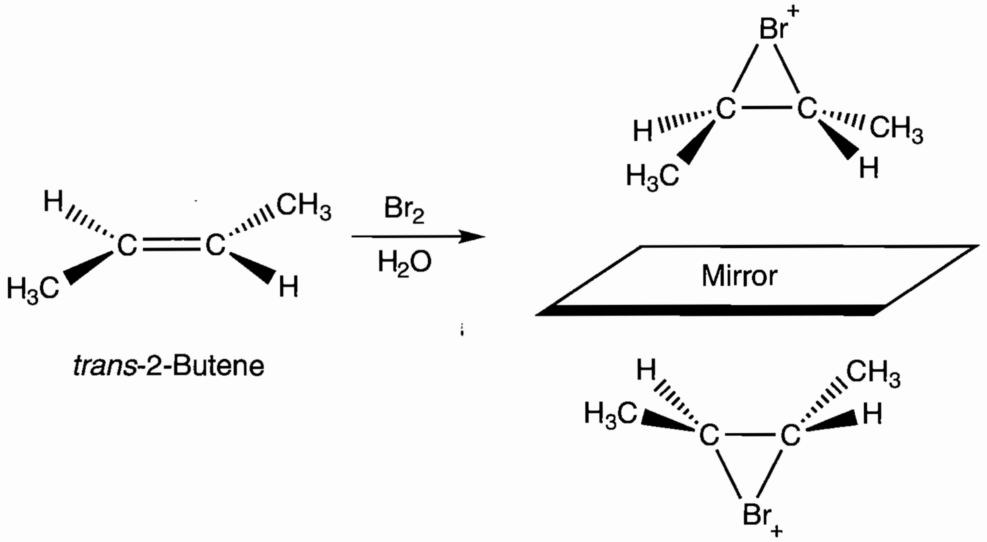


A

B (C_4H_8O)

The keys to seeing this step of the problem are remembering that NaH is a useful base for forming alkoxides, and the recognition that an HBr is lost in going from C_4H_9OBr to C_4H_8O.

The *trans*-2-butene undergoes exactly the same reaction sequence, but the stereochemical relationships are different. The bromonium ion can be formed by addition of the bromine from either the top or bottom of the alkene to give a pair of enantiomeric ions.



trans-2-Butene

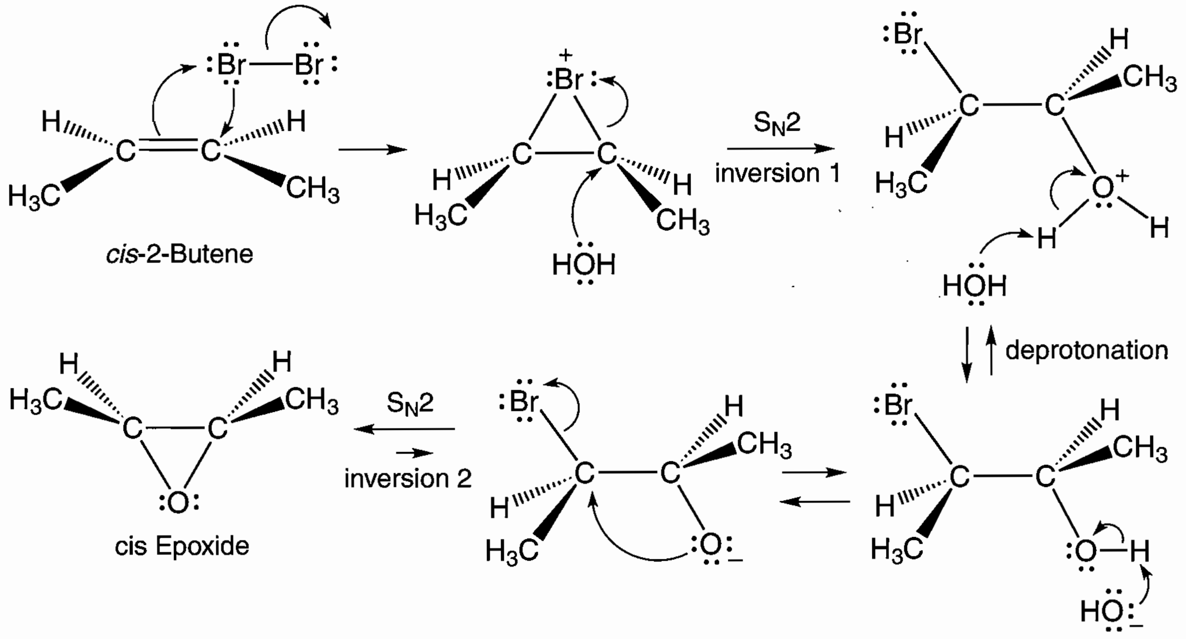
Addition of "Br^+" from "top"

These intermediates are enantiomers— the mixture is racemic

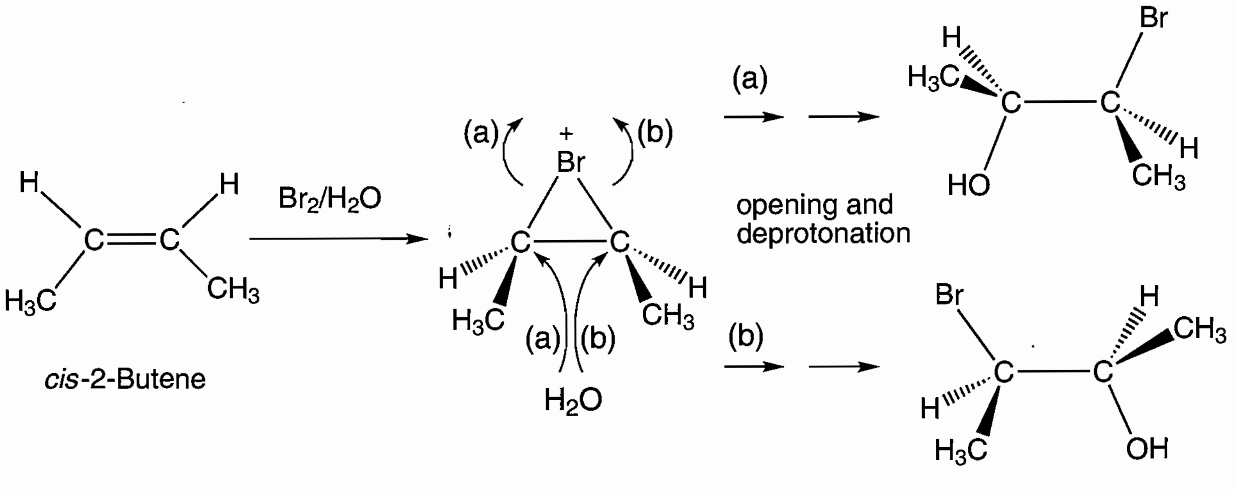
Addition of "Br^+" from "bottom"

(continued)

Problem 11.51 First of all, what are the basic mechanisms of bromohydrin formation and epoxide formation from the bromohydrin? The first part is a straightforward addition reaction covered many times already. In the second and more difficult part of the problem, alkoxide formation is followed by intramolecular displacement of bromide in S_N2 fashion. Thus, this process involves *two* inversions of configuration. Two inversions result in net retention of configuration as cis alkene becomes the cis epoxide. A mechanistic analysis should make this clear.

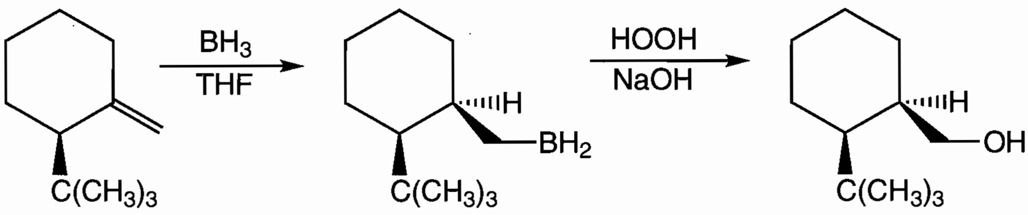


Problem 11.52 Formation of the bromonium ion and opening by water leads to a racemic mixture of bromohydrins (3-bromo-2-butanol, **A**).

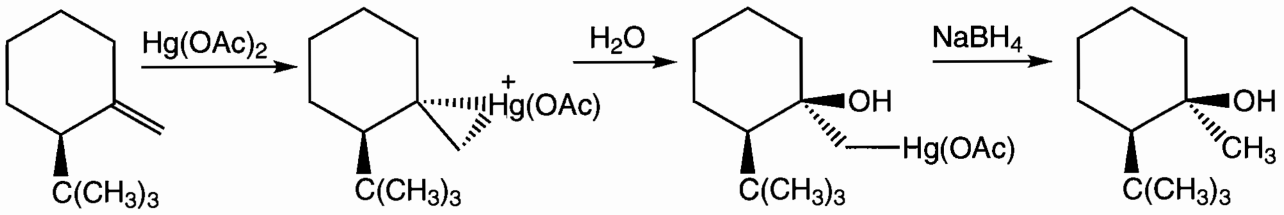


Product **A**, C_4H_9OBr, is a racemic mixture of bromides

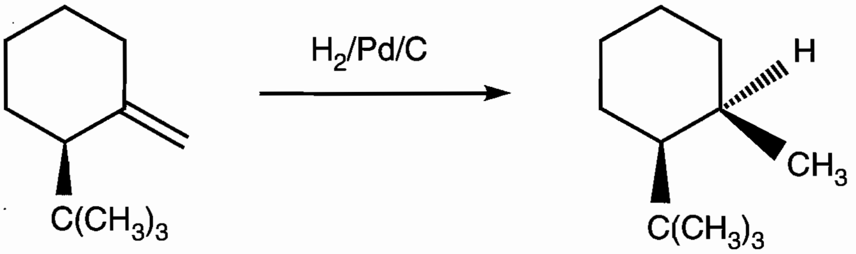
Addition of BH_3 will be from the side away from the the *tert*-butyl group. Accordingly, the final product will have the cis stereochemistry shown:



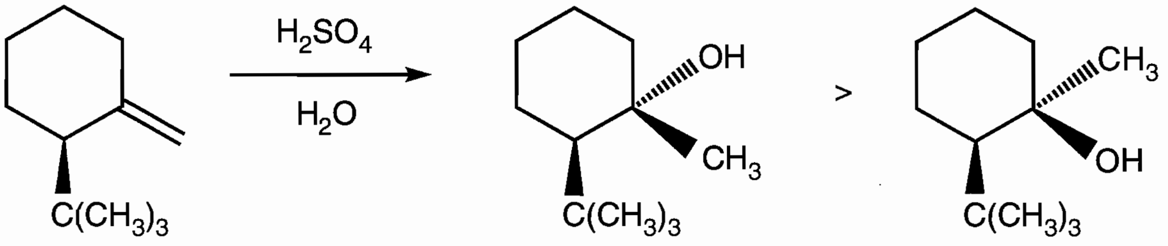
The mercurinium ion will form anti to the *tert*-butyl group. Opening by water at the more hindered position followed by borohydride reduction will lead to the compound with the OH cis to the *tert*-butyl group.



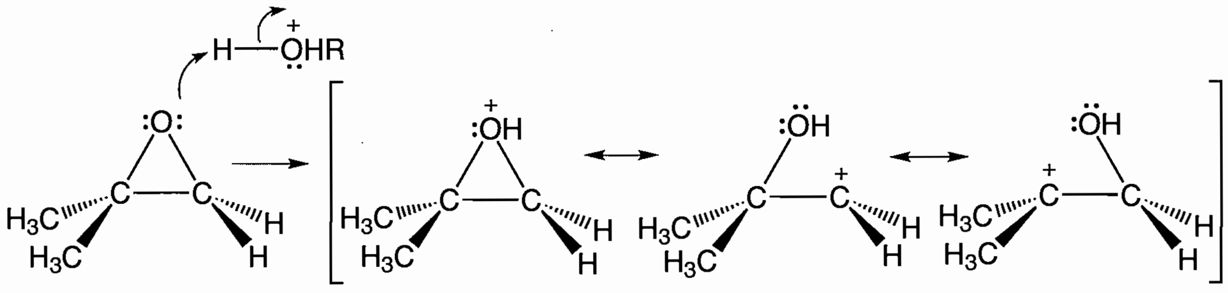
Hydrogenation will occur preferentially from the side away from the large *tert*-butyl group.



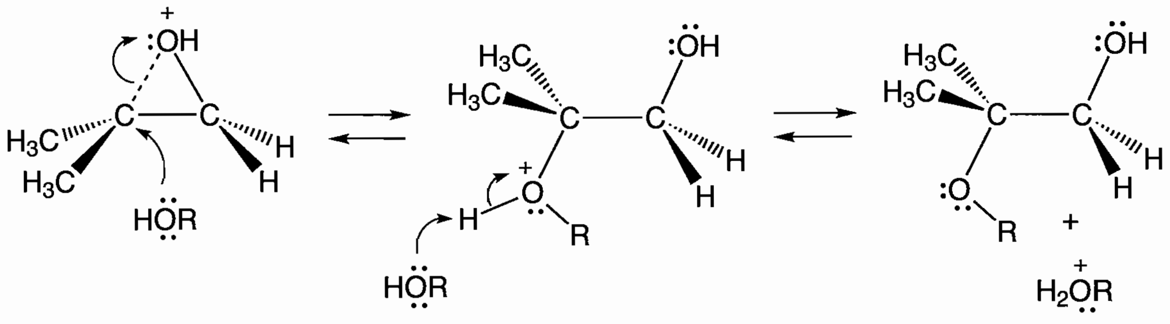
The major—not exclusive—product will come from addition of water to the intermediate carbocation from the side away from the large *tert*-butyl group. There could be a hydride shift—what product would that give?



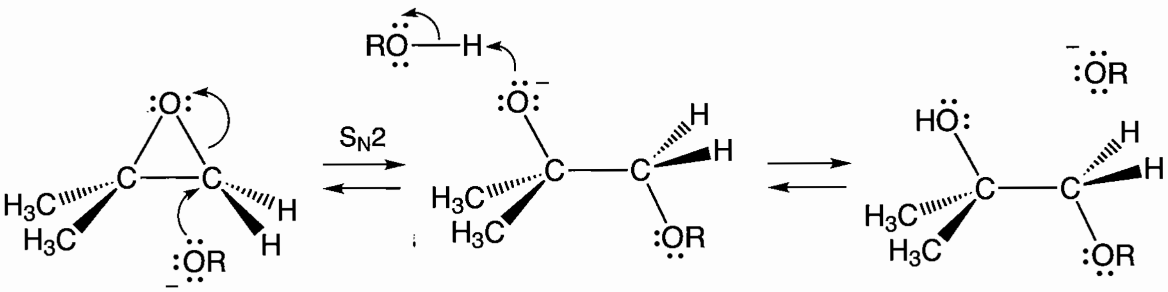
Problem 11.49 In the acid-catalyzed reaction, the first step is the protonation of the epoxide oxygen to give a resonance-stabilized cation. The two bonds from carbon to oxygen are different as the tertiary carbon will have a greater share of the positive charge than will the primary carbon.



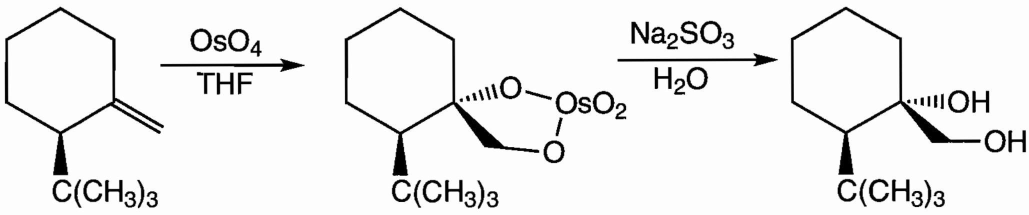
The alcohol will add predominately to break the longer and weaker, more substituted carbon–oxygen bond. Deprotonation of the intermediate oxonium ion leads to the product and regenerates the catalyst, the protonated alcohol.



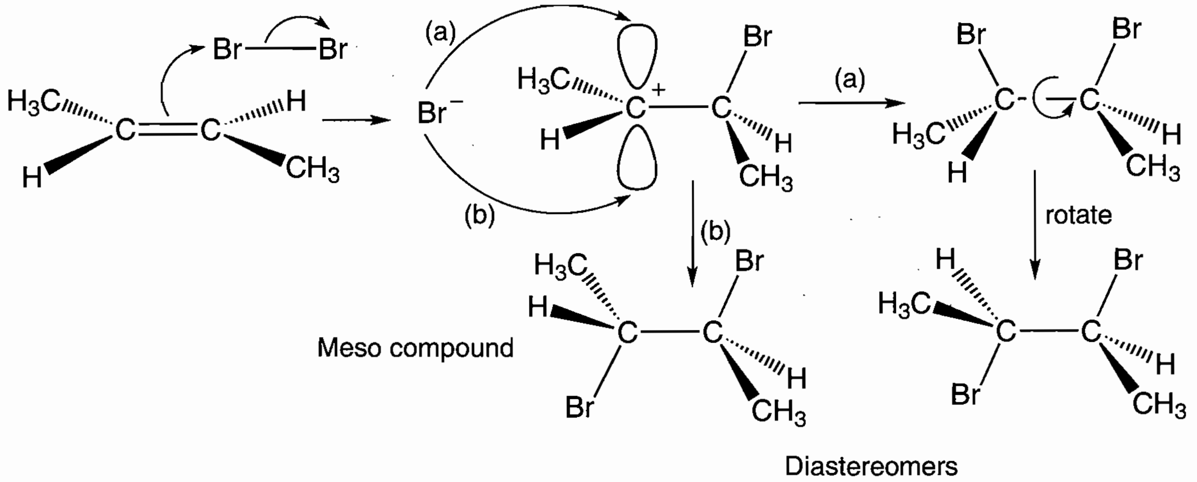
The base-catalyzed reaction is a straightforward S_N2 displacement of a leaving group by a negatively charged nucleophile. The epoxide opens from the less hindered side. Proton transfer completes the reaction and regenerates a molecule of alkoxide.



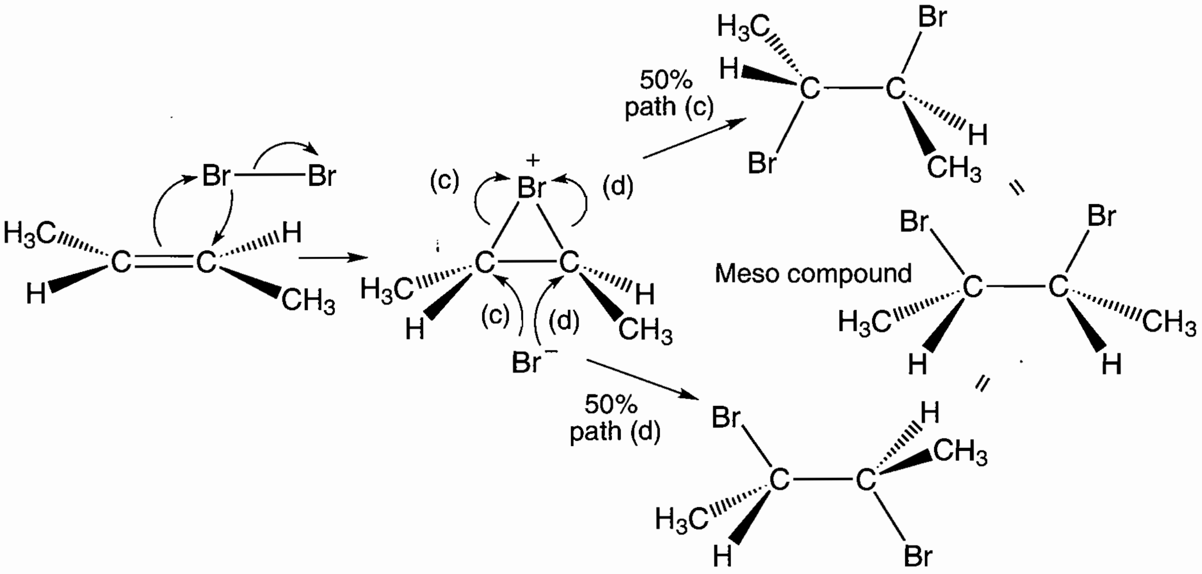
Problem 11.50 The cyclic osmium intermediate will be preferentially formed anti to the *tert*-butyl group, so opening will give the product shown:



Similarly, in the addition to *trans*-2-butene, an open carbocation must lead to two products, a result not observed experimentally:

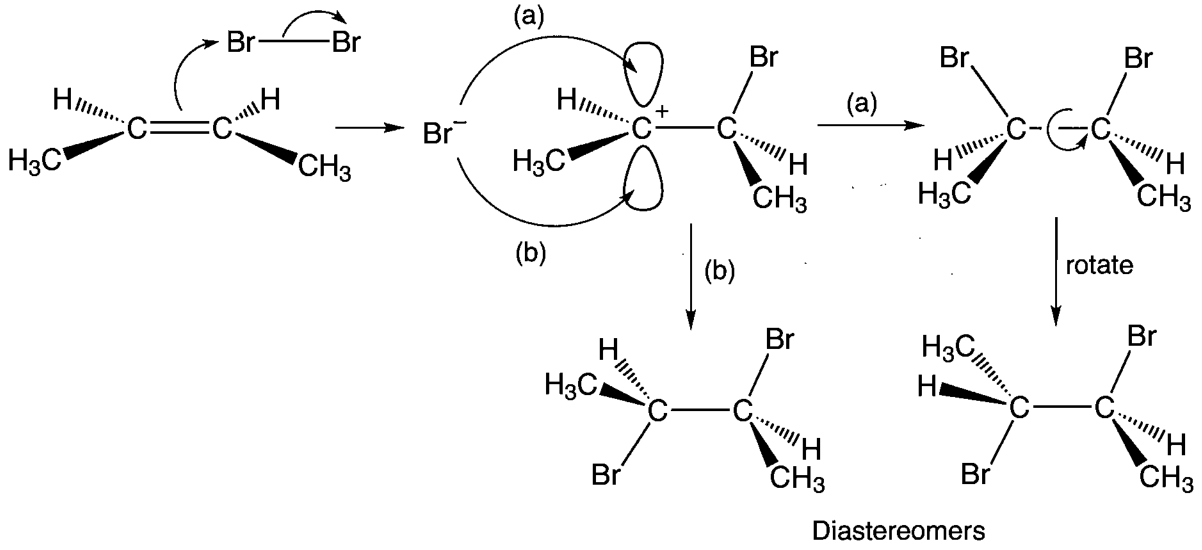


A bromonium ion shows how the experimentally observed single product, a meso compound, is formed.

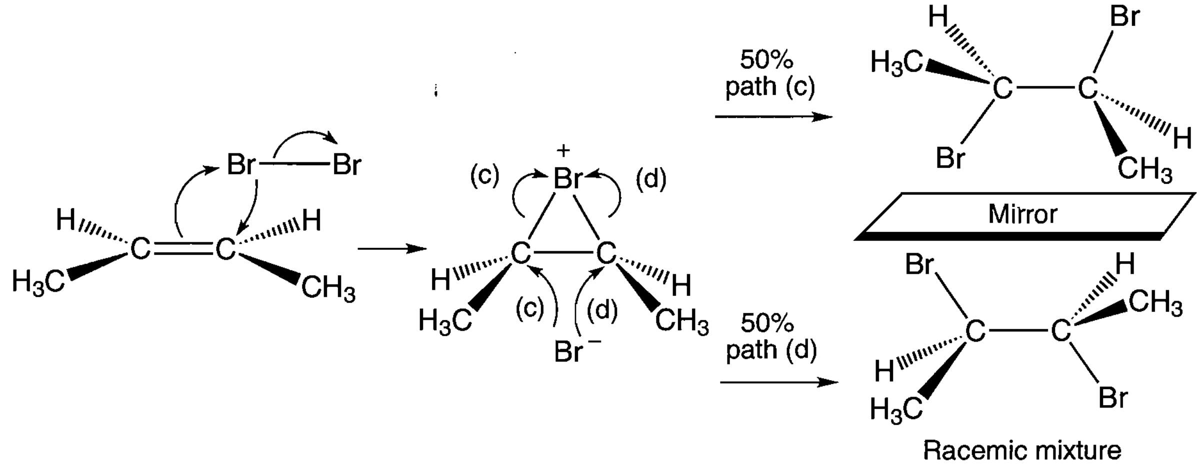


Problem 11.47 Each of the potential products shown in Problem 11.46 would be formed as a single enantiomer. The stereogenic carbon in the starting material is the (*R*) configuration, and it does not change throughout the reaction. Forming a racemic mixture would mean that the isomer with methyl in the (*S*) configuration would also have to be present.

Problem 11.48 In the addition of Br_2 to *cis*-2-butene, an open carbocation must give two diastereomeric products.



As this result is not observed, this mechanism must be wrong. Formation of a bromonium ion that opens up in an S_N2-like fashion solves the problem. The bromonium ion must open by addition of bromide from the rear, and this reaction leads to racemic dibromide when *cis*-2-butene is the starting material.



(g) Start with (d): PBr_3

(h) 1. CF_3COOOH 2. $^{-}OH/H_2O$

(i) Br_2/CH_3OH

(j) Start with (b): 1. O_3 2. HOOH

Problem 11.45 Once again, there are many possible correct answers. Here are some. Mrs. Tao's eels, though incredibly delicious, are ineffective.

(a) 1. BH_3 2. $HOOH/HO^-$

(b) H_3O^+/H_2O

(c) HBr

(d) Compound (a) and PBr_3

(e) 1. OsO_4 2. Na_2SO_3/H_2O

(f) 1. $H_2/CaCO_3/Pb/Pd$ 2. CH_2N_2, light or heat

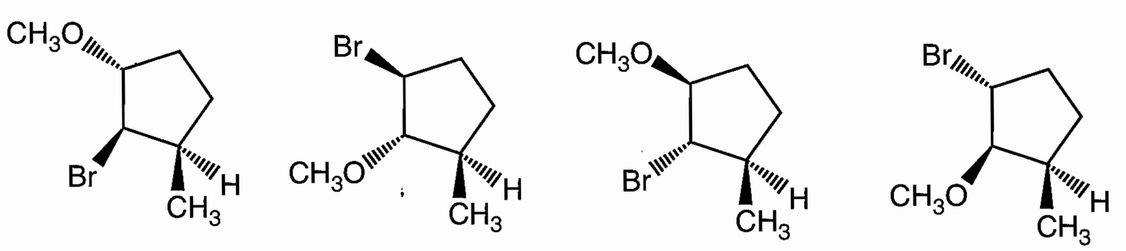
(g) 1. NH_3/Na 2. CF_3COOOH

(h) H_3O^+/H_2O

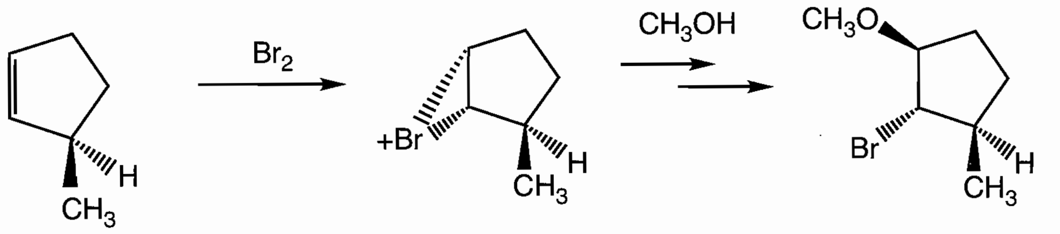
(i) 1. $H_2/CaCO_3/Pb/Pd$ 2. O_3 3. H_2/Pd

(j) 1. NH_3/Na 2. O_3 3. Zn

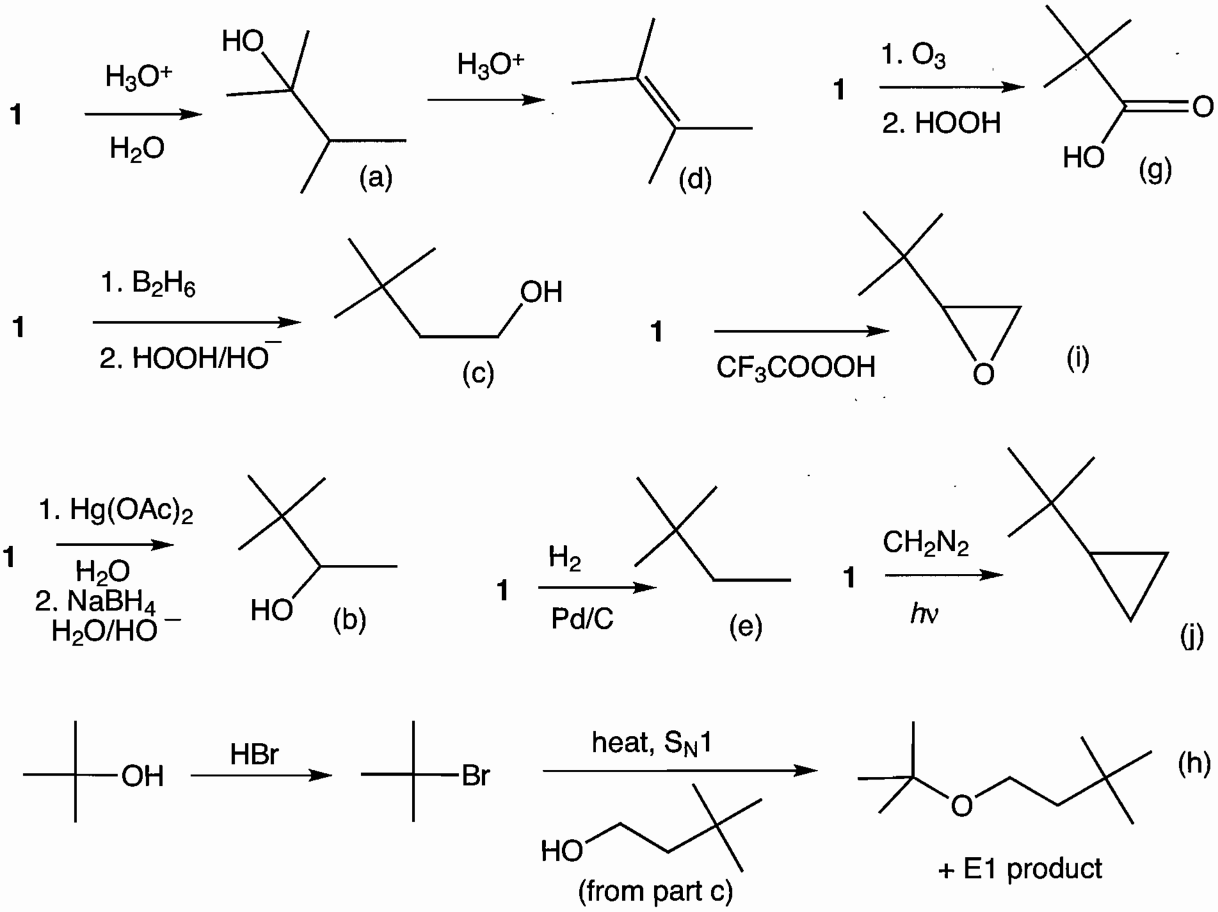
Problem 11.46 Formation of a bromonium ion could, in principle, occur in two ways: syn to the methyl group or anti to the methyl group. Opening, again in principle, could occur through an S_N2 reaction in two ways for each bromonium ion. Here are the four possibilities:



Steric factors will favor the anti bromonium ion. Opening by methanol, followed by deprotonation, will occur at the less sterically hindered position with inversion to give the product shown.



Problem 11.42



Problem 11.43

(a) HBr/ether

(b) Br_2/CH_3CH_2OH

(c) catalytic H_2SO_4/CH_3CH_2OH

(d) 1. BH_3/THF 2. $NaOH/H_2O_2$ 3. NaH 4. CH_3CH_2Br

Problem 11.44 There are many correct answers to these questions. The following suggestions are not exhaustive. Think about other possibilities.

(a) H_2/Pd/C

(b) catalytic H_2SO_4, heat

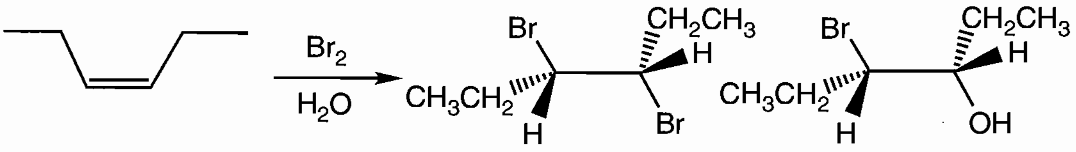
(c) Start with (b): 1. BH_3 2. $HOOH/HO^-$

(d) 1. BH_3 2. $HOOH/HO^-$

(e) H_3O^+/H_2O

(f) 1. O_3 2. H_2O/HOOH

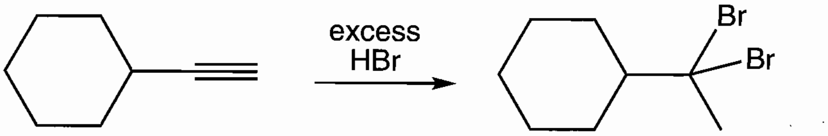
(d)



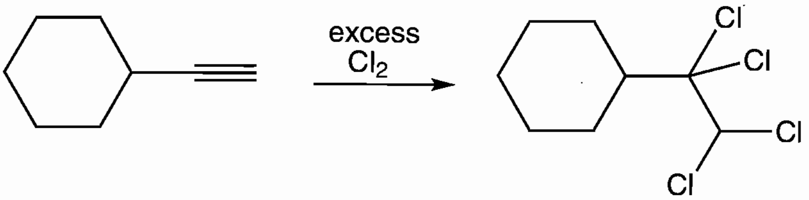
both racemic

Problem 11.41

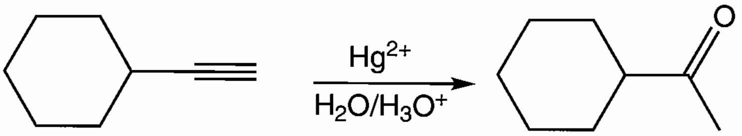
(a)



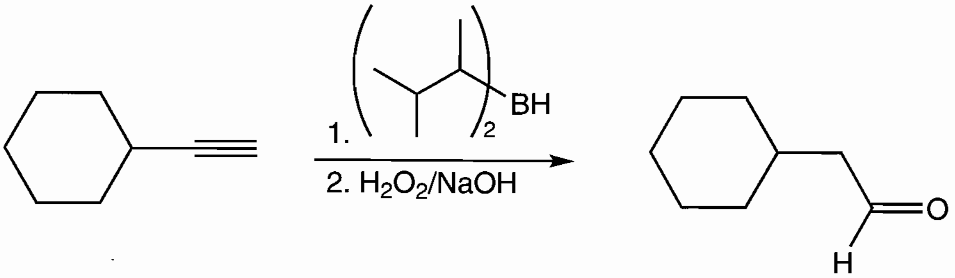
(b)



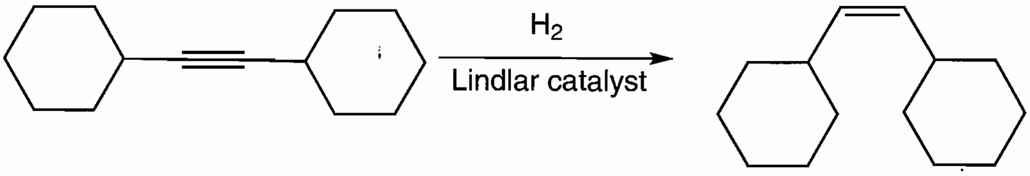
(c)



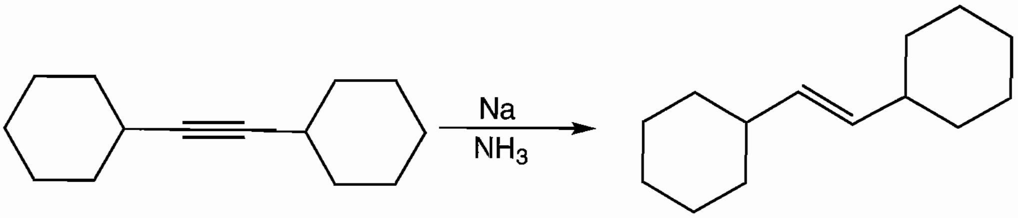
(d)



(e)

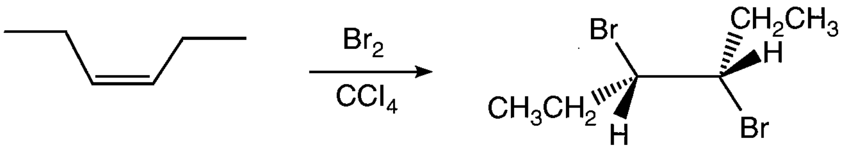


(f)



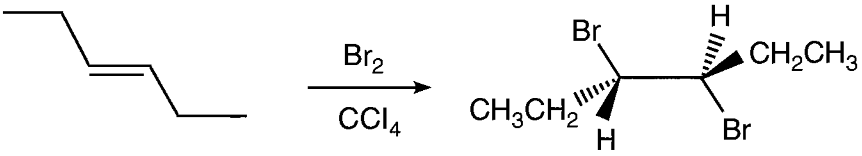
Problem 11.38 *(continued)*

(c)



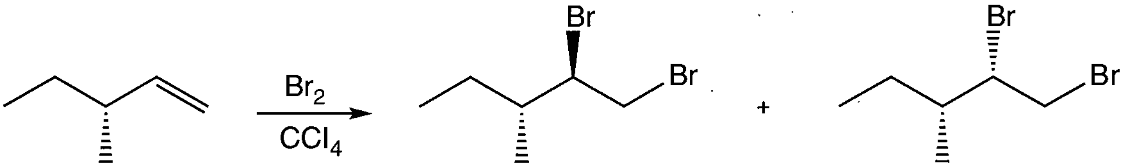
racemic

(d)



meso

(e)

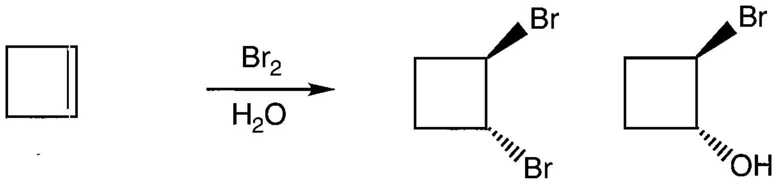


Optically active Optically active

Problem 11.39 The products in Problem 11.38(a), (b), and (c) are chiral and are formed as racemic mixtures in each case. The single product in 11.38 d is a meso compound, therefore it is achiral. The starting material in 11.38 e is an optically active molecule with (*R*) configuration. Because the reaction generates a new stereogenic center, there will be two diastereomers formed, (2*R*,3*R*)-1,2-dibromo-3-methylpentane and (2*S*,3*R*)-1,2-dibromo-3-methylpentane. Each will be formed as a single enantiomer.

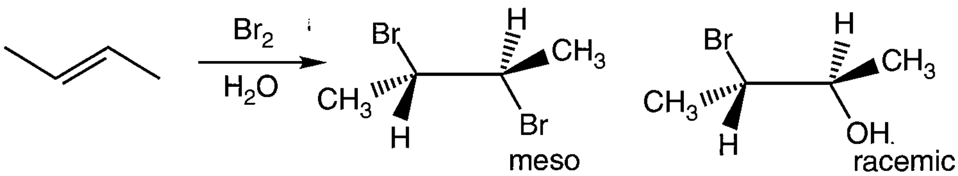
Problem 11.40 In each case, an intermediate bromonium ion is opened either by bromide ion or water to give the products shown. As all starting materials are achiral, there can be no net optical activity in the products. Since water is the solvent, we predict the major product in each case will be the halohydrin.

(a)



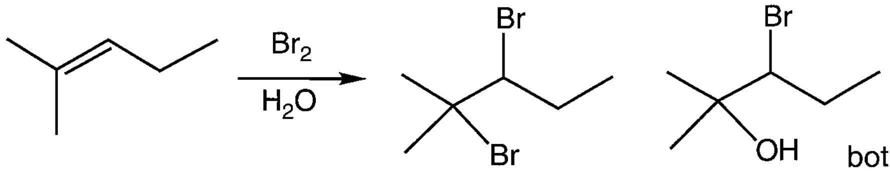
both racemic

(b)



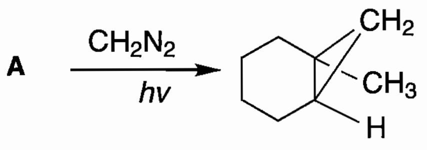
meso racemic

(c)

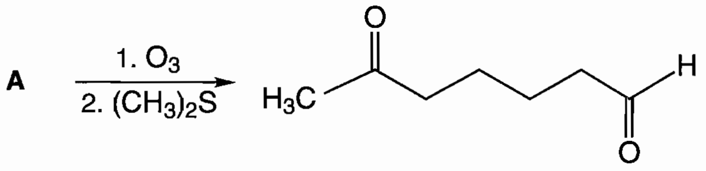


both racemic

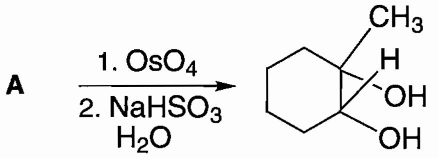
(g)



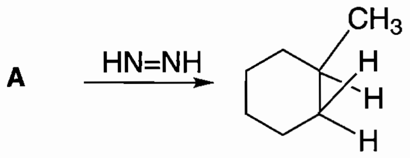
(h)



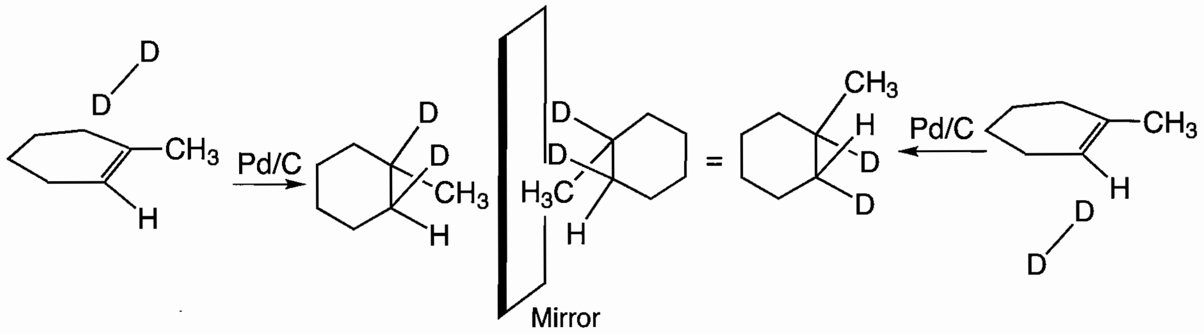
(i)



(j)

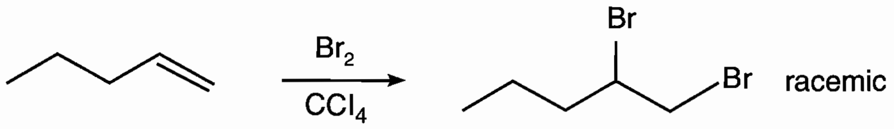


Problem 11.37 Deuterium can be delivered from either side of the planar double bond. The two enantiomers of the methylcyclohexane product result.

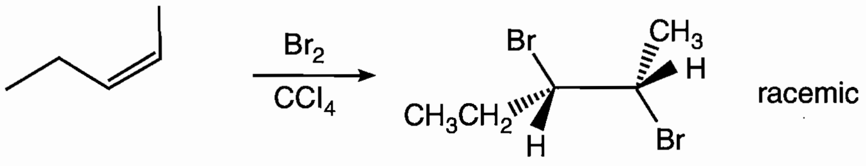


Problem 11.38 In each case, an intermediate bromonium ion is opened by bromide addition at the more substituted carbon. In (b), (c), and (d) ring-opening will occur at both possible positions.

(a)

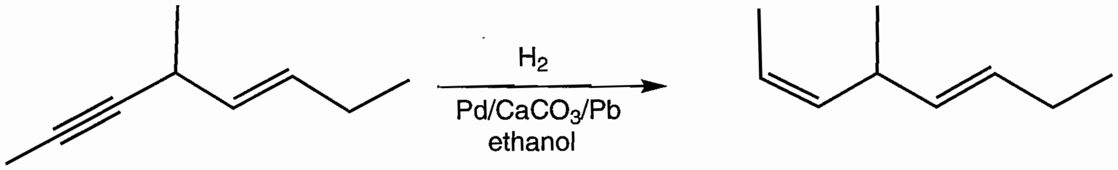


(b)



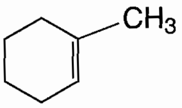
(continued)

Problem 11.35 The use of poisoned palladium to catalyze hydrogenation of an alkyne results in syn addition to give the cis alkene. The cis alkene does not react further. Therefore, we predict that the poisoned palladium will not hydrogenate the trans alkene either.

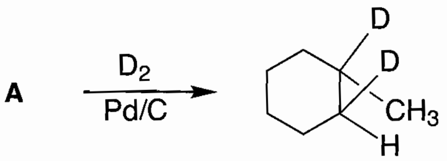


Problem 11.36 These are all one- or two-step syntheses. There is nothing tricky here, only remembering the reactions. If you forget, fall back on a mechanistic analysis, and this should lead you to the product in most cases. Remember, we start with achiral materials, and in *all* cases racemic mixtures must result. In the answers, only one enantiomer is shown.

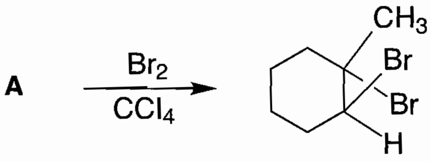
A =



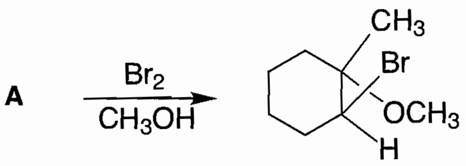
(a)



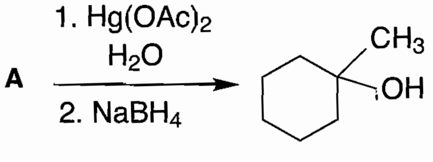
(b)



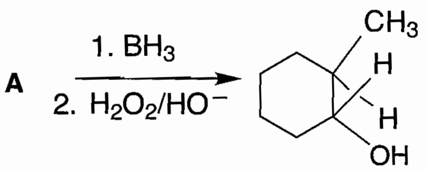
(c)



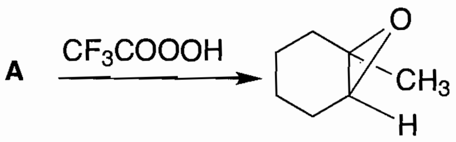
(d)



(e)

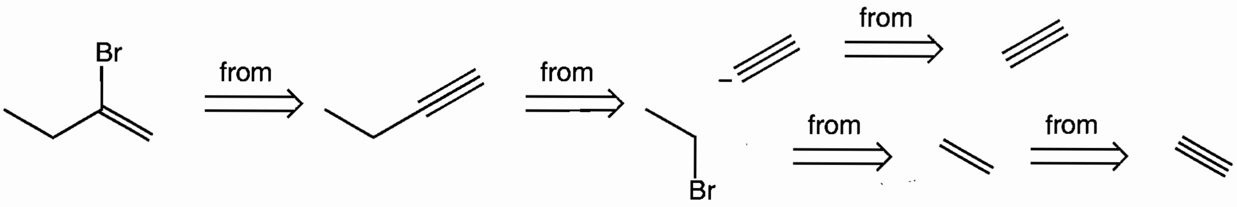


(f)

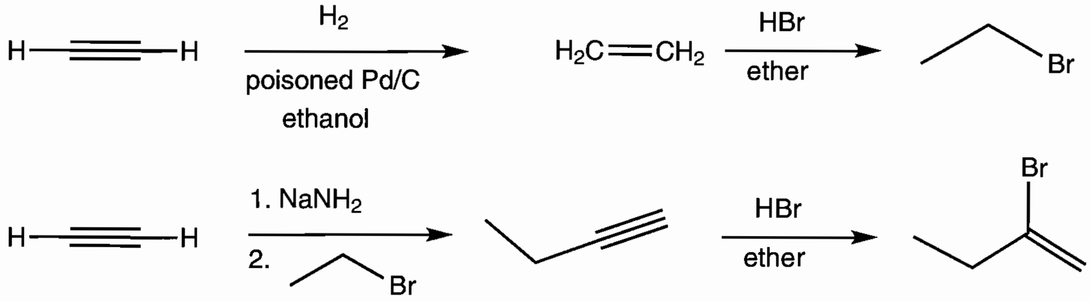


Additional Problem Answers

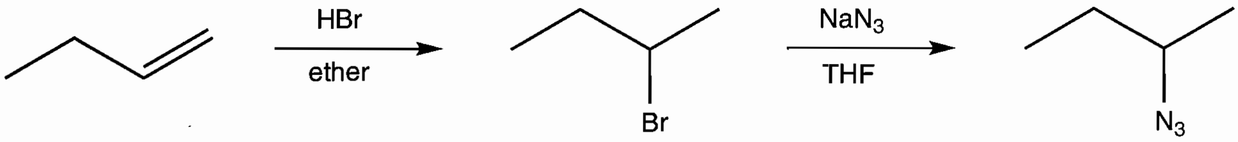
Problem 11.32 We should be able to make the vinyl bromide 2-bromo-1-butene from the corresponding 1-butyne using one equivalent of HBr. The 1-butyne can be obtained from S_N2 reaction between acetylide anion and ethyl bromide. The ethyl bromide can be obtained from ethylene, and that in turn can come from acetylene.



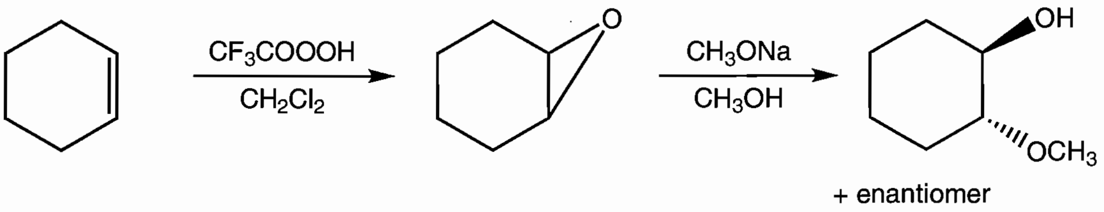
The reactions are shown in the following scheme:



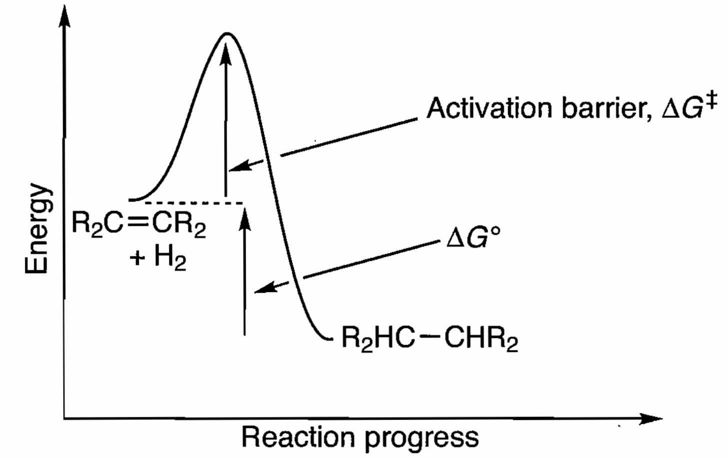
Problem 11.33 Displacement of a good leaving group such as bromide or iodide by azide ion would work. The halide can be made from 1-butene through the addition of HBr or HI to 1-butene.



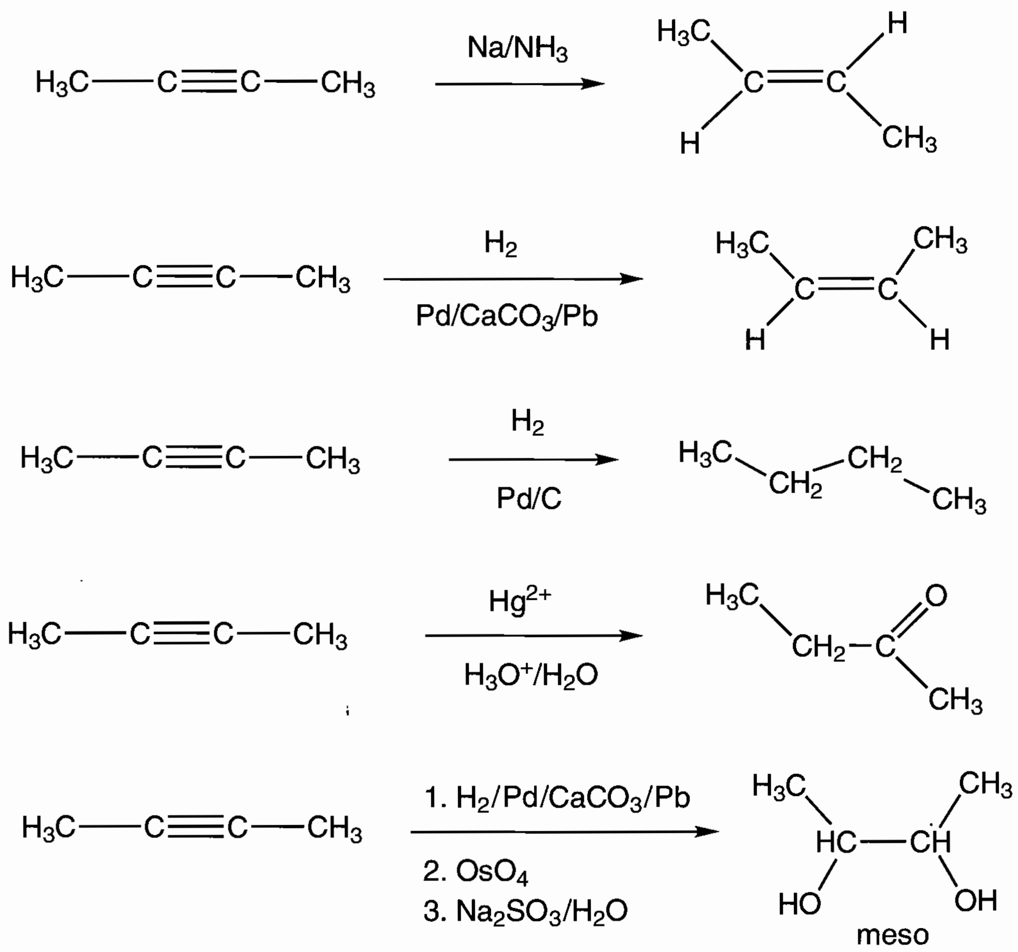
Problem 11.34 Opening of cyclohexene epoxide must give the trans compound because the S_N2 reaction always goes with inversion.



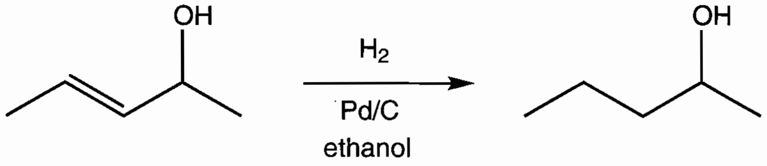
Problem 11.30 *(continued)*



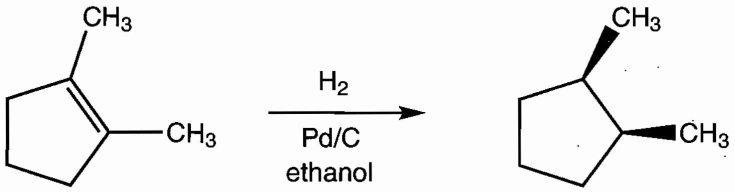
Problem 11.31 This problem is just an exercise in remembering reagents.



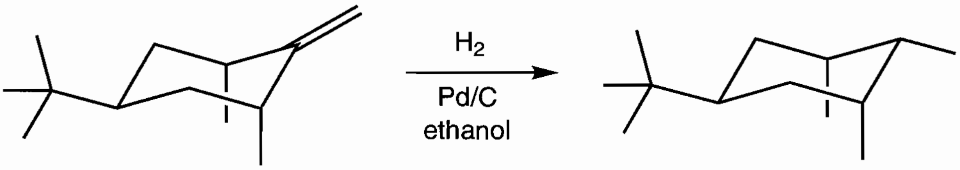
(c) An alcohol does not participate (is not changed) in the hydrogenation reaction.



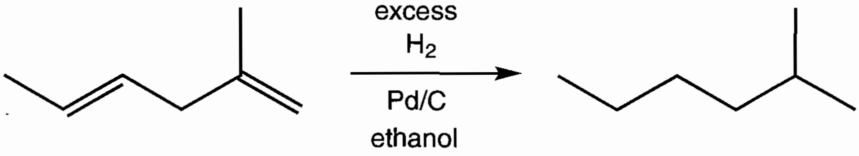
(d) We can confirm that hydrogenation is a syn addition using 1,2-dimethylcyclopentene. The product is achiral. Adding hydrogen to the top face of the alkene will give the same product, which is *cis*-1,2-dimethylcyclopentane.



(e) The hydrogenation of this methylene-substituted cyclohexane will occur from the less hindered side of the alkene. In this case, that side is the top of the molecule. The methyl groups that are axial on either side of the alkene will block that side of the alkene. Adding hydrogen to the top face will push the new methyl group into the equatorial position.



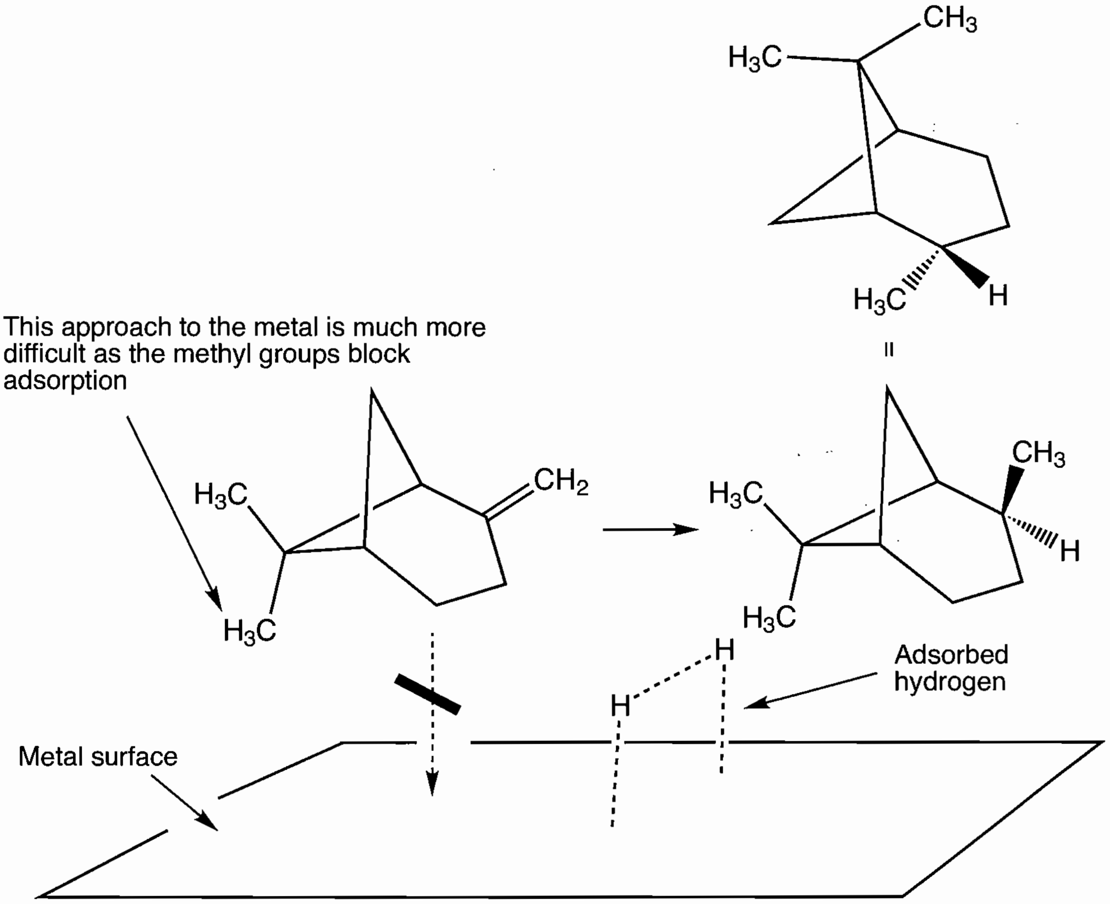
(f) Both alkenes will be hydrogenated in (*E*)-2-methyl-1,4-hexadiene. It would be difficult to control monohydrogenation of this reagent. It is usually steric factors that regulate hydrogenation, and both alkenes in this molecule are both disubstituted.



Problem 11.30 The reaction does not occur spontaneously because there is an activation energy barrier (Chapter 7, p. 281). It is not enough that the starting material, here alkene plus hydrogen, be higher in energy than the product, here alkane. There must be energy enough to surmount the barrier. The role of the catalyst is to provide a lower energy mechanistic pathway leading to product; a trail on a lower slope of the activation mountain (Fig. 10.39, p. 461).

(continued)

Problem 11.28 *(continued)*

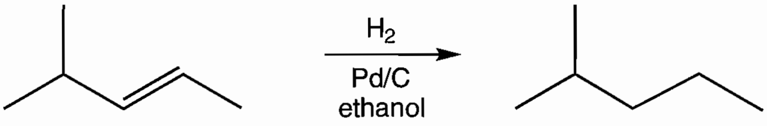

This approach to the metal is much more difficult as the methyl groups block adsorption

Adsorbed hydrogen

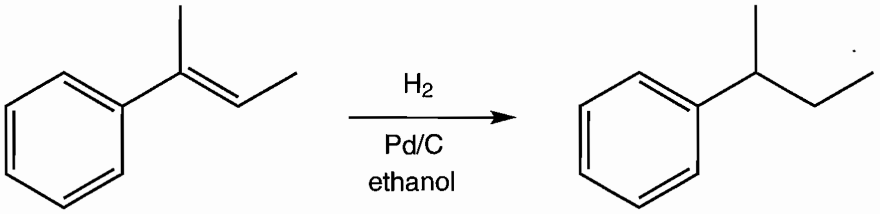
Metal surface

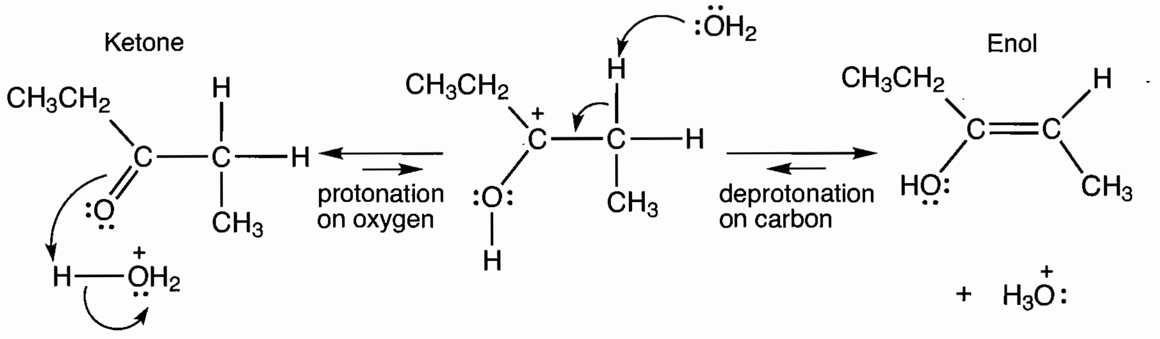
Problem 11.29

(a)

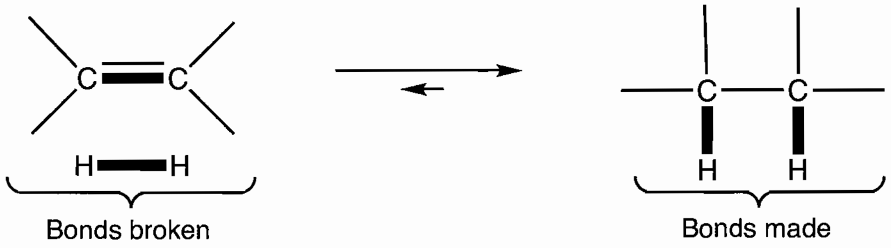


(b) The hydrogenation of an alkene is much easier than the hydrogenation of an aromatic ring. The π bonds of the aromatic ring will hydrogenate with the Pd catalyst only if we apply higher temperatures and pressure. Even with excess H_2, this reaction will give 2-phenylbutane as the product.





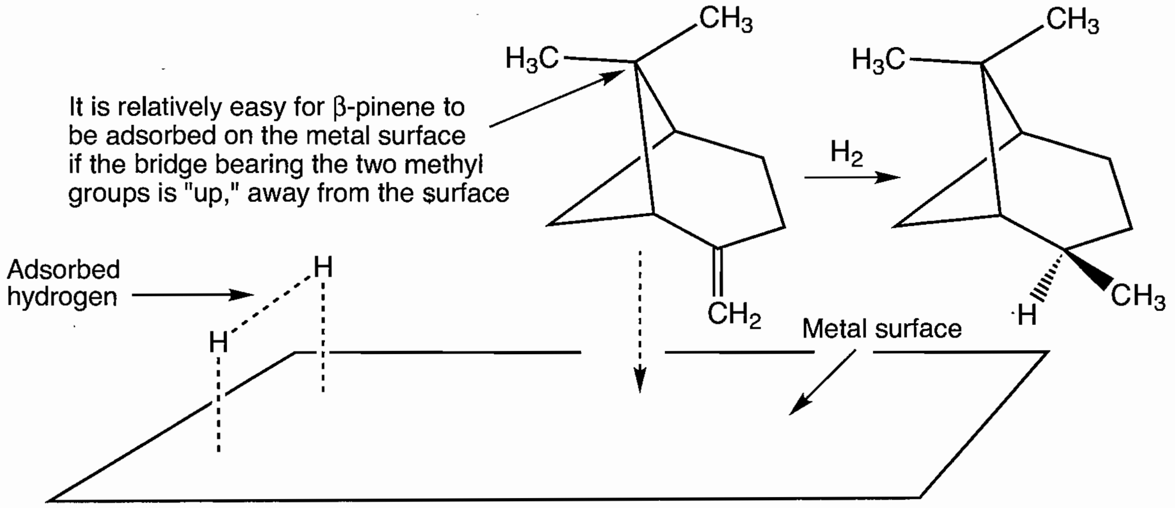
Problem 11.27 Why do we press this point so relentlessly? You should get into the habit of asking this question about any new reaction. The analysis is always the same: Compare the bond energies of the bonds broken and made in the reaction. The bonds broken are the π bond of ethylene and the σ bond of hydrogen. Two new carbon–hydrogen σ bonds are made. The reaction is exothermic by about 30 kcal/mol, and Δ*H* is negative for this reaction.



π bond = 66 kcal/mol σ bond = 104 kcal/mol Two C—H σ bonds = about 200 kcal/mol

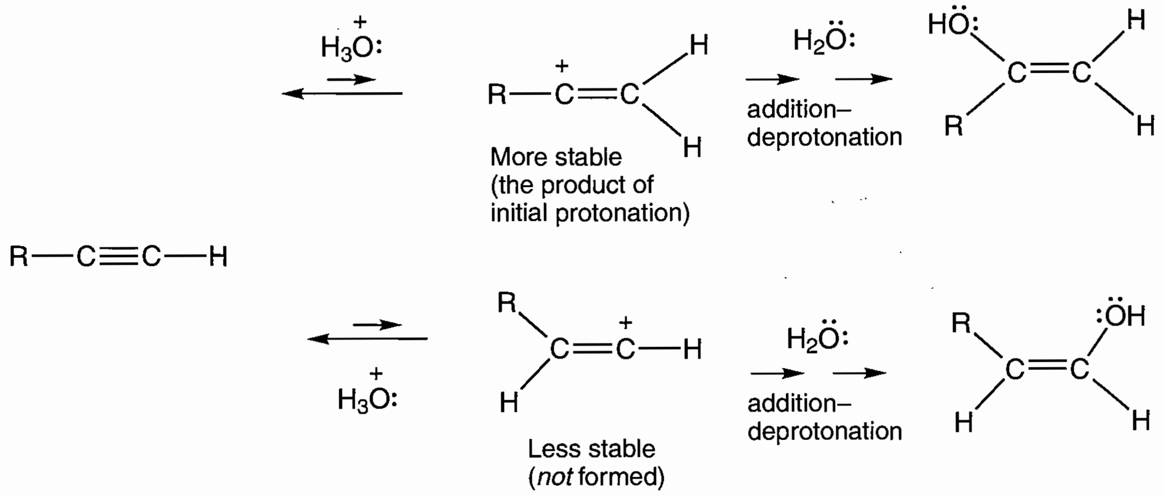
200 − 170 = 30 kcal/mol exothermic, $\Delta H = -30$ kcal/mol

Problem 11.28



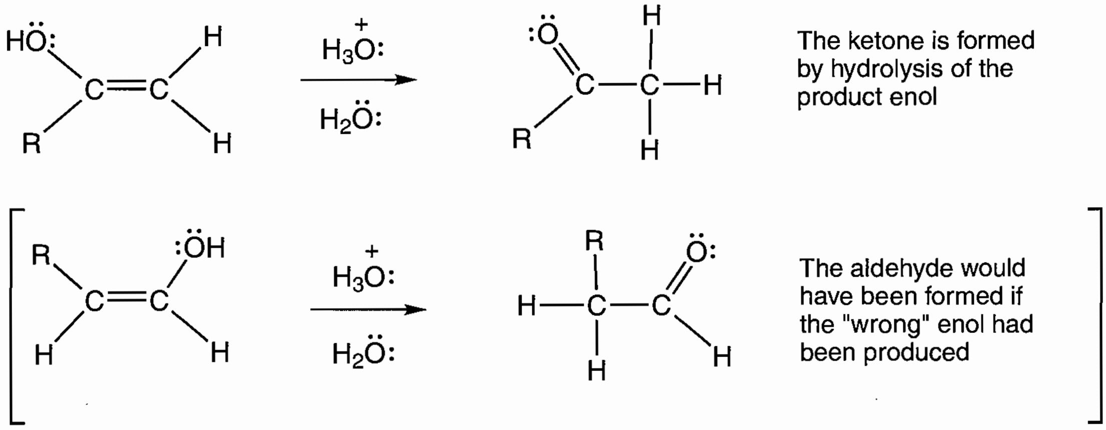
(continued)

Problem 11.25 Follow through the two mechanisms, look for the point at which the pathways diverge, and try to see why the pathway to the ketone is favored. In this case, it is the initial protonation of the alkyne that determines the final product. Protonation gives the more substituted, more stable vinyl cation (or a cyclic intermediate in which the more substituted position bears most of the positive charge). Addition of water to give the enol is followed by conversion of the enol into the final product, the ketone (see Fig. 11.66 for mechanistic details of the formation of the ketone from the enol).



More stable (the product of initial protonation)

Less stable (*not* formed)

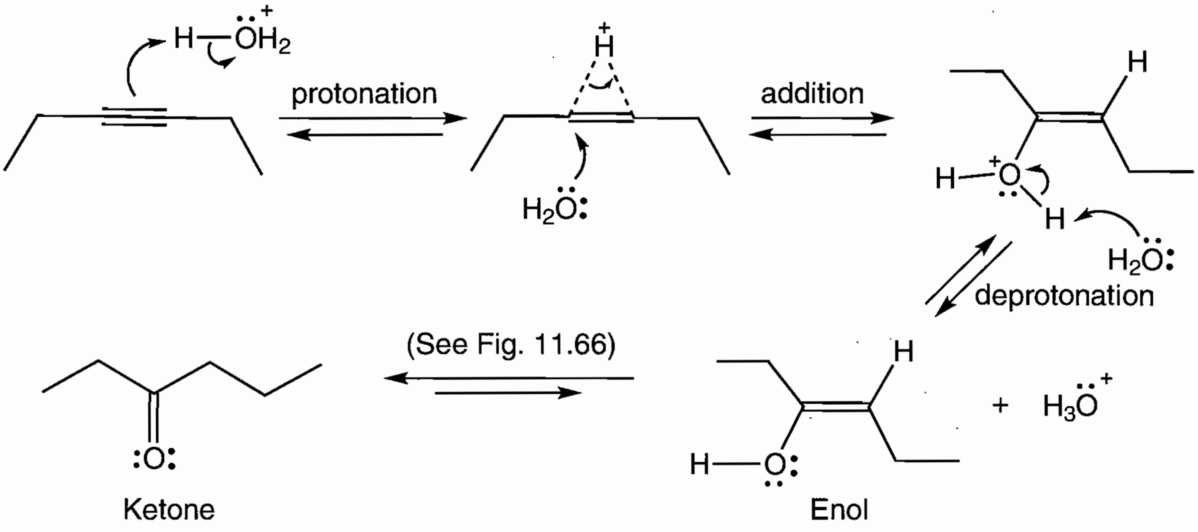


The ketone is formed by hydrolysis of the product enol

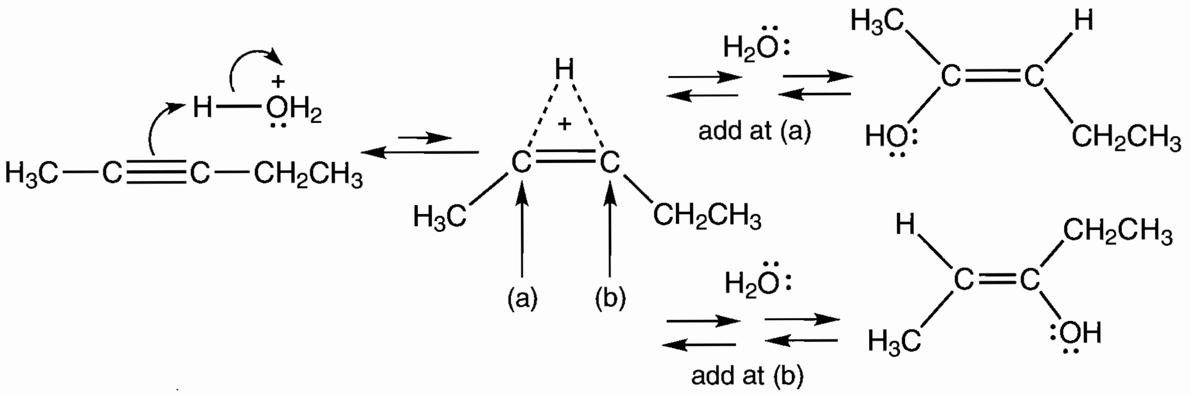
The aldehyde would have been formed if the "wrong" enol had been produced

Problem 11.26 The best way to learn mechanisms is to write them backward. This problem presents an opportunity to do that for the mechanism of ketone formation from enols by asking you to do the reverse reaction. Remember, if you have written the mechanism in one direction, you have automatically written it in the other. All you need to do is to read the first one backward. So you could take the mechanism of Figure 11.66 as your answer.

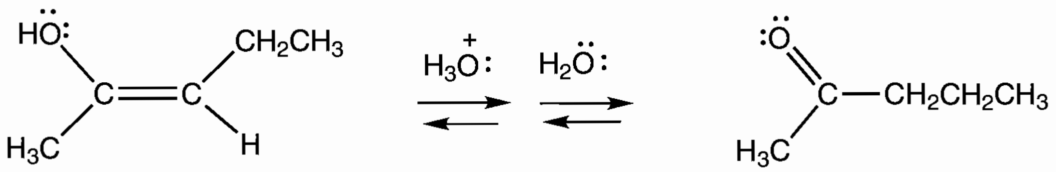
Problem 11.22 Protonation gives an intermediate, probably a cyclic cation of some kind, which can be captured by water to give the enol after deprotonation. Continued reaction of the enol will eventually produce the ketone.

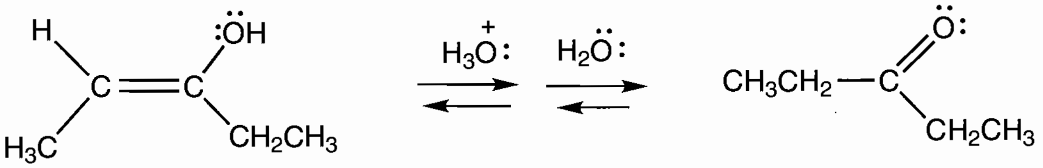


Problem 11.24 In the cyclic intermediate for this reaction, both carbons will share the positive charge by approximately the same amount because the two carbons are equally substituted. Accordingly, addition of the nucleophile will occur at both carbons to give, ultimately, two enols in roughly equal amounts.

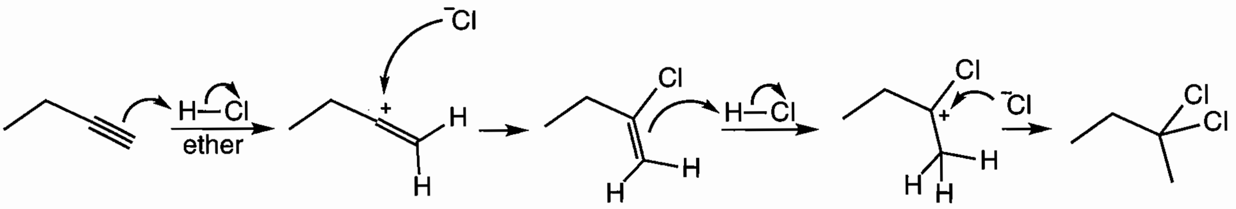


Conversion of the enols into ketones will give *two* ketones (for a mechanism, see Fig. 11.66). This reaction is *not* a useful synthetic process.

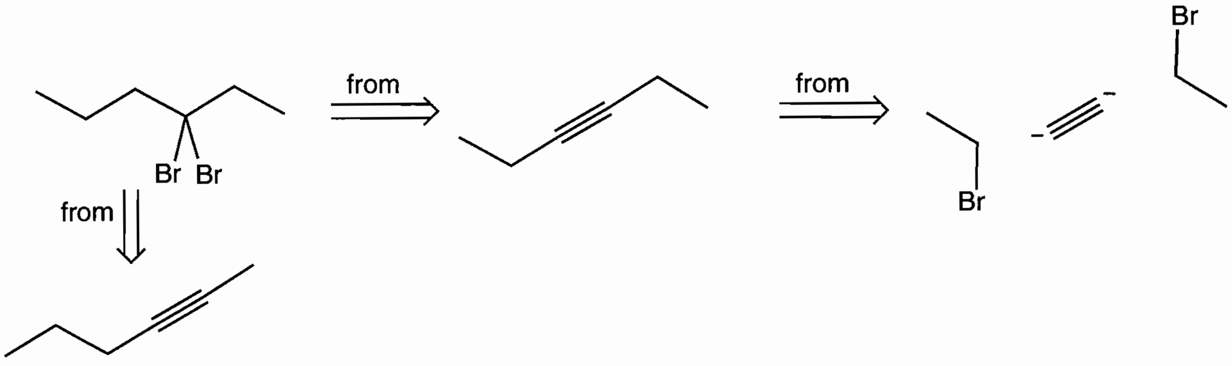




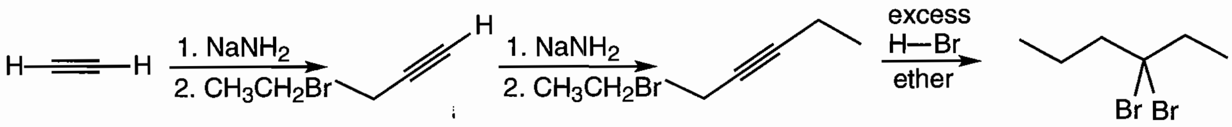
Problem 11.20 The first step of the reaction will form the unstable vinyl carbocation. This ion might be a cyclic species, as shown in Figure 11.60. The second addition of HCl will proceed via the more stable carbocation because it is stabilized by resonance.



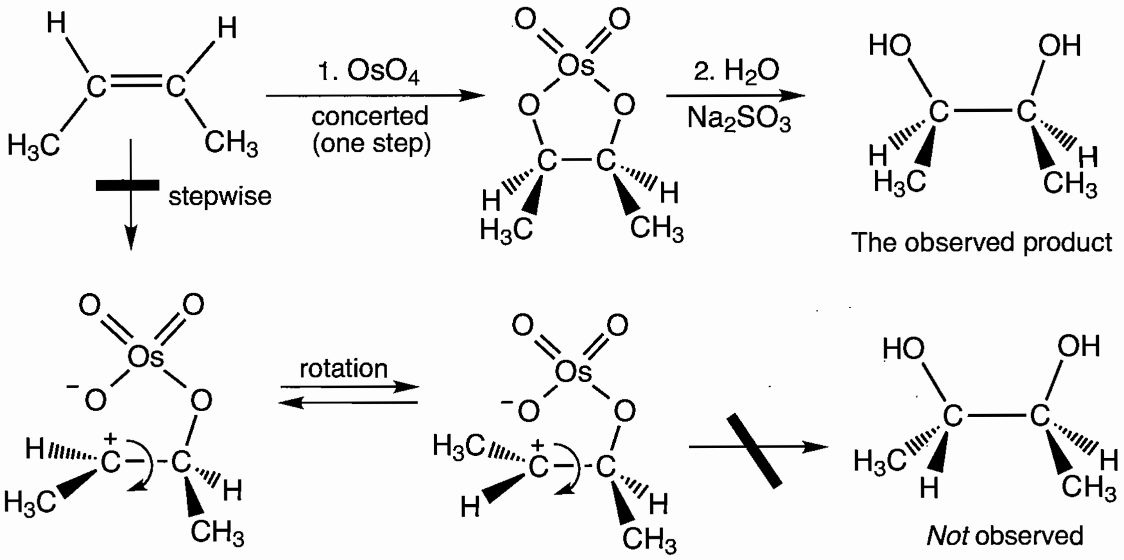
Problem 11.21 The 3,3-dibromohexane can come from the reaction of excess HBr with either 3-hexyne or from 2-hexyne. But you will notice that the 2-hexyne will also produce 2,2-dibromohexane, whereas the 3-hexyne—because of its symmetry—will only give the desired 3,3-dibromohexane. Therefore, we want to think about making 3-hexyne in order to solve this problem. Fortunately, the 3-hexyne comes easily from S_N2 reaction of the acetylide with ethyl bromide on both ends of the acetylene.



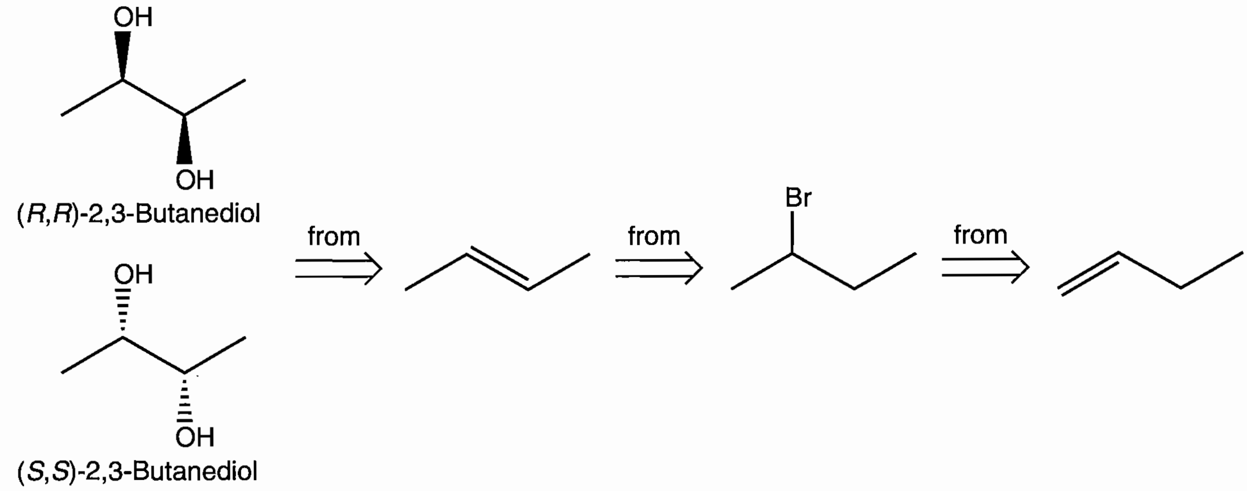
The forward reactions are shown.



Problem 11.18 The stereochemical relationship of the methyl groups does not change. The cis alkene gives a cis-substituted five-membered ring. There can be no steps in the reaction that allow rotation. If there were, a different diol would also be isolated. The initial reaction of OsO_4 with *cis*-2-butene must be one-step (concerted):



Problem 11.19 Racemic 2,3-butanediol must be the mixture of (*R*, *R*)- and (*S*, *S*)-2,3-butanediol, because the (*R*, *S*)- and (*S*, *R*)-2,3-butanediol are equivalent and not chiral. The (*R*, *R*) and (*S*, *S*) enantiomers come from a syn-dihydroxylation of (*E*)-2-butene.



Therefore, the question we need to answer is, How can we make (*E*)-2-butene? We know that an E2 reaction will work well, which requires 2-bromobutane. We can make the 2-bromobutane from 1-butene.

The reactions starting with 1-butene are