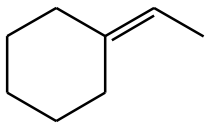
# 21

# Alkenes and alkynes: electrophilic addition and pericyclic reactions

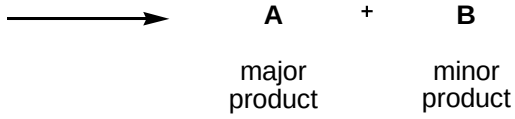
## Answers to worked examples

**WE 21.1 Forming structural isomers by addition reactions (on p. 972 in *Chemistry*[3])**

Addition of HCl to the C=C bond of ethylidenecyclohexane forms products **A** and **B** in unequal amounts. Neither product arises from a rearrangement of a carbocation intermediate. Suggest structures for **A** and **B** and explain why **A** is formed in higher yield than **B**.



ethylidenecyclohexane



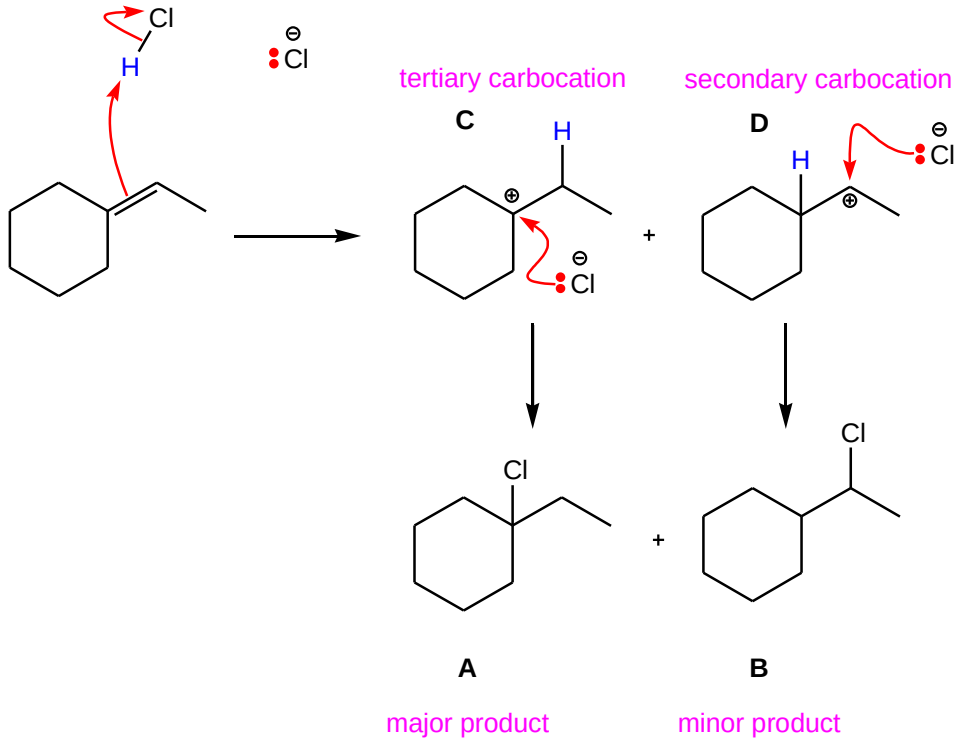

Strategy

Addition of an unsymmetrical reagent, such H-Cl, to an unsymmetrical alkene, like ethylidenecyclohexane, gives two isomeric products in an unequal amount. In order to deduce the major product of this reaction, work out the structures of the intermediate carbocations, formed from the protonation of this alkene with H-Cl. The mechanism for this process is given on p. 966 in *Chemistry*[3].

Solution

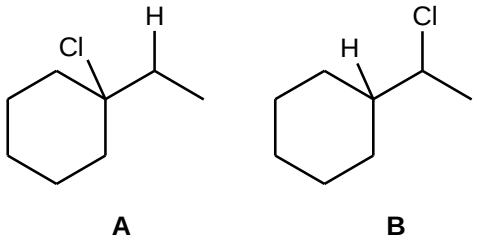
Protonation of ethylidenecyclohexane with H-Cl leads to two carbocations, **C** and **D**. The tertiary carbocation, **C**, is more stable than the isomeric secondary carbocation, **D**, because

of the extra hyperconjugation from its three alkyl substituents. Nucleophilic addition of the resulting chloride counter ion, $Cl^-$, to both carbocations, **C** and **D**, lead to the products, **A** and **B**, respectively. The major product, **A**, is formed preferentially as it is derived from the more stable tertiary carbocation **C**. The mechanism of this shown below:




Answer

Addition of $H^+$ to the C=C bond of ethylidenecyclohexane produces a secondary carbocation or a tertiary carbocation. Compound **A** is formed by addition of $Cl^-$ to a tertiary carbocation. Compound **B** is formed by addition of $Cl^-$ to a secondary carbocation. The tertiary carbocation is selectively formed because this is more stable than the secondary carbocation, and therefore compound **A** is the major product.



**WE 21.2 Opening bromonium ions (on p. 979 in *Chemistry*$^3$)**

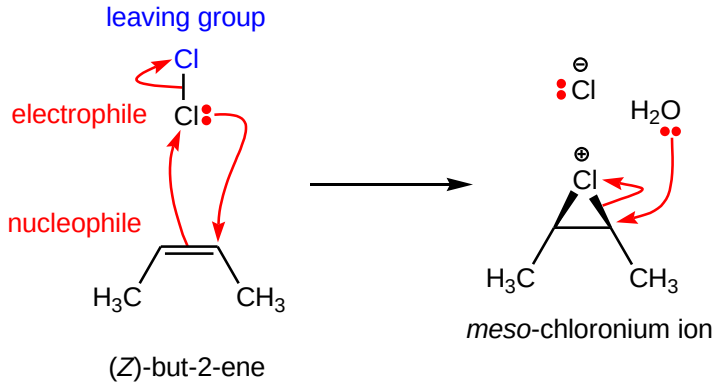
$Cl_2$ reacts with C=C bonds to form intermediate chloronium ions which are converted into 1,2-dichlorides. Assuming that, in the presence of water, both $Cl_2$ and $Br_2$ react with C=C bonds by the same type of mechanism, suggest a mechanism for the reaction of (*Z*)-but-2-ene with $Cl_2$ and water, and give the structure of the major product.

Strategy

Draw out the structure of (*Z*)-but-2-ene and $Cl_2$. From these reagents, identify which are the nucleophile and electrophile, and any leaving group. Draw a curly arrow from the nucleophile to the electrophile (→). [Ensure that the valency is correct as you may need to draw an additional "curly arrow" to any potential leaving group.] If any intermediates are formed; identify any nucleophile/electrophile combinations which lead to more stable products. Draw the structure of the major product. [A related mechanism for this process is given on p. 972 in *Chemistry*$^3$.]

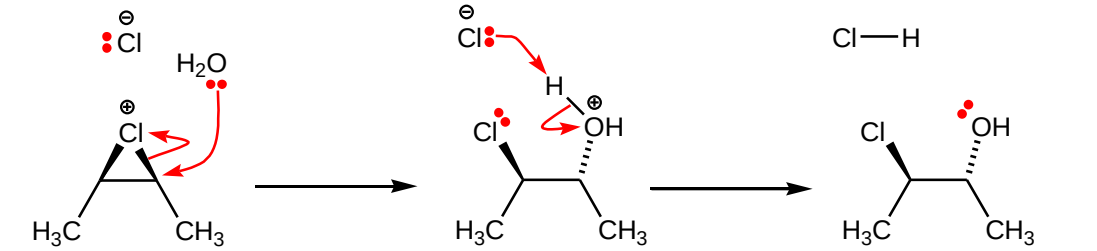
Solution

Electrophilic addition of molecular chlorine ($Cl_2$) to this alkene gives an intermediate *meso*-chloronium ion. [Note: this *meso*-chloronium ion contains a vertical plane of symmetry.]



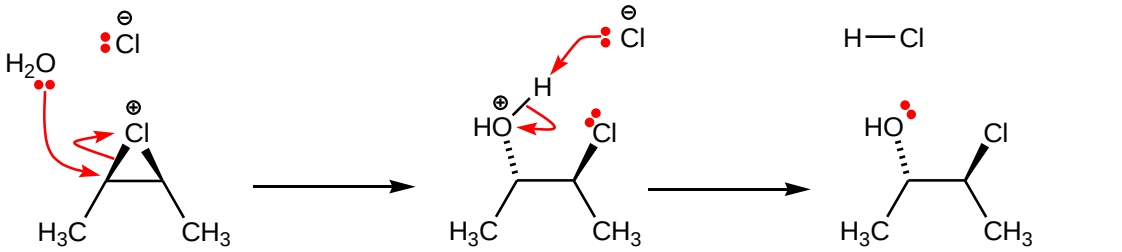

Ring-opening of this *meso*-chloronium ion (on either side) with water leads to racemic mixture of 3-chlorobutan-2-ol. The mechanism of this is shown below.

*Ring opening on the right-hand side*



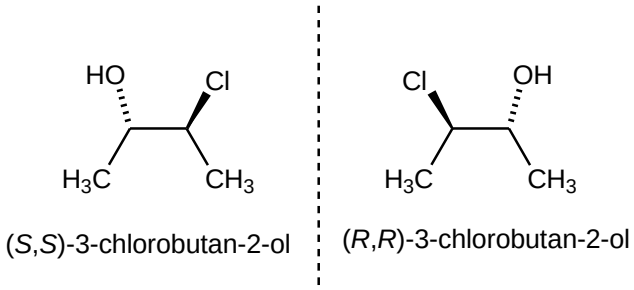

*meso*-chloronium ion (*R*,*R*)-3-chlorobutan-2-ol

*Ring opening on the left-hand side*




*meso*-chloronium ion (*S*,*S*)-3-chlorobutan-2-ol

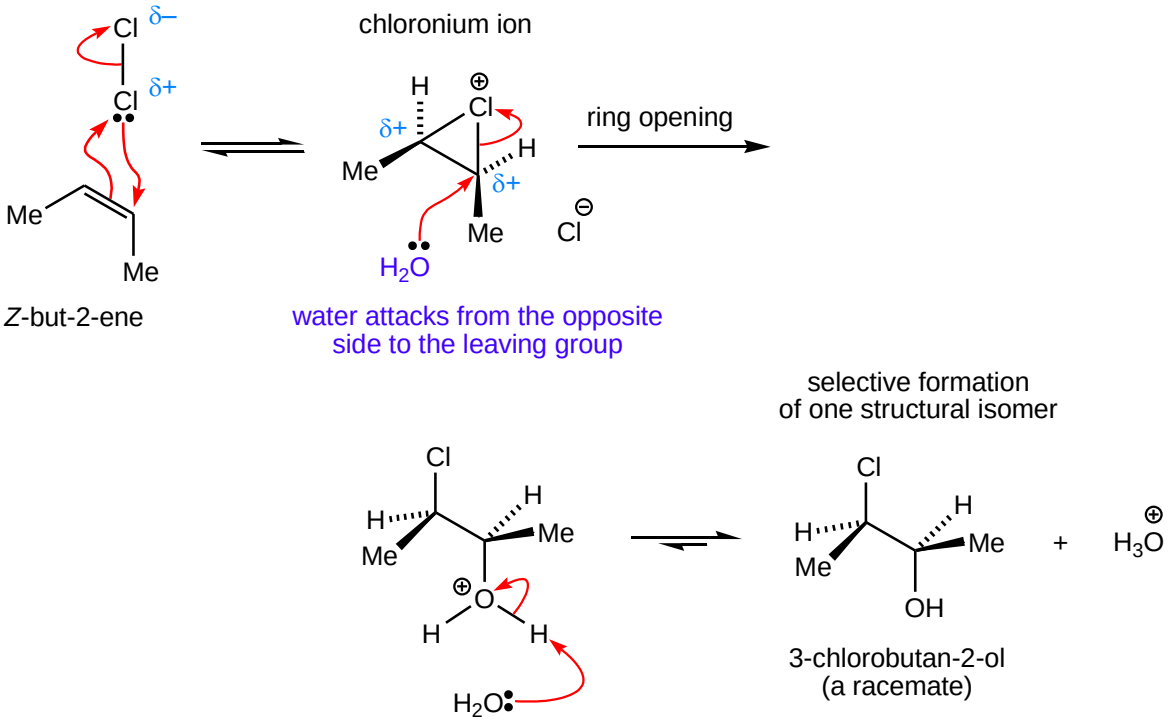
Ring opening on the right- and left-hand sides leads to the (*R*,*R*)- and (*S*,*S*)-enantiomer of 3-chlorobutanol-2-ol, respectively. As this ring opening occurs equally on both sides (as they can be related by a vertical mirror plane); this will lead to an equal amount of both enantiomers of 3-chlorobutanol-2-ol. Therefore, this mixture will be racemic.




(*S*,*S*)-3-chlorobutan-2-ol (*R*,*R*)-3-chlorobutan-2-ol

racemic mixture

Answer




**WE 21.3 Selectivities in hydroboration–oxidation reactions (on p. 985 in *Chemistry*[3])**

2-Methylhex-2-ene is treated with diborane, and then with a solution of hydrogen peroxide in aqueous sodium hydroxide.

(a) Suggest a structure for the major product of this reaction.

Strategy

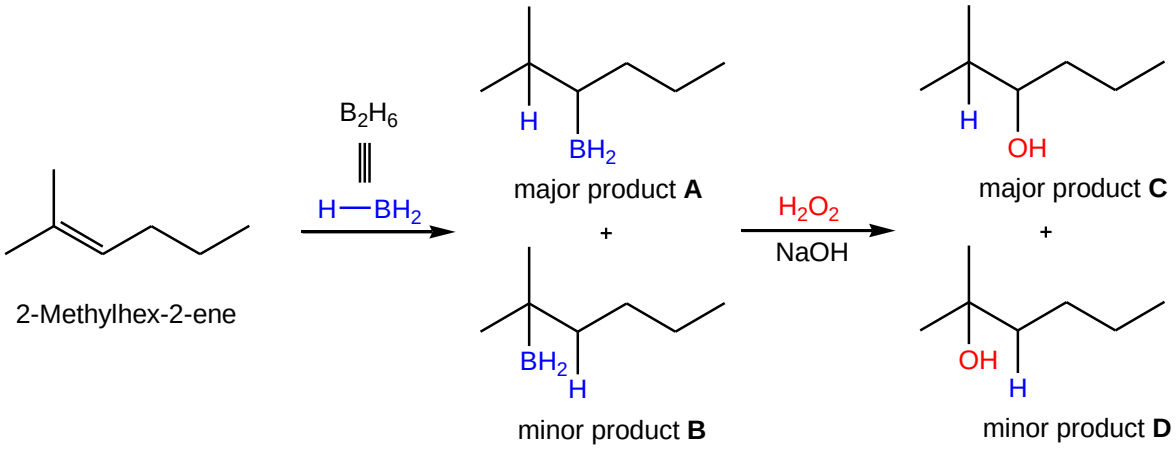
Draw out the structure of 2-methylhex-2-ene and borane (the active component of diborane). Addition of an unsymmetrical reagent, such $BH_2$-H, to an unsymmetrical alkene, like 2-methylhex-2-ene, gives two isomeric borane products in an unequal amount. [Drawing a reaction mechanism can sometimes help you decide which pathway is favoured; from these reagents, identify which is the nucleophile and electrophile, and any leaving group. Draw a curly arrow from the nucleophile to the electrophile (→).]

Draw the structure of the major borane product. A related process is given on p. 978 in *Chemistry*[3].

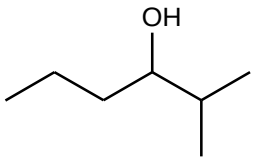
In the second step, addition of $H_2O_2$/NaOH to these boranes, stereospecifically converts the borane "C-$BH_2$" group into an alcohol "C-OH" group (with retention of configuration).

Solution

*syn*-Addition of borane ($BH_3$) to 2-methylhex-2-ene gives two substituted boranes **A** and **B** (ratio >99:1). This addition process is highly regioselective in favour of borane **A**, as its transition state is electronically and sterically preferred. Oxidative cleavage of the resulting boranes using $H_2O_2$/NaOH, leads to the corresponding alcohols **C** (major) and **D** (minor). The major product from this reaction is alcohol **C**. The mechanism of a related process is given on p. 976 in *Chemistry*$^3$.




Solution




(b) Explain why this process is regioselective

Strategy

For a step to be regioselective, it must involve the formation of regioisomers and it must be selective; *i.e.*, **regioselective**. If there is a **choice** within its mechanism, then it will always be **selective**.

Solution

Step 1: hydroboration of 2-methylhex-2-ene using borane.

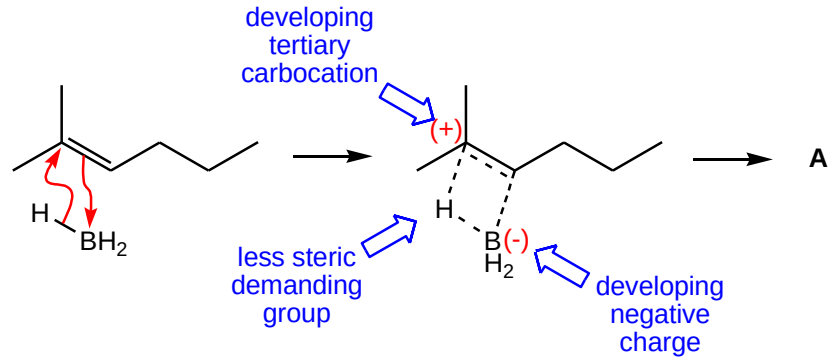
This process is regioselective because it has the potential to form TWO regioisomeric boranes **A** and **B**. It selectively forms borane **A**, which leads to the formation of the major product **C** (in step 2).

Step 2: oxidative cleavage of boranes **A** and **B** with $H_2O_2$/NaOH.

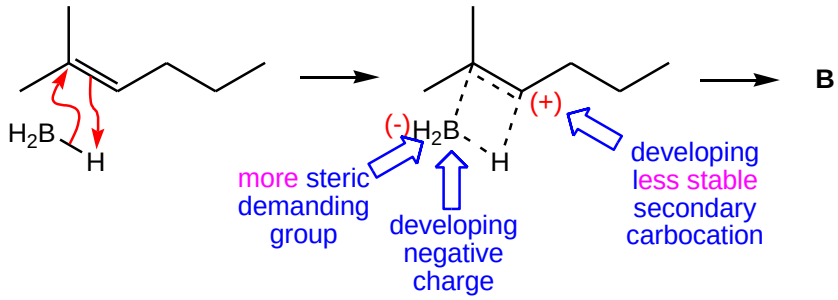
This step does not involve regiochemistry and can be ignored.

Step 1 is regioselective as addition of an unsymmetrical reagent, such as borane, across an unsymmetrical alkene, like 2-methylhex-2-ene leads to two substituted boranes **A** and **B** (ratio >99:1). This addition process is highly regioselective in favour of borane **A**, as its transition state is electronically and sterically preferred. The mechanism for the formation of boranes **A** and **B** are given below.

*Formation of the major borane **A***



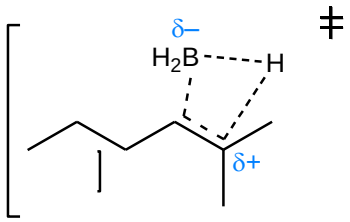

*Formation of the minor borane **B***




Answer

The hydration is regioselective. $BH_3$ adds to the unsymmetrical C=C bond in 2-methylhex-2-ene to form a four-membered transition state that has a partial positive charge on the more substituted carbon. This is also favoured for steric reasons because

the $BH_2$ group is larger than an H atom. The C–B bond that is formed is subsequently converted into a C–OH bond on reaction with $H_2O_2/HO^-$.




four-membered transition state

**WE 21.4 Oxidation of C=C bonds (on p. 992 in *Chemistry*$^3$)**

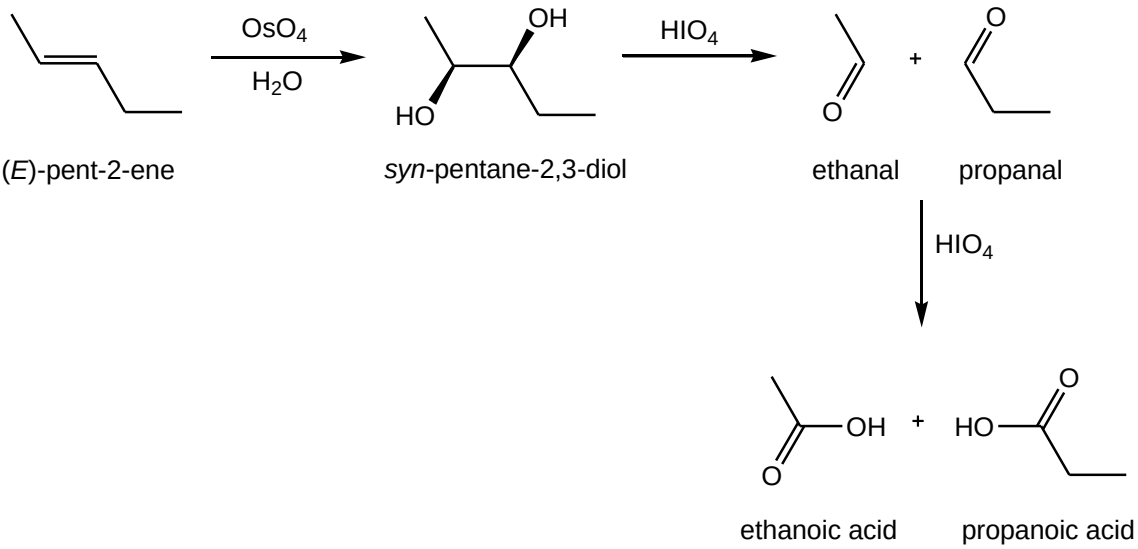
Give the structures of the products from reaction of (*E*)-pent-2-ene with $OsO_4/H_2O$ followed by $HIO_4$.

Strategy

Draw out the starting material, (*E*)-pent-2-ene, and identify the reaction types.
Work out the structures of these products from this reaction.

Solution

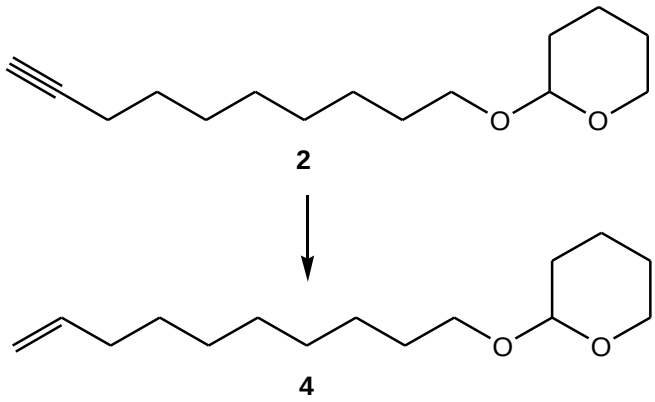
Dihydroxylation of (*E*)-pent-2-ene using $OsO_4$ and $H_2O$ leads to *syn*-pentane-2,3-diol. This 1,2-diol is fragmented oxidatively with $HIO_4$ to give ethanal and propanal. However, under these conditions, these are oxidised to give ethanoic and propanoic acids, respectively. The products from this reaction are ethanoic acid and propanoic acid. The mechanism of this reaction using a related substrate can be found on p. 984 in *Chemistry*$^3$.




Answer


**WE 21.5 Synthesis of a pheromone (on p. 996 in *Chemistry*$^3$)**

Suggest reagents for converting alkyne **2** into compound **4**.

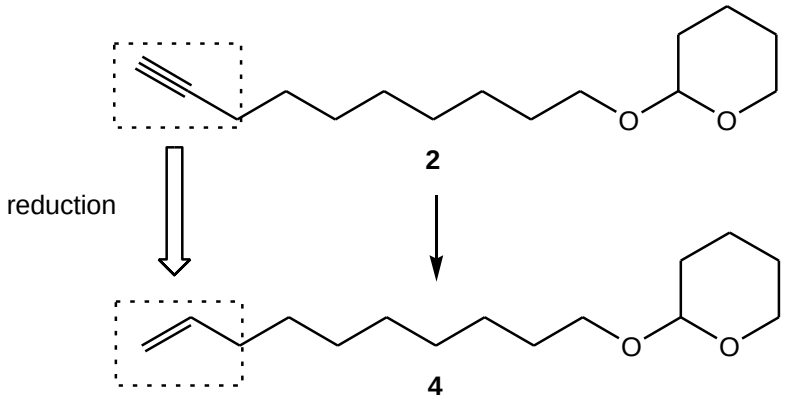



Strategy

Work out if any functional groups have changed during this reaction, and deduce if they involve oxidation, reduction or neither. Suggest potential reagents for any change in functionality.

Solution

This reaction involves the reduction of an alkyne (-C≡C-) to an alkene (-CH=CH-). Simple hydrogenation ($H_2$, Pd) gives access to this alkene; however, over reduction of this alkene leads to corresponding alkane (-$CH_2$-$CH_2$-). To stop this reduction at the required alkene stage, a less electrophilic catalyst is needed; the most widely used being Lindlar's catalyst, which is a poisoned palladium metal catalyst.




Answer

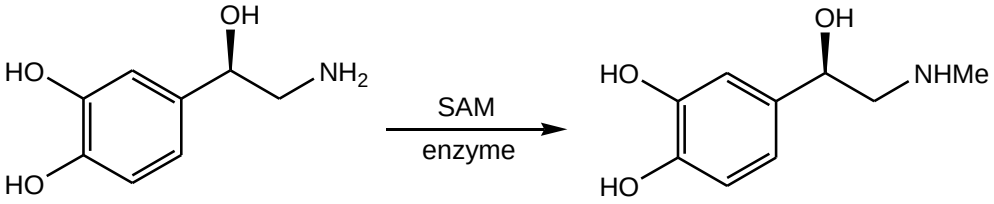
Conversion of molecules **2** → **4**: $H_2$, Lindlar's catalyst.

# Answers to boxes

## Box 21.1 Ethene production in plants (on p. 965 in *Chemistry*$^3$)

In living cells, *S*-adenosylmethionine (SAM) acts as an efficient methylating agent. Methylation reactions in the body regulate the biological activities of various hormones and neurotransmitters. For example, SAM reacts with norepinephrine in the presence of an enzyme to form epinephrine, which triggers a rise in blood pressure and heart rate in the body.

Suggest a mechanism for the reaction below and explain why SAM is such a reactive methylating agent. [*Hint*: use your knowledge of nucleophilic substitution reactions (see section 20.3 on p. 924 in *Chemistry*$^3$) to help you propose a mechanism.]




norepinephrine (noradrenaline)

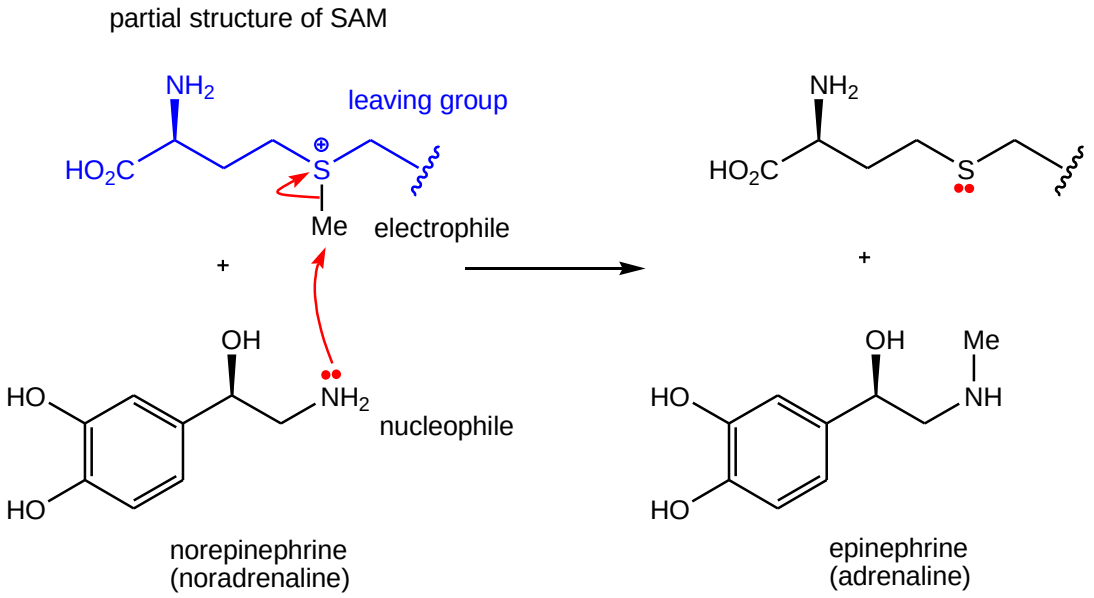
epinephrine (adrenaline)

Strategy

Exam norepinephrine and epinephrine, and work out where this methylation had occurred. Work out which reagent is the nucleophile and electrophile. [Remember, the "curly arrow" flows from the nucleophile (→) to the electrophile.] Nucleophiles contain non-bonded electrons (which sometimes can be depicted by negative charge) and electrophiles have low-lying empty orbitals (which often contain a leaving group). Draw the mechanism of this reaction, and suggest why (*S*)-adenosylmethionine (SAM) is an efficient alkylating agent.

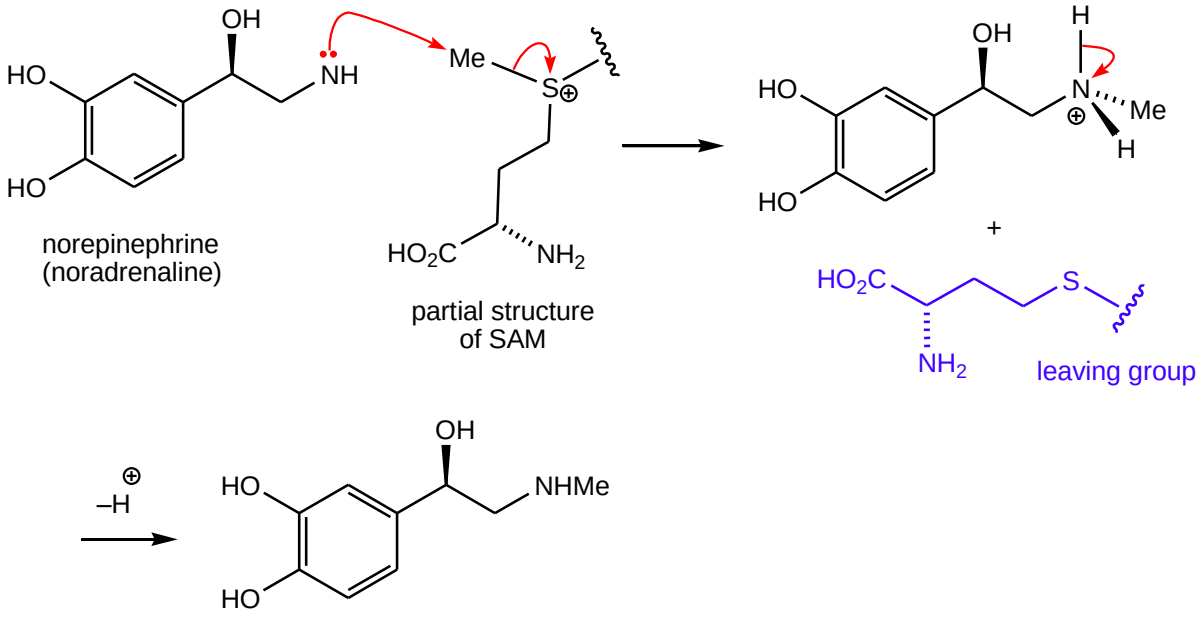
Solution

Methylation occurs on the amino-group of norepinephrine; the overall transformation is $-NH_2 \rightarrow -NHMe$. The mechanism of this reaction is shown below, where the nucleophile is norepinephrine, and the electrophile is SAM.




SAM is an efficient methylating agent as it is positively charged and has a high-ground state energy (*i.e.,* it is reactive), and after methylation the leaving group is neutral and has low-ground state energy.

Answer




SAM is a reactive alkylating agent because (a) it is positively charged (the positively charged S atom attracts electrons away from the –Me group, making it a good

electrophile and susceptible to attack by the nucleophilic $-NH_2$ group; and (b) the alkylation produces a stable neutral leaving group.

**Box 21.2 Adding HBr to alkenes in the presence of peroxides (on p. 973 in *Chemistry*$^3$)**

For hydrogen halides to add to a C=C bond in a radical reaction, both addition and abstraction steps must be exothermic. If either step is endothermic, then the propagation step is too slow for the chain reaction to proceed. Reaction of HCl or HI with a terminal alkene, in the presence of peroxide, does not produce the anti-Markovnikov addition products. Using the approximate bond enthalpies given below, explain why HCl or HI does not add to a C=C bond in a radical chain reaction.

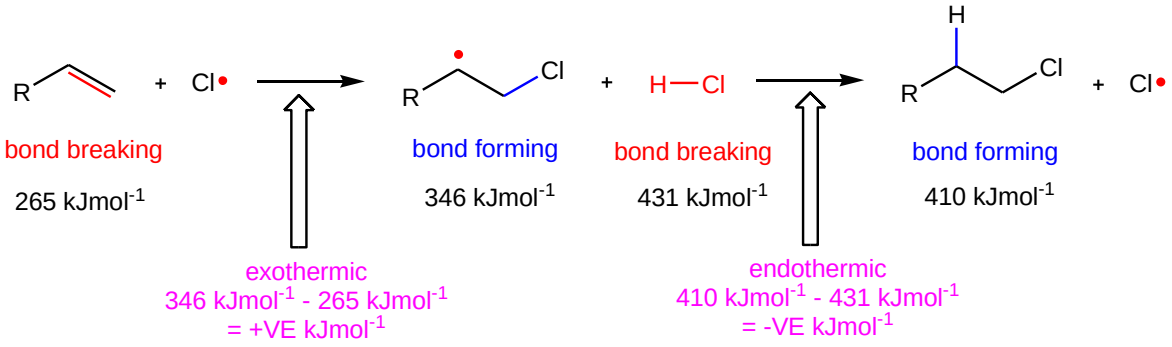
| H—Cl | C—Cl | H—I | C—I |
|---|---|---|---|
| 431 kJmol$^{-1}$ | 346 kJmol$^{-1}$ | 298 kJmol$^{-1}$ | 228 kJmol$^{-1}$ |

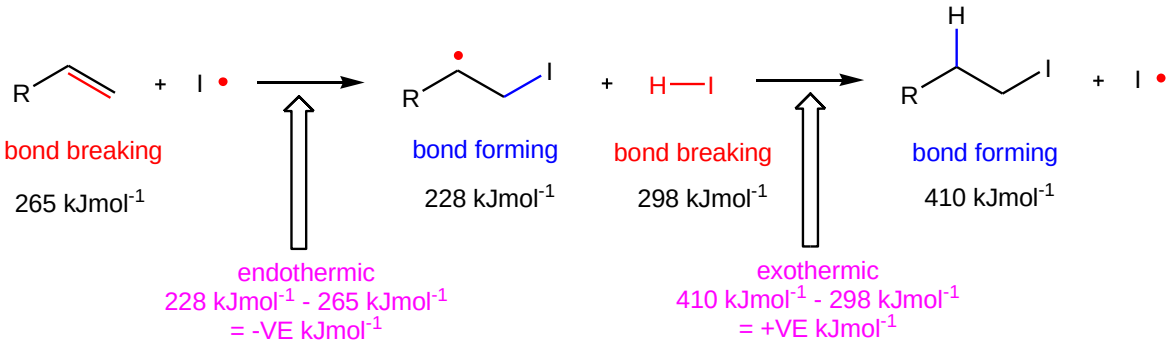
Strategy

Draw out both reactions schemes. Work out which bonds are being formed and broken in these processes. As a rule of thumb, for all other things being equal, exothermic reactions are generally more favoured than endothermic reactions. [Remember, for exothermic reactions, energy is given out, and in endothermic reactions, energy is taken in.]

Solution

The schemes for both processes are shown below. If either step is endothermic, then the propagation step is too slow for the chain reaction to proceed. For the radical addition of HCl to an alkene, the second step is endothermic (the H-Cl bond is stronger than the newly formed C-H bond). Whereas, for radical addition of HI, the first step is endothermic (the pi-component of the C=C bond is stronger than the newly formed C-I bond). Therefore, these chain propagation steps are too slow to be synthetically useful for the addition of H-Cl and H-I across alkenes.

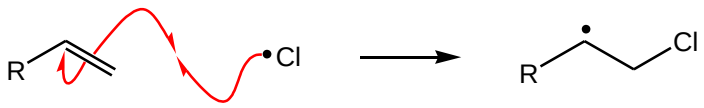


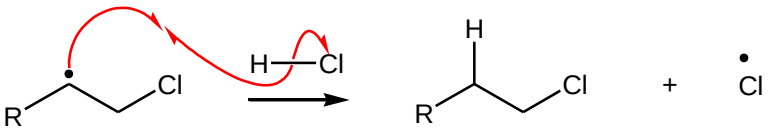

Answer

HCl does not add to a C=C bond in a radical chain reaction because the abstraction step is endothermic.

Addition is **exothermic.** The C–Cl bond (346 kJ $mol^{-1}$) is stronger than the C=C π-bond (~265 kJ $mol^{-1}$)



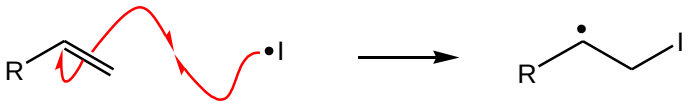

Abstraction is **endothermic**. The C–H bond (~410 kJ $mol^{-1}$) is weaker than the H–Cl bond (431 kJ $mol^{-1}$)



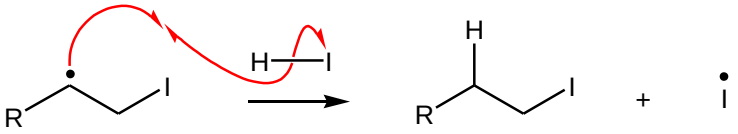

HI does not add to a C=C bond in a radical chain reaction because the addition step is endothermic.

(For the radical addition of HBr to a C=C bond, both the addition and the abstraction steps are exothermic).

Addition is **endothermic**. The C–I bond (228 kJ mol$^{-1}$) is weaker than the C=C π-bond (~265 kJ mol$^{-1}$)

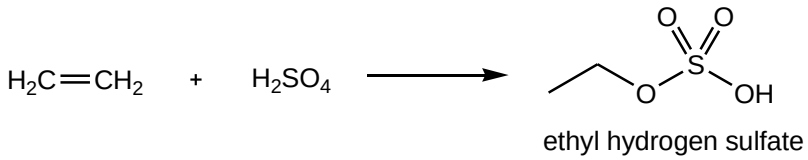



Abstraction is **exothermic**. The C–H bond (~410 kJ mol$^{-1}$) is stronger than the H–I bond (298 kJ mol$^{-1}$)

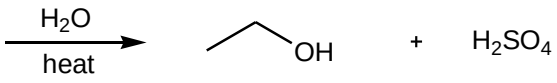



**Box 21.3 Making ethanol on a large scale (on p. 980 in *Chemistry*$^3$)**

Concentrated sulfuric acid reacts with ethene to form ethyl hydrogen sulfate, which can be converted into ethanol by reaction with water as shown below. Suggest a mechanism for the formation of ethyl hydrogen sulfate.




ethyl hydrogen sulfate

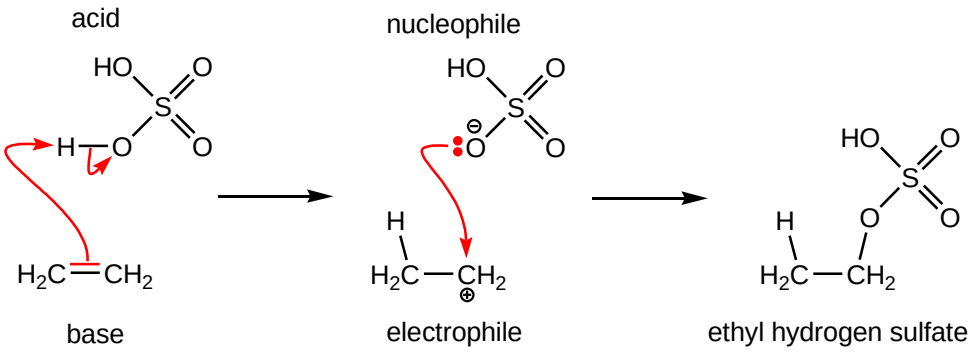



Strategy

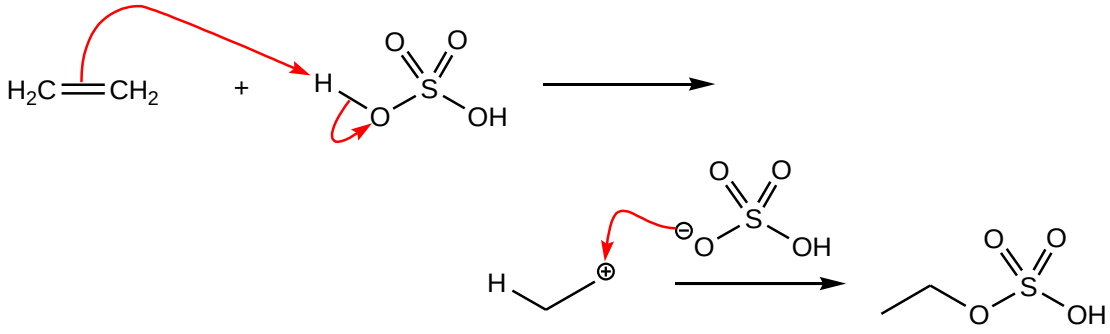
For each step, you will need to decide whether the reaction involves an electrophile/nucleophile or acid/base combination. Acid and base processes involve proton exchange, whereas, electrophile and nucleophile processes involve bond-breaking and bond-making. Draw a curly arrow from the nucleophile or base to the electrophile or acid (→).

Solution

The first step must involve an acid/base combination, as sulfuric acid ($H_2SO_4$) is the acid and ethene ($CH_2$=$CH_2$) is the base. The second step involves an electrophile/nucleophile combination. This mechanism is shown below.




Answer



**Box 21.4 Why is benzene carcinogenic (on p. 988 in *Chemistry*$^3$)?**

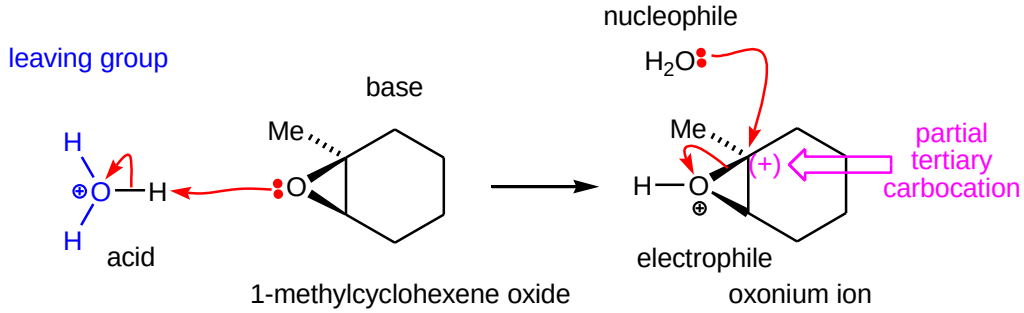
Suggest a mechanism for the reaction of 1-methylcyclohexene oxide with aqueous acid and give the structure of the product.

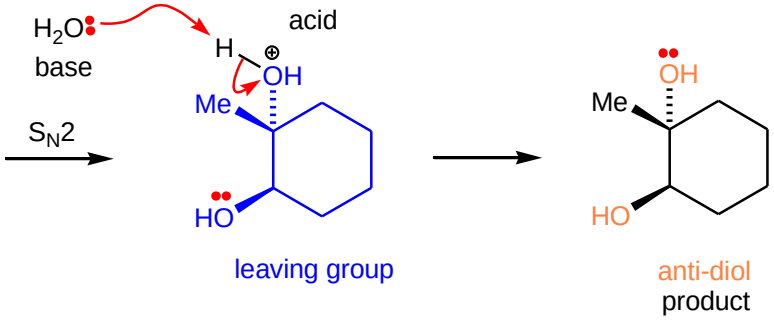
Strategy

Draw out the starting material, 1-methylcyclohexene oxide. Aqueous acid can be considered as "$H^{+}$" and "$H_2O$" (or $H_3O^{+}$). The water, $H_2O$, can act as a base or nucleophile. For each step, you will need to decide whether the reaction involves an electrophile/nucleophile or acid/base combination. Acid and base processes involve proton exchange, whereas, electrophile and nucleophile processes involve bond-breaking and bond-making. Draw a curly arrow from the nucleophile or base to the electrophile or acid (→).

Solution

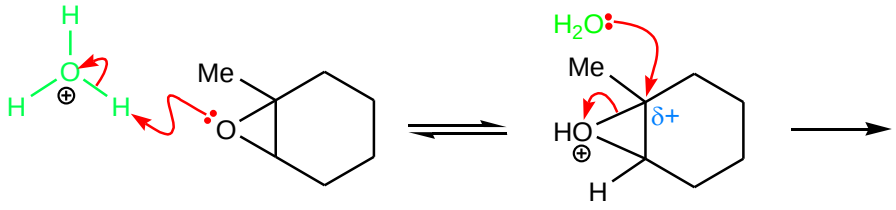
This reaction involves the ring-opening of epoxide, 1-methylcyclohexene, under acid-catalysed conditions. The general mechanism of this process using a related alkene is discussed on p. 980 in *Chemistry*[3]. Protonation of 1-methylcyclohexene with $H_3O^+$ gives the activated epoxide (oxonium ion); $S_N2$ ring-opening of this electrophilic oxonium ion, with water, at the more electronically activated and more substituted side, leads to the anti-diol product. This $S_N2$ ring-opening stereospecifically forms the *anti*-diol and not the *syn*-diol.




Answer

Using drawings that do not show the conformation of molecules

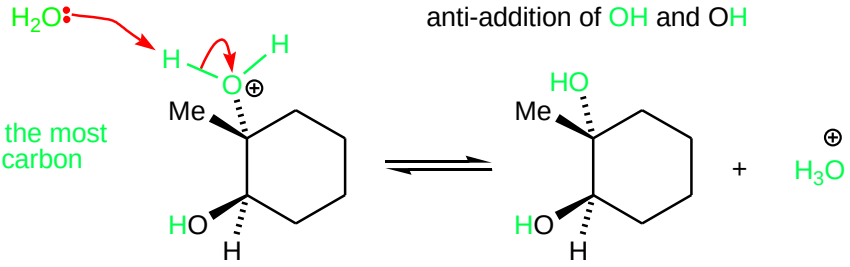



1-methylcyclohexene oxide

unsymmetrical epoxide

unsymmetrical bromonium ion

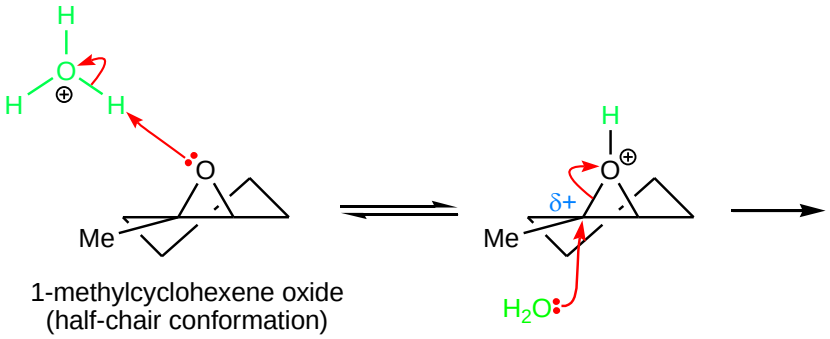
anti-addition of OH and OH




water attacks the most substituted carbon

*trans*-1-methylcyclohexane-1,2-diol (chair conformation) as a racemate

Using drawings that show the conformation of molecules

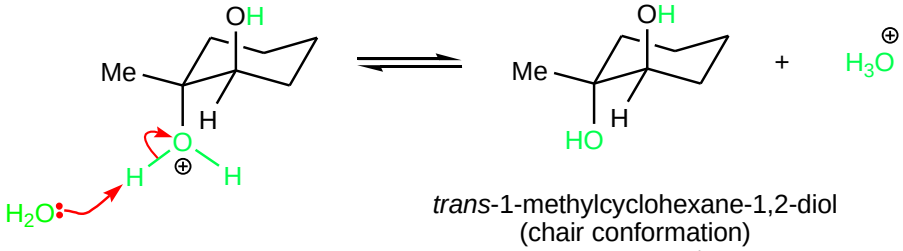



1-methylcyclohexene oxide
(half-chair conformation)

unsymmetrical
epoxide

water attacks the most
substituted carbon

anti-addition of OH and OH

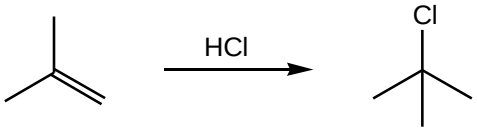



*trans*-1-methylcyclohexane-1,2-diol
(chair conformation)
as a racemate

# Answers to end of chapter questions (on p. 999 in *Chemistry*[3])

**1.** Suggest mechanisms for the following electrophilic addition reactions.

(a)

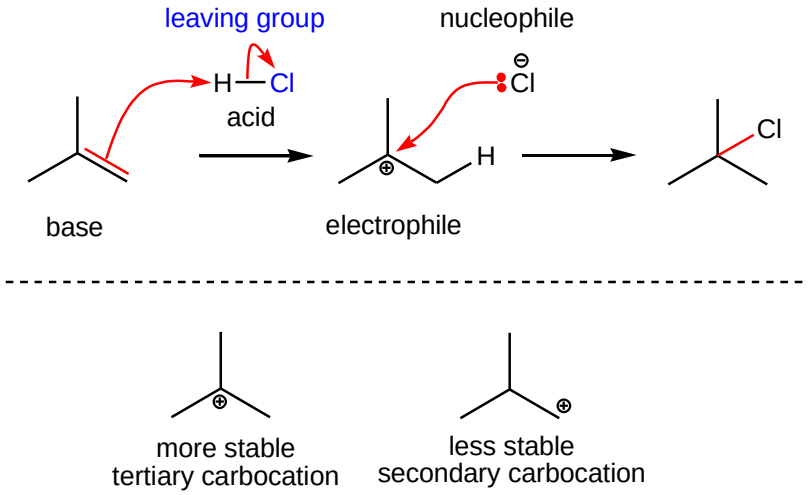



Strategy

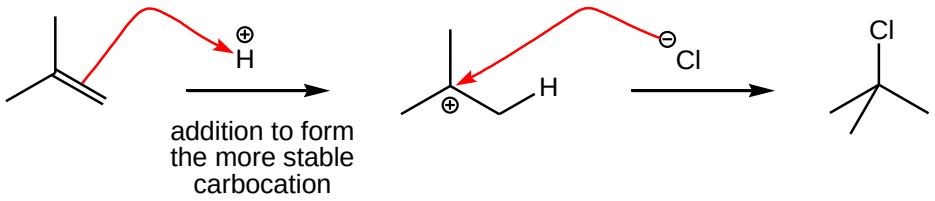
You will need to decide whether the reaction involves an electrophile/nucleophile or acid/base combination. Acid and base processes involve proton exchange, whereas, electrophile and nucleophile processes involve bond-breaking and bond-making. Draw a curly arrow from the nucleophile or base to the electrophile or acid (→).

Solution

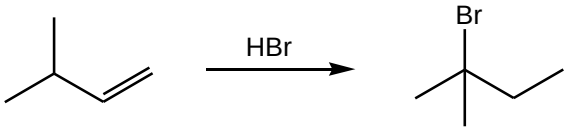
The alkene acts as the base, H-Cl acts as the acid, and the chloride anion, $Cl^-$, as the leaving group. Protonation of this unsymmetrical alkene leads to the more substituted tertiary carbocation (as drawn). Nucleophilic addition of chloride to this tertiary carbocation gives the required product. The product derived from the less stable secondary carbocation is the minor product. This mechanism is shown below.



Answer




(b)



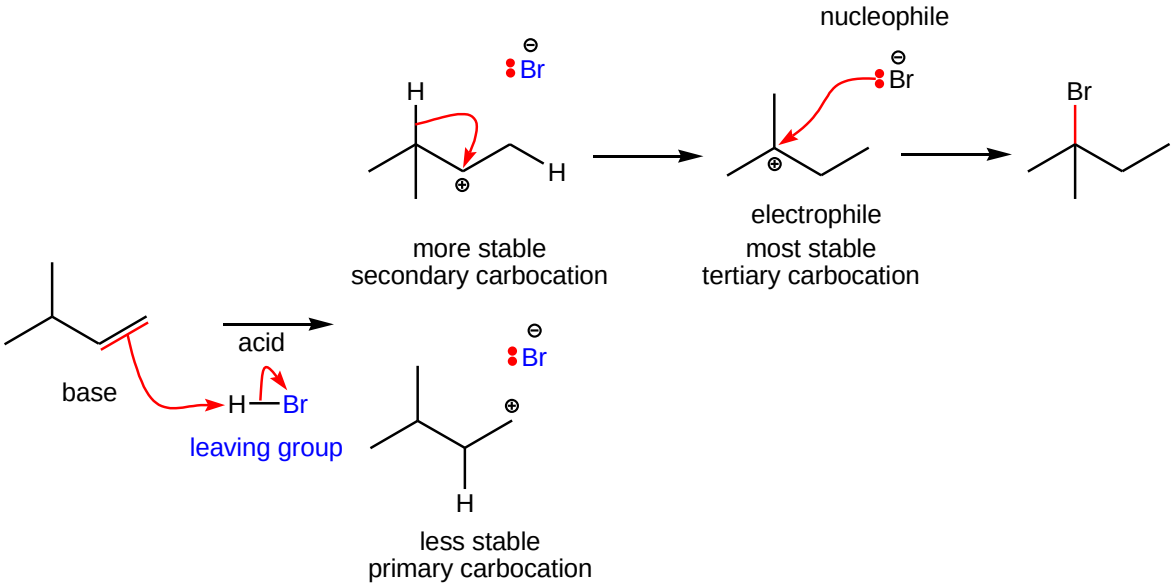

Strategy

You will need to decide whether the reaction involves an electrophile/nucleophile or acid/base combination. Acid and base processes involve proton exchange, whereas, electrophile and nucleophile processes involve bond-breaking and bond-making. Draw a curly arrow from the nucleophile or base to the electrophile or acid (→).

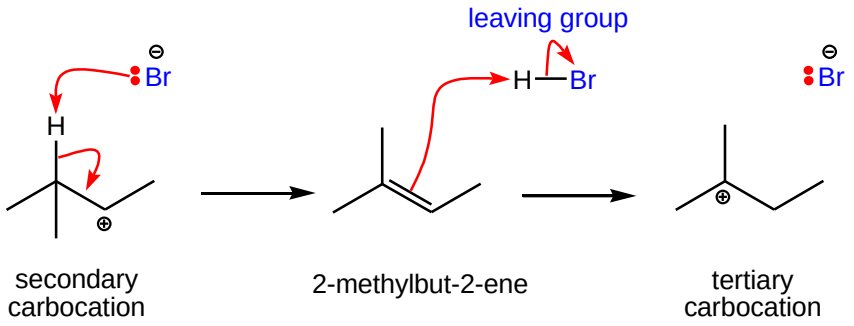
There may be a rearrangement in this reaction, as the hydrocarbon skeleton has changed; the original C-H bond has been replaced with a C-Br bond, and the alkene has been reduced! Do not overly focus on a potential rearrangement; let the "curly arrows" guide you through this mechanism.

Solution

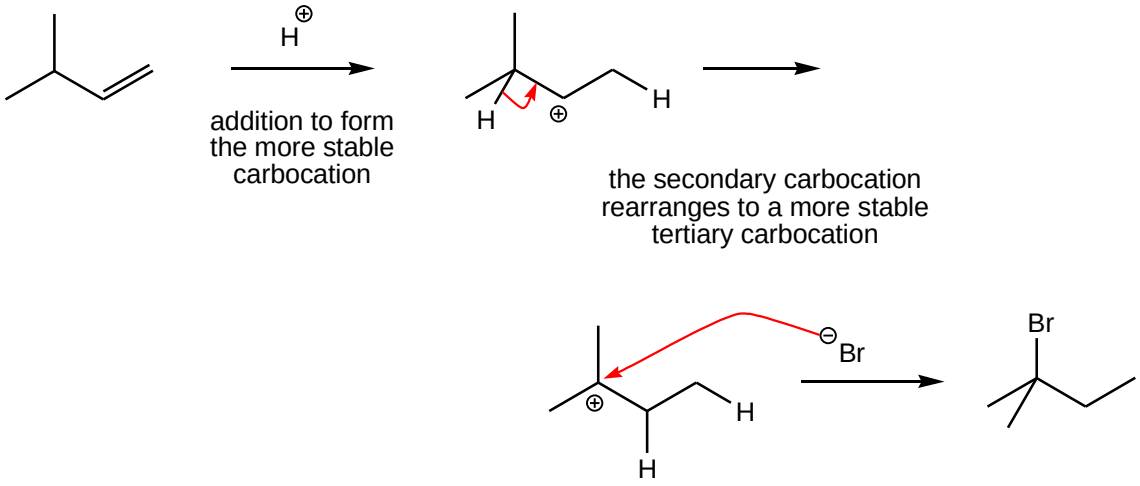
The alkene acts as the base, H-Br acts as the acid, and the bromide anion, $Br^-$, as the leaving group. Protonation of this unsymmetrical alkene leads to the more substituted secondary carbocation; competitive formation of the less substituted and less stable primary carbocation does not occur. Formation of the product must come from the corresponding tertiary carbocation; access to this presumably comes from a 1,2-CH shift involving the initial secondary carbocation. Nucleophilic addition of bromide to this tertiary carbocation gives the required product. The products derived from the less stable secondary and primary carbocations are minor products. These mechanisms are shown below.



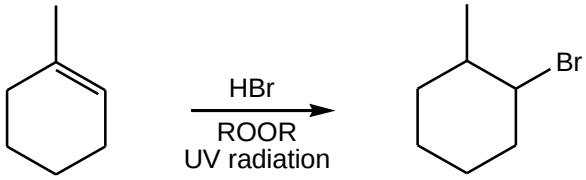

Rearrangement of this secondary carbocation to the more stable tertiary carbocation could also occur by a deprotonation-reprotonation mechanism, as outlined below.




Answer



(c)




Strategy

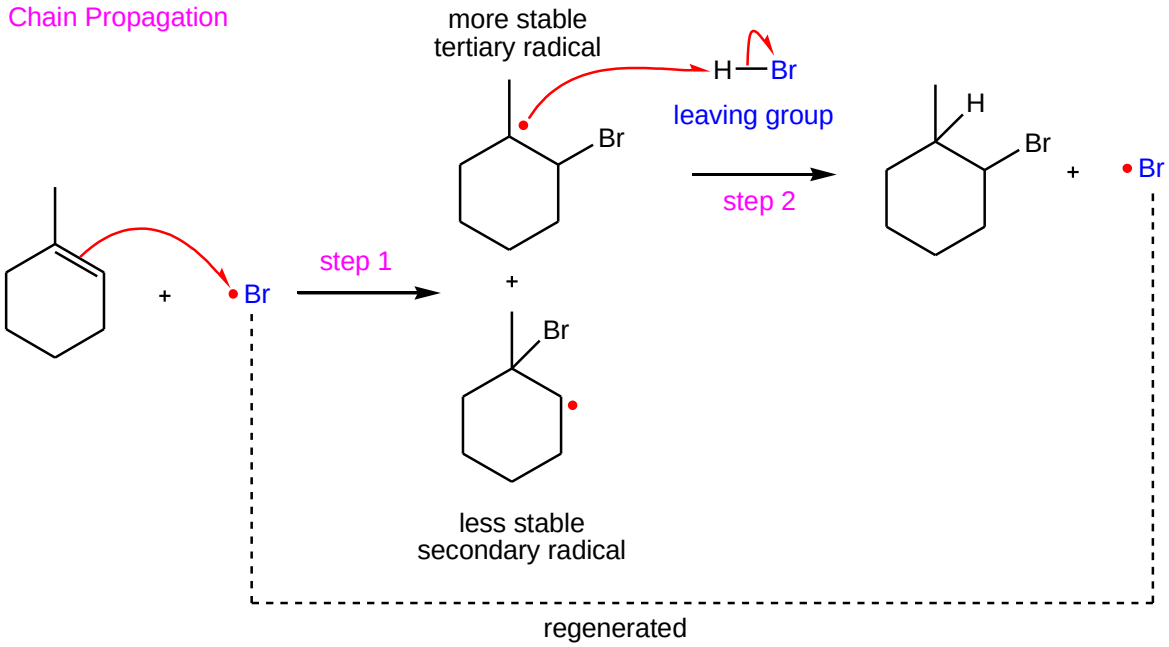
You will need to decide whether this reaction involves radical bromination (homolytic cleavage) or electrophilic/nucleophilic bromination (heterolytic cleavage). Draw a curly arrow from the nucleophile or radical to the electrophile or radical; remember a double-headed arrow is needed for a nucleophile (→) and a single headed arrow for a radical (□).

Look at the reaction conditions as these might give you a clue; this reaction involves an organic peroxide with UV radiation. More than likely this reaction will involve radical bromination.

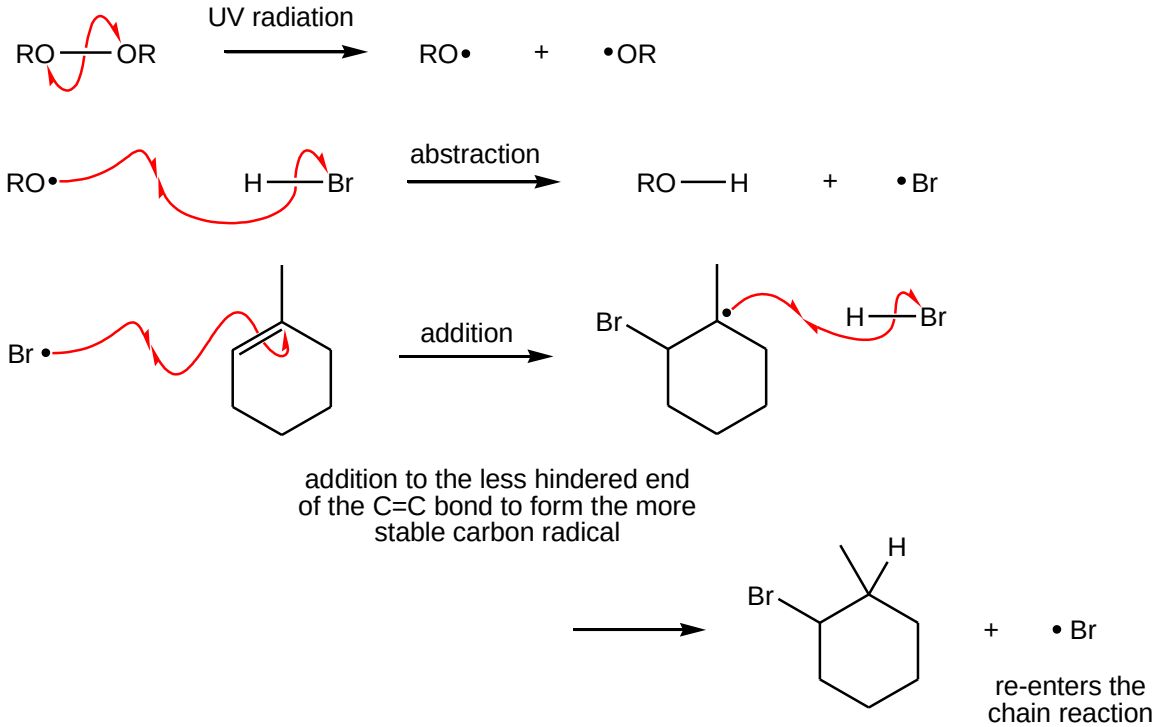
Solution

The product forming step is the propagation step. If you need to recap, the initiation and termination steps for radical addition of HBr across an alkene see p. 967 in *Chemistry*[3].

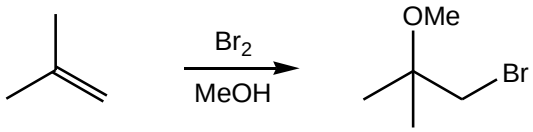
In the first propagation step, radical bromination of 1-methylcyclohexene with Br▪ gives the more stable tertiary radical through bromination of the less hindered carbon atom of this alkene group. Formation of the required product occurs in the second propagation step through radical hydrogen abstraction of HBr using the more stable tertiary radical (generated in step 1). Radical addition of HBr across this alkene, 1-methylcyclohexene, gives the anti-Markovnikov addition product. Markovnikov radical addition of HBr to this alkene **does not** occur as the intermediate secondary radical (in step 1) is too unstable to lead to efficient product formation.




Answer



(d)



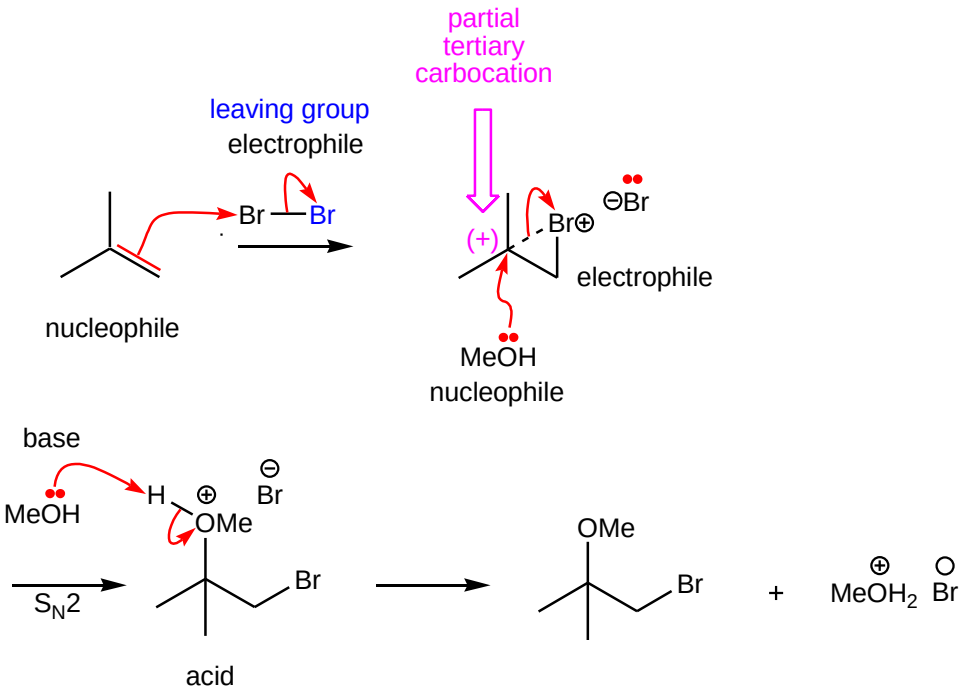

Strategy

You will need to decide whether the reaction involves an electrophile/nucleophile or acid/base combination. Acid and base processes involve proton exchange, whereas, electrophile and nucleophile processes involve bond-breaking and bond-making. Draw a curly arrow from the nucleophile or base to the electrophile or acid (→).

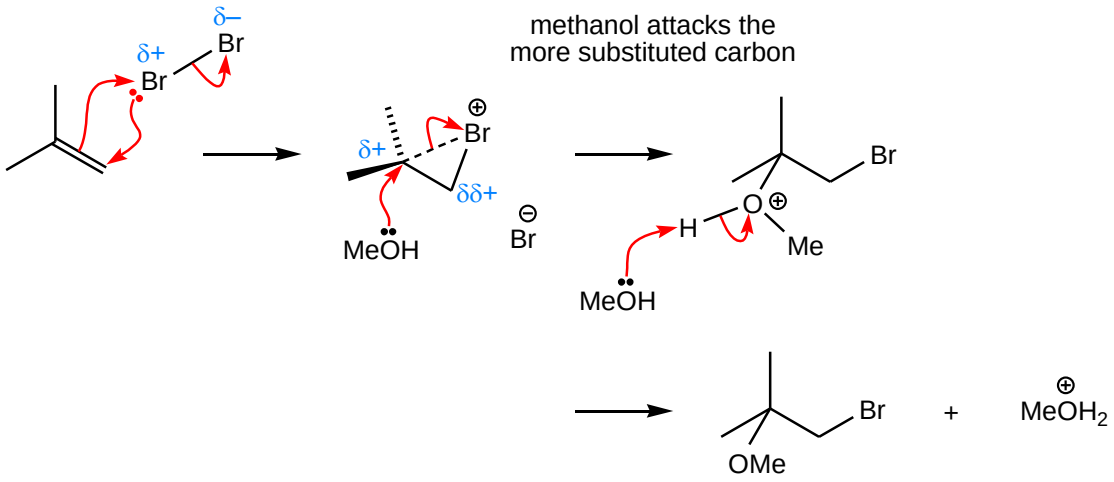
Bromine is generally a good electrophile, and alkenes are good nucleophiles.

Solution

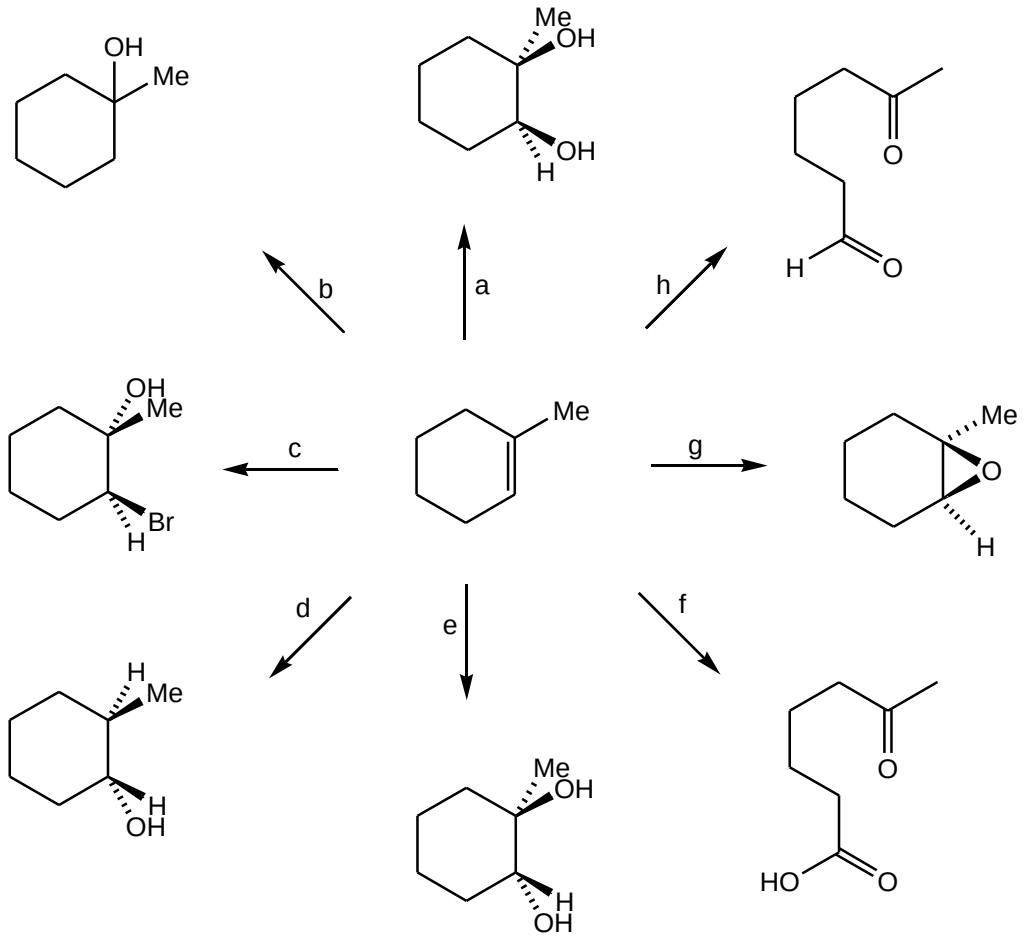
Electrophilic bromination of 2-methylpropene gives an intermediate bromonium ion. Ring-opening this, with the nucleophilic solvent MeOH, at the more substituted and electronically activated position leads to the required product. Competitive ring-opening of this bromonium ion with bromide to give the corresponding 1,2-dibromide is slow due to the lower concentration of bromide (relative to the solvent, MeOH).



Answer



**2.** Suggest reagents (a–h) for the following transformations. More than one step may be required for each transformation. (The relative stereochemistry of these products is shown below, not the absolute stereochemistry.)



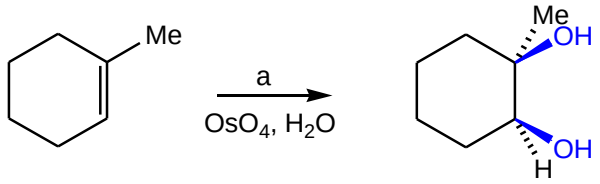

Strategy

Examine each product derived from the reactions (a)-(h), and the starting alkene, 1-methylcyclohexene. Work out if each reaction is an oxidation, reduction or neither, and suggest likely reagents. Pay close attention to the relative stereochemistry of the products derived from reactions a, c, d, e and g.

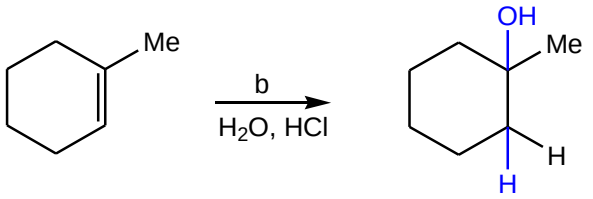
Solution

(a) This reaction is an oxidation and involves *syn*-(same face)-dihydroxylation (addition of two OH groups) of 1-methylcyclohexene. The reagents for this transformation are $OsO_4$ and $H_2O$; the mechanism of this reaction is discussed at length on p. 984 in

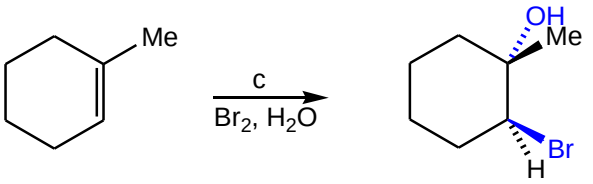
*Chemistry*$^3$. Alternatively, $KMnO_4$ under basic conditions (NaOH, $H_2O$) can be used; see p. 982 in *Chemistry*$^3$ for a comprehensive example of this reaction. For *anti*-(opposite face)-dihydroxylation, see part (e).




(b) This reaction is neither an oxidation nor a reduction; it is an informal disproportionation reaction, where one carbon is oxidised and the other is reduced. The reagents for this transformation are $H_2O$ and mild mineral acid (dilute HCl); the mechanism of this reaction is discussed at length on p. 973 in *Chemistry*$^3$. This reaction is regioselective as the OH group has been added to the more substituted position of this alkene, 1-methylcyclohexene. For the formation of the minor regioisomeric product, see part (d).

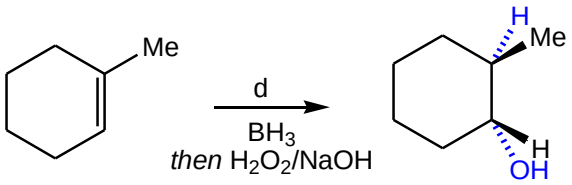



(c) This reaction is an oxidation, and involves the *anti*-addition of OH and Br groups. The reagents for this transformation are $Br_2$ and $H_2O$; the mechanism of this reaction is discussed at length on p. 972 in *Chemistry*$^3$. This reaction is regioselective as the OH group has been added to the more substituted position of this alkene (1-methylcyclohexene) by addition of $H_2O$ to the more substituted and electronically activated position of the intermediate bromonium ion.

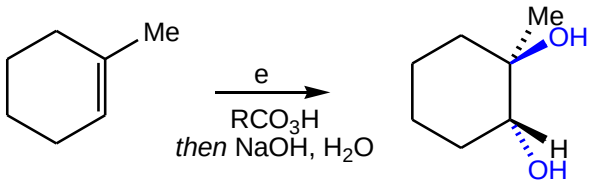



(d) This reaction is neither an oxidation nor a reduction; it is an informal disproportionation reaction, where one carbon is oxidised and the other is reduced. The reagents for this transformation are $BH_3$ (or $B_2H_6$) to form the corresponding borane, followed by oxidative cleavage ($H_2O_2$/NaOH) to give stereospecifically this alcohol; the mechanism of this reaction is discussed at length on p. 975 in *Chemistry*$^3$. This reaction is

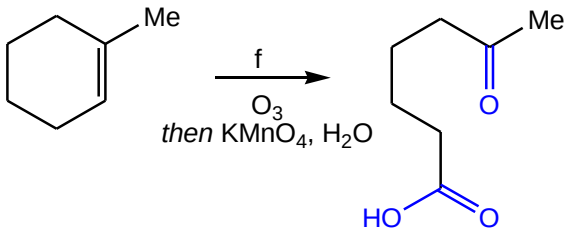
regioselective as the OH group has been added to the less substituted position of this alkene, 1-methylcyclohexene. For the formation of the complementary regioisomeric product, see part (b).




(e) This reaction is an oxidation and involves *anti*-(opposite face)-dihydroxylation (addition of two OH groups) of 1-methylcyclohexene. The reagents for this transformation are peracid, $RCO_3H$, to give the corresponding epoxide, followed by base-catalysed ($NaOH/H_2O$) ring-opening to give the *anti*-1,2-diol; the mechanisms for this reaction are discussed at length on p. 980 in *Chemistry*$^3$. $S_N2$ ring-opening of this intermediate epoxide, with hydroxide, gives the required 1,2-diol with *anti*-stereochemistry. For *syn*-(same face)-dihydroxylation, see part (a).

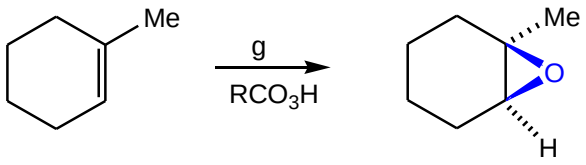



(f) This reaction is an oxidation; it involves oxidative cleavage of this alkene (C=C) group to give a ketone C=O and a carboxylic acid (C=O)OH. The principal reaction in this transformation is **ozonolysis**; the reagents are ozone ($O_3$) (to give the required ketone and an intermediate aldehyde), followed by $KMnO_4$ in $H_2O$ (to oxidise the aldehyde to the carboxylic acid). The mechanisms for this reaction are discussed at length on p. 985 in *Chemistry*$^3$. This reaction can be stopped at the ketone and aldehyde stage by working the reaction up with dimethylsulfide; see part (h).

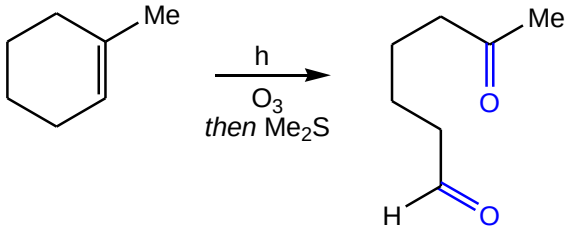



(g) This reaction is an oxidation; it involves epoxidation of the alkene to give an epoxide. The reagent for this transformation is peracid ($RCO_3H$); the mechanism for this reaction

is discussed at length on p. 979 in *Chemistry*$^3$. Epoxides are versatile intermediates in synthesis as they can be converted into *anti*-1,2-diol by simple treatment with aqueous NaOH; see part (e).




(h) This reaction is an oxidation; it involves oxidative cleavage of this alkene (C=C) group to give a ketone C=O and an aldehyde (C=O)H. The principal reaction in this transformation is **ozonolysis**; the reagents are ozone ($O_3$), followed by dimethylsulfide, $Me_2S$, to give the required ketone and an aldehyde. Alternatively, Zn or $PPh_3$ can be used instead of $Me_2S$. The mechanisms for this reaction are discussed at length on p. 985 in *Chemistry*$^3$. This product can be oxidised further, if need be, by treatment with $KMnO_4$ to give the ketone and carboxylic acid, see part (f).




Answer

(a) $OsO_4$, $H_2O$ or $KMnO_4/HO^-/H_2O$ at low temperature

(b) $H^+$, $H_2O$

(c) $Br_2$, $H_2O$

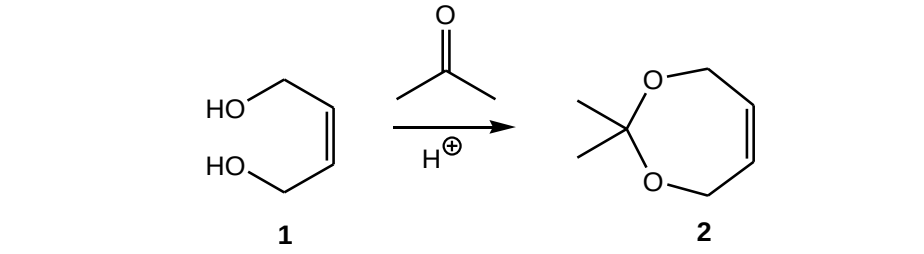
(d) $BH_3$ then $H_2O_2$, $HO^-$

(e) $RCO_3H$ then $H^+$, $H_2O$ (or $HO^-$, $H_2O$)

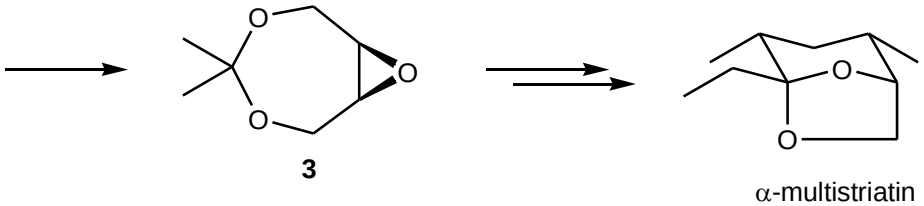
(f) $O_3$ then $H_2O_2$ (or $KMnO_4$, heat)

(g) $RCO_3H$

(h) $O_3$ then $Me_2S$ (Zn or $PPh_3$)




**1** **2**




**3**

(The relative stereochemistry is shown)

α-multistriatin

(A 1:1 mxture of enantiomers)

**3.** An outline of a racemic synthesis of α-multistriatin, a pheromone of the elm bark beetle, is shown below.

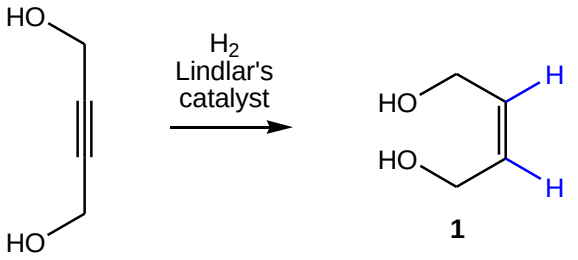
(a) Suggest reagents for a one-step synthesis of **1** from but-2-yne-1,4-diol.

Strategy

Draw out the starting material, but-2-yne-1,4-diol, and deduce what functional groups have changed in this reaction. Work out if this reaction is an oxidation, reduction or neither, and suggest likely reagents. [Remember, more than one reagent may be required for each synthetic step.]

Solution

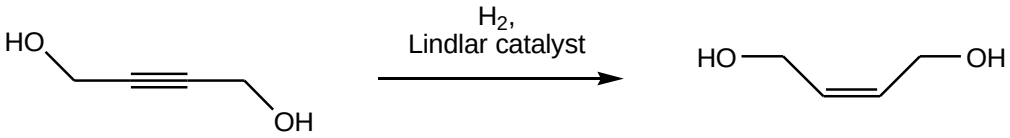
This reaction is a reduction, and must involve the addition of hydrogen across the alkyne group to give the required *cis*-alkene **1**. A transition metal-based catalyst is required, as molecular hydrogen ($H_2$) is inert and **does not** directly add to an alkyne. However, this catalyst must be poorly electrophilic to prevent further reduction of the product, alkene, to give the corresponding alkane. One of the best catalysts for this selective reduction is Lindlar's catalyst (as it contains powdered $CaCO_3$ coated with Pd and poisoned with lead). The required reactions for this step are $H_2$ and Lindlar's catalyst.




but-2-yne-1,4-diol **1**

Answer

$H_2$, Lindlar catalyst



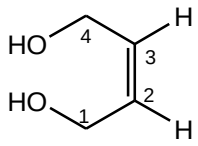

(b) Give the IUPAC name of compound **1**.

Strategy

1. Identify the longest continuous carbon chain. All alkene names end with –ene.
2. Number the carbon atoms starting at the end nearest to a branch point (to ensure the substituents have the lowest possible numbers).
3. Write down the complete name, and ensure that any substituents listed (if any) are in alphabetical order.

Solution

1. The longest continuous carbon chain has FOUR carbon atoms. This molecule is an alkene, it has (*Z*)-stereochemistry, and the double bond is at carbon 2 (→3). Therefore, its suffix is but-2-ene.
2. There are TWO hydroxy groups at carbons-1 and -4.
3. The name of this compound is (*Z*)-but-2-ene-1,4-diol. It is not (*Z*)-1,4-dihydroxybut-2-ene as the suffix –ol has higher priority than –ene.




**1**

(*Z*)-but-2-ene-1,4-diol

Answer

(*Z*)-but-2-ene-1,4-diol

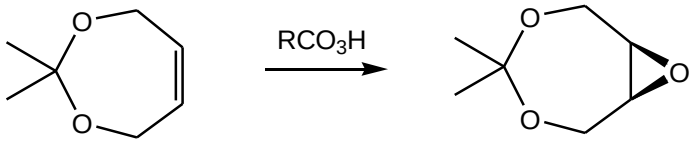
(c) Suggest a reagent for a one-step synthesis of **3** from **2.**

Strategy

Draw out the starting material, **2**, and product, **3**, and deduce what functional groups have changed in this reaction sequence. Work out if this reaction is an oxidation, reduction or neither, and suggest likely reagents. [Remember, more than one reagent may be required for each synthetic step.]

Solution

This reaction is an oxidation; it involves epoxidation of the alkene, **2**, to give the epoxide, **3**. The reagent for this transformation is peracid ($RCO_3H$); the mechanism for this reaction is discussed at length on p. 979 in *Chemistry*$^3$.




**2** **3**

(the relative stereochemistry is shown)

Answer

$RCO_3H$

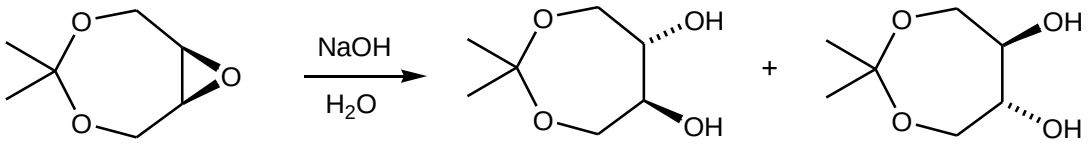
(d) Suggest a structure of the product formed from the reaction of **3** with $HO^-/H_2O$.

Strategy

Work out which reagent is the nucleophile or electrophile. Nucleophiles contain non-bonded electrons (which sometimes can be depicted by a negative charge) and electrophiles have low-lying empty orbitals (which often contain a leaving group). [Remember, drawing a reaction mechanism can sometimes help you decide which pathway is favoured.]

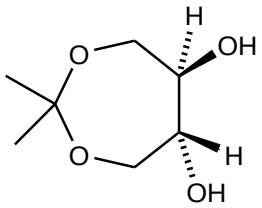
Solution

Hydroxide (HO-) is the nucleophile and the epoxide **3** is the electrophile. [Ring-opening of epoxides to give 1,2-diols can be either acid or base catalysed; the mechanisms for these reactions are discussed at length on p. 980 in *Chemistry*[3].] In this particular example, this process is base-catalysed; nucleophilic addition of hydroxide to the top and bottom carbon atoms of this *meso*-epoxide, **3**, leads to an equimolar mixture of two enantiomeric *anti*-1,2-diols by $S_N2$ ring-opening of the strained epoxide ring. The ketal group in **3** remains unchanged.




**3** 1:1 ratio of enantiomers

Answer



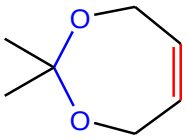

(e) Name the functional groups that is present in compounds **2**, **3**, and α-multistriatin.

Strategy

Carefully consider the functionality of these molecules. It is important to note the alkane backbone of these molecules is not a functional group but a carbon skeleton. A functional group, as its name suggests is a group, which can be functionalised.

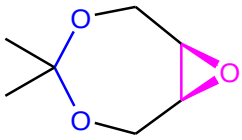
Solution

The common functionality of all these molecules is the ketal group; this functional group is sometimes inadvertently called an acetal group. Molecules **2** and **3** also contain an alkene and an epoxide, respectively.



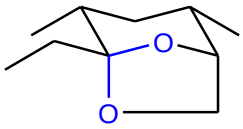
**2**

ketal
alkene



**3**

ketal
epoxide



α-multistriatin

ketal

Answer

A ketal (but sometimes called an acetal).

**4.** Draw the product from reaction of prop-1-yne ($HC{\equiv}CCH_3$) with each of the following reagents

(a) HBr (2 equivalents)

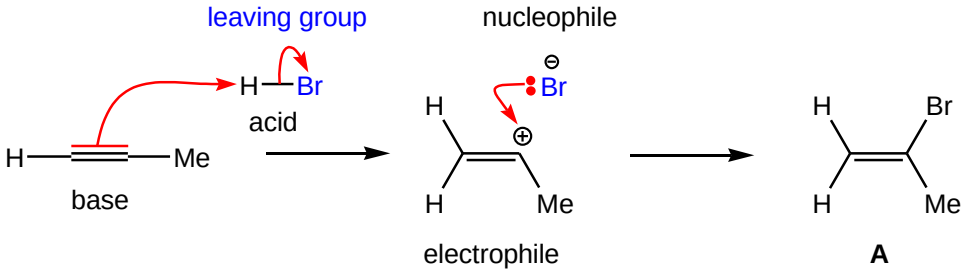
Strategy

From these reagents, prop-1-yne ($HC{\equiv}CCH_3$) and HBr, you will need to decide whether the reaction involves an electrophile/nucleophile or acid/base combination. Acid and base processes involve proton exchange, whereas, electrophile and nucleophile processes involve bond-breaking and bond-making. Draw a curly arrow from the nucleophile or base to the electrophile or acid (→). [Remember, drawing a reaction mechanism can sometimes help you decide which pathway and product is favoured.]

Solution

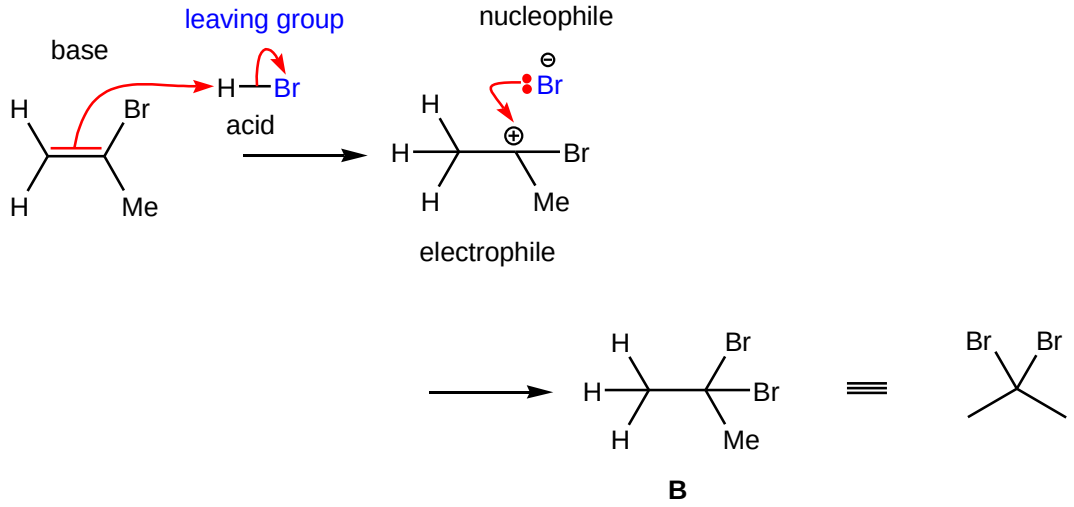
HBr is the acid and prop-1-yne ($HC{\equiv}CCH_3$) is the base. Regioselective protonation of this alkyne, on the less substituted carbon atom, leads to the more stable secondary vinyl carbocation. Nucelophilic addition of the resulting bromide anion to this carbocation, gives the intermediate vinyl bromide **A**. [Note: HBr has been added regioselectively across this alkyne.]

*1st equivalent of HBr*

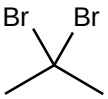



Regioselective addition of the remaining second equivalent of HBr to this vinyl bromide **A** gives the dibromoalkane **B** as the final product. Regioselective protonation of this vinyl bromide occurs on the less substituted carbon atom to give the more stable secondary carbocation, which is stabilised through hyperconjugation (+I effect from Me groups) and resonance (+M effect from the Br atom). These reactions are discussed using related substrates on p. 988 in *Chemistry*[3].

*2nd equivalent of HBr*




Answer




(b) $NaNH_2$ then $PhCH_2Br$ followed by $Na/NH_3$.

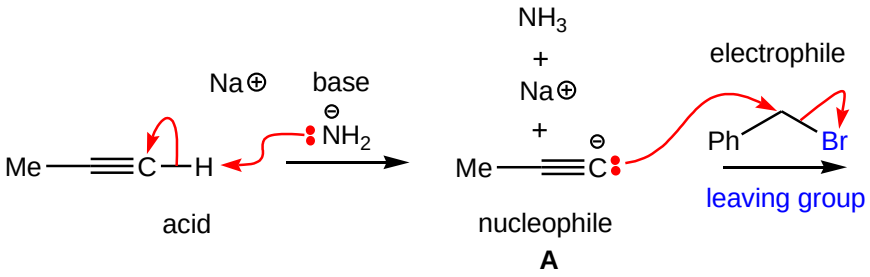
Strategy

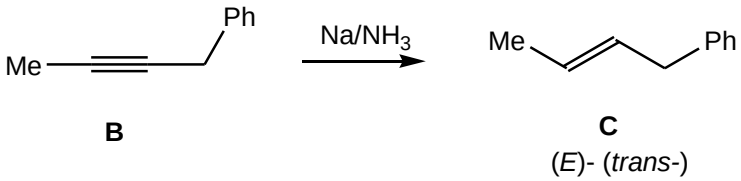
From these reagents, prop-1-yne ($HC{\equiv}CCH_3$) and $NaNH_2$, and so on, you will need to decide whether the reaction involves an electrophile/nucleophile or acid/base combination.

Acid and base processes involve proton exchange, whereas, electrophile and nucleophile processes involve bond-breaking and bond-making. Draw a curly arrow from the nucleophile or base to the electrophile or acid (→). [Remember, drawing a reaction mechanism can sometimes help you decide which pathway and product is favoured.]

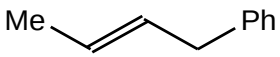
Solution

Sodium amide ($NaNH_2$) is the base, and prop-1-yne ($HC{\equiv}CCH_3$) is the acid. Deprotonation of this terminal alkyne (p$K_a$ 25) using $NaNH_2$ gives the sodium carbanion **A** and $NH_3$. This can be alkylated efficiently with benzyl bromide ($PhCH_2Br$) to give the intermediate di-substituted alkyne **B**. Stereoselective reduction using sodium in ammonia leads to the overall product, *trans*-alkene **C**. These reactions are discussed using related substrates on p. 961 in *Chemistry*[3].




Answer




(c) $NaNH_2$ then EtI followed by $H_2$/Pd/C.

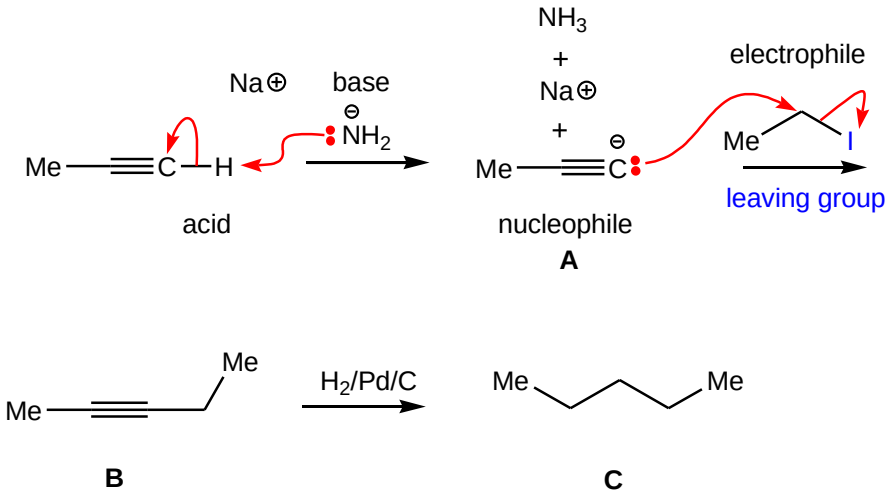
Strategy

From these reagents, prop-1-yne ($HC{\equiv}CCH_3$) and $NaNH_2$, and so on, you will need to decide whether the reaction involves an electrophile/nucleophile or acid/base combination. Acid and base processes involve proton exchange, whereas, electrophile and nucleophile processes involve bond-breaking and bond-making. Draw a curly arrow from the

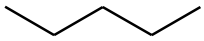
nucleophile or base to the electrophile or acid (→). [Remember, drawing a reaction mechanism can sometimes help you decide which pathway and product is favoured.]

Solution

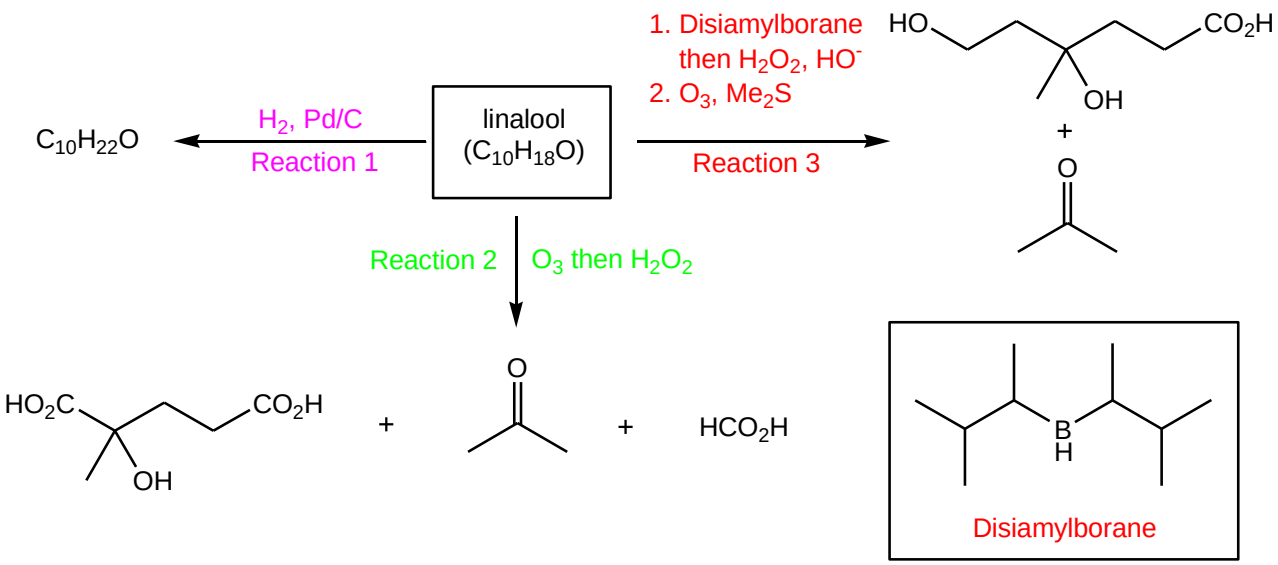
Sodium amide ($NaNH_2$) is the base, and prop-1-yne ($HC{\equiv}CCH_3$) is the acid. Deprotonation of this terminal alkyne ($pK_a$ 25) using $NaNH_2$ gives the sodium carbanion **A** and $NH_3$. This can be alkylated efficiently with ethyl iodide ($MeCH_2I$) to give the intermediate di-substituted alkyne **B**. Reduction of this alkyne, using molecular hydrogen ($H_2$) and palladium-on-carbon (Pd/C), leads to the overall product, hexane **C**. These reactions are discussed using related substrates on p. 961 in *Chemistry*[3].




Answer



**5.** Linalool ($C_{10}H_{18}O$) is found in lavender flowers and is one of the constituents of lavender oil. It has a single chiral centre and both (*R*)- and (*S*)-enantiomers (see p. 839 in *Chemistry*[3]) are found in lavender oil. To determine the structure of linalool, the following reactions were carried out.




(a) Use the information in reaction 1 to determine the number of C=C bonds in linalool.

Strategy

Work out how many equivalents of molecular hydrogen ($H_2$) have been added to linalool, $C_{10}H_{18}O$, to give the product, $C_{10}H_{22}O$. If two (or more) equivalents of molar hydrogen are needed for this reduction, then this could mean than two (or more) double bonds or a triple bond is present.

Solution

Subtracting linalool, $C_{10}H_{18}O$, from the product, $C_{10}H_{22}O$, reveals that "$H_4$" or "$2 \times H_2$" has been added. Linalool must contain either two double C=C bonds or a triple C≡C bond. Alternatively, this can be determined from the number of double bond equivalents present in the molecular formula of linalool, $C_{10}H_{18}O$; the formula for calculating this is on p. 598 in *Chemistry*$^3$. Using this formula, there are two double bond equivalents in linalool. Assuming these are double bonds and not a triple bond (from reaction 2), there are two double bonds in linalool.

Answer

On catalytic hydrogenation, four hydrogen atoms add to linalool. This tells you that there are two C=C bonds in linalool.

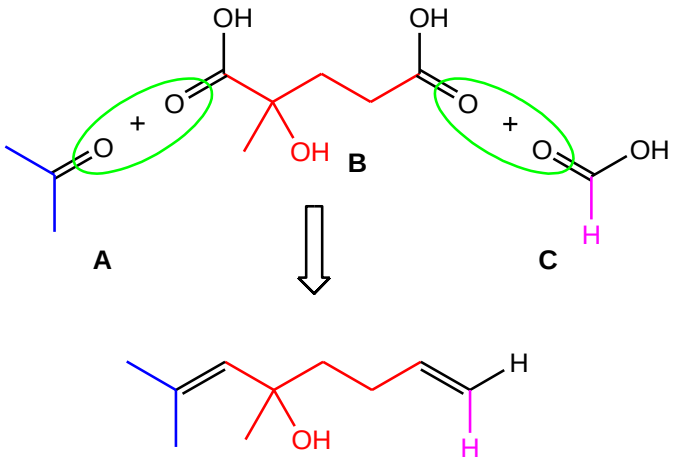
(b) From the products in reaction 2, what are the two possible structures of linalool?

Strategy

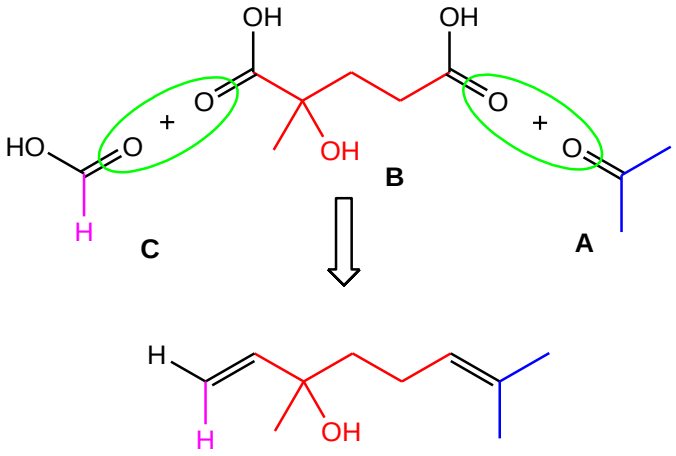
Reaction 2 is an oxidative ozonolysis ($O_3$, *then* $H_2O_2$); each carbon-carbon double (C=C) bond will be converted into two carbonyl groups (C=O + O=C). From this reaction, there must be an even number of carbonyl groups formed. If one (or more) of the resulting carbonyl groups is an aldehyde, this will be oxidised to a carboxylic acid. A ketone group will remain unchanged under these oxidative reaction conditions.

Solution

From the three products, there are four carbonyl groups; three carboxylic acid groups and one ketone group. The tertiary alcohol must have originally been present in the structure of linalool. Reconnecting these four carbonyl groups together from these three molecules, **A**, **B** and **C**, in an **ABC** and a **CBA** fashion, gives the two potential structures of linalool, **D** and **E**, respectively.



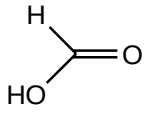

potential structure **D**



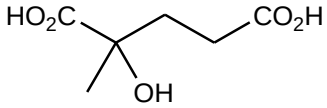

potential structure **E**

Answer

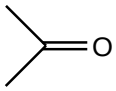
The two C=C bonds are cleaved under oxidising conditions to give three products.



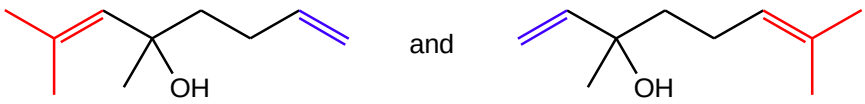

produced from a terminal $H_2C$=C group




produced from the central part of the molecule




produced from a terminal $Me_2C$=C group




(c) Use the information in reaction 3 to determine the structure of linalool. (*Hint*: disiamylborane reacts with the C=C bond.)

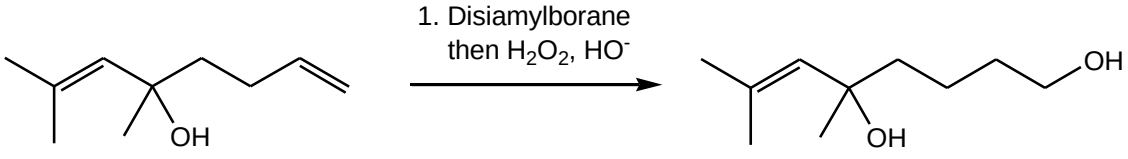
Strategy

Reaction 3 is a two step procedure. Step 1 involves oxidative hydroboration (disiamylborane, *then* $H_2O_2/HO^-$); this procedure will result in the hydration of the less sterically demanding alkene by an *anti*-Markovnikov addition. For additional information about this procedure and its mechanism, see p. 975 in *Chemistry*$^3$. Step 2 involves ozonolysis ($O_3$, *then* $Me_2S$); each carbon-carbon double (C=C) bond will be converted into two carbonyl groups (C=O + O=C). From this reaction, there must be an even number of carbonyl groups formed, and under these "neutral" conditions, the aldehyde group will remain unchanged.

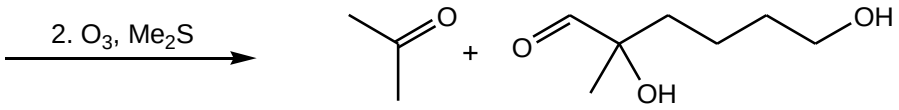
Solution

Oxidative hydroboration of the terminal alkenes in **D** and **E** with the steric demanding disiamylborane, followed by oxidative cleavage of the resulting C-B bonds, with $H_2O_2/HO^-$, gives the primary alcohols in **F** and **H**, respectively. Ozonolysis of the remaining trisubstituted alkenes in **F** and **H** with $O_3$, followed by $Me_2S$, gives the di-hydroxy aldehydes **G** and **I**, respectively, and acetone. From the answer given in the question above, the structure of linalool must be **E**, as this leads to the required products, acetone and di-hydroxy aldehyde **I**. These synthetic sequences are given below for both proposed structures of linalool, **D** and **E**.

*Reaction 3 for proposed structure **D***

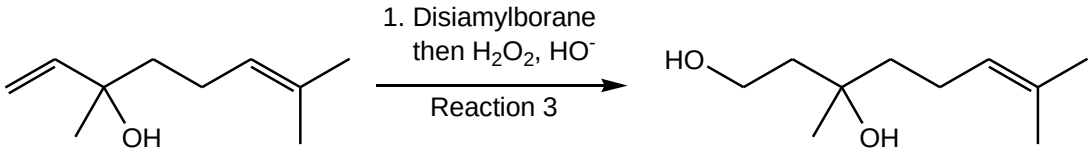



Potential structure **D** **F**

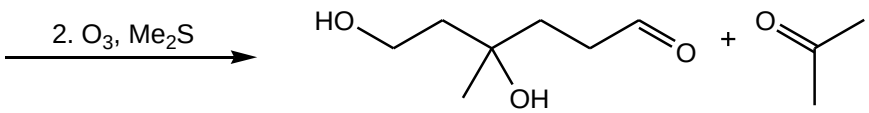



**G**

*Reaction 3 for proposed structure **E***



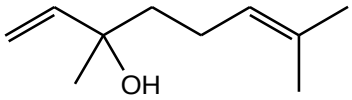

Potential structure **E** **H**




**I**

Answer

In reaction 3, hydration of the less substituted C=C bond (step 1) is followed by oxidative cleavage of the more substituted C=C bond (step 2). (Notice that disiamylborane has a single B–H bond, so it can only add to one C=C bond).



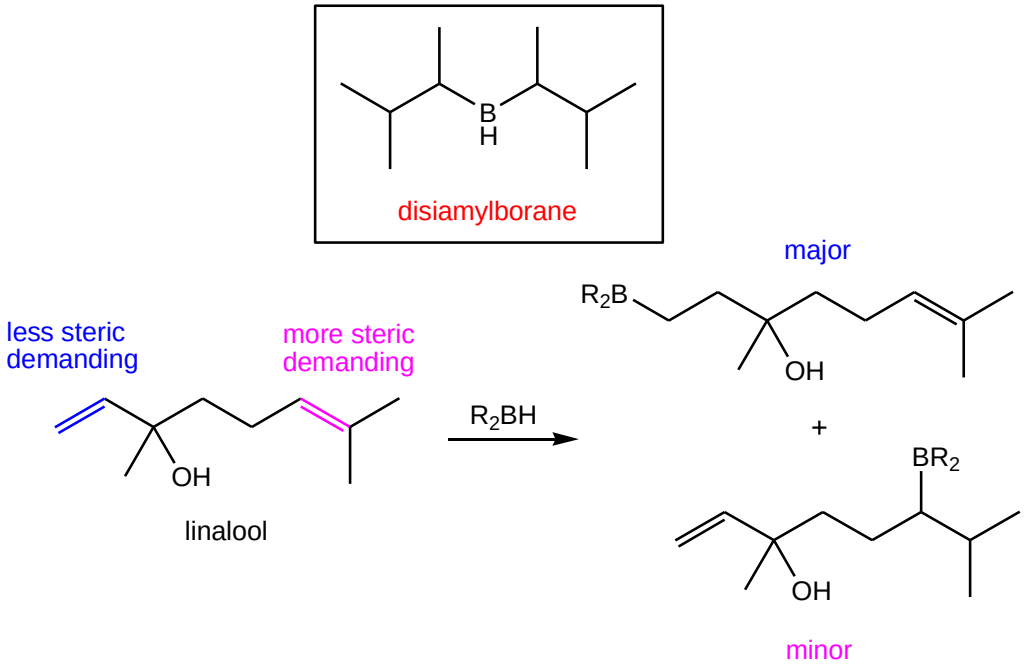

(d) Explain why the reaction of disiamylborane with linalool is chemoselective. (*Hint*: Consider the size of disiamylborane.)

Strategy

For a step to be chemoselective (or chemical selective), the reagent must be able to distinguish between chemicals through reactivity, and it must be selective; *i.e.*, **chemoselective**. If there is a product **choice** within the reaction, then it will always be **selective**.

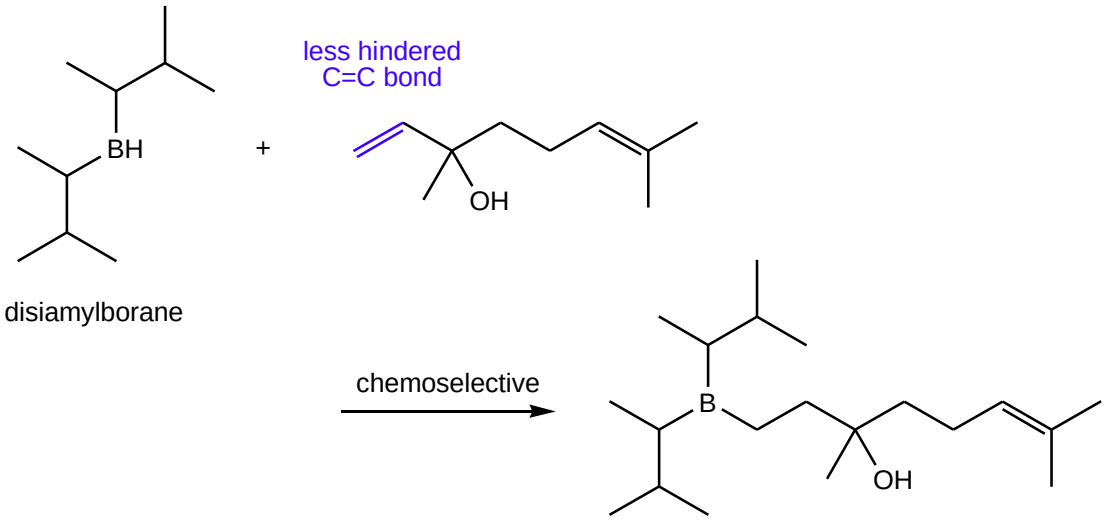
Solution

This hydroboration is chemoselective as it occurs on the less steric demanding mono-substituted alkene and NOT on the more hindered tri-substituted alkene. The use of a large and bulky borane, like disiamylborane, ensures that the chemoselectivity for this reaction is high (>99:1).




Answer

In linalool, one C=C bond is mono-substituted and the other C=C bond is tri-substituted. In reaction 3, the mono-substituted C=C bond in linalool reacts selectively with disiamylborane (a bulky borane) because this C=C bond is less substituted and so there is less steric hindrance.




Solutions provided by J. Eames (j.eames@hull.ac.uk)