

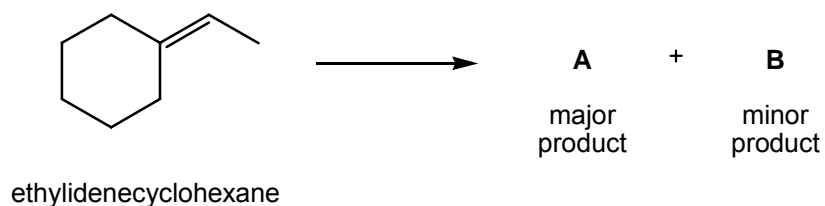
21

Alkenes and alkynes: electrophilic addition and pericyclic reactions

Answers to worked examples

WE 21.1 Forming structural isomers by addition reactions (on p. 968 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**.



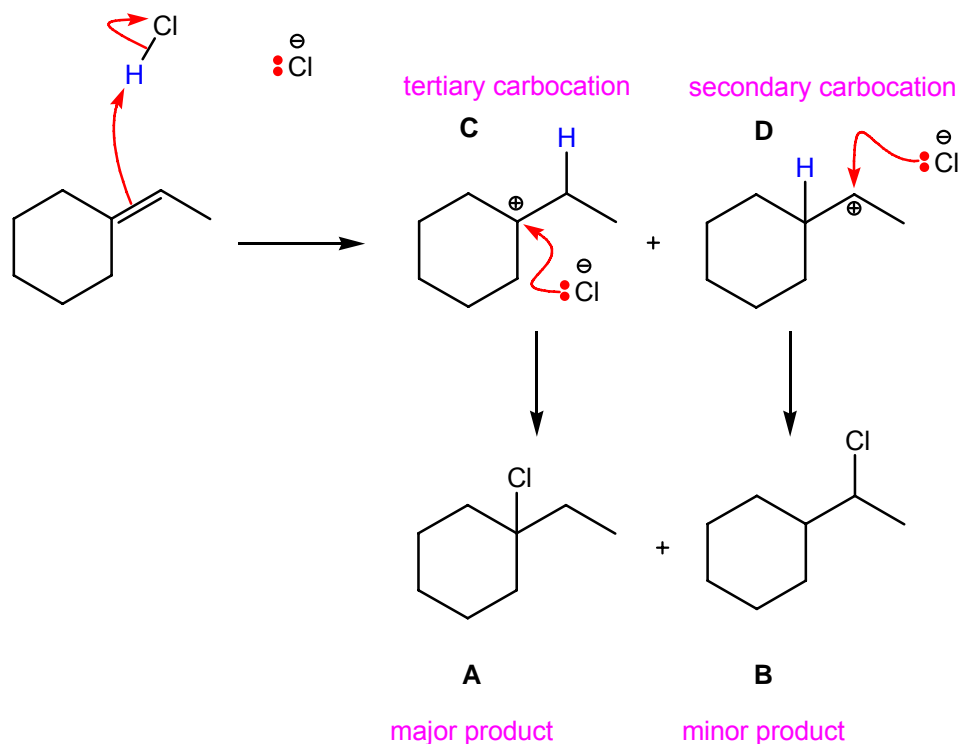
Strategy

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. 968 in *Chemistry*³.

Solution

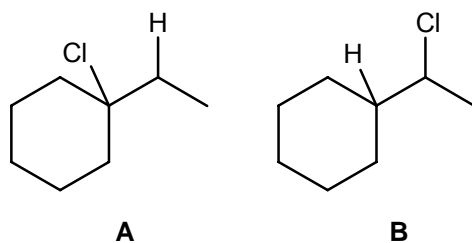
Protonation of ethylidenecyclohexane with H-Cl leads to two carbocations, **C** and **D**. The tertiary carbocation, **C**, is more stable than the isomeric secondary carbocation, **D**, because

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 $\text{C}=\text{C}$ 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 21.3 Selectivities in hydroboration–oxidation reactions (on p. 980 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

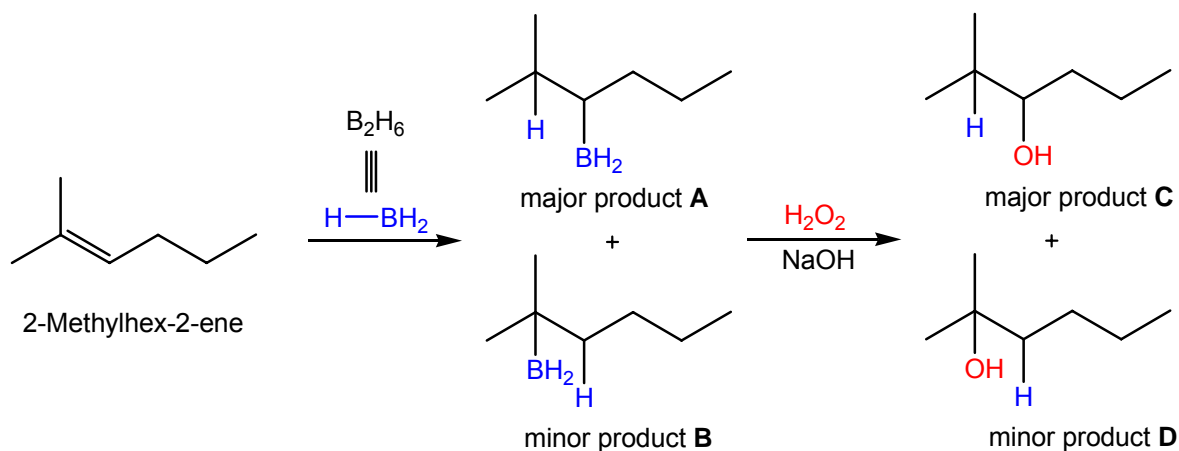
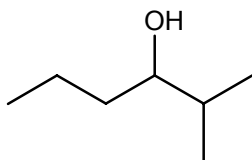
Draw out the structure of 2-methylhex-2-ene and borane (the active component of diborane). Addition of an unsymmetrical reagent, such $\text{BH}_2\text{-H}$, to an unsymmetrical alkene, like 2-methylhex-2-ene, gives two isomeric borane products in an unequal amount. [Drawing a reaction mechanism can 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 (\rightarrow).]

Draw the structure of the major borane product. A related process is given on p. 980 in *Chemistry*³.

In the second step, addition of $\text{H}_2\text{O}_2/\text{NaOH}$ to these boranes, stereospecifically converts the borane “C-BH₂” 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 $\text{H}_2\text{O}_2/\text{NaOH}$, 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. 978 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).

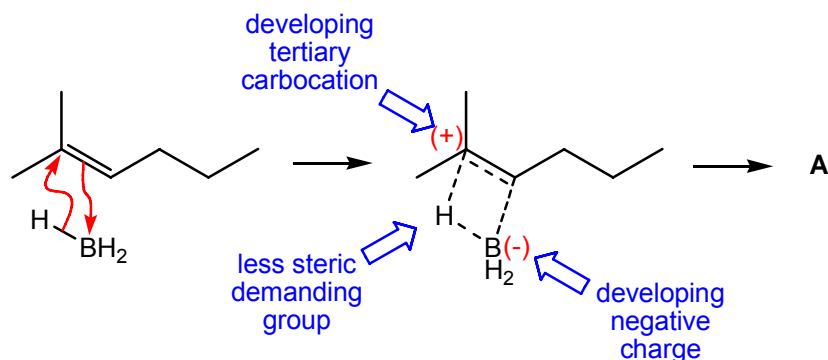
Step 2: oxidative cleavage of boranes **A** and **B** with $\text{H}_2\text{O}_2/\text{NaOH}$.

This step does not involve regiochemistry and can be ignored.

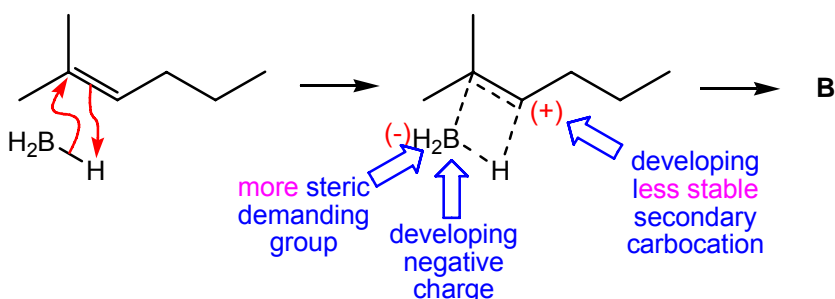
Step 1 is regioselective as addition of an unsymmetrical reagent, such as borane, across an unsymmetrical alkene, like 2-methylhex-2-ene leads to two substituted boranes **A** and **B** (ratio >99:1). This addition process is highly regioselective in favour of borane **A**, as its

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

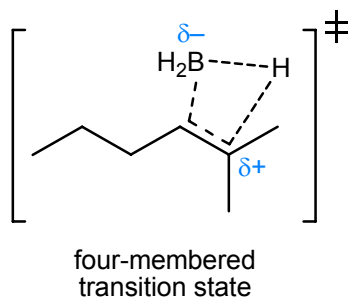


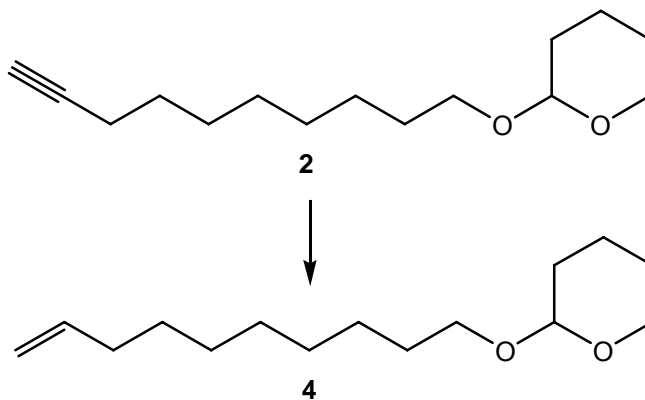
Formation of the minor borane B



Answer

The hydration is regioselective. BH_3 adds to the unsymmetrical $\text{C}=\text{C}$ 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 $\text{C}-\text{B}$ bond that is formed is subsequently converted into a $\text{C}-\text{OH}$ bond on reaction with $\text{H}_2\text{O}_2/\text{HO}^-$.

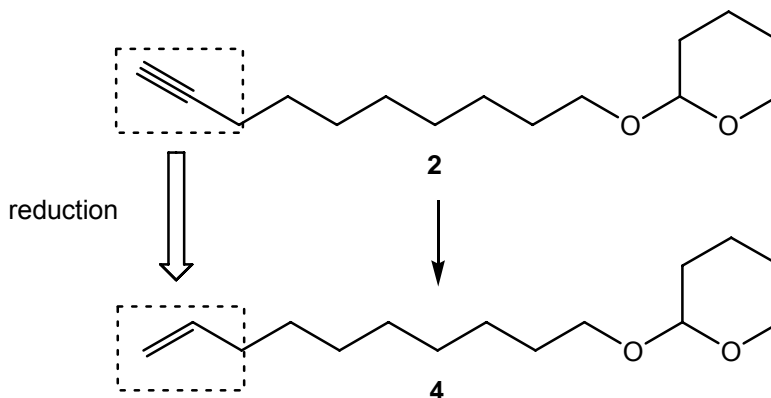


WE 21.5 Synthesis of a pheromone (on p. 991 in *Chemistry*³)Suggest reagents for converting alkyne **2** into compound **4**.Strategy

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 ($-\text{C}\equiv\text{C}-$) to an alkene ($-\text{CH}=\text{CH}-$). Simple hydrogenation (H_2 , Pd) gives access to this alkene; however, over reduction of this alkene leads to corresponding alkane ($-\text{CH}_2-\text{CH}_2-$). 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

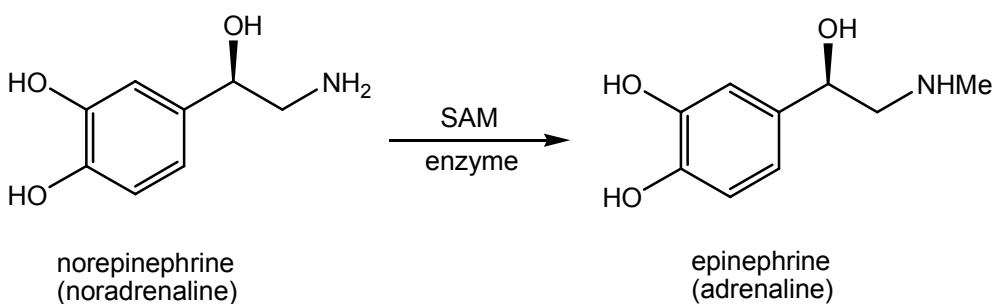
Conversion of molecules **2** → **4**: H₂, Lindlar's catalyst.

Answers to boxes

Box 21.1 Ethene production in plants (on p. 961 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. 925 in *Chemistry*³) to help you propose a mechanism.]

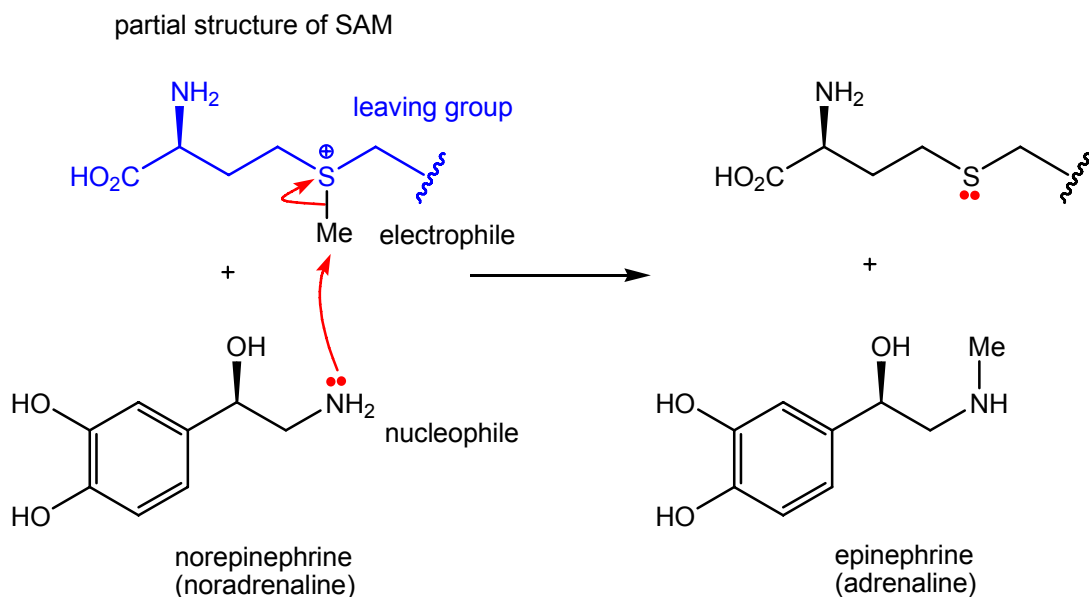


Strategy

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 (\rightarrow) 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.

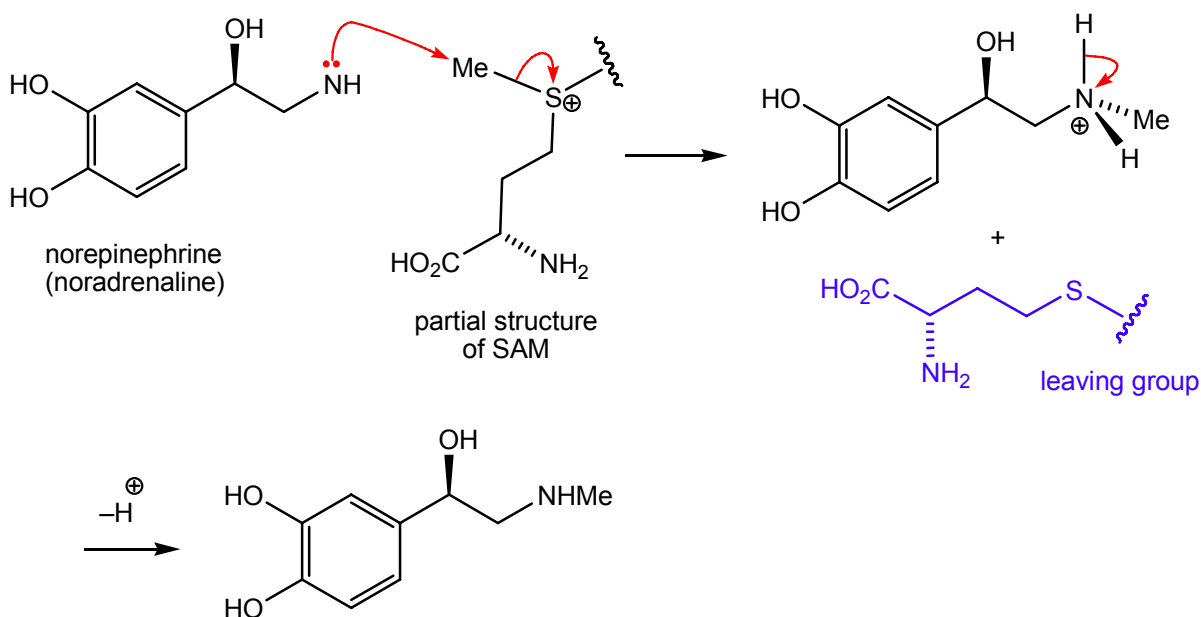
Solution

Methylation occurs on the amino-group of norepinephrine; the overall transformation is $-\text{NH}_2 \rightarrow -\text{NHMe}$. 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

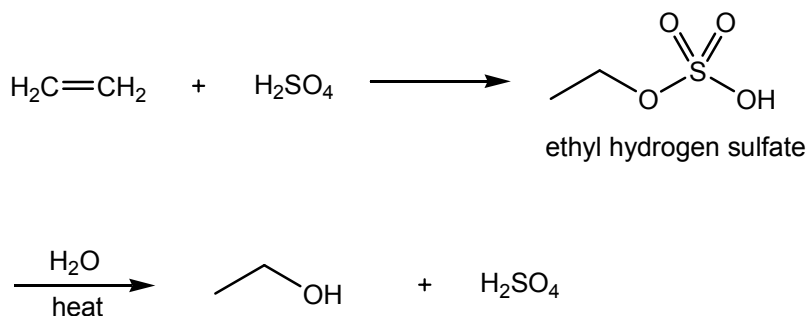


SAM is a reactive alkylating agent because (a) it is positively charged (the positively charged S atom attracts electrons away from the $-Me$ group, making it a good

electrophile and susceptible to attack by the nucleophilic $-\text{NH}_2$ group; and (b) the alkylation produces a stable neutral leaving group.

Box 21.3 Making ethanol on a large scale (on p. 976 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.

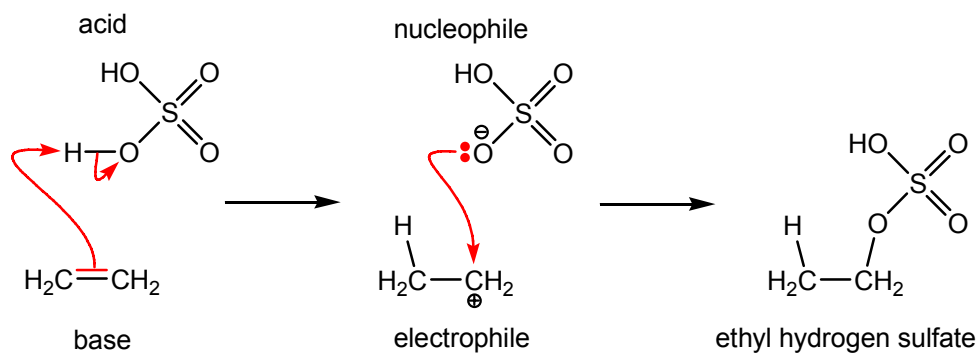


Strategy

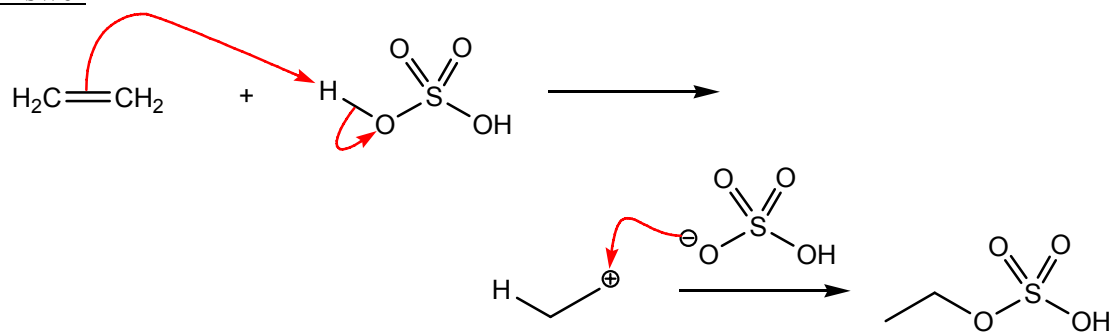
For each step, you will need to decide whether the reaction involves an electrophile/nucleophile or acid/base combination. Acid and base processes involve proton exchange, whereas, electrophile and nucleophile processes involve bond-breaking and bond-making. Draw a curly arrow from the nucleophile or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

Solution

The first step must involve an acid/base combination, as sulfuric acid (H_2SO_4) is the acid and ethene ($\text{CH}_2=\text{CH}_2$) is the base. The second step involves an electrophile/nucleophile combination. This mechanism is shown below.

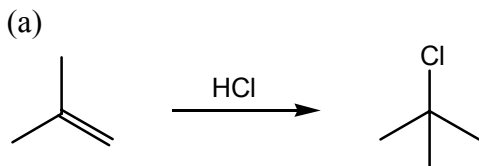


Answer



Answers to end of chapter questions (on p. 994 in *Chemistry*³)

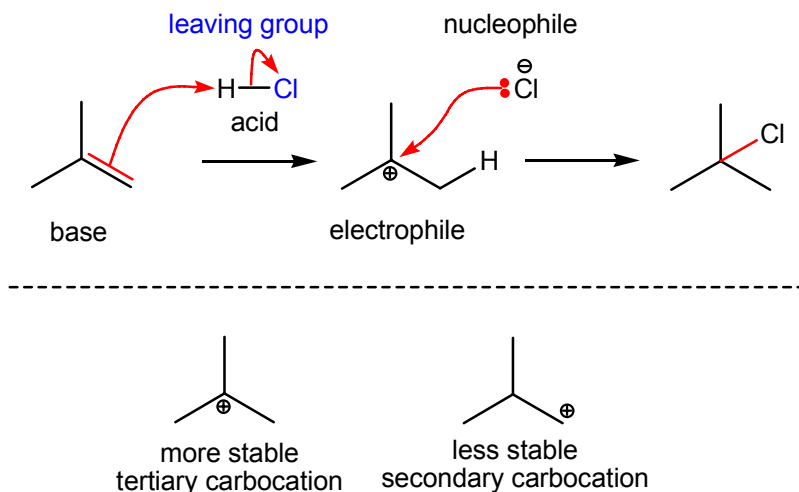
1. Suggest mechanisms for the following electrophilic addition reactions.

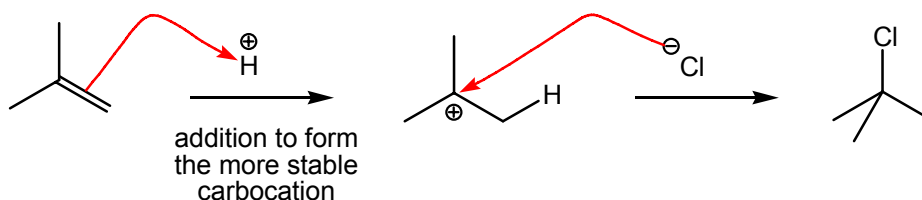
Strategy

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 (\rightarrow).

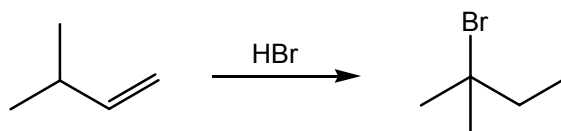
Solution

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)

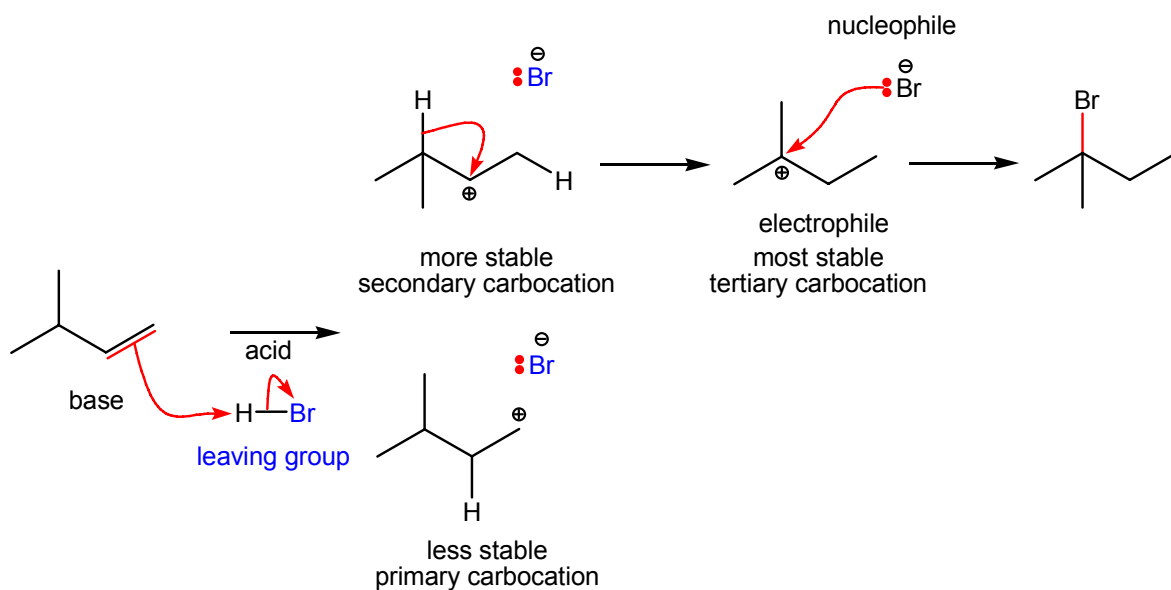
Strategy

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 (\rightarrow).

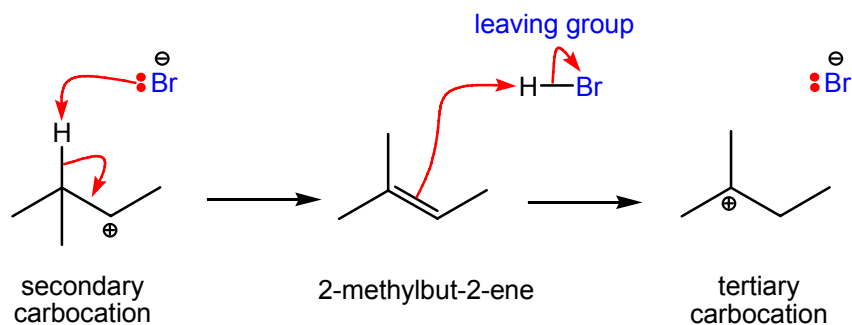
There may be a rearrangement in this reaction, as the hydrocarbon skeleton has changed; the original C-H bond has been replaced with a C-Br bond, and the alkene has been reduced! Do not overly focus on a potential rearrangement; let the “curly arrows” guide you through this mechanism.

Solution

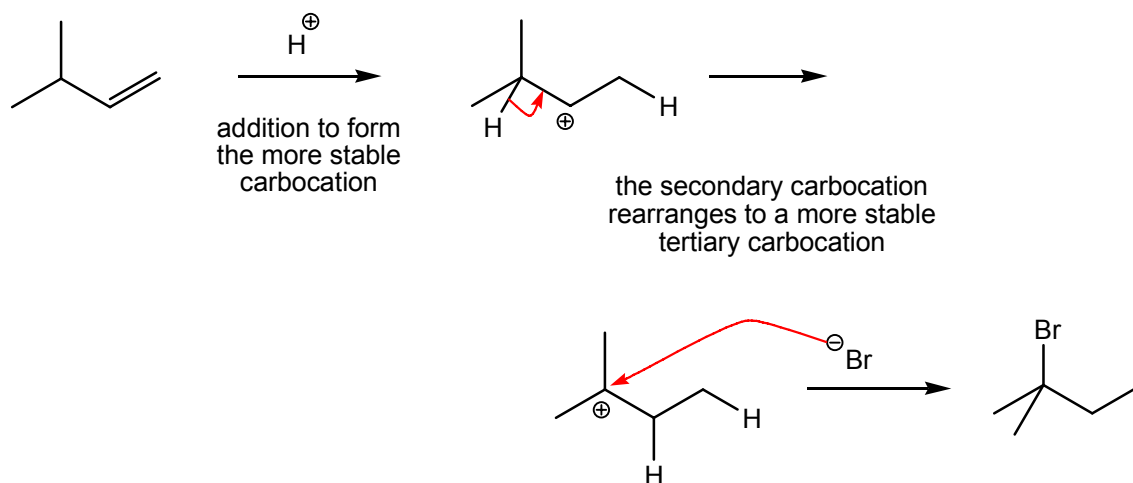
The alkene acts as the base, H-Br acts as the acid, and the bromide anion, Br^- , as the leaving group. Protonation of this unsymmetrical alkene leads to the more substituted secondary carbocation; competitive formation of the less substituted and less stable primary carbocation does not occur. Formation 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.



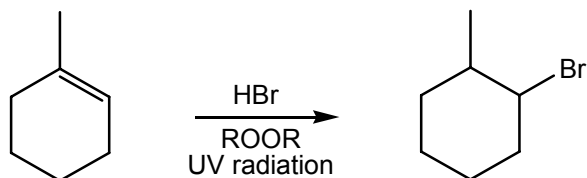
Rearrangement of this secondary carbocation to the more stable tertiary carbocation could also occur by a deprotonation-reprotonation mechanism, as outlined below.



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 (\rightarrow) and a single headed arrow for a radical (\square).

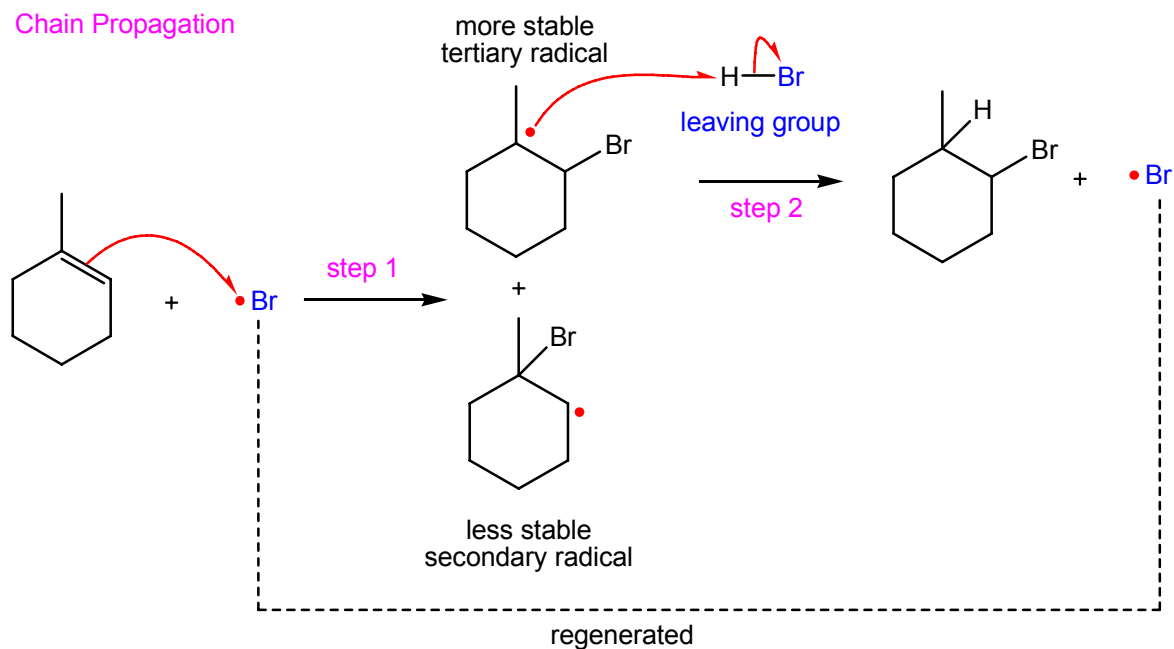
Look at the reaction conditions as these might give you a clue; this reaction involves an organic peroxide with UV radiation. More than likely this reaction will involve radical bromination.

Solution

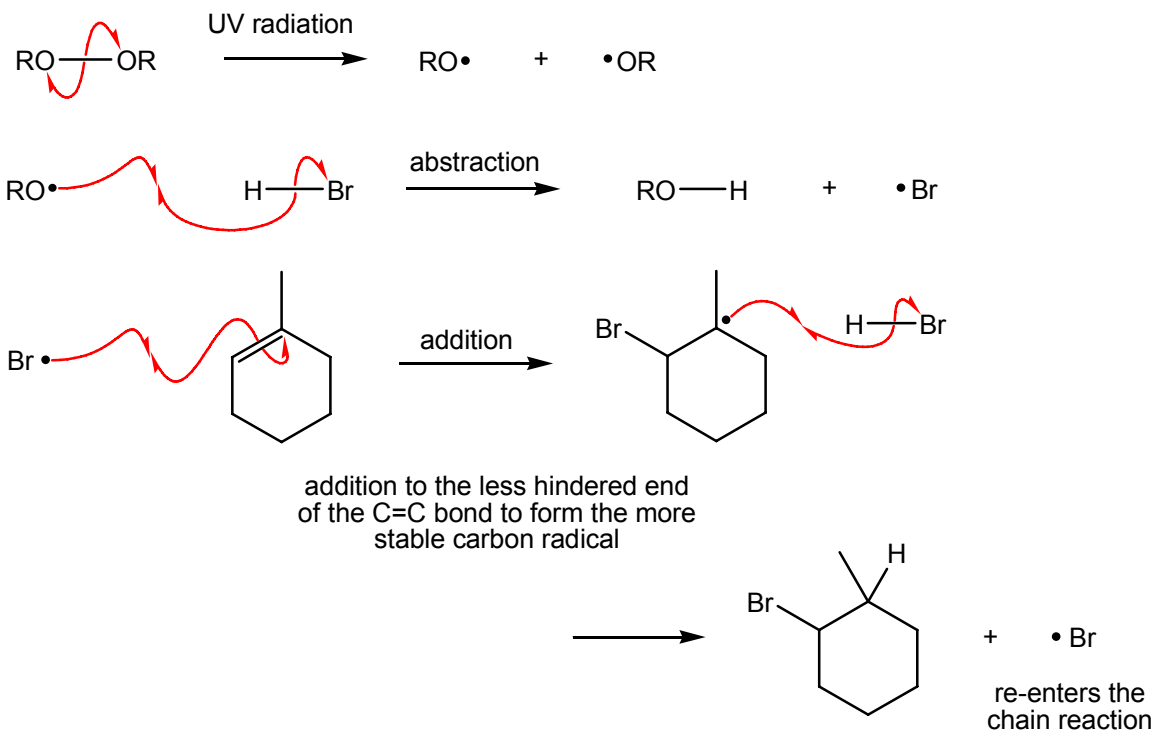
The product forming step is the propagation step. If you need to recap, the initiation and termination steps for radical addition of HBr across an alkene see p. 969 in *Chemistry*³.

In the first propagation step, radical bromination of 1-methylcyclohexene with $\text{Br}\cdot$ 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.

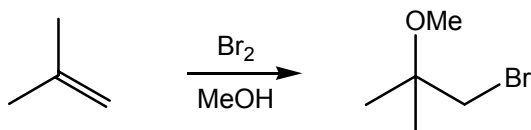
Chain Propagation



Answer



(d)

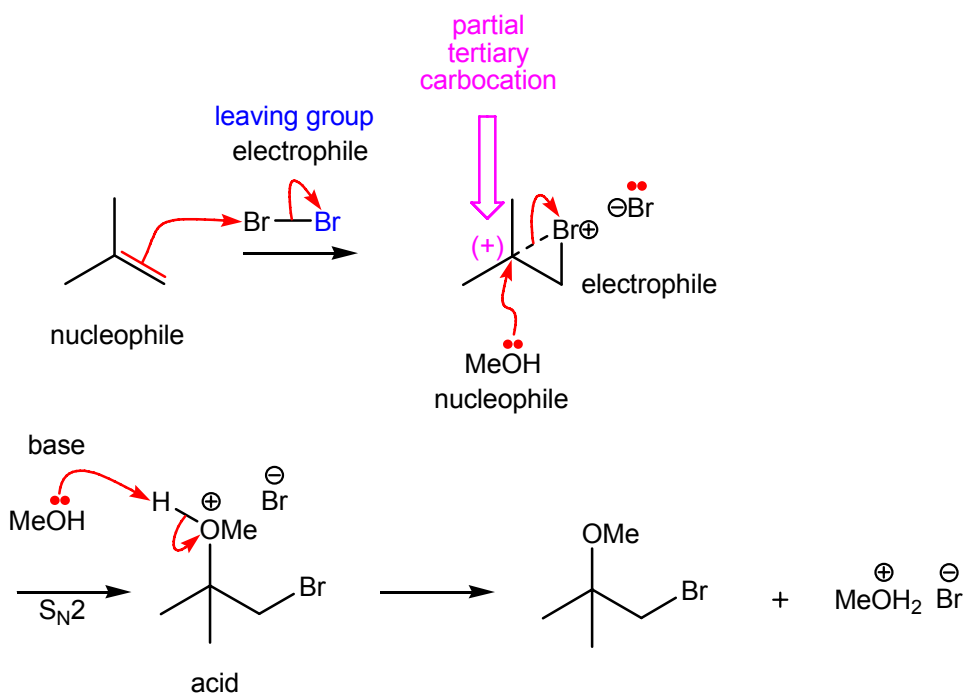
Strategy

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 (\rightarrow).

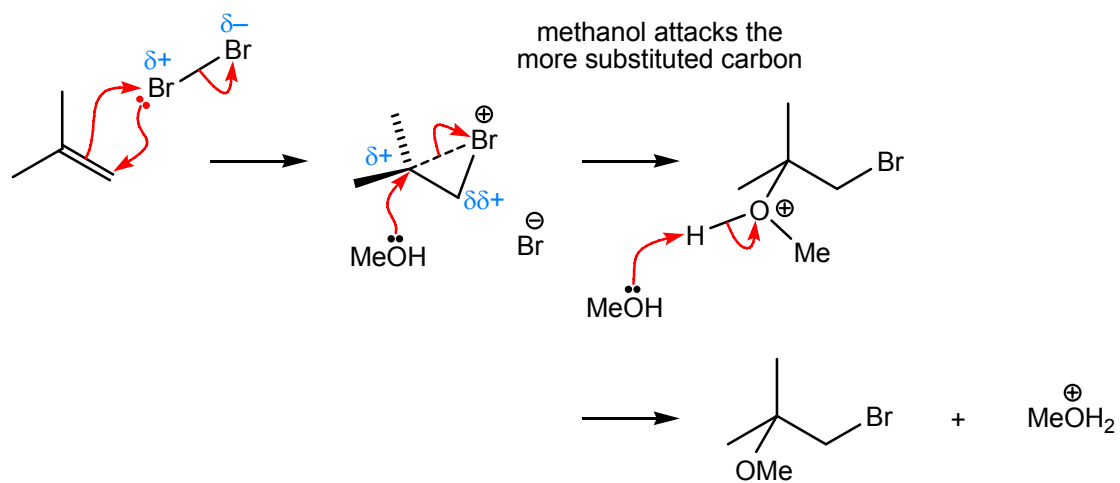
Bromine is generally a good electrophile, and alkenes are good nucleophiles.

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



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

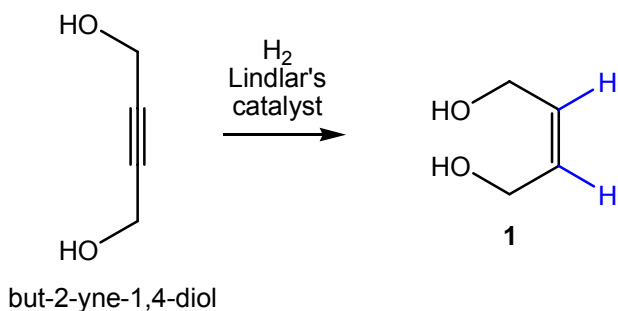
(a) Suggest reagents for a one-step synthesis of **1** from but-2-yne-1,4-diol.

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.]

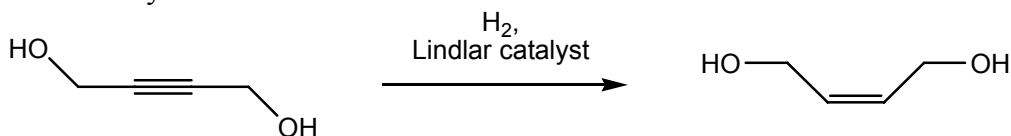
Solution

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.



Answer

H_2 , Lindlar catalyst



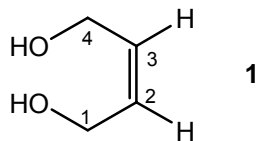
(b) Give the IUPAC name of compound **1**.

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.



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

Answer

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

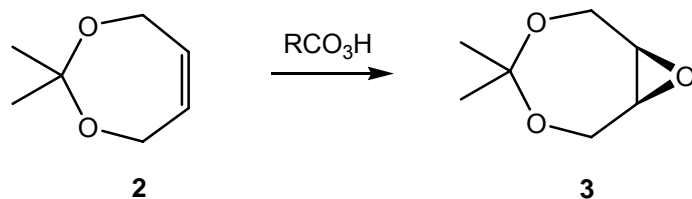
(c) Suggest a reagent for a one-step synthesis of **3** from **2**.

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. 981 in *Chemistry*³.



(the relative stereochemistry is shown)

Answer

RCO_3H

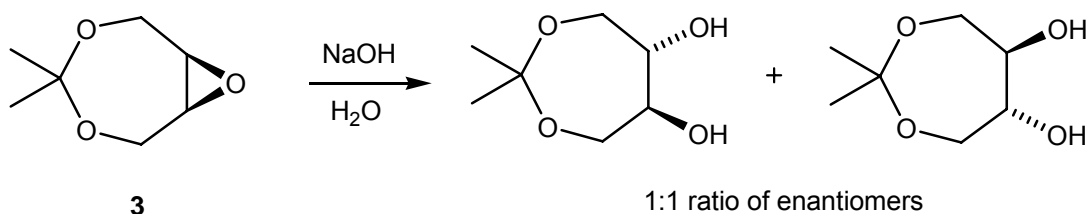
(d) Suggest a structure of the product formed from the reaction of **3** with $\text{HO}^-/\text{H}_2\text{O}$.

Strategy

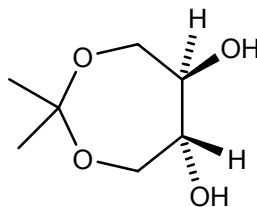
Work out which reagent is the nucleophile or electrophile. Nucleophiles contain non-bonded electrons (which sometimes can be depicted by a negative charge) and electrophiles have low-lying empty orbitals (which often contain a leaving group). [Remember, drawing a reaction mechanism can sometimes help 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. 982 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 $\text{S}_{\text{N}}2$ ring-opening of the strained epoxide ring. The ketal group in **3** remains unchanged.



Answer



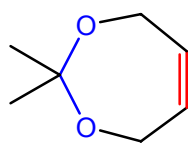
(e) Name the functional groups that is present in compounds **2**, **3**, and α -multistriatin.

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.

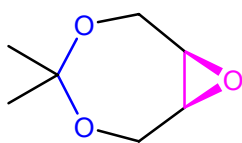
Solution

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.



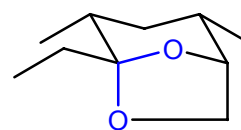
2

ketal
alkene



3

ketal
epoxide



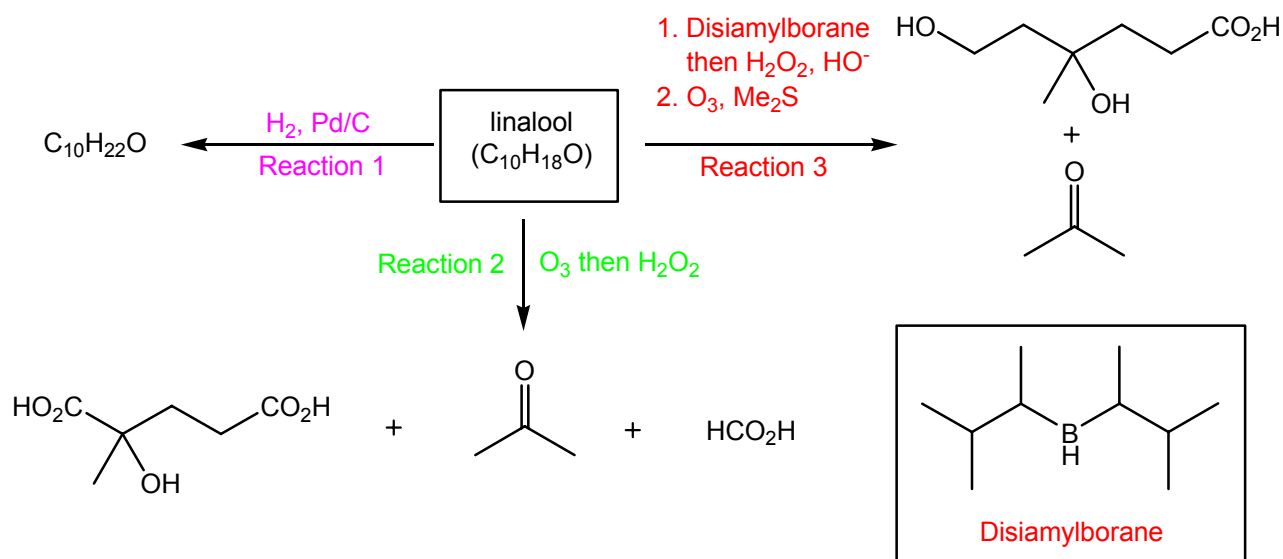
α -multistriatin

ketal

Answer

A ketal (but sometimes called an acetal).

4. 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. 480 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, $\text{C}_{10}\text{H}_{18}\text{O}$, to give the product, $\text{C}_{10}\text{H}_{22}\text{O}$. If two (or more) equivalents of molar hydrogen are needed for this reduction, then this could mean that two (or more) double bonds or a triple bond is present.

Solution

Subtracting linalool, $\text{C}_{10}\text{H}_{18}\text{O}$, from the product, $\text{C}_{10}\text{H}_{22}\text{O}$, reveals that “ H_4 ” or “ $2 \times \text{H}_2$ ” 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, $\text{C}_{10}\text{H}_{18}\text{O}$; the formula for calculating this is on p. 649 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.

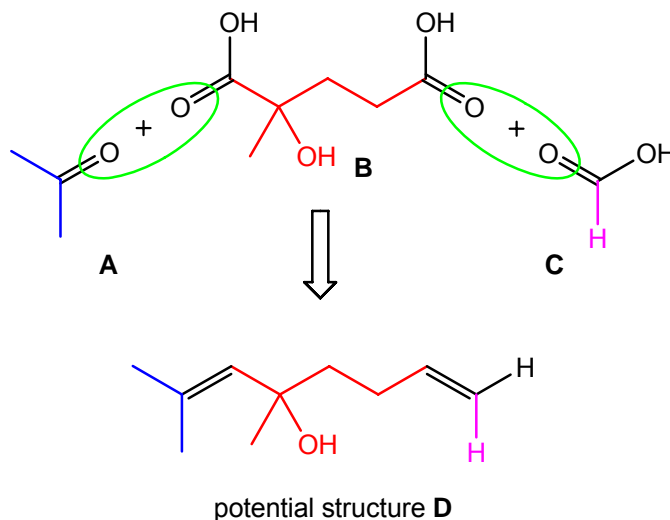
(b) From the products in **reaction 2**, what are the two possible structures of linalool?

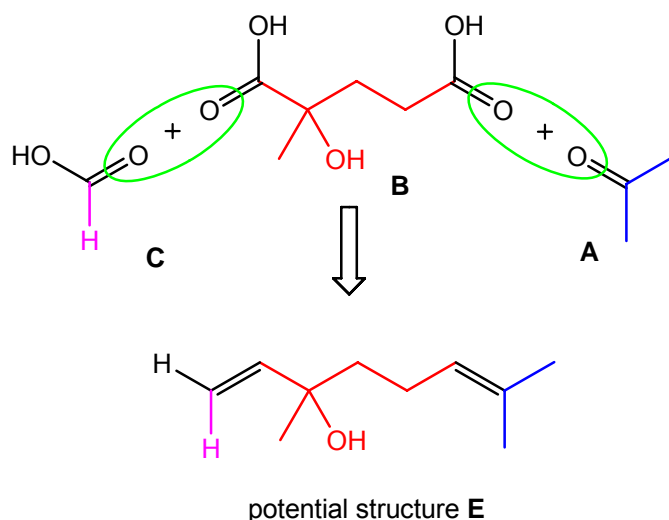
Strategy

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.

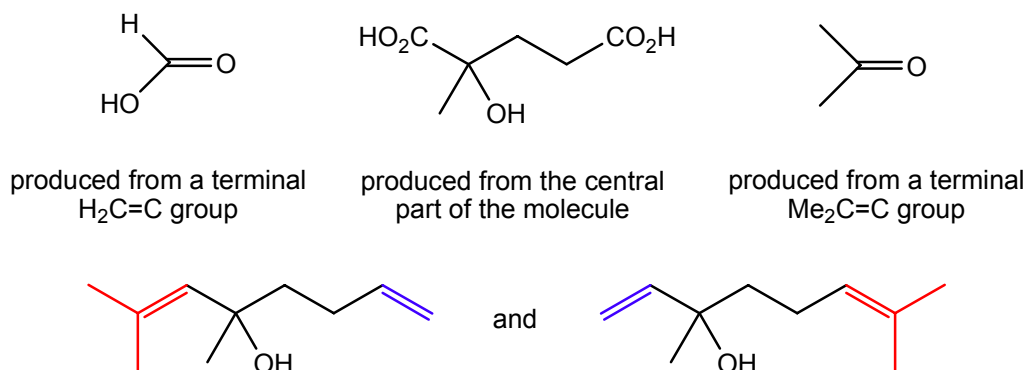
Solution

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.



Answer

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



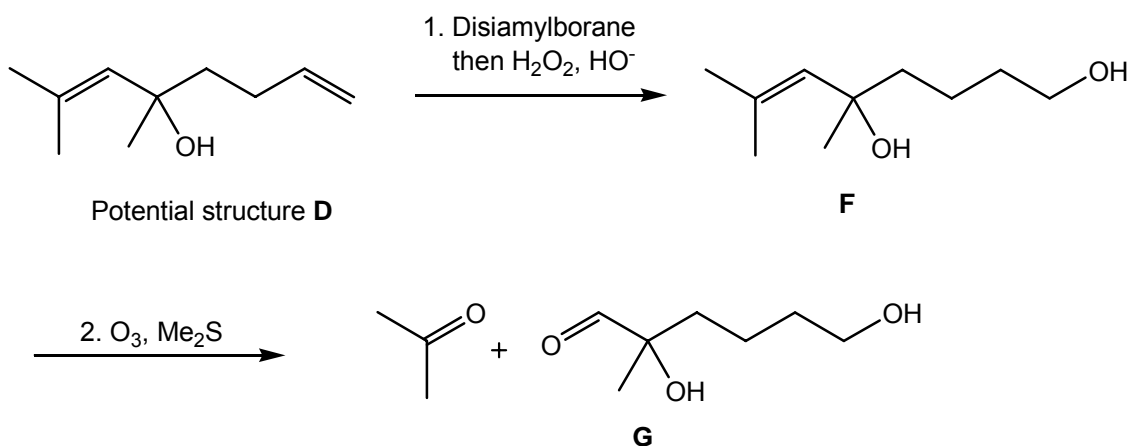
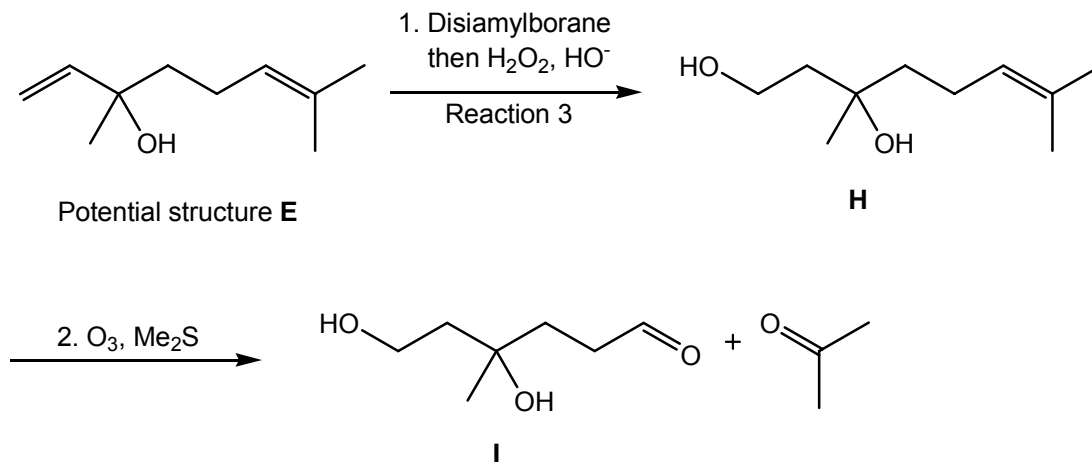
- (c) Use the information in **reaction 3** to determine the structure of linalool. (*Hint*: disiamylborane reacts with the C=C bond.)

Strategy

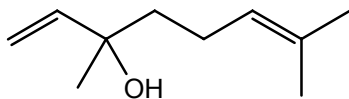
Reaction 3 is a two step procedure. Step 1 involves oxidative hydroboration (disiamylborane, *then* H₂O₂/HO⁻); this procedure will result in the hydration of the less sterically demanding alkene by an *anti*-Markovnikov addition. For additional information about this procedure and its mechanism, see p. 977 in *Chemistry*³. Step 2 involves ozonolysis (O₃, *then* Me₂S); 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 $\text{H}_2\text{O}_2/\text{HO}^-$, 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 dihydroxy 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*Reaction 3 for proposed structure E*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).



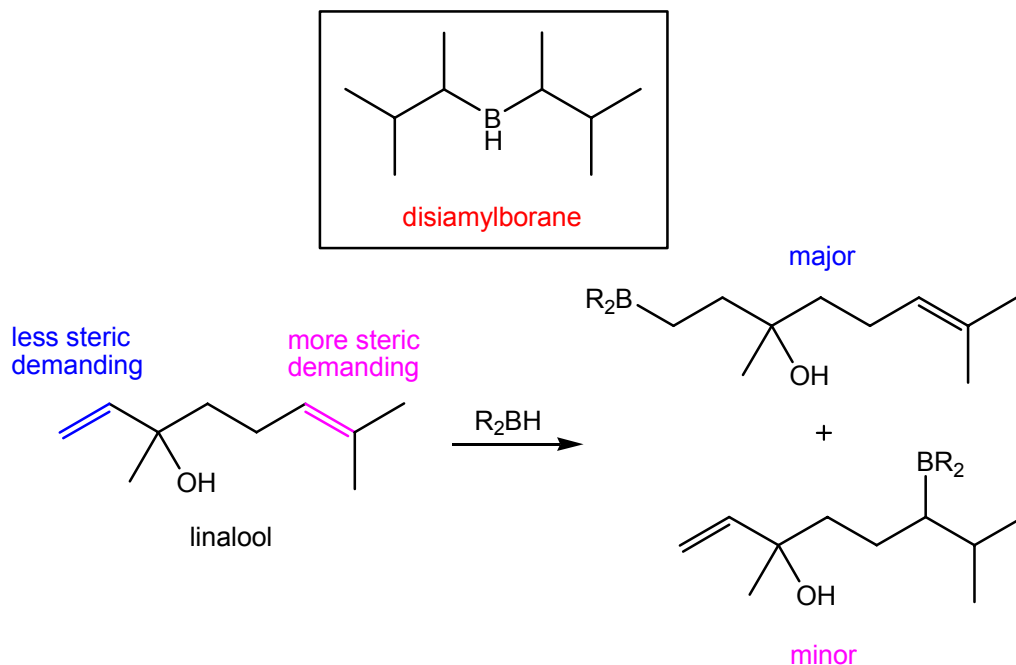
- (d) Explain why the reaction of disiamylborane with linalool is chemoselective. (*Hint*: Consider the size of disiamylborane.)

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**.

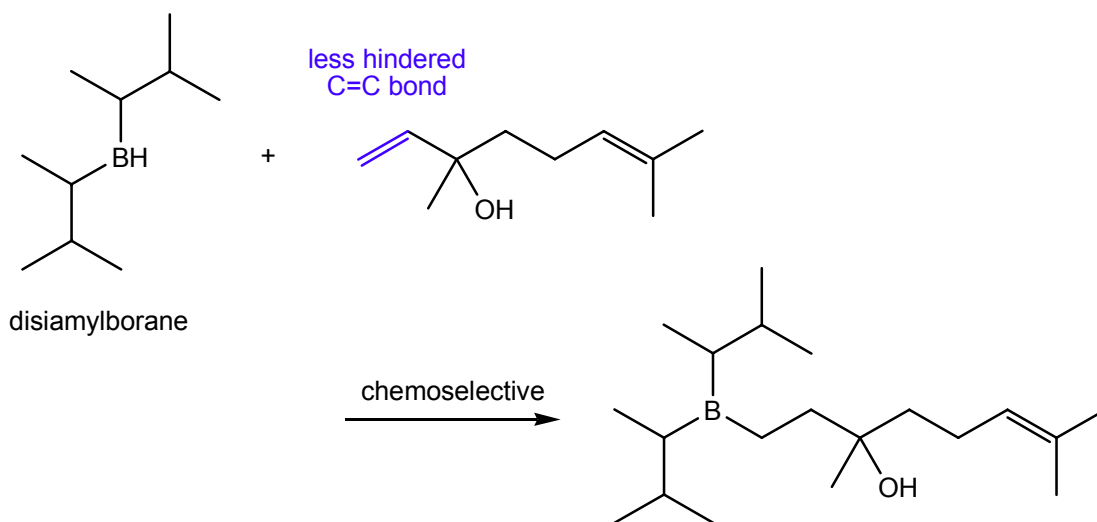
Solution

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)