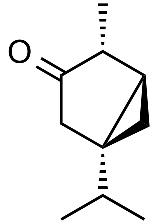
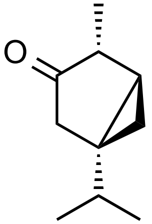


Chemistry 2600

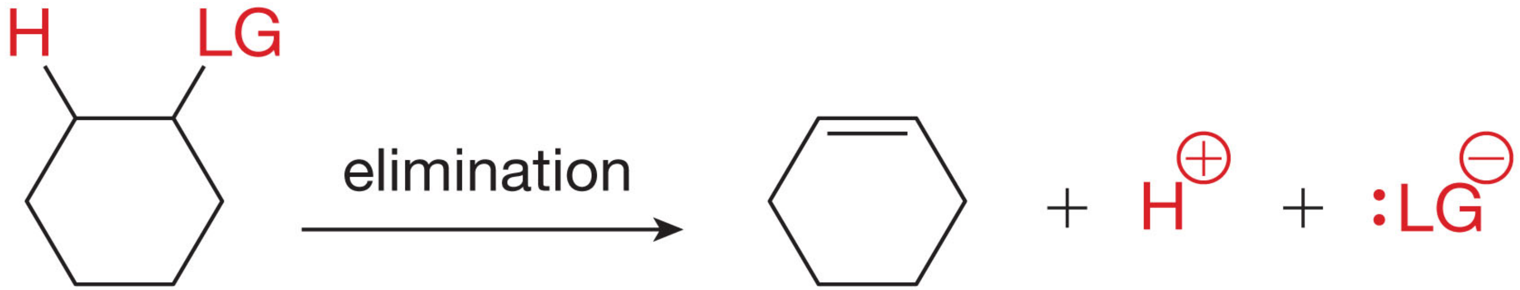
Chapter 12

Formation of π Bonds by Elimination Reactions

E2 Elimination Reactions

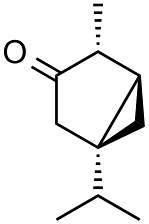


- ***Elimination reactions*** involve the removal of hydrogens and leaving groups from adjacent carbon atoms to form π bonds.

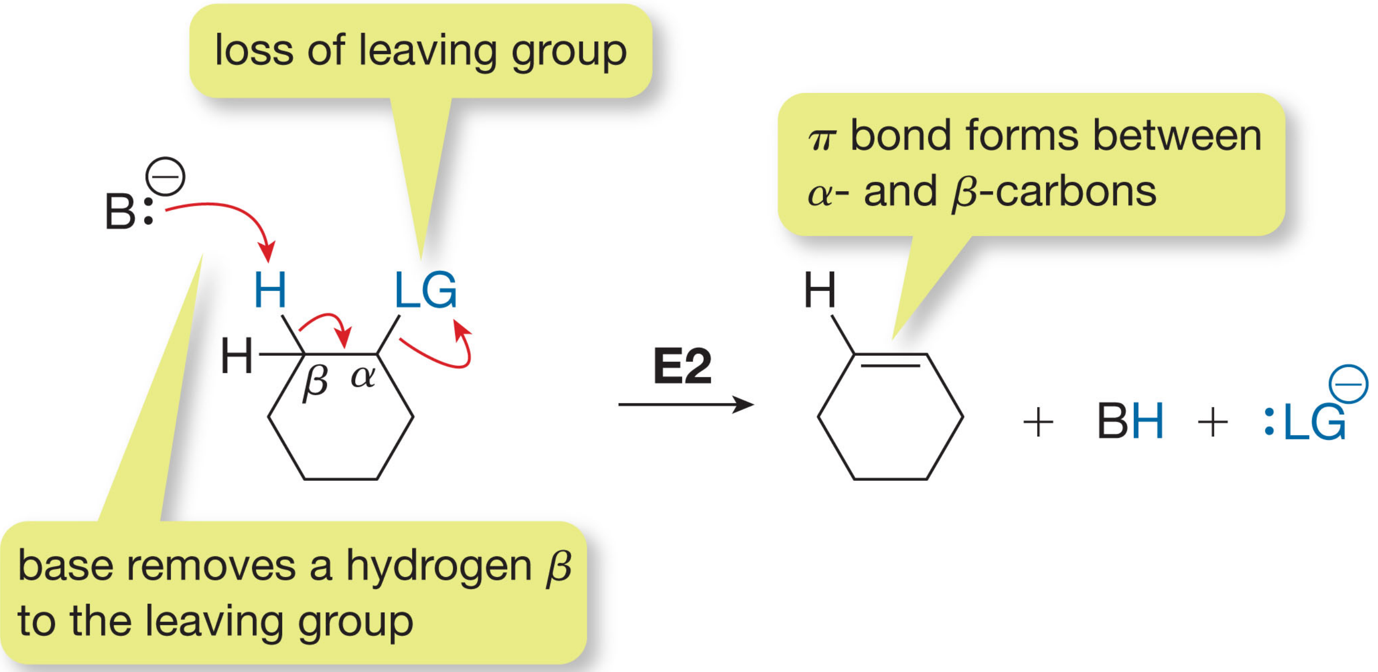


- The simplest mechanism is the E2 (elimination, bimolecular) reaction.
- Bimolecular refers to 2 reactants involved in the RDS.

E2 Elimination Reactions



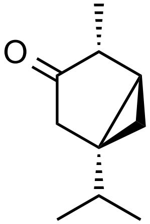
- In an E2 elimination reaction, a strong base removes a hydrogen atom from a carbon that is β to the leaving group and simultaneously ejects the leaving group to form a π bond between the α and β carbon atoms.


loss of leaving group

π bond forms between α- and β-carbons

base removes a hydrogen β to the leaving group

E2 Elimination Reactions



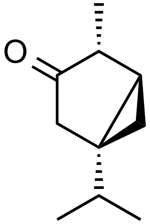
- Experimental measurements provide the following rate expression for this reaction:

$$\text{rate} = k[\text{substrate}][\text{base}]$$

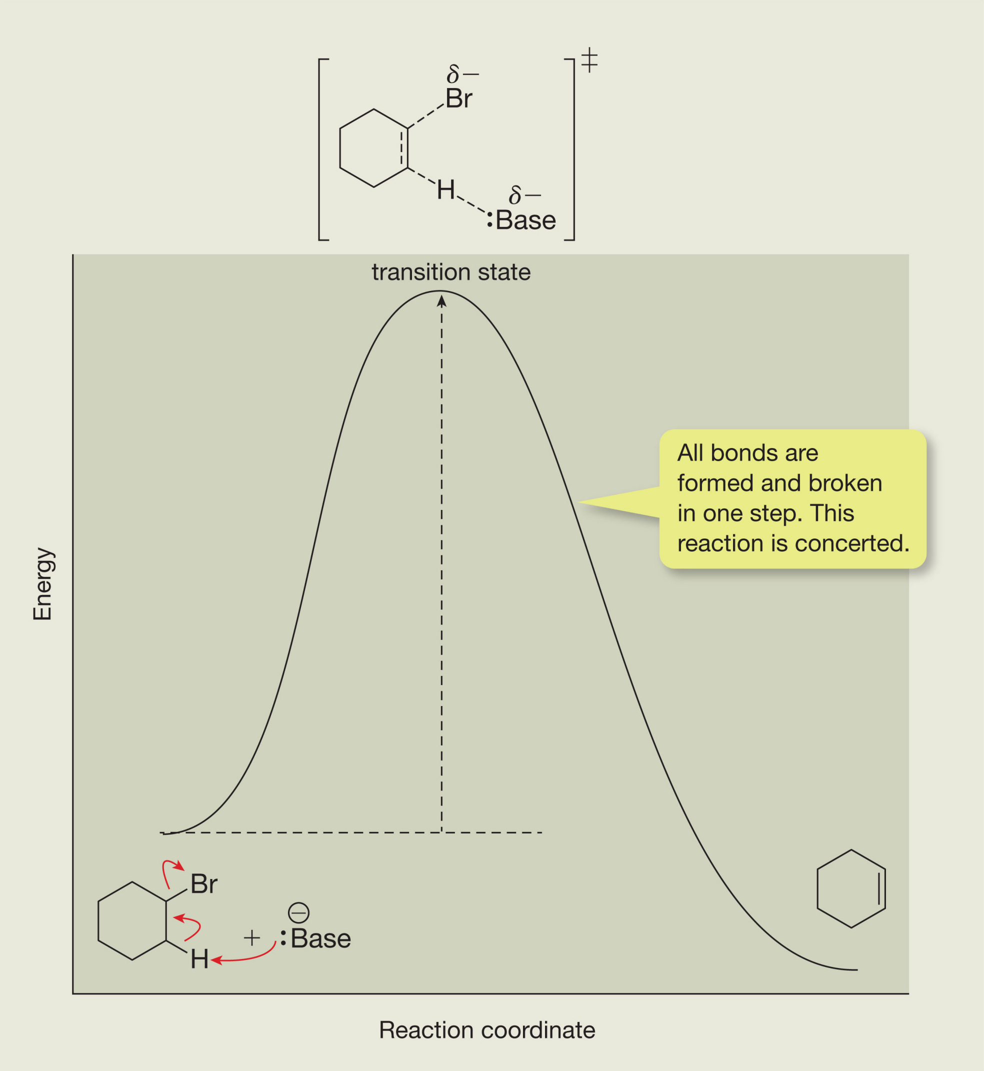
rate of the elimination depends on the concentration of the substrate and the base

- This type of reaction is designated E2 (elimination, bimolecular).
- The rate law implies that both the base and substrate are involved in the RDS and that the elimination occurs in one step (concerted).

E2 Reaction Diagram

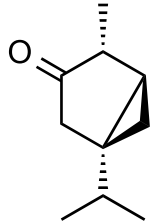


- E2 reactions typically occur with strong bases; H^-, HO^-, RO^-.
- This E2 reaction diagram is similar to that of the S_N2 reaction diagram.
- E2 and S_N2 reactions often compete with each other.

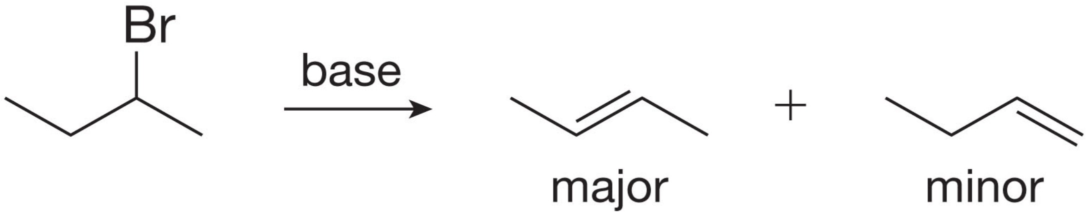


All bonds are formed and broken in one step. This reaction is concerted.

Regioselectivity in E2 Reactions



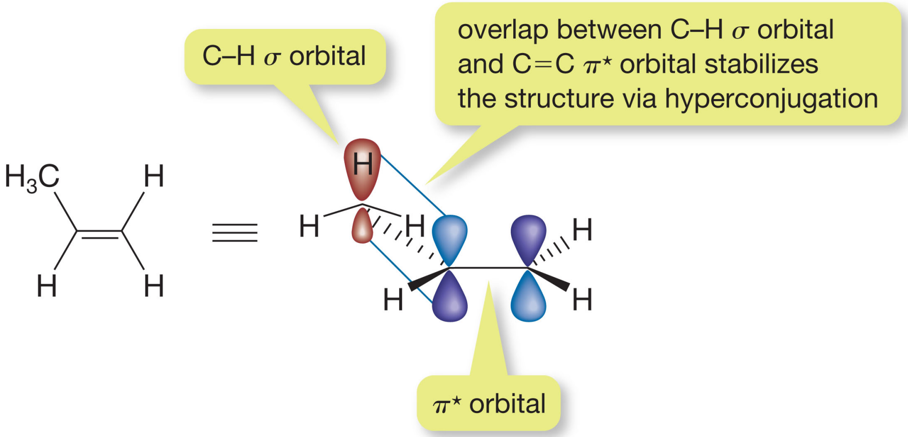
- For unsymmetrical substrates, a mixture of alkenes is possible.



- The favoured product is know as the ***Zaitsev product*** and can be predicted by ***Zaitsev's rule*** which states that the favoured product will be the most stable alkene.
- Often, the most stable alkene is one that is the most substituted.
- This means then that the Zaitsev product is the ***thermodynamic product*** (see Chapter 8)

Regioselectivity in E2 Reactions

- Alkenes are stabilized by two general methods:
- Hyperconjugation:

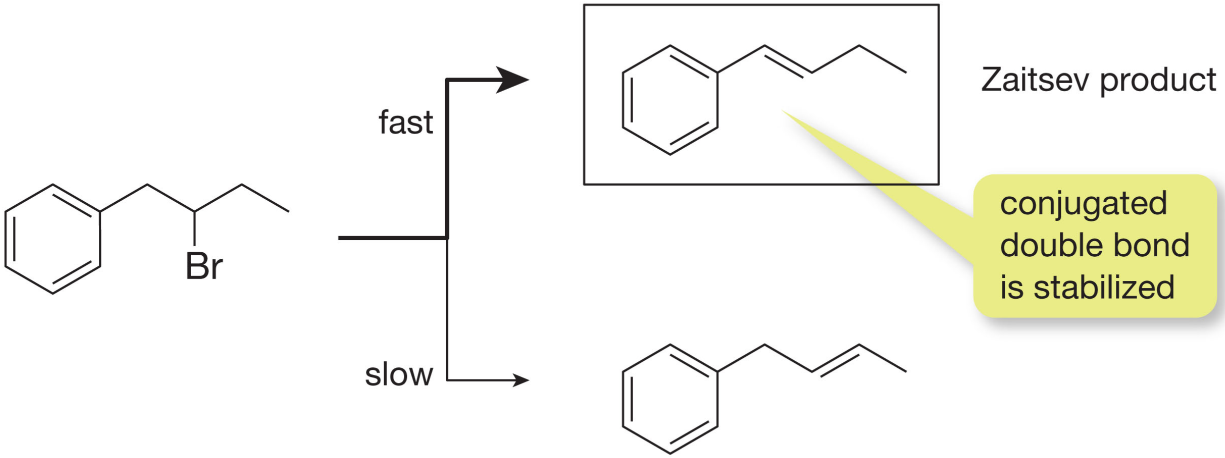


C–H σ orbital

overlap between C–H σ orbital and C=C π^* orbital stabilizes the structure via hyperconjugation

π^* orbital

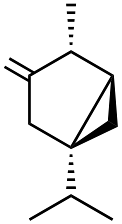
- Delocalization:



Zaitsev product

conjugated double bond is stabilized

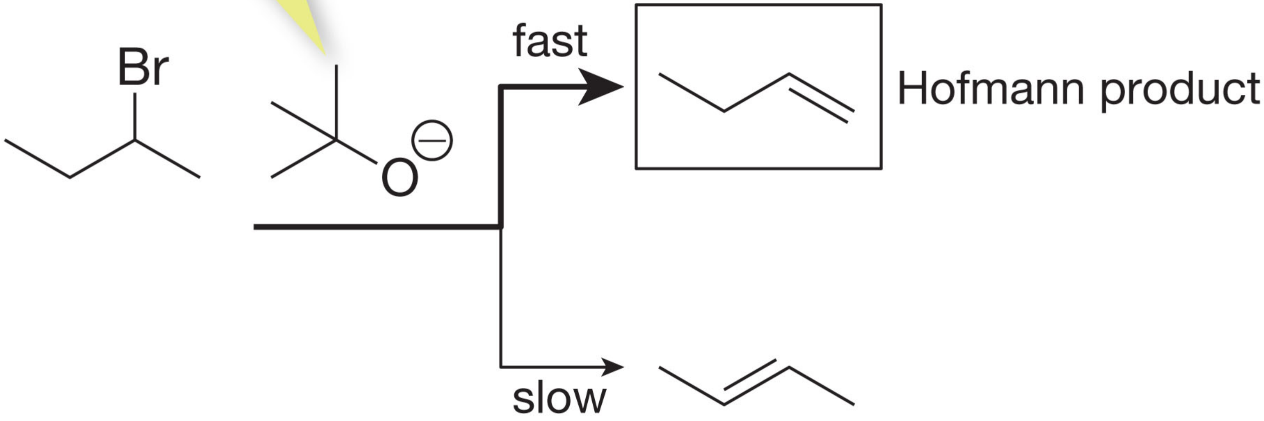
Regioselectivity in E2 Reactions



- By using large, bulky bases, the regioselectivity of the E2 reactions can be altered.
- *tert*-butoxide (*t*-BuO$^-$) is a strong base and will promote an E2 mechanism, however, because it is also large and bulky, it cannot easily reach the more sterically hindered hydrogen atoms.
- Large, bulky bases such as this remove hydrogen atoms from less crowded positions and produce less substituted alkenes.

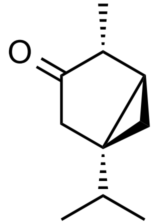
Regioselectivity in E2 Reactions

- The less substituted (less stable) alkene product is called the ***Hofmann product***.
- In this case, the Hofmann product is the kinetic product.



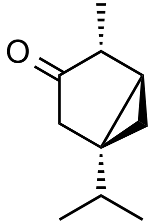
large base (t-BuO$^{\ominus}$) can only reach the more accessible hydrogens at the less substituted position

Stereochemistry of E2 Reactions



- ***Stereoselectivity*** refers to the preferential formation of one stereoisomer over another in a chemical reaction.
- In elimination reactions, alkene products can often be formed in both the *E* or *Z* conformation, however, the *E* isomer is often preferred.
- The are two main reasons for this observed selectivity:
  - The relative orientation of the bonds involved in the reaction
  - The conformation of the molecule

Stereochemistry of E2 Reactions

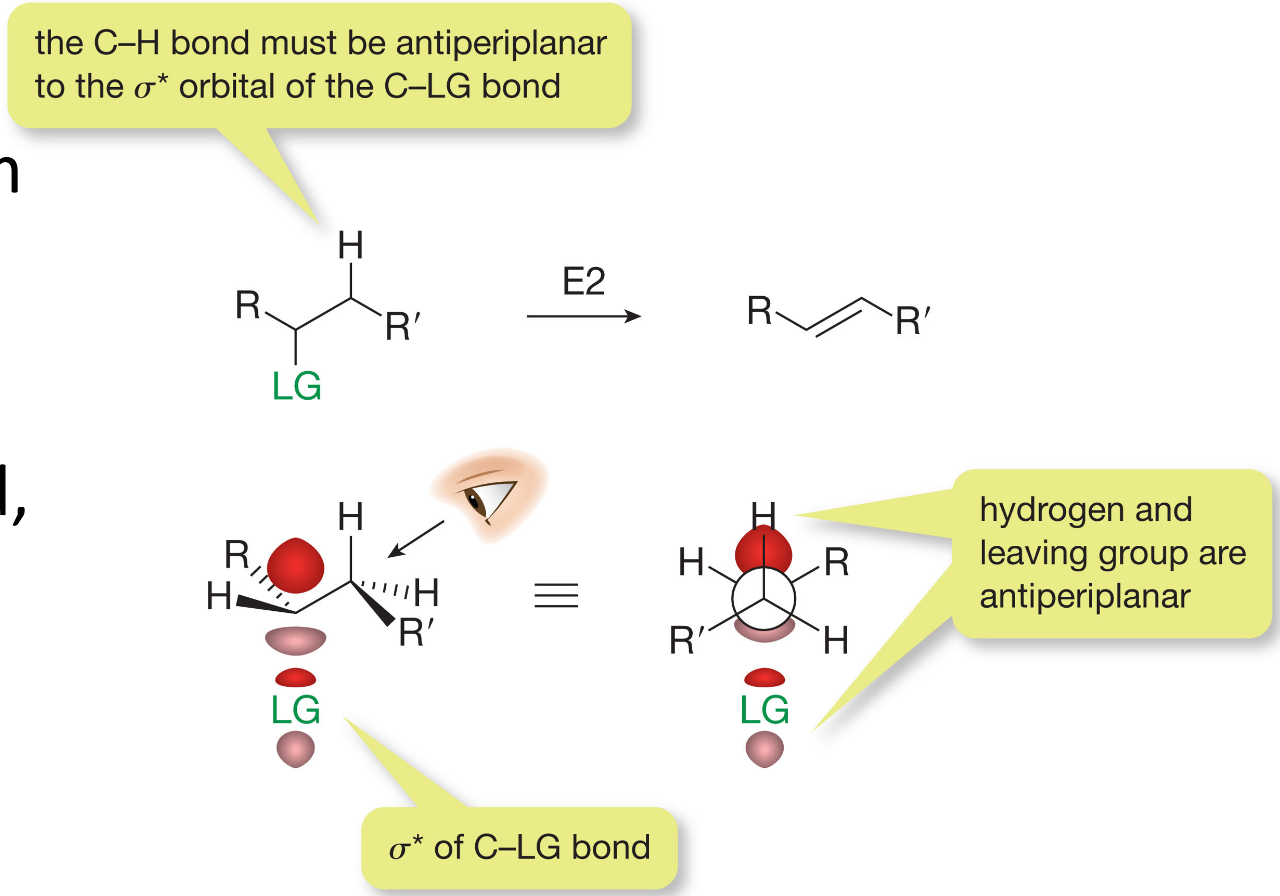


Bond Orientation

- Recall that for S_N2 reactions, the nucleophile must attack from the backside of the carbon-leaving group bond in order for the reaction to proceed.
- In E2 reactions, the 4 involved atoms; the hydrogen, the 2 carbon atoms, and the leaving group, must all lie in the same plane with the C-H bond and the C-LG bond ***anti*** (180°) to each other.
- This allows for the best overlap of the orbitals involved.

Stereochemistry of E2 Reactions

- As the C-H bond breaks, electrons from this bond can flow into the σ^* orbital of the C-LG bond, thus breaking this bond.


the C–H bond must be antiperiplanar to the σ^* orbital of the C–LG bond

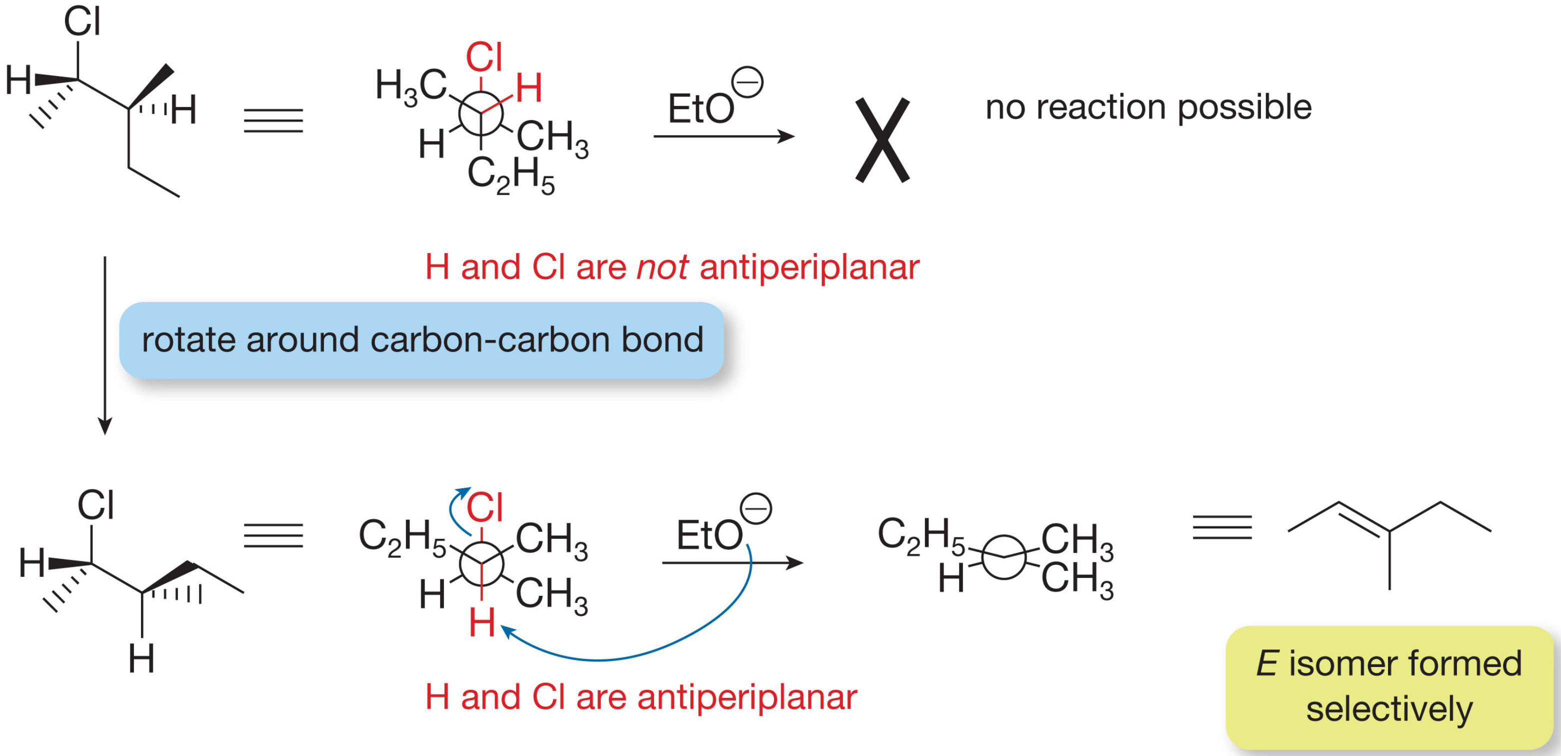
hydrogen and leaving group are antiperiplanar

σ^* of C–LG bond

Stereochemistry of E2 Reactions

Molecular Conformation

- If the H atom and LG are not antiperiplanar, the molecule must rotate, if possible, into a conformation that provides the correct alignment.



no reaction possible

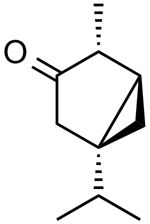
H and Cl are *not* antiperiplanar

rotate around carbon-carbon bond

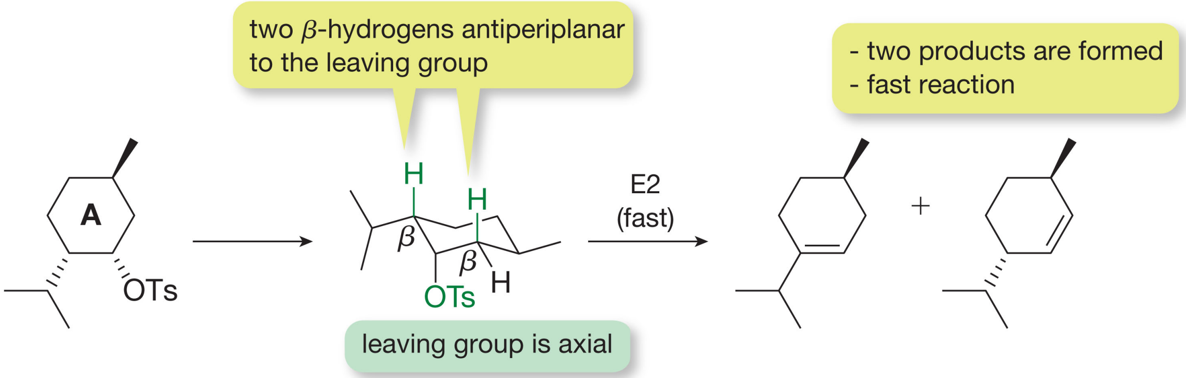
H and Cl are antiperiplanar

E isomer formed selectively

Stereochemistry of E2 Reactions



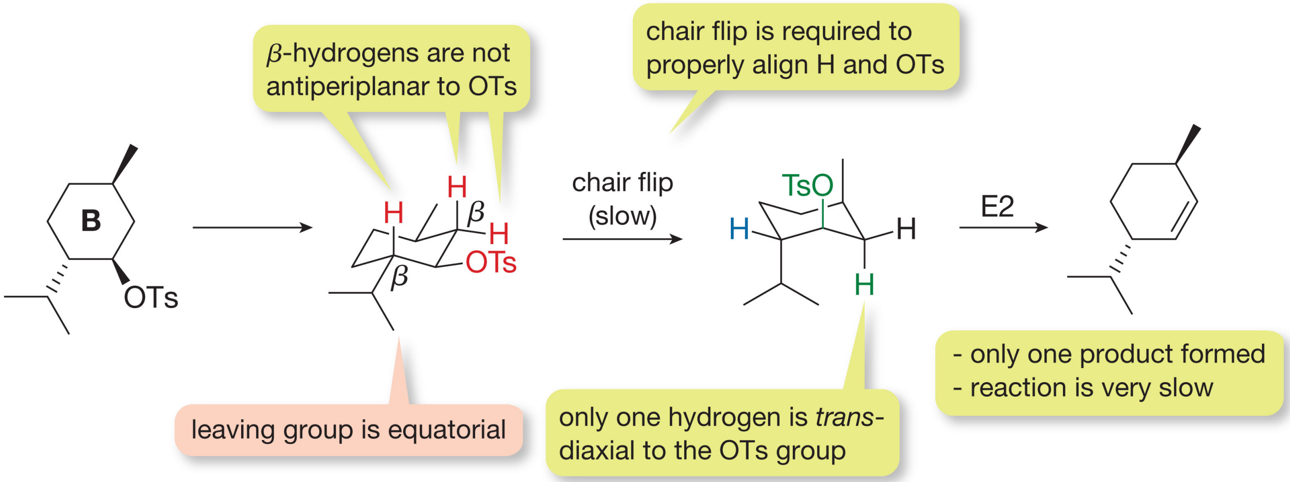
- These stereochemical requirements are commonly seen in substituted cyclohexane reactants:



two *β*-hydrogens antiperiplanar to the leaving group

leaving group is axial

- two products are formed
- fast reaction



β-hydrogens are not antiperiplanar to OTs

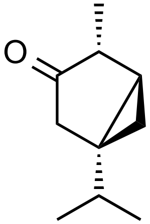
chair flip is required to properly align H and OTs

leaving group is equatorial

only one hydrogen is *trans*-diaxial to the OTs group

- only one product formed
- reaction is very slow

E1 Elimination Reactions



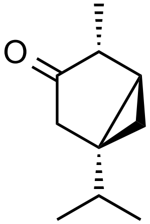
- Alkenes are also formed by E1 reactions (elimination, bimolecular).
- Experimental measurements provide the following rate expression for this reaction:

$$\text{rate} = k[\text{substrate}]$$

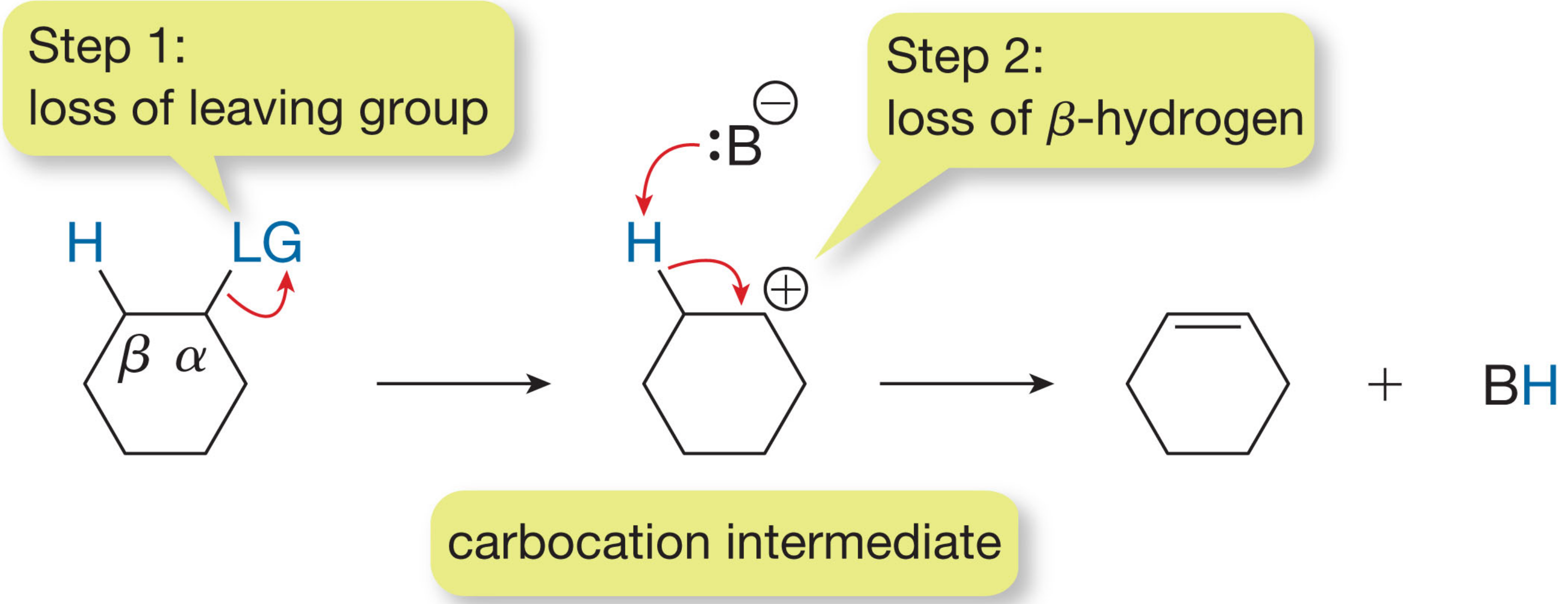
rate of an E1 elimination depends only on the concentration of the substrate

- This rate law implies that only the substrate is involved in the RDS and that the elimination occurs in two steps.

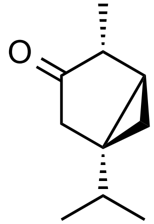
E1 Elimination Reactions



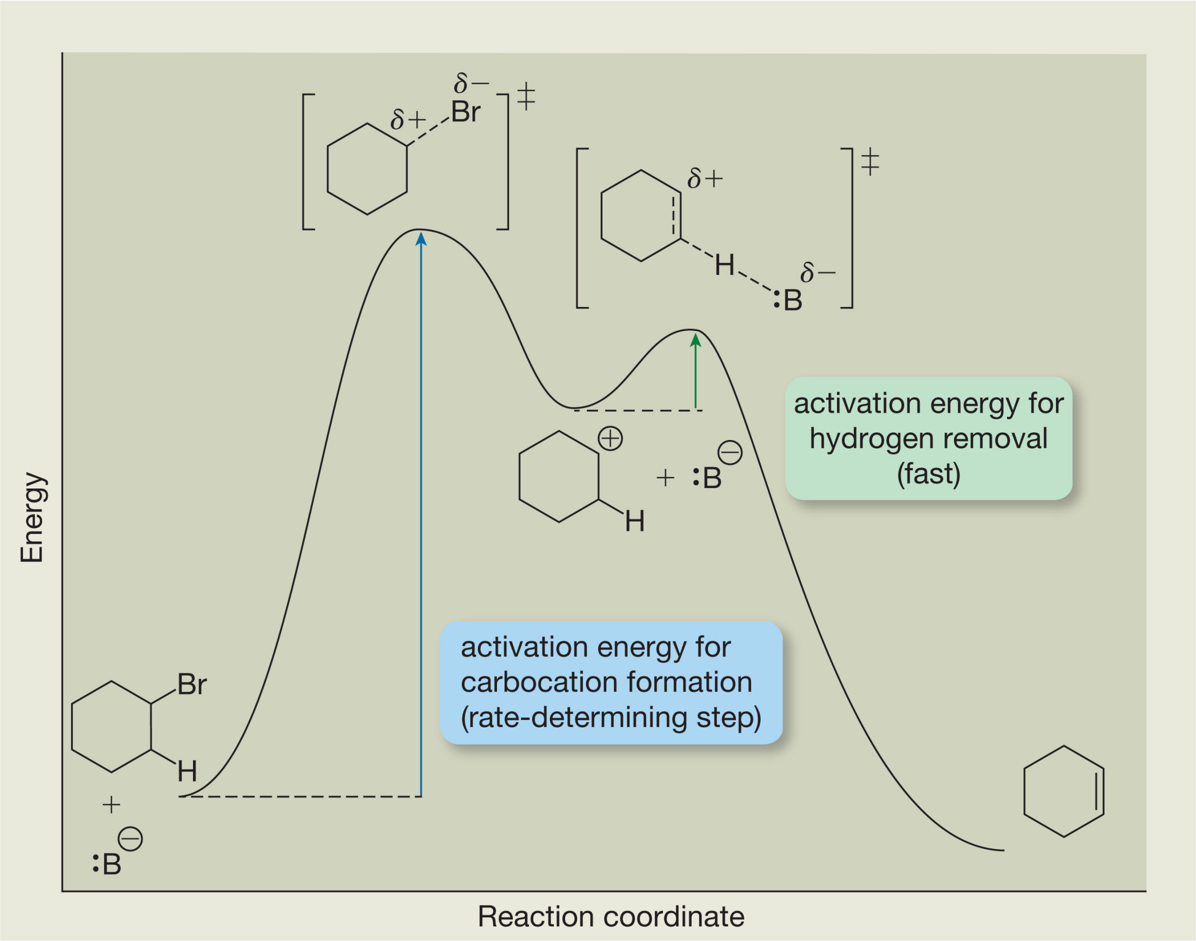
- The mechanism of an E1 reaction is similar to that of an S_N1 mechanism.



E1 Elimination Reactions

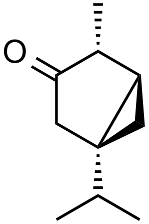


- This E1 reaction diagram is similar to that of the S_N1 reaction diagram.
- E1 and S_N1 reactions often compete with each other.



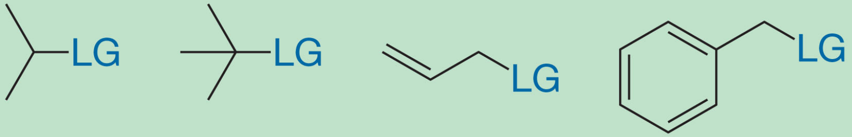
activation energy for hydrogen removal (fast)

activation energy for carbocation formation (rate-determining step)

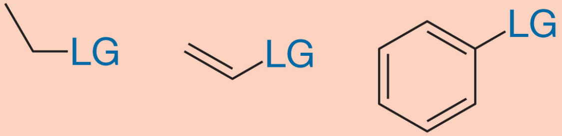


E1 Elimination Reactions

- Substrates that can form stable carbocation intermediates (secondary, tertiary, allylic, and benzylic) favour the E1 pathway (just as they favour the S_N1 mechanism).
- Primary, vinyl, and aryl substrates do not react via E1 elimination reactions as they cannot form stable carbocations.

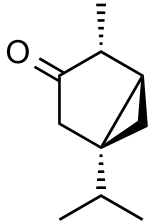


good E1 substrates



inappropriate E1 substrates

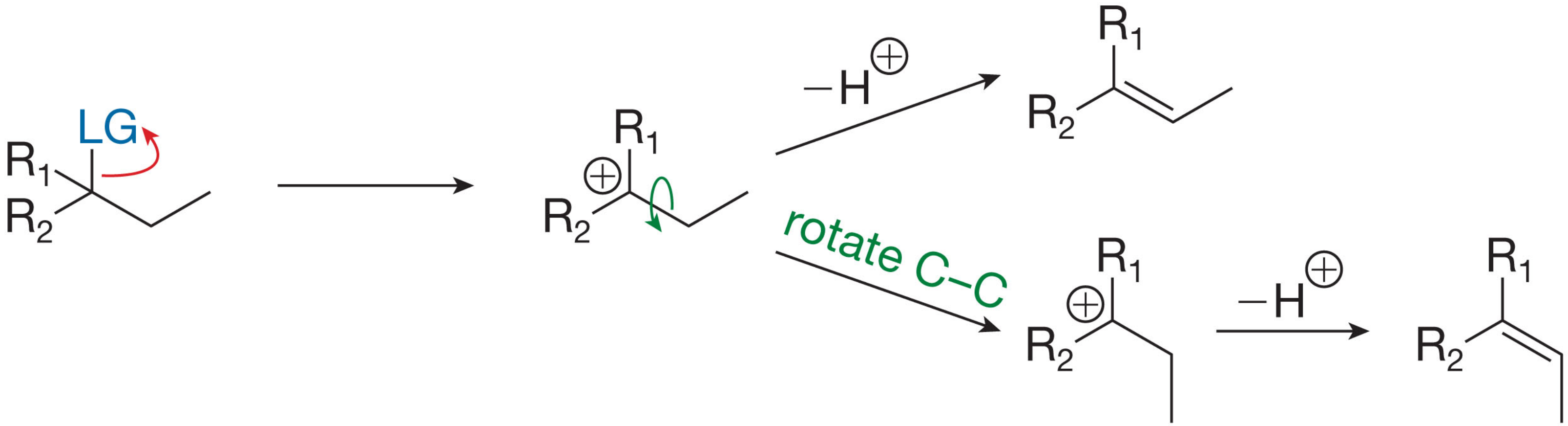
E1 Elimination Reactions



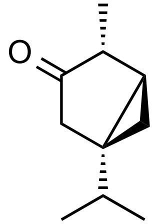
- Just as in substitution reactions, good leaving groups are needed for elimination reactions – halides, water, sulfonate esters, etc.
- Unlike E2 eliminations, strong bases are not required for E1 reactions. This is because the hydrogen atom β to the carbocation is much more acidic and therefore easier to remove than a typical carbon-bonded hydrogen.

Selectivity in E1 Reactions

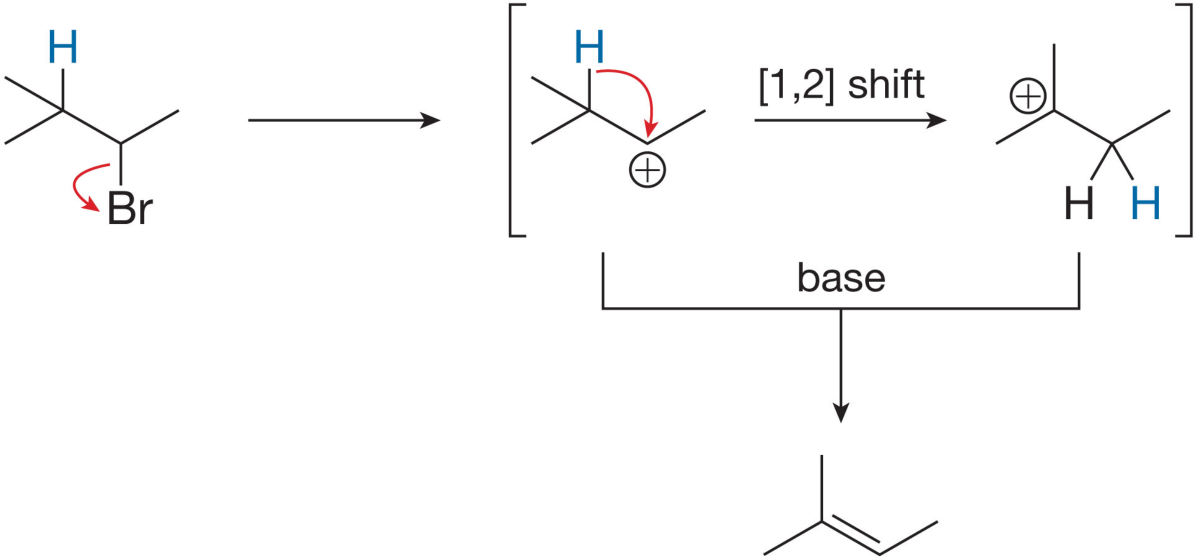
- E1 elimination reactions follow Zaitsev's rule of the preferential formation of the most stable alkene.
- E1 reactions are generally less stereoselective than E2 reactions. This is because E1 reactions proceed via carbocation intermediates, which are flat and free to rotate about carbon-carbon single bonds.



Rearrangements in E1 Reactions

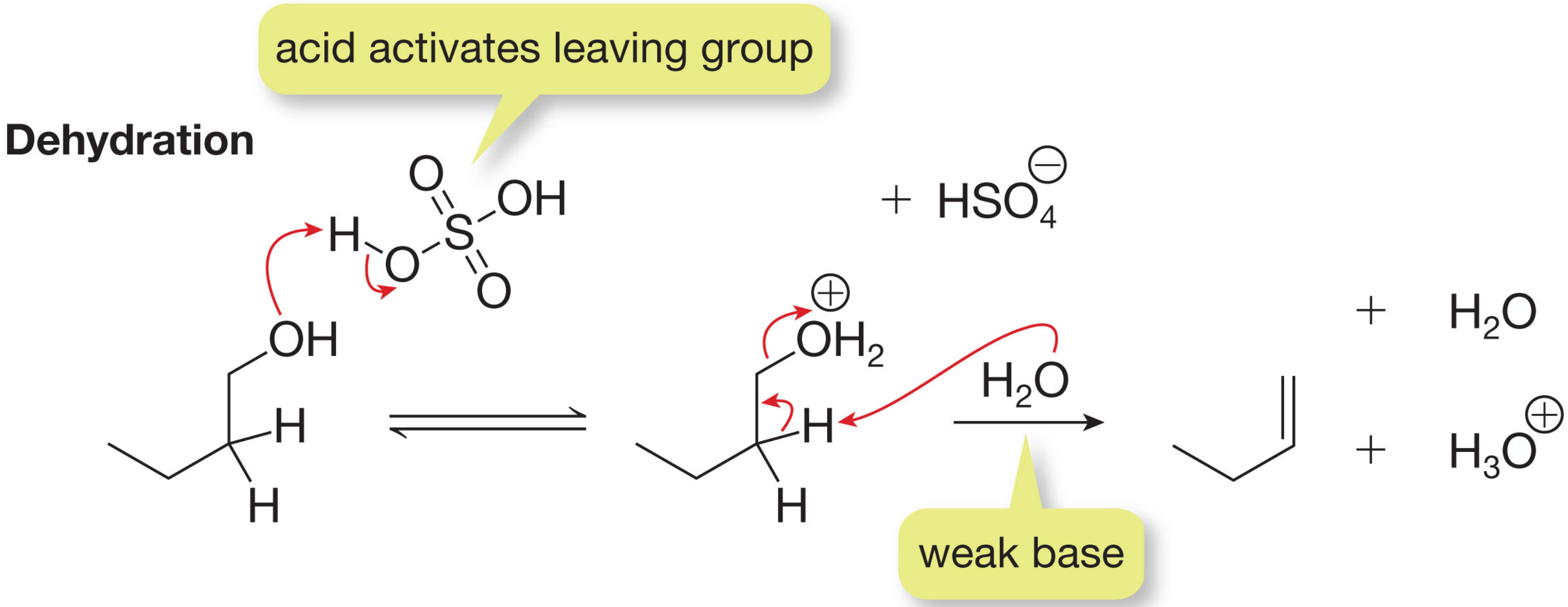


- Carbocation rearrangements can occur during E1 reactions.
- This is true for any reactions involving carbocation intermediates.
- Note that for elimination reactions, not all rearrangements will lead to different products.

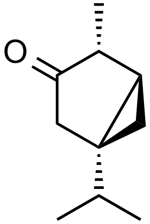


E1 Reactions of Alcohols

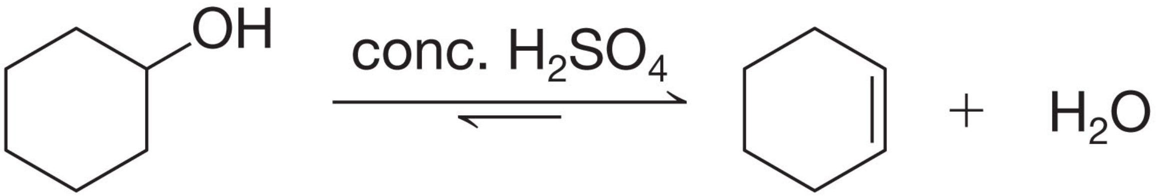
- Dehydration is the loss of water to produce an alkene from an alcohol.
- For the reaction to proceed, the alcohol leaving group must first be made into a better leaving group:



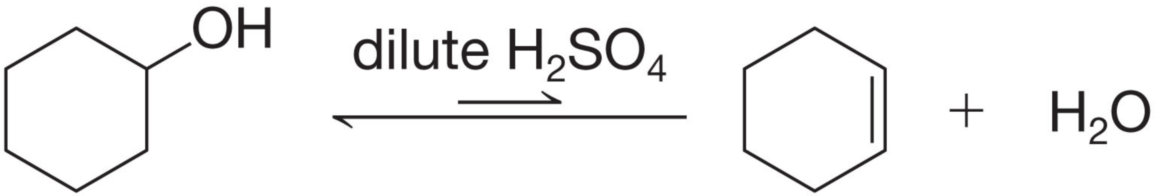
E1 Reactions of Alcohols



- The mechanism of E1 dehydration is the reverse of the mechanism of hydration of an alkene (Chapter 8).

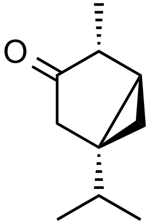


dehydration is favoured



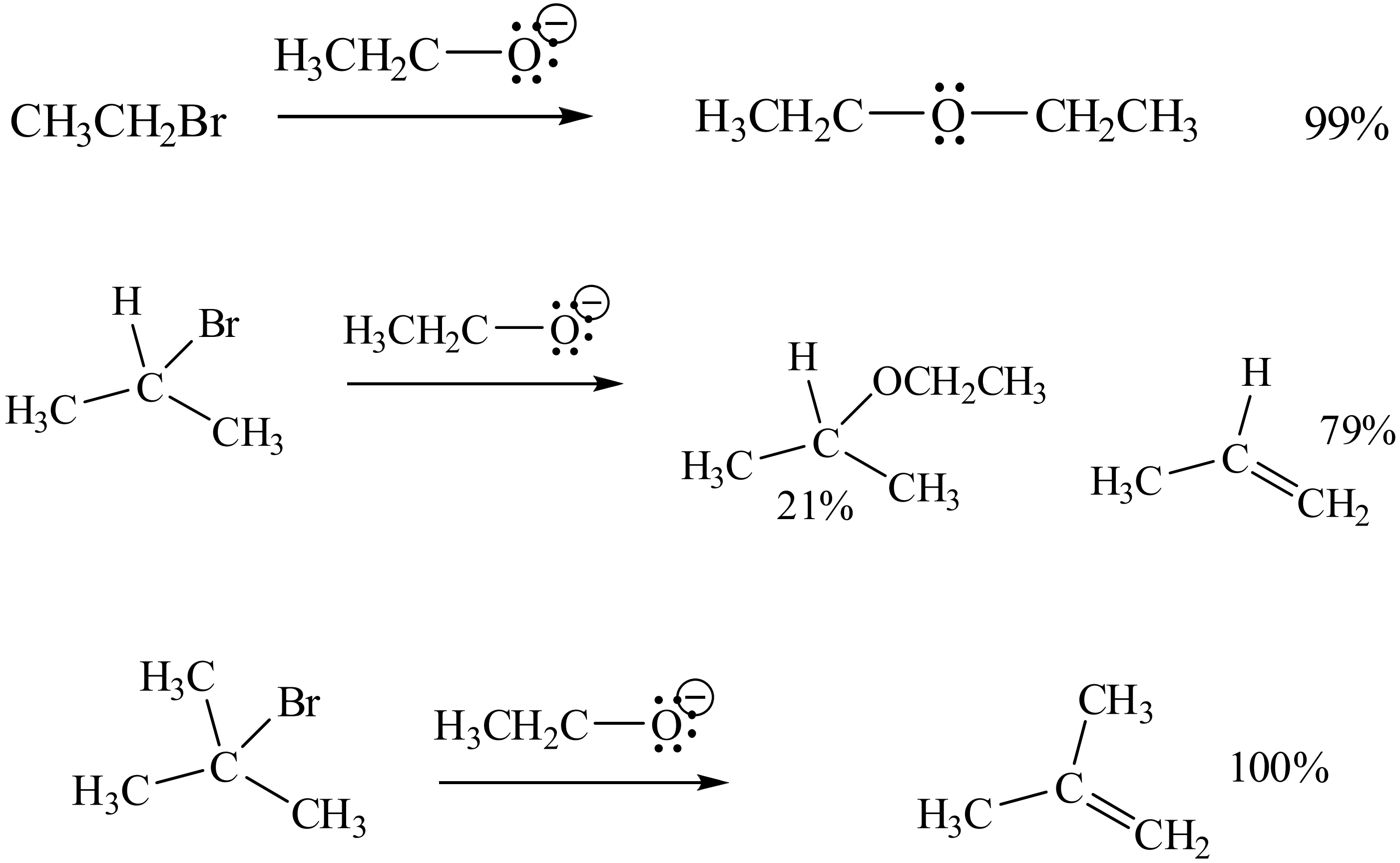
hydration is favoured

E2/E1 versus S_N2/S_N1 Reactions

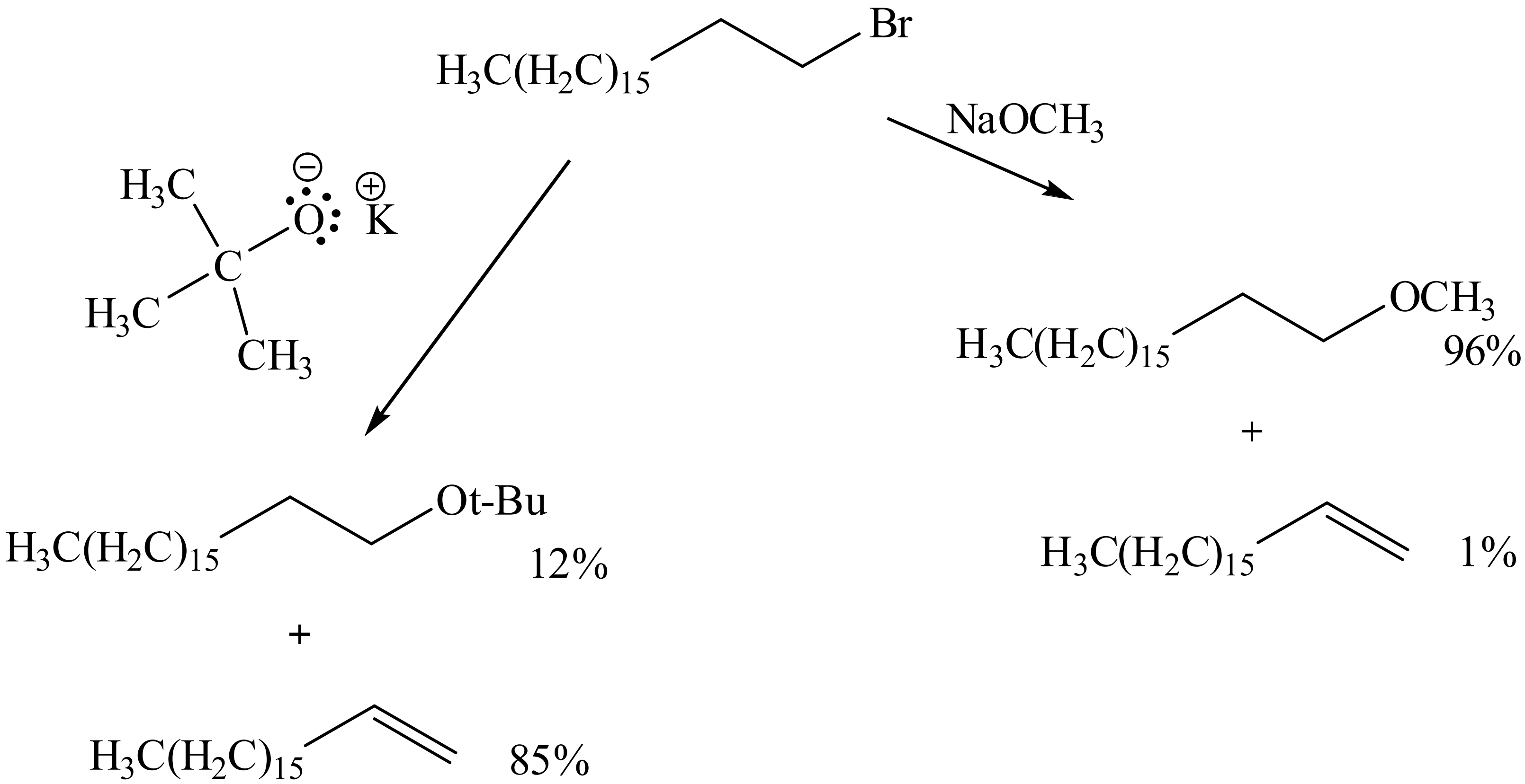


- Because Nu^- and B^- are by definition ‘electron pair donors’, it is important to understand that substitution and elimination reactions compete with each other.
  - To favour E1 over S_N1 for alcohols, use an acid with a non-nucleophilic conjugate base (H_2SO_4, H_3PO_4). To favour S_N1 over E1, use an acid with good nucleophilic conjugate base (HBr).
  - To favour E2 over S_N2, use a strong, bulky non-nucleophilic base (tBuO$^-$). To favour S_N2 over E2, use good nucleophiles that are relatively weak bases (Br^-).
  - Before you even consider the possibility of an elimination reaction, make sure there are β–hydrogen atoms available to eliminate.

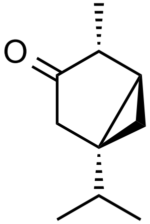
E2/E1 versus S_N2/S_N1 Reactions



E2 versus S_N2 Reactions

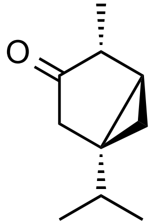


E2/E1 versus S_N2/S_N1 Reactions

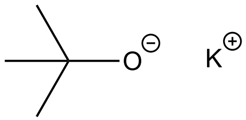


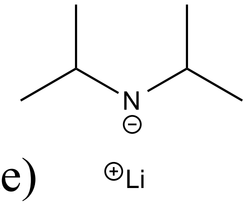
	S_N1	S_N2	E1	E2
Mechanism	2 or more steps involving carbocation intermediate	1 step bimolecular process	2 or more steps involving carbocation intermediate	1 step bimolecular process
Kinetics	First order in substrate	Second order, first in substrate and nucleophile	First order in substrate	Second order, first in substrate and base
Substrate Dependence	Substrates that form stable carbocations: 3°, allylic, benzylic	Substrates that are uncluttered at the reaction site: 1°, 2°	Substrates that form stable carbocations: 3°, allylic, benzylic	Requires strong base and any substrate with beta proton.
Stereochem	Racemization.	Inversion of configuration at the α-carbon.	Usually mixtures.	Stereoselective
Importance of Base/nucleophile	Not involved in RDS, but less basic form of nucleophile will limit E2.	Reactivity of nucleophile is important since it is involved in RDS.	If a good, non-basic nucleophile is present (halides, H_2S) then S_N1.	Strong, non-nucleophilic bases (KOtBu, LDA) best to limit S_N2.
Importance of Leaving group	Involved in RDS so is important.	Involved in RDS so is important.	Involved in RDS so is important.	Involved in RDS so is important.
Competes with…	E1 and E2	E2 when basic nucleohiles employed.	S_N1	S_N2
Solvent	Polar protic best	Polar aprotic best	Polar protic best	Varies.

E2/E1 versus S_N2/S_N1 Reactions

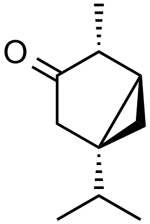


Weak Base/Poor Nu:	H_2O, ROH
Weak Base/Good Nu:	Cl^-, Br^-, I^-, RSH, H_2S
Moderate-Strong Base/Good Nu:	RNH_2, NH_3 $N{\equiv}C^-$ (cyanide), $RC{\equiv}C^-$ (acetylide) RS^-, RO^-, HO^-, N_3^-
Strong Base/Poor Nu:	*t*BuO$^-$ (tert butoxide) LDA (lithium diisopropylamide)

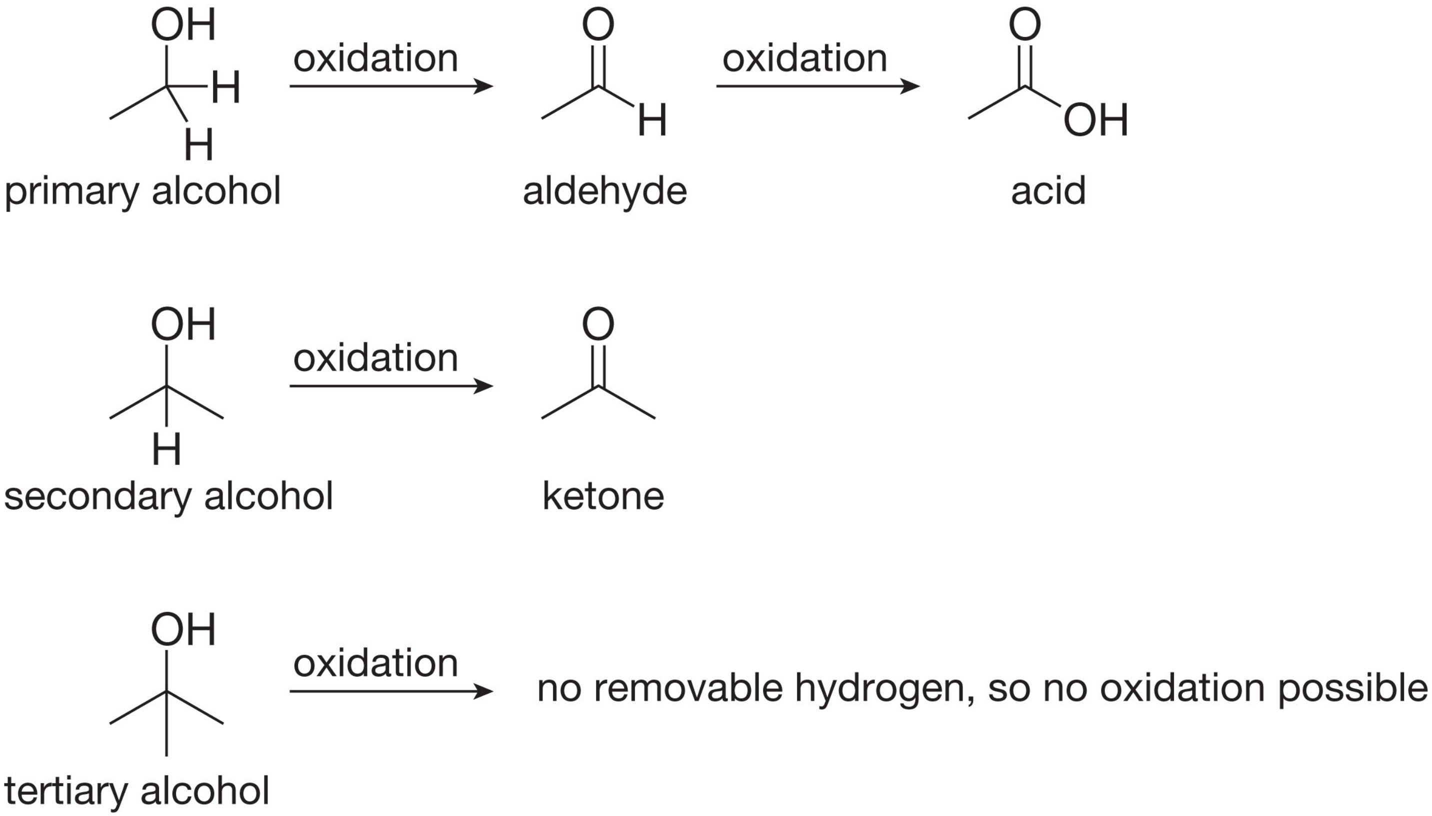




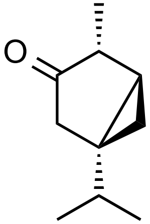
Oxidation of Alcohols



- The oxidation of alcohols is a type of elimination reaction.

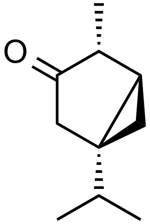


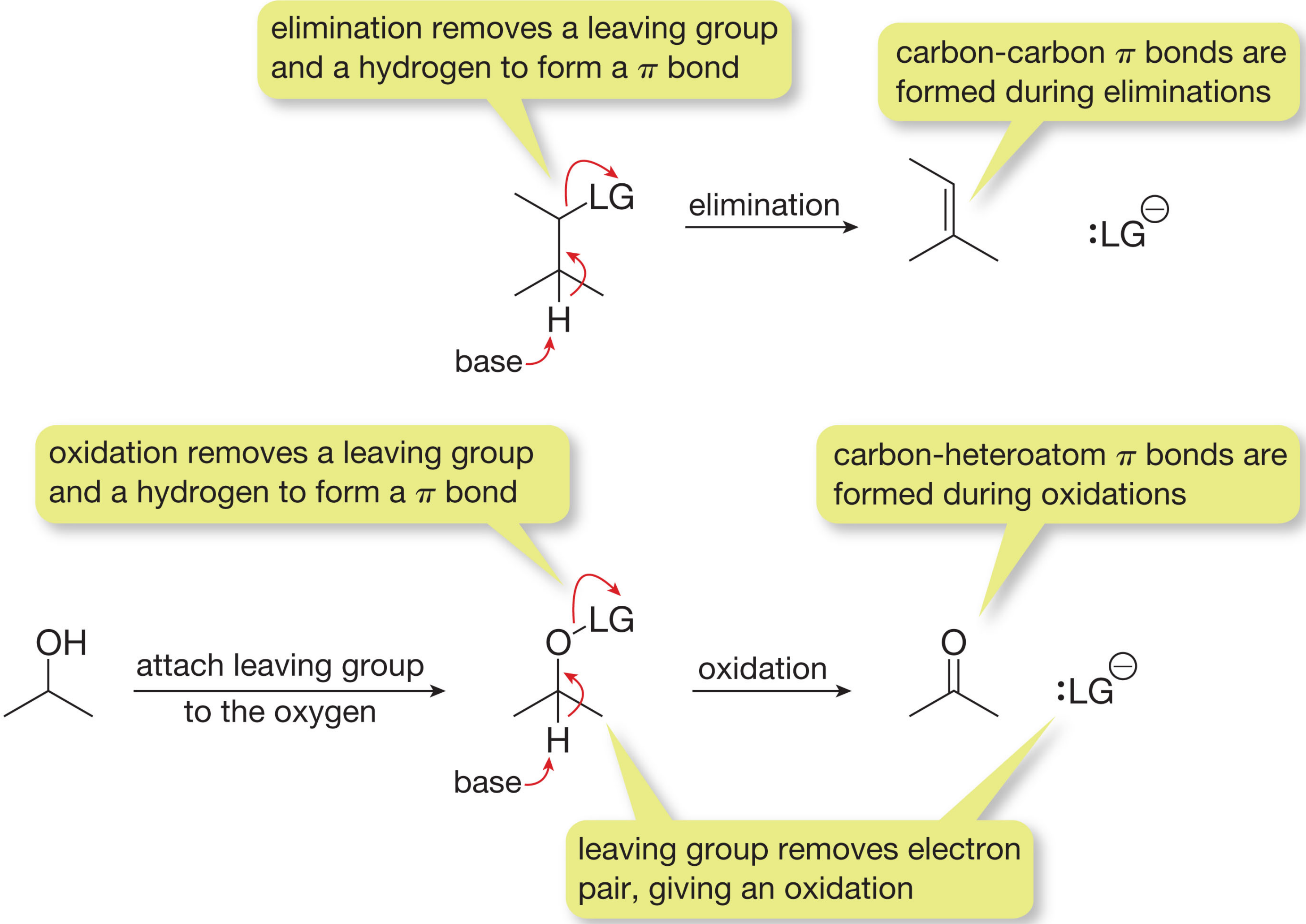
Oxidation of Alcohols



- When the LG in an oxidation departs, it takes with it a pair of electrons. The substrate loses electrons and is by definition oxidized.
- Typically the term elimination is used when a new π bond is formed between 2 carbon atoms.
- When the π bond involves a heteroatom, the reaction is called an oxidation.
- Regardless of the terminology used, the mechanism (electron flow) in the two processes is the same.

Oxidation of Alcohols





elimination removes a leaving group and a hydrogen to form a π bond

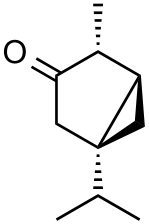
carbon-carbon π bonds are formed during eliminations

oxidation removes a leaving group and a hydrogen to form a π bond

carbon-heteroatom π bonds are formed during oxidations

leaving group removes electron pair, giving an oxidation

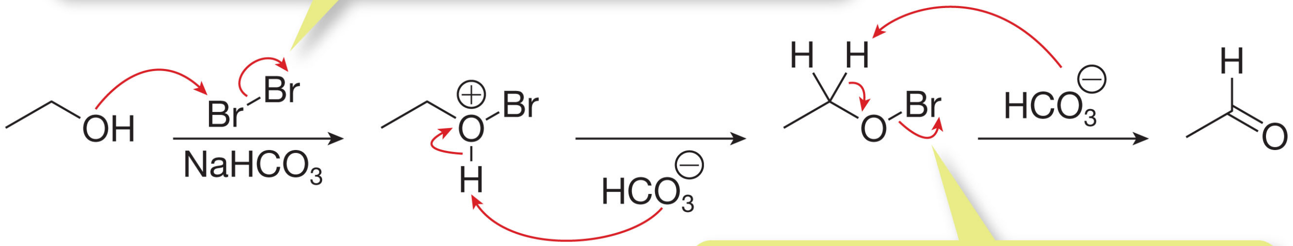
Oxidation of Alcohols



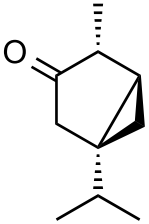
- The general mechanism of oxidation:
  1) Attach a good leaving group to one of the atoms that eventually forms a π bond (usually the heteroatom). The reagent that installs the LG is an oxidizing agent.
  2) Elimination to form the π bond.

The oxidation of 1° alcohols can be accomplished using Br_2 and $NaHCO_3$ in anhydrous methanol.

oxidant attaches a leaving group onto the heteroatom

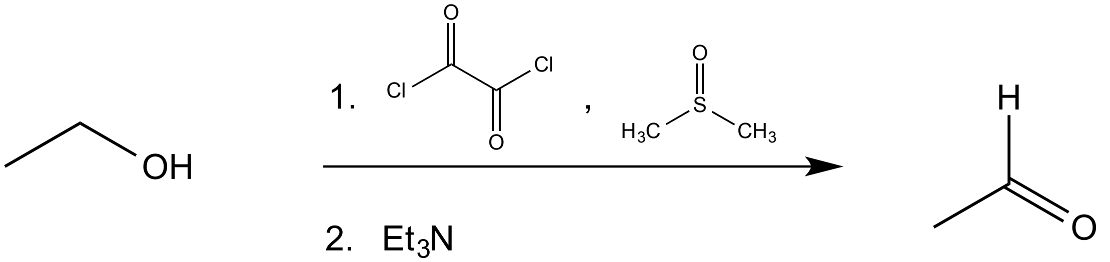


base carries out an elimination to form a π bond and complete the oxidation

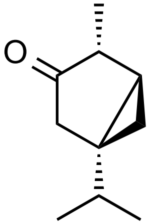


Oxidation of Alcohols

- The Swern oxidation is a very reliable way of oxidizing 1° alcohols to aldehydes:

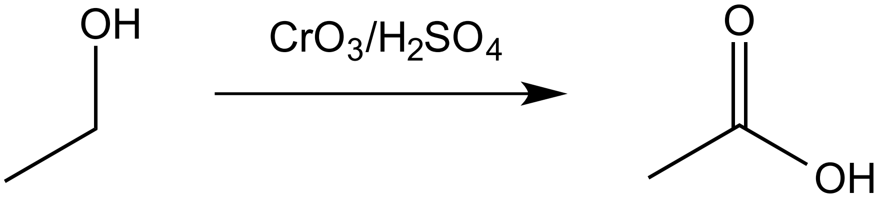


Oxidation of Alcohols

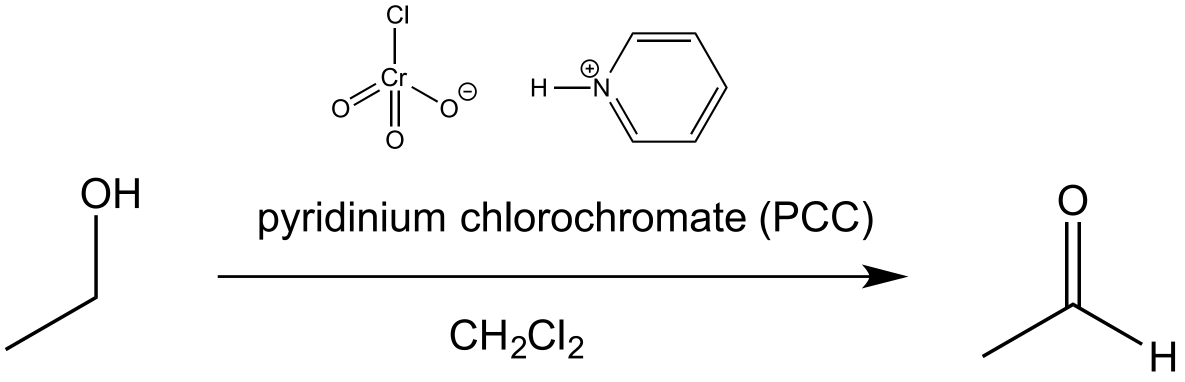


- Chromium reagents make effective oxidizing agents, however, because of their toxicity, chemists try and use alternatives when possible.

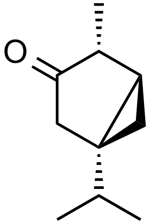
Jones Reagent (CrO_3/H_2SO_4):



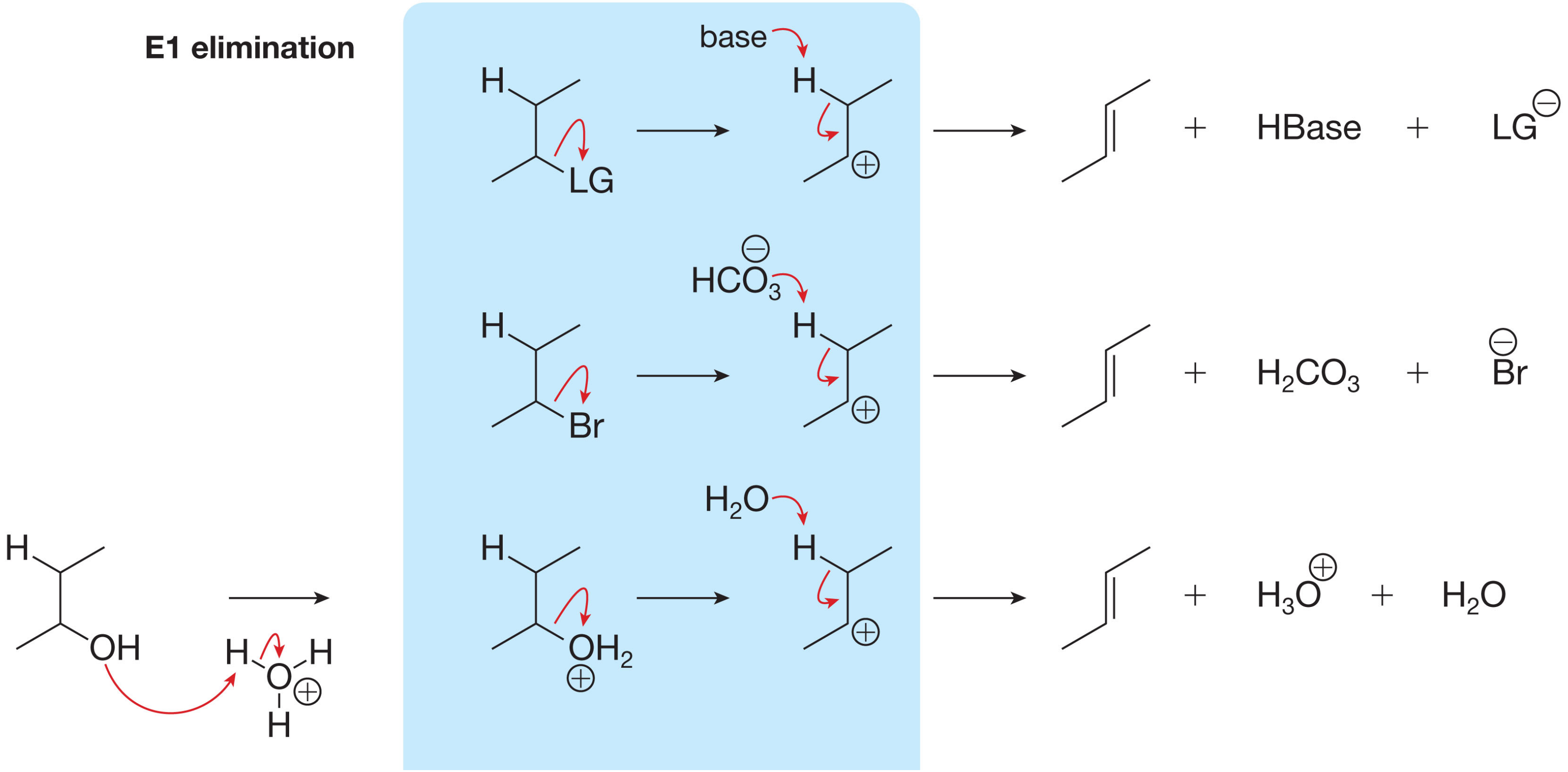
Pyridinium Chlorochromate/CH_2Cl_2 (PCC):



Patterns in Elimination Reactions

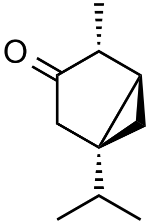


- Elimination reactions can follow one of two general mechanisms, E1 or E2. Both involve the removal of a hydrogen atoms and LG to form a new π bond.

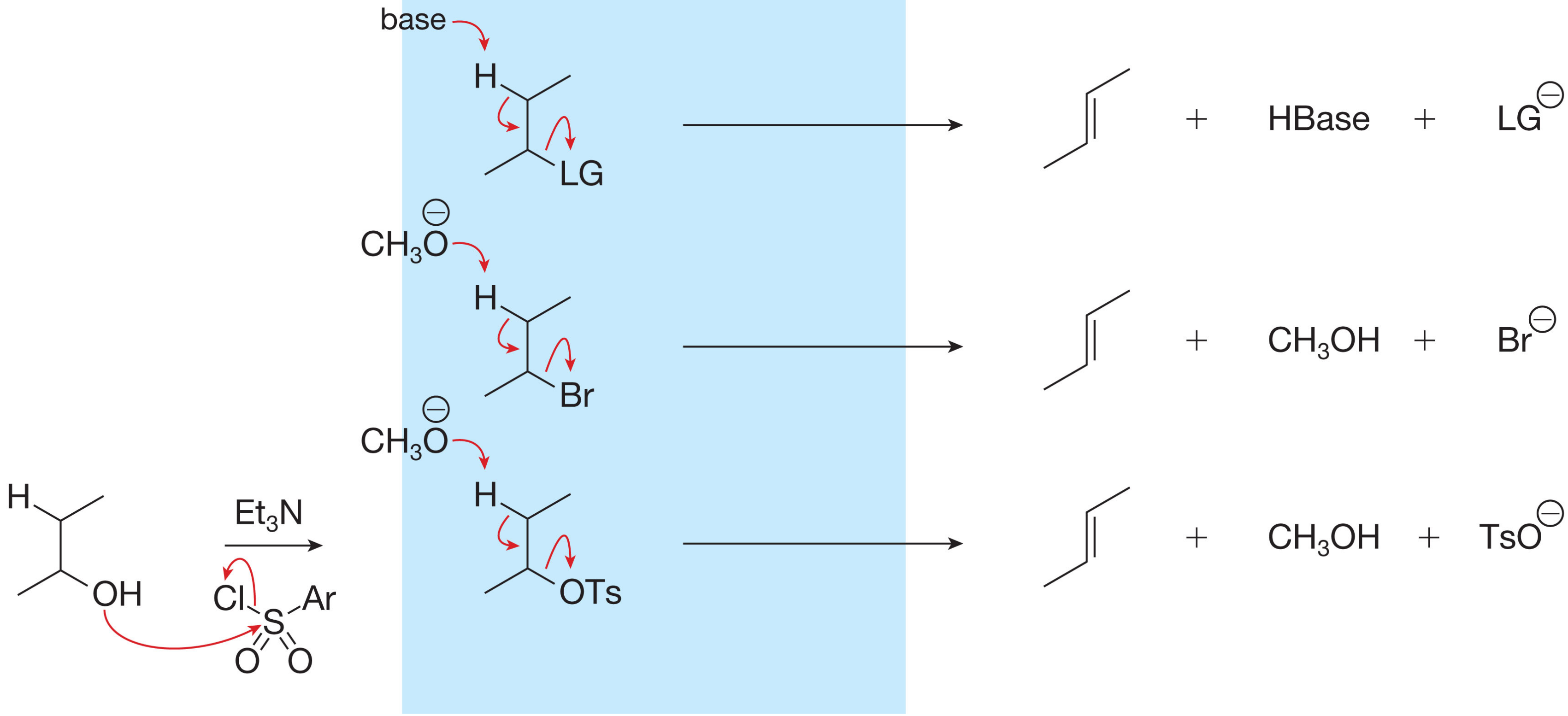


E1 elimination

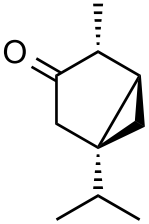
Patterns in Elimination Reactions



E2 elimination



Patterns in Elimination Reactions



- Notice how the electron flow for the oxidation of alcohols is essentially the same as E2.