Elimination Reactions

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ELIMINATION REACTIONS

Definition: Elimination reaction defined as the reaction in which atom or groups are eliminated to form a new bond.

Every elimination reactions under goes two common steps

- Departure of leaving groups with its electron pair
- Removal of proton by base(leaving behind electrons to form a new bond)

Types of elimination reactions

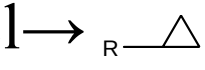
α-Elimination where atoms or groups are eliminated from the same atom

$CHCl_3 \rightarrow :CCl_2 + HCl$

β-Elimination where atoms or groups are eliminated from the adjacent positions

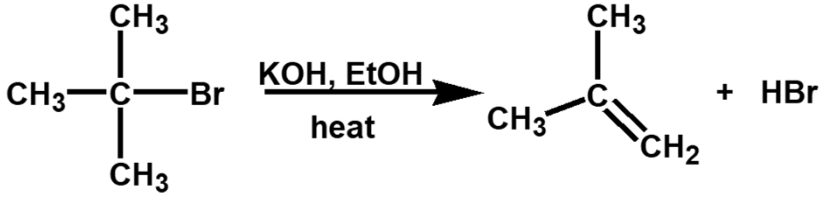
$RCH_2\text{-}CH_2Cl \rightarrow CH_2{=}CH_2 + HCl$

√-Elimination where atoms or groups are eliminated from the alternate atoms/positions

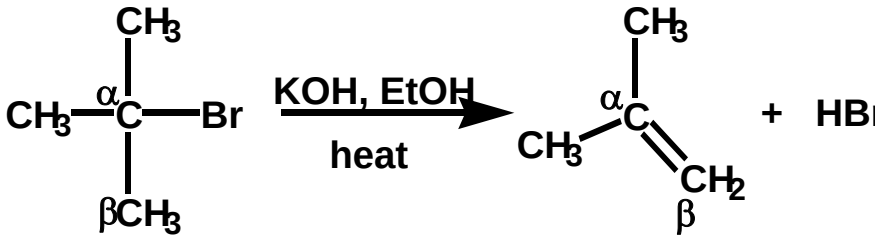
$RCH_2CH_2CH_2Cl \rightarrow$ 

Alkyl halides

Alkyl halides undergo elimination of HX when treated with base. The products are Alkenes.



Elimination reactions usually require forcing conditions, i.e. heat and strong base. The elimination reactions which alkyl halides undergo are known as **1,2-eliminations or β-eliminations**.

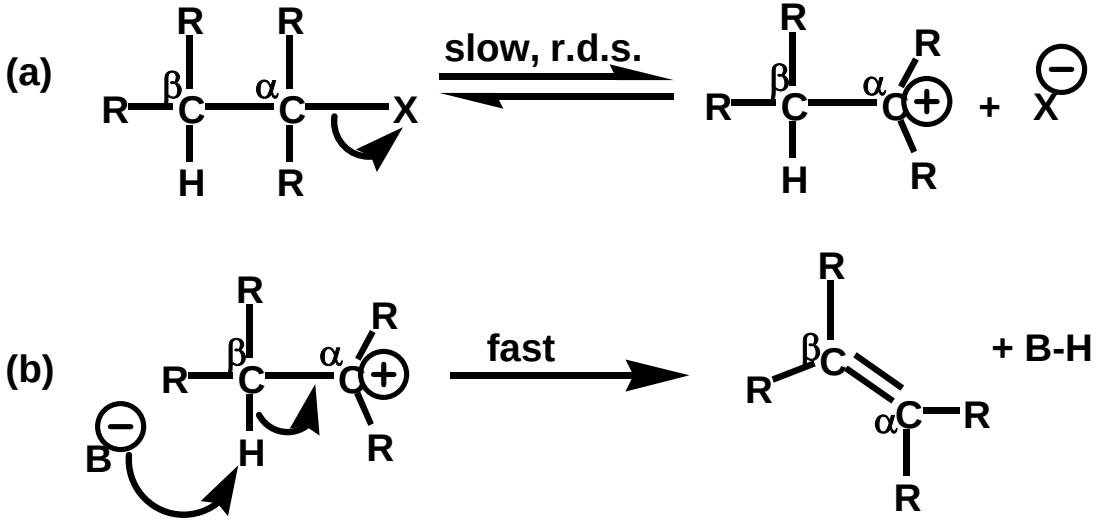


B-Elimination reaction

- The elements of HX are lost from neighboring carbon atoms and a C=C is formed. The head carbon of the alkyl halide is termed α ("alpha") and the carbon atom or atoms next to it are designated β ("beta"). The halogen atom is lost from the α carbon, and the hydrogen from one of the β carbons.
- important mechanisms by which alkyl halides undergo elimination reactions are:
- The **E1 mechanism** (unimolecular);
- The **E2 mechanism** (bimolecular)

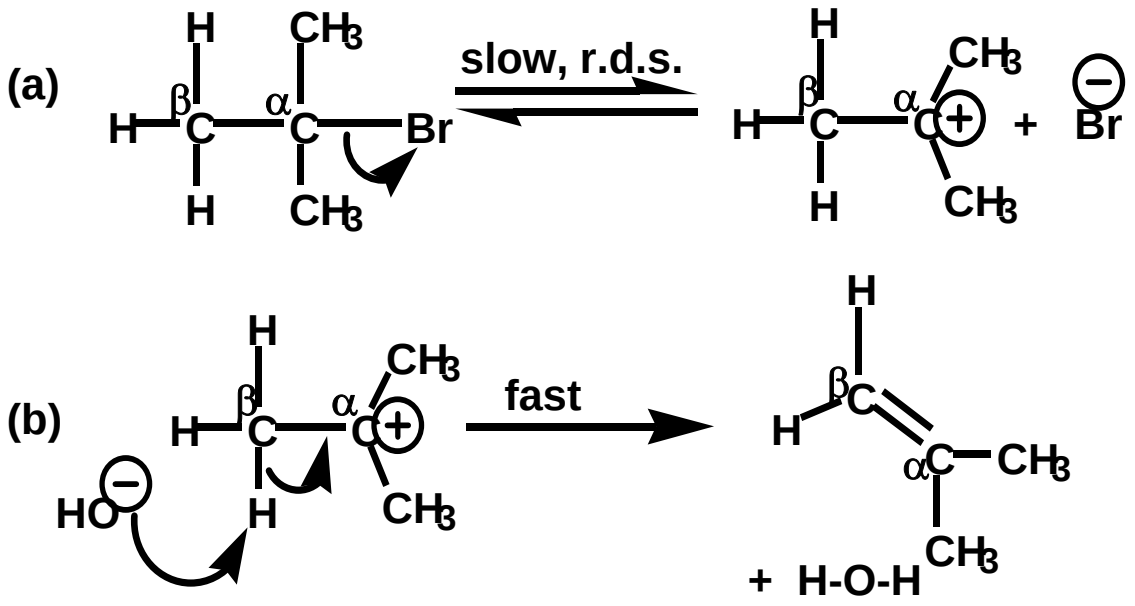
The unimolecular mechanism (E1)

- **The slow, rate determining step entails one species – the alkyl halide.**
- **The rate of the reaction = k[alkyl halide], and the carbocation intermediate**



E1 mechanism

A ***carbocation intermediate*** is formed when alkyl halides undergo elimination via the E1 (unimolecular) mechanism.3^{o} alkyl halides are likely to lose HX via this mechanism. For *t*-butyl bromide in aqueous alcoholic KOH:



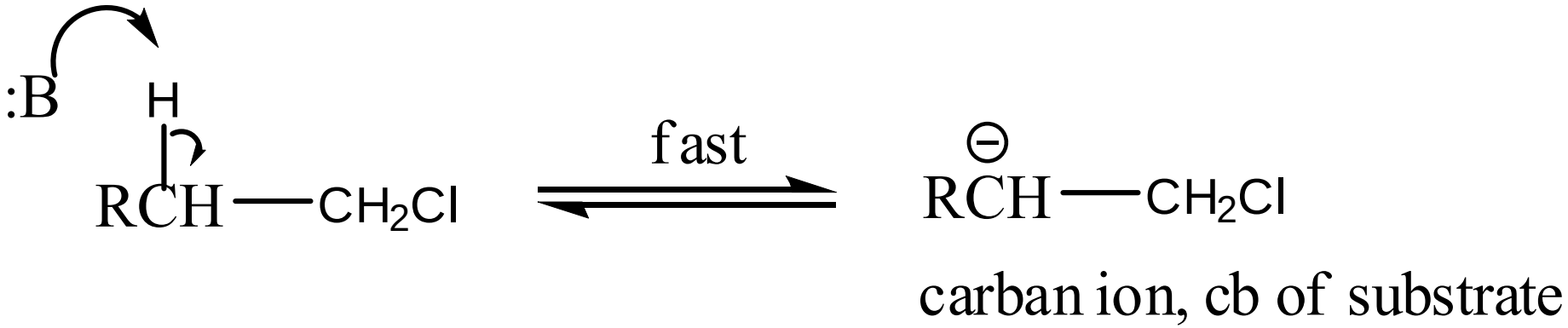
Evidences for E1 mechanism

- It follows first order kinetics as rate of reaction depends only on concentration of substrate and is unimolecular
- Not accompanied by H-isotope effect, which is not expected in E1 as proton is removed in fast second step, whose rate is negligible
- Rate of reaction depends on the stability of carbo cation$3^0>2^0>1^0$)
- When substrate structure permits it undergo rearrangement by hydride or alkyl shift e.g. neo pentyl bromide
- E1 reactions are nonstereospecific
- Ease of formation of alkene is R2C=CR2>CR2=CHR> RCH=CHR> CR2=CH2> RCH=CH2> CH2=CH2
- Potential energy diagram of PE vs Reaction progress

E1Cb mechanism:

In E1cb mechanism in a fast first step base abstracts the proton in a forming carban ion i.e. conjugate base of a substrate, which is under equilibrium with substrate. Rate of reaction depends on the concentration of carban ion, therefore the name given Unimolecular Elimination via Conjugate base.

Step 1



E1cb

We can establish Keq=[anion]/[base][substrate]----1

In the second slow step leaving group departs with its electron pair to form a new bond

Now rate α [anion]------2

So rate=K1[anion]--------3

And [anion]=Keq[base][substrate]---4

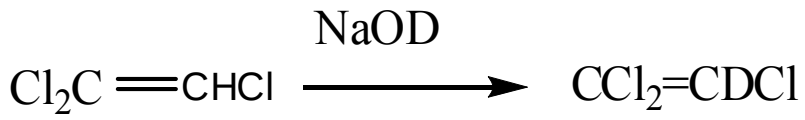
From 1 and 4 we have Rate = K1.Keq[base][substrate]

Establishing new constant K for K1.Keq we have

Rate = K[base][substrate]

E1cb

This is same as bimolecular rate law for E2 reaction, which is evident by following reaction, Deuteriated product is only possible if it follows second order kinetics.



Increasing acidity of B-proton leading to the spectrum towards E1cb reaction.

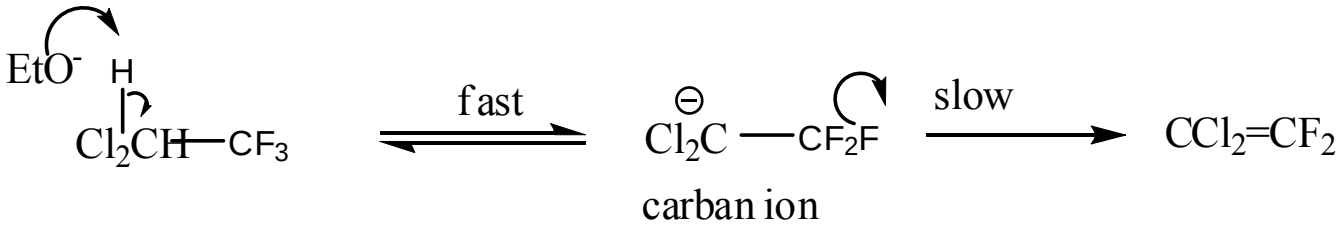
High electro withdrawing nature of leaving group increases the acidity of B-proton.

Use of stronger base and base concentration also increase E1cb reaction to occur.

E1cb

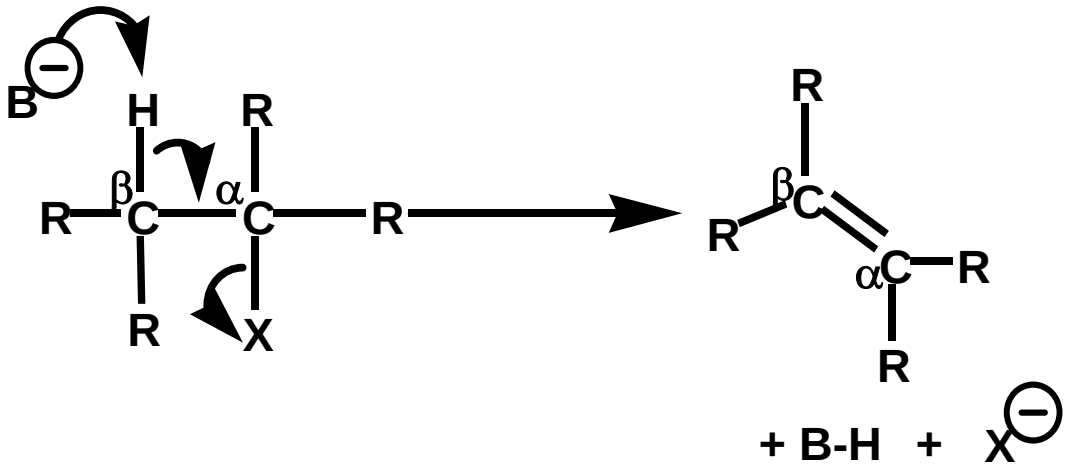
This much likely to occur when triple bond is formed, since the H of SP3 is less acidic H of SP2, so triple bond is more readily formed.

e.g.



The bimolecular mechanism (E2)

This is a *concerted* reaction. Bond formation and bond breaking take place simultaneously.the rate determining step entails the base and the alkyl halide.



Where rate = k[alkyl halide][base]

Evidences for E2 mechanism

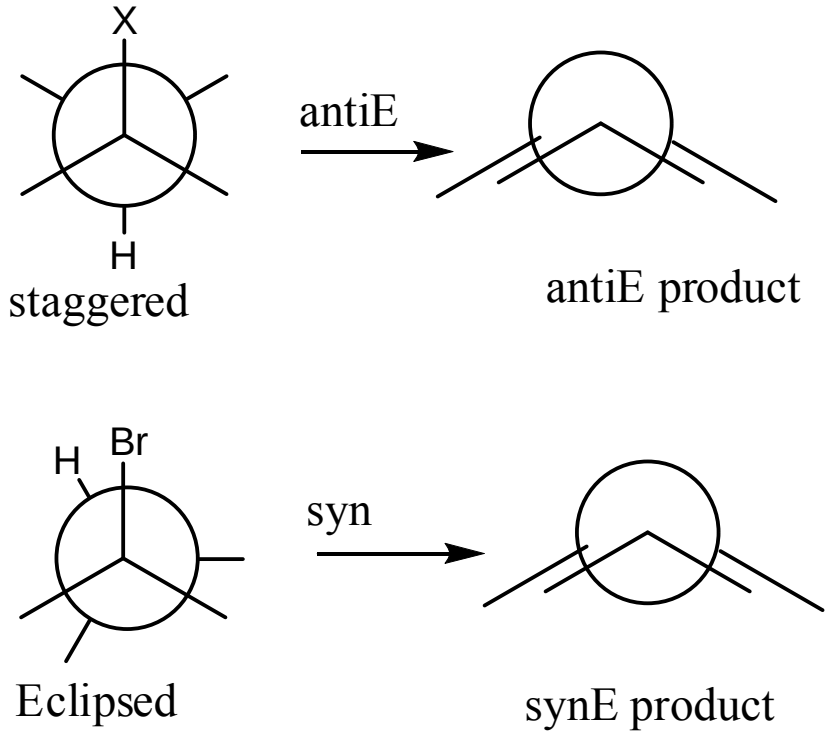
- It follows second order kinetics as rate of reaction depends only on concentration of substrate and base i.e. bimolecular Rate=[substrate][base]
- Accompanied by H-isotope effect, which expected in E2as proton is removed in the same step
- If H is replaced by D, rate of reaction is slower down as breaking of C-H bond is faster than C-D bond
- Not accompanied by rearrangement
- E1 reactions are stereospecific
- Ease of formation of alkene is R2C=CR2>CR2=CHR> RCH=CHR> CR2=CH2> RCH=CH2> CH2=CH2
- Potential energy diagram of PE vs Reaction progress

Stereochemistry of E2 mechanism:

- Syn and Anti elimination in E2 mechanism:
- In the case of bimolecular elimination reaction the eliminating groups eliminate either from the same side or from the opposite sides. If they eliminate from the opposite sides i.e. anti in position the elimination is known as anti elimination.
- If they eliminate from the same side i.e. syn in position the elimination is known as syn elimination.
- In anti E substrate has staggered conformation while that of in syn is eclipsed. In staggered conformation C-X, C-C and C-H bonds are in the same plane making an angle of 180^0, therefore electron pair to B-carbon is made easily available for the formation of new bond.

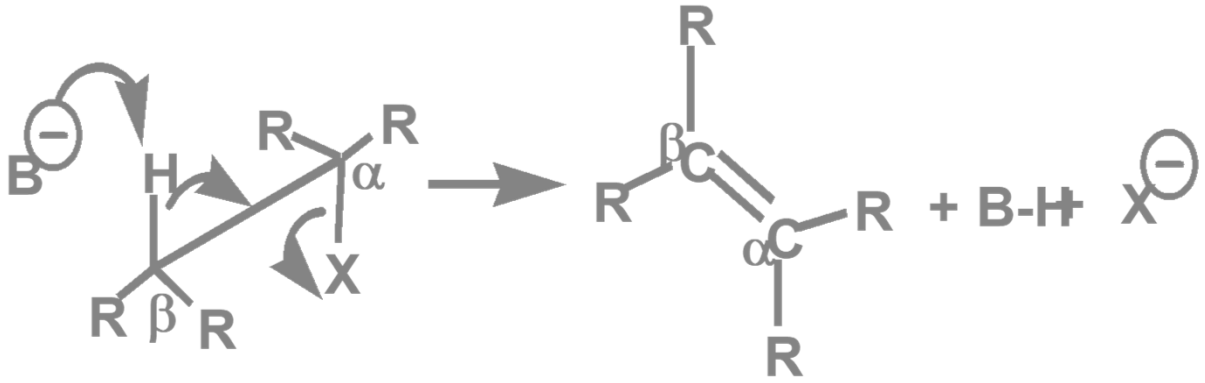
Sterechemistry of E2

E2 reactions are highly stereospecific and anti elimination is preferred over syn elimination as substrate has to adopt an eclipsed conformation, which is higher in energy, eliminating groups are eclipsing in position making 0^0 angle.



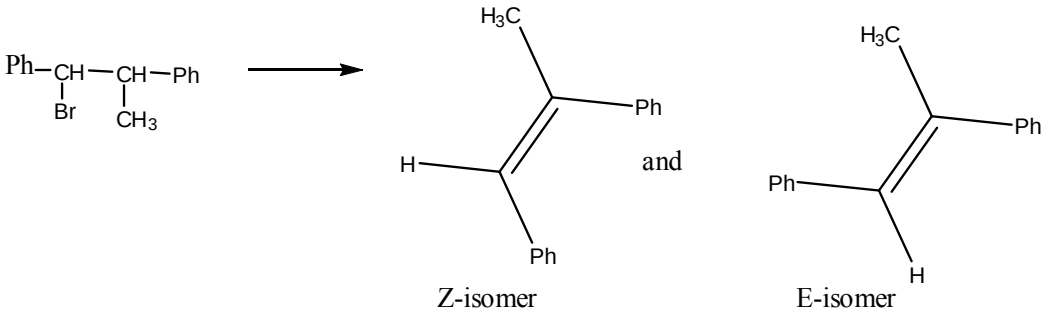
Anti elimination in E2

A very important feature for an alkyl halide to undergo elimination via the E2 mechanism, the H and X groups must be ***anti*** to each other and be in the same plane with each other and the carbon atoms to which they are attached. The elements of H-X must be ***antiperiplanar.***

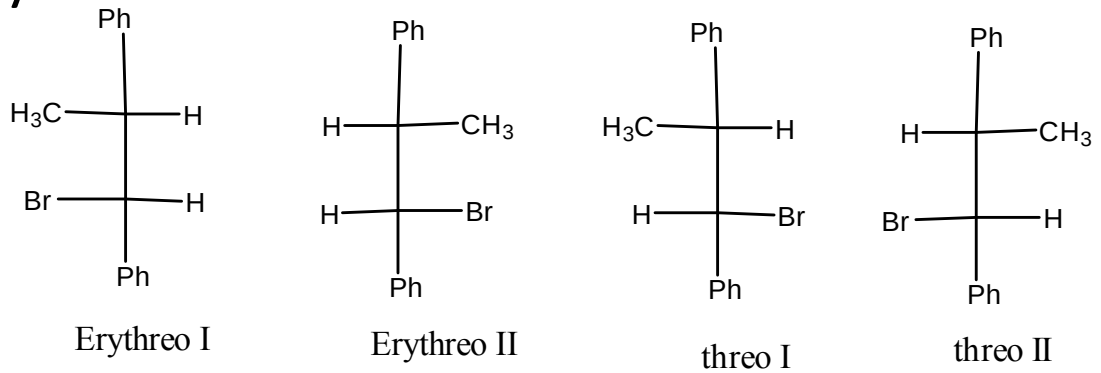


Evidences for anti elimination in E2:

1,2-Diphenyl-1-bromopropane undergoes elimination to form Z and E-1,2-diphenylprop-2-ene.



Ph-C(Br)-CH(CH3)-Ph. It can exist as erythro and threo isomers. In addition each erythro and threo isomers exists as enantiomers.

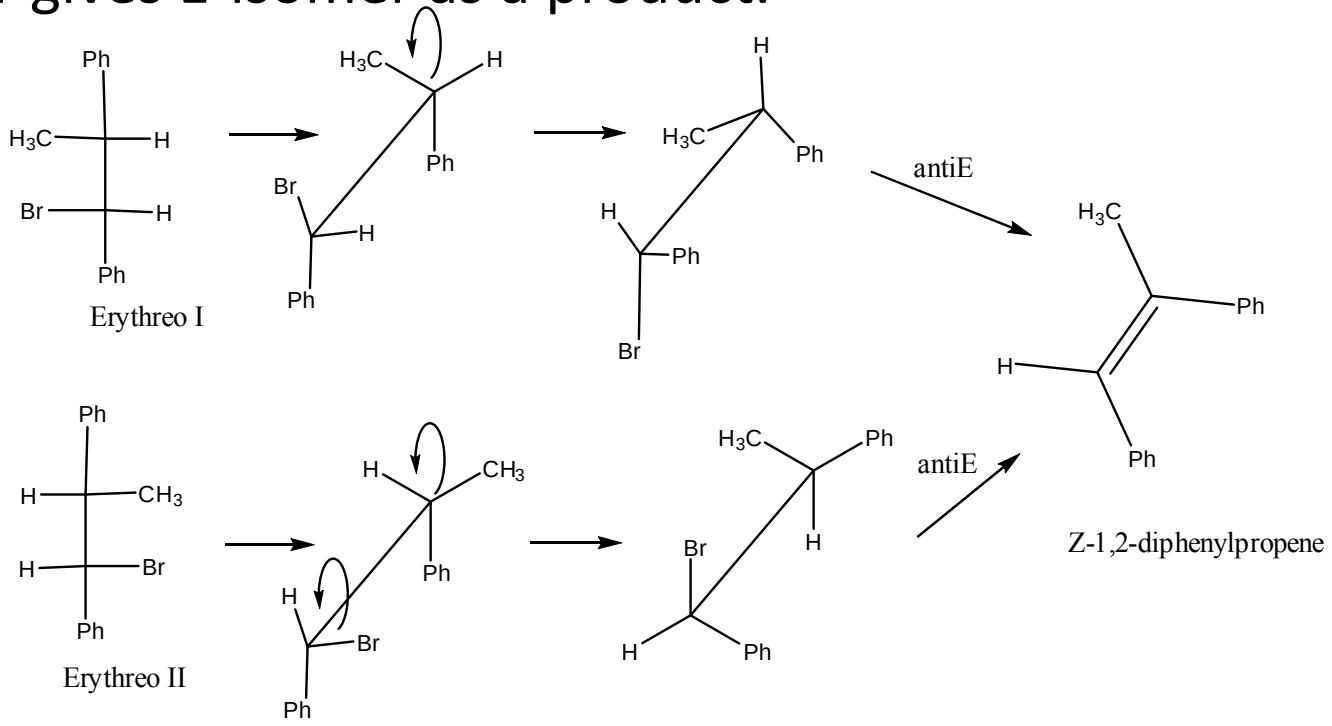


a pair of enantiomers dlpair 1

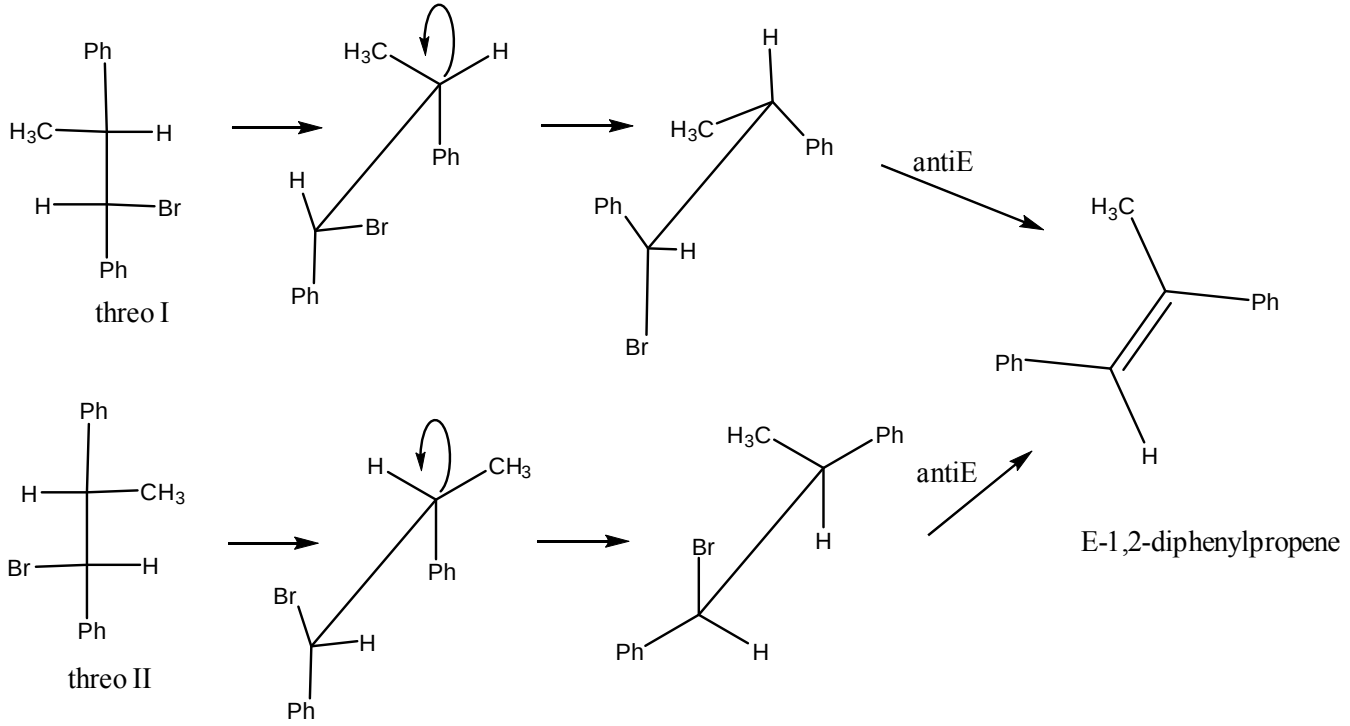
a pair of enantiomers dl pair 2

Stereochemistry of E2

In anti elimination atoms or groups are removed from opposite sides. Erythro isomer undergoes elimination to give Z-isomer and threo isomer gives E-isomer as a product.

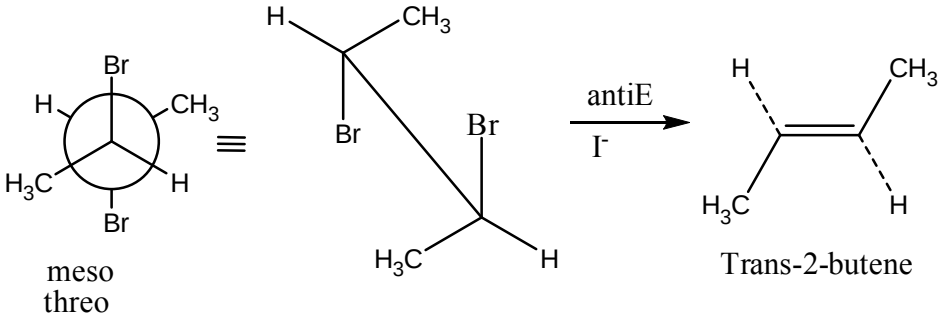


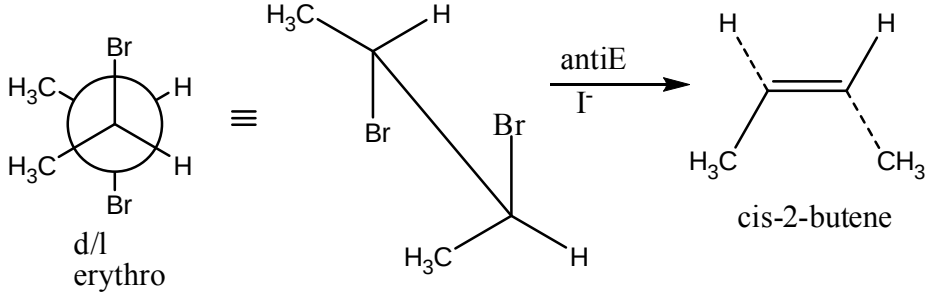
Threo isomer gives E-olefin



This results are only obtained if anti elimination occurs.

2) Reaction of meso-2,3-dibromobutane in presence of iodide ion gives trans-2-butene, where as d/l 2,3-dibromobutane gives cis-2-butene



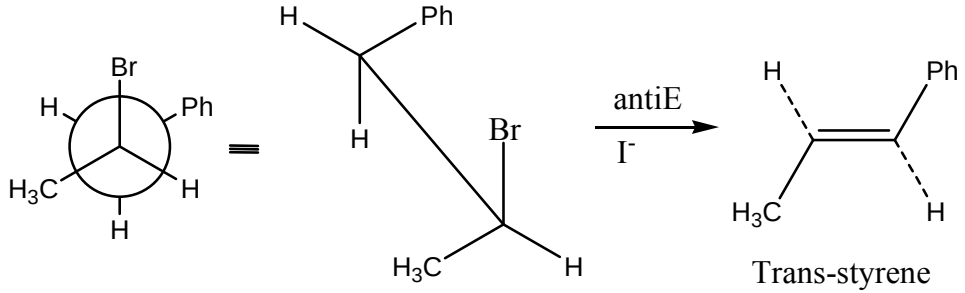


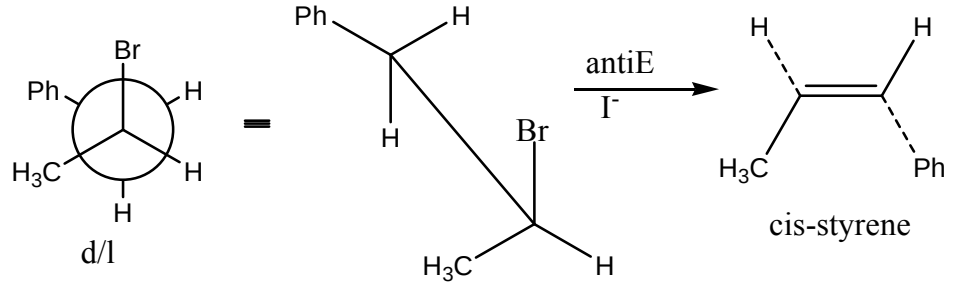
Reaction of meso-2,3-dibromobutane in presence of iodide ion as base gives trans-2-butene, where iodide ion abstracts the bromonium ion(Br^+) as base abstracts the proton, and bromanium ion(Br^-) departs as a leaving group with its electron pair. d/l 2,3-Dibromobutane under same condition gives cis-2-butene. Meso compound undergoes reaction at the double rate than dl pair as bulky methyl groups are in opposite sides(threo), while that of dl pair are in the same side(erythro) lowering the rate of reaction.

Eclipsing effect in E2

- Lowering the rate of reaction in E2 reactionsdue to steric effect is known as eclipsing effect in E2.
- If CH_3 groups are replaced by Phenyl groups, rate of reaction decreases 100 times. Steric effect lowering the rate of E2 is known as eclipsing effect in E2.

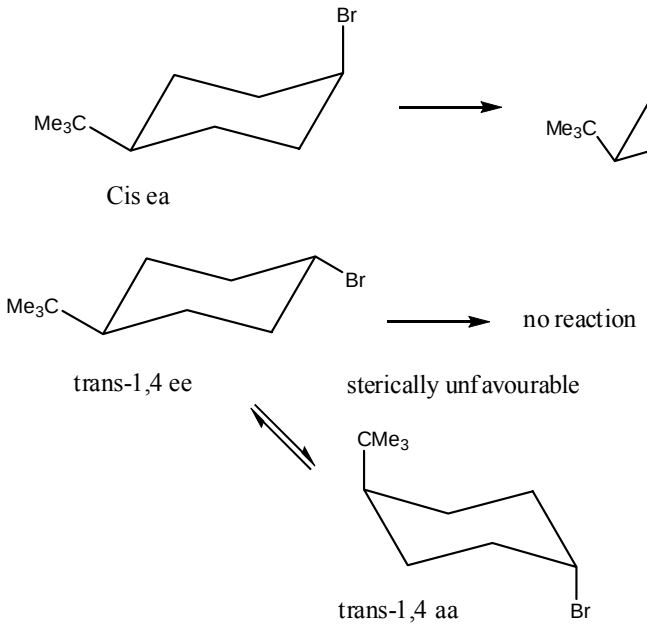
3) Reaction of 2-bromo-1-phenylprapane in presence of alkoxide as base gives styrene. Threo isomer gives trans product whereas erythro gives cis product. Among threo undergo reaction at a faster rate.





In threo isomer they are on the opposite side. While in erythreo isomer bulky Ph and Me groups are on the same side, that causes steric effect leading to the partial eclipsing conformation, which is less stable conformer and undergoes reaction at a lower rate than threo isomer. In this case eclipsing effect plays important role.

Cis-tert-butylcyclohexylbromide under goes elimination reaction to give Cis-tert-butylcyclohexene, where as its trans isomer does not undergo reaction at all-justify



1,2-dimethylcyclohexane	trans	aa ee
	cis	ea ae
1,3-dimethyl	trans	ea ae
	cis	aa ee
1,4-dimethyl	trans	aa ee
	cis	ea ae

For Cis-tert-butylcyclohexylbromide ea or ae conformations are possible.

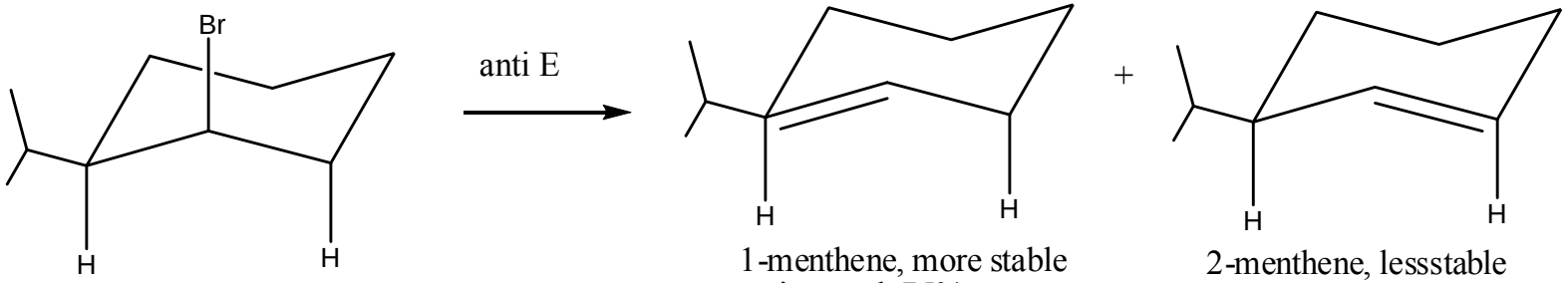
E2 elimination in six membered ring proceeds best when adjacent trans group can adopt antiperiplanar conformation, even if this is higher energy conformation.

The stable conformation having bulky tert-butyl in equatorial position and bromide in axial position, in which Br-C, C-C and C-H bonds have antiperiplanar relationship and can easily undergo E2 reaction to give Cis-tert-butylcyclohexene.

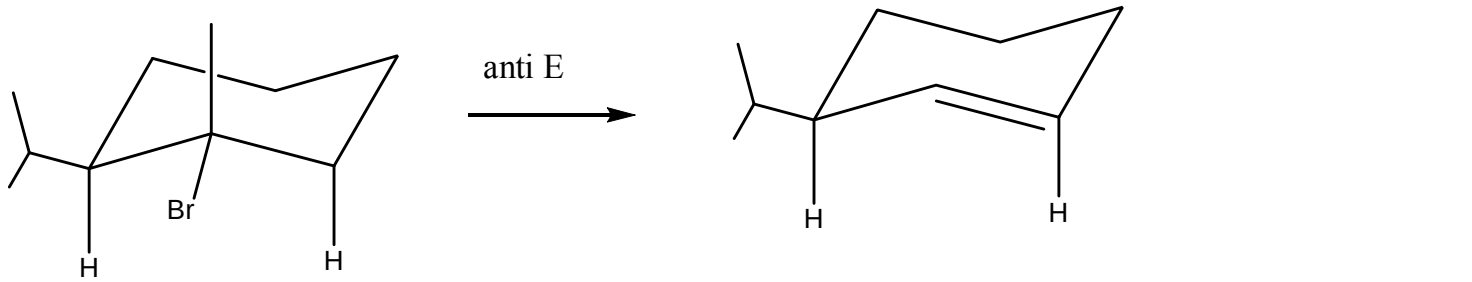
Whereas, in case of trans-tert-butylcyclohexylbromide aa or ee conformations are possible. The stable conformation having bulky tert-butyl and bromide both in equatorial position.

To adopt antiperiplanar relationship for Br-C, C-C and C-H bonds, ee conformation to be converted aa conformation, where tert-butyl group has to be equatorial, that is sterically unfavourable, therefore it can not undergo E2 elimination at all.

Neomenthyl bromide when undergoes E2 elimination reaction to give 1-menthene(more stable, major prod 75%) and 2menthene(less stable minor prod 25%), while menthyl bromide under goes E2 elimination reaction to give only 2-menthene as a product-justify.



H at C1 and C3 are anti to Br



menthylbromide

2-menthene, only prod minorprod as only H at C3 is anti to Br

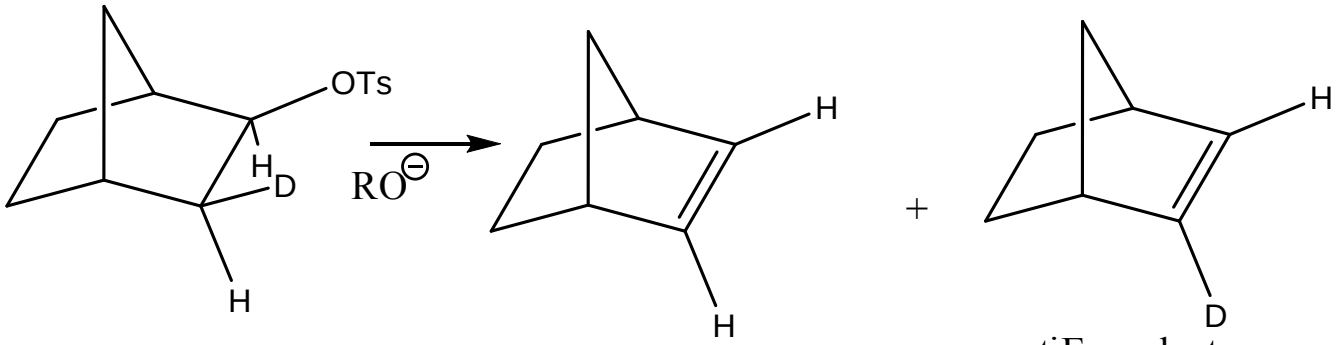
E2 in menthylchloride and neomenthylchloride

- E2 elimination in six membered ring proceeds best when adjacent trans group can adopt antiperiplanar conformation, even if this is higher energy conformation.
- In neomenthyl bromide bulky iso-propyl group tends to remain equatorial, Br is axial and two axial H atoms on neighboring carbon are axial and anti to Br for E2 anti elimination.
- Where as in menthylchloride bulky iso-propyl group tends to remain equatorial, Br is also equatorial. For Br, To become axial it has to convert iso-prop group from equatorial to axial which is sterically unfavourable, and can have only one axial H atom on neighboring carbon anti to Br for E2 anti elimination.
- In addition 1-menthene is obtained as a major product according to Sayzeff's orientation rule.

Syn elimination in E2:

- In certain rigid system eliminating groups do not contain antiperiplanar arrangement, then the elimination follows different path. When eliminating groups are on the same side making an angle of 0^0 having syn periplanar arrangement they follow syn elimination.

1. Deuteriated norbordyl tosylate when undergoes E2 elimination reaction syn product is obtained without D (major) and anti product with retention of D (minor). Ion pairing in ionizing solvent promotes syn E.



synE product

D and OTs are removed

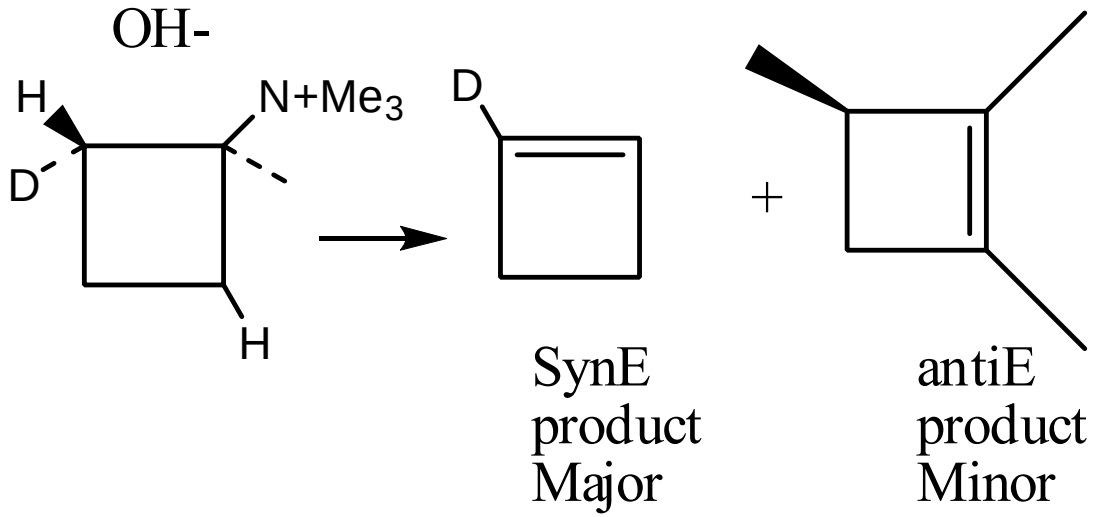
70% in presence of 18-C-6

antiE product

H and OTs are removed, no 180 but 120

30% in presence of 18-C-6

2. When cyclobutyltrimethylammonium hydroxide undergoes E2 elimination, following syn and anti products are obtained.

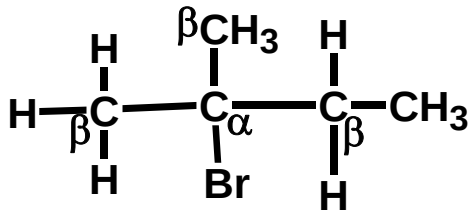


Other aspects of E1 and E2 reactions

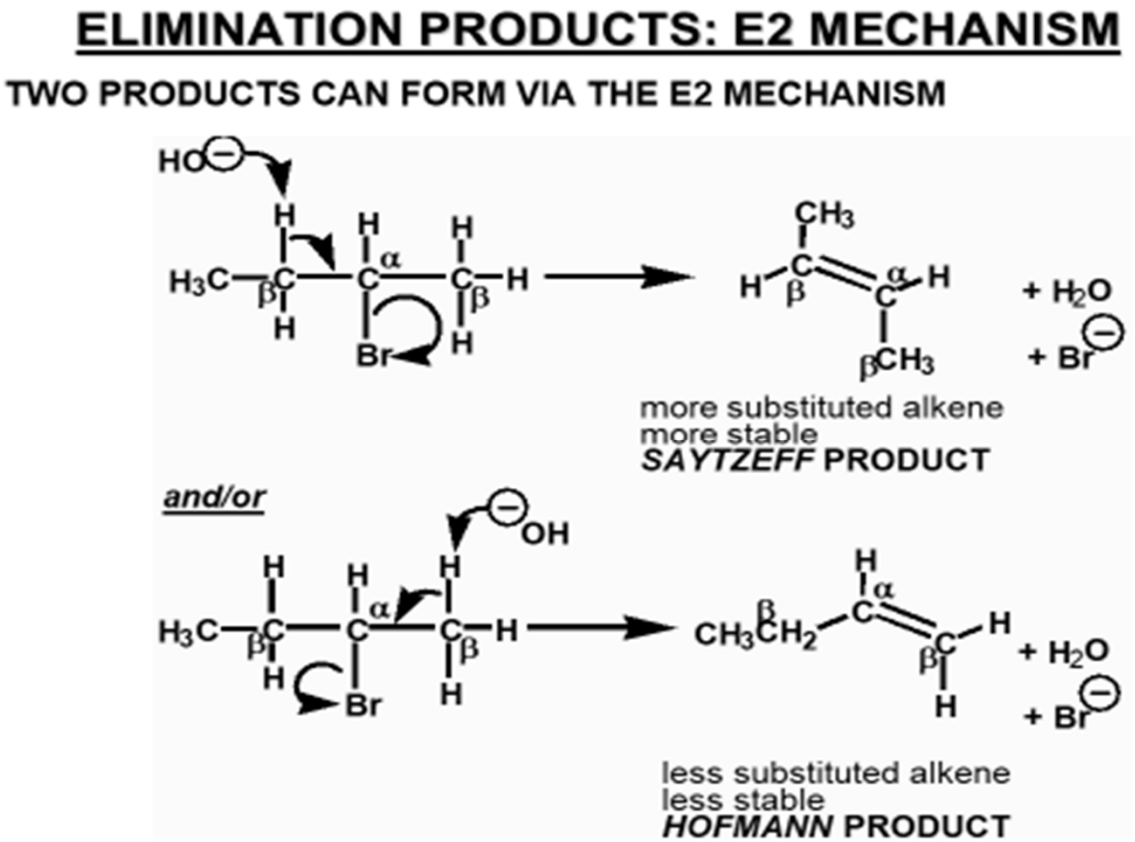
- The distinction between the E1 and E2 mechanisms is not as clear as the distinction between the SN1 and SN2 mechanisms.
- 3^o and 2^o alkyl halides will eliminate H-X via both the E1 and E2 mechanisms, the elimination of H-X from 1^o alkyl halides takes place via the E2 mechanism only.
- For both E1 and E2 mechanisms, the rates follow the trend:
- 3^o R-X **>** 2^o R-X **>** 1^o R-X (do not react via E1)

For many alkyl halides, there are two possible elimination products.

The 3° alkyl halide below has three β carbons; two are identical methyl (Me) groups, and the 3rd



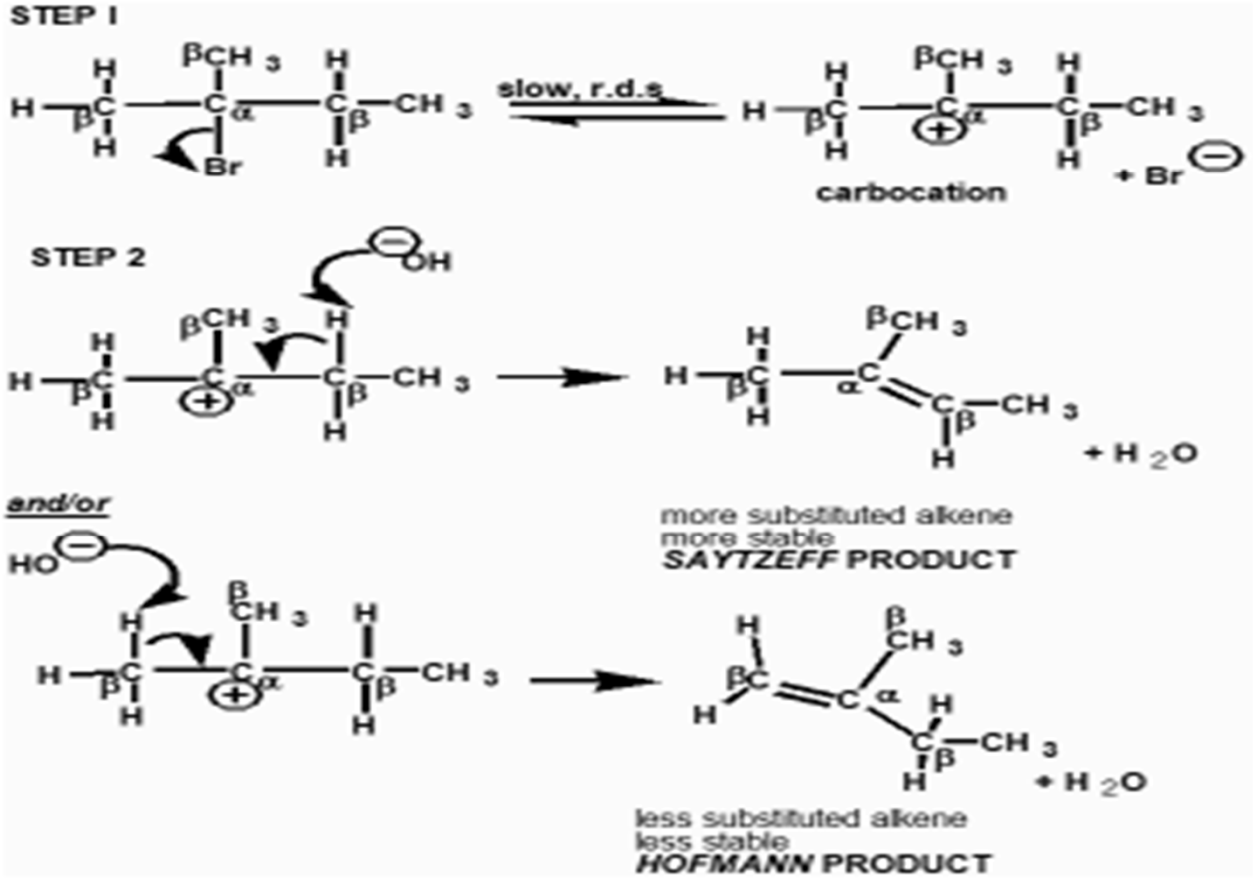
e.g.the elimination of HBr from this compound via the E1 mechanism.



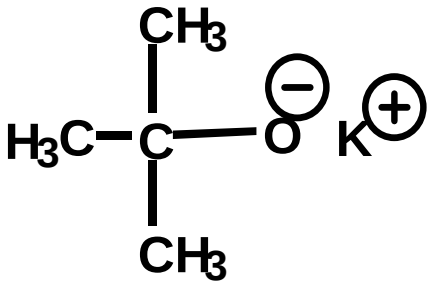
The proportion of the less substituted alkene (Hofmann product) can be increased by using a very bulky base. Two examples of bulky bases are shown

ELIMINATION PRODUCTS: E1 MECHANISM

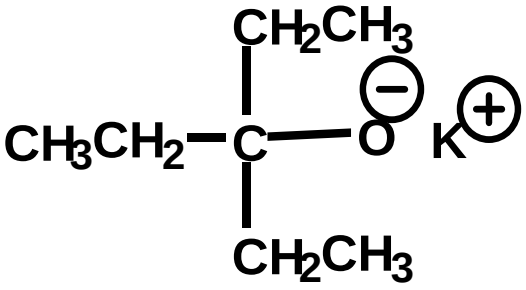
Two products can result from the loss of H-Br



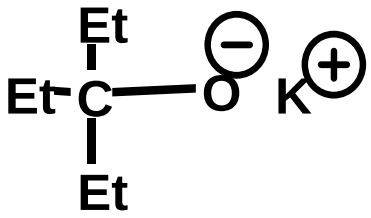
Bulky bases increase the proportion of the less substituted alkene (Hofmann product) formed in elimination reactions.



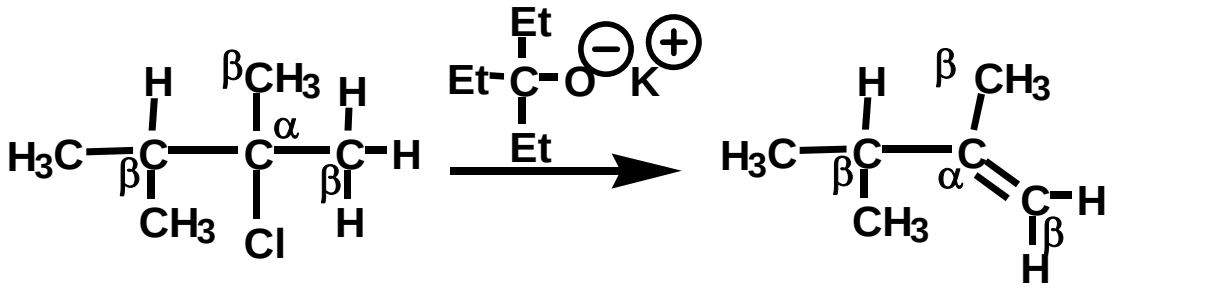
potassium *t*-butoxide



potassium 3-ethyl-3-pentoxid



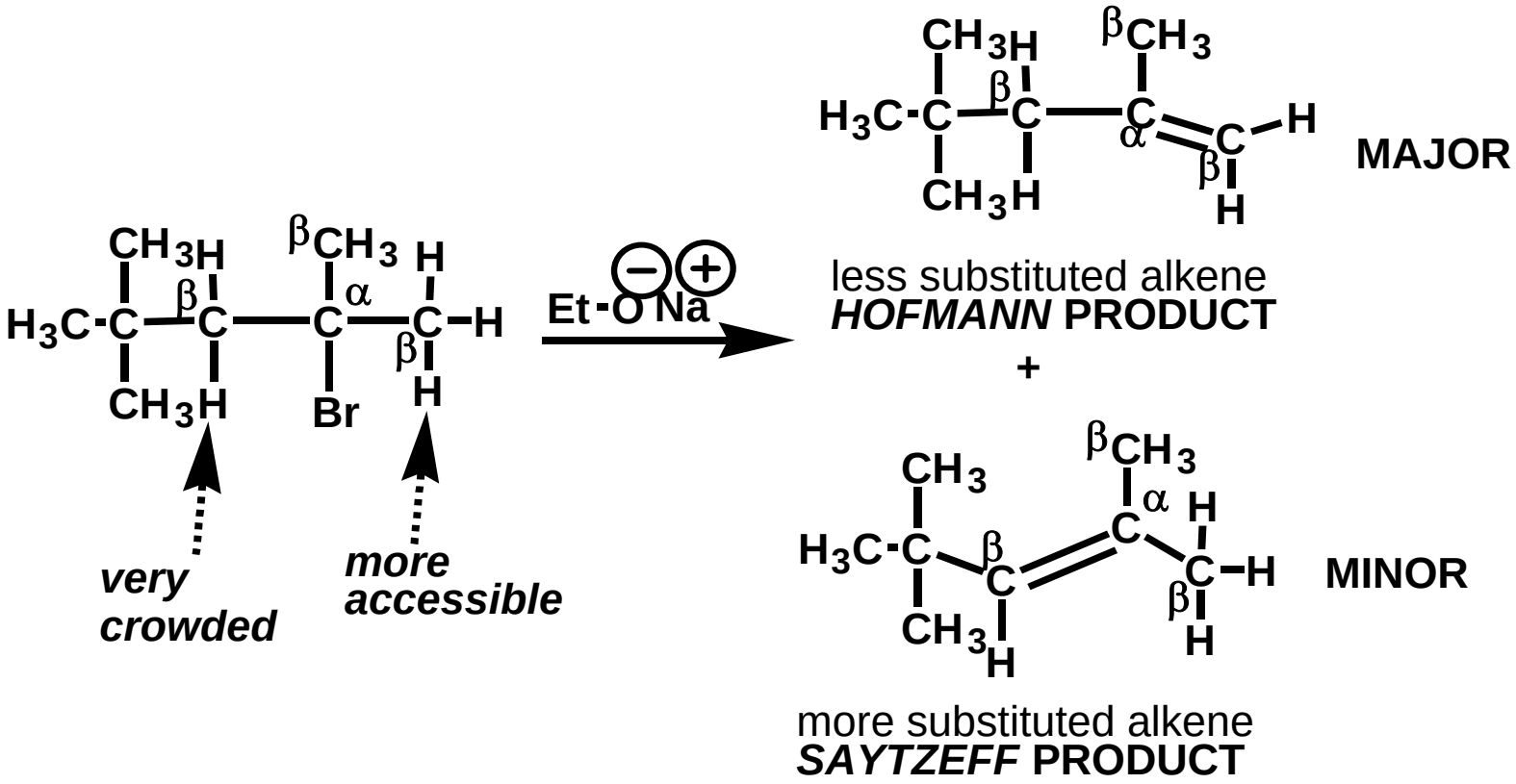
The H's on the less substituted β carbon are more sterically accessible to the base than are the H's on the more substituted β carbon. When the base is very bulky, then the H's on the less substituted β carbon are almost exclusively removed, and the less substituted (Hofmann) alkene product predominates.



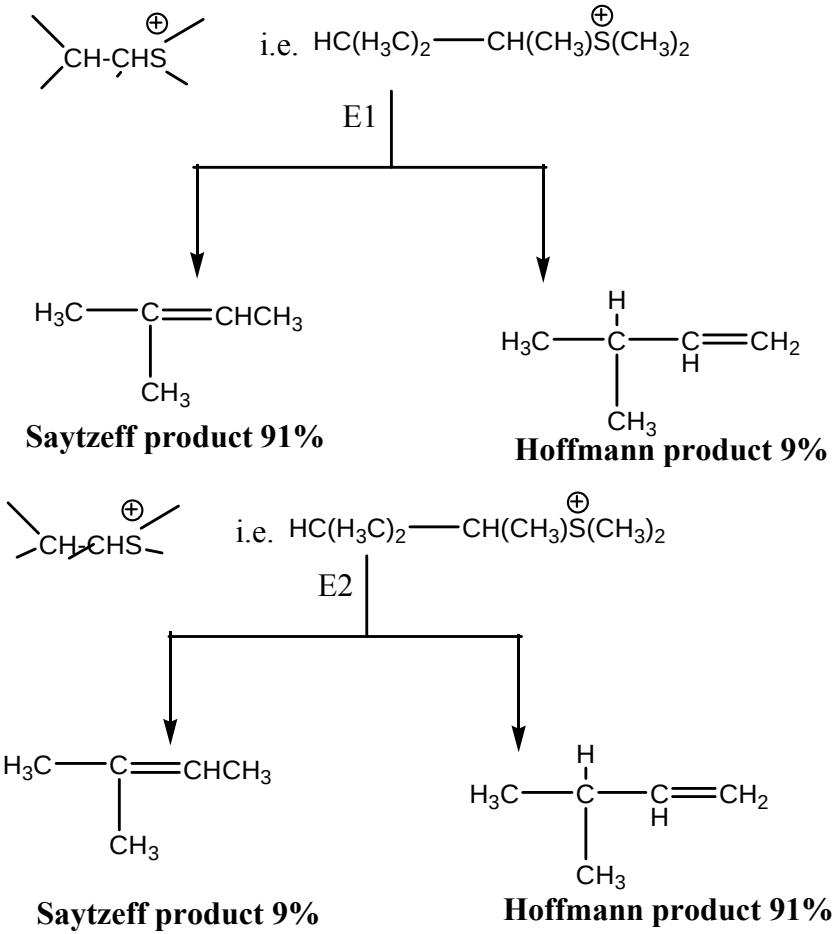
97% less substituted alkene
***HOFMANN* PRODUCT**

Elimination products: Hofmann vs. Saytzeff

Steric accessibility of the β h affects the outcome of elimination reactions. If the h on the β carbon whose elimination leads to the more substituted alkene is very crowded, then the proportion of the less substituted alkene product will be high.

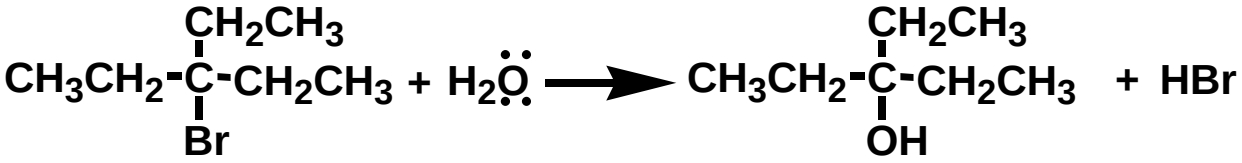


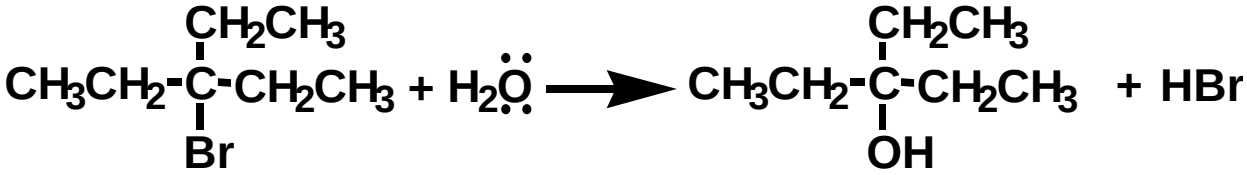
When $Me_2CHCH(Me)S^+(Me)_2$ undergoes elimination under E1 condition it favors Saytzeff's product, where as under E2 condition it favors Hoffmann product formation.



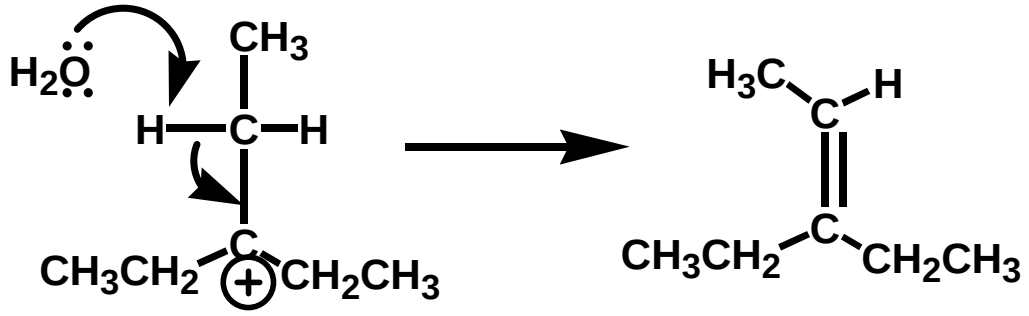
Substitution versus elimination: SN1 vs E1

When substitution reactions are carried out on 3^{o} alkyl halides (SN1 reactions), products of elimination (alkenes) are almost inevitably formed. Let us consider the following reaction.





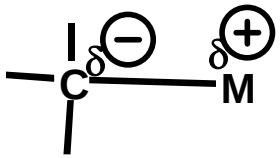
In this reaction the carbocation intermediate, once it is formed, can lose a proton by reaction with a weak a base as H_2O to give appreciable quantities of the alkene (elimination) product.



Substitution versus elimination: E2 vs SN2

- **It is easier to create conditions which favor the E2 mechanism over the SN2 mechanism, or *vice versa.***
- ***very strong base*** (ethoxide as opposed to hydroxide)
- ***Relatively non-polar solvents***
- (e.g. ethanol in preference to water)
- ***Higher temperature***
- will favor the E2 mechanism over the SN2 mechanism.

Organometallic compounds



Compounds in which a metal is directly bonded to carbon are known as ***organometallic compounds***. The metal-carbon bond is polarized as shown.metals are less electronegative than carbon; larger differences in electronegativity between the metal and carbon increase the ionic character of the metal-carbon bond. Ionic character of metal carbon bonds follows the trend is

Na > Li > Mg > Al > Rn > Cd > Hg

Alkyl derivatives of almost all metals have been prepared.these are named as "alkylmetals"

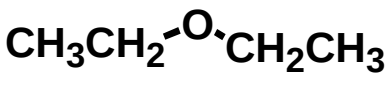
$(Me)_2Hg$ dimethylmercury

(liquid; bp 92 ^{o}c; neurotoxin; environmental contaminant)

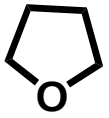
$(Et)_4Pb$ tetraethyllead (liquid; bp ~ 220 ^{o}c; toxic; formerly used as a gasoline additive)

Grignard reagents

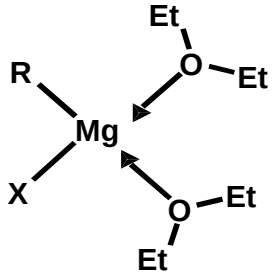
Alkylmagnesium halides, R-Mg-X, are known as ***grignard reagents***. Grignard reagents are prepared by reacting alkyl halides with excess magnesium metal in dry alcohol-free diethyl ether or tetrahydrofuran (THF). Diethyl ether and THF are solvents.



diethyl ether



tetrahydrofuran (THF), a cyclic ether



R-X + Mg $\rightarrow$ R-Mg-X (radical mechanism)

Ease of formation follows the trends shown below

R-I > R-Br > R-Cl.

$CH_3X > C_2H_5X > C_3H_7X$

Grignard reagents are usually closely associated with two molecules of the ethereal solvent in which they have been prepared.