

Introduction

In this module, different types of elimination reactions are described. From a practical standpoint, elimination reactions widely used for the generation of double and triple bonds in compounds from a saturated precursor molecule. The presence of a good leaving group is a prerequisite in most elimination reactions. Traditional classification of elimination reactions, in terms of the molecularity of the reaction is employed. How the changes in the nature of the substrate as well as reaction conditions affect the mechanism of elimination are subsequently discussed. The stereochemical requirements for elimination in a given substrate and its consequence in the product stereochemistry is emphasized.

ELIMINATION REACTIONS

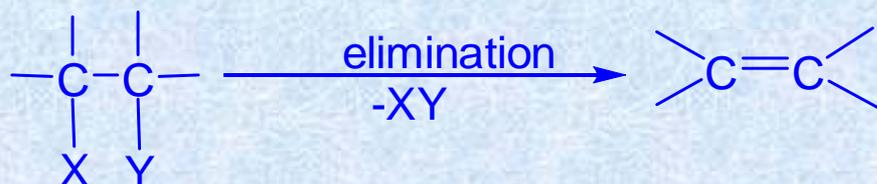
Objective and Outline

- beta-eliminations*
- E1, E2 and E1_cB mechanisms*
- Stereochemical considerations of these reactions*
- Examples of E1, E2 and E1_cB reactions*
- Alpha eliminations and generation of carbene*

I. Basics

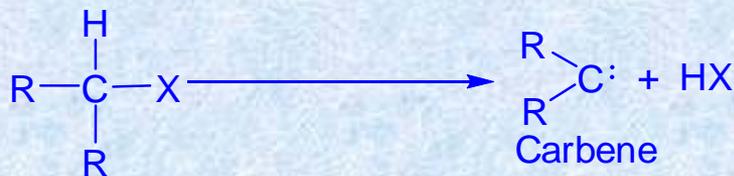
Elimination reactions involve the loss of fragments or groups from a molecule to generate multiple bonds.

A generalized equation is shown below for 1,2-elimination wherein the X and Y from two adjacent carbon atoms are removed,



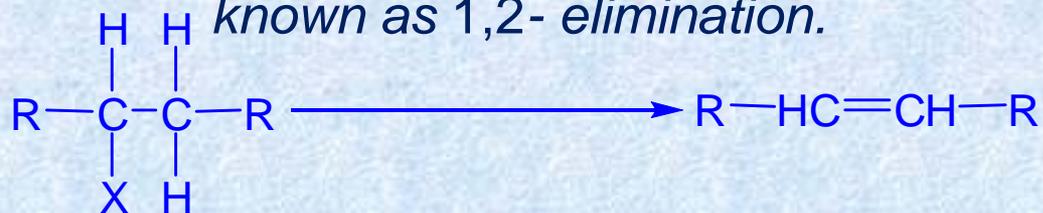
Three major types of elimination reactions are:

α -elimination: two atoms or groups are removed from the same atom.
It is also known as 1,1-elimination.

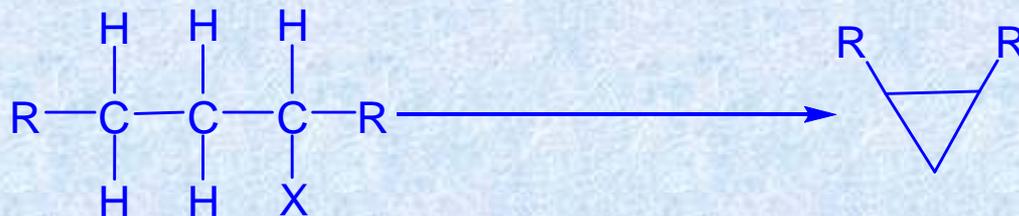


Both H and X are removed from carbon atom here

β -elimination: loss of atoms or groups on adjacent atoms. It is also known as 1,2- elimination.



γ -elimination: loss of atoms or groups from the 1st and 3rd positions as shown below. Generally such elimination reactions result in cyclic compounds.



Apart from these three, there is one more way i.e., extrusion reaction in which a fragment is lost either from a chain or a ring.



II. More details on β -eliminations

β -eliminations can be further subdivided into three categories depending upon the mechanistic pathway. The important aspect is to establish the number of molecules taking part in the elimination step (molecularity of the reaction)

The types of β -eliminations are

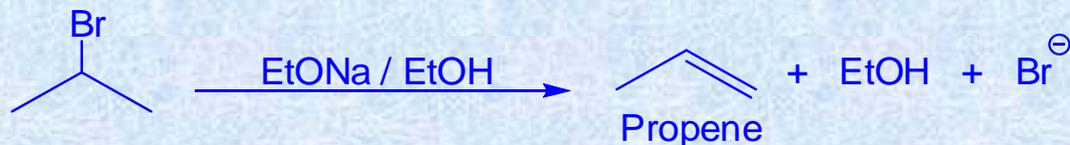
- 1) E2
- 2) E1
- 3) E1cB

These are read as “Elimination bimolecular E2”, “Elimination unimolecular” and “Elimination unimolecular conjugate base”

II. (1) E2 Eliminations

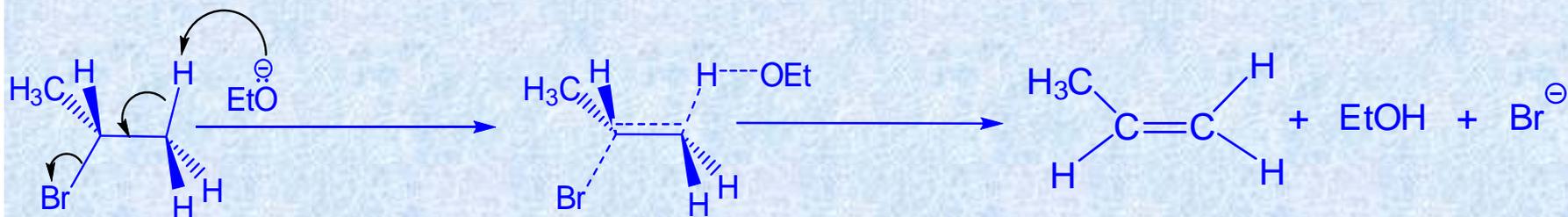
Key mechanistic features in this family are

- two groups depart simultaneously
- Involves one step (in other words, no intermediates are involved)
- bimolecular reaction i.e., both substrate and nucleophile participate in a single step
- The base abstracts the β hydrogen and leaving group simultaneously leaves such that it forms a multiple bond between α and β carbon atoms.



In the example given above, sodium ethoxide acts as the base, abstracting β -hydrogen. Bromine is the leaving group.

An illustration of a common elimination reaction is given below,

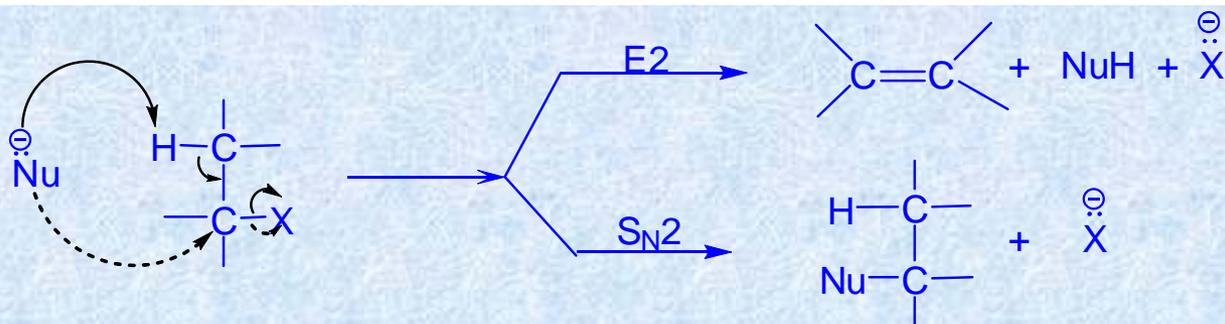


The sequence of events involved are,

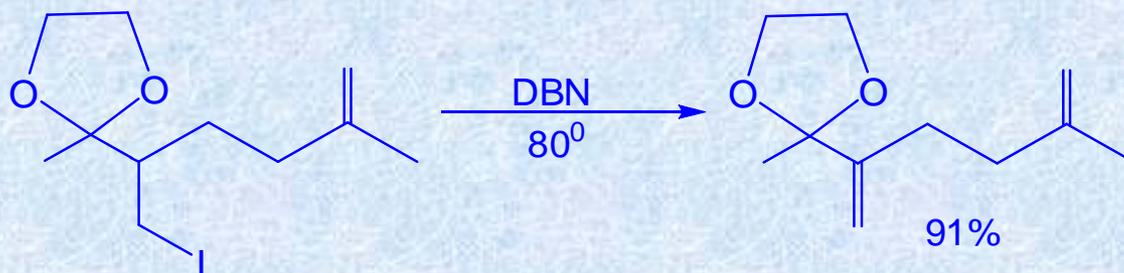
- The attack of ethoxide on β hydrogen and its abstraction as a proton is the first event. This will leave two electrons of the C-H bond available for the formation of a new double bond between the carbon atoms.
- As the new double bond is created, the C-Br bond begins to break away (leaving group). This will result in the departure of the bromide ion.

The events summarized above are the general steps, the extent of bond formation/breaking would depend on a number of factors described later.

Note: Often times, E2 elimination competes with S_N2 reactions. This is due to the inherent propensity of the incoming nucleophile also to attack the carbon atom bearing the leaving group. Such situations will lead to substitution products.

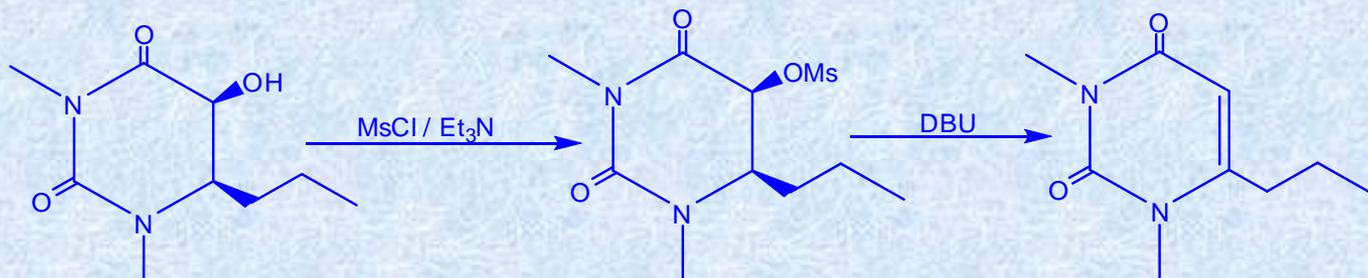
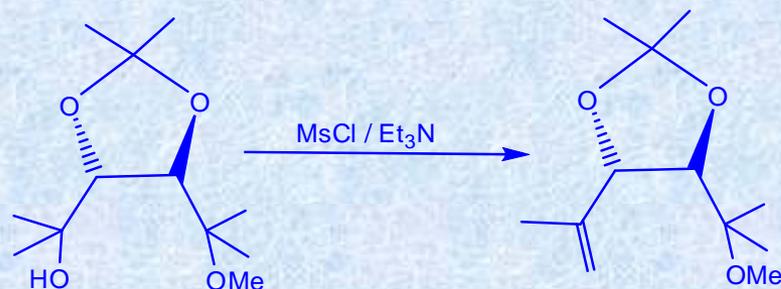


Examples of E2 elimination :



Note that examples given here are non-traditional, selected from the list of recently available examples. Standard examples can be found in basic text books

Additional Examples for E2 eliminations



Suggestions on **problem solving skills**:

Look at the given reaction and reagents first. Do not worry about the complexity of the given substrates. Focus on the 'site-of-reaction'

In the above examples, Et_3N is obviously the base, and 'OH-group' should be removed. Now, note that OH is a poor leaving group and conversion to O-mesyl is required here (achieved through the use of mesyl chloride, MsCl).

II. (2) E1 Eliminations

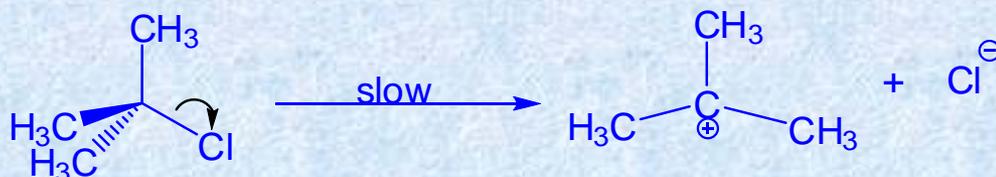
Important characteristics include,

it is two step reaction.

- *First step is similar to that of S_N1 reaction i.e., the generation of carbocation intermediate. Subsequently, hydrogen is abstracted by the base rather than attack on the carbocation as in S_N1*
- *only one of the substrates is involved in the rate determining step i.e., unimolecular reaction.*



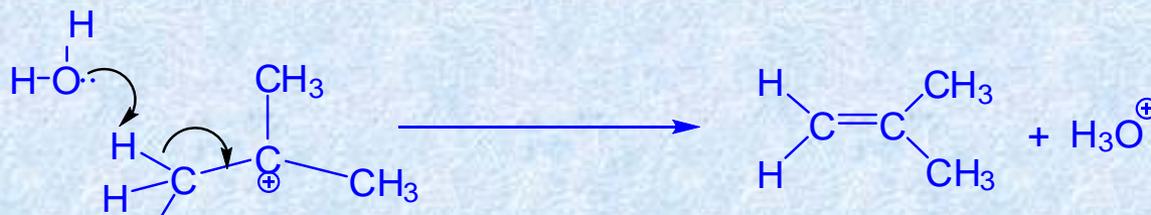
Step 1 :



*departure of chlorine with
bonding electron pair*

*stable carbocation
(tertiary)*

Step 2 :



attack of water or solvent molecule on the β hydrogen and subsequent movement of electron pair to the developing carbon carbon double bond.

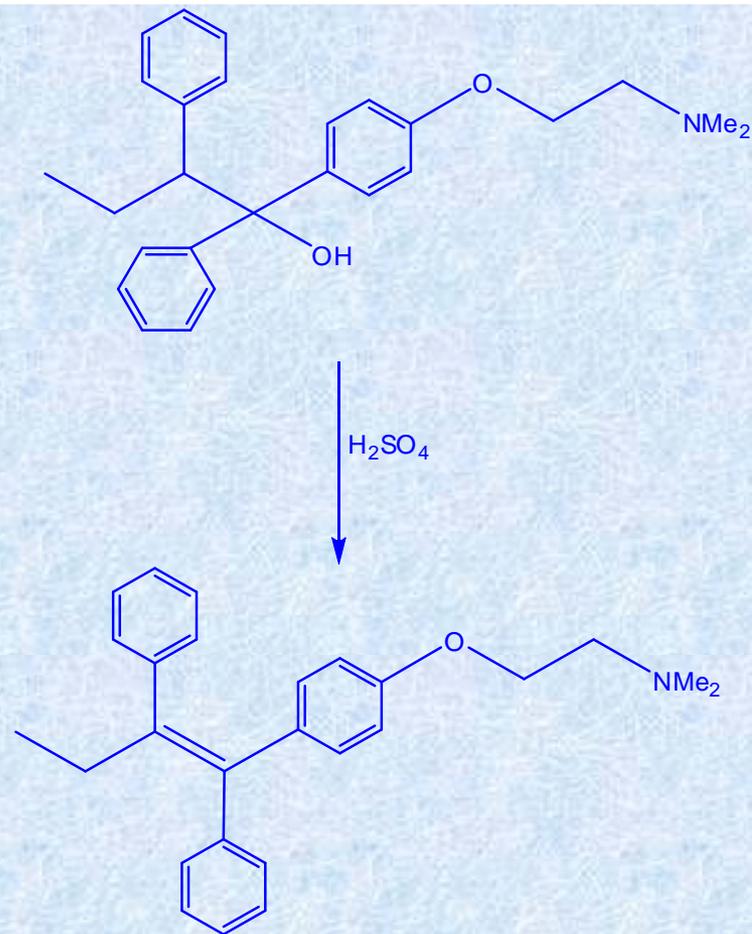
Note: Even though a sp^3 C-H bond is not acidic in a general sense, the presence of a carbocationic center adjacent to it renders increased acidity such that even a weak base such as water can deprotonate.

Similar to the competition between E2 and S_N2 pathways, E1 mechanism competes with S_N1.

Formation of carbocation is a slower process, as compared to the reaction between a 'reactive-carbocation' and a base/solvent. Hence, carbocation formation is the rate determining step.

Ideal conditions are for E1 mechanism are (a) highly substituted carbon atom for the carbocation center, such as a tert-carbon atom, (b) use of polar solvents (which can stabilize the resulting carbocation in addition to stabilizing a polar transition state involved in the heterolytic bond cleavage).

Examples for E1 elimination:



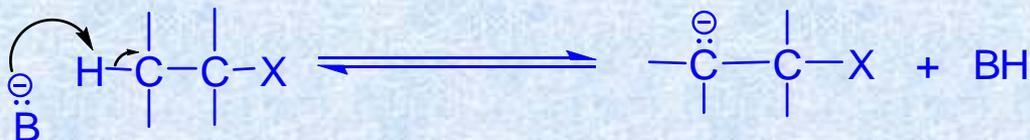
It can be readily noticed that the carbocation generated in the first step would be a stabilized species due to effective delocalization promoted by the presence of two phenyl groups on the tert-carbon.

III. *E1cB* Eliminations

- *This is a two step base-induced β elimination.*
- *In this reaction base first abstracts the β hydrogen, giving rise to a carbanion or **conjugate base** of the substrate from which the leaving group departs subsequently to form the product.*
- *An interesting comparison can be done with the *E1* pathway. The timing of departure of the groups is reversed as compared to that in *E1* reaction. In *E1cB*, the deprotonation occurs ahead of leaving group departure*
- *Reaction usually follows second order kinetics but is designated as *E1cB* to indicate that the departure of the leaving group is from the initially formed conjugate base (i.e., carbanion).*

Illustration of E1cB mechanism

Step 1 :

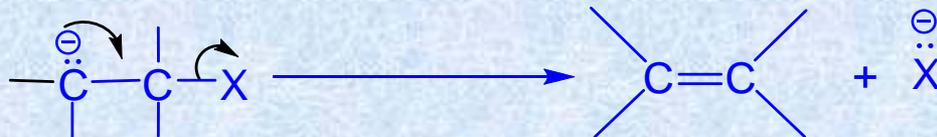


attack of the base on the β hydrogen.

β hydrogen leaves without its carbon electron pair forming a carbanion.

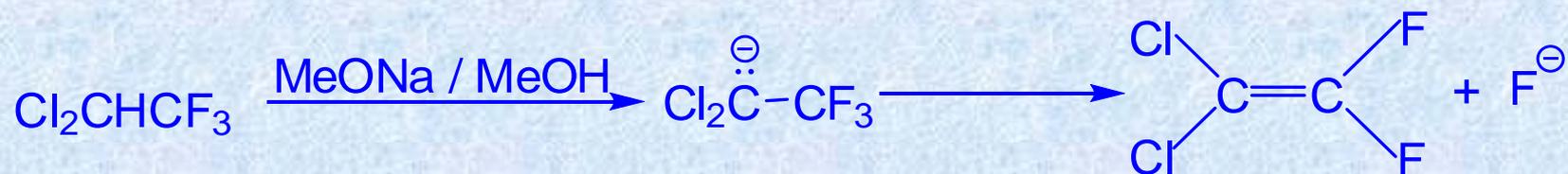
The electron pair then move towards the new C-C double bond to be generated.

Step 2



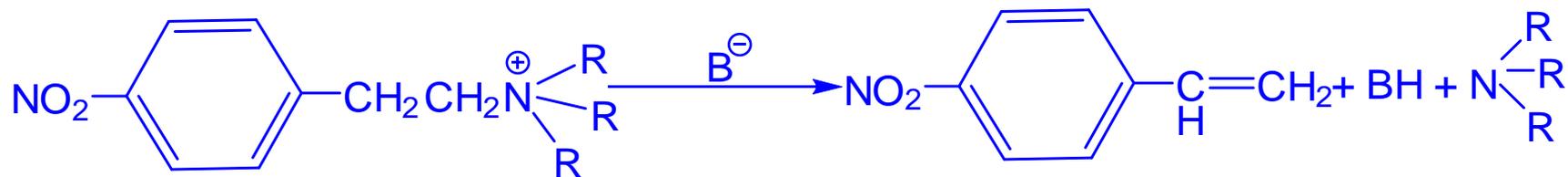
departure of the leaving group to give product.

These reactions require substrate which contain groups that can stabilize carbanions i.e., presence of electron withdrawing group

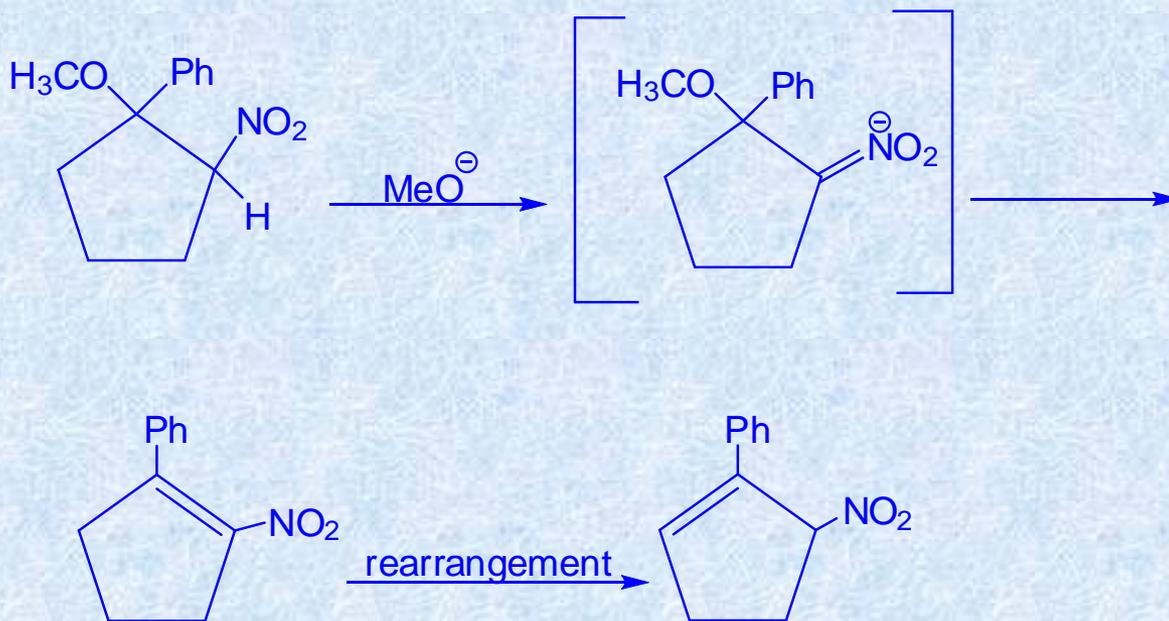


Additional Details on E1cB: Depending on the nature of the rate-determining step, there are different ways by which reaction can proceed,

- a. *Carbanion returns to the starting material faster than the product formation. Step 1 is reversible and step 2 is slow. It is designated as (E1cB)_R.*
- b. *Product formation is faster as compared to return of proton to carbanion. Step 2 is irreversible and step 1 is slow. It is designated as (E1cB)_I.*



- c. *Carbanion goes slowly to product formation as it is very stable. Step 1 is rapid and irreversible. It is designated as (E1)_{anion}.*



Mechanistic Continuum

Thus far we have studied three major classes of elimination reactions. E2, E1, and E1cB can be regarded as ‘extremities’ or ‘ideal’ situations.

In reality, dependence on the nature of substrates and reaction conditions have a huge influence on the course of the reaction.

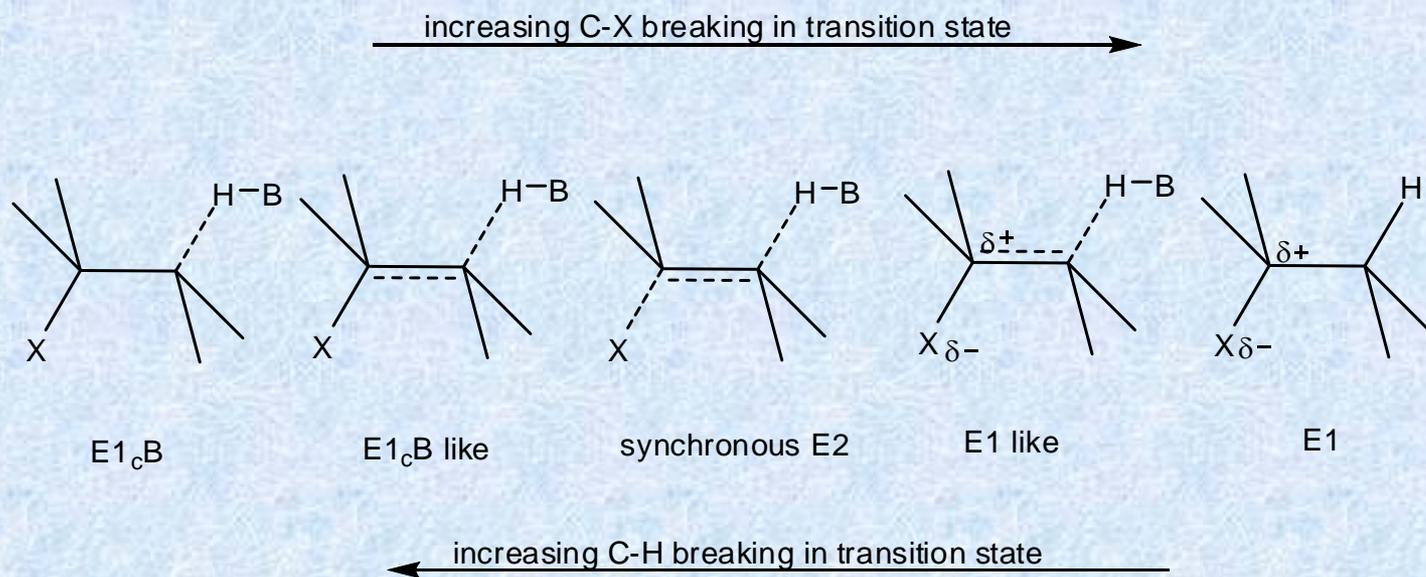
*In fact, one can use what is known as ‘**variable E2 transition state theory**’ to explain the continuum of mechanistic possibilities. In other words, clear demarcation between these mechanistic types are difficult.*

For additional reading: refer to “**More O’Ferrall Diagram**”

IV. Variable transition state theory for elimination reaction

Many β elimination reactions proceed via mechanisms, which are intermediate between the extremities such as $E1cB$ and $E1$. This is called variable $E2$ transition state theory.

The timing of deprotonation and departure of the leaving group is the key to the following mechanistic continuum

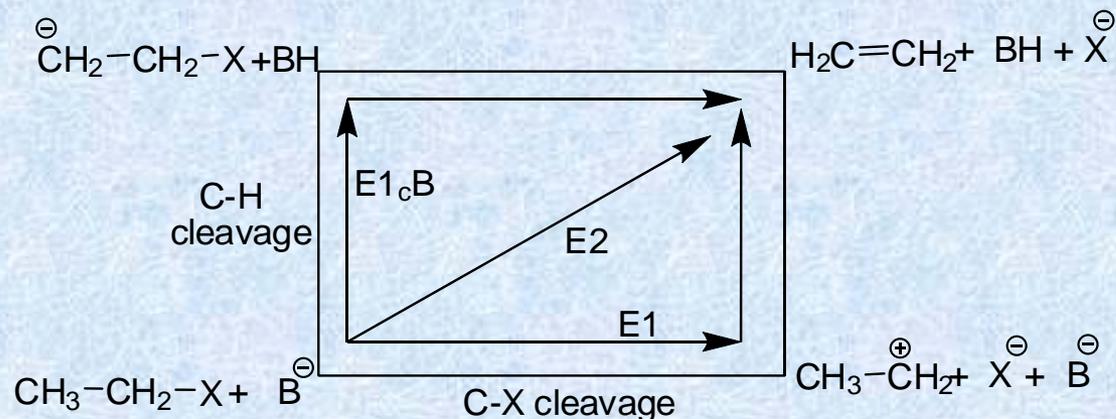


The other way to depict the variable transition state theory is to construct three dimensional potential energy diagram.

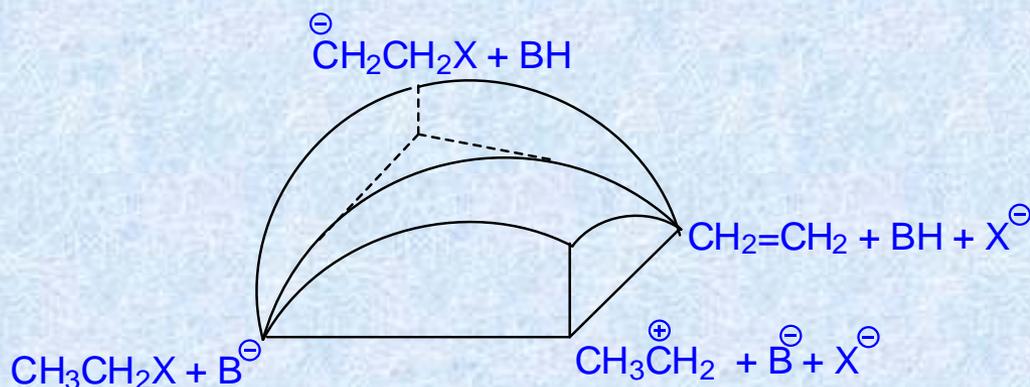
Consider example of ethyl halide. The two intermediates involved in two extreme processes are;



When there are no suitable stabilizing groups, both primary carbocation and primary carbanion are highly unstable. If we construct a diagram in which progress of C-H bond breaking is one dimension, progress of C-X bond breaking is second dimension and energy of reactant system is third dimension, then following diagram is obtained.



This is two dimensional representation which shows that **E1** corresponds to complete C-X breakage before C-H bond breaking while **E1cB** corresponds to complete C-H breakage before C-X. When energy axis is also included in this diagram it looks like



three dimensional diagram depicting transition state locations for E1, E1cB and E2 mechanisms

In this diagram, E1 and E1cB intermediates are respectively placed at front right and back left corners. These two are high energy intermediates.

The lowest energy path is a concerted E2 path which is almost diagonally across energy surface. Reason for this is that double bond character developing between α and β carbon compensates for the energy required for breaking the C-H and C-X bonds.

Following paragraph is only for additional reading

If the substituent can stabilize the developing carbocation, then that would cause lowering of right front corner of diagram. The E2 transition state will then move closer to point where it resembles E1 transition state.

Similarly, for substituents which can stabilize the developing carbanion, will lower the back left corner of diagram and subsequently E2 transition state will begin to resemble closely to that of E1cB transition state.

In E1 like transition state C-X bond cleavage is more advanced than C-H bond cleavage and vice versa for E1cB transition state.

Important factors that influence the reaction mechanism

E1

- i. electron donating ability of substituents*
- ii. good leaving group*
- iii. solvents of high polarity*

These factors will favor E1 pathway. Base is not important in the rate determining step but its presence is important.

E2

Base participates in the rate-determining step

- i. strength of base*
- ii. nature of leaving group*
- iii. nature of the solvent*

If strong base is used reaction will move towards E1cB like pathway whereas good leaving group with strongly ionizing solvent will cause it to move towards E1 pathway.

V. Orientation of double bond

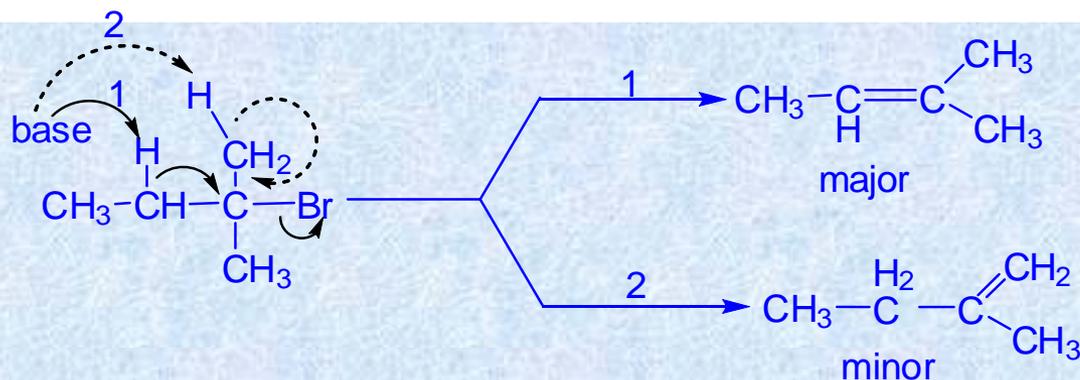
In a substrate where the double bond can be generated in different regions of the molecule, the obvious question is whether one can predict which one is likely to be the major product. Here comes the issue of 'regio' 'selectivity'

Regioselectivity:

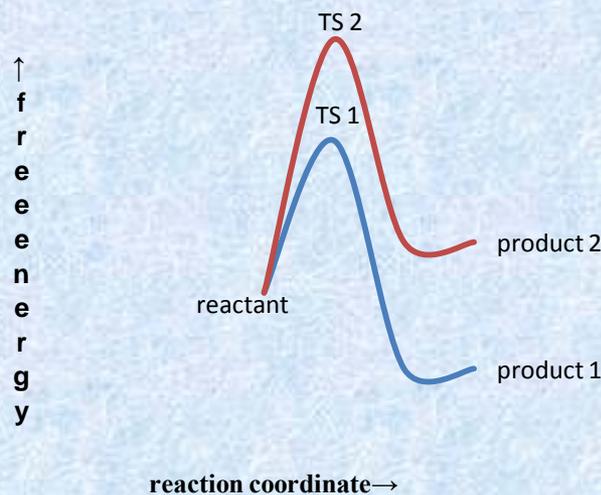
*In many substrate, more than one kind of β hydrogens can be removed in an elimination reaction. Which of the β hydrogens is lost depends on various factors. Three **rules** generally **govern regiochemistry**.*

(1) Zaitsev's Rule, (2) Hofmann Rule, (3) Bredt's Rule

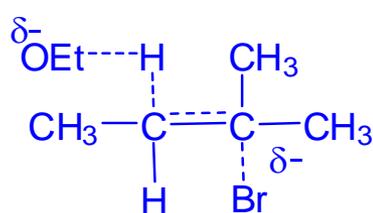
Zaitsev's rule: In an elimination reaction, the major product formed will be a more substituted alkene. This means that removal of the hydrogen from the more substituted β carbon atom should occur.



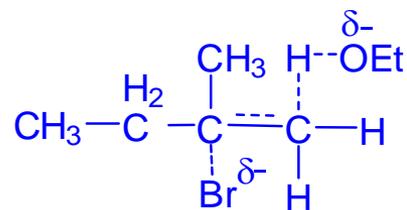
Transition state for path 1 leading to more substituted olefin is lower in energy than in path 2.



The relative positions (energies) of TS-I and TS-II can be explained as follows,



T S (I)



T S (II)

more stable

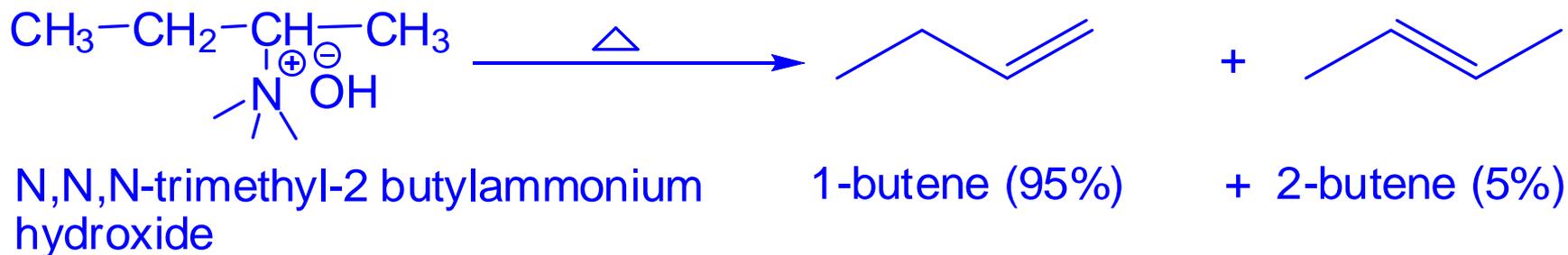
resembles trisubstituted alkene

less stable

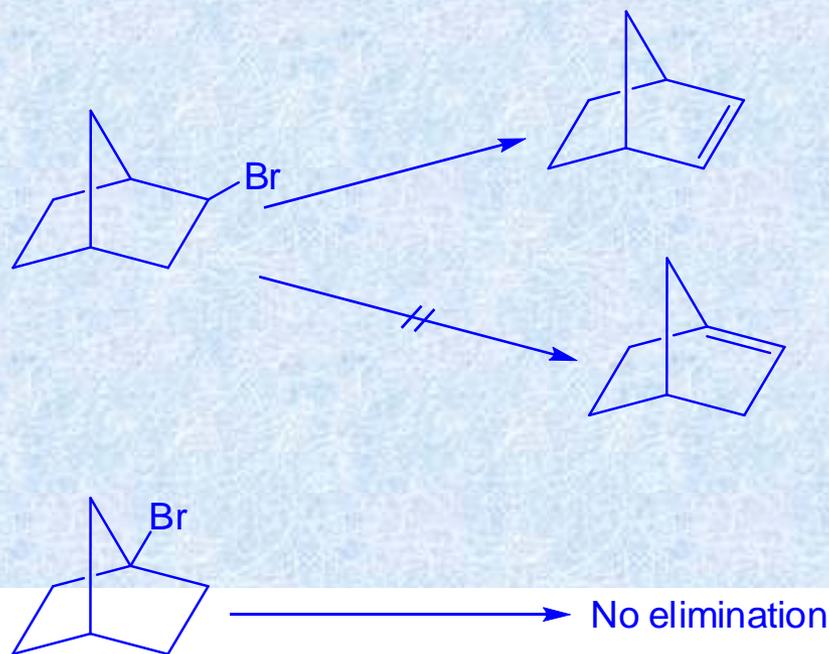
resembles disubstituted alkene

Additional information: The product stability (more substituted olefin generated as a result of the elimination reaction) can be explained using the concept of orbital interaction between the CH₃ orbitals and that of the pi-bond

2. Hofmann rule: Although most compounds seem to follow Zaitsev's rule, some give product according to Hofmann rule i.e., less substituted alkene. Hofmann elimination is observed for compounds containing bulky leaving groups such as **quaternary ammonium or sulfonium salts**.



3. Bredt's rule: No double bond can be generated on a bridge head carbon of bicyclic compounds unless size of ring is sufficiently large.

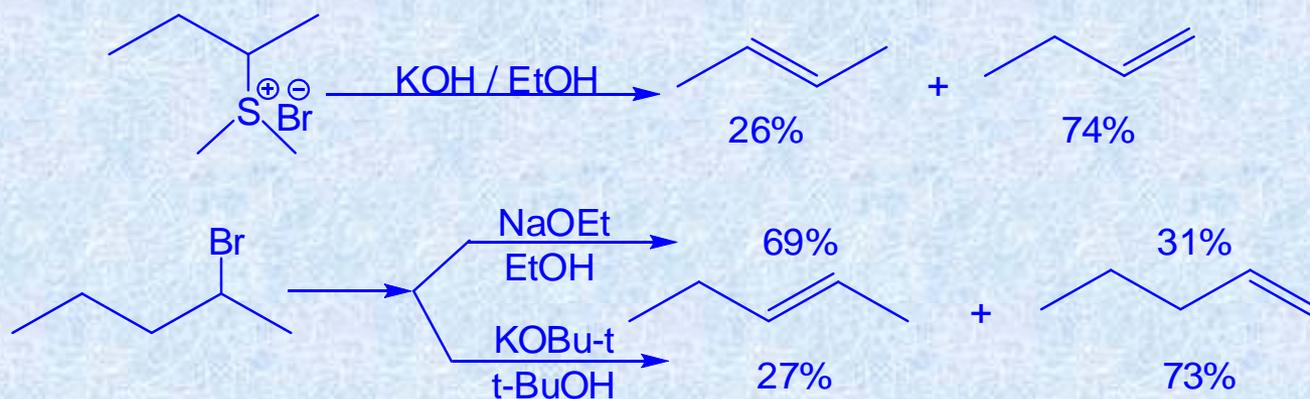


Note: The origin of why Bredt's rule can be rationalized by considering the need for lateral overlap between two adjacent p-orbitals. Two p-orbitals can't remain parallel due to the bridged bicyclic structure.

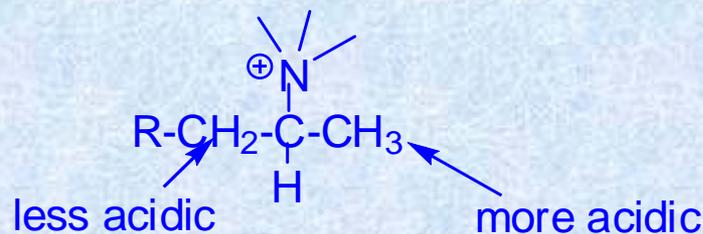
Other features of directionality of elimination reactions

- 4. If compound already contains C=C or C=O functional groups, then the newly generated double bond tends to maintain conjugation with it.*

Many factors are responsible for regioselectivity. One of them is steric interaction. In E2 reaction when leaving group is bulky approach of base towards β hydrogen is more likely to take place from less hindered side to produce less substituted alkene. Similarly, large base favors formation of Hofmann product.



Acidity of terminal and internal β hydrogen is also important factor in determining the product ratios. Terminal hydrogens are more acidic, producing less substituted product, particularly in quaternary ammonium or sulfonium group containing compound.



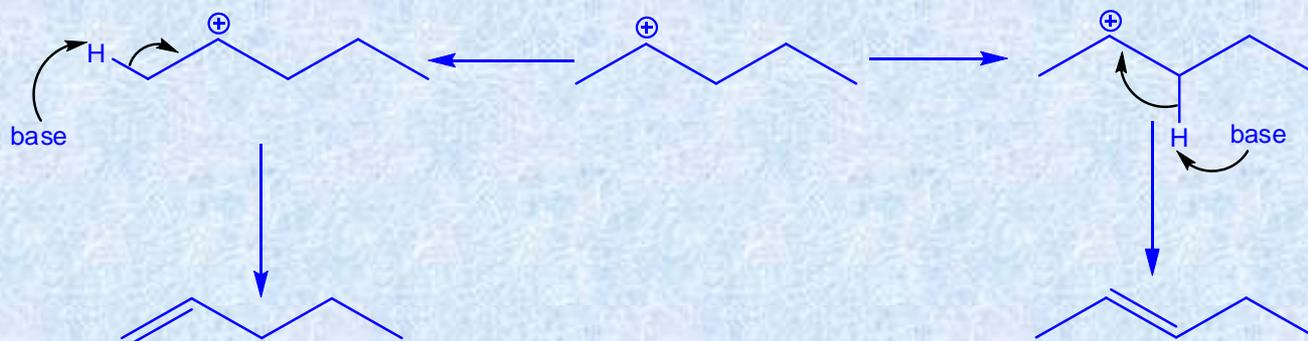
In case of E1 reaction, the rate controlling step is the formation of carbocation which is followed by product formation. Carbocation generated hence has choice to adopt more stable arrangement, before the removal of the proton.

In most E1 reaction, the product predominantly will be in accordance with Zaitsev`s rule i.e., thermodynamically more stable, highly substituted alkene. In general, Zaitsev`s rule is directly applicable to molecules containing small leaving groups such as bromide.

E1 reaction :

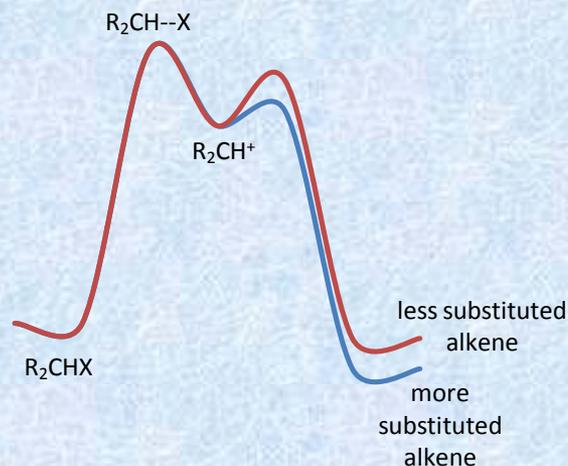
In E1 reaction C-X bond breaking is more advanced (or ahead of) than C-H bond breaking.

Hence, structure of carbocation will decide the fate of elimination reaction.



E1 reaction mainly favors more substituted alkene because energies of transition states are similar to those of isomeric alkenes. But, activation energy for removal of hydrogen is low, hence transition state should resemble carbocation and not alkene. Each β hydrogen is hyperconjugation with the carbocation.

Thus, there is more weakening of C-H bonds and more double bond character at highly substituted carbon. This structural effect will govern direction of elimination as shown below.



E1cB reaction :

In E1cB reaction, the direction of elimination is governed by the acidity of β protons, which in turn, is determined by polar and resonance effect of substituents and degree of steric effect to approach of base. Alkyl substituents retard approach and proton essentially from less substituted carbon is abstracted, forming less substituted alkene.

E2 reaction :

In E2 reaction, the direction of elimination depends on the nature of the transition state. When E2 reaction resembles E1cB transition state, then direction of elimination is governed by the ease of proton removal and usually less substituted alkene predominates.

When E2 reaction resembles E1 transition state, then highly substituted alkene dominates.

In synchronous E2 reaction, double bond is formed in the transition state at expense of rupture of C-X and C-H bonds. It favors more substituted alkene.

Additional note of the usage of 'E1cB-like' or 'E1-like': *When the geometry of the transition state is similar to that of reactant, it is described as "reactant-like" and when it is similar to that of the product, "product-like" is used. In the context of elimination reactions, any transition state structures other than the synchronous E2, will resemble either of the extremities like E1cB or E1. Depending on their structural similarity, these are termed as "E1cB-like" or "E1-like"*

VI. More details on the stereochemical aspects of elimination reactions

Stereoselectivity:

The product formed can either be E isomer or Z isomer, depending on the stereochemical course of the reaction.

Coplanarity of departing group is an important criterion i.e., five atoms in the transition state inclusive of base, β hydrogen, α and β carbon atoms and the leaving group, should lie in the same plane. This is necessary for the orbitals to lie in proper orientation to overlap between each other to form the new double bond.

Two major stereochemical pathways are possible,

- *Anti elimination and Syn elimination*
- *Characteristics of these modes of elimination are give below*

1. *Antiperiplanar transition state (anti-periplanar between the proton being abstracted and the leaving group in the following example) (180° dihedral angle between H and X)*
2. *Staggered conformation— low energy*
3. *Anti-eliminations are more favored and more widely found*



- Syn elimination :

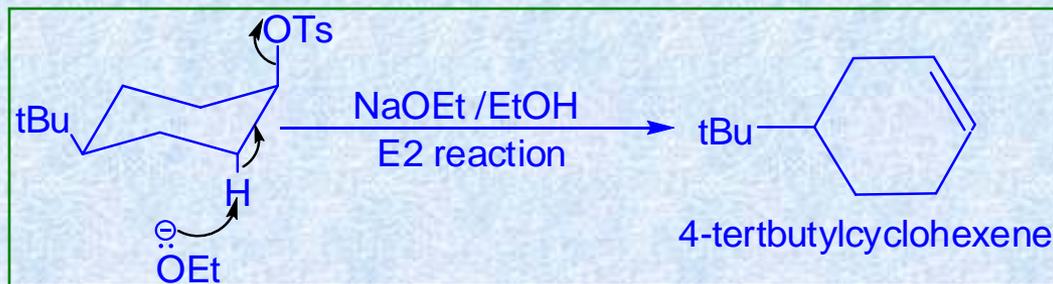
1. *Syn periplanar transition state*
2. *Eclipsed conformation*
3. *Possible only with certain rigid molecules*
4. *H and X are cis to each other (0° dihedral angle)*



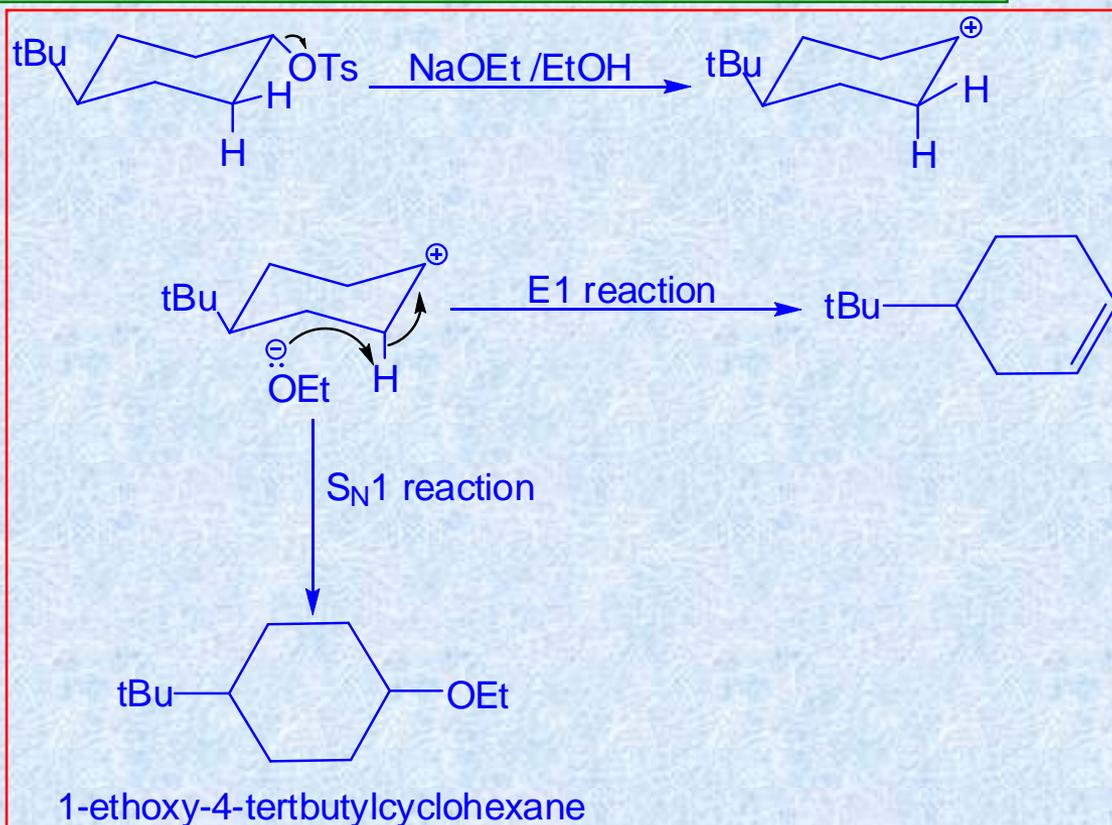
Examples for *anti* elimination :

In cyclic compounds like 4-tertbutyl-cyclohexyltosylate following two results are obtained according to isomer under study.

cis-isomer →



trans-isomer →

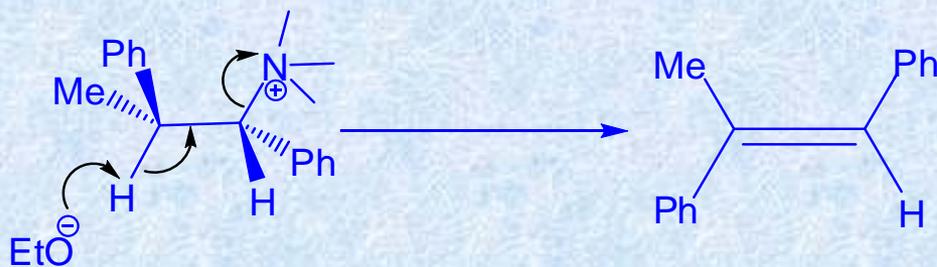
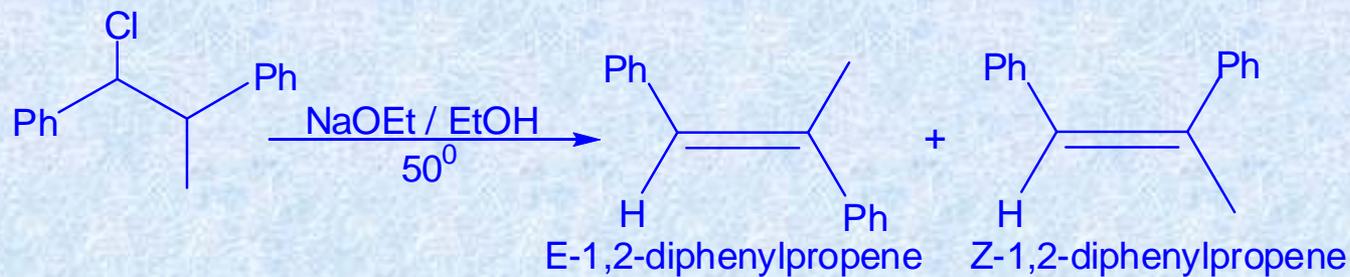


*In the case of the cis isomer, the tosylate group and β hydrogen are far apart with dihedral angle of 180° . This spatial arrangement is known as **antiperiplanar**. This geometric arrangement is ideal for E2 elimination leading to exclusive formation of 4-tertbutylcyclohexene.*

Such spatial arrangement of the two departing groups is not possible in the case of the trans isomer. Hence, elimination proceeds mainly by E1 mechanism and is usually accompanied by S_N1 reaction.

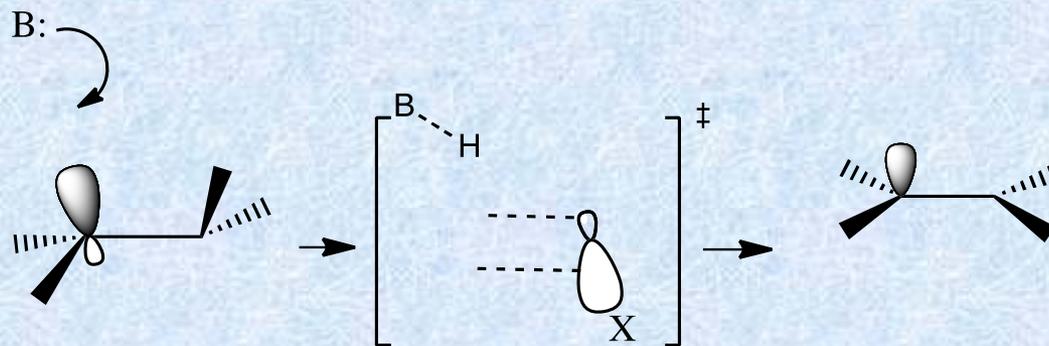
More remarkable example is provided by acyclic substrates. In these free rotation about C-C single bond is possible, yet elimination is preferably anti.

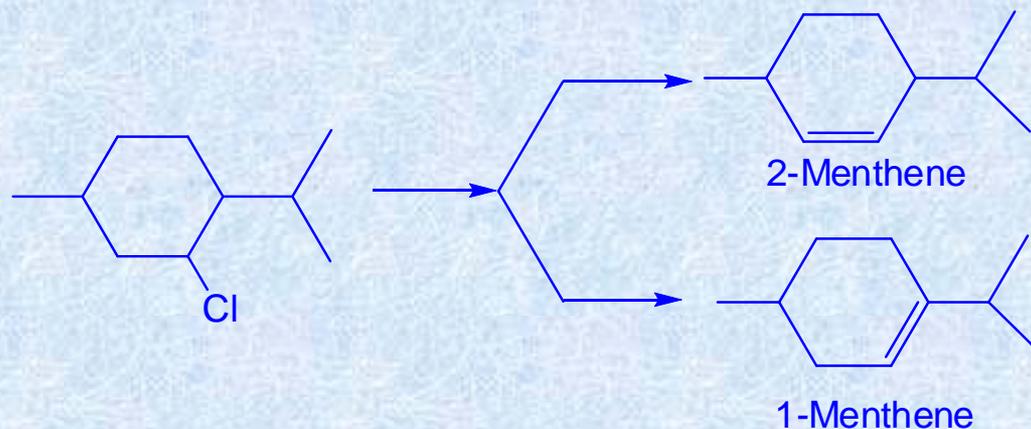
Examples for anti-elimination



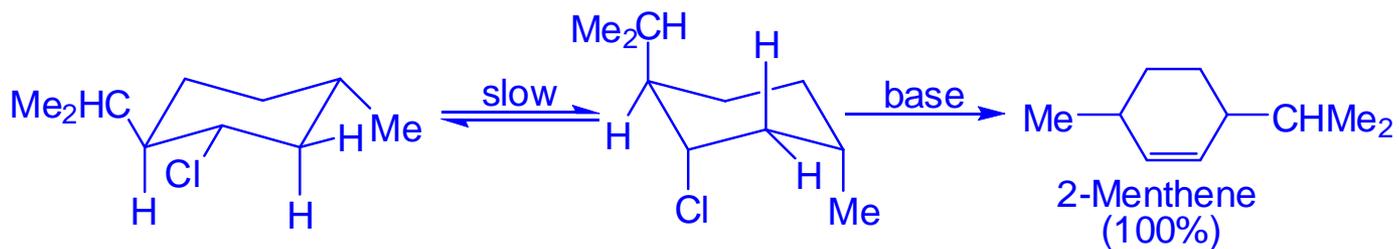
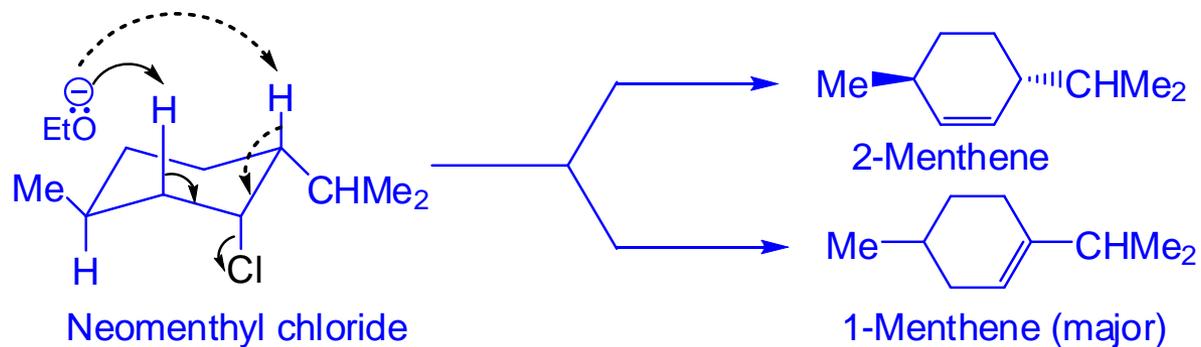
Orbital Interaction

In an elimination reaction such as the one given below, electrons from the sigma bond at the β carbon will delocalize into empty orbital forming pi bond at α carbon atom. p orbitals of pi bonds are coplanar. Also, steric interactions are minimum when two departing groups are on the opposite side.





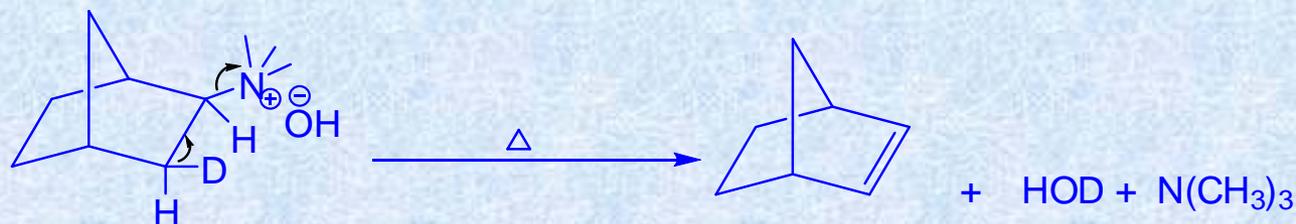
β hydrogen and leaving group on cyclohexane ring can assume anti periplanar conformation, if both are axial.



Syn elimination :

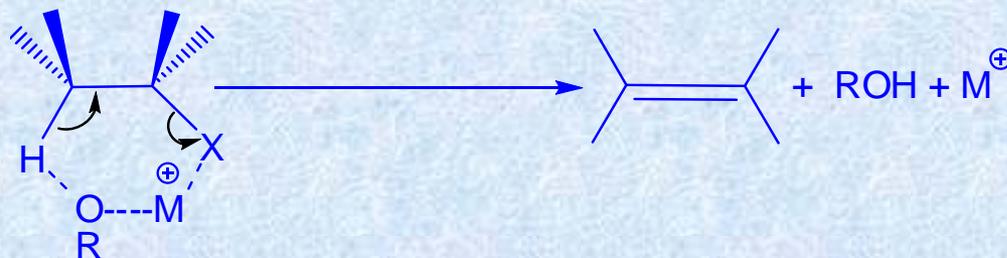
In certain rigid molecules, antiperiplanar arrangement of the departing groups can not be attained. In such molecules, departing groups may be on the same side i.e., syn periplanar and process is called syn elimination.

In the example below deuterium is coplanar with the leaving group while hydrogen is not. Hence, though deuterium is syn to ammonium group, it is lost to give elimination product.



N,N,N-trimethyl-3-deuteriobicyclo
[2.2.1]-2-heptylammonium hydroxide

Bicyclo[2.2.1]-2-heptene
(94%)



Ion pair promoters are suggested as capable of syn elimination of anionic leaving group.

This can be explained by proposing transition state in which anion functions as a base and the cation assists in the departure of the leaving group.

Ion pair interpretation is also supported by the fact that addition of specific metal ion complexing agents such as crown ethers resulted in diminished amount of syn elimination.

Another factor which affects syn to anti ratio is the strength of the base used. Strong bases exhibit high proportion of syn elimination.

Steric effect is also important in determining syn to anti ratio.

VII. Elimination v/s substitution

Elimination and substitution reactions are closely related and competitive but form different products.

However, substitution becomes favorable as it involves less bond reorganization and energetically being more favorable.

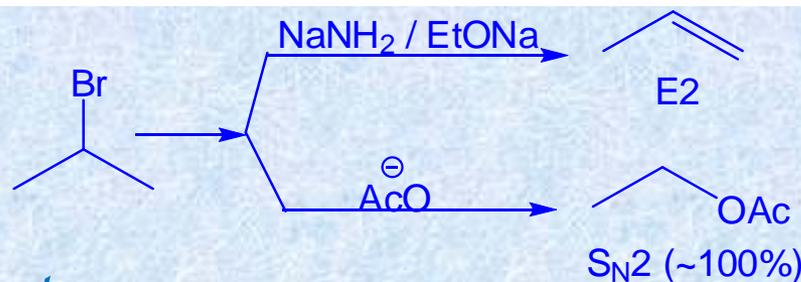
1) Basicity and nucleophilicity:

*For elimination reaction **basicity** of nucleophile or base is important while for substitution it is **nucleophilicity** that matters more.*

Therefore, strongly basic conditions favor elimination reaction and use of strong bases is advisable. If some compounds which are not strong bases but are good nucleophiles are used, then substitution predominates.

Use of strong and slightly polarizable base such as amide or alkoxide favors elimination over substitution.

Basicity and nucleophilicity: Basicity is the ability of an atom or molecule to donate a lone pair of electrons to a proton (H⁺). Nucleophilicity is the ability of an atom or molecule to donate a lone pair of electrons to carbon.

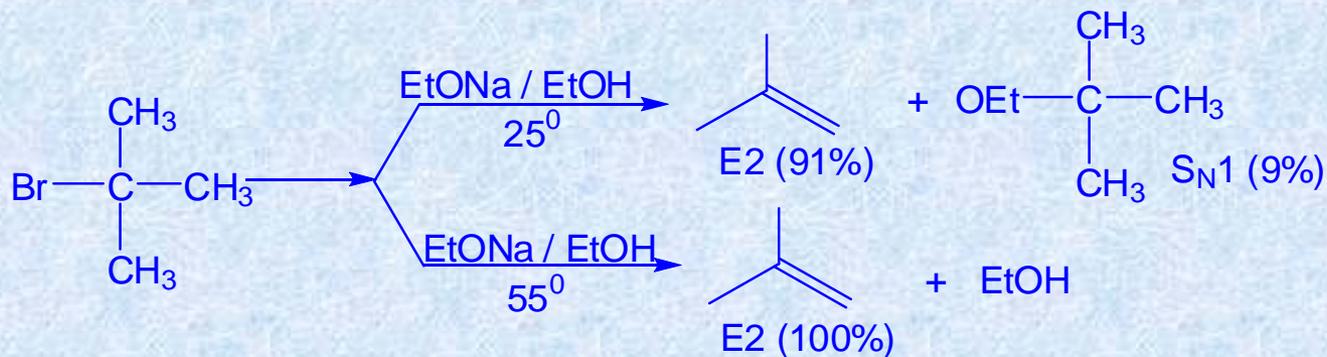
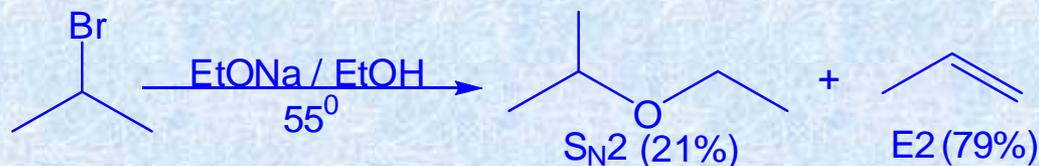
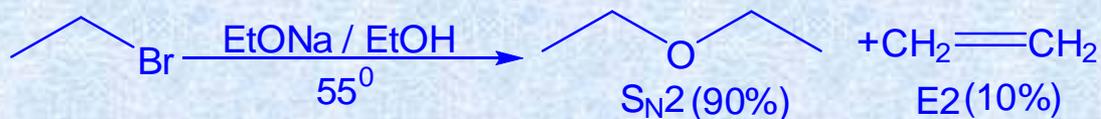


2) Substrate structure :

Crowded reactant favors elimination reaction over substitution due to hindrance to approach of nucleophile. In primary alkyl halides, easy approach of nucleophile is possible hence substitution is favored over elimination. In secondary alkyl halides, substitution is difficult due to steric hindrance and elimination is favored. Whereas, in case of tertiary halides $\text{S}_{\text{N}}2$ reaction is not possible, elimination is favored particularly at elevated temperature. If substitution occurs, then it is by $\text{S}_{\text{N}}1$ pathway.

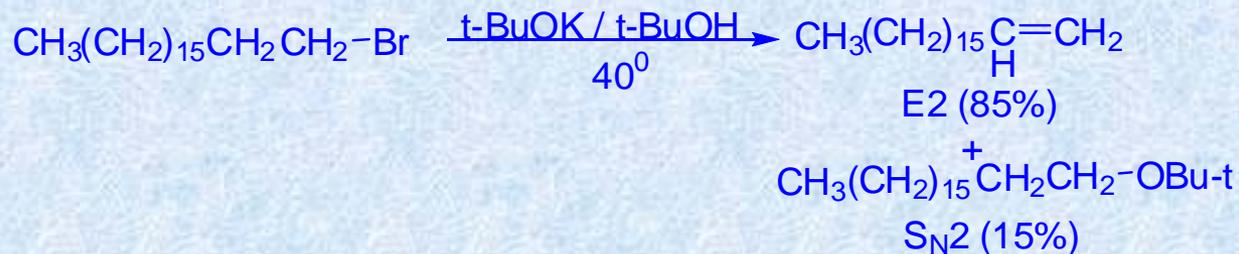
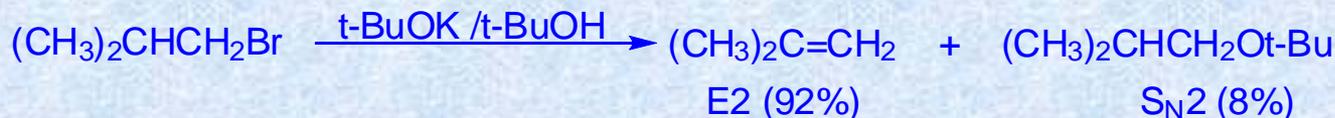
Elimination can also be favored by stability of product formed.

More examples: distribution of elimination and substitution products



More examples: nature of the base

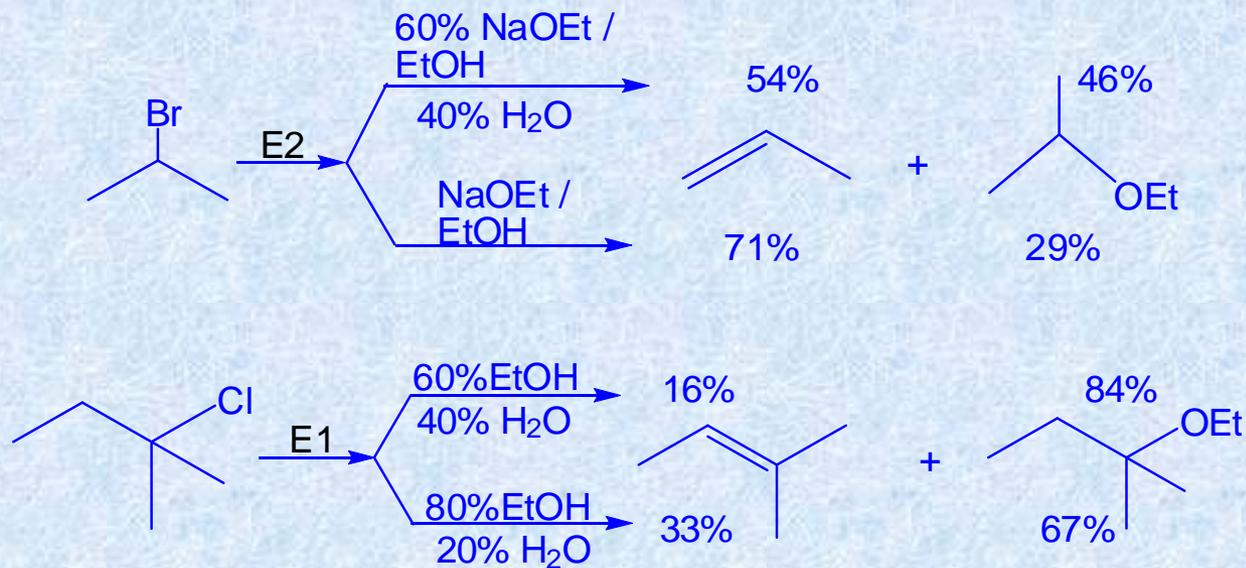
Structure of base has similar effect on the ratio of substitution or elimination reaction. A more crowded base of similar strength favors elimination over a less crowded base. Therefore, tert-butoxide gives more of elimination product than substitution whereas ethoxide shows opposite effect altogether.



More examples: nature of the solvent

3) Solvent :

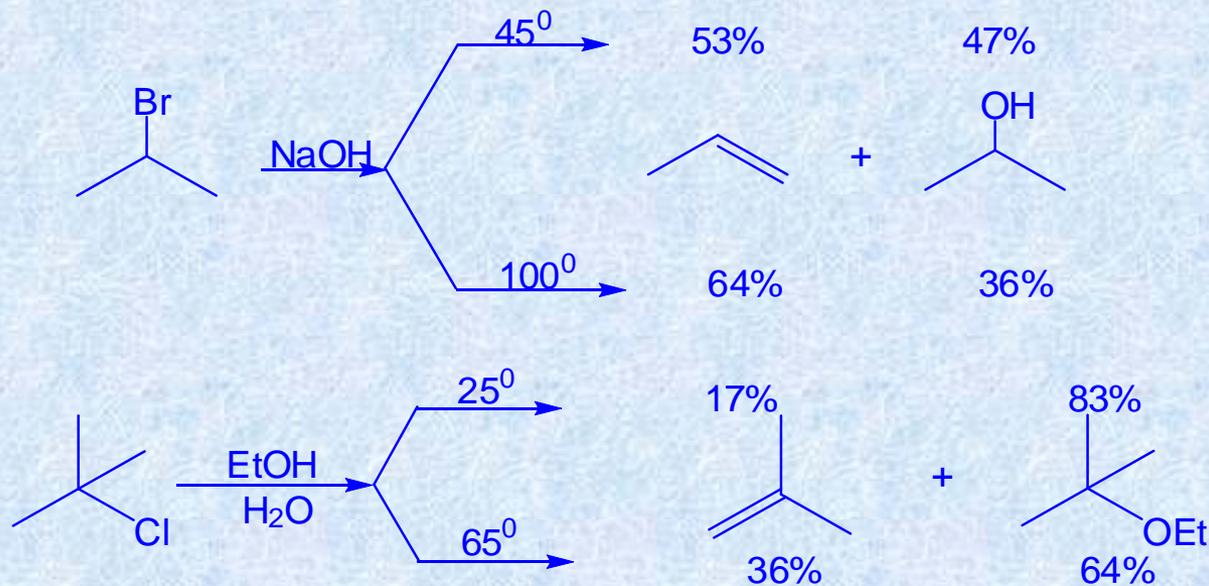
In E2 reaction, five atoms are involved, thus, charge is more dispersed due to which less polar solvents favor E2 elimination over S_N2 reaction. (Similar is the case with E1 reaction).



More examples: role of temperature

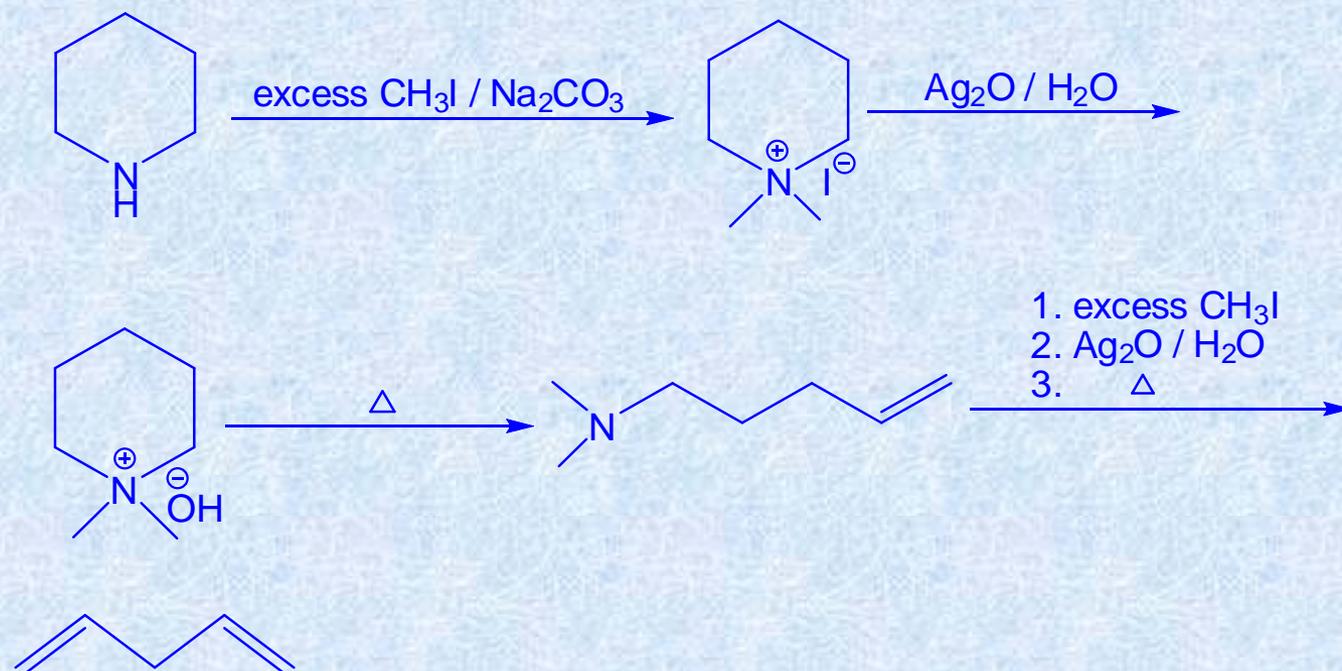
4) Temperature :

Elimination reactions are favored at higher temperature than substitution reaction because elimination reaction has high free energies of activation than substitution due to higher degree of bond reorganization (or change in the bonding pattern) i.e., more bonds are broken and formed.



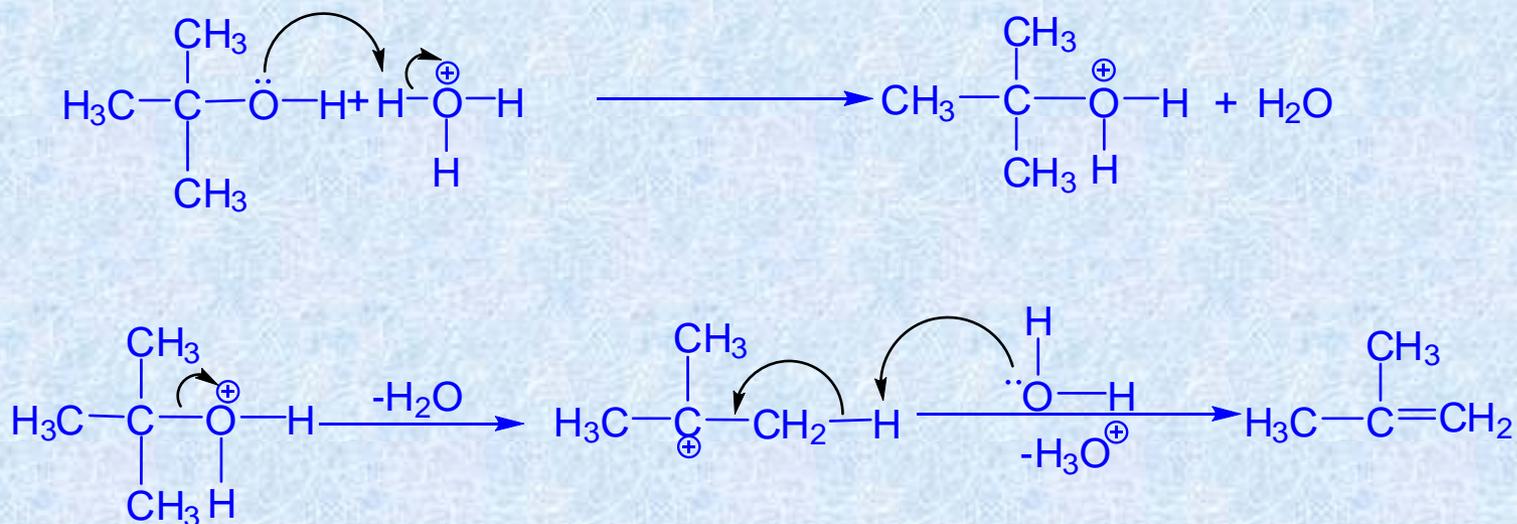
More examples for elimination reactions

(a) Hofmann degradation :

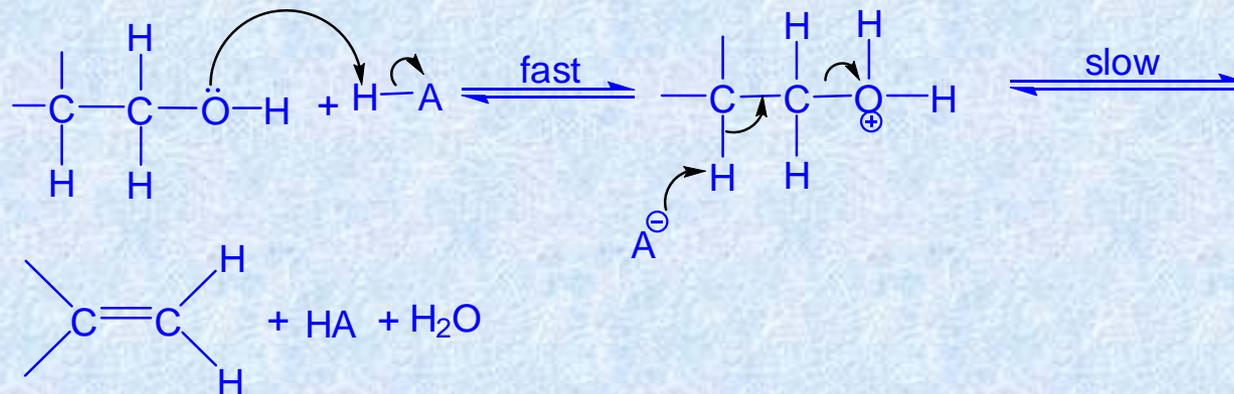


(b) Dehydration of alcohols :

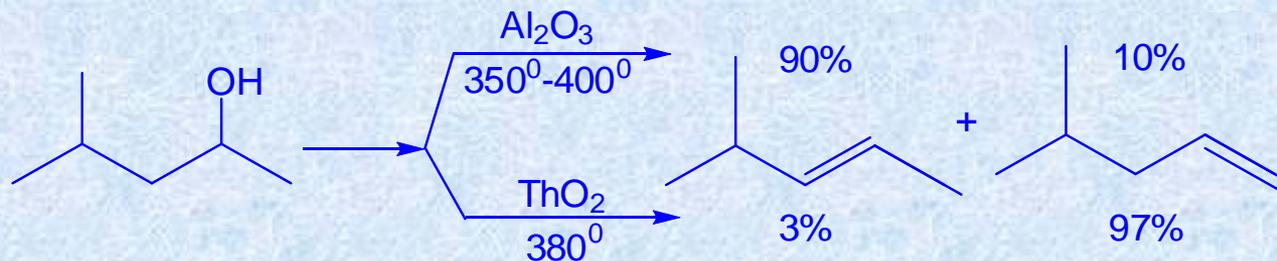
- *elimination reaction favored at high temperature*
- *catalyzed by acid (H_2SO_4 , H_3PO_4 , PBr_3 , SOCl_2 etc.)*
- *For secondary and tertiary alcohols, the mechanism goes through carbocation intermediate, which explains why the rate of dehydration of tertiary alcohols is greater than that of secondary and primary alcohols (E1 reaction)*



- Whereas, dehydration of primary alcohol is supposed to proceed through E2 mechanism. In a protonated alcohol, the Lewis base removes β hydrogen, simultaneously an olefinic bond is formed and protonated hydroxyl group is departs as 'water'.

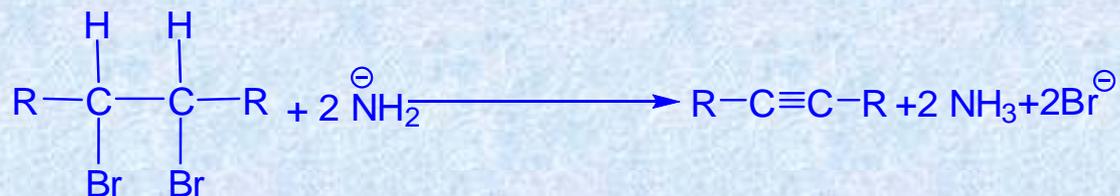


Metal oxides are excellent and widely used catalysts for dehydration of alcohol. Different products are formed due to different catalytic properties of these oxides or different reaction conditions.

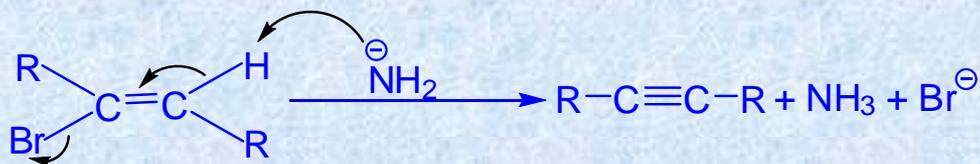
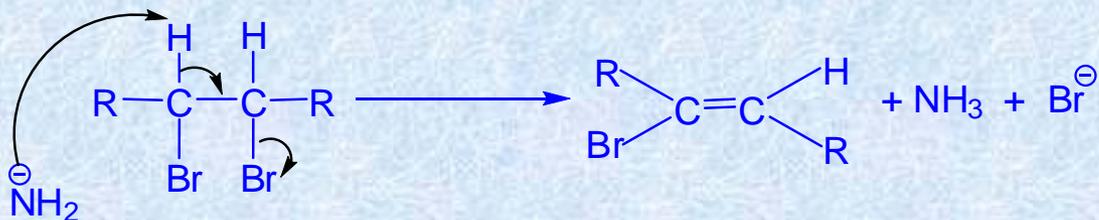


(c) Synthesis of alkynes :

Usually follows antistereochemical pathway.

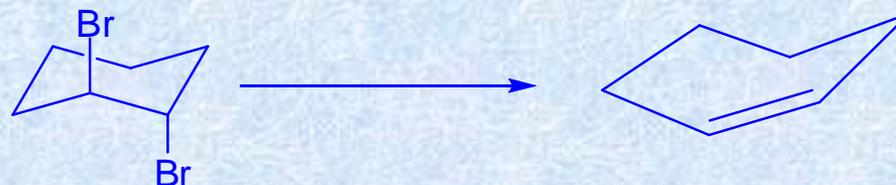


Here, a strong base such as an amidate ion triggers the elimination, first by abstracting the proton as shown.



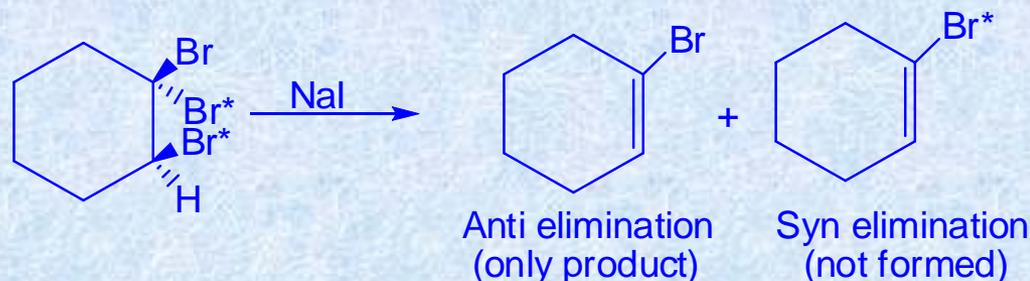
(d) Debromination of vicinal dibromides:

Vicinal dibromides can be debrominated by treating them with reducing agents such as iodide or zinc.

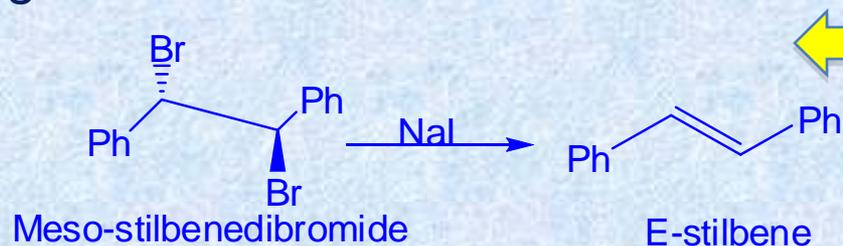


Dehalogenation by iodide is stereospecific and goes through an anti pathway.

In a reaction of NaI with 1,1,2-tribromocyclohexane, syn elimination will give labeled product (bromine with a * is the labelled one). Whereas, anti elimination will give non labeled product. It is found that debromination using NaI is purely anti. However with zinc, the major product is anti, but some syn is also formed elimination.

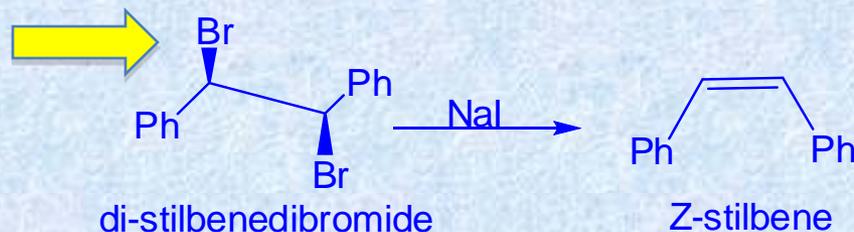


Meso stilbene dibromide gives E-stilbene and d,l-stilbenedibromide gives Z-stilbene.



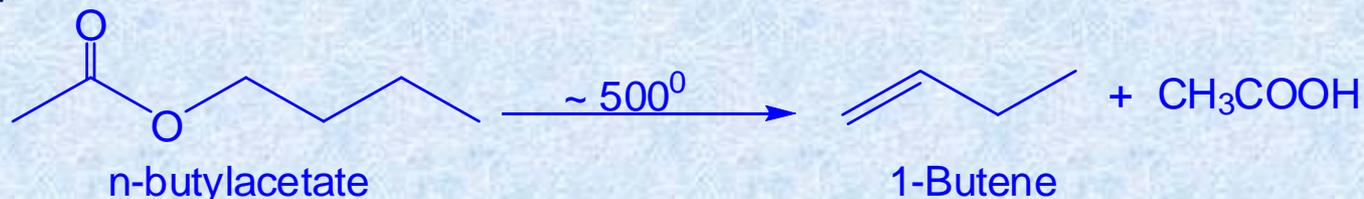
It is important realize that the anti-periplanar geometries of H and Br are required for this elimination. In the given stereoisomer, this is possible and hence it leads to a E-stilbene as the product

For the anti-periplanar arrangement in this stereoisomer, the molecule should rotate along the C-C bond first such that both Ph comes on the same side and hence it leads to a Z-stilbene as the product

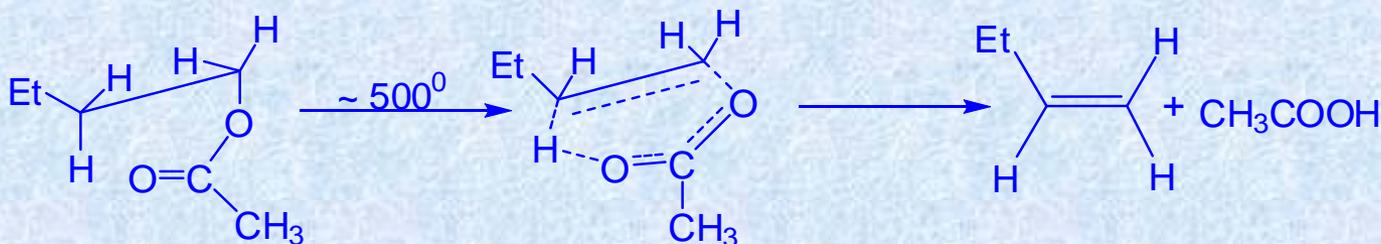


(e) Pyrolytic elimination :

Some substrates such as **esters** and **amine oxides** do not require any external agent for elimination. Simply heating such substrates provides elimination product. These reactions are known as **pyrolytic Elimination**.



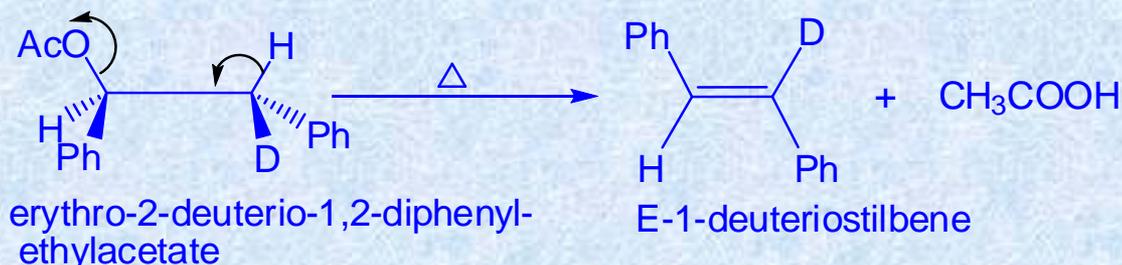
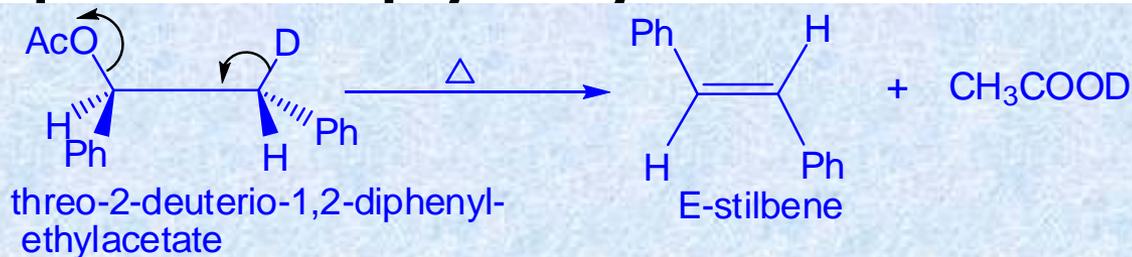
These reactions are suggested to proceed through a concerted, cyclic, six membered transition state. They are often designated as E_i (i.e., Elimination internal)



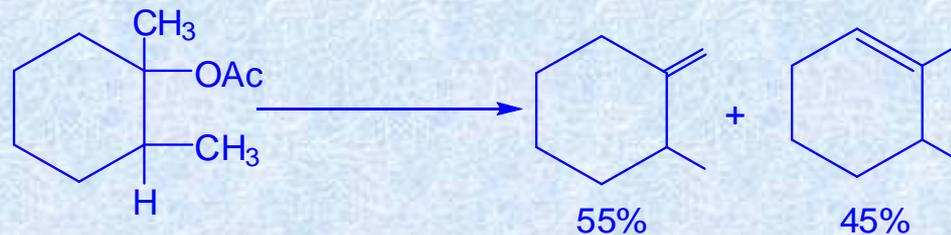
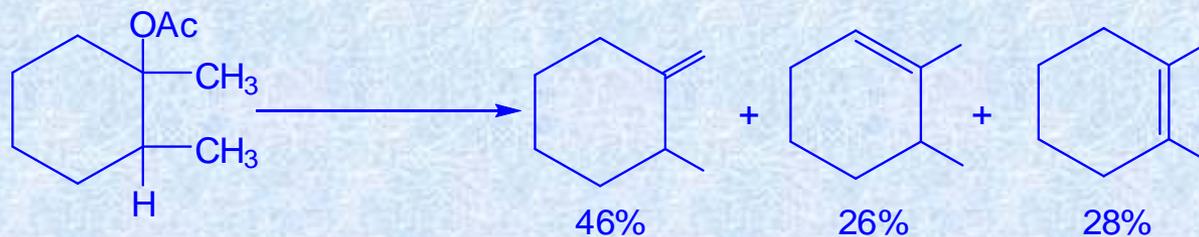
These reactions follow stereospecific syn elimination pathway i.e. leaving group must assume syn periplanar conformation with respect to each other

Examples for pyrolytic eliminations

Example-1



Example-2

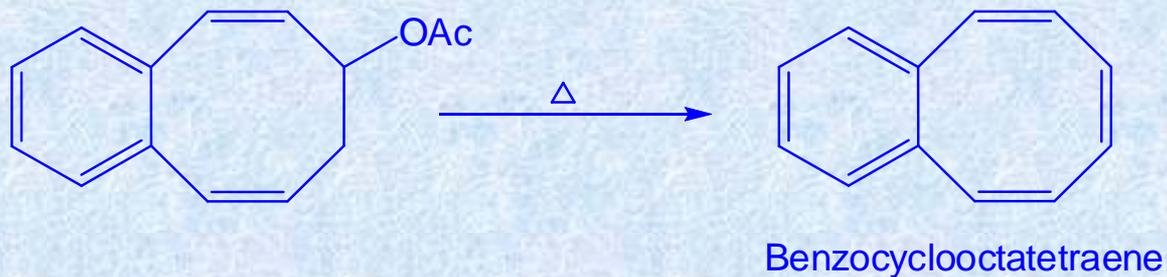


The readers are expected to write the mechanism for these additional examples, based on the earlier description in this module

Example-3



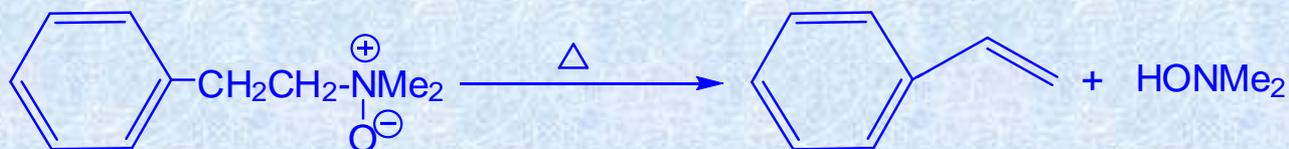
Example-4



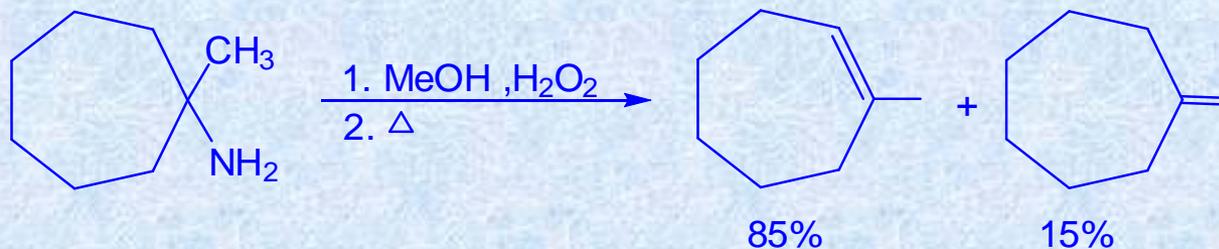
DePuy, C. H.; King, R. W. Chem. Rev. 1960, 60, 431-457.

(f) Cope reaction :

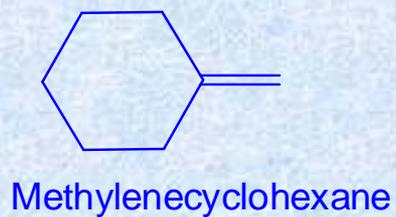
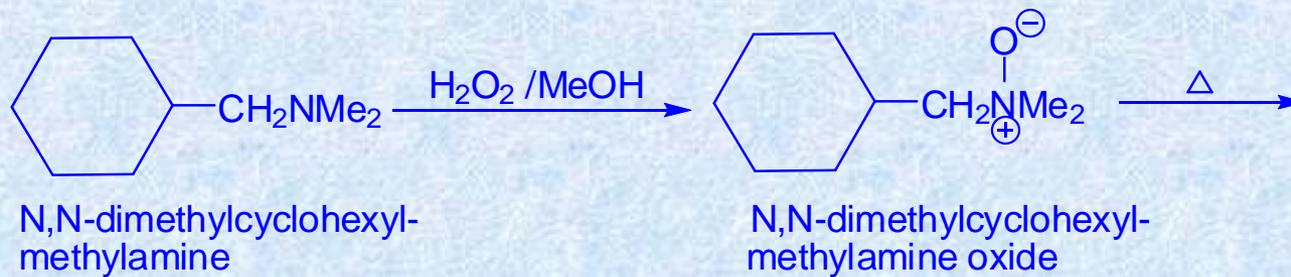
Pyrolytic elimination of amine oxide can be done under mild conditions, to give olefin. This reaction is called as **Cope reaction**.



Internal base attacks β proton, so highly basic nucleophile is not required.



Additional example on Cope elimination



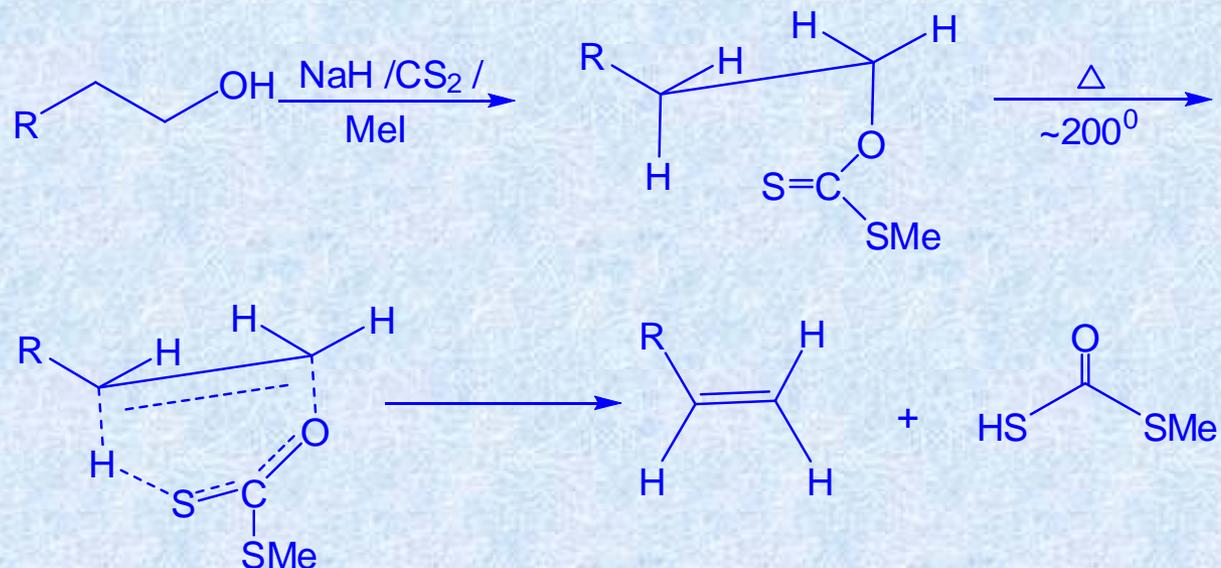
(g) Chugaev reaction:

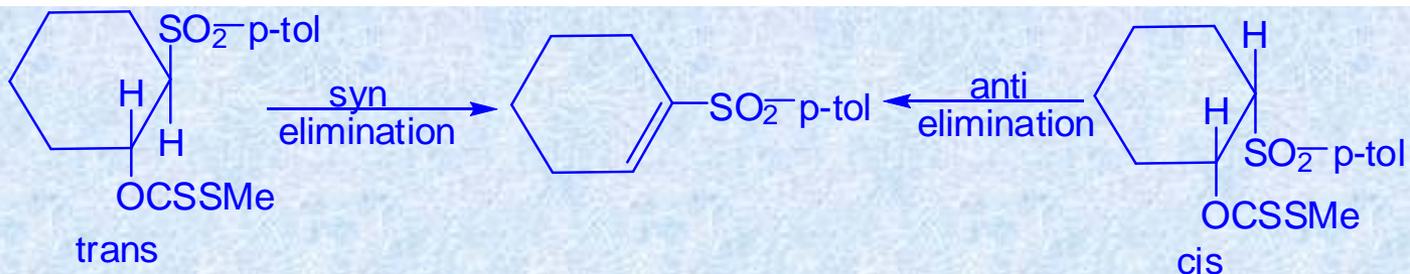
In these reactions, O-alkyl-S-methyl xanthates are pyrolysed to olefin, (oxysulfide and methanethiol) at about 200°C.

These reactions are of particular use due to its relatively milder reaction conditions as compared to other pyrolytic eliminations.

Using this method, alkenes which are labile or tend to undergo rearrangement can be prepared.

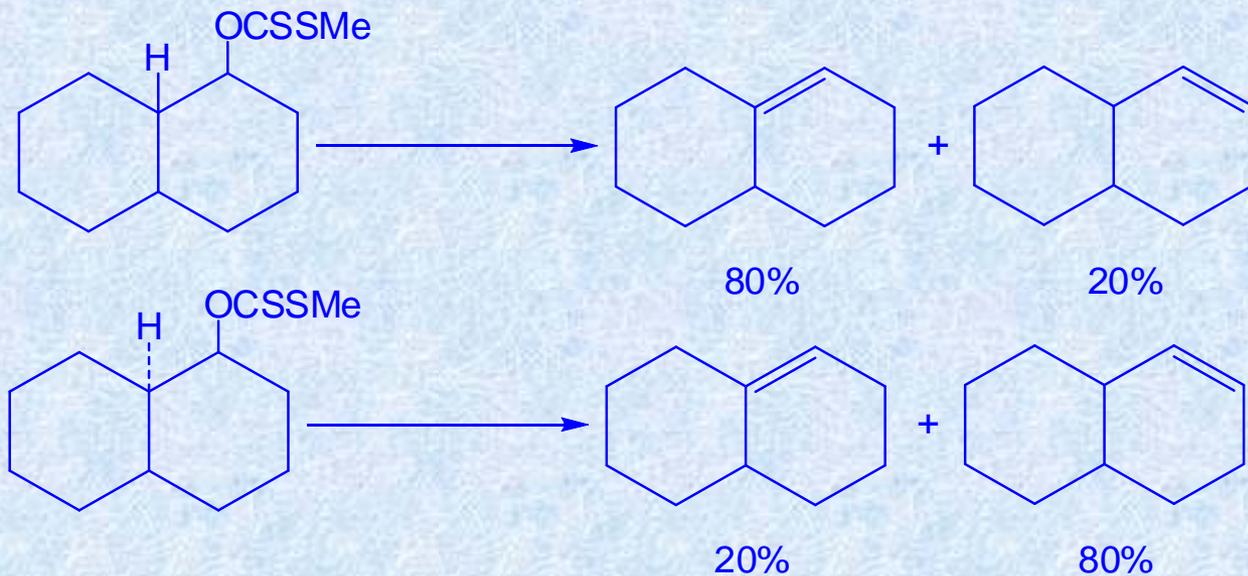
These reactions take place via six membered cyclic transition state and generally proceed through syn elimination, although anti elimination is also reported.





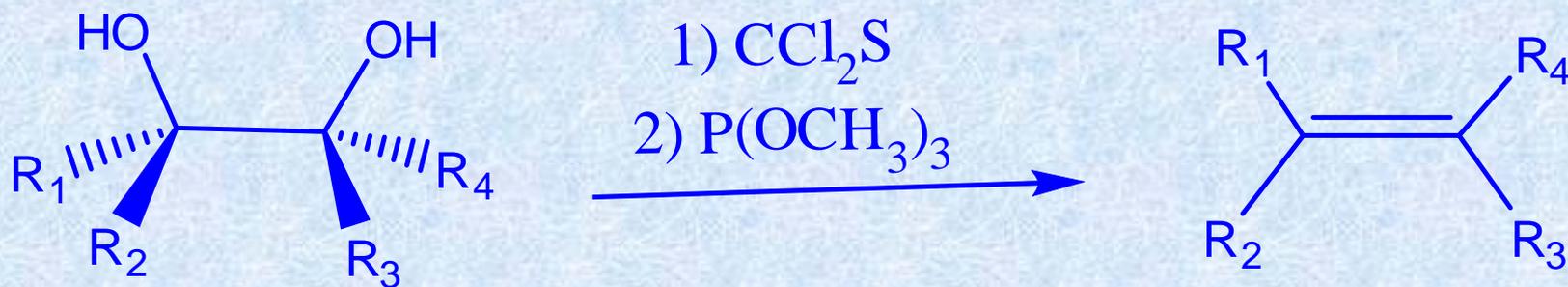
F. G. Brodwell; P. S. Zandis, *J.A.C.S.*, **1958**, 80, 2450-2453.

C. H. DePuy; R. W. King, *Chem.Rev.*, **1960**, 60, 431-457.



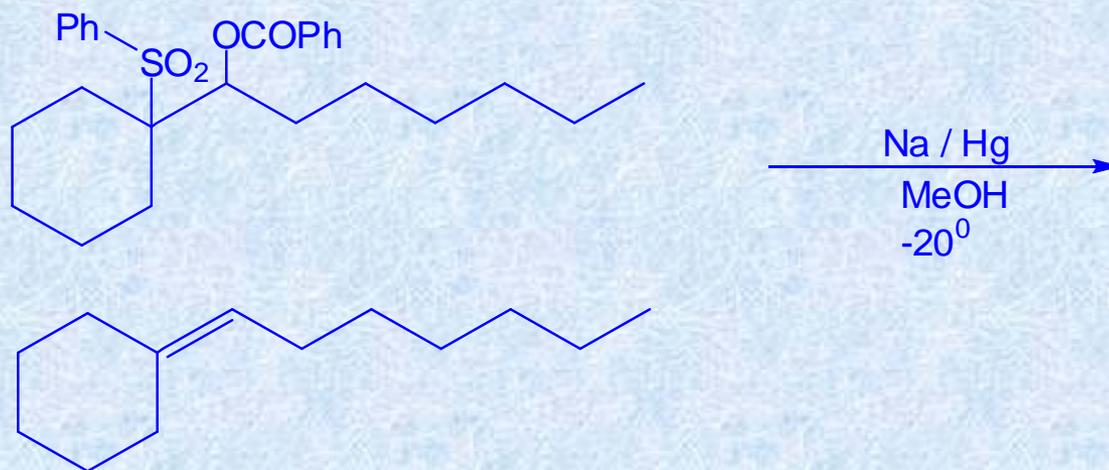
(h) Corey-Winter reaction:

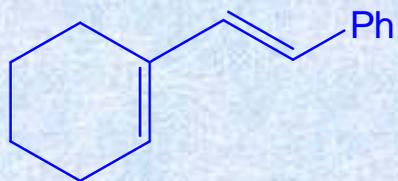
Vicinal diols are first converted into cyclic thiocarbonates which on heating in trimethylphosphite gives an olefin. It is a syn elimination reaction.



(i) Julia olefination :

Regioselective elimination of phenylsulfonyl and benzoate from substrate containing phenylsulfonyl group adjacent to leaving group. It is mainly promoted by reducing agents such as sodium amalgam. Leaving groups are carboxylates, acetates or benzoates.



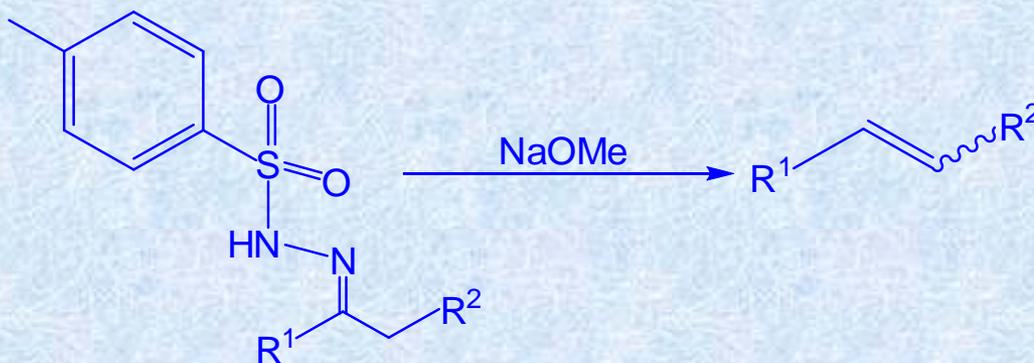


93%

(j) Bamford-Stevens reaction:

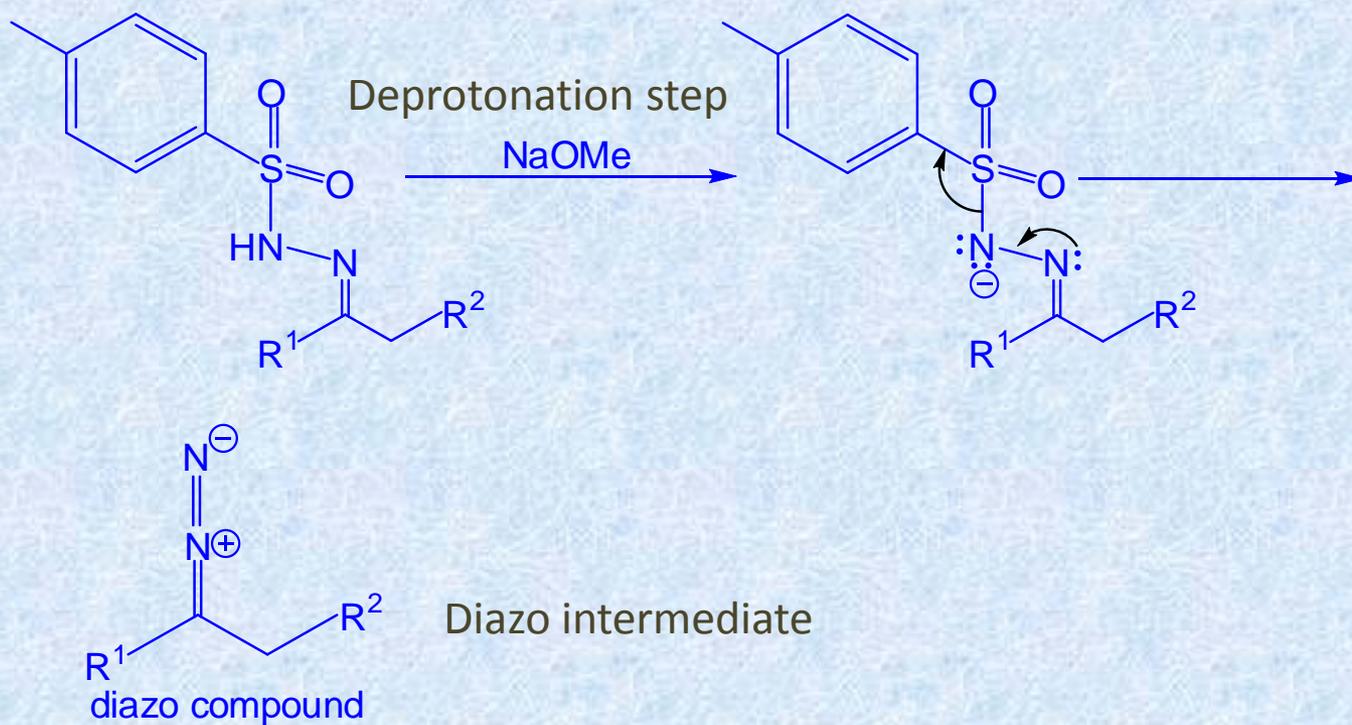
Treatment of tosylhydrazone with a strong base gives alkene, this reaction is called Bamford-Stevens reaction.

Aprotic solvent mainly gives Z-alkenes while protic solvents give mixture of E and Z alkene.



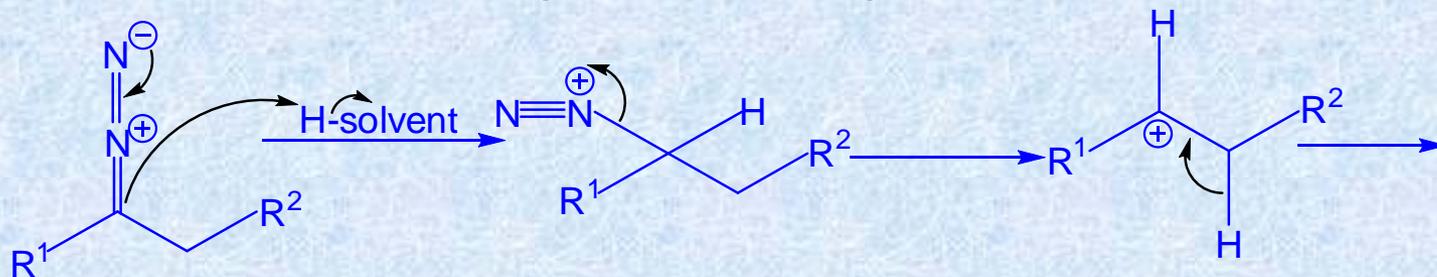
Mechanism of reaction is as follows

Step 1 : *Formation of diazo compound*

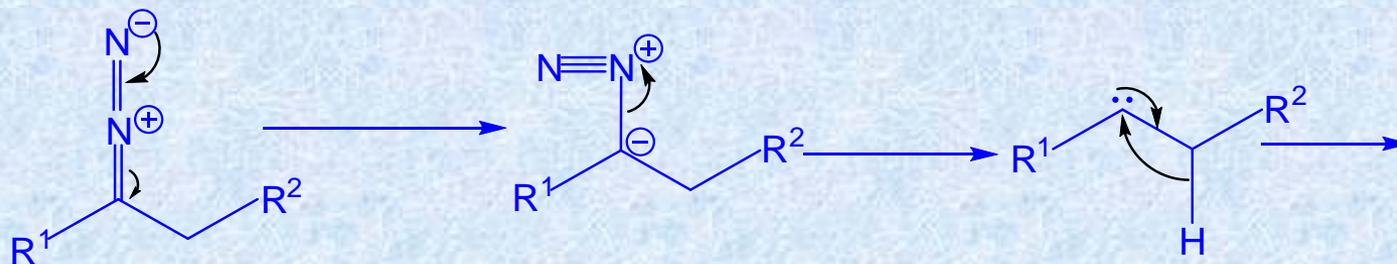


Step-II (olefination)

In protic solvent, diazo compound decomposes to carbocation



In aprotic solvent, diazo compound decomposes to carbene

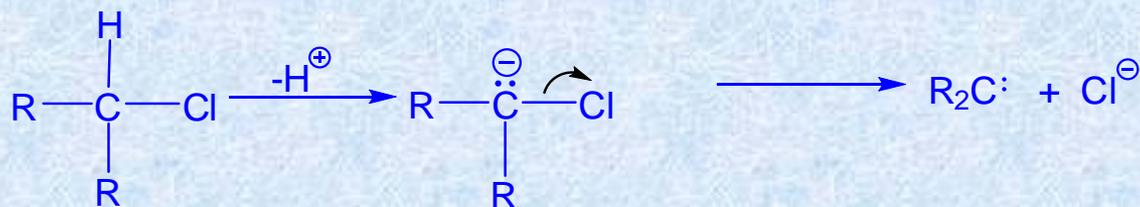


VIII. α -elimination

Very small number of reactions are known in which 1,1 or α elimination occurs.

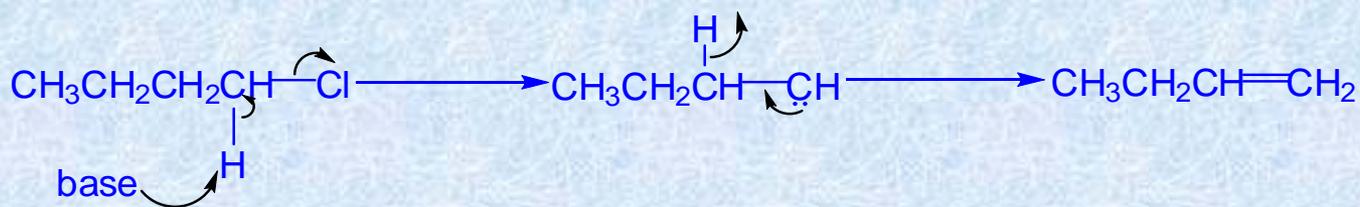
These reactions follow mechanism similar to E1cB. A strong base removes acidic protons followed by loss of leaving group i.e. first a group or atom without its electron pair is lost, usually proton and then a group with its electron pair is lost.

First step generates carbanion which may be stabilized by electron withdrawing group.



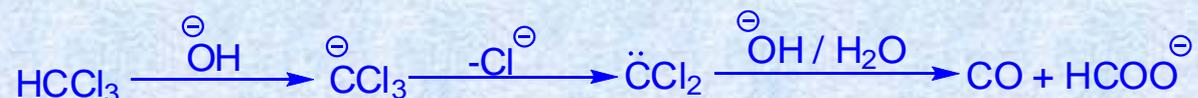
These reactions are favored by

- *Presence of electron withdrawing group on α carbon atom (i.e. acidity of α hydrogen is increased). It is supported by the fact that reaction of alkyl bromides or iodides with base gave very less α elimination product than that of corresponding alkyl chlorides.*
- *Use of very strong base favors α elimination. PhNa, a very strong base gave α elimination product in following reaction up to 94% whereas NaNH_2 or NaOMe did not give much yields.*



- *Absence of β hydrogen atom, though not necessary, favors 1,1-elimination.*

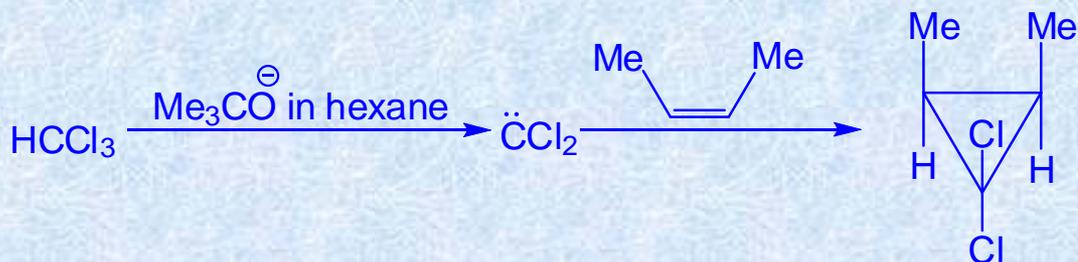
e.g. Hydrolysis of haloforms



Loss of proton and chloride to generate carbene in α elimination is proposed to proceed by a concerted mechanism. This step will be followed by a migration of β hydrogen with its electron pair to give an alkene as the product.

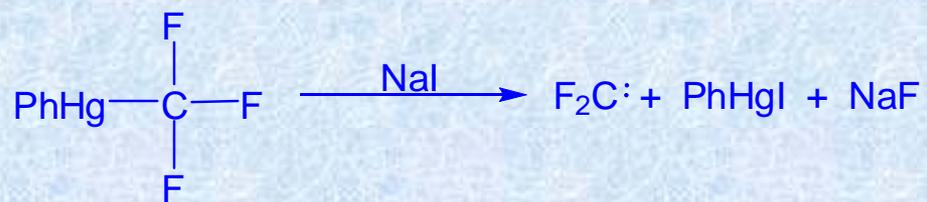
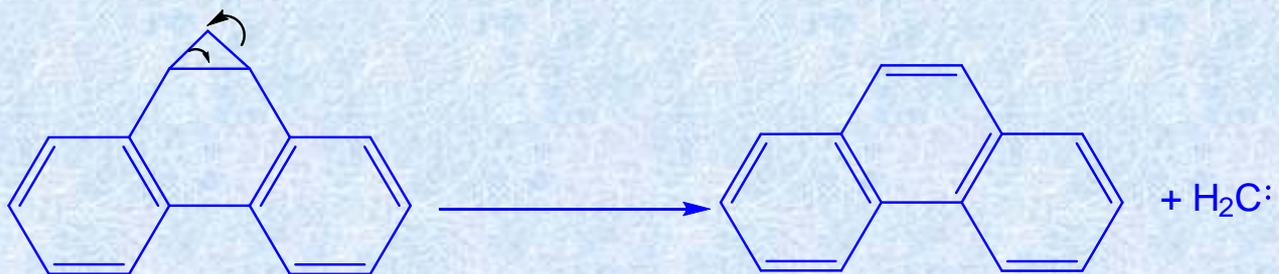
1,1-elimination can be distinguished from 1,2-elimination by isotopic labeling.

Presence of carbenes can be detected by various reactions like trapping or insertion reactions.



Other preparative use is in electrophilic attack on phenol such as in Reimer-Tiemann reaction.

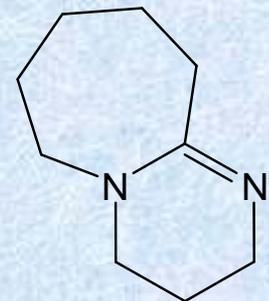
However, in protic solvents, with use of common bases and with substrates containing β hydrogen, α elimination is found to be less prominent.



Further Reading: Some common bases and protecting groups

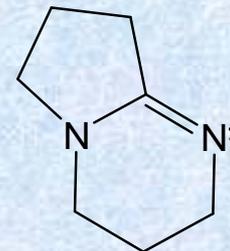
DBU: Diazabicycloundecene

- Nucleophilic, bulky base.
- Stable, water soluble and air sensitive.
- Tends to attack proton which is at periphery rather than deeper in molecule.
- Incompatible with strong oxidizing agents, acids, acid chlorides and acid anhydrides.



DBN: Diazabicyclononene

- Strong amidine base.
- Usually used for nucleophilic substitution and elimination reactions.



NaHMDS : Sodiumhexamethyldisilylamide

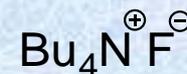
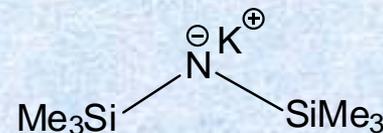
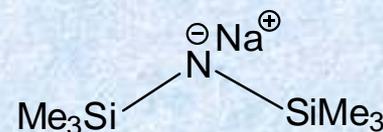
- *Strong base used for deprotonation and base catalyzed reactions.*
- *Water soluble*

KHMDS: Potassiumhexamethyldisilylamide

- *Strong non-nucleophilic base.*
- *pKa 26 as compared to that of LDA 36.*

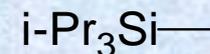
TBAF: Tetra-n-butylammoniumfluoride

- *Quaternary ammonium salt*
- *Mild non-nucleophilic base.*
- *Used for deprotection of silyl ether protecting groups and phase transfer catalyst.*



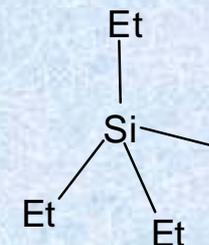
TIPS: Triisopropylsilyl

- Used as alcohol protecting group.
- More stable to hydrolysis than TMS.



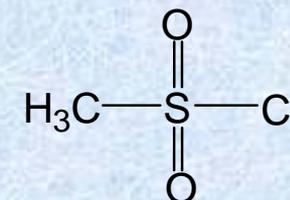
TES: Triethylsilyl

- Used as alcohol protecting groups.
- Considerably more stable than TMS.
- Can be selectively removed in presence of more robust silyl ethers with fluoride and mild acid.



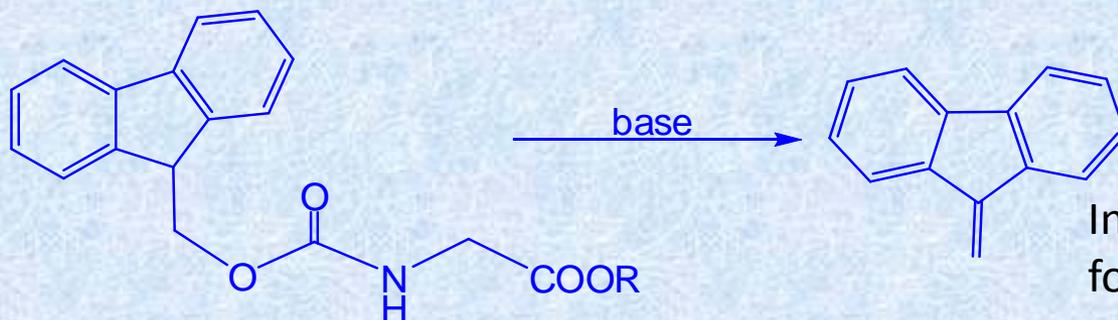
MsCl: Mesyl chloride

- Protecting group for alcohol.
- Excellent leaving group.
- Stable to acids and can be removed with use of sodium amalgam.



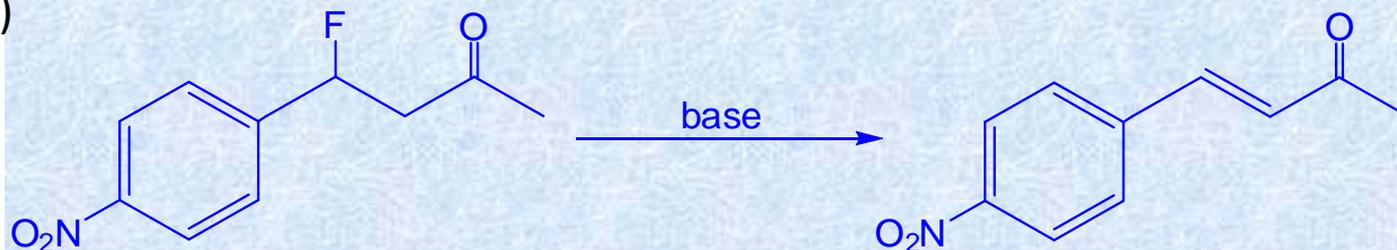
Additional/Practice Problems:

(1)



In both these examples, the formation of initial carbanion is quite feasible, as such species will be stabilized due to conjugation.

(2)



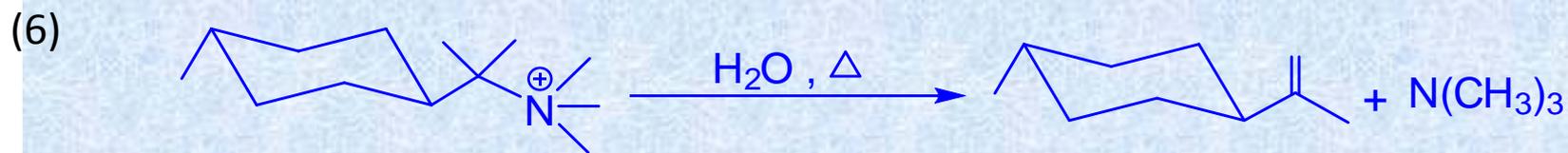
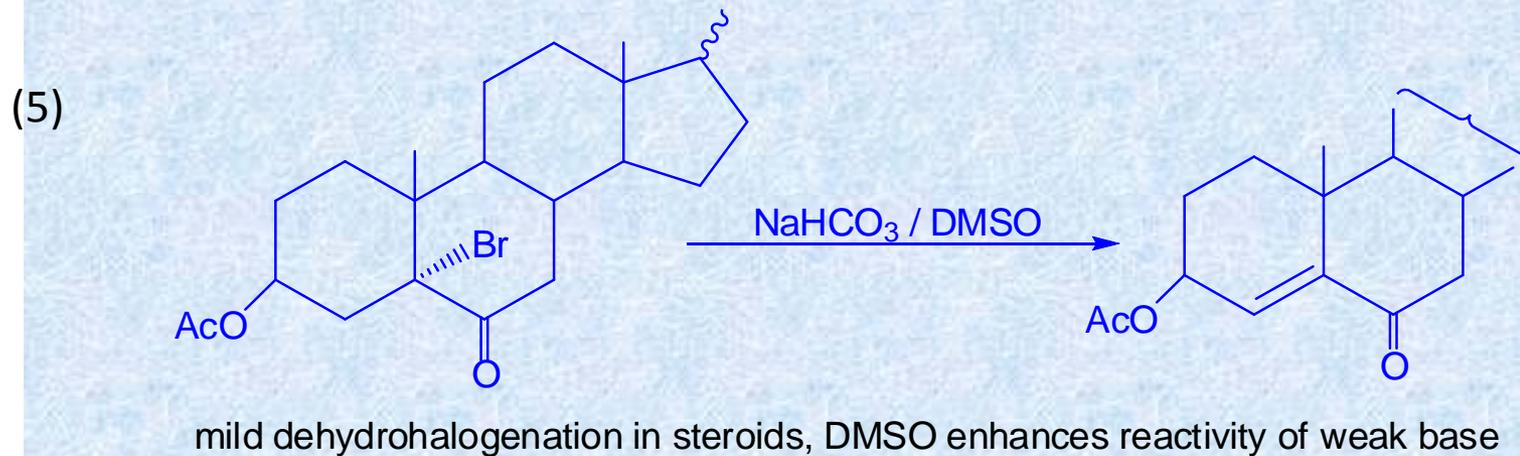
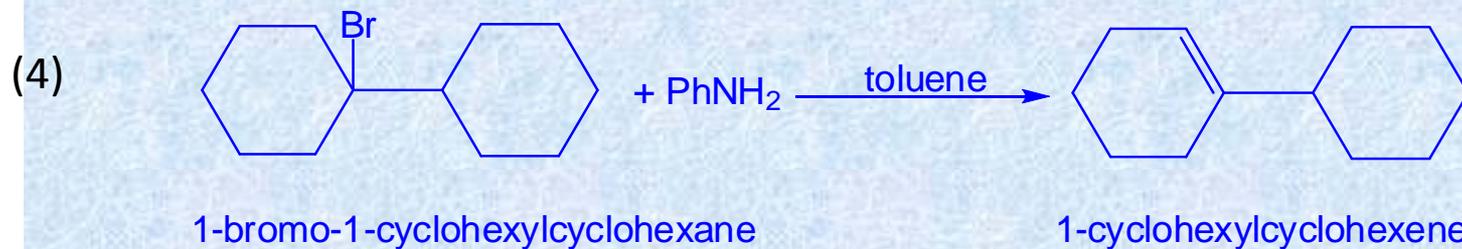
Reyberg, P; Matson, O. *J. Am. Chem. Soc.*, **2001**, 123, 2712-2718.

(3)

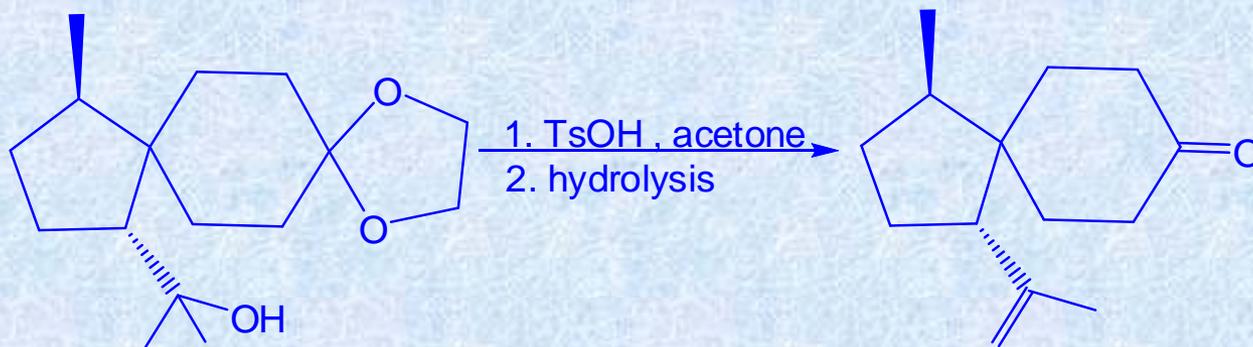


Cho, R. B.; Chul Oh, Y.; Lee, S. H.; Park, Y. J. *J. Org. Chem.*, **1996**, 61, 5656-5658.

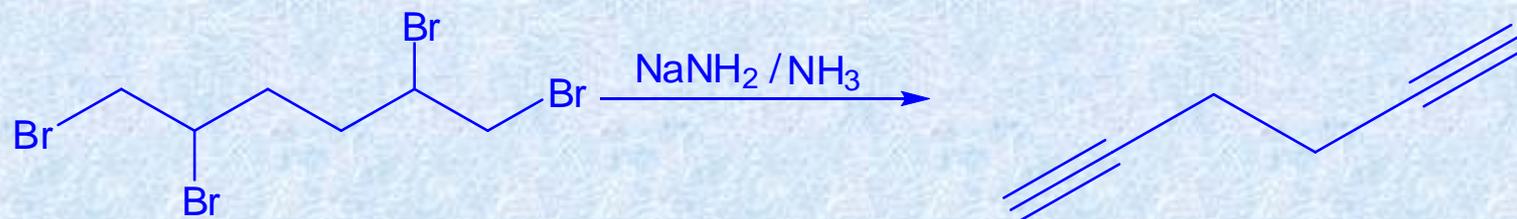
Additional/Practice Problems:



(7)



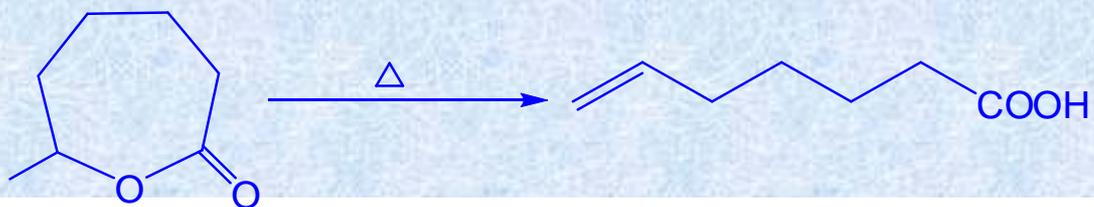
(8)



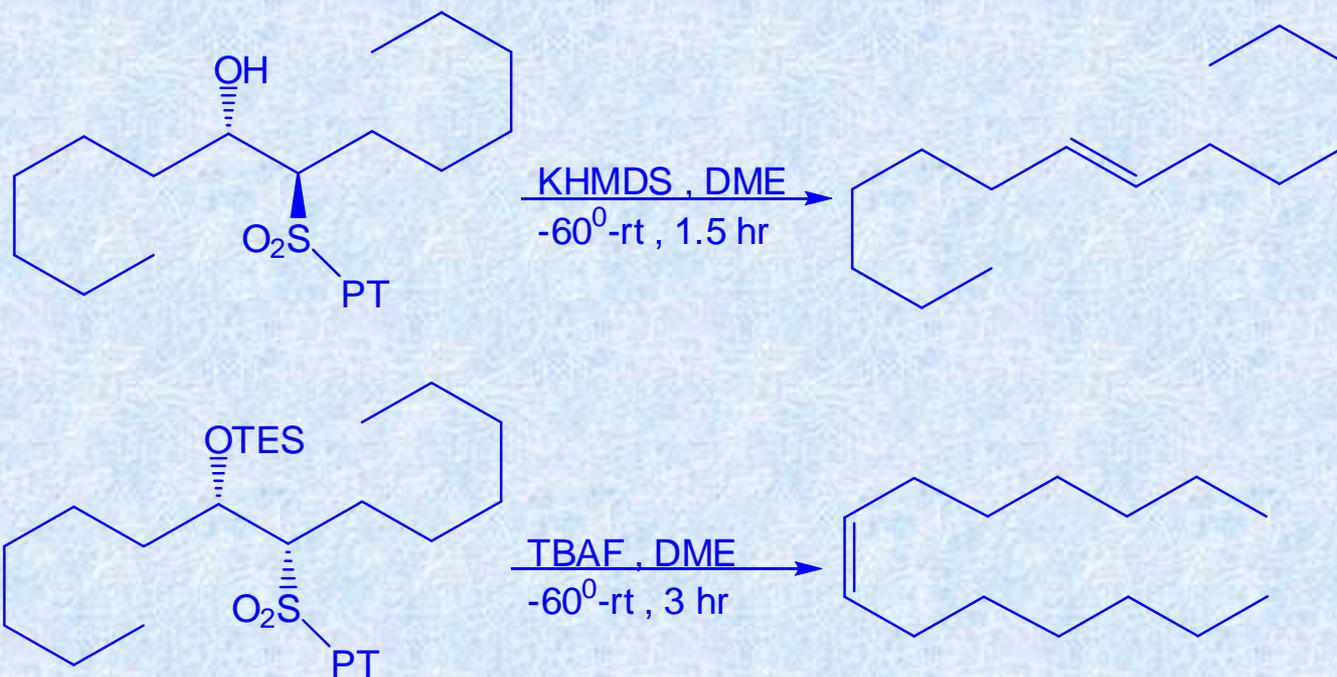
(9)



(10)



(11)



PT=1-phenyl-1H-tetrazol-5-yl .

J.Chem.Soc.,Perkin Trans, 1, 2002, 2563-2585.