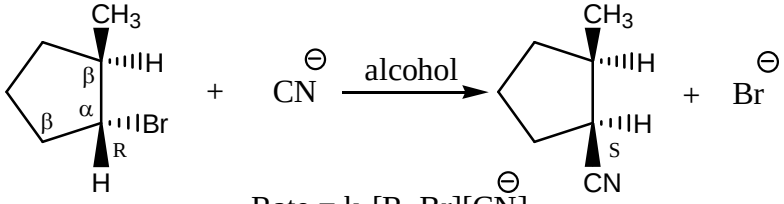
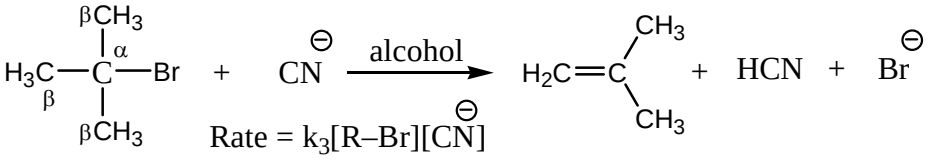
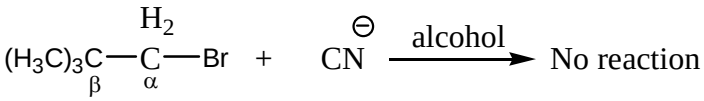
2. 

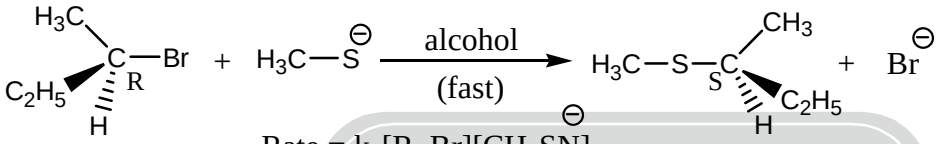
2°-bromide

Rate = $k_2[R–Br][CN^-]$

3. 

Rate = $k_3[R–Br][CN^-]$

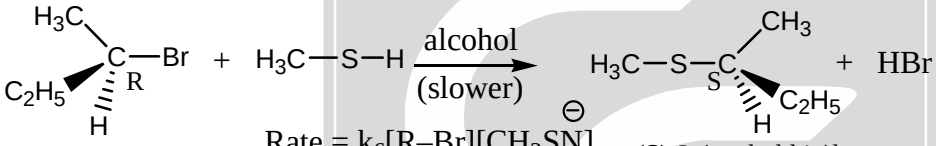
4. 

5. 

(R)-2-bromobutane

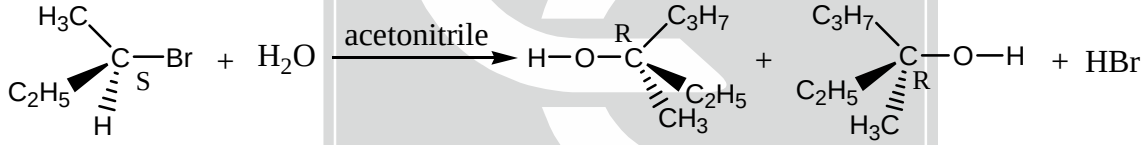
Rate = $k_5[R–Br][CH_3SN^-]$

(S)-2-(methylthio)butane

6. 

Rate = $k_6[R–Br][CH_3SN^-]$

(S)-2-(methylthio)butane

7. 

(S)-3-bromo-3-methylhexane

Rate = $k_7[R–Br]$

racemic 3-methyl--hexanol

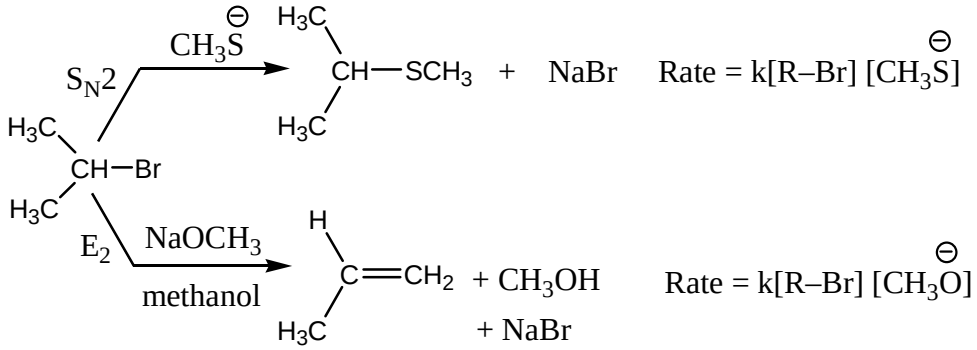
5.4. Elimination reaction:

Types of Elimination reaction:

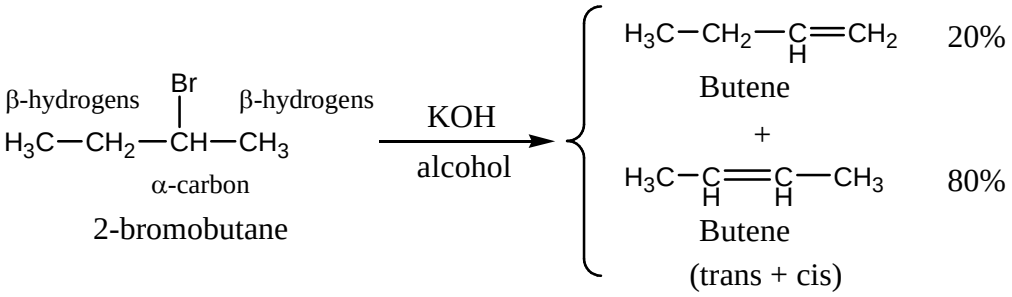
(1) **The E2 Reaction:** We have not yet considered the factors that influence elimination reactions, such as example 3 in the group presented at the beginning of this section. Elimination of second order is called E_2 reaction.

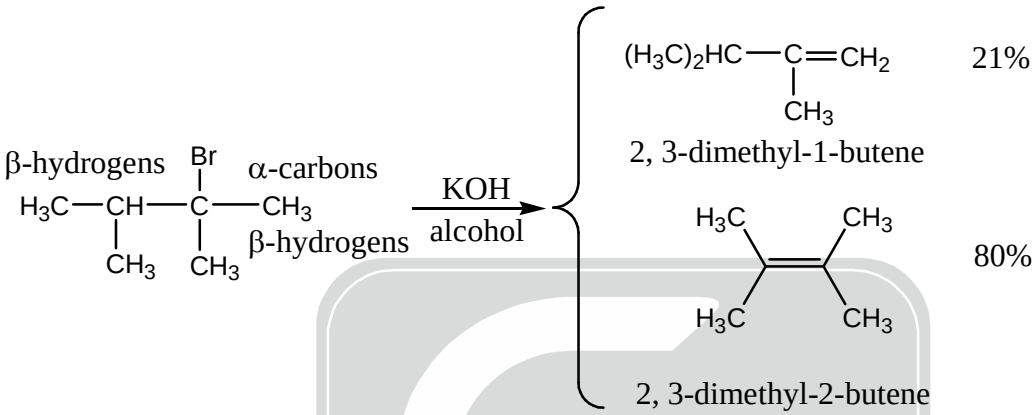
$$(CH_3)_3C-Br + CN^- \longrightarrow (CH_3)_2C=CH_2 + Br^- + HCN$$

For E_2 reaction, there is no formation of intimate ion pair that is carbocation (if formed) is not stable.



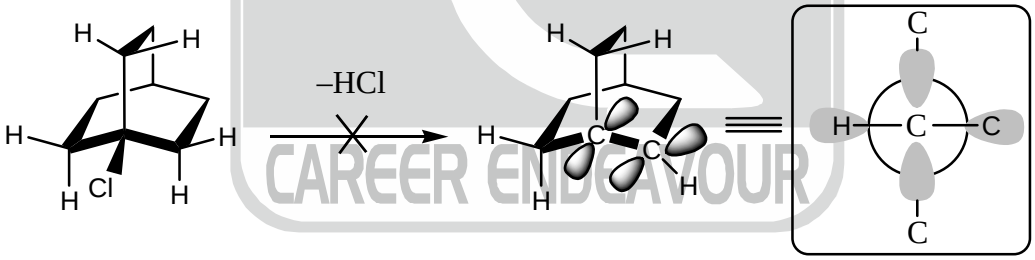
If two or more structurally distinct groups of beta-hydrogens are present in a given reactant, then several constitutionally isomeric alkenes may be formed by an E_2 elimination. This situation is illustrated by the 2-bromobutane and 2-bromo-2,3-dimethylbutane elimination examples given below.



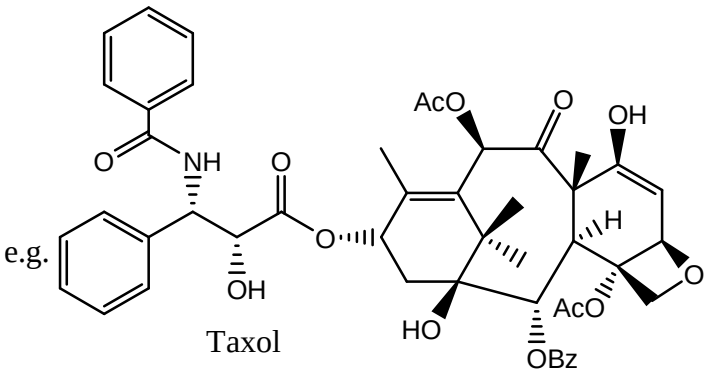


These results point to a strong regioselectivity favoring the more substituted double bond, an empirical statement generally called the **Zaitsev's Rule**.

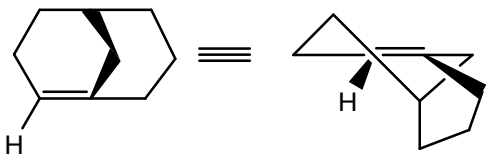
Bredt's Rule: **Double bond can never be formed to bridge head carbons in bicyclic system due to impossibility of formation of planarity at bridge head carbon.**



Note: Bridged-head double bond is possible in large ring compounds.



Taxol

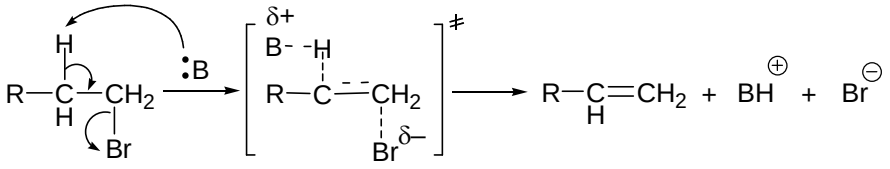


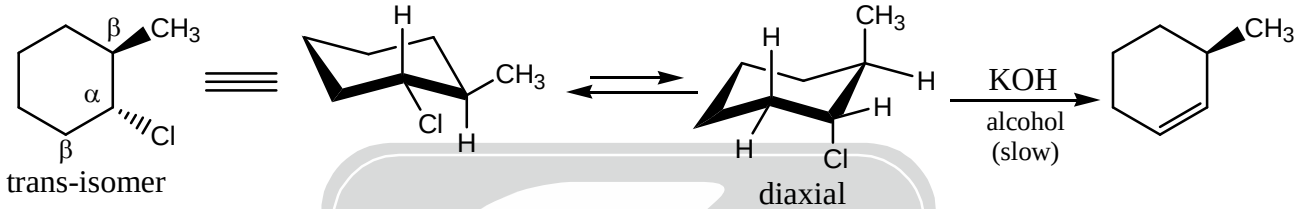
A brigehead double bond
in 1-bicyclo[3, 3, 1]octene

2. Stereochemistry of the E2 Reaction:

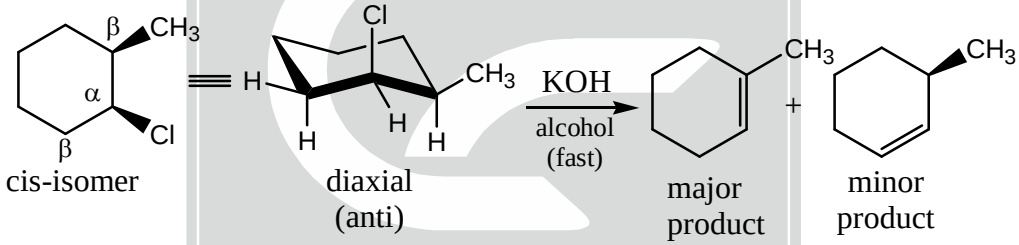
E_2 elimination reactions of certain isomeric cycloalkyl halides show unusual rates and regioselectivity that are not explained by the principles thus far discussed. For example, trans-2-methyl-1-chlorocyclohexane reacts with alcoholic KOH at a much slower rate than does its cis-isomer. Furthermore, the product from elimination of the trans-isomer is 3-methylcyclohexene (not predicted by the Zaitsev rule), whereas the cis-isomer gives the predicted 1-methylcyclohexene as the chief product.

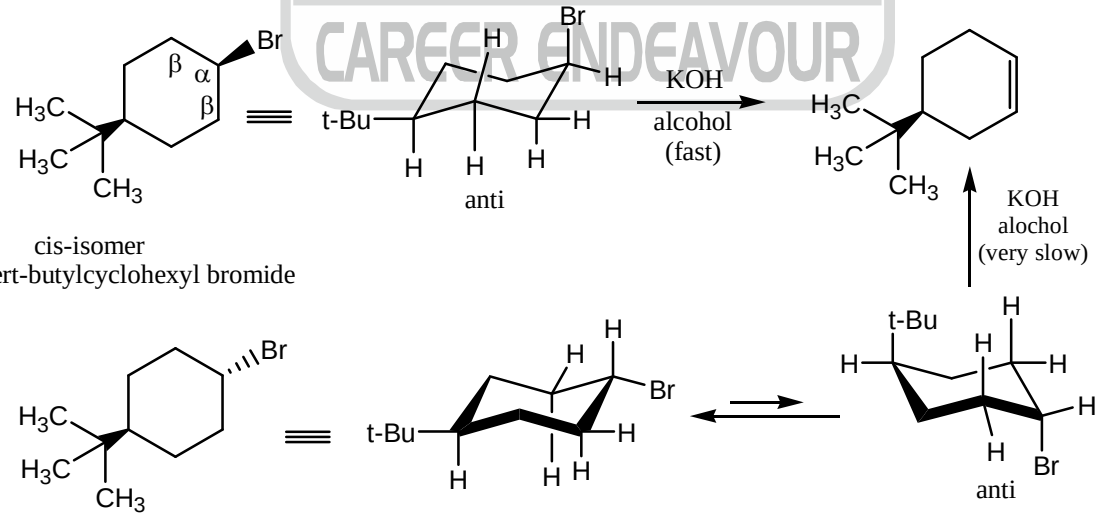
Unlike open chain structures, cyclic compounds generally restrict the spatial orientation of ring substituents to relatively few arrangements.





1-chloro-2-methylcyclohexane

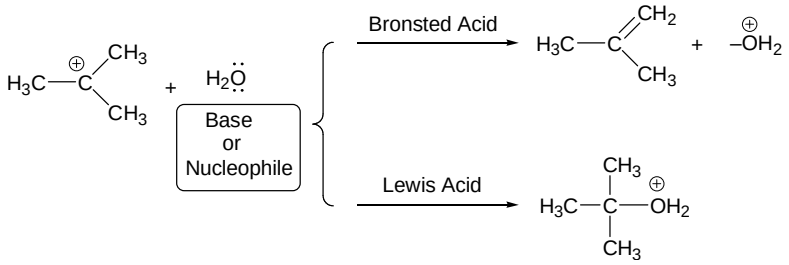




Note: Both eleminating group must be antiperiplanar to each other.

3. The E1 Reaction:

Just as there were two mechanisms for nucleophilic substitution, there are two elimination mechanisms. The E_1 mechanism is nearly identical to the S_N1 mechanism, differing only in the course of reaction taken by the carbocation intermediate. As shown by the following equations, a carbocation bearing beta-hydrogens may function either as a Lewis acid (electrophile), as it does in the S_N1 reaction, or a Brønsted acid, as in the E_1 reaction.



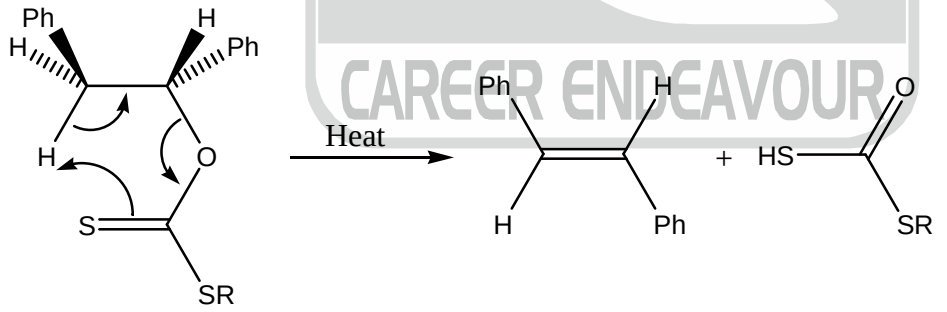
$$(CH_3)_3C-Cl + H_2O \longrightarrow [(CH_3)_3C^+)] + Cl^- + H_2O \longrightarrow (CH_3)_3C-OH + (CH_3)_2C=CH_2 + HCl + H_2O$$

To summarize, when carbocation intermediates are formed one can expect them to react further by one or more of the following modes:

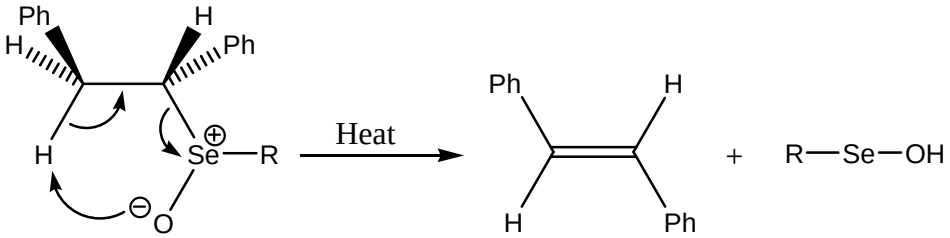
1. The cation may bond to a nucleophile to give a substitution product.
2. The cation may transfer a beta-proton to a base, giving an alkene product.
3. The cation may rearrange to a more stable carbocation, and then react by mode E_1 or E_2.
Since the S_N1 and E_1 reactions proceed via the same carbocation intermediate.
The most important being the structure of the alkyl group and the nature of the nucleophilic reactant.

Pyrolytic syn-eliminations:

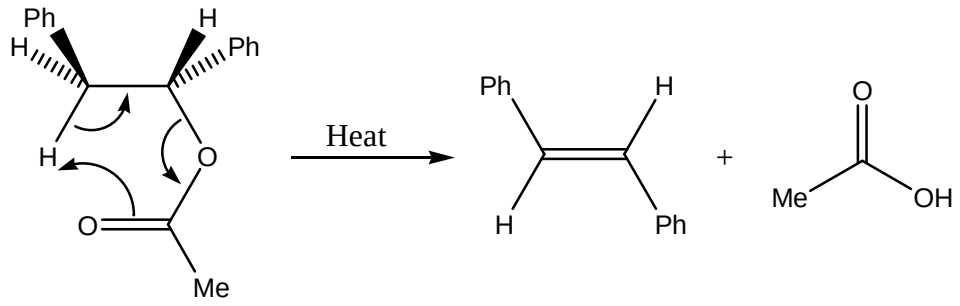
Pyrolytic eliminations take place in a concerted manner via cyclic transition state and therefore proceed with syn-stereochemistry i.e. H-atom and leaving group depart from same side. (**Note:** Less crowded transition state is favoured). e.g.



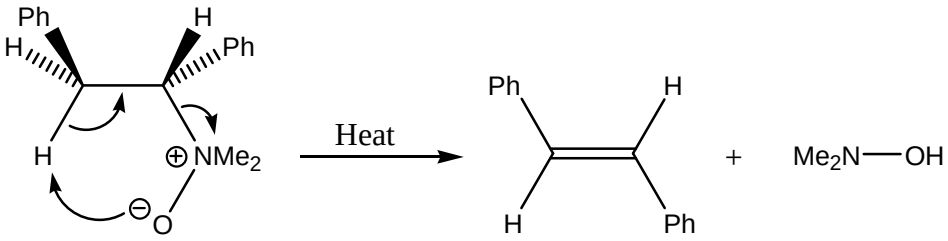
Xanthate Elimination



Selenoxide Elimination



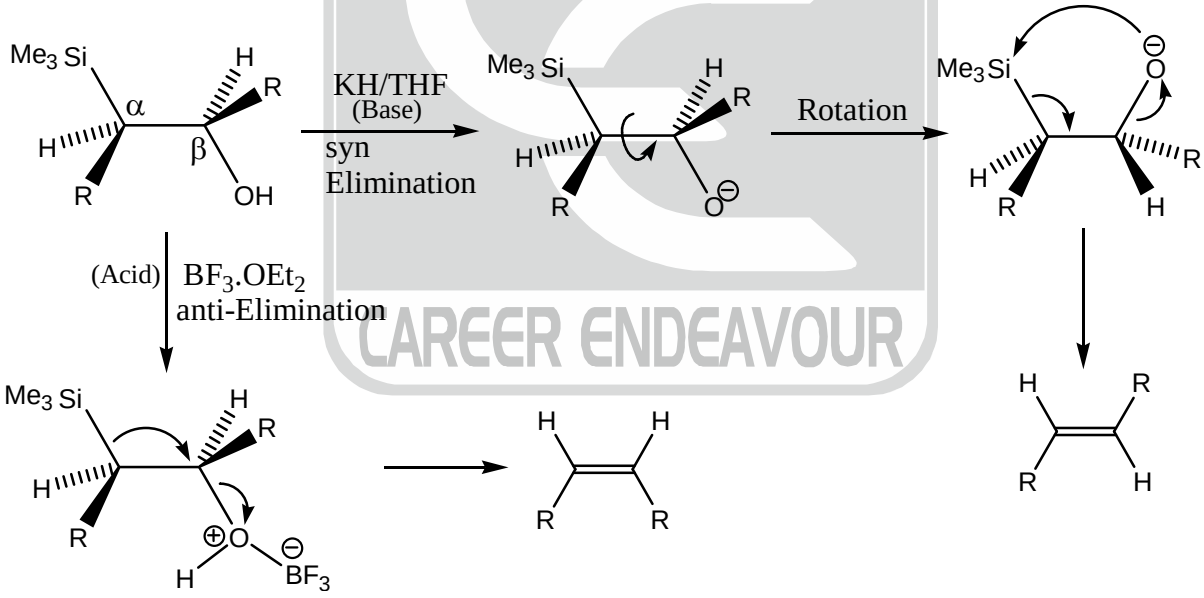
Acetate Elimination



N-Oxide
Cope-Elimination

Peterson Elimination Reaction:

Elimination reactions of β-hydroxy silane:



Note that halogens bonded to sp^2 or sp hybridized carbon atoms do not normally undergo substitution or elimination reactions with nucleophilic reagents.

Nucleophile	Non-Basic Anionic Nucleophile	Basic Anionic Nucleophile	Neutral Nucleophile
Alkyl Group	(Weak Bases: I^-, Br^-, SCN^-, N_3^- ,$CH_3CO_2^-$, RS^-, CN^- etc.) pKa's from -9 to 10 (left to right)	(Strong Bases: HO^-, RO^-) pKa's > 15	(H_2O, ROH, RSH, R_3N) pKa's ranging from -2 to 11
Primary RCH_2^-	Rapid S_N2 substitution. The rate may be reduced by substitution of β-carbons, as in the case of neopentyl.	Rapid S_N2 substitution. E_2 elimination may also occur. *e.g.* $ClCH_2CH_2Cl + KOH \rightarrow CH_2=CHCl$	S_N2 substitution. ($SH^- > NH_2^- > OH^-$)
Secondary R_2CH^-	S_N2 substitution and / or E_2 elimination (depending on the basicity of the nucleophile). Bases weaker than acetate (pKa = 4.8) give less elimination. The rate of substitution may be reduced by branching at the β carbons, and this will increase elimination.	E_2 elimination will dominate.	S_N2 substitution. ($SH^- > NH_2^- > OH^-$) In high dielectric ionizing solvents, such as water, dimethyl sulfoxide & acetonitrile, S_N1 and E_1 products may be formed slowly.
Tertiary R_3C^-	E_2 elimination will dominate with most nucleophiles (even if they are weak bases). No S_N2 substitution due to steric hindrance. In high dielectric ionizing solvents, such as water, dimethyl sulfoxide & acetonitrile, S_N1 and E_1 products may be expected.	E_2 elimination will dominate. No S_N2 substitution will occur. In high dielectric ionizing solvents S_N1 and E_1 products may be formed.	E_2 elimination with nitrogen nucleophiles (they are bases). No S_N2 substitution. In high dielectric ionizing solvents S_N1 and E_1 products may be formed.
Allyl $H_2C=CH-CH_2$	Rapid S_N2 substitution for 1º and 2º -halides. For 3º -halides a very slow S_N2 substitution or, if the nucleophile is moderately basic, E_2 elimination. In high dielectric ionizing solvents, such as water, dimethyl sulfoxide and acetonitrile, S_N1 and E_1 products may be observed.	Rapid S_N2 substitution for 1º halides. E_2 elimination will compete with substitution in 2º - halides, and dominate in the case of 3º-halides. In high dielectric ionizing solvents S_N1 and E_1 products may be formed.	Nitrogen and sulfur nucleophiles will give S_N2 substitution in the case of 1º and 2º -halides. 3º-halides will probably give E_2 elimination with nitrogen nucleophiles (they are bases). In high dielectric ionizing solvents S_N1 and E_1 products may be formed. Water hydrolysis will be favorable for 2º & 3º-halides.
Benzyl $C_6H_5CH_2^-$	Rapid S_N2 substitution for 1º and 2º -halides. For 3º -halides a very slow S_N2 substitution or, if the nucleophile is moderately basic, E_2 elimination. In high dielectric ionizing solvents, such as water, dimethyl sulfoxide & acetonitrile, S_N1 and E_1 products may be observed.	Rapid S_N2 substitution for 1º halides (note there are no β hydrogens). E_2 elimination will compete with substitution in 2º-halides, and dominate in the case of 3º-halides. In high dielectric ionizing solvents S_N1 and E_1 products may be formed.	Nitrogen and sulfur nucleophiles will give S_N2 substitution in the case of 1º and 2º-halides. 3º-halides will probably give E_2 elimination with nitrogen nucleophiles (they are bases). In high dielectric ionizing solvents S_N1 and E_1 products may be formed. Water hydrolysis will be favorable for 2º and 3º halides.

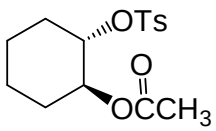
5.5. Neighbouring Group Participation:

The presence of nucleophilic groups in molecule undergoing nucleophilic substitution affects the kinetics and stereochemistry of reaction. The involvement of nearby nucleophilic substitutents such as lone pair electrons of group, in a substitution process is called neighbouring group participation.

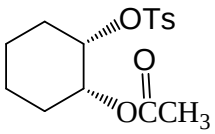
The leaving group and participating group are in the trans-position.

1. Acetoxy $\left(CH_3-\overset{\overset{O}{\|}}{C}-O\right)$ group:

The rate of solvolysis of the cis and trans isomers of 2-acetoxy cyclohexyl p- toluene sulfonate differs by a factor of about 670, trans isomers being more reactive one and the products obtained are also different.

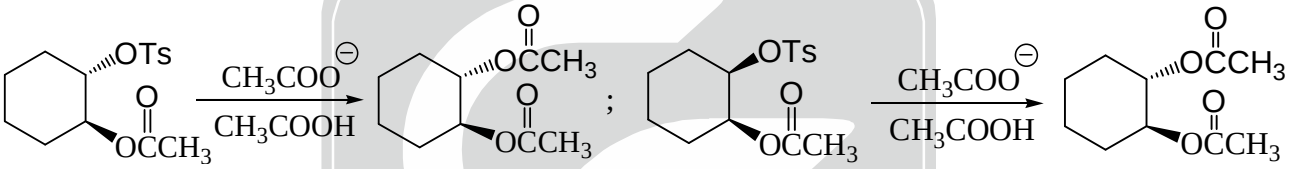


$K = 1.9 \times 10^{-4} S^{-1} (100^oC)$



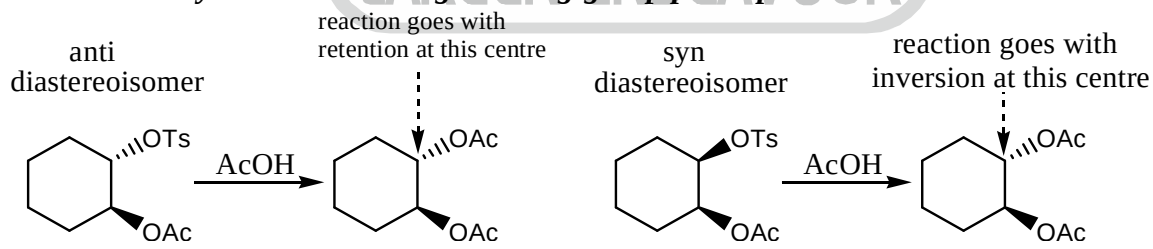
$K = 2.9 \times 10^{-7} S^{-1} (100^oC)$

The diacetate obtained from the cis isomer is the trans-isomer (inverted stereochemistry) whereas retention of configuration is observed for the trans isomer.



The results can be explained by the participation of the trans acetoxy group in the ionisation process. The assistance provided by the acetoxy carbonyl group facilitates the ionisation of the tosylate group, accounting for the rate enhancement. This kind of backside participation by adjacent acetoxy group is both sterically and energetically favorable. The cation which is formed by participation is stabilised by two oxygen atoms and is for more stable than a secondary carbocation. The acetoxonium ion is subsequently opened by nucleophilic attack with inversion at one of the two equivalent carbons leading to the observed trans product. Whereas in case of cis isomer, simple S_N2 mechanism is involved.

Stereochemistry can indicate neighbouring group participation:



To explain this, we should first draw the six-membered rings in their real conformation. For the anti compound, both substituents can be equatorial.

However, not much can happen in this conformation–but, if we allow the ring to flip, you can see immediately that the acetate substituent is ideally placed to participate in the departure of the tosylate group.