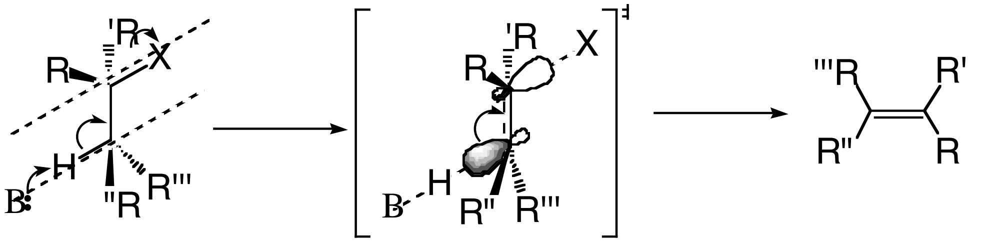
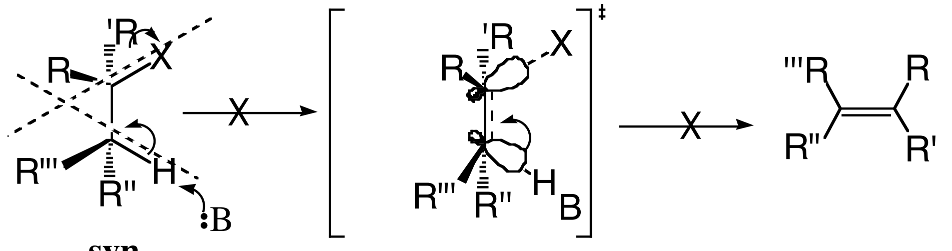
Elimination Reactions, E2

The E2 elimination is a concerted reaction involving the deprotonation of a carbon adjacent to a carbon bearing a good leaving group. As the negative charge develops on the deprotonated carbon, the nascent lone pair acts as a nucleophile to displace the leaving group (X) from the adjacent carbon.

- This is also known as *concerted* a 1,2 elimination reaction.
- Note that, in principle, this reaction can occur with the hydrogen either syn or anti relative to the leaving group as shown below.
- The elimination generally occurs from the anti configuration. However, few rare exceptions do exist when the elimination ocurs from the syn configuration.



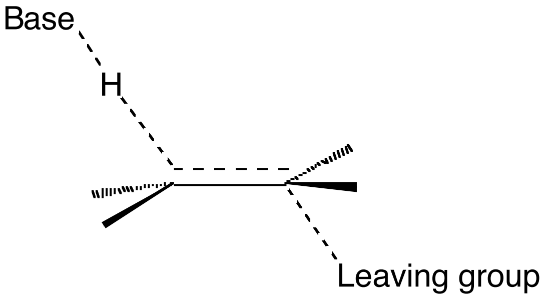
anti periplanar "backside attack" stereospecific reaction

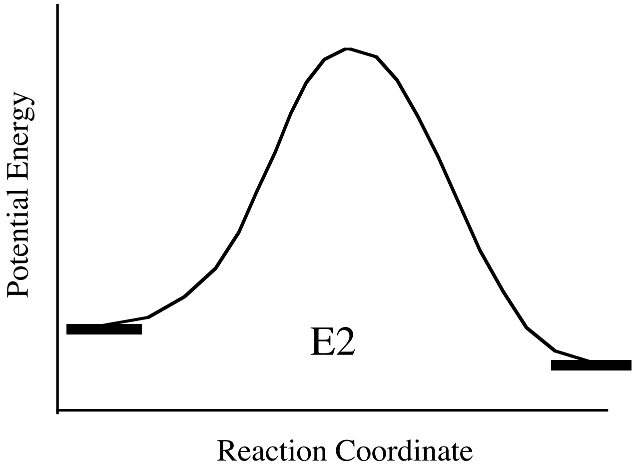


syn

Note that R groups are eclipsed in the syn configuration which is higher in energy and that backside attack is preferred (by analogy to the S_N2 reaction).

The Transition State for an E2 Reaction





Since the rate determining step involves a collision between the base and the starting material, the rate equation for the disappearance of starting material is:

$$d[\text{starting material}]/dt = -k[\text{starting material}][\text{base}]$$

Therefore, the rate depends on the concentration of both the starting material and the base and is second order overall.

The E2 Reaction in Detail

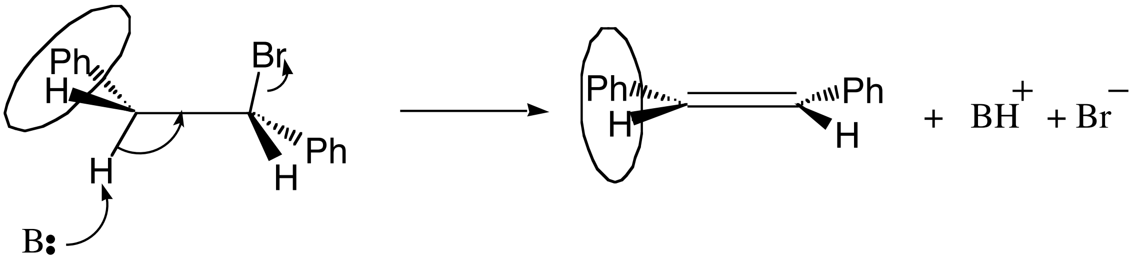
1. Because the base has to closely interact with the starting materials, in order to remove the proton, the starting material cannot be too sterically hindered, *especially if a hindered base is used.*
2. In the rate determining step, the base removes the proton in an **antiperiplanar** configuration to the leaving group.

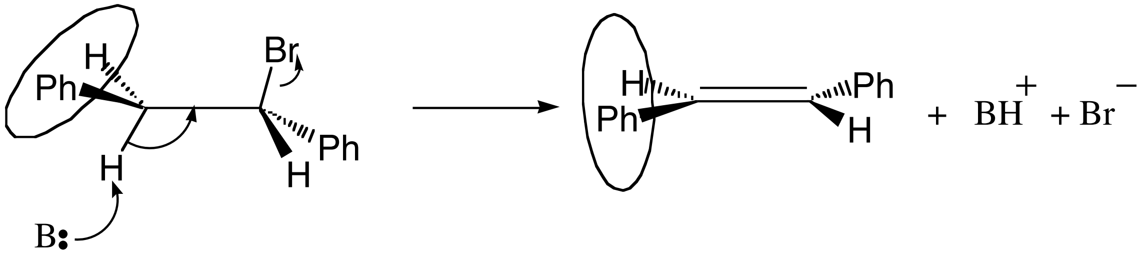
Why is anti elimination preferred?

- The elimination occurs from a staggered conformation which is lower in energy than an eclipsed conformation needed for syn elimination. In this manner the steric interaction between the base and the leaving group are also minimized.
- Anti elimination is favorable from a molecular orbital perspective (somewhat beyond the scope of this course).

3. The configuration of the starting materials will determine whether you obtain the E or Z isomer of the double bond. Hence the reaction is stereospecific.

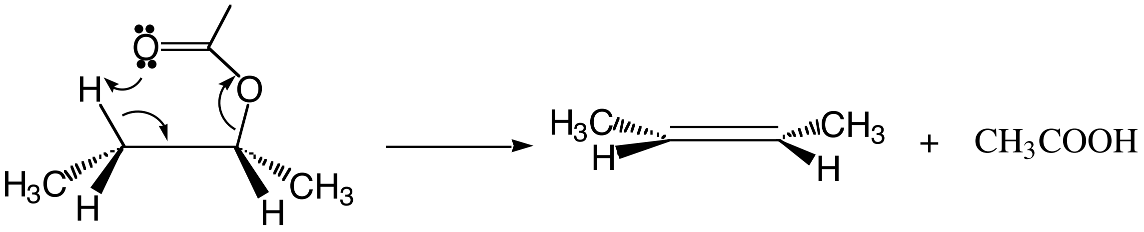
Stereospecificity of the E2 reaction





- Leaving group effects are very similar to those for the S_N2 reaction (i.e. weak bases are favorable).

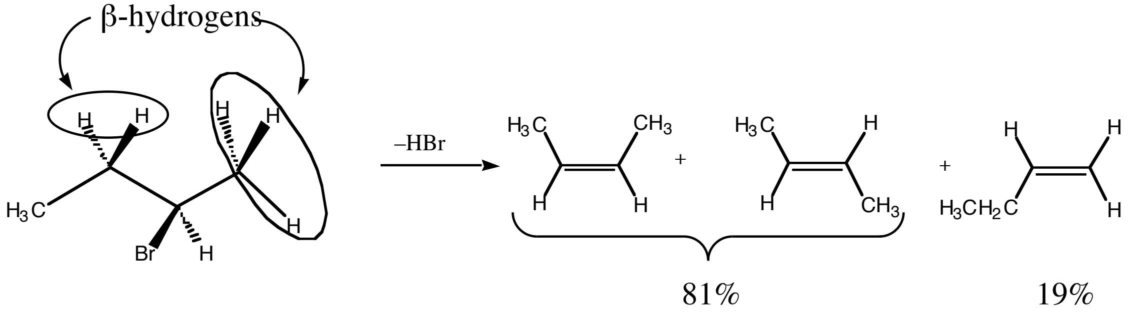
Note: all concerted eliminations are anti, with the exception of the case where the base and the leaving group are one in the same as shown below.



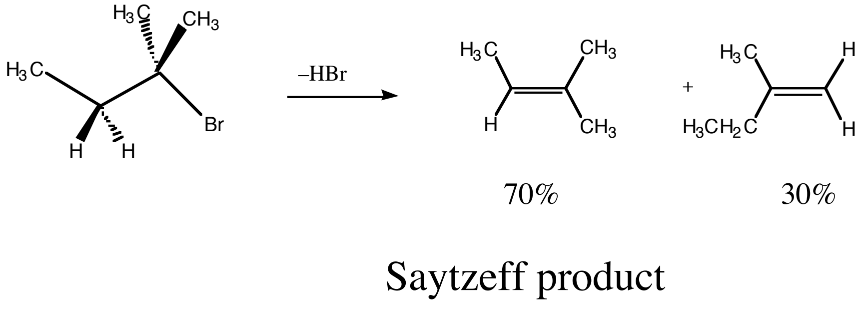
Saytzeff Elimination

If more than one type of β hydrogen is present, in general, the most stable (most substituted) alkene will be preferentially formed. This is known as **Saytzeff Elimination.** Thus, the Saytzeff elimination is a *regiselective reaction.*

Unfortunately, the most substituted isomer is often not exclusively formed as shown below (i.e. the reaction is not regiospecific). Thus, this reaction is really only of synthetic value if only one type of β hydrogen is present.



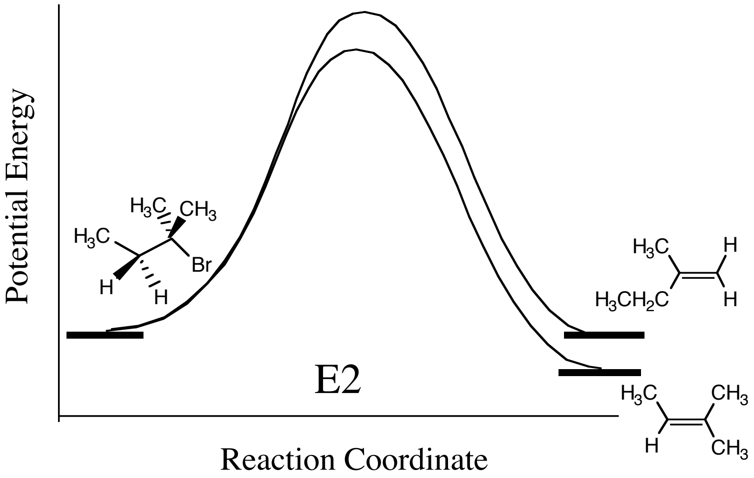
Saytzeff products



Saytzeff product

Why is the more stable alkene the major product of the reaction?

- It is likely that there may be a relatively late transition state such that the relative stability of the various products are manifested in the relative stabilities of the transition states leading to these products.



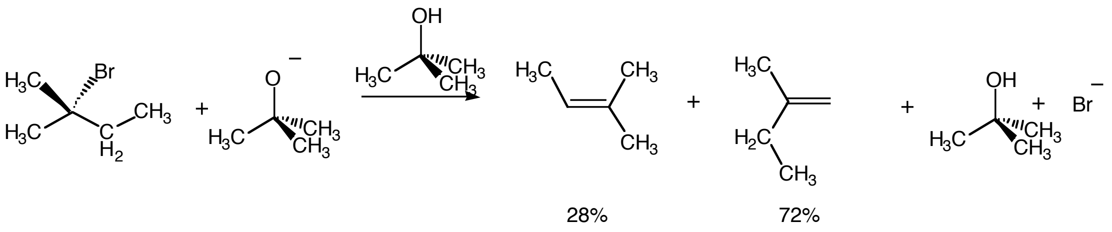
- The pattern is most consistent with the fact that E2 elimination requires good leaving groups. This implies that substantial bond breaking has occurred in the transition state.

Could the selectivity of Saytzeff elimination be the result of equilibration subsequent to elimination?

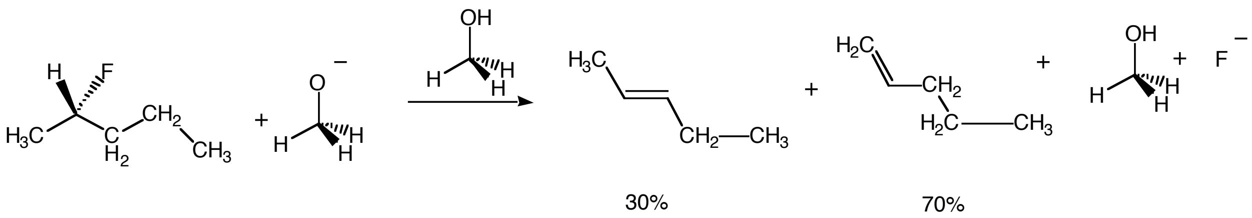
- This is unlikely since E2 reactions are run under basic conditions that would effectively preclude the re-addition of, for example, HBr to the double bond.

Exception to Saytzeff Elimination Products

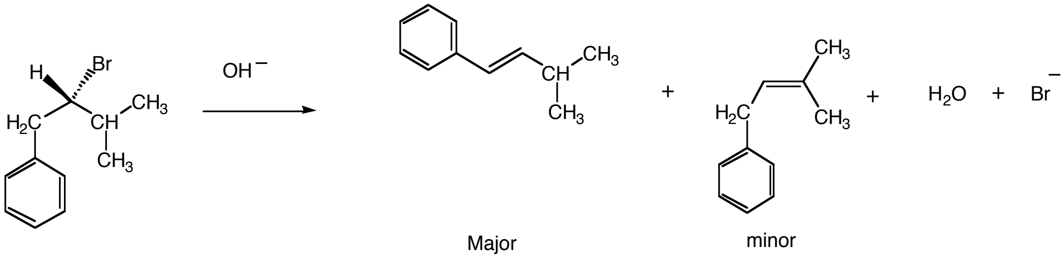
If the base is very hindered (for example $(CH_3)_3CO^-$), *t*-butoxide the approach to the protons that produce the most stable alkene will be blocked. In this case the, *t*-butoxide will deprotonate the most accessible hydrogens.



Also if there is a poor leaving group, for example F^-, then the least substituted alkene will be the major product. In this case this is an early transition state which has significant deprotonation character. If this is the case, the *least substituted carbon will build up the least amount of negative charge and will create the most stable transition state which leads to the formation of the less stable alkene product.*

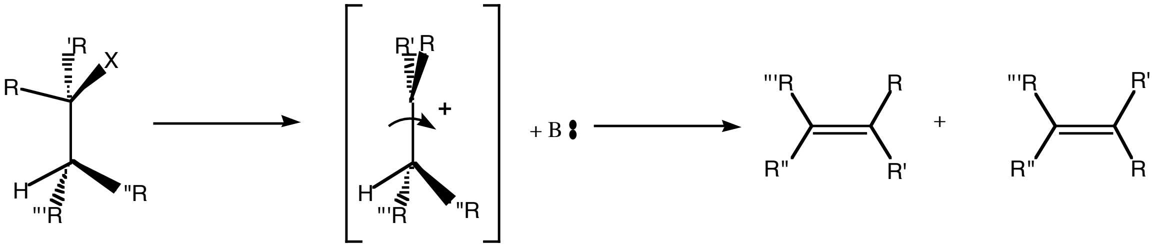


- If elimination can make a conjugated double bond then this could be the thermodynamically most stable product even if it is less substituted and it will be the major product.



Elimination Reactions, E1

The E1 elimination reactions parallels the S_N1 reaction in that, in the first (rate determining step), a starting material with a very good leaving group ionizes to give a carbocation.



Note that in the rate determining step the C-X bond is broken heterolytically, and it is **after** this that the base comes in and removes a proton.

Implications:

1. If you start out with an optically active starting material, you can end up with either Z or E isomers about the double bond since there is free rotation about the single bond between the carbon bearing R''' and R" and the carbocationic carbon.

2. This type of elimination reaction will only occur when a stable carbocation can be formed. Therefore, you will never see this type of elimination reaction with primary carbocations.

3. Since the rate determining step involves only a single species the rate equation for the disappearance of starting material is:

   $$d[\text{starting material}]/dt = -k[\text{starting material}]$$

   there is no dependence of the rate on the base.
4. Nucleophiles that can act as strong bases favor elimination reactions over substitution reactions.

Competition between E2 and E1 Reactions

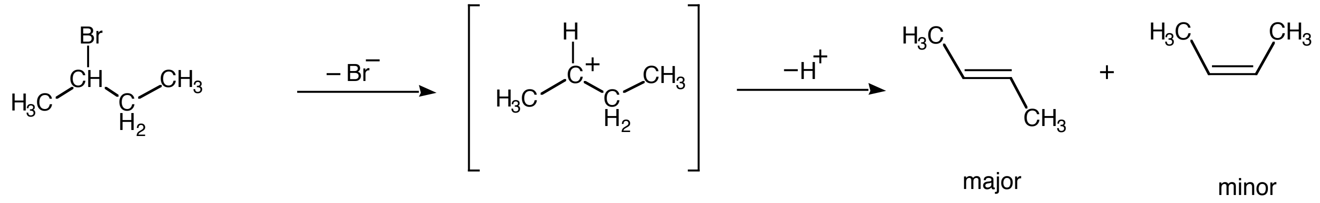
The same factors that determine whether an S_N1 or S_N2 reaction will occur will determine whether an E1 or E2 reaction will occur.

Namely:

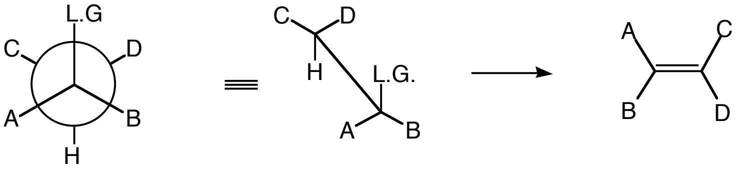
- primary alkyl halides will only go by E2
- secondary alkyl halides will go by E1 or E2 depending on leaving group and conditions
- tertiary alkyl halides will go by E1 or E2 depending on leaving group and conditions
- a high concentration of a strong base will favor E2
- an polar aprotic solvent will favor E2
- a protic solvent that is also a weak base will favor E1

Stereochemistry of E1 and E2 Reactions

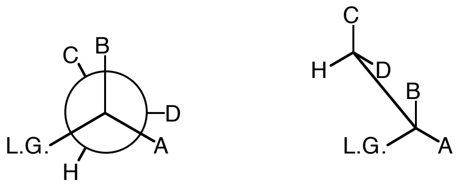
For an E1 reaction, an intermediate carbocation is formed and so the stereochemistry of the starting material will not determine the stereochemistry of the final product. The products formed though, will favor having the two bulky group on the opposites side of the double bond (the E alkene).



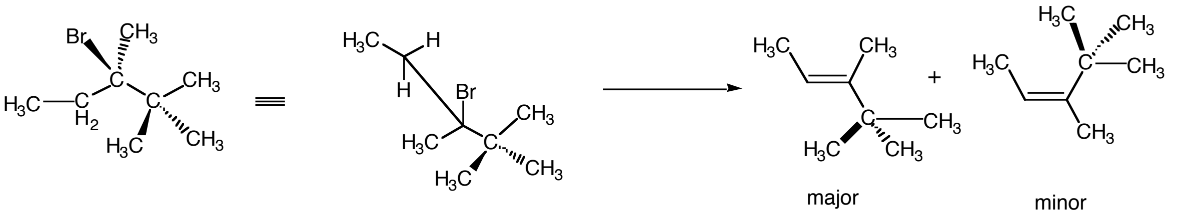
For the E2 elimination, the products formed will result from the conformation of the starting materials where the H and the leaving group are anti-periplanar.



Products resulting from the starting material in the syn conformation will not be favored as explained before.



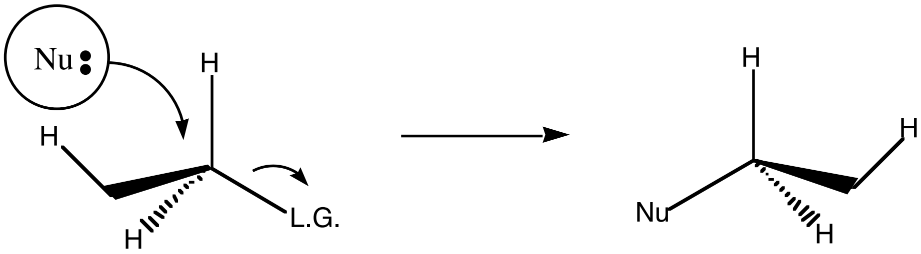
In general with the anti periplanar conformation, if there is a choice the molecule formed will result from having the two biggest groups anti to each other, resulting in a double bond with the bulky groups trans to each other (E alkene).



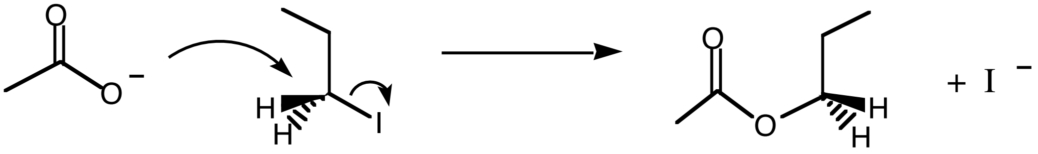
Factors Influencing Whether Substitution or Elimination Occur

S_N2 and E2 reactions can compete to give different products. The course of the reaction is determined by both the substrate and the nucleophile as described below.

1. Primary or secondary carbons substituted with good leaving groups, no branching on β carbons, that are attacked by small, non-basic nucleophiles favor S_N2.



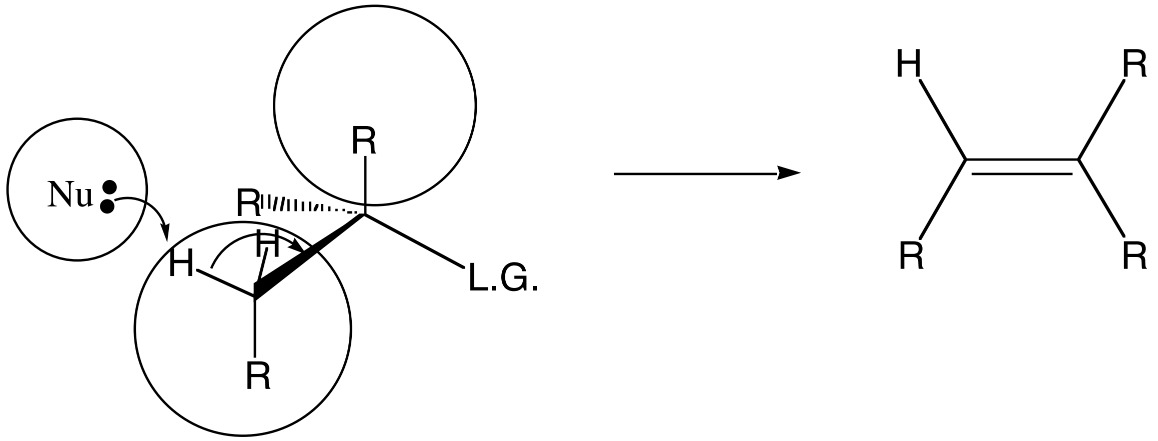
Example:



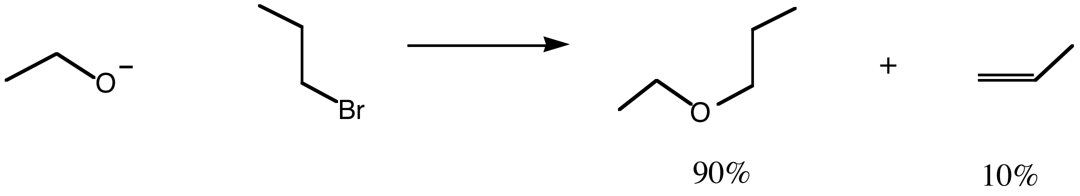
Factors Influencing Whether Substitution or Elimination Occur cont.

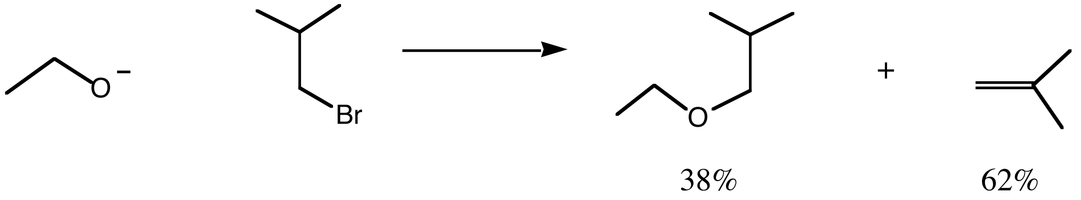
2. Nucleophiles that are also strong bases favor elimination, while nucleophiles that are weak bases favor S_N2, for example ethoxide

Alkyl branching at either the α or β carbons favor the E2 reaction.



The balls indicate steric congestion—this could, in fact, be at either the α or β carbon.

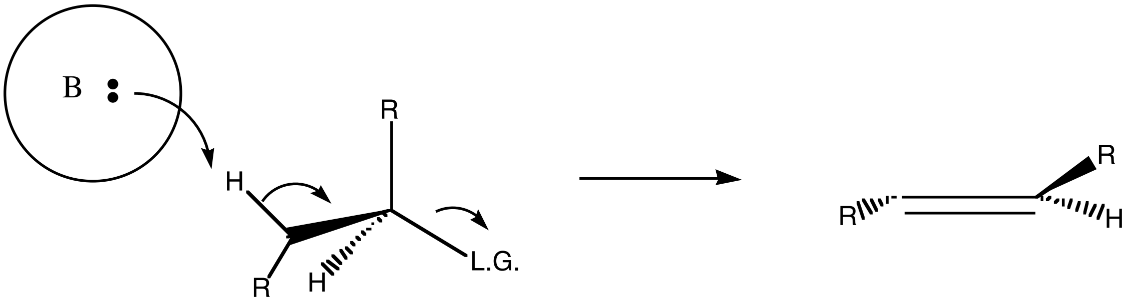




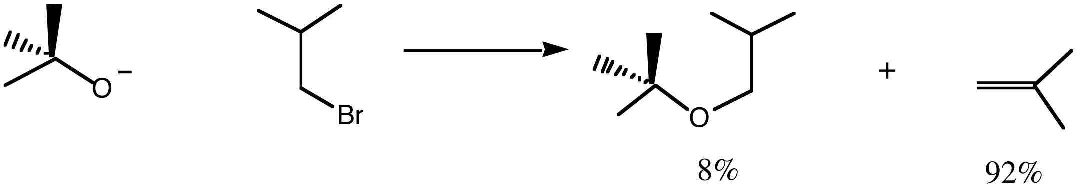
Example:

Factors Influencing Whether Substitution or Elimination Occur cont.

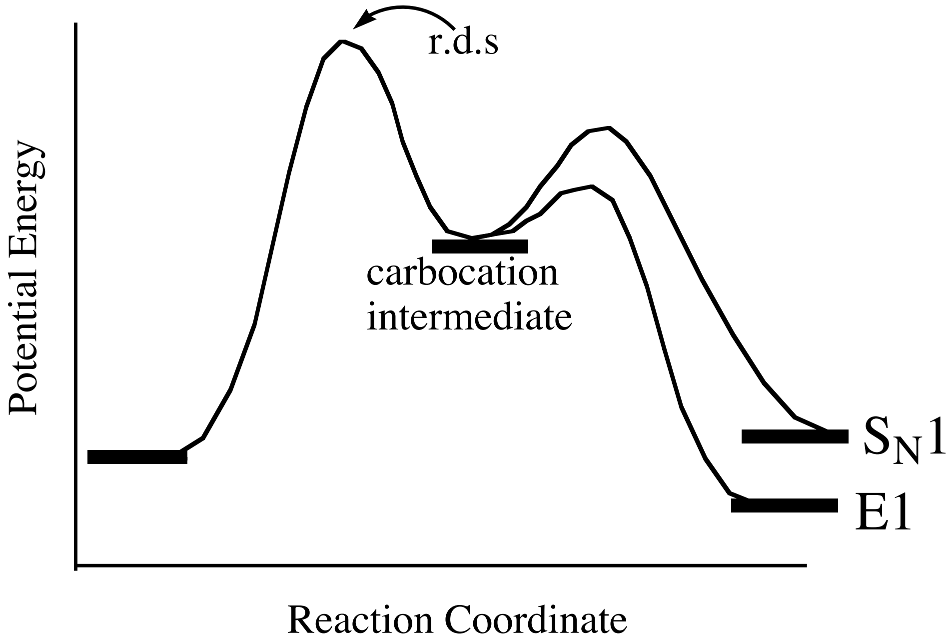
3. Nucleophiles that are hindered bases favor the E2 reaction.



Example:

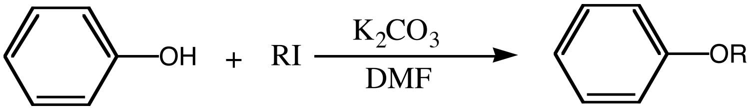


- Whether the product results from E1 vs. S_N1 is determined by the relative rates of deprotonation vs. nucleophilic attack on carbocation intermediate as shown below.


r.d.s
carbocation
intermediate
Potential Energy
S_N1
E1
Reaction Coordinate

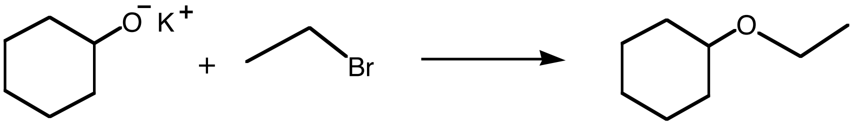
Williamson Ether Synthesis

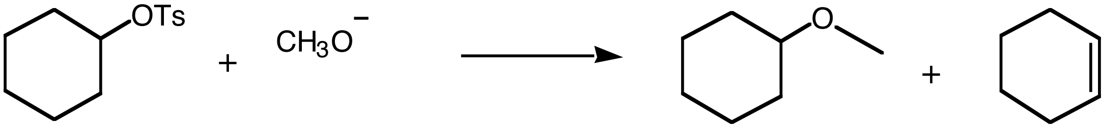
Williamson Ether Synthesis: unhindered primary alkyl halides or tosylates react with simple (unhindered) alkoxides to form ethers by an S_N2 mechanism. The alkyl halide or tosylate must have no β-branches or elimination will be likely.



$$R'{-}OH \qquad RI \xrightarrow[DMF]{K_2CO_3} R'{-}O{-}R$$

Examples:





5% 85%

- With secondary halides there will be a competition between addition and elimination.
- In general, if one group is somewhat bulky for ether synthesis it is better for this to be the alkoxide than the alkyl halide. The above examples illustrate this point.

Some sulfides can be prepared in an analogous manner:

$$R'{-}SH + R{-}OTs \xrightarrow{\text{base}} R'{-}S{-}R$$

Guide to Displacement Reactions

Reactivity

Type of carbon	SN1 (carbocation intermediate)	E1 (carbocation intermediate)	SN2 (concerted)	E2 (concerted)
1 °			• good LG • good Nu: • polar aprotic solvent	• strong, bulky bases
2 °	• good LG • poor Nu: • polar protic solvent •possibility for rearrangements •tends to racemizes optically active starting materials	• competes with SN1 when base is present • good leaving group needed	• good LG • good Nu: (weaker base than HO^- and high polarizable) • polar aprotic solvent •stereochemistry determined by starting configuration •backside attack	• competes with SN2 • favored by bulky bases stronger than HO^- •favor by hindered carbons with leaving groups •stereochemistry determined by starting configuration
3 °	• good LG • any Nu: • polar protic solvent	• competes with SN1 when base is present		• unlikely to occur

Nucleophilicity

Classification	Nucleophiles	Rel. React.
Excellent	I^-, HS^-, RS^- RSe^-	$>10^5$
Good	Br^-, HO^-, RO^-, CN^-, N_3^-	10^4
Fair	NH_3, Cl^-, F^-, RCO_2^-	10^3
Weak	H_2O, ROH	1
Very Weak	RCO_2H	10^{-2}

Leaving Groups

Classification	Leaving Groups
Excellent	$ROSO_2^-$, H_2O, ROH, N_2
Good	I^-, Br^-, Cl^-, NR_3, RCO_2^-
Poor	HO^-, RO^-, F^-, CN^-, NH_2