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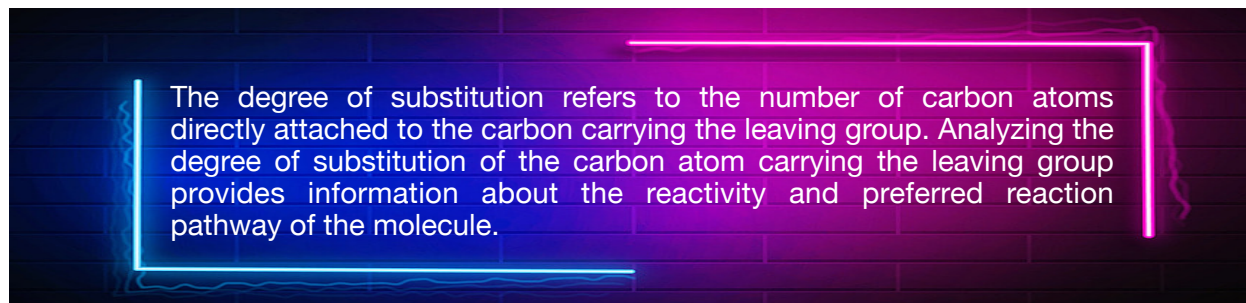
## Lesson 5: Substitution and elimination reactions

Analyzing the presence of functional groups is a crucial initial step in evaluating any reaction. Substitution and elimination reactions primarily involve alkyl halides or alcohols as starting materials. These reactions encompass various types, including:

- SN1 unimolecular nucleophilic substitution
- SN2 bimolecular nucleophilic substitution
- E1 unimolecular beta elimination
- E2 bimolecular beta elimination.

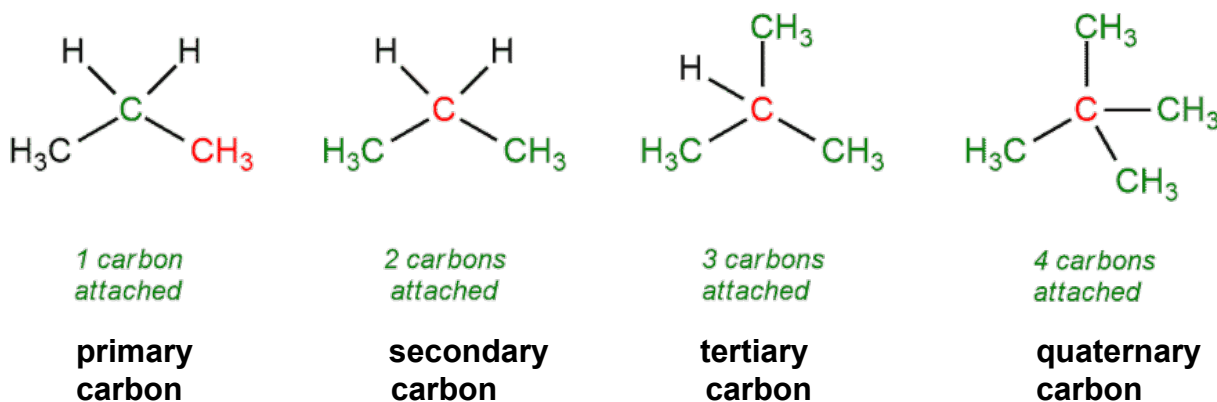
To differentiate between substitution and elimination reactions, it is essential to assess the degree of substitution of the carbon atom carrying the leaving group. The leaving group, such as Br, comprises an atom or group of atoms that separates from the molecule, along with the shared electron pair in the bond.

THINK! Why is it necessary to analyze the degree of substitution of the carbon atom carrying the leaving group when distinguishing between substitution and elimination reactions?



Go to <https://www.khanacademy.org/science/organic-chemistry>  
 Watch the videos on Substitution and elimination reactions

There are **five types of carbons** based on the degree of substitution. The name depends on the number of **carbons** directly attached to the **red** carbon.



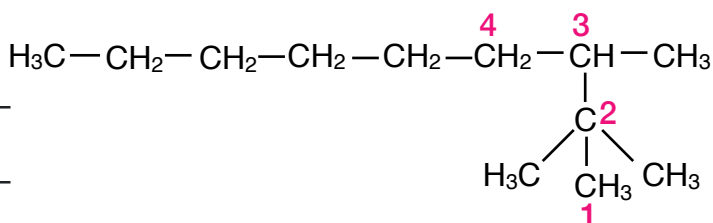
1. Build the molecule shown to the right. Identify each numbered carbon atom as primary, secondary, tertiary, or quaternary.

C1 \_\_\_\_\_

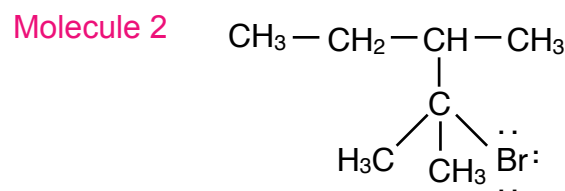
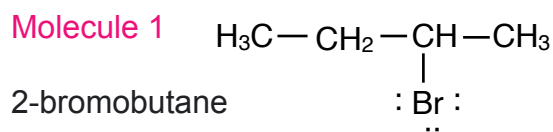
C2 \_\_\_\_\_

C3 \_\_\_\_\_

C4 \_\_\_\_\_



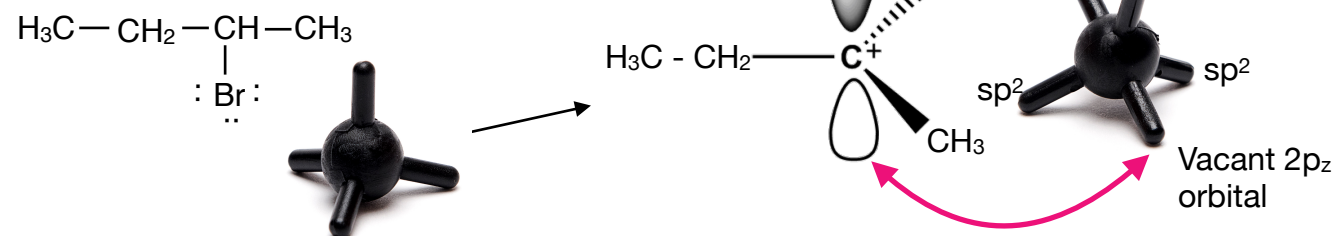
2. Divide the molecule above into two smaller molecules and attach a leaving group (Br) to each molecule. Identify the carbon atom with the leaving group as primary, secondary, tertiary or quaternary.



Both substitution reactions and elimination reactions occur with an alkyl halide or alcohol. Both SN1 and E1 reactions start the same, with the dissociation of a leaving group, forming a stable carbocation. A carbocation is an intermediate that has a carbon atom with a positive charge and three bonds (instead of four) in a trigonal planar arrangement. The carbocation can be attacked by a nucleophile for a SN1 reaction. A nucleophile is a molecule or an ion, that donates a pair of electrons to form a new covalent bond with another atom or molecule. Nucleophiles can replace a leaving group on a carbon atom, leading to the formation of a new bond. On the other hand, a base can pull a beta-hydrogen from the carbocation for an E1 reaction. A beta-hydrogen refers to a hydrogen atom that is directly bonded to the carbon atom adjacent to a functional group or a leaving group in a molecule.

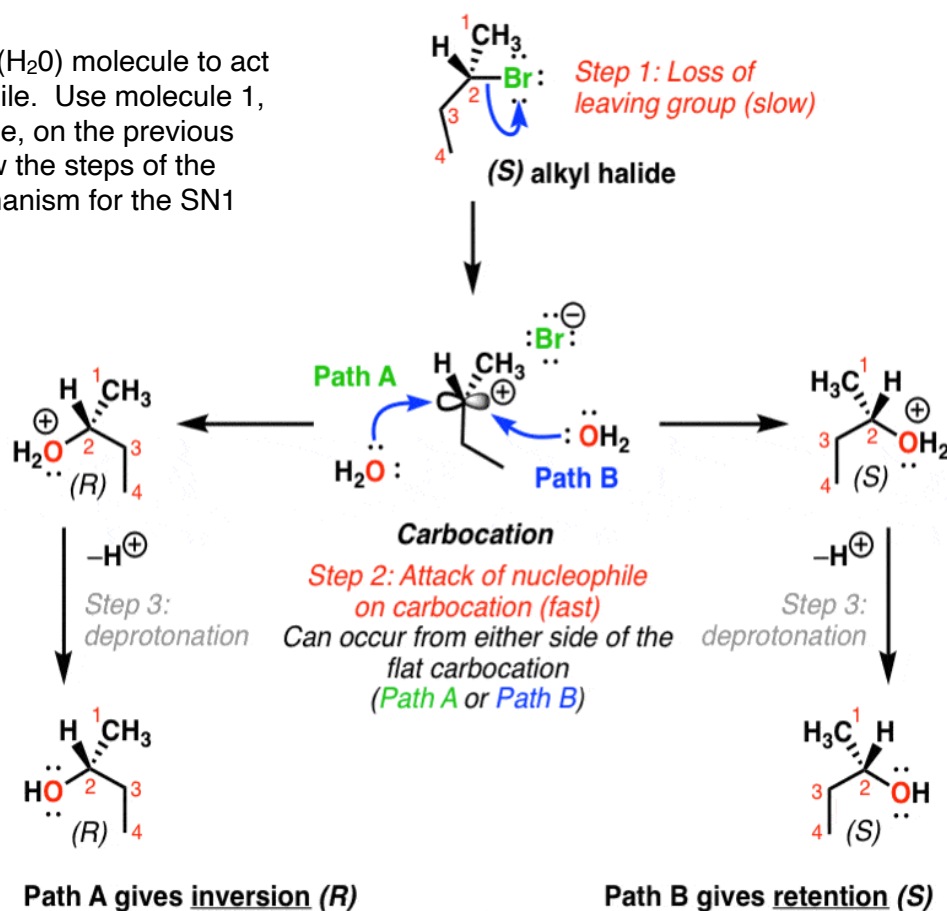
### Carbocation formation

The carbon atom bonded to Br has four sp<sup>3</sup> hybrid orbitals. When Br leaves, the carbocation forms with one vacant unhybridized p orbital and three sp<sup>2</sup> hybrid orbitals.



## SN1 Mechanism

3. Build a water ( $\text{H}_2\text{O}$ ) molecule to act as a nucleophile. Use molecule 1, 2-bromobutane, on the previous page, to follow the steps of the reaction mechanism for the SN1 reaction.



(Original source: MasterOrganicChemistry.com)

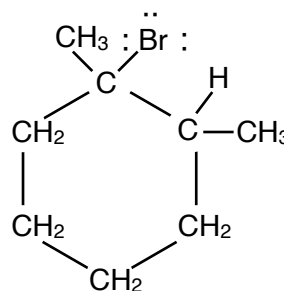
## Clues for SN1 reaction

- There is a mixture of products where the stereochemistry is the same as the starting material (retention) or opposite (inversion).
- The rate of the reaction is only dependent on the concentration of the substrate.
- Since tertiary carbocations are the most stable, tertiary substrates are faster than secondary, which are in turn faster than primary.

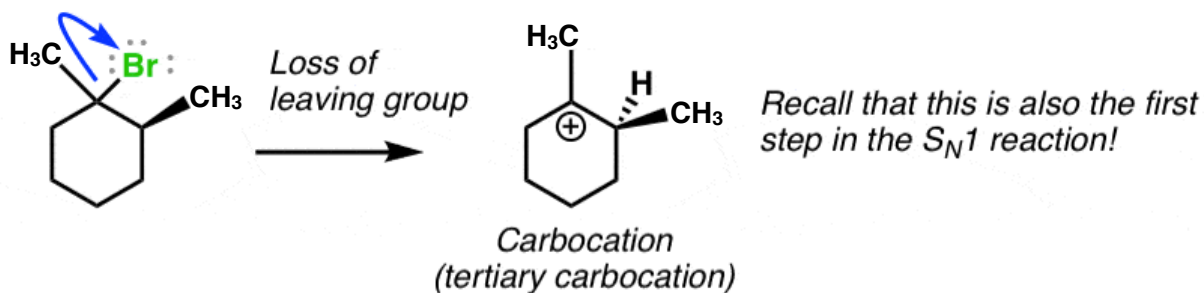
Disassemble the molecules.

## E1 Mechanism

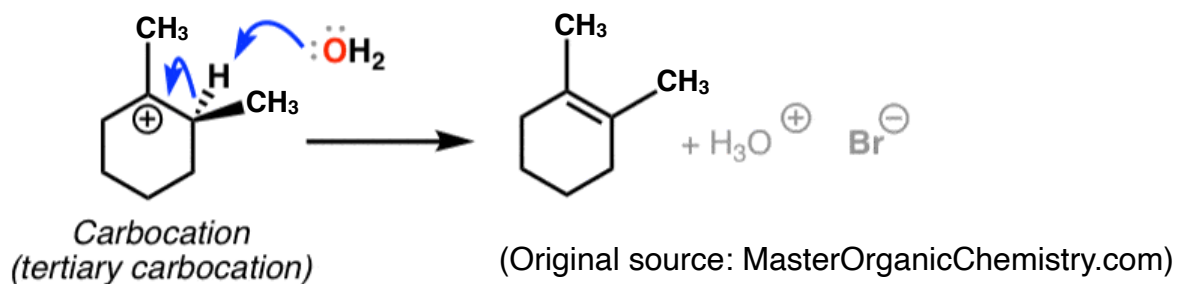
4. Build the molecule shown to the right and a water molecule to act as a base.
5. Use the molecules to follow the steps of the reaction mechanism for the E1 reaction.



First, the leaving group leaves to form a carbocation:



Second, a proton is removed by base to give the alkene:



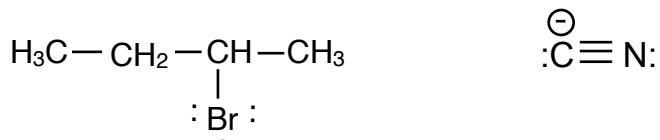
### Clues for E1 reaction

- The rate of the reaction is dependent on the concentration of substrate.
- The rate proceeds in the order tertiary (fastest) > secondary >> primary (slowest)
- The reaction is proposed to occur in two steps: first, the leaving group leaves, forming a carbocation. Second, base removes a proton, forming the alkene.
- The loss of the leaving group is also the first step in the S<sub>N</sub>1 reaction. S<sub>N</sub>1 products may be observed amongst the products.

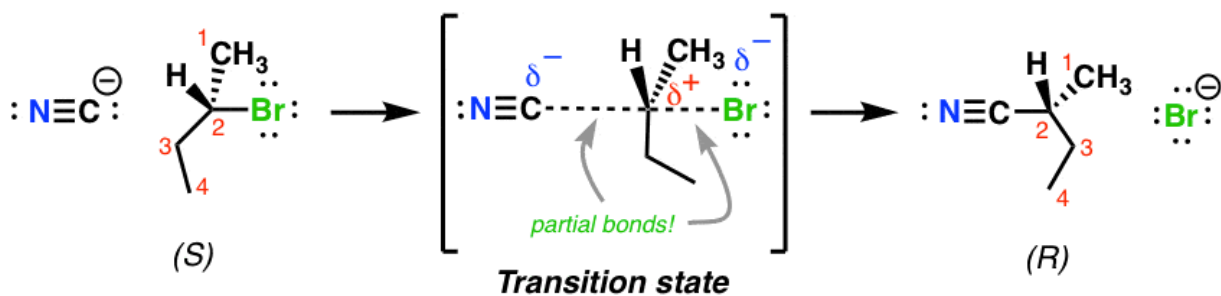
Disassemble the molecules.

### S<sub>N</sub>2 Mechanism

6. Build the molecule below and a nucleophile, the cyanide ion.



7. Use the substrate molecule and the nucleophile to simulate the S<sub>N</sub>2 reaction mechanism. The nucleophile attacks the substrate from the backside in a single step, resulting in inversion in configuration. This change of the molecule from one enantiomeric form to another is called the Walden inversion. It is the reversal of a chiral center of the molecule during the S<sub>N</sub>2 reaction.



(Original source: MasterOrganicChemistry.com)

### Clues for SN2 reaction

- The rate of the reaction is dependent on both the concentration of the nucleophile and that of the substrate. In other words, it's a second-order reaction.
- The reaction rate of the SN2 reaction is fastest for small alkyl halides (methyl > primary > secondary >> tertiary). The reaction is slowed by steric hindrance (bulky groups slow down the backside attack).

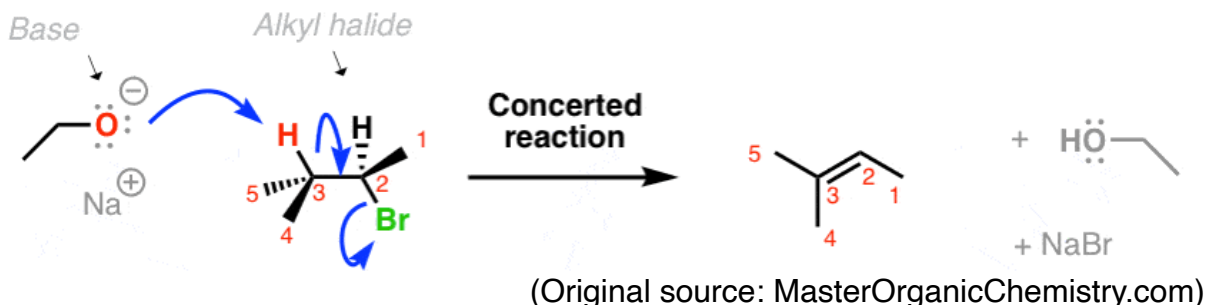
### E2 Mechanism

Both SN2 and E2 reactions are bimolecular reactions. Both reactions are single-step reactions. The key difference between SN2 and E2 reactions is that SN2 reactions are nucleophilic substitution reactions whereas E2 reactions are elimination reactions.

8. Build the substrate molecule and the base below.



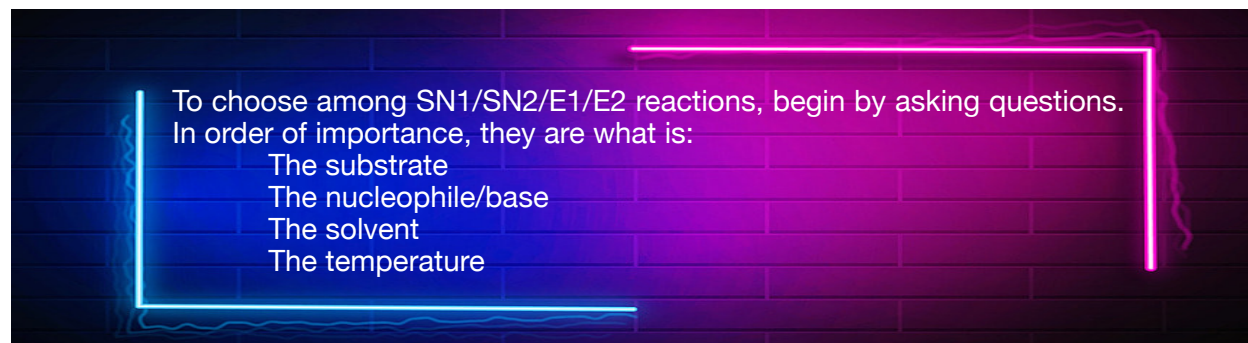
9. Use the substrate molecule and the base to simulate the E2 reaction mechanism. A concerted reaction takes place in a single step.



### Clues for E2 reaction

- The rate depends on the concentration of both the substrate and the base.
- The stereochemistry of the C-H bond and the leaving group is "anti", that is the H and Br are oriented at 180° to each other.

THINK! What are the key considerations in choosing among SN1, SN2, E1, and E2 reactions?



### The Substrate

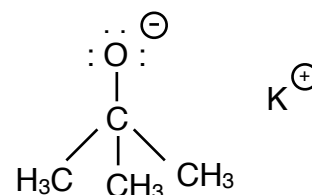
Look at the molecule and find the carbon with the best leaving group, usually Cl, I, or Br. Determine whether the carbon is methyl, primary, secondary, or tertiary. Methyl carbons always proceed through SN2. For primary carbons, rule out SN1 and E1 reactions because primary carbocations are unstable. Tertiary carbons increase steric hinderance (crowding at the reaction site), so rule out SN2 reactions.

Allylic halides are the halides in which the halogen atom is bonded to sp<sup>3</sup>-hybridized carbon atom next to carbon-carbon double bond (C=C). Primary allylic halides show high reactivity towards Sn1/E1 reactions due to stabilization of carbocation intermediates as a result of resonance.

### The Nucleophile/base

A nucleophile is a reactant that donates a pair of electrons to form a new covalent bond. A compound like NaOH is both a strong base and a good nucleophile. When it forms a bond to carbon (as in a substitution reaction), it acts as a nucleophile. When it forms a bond to hydrogen (as in an elimination reaction), it acts as a base. Charged bases/nucleophiles are compounds containing Na, K, or Li and tend to perform SN2/E2 reactions. A bulky base such as tBuOK, shown below, will tend to give elimination products, E2.

Reactions where neutral bases/nucleophiles, such as H<sub>2</sub>O or CH<sub>3</sub>OH, are involved tend to go through carbocations and be SN1/E1 reactions.



### The Solvent

There are three types of solvents for these reactions.

- 1) Polar protic (water, alcohol, and ammonia)

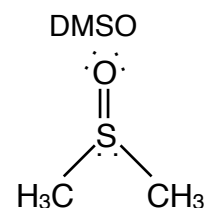
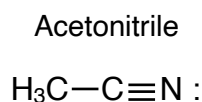
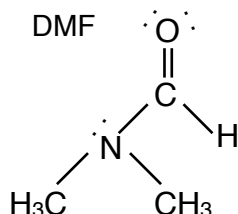
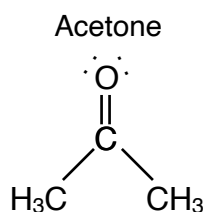
Polar protic solvents are capable of hydrogen bonding because there is a highly electronegative atom such as O or N directly bonded to hydrogen.

E2 reactions are favored over SN2 reactions.

- 2) Polar aprotic (acetone, DMF, acetonitrile, DMSO)

SN2 reactions are favored over E2 reactions.

## Polar aprotic solvents



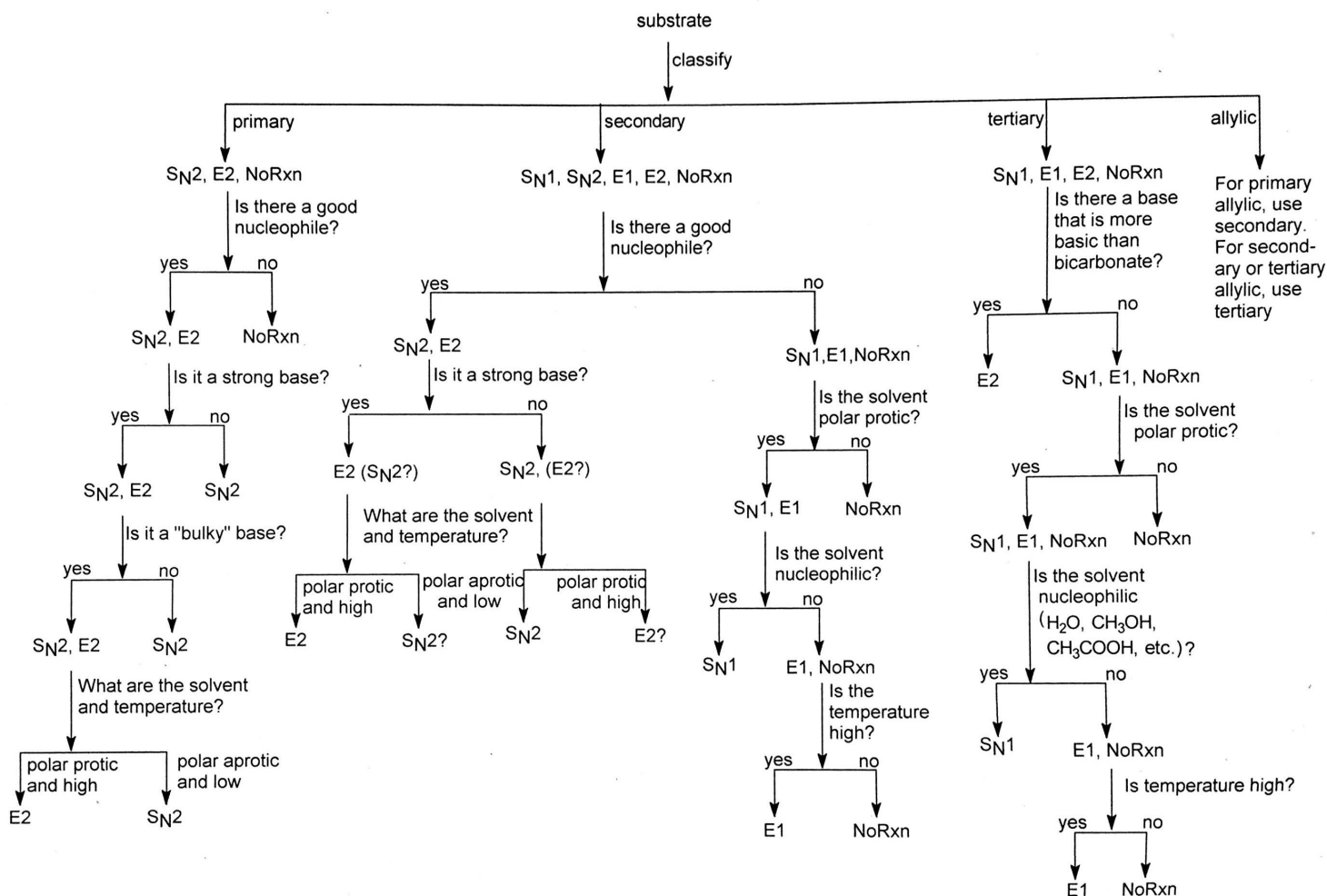
### 3) Nonpolar (hydrocarbons, chloroform, diethyl ether)

Polar protic and polar aprotic solvents are more likely found in substitution and elimination reactions.

## The Temperature

In practice a mixture of both SN1 and E1 products are found when the reaction proceeds through the formation of a carbocation. Heat is added when the elimination reaction is desired.

Use the flow-chart below and/or the chart on the following page to determine the favored type of substitution or elimination reaction.



(Original source: University of New Mexico Center for Academic Support)

	SN1	E1	SN2	E2
Reaction mechanism	2 step with carbocation	2 step with carbocation	Concerted	Concerted
Leaving group ability	Must be great	Must be great	Can be mediocre	Can be mediocre
Primary substrate	No reaction	No reaction	Highly favored	Favored only with a strong base
Secondary substrate	Only with a non-basic nucleophile or if the carbocation is resonance stabilized	Only if the carbocation is resonance stabilized	Need strong non-basic nucleophile, otherwise will compete with E2	Favored with strong base
Tertiary substrate	Favored with non-basic nucleophile	Competes with SN1	No reaction	Can occur but ONLY with a strong base
Strength of nucleophile	Can be mediocre, must be non-basic	Can be mediocre, must be basic	Strong, non-basic, non-bulky	Strong AND basic
Solvent	Polar protic	Polar protic	Polar aprotic	Polar aprotic
Stereochemistry	Gives (almost) totally racemic (see #2 below)	Bulky groups will prefer opposite sides	Walden inversion	"H" must be antiperiplanar (see #3 below)

#### What are the leaving groups?

Great: I<sup>-</sup>, Br<sup>-</sup>, Cl<sup>-</sup>, OTs<sup>-</sup>, OCF<sub>3</sub><sup>-</sup>, OMs<sup>-</sup>, and H<sub>2</sub>O (not OH<sup>-</sup>)

Mediocre: F<sup>-</sup>, CH<sub>3</sub>COO<sup>-</sup>, NH<sub>2</sub><sup>-</sup> (not NH<sub>2</sub><sup>-</sup>)

Bad: OH<sup>-</sup>, OCH<sub>3</sub><sup>-</sup>, NH<sub>2</sub><sup>-</sup>

#### What are the solvents?

Polar Protic: Acetic acid, H<sub>2</sub>O, ROH, NH<sub>3</sub>.

Polar Aprotic: DMF, nitromethane, acetone, acetonitrile, DMSO, ethyl acetate.

Non-polar: alkanes, cycloalkanes, toluene, benzene, ether.

#### What are the nucleophiles?

VERY GOOD Nu: I<sup>-</sup>, HS<sup>-</sup>, RS<sup>-</sup>

Good Nu: Br<sup>-</sup>, HO<sup>-</sup>, RO<sup>-</sup>, CN<sup>-</sup>, N<sub>3</sub><sup>-</sup>

Fair Nu: NH<sub>3</sub>, Cl<sup>-</sup>, F<sup>-</sup>, RCO<sub>2</sub><sup>-</sup>

Weak Nu: H<sub>2</sub>O, ROH

VERY Weak Nu: RCO<sub>2</sub>H

#### What are the bases?

Very Strong: NH<sub>2</sub><sup>-</sup>, H<sup>-</sup>, HC≡C<sup>-</sup>

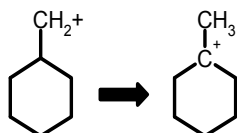
Strong: RO<sup>-</sup>, HO<sup>-</sup>,

Mediocre: RNH<sub>2</sub>, Na<sub>2</sub>CO<sub>3</sub>

Weak: NH<sub>3</sub>, CN<sup>-</sup>, RCOO<sup>-</sup>, Cl<sup>-</sup>, Br<sup>-</sup>, I<sup>-</sup>, NaHCO<sub>3</sub>

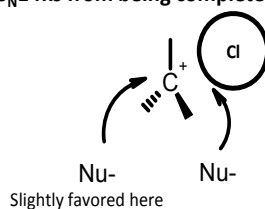
#### And don't forget....

1) Carbocations WILL rearrange if they can



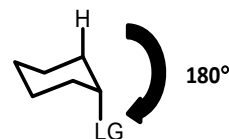
Will rearrange to a more stable cation.

2) Solvent-Separate Ion Pairs (SSIP) Keep S<sub>N</sub>1 rxns from being completely racemic



The leaving groups partially blocks one face, keeping it from being totally racemic.

3) E2 need antiperiplanar H's, or no rxn.



Must be able to rotate the H into a 180° angle or no rxn. Can happen with rings sometimes.

**racemic**: composed of equal amounts of left- and right-handed enantiomers of a chiral molecule.

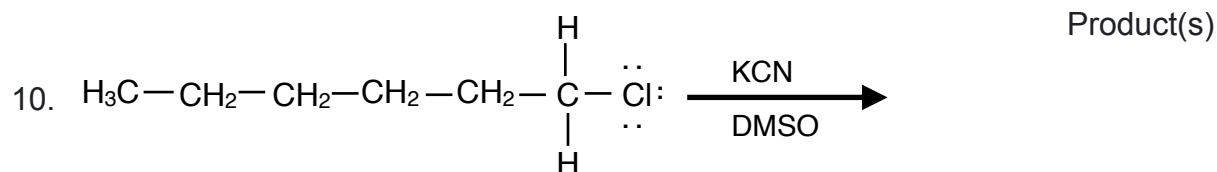
(Original source: aceorganicchem.com)



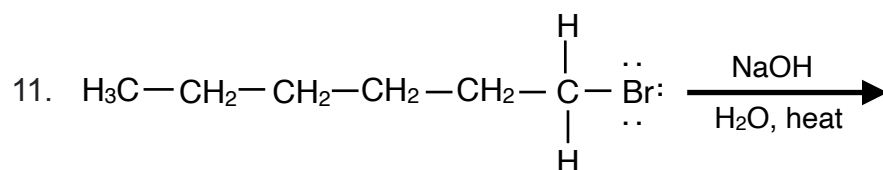
Determine and record the favored reaction mechanism. Simulate the favored reaction mechanism to determine the products for each reaction. Draw the product(s). Use the following symbols:

⋮ Wedge-hash = behind the plane of the page

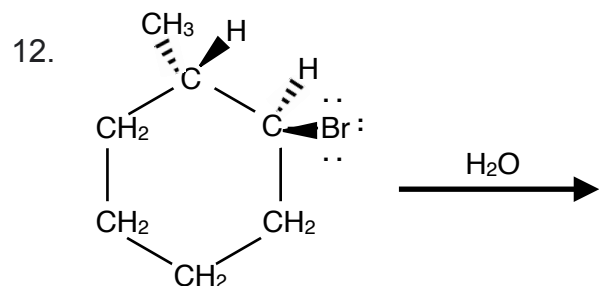
▼ Wedge-solid = in front of the plane of the page



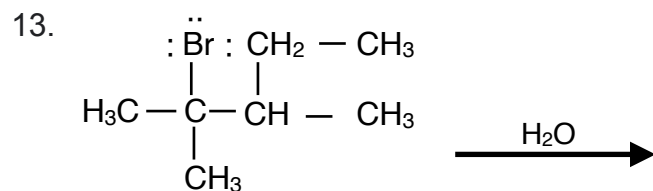
Reaction mechanism: \_\_\_\_\_



Reaction mechanism: \_\_\_\_\_

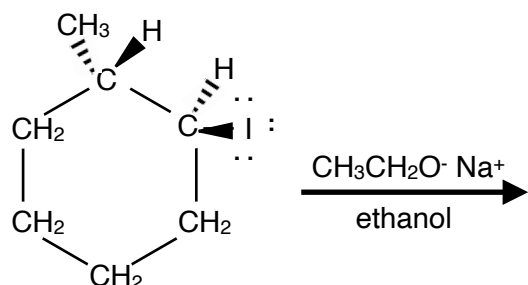


Reaction mechanism: \_\_\_\_\_



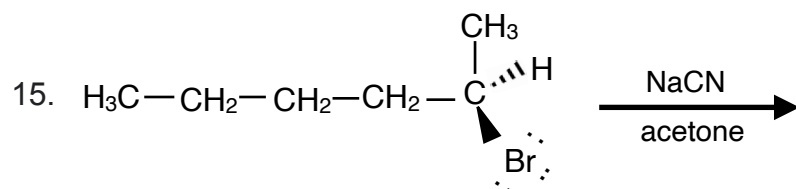
Reaction mechanism: \_\_\_\_\_

14.



Product(s)

Reaction mechanism: \_\_\_\_\_



Reaction mechanism: \_\_\_\_\_

Lesson five discussed the concepts and considerations related to substitution and elimination reactions. It highlighted the importance of analyzing the degree of substitution of the carbon atom carrying the leaving group in order to differentiate between the types of reactions. The lesson also provided a detailed explanation of various reaction mechanisms, including SN1, E1, SN2, and E2, along with their characteristic clues and features. Additionally, it explored the role of the substrate, nucleophile/base, solvent, and temperature in determining the favored reaction pathway. By addressing these factors and asking relevant questions, chemists can make informed decisions regarding the type of reaction to expect.