# Module 3  Alkanes and Alkyl Halides
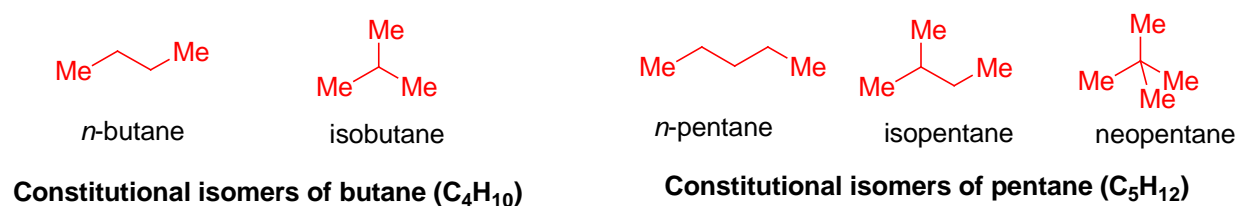
# Lecture 4 Alkanes

## 3.1 Introduction

Alkanes are hydrocarbons i.e. compounds made of carbon and hydrogen only. There are two kinds of alkanes-linear and cyclic alkanes or cycloalkanes. The linear alkanes have the general formula $C_nH_{2n+2}$, while cycloalkanes have the general formula $C_nH_{2n}$. Besides the simple monocyclic cycloalkanes, there are other forms such as bicyclic and tricyclic cycloalkanes with bridges containing any or no carbon atom. Another special class of cycloalkanes is the so called spiroalkanes, which have one carbon atom common between two rings.

Alkanes show both constitutional and conformational isomerism. The conformational isomerism manifests itself as early as the second member of the alkane family-ethane while constitutional isomerism first appears for butane. The issue of conformational isomerism is discussed separately under stereoisomerism.

Constitutional isomerism arises due to compounds having same molecular formula but different bond connectivity. Butane has two constitutional isomers: *n*-butane and *iso*butane. Similarly, pentane has 3 constitutional isomers: *n*-pentane, *iso*pentane and *neo*pentane (Scheme 1).



*n*-butane          isobutane          *n*-pentane          isopentane          neopentane

**Constitutional isomers of butane (C₄H₁₀)**     **Constitutional isomers of pentane (C₅H₁₂)**

Scheme 1

Carbon atoms in alkanes are sometimes labeled as primary (1°), secondary (2°) and tertiary (3°) carbon. This classification is based on the number of carbon atoms attached to the carbon atom. If a carbon atom is attached to one carbon atom, then it is called a primary carbon. Similarly, a carbon atom which is attached to two and three other carbon atoms is called secondary and tertiary carbon, respectively.
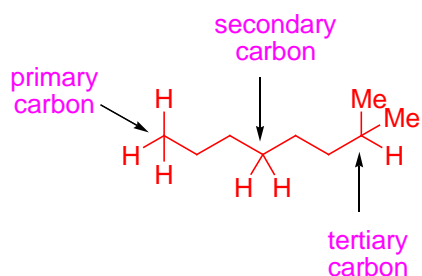


## 3.2 Nomenclature

Alkanes are usually referred by their trivial names. However, the IUPAC lays down certain rules for the nomenclature of alkanes. These rules are:

**Rule 1.** The name of an alkane consists of two parts- a prefix and a root. The prefix will denote the number of carbons present in the chain. Some prefixes for common alkanes are given below along with the number of carbons they represent (Table 1).The root is always *ane*. The moiety generated by removing a hydrogen from an alkane is called an alkyl group. Its name is given based on the name of parent hydrocarbon from which it is derived.
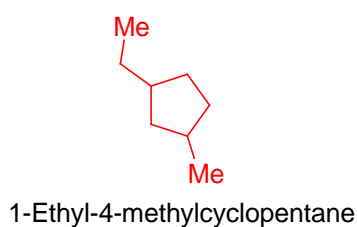
**Table 1**

| Number of Carbons | IUPAC Prefix | Name of Hydrocarbon | Name of Moiety Generated by Removing a Hydrogen |
|:---:|:---:|:---:|:---:|
| 1 | Meth | Methane ($CH_4$) | Methyl($CH_3$) |
| 2 | Eth | Ethane ($C_2H_6$) | Ethyl( $C_2H_5$) |
| 3 | Prop | Propane ( $C_3H_8$) | Propyl($C_3H_7$) |
| 4 | But | Butane ($C_4H_{10}$) | Butyl($C_4H_9$) |
| 5 | Pent | Pentane ($C_5H_{12}$) | Pentyl( $C_5H_9$) |

**Rule 2.** In case of cycloalkanes, the word cyclo should be prefixed with the name of alkane. Thus, a cycloalkane containing three carbon atoms is called cyclopropane.

Cyclopropane    Cyclohexane    Cycloheptane
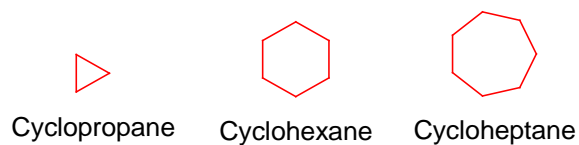
For substituted cyclohexanes, the name of the substituents is added as prefixes to the name of parent hydrocarbon.

1-Ethyl-4-methylcyclopentane

**Rule 3.** In case of branched alkanes, the longest carbon chain gives the name of the parent alkane. The substituents are to be prefixed using suitable locants. If there are multiple same substitutents, then the prefixes *di-, tri, tetra-* etc are added before the substituent name. Thus, the name of **1** is 2,3,7,8-tetramethylnonane.



**1**
— longest carbon chain
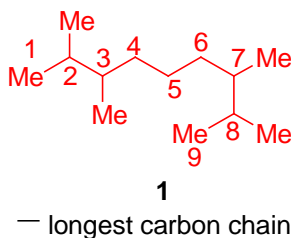
If there is more than one type of substituents, then they are usually arranged in an alphabetical order. Thus, in compound **2**, ethyl group is mentioned before the methyl groups.
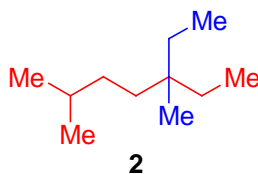


**2**
5-Ethyl-2,5-dimethylheptane

If more than one substituent is attached to the parent hydrocarbon, the chain is numbered in that direction that will result in the lowest number in the name of the compound (Rule of lowest locants).
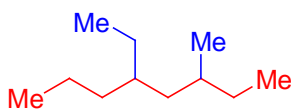


5-ethyl-3-methyloctane
*but not*
4-ethyl-6 methyloctane
as 3>4

**Rule 4.** In case of bridged cycloalkanes, the naming is to be done in the following manner-

I.  The number of rings is to be identified. The two rings in compounds **1** and 2 are depicted in different colours. The prefix bicyclo is to be added for these compounds.
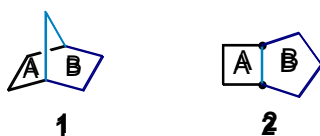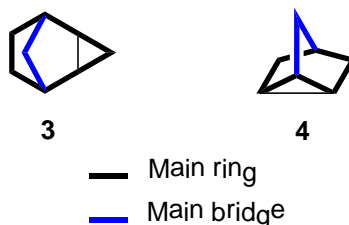


II. The number of carbon atoms in each ring is to be counted including the carbons in the bridge but excluding those at bridge heads. Thus, in compound **1**, there are 2 carbons in both rings **A** and **B** while only 1 carbon in the bridge. Similarly, in compound **2**, there are 2 carbons in the ring **A** while 3 carbon atoms in the ring **B** but no carbons in bridge. This number of carbon atoms in each ring is written in a square bracket separated by a dot after the prefix bicycle in a descending order.



Bicyclo[2.2.1]   Bicyclo[3.2.0]
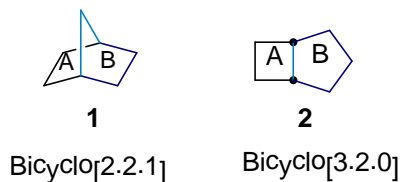
III. The suffix consists of the name of alkane as described for linear alkanes. The number of carbons (for determining the prefix of alkane's name) is determined by the formula: $x + y + z + 2$ where x and y are the number of carbon atoms in each of the rings and z is the number of carbons in the bridge. Thus, the name for compound **1** ($x + y + z + 2 = 2+2+1+2 = 7$) is bicyclo[2.2.1]heptane while that for compound **2** ($x + y + z + 2 = 3+2+0+2 = 7$) is bicyclo[3.2.0]heptane.



Bicyclo[2.2.1]heptane   Bicyclo[3.2.0]heptane
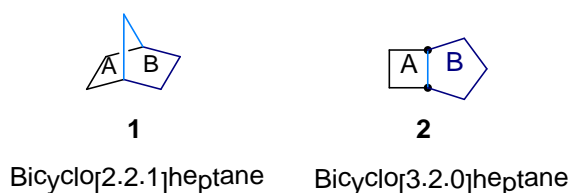
IV.   If there is more than one bridge, as in case of polycyclic compounds, a main ring and a main bridge is to be selected. The main ring should contain as many carbon atoms as possible from the main skeleton.  This count should begin from one of the bridge heads. If there is more than one bridge, then a main bridge is selected to include as many atoms as possible which are not contained in the main ring.



**3**                    **4**

▬ Main ring
▬ Main bridge

A prefix indicating the number of rings is to be prefixed. Thus, **3** and **4** both have 3 rings (tricyclo). Numbers for indicating lengths of carbon chains in each ring are to be placed in square brackets as in case of bicyclic compounds. In this case the secondary bridges are to be neglected while counting the atoms in the main ring. If however, there are secondary bridges, there should be additional superscript locants (the rule of lowest locants is valid) are to be written. The $x + y + z + 2$ rule may be also applied here to find the parent name of the alkane.



**3**                    **4**

Tricyclo[3.2.1.0$^{2,4}$]octane          Tricyclo[2.2.1.0$^{2,6}$]heptane
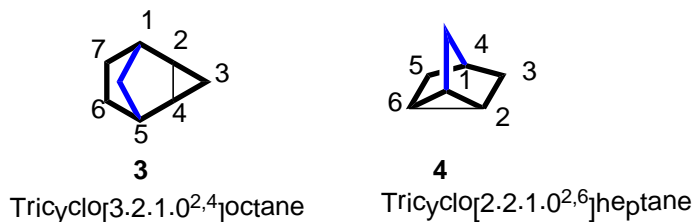
## 3.3 Physical Properties

The lower members of alkanes are gases. As the molecular weight increases, they become liquids while still higher members are solids. Thus, the physical state changes from gas to liquid to solid as the molecular weight increases. Branching of alkanes also leads to lower boiling points. Thus, among the isomers of n-pentane, neopentane has the lowest boiling point.  A similar effect is noticed in case of alkyl halides.

   Alkanes are non-polar compounds and as such they are insoluble in water. In fact, solid alkanes behave as water repellents. Thus, the water proofing property of wax is an example of this property.

## *3.4 Preparation of Alkanes*

The principal source of alkanes is naturally occurring petroleum and gas. Natural gas consists of mainly methane whereas petroleum consists of a complex mixture of various hydrocarbons which are then fractionally distilled to obtain either a mixture of hydrocarbons corresponding to boiling range or a pure hydrocarbon. Some of important constituents obtained by fractional distillation of petroleum are listed below (Table 2).

**Table 2**

| Names of Fraction | Carbon Atoms Present | Boiling Range (°C) | Use |
|---|---|---|---|
| Fuel gas, LPG | 1-4 | <25 | Used as fuel for domestic purposes |
| Petrol | 5-7 | 25-75 | Fuel for light automobiles |
| Naphtha | 6-10 | 75-190 | Feedstock for cracking |
| Kerosene | 10-16 | 190-250 | Domestic fuel, Air turbine fuel |
| Diesel | 14-20 | 250-350 | Fuel for heavy automobiles |
| Residue (Fuel oil, lubricating oil, waxes) | 20-70 | >350 | Used as lubricating agents for machinery |
| Asphalt | Over 70 | Non volatile | Used on roads |

The high boiling or non-volatile higher fractions obtained by fractional distillation of petroleum can be further converted into useful lower hydrocarbons by cracking. The process involves treatment of these non-volatile components under high pressure and temperature to generate the smaller hydrocarbons (thermal cracking). In hydrocracking, the reaction is carried out in presence of hydrogen and catalyst. This process requires a much lower temperature (250-450 °C) as compared to thermal cracking.  Similarly, catalytic cracking (a process to improve the quality of petrol) involves treatment of high boiling petroleum fractions with a finely divided silica–alumina catalyst.

Some other methods for preparation of alkanes are discussed below. These methods are mostly used only in the laboratory as most of the industrial supply is obtained from naturally occurring petroleum.

1. **Halogenation of alkenes.** Alkenes can be hydrogenated by hydrogen gas in the presence of a finely divided metal catalyst. The most commonly used metals include Pt, Pd or Ni.

2. **Reaction of alkyl halides with organometallic reagents.**  This method involves the treatment of an alkyl halide with another organometallic reagent usually an organocopper reagent (Corey-House method). For good yields, the alkyl halide should be a primary halide but there is no constraint on the alkyl group in the organocopper reagent (Scheme 2).
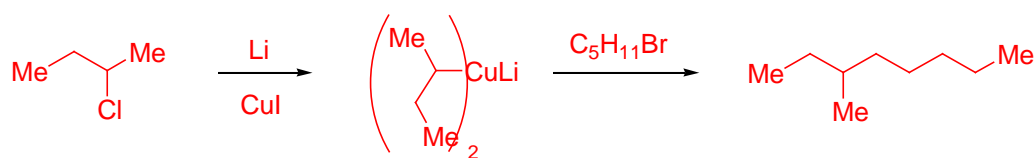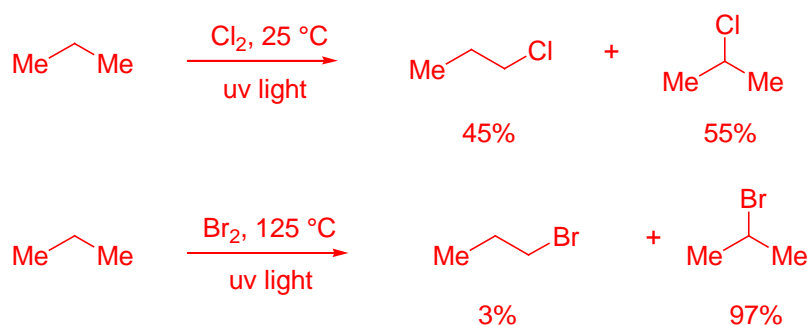


**Scheme 2**

3. **Reduction of alkyl halides.** The reduction of alkyl halides can be carried out in the presence of a metal and acid (Scheme 3).
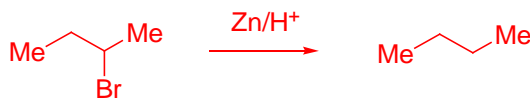


**Scheme 3**

## 3.5 Reactions of Alkanes

The halogenation of alkanes to generate alkyl halides is an important reaction. However, it is seldom of any preparative value. This is because alkanes usually give a mixture of isomeric alkyl halides when they are treated with a halogen. Usually, chlorine is more reactive towards the alkane than bromine. Among the alkanes, the reactivity decrease on going from tertiary to secondary to primary alkanes. Thus, when propane is chlorinated in the presence of chlorine gas under photochemical conditions, both 1-chloropropane and 2-chloropropane are formed. An analogous result is observed for bromination of propane (Scheme 4). The selectivity observed in case of bromination is due to the lower reactivity of the bromine atoms compared to the chlorine atoms.



**Scheme 4**

The mechanism for the halogenation of alkanes follows the pathway of radical initiated reaction and thus it consists of the following steps:
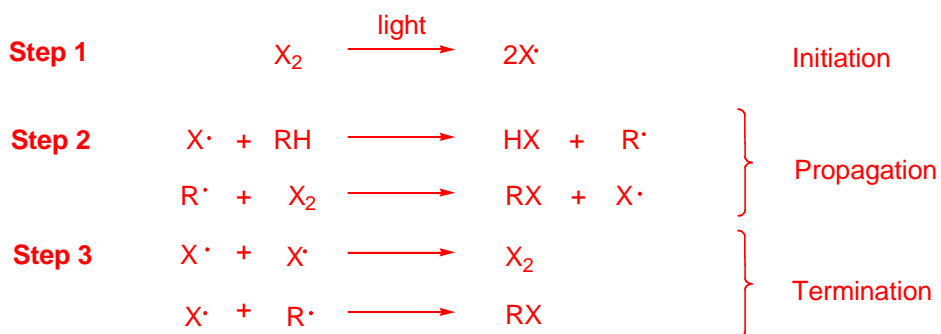


The abstraction of the proton is the rate limiting step in this reaction.

The combustion of alkanes generates carbon dioxide and water on complete oxidation. The energy liberated (known as heat of combustion) for this complete oxidation is an important factor determining the efficiency of a hydrocarbon as fuel. The reaction is exothermic in nature but requires a very high temperature for its initiation. Heats of combustion of some hydrocarbons are given in Table 3.

**Table 3.**

| Alkane | Heat of Combustion ($\Delta H_{comb}$) (kJmol$^{-1}$) |
| --- | --- |
| Methane | -802 |
| Ethane | -1560 |
| Butane | -2874 |
| Isooctane | -5466 |
| Hexadecane (Cetane) | -10699 |

Most automobiles use petrol or diesel as a fuel. The efficiency of an internal combustion engine depends upon the compression ratio of the fuel-air mixture in the engine. However, increasing this ratio leads to "knocking"( knocking, in an internal-combustion engine, sharp sounds caused by premature combustion of part of the compressed air-fuel mixture in the cylinder) where the power of the engine is greatly reduced. The problem of knocking can be met with in two different ways: (a) proper selection of hydrocarbons in fuel and (b) addition of additives. The second approach employed the addition of tetraethyl lead (TEL) as an additive but recent concern about environmental pollution has seen the decline of its use. The first approach is still used. It employs addition of specific hydrocarbons having high octane number (octane number is measure of the ability of a fuel to resist knocking when ignited in a mixture with air in the cylinder of an internal-combustion engine).

# Module 3  Alkanes and Alkyl Halides

## Lecture 5 Alkyl Halides

### 3.6 Introduction

Alkyl halides are compounds containing one or more halogen atoms. They resemble the alkanes in structure but contain one or more halogen atoms instead of hydrogen atoms. The linear alkyl halides having one halogen atom have formula $C_nH_{2n+1}X$ where X is a halogen atom. Similarly, the cyclohaloalkanes have general formula $C_nH_{2n-1}X$.

### 3.7 Nomenclature

Alkyl halides can also be named by following the rules of IUPAC nomenclature. The generic name for alkyl halides is haloalkanes according to IUPAC. Thus, the name of haloalkane constitutes of two parts-the prefix which contain the number and identity of the halogen atom attached and the suffix which states from what alkane is the name derived. Thus, for an alkyl halide of formula $C_2H_5Cl$, IUPAC name is chloroethane. If more than one halogen atom is attached, then the prefixes *di, tri, tetra, penta* etc are added to denote the number of halogen atoms. The rule of lowest locants is also valid here.
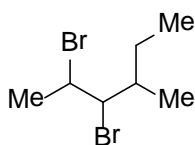


2,3-Dibromo-4-methylhexane

   If the alkyl halide contains more than one type of halogen, the halogen names are prefixed in an alphabetical order. Thus, the IUPAC name for compound **6** should be 2-bromo-3-chlorobutane.
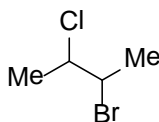


**6**
2-Bromo-3-chlorobutane

## *3.8 Preparation of Alkyl Halides*

The most common method for preparation of alkyl halides is by treatment of alcohols with hydrogen halides. The order of reactivity hydrogen halides parallels their acid strength i.e. $HI > HBr > HCl >> HF$. Thus, this method cannot be used for making alkyl fluorides. Among primary, secondary and tertiary alcohols, it is found that tertiary alcohols are most reactive (Schme 1). Instead of using the hydrogen halides, phosphorus halides may also be used.
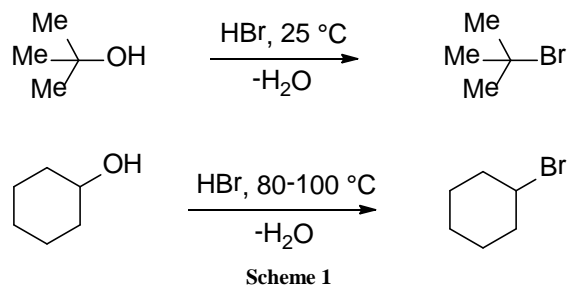


**Scheme 1**

Another method that can be used for preparation of only certain alkyl halides is the direct halogenation of alkanes using molecular chlorine or bromine under photochemical conditions (Scheme 2).
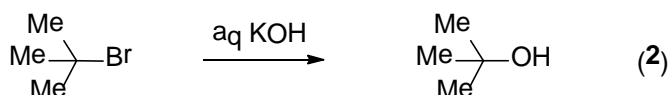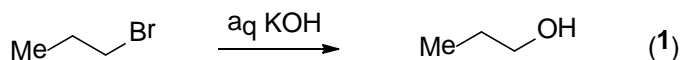


**Scheme 2**
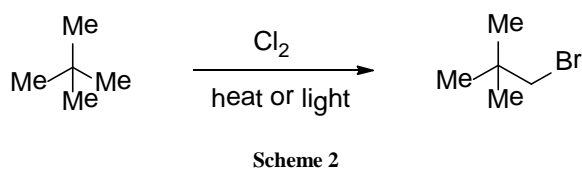
## 3.9 Reactions of Alkyl halides

The most important reaction for alkyl halides is the nucleophillic displacement (substitution) reaction. When an alkyl halide is treated with a nucleophile, it displaces the halide ion. The general reaction may be represented as:

$$RX \ + \ Nu: \longrightarrow \ RNu \ + \ X^-$$
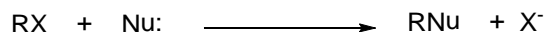
Some examples of this reaction follow:



Though the above two reactions looks identical in nature, but they differ widely in the mechanistic pathway. If the first reaction is carried out by increasing the amount of either nucleophile or substrate, then there is an increase in the rate of the reaction. However, in the second case, there is hardly any effect in the rate of the reaction on increasing the concentration of nucleophile but the rate increases on increasing the concentration of substrate. So, for reaction (**1**), the rate law may be written as:

$$Rate = k[RBr][OH^-]$$

This indicates that both the substrate and the nucleophile are involved in rate determining step. In other words, it is a second order reaction. Traditionally, this type of reactions are called $S_N^2$ (Substitution Nuclephilic Bimolecular) reactions. This type of reaction is therefore concerted in nature and, therefore, must involve only one transition state. Quantum mechanical calculations predict that an approach by the nucleophile along the lines of centers of the carbon and bromine is of least energy requirement. This may be represented as (Scheme 3):
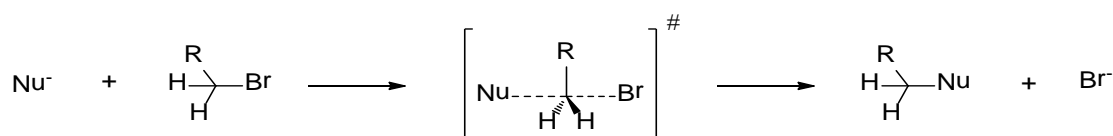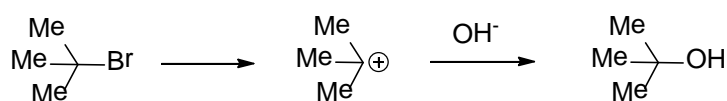


**Scheme 3**

In reaction (**2**) the rate law has to be written as:

$$\text{Rate} = k[\text{RBr}]$$

Since the rate of reaction is independent of the concentration of nucleophile, therefore, the reaction must have more than one step involving at least one intermediate. This type of reaction is depicted as $S_N^1$ (Substitution Nucleophilic Unimolecular) reaction. It has been observed that these reactions involve the actual formation of a carbocation in the slow rate limiting step. The carbocation so formed reacts with nucleophile in a fast step to give the product. The mechanism may thus be depicted as (Scheme 4):



**Scheme 4**

Since $S_N^1$ reactions involve the formation of a carbocation, so factors stabilizing the carbocation would make the reaction more facile. One such factor is the effect of solvent. Polar solvents having high dielectric constants will stabilize the carbocation and, hence, increase the rate of the reaction. Thus, the rate of solvolysis of tertiary halide, $(CH_3)_3Br$ is found to be 30000 times faster in 50% aqueous ethanol than in pure ethanol. This is due to the fact that the charge is developed and concentrated in the transition state (T.S.) as compared to the starting material. The energy requirement for this process can be decreased by increasing the dielectric constant of the solvent. The process is also facilitated by solvation by the solvent molecules.
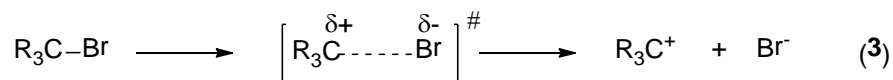


The effect of solvent in $S_N^2$ reaction is much less pronounced than in case of $S_N^1$ reactions as the reaction proceed through a transition state having no new charge separation but rather the existing charge is being dispersed. Thus, the solvation of the T.S. may only slightly be unfavoured as compared to the nucleophile. This leads to only a marginal decrease in the rate of $S_N^2$ reactions on going from non-polar to polar solvent.
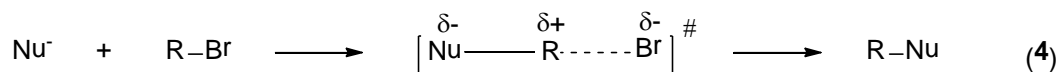
However, there is a pronounced effect on the rate of $S_N^2$ reactions on going from polar protic to polar aprotic solvent. This is because in a polar protic solvent like methanol, the nucleophile is solvated efficiently as compared to a polar aprotic solvent like *N,N*-dimehylformamide. This solvation reduces the nucleophililicity of the nucleophile.

Another factor that decides whether a particular nucleophilic substitution will follow $S_N^1$ or $S_N^2$ pathway is the structure of the substrate. If the structure of the substrate that the carbocation generated from it has some degree of stabilization owing to some factors, then it is quite possible for the substrate to follow $S_N^1$ pathway. In the hydrolysis of series of the given alkyl halides, the following trends are observed:



      (1)           (2)           (3)           (4)
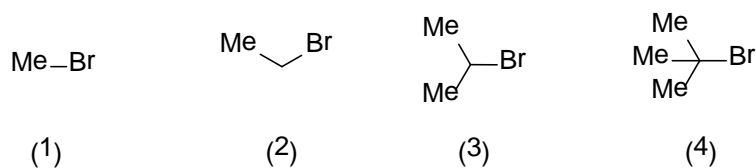
1. The alkyl halides (1) and (4) readily undergo hydrolysis.
2. The $S_N^1$ rates increase from left to right in the series and the $S_N^2$ rates decrease in the same direction.
3. The alkyl halides (2) and (3) are following a mixed $S_N^2$ and $S_N^1$ rate laws. The rate of $S_N^2$ reaction is increased by increasing the concentration of the nucleophile.

Methyl bromide (1) undergoes reaction by $S_N^2$ pathway. Now as the substitution is increased at the α-carbon it becomes increasingly difficult for the nucleophile to approach the carbon center to attack. Thus, there is a drop in the $S_N^2$ reaction rate progressively along the series. In (4), however, there is a very significant crowding the T.S. for $S_N^2$ pathway having 5 bulky groups around a carbon center as compared to 4 in the starting material. Such steric crowding increases the energy of T.S. and, thus, it is less likely to be formed and hence slows the $S_N^2$ reaction extremely.

Now in a $S_N^1$ attack, there is considerable charge separation on going from substrate to the T.S. to the carbocation intermediate. Thus, factors which stabilize the carbocation will evidently increase the rate of the reaction. In the series depicted above, the stabilization of the carbocation on account of electron donating inductive effect and hyperconjugation

progressively increases from left to right across the series. In steric terms, the formation of a planar carbocation with 3 substituents on the central carbon as compared to alkyl halide having 4 substituents on the same carbon is less demanding sterically (as compared to the T.S. for $S_N^2$). The steric factor gets more emphasis from the fact that on going from left to right across the series, the relative relief in steric strain on going from alkyl halide to planar carbocation is more ($CH_3$ is more bulky than H). These factors is turn stabilized the carbocation intermediate and consequently the $S_N^1$ pathway is preferred on going from left to right in the series (Scheme 5).
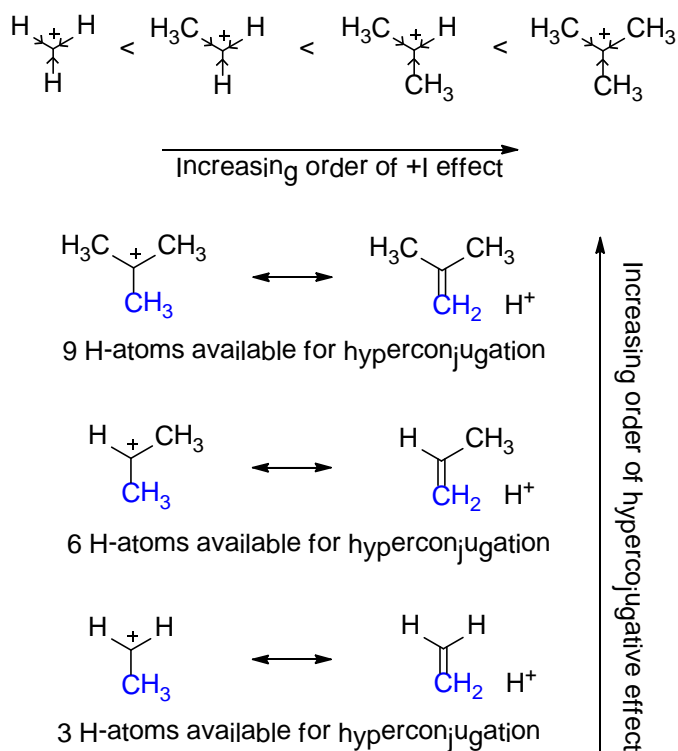


**Scheme 5**

The effect of substitution at α-carbon of an alkyl halide is much more pronounced than substitution at the β-carbon. However, steric factors do play role in determining the reactivity of alkyl halides substituted at the β-carbon. Thus, in the following series of alkyl halides, for the solvolysis by ethanol, the given order of relative rates of reaction was observed. It must be noted that these are all $S_N^2$ rates.



| | (5) | (6) | (7) | (8) |
|---|---|---|---|---|
| Rate: | 1 | 0.28 | 0.03 | 0.0000042 |
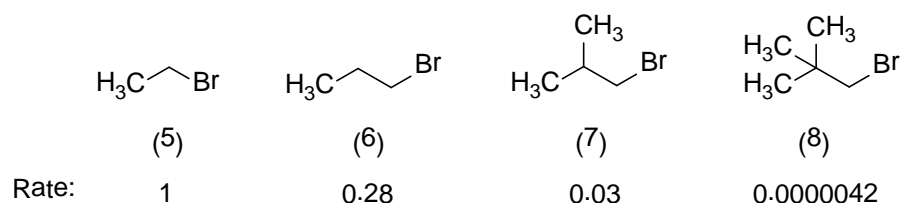
This occurs because of increase in relative crowding in T.S. of the $S_N^2$ reaction, which makes it increasingly difficult for the nucleophile to approach the α-carbon carrying the bromide ion for attack "from the back". The steric effect is not very pronounced till there is a possibility of adoption of a conformation (by rotation along the $C_\alpha$-$C_\beta$ bond). The large difference on going from (7) to (8) is that there is no scope for the $C_\alpha$-$C_\beta$ bond to adopt a favourable conformation in (8) as all conformations are equally crowded while in (6) and (7) there is at least one conformation where the nucleophile $C_2H_5O^-$ is hindered by only one hydrogen.



(7*)          (8*)
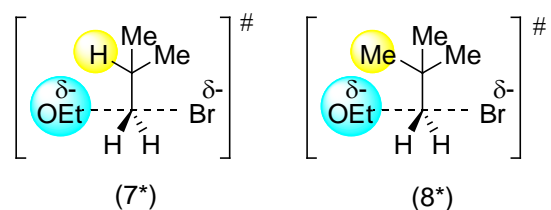
The structure of a compound also plays an important role in the rate of the reaction. Thus, alkyl halides bearing the halogen at bridge head carbons undergo hydrolysis extremely slowly. The more is the rigidity of the structure, the less is the rate of substitution. Thus, among the alkyl halides, 1-bromobicyclo[2.2.1]heptane (9) and 1-bromobicyclo[2.2.2]octane (10), for the solvolysis by ethanoate anion, the latter exhibits improved rate of reaction compared to the former, however, both the alkyl halides are extremely slow in undergoing solvolysis. These two compounds evidently undergo reaction by $S_N^1$ pathway as both the halides are 3° halides which rules out any possibility of attack from the back by nucleophile ($S_N^2$ pathway). But the possibility of forcing these

rigid structures to adopt a planar conformation required for the carbocation is also very demanding and has a very high energy requirement. This causes the carbocation to be formed only reluctantly at a very slow rate which explains the slow rate of the reaction. The improvement of rate for (10) as compared to (9) is due to less rigidity in the ring (2 carbons in bridge in (10) compared to one in (9))



(9)          (10)
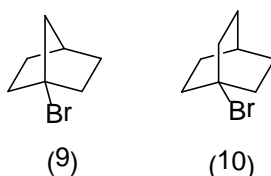
The presence of electron donating and electron withdrawing groups on the substrates also effect the rate of reaction. For an $S_N^1$ reaction, electron donating groups stabilize the carbocation and thus it increases the rate of reaction while electron withdrawing groups tend to reduce it. In $S_N^2$ reactions, however, no simplistic trend could be observed. This is because both the bond forming and bond breaking processes, which act in opposite directions, are important in an $S_N^2$ reaction in the same step.

The strength of a nucleophile can be made to dictate whether a reaction will proceed through $S_N^1$ or $S_N^2$ pathway. A stronger nucleophile will favour $S_N^2$ as compared to $S_N^1$ pathway. Thus changing the nucleophile from $CH_3COOH$ to $CH_3COO^-$ will probably shift the pathway towards $S_N^2$ provided all other factors favour this change.

Since the departure of the leaving group is involved in the rate determining step of both $S_N^2$ and $S_N^1$ pathways, the strength of the carbon- leaving group(C-L) bond, the polarizibility of this bond and the stability of leaving group ($L^-$) as well as its degree of solvation by the solvent are key factors for the rate of reactions. In the series of alkyl halides it has been observed that the rate falls on going from alkyl iodides to alkyl bromides to alkyl chlorides. Alkyl fluorides are the most unreactive. This is not only in accordance to the order of the strength and polarizibilty of the bond but also follows the order of the relative acid strengths of the conjugate acids of the leaving groups. The effect of the strength of conjugate acid is an important fact in the determination of the effectiveness of an "oxygen acid" such as acetate or triflate to act as a leaving group.
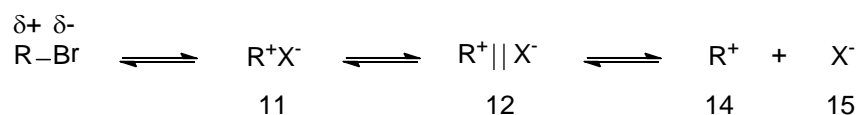
Since a $S_N^1$ pathway involves the formation of a carbocation, it may at times lead to rearrangement of the carbocation to more stable carbocation (1° to 2° or 2° to 3°) before being attacked by the nucleophile to give the product. Thus, when neopentyl bromide (1-bromo-2,2-dimethylpropane) is subjected to solvolysis in ethanol, it gives ethyl-*t*-pentyl ether (2-ethoxy-2-methylbutane) along with other rearrangement products (Scheme 6).



**Scheme 6**
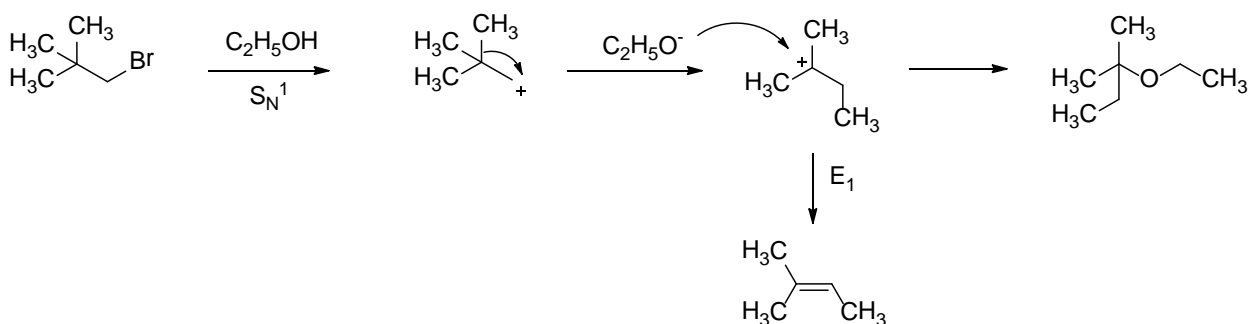
With regard to the stereochemical implications of aliphatic nucleophilic substitution, it must be noted that $S_N^2$ reactions proceed with an inversion of configuration at the attacking carbon, while a $S_N^1$ pathway understandably leads to racemization. The proof of complete inversion of configuration for $S_N^2$ reactions is obtained from an ingenious experiment where (+)-2-iodooctane was treated with isotopically labelled iodine (Scheme 7). If $S_N^2$ pathway leads to inversion of configuration, as postulated, then optical activity should fall to zero due to formation of a racemate. Thus, the observed rate of racemization will be double the rate of inversion. The reaction was monitored polarimetrically and it was found that the rate of inversion is same as the rate of the reaction.
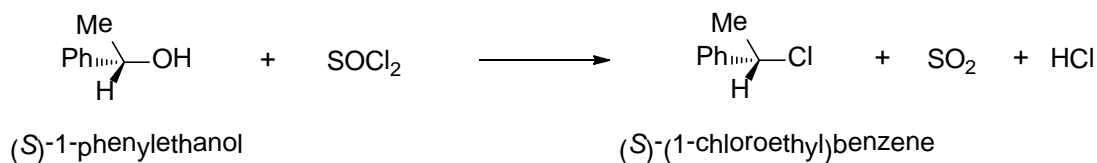


**Scheme 7**
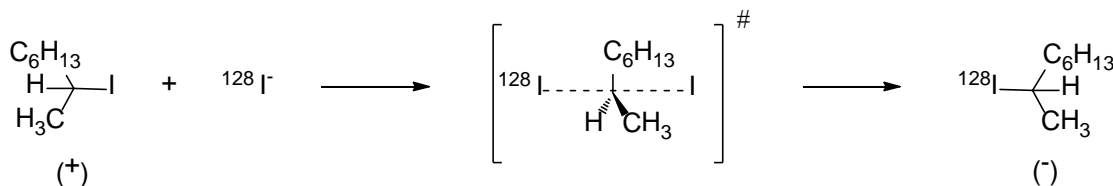
As for $S_N^1$ reaction, the formation of carbocation in the slow rate limiting step should lead to racemization of the product. This is because, once the carbocation is formed there is an equal probability of attack on both sides by the nucleophile thereby leading to a 1:1 mixture of both enantiomers. However, when (+)-(1-chloroethyl)benzene was subjected to solvolysis in 4:1 acetone water mixture, 98% racemization was observed while when water alone was used only 80% racemization was observed. This result can be explained by the effect of solvent in solvating the ions formed in this reaction. The rate limiting ionization of $S_N^1$ is assumed to proceed in the following manner:

$$\overset{\delta+ \ \ \delta-}{R-Br} \ \rightleftharpoons \ \underset{11}{R^+X^-} \ \rightleftharpoons \ \underset{12}{R^+||X^-} \ \rightleftharpoons \ \underset{14}{R^+} \ + \ \underset{15}{X^-}$$

Here, (11) is an intimate ion pair where the jointly solvated ion pair where the ions are in close association with each other with no solvent molecules between them, (12) is a solvent separated ion-pair while the latter are completely separated ion pair. Thus, the degree of racemization is dependent on the fact that at what stage does the nucleophile attacks the carbocation predominantly. If the attack takes place in (11) then it has to be from one direction only. However, if the nucleophile attacks in (12), then this would lead to racemization. Now, the more stable a carbocation is, it will reach the state represented by (12) and thus more will be racemization. However, more nucleophilic is the solvent more will be the attack in the state represented by (11) leading to inversion. This explains the results stated above.

A third kind of nucleophilic substitution pathway is also known. In some nucleophilic substitutions, the reactant proceed the reaction with retention of configuration. The pathway for these reactions is known as $S_N^i$ (Substitution Nucleophillic Internal). One reaction where this mechanism is found to operate is the chlorination of (*S*)-1-phenylethanol with thionyl chloride (Scheme 8).
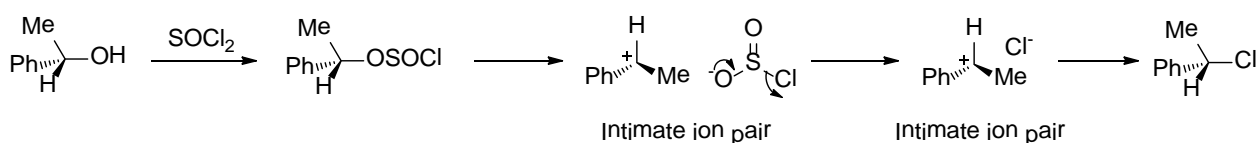


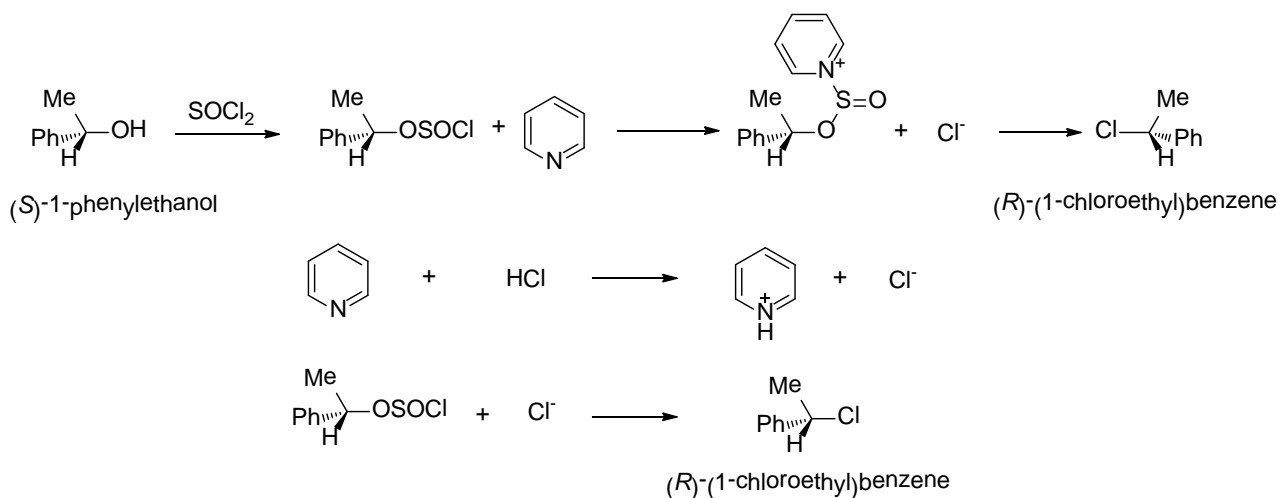Scheme 8

The rate law for this transformation is given by:

$$Rate = k[ROH][SOCl_2]$$

Now the mechanism of this reaction was determined by isolating the intermediate ROSOCl which then decomposes to give the product. Now in this reaction the formation of intermediate proceeds with retention of configuration as none of the bonds with the chiral center are broken. The decomposition of the intermediate takes place in an intimate ion pair (11) where the nucleophile can attack only from the same side from where the OSOCl moiety has departed leads to overall retention in configuration (Scheme 9).



**Scheme 9**

The evidence for this mechanism comes from the fact addition of pyridine to generate the naked $Cl^-$ anion leads the reaction to proceed by $S_N^2$ pathway leading to inversion. The role of pyridine is to combine with either the ROSOCl to form $ROSOpy^+$ or HCl generated as a byproduct of the original $S_N^i$ reaction to form pyridinium cation, thereby allowing the free chloride ion to attack from the back leading to inversion of configuration (Scheme 10).
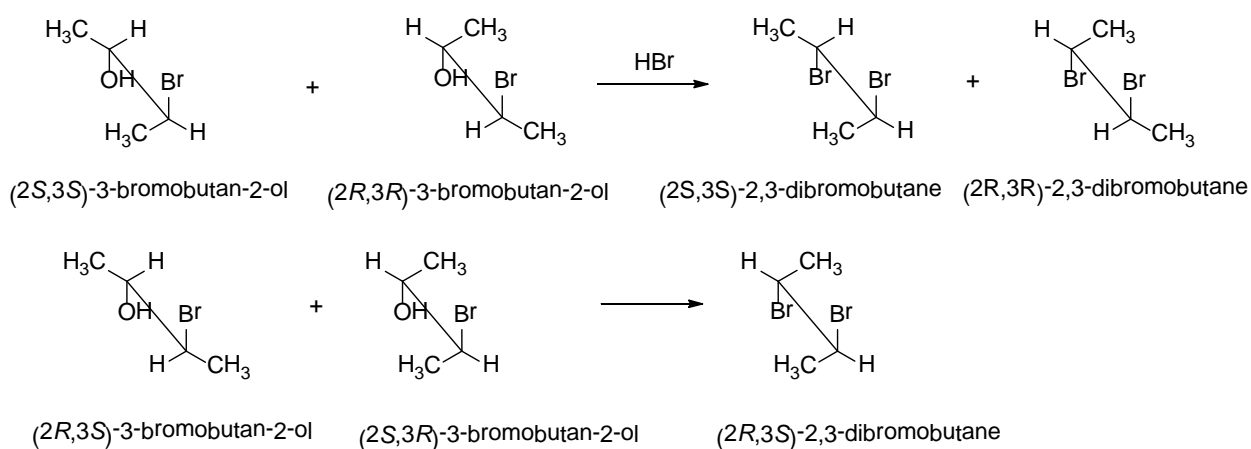


**Scheme 10**

# Module 3  Alkanes and Alkyl Halides
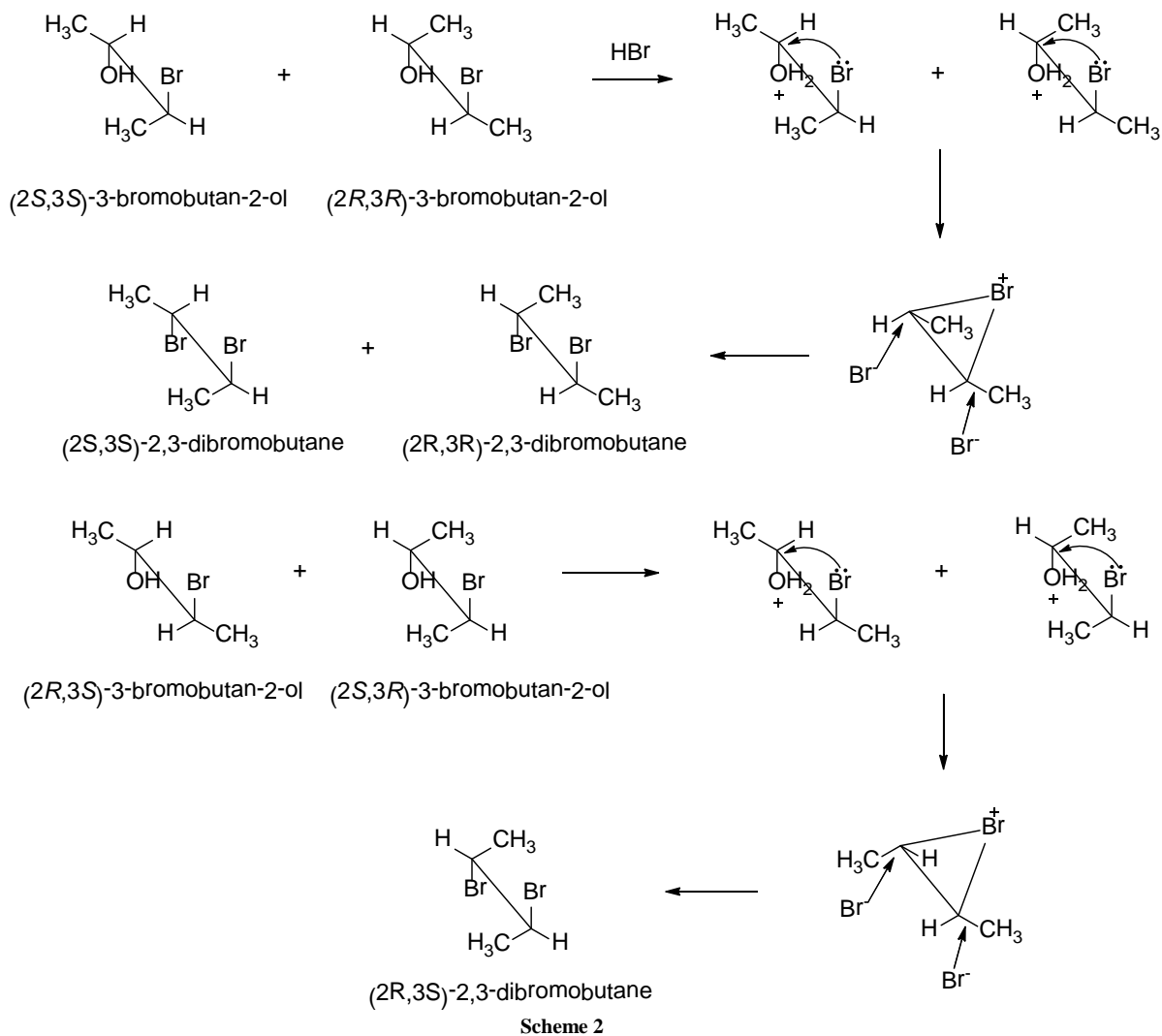
# Lecture 6 Alkyl Halides

## *3.9 Reactions of Alkyl halides*

An intriguing result is obtained when the result of treatment of a racemic mixture of (2*R*,3*R*)-3-bromobutan-2-ol and (2*S*,3*S*)-3-bromobutan-2-ol with hydrogen bromide is compared with a similar reaction of (2*R*,3*S*)-3-bromobutan-2-ol and (2*R*,3*S*)-3-bromobutan-2-ol with hydrogen bromide. In the former case,  a racemic mixture of (2*R*,3*R*)-2,3-dibromobutane  and (2*S*,3*S*)-2,3-dibromobutane is obtained while in the latter case (2*R*,3*S*)-2,3-dibromobutane(meso isomer) is obtained as the only product (Scheme 1). It is thus clear that retention of configuration has occurred in both cases. More importantly, even when one of the enantiomers (2*R*,3*R*)-3-bromobutan-2-ol or (2*S*,3*S*)-3-bromobutan-2-ol was treated with hydrogen bromide  both the (2*R*, 3*R*)- and (2*S*, 3*S*) isomers are obtained. This suggests that the reaction proceeds through a symmetrical intermediate. It is also reasonable to assume that the reaction follows a $S_N^1$ pathway.
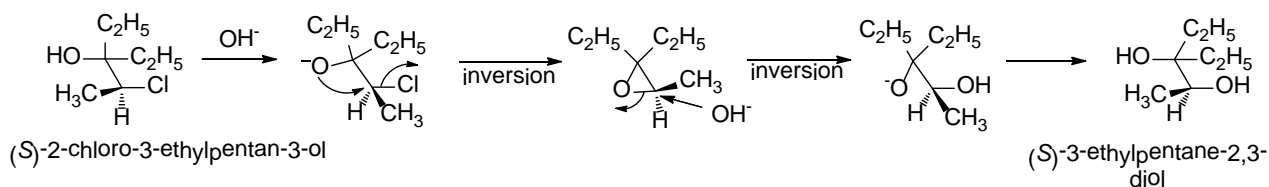


**Scheme 1**

This observation can be explained by the formation of a symmetrical bromonium ion intermediate formed by the internal attack of bromide. This is an example of neighbouring group participation (NGP) by the bromide ion (Scheme 2).

(2S,3S)-3-bromobutan-2-ol    (2R,3R)-3-bromobutan-2-ol

(2S,3S)-2,3-dibromobutane    (2R,3R)-2,3-dibromobutane

(2R,3S)-3-bromobutan-2-ol    (2S,3R)-3-bromobutan-2-ol

(2R,3S)-2,3-dibromobutane

**Scheme 2**

Another consequence of NGP is rearrangement in the product in unsymmetrical intermediates leading to the nucleophile to be attached at a different place than where the leaving group was actually attached. Similarly, the hydrolysis of (*S*)-2-chloro-3-

ethylpentan-3-ol proceeds with retention of configuration due to the anchimeric assistance provided by the internal nucleophilic OH group (Scheme 3).



**Scheme 3**

In some cases, the nucleophile may have more than one reactive center through which it may attack the substrate. Such nucleophiles are called ambident nucleophiles. Obviously the regioselectivity becomes a key noticeable fact in the operation of ambident nucleophiles. Cyanide ion ($CN^-$) provides an ideal example of this kind. In a reaction with an alkyl halide, it may attack through the carbon or through nitrogen leading to alkyl cyanides and alkyl isocyanides, respectively. The preference whether cyanide will attack seems to depend on the HSAB principle. In a $S_N^1$ reaction a carbocation (hard acid) with a "naked" charge is involved, so cyanide attacks through its hard centre nitrogen leading to the formation of alkyl isocyanide. If however, the reaction proceeds through $S_N^2$ then the attack is through the softer carbon centre leading to alkyl cyanides.
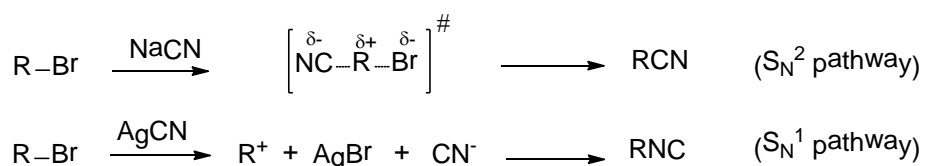


If the reaction of alkyl halide with sodium hydroxide is carried out in an alcoholic solution instead of aqueous medium, elimination occurs to give an alkene as a product. This is a new class of reactions known as *elimination reactions*. Since several nucleophiles are also potential bases, thus there is a continuous competition between aliphatic nucleophilic substitution and elimination reactions. The factor which decides in whose favour the scales will tilt seems to be a combination of solvent, strength of the nucleophile/base and structure of substrate.

The class of reactions known as elimination reactions are also an important reaction of alkyl halides. These reactions evidently lead to elimination of two moieties from an alkyl halide leading to formation of carbon-carbon multiple bonds. The most common type of

elimination involves 1,2-elimination where the groups are lost from adjacent carbon atoms. Three different pathways have been envisaged for 1,2-elimination reactions.
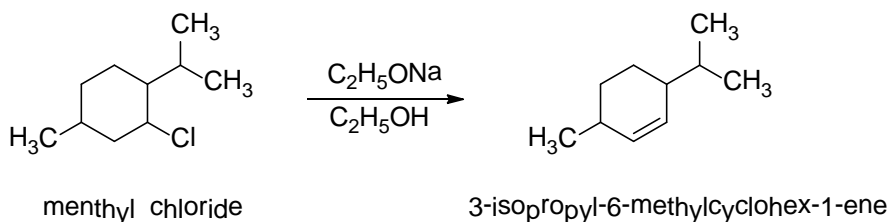
1. E2 (Elimination Bimolecular) pathway: Here both the leaving groups are detached from the alkyl halide at the same time with simultaneous formation of the new bond i.e. the H-C and C-Y (Y = leaving group) are broken simultaneously while the new C=C is formed. This pathway does not involve any intermediate but passes only through a 5 center transition state (T.S). It may be represented as:
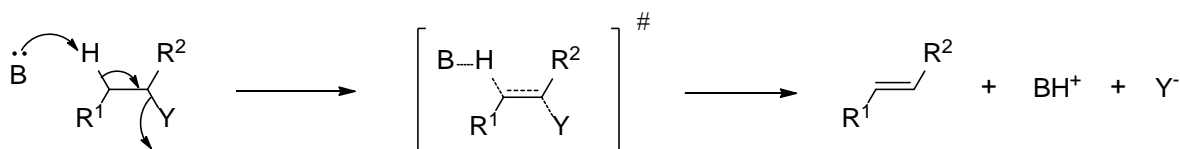


The rate law for this pathway both the bond forming and bond breaking may be represented as:
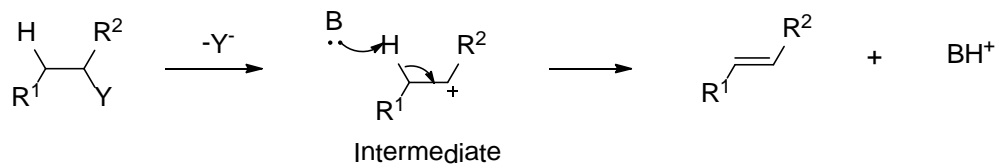
$$\text{Rate} = k[\mathbf{RY}][\mathbf{B:}]$$

**The formation of 3-isopropyl-6-methylcyclohex-1-ene from menthyl chloride follows E2 pathway:**



menthyl chloride                      3-isopropyl-6-methylcyclohex-1-ene

2. E1(Elimination Unimolecular) pathway: Here, the substrate undergoes elimination of the leaving group (Y) to form a carbocation which then undergoes elimination of a proton to give the alkene as the product. This pathway therefore

involves the formation of an intermediate from which the proton is abstracted by the base. This may be represented as:



In this case only the formation of the carbocation is involved in the slow rate limiting step and, thus, its rate law is represented as:

$$\text{Rate} = k[RY]$$

The solvolysis of 2-bromo-2-methylbutane by ethanol is an example of this pathway in operation:



2-bromo-2-methylbutane

2-methylbut-2-ene
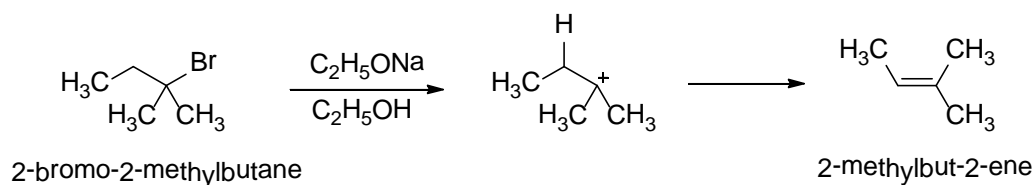
3. E1cB (Elimination Unimolecular Conjugate Base) pathway: Like E1, this pathway also involves two steps. In this pathway, the base abstracts a proton from the substrate to generate a carbanion which then undergoes elimination of the leaving group (Y) to give the corresponding alkene as product. This mechanism is relatively rare and operates only in substrates where the carbanion is stabilized by electron withdrawing groups. This may be represented as:
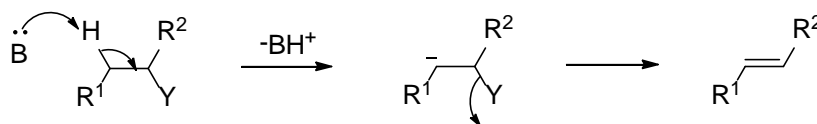


In this case, the elimination of the leaving group (Y) occurs in the slow rate limiting step and, thus, the rate law may be expressed as:

$$\text{Rate} = k[RY][B:]$$

The elimination of HF from 2,2-dichloro-1,1,1-trifluoroethane serves as an example for the operation of E1cB pathway.

2,2-dichloro-1,1,1-trifluoroethane                                1,1-dichloro-2,2-difluoroethene
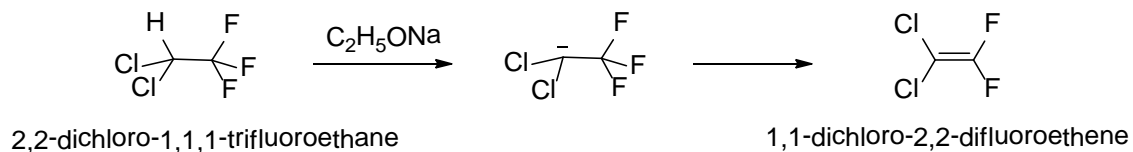
In relation to stereochemistry of the elimination reactions, E2 pathway is stereospecific in nature leading to elimination in an *anti*-periplanar conformation where the hydrogen abstracted by the base and the leaving group are *anti* to each other. This can be inferred from the fact that elimination of HBr from (1*R*,2*S*)-1,2-dibromo-1,2-diphenylethane gave exclusively (*E*)-2-bromostillbene while any of the optically active enantiomeric dibromides provided the (*Z*)-alkene as the only product (Scheme 4).
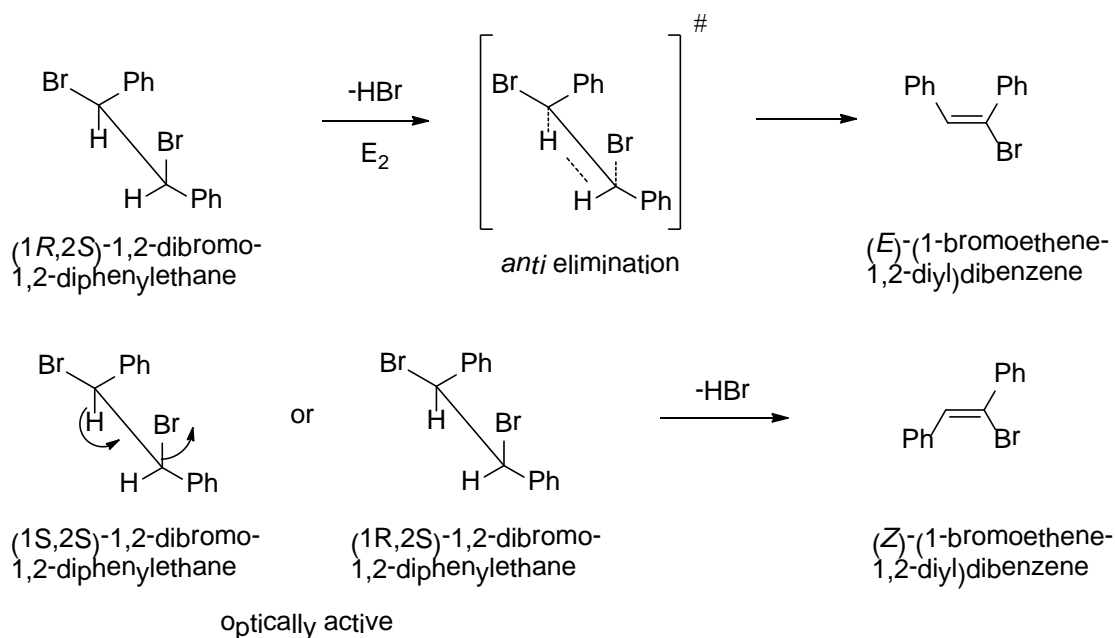


**Scheme 4**

The reason for this observation lies in the fact that the *anti*-periplanar (staggered) conformation is more stable than the *syn*-periplanar (eclipsed) conformation and thus it allows the elimination to take place in a state of low energy. Furthermore, in this conformation, the attacking base B:, and the departing group (Y⁻) are as far from each other as possible in the T.S.

As both the E1 and E1cB pathways involve planar carbocation and carbanion intermediates respectively, so there is no element of stereoselectivity involved in these pathways.

In a case of comparison of the products formed by E2 elimination of 2-bromobutane and *N,N,N*-trimethylbutan-2-aminium ion, it is found that the former yields but-2-ene as the major product while the latter yields but-1-ene as the major product. The prediction which alkene will be formed depends on the nature of the leaving group. There are two specific rules in this regard known as **Saytzeff** rule and **Hoffman** rule. Hoffman rule states that the alkene having least alkyl substituents on the double bond will predominate while Saytzeff rule states that the alkene having least alkyl substituents on the double bond will predominate. Though these two rules appear contradictory in nature but both are true as is shown in the above example (but-1-ene is Hoffman product while but-2-ene is Saytzeff product). Saytzeff elimination seems to occur when Y is neutral in nature. In these reactions, the reaction is believed to proceed via a T.S which does possess a considerable degree of "alkene character" which leads the stabilizing effect of the alkyl groups to play a role in lowering the energy of the T.S.
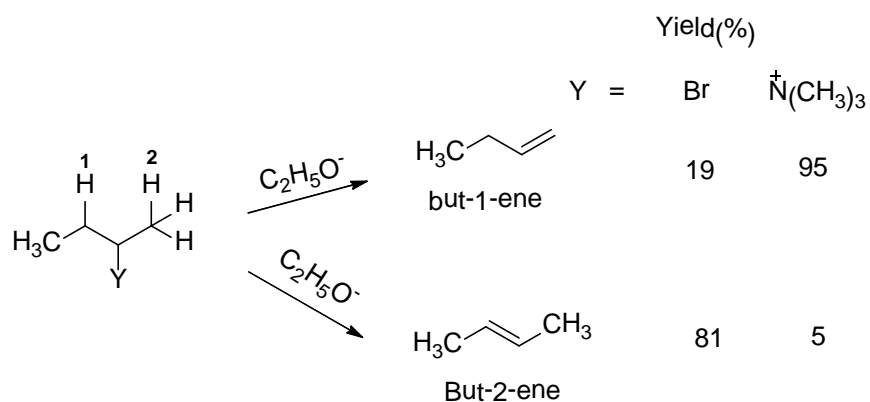
On the contrary, a positively charged Y would exert strong electron withdrawing inductive effect thereby increasing the acidity of the β-protons **1** and **2**. The effect is somewhat nullified by the electron donating inductive effect of the methyl group for protons marked **1** but not for protons marked **2**. Thus, now the reaction proceeds through a T.S having a "carbanion character".



Saytzeff T.S.        Hoffman T.S.

**1**      **2**
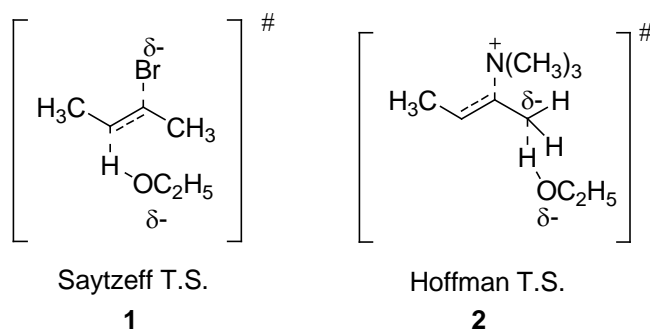
Another example Hoffman elimination vs Saytzeff elimination is that, where there is more than one potential $RN(CH_3)_2$ leaving groups, the elimination occurs in such a fashion to yield the least substituted alkene.
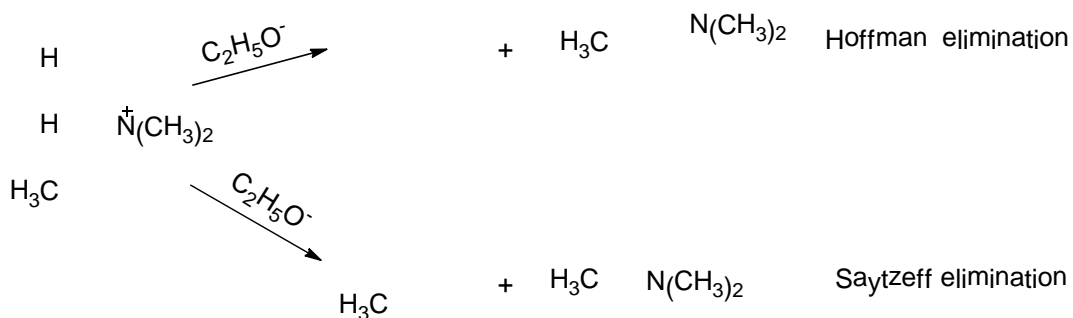
Increase of steric crowding in the T.S of E2 elimination also favours the formation of Hoffman product over Saytzeff product progressively. This crowding can be either in alkyl halide (R groups), leaving groups (Y) and attacking base (B:). Thus in the E2 elimination of 2-bromo-2-methylbutane, with the increase in steric bulk in the attacking base, the proportion of Hoffman elimination product increases.
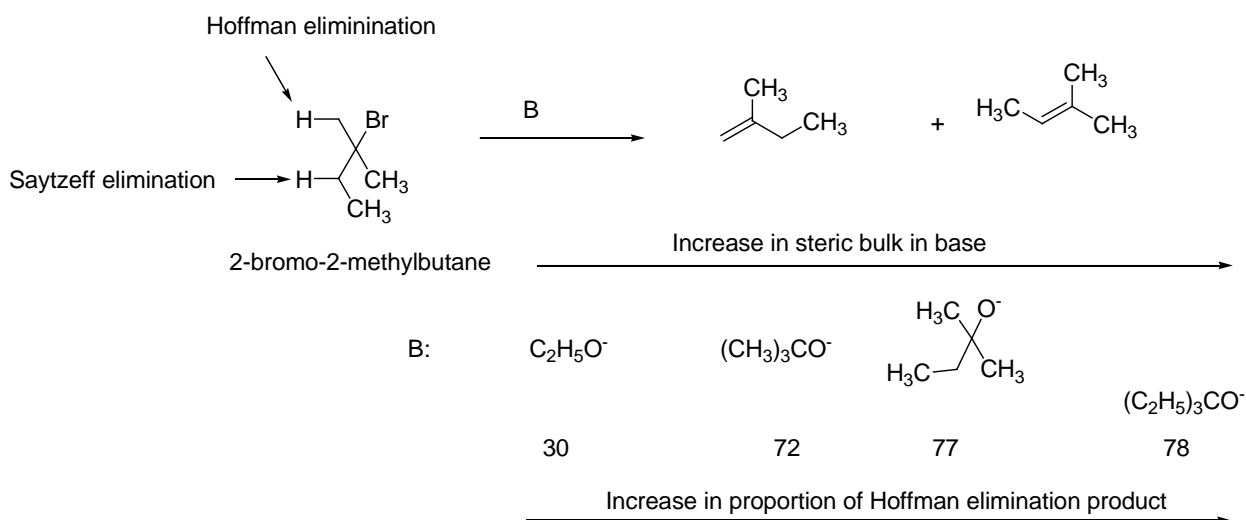


It must be considered that the aliphatic nucleophilic substitution and elimination reaction of alkyl halides have a striking similarities in terms of the reactants involved since a nucleophile can also act as a base. Thus, in a given reaction elimination vs substitution ratio can be of importance. There may be five considerations in determining the elimination to substitution ratio.

- In terms of reactant structure, branching in the reactant structure, especially leading to increase in steric bulk at carbon next to leaving group leads to increase in $E2/S_N^2$ ratios. This is reflected in the fact that 3° alkyl halides seldom undergo substitution.

- In terms of the attacking species, a species which can act as a strong base favours elimination over substitution. This is also aided by the fact that strong bases are seldom good nucleophiles.

- In terms of the leaving group, the correlation between elimination vs substitution ($E2$ vs $S_N^2$) is not very clear. However, it seems that a better leaving group slightly favours the $E2/S_N^2$ ratio. On the other hand positive charged leaving groups greatly enhance the rate of elimination reactions.

- In terms of solvent polarity, increase in solvent polarity leads to decrease in elimination vs substitution for second order reactions. For the first order reactions substitution is usually favoured in all solvents. E1 reactions are favoured in polar solvents which do not act as nucleophiles.

- On increasing the temperature, elimination reactions are usually favoured over substitution reactions. This is on account of the fact that the activation energies of eliminations are higher than substitution reactions.

A relatively less examples have been observed for 1,1-eliminations i.e.; elimination reactions in which both the leaving group(Y) and the proton abstracted by the base were on the same carbon. They tend to be favoured by powerful electron withdrawing leaving groups and by strong bases. In examples of this type of eliminations, there are instances of formation of carbene intermediates. Thus, when 1-chlorobutane is treated with phenylsodium, the corresponding 1,1-elimination product is obtained. The formation of a carbene intermediate in this case is inferred from the side product 1-methylcyclopropane
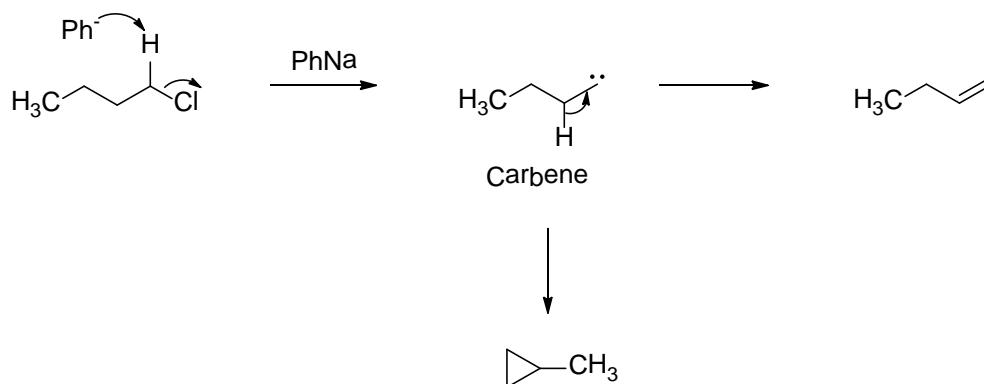


Grignard reagents, a very important class of organometallic reagents are prepared by the reaction of alkyl halides with magnesium metal.