CHAPTER 6

Aliphatic Nucleophilic Substitution

❖ The SN₂, SN₁, Mixed SN₁ and SN₂, SNᵢ, SN₁', SN₂', SNᵢ' and SET Mechanisms

Although the number of mechanisms by which the nucleophilic substitutions proceed is very large, certain patterns can still be used to profile them for more systematic and simplistic analysis. Some of the prominent types of aliphatic nucleophilic substitutions are given below.

➢ SN₂ (Substitution Nucleophilic Bimolecular) Mechanism

In SN₂ reactions, the "SN" stands for "nucleophilic substitution", and "2" means that the rate-determining step is bimolecular. In other words, a stronger nucleophile displaces a weaker one via the formation of a transition state.

Illustrative reaction: One of the most common examples of the SN₂ reaction is the attack of Br⁻ on ethyl chloride results in ethyl bromide, with chloride ejected as the leaving group.

\[
\begin{array}{c}
\text{H} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{Cl}
\end{array}
\quad +
\begin{array}{c}
\text{Br}^-
\end{array}
\quad \rightarrow
\begin{array}{c}
\text{H} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{Br}
\end{array}
\quad +
\begin{array}{c}
\text{Cl}^-
\end{array}
\]

Mechanism involved: The proposed mechanism for the reaction given above involves a single step which must be discussed before we give the salient features of the same. The process occurs most often at the \(sp^3\) hybridized carbon with a stable electronegative leaving group attached to it (usually halide \(X^-\)).

\[
\begin{array}{c}
\text{H} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{Cl}
\end{array}
\quad +
\begin{array}{c}
\text{Br}^-
\end{array}
\quad \rightarrow
\begin{array}{c}
\text{H} \\
\text{H} \\
\text{H} \\
\text{H} \\
\text{Br}
\end{array}
\quad +
\begin{array}{c}
\text{Cl}^-
\end{array}
\]

The breaking of the carbon–halogen bond and the formation of the new covalent bond takes place simultaneously via a transition state in which the carbon under nucleophilic attack is in 5-coordination with probable \(sp^2\) hybridization. The nucleophilic attack at the carbon takes place at 180° w.r.t the leaving group to provides a good overlap between the nucleophile's lone pair and the antibonding orbital (\(\sigma^*\)) C–X bond. The leaving group is then detached from the opposite side and the product is formed with inversion of the tetrahedral geometry at the central carbon atom if the substrate is chiral.
**Salient Features:** The main features of the mechanism involved in nucleophilic substitution bimolecular or SN₂ type reactions are given below.

i) SN₂ reactions follow second-order kinetics with the rate law

\[
Rate = k[RX][Nu]
\]

Where \( k \) is the rate constant. The symbol \([RX]\) and \([Nu]\) represent the molar concentration of the substrate and attacking nucleophiles, respectively.

ii) If the alkyl halide is chiral, then this often leads to an inversion of configuration, called the Walden inversion.

iii) The rate of the substitution becomes independent of the concentration of the attacking reagent if its concentration is extremely high in comparison to the substrate.

iv) The rate of the substitution increases as the steric bulk around the carbon center decreases.

v) The SN₂ reactions are favored in polar aprotic solvents.

➢ **SN₁ (Substitution Nucleophilic Unimolecular) Mechanism**

In SN₁ reactions, the word "SN" stands for "nucleophilic substitution", and "1" means that the rate-determining step is unimolecular in nature. In other words, a stronger nucleophile displaces a weaker one via the formation of an intermediate.

**Illustrative reaction:** The most common example of an SN₁ reaction is the formation of alcohols from alkyl halides as shown below.

**Mechanism involved:** The proposed mechanism for the reaction given above involves two steps which must be discussed before we give salient features of the same.

i) **Formation of intermediate:**

The carbocation formed during this step is trigonal planar in geometry and is open for attack from both sides. Now since the carbocations are electron-deficient species and very reactive, The OH⁻ will attack from either side to give the same product, which will be the second step of the reaction.
ii) Attack by the Nucleophile:

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{CH}_3 \\
\text{OH}^- & \quad \text{CH}_3
\end{align*}
\]

Now since the faces of the carbocations formed are homotopic, the OH\(^-\) can attack from either side to give the same product.

**Salient Features:** The main features of the mechanism involved in nucleophilic substitution unimolecular or SN\(_1\) type reactions are given below.

i) **SN\(_1\) reactions** follow first-order kinetics with the rate law

\[
Rate = k[RX]
\]

Where \(k\) is the rate constant and \([RX]\) represents the molar concentration of the substrate (tert-butyl halide in this case).

ii) If the alkyl halide has one or more asymmetric carbons, two stereoisomers (diastereomers or enantiomers) will be formed.

iii) The rate of the nucleophilic substitution unimolecular is almost independent of the concentration of the attacking reagent.

iv) The rate of the substitution increases as the steric bulk around the carbon center increases.

v) Since an unstable intermediate carbocation is formed in course of the SN\(_1\) reactions (rate-determining step), any factor that can support this will boost up the rate. Normal solvents of choice are both protic (to hydrolyze the leaving group in particular) and polar (to simply stabilize ionic intermediates). Archetypal polar protic solvents include alcohol and water, which are also capable of acting as nucleophiles (i.e. support solvolysis). Therefore, we can conclude that the SN\(_1\) reactions are favored in polar and protic solvents.

vi) Since the intermediate formed is carbocation, the possibility of rearrangement to form more stable carbocation and yielding different products is also there.

vii) The substitution at bridgehead carbon is either absent or takes place very slowly because the carbocation in such cases cannot attain planar geometry.

viii) In asymmetric alkyl halides, racemization does not take place fully all the time because the nucleophile attacks even before the complete detachment of leaving group. This leads to some inversion also causing unequal racemic mixture.
CHAPTER 6: Aliphatic Nucleophilic Substitution

➢ Mixed SN\textsubscript{1} and SN\textsubscript{2} Mechanism

Most of the organic reactions are either SN\textsubscript{1} or SN\textsubscript{2} over a vast range of experimental conditions. However, some reactions show both types of characteristic features under certain conditions indicating that they are neither SN\textsubscript{1} nor SN\textsubscript{2} but a mixture of two. In other words, some nucleophilic substitution reactions proceed via mixed SN\textsubscript{1} and SN\textsubscript{2} mechanisms.

Illustrative reaction: The common depictive example of SN\textsubscript{1}-SN\textsubscript{2} mixed-mechanism is shown below.

Mechanism involved: There are two theories that are typically used to rationalize the borderline nucleophilic substitution mechanism as given below.

i) Simultaneity of SN\textsubscript{1} and SN\textsubscript{2}: As the name suggests, this theory says that the reaction proceeds simultaneously via SN\textsubscript{1} and SN\textsubscript{2} pathways. The pictorial representation of this theory is given below.

ii) Intermediatory mechanism: This theory assumes that the reaction takes place via the formation of an intermediary ion-pair as shown below.

When the formation of ion-pair is the rate-determining step, the reaction becomes SN\textsubscript{1}; whereas, if the conversion of ion-pair into the product is the rate-determining step, the reaction becomes SN\textsubscript{2}; if \( k_1 = k_2 \), we get a borderline case.

Salient Features: The main features of the mixed SN\textsubscript{1} and SN\textsubscript{2} mechanism are given below.

i) SN\textsubscript{1} pathway competes with the SN\textsubscript{2} route to dominate the products’ ratio for asymmetric reactants.

ii) The ion-pair theory can be applied to both SN\textsubscript{1} and SN\textsubscript{2} as well.
 ➢ **SN<sub>i</sub> (Substitution Nucleophilic Internal) Mechanism**

In SN<sub>i</sub> reactions, the "SN" stands for "nucleophilic substitution", and the "i" means that the substitution takes place internally in the molecule.

**Illustrative reaction:** One of the most common examples of the SN<sub>i</sub> reaction is the displacement of OH<sup>-</sup> of alcohols by Cl<sup>-</sup> in the presence of SOCl<sub>2</sub>.

![Illustrative reaction diagram]

**Mechanism involved:** The SOCl<sub>2</sub> first reacts with the alcohol to give rise to an alkyl chloro sulfite (i.e. intimate ion pair). The next step is concerted and involves the loss of an SO<sub>2</sub> molecule and its displacement by its own chloride group.

![Mechanism involved diagram]

The major point of difference between SN<sub>i</sub> and SN<sub>1</sub> is actually that the ion pair is not completely separate, and therefore, no actual carbocation is generated (otherwise we would have got racemized product).

**Salient Features:** The main features of the mechanism involved in nucleophilic substitution internal or SN<sub>i</sub> type reactions are given below.

<i>)** SN<sub>i</sub> reactions follow second-order kinetics with the rate law**

\[
Rate = k[ROH][SOCl_2]
\]

Where \( k \) is the rate constant. The symbol \([ROH]\) and \([SOCl_2]\) represent the molar concentration of the substrate and species with attacking nucleophiles, respectively.

\(<ii>)** If the alcohol is chiral, then this leads to the retention of configuration.**
SN₁' (Substitution Nucleophilic Unimolecular Prime) Mechanism

In SN₁' reactions, the word "SN" stands for "nucleophilic substitution", "1" means that the rate-determining step is unimolecular in nature, and prime indicates that there is a double bond in the vicinity of leaving group. In other words, a stronger nucleophile displaces a weaker one via the formation of an intermediate that has a delocalization of π-electron density.

Illustrative reaction: The most common example of SN₁' reaction is the formation of but-2-ene-1-ol from 3-bromobuta-1-ene as shown below.

\[
\begin{align*}
\text{3-bromobuta-1-ene} & \quad \xrightarrow{\text{OH}} \quad \text{(E)-but-2-ene-1-ol} \\
\text{+ Br}^- & \\
\end{align*}
\]

Mechanism involved: The proposed mechanism for the reaction given above involves two steps which must be discussed before we give salient features of the same. At first, the detachment of bromide ion gives rise to an allylic carbocation system in which the positive charge is distributed at 1st and 3rd carbon atoms. Now since the terminal carbon is primary but 3rd carbon is secondary, the first carbon is more electron deficient, and therefore, will become the first choice for attacking nucleophile to yield our product.

Salient Features: Almost all of the features of SN₁' prime are similar to the SN₁ mechanism with some exceptions as given below.

i) The carbolination formed in SN₁ was simple but rearrangeable in the case of allylic systems.

ii) The nucleophile attack on γ-carbon rather than the α-one.
**SN$_2'$ (Substitution Nucleophilic Bimolecular Prime) Mechanism**

In SN$_2'$ reactions, the "SN" stands for "nucleophilic substitution", "2" means that the rate-determining step is bimolecular, and prime indicates that there is a double bond in the vicinity of the leaving group. In other words, a stronger nucleophile displaces a weaker one via the formation of a transition state; though the attachment and detachment are at different carbons.

**Illustrative reaction:** One of the most common examples of the SN$_2'$ reaction is the conversion of 3-bromo-3-methylcyclohex-1-ene into 3-methylcyclohex-2-en-1-ol, with bromide ejected as the leaving group.

![Illustrative reaction diagram]

**Mechanism involved:** The proposed mechanism for the reaction given above involves the use of a double bond as a relay system of electron density. Instead of attacking at the 3rd carbon in the cycle (would have yielded normal SN$_2$ product), the incoming nucleophile attacks at 1st carbon due to its greater electron deficiency than the 3rd one which is obviously caused by electrons' relay from first carbon to bromine.

One more reason why the methoxide ion did not attack at the 3rd carbon to give normal SN$_2$ is that there is more steric hindrance at the 3rd carbon than what it is at 1st. In other words, the greater electron deficiency and a less steric hindrance at first carbon make it a better site for nucleophilic attack.

**Salient Features:** Almost all of the features of SN$_2'$ prime are similar to the SN$_2$ mechanism with some exceptions as given below.

1. The nucleophilic attack and the detachment of leaving group takes place at different carbon atoms.
2. The double bond is used as an electrons’ relay system.
CHAPTER 6: Aliphatic Nucleophilic Substitution

SN′ (Substitution Nucleophilic Internal Prime) Mechanism

In SN′ reactions, the "SN" stands for "nucleophilic substitution", the "i" means that the substitution takes place internally in the molecule, and prime indicates that there is a double bond in the vicinity of leaving group.

Illustrative reaction: One of the most common examples of the SN′ reaction is the displacement of OH of in but-3-en-2-ol by Cl in the presence of SOCl₂.

\[
\text{OH} + \text{SOCl}_2 \rightarrow \text{Cl} - \text{HCl} \rightarrow (E)-1\text{-chlorobut-2-ene} + \text{SO}_2
\]

Mechanism involved: The proposed mechanism for the reaction given above initially proceed normally like SN; however, the detachment of sulfurochloridite ion gives rise to an allylic carbocation system in which the positive charge is distributed at 1st and 3rd carbon atoms. Now since the terminal carbon is primary but 3rd carbon is secondary, the first carbon is more electron deficient, and therefore, will become the first choice for attacking nucleophile to yield our product.

Salient Features:

i) The carbonation formed in SN was simple but rearrangeable in the case of allylic systems.

ii) The nucleophile attack on the 1st carbon rather than the 3rd one.
**SET (Single-Electron Transfer) Mechanism**

SET (single electron transfer) reactions may simply be defined as the organic reaction mechanism in which an electron-rich molecule gives away one of its electrons to an electron-poor molecule to form radical cation and radical anion, respectively. Furthermore, these radical anions and cations can bind to give new bonds or may react in some other way to yield strange products.

**Illustrative reaction:** One of the most common examples of the SET reactions is the transformation of benzophenone into 1,1-diphenylmethanol in the presence of metallic sodium.

**Mechanism involved:** The proposed mechanism for the reaction given above involves four steps which must be discussed before we give salient features of the same. The process occurs most often via the formation of benzophenone anion and dianion as given below.

At this stage, some protons are added in the form of very weak (NH₄Cl) or strong acid (HCl). The protonation of benzophenone dianion would yield 1,1-diphenylmethanol.

**Salient Features:** The main features of the mechanism involved in simple electric transfer or SET type reactions are given below.

i) The electron transfer results in radical cation and radical cation.

ii) The SET mechanisms can be distinguished from polar mechanisms by careful analysis of end products.
Want to study chemistry for CSIR UGC - NET JRF, IIT-GATE, M.Sc Entrance, IIT-JAM, IIT-JEE, NEET, 11th and 12th?

Are you interested in books (Print and E-book) published by Dalal Institute? READ MORE

Want video lectures in chemistry for CSIR UGC - NET JRF + IIT-GATE; IIT-JAM + M.Sc Entrance; IIT-JEE + NEET + 11th + 12th; and all other postgraduate, undergraduate & senior-secondary level examinations where chemistry is a paper? READ MORE

Postgraduate Level

CSIR UGC - NET JRF & IIT-GATE
First Chemistry Batch
(1st January – 31st May)
Second Chemistry Batch
(1st July – 30th November)

Regular Program
Online Course
Result

Senior-Secondary Level

11TH, 12TH, NEET & IIT-JEE
First Chemistry Batch
(1st April – 31st August)
Second Chemistry Batch
(1st October – 28th February)

Regular Program
Online Course
Result

Undergraduate Level

M. Sc Entrance & IIT-JAM
First Chemistry Batch
(1st February – 30th June)
Second Chemistry Batch
(1st August – 31st December)

Regular Program
Online Course
Result

Join the revolution by becoming a part of our community and get all of the member benefits like downloading any PDF document for your personal preview.

Sign Up

Dalal Institute

Main Market, Sector 14, Rohtak, Haryana 124001, India
(+91-9802825820, info@dalalinstitute.com)
www.dalalinstitute.com

Join the revolution from Beast to Buddha

..... India's Best Coaching Center for Academic and Competitive Chemistry Exams.....
(CSIR UGC – NET JRF + IIT-GATE; IIT-JAM + M.Sc Entrance; IIT-JEE + NEET + 11th + 12th; and all other postgraduate, undergraduate & senior-secondary level examinations where chemistry is a paper)
# Table of Contents

## CHAPTER 1 ................................................................................................................................. 11

**Nature of Bonding in Organic Molecules** ................................................................................. 11
- Delocalized Chemical Bonding ....................................................................................................... 11
- Conjugation .................................................................................................................................... 14
- Cross Conjugation .......................................................................................................................... 16
- Resonance ..................................................................................................................................... 18
- Hyperconjugation .......................................................................................................................... 27
- Tautomerism ................................................................................................................................. 31
- Aromaticity in Benzenoid and Nonbenzenoid Compounds ......................................................... 33
- Alternant and Non-Alternant Hydrocarbons ............................................................................... 35
- Huckel’s Rule: Energy Level of $\pi$-Molecular Orbitals ................................................................. 37
- Annulenes ....................................................................................................................................... 44
- Antiaromaticity .............................................................................................................................. 46
- Homoaromaticity ........................................................................................................................... 48
- PMO Approach .............................................................................................................................. 50
- Bonds Weaker Than Covalent ........................................................................................................ 58
- Addition Compounds: Crown Ether Complexes and Cryptands, Inclusion Compounds, Cyclodextrins ......................................................................................................................... 65
- Catenanes and Rotaxanes .............................................................................................................. 75
- Problems ....................................................................................................................................... 79
- Bibliography ................................................................................................................................. 80

## CHAPTER 2 ......................................................................................................................................... 81

**Stereochemistry** ......................................................................................................................... 81
- Chirality ......................................................................................................................................... 81
- Elements of Symmetry ...................................................................................................................... 86
- Molecules with More Than One Chiral Centre: Diastereomerism .................................................. 90
- Determination of Relative and Absolute Configuration (Octant Rule Excluded) with Special Reference to Lactic Acid, Alanine & Mandelic Acid ................................................................. 92
- Methods of Resolution .................................................................................................................... 102
- Optical Purity ................................................................................................................................ 104
- Prochirality .................................................................................................................................... 105
- Enantiotopic and Diastereotopic Atoms, Groups and Faces .......................................................... 107
- Asymmetric Synthesis: Cram’s Rule and Its Modifications, Prelog’s Rule ...................................... 113
- Conformational Analysis of Cycloalkanes (Upto Six Membered Rings) ......................................... 116
- Decalins ........................................................................................................................................... 122
- Conformations of Sugars ............................................................................................................... 126
- Optical Activity in Absence of Chiral Carbon (Biphenyls, Allenes and Spiranes) ......................... 132
- Chirality Due to Helical Shape ....................................................................................................... 137
- Geometrical Isomerism in Alkenes and Oximes .............................................................................. 140
- Methods of Determining the Configuration .................................................................................... 146
CHAPTER 3 ............................................................................................................................................... 153

Reaction Mechanism: Structure and Reactivity ................................................................................. 153

- Problems........................................................................................................................................... 151
- Bibliography..................................................................................................................................... 152

CHAPTER 4 ............................................................................................................................................... 221

Carbohydrates................................................................................................................................. 221

- Types of Naturally Occurring Sugars............................................................................................... 221
- Deoxy Sugars................................................................................................................................. 227
- Amino Sugars................................................................................................................................. 229
- Branch Chain Sugars...................................................................................................................... 230
- General Methods of Determination of Structure and Ring Size of Sugars with Particular Reference to Maltose, Lactose, Sucrose, Starch and Cellulose....................................................... 231
- Problems....................................................................................................................................... 239
- Bibliography................................................................................................................................... 240

CHAPTER 5 ............................................................................................................................................... 241

Natural and Synthetic Dyes ............................................................................................................... 241

- Various Classes of Synthetic Dyes Including Heterocyclic Dyes..................................................... 241
- Interaction Between Dyes and Fibers............................................................................................... 245
- Structure Elucidation of Indigo and Alizarin...................................................................................... 247
- Problems....................................................................................................................................... 252
- Bibliography................................................................................................................................... 253

CHAPTER 6 ............................................................................................................................................... 254

Aliphatic Nucleophilic Substitution.................................................................................................. 254

- The SN2, SN1, Mixed SN1 and SN2, SNi, SNi’, SN2’, SNi’ and SET Mechanisms............................. 254
The Neighbouring Group Mechanisms ................................................................. 263
Neighbouring Group Participation by $\pi$ and $\sigma$ Bonds ........................................ 265
Anchimeric Assistance ................................................................................................. 269
Classical and Nonclassical Carbocations .................................................................... 272
Phenonium Ions ........................................................................................................... 283
Common Carbocation Rearrangements ...................................................................... 284
Applications of NMR Spectroscopy in the Detection of Carbocations ....................... 286
Reactivity – Effects of Substrate Structure, Attacking Nucleophile, Leaving Group and Reaction Medium ................................................................. 288
Ambident Nucleophiles and Regioselectivity .............................................................. 294
Phase Transfer Catalysis .............................................................................................. 297
Problems ....................................................................................................................... 300
Bibliography .................................................................................................................. 301
CHAPTER 7 .................................................................................................................. 302
Aliphatic Electrophilic Substitution ........................................................................... 302
- Bimolecular Mechanisms – $SE_2$ and $SE_1$ .............................................................. 302
- The $SE_1$ Mechanism ............................................................................................... 305
- Electrophilic Substitution Accompanied by Double Bond Shifts ............................... 307
- Effect of Substrates, Leaving Group and the Solvent Polarity on the Reactivity ... 308
- Problems ..................................................................................................................... 310
- Bibliography ................................................................................................................ 311
CHAPTER 8 .................................................................................................................. 312
Aromatic Electrophilic Substitution ........................................................................... 312
- The Arenium Ion Mechanism ................................................................................... 312
- Orientation and Reactivity ......................................................................................... 314
- Energy Profile Diagrams .......................................................................................... 316
- The Ortho/Para Ratio ............................................................................................... 317
- $ipso$-Attack .............................................................................................................. 319
- Orientation in Other Ring Systems .......................................................................... 320
- Quantitative Treatment of Reactivity in Substrates and Electrophiles ...................... 321
- Diazonium Coupling ............................................................................................... 325
- Wilsmeier Reaction .................................................................................................. 326
- Gattermann-Koch Reaction ..................................................................................... 327
- Problems ..................................................................................................................... 329
- Bibliography ................................................................................................................ 330
CHAPTER 9 .................................................................................................................. 331
Aromatic Nucleophilic Substitution ........................................................................... 331
- The ArSN$_1$, ArSN$_2$, Benzyne and S$_8$N$_1$ Mechanisms ....................................... 331
- Reactivity – Effect of Substrate Structure, Attacking Nucleophile, Leaving Group and Attack Medium ................................................................. 336
- The von Richter, Sommelet-Hauser, and Smiles Rearrangements ......................... 339
- Problems ..................................................................................................................... 343
- Bibliography ................................................................................................................ 344
Mandeep Dalal is an Indian research scholar who is primarily working in the field of Science and Philosophy. He received his Ph.D in Chemistry from Maharshi Dayanand University, Rohtak, in 2018. He is also the Founder of "Dalal Institute" (India’s best coaching centre for academic and competitive chemistry exams), the organization that is committed to revolutionize the field of school-level and higher education in Chemistry across the globe. He has published more than 40 research papers in various international scientific journals, including mostly from Elsevier (USA), IOP (UK), and Springer (Netherlands).

Other Books by the Author

A TEXTBOOK OF INORGANIC CHEMISTRY - VOLUME I, II, III, IV
A TEXTBOOK OF PHYSICAL CHEMISTRY - VOLUME I, II, III, IV
A TEXTBOOK OF ORGANIC CHEMISTRY - VOLUME I, II, III, IV