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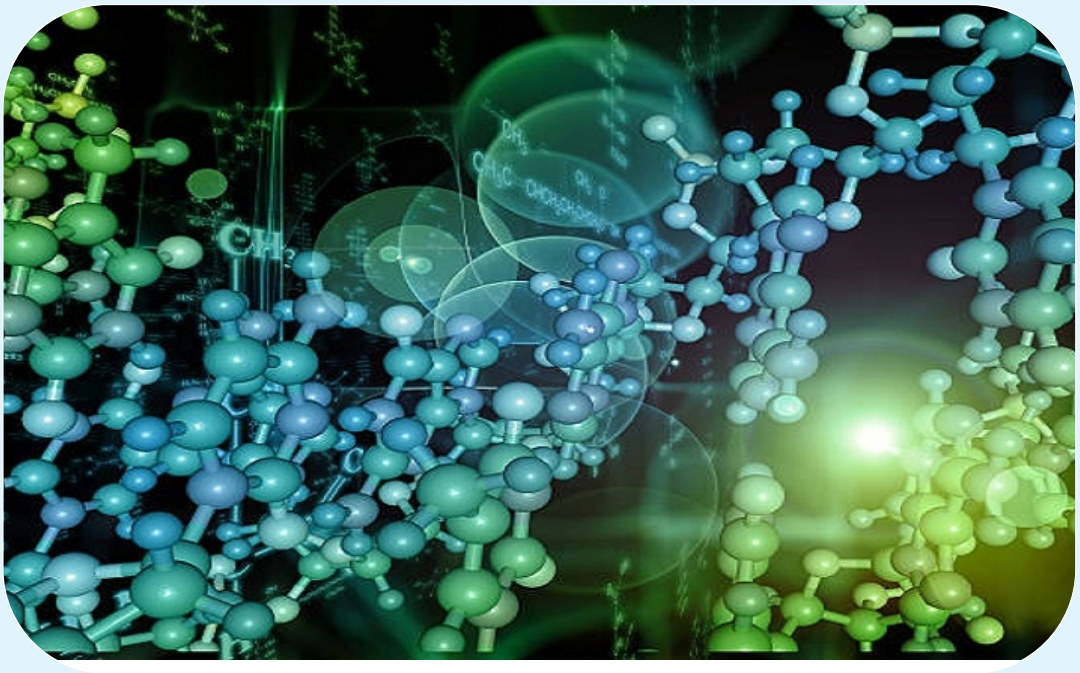
Organic & Physical Chemistry I

Bachelor of Science (B.Sc.)
Semester - 4



SELF LEARNING MATERIAL

CC 403

Organic & Physical Chemistry

MATS University

Organic & Physical Chemistry

ODL/MSS/BSCB/403

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The entire syllabus has organized into four modules. Module 01 focuses on organic compounds like alkyl halides, aryl halides, alcohols, and phenols. It covers their structures, synthesis methods, reactivity, and applications. Module 02 explores carbonyl compounds, such as aldehydes and ketones, as well as carboxylic acids and their derivatives, highlighting their properties, synthesis, and chemical behavior. Module 03 introduces the concepts of chemical and phase equilibria, focusing on equilibrium constants, factors that affect equilibrium, and applications in reversible reactions. Finally, Module 04 covers photochemical reactions and their real-world applications, along with the study of liquid-liquid mixtures and the Nernst Distribution Law for solute distribution.

MODULE -1

HALIDES, ALCOHOLS, AND PHENOLS

1.0 Objective

- Understand the preparation and reactions of alkyl and aryl halides.
- Learn about nucleophilic substitution reactions and their mechanisms.
- Study the nomenclature, preparation, properties, and reactions of alcohols and phenols.
- Explore the mechanisms of important reactions like Williamson's ether synthesis, Fries rearrangement, and Reimer-Tiemann reaction.

Unit - 1 Alkyl Halides:

A particularly important class of organic compounds with carbon halogen bonds are the alkyl halides. The chemical reactivity of these compounds gives them the potential to serve as versatile synthetic intermediates in organic chemistry, undergoing a variety of transformation in differing reaction conditions. They are easy to prepare from alkenes and alcohols, and they undergo a variety of nucleophilic substitution reactions that enable the introduction of a wide range of functional groups. Mechanism, stereochemistry and factors of these reactions help in predicting the reaction and designing the synthetic pathway. Covering the preparation, nucleophilic substitution reactions, mechanisms and stereochemistry, this in-depth article and infographic also covers the factors that affect the reactivity of alkyl halides.

Preparation of Alkyl Halides

Alkyl halides can be synthesized through various methods, with preparation from alkenes and alcohols being among the most common and synthetically useful approaches.

Preparation from Alkenes

Alkenes serve as excellent precursors for alkyl halides through addition reactions across the carbon-carbon double bond. These additions typically follow Markovnikov's rule

unless specific reagents or conditions are employed to achieve anti-Markovnikov addition.

1. Addition of Hydrogen Halides (HX)

The addition of hydrogen halides (HX, where X = Cl, Br, I) to alkenes represents one of the most straightforward methods for preparing alkyl halides. This reaction proceeds via electrophilic addition mechanism:

R, C=CR, + HX '! R, CX-CR, H

For example, the addition of HBr to propene yields 2-bromopropane (isopropyl bromide) as the major product, following Markovnikov's rule:

CH*f* CH=CH, + HBr '! CH*f* CHBr-CH*f*

This reaction is in accordance with Markovnikov's rule which states that when HX adds to unsymmetrical alkenes, electrophilic hydrogen of HX goes to less substituted carbon of double bond and halide goes to more substituted carbon and results into more stable carbocation intermediate. So, in contrast, the order of reactivity of hydrogen halides is: HI > HBr > HCl > HF, correlating with their acid strengths and nucleophilicity of the halide anions.

2. Anti-Markovnikov Addition (Peroxide Effect)

When the addition of HBr is carried out in the presence of peroxides (ROOR), the reaction proceeds via a radical mechanism, resulting in anti-Markovnikov addition. This phenomenon is known as the peroxide effect or Kharasch effect:

CH*f* CH=CH, + HBr + ROOR '! CH*f* CH, CH, Br

In this reaction, the bromine attaches to the less substituted carbon, contrary to Markovnikov's rule. The peroxide initiates a radical chain reaction by generating bromine radicals that attack the alkene to form the more stable radical intermediate.

3. Halogenation of Alkenes

Alkenes react with halogens (X, , where X = Cl, Br) to form vicinal dihalides through an anti addition mechanism. This reaction proceeds through a cyclic halonium ion intermediate:

R, C=CR, + X, '! R, CX-CXR,

For instance, the reaction of ethene with bromine yields 1,2-dibromoethane:

CH, =CH, + Br, '! BrCH, -CH, Br

4. Halohydrin Formation

Alkenes react with halogens in aqueous medium to form halohydrins, which are compounds containing both a halide and a hydroxyl group on adjacent carbon atoms:

R, C=CR, + X, + H, O '! R, CX-CR, OH + HX

For example, the reaction of propene with bromine in water produces 1-bromo-2-propanol:

CH*f* CH=CH, + Br, + H, O '! CH*f* CHBr-CH, OH + HBr

Preparation from Alcohols

Alcohols serve as excellent precursors for alkyl halides through various substitution reactions. The hydroxyl group (-OH) in alcohols can be replaced by a halogen atom under appropriate conditions.

1. Reaction with Hydrogen Halides (HX)

Alcohols react with hydrogen halides (HX, where X = Cl, Br, I) to form alkyl halides and water:

R-OH + HX '! R-X + H, O

The reactivity of alcohols toward hydrogen halides follows the order: tertiary > secondary > primary, corresponding to the stability of the carbocation intermediates formed during the reaction. Similarly, the reactivity of hydrogen halides follows: HI > HBr > HCl > HF.

For example, the reaction of 2-propanol with HBr yields 2-bromopropane:

CH*f* CHOH-CH*f* + HBr '! CH*f* CHBr-CH*f* + H, O

2. Reaction with Phosphorus Halides (PX*f* , PX…)

Alcohols react with phosphorus halides such as PCl*f* , PCl… , PBr*f* , and PI*f* to form alkyl halides:

3R-OH + PX*f* '! 3R-X + H*f* PO*f* R-OH + PX… '! R-X + POX*f* + HX

For instance, the reaction of ethanol with phosphorus tribromide yields bromoethane:

3CH*f* CH, OH + PBr*f* '! 3CH*f* CH, Br + H*f* PO*f*

Phosphorus halides are particularly useful for converting primary and secondary alcohols to alkyl halides without significant rearrangement.

3. Reaction with Thionyl Chloride (SOCl,)

Alcohols react with thionyl chloride (SOCl,) in the presence of a base such as pyridine to form alkyl chlorides:

R-OH + SOCl, '! R-Cl + SO, + HCl

For example, the reaction of 1-butanol with thionyl chloride yields 1-chlorobutane:

CH*f* CH, CH, CH, OH + SOCl, '! CH*f* CH, CH, CH, Cl + SO, + HCl

This method is particularly advantageous because the byproducts (SO, and HCl) are gases that escape from the reaction mixture, driving the equilibrium toward the product.

4. Reaction with Sulfonyl Chlorides

Alcohols can be converted to alkyl halides via tosylate or mesylate intermediates. The alcohol is first converted to a tosylate or mesylate, which then undergoes nucleophilic substitution with a halide ion:

R-OH + TsCl '! R-OTs + HCl R-OTs + X{ '! R-X + TsO{

This two-step process is particularly useful for converting alcohols that are prone to rearrangement or elimination reactions.

Nucleophilic Substitution Reactions of Alkyl Halides

Alkyl halides undergo a variety of nucleophilic substitution reactions, wherein the halogen atom is replaced by a nucleophile. These reactions are central to organic synthesis as they allow for the introduction of various functional groups.

Alcohol Formation

Alkyl halides react with aqueous bases such as NaOH or KOH to form alcohols:

R-X + OH{ '! R-OH + X{

For example, the reaction of 1-bromobutane with sodium hydroxide yields 1-butanol:

CHf CH, CH, CH, Br + NaOH '! CHf CH, CH, CH, OH + NaBr

This reaction proceeds via an SN2 mechanism for primary and secondary alkyl halides, while tertiary alkyl halides may undergo elimination (E2) as a competing reaction.

Ester Formation

Alkyl halides react with carboxylate ions to form esters:

R-X + R'COO{ '! R'COOR + X{

For instance, the reaction of methyl bromide with sodium acetate yields methyl acetate:

CHf Br + CHf COO{ Naz '! CHf COOCHf + NaBr

This reaction is useful in organic synthesis for preparing esters from alkyl halides and carboxylic acid salts.

Nitrile Formation

Alkyl halides react with cyanide ions (CN{) to form nitriles (alkyl cyanides):

R-X + CN{ '! R-CN + X{

For example, the reaction of 1-chlorobutane with potassium cyanide yields pentanenitrile:

CHf CH, CH, CH, Cl + KCN '! CHf CH, CH, CH, CN + KCl

Nitriles are valuable intermediates in organic synthesis as they can be hydrolyzed to carboxylic acids or reduced to amines.

Isonitrile Formation

Alkyl halides react with silver isocyanide (AgNC) to form isonitriles (isocyanides):

R-X + AgNC '! R-NC + AgX

For instance, the reaction of methyl iodide with silver isocyanide yields methyl isocyanide:

CH*f* I + AgNC '! CH*f* NC + AgI

Isonitriles, characterized by their pungent odor, serve as important intermediates in heterocyclic compound synthesis and multicomponent reactions.

Williamson's Ether Synthesis

The Williamson ether synthesis represents one of the most reliable methods for preparing ethers. In this reaction, an alkyl halide reacts with an alkoxide ion to form an ether:

R-X + R'O{ '! R-O-R' + X{

For example, the reaction of bromoethane with sodium methoxide yields methyl ethyl ether:

CH*f* CH, Br + CH*f* O{ Naz '! CH*f* CH, OCH*f* + NaBr

For optimal results, primary alkyl halides are preferred as they minimize competing elimination reactions. The reaction proceeds via an SN2 mechanism, leading to inversion of configuration at the stereogenic center if present in the alkyl halide.

Mechanism and Stereochemistry of Nucleophilic Substitution Reactions

Nucleophilic substitution reactions of alkyl halides primarily proceed through two distinct mechanisms: SN1 (Substitution Nucleophilic Unimolecular) and SN2 (Substitution Nucleophilic Bimolecular). Understanding these mechanisms is crucial for predicting reaction outcomes, including stereochemistry.

SN2 Mechanism

The SN2 mechanism involves a concerted process where the nucleophile attacks the carbon bearing the halogen from the side opposite to the leaving group, resulting in inversion of stereochemistry. This mechanism occurs in a single step without the formation of intermediates.

Key features of the SN2 mechanism include:

1. **Rate Law**: The reaction rate depends on the concentrations of both the substrate and the nucleophile, indicating a bimolecular process:

   Rate = k[R-X][Nu{]

2. **Stereochemistry**: The SN2 mechanism proceeds with inversion of configuration at the stereogenic center, often described as an "umbrella-like" inversion or "Walden inversion." If the reaction occurs at a stereogenic center, the product will have the opposite configuration:

   R-X + Nu{ '! [Nu—C—X]‡ '! Nu-R + X{

For example, when (R)-2-bromobutane reacts with hydroxide ion, (S)-2-butanol is formed:

(R)-CH*f* CH, CHBrCH*f* + OH{ '! (S)-CH*f* CH, CHOHCH*f* + Br{

3. **Transition State**: The transition state involves a pentacoordinate carbon atom with partial bonds to both the nucleophile and the leaving group, resulting in a trigonal bipyramidal geometry.

4. **Substrate Reactivity**: The reactivity of alkyl halides in SN2 reactions follows the order: methyl > primary > secondary > tertiary. This trend reflects the steric hindrance encountered by the nucleophile during its approach to the carbon center.

SN1 Mechanism

The SN1 mechanism involves a stepwise process where the departure of the leaving group precedes the attack of the nucleophile, resulting in the formation of a carbocation intermediate. This mechanism consists of two distinct steps.

Key features of the SN1 mechanism include:

1. **Rate Law**: The reaction rate depends only on the concentration of the substrate, indicating a unimolecular process:

   Rate = k[R-X]

2. **Stereochemistry**: The SN1 mechanism typically results in racemization with a slight predominance of inversion due to the presence of the departing leaving group on one face of the planar carbocation, partially hindering nucleophilic attack from that side:

   R-X '! Rz + X{ Rz + Nu{ '! R-Nu

   For example, when (R)-2-bromobutane undergoes SN1 reaction with water, a mixture of (R)- and (S)-2-butanol is formed, with a slight excess of the (S)-isomer.

3. **Carbocation Intermediate**: The carbocation intermediate is planar and sp^2-hybridized, allowing the nucleophile to attack from either face. However, the departing leaving group may shield one face, leading to partial inversion.

4. **Substrate Reactivity**: The reactivity of alkyl halides in SN1 reactions follows the order: tertiary > secondary > primary > methyl. This trend corresponds to the stability of the carbocation intermediates: tertiary > secondary > primary > methyl.

5. **Rearrangements**: Carbocation intermediates may undergo rearrangements (hydride or alkyl shifts) to form more stable carbocations before nucleophilic attack, potentially leading to unexpected products.

Factors Affecting SN1 and SN2 Reactions

Several factors influence the rates and outcomes of SN1 and SN2 reactions, determining which mechanism predominates under given conditions.

Nature of the Substrate

The structure of the alkyl halide significantly impacts the reaction mechanism:

1. **Steric Hindrance**: Increasing steric hindrance around the reaction center favors SN1 over SN2:
    - Primary alkyl halides predominantly undergo SN2 reactions due to minimal steric hindrance.
    - Secondary alkyl halides can undergo both SN1 and SN2 reactions depending on other factors.
    - Tertiary alkyl halides predominantly undergo SN1 reactions due to significant steric hindrance that impedes nucleophilic attack in an SN2 fashion.
2. **Carbocation Stability**: The stability of the potential carbocation intermediate strongly influences the likelihood of an SN1 mechanism:
    - Tertiary carbocations are relatively stable due to hyperconjugation and inductive effects from alkyl groups.
    - Secondary carbocations are moderately stable.
    - Primary carbocations are highly unstable and generally do not form under normal conditions.
    - Methyl carbocations are extremely unstable and essentially do not form.
3. **Leaving Group Ability**: The ability of the halide to depart as a leaving group affects both mechanisms:
    - The leaving group ability of halides follows: I{ > Br{ > Cl{ > F{, corresponding to their decreasing polarizability and increasing basicity.
    - Better leaving groups facilitate both SN1 and SN2 reactions but have a more pronounced effect on SN1 reactions as the rate-determining step involves leaving group departure.

Nature of the Nucleophile

The characteristics of the nucleophile significantly impact the reaction pathway:

1. **Nucleophilicity**: Stronger nucleophiles favor SN2 reactions:
    - Nucleophilicity generally follows the trend: R*f* P > R*f* N > RS{ > I{ > CN{ > Br{ > HO{ > Cl{ > F{ > ROH > H, O
    - Factors affecting nucleophilicity include:
        - Ø Basicity: Higher basicity often correlates with higher nucleophilicity, especially within the same row of the periodic table.
        - Ø Polarizability: More polarizable species tend to be better nucleophiles, especially in aprotic solvents.
        - Ø Charge: Negatively charged species are generally stronger nucleophiles than their neutral counterparts (e.g., HO{ > H, O).
2. **Steric Bulk**: Bulky nucleophiles favor SN1 reactions as they encounter greater steric hindrance in approaching the carbon center in an SN2 fashion.
3. **Concentration**: Higher nucleophile concentration favors SN2 reactions as the rate of SN2 reactions depends on nucleophile concentration, while SN1 reactions are independent of it.

Solvent Effects

The solvent plays a crucial role in determining the reaction mechanism:

1. **Polar Protic Solvents** (e.g., water, alcohols, carboxylic acids):
    - Favor SN1 reactions by:
        - Ø Stabilizing the carbocation through solvation
        - Ø Stabilizing the leaving group through hydrogen bonding
        - Ø Decreasing nucleophilicity through hydrogen bonding with the nucleophile
    - Examples include water, methanol, ethanol, and formic acid.

2. **Polar Aprotic Solvents** (e.g., acetone, DMF, DMSO, acetonitrile):
    - Favor SN2 reactions by:
        - Ø Not forming hydrogen bonds with nucleophiles, leaving them "naked" and more reactive
        - Ø Solvating cations effectively, increasing nucleophile reactivity
    - Examples include dimethylformamide (DMF), dimethyl sulfoxide (DMSO), acetone, and acetonitrile.
3. **Nonpolar Solvents** (e.g., hexane, benzene, carbon tetrachloride):
    - Generally disfavor both SN1 and SN2 reactions due to poor solvation of ionic species
    - May support SN2 reactions with strong, neutral nucleophiles

Temperature Effects

Temperature influences the competition between SN1 and SN2 mechanisms:

1. **Higher Temperatures**:
    - Generally favor SN1 reactions due to the higher activation energy associated with bond breaking in the rate-determining step.
    - Also favor competing elimination reactions (E1 and E2) over substitution reactions.
2. **Lower Temperatures**:
    - Generally favor SN2 reactions, especially with good nucleophiles and primary or secondary substrates.
    - Minimize competing elimination reactions.

Competitive Elimination Reactions

Substitution reactions often compete with elimination reactions:

1. **E1 (Elimination Unimolecular)**:

- Competes with SN1 and involves the same carbocation intermediate
- Favored by higher temperatures, stronger bases, and bulkier substrates
- Results in the formation of alkenes

2. **E2 (Elimination Bimolecular)**:
    - Competes with SN2 and involves a concerted mechanism
    - Favored by strong, sterically hindered bases, higher temperatures, and tertiary substrates
    - Results in the formation of alkenes with predominantly anti elimination

The competition between substitution and elimination can be controlled by adjusting reaction conditions:

- To favor substitution: Use weaker bases/better nucleophiles, lower temperatures, and polar aprotic solvents.
- To favor elimination: Use stronger bases, higher temperatures, and bulkier bases.

Practical Applications of Alkyl Halide Reactions

Understanding the preparation and reactivity of alkyl halides enables their effective use in various synthetic applications:

1. **Synthetic Intermediates**: Alkyl halides serve as versatile intermediates in the synthesis of various organic compounds, including alcohols, ethers, esters, amines, and nitriles.
2. **C-C Bond Formation**: Alkyl halides participate in numerous carbon-carbon bond-forming reactions, such as the Wurtz reaction, Grignard reaction, and various coupling reactions.
3. **Pharmaceuticals**: Many pharmaceutical compounds are synthesized using alkyl halide intermediates due to their versatile reactivity.

4. **Agrochemicals**: Numerous pesticides, herbicides, and fungicides contain halogenated compounds or are synthesized using alkyl halide intermediates.

5. **Materials Science**: Halogenated polymers and materials exhibit unique properties, making them valuable in various applications.

Alkyl halides are one of the main classes of organic compounds with broad synthetic applications. Their synthetic availability from alkenes and alcohols affords simple procedures for the installation of halogen atoms into organic structures. In fact there are full series of nucleophilic substitution reactions performed on alkyl halides which enables the formation of alcohols, esters, nitriles, isonitriles and Williamson's ether synthesis etc. Mechanistic understanding and stereochemistry of SN1 and SN2 reactions. The driving forces behind these reactions—and substrate structure, nucleophile properties, and solvent and temperature effects—give chemists the ability to tune reaction conditions to favour the pathway of choice. As an organic chemist, the more you learn about the fundamental principles that govern alkyl halide chemistry, the more you will be able to leverage these remarkable intermediates for the development of the intricate molecules utilized in human society ranging from medicines to agrochemicals to the plastics that deliver them. LINOWSKI, DR; Strength during the trauma response and symptom severity related to adolescent enhancement and incrementation of drug-seeking behavior.

Unit - 2 Aryl Halides:

Aryl halides are aromatic compounds where one or more hydrogen atoms directly bonded to an aromatic ring system are variable for halogen atoms (fluorine, chlorine, bromine, or iodine). The simplest aryl halide is halobenzene, in which one of the hydrogen atoms in a benzene ring is replaced by a halogen atom. They serve as important building blocks in organic synthesis for a range of transformations. They have unique reactivity patterns due to the presence of the aromatic ring system affecting the carbon-halogen bond, unlike the reactivity of alkyl halides. Aryl halides are a prime example of a class of compounds whose chemistry is dominated by a resonance-stabilized aromatic ring that affects bond strength, nucleophilic reactivity, and involvement in a range of mechanistic pathways. Chlorobenzene is the first chlorinated

aromatic compound and should be taken as a prototypical example for this class of compounds in terms of its chemical reactivity.

Preparation of Chlorobenzene

There are several methods of synthesizing chlorobenzene; the most important industrial and laboratory procedures are aromatic halogenation and the Sandmeyer reaction.

Aromatic Halogenation

The llegar halogen, is the direct introduction of a halogen atom into the aromatic ring. For the synthesis of chlorobenzene, this has been primarily done via electrophilic aromatic substitution. This reaction is carried out with benzene and chlorine in the presence of a Lewis acid catalyst (FeCl*f* , AlCl*f* , iron fillings).

The mechanism of aromatic halogenation follows the general pathway of electrophilic aromatic substitution:

1. **Electrophile Generation**: The Lewis acid catalyst (FeCl*f*) interacts with molecular chlorine (Cl,) to generate a more electrophilic species, enhancing the polarization of the Cl-Cl bond and creating an electrophilic Clz species:

   Cl, + FeCl*f* '! Clz + [FeCl,,]{

2. **Electrophilic Attack**: The electrophilic Clz attacks the ð-electron system of benzene, forming a resonance-stabilized carbocation intermediate (arenium ion or ó-complex):

   C† H† + Clz '! [C† H† Cl]z

3. **Deprotonation**: The carbocation intermediate loses a proton to a base (typically [FeCl,,]{) to restore aromaticity:

   [C† H† Cl]z + [FeCl,,]{ '! C† H… Cl + HCl + FeCl*f*

The overall reaction can be represented as:

C† H† + Cl, + FeCl*f* '! C† H… Cl + HCl

This method is effective but has limitations including lack of regioselectivity in substituted benzenes, potential for multiple halogenation, and the production of HCl as a byproduct, which can be corrosive and environmentally problematic.

Sandmeyer Reaction

The Sandmeyer reaction provides a more controlled method for synthesizing aryl halides, including chlorobenzene. This reaction involves the conversion of an aromatic diazonium salt to an aryl halide. The process typically follows these steps:

1. **Diazotization**: Aniline (or another primary aromatic amine) is treated with sodium nitrite (NaNO,) in the presence of a strong acid (usually HCl) at low temperatures (0-5°C) to form a diazonium salt:

   C† H… NH, + NaNO, + 2HCl '! C† H… N, z Cl{ + NaCl + 2H, O

2. **Halogenation**: The diazonium salt is then treated with copper(I) chloride (CuCl) to form chlorobenzene:

   C† H… N, z Cl{ + CuCl '! C† H… Cl + N, + Cuz

The overall reaction can be represented as:

C† H… NH, '! C† H… N, z '! C† H… Cl

The Sandmeyer reaction proceeds via a radical mechanism involving single-electron transfer steps. The copper(I) salt acts as both a source of the halide nucleophile and as a catalyst for the decomposition of the diazonium ion.

Advantages of the Sandmeyer reaction include:

- Superior regioselectivity, as the position of halogenation is determined by the initial position of the amino group
- Versatility in introducing various functional groups (not just halogens)
- Milder reaction conditions compared to direct halogenation

However, the Sandmeyer reaction has drawbacks such as:

- A multi-step process requiring careful temperature control

- Formation of unstable and potentially explosive diazonium intermediates
- Necessity of copper catalysts, which can be environmentally concerning

Aromatic Nucleophilic Substitution Involving Benzyne Mechanism

Base does not form on the side of solvent non-volatile - to that a method use derives on nucleophilic substitutions because that are obtained the more positive charge on the second carbon of the aryl haloginol takes place because that as that solvent is less volatile. A notable way is via benzyne mechanism, which takes place using very strong bases like with potassium amide (KNH,) or sodium amide (NaNH,) in liquid ammonia.

The Benzyne Mechanism

The benzyne mechanism of aromatic nucleophilic substitution in chlorobenzene using KNH, /NH*f* proceeds through the following steps:

1. **Deprotonation**: The strong base (NH, {) abstracts a proton from the carbon adjacent to the carbon bearing the halogen (ortho position), rather than directly attacking the carbon-halogen bond:

   C† H… Cl + NH, { ’! [C† H,, Cl]{ + NH*f*

2. **Elimination**: The resulting carbanion undergoes an elimination reaction, losing the chloride ion and forming a highly reactive benzyne intermediate with a formal triple bond:

   [C† H,, Cl]{ ’! C† H,, (benzyne) + Cl{

3. **Nucleophilic Addition**: The nucleophile (NH, {) adds to the strained triple bond of the benzyne intermediate, which can occur at either carbon of the former triple bond:

   C† H,, + NH, { ’! [C† H,, NH,]{

4. **Protonation**: The resulting anion is protonated by the solvent (NH*f*) to form the final product:

   [C† H,, NH,]{ + NH*f* ’! C† H… NH, + NH, {

The overall reaction can be represented as:

C† H… Cl + 2NH, { '! C† H… NH, + Cl{ + NH*f*

Several key characteristics of the benzyne mechanism include:

- **Regioselectivity**: Since the nucleophile can attack either carbon of the triple bond in the benzyne intermediate, the reaction often leads to a mixture of products when substituted aryl halides are used. For monosubstituted benzenes, meta-substitution is preserved, while ortho and para substitutions can interchange.
- **Base Strength Requirement**: The mechanism requires extremely strong bases (like KNH,) to abstract a proton from the relatively non-acidic benzene ring.
- **Temperature Considerations**: The reaction typically requires low temperatures due to the use of liquid ammonia as a solvent.
- **Evidence for Benzyne**: The existence of benzyne intermediates has been confirmed through various experimental methods, including trapping experiments and isotopic labeling studies.

Applications and Limitations of the Benzyne Mechanism

The benzyne mechanism provides a valuable route for nucleophilic substitution in aryl halides that are otherwise resistant to such transformations. However, it has several limitations:

- **Limited Substrate Scope**: The reaction works best with aryl halides that possess hydrogen atoms at the ortho positions.
- **Regioselectivity Issues**: The reaction often produces a mixture of isomers due to the lack of regioselectivity in the nucleophilic addition step.
- **Harsh Conditions**: The requirement for extremely strong bases and low temperatures limits practical applications.

- **Competing Reactions**: Side reactions, including polymerization of the highly reactive benzyne intermediate, can reduce yields.

Despite these limitations, benzyne chemistry has found applications in the synthesis of complex aromatic compounds, particularly those with substituents that would be difficult to introduce through conventional methods.

Reactivity and Relative Strength of C-Halogen Bonds

The reactivity of halogenated compounds is intimately connected to the strength of the carbon-halogen bond. Understanding the relative bond strengths in different classes of halogenated compounds—aryl halides, alkyl halides, and vinyl halides—provides critical insights into their chemical behavior.

Carbon-Halogen Bond Strength in Different Classes

The carbon-halogen bond strengths follow this general order:

Aryl-X > Vinyl-X > Alkyl-X

Where X represents a halogen atom (F, Cl, Br, or I).

This ordering can be explained by considering the hybridization state of the carbon atom and the influence of resonance effects:

1. **Aryl Halides (C† H… -X)**:
    - The carbon-halogen bond is formed between an sp^2 hybridized carbon of the aromatic ring and the halogen.
    - The bond is strengthened by resonance interaction between the ð-electrons of the aromatic ring and the p-orbitals of the halogen.
    - This resonance contribution gives the carbon-halogen bond partial double-bond character, increasing its strength.
    - The electron-withdrawing nature of the aromatic ring also reduces electron density at the carbon-halogen bond, decreasing its polarization and making it less susceptible to nucleophilic attack.

2. **Vinyl Halides (CH, =CH-X)**:
   - The carbon-halogen bond involves an sp^2 hybridized carbon.
   - There is some resonance stabilization due to the interaction between the ð-bond and the p-orbitals of the halogen, though less extensive than in aryl halides.
   - This limited resonance contribution still provides some additional bond strength compared to alkyl halides.
3. **Alkyl Halides (R-X)**:
   - The carbon-halogen bond involves an sp^3 hybridized carbon.
   - No resonance stabilization is possible.
   - The bond is more polarized due to the electronegativity difference between carbon and halogen, making it more susceptible to nucleophilic attack.

Quantitative Bond Strength Comparison

In terms of bond dissociation energies:

1. **Aryl-Cl Bond**: ~96 kcal/mol
2. **Vinyl-Cl Bond**: ~94 kcal/mol
3. **Alkyl-Cl Bond**: ~85 kcal/mol

Similar trends are observed for other halogens, though the absolute values differ.

Effect of Halogen Identity on Bond Strength

Within each class of halogenated compounds, the carbon-halogen bond strength follows the order:

C-F > C-Cl > C-Br > C-I

This ordering correlates with the electronegativity and atomic size of the halogens:

- Carbon-fluorine bonds are the strongest due to fluorine's high electronegativity and small size, allowing for effective orbital overlap.
- As atomic size increases down the halogen group, orbital overlap becomes less effective, and bond strength decreases.

Implications for Reactivity

The differences in carbon-halogen bond strengths have significant implications for the reactivity of these compounds:

1. **Nucleophilic Substitution (S™ 2 and S™ 1)**:
    - Alkyl halides readily undergo nucleophilic substitution due to their weaker C-X bonds and the accessibility of the ó* antibonding orbital.
    - Aryl halides are highly resistant to nucleophilic substitution under standard conditions due to their stronger C-X bonds, the steric hindrance provided by the aromatic ring, and the lack of accessibility to the ó* antibonding orbital.
    - Vinyl halides show intermediate reactivity but are generally resistant to standard nucleophilic substitution conditions.
2. **Elimination Reactions**:
    - Alkyl halides readily undergo elimination reactions (E1 and E2).
    - Aryl halides require special conditions, such as very strong bases (as in the benzyne mechanism), to undergo elimination.
    - Vinyl halides can undergo elimination but typically require stronger bases compared to alkyl halides.
3. **Reduction Reactions**:
    - The ease of reduction follows the order: Alkyl-X > Vinyl-X > Aryl-X, directly correlating with the inverse of bond strength.
4. **Metal-Catalyzed Coupling Reactions**:

- Aryl and vinyl halides participate effectively in various metal-catalyzed coupling reactions (Suzuki, Heck, Stille, etc.).
- In these reactions, the reactivity generally follows the order: Aryl-I > Aryl-Br > Aryl-Cl, reflecting the ease of oxidative addition which is inversely related to bond strength.

Role of Bond Strength in Reaction Mechanisms

The strength of the carbon-halogen bond plays a crucial role in determining the dominant reaction mechanisms for different classes of halogenated compounds:

1. **Alkyl Halides**:
   - Weaker C-X bonds and higher polarization favor both S™ 2 and S™ 1 mechanisms.
   - Primary alkyl halides typically react via S™ 2, while tertiary alkyl halides favor S™ 1.
2. **Aryl Halides**:
   - Stronger C-X bonds and resonance stabilization generally make conventional S™ 2 or S™ 1 mechanisms unfavorable.
   - Instead, these compounds often react via:
     - Ø Addition-elimination mechanisms (nucleophilic aromatic substitution) when strong electron-withdrawing groups are present at ortho/para positions
     - Ø Benzyne mechanisms with very strong bases
     - Ø Metal-catalyzed coupling reactions
3. **Vinyl Halides**:
   - Like aryl halides, vinyl halides are resistant to standard nucleophilic substitution.
   - They typically react via addition-elimination pathways or metal-catalyzed processes.

Activating and Deactivating Effects in Aryl Halides

The reactivity of aryl halides is significantly influenced by the electronic effects of the halogen substituent on the aromatic ring. Halogens exert both inductive and resonance effects, which have opposing influences on the reactivity of the aromatic system.

Inductive Effects

Halogens are electronegative elements that withdraw electron density through the sigma bond framework (inductive effect):

- This inductive withdrawal makes the aromatic ring electron-deficient.
- The strength of this effect decreases with distance and follows the electronegativity trend: F > Cl > Br > I.
- The electron-withdrawing inductive effect deactivates the aromatic ring toward electrophilic substitution.

Resonance Effects

Halogens possess lone pairs of electrons that can participate in resonance with the aromatic ð-system:

- This resonance donation of electron density enriches the ortho and para positions of the aromatic ring.
- The strength of this effect depends on the effective overlap between the halogen's p-orbitals and the aromatic ð-system.
- The resonance effect activates the aromatic ring toward electrophilic substitution, particularly at the ortho and para positions.

Net Effect on Electrophilic Aromatic Substitution

The net effect of halogen substituents on electrophilic aromatic substitution is:

- **Moderate Deactivation**: The inductive withdrawal slightly outweighs the resonance donation, making halobenzenes less reactive than benzene toward electrophilic substitution.

- **ortho/para Direction**: Despite the overall deactivation, the resonance effect directs incoming electrophiles primarily to the ortho and para positions.

This combination of moderate deactivation and ortho/para direction places halogens in a unique category among aromatic substituents.

Applications of Aryl Halides

Aryl halides find extensive applications in various fields due to their versatile reactivity and the valuable products that can be derived from them.

Synthetic Intermediates

Aryl halides serve as crucial intermediates in organic synthesis:

1. **Cross-Coupling Reactions**: Aryl halides are essential substrates for numerous metal-catalyzed cross-coupling reactions, including:
    - Suzuki-Miyaura coupling (with boronic acids)
    - Heck reaction (with alkenes)
    - Sonogashira coupling (with terminal alkynes)
    - Stille coupling (with organostannanes)
    - Negishi coupling (with organozinc compounds)
    - Buchwald-Hartwig amination (with amines)
2. **Grignard Reagent Formation**: Aryl halides can be converted to aryl Grignard reagents, which are versatile nucleophiles for carbon-carbon bond formation.
3. **Lithiation**: Aryl halides can undergo halogen-lithium exchange to form aryllithium compounds, which are highly reactive nucleophiles.

Industrial and Commercial Applications

1. **Pharmaceuticals**: Many pharmaceutical compounds contain aryl halide moieties or are synthesized using aryl halide intermediates.

2. **Agrochemicals**: Numerous pesticides, herbicides, and fungicides incorporate aryl halide structures.
3. **Polymers**: Chlorobenzene and its derivatives are used in the production of polymers like polychlorobiphenyls (PCBs) and polysulfones.
4. **Solvents**: Chlorobenzene serves as a solvent for various industrial processes, particularly those involving high-temperature reactions.
5. **Flame Retardants**: Brominated aryl compounds are widely used as flame retardants in various materials.

Environmental Considerations

Despite their utility, many aryl halides pose environmental concerns:

- **Persistence**: Many aryl halides, especially chlorinated and brominated compounds, are resistant to biodegradation.
- **Bioaccumulation**: Lipophilic aryl halides can accumulate in fatty tissues of organisms.
- **Toxicity**: Some aryl halides have been associated with various toxic effects, including endocrine disruption and carcinogenicity.

These concerns have led to increased regulation and the development of greener alternatives in many applications.

Analytical Methods for Aryl Halides

The identification and characterization of aryl halides involve various analytical techniques, which exploit their physical and chemical properties.

Spectroscopic Methods

1. **Infrared (IR) Spectroscopy**:
   - C-Hal stretching vibrations: C-F (1400-1000 cm{ ¹), C-Cl (800-600 cm{ ¹), C-Br (600-500 cm{ ¹), C-I (500-400 cm{ ¹)

- Characteristic aromatic C-H out-of-plane bending patterns that are affected by the halogen substitution pattern

2. **Nuclear Magnetic Resonance (NMR) Spectroscopy**:
   - ^{1}H-NMR: Halogen substituents cause deshielding of ortho protons due to their electronegativity
   - ^{13}C-NMR: Carbon atoms bearing halogens show characteristic chemical shifts
   - Coupling constants between protons in halogenated aromatic rings provide information about substitution patterns
3. **Mass Spectrometry (MS)**:
   - Distinctive isotope patterns due to the natural isotopic distribution of halogens (especially chlorine and bromine)
   - Fragmentation patterns often involve the loss of halogen radicals

Chemical Tests

1. **Beilstein Test**: Copper wire is heated in a flame, dipped in the sample, and reheated. A green flame indicates the presence of halogen.
2. **Silver Nitrate Test**: After fusion with sodium metal, the sample is extracted with water and treated with silver nitrate. Formation of a silver halide precipitate confirms the presence of a halogen.
3. **Reaction with Alcoholic KOH**: Different classes of halogenated compounds show varying reactivity with alcoholic KOH, helping to distinguish between aryl, vinyl, and alkyl halides.

Structurally different from other compoundsAril halides compose an interesting group of compounds with specific structural characteristics and reactivity patterns. Aromatic halogenation and the Sandmeyer reaction The preparation methods mentioned above (aromatic halogenation and the Sandmeyer reaction) illustrate distinct strategies for attaching halogen atoms to aromatic rings, one of which has certain proficiencies/ limitations. The aryl halides are known to be resistant to nucleophilic substitution;

however the benzyne mechanism reveals how they can participate in such reactions given the right set of circumstances. This mechanism highlights both the versatility of aryl halides in organic synthesis as well as how reaction conditions can significantly influence the pathways of reactions. The relative reactivities of different classes of halogenated compounds (aryl, vinyl and alkyl halides) can be understood by discussing carbon-halogen bond strengths. Aryl halides possess particularly strong carbon-halogen bonds, which benefit from their resonance interactions with the aromatic system, resulting in their unique chemical properties, such as their resilience towards traditional nucleophilic substitution pathways and their broad applications in metal-catalyzed coupling reactions.

In the context of electrophilic aromatic substitution reactions, the dual electronic effects of halogen substituents on aromatic rings include the electron-withdrawing inductive effect combined with the electron-donating resonance effect, that adds complexity to the chemistry of aryl halides as substituents. The chemistry of aryl halides is of not only theoretical significance, but also wide applications in pharmaceutical synthesis, material science, and industrial chemistry. While synthetic methodologies improve, aryl halides are timeless and significance building blocks in the hands of the organic chemist, allowing viable assembly of complex molecular structures through selective carbon–carbon and carbon–heteroatom bond formation.

Unit - 3 Alcohols

Monohydric Alcohols

Monohydric monohydric alcohols contain a single hydroxyl (-OH) group bonded to a saturated carbon atom. Their general formula is R-OH, where R is an alkyl group. These alcohols may then be classified as primary (1°), secondary (2°), or tertiary (3°) depending on the number of carbon atoms attached to the carbon atom which contains the hydroxyl group.

Nomenclature

Alcohols are named according to the IUPAC nomenclature by replacing the terminal "-e" (the final letter of the name of the alkane) with the suffix "-ol". A number prefix indicates the position of the hydroxyl group. Thus, we have CH*f* CH, OH being ethanol, CH*f* CH(OH)CH*f* being propan-2-ol (or isopropyl alcohol); and (CH*f*)*f*

COH being 2-methylpropan-2-ol (or tert-butyl alcohol). The common names of alcohols are given by naming the alkyl group, followed by alcohol. For example, CH*f* OH is methyl alcohol, CH*f* CH, OH is ethyl alcohol, and (CH*f*)*f* COH is tert-butyl alcohol.

Methods of Formation

1. **Hydration of Alkenes**: Alkenes react with water in the presence of acids like H, SO,, or H*f* PO,, to form alcohols. This reaction follows Markovnikov's rule, where the hydroxyl group attaches to the more substituted carbon atom.

2. CH, =CH, + H, O '! CH*f* CH, OH

3. **Hydrolysis of Alkyl Halides**: Alkyl halides undergo nucleophilic substitution when treated with aqueous NaOH or KOH to yield alcohols.

4. CH*f* CH, Br + NaOH '! CH*f* CH, OH + NaBr

5. **Reduction of Carbonyl Compounds**: Aldehydes and ketones can be reduced to alcohols using reducing agents like LiAlH,, , NaBH,, , or through catalytic hydrogenation.

6. CH*f* CHO + H, '! CH*f* CH, OH (primary alcohol)

7. CH*f* COCH*f* + H, '! CH*f* CH(OH)CH*f* (secondary alcohol)

8. **Grignard Reaction**: Alcohols can be synthesized by treating carbonyl compounds with Grignard reagents (RMgX) followed by hydrolysis.

9. HCHO + RMgX '! RCH, OH (primary alcohol)

10. RCHO + R'MgX '! RR'CHOH (secondary alcohol)

11. RCOR' + R"MgX '! RR'R"COH (tertiary alcohol)

12. **Reduction of Carboxylic Acids and Esters**: These compounds can be reduced to primary alcohols using powerful reducing agents like LiAlH,, .

13. RCOOH '! RCH, OH

14. RCOOR' '! RCH, OH + R'OH

15. **Oxymercuration-Demercuration**: This two-step process involves treating an alkene with mercuric acetate in water, followed by reduction with NaBH,, , resulting in Markovnikov addition.

16. CH, =CH, + Hg(OAc), /H, O '! CH*f* CH, OH

17. **Hydroboration-Oxidation**: This process involves the addition of borane to an alkene followed by oxidation with hydrogen peroxide, resulting in anti-Markovnikov addition.

18. CH, =CH, + BH*f* followed by H, O, /NaOH '! CH*f* CH, OH

Physical Properties

1. **Boiling Points**: Alcohols have higher boiling points compared to alkanes of similar molecular weight due to hydrogen bonding. The boiling points increase with increasing molecular weight within a homologous series.

2. **Solubility**: Lower alcohols (C -C*f*) are completely miscible with water due to hydrogen bonding. As the carbon chain length increases, solubility in water decreases while solubility in organic solvents increases.

3. **Density**: Most alcohols have densities slightly less than water, except methanol.

4. **Viscosity**: Alcohols have higher viscosities compared to corresponding alkanes due to hydrogen bonding.

Chemical Reactions

1. **Reaction with Active Metals**: Alcohols react with active metals like sodium and potassium to form alkoxides and hydrogen gas.

2. 2ROH + 2Na '! 2RONa + H,

3. **Reaction with Mineral Acids**: Alcohols react with HX (X = Cl, Br, I) to form alkyl halides.

4. ROH + HX '! RX + H, O

The reactivity order is 3° > 2° > 1° due to the stability of the carbocation intermediate.

5. **Dehydration**: When heated with concentrated H, SO,, or H*f* PO,, , alcohols undergo dehydration to form alkenes. The ease of dehydration follows: 3° > 2° > 1°.

6. ROH + Hz '! Rz + H, O '! Alkene + Hz

7. **Oxidation**: Alcohols can be oxidized to form carbonyl compounds.

   · Primary alcohols are oxidized to aldehydes and then to carboxylic acids using oxidizing agents like K, Cr, O‡ /H, SO,, or KMnO,, .

   · RCH, OH '! RCHO '! RCOOH

   · Secondary alcohols are oxidized to ketones.

   · R, CHOH '! R, CO

   · Tertiary alcohols resist oxidation under normal conditions due to the absence of a hydrogen atom on the carbon bearing the hydroxyl group.

8. **Esterification**: Alcohols react with carboxylic acids in the presence of a catalyst (usually concentrated H, SO,,) to form esters.

9. ROH + R'COOH Ì! R'COOR + H, O

10. **Reaction with PCl*f* , PCl… , and SOCl,** : These reagents convert alcohols to alkyl halides.

11. 3ROH + PCl*f* '! 3RCl + H*f* PO*f*

12. ROH + PCl… '! RCl + POCl*f* + HCl

13. ROH + SOCl, '! RCl + SO, + HCl

14. **Reaction with Carboxylic Acid Anhydrides and Acid Chlorides**: Alcohols react with these compounds to form esters.

15. ROH + R'COCl '! R'COOR + HCl

16. ROH + (R'CO), O '! R'COOR + R'COOH

Distinction Between Primary, Secondary, and Tertiary Alcohols

Several tests can be used to distinguish between primary, secondary, and tertiary alcohols:

1. **Lucas Test**: A mixture of concentrated HCl and ZnCl, (Lucas reagent) reacts differently with the three classes of alcohols:
   - Tertiary alcohols react immediately, forming a cloudy solution due to the formation of insoluble alkyl chlorides.
   - Secondary alcohols react within 5-10 minutes.
   - Primary alcohols (except benzyl and allyl alcohols) react very slowly or not at all at room temperature.
2. **Victor Meyer's Test**: This test involves treating the alcohol with a mixture of red phosphorus and iodine to form alkyl iodides, which are then hydrolyzed to form nitroalkanes.
   - Primary alcohols form primary nitroalkanes, which give a red color with sodium nitrite and dilute HCl.
   - Secondary alcohols form secondary nitroalkanes, which give a blue color.
   - Tertiary alcohols do not react.
3. **Oxidation Test**: Treatment with K, Cr, O‡ /H, SO,, or KMnO,, :
   - Primary alcohols are oxidized to aldehydes (which can be detected by Schiff's reagent) and then to carboxylic acids.
   - Secondary alcohols are oxidized to ketones.
   - Tertiary alcohols resist oxidation.
4. **Chromic Acid Test**: A solution of chromic anhydride in concentrated H, SO,, gives different color changes:

- Primary and secondary alcohols cause the orange solution to turn green due to the formation of chromium(III) ions.
- Tertiary alcohols show no color change.

5. **Dehydration Rate**: The ease of dehydration follows: 3° > 2° > 1°, which can be used as a distinguishing test.

Dihydric Alcohols (Glycols)

Dihydric alcohols, or glycols, contain two hydroxyl groups attached to different carbon atoms. The most common example is ethylene glycol (1,2-ethanediol).

Nomenclature

Dihydric alcohols are named by replacing the terminal "-e" of the corresponding alkane with "-diol" and indicating the positions of the hydroxyl groups using number prefixes. For example, HOCH, CH, OH is ethane-1,2-diol (ethylene glycol), and HOCH, CHOHCH, OH is propane-1,2,3-triol (glycerol).

Common names are often derived from the parent compounds. For instance, ethylene glycol derives its name from ethylene.

Methods of Formation of Ethylene Glycol

1. **From Ethylene**: Ethylene can be oxidized to ethylene oxide using oxygen or air in the presence of a silver catalyst, followed by hydrolysis of the oxide to ethylene glycol.

2. CH, =CH, + ½O, '! CH, -CH, '! HOCH, CH, OH

3. \O/

4. **From Epoxide**: Direct hydrolysis of ethylene oxide under acidic or basic conditions yields ethylene glycol.

5. CH, -CH, + H, O '! HOCH, CH, OH

6. \O/

7. **From Ethylene Dibromide**: Ethylene dibromide can be hydrolyzed with aqueous sodium or potassium hydroxide to form ethylene glycol.

8. BrCH, CH, Br + 2NaOH '! HOCH, CH, OH + 2NaBr

9. **From Ethylene Diamine**: Ethylene diamine can be treated with nitrous acid to form ethylene glycol.

10. H, NCH, CH, NH, + 2HNO, '! HOCH, CH, OH + 2N, + 2H, O

Chemical Reactions of Vicinal Glycols

1. **Reaction with Carbonyl Compounds**: Vicinal glycols react with carbonyl compounds like aldehydes and ketones to form cyclic acetals and ketals.

2. HOCH, CH, OH + O=CH, '! O-CH,

   |

   O-CH,

3. **Dehydration**: When heated with concentrated H, SO,, or P, O… , glycols undergo dehydration to form either aldehydes, ketones, or unsaturated alcohols, depending on the conditions.

4. HOCH, CH, OH '! CH, =CHOH '! CH*f* CHO

5. **Oxidative Cleavage with Lead Tetraacetate (Pb(OAc),,)**: Vicinal glycols undergo oxidative cleavage with Pb(OAc),, to form carbonyl compounds.

6. HOCH, CH, OH + Pb(OAc),, '! 2CH, O + Pb(OAc), + 2HOAc

7. **Oxidative Cleavage with Periodic Acid (HIO,,)**: Similar to lead tetraacetate, periodic acid cleaves vicinal glycols to form carbonyl compounds.

8. HOCH, CH, OH + HIO,, '! 2CH, O + HIO*f* + H, O

9. **Pinacol-Pinacolone Rearrangement**: This rearrangement involves the acid-catalyzed dehydration and rearrangement of vicinal diols, particularly 2,3-dimethyl-2,3-butanediol (pinacol), to form ketones.

10. CH*f* CH*f*

| |

CH*f* -C-OH | Hz CH*f* -C=O

| | ’! |

| | |

CH*f* -C-OH | CH*f* -C-CH*f*

| |

CH*f* CH*f*

(Pinacol) (Pinacolone)

Mechanism of Pinacol-Pinacolone Rearrangement:

a. Protonation of one of the hydroxyl groups:

CH*f* CH*f*

| |

CH*f* -C-OH | Hz CH*f* -C-OH, z

| | ’! |

| | |

CH*f* -C-OH | CH*f* -C-OH

| |

CH*f* CH*f*

b. Dehydration to form a carbocation:

CH*f* CH*f*

| |

CH*f* -C-OH, z | CH*f* -Cz

| | ’! |

| | |

CH*f* -C-OH | CH*f* -C-OH

| |

CH*f* CH*f*

c. Methyl migration to the electron-deficient carbon:

CH*f* CH*f*

| |

CH*f* -Cz | CH*f* -C=O

| | ’! |

| | |

CH*f* -C-OH | C-CH*f*

| |

CH*f* CH*f*

d. Deprotonation to form the final ketone product:

CH*f* CH*f*

| |

CH*f* -C=O | Hz CH*f* -C=O

| | ’! |

| | |

HC-CH*f* | CH*f* -C-CH*f*

| |

CH*f* CH*f*

Trihydric Alcohols

Trihydric alcohols contain three hydroxyl groups attached to different carbon atoms. The most common example is glycerol (propane-1,2,3-triol).

Nomenclature

Trihydric alcohols are named by replacing the terminal "-e" of the corresponding alkane with "-triol" and indicating the positions of the hydroxyl groups using number prefixes. For example, HOCH, CHOHCH, OH is propane-1,2,3-triol (glycerol).

Common names are often derived historically. For instance, glycerol derives its name from the Greek word "glykys," meaning sweet.

Methods of Formation of Glycerol

1. **Hydrolysis of Fats and Oils**: Glycerol is formed as a byproduct during the saponification of fats and oils (triglycerides) with alkalies like NaOH or KOH.
2. Triglyceride + 3NaOH '! 3RCOONa + Glycerol

3. **From Propene**: Propene can be chlorinated to form allyl chloride, which is then hydrolyzed to allyl alcohol. Subsequent oxidation with KMnO,, or OsO,, followed by reduction yields glycerol.
4. CH, =CHCH*f* '! CH, =CHCH, Cl '! CH, =CHCH, OH '! HOCH, CHOHCH, OH

5. **From Acrolein**: Acrolein (propenal) can be oxidized to form glyceraldehyde, which is then reduced to glycerol.
6. CH, =CHCHO '! HOCH, CHOHCHO '! HOCH, CHOHCH, OH

7. **Synthetic Methods**: Glycerol can be synthesized from propene by various industrial processes, including chlorination followed by hydrolysis, or epoxidation followed by hydrolysis.

Chemical Reactions of Glycerol

1. **Reaction with PCl…** : Glycerol reacts with phosphorus pentachloride to form trichloropropane.

2. HOCH, CHOHCH, OH + 3PCl… '! ClCH, CHClCH, Cl + 3POCl*f* + 3HCl

3. **Reaction with HI**: Glycerol reacts with hydroiodic acid to form propane or isopropyl iodide, depending on the conditions.

4. HOCH, CHOHCH, OH + 3HI '! CH*f* CH, CH*f* + 3I, + 3H, O

5. **Oxidation**: Glycerol can be oxidized to form various products depending on the oxidizing agent and conditions.

   · With dilute HNO*f* , glycerol is oxidized to glyceric acid.

6. HOCH, CHOHCH, OH + HNO*f* '! HOCH, CHOHCOOH + H, O

   · With KMnO,, , glycerol can be oxidized to tartronic acid or mesoxalic acid.

7. HOCH, CHOHCH, OH + KMnO,, '! HOOCCHOHCOOH

   · With biological oxidation, glycerol can be converted to pyruvic acid and then to lactic acid.

8. **Dehydration**: When heated with dehydrating agents like KHSO,, , glycerol can lose water to form acrolein.

9. HOCH, CHOHCH, OH '! CH, =CHCHO + 2H, O

10. **Nitration**: Glycerol reacts with concentrated nitric acid in the presence of concentrated sulfuric acid to form glyceryl trinitrate (nitroglycerin), a powerful explosive.

11. HOCH, CHOHCH, OH + 3HNO*f* '! (O, NO)CH, CH(ONO,)CH, (ONO,) + 3H, O

12. **Esterification**: Glycerol can be esterified with carboxylic acids to form mono-, di-, or triesters (glycerides).

13. HOCH, CHOHCH, OH + 3RCOOH '! RCOOCH, CH(OCOR)CH, OCOR + 3H, O

14. **Formation of Cyclic Acetals and Ketals**: Glycerol reacts with aldehydes and ketones to form cyclic acetals and ketals.

15. HOCH, CHOHCH, OH + O=CH, '! OCH,

|

O-CH,

|

CH, OH

Uses and Applications of Glycerol

1. **Pharmaceuticals and Cosmetics**: Glycerol is used as a solvent, sweetening agent, and moisturizer in pharmaceuticals and cosmetics.
2. **Food Industry**: It serves as a humectant, solvent, and sweetener in various food products.
3. **Explosives**: Glycerol is used to manufacture nitroglycerin, an explosive.
4. **Tobacco Industry**: It is used as a moistening agent in tobacco.
5. **Plastics**: Glycerol is a raw material for the synthesis of polyesters and alkyd resins.
6. **Antifreeze**: Due to its low freezing point, glycerol is used as an antifreeze in automotive applications.
7. **Lubricants**: It serves as a base for various lubricants.
8. **Textiles**: Glycerol is used in the textile industry for sizing and as a softening agent.

9. **Chemical Synthesis**: It is an important starting material for the synthesis of various chemicals.

10. **Medical Applications**: Glycerol is used in medical applications like suppositories, cough syrups, and as a vehicle for drug delivery.

In conclusion, alcohols represent a diverse and important class of organic compounds with wide-ranging applications in various industries. Their reactivity, determined by the presence of the hydroxyl group, allows them to participate in numerous chemical reactions, making them versatile starting materials for the synthesis of many other organic compounds. Understanding the structures, properties, and reactions of alcohols is essential for comprehending the broader landscape of organic chemistry.

Unit -4 Phenols

Phenols are organic compounds characterized by a hydroxyl (-OH) group attached directly to an aromatic ring. The simplest and most common phenol is hydroxybenzene, commonly referred to simply as "phenol." These compounds form an important class of organic substances with wide-ranging applications in synthetic chemistry, pharmaceuticals, and industrial processes. Their unique properties stem from the interaction between the hydroxyl group and the aromatic ring, creating distinctive chemical behaviors that differ significantly from both alcohols and aromatic hydrocarbons individually.

Nomenclature of Phenols

The naming of phenols follows systematic rules established by IUPAC (International Union of Pure and Applied Chemistry). For simple phenols, the parent compound hydroxybenzene is commonly called "phenol," while substituted phenols are named by indicating the position and identity of substituents on the aromatic ring.

When phenol acts as the parent structure, other substituents are named as prefixes, with their positions indicated by numbers. The carbon bearing the hydroxyl group is designated as C-1 (though this number is usually omitted in simple cases). For example, 2-methylphenol (also known by its common name, o-cresol) has a methyl group at position 2 relative to the hydroxyl group.

For dihydroxybenzenes, special common names are frequently used:

- 1,2-dihydroxybenzene is called catechol (or pyrocatechol)
- 1,3-dihydroxybenzene is known as resorcinol
- 1,4-dihydroxybenzene is referred to as hydroquinone (or quinol)

When the phenolic group is considered as a substituent on a more complex structure, it is named as a "phenol" or "hydroxyphenyl" group. For instance, 4-phenylphenol contains a phenyl group attached to position 4 of a phenol ring.

Common names persist in scientific literature for many phenolic compounds, particularly those with historical significance or industrial importance. Examples include cresols (methylphenols), xylenols (dimethylphenols), and thymol (2-isopropyl-5-methylphenol, found in thyme oil).

Methods of Formation of Phenols

Several synthetic routes are available for the preparation of phenols, each with specific advantages depending on the starting materials and desired product.

1. From Haloarenes (Dow Process)

One of the most important industrial methods involves the hydrolysis of aryl halides under harsh conditions. This reaction typically requires high temperature and pressure in the presence of copper catalysts:

ArX + NaOH '! ArOH + NaX

For example, chlorobenzene can be converted to phenol using sodium hydroxide at around 350°C and 300 atm pressure with copper catalysts. This process, known as the Dow process, is particularly valuable for industrial production.

2. From Diazonium Salts

Aromatic diazonium salts undergo hydrolysis in acidic conditions to yield phenols:

ArN, z X{ + H, O '! ArOH + N, + HX

This method is especially useful in laboratory-scale synthesis and allows for the introduction of a hydroxyl group at a specific position in the aromatic ring. The

diazonium salt itself is typically prepared from an aniline derivative through diazotization using nitrous acid (generated in situ from sodium nitrite and a mineral acid).

3. From Sulphonic Acids

Aromatic sulphonic acids can be converted to phenols by fusion with sodium hydroxide at high temperatures (300-350°C):

ArSO*f* H + 2NaOH '! ArONa + Na, SO*f* + H, O ArONa + HCl '! ArOH + NaCl

This method has historical significance and remains valuable for certain synthetic applications.

4. From Cumene (Industrial Method)

The cumene process is the predominant industrial method for phenol production. It involves the air oxidation of cumene (isopropylbenzene) to cumene hydroperoxide, followed by acid-catalyzed rearrangement to yield phenol and acetone:

C† H… CH(CH*f*), + O, '! C† H… C(OOH)(CH*f*), C† H… C(OOH)(CH*f*), + Hz '! C† H… OH + (CH*f*), CO

This process is economically advantageous as it produces two valuable industrial chemicals simultaneously.

5. From Benzene Sulphonic Acid

Benzene is first sulphonated with concentrated sulphuric acid to form benzene sulphonic acid, which is then fused with sodium hydroxide to yield sodium phenoxide. Acidification of sodium phenoxide produces phenol:

C† H† + H, SO,, '! C† H… SO*f* H + H, O C† H… SO*f* H + 2NaOH '! C† H… ONa + Na, SO*f* + H, O C† H… ONa + HCl '! C† H… OH + NaCl

6. From Grignard Reagents

Phenols can be synthesized by treating aryl magnesium halides (Grignard reagents) with oxygen, followed by acidification:

ArMgX + O, '! ArOOMgX ArOOMgX + Hz '! ArOH + Mg²z + X{

7. From Aryl Ethers (Cleavage Reactions)

Aryl alkyl ethers undergo cleavage with hydroiodic acid or hydrobromic acid to produce phenols:

ArOR + HI '! ArOH + RI

This reaction proceeds through nucleophilic attack at the alkyl carbon, with the weaker phenol being a better leaving group than the alkoxide.

Physical Properties of Phenols

Phenols exhibit distinctive physical characteristics that reflect the influence of both the aromatic ring and the hydroxyl group.

State and Appearance

The simplest phenol (hydroxybenzene) is a colorless crystalline solid, which possesses a noticeably medicinal odor at room temperature. Most simple substituted phenols are crystalline solids, although some of the lower molecular weight compounds will be liquids. Many phenols darken when they are exposed to air and light because of oxidation.

Melting and Boiling Points

Due to hydrogen bonding between the hydroxyl groups, phenols engage in intermolecular hydrogen bonding, confer high melting and boiling points relative to similarly sized hydrocarbons. As an example, phenol (C† H… OH) melts at 40.5°C and boils at 181.7°C, much higher than toluene (C† H… CH*f*), which has an analogous molecular weight, but has a melting point of -95°C and a boiling point of 110.6°C. This ability to form hydrogen bonds is so strong that it makes the physical properties of phenols more like those of alcohols than aromatic hydrocarbons in some ways. Their boiling points are generally higher than comparable size alcohols due to additional ð-ð interactions between aromatic rings.

Solubility

The hydroxyl group of phenols imparts some water solubility to these compounds by hydrogen bonding to water molecules. Simple phenols, such as phenol, are moderately

soluble in water (albeit much less so than alcohols, with about 8.3 g/100 mL for phenol at 20 °C). This solubility decreases as the size of the hydrophobic portion of the molecule increases. Phenols are also soluble in alcohols, ethers, and most organic solvents; this is because of their ability to form hydrogen bonds with these molecules and because non-polar environments are tolerated by the aromatic ring. One interesting property of phenols is that they are much more soluble in aqueous sodium hydroxide than in plain water, the reason being that phenoxide ions, which are formed by deprotonation of the hydroxy group, are more water-soluble than the neutral species (phenol molecules).

Hydrogen Bonding

The hydroxyl ("OH) group of phenols can undergo hydrogen bonding both with other phenol molecules (intermolecular) and with appropriate acceptors. Hydrogen bonding is responsible for the fairly high melting and boiling points of phenols, as well their solubility behavior. Since phenols are aromatic compounds, this causes a decrease in the electron density on the hydroxyl oxygen, leading to somewhat weaker hydrogen bonding compared to alcohols.

Spectroscopic Properties

In the infrared spectrum, phenols exhibit a characteristic O-H stretching band at the higher end of about 3500–3600 cm{ ¹ that is much broader than that of alcohols due to stronger hydrogen-bonding interactions. The C-O stretching of the aromatic appears at approximately 1230-1250 cm{ ¹. In ¹H NMR spectroscopy, phenolic hydroxyl protons usually appear as singlets in the region of 4-7 ppm, though their position varies broadly with concentration, solvent, and temperature because of hydrogen bonding effects. Aromatic protons resonate between 6.5 to 7.5 ppm, in coupling patterns that mirror substitution on the ring.

Acidic Character of Phenols

Phenols are more acidic compared to alcohols which is one of their most unique functional characteristics. Although now the alcohols are very neutral compounds (pKa H" 16-19), the phenols are weak acids with pKa values of about 9 to 11.

Phenol is a structure above ethanol that has a pKa on the order of about 10 so phenol is something like a 10^6 times more acidic than ethanol.

Factors Affecting Acidity

These factors could include(r) the increased acidity of phenols:

Electronics of the Aromatic Ring: the benzene ring is electron-withdrawing compared to an alkyl group, facilitating the stabilization of the negative charge on the deprotonated phenoxide ion.

Hybridization effect: The oxygen atom of phenol is sp^2 hybridized as it is joined to the aromatic ring by resonance, while the oxygen in alcohol is sp^3 hybridized. With more s-character, the sp^2 hybridized orbital brings electrons closer to the nucleus, allowing them less availability for bonding with hydrogen and making the O-H bond weaker. Resonance Stabilization of the Phenoxide Ion: By far the most important factor contributing to the increased acidity of phenols is the ability of the phenoxide ion to delocalize the negative charge by resonance with the aromatic ring.

Comparative Acidity

Phenols are intermediate in acidity between alcohols and carboxylic acids. The fact that phenols are only weakly acidic means that they react with more strongly basic compounds; both sodium hydroxide or sodium hydride can be reacted, with phenoxide salts created instead, but, unlike carboxylic acids, weaker bases like sodium bicarbonate do not react with them.

The acidity of phenols is also sufficient for them to react with aqueous sodium hydroxide, forming water-soluble phenoxide salts:

C† H… OH + NaOH '! C† H… O{ Naz + H, O

This reaction is reversible, and acidification of phenoxide salts regenerates the phenol:

C† H… O{ Naz + HCl '! C† H… OH + NaCl

Effect of Substituents on Acidity

The acidity of phenols is significantly influenced by substituents on the aromatic ring:

1. **Electron-withdrawing groups** (e.g., -NO, , -CN, -COOH, -CHO) increase acidity by stabilizing the phenoxide ion through inductive and/or resonance effects. For example, p-nitrophenol (pKa H" 7.15) is considerably more acidic than phenol (pKa H" 10).

2. **Electron-donating groups** (e.g., -CH*f* , -OCH*f* , -NH,) decrease acidity by destabilizing the phenoxide ion. For instance, p-cresol (pKa H" 10.3) is slightly less acidic than phenol.

3. **Position of substituents** affects the acidity, with the effect being generally strongest for para and ortho positions due to direct resonance interactions with the phenoxide oxygen.

Multiple substituents can have cumulative effects. For example, 2,4,6-trinitrophenol (picric acid) is highly acidic (pKa H" 0.25) due to the strong electron-withdrawing effect of three nitro groups.

Practical Applications of Phenol Acidity

The acidic character of phenols has several practical implications:

1. **Extraction and Purification**: The ability of phenols to form water-soluble salts with bases allows for their separation from non-acidic organic compounds through extraction techniques.

2. **Analytical Chemistry**: The acidity of phenols makes them useful as acid-base indicators in certain pH ranges.

3. **Synthetic Chemistry**: The phenoxide ion is a good nucleophile, enabling various substitution and condensation reactions useful in organic synthesis.

4. **Material Science**: The acidic hydroxyl group in phenols allows for the formation of various polymers like phenol-formaldehyde resins (Bakelite).

Resonance Stabilization of Phenoxide Ion

Their greater acidity to alcohols is due in part to the better stability of the phenoxide ion (C† H… O{) than of any alkoxide ions. This stability comes mainly from the resonance delocalization of the negative charge.

Resonance Structures

When phenol loses proton it forms phenoxide ion which is very much resonance stabilized. The negative charge on the oxygen atom is delocalized into the aromatic ring via conjugation, allowing the charge to be spread over multiple atoms, thus stabilizing the compound.

In this case, the resonance structures of the phenoxide ion are:

The negative charge is found on an oxygen atom in the primary resonance structure. When you are adding the resonance structures it can dois so that the -ve charge is delocalized in the ortho and para (positions 2, 4 and 6 respectively of the aromatic ring.

The negative charge is transferred to one of the sp-carbons, and pi-electrons are re-distributed to maintain aromatic sextet character, thus generating additional resonance structures. and the primary structure (oxygen having charge) making the most important contribution to it, since the real electronic structure of the phenoxide ion is actually a weighted average of all of these resonance structures.

Evidence for Resonance Stabilization

Several experimental observations support the resonance stabilization of the phenoxide ion:

1. **Acidity Measurements**: The significantly higher acidity of phenols compared to alcohols (by a factor of approximately 10v) cannot be explained by inductive effects alone and provides strong evidence for resonance stabilization.
2. **Spectroscopic Data**: UV-visible spectroscopy shows that phenoxide ions absorb at longer wavelengths than phenols, indicating extended conjugation.
3. **X-ray Crystallography**: Structural studies of phenoxide salts reveal C-O bond lengths intermediate between typical single and double bonds, consistent with partial double bond character due to resonance.

4. **Substituent Effects**: The influence of ring substituents on acidity correlates well with their expected effects on resonance stabilization. For example, electron-withdrawing groups at para positions greatly enhance acidity by stabilizing the negative charge through resonance.

Quantitative Aspects of Stabilization

The resonance stabilization energy of the phenoxide ion has been estimated to be approximately 20-25 kcal/mol. This substantial stabilization explains why phenols can be deprotonated by bases like sodium hydroxide, while alcohols cannot.

The extent of charge delocalization is not uniform across all carbon atoms of the ring. Calculations and experimental evidence indicate that the negative charge density is highest at the oxygen atom, followed by the ortho and para positions. The meta positions (3 and 5) have relatively little negative charge density because they cannot participate directly in resonance with the oxygen atom.

Implications of Resonance Stabilization

The resonance stabilization of phenoxide ions has several important implications:

1. **Regioselectivity in Reactions**: Electrophilic aromatic substitution in phenols occurs preferentially at ortho and para positions due to the enhanced electron density at these sites in both phenol and its conjugate base.

2. **Enhanced Nucleophilicity**: The phenoxide ion is a stronger nucleophile than comparable alkoxide ions in reactions at carbon centers, though the oxygen atom itself may be less nucleophilic due to delocalization of its electron pair.

3. **Colorimetric Applications**: Many phenols form intensely colored complexes with iron(III) ions due to the ability of the phenoxide to coordinate with the metal through resonance-stabilized structures. This property is the basis for colorimetric tests for phenols.

4. **Biological Activity**: Many biological systems utilize phenolic compounds as antioxidants because the phenoxide ion formed after hydrogen atom abstraction is stabilized by resonance, making phenols effective radical scavengers.

Phenols are an interesting group of organic compounds in which a phenolic hydroxyl group interacts with an aromatic ring to define a specific chemical property. Their nomenclature adheres to systematic IUPAC rules but retains historically significant common names. There are many synthetic routes to form phenolic structures for applications in forest products, pesticides, plastics, and pharma; however, the cumene process is the industrial method of choice. The aromatic nature of phenols and hydrogen-bonding capacity are also reflected in their physical properties, which result in unusual solubility trends and higher melting and boiling points. The acidic character of phenols, however, is what sets them apart from alcohols, making them useful reagents in organic synthesis and other practical applications. The higher acidity of phenols is due to, among others, the resonance stabilization of the phenoxide ion. This stabilization, by delocalizing the negative charge over the aromatic system is a clear representation of a fundamental tenet of organic chemistry: that delocalization of charge or electron density tends to lead to greater stability. These types of resonance effects can help predict and explain chemistry as the formation of stable phenoxide ions can lead to many reactions and applications not possible using simple alcohols. Due to their unique chemical properties, phenols are still used widely in industry, ranging from drug development to polymer synthesis, highlighting the importance of this class of organic compound.

Acidic Strength of Alcohols and Phenols — Comparison

Both alcohols and phenols are important classes of organic compounds including the hydroxyl (-OH) functional group, but they have very different acidities. Such an inconsistency is based on their structure differences and the electronic environments around the hydroxyl group.

Structural Comparison

Alcohols contain an -OH group attached to an sp^3 hybridized aliphatic carbon atom, while phenols feature an -OH group directly bonded to an sp^2 hybridized carbon atom of an aromatic ring. This fundamental structural difference creates significant disparities in their chemical behavior, particularly their acidic properties.

Quantitative Acid Strength Comparison

The acid dissociation constant (Ka) provides a quantitative measure of acid strength. Phenols are considerably stronger acids than alcohols:

- Typical pKa values for phenols: 9-10
- Typical pKa values for alcohols: 16-19

This difference of approximately 7-9 pKa units represents a significant gap in acid strength, with phenols being 10w -10y times more acidic than alcohols.

Factors Influencing Acidic Strength

1. Resonance Stabilization

The primary factor for phenol's enhanced acidity is resonance stabilization of its conjugate base, the phenoxide ion. When phenol loses a proton, the resulting negative charge delocalizes throughout the aromatic ring through multiple resonance structures:

- The negative charge distributes across the ortho and para positions of the ring.
- This charge delocalization stabilizes the phenoxide ion, lowering its energy.
- Lower energy of the conjugate base drives the equilibrium toward dissociation.

In contrast, alkoxide ions from alcohols lack this resonance stabilization. The negative charge remains concentrated on the oxygen atom, making the conjugate base less stable and the deprotonation less favorable.

2. Inductive Effects

Electronegative substituents affect the acidic strength through the inductive effect:

- Electron-withdrawing groups increase acidity by stabilizing the negative charge.
- Electron-donating groups decrease acidity by destabilizing the negative charge.

Examples in phenols:

- p-nitrophenol (pKa H" 7.2) is more acidic than phenol (pKa H" 10) due to the electron-withdrawing nitro group.

- p-cresol (pKa H" 10.3) is slightly less acidic than phenol due to the electron-donating methyl group.

Examples in alcohols:

- 2,2,2-trifluoroethanol (pKa H" 12.5) is more acidic than ethanol (pKa H" 16) due to the electron-withdrawing fluorine atoms.
- tert-butanol (pKa H" 18) is slightly less acidic than ethanol due to the electron-donating alkyl groups.

3. Hybridization Effects

The hybridization of the carbon atom attached to the hydroxyl group affects acidity:

- The sp^2 hybridized carbon in phenols has more s-character (33.3%) than the sp^3 hybridized carbon in alcohols (25%).
- Greater s-character makes the C-O bond more polarized, facilitating proton removal.
- This hybridization effect contributes to phenol's higher acidity but is secondary to the resonance effect.

4. Position and Nature of Substituents

For substituted phenols, both the position and nature of substituents impact acidity:

- Ortho-substituted phenols often show anomalous behavior due to steric effects and potential hydrogen bonding.
- Para-substituted phenols demonstrate more predictable electronic effects.
- Meta-substitution has a primarily inductive effect with minimal resonance contribution.

The Hammett equation quantifies these substituent effects, allowing prediction of acidity changes based on substituent constants.

Acidity Trends Within Groups

Trend Among Alcohols:

Primary > Secondary > Tertiary

This subtle trend is explained by:

- Increasing alkyl substitution provides greater electron density to the oxygen atom.
- Greater electron density destabilizes the alkoxide ion, decreasing acidity.
- However, these differences are relatively minor (typically less than 1 pKa unit).

Trend among Phenols Based on Substituents:

Polynitrophenols > Nitrophenols > Halophenols > Phenol > Alkylphenols

This more pronounced trend reflects the significant impact of substituents on the stability of the phenoxide ion.

Chemical Consequences of Acidity Differences

The substantial acidity difference leads to distinct chemical behaviors:

1. **Base Reactivity**: Phenols react with weak bases like NaOH and Na, CO*f* , while alcohols typically require stronger bases like sodium metal or sodium hydride.
2. **Nucleophilicity**: Phenoxide ions are weaker nucleophiles than alkoxide ions due to resonance delocalization of the negative charge.
3. **Hydrogen Bonding**: Phenols form stronger hydrogen bonds than alcohols, affecting physical properties like boiling points and solubility.
4. **Biological Activity**: Many phenolic compounds act as weak acids in biological systems, participating in important biochemical processes where alcohols cannot.

The comparative understanding of these acidic properties provides the foundation for predicting reactivity patterns and designing synthetic pathways involving these important functional groups.

Electrophilic Aromatic Substitution, Acetylation, and Carboxylation

Electrophilic Aromatic Substitution: Fundamental Mechanism

Electrophilic aromatic substitution (EAS) represents one of the most important reaction classes for functionalizing aromatic compounds. These reactions follow a general mechanism consisting of two primary steps:

Step 1: Electrophilic Attack and Formation of Arenium Ion

- The ð-electrons of the aromatic ring attack an electrophile (Ez).
- This forms a resonance-stabilized carbocation intermediate called the sigma complex or arenium ion.
- This step disrupts aromaticity, creating a high-energy intermediate.
- The intermediate has three significant resonance structures, distributing the positive charge at ortho and para positions.

Step 2: Deprotonation and Rearomatization

- Base-mediated removal of a proton from the sp^3 hybridized carbon.
- Restoration of aromaticity by reforming the ð-system.
- This step is typically fast and energetically favorable.

The rate-determining step is usually the formation of the sigma complex, which depends on both the nucleophilicity of the aromatic ring and the reactivity of the electrophile.

Directing Effects in Electrophilic Aromatic Substitution

Substituents already present on the aromatic ring significantly influence the reaction outcome:

Activating Groups (Electron-Donating)

- Groups like -OH, -NH, , -NHR, -NR, , -OR, and -R.
- Increase electron density in the ring, enhancing reactivity toward electrophiles.
- Direct substitution primarily to ortho and para positions through resonance stabilization of the intermediate.

Deactivating Groups (Electron-Withdrawing)

- Groups like -NO, , -CN, -SOf H, -CHO, -COR, -COOH, and halogens (except for directing effects).
- Decrease electron density in the ring, reducing reactivity.
- Most direct substitution to meta position due to destabilization of ortho/para intermediates.

Special Case: Halogens

- Deactivating through inductive effects but ortho/para directing through resonance.
- This dual nature makes them unique among substituents.

Acetylation: Friedel-Crafts Acylation

Acetylation introduces an acetyl group (COCHf) onto an aromatic ring through the Friedel-Crafts acylation reaction.

Mechanism of Friedel-Crafts Acetylation:

1. **Activation of Acylating Agent**:
    - Lewis acid (typically AlClf) coordinates to the carbonyl oxygen of acetyl chloride or acetic anhydride.
    - This coordination enhances the electrophilicity of the carbonyl carbon.
    - Formation of the acylium ion (CHf COz) as the active electrophile.
2. **Electrophilic Attack**:
    - The aromatic ð-system attacks the acylium ion.
    - Formation of a resonance-stabilized sigma complex.
3. **Deprotonation and Rearomatization**:
    - Loss of a proton from the sigma complex.
    - Regeneration of aromaticity, yielding the acetylated product.
    - Release of HCl and regeneration of the Lewis acid catalyst.

Key Features of Acetylation:

1. **Self-Limiting Nature**:
   - Unlike alkylation, acetylation is typically mono-selective.
   - The introduced acetyl group deactivates the ring toward further substitution.
   - This prevents polysubstitution, a common problem in Friedel-Crafts alkylation.
2. **Substrate Limitations**:
   - Requires moderately to highly activated aromatic rings.
   - Does not work with strongly deactivated systems like nitrobenzene.
   - Fails with substrates containing strong Lewis basic sites that would deactivate the catalyst.
3. **Regioselectivity**:
   - Follows standard directing effects of existing substituents.
   - Preferentially occurs at positions of highest electron density.
4. **Practical Applications**:
   - Production of acetophenone derivatives for fragrances.
   - Synthesis of pharmaceutical intermediates.
   - Preparation of acetylsalicylic acid (aspirin) from salicylic acid.

Carboxylation: Introduction of Carboxyl Groups

Carboxylation introduces a carboxyl group (-COOH) to aromatic rings, primarily through the Kolbe-Schmitt reaction.

Kolbe-Schmitt Reaction Mechanism:

1. **Formation of Phenoxide**:

- Treatment of phenol with a strong base (typically NaOH) generates sodium phenoxide.
- The phenoxide ion has enhanced nucleophilicity compared to phenol.

2. **CO, Coordination and Attack**:
   - Carbon dioxide coordinates with the phenoxide oxygen.
   - The ortho or para position of the aromatic ring attacks the electrophilic carbon of CO_2.
   - Formation of a cyclic transition state that guides the regioselectivity.
3. **Rearrangement and Protonation**:
   - Rearrangement of the initial adduct.
   - Acidification during workup protonates the carboxylate salt to form the carboxylic acid.

Distinctive Features of the Kolbe-Schmitt Reaction:

1. **Unusual Regioselectivity**:
   - Predominantly yields ortho-hydroxybenzoic acid (salicylic acid).
   - This contrasts with typical ortho/para directing effects, where para products often predominate due to reduced steric hindrance.
   - The ortho selectivity is attributed to the coordination between the phenoxide oxygen and CO_2, creating a guided delivery mechanism.
2. **Reaction Conditions**:
   - Typically requires elevated temperature (125-140°C) and pressure.
   - Often performed in autoclaves with sodium bicarbonate or sodium carbonate.
   - Industrially important for the synthesis of salicylic acid, a precursor to aspirin.

3. **Substrate Scope**:
   - Limited primarily to phenols and activated derivatives.
   - Alkylphenols and naphthols also undergo the reaction with varying efficiency.
4. **Modern Variations**:
   - Catalytic versions using transition metals.
   - Microwave-assisted protocols for accelerated reaction rates.
   - Flow chemistry adaptations for industrial scale-up.

Comparative Analysis and Synthetic Utility

Both acetylation and carboxylation provide valuable methods for functionalizing aromatic rings:

1. **Electrophile Nature**:
   - Acetylation uses a discrete, highly reactive acylium ion.
   - Carboxylation employs CO, , a milder electrophile requiring more nucleophilic substrates.
2. **Catalyst Requirements**:
   - Acetylation requires stoichiometric or catalytic Lewis acids.
   - Carboxylation typically needs basic conditions without additional catalysts.
3. **Product Utility**:
   - Acetylation yields ketones useful in fragrance chemistry and as synthetic intermediates.
   - Carboxylation produces carboxylic acids valuable in pharmaceutical synthesis, particularly for anti-inflammatory drugs.
4. **Green Chemistry Considerations**:

- Modern adaptations of both reactions focus on catalyst recyclability, reduced waste, and energy efficiency.
- Carboxylation has gained attention for carbon capture applications, utilizing CO, as a renewable C1 source.

Understanding these electrophilic aromatic substitution pathways provides essential tools for strategic functionalization of aromatic compounds in complex organic synthesis.

Mechanism of Fries Rearrangement, Claisen Rearrangement, and Reimer-Tiemann Reaction

Fries Rearrangement

The Fries rearrangement is a Lewis acid-catalyzed transformation that converts phenolic esters to hydroxyaryl ketones. This reaction provides a valuable synthetic route to ortho- and para-hydroxyphenyl ketones, important intermediates in pharmaceutical and fine chemical synthesis.

Detailed Mechanism:

1. **Lewis Acid Coordination**:
   - Aluminum chloride (AlCl*f*) coordinates to the carbonyl oxygen of the phenyl ester.
   - This complexation enhances the electrophilicity of the carbonyl carbon.
   - The coordination weakens the acyl-oxygen bond, facilitating subsequent steps.
2. **C-O Bond Cleavage**:
   - The acyl-oxygen bond breaks heterolytically.
   - This generates an acylium ion (R-C=Oz) and a phenolic aluminum complex.
   - The strength of the Lewis acid and reaction conditions influence the extent of this dissociation.

3. **Electrophilic Attack**:
    - The acylium ion functions as an electrophile.
    - It attacks the aromatic ring, primarily at ortho or para positions.
    - This forms a resonance-stabilized ó-complex (arenium ion).
4. **Deprotonation and Rearomatization**:
    - Loss of a proton from the ó-complex restores aromaticity.
    - The aluminum complex is cleaved during aqueous workup.
    - This yields the final hydroxyaryl ketone product.

Regioselectivity Factors:

The Fries rearrangement exhibits interesting regioselectivity patterns:

1. **Temperature Effects**:
    - Lower temperatures (60-80°C) typically favor ortho-substitution.
    - Higher temperatures (150-200°C) generally favor para-substitution.
    - This temperature dependence suggests different mechanistic pathways.
2. **Mechanistic Implications**:
    - **Intramolecular Pathway**: At lower temperatures, the acylium ion may remain loosely associated with the phenolic oxygen through the aluminum complex, directing attack to the ortho position. This represents a directed delivery mechanism.
    - **Intermolecular Pathway**: At higher temperatures, complete dissociation allows the acylium ion to attack the most electron-rich position (typically para) without directional constraints.
3. **Substrate Effects**:

- Electron-donating substituents enhance reactivity and influence regioselectivity.
- Steric factors can override electronic preferences, particularly for ortho-substitution.
- Pre-existing substituents direct the incoming acyl group according to standard directing effects.

Variations and Applications:

1. **Photo-Fries Rearrangement**:
   - UV irradiation induces homolytic cleavage of the acyl-oxygen bond.
   - Proceeds through radical intermediates rather than ionic species.
   - Often provides different product distributions than thermal Fries rearrangement.
2. **Catalytic Variations**:
   - Modern developments include catalytic variants using substoichiometric Lewis acids.
   - Solid-supported catalysts facilitate easier purification and potential recycling.
   - Metal triflates and other strong Lewis acids can provide enhanced selectivity.
3. **Synthetic Applications**:
   - Synthesis of anti-inflammatory agents like fenbufen.
   - Preparation of UV stabilizers for polymers.
   - Production of agrochemical intermediates.

Claisen Rearrangement

The Claisen rearrangement is a [3,3]-sigmatropic rearrangement that converts allyl phenyl ethers to ortho-allylphenols. Unlike the Fries rearrangement, it proceeds through a concerted pericyclic mechanism without requiring external catalysts.

Detailed Mechanism:

1. **Conformational Alignment**:
   - The allyl phenyl ether adopts a conformation aligning the allyl ð-system parallel to the aromatic ð-orbitals.
   - This arrangement facilitates optimal orbital overlap in the transition state.
   - The conformational adjustment establishes the stereochemical course of the reaction.
2. **Concerted Rearrangement**:
   - A concerted [3,3]-sigmatropic shift occurs through a cyclic six-membered transition state.
   - The C-O bond breaks as a new C-C bond forms between the allyl terminus and the ortho position.
   - Electron redistribution maintains the proper bond count throughout the process.
3. **Dienone Formation and Tautomerization**:
   - The initial product is a cyclohexadienone intermediate.
   - This intermediate rapidly tautomerizes to the more stable ortho-allylphenol.
   - The tautomerization restores aromaticity, providing a significant driving force.

Key Characteristics:

1. **Thermal Requirement**:

- Typically requires elevated temperatures (150-200°C) to overcome the activation barrier.
- The high energy requirement reflects the temporary loss of aromaticity in the transition state.
- Modern modifications employ microwave irradiation or metal catalysts to accelerate the process.

2. **Stereochemical Aspects**:
   - The reaction proceeds with high stereoselectivity.
   - Chirality in the allyl group is preserved through a suprafacial process.
   - This stereospecificity makes the Claisen rearrangement valuable for stereoselective synthesis.
3. **Solvent Effects**:
   - Polar solvents generally accelerate the reaction by stabilizing the polar transition state.
   - Hydrogen-bonding solvents can influence the equilibrium between the dienone intermediate and the final phenolic product.
   - High-pressure conditions can enhance reaction rates by favoring the more compact transition state.

Variations and Related Rearrangements:

1. **Aromatic Claisen vs. Aliphatic Claisen**:
   - The aromatic Claisen applies specifically to allyl phenyl ethers.
   - The aliphatic Claisen involves allyl vinyl ethers, yielding ã,ä-unsaturated carbonyl compounds.
2. **Ortho-Claisen vs. Para-Claisen**:
   - The standard outcome is ortho-substitution (ortho-Claisen).

- In certain blocked substrates, para-migration can occur (para-Claisen), though with higher activation energy.

3. **Related Rearrangements**:

   - **Cope Rearrangement**: Similar [3,3]-sigmatropic shift involving 1,5-dienes.
   - **Johnson-Claisen**: Uses orthoester reagents to generate the requisite allyl vinyl ether in situ.
   - **Ireland-Claisen**: Applies to allyl esters via silyl ketene acetal intermediates.

SELF ASSESSMENT QUESTIONS

Multiple Choice Questions (MCQs)

1. What type of reaction is Williamson's ether synthesis?

a) Electrophilic substitution

b) Nucleophilic substitution

c) Free radical reaction

d) Elimination reaction

2. The SN2 reaction is favored by:

a) Weak nucleophiles

b) Sterically hindered substrates

c) Polar aprotic solvents

d) Carbocation stability

3. What is the major product when chlorobenzene reacts with $NaNH_2$ in liquid ammonia?

a) Benzylamine

b) Phenol

c) Aniline

d) Benzyne

4. The oxidation of primary alcohols yields:

a) Ketones

b) Aldehydes

c) Esters

d) Ethers

5. Phenols exhibit higher acidity than alcohols due to:

a) Inductive effect

b) Resonance stabilization

c) Hyperconjugation

d) Steric hindrance

6. Which reagent is used in the Reimer-Tiemann reaction?

a) ZnCl,

b) Chloroform and NaOH

c) KMnO,,

d) PCl…

7. Which alcohol undergoes the fastest reaction in Lucas test?

a) Primary alcohol

b) Secondary alcohol

c) Tertiary alcohol

d) Dihydric alcohol

8. The Pinacol-Pinacolone rearrangement involves:

a) Dehydration of alcohol

b) Rearrangement of glycol

c) Formation of ester

d) None of the above

9. The most reactive compound in SN1 reaction is:

a) Methyl chloride

b) Benzyl chloride

c) Ethyl chloride

d) Vinyl chloride

10. The Fries rearrangement is used to prepare:

a) Ketones

b) Aldehydes

c) Hydroxy aryl ketones

d) Alcohols

Short Answer Questions

1. Define SN1 and SN2 reactions with examples.
2. What is the effect of solvent on SN2 reactions?
3. Explain the acidic nature of phenols compared to alcohols.
4. Write the mechanism of the Reimer-Tiemann reaction.
5. Why do tertiary alcohols react faster with Lucas reagent?
6. Differentiate between Williamson's ether synthesis and nucleophilic substitution.
7. What is the role of $NaNH_2$ in the Benzyne mechanism?

8. Explain the structure and bonding in phenoxide ion.
9. How does the presence of electron-withdrawing groups affect the acidity of phenols?
10. What are the key differences between electrophilic and nucleophilic substitution reactions?

Long Answer Questions

1. Explain in detail the SN1 and SN2 reaction mechanisms with suitable examples.
2. Describe the methods of preparation of alcohols and their physical and chemical properties.
3. Write a detailed note on the electrophilic substitution reactions of phenol.
4. Discuss the mechanisms of Fries rearrangement, Claisen rearrangement, and Reimer-Tiemann reaction.
5. Explain the concept of resonance stabilization in phenols and phenoxide ions.
6. Compare and contrast the acidic strength of alcohols and phenols with experimental evidence.
7. Describe the method of preparation and properties of dihydric and trihydric alcohols.
8. Explain the oxidation reactions of alcohols and their industrial importance.
9. Discuss the role of solvents in nucleophilic substitution reactions.
10. Explain the factors affecting the reactivity of alkyl and aryl halides in substitution reactions.

MODULE- 2

ALDEHYDES, KETONES, AND ACIDS & THEIR DERIVATIVES

2.0 Objective

- Understand the nomenclature and structure of aldehydes, ketones, carboxylic acids, and their derivatives.
- Learn about the acidity of á-hydrogens and the concept of enolate formation.
- Study the preparation and reactions of aldehydes, ketones, and carboxylic acids.
- Explore important reactions like Cannizzaro, Perkin, and Wittig reactions.

Unit -5 Aldehydes & Ketones

The class of organic compounds known as aldehydes and ketones is defined by the presence of a carbonyl group. The distinguishing feature that underpins the physical properties and chemical reactivity of these compounds is the carbonyl functionality, wherein a carbon atom is double-bonded to an oxygen atom. The carbonyl group possesses unique properties due to its polarity and reactivity toward nucleophiles, establishing aldehydes and ketones as crucial intermediates in organic synthesis and biochemical pathways. The general properties of aldehydes and ketones are covered in this segment, along with their naming, structure and synthesis as well as the acidity of alpha hydrogens, the ways to generate enolates and important oxidation-reduction reactions we hope to see.

Carbonyl Group: Nomenclature and Structure

Aldehydes and ketones are characterized by the carbonyl group (C=O), which is a carbon atom connected to an oxygen atom through a double bond. This structural configuration gives rise to a planar disposition around the carbonyl carbon, with bond angles approaching 120° in line with sp2 hybridization. Because of the electronegativity difference between carbon and oxygen, a carbon-oxygen double bond is very polar and leads to partial positive charge on the carbon and partial

negative charge on the oxygen. That polarization is key to reactivity of the carbonyl group, especially it's ability to undergo nucleophilic addition reactions. In aldehydes, there is at least one hydrogen atom bonded to the carbonyl carbon, whereas in ketones, the carbonyl carbon is bonded only to carbon atoms. This structural difference is why they are named as they are and why they have different reactivity. Aldehydes are more electrophilic than ketones due to the presence of a hydrogen atom attached directly to the carbonyl carbon, making them more reactive to nucleophilic addition and more easily oxidized. The internationally accepted naming nomenclature is set out by the IUPAC. Aldehydes: For aldehydes, the suffix "-al" is added to the parent alkane name to denote the presence of the aldehyde functional group. Carbonyl carbon is given position 1 in the carbon chain numbering. So, for example, CH*f* CHO is ethane converted to ethanal, while CH*f* CH, CHO is propane converted to propanal. For complex aldehydes with substituents, the locants of these substituents are given by numbers, beginning with the carbonyl carbon. For example, you have 3-methylbutanal, an aldehyde with a methyl group on carbon 3 of a four-carbon chain.

Unlike aldehydes, however, ketones cannot react with oxidizing agents to form higher-carbon ketones, as they have no hydrogen atom attached to the carbonyl carbon to remove. CH*f* COCH*f* , for example, is called propanone (better known as acetone), from propane. For larger ketones, the carbonyl position needs to be indicated: CH*f* CH, COCH*f* is 2-butanone, indicating the carbonyl group on the 2 position of a four-carbon chain. When substituents are present, their positions are indicated by numbers, as in 4-methyl-2-pentanone, which describes a ketone with a methyl substituent at position 4 of a five-carbon chain whose carbonyl is at position 2. Some aldehydes and ketones, especially those that are significant historically or of industrial importance, still retain their common or trivial names. Some widely used trivial names still remain in use today along with their systematic IUPAC names, such as formaldehyde (methanal), acetaldehyde (ethanal), acetone (propanone), and benzaldehyde. As one can imagine, the physical characteristics of both aldehydes and ketones are greatly affected by the existence of the carbonyl group. The carbonyl bond possesses a polar character and dipole-dipole interactions between carbonyl molecules are stronger than dispersion forces, resulting in higher boiling points than their alkane counterparts with the same molecular weight. For this reason, aldehydes and ketones cannot form hydrogen bonds with themselves (unlike the alcohols), and

thus have boiling points that are lower than those of alcohols of comparable molecular weight. The smaller aldehydes and ketones are appreciably soluble in water due to hydrogen bonding between the carbonyl oxygen and water, and higher homologs are more hydrophobic and less water-soluble with increasing carbon chain length.

The carbonyl group gives unmistakable spectroscopic signatures that enable their identification and have aided in the characterization of aldehydes and ketones. The C=O stretching vibration results in a strong absorption band around 1700-1750 cm{ [1] for aldehydes and around 1680-1720 cm{ [1] for ketones in an infrared (IR) spectrum. With respect to nuclear magnetic resonance (NMR) spectroscopy, the aldehydic proton is observed as a unique downfield signal in the region of around 9-10 ppm and the carbonyl carbon resonates around 190-200 ppm for aldehydes and 205-220 ppm for ketones (Fig. 3; ^{13}C NMR spectra). The spectroscopic features find important use in explaining the structure and checking the purity of carbonyl compounds.

Preparation of Aldehydes and Ketones

The synthesis of aldehydes and ketones covers a wide variety of different approaches that can be classified depending on the type of transformation. Synthetic methodologies such as oxidation of alcohols, reduction of carboxylic acid derivatives, ozonolysis of alkenes, and an array of carbon–carbon bond forming reactions can be employed. The choice for a particular synthetic pathway depends on the complexity of the target's structure and the types of functional groups as well as the accessibility of reactants. One of the most direct and widely used methods for the preparation of carbonyl compounds is the oxidation of alcohols. Primary alcohols can therefore be oxidised to aldehydes under very controlled conditions, so as to avoid further oxidation to carboxylic acid. A common selective oxidation is offered by pyridinium chlorochromate (PCC) in dichloromethane, giving the possibility to isolate the intermediate aldehyde. The reaction involves formation of a chromate ester intermediate which then undergoes elimination to produce the aldehyde product. For instance, when 1-butanol is oxidized with PCC, you would get butanal:

CH*f* CH, CH, CH, OH + PCC '! CH*f* CH, CH, CHO + Cr(III) compounds

Secondary alcohols undergo oxidation to form ketones using oxidizing agents such as potassium dichromate (K, Cr, O‡) in acidic conditions or Jones reagent (CrO*f* in aqueous H, SO,,). The oxidation of 2-butanol, for instance, yields 2-butanone:

CH*f* CH(OH)CH, CH*f* + K, Cr, O‡ /Hz '! CH*f* COCH, CH*f* + H, O + Cr(III) compounds

Milder oxidizing agents such as Dess-Martin periodinane (DMP) and 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) with a secondary oxidant have gained prominence in modern synthetic chemistry due to their selectivity and compatibility with sensitive functional groups.

The reduction of carboxylic acid derivatives provides an alternative pathway for the synthesis of aldehydes and ketones. Acid chlorides can be reduced to aldehydes using lithium tri-tert-butoxyaluminum hydride (LiAlH(O-t-Bu)*f*) or diisobutylaluminum hydride (DIBAL-H) at low temperatures. These reagents serve as milder reducing agents compared to lithium aluminum hydride, allowing for the controlled reduction to the aldehyde oxidation state without further reduction to the alcohol. For example, the reduction of butanoyl chloride with DIBAL-H at -78°C produces butanal:

CH*f* CH, CH, COCl + DIBAL-H '! CH*f* CH, CH, CHO + isobutylaluminum byproducts

Nitriles (R-CN) can be reduced to aldehydes using DIBAL-H through the formation of an imine intermediate that undergoes hydrolysis during workup. This approach is particularly valuable for the synthesis of aldehydes that might be difficult to access through alcohol oxidation. The reduction of butanenitrile, for instance, yields butanal:

CH*f* CH, CH, CN + DIBAL-H '! CH*f* CH, CH, CH=NH '! CH*f* CH, CH, CHO

Acyl chlorides can be converted to ketones via Friedel-Crafts acylation of aromatic compounds, a process that is mediated by Lewis acids like AlCl*f* . (N-FCl was used in some literature instead of NOCl as a mild electrophilic aromatic substitution has been formed so if there is an activating group, it may also attack the aromatic ring.) For example, the acylation of benzene with acetyl chloride results in acetophenone:

C† H† + CH*f* COCl + AlCl*f* '! C† H… COCH*f* + HCl + AlCl*f*

N-Methoxy-N-methylamides (also called a Weinreb amide) are key intermediates in the synthesis of ketones via Grignard or organolithium reagents. The tetrahedral intermediate of this reaction is stable until the aqueous workup stage, which means over-addition does not occur, leading to the formation of the desired ketone product. This approach is especially useful for the synthesis of unsymmetrical ketones:

R-CON(OCH*f*)CH*f* + R'-MgX '! R-CO-R' + Mg(X)N(OCH*f*)CH*f*

Ozonolysis of alkenes is a reaction that cleaves carbon-carbon double bonds of the alkene to form carbonyl compounds. The reaction, which proceeds through the formation of an ozonide intermediate, is subsequently reduced with zinc in acetic acid or dimethyl sulfide. Ozonolysis can yield either aldehydes, ketones, or a mixture of both depending on the overall substitution pattern of the alkene. For example, the ozonolysis of 2-methyl-2-butene subsequently followed by reductive workup yields acetone and acetaldehyde:

(CH*f*), C=CHCH*f* + O*f* '! (CH*f*), C=O + CH*f* CHO

This reaction — the Wacker oxidation (named after the Wacker Chemie company) — allows for the oxidative transformation of terminal alkenes into methyl ketones with palladium(II) chloride and copper(II) chloride and oxygen. This process is facilitated by a ð-complex formed between the alkene and palladium(II) followed by nucleophilic attack of water and rearrangement to yield the ketone. For example, the Wacker oxidation of 1-butene gives 2-butanone:

CH*f* CH, CH=CH, + PdCl, + CuCl, + H, O + O, '! CH*f* CH, COCH*f* + Pd + CuCl + HCl

The Aldol condensation and the Claisen condensation are examples of carbon-carbon bond-forming reactions that lead to â-hydroxy carbonyl compounds that may be subsequently dehydrated to yield á,â-unsaturated carbonyl compounds. Identification of the general reaction scheme and the fact that that you fully developed the carbon nucleophile, either an enolate or enol, and then perform a nucleophilic addition to the carbonyl compounds to generate a new C-C bond. The aldol condensation of acetaldehyde, for instance, affords 3-hydroxybutanal, which can also be dehydrated to crotonaldehyde:

2 CH*f* CHO '! CH*f* CH(OH)CH, CHO '! CH*f* CH=CHCHO + H, O

Reactivity of organometallic reagents with aldehydes and ketones provides further variability. Acylation with acid chlorides of organocopper reagents (Gilman reagents) represents a method to form ketones without the double addition observed with Grignard reagents. As an example, the reaction of lithium dimethylcuprate with acetyl chloride generates acetone:

(CH*f*), CuLi + CH*f* COCl '! CH*f* COCH*f* + LiCl + Cu

Collectively, these synthetic methods — and their many variations and more recent developments — offer an extensive toolbox for the synthesis of aldehydes and ketones with different combinations of structural features and functional groups. The choice of any given synthetic route is dependent on factors like functional group tolerance, stereochemical control, and overall synthesis towards complex targets.

Acidity of Alpha Hydrogens and Formation of Enolates

The carbonyl group plays a major role in this, as the alpha-hydrogens (those that are on the alpha carbon, which is the first carbon attached to a carbonyl carbon) are much more acidic. The greater acidity of á-hydrogens in carbonyl compounds compared to their non-carbonyl counterparts is due to the stabilizing resonance and inductive effects of the carbonyl group on the carbanion that results when these hydrogens are removed. The alpha hydrogens of aldehydes and ketones have pKa values of ~ 16-20, which makes them significantly more acidic than simple alkanes (pKa H" 50) but much less than carboxylic acids (pKa H" 4-5).

When aldehydes and ketones are treated with appropriate bases, the alpha hydrogens can be deprotonated, forming enolate anions due to their acidic nature. These enolate ions act as nucleophiles in various carbon-carbon bond-forming reactions such as aldol condensations, Claisen condensations and alkylation reactions. The generation and reactivity of enolates are key features of carbonyl chemistry highly relevant in organic synthesis and biological processes.

Because this carbanion can be managed with a hybrid orbital that has resonance stabilization across the base form, the alpha hydrogens are more acidic. If the proton on the alpha carbon is removed (deprotonation), the negative charge can delocalize

between the alpha carbon and the carbonyl oxygen, forming an enolate (which is resonance-stabilized). This resonance stabilization delocalizes the negative charge between two atoms, lowering the energy of the system and stabilizing the enolate compared to a localized carbanion. The enolate ion resonance structures can be drawn as:

R, CH-CR'=O ÷' R, C=CR'-O{

Another factor is the carbonyl group has an inductive effect on the attached alpha carbon, pulling electron density away from it through sigma bond network and increasing alpha hydrogens acidity. This inductive effect adds to the resonance stabilization and further lends to the acidifying effect of the carbonyl group.

Enolates are usually formed with strong bases like lithium diisopropylamide (LDA), sodium hydride (NaH) or potassium tert-butoxide (t-BuOK). Base selection is based on regiosectivity, stereoselectivity and other functional group present. For instance, a sterically hindered strong base such as LDA (pKa H" 36) is able to deprotonate alpha hydrogens without nucleophilic addition to the carbonyl moiety. LDA reacts with acetone at low temperature to form the lithium enolate of acetone:

CH*f* COCH*f* + LiN(i-Pr), '! CH*f* COCH, { Liz + HN(i-Pr),

Aggregation state, sulubility, and reactivity of the enolate is dependent on the counter ion (Liz , Naz , Kz) in the enolate. For example, lithium enolates are prone to aggregate in solution as the hard lithium cation strongly interacts with the enolate's oxygen atom. These types of aggregation effects can also influence the stereochemical outcome of other reactions.

With unsymmetrical ketones having more than one pair of alpha hydrogens, regioselectivity for enolate formation becomes an issue. Kinetic deprotonation favors formation of the less substituted enolate (the kinetic enolate), whereas thermodynamic conditions yield the more substituted and therefore more stable enolate (the thermodynamic enolate). Here is a list of very simple turnovers: 2-butanone can generate two different enolates:

CH*f* COCH, CH*f* + LDA '! CH*f* COCH{ CH*f* (kinetic enolate) or CH*f* CO{ C(CH*f*), (thermodynamic enolate)

Regioselectivity is tunable by adjusting the base, solvent, temperature, and reaction time. LDA in tetrahydrofuran (THF) at "78 °C usually leads to kinetic deprotonation whereas potassium tert--butoxide in tert-butanol at higher temperatures favors thermodynamic enolate formation.

Enolate reactivity includes alkylation, aldol condensation, Claisen condensation, and Michael addition. Enolates react with alkyl halides in alkylation reactions that generate carbon-carbon bonds at the alpha position. For example, alkylation of the lithium enolate of acetone with methyl iodide gives 2-butanone:

CH*f* COCH, { Liz + CH*f* I '! CH*f* COCH(CH*f*), + LiI

There are several other variations of the aldol condensation reaction, in which the enolate is formed and then adds to the carbonyl carbon of another aldehyde or ketone to form the â-hydroxy carbonyl compound (aldol product). This reaction can be followed by dehydrating to yield an á,â-unsaturated carbonyl compound. The aldol condensation is a fundamental reaction for Carbon-Carbon bond formation and finds widespread applicability in organic synthesis and biological systems. An example of this transformation is the reaction of acetaldehyde enolate with another molecule of acetaldehyde:

CH*f* CHO + { CH, CHO '! CH*f* CH(OH)CH, CHO

A related transformation to this is the Claisen condensation where an ester enolate reacts with another ester, resulting in a â-keto ester. This reaction gives access to attractive synthetic precursors, with potential applications in the synthesis of complex molecules. For example, the Claisen condensation of ethyl acetate produces ethyl acetoacetate:

2 CH*f* COOC, H… + NaOC, H… '! CH*f* COCH, COOC, H… + C, H… OH + NaOC, H…

The formation and reactivity of enolates is a key theme in carbonyl chemistry, offering a mechanistic foundation for many synthetic transformations that allow the forging of complex molecules. Regioselectivity and stereoselectivity during enolate formation

and downstream transformations are powerful tools in organic synthesis, with applications in drug discovery and materials science.

Concept of Reactive Methylene Group, Keto-Enol Tautomerism in Acetoacetic Ester

A reactive methylene group describes a methylene (-CH, -) group located between two electrophilic groups, most commonly a carbonyl or cyano group, that greatly activate the acidity of the methylene hydrogens. This increased acidity is due to the stabilizing effects of both neighboring groups on the resulting carbanion, giving a pKa as low as 10-13 for compounds containing reactive methylene groups. Examples of such compounds include acetylacetone (2,4-pentanedione), diethyl malonate, and acetoacetic ester (ethyl acetoacetate).

The carbanion that forms upon deprotonation of these groups is stabilized by resonance through the two electron-withdrawing groups. A methylene bridge between a ketone and an ester functionality renders it more acidic, such as in acetoacetic ester (ethyl acetoacetate, CH*f* COCH, COOC, H…) After deprotonation, the negative charge can be delocalized over both carbonyl oxygen atoms, resulting in a highly stabilized anion:

CH*f* COCH, COOC, H… + B{ ’! CH*f* CO{ =CHCOOC, H… ÷’ CH*f* CO=CH{ COOC, H… + BH

This increased acidity makes reactive methylene units valuable synthetic handle for carbon”carbon bond-forming reactions. Carbanions originating from these species can also act as nucleophiles in a variety of other reactions, including but not limited to alkylation, aldol condensation, and Michael addition, affording more complex molecules. A prime example of this is alkylation of the anion of diethyl malonate with an alkyl halide, followed by hydrolysis and decarboxylation to give a carboxylic acid by a reaction known as malonic ester synthesis.:

CH, (COOC, H…), + NaOC, H… ’! { CH(COOC, H…), Naz + C, H… OH { CH(COOC, H…), Naz + RX ’! RCH(COOC, H…), + NaX RCH(COOC, H…), + 2 NaOH ’! RCH(COO{ Naz), + 2 C, H… OH RCH(COO{ Naz), + Hz , heat ’! RCH, COOH + CO, + Naz

Keto-enol tautomerism is a dynamic equilibrium between the keto form (with a carbonyl group) and the enol form (with a hydroxyl group bonded to a double bond) of a compound. This is an example of tautomerization, which is the migration of a proton and a shift in a double bond but does not involve a change in the molecular formula. Tautomerism is different from resonance in that tautomers are separate, isolable structures that can interconvert, while resonance structures are just different pictures of the same molecule.

In the case of acetoacetic ester (ethyl acetoacetate), keto-enol tautomerism involves the equilibrium between the keto form (CH*f* COCH, COOC, H…) and the enol form (CH*f* C(OH)=CHCOOC, H…). The enol form features a hydroxyl group and a carbon-carbon double bond in place of the ketone and methylene groups in the keto form. This equilibrium can be represented as:

CH*f* COCH, COOC, H… ÷' CH*f* C(OH)=CHCOOC, H…

The stability of this equilibrium is dependent on several factors, such as the structure of the compound, the solvent it is in and the temperature. For simple ketones, however, the keto form is favored at equilibrium because the C=O bond is stronger than the C=C bond. Again, however, for reactive methylene compounds, enol content can be substantial due to stabilizing intramolecular hydrogen bonding and extended conjugation (e.g., with acetoacetic ester).

Both intra molecular H-bonding between the enolic -OH and the ester C=O, as well as extended conjugation of the ð electrons through the C=C-C=O system stabilize the enol form in acetoacetic ester. This stabilization raises the enol content compared to simple ketones. The enol content of acetoacetic ester in non-polar solvents can be determined at room temperature, and the amount can be approximately be around 7-8%.

Keto-enol interconversion can occur by acid-catalyzed or base-catalyzed mechanisms. In acid catalysis, the carbonyl oxygen can be protonated — this increases the acidity of the alpha hydrogen, so it can be removed in the formation of the enol intermediate. In base catalysis, the alpha position is deprotonated to generate an enolate intermediate, which can undergo protonation at the oxygen to produce the enol.

Keto-enol tautomerism is common in acetoacetic ester and similar compounds and has important consequences for their reactivity. Of even higher grounds is the fact that the keto and enol forms will not react in the same ways, and can be used as different nucleophiles in an electrophilic substitution reaction. Because the nucleophilic C=C double bond of the enol is available, it undergoes halogenation, nitrosation, and coupling with diazonium salts. Thus, for instance, the bromination of acetoacetic ester without base is carried out predominantly at the alpha position via enol form:

CH*f* C(OH)=CHCOOC, H… + Br, '! CH*f* C(OH)=CBrCOOC, H… + HBr '! CH*f* COCBr, COOC, H…

Tautomerism of keto-enol nature for acetoacetic ester will also play a role in its performances as a good condensation agent. The increased nucleophilicity of the enol form allow it to react with electrophiles, like aldehydes and ketones, giving rise to the formation of carbon-carbon bonds. Moreover, the acidity of the á-hydrogen allows acetoacetic ester to undergo aldol-type condensations and related reactions.

The reactivity of the methylene group, and keto-enol tautomerism, is not limited to acetoacetic ester, but extends to other compounds with comprises similar structural characteristics, namely, malonic esters, 1,3-diketones, and â-keto nitriles. The enhanced acidity of the methylene hydrogens and potential for keto-enol tautomerism give these compounds versatility as synthetic intermediates in organic chemistry.

Additionally, reactive methylene groups are well known for their synthetic utility, with a classic synthetic method being the acetoacetic ester synthesis — Deriving its utility based on the reactivity of the methylene group in ethyl acetoacetate. Its synthetic method is the alkylation of the sodium enolate of acetoacetic ester and the subsequent hydrolysis and decarboxylation to give methyl ketones. This sequence of reactions can be summarized as follows:

CH*f* COCH, COOC, H… + NaOC, H… '! CH*f* COCH{ COOC, H… Naz + C, H… OH CH*f* COCH{ COOC, H… Naz + RX '! CH*f* COCHR'COOC, H… + NaX CH*f* COCHR'COOC, H… + NaOH '! CH*f* COCHR'COO{ Naz + C, H… OH CH*f* COCHR'COO{ Naz + Hz , heat '! CH*f* COCHR, + CO, + Naz

The preparation of a number of methyl ketones, including structural motifs that might be difficult to prepare by other means, can be achieved using this synthetic sequence. The acetoacetic ester synthesis is an example of how the notion of the reactive methylene group informs a synthetic methodology that is useful and widely applicable across organic synthesis.

Oxidation of Aldehydes by KMnO4, and Tollen's Reagent, Reduction of Aldehydes by LiAIH4 and NaBH4

The characteristic oxidation and reduction reactions of aldehydes are what separate them from ketones and offer many useful ways in which aldehydes can be transformed to other functional groups. The hydrogen in aldehydes makes them more easily oxidized than ketones that do not have a hydrogen attached to their carbonyl carbon. Aldehydes and ketones are also reduced to alcohols, and the choice of reducing agent will affect selectivity and compatibility with other functional groups.

A classic example of aldehyde oxidation to carboxylic acids is the oxidation of aldehydes by potassium permanganate (KMnO,,). This process is the conversion of the -CHO group to the -COOH group when a strong oxidizer, such as KMnO,, , is utilized. The permanganate ion (MnO,, {) acts as the oxidant in a reaction that usually takes place under alkaline conditions and is reduced to manganese dioxide (MnO,).:

RCHO + 2 KMnO,, + H, O '! RCOOH + 2 MnO, + 2 KOH

The mechanism of this oxidation involves the nucleophilic attack of hydroxide ion on the carbonyl carbon, followed by electron transfer to the permanganate ion. The intermediate formed undergoes further oxidation to yield the carboxylic acid product. For example, the oxidation of benzaldehyde with alkaline KMnO,, produces benzoic acid:

C† H… CHO + 2 KMnO,, + H, O '! C† H… COOH + 2 MnO, + 2 KOH

The oxidation of aldehydes by Tollens' reagent (silver ammonium complex, [Ag(NH*f*),]z) provides a selective method for distinguishing aldehydes from ketones and

serves as a qualitative test known as the silver mirror test. Tollens' reagent is prepared by adding ammonia solution to silver nitrate, resulting in the formation of the silver ammonium complex:

AgNOf + 2 NHf '! [Ag(NHf),]z NOf {

When an aldehyde is treated with Tollens' reagent, the aldehyde is oxidized to a carboxylic acid (or its salt under the basic conditions of the reaction), while the silver(I) ion is reduced to metallic silver, which deposits as a silver mirror on the walls of the reaction vessel:

RCHO + 2 [Ag(NHf),]z + 3 OH{ '! RCOO{ + 2 Ag + 4 NHf + 2 H, O

The mechanism involves the formation of a silver-coordinated hemiacetal intermediate, followed by the transfer of hydride from the hemiacetal to the silver ion. For example, the reaction of propionaldehyde with Tollens' reagent produces propionate ion and metallic silver:

CHf CH, CHO + 2 [Ag(NHf),]z + 3 OH{ '! CHf CH, COO{ + 2 Ag + 4 NHf + 2 H, O

Notably, ketones do not react with Tollens' reagent under typical conditions because they lack a hydrogen atom on the carbonyl carbon. In qualitative analysis, aldehydes and ketones can be distinguished from one another due to this differential reactivity. A positive aldehyde test results in the formation of a silver mirror or dark precipitate for ketones or non-aldehyde carbonyl compounds. Common oxidizing agents for the conversion of aldehydes to carboxylic acids include chromic acid (H, CrO,, , generated from potassium dichromate and sulfuric acid), Jones reagent (CrOf in aqueous sulfuric acid), and sodium chlorite (NaClO,). Many of these reagents show different selectivity profiles as well as compatibility with other functional groups, permitting and thereby providing valuable options for von the oxidation of aldehydes in the context of complex molecules.

Aldehyde and ketone reduction is another critical reactivity within their general reactivity, allowing them to be converted into primary and secondary alcohols, respectively. Lithium aluminum hydride (LiAlH,,) and sodium borohydride (NaBH,,) are two

frequently used reducing agents for this transformation with differing reactivity, selectivity, and compatibility with other functional groups. Lithium aluminum hydride ($LiAlH_4$) is a very strong reducing agent and can reduce most carbonyl compounds such as aldehydes, ketones, esters, carboxylic acids and amides. The initiating reducing strength comes from the highly polarized aluminum-hydrogen bonds that deliver hydride (H^-) to the electrophilic carbonyl carbon. The broader equation for the reduction of an aldehyde or ketone with $LiAlH_4$ can be written as:

$$4\ R,C{=}O + LiAlH_4 \rightarrow (R,CHO)_4AlLi \quad (R,CHO)_4AlLi + 4\ H_2O \rightarrow 4\ R,CHOH + LiOH + Al(OH)_3$$

The mechanism involves the nucleophilic attack of hydride on the carbonyl carbon, resulting in the formation of an alkoxide intermediate. After the consumption of all four hydrides from $LiAlH_4$, the resulting aluminum alkoxide complex undergoes hydrolysis during workup to release the alcohol product. For example, the reduction of butanal with $LiAlH_4$ produces 1-butanol:

$$4\ CH_3CH_2CH_2CHO + LiAlH_4 \rightarrow (CH_3CH_2CH_2CH_2O)_4AlLi \quad (CH_3CH_2CH_2CH_2O)_4AlLi + 4\ H_2O \rightarrow 4\ CH_3CH_2CH_2CH_2OH + LiOH$$

Nucleophilic Additions to Carbonyl Group and Related Reactions

The carbonyl group (C=O) is one of the most versatile functional groups in organic chemistry and underlies many synthetic transformations. This makes the carbon-oxygen double bond polarized, as the O atom is more electronegative than C, pulling electron density away from the carbon atom. This polarization makes the carbon electrophilic and exposes it to nucleophile attack, and the oxygen can stabilize negative charges that form throughout reaction sequences. This basic feature of the carbonyl group allows for a multitude of addition reactions which form the foundation of organic synthesis.

Nucleophilic Addition to the Carbonyl Group

When a nucleophile attacks the electrophilic carbon atom of a C=O bond, it is referred to as nucleophilic addition to a carbonyl group. There are several steps in the general mechanism. First, the nucleophile donates a pair of electrons to the

carbon atom at the carbonyl group, leading to a tetrahedral intermediate where the sp^2 carbon becomes a tetrahedral sp^3 carbon. This intermediate often carries a negative charge on the oxygen atom, which under acidic conditions becomes protonated to produce the final addition product. The Reactivity of Carbonyl Compounds Towards Nucleophilic Addition Depends on Very Fundamental Structural Aspects Aldehydes are more reactive than ketones because of steric and electronic effects. In contrast, with only one substituent on the carbonyl carbon, nucleophilic approach is less hindered for aldehydes due to reduced steric hindrance. Furthermore, alkyl groups in ketones have an electron-donating effect, which partially offsets the positive charge on the carbonyl carbon and reduces its electrophilicity.Nucleophilic addition reactions are controlled by a variety of factors. The basicity of the nucleophile, as well as nucleophilicity, are important factors influencing rates of reactions and the products formed. Reactivity is significantly affected by the particular structure of the carbonyl compound, or the steric and electronic properties of the substituents adjacent to the carbonyl group. In addition, reaction conditions in terms of solvent polarity, temperature, and the introduction of catalysts or promoters can also change dramatically the reaction pathways and product distributions.

Aldol Reaction

Known as the aldol reaction, the process is one of the most significant of carboncarbon bond-forming reactions in organic chemistry. The aldol condensation 3 is a condensation reaction between carbonyl compounds. This reaction progresses through a series of characteristic mechanistic steps, and it also illustrates the ambident nature of carbonyl compounds (they can act as both nucleophiles—after enolate formation—and electrophiles). Aldol reaction mechanism formation of trivial molecule A by enolate ion of carbonyl with alpha H atoms In the presence of a base, a basic condition abstracts an acidic á”hydrogen from the carbonyl compound to produce the resonance-stabilized enolate ion. In this step, this enolate acts as a nucleophile and attacks an electrophilic carbonyl carbon of another molecule to generate a new carbon-carbon bond. The intermediate alkoxide ion is subsequently protonated on workup, giving the â-hydroxy carbonyl product.

For example, in the base-catalyzed aldol reaction of acetaldehyde, the mechanism unfolds as follows:

1. Base abstracts an á-hydrogen from acetaldehyde, generating an enolate ion.
2. The enolate nucleophilically attacks the carbonyl carbon of a second acetaldehyde molecule.
3. The resulting alkoxide intermediate undergoes protonation to form 3-hydroxybutanal (aldol product).

One reaction that can create carbon–carbon bonds is known as the aldol reaction, which is highly versatile: it can involve many different carbonyl compounds as substrates. Aldehydes are more reactive than ketones for aldol reaction due to lower steric hindrance and higher electrophilicity for the carbonyl carbon. Mixed aldol reactions, with different carbonyl compounds, can produce several products although precise control of reaction conditions will often lead to a preferred one. Under particular conditions, aldol products can lose the elements of H2O or H from the â position to give á,â-unsaturated carbonyl compounds. This dehydration usually goes more easily when heating the reaction mixture or in an acidic environment. The resulting conjugated systems serve as useful intermediates in other synthetic transformations. There are many variants of the aldol reaction to solve specific synthetic problems. (2"3) The directed aldol reaction uses preformed enolates to dictate regioselectivity for unsymmetrical ketones. The Mukaiyama aldol reaction employs silyl enol ethers as nucleophiles, providing milder reaction conditions and frequently better stereoselectivity. The Evans aldol reaction employs chiral auxiliaries to yield high stereochemical control and has proven to be invaluable in complex natural product synthesis.

Perkin Reaction

Perkin reaction is a classical reaction to afford á,â-unsaturated carboxylic acids via the condensation of aromatic aldehydes with acid anhydrides in the presence of base. First observed by William Henry Perkin in 1868 while attempting to synthesize quinine, this reaction has become one of the most important methods of constructing carbon-carbon bonds adjacent to aromatic rings in organic synthesis. The Perkin Reaction Mechanism0The mechanism for the Perkin reaction starts with the formation of a carbanion from the acid anhydride (usually acetic anhydride). The common initial catalyst, typically the sodium/potassium salt of the corresponding carboxylic acid,

abstracts a proton from the á-carbon of the anhydride, resulting in an enolate-like intermediate. The nucleophilic species then reacts with the carbonyl carbon of the aromatic aldehyde to yield the new carbon-carbon bond. The resulting alkoxide intermediate undergoes intramolecular acyl transfer, followed by elimination to provide the á,â-unsaturated carboxylic acid product upon hydrolysis.

In greater detail, the mechanism proceeds as follows:

1. The base (often sodium acetate) removes an acidic á-hydrogen from acetic anhydride, generating a resonance-stabilized carbanion.
2. This carbanion acts as a nucleophile and attacks the carbonyl carbon of the aromatic aldehyde.
3. The resulting alkoxide intermediate undergoes an intramolecular acyl transfer.
4. Subsequent elimination of a carboxylate group leads to the formation of the á,â-unsaturated structure.
5. Hydrolysis during workup yields the final cinnamic acid derivative.

The Perkin reaction demonstrates substrate specificity, working most effectively with aromatic aldehydes. Aliphatic aldehydes generally prove less suitable due to competing side reactions such as self-condensation. The reaction typically favors the formation of the trans (E) isomer of the á,â-unsaturated carboxylic acid, driven by thermodynamic stability. Various modifications of the Perkin reaction have expanded its synthetic utility. The use of different acid anhydrides allows for the introduction of diverse substituents at the á-position of the product. The incorporation of phase-transfer catalysts has improved reaction efficiency in certain cases, while microwave irradiation has been employed to reduce reaction times significantly.

Knoevenagel Reaction

The Knoevenagel reaction is a well known example of the aldol condensation where the active methylene compound performs a nucleophilic addition to the carbonyl followed by dehydration. However, it is an essential reaction in the toolkit for the synthesis of á,â-unsaturated compounds in many areas of synthetic chemistry from pharmaceutical development to materials science, and is named after Emil Knoevenagel

who first published in this reaction in 1894. Mechanistically, the formation of the Knoevenagel reaction begins with the abstraction of a proton from an active methylene compound by a base, generally, a secondary amine such as piperidine or a tertiary amine, triethylamine. Active methylene compounds encompass a range of structures containing electron-withdrawing substituents on either side of the methylene unit, including malonates, â-ketoesters, and cyanoacetates. The resultant carbanion then attacks the carbonyl carbon of an aldehyde or ketone to produce an alkoxide intermediate. Dehydration follows,typically by action of the amine catalyst or another dehydration agent to give the á,â-unsaturated product.

Here is how the full mechanism plays out:

- The generation of the resonance-stabilized carbanion is generated via deprotonation of the active methylene compound by the amine catalyst.
- The nucleophilic carbanion attacks the electrophilic carbonyl carbon.
- The resulting alkoxide intermediate is then deprotonated at the á-position.
- Hydroxyl group elimination yields the desired á,â-unsaturated species, typically with assistance from the amine catalyst via iminium ion formation.

Knoevenagel reaction can depend on many factors. The viscosity in reaction rates of the active methylene compound has been proved to be very significant, where more acidic substrates (the electron-withdrawing groups) will undergo reactions readily. An important factor is the electrophilicity of the carbonyl component, which also contributes to the relative reactivity of the two components : there is a general trend for aldehydes to be more reactive than ketones as a result of lower steric hindrance and more electrophilic carbon of the carbonyl. Often conducted at room temperature or with mild heating, the Knoevenagel reaction proceeds under mild conditions. Traditional catalysts consist of amines, but more recently a number of alternative catalytic systems have been developed in order to broaden the substrate scope of such reactions and improve their efficiency, including ionic liquids, solid supports and metal-organic frameworks. Numerous variants of the Knoevenagel reaction have been designed for specific synthetic applications. Another variation, the Doebner modification, uses malonic acid rather than malonic esters to produce

á,â-unsaturated carboxylic acids directly with concurrent decarboxylation. The nitroaldol and Knoevenagel processes are combined via the Henry-Knoevenagel tandem reaction to access complex molecular architectures. The Knoevenagel-Cope sequence allows the coupling of Knoevenagel condensation with the successive Cope rearrangement in order to build complex carbon skeletons.

Wittig Reaction

One of the most useful techniques are Wittig reactions, whereby carbonyl compounds are converted to alkenes with defined position of double bonds. This reaction, which was developed by Georg Wittig in the 1950s (for which he was awarded the Nobel Prize in Chemistry in 1979), has transformed organic synthesis because it offers a dependable way to create carbon-carbon double bonds having definite configuration. The Wittig reaction involves phosphonium ylides (or Wittig reagents) and aldehydes or ketones. Phosphonium ylides are wrought from alkyl halides and triphenylphosphine to produce phosphonium salts, followed by treatment with a strong base (e.g. butyllithium or sodium hydride) to deprotonate}. These ylides have a carbon atom which has one pair of electrons which are not shared and is stabilized by the adjacent phosphorus atom. Although a detailed discussion of the mechanism is beyond the scope of our present work, we shall highlight that the reaction proceeds via the formation of an oxaphosphetane intermediate that can then decompose to provide the alkene product and triphenylphosphine oxide. The driving force behind this reaction is formation of the strong phosphorus-oxygen bond in the triphenylphosphine oxide byproduct.

The stereochemical outcome of the Wittig reaction is most dependent on the type of ylide. Unstabilized ylides (carbanions that do not have electron-withdrawing groups adjacent to them) give predominantly Z-alkenes but stabilized ylides (carbanions that are adjacent to electron-withdrawing groups, such as carbonyl or cyano) yield predominantly E-alkenes. This often gives mixtures of geometric isomers with semi-stabilized ylides. The Wittig reaction is a highly functional group tolerant process and is applicable to a broad range of substrates featuring a variety of reactivity sensitive functionalities. The direct double bond formation at a defined position and with

predictable stereochemistry makes this method an excellent tool in the synthesis of complex molecules such as natural products, pharmaceuticals and agrochemicals.

Mannich Reaction

The Mannich reaction is a versatile three-component condensation forming aminoalkylated products from an amine, formaldehyde (or some other aldehyde), and a compound with an acidic hydrogen. Now this reaction has found its way into the synthesis of alternative nitrogen-containing compounds, such as pharmaceuticals, alkaloids, and a variety biologically active molecules, as described by Carl Mannich at the beginning of the 20th century. When enolizable aldehydes, ketones or other acidic compounds are used as substrates in the Mannich reaction â-amino carbonyl compounds are obtained. The reaction tolerates a range of primary and secondary amines, including ammonia, and can use a variety of aldehydes although formaldehyde is the preferred reagent often. We will not go into the detailed mechanism of this process here, but be aware that it usually occurs through the intermediacy of an iminium ion between the amine and the aldehyde, which is subsequently subject to nucleophilic attack by the enolized acidic partner. This reaction builds a new carbon-carbon bond and adds an amino group at the á-position of the acid substrate.

The Mannich reaction has a broad range of synthetic utility. It is an important step in medicinal chemistry to prepare a wide range of pharmaceutical agents – such as analgesics, anticonvulsants and antimalarials. The reaction is also useful for obtaining complex alkaloid structures and other naturally occurring products with aminoalkyl functionalities. Moreover, Mannich bases are versatile synthetic intermediates, being able to be converted into á,â-unsatured carbonyls through elimination reactions, reduced to amino alcohols, and employed in cycloaddition reactions. A variety of variations of the classical Mannich reaction have broadened its scope and increased its efficiency. Preformed iminium salts can improve reaction control and reduce side reactions. Chiral catalysts have permitted asymmetric varieties of the Mannich reaction, furnishing access to enantioenriched products. More recent one-pot, multi-component variations have also greatly simplified these synthetic processes, and solid-support strategies combined with increased synthesis throughput have opened more possibilities.

Baeyer-Villiger Oxidation

The Baeyer-Villiger oxidation is one of the most important transformations in organic chemistry, first described by Adolf von Baeyer and Victor Villiger in 1899, in which ketones are converted to esters and cyclic ketones to lactones via insertion of an oxygen atom adjacent to the carbonyl group. This reaction has been rewarding in synthetic organic chemistry, especially in the construct of complex molecular scaffolds and in natural product synthesis. Baeyer—Villiger oxidation usually uses peroxy acids including meta-chloroperoxybenzoic acid (mCPBA), peroxyacetic acid or hydrogen peroxide and an acid catalyst. Even for similar classes of oxidant, the reactivity differs, and more electrophilic peroxy acids in general lead to faster reactions and higher selectivity. While we won't address the mechanism in detail here, it is worth mentioning that the reaction shows a fine degree of regioselectivity for unsymmetrical ketones. The migratory ability of substituents adjacent to the carbonyl group often follows the trend: tertiary alkyl > secondary alkyl > aryl > primary alkyl > methyl. This migration preference reflects the capacity of various groups to stabilize positive charge character through the rearrangement process.

The Baeyer-Villiger oxidation has broad synthetic applications in many branches of chemistry. It is one of the crucial steps applied in the construction of a variety of natural products like macrolides, steroids, and terpenoids. The reaction gives access to compounds that would be difficult to synthesize by other means, especially some esters and lactones with particular substitution patterns. Moreover, Baeyer-Villiger oxidation provides a valuable route for functional group interconversion, allowing strategic elaboration in the synthesis of complex molecules. Recent developments have increased the scope of the Baeyer-Villiger oxidation. Mild condition highly enantioselective transformations have also been achieved by employing Baeyer-Villiger monooxygenases (BVMOs) as an enzymatic counterpart. Catalytic systems, such as metal catalysts and organocatalysts, are openly developed while reaction efficiency and selectivity are enhanced. Green chemistry concerns have been addressed by environmentally benign variants that replace hypochlorite with hydrogen peroxide along with sustainable catalysts.

Cannizaro Reaction

In the presence of strong bases, aldehydes without á-hydrogens undergo simultaneous oxidation and reduction in what is known as the Cannizaro reaction, a recognized example of disproportionation. First observed by Stanislao Cannizaro in 1853,6 this reaction has evolved into an essential reaction in organic chemistry7 and is particularly useful for aldehydes that are precluded from undergoing aldol condensations owing to the lack of enolizable hydrogens.

Mechanism of the Cannizaro Reaction

The Cannizaro reaction mechanism involves multiple steps.

- Aldehyde attack by the base (usually a concentrated form of either sodium or potassium hydroxide) to the carbonyl carbon, developing a tetrahedral intermediate.
- This intermediate donates a hydride ion to a second aldehyde molecule.
- The hydride acceptor is reduced to the corresponding primary alcohol.
- The hydride donor gets oxidized to a carboxylate salt.

Acidification during workup transforms the carboxylate salt into the carboxylic acid.

The first step is a nuclophilic attack of hydroxide on the carbonyl carbon leading to the formation of an alkoxide intermediate. This tetrahedral intermediate then donates a hydride ion to another aldehyde molecule, in a complicated series of steps which may include several transition states. The final hydride transfer reduces the accepting aldehyde directly to an alkoxide, which further protonates to give the primary alcohol. At the same time, the donor aldehyde is oxidized (losing a hydrido) to a carboxylic acid salt. During workup, this salt is acidified to generate the free carboxylic acid. The Cannizaro reaction is mainly performed on aromatic aldehydes and some branched aliphatic aldehydes that contain no á-hydrogens. Although formaldehyde lacks á-hydrogens, this type of reaction is generally quite slow due to its inherent electronic properties. Mixed Cannizaro reactions with different aldehydes show intriguing selectivity trends in which the more electrophilic aldehyde is the preferential hydride acceptor.

The Cannizaro reaction is affected by various factors. Higher concentrations of the base usually speed up reaction rates, while lower concentrations slow them down. Importantly, the electronic properties of the aldehydes are key factors, as electron-withdrawing substituents promote electrophile character, thereby resulting in enhanced hydride acceptance. The resulting reaction usually needs high temperatures to surpass early energy barriers, although in some instances, the specific structural characteristics of a material allow for a transformation that can set in at room temperature. The Cannizaro reaction has been extended in various ways. The crossed Cannizaro reaction utilizes formaldehyde as a sacrificial hydride donor, facilitating the selective reduction of other aldehydes. A related process catalyzed by aluminum alkoxides that forms esters instead of alcohol-acid pairs is the Tishchenko reaction. Similar in mechanism to the Cannizaro reaction, the Meerwein-Ponndorf-Verley reduction merely serves to reduce ketones to alcohols using aluminum isopropoxide.

In an MPV reduction, the carbonyl compound is reduced with sodium metal or an alkaline borohydride, in the presence of isopropanol.

The Meerwein-Ponndorf-Verley (MPV) reduction is a highly selective process for the reduction of aldehydes and ketones to their corresponding alcohols using aluminum alkoxides as reducing reagents and alcohols as sources of hydride. Initially discovered independently by Meerwein, Ponndorf, and Verley in the 1920s, this reaction provides a useful alternative to metal hydride reductions, especially for substrates containing sensitive functional groups. Similarly, the MPV reduction proceeds via a cyclic transition state mechanism, not discrete intermediates. An aluminum isopropoxide (or another aluminum alkoxide) coordinates to oxygen of the carbonyl in substrate, making it more reactive toward hydride transfer. At the same time, the alkoxide part of the aluminum reagent brings its á-hydrogen close to carbonyl carbon. The hydride is transferred from the á-carbon of the alkoxide to the carbonyl carbon in a concerted process, and the alkoxide oxygen forms a stronger bond to aluminum. This reaction effectively reduces the carbonyl compound to an aluminum alkoxide of the product alcohol, which upon workup hydrolyzes to give the free alcohol.

The response shows very high chemoselectivity, favorably minimizing aldehydes and ketones while keeping various other practical groups, which include esters, amides,

nitro teams, and carbon-carbon multiple connections unaffected. This selectivity profile renders the MPV reduction particularly useful in the late-stage functionalisation of complex molecules with multiple reactive sites. The MPV reduction functions in rather mild, neutral conditions and usually only requires mild heating in solvents such as toluene or isopropanol. The reaction is generally faster with aldehydes than with ketones due to decreased steric hindrance and increased electrophilicity at the reaction site. The presence of groups that withdraw electrons adjacent to carbonyls increases reactivity through enhanced electrophilicity, while sterics in proximity to the reaction center can profoundly inhibit the process. When applied to alcohols, this mechanistic framework is exploited by the reverse reaction, the Oppenauer oxidation, in which aluminum alkoxides and ketones act as oxidants to form carbonyl compounds. The MPV reduction and Oppenauer oxidation are in equilibrium, and this can be driven in either direction by using an excess of the alcohol (to reduce) or of the ketone (to oxidize). Recent advances improved the speed and the magnitude of MPV reduction. Aluminum reagents are also incorporated in stoichiometric quantities but catalytic variants using alternative transition metals have reduced this requirement. Asymmetric approaches have allowed for the preparation of enantioenriched alcohols from prochiral ketones. Examples include modified zeolites and metal-organic frameworks, which are heterogeneous catalysts that have contributed to continuous-flow processes and enhanced recyclability.

Clemmensen Reduction

The Clemmensen reduction is a powerful method to convert carbonyl groups of aldehydes and ketones to methylene (CH,) groups in strongly acidic conditions. Originally described by Erik Christian Clemmensen in 1913, this transformation has become a useful method in organic synthesis, especially for the deoxygenation of base-sensitive carbonyl compounds. The Clemmensen reduction uses amalgamated zinc (zinc with mercuric chloride adsorbed onto it) in concentrated hydrochloric acid. The reaction is typically performed at high temperatures with extended reaction times, particularly for sterically highted substrates. 7 Although the exact pathways are still debated, the hypothesis is formed on the basis of organozinc complexation at the metal surface followed by stepwise electron and proton transfers. This reduction is especially useful in a variety of scenarios. It is a very useful and selective reduction of

aryl ketones and aldehydes to their corresponding complex alkylbenzenes which makes a rich source for aromatic compounds with defined substitution. This reaction has proven advantageous for substrates that would otherwise novelty undergo unwanted sidereactions in basic conditions; those prone to aldol condensations, concur. The Clemmensen reduction is also an important step in a number of natural product syntheses, as it allows the strategic removal of carbonyl functionalities.

The efficiency of the Clemmensen reduction is affected in several ways. The frequency of reactions is greatly influenced by the surface area of the zinc amalgam in the reaction, as maximally galked, freshly prepared and finely divided metal performs the best. The choice of solvent is critical, as the addition of cyclohaxane or diethyl ether typically helps to improve the solubility of substrate in the biphasic reaction system. We know that electronic factors present in the substrate can have very dramatic effects on the reactivity, leading to the generalization that electron-withdrawing groups tend to promote reductions (note the electron-deficient behavior of the cation transition state). Raffinose ether reduction and other variations of the Clemmensen reduction for certain synthetic problems have been reported. An alternative procedure for some sensitive substrates employs zinc dust with acetic anhydride in acetic acid. Ultrasound-assisted methods have made successful attempts to enhance reaction progress by improving mass transfer and the activation of the metal surface. Continuous-flow methodologies allow for safer handling of the mercury-containing reagents while improving scalability.

Wolff-Kishner Reduction

The Wolff-Kishner reduction is a complementary method to the Clemmensen reduction for reduction of carbonyl compounds to (methylene) groups, but occurring under strongly basic instead of acidic conditions. This reaction, independently described by Nikolai Kishner in 1911 and Ludwig Wolff in 1912, is now a routine method in organic synthesis, particularly for substrates sensitive to acidic conditions. The Wolff-Kishner is conducted using hydrazine (often its hydrate) in high boiling basic solvent like ethylene glycol or diethylene glycol with potassium or sodium hydroxide as the base. The reaction occurs at elevated temperatures, typically above 180 °C, to encourage the removal of nitrogen gases. The reaction mechanism starts with the nucleophilic attack by hydrazine on the carbonyl group of the ketone or aldehyde,

leading to the formation of a hydrazone intermediate. Deprotonation of the terminal nitrogen of the hydrazone occurs under strongly basic conditions, resulting in a series of electron transfers that allows for loss of nitrogen gas to provide a carbanion. This carbanion abstracts a proton from the solvent or from other acid source resulting in the final reduced product.

The Wolff-Kishner reduction is especially useful in certain situations. It efficiently reduces aldehydes and ketones that are resistant to other reduction techniques, including sterically hindered carbonyl species. When applied to substrates with acidic- or metal-hydride-sensitive functional groups, such as some heterocycles and acid-labile protecting groups, the reaction demonstrates utility. The Wolff-Kishner reduction is also important in total synthesis of various molecules where strategic deoxygenation of carbonyls is required in the context of complex molecular architectures. There are a few factors that determine the efficiency of Wolff-Kishner reduction. The concentration of base can significantly affect reaction rates, with greater concentrations generally speeding up the process. Temperature control becomes critical: if the substrate is not heated adequately, the reaction may not go to completion, while if an excessive temperature is used, sensitive substrates may start to decompose. We have to take care about the water content of the reaction mixture because later stages of the mechanism can be obstructed by by-products. Numerous modifications have made the Wolff-Kishner reduction more practical, and provided it with a wider scope. In contrast, the Huang-Minlon modification makes the hydrazone at lower temperatures via a temperature-programmed process, heating for the reduction step, which improves yields in the scene of sensitive substrates. There are many variations of this reaction and one notable example is the Myers modification which instead of hydrazine uses trimethylsilyldiazomethane to generate the same carbonyl unit, which gives milder reaction conditions and better functional group compatibility. Microwave-assisted protocols have generally resulted in reaction times ranging from several minutes to a few hours at most without sacrificing good yields for most of the substrates.

Analysis and Synthetic Applications

The reactions reviewed here represent paradigm shifts in carbonyl chemistry, each with unique strengths and weaknesses with respect to addressing particular synthetic

challenges. Knowledge of their relevant features allows organic chemists to make appropriate choices of methods for specific target molecules. The aldol, Perkin, and Knoevenagel reactions form carbon-carbon bonds via nucleophilic addition to carbonyl functionalities but differ in their respective nucleophilic coupling partners and reaction conditions. Enolates from carbonyl compounds are used in the aldol reaction, carbanions from acid anhydrides in the Perkin reaction, and active methylene compounds stabilized via electron-withdrawing groups in the Knoevenagel reaction. These differences translate into unique products in terms of structures and stereochemistry, thereby serving as complementary tools to construct carbon networks of different kinds. The Wittig and Mannich reactions contribute two unique functional groups during carbon-carbon bond formation, thus broadening the synthetic arsenal. The Wittig reaction introduces carbon-carbon double bonds, with defined geometry, and the Mannich reaction adds amino substitutes when they are adjacent to the carbonyl moiety. Venture phosporation-reduction and anti-Wurtz reaction: The transformations are extremely valuable for obtaining complex molecular architectures, especially scaffolds encased with stereochemical moieties or heteroatom-embedded carbon centers. The carbony reductive methods—LeClemmensen and Wolff-Kishner reductions—represent complementary strategies to convert carbonyl groups to methylene units in either acidic or basic conditions, respectively. The choice among these methods typically hinges upon the sensitivity of the substrate to specific reaction environments and the presence of other functionality. The reduction of MPVs offers a milder approach for reducing carbonyls to alcohols while leaving other reactive functionalities intact.

Carbonyl chemistry offers a lot more than just simple additions, and the Baeyer-Villiger oxidation and the Cannizaro reaction are prominent examples of carbonyl's ability towards strategic oxidative transformations. Baeyer-Villiger oxidation adds oxygen next to carbonyls, transforming certain ketones into esters, and Cannizaro reactions disproportionate aldehydes into alcohols and carboxylic acids. This utility becomes especially important during functional group interconversions and oxidation state manipulations upon synthesis of complex molecules. Such elementary carbonyl transformations have been widely applied in natural product synthesis, pharmaceutical development and material chemistry. By forming carbon-carbon connections after

adding functional groups strategically site-selectively and managing oxidation states, they empower the assembly of elaborate molecular edifices. Ongoing iterations of catalyst development, asymmetric modifications, and conditions optimizations also ensure their continued utility in modern organic synthesis.

Unit -6 **Carboxylic Acids**

(i) Carboxylic Acids

- Nomenclature, structure, physical properties, acidity of carboxylic acids, effect of substituent on acid strength, method of preparation and chemical reaction.
- Hell-Volhard-Zeilinsky (HVZ) reaction, Reduction of carboxylic acids
- Mechanism of decarboxylation. Di carboxylic acids: - Methods of formation and chemical reactions, effect of heat and Dehydrating agents.

(ii) Carboxylic Acid Derivatives

- Structure, method of preparation & physical properties of acid chlorides, esters, amides (Urea) and acid anhydrides.
- Relative stability of acyl derivatives.

2.2 Acid & its Derivatives

(i) Carboxylic Acids

Carboxylic acids represent one of the most important classes of organic compounds, characterized by the presence of a carboxyl group (-COOH) attached to an alkyl or aryl group. These versatile compounds serve as precursors for numerous derivatives and play crucial roles in biological systems, industrial processes, and organic synthesis.

Nomenclature

Carboxylic acids have systematic IUPAC names, with the base hydrocarbon name modified by replacing the terminal "e" with the "oic acid" suffix. As an illustration, CH*f* COOH is termed ethanoic acid (or acetic acid) and C† H… COOH is referred to as benzoic acid! Numbering of substituted acids begins from the carboxyl carbon, which is always given position 1.

As a general nomenclature, lower carboxylic acids keep historical names based on where they were found in nature. Others are formic acid (from the Latin formica, which means ant), butyric acid (from the Latin butyrum, which means butter) and propionic acid (from the Greek protos pion, which means first fat). Dicarboxylic acid names end with "dioic acid"; examples are hexanedioic acid (adipic acid) and butanedioic acid (succinic acid) When necessary, especially for complex structures, the positions of the carboxyl groups are specified using numbers.

Structure

The functional group of carboxylic acids is the carboxyl group, which is a carbonyl (C=O) directly attached to a hydroxyl (-OH) group. This configuration leads to a quasi planar environment around the carboxyl carbon through sp^2 hybridization. The C=O bond has a partial double bond character with a bond length of <"1.20 Å; the C"O bond of the hydroxyl group has a length of <"1.34 Å. Dimers are widely formed in both solid and vapor phases of low molecular weight carboxylic acids due to the hydrogen bonding between two carboxyl groups. This dimerization has an important influence on their physical properties, such as boiling points and solubility trends. Carboxylic acids have resonance structures that show delocalization of electrons over the carboxyl group. This delocalization of electrons stabilizes the carboxylate anion that is formed through deprotonation and makes these compounds acidic.

Physical Properties

Carboxylic acids exhibit distinct physical characteristics influenced by their molecular structure and hydrogen-bonding capabilities:

1. **State of Matter**: Lower molecular weight carboxylic acids (C -C,,) are colorless liquids with pungent odors at room temperature. As the carbon chain length increases (C… -C‰), they become oily liquids with increasingly unpleasant odors. Higher members (C € and above) exist as waxy solids with minimal odor.

2. **Boiling Points**: Carboxylic acids have unusually high boiling points compared to alcohols and alkanes of similar molecular weights. This is attributed to the extensive hydrogen bonding that creates dimeric structures, effectively doubling their molecular mass. For instance, acetic acid (MW 60) boils at 118°C, while propanol (MW 60) boils at only 97°C.

3. **Solubility**: Lower carboxylic acids (up to C,,) demonstrate complete water solubility due to their ability to form hydrogen bonds with water molecules. As the hydrocarbon chain lengthens, water solubility decreases due to the increasing hydrophobic character. All carboxylic acids dissolve readily in less polar solvents like alcohols, ethers, and chloroform.

4. **Density**: Most carboxylic acids have densities slightly greater than water, with values typically between 1.0-1.1 g/cm³ for the lower members of the series.

Acidity of Carboxylic Acids

Carboxylic acids are moderately strong acids with pKa values ranging from 3 to 5, making them significantly stronger than alcohols (pKa ~16-18) but weaker than mineral acids like HCl (pKa ~-7). Their acidic character arises from the ability to release a proton from the carboxyl group to form a resonance-stabilized carboxylate anion:

RCOOH Ì! RCOO{ + Hz

The acidity of carboxylic acids can be explained by:

1. **Resonance Stabilization**: The negative charge in the carboxylate ion is delocalized over two oxygen atoms through resonance, distributing the charge and stabilizing the anion.

2. **Electronegativity**: The electronegative oxygen atoms within the carboxyl group pull electron density away from the O-H bond, weakening it and facilitating proton donation.

3. **Solvation Effects**: The carboxylate ion forms strong hydrogen bonds with water molecules, further stabilizing the anion and driving the equilibrium toward dissociation.

Effect of Substituents on Acid Strength

The acidity of carboxylic acids is significantly influenced by substituents attached to the carbon chain:

1. **Electron-Withdrawing Groups (EWG)**: Substituents like halogens (-F, -Cl, -Br), nitro (-NO,), and cyano (-CN) increase acid strength by inductively withdrawing electron density from the carboxyl group, stabilizing the carboxylate anion. This effect diminishes with distance from the carboxyl group. For example, trifluoroacetic acid (pKa 0.23) is much stronger than acetic acid (pKa 4.76).

2. **Electron-Donating Groups (EDG)**: Groups like alkyl (-CH*f* , -C, H…) slightly decrease acidity by pushing electron density toward the carboxyl group through an inductive effect, destabilizing the carboxylate anion. This explains why formic acid (pKa 3.77) is stronger than acetic acid (pKa 4.76).

3. **Resonance Effects**: Aromatic rings can either increase or decrease acidity depending on the substituents. For instance, p-nitrobenzoic acid (pKa 3.44) is more acidic than benzoic acid (pKa 4.19) due to the electron-withdrawing nitro group, while p-methoxybenzoic acid (pKa 4.47) is less acidic due to the electron-donating methoxy group.

The relative acid strengths follow this general trend: CF*f* COOH > CCl*f* COOH > CHCl, COOH > CH, ClCOOH > CH*f* COOH

Methods of Preparation

Carboxylic acids can be synthesized through various routes:

1. **Oxidation of Primary Alcohols and Aldehydes**: Primary alcohols and aldehydes can be oxidized to carboxylic acids using strong oxidizing agents

like potassium permanganate (KMnO,,), potassium dichromate (K, Cr, O‡), or nitric acid (HNO*f*).

R-CH, OH + [O] '! R-COOH + H, O R-CHO + [O] '! R-COOH

2. **Oxidation of Alkyl Benzenes**: Side chains in alkyl benzenes can be oxidized to carboxyl groups using potassium permanganate or dichromate under reflux conditions, regardless of the alkyl chain length.

   C† H… -CH, R + 3[O] '! C† H… -COOH + R-COOH

3. **Hydrolysis of Nitriles**: Nitriles undergo hydrolysis in the presence of acids or bases to form carboxylic acids. Acid hydrolysis yields the carboxylic acid directly, while base hydrolysis first forms a carboxylate salt that requires acidification.

   R-CN + H, O + Hz '! R-COOH + NH,, z R-CN + 2NaOH + H, O '! R-COONa + NH*f* (followed by acidification)

4. **Carbonation of Grignard Reagents**: Grignard reagents react with carbon dioxide to form carboxylate salts, which upon acidification yield carboxylic acids.

   RMgX + CO, '! RCOO{ MgXz RCOO{ MgXz + Hz '! RCOOH + Mg²z + X{

5. **Hydrolysis of Esters**: Esters undergo hydrolysis in acidic or basic conditions to form carboxylic acids. Base hydrolysis (saponification) requires subsequent acidification.

   RCOOR' + H, O + Hz '! RCOOH + R'OH RCOOR' + NaOH '! RCOONa + R'OH (followed by acidification)

6. **Oxidation of Alkenes**: Vigorous oxidation of alkenes with potassium permanganate or ozone followed by oxidative workup cleaves the double bond, forming carboxylic acids.

   RCH=CHR' + [O] '! RCOOH + R'COOH

7. **From Alkyl Halides via Malonic Ester Synthesis**: This multi-step process involves alkylation of diethyl malonate followed by hydrolysis and decarboxylation.

   CH, (COOEt), + NaOEt '! CHNa(COOEt), CHNa(COOEt), + RX '! CR(COOEt), + NaX CR(COOEt), + 2NaOH '! CR(COONa), + 2EtOH CR(COONa), + Hz '! CR(COOH), CR(COOH), + heat '! RCOOH + CO,

Chemical Reactions

Carboxylic acids participate in various chemical transformations:

1. **Salt Formation**: Carboxylic acids react with bases to form carboxylate salts.

   RCOOH + NaOH '! RCOONa + H, O

2. **Esterification**: Carboxylic acids react with alcohols in the presence of acid catalysts to form esters (Fischer esterification).

   RCOOH + R'OH Ì! RCOOR' + H, O

3. **Formation of Acid Chlorides**: Treatment with thionyl chloride (SOCl,) or phosphorus pentachloride (PCl…) converts carboxylic acids to acid chlorides.

   RCOOH + SOCl, '! RCOCl + SO, + HCl RCOOH + PCl… '! RCOCl + POCl*f* + HCl

4. **Formation of Acid Anhydrides**: Carboxylic acids react with dehydrating agents like P, O… or can be converted to acid anhydrides via acid chlorides.

   2RCOOH + P, O… '! (RCO), O + H*f* PO,, RCOCl + RCOONa '! (RCO), O + NaCl

5. **Formation of Amides**: Carboxylic acids react with ammonia or amines, often via the acid chloride, to form amides.

   RCOOH + NH*f* '! RCONH, + H, O (requires heating) RCOCl + NH*f* '! RCONH, + HCl

6. **Reduction**: Carboxylic acids can be reduced to alcohols using lithium aluminum hydride (LiAlH,,) or borane (BH*f*).

   RCOOH + LiAlH,, '! RCH, OH

7. **Decarboxylation**: Heating carboxylic acids with soda lime (NaOH + CaO) or certain catalysts leads to decarboxylation, producing hydrocarbons.

   RCOOH + NaOH/CaO '! RH + Na, CO*f*

Hell-Volhard-Zelinsky (HVZ) Reaction

The Hell-Volhard-Zelinsky reaction is a method for á-halogenation of carboxylic acids. The reaction proceeds through the following steps:

1. The carboxylic acid is treated with a catalytic amount of phosphorus (or phosphorus tribromide/trichloride) and halogen (chlorine or bromine).
2. This forms an acid halide intermediate that undergoes enolization.
3. The enol form reacts with the halogen to produce an á-halogenated acid halide.
4. Hydrolysis yields the á-halogenated carboxylic acid.

The general reaction can be represented as: RCOOH + X, /P '! RCHXCOOH (where X = Cl, Br)

For example, propionic acid can be converted to á-bromopropionic acid: CH*f* CH, COOH + Br, /P '! CH*f* CHBrCOOH

The HVZ reaction is highly regioselective, occurring specifically at the á-position, and can be used to introduce multiple halogens through repeated applications of the procedure.

Reduction of Carboxylic Acids

Carboxylic acids can be reduced to various functional groups depending on the reducing agent employed:

1. **Lithium Aluminum Hydride (LiAlH,,)**: This powerful reducing agent converts carboxylic acids to primary alcohols through a two-electron reduction process. The reaction occurs via an aldehyde intermediate that is further reduced in situ.

   RCOOH + 2LiAlH,, '! RCH, OH + Li, O + 2Al + 3H,

2. **Borane (BH*f* ·THF)**: This selective reducing agent also converts carboxylic acids to primary alcohols but with greater functional group tolerance than LiAlH,, .

   RCOOH + BH*f* ·THF '! RCH, OH

3. **Sodium Borohydride (NaBH,,)**: Unlike LiAlH,, , NaBH,, alone is not strong enough to reduce carboxylic acids. However, when activated by iodine or when the acid is first converted to an acid chloride, reduction can proceed.

   RCOOH '! RCOCl '! RCH, OH (with NaBH,, /I,)

4. **Catalytic Hydrogenation**: Using hydrogen gas with catalysts like copper chromite or Raney nickel under high pressure and temperature, carboxylic acids can be reduced to alcohols or even alkanes depending on conditions.

   RCOOH + H, /catalyst '! RCH, OH (moderate conditions) RCOOH + H, /catalyst '! RCH*f* (harsh conditions)

5. **Rosenmund Reduction**: This specialized method reduces acid chlorides to aldehydes using hydrogen gas and a poisoned palladium catalyst, allowing for a controlled partial reduction.

   RCOCl + H, /Pd-BaSO,, '! RCHO + HCl

Mechanism of Decarboxylation

Decarboxylation is the process by which carboxylic acids lose carbon dioxide to form hydrocarbons or derivatives. The mechanism varies depending on the substrate and conditions:

1. **Thermal Decarboxylation**: Simple aliphatic carboxylic acids typically require high temperatures (>200°C) for decarboxylation to occur. The mechanism involves breaking the C-C bond between the carboxyl group and the á-carbon:

   R-CH, -COOH + heat '! R-CH*f* + CO,

2. **Beta-Keto Acid Decarboxylation**: â-keto acids undergo facile decarboxylation at much lower temperatures due to the formation of a stable six-membered cyclic transition state. The process is driven by the formation of an enol intermediate that rapidly tautomerizes to the ketone:

   R-CO-CH, -COOH '! R-CO-CH*f* + CO,

3. **Alpha,Beta-Unsaturated Acid Decarboxylation**: These acids decarboxylate relatively easily because the reaction forms a resonance-stabilized intermediate:

   R-CH=CH-COOH '! R-CH=CH, + CO,

4. **Malonic Acid Derivatives**: Compounds with two carboxyl groups attached to the same carbon undergo decarboxylation readily through a cyclic transition state:

   R-CH(COOH), '! R-CH, -COOH + CO,

5. **Catalyzed Decarboxylation**: Certain transition metals (Cu, Ag) or enzymes can facilitate decarboxylation by coordinating with the carboxyl group, weakening the C-C bond.

The ease of decarboxylation follows this general trend: â-keto acids > á,â-unsaturated acids > á-amino acids > dicarboxylic acids > simple monocarboxylic acids

Dicarboxylic Acids: Methods of Formation

Dicarboxylic acids contain two carboxyl groups and are important in various biological and industrial processes. Common methods of preparation include:

1. **Oxidation of Cyclic Alkenes**: Vigorous oxidation of cyclic alkenes with potassium permanganate or ozone cleaves the ring, forming dicarboxylic acids.

   Cyclohexene + KMnO,, /Hz '! HOOC-(CH,),, -COOH (adipic acid)

2. **Oxidation of Diols**: Primary diols can be oxidized to dicarboxylic acids using strong oxidizing agents like nitric acid or potassium permanganate.

   HO-CH, -(CH,)n-CH, -OH + [O] '! HOOC-(CH,)n-COOH

3. **Oxidation of Dicarbonyl Compounds**: Aldehydes with two carbonyl groups can be oxidized to form dicarboxylic acids.

   OHC-(CH,)n-CHO + [O] '! HOOC-(CH,)n-COOH

4. **Hydrolysis of Dinitriles**: Dinitriles undergo hydrolysis to form dicarboxylic acids.

   NC-(CH,)n-CN + 2H, O + Hz '! HOOC-(CH,)n-COOH + 2NH,, z

5. **Malonic Ester Synthesis**: This method allows for the preparation of substituted malonic acids, which can be hydrolyzed to dicarboxylic acids.

   CH, (COOEt), + 2RX '! CR, (COOEt), '! CR, (COOH),

6. **Grignard Reaction with CO,** : Di-Grignard reagents can react with carbon dioxide to form dicarboxylic acids after acidification.

   X-(CH,)n-X '! XMg-(CH,)n-MgX '! HOOC-(CH,)n-COOH

7. **Diels-Alder Reaction**: Cyclic dienes can undergo Diels-Alder reactions with dienophiles, followed by oxidation to yield dicarboxylic acids.

Chemical Reactions of Dicarboxylic Acids

Dicarboxylic acids exhibit reactions similar to monocarboxylic acids but with some distinctive features:

1. **Acid Strength**: The first carboxyl group in dicarboxylic acids typically has a lower pKa than the second due to the electron-withdrawing effect of the

adjacent carboxyl group. For example, in oxalic acid, pKa = 1.23 and pKa, = 4.19.

2. **Salt Formation**: Dicarboxylic acids can form either acid salts (with one carboxyl group neutralized) or normal salts (with both groups neutralized).

   HOOC-(CH,)n-COOH + NaOH '! HOOC-(CH,)n-COONa + H, O
   HOOC-(CH,)n-COONa + NaOH '! NaOOC-(CH,)n-COONa + H, O

3. **Esterification**: Similar to monocarboxylic acids, dicarboxylic acids can undergo esterification to form diesters, or selective conditions can produce monoesters.

   HOOC-(CH,)n-COOH + 2R'OH '! R'OOC-(CH,)n-COOR' + 2H, O

4. **Formation of Acid Chlorides**: Treatment with thionyl chloride converts both carboxyl groups to acid chlorides.

   HOOC-(CH,)n-COOH + 2SOCl, '! ClOC-(CH,)n-COCl + 2SO, + 2HCl

5. **Decarboxylation**: Dicarboxylic acids undergo selective decarboxylation depending on their structure. á,ù-Dicarboxylic acids typically lose one carboxyl group when heated.

   HOOC-(CH,)n-COOH + heat '! CH*f* -(CH,)n-COOH + CO,

6. **Reduction**: Dicarboxylic acids can be reduced to diols with LiAlH,, or BH*f* .

   HOOC-(CH,)n-COOH + 4H '! HO-CH, -(CH,)n-CH, -OH

Effects of Heat and Dehydrating Agents on Dicarboxylic Acids

When subjected to heat or dehydrating agents, dicarboxylic acids undergo characteristic transformations depending on the distance between the carboxyl groups:

1. **Oxalic Acid (HOOC-COOH)**: When heated, oxalic acid decomposes to form carbon monoxide, carbon dioxide, and water.

HOOC-COOH '! CO + CO, + H, O

2. **Malonic Acid (HOOC-CH, -COOH)**: Easily undergoes decarboxylation upon heating to form acetic acid and carbon dioxide.

   HOOC-CH, -COOH '! CH*f* COOH + CO,

3. **Succinic Acid (HOOC-(CH,), -COOH)**: When heated strongly or treated with dehydrating agents like P, O… or acetic anhydride, succinic acid forms succinic anhydride.

   HOOC-(CH,), -COOH '! O(CO-(CH,), -CO)O + H, O

4. **Glutaric Acid (HOOC-(CH,)*f* -COOH)**: Forms glutaric anhydride when heated or treated with dehydrating agents, though less readily than succinic acid.

   HOOC-(CH,)*f* -COOH '! O(CO-(CH,)*f* -CO)O + H, O

5. **Adipic Acid (HOOC-(CH,),, -COOH)**: Does not readily form cyclic anhydrides due to the unfavorable formation of a seven-membered ring. Instead, it may undergo partial decarboxylation or form polymeric anhydrides.

6. **Phthalic Acid (ortho-dicarboxybenzene)**: Readily forms phthalic anhydride when heated, due to the proximity of the carboxyl groups on the benzene ring.

   C† H,, (COOH), '! C† H,, (CO), O + H, O

Cyclic anhydrides are formed most readily where a stable five- or six-membered ring can be generated (as with succinic, glutaric, and phthalic acids). Commonly, upon heating, some dicarboxylic acids, unable to close the rings, would undergo decarboxylation or decomposition. Dicarboxylic acids may be first converted into their anhydrides on treatment with strong dehydrating agents such as P, O… or acetic anhydride at low temperatures, but further decomposition occurs at elevated temperatures. The exact result is determined by the acid structure as well as the specific reaction conditions used.

Carboxylic acids are a class of organic compounds that have a flagrant ability to discernible roles in both industrial and biological systems. Broader transformations are possible owing to the very structure of amino acids and the presence of the function group carboxyl, giving rise to unique physical and chemical properties. Carboxylic acids are the building blocks for understanding their derivatives, so Familiarity with their nomenclature, structure, physical properties, acidity, formation, and chemical reactions provides a foundation for exploring their derivatives and applications in organic synthesis, medicine, polymers, and many more areas.

Unit 6 Carboxylic Acid Derivatives

So derivatives of carboxylic acid are those functional groups which can be derived from carboxylic acid by replacing OH group of a carboxylic acid. Capsule Classes: Acid chlorides; esters; amides (urea included); acid anhydrides All of these compounds contain acyl groups (R-CO-) as a common structural feature, but they differ in what is attached to the carbonyl carbon.

Carboxylic Acid Derivatives Structure

Table of ContentsHideAcid Chlorides (Acyl Chlorides)

Acid chlorides are derivatives of carboxylic acids in which the hydroxyl group -OH is replaced with a chlorine atom and they have the general formula of R-COCl (where R is an organic group or hydrocarbon chain). Resonance gives the carbon-oxygen bond considerable double bond character. The oxygen and chlorine both function as electron-withdrawing groups; therefore, the carbonyl carbon is significantly electrophilic and reacts readily toward any nucleophile.

Esters: The general formula for Esters is: R-COOR' where R is the alkyl or aryl group from the acid and R' is the alkyl or aryl group from the alcohol. It contains a carbonyl group in which an alkoxy group (-OR') is bound to the carbon of the carbonyl. Between carbonyl group and hydroxy oxygen lone pair resonance stabilization occurs.

Amides: The general structure of amides is R-CONH, (primary amide), R-CONHR' (secondary amide) and R-CONR'R" (tertiary amide). They contain a carbonyl group, with a nitrogen atom bonded to the carbonyl carbon. The lone pair of electrons on the

nitrogen atom in an amide participates in resonance with the carbonyl—this imparts some double bond character to the C-N bond and thus restricts rotation about this bond.

Urea: Urea is a special type of amide with a formula of(NH, CO), ; it can also be considered as a diamide of carbonic acid. It is composed of a carbonyl group bonded to two amino groups. Resonance causes the molecule to be planar; however, the lone pairs on both nitrogen atoms can delocalize into the carbonyl group.

Acid Anhydrides

Acid anhydrides have the general formula R-CO-O-CO-R' (simple anhydrides when R=R') or R-CO-O-CO-R' (mixed anhydrides when R'"R'). They can be viewed as two acyl groups linked by an oxygen atom, formed by the condensation of two carboxylic acid molecules with the loss of water.

Methods of Preparation

Acid Chlorides

1. **From Carboxylic Acids using Thionyl Chloride (SOCl,)**:

2. R-COOH + SOCl, '! R-COCl + SO, + HCl

   This is the preferred method as the byproducts (SO, and HCl) are gases and easily removed.

3. **From Carboxylic Acids using Phosphorus Pentachloride (PCl…)**:

4. R-COOH + PCl… '! R-COCl + POCl*f* + HCl

5. **From Carboxylic Acids using Phosphorus Trichloride (PCl*f*)**:

6. 3 R-COOH + PCl*f* '! 3 R-COCl + H*f* PO*f*

Esters

1. **Fischer Esterification**: Direct reaction of carboxylic acids with alcohols in the presence of a strong acid catalyst (usually H, SO,, or dry HCl):

2. R-COOH + R'-OH Ì! R-COOR' + H, O

This is a reversible reaction, and the equilibrium is shifted toward products by removing water or using excess alcohol.

3. **From Acid Chlorides (Schotten-Baumann Reaction)**:

4. R-COCl + R'-OH '! R-COOR' + HCl

Often carried out in the presence of a base like pyridine to neutralize the HCl formed.

5. **From Acid Anhydrides**:

6. (R-CO), O + R'-OH '! R-COOR' + R-COOH

7. **Alcoholysis of Nitriles**:

8. R-Ca"N + R'-OH + Hz '! R-COOR' + NH*f*

Amides

1. **From Acid Chlorides with Ammonia or Amines**:

2. R-COCl + NH*f* '! R-CONH, + HCl

3. R-COCl + R'NH, '! R-CONHR' + HCl

4. R-COCl + R'R"NH '! R-CONR'R" + HCl

5. **From Esters with Ammonia or Amines (Aminolysis)**:

6. R-COOR' + NH*f* '! R-CONH, + R'-OH

7. R-COOR' + R"NH, '! R-CONHR" + R'-OH

8. **From Carboxylic Acids and Amines using Coupling Reagents**:

9. R-COOH + R'NH, + DCC '! R-CONHR' + DCU + H, O

DCC (Dicyclohexylcarbodiimide) is a common coupling agent; DCU is dicyclohexylurea.

10. **Dehydration of Ammonium Carboxylates**:

11. R-COONH,, '! R-CONH, + H, O

This requires heating to remove water.

Urea

1. **Industrial Preparation (Wöhler Synthesis)**:

2. NH,, NCO '! NH, CONH,

Ammonium cyanate undergoes rearrangement to form urea.

3. **From Phosgene**:

4. COCl, + 2 NH*f* '! NH, CONH, + 2 HCl

5. **From Carbon Dioxide and Ammonia**:

6. CO, + 2 NH*f* '! NH, CONH, + H, O

This reaction occurs at high temperature and pressure.

Acid Anhydrides

1. **From Acid Chlorides and Carboxylate Salts**:

2. R-COCl + R'-COO{ Naz '! R-CO-O-CO-R' + NaCl

3. **Dehydration of Carboxylic Acids**:

4. 2 R-COOH '! (R-CO), O + H, O

This requires a dehydrating agent like P, O… , acetic anhydride, or ketene.

5. **From Ketene**:

6. CH, =C=O + CH*f* COOH '! (CH*f* CO), O

Ketene reacts with acetic acid to form acetic anhydride.

Physical Properties

Acid Chlorides

1. **Physical State**: Lower members (up to C‰) are colorless liquids with pungent odors; higher members are solids.

2. **Boiling Point**: Higher than corresponding hydrocarbons due to dipole-dipole interactions but lower than corresponding carboxylic acids due to absence of hydrogen bonding.
3. **Solubility**: Insoluble in water due to hydrolysis but soluble in organic solvents like ethers, benzene, and chloroform.
4. **Density**: Generally greater than 1 g/cm³, denser than water.
5. **Reactivity**: Highly reactive and moisture-sensitive, undergo rapid hydrolysis when exposed to water.

Esters

1. **Physical State**: Lower members (up to C,,) are colorless liquids with pleasant, fruity odors; higher members are solids.
2. **Boiling Point**: Higher than corresponding alkanes due to dipole-dipole interactions but lower than corresponding carboxylic acids and alcohols due to absence of hydrogen bonding.
3. **Solubility**: Lower members are slightly soluble in water; solubility decreases with increasing carbon chain length. All esters are soluble in organic solvents.
4. **Density**: Generally less than 1 g/cm³, less dense than water.
5. **Volatility**: More volatile than corresponding carboxylic acids due to absence of hydrogen bonding.

Amides

1. **Physical State**: Lower members are colorless solids with high melting points; higher members are waxy solids.
2. **Boiling Point and Melting Point**: Much higher than corresponding esters and acid chlorides due to strong hydrogen bonding between amide molecules.
3. **Solubility**: Lower amides are soluble in water due to hydrogen bonding with water molecules; solubility decreases with increasing carbon chain length. All amides are soluble in polar organic solvents.

4. **Dipole Moment**: High dipole moment due to the polar C=O and C-N bonds.
5. **Hydrogen Bonding**: Primary and secondary amides can form hydrogen bonds through their N-H groups, leading to higher melting and boiling points.

Urea

1. **Physical State**: White crystalline solid.
2. **Melting Point**: 132-135°C (decomposes).
3. **Solubility**: Highly soluble in water (about 1080 g/L at 20°C) due to extensive hydrogen bonding; moderately soluble in alcohols; insoluble in non-polar solvents.
4. **Crystal Structure**: Forms an extensive hydrogen-bonded network in its crystal structure.
5. **Hygroscopic Nature**: Absorbs moisture from the atmosphere.

Acid Anhydrides

1. **Physical State**: Lower members are colorless liquids with pungent odors; higher members are solids.
2. **Boiling Point**: Higher than corresponding esters but lower than corresponding carboxylic acids.
3. **Solubility**: Generally insoluble in water due to hydrolysis; soluble in organic solvents.
4. **Reactivity**: Reactive toward water and alcohols, but less reactive than acid chlorides.
5. **Odor**: Characteristic sharp, irritating odor, especially in lower members like acetic anhydride.

Relative Stability of Acyl Derivatives

The relative stability of carboxylic acid derivatives can be ranked based on the leaving group ability, resonance stabilization, and electronic effects. From least stable (most reactive) to most stable (least reactive):

1. **Acid Chlorides (Least Stable)**:
    - Chloride is an excellent leaving group due to its weak basicity.
    - The C-Cl bond is polarized, making the carbonyl carbon highly electrophilic.
    - No significant resonance stabilization from the chlorine atom.
    - Highly susceptible to nucleophilic attack.
2. **Acid Anhydrides**:
    - The carboxylate anion is a moderate leaving group.
    - Some resonance stabilization exists but is insufficient to significantly reduce reactivity.
    - The carbonyl carbon remains quite electrophilic.
3. **Esters**:
    - Alkoxide is a poorer leaving group than chloride or carboxylate.
    - The lone pairs on the alkoxy oxygen participate in resonance with the carbonyl group, stabilizing the ester.
    - This resonance reduces the electrophilicity of the carbonyl carbon.
4. **Amides (Most Stable)**:
    - Amide ion is a very poor leaving group due to its high basicity.
    - Extensive resonance stabilization occurs between the nitrogen lone pair and the carbonyl group.
    - This strong resonance gives the C-N bond partial double bond character.

- The carbonyl carbon is significantly less electrophilic.
- Amides are the most stable of the carboxylic acid derivatives.

The relative reactivity toward nucleophilic acyl substitution follows the reverse order of stability:

Acid Chlorides > Acid Anhydrides > Esters > Amides

This order of reactivity is reflected in the ease of hydrolysis, with acid chlorides hydrolyzing rapidly even at room temperature, while amides require strong acids or bases and heating for hydrolysis.

The stability order can also be explained using resonance structures. In amides, the nitrogen atom with its lone pair participates strongly in resonance with the carbonyl group, significantly stabilizing the molecule. In esters, similar resonance occurs with the alkoxy oxygen, but it's less effective than in amides. In acid anhydrides and acid chlorides, the resonance stabilization is much weaker or absent, making them more reactive.

The relative stability also correlates with carbonyl stretching frequencies in IR spectroscopy, with more reactive derivatives showing higher C=O stretching frequencies due to less resonance delocalization:

- Acid chlorides: ~1800 cm{ ¹
- Acid anhydrides: ~1760 cm{ ¹
- Esters: ~1735 cm{ ¹
- Amides: ~1650 cm{ ¹

This trend in IR frequencies provides experimental evidence for the relative stability of these derivatives.

SELF ASSESSMENT QUESTIONS

Multiple Choice Questions (MCQs)

1. Which of the following is most reactive towards nucleophilic addition?

a) Acetone

b) Formaldehyde

c) Acetic acid

d) Benzophenone

2. Aldol condensation requires:

a) á-Hydrogen

b) Strong acid

c) Aromatic aldehyde

d) Dry ether

3. The Cannizzaro reaction is given by:

a) Formaldehyde

b) Acetone

c) Benzophenone

d) Acetic acid

4. The HVZ reaction is used for:

a) Halogenation of alkanes

b) Halogenation of carboxylic acids

c) Hydroxylation of alcohols

d) Oxidation of ketones

5. The reagent used in Clemmensen reduction is:

a) Zn/HCl

b) LiAlH,,

c) $NaBH_4$

d) $KMnO_4$

6. The product of Wolff-Kishner reduction of acetophenone is:

a) Benzyl alcohol

b) Ethanol

c) Toluene

d) Phenol

7. Keto-enol tautomerism is observed in:

a) Formaldehyde

b) Acetic acid

c) Acetoacetic ester

d) Methanol

8. The Baeyer-Villiger oxidation converts ketones into:

a) Aldehydes

b) Carboxylic acids

c) Esters

d) Alcohols

9. Which of the following acids is strongest?

a) Acetic acid

b) Chloroacetic acid

c) Formic acid

d) Propionic acid

10. Which reaction does NOT involve nucleophilic attack?

a) Aldol condensation

b) Perkin reaction

c) Cannizzaro reaction

d) Clemmensen reduction

Short Answer Questions

1. Explain the mechanism of Aldol condensation.
2. What is the effect of resonance on the acidity of carboxylic acids?
3. Describe the structure and reactivity of the carbonyl group.
4. How does the presence of á-hydrogen affect keto-enol tautomerism?
5. Write the mechanism of the Perkin reaction.
6. Explain the Clemmensen reduction and its applications.
7. What is the role of Tollen's reagent in aldehyde oxidation?
8. Differentiate between acid chlorides and acid anhydrides.
9. Describe the effect of electron-withdrawing groups on carboxylic acid strength.
10. What is the mechanism of decarboxylation of carboxylic acids?

Long Answer Questions

1. Explain the different methods of preparation of aldehydes and ketones.
2. Discuss the oxidation and reduction reactions of aldehydes and ketones.
3. Describe the mechanisms of the Cannizzaro reaction and Baeyer-Villiger oxidation.
4. Compare the acidity of carboxylic acids and phenols with examples.
5. Explain the formation of enolate ions and their role in condensation reactions.

6. Discuss the synthetic applications of the Wittig reaction.
7. Write a detailed note on the different carboxylic acid derivatives and their reactivity.
8. Describe the HVZ reaction and its significance in organic synthesis.
9. Explain the mechanisms of Clemmensen and Wolff-Kishner reductions.
10. Discuss the decarboxylation reaction and its industrial applications.

MODULE- 3

EQUILIBRIUM

3.0 Objective

- Understand the concept of equilibrium in chemical and ionic systems.
- Learn about equilibrium constants and their dependence on temperature, pressure, and concentration.
- Study Le Chatelier's principle and its applications.
- Explore ionic equilibrium, pH, buffer solutions, and solubility product.
- Understand the phase rule and its applications in one- and two-component systems.

Unit- 8Chemical equilibria

Dynamic Nature of Equilibrium in Physical and Chemical Processes

To achieve chemical equilibrium, rates of the forward and reverse reactions must become equal, and concentrations of the reactants and products no longer show a net change over time. This idea holds true for physical processes (such as the equilibrium between different phases of matter) as well as chemical reactions. In looking at equilibrium at the molecular level, one needs to realize that it is not a static condition where the reactions have ceased. Instead, it is a dynamic state where both forward and reverse processes continue to occur at an equilibrium rate. The fact that equilibrium can change with time is crucial to understanding how it reacts to external perturbations.

Suppose one considers the evaporation of water in a closed system:

H, O(l) Ì! H, O(g)

Initially, molecules of liquid water enter the gas phase via evaporation. As more and more water molecules enter the gas phase, others start returning to their liquid state through the process of condensation. As time goes on, these rates become equal,

leading to dynamic equilibrium. Even as individual molecules move back and forth between phases, the macroscopic conditions (pressure, concentration, and so on) are statistically frozen.Paved with turbulent roadsSo how's this equilibrium breaking down in an exploding system?

The same principle applies to chemical reactions. For a general reaction:

aA + bB Ì! cC + dD

At equilibrium, the rate at which A and B form C and D equals the rate at which C and D revert to A and B. This balance creates a stable system despite ongoing molecular activity.

Law of Mass Action and Equilibrium Constants

The law of mass action, formulated by Cato Maximilian Guldberg and Peter Waage in 1864, provides a mathematical relationship between reactant and product concentrations at equilibrium. For the general reaction above, the equilibrium constant (K) is expressed as:

K = [C]œ"[D]H" / [A]C"[B]G"

Where [A], [B], [C], and [D] represent the molar concentrations of each species at equilibrium, and a, b, c, and d are their stoichiometric coefficients.

For gas-phase reactions, we often use partial pressures instead of concentrations, giving us Kš :

Kš = (P_C)œ"(P_D)H" / (P_A)C"(P_B)G"

The relationship between Kc and Kp is:

Kš = Kc(RT)^Än

Where Än is the change in the number of moles of gas (products - reactants) and R is the gas constant.

The magnitude of K indicates the extent of the reaction:

- K >> 1: The equilibrium favors products

- K << 1: The equilibrium favors reactants
- K H" 1: Substantial amounts of both reactants and products are present

Different types of equilibrium constants exist for various scenarios:

- Kc: Based on molar concentrations
- Kp: Based on partial pressures
- Ksp: Solubility product constant for dissolution equilibria
- Ka and Kb: Acid and base dissociation constants
- Kw: Water auto-ionization constant

Temperature, Pressure, and Concentration Effects on Equilibrium Constants

The equilibrium constant is not truly constant under all conditions—it varies with temperature according to the van't Hoff equation:

ln(K, /K) = (ÄH°/R)(1/T - 1/T,)

Where:

- K and K, are equilibrium constants at temperatures T and T,
- ÄH° is the standard enthalpy change for the reaction
- R is the gas constant (8.314 J/mol·K)

For exothermic reactions (ÄH < 0), K decreases as temperature increases. For endothermic reactions (ÄH > 0), K increases with temperature.

While K changes with temperature, it's important to note that it does not change with pressure or concentration changes. These factors affect the equilibrium position (the actual concentrations of reactants and products) but not the equilibrium constant itself. Changes in pressure particularly affect gas-phase reactions with unequal numbers of gaseous molecules on the reactant and product sides. However, these changes shift the equilibrium position within the constraint of the same equilibrium constant value at a given temperature. Similarly, adding or removing reactants or products shifts the

equilibrium position as the system adjusts to maintain the same value of K, but doesn't change K itself.

Factors Affecting Equilibrium - Le Chatelier's Principle

Le Chatelier's principle, formulated by French chemist Henry Louis Le Chatelier in 1884, states that when a system at equilibrium is subjected to a change, the system will adjust to partially counteract the effect of the change and establish a new equilibrium.

This principle helps predict how chemical equilibria respond to disturbances like changes in concentration, pressure, temperature, or the addition of catalysts:

1. **Concentration Changes:** When concentration of a reactant or product is altered, the equilibrium shifts to counteract this change.
    - Increasing reactant concentration shifts equilibrium toward products
    - Increasing product concentration shifts equilibrium toward reactants
    - Removing a product shifts equilibrium toward products
    - Removing a reactant shifts equilibrium toward reactants
2. **Pressure Changes:** Pressure changes affect gas-phase reactions with unequal numbers of gas molecules on each side.
    - Increasing pressure favors the reaction direction that produces fewer gas molecules
    - Decreasing pressure favors the reaction direction that produces more gas molecules
    - For reactions with equal numbers of gas molecules on both sides, pressure changes have negligible effects
3. **Temperature Changes:** Temperature directly affects the equilibrium constant.
    - For exothermic reactions (ÄH < 0), increasing temperature shifts equilibrium toward reactants

- For endothermic reactions (ÄH > 0), increasing temperature shifts equilibrium toward products
- This can be understood as the system "absorbing" some of the added heat in endothermic reactions or releasing heat to compensate for cooling in exothermic reactions

4. **Catalysts:** Catalysts increase the rates of both forward and reverse reactions equally, without changing the equilibrium position or equilibrium constant. They help the system reach equilibrium faster but don't affect the final concentrations.
5. **Addition of Inert Gases:** Adding an inert gas at constant volume doesn't affect equilibrium. However, adding an inert gas at constant pressure (which increases total volume) effectively decreases the partial pressures of reactants and products, potentially shifting gas-phase equilibria.

Quantitative Applications of Equilibrium Constants

Equilibrium constants allow us to calculate equilibrium concentrations from initial conditions, predict the direction of reactions, and determine the extent of reaction completion.

For instance, the reaction quotient Q, which has the same form as K but uses non-equilibrium concentrations, helps predict reaction direction:

- Q < K: Reaction proceeds toward products
- Q > K: Reaction proceeds toward reactants
- Q = K: System is at equilibrium

The position of equilibrium can also be expressed using the extent of reaction (î) or percent conversion, which indicates how far a reaction has progressed toward completion.

Industrial Applications and Optimizations

Understanding equilibrium principles is crucial for industrial process optimization. The Haber-Bosch process for ammonia synthesis (N, + 3H, Ì! 2NH*f*) illustrates this well:

- The reaction is exothermic, so lower temperatures favor product formation (higher K)
- The reaction reduces the number of gas molecules, so higher pressures favor product formation
- However, very low temperatures make the reaction too slow to be practical
- The industrial compromise uses moderate temperatures (400-450°C), high pressures (150-300 atm), and iron-based catalysts to achieve reasonable yields and reaction rates

In the same manner as how the Contact Process for sulfuric acid production and the Ostwald Process for nitric acid use equilibrium management to optimize efficiency and yield.

Understanding of complex systems, from industrial processes, and building blocks of the chemical industry, to biological reactions, acid-base chemistry, solubility, and electrochemical cells is based on concepts of chemical equilibrium. Dynamic equilibrium and Le Chatelier's principle are important for designing and controlling reactions in these many applications, both basic and applied.

3.2 Ionic Equilibria

Ionic equilibria form a fundamental aspect of chemical processes, governing the behavior of electrolytes in solution. These equilibria determine the extent to which compounds dissociate into ions, influencing properties like conductivity, acidity, and solubility. This chapter explores the principles of ionic equilibria, from basic acid-base ionization to complex buffer systems and their applications.

Ionization of Acids and Bases

Ionization refers to the process by which a neutral molecule splits into charged ions when dissolved in a suitable solvent, typically water. This phenomenon is particularly important for acids and bases.

Acids are substances that donate protons (Hz) when dissolved in water. For example, hydrochloric acid ionizes as follows: HCl(aq) '! Hz (aq) + Cl{ (aq)

Bases are substances that accept protons or donate hydroxide ions (OH{). For example, sodium hydroxide ionizes as: NaOH(aq) '! Naz (aq) + OH{ (aq)

The Brønsted-Lowry theory defines acids as proton donors and bases as proton acceptors. According to this theory, acid-base reactions involve the transfer of protons from an acid to a base. When an acid donates a proton, it forms its conjugate base, and when a base accepts a proton, it forms its conjugate acid.

For example, in the ionization of acetic acid in water: CH*f* COOH(aq) + H, O(l) Ì! CH*f* COO{ (aq) + H*f* Oz (aq)

Here, CH*f* COOH acts as an acid by donating a proton to water, which acts as a base. After the proton transfer, CH*f* COO{ becomes the conjugate base of the acid, and H*f* Oz becomes the conjugate acid of the base.

Strong and Weak Electrolytes

Electrolytes are substances that, when dissolved in water, produce a solution capable of conducting electricity due to the presence of ions. They can be classified as strong or weak based on their degree of ionization.

Strong Electrolytes undergo complete or nearly complete ionization in solution. The concentration of undissociated molecules is negligible compared to the concentration of ions. Examples include:

- Strong acids: HCl, HBr, HI, HNO*f* , H, SO,, , HClO,,
- Strong bases: NaOH, KOH, Ca(OH), , Ba(OH),
- Most soluble salts: NaCl, KNO*f* , MgCl,

For instance, when sodium chloride dissolves in water, it completely dissociates: NaCl(s) '! Naz (aq) + Cl{ (aq)

Solutions of strong electrolytes conduct electricity effectively due to the high concentration of mobile ions.

Weak Electrolytes only partially ionize in solution, establishing an equilibrium between the undissociated molecules and their constituent ions. Examples include:

- Weak acids: CH*f* COOH (acetic acid), HCOOH (formic acid), H, CO*f* (carbonic acid)
- Weak bases: NH*f* (ammonia), CH*f* NH, (methylamine)

For example, acetic acid establishes the following equilibrium: CH*f* COOH(aq) Ì! CH*f* COO{ (aq) + Hz (aq)

Solutions of weak electrolytes conduct electricity less effectively than strong electrolytes due to the lower concentration of ions.

Non-electrolytes do not produce ions when dissolved in water and therefore do not conduct electricity. Examples include glucose, sucrose, alcohol, and most organic compounds.

Degree of Ionization

The degree of ionization (á) quantifies the extent to which an electrolyte dissociates into ions. It is defined as the fraction of the total electrolyte that has ionized:

á = Number of molecules ionized / Total number of molecules dissolved

Alternatively, it can be expressed in terms of concentrations:

á = Concentration of ionized molecules / Initial concentration of electrolyte

For strong electrolytes, á H" 1 (or 100%), indicating complete ionization. For weak electrolytes, á < 1, typically ranging from 0.01 to 0.1 (1% to 10%), depending on the specific electrolyte and its concentration.

The degree of ionization depends on several factors:

1. **Nature of the electrolyte**: Stronger acids and bases have higher degrees of ionization.
2. **Concentration of the solution**: The degree of ionization generally decreases with increasing concentration due to the common ion effect and increased

ionic interactions.

3. **Temperature**: Higher temperatures typically increase the degree of ionization.
4. **Presence of common ions**: The addition of a common ion decreases the degree of ionization of a weak electrolyte.

For a weak acid HA with initial concentration C€ , the degree of ionization can be related to the acid dissociation constant (K) by the expression:

á = "(K /C€) (when á is small, typically < 0.05)

This relationship indicates that the degree of ionization decreases with increasing concentration, which is known as the dilution law.

Ionization Constant and Ionic Product of Water

Ionization Constant

The ionization constant (also called the dissociation constant) quantifies the extent of ionization of a weak electrolyte at equilibrium. For a weak acid HA that dissociates according to the equation:

HA(aq) Ì! Hz (aq) + A{ (aq)

The acid dissociation constant (K) is defined as:

K = [Hz][A{]/[HA]

Where [Hz], [A{], and [HA] represent the molar concentrations of hydrogen ions, anions, and undissociated acid at equilibrium, respectively.

Similarly, for a weak base B that ionizes according to:

B(aq) + H, O(l) Ì! BHz (aq) + OH{ (aq)

The base dissociation constant (K') is defined as:

K' = [BHz][OH{]/[B]

The magnitude of these constants provides insight into the strength of the acid or base. Larger values of K or K' indicate stronger acids or bases, respectively.

Ionic Product of Water

Pure water undergoes self-ionization (autoionization) to a small extent:

H, O(l) + H, O(l) Ì! H*f* Oz (aq) + OH{ (aq)

Often simplified as:

H, O(l) Ì! Hz (aq) + OH{ (aq)

At equilibrium, the product of the concentrations of hydrogen and hydroxide ions is constant at a given temperature. This constant is known as the ionic product of water (K!"):

K!" = [Hz][OH{]

At 25°C, K!" = 1.0 × 10{ ¹t mol²/L².

In pure water at 25°C, [Hz] = [OH{] = 1.0 × 10{ w mol/L, indicating a neutral solution. In acidic solutions, [Hz] > 10{ w mol/L and [OH{] < 10{ w mol/L. In basic solutions, [Hz] < 10{ w mol/L and [OH{] > 10{ w mol/L.

The value of K!" increases with temperature because the ionization of water is an endothermic process. For example, at 100°C, K!" H" 1.0 × 10{ ¹² mol²/L².

Ionization of Weak Acids and Bases

Weak Acids

Weak acids partially ionize in aqueous solutions, establishing an equilibrium between the undissociated acid and its ions. Consider a generic weak acid HA:

HA(aq) + H, O(l) Ì! H*f* Oz (aq) + A{ (aq)

The acid dissociation constant (K) for this equilibrium is:

K = [H*f* Oz][A{]/[HA]

For simplicity, H*f* Oz is often written as Hz , and the equilibrium becomes:

HA(aq) Ì! Hz (aq) + A{ (aq) K = [Hz][A{]/[HA]

If the initial concentration of the acid is C€ and the degree of ionization is á, then at equilibrium:

- [HA] = C€ (1-á)
- [Hz] = [A{] = C€ á

Substituting these values into the expression for K :

K = (C€ á)(C€ á)/(C€ (1-á)) = C€ á²/(1-á)

For weak acids where á << 1, the expression simplifies to:

K H" C€ á² á H" "(K /C€)

This relationship indicates that the degree of ionization decreases with increasing concentration, which is known as Ostwald's dilution law.

Examples of weak acids and their dissociation constants at 25°C:

- Acetic acid (CH*f* COOH): K = 1.8 × 10{ u
- Formic acid (HCOOH): K = 1.8 × 10{ t
- Carbonic acid (H, CO*f*): K = 4.3 × 10{ w

Weak Bases

Weak bases also partially ionize in aqueous solutions. Consider a generic weak base B:

B(aq) + H, O(l) Ì! BHz (aq) + OH{ (aq)

The base dissociation constant (K') for this equilibrium is:

K' = [BHz][OH{]/[B]

Similar to weak acids, if the initial concentration of the base is C€ and the degree of ionization is á, then at equilibrium:

- [B] = C€ (1-á)
- [BHz] = [OH{] = C€ á

Substituting these values:

K‘ = (C€ á)(C€ á)/(C€ (1-á)) = C€ á²/(1-á)

For weak bases where á << 1:

K‘ H” C€ á² á H” “(K‘ /C€)

Examples of weak bases and their dissociation constants at 25°C:

- Ammonia (NH*f*): K‘ = 1.8 × 10{ u
- Methylamine (CH*f* NH,): K‘ = 4.4 × 10{ t
- Pyridine (C… H… N): K‘ = 1.7 × 10{ y

Polyprotic Acids

Polyprotic acids can donate multiple protons sequentially. Each ionization step has its own dissociation constant, with K > K, > K*f* and so on.

For example, phosphoric acid (H*f* PO,,) ionizes in three steps:

H*f* PO,, (aq) Ì! Hz (aq) + H, PO,, { (aq) K = 7.5 × 10{ ³ H, PO,, { (aq) Ì! Hz (aq) + HPO,, ²{ (aq) K, = 6.2 × 10{ x HPO,, ²{ (aq) Ì! Hz (aq) + PO,, ³{ (aq) K*f* = 4.8 × 10{ ¹³

The significant decrease in dissociation constants with each successive step is due to the increasing difficulty of removing a proton from an increasingly negatively charged species.

pH Scale

The pH scale provides a convenient way to express the acidity or basicity of a solution based on the concentration of hydrogen ions.

pH is defined as the negative logarithm (base 10) of the hydrogen ion concentration:

pH = -log € [Hz]

Similarly, pOH represents the negative logarithm of the hydroxide ion concentration:

pOH = -log € [OH{]

Given that K!" = [Hz][OH{] = 10{ ¹t at 25°C, taking the negative logarithm of both sides:

-log € (K!") = -log € ([Hz][OH{]) -log € (10{ ¹t) = -log € [Hz] - log € [OH{] 14 = pH + pOH

Therefore, at 25°C, the sum of pH and pOH is always 14.

The pH scale typically ranges from 0 to 14, with:

- pH < 7 indicating an acidic solution ([Hz] > 10{ w mol/L)
- pH = 7 indicating a neutral solution ([Hz] = 10{ w mol/L)
- pH > 7 indicating a basic solution ([Hz] < 10{ w mol/L)

It's important to note that pH values outside the range of 0-14 are possible for very strong acids or bases or in non-aqueous solutions.

Calculating pH for Different Types of Solutions

1. **Strong Acids**: For a strong acid with concentration C€ , assuming complete ionization: [Hz] = C€ pH = -log € (C€)
2. **Strong Bases**: For a strong base with concentration C€ , assuming complete ionization: [OH{] = C€ pOH = -log € (C€) pH = 14 - pOH = 14 + log € (C€)
3. **Weak Acids**: For a weak acid HA with concentration C€ and dissociation constant K : [Hz] H" "(K × C€) (when á << 1) pH = -log € [Hz] = -log € ("(K × C€)) = -½log € (K × C€)
4. **Weak Bases**: For a weak base B with concentration C€ and dissociation constant K' : [OH{] H" "(K' × C€) (when á << 1) pOH = -log € [OH{] = -½log € (K' × C€) pH = 14 - pOH = 14 + ½log € (K' × C€)

The pH scale is extensively used in various fields, including chemistry, biology, medicine, agriculture, and environmental science, to monitor and control the acidity or basicity of solutions.

Common Ion Effect and Solubility Product

Common Ion Effect

The common ion effect refers to the suppression of the ionization of a weak electrolyte due to the presence of a common ion (an ion that is also produced by the ionization of the weak electrolyte). According to Le Chatelier's principle, when a stress is applied to a system at equilibrium, the system adjusts to partially counteract the stress. In the context of ionic equilibria, adding a common ion shifts the equilibrium toward the undissociated form, reducing the degree of ionization.

For example, consider the ionization of acetic acid: CH*f* COOH(aq) Ì! CH*f* COO{ (aq) + Hz (aq)

If sodium acetate (CH*f* COONa), which dissociates to produce CH*f* COO{ ions, is added to an acetic acid solution, the equilibrium shifts to the left, decreasing the ionization of acetic acid and consequently decreasing the concentration of Hz ions, resulting in a higher pH.

Similarly, for a weak base like ammonia: NH*f* (aq) + H, O(l) Ì! NH,, z (aq) + OH{ (aq)

The addition of ammonium chloride (NH,, Cl), which provides NH,, z ions, shifts the equilibrium to the left, decreasing the concentration of OH{ ions and resulting in a lower pH.

Solubility Product

The solubility product (Ksp) is an equilibrium constant that describes the solubility of a sparingly soluble ionic compound. For a general salt A "Ž B g"Ž that dissociates according to:

A "Ž B g"Ž (s) Ì! xAz n(aq) + yB{ P"(aq)

The solubility product is defined as:

Ksp = [Az n]ã[B{ P"]¸

Where [Az n] and [B{ P"] are the molar concentrations of the ions at equilibrium.

For example, for silver chloride: AgCl(s) Ì! Agz (aq) + Cl{ (aq) Ksp = [Agz][Cl{]

For calcium phosphate: Ca*f* (PO,,), (s) Ì! 3Ca²z (aq) + 2PO,, ³{ (aq) Ksp = [Ca²z]³[PO,, ³{]²

The value of Ksp provides information about the solubility of the compound. A higher Ksp indicates greater solubility, while a lower Ksp indicates lower solubility.

Relationship between Solubility and Solubility Product

The molar solubility (S) of a salt is the number of moles of the salt that dissolve in one liter of solution to form a saturated solution. The relationship between the molar solubility and the solubility product depends on the stoichiometry of the salt.

For a salt A "Ž B g"Ž :

- [Az n] = xS
- [B{ P"] = yS

Substituting into the Ksp expression: Ksp = (xS)ã(yS)¸ = x^x × y^y × S^(x+y)

Rearranging to solve for S: S = [(Ksp)/(x^x × y^y)]^[1/(x+y)]

For example, for silver chloride (AgCl): If S is the molar solubility, then [Agz] = [Cl{] = S Ksp = [Agz][Cl{] = S × S = S² S = "Ksp

For calcium phosphate (Ca*f* (PO,,),): [Ca²z] = 3S and [PO,, ³{] = 2S Ksp = [Ca²z]³[PO,, ³{]² = (3S)³(2S)² = 108Su S = [(Ksp)/108]^(1/5)

Common Ion Effect on Solubility

The common ion effect also influences the solubility of ionic compounds. The presence of a common ion decreases the solubility of a sparingly soluble salt. For example, the solubility of silver chloride (AgCl) decreases in the presence of sodium chloride (NaCl) due to the common Cl{ ion. Similarly, the solubility of calcium carbonate (CaCO*f*) decreases in the presence of calcium chloride (CaCl,) due to the common Ca²z ion.

Mathematically, if a sparingly soluble salt A “Ž B g”Ž is dissolved in a solution already containing one of its ions (e.g., Az n with a concentration [Az n]€), the molar solubility (S) can be calculated using the solubility product (Ksp):

Ksp = [Az n]ã[B{ P”]¸ = ([Az n]€ + xS)ã(yS)¸

If [Az n]€ >> xS, the equation simplifies to: Ksp H” [Az n]€ ã(yS)¸

Solving for S: S H” [(Ksp)/([Az n]€ ã × y^y)]^(1/y)

Illustrative Examples

Example 1: Calculating Solubility from Ksp Calculate the molar solubility of calcium fluoride (CaF,) in water at 25°C, given that Ksp = 3.9 × 10{ ¹¹.

Solution: CaF, (s) Ì! Ca²z (aq) + 2F{ (aq)

Let S be the molar solubility of CaF, . At equilibrium: [Ca²z] = S [F{] = 2S

Ksp = [Ca²z][F{]² = S(2S)² = 4S³ 3.9 × 10{ ¹¹ = 4S³ S³ = (3.9 × 10{ ¹¹)/4 = 9.75 × 10{ ¹² S = “(9.75 × 10{ ¹²) = 2.13 × 10{ t mol/L

Example 2: Common Ion Effect on Solubility Calculate the molar solubility of calcium fluoride (CaF,) in a 0.10 M CaCl, solution at 25°C, given that Ksp = 3.9 × 10{ ¹¹.

Solution: In a 0.10 M CaCl, solution, [Ca²z]€ = 0.10 M (from CaCl,).

Let S be the molar solubility of CaF, in this solution. At equilibrium: [Ca²z] = 0.10 + S H” 0.10 (since S is expected to be very small) [F{] = 2S

Ksp = [Ca²z][F{]² = (0.10)(2S)² = 0.40S² 3.9 × 10{ ¹¹ = 0.40S² S² = (3.9 × 10{ ¹¹)/0.40 = 9.75 × 10{ ¹¹ S = “(9.75 × 10{ ¹¹) = 3.12 × 10{ v mol/L

Comparing the results from both examples, the molar solubility of CaF, decreases from 2.13 × 10{ t mol/L in pure water to 3.12 × 10{ v mol/L in 0.10 M CaCl, solution, demonstrating the common ion effect.

Salt Hydrolysis

Salt hydrolysis refers to the reaction of the cation or anion (or both) of a dissolved salt with water, resulting in a solution that is not neutral. The pH of a salt solution depends on the nature of the constituent ions.

Salts can be categorized into four types based on the nature of the acid and base from which they are derived:

1. Salts of strong acid and strong base (e.g., NaCl)
2. Salts of strong acid and weak base (e.g., NH,, Cl)
3. Salts of weak acid and strong base (e.g., CH*f* COONa)
4. Salts of weak acid and weak base (e.g., NH,, CH*f* COO)

Salts of strong acid and strong base do not undergo hydrolysis, and their solutions are neutral (pH = 7). The other types of salts undergo hydrolysis to varying extents, resulting in solutions that are either acidic or basic.

Hydrolysis of Salts of Strong Acid and Weak Base

When a salt derived from a strong acid and a weak base dissolves in water, the cation (the conjugate acid of the weak base) undergoes hydrolysis, while the anion (the conjugate base of the strong acid) does not.

Consider ammonium chloride (NH,, Cl), a salt of the strong acid HCl and the weak base NH*f* :

NH,, Cl(s) '! NH,, z (aq) + Cl{ (aq)

The ammonium ion undergoes hydrolysis: NH,, z (aq) + H, O(l) Ì! NH*f* (aq) + H*f* Oz (aq)

This reaction produces hydronium ions, making the solution acidic (pH < 7).

The hydrolysis constant (Kh) for this reaction is related to the dissociation constant of the weak base (K‘) and the ionic product of water (K!"):

Kh = K!"/K‘

For the ammonium ion: Kh = K!"/K‘ (NH*f*) = 10{ ¹t /1.8 × 10{ u = 5.56 × 10{ ¹p

The degree of hydrolysis (h) is defined as the fraction of salt that undergoes hydrolysis:

h = Concentration of hydrolyzed salt / Initial concentration of salt

For a salt of a strong acid and a weak base with initial concentration C:

h = “(Kh/C) (when h << 1)

The pH of the solution can be calculated as:

pH = -log € [Hz] = -log € (h × C) = -log € (“(Kh × C))

Calculation of Hydrolysis Constant and Degree of Hydrolysis for Salt of Strong Acid and Weak Base

Let’s consider a specific example: a 0.10 M solution of ammonium chloride (NH,, Cl) at 25°C, where K‘ for NH*f* is 1.8 × 10{ u .

Step 1: Calculate the hydrolysis constant (Kh). Kh = K!”/K‘ = 10{ ¹t /1.8 × 10{ u = 5.56 × 10{ ¹p

Step 2: Calculate the degree of hydrolysis (h). h = “(Kh/C) = “(5.56 × 10{ ¹p / 0.10) = “(5.56 × 10{ y) = 7.46 × 10{ u

This means that approximately 0.00746% of the NH,, z ions undergo hydrolysis.

Step 3: Calculate the pH of the solution. [Hz] = h × C = (7.46 × 10{ u)(0.10) = 7.46 × 10{ v mol/L pH = -log € [Hz] = -log € (7.46 × 10{ v) = 5.13

The solution is slightly acidic, as expected for a salt of a strong acid and a weak base.

Hydrolysis of Other Types of Salts

Salts of Weak Acid and Strong Base: The anion undergoes hydrolysis, producing hydroxide ions and making the solution basic (pH > 7).

For example, sodium acetate (CH*f* COONa): CH*f* COONa(s) ’! Naz (aq) + CH*f* COO{ (aq)

The acetate ion undergoes hydrolysis: CH*f* COO{ (aq) + H, O(l) Ì! CH*f* COOH(aq) + OH{ (aq)

The hydrolysis constant is: Kh = K!"/K (CH*f* COOH) = 10{ ¹t /1.8 × 10{ u = 5.56 × 10{ ¹p

Salts of Weak Acid and Weak Base: Both the cation and anion undergo hydrolysis. The pH of the solution depends on the relative strengths of the acid and base.

For example, ammonium acetate (NH,, CH*f* COO): NH,, CH*f* COO(s) '! NH,, z (aq) + CH*f* COO{ (aq)

Both ions undergo hydrolysis: NH,, z (aq) + H, O(l) Ì! NH*f* (aq) + H*f* Oz (aq) CH*f* COO{ (aq) + H, O(l) Ì! CH*f* COOH(aq) + OH{ (aq)

The pH of the solution depends on the relative values of K (acid) and K‘ (base):

- If K > K‘ , the solution is acidic (pH < 7).
- If K < K‘ , the solution is basic (pH > 7).
- If K = K‘ , the solution is neutral (pH = 7).

Buffer Solutions: Introduction and Henderson-Hasselbalch Equations

Buffer solutions play an important role as a chemical system that resist changes in pH upon the addition of small amounts of acid or base. Such solutions are important in numerous biological processes, lab exercises, and industrial applications where control over pH is needed for proper operation.

When a weak acid, and its conjugate base, or a weak base and its conjugate acid are present in appreciable and comparable concentrations, we have a buffer solution. Hence adding the buffer enables this combination to wipe out more hydrogen hydroxide ions (OH-) or hydrogen ions (H+) strong, which step down the pH leaps.

Buffer Composition and Function

Some of the important factors that influence the effectiveness of a buffer include the relative concentrations of the buffer components and the correlation between the pH of the buffer and the pKa (or pKb) of the acidic (or basic) species involved in the

system. Buffers function best when the pH is about one unit on either side of the pKa of the weak acid part.

pH = pKa + log [A"]/[HA] (2.2) When a small amount of strong acid is added to the buffer, conjugate base component of the buffer reacts with the added H+ ions to convert them to the weak acid form. In contrast, as you add a small amount of strong base, the weak acid component of the buffer gives up protons to neutralize the added OH- ions, resulting in water and converting some of the weak acid into its conjugate base form.

The Henderson-Hasselbalch Equation for Acidic Buffers

The Henderson-Hasselbalch equation, which defines the relationship between the pH of a buffer solution and the concentrations of the respective acidic and conjugate base components. For an acidic buffer that consists of a weak acid (HA) and it conjugate base (A-), the equation is:

pH = pKa + log([A-]/[HA])

Where:

- pH is the negative logarithm of the hydrogen ion concentration
- pKa is the negative logarithm of the acid dissociation constant
- [A-] is the molar concentration of the conjugate base
- [HA] is the molar concentration of the weak acid

This equation is derived from the acid dissociation equilibrium: HA Ì! H+ + A-

The equilibrium constant for this reaction, Ka, is given by: Ka = [H+][A-]/[HA]

Taking the negative logarithm of both sides: -log(Ka) = -log([H+]) - log([A-]/[HA])

Which rearranges to: pH = pKa + log([A-]/[HA])

The Henderson-Hasselbalch Equation for Basic Buffers

For a basic buffer composed of a weak base (B) and its conjugate acid (BH+), the Henderson-Hasselbalch equation takes a slightly different form:

pOH = pKb + log([BH+]/[B])

Where:

- pOH is the negative logarithm of the hydroxide ion concentration
- pKb is the negative logarithm of the base dissociation constant
- [BH+] is the molar concentration of the conjugate acid
- [B] is the molar concentration of the weak base

Since pH + pOH = 14 (in aqueous solutions at 25°C), we can convert this to pH:

pH = 14 - pKb - log([BH+]/[B])

Alternatively, using the relationship pKa + pKb = 14 for conjugate acid-base pairs, we can express the equation as:

pH = pKa - log([BH+]/[B])

This form of the equation is often more convenient, as it allows consistent use of pKa values for both acidic and basic buffers.

Buffer Capacity and Preparation

The buffer capacity refers to the amount of acid or base a buffer can neutralize before significant pH changes occur. It is highest when the concentrations of the weak acid and its conjugate base are equal, which occurs when pH = pKa.

To prepare a buffer solution with a specific pH, the Henderson-Hasselbalch equation can be rearranged to determine the required ratio of conjugate base to acid:

[A-]/[HA] = 10^(pH - pKa)

Practical buffer preparation often involves:

1. Selecting an appropriate weak acid with a pKa near the desired pH
2. Calculating the required ratio of conjugate base to acid
3. Preparing solutions of the weak acid and its conjugate base, or

4. Preparing a solution of the weak acid and partially neutralizing it with a strong base to generate the conjugate base in situ

Common buffer systems include acetate buffers (acetic acid/acetate), phosphate buffers, and TRIS buffers, each suitable for different pH ranges.

In biological systems, buffers play crucial roles in maintaining the pH of blood (primarily through the bicarbonate buffer system) and intracellular fluids, ensuring optimal conditions for enzymatic reactions and other biochemical processes.

Unit -9 Phase Equilibrium

- Gibbs phase (no derivation), phase, component and degree of freedom
- Application of phase rule to one component system (water system and Sulphur systems), Reduced phase rule
- Application of phase rule to two component systems: Pb-Ag system.
- Congruent Ferric chloride system.

Phase Equilibrium

Gibbs Phase Rule, Phases, Components, and Degrees of Freedom

The freedom degree is the number of independent intensive variables (like, temperature, pressure and composition) which could be changed, without disturbing the equilibrium state of the system. To characterize the state of a system, we need to specify these variables.

The number 2 in the Gibbs Phase Rule equation corresponds to the two most common external parameters of phase equilibria: temperature and pressure. Neutron pipes are made of transparent, homogeneous material so that Neutron phase equilibrium is a crucial rule in trying to penetrate different matter. Before getting into phase equilibrium, we need to understand the Gibbs Phase Rule.

The Gibbs Phase Rule relates the number of degrees of freedom (F) in a system at equilibrium to the number of components (C) and the number of phases (P):

$F = C - P + 2$

It is the basis of the analysis of phase equilibria in systems of this type. Let us tease out the individual terms in this equation:

A phase is a physically separate, homogeneous body of matter in which all physical and chemical properties are the same throughout the system. Known examples may involve solid, liquid and gas phases, although a system may consist of multiple solid phases with different crystal arrangements or multiple liquid phases that do not mix. A component is a chemically independent part of a system. The minimum number of independent chemical species required to define the composition of all phases in the system is the number of components. For uncomplicated systems, this often corresponds to the number of unique chemical substances, but for systems with chemical reactions or constraints, it may be lesser number of components.

Application of Phase Rule to One-Component Systems

Water System

The water system is a classic example of a one-component system (C = 1) that exhibits rich phase behavior. Applying the Gibbs Phase Rule:

$F = 1 - P + 2 = 3 - P$

For this system, the maximum number of phases that can coexist in equilibrium is three (when F = 0), which occurs at the triple point where solid, liquid, and vapor phases coexist at a specific temperature (0.01°C) and pressure (611.73 Pa).

The phase diagram of water displays several noteworthy features:

1. **Triple point**: Where ice, liquid water, and water vapor coexist (F = 0)
2. **Critical point**: Where the distinction between liquid and vapor phases disappears (T = 374°C, P = 218 atm)
3. **Sublimation curve**: Direct transition between solid and vapor phases
4. **Melting curve**: Transition between solid and liquid phases
5. **Vapor pressure curve**: Transition between liquid and vapor phases

A unique characteristic of the water system is the negative slope of the solid-liquid equilibrium line, indicating that ice melts under pressure. This unusual property arises because water expands upon freezing, unlike most substances. Along any phase boundary (where two phases coexist), F = 1, meaning only one variable (either temperature or pressure) can be independently varied while maintaining equilibrium between the two phases.

Sulfur System

The sulfur system presents a more complex one-component system due to sulfur's allotropy (existence in different solid forms). The main phases in the sulfur system include:

1. **Rhombic sulfur (Sá)**: Stable below 95.5°C
2. **Monoclinic sulfur (Sâ)**: Stable between 95.5°C and 119°C
3. **Liquid sulfur**: Exists above melting points of solid phases
4. **Sulfur vapor**: Gaseous phase

Applying the Gibbs Phase Rule to the sulfur system:

F = 1 - P + 2 = 3 - P

Similar to water, the maximum number of phases that can coexist at equilibrium is three, which occurs at transition points.

The phase diagram of sulfur features:

1. **Triple points**: Where three phases coexist (F = 0)
    - Rhombic sulfur, monoclinic sulfur, and vapor
    - Rhombic sulfur, monoclinic sulfur, and liquid sulfur
    - Monoclinic sulfur, liquid sulfur, and vapor
2. **Phase boundaries**: Where two phases coexist (F = 1)
    - Rhombic-monoclinic transition line
    - Solid-liquid transition lines

- Solid-vapor and liquid-vapor transition lines

The existence of multiple solid phases makes the sulfur system a rich example for studying phase transformations in single-component systems.

Reduced Phase Rule

In certain situations, we may wish to analyze phase equilibria at constant pressure or constant temperature, leading to the Reduced Phase Rule:

For constant pressure: $F' = C - P + 1$ For constant temperature: $F' = C - P + 1$

Where F' represents the reduced degrees of freedom. This simplification is particularly useful when working with phase diagrams that are commonly constructed at either constant pressure or constant temperature.

For example, in a one-component system at constant pressure: $F' = 1 - P + 1 = 2 - P$

This implies that a maximum of two phases can coexist at equilibrium under isobaric conditions.

Application of Phase Rule to Two-Component Systems

Two-component systems (C = 2) introduce compositional variables, making their phase diagrams more complex and typically requiring three-dimensional representation. However, by fixing one variable (usually pressure), we can analyze these systems using two-dimensional phase diagrams.

Applying the Gibbs Phase Rule to a two-component system:

$F = 2 - P + 2 = 4 - P$

At constant pressure, the reduced phase rule gives: $F' = 2 - P + 1 = 3 - P$

Lead-Silver (Pb-Ag) System

The lead-silver system is a classic example of a two-component system with limited solid solubility and a eutectic point. Key features of this system include:

1. **Liquid phase**: Homogeneous mixture of molten Pb and Ag

2. **Solid phases**: Almost pure Pb and Ag with limited solid solubility
3. **Eutectic point**: Where the liquid phase solidifies directly into a mixture of two solid phases

At constant pressure, applying the reduced phase rule: F' = 2 - P + 1 = 3 - P

The phase diagram consists of several regions:

1. **Single-phase regions** (F' = 2):
   - Liquid solution (L): Requires specifying both temperature and composition
   - Solid solution rich in Ag (á): Limited solubility of Pb in Ag
   - Solid solution rich in Pb (â): Limited solubility of Ag in Pb
2. **Two-phase regions** (F' = 1):
   - L + á: Liquid in equilibrium with solid á phase
   - L + â: Liquid in equilibrium with solid â phase
   - á + â: Two solid phases in equilibrium
3. **Three-phase point** (F' = 0):
   - Eutectic point: Where L, á, and â phases coexist at a specific temperature (303°C) and composition (2.6 wt% Ag)

The eutectic composition represents the lowest melting point in the system. The phase diagram guides understanding how the Pb-Ag system behaves during cooling or heating:

- Above the liquidus line: Only liquid phase exists
- Between liquidus and solidus: Two phases coexist (liquid + solid)
- Below the solidus: Only solid phases exist

For any overall composition, the lever rule can be applied to determine the relative amounts of phases present in two-phase regions.

Ferric Chloride System (Congruent Melting)

The ferric chloride-water system (FeCl*f* -H, O) exhibits congruent melting behavior, which occurs when a solid compound melts to form a liquid of the same composition. This system features several solid hydrates of ferric chloride with different water content.

Applying the reduced phase rule at constant pressure: F' = 2 - P + 1 = 3 - P

The phase diagram of the FeCl*f* -H, O system includes:

1. **Single-phase regions** (F' = 2):
    - Liquid solution: Homogeneous mixture of FeCl*f* and H, O
    - Solid phases: Various hydrates like FeCl*f* ·6H, O, FeCl*f* ·4H, O, FeCl*f* ·2.5H, O, etc.
2. **Two-phase regions** (F' = 1):
    - Liquid in equilibrium with a solid phase
3. **Three-phase points** (F' = 0):
    - Eutectic points: Where liquid and two solid phases coexist
    - Peritectic points: Where a solid phase decomposes upon heating to form a different solid phase and liquid

A key feature of this system is the congruent melting point of the FeCl*f* ·6H, O hydrate at around 37°C. At this point, the hydrate melts to form a liquid of identical composition without decomposition.

The phase diagram for this system displays multiple thermal arrest points corresponding to eutectic and peritectic transformations. These transitions are critical in understanding the behavior of the system during processes like crystallization, dissolution, and hydration/dehydration.

Practical Significance of Phase Equilibria

Understanding phase equilibria has numerous practical applications:

1. **Materials processing**: Controlling phase transformations during heat treatment, casting, and solidification
2. **Separation processes**: Designing distillation, extraction, and crystallization operations
3. **Alloy design**: Developing materials with desired microstructure and properties
4. **Geological processes**: Understanding mineral formation and metamorphism
5. **Chemical reactions**: Optimizing reaction conditions for desired products

The Gibbs Phase Rule provides a powerful framework for analyzing and predicting the behavior of systems under various conditions, making it an essential tool in thermodynamics, materials science, and chemical engineering.

By systematically applying the phase rule to increasingly complex systems—from one-component systems like water and sulfur to two-component systems like Pb-Ag and FeCl*f* -H, O—we gain insights into the fundamental principles governing phase transformations and equilibria in matter.

SELF ASSESSMENT QUESTIONS

Multiple Choice Questions (MCQs)

1. The equilibrium constant for a reaction is affected by:

a) Temperature

b) Catalyst

c) Pressure

d) Both (a) and (c)

2. Le Chatelier's principle states that:

a) Equilibrium shifts to oppose changes

b) Reaction rate remains constant

c) Equilibrium favors reactants

d) Temperature has no effect

3. A weak acid has:

a) Low pKa value

b) High degree of ionization

c) Strong conjugate base

d) Partial dissociation in water

4. The common ion effect is observed in:

a) Buffered solutions

b) Solutions of weak acids and their salts

c) Neutral solutions

d) None of the above

5. The solubility of a salt decreases if:

a) The temperature is increased

b) A common ion is added

c) Pressure is increased

d) pH is increased

6. Henderson-Hasselbalch equation is used to calculate:

a) Solubility

b) pH of buffer solutions

c) Gibbs free energy

d) Equilibrium constant

7. Which is NOT an example of a one-component system?

a) Water system

b) Sulfur system

c) Pb-Ag system

d) CO, system

8. The number of phases in a water system at 0°C and 1 atm pressure is:

a) 1

b) 2

c) 3

d) 4

9. In the Pb-Ag system, the phase rule applies to:

a) A pure substance

b) A binary system

c) A ternary system

d) A non-equilibrium system

10. The solubility product is applicable for:

a) All electrolytes

b) Strong electrolytes

c) Sparingly soluble salts

d) None of the above

Short Answer Questions

1. Define the law of mass action and its significance in equilibrium.

2. Explain the effect of temperature on equilibrium constants.
3. What is Le Chatelier's principle? Give an example.
4. Define pH and write the Henderson-Hasselbalch equation.
5. What is the common ion effect? How does it affect solubility?
6. Explain the significance of solubility product in precipitation reactions.
7. Differentiate between strong and weak electrolytes with examples.
8. How does the phase rule apply to the water system?
9. What is the reduced phase rule?
10. Describe the concept of salt hydrolysis and its effect on solution pH.

Long Answer Questions

1. Derive the expression for the equilibrium constant and explain its significance.
2. Explain Le Chatelier's principle with industrial examples.
3. Discuss the concept of ionic equilibrium and the dissociation of weak acids and bases.
4. Explain the common ion effect and its applications in chemical equilibrium.
5. Describe the solubility product and its significance in qualitative analysis.
6. Derive the Henderson-Hasselbalch equation and explain its applications.
7. Explain the Gibbs phase rule and its applications in one- and two-component systems.
8. Describe the phase diagram of the Pb-Ag system and its industrial importance.
9. Discuss the importance of buffer solutions in biological and industrial applications.
10. Explain how the solubility of a salt is affected by temperature, pressure, and pH.

MODULE -4

PHOTOCHEMISTRY AND LIQUID-LIQUID MIXTURES

4.0 Objective

- Understand the interaction of radiation with matter.
- Differentiate between thermal and photochemical reactions.
- Learn the laws governing the absorption of light and photochemical reactions.
- Study the Jablonski diagram, quantum yield, and examples of photochemical reactions.
- Understand liquid-liquid mixtures, ideal solutions, Raoult's law, and Henry's law.

Unit -10 Photochemistry

Radiation with Matter

Depending on the nature of the interaction, electromagnetic radiation may either pass through matter, be absorbed by matter, be reflected by matter, scatter off matter, or a combination of these processes. Key processes involved are absorption, reflection, refraction, scattering, and transmission. Absorption is the most important of these for photochemistry. Molecules absorb indeed photons of the right amount of energy and the electrons go from their ground states to excited states. Photo-excitation is also very selective, as this energy absorption takes place only at particular wavelengths, which correspond to the difference in energy between the electronic states of the molecule. The energy absorbed in the absorption events can then be released into the environment via different pathways, for example through photochemical processes (the energy is used to break/form chemical bonds) or photophysical processes (the energy is released in the form of radiation through fluorescence and phosphorescence).

Since the energy state of molecules are quantized molecules can exist in discrete energy levels. When radiation interacts with matter, only photons of energy precisely equal to the energy difference between these quantised states can be absorbed. This

principle is responsible for the selectivity of photochemical reactions and, therefore, for the differing reactions by different molecules to different wavelengths of light. Absorption of UV-Vis irradiation, which excites organic molecules, resides in the electronic energy levels range; hence of immediate interest, whilst infrared radiation induces vibrational transitions and microwave radiation-excites rotational transitions.

Thermal Reactions vs Photochemical Reactions

Reactions based on thermal and photochemical mechanisms activate by different paths and have different reaction networks. At high temperatures, the kinetic energy transfer between colliding molecules induces thermal reactions. The energy gets split among all the available vibrational modes of the molecule according to the Boltzmann distribution. Consequently, thermal reactions typically take place along the minimum energy reaction coordinate of the ground state potential energy surface, yielding the most thermodynamically stable products. Unlike these nonradiative processes, photochemical reactions begin with the absorption of photons which results in the electronic excitation of molecules to higher energy states. This electronic excitation is not random, and localized, the way that thermal processes spread energy out in a soup. Excited states function the same way after photochemical reactions, with different electronic configurations, and different potential energy surfaces with respect to the ground state. It thus allows for reaction pathways that are otherwise unattainable under thermal reactions, leading to the formation of thermodynamically disfavored products. Photochemical reactions are also possible at low temperatures because instead of thermal energy, the activation in photoreactions is provided by light energy.

A further important difference is in reaction selectivity. For example, thermal reactions follow the Woodward-Hoffmann rules for pericyclic reactions, but photochemical reactions typically show reverse stereoselectivity because of the differing orbital symmetry requirements of a singlet state versus a triplet state. This transition is responsible for the photochemical utility of certain thermally forbidden cycloaddition reactions that become photochemically available. Because of the high degree of specificity of photochemical reactions with respect to the range of light used, it is possible to control pathways to the formation of products by performing the reactions at the right wavelengths of light, making photochemical methods extremely useful in

organic synthesis especially in the preparation of structures that may be otherwise difficult to access using standard thermal methods.

Principles of the Absorption of Light

Several universal laws govern the way that matter absorbs light. The most well-known of these is the Beer-Lambert Law which relates the amount of light absorbed by a sample to its properties. It says that the absorbance (A) is directly proportional to the concentration (c) of the absorbing species and the pathlength (l) of the sample: A = åcl, where å is the molar absorption coefficient (or molar absorptivity), which is specific to each substance at a specific wavelength. Beer's Law is used to quantitatively relate concentrations of absorbing species determined via spectrophotometric methods.

The Grotthuss-Draper Law (also called the First Law of Photochemistry) states that a compound must absorb light in order for a photochemical reaction to take place. This is expressed in the principle that only absorbed but not incident photons can trigger a photochemical process. Complementing this is the Stark-Einstein Law, or Second Law of Photochemistry, which states that for each photon of light absorbed by a chemical system, only one molecule gets activated for later reaction. This creates one-to-one correspondence between the absorbed photons and the activated molecules, even though, depending on competing deactivation pathways, the final chemical event might be different. Moreover light absorption obeys quantum mechanical selection rules. The transition probability between electronic states is mediated by the overlap of their vibrational wavefunctions (Franck-Condon principle), as well as by spin conservation (spin selection rules). These determine the allowed and forbidden transitions, which affect the degree of intensity observed in absorption spectra. Knowledge of these laws is foundational for interpreting spectroscopic data as well as being able to design efficient photochemical processes.

Laws of Photochemistry

Photochemistry is a discipline governed by a few fundamental laws that apply to the interaction of light with matter and subsequent transformations. The making of a new rule and a Grotthuss-Draper Law in photochemistry comes from the early 19th

century. Only the light absorbed by a molecule can produce photochemical change. This is a basic principle because it asserts that only when light is absorbed by the system will a photochemical reaction be processed rather than when just arrive at system. The absorption process depends on the wavelength, which is given by the molecular species (determined by the electronic structure). The Stark-Einstein Law (also called the Second Law of Photochemistry or the Photochemical Equivalence Law) gives this quantitative link. It says, for every quanta of radiation absorbed by a chemical system, only a single molecule is permitted activation for follow-up reaction. 11, 12 More specifically, it means that one mole of a substance undergoing photochemical reaction absorbs one einstein(6.022×10^{23} photons) of radiation. This law defined the primary quantum yield as theoretically no greater than unity; however, secondary processes may result in apparent deviation.

The Bunsen-Roscoe Law of Reciprocity states that the photochemical effect is proportionate to the total energy dose, no matter how that dose is administered. So, the same photochemical principle should work when exposing a system to a strong light (high intensity) for a short period of time, in comparison of low intensity light for a proportionally longer period of time, given that the total delivered energy in both cases is the same. This law, however, is limited and fails to hold true under very high or low intensities or when other processes compete at different rates. It states that for luminescence, the quantum yield is generally independent of the excitation wavelength (Kasha-Vavilov Rule). This implies that regardless of the excited state which was initially populated, there is normally a rapid internal conversion to the lowest excited state of the same multiplicity before emission. Hence, fluorescence normally takes place from S , the lowest excited singlet state (T , lowest triplet state), regardless of where the initial excitation is.

The Jablonski Diagram Showing Different Processes

This visualizes the electronic states of molecules as well as transitions between them; it is called a Jablonski diagram. It is a basic tool to understand photophysical and photochemical processes. In the diagram, energy levels are represented as horizontal lines, often with the ground singlet state (S€) at the bottom, then the next higher singlet states (S , S, , etc.) and the lower triplet states (T , T, , etc.). There are also several vibrational levels that the electronic states can be in, shown as thinner lines within each electronic state. Most molecules upon absorption of a photon are

promoted from S€ to one of the vibrational levels of S or S, , a process that takes place on the femtosecond time scale. After this first excitation, there are multiple routes to dissipate the energy. Vibrational relaxation (VR) describes the process by which the molecule undergoes a rapid cascade from higher to lower vibrational levels of a given electronic state with excess energy released into the surrounding medium as heat. And this happens in the span of picoseconds. 9. Internal conversion (IC) is a radiationless transition between electronic states of the same spin multiplicity, i.e. from higher to lower energy states (e.g. S, to S). This process is also very fast taking place in the range of picoseconds to nanoseconds.

In other words, fluorescence is a radiative transition from the lowest vibrational level of S to the ground state (S€) with emission of a photon. This fluorescence is generally emitted on the nanosecond timescale and at longer wavelengths/lower energy than absorption, due to the loss of energy from vibrational relaxation i.e., Stokes shift. Intersystem crossing (ISC) is a non-radiative path from an excited state (e.g. S) to a different lower state (e.g. T) of different spin multiplicity. This spin-forbidden process is typically slower than internal conversion, but can be facilitated by the presence of heavy atoms or paramagnetic species. It is worth noting that phosphorescence is a radiative transition from T to S€ , which is spin-forbidden and therefore occurs significantly slower than fluorescence, across timescales from microseconds to seconds at low temperatures and longer. Triplet states have a longer lifetime; therefore, they are of particular importance for photochemistry because they allow sufficient time for chemical reactions to happen. The Jablonski diagram also provides information regarding non-radiative decay from T to S€ and photochemical pathways that may branch off of excited states, thereby providing a complete overview of excited state dynamics.

Quantum Yield

Quantum yield (Ö) is a key parameter in photochemistry quantifying the efficiency of a photochemical process. The quantum yield is defined as the ratio of the number of individual molecules that undergo a specific photochemical reaction to the number of photons absorbed by the system. Quantum yield, for a photochemical reaction that yields a given product, is given by:

Ö = Number of molecules reacted or products formed / Number of photons absorbed.

This is a dimensionless ratio that directly quantifies the efficiency of light energy absorption into chemical change. A quantum yield of 1.0 corresponds to total efficiency, where every absorbed photon causes one molecule to react. Quantum yields less than 1.0 denote that counteracting deactivation processes are extracting energy from the photochemical reaction pathway we want most, whereas values greater than 1.0 inform us of chain reactions or secondary thermal processes that are amplifying the initial photochemical step. Depending on reactant molecular types, reaction environment (temperature, pressure, solvent) and type of incoming radiation, quantum yield is a function. Different photochemical processes from the same excited state will usually compete with each other (19), and thus their individual quantum yields will sum to the total quantum yield determined for deactivation of that state. In the absence of photochemical reactions, the sum of the quantum yields for the primary photophysical processes (e.g., fluorescence, phosphorescence, intersystem crossing) will equal unity. Quantum yield is an important indicator of the potential and efficiency of photochemical processes in applications, from synthetic organic chemistry to solar energy conversion. This enables researchers to optimize both reaction conditions and photosensitizer to design more efficient photochemical systems. In addition, the determination of quantum yields offers fundamental information on reaction mechanisms and competition between the different deactivation processes of excited states.

Quantitative Study of Reaction Quantum Yields

Accurate estimation of quantum yield is crucial for unraveling photochemical reaction mechanisms and designing efficient photochemical systems. There are several methods for doing this, each with their own specific use cases and limitations. The most basic method is measuring how many photons are absorbed and what photochemical change was generated. The actinometric methods are broadly applicable in measuring quantum yields. Chemical actinometers (e.g., potassium ferrioxalate, uranyl oxalate, 2,2'-dimethoxybenzoin) are defined quantum yield systems that should be used as references. By placing the same excitation source on the sample and the actinometer

(in the same conditions) and using the response of the actinometer, the photon flux can be calculated. Subsequently, the quantum yield of the sample reaction is determined by comparing the extent of reaction in the sample to the evolution of the actinometer, correcting for differences in absorption. Alternatively, one can use specialized equipment such as quantum yield determination systems that combine light sources, monochromators, sample chambers, and detection systems. These configurations closely regulate the irradiation conditions and measure the incident light intensity (using calibrated photodiodes) and the sample's absorption, and progress of reaction directly. Moreover, time-resolved spectroscopy is able to provide detailed information about the lifetimes and concentrations of such transient species, which together can be used to determine the quantum yields for complex photochemical processes.

For fluorescence quantum yields, standard methods relying on an appropriate standard of known quantum yield are widely adopted. The sample and the standard are prepared at equal absorbance at the excitation wavelength, and their fluorescence emission spectra are measured under the same conditions. The fluorescence quantum yield of the sample relative to that of the standard can be determined by comparing the integrated emission intensities while correcting for the differences in absorption and refractive indices of the solvents. R, where \Phi is the quantum efficiencies evaluated for the observed photochemical reaction method, which examine the calorimetric heat (phonons/photons or other) released relative to the energy of the incident photons. This is particularly valuable for systems in which shaking off traditional analytical methods is hard. Regardless of the spectroscopic method chosen for measuring quantum yield, accurate quantum yield determination requires a close attention to experimental conditions including monochromatic light sources, uniform irradiation, accurate measurement actinometry, and secondary thermal reactions that may occur after the primary photochemical step.

Low and High Quantum Yields Explained

A photochemical reaction's quantum yield can range widely from system to system and conditions to conditions, taking values far below unity, to values well in excess of 100. This understanding of the low or high quantum yields sheds light on the reaction mechanisms and allows designing of more efficient reaction photochemical processes. Low quantum yields (Ö 1) represent that the number of produced molecules is higher

than apparent photons absorbed by the reaction system, which also would imply the existence of chain reactions or secondary processes. In these scenarios, chain reactions occur when the first photochemical step produces chemically reactive intermediates (radicals), causing the photonic energy to propagate through multiple thermal reaction cycles until termination. As an example, quantum yields on the order of several thousand are possible for the photodissociative chlorination of methane, where each photochemically generated chlorine radical initiates a cascade of consecutive propagation steps. Photosensitization processes wherein excited sensitizer molecules transfer energy to substrate molecules that subsequently undergo chemical reaction can also produce apparent quantum yields greater than unity so long as the sensitizer is regenerated and available for multiple energy transfer events.

Quantum yield is a phenomenon that is critically dependent on experimental conditions. Temperature impacts the rates of competing processes and the stability of reactive intermediates. The solvent characteristics play a critical role in stabilizing excited states and reactive intermediates, and concentration effects can either promote or inhibit intermolecular interactions. Especially critical is the wavelength of excitation, which sets the initial excited state and its energy content. Insights into these factors not only account for measured quantum yields, but also inform design strategies to optimize photochemical reactions for target applications, spanning organic synthesis, solar energy conversion systems, etc.

Grid-Gated X-ray Source Based on Quantum Yield Principles

Quantum yield control has opened most significant innovations in numerous fields of science and technology. Inspired by nature, which has evolved complex light-harvesting complexes with near-unity quantum yield energy transfer in photosynthetic systems, artificial photosynthetic systems for solar energy conversion has been developed. Biomimetic systems take advantage of arrayed chromophores and energy funneling to accomplish well-characterized functions such as efficient light harvesting and charge separation, which are important for solar cells and photocatalytic systems. Because of the role of quantum yield on efficacy, quantum yield design is of paramount importance in the design of PDT agents for cancer. Photosensitizers designed for PDT should have sufficient quantum yields for intersystem crossing, allow populations for reactive triplet states to be > 10% as these react with molecular oxygen to form cytotoxic singlet oxygen. Porphyrins and

phthalocyanines were subsequently optimized for this purpose, and structural improvements to enhance the efficiency of intersystem crossing and thus therapeutic action were made. In materials science, the principles governing quantum yield underpin the development of efficacious OLED (organic light-emitting diodes) and luminescent materials. Phosphorescent compounds with internal quantum efficiencies approaching 100% have been realized through strategies to limit non–radiative decay pathways and augment radiative transitions. This has been accomplished by incorporation of heavy atoms for enhanced intersystem crossing and through placing rigidities in the molecular structure to block the vibrational modes contributing to the non-radiative decay.

Another major application area is photoinitiators for polymerization processes. They are intended to maximize quantum yields of radical or cationic species produced via irradiation for effective chain initiation in photopolymerization reactions in the fields of 3D printing, coatings, and adhesives. Bimolecular reactions between an excited photosensitizer and a co-initiator can also improve quantum yields through optimized processes of electron or hydrogen transfer (Type II photoinitiators). Compounds with high quantum yields (QY) for well defined photochemical transformations undergoes the molecular switches and the photochromic materials. Irradiation induces reversible conformational transitions in molecules such as azobenzenes, diarylethenes, and spiropyrans with quantum yields varying significantly depending on the specific structure. These compounds serve as the foundation for optical data storage, smart materials, and molecular machines that react to light stimuli. The principles of quantum yield also underpin newer technologies such as upconversion processes, where triplet-triplet annihilation or lanthanide-based systems convert several lower-energy photons into a single higher-energy photon. Although heavily compromised by poor efficiencies in earlier years, new advancements in relevant molecular design and nanomaterials have drastically increased upconversion quantum yields to create paths toward solar cells, bioimaging and photocatalysis utilizing low energy terrestrial light sources.

Heterocycles in Photochemistry: Environmental and Practical Considerations

While application of photochemical principles to address environmental problems has gained ground during the last few decades, they achieved particular momentum in the water treatment sector. Advanced oxidation processes (AOPs) utilize

photochemical methods to produced highly active hydroxyl radicals for degradation of organic micropollutants. A key parameter is the quantum yield for hydroxyl radical production, as this governs the efficiency of these reactions. In this sense, photocatalytic systems — generally employing semiconductors such as titanium dioxide — are now working in order to achieve the highest possible quantum yields for converting pollutants under solar irradiation, thus providing a sustainable solution in water purification. Atmospheric photochemistry controls a wide variety of processes important to the environment of our home planet from Ozone layer dynamics to smog formation. The rates of these processes and hence their environmental impact are strongly dependent on both quantum yields of key reactions like the photolysis of nitrogen dioxide or volatile organic compounds. These quantum yields are crucial for accurate atmospheric modelling and predicting the impacts of anthropogenic emissions on air pollution and climate change. In home/factory photochemistry, down- or up-scaling is another issue to be considered in the quantum yield optimization. Light penetration is reduced in large reaction volumes, and thus specialized reactor designs such as falling film reactors, spinning disc reactors, or microflow systems that highlight surface-to-volume ratios are required for efficiency. Furthermore, for industrial photochemical processes to be economically viable, it is critical to ensure high quantum yields and efficient light utilization, leading to innovations in light sources, efficient reactors, and catalysts.

Visible light photoredox catalysis has provided groundbreaking ways to conduct difficult transformations in synthetic organic chemistry under mild conditions. Catalysts include transition metal complexes and organic dyes that can achieve high quantum yields for photoinduced electron transfer and carry out single-electron transfer processes to enable many types of reactions. The migration of these methodologies to the photocatalytic family rely on understanding and controlling quantum yields of crucial steps in the catalytic cycle, such as excitation, electron transfer or catalyst regeneration. Photochemical stability is of key importance in many applications ranging from pharmaceuticals to sunlight-exposed materials. Some compounds that shown high quantum yields for photodegradation, possess a shorter shelf life and cannot be use at outdoors. Hence, stabilization strategies such as the addition of UV absorbers, quenchers or physical barriers are applied to suppress undesired photochemical reactions. Accelerated photostability testing, wherein the quantum yields of new compounds are correlated under exaggerated conditions to their likely real-world

performance, has since become standard practice in pharmaceutical, coating and plastics industries. Such practical considerations underscore the importance of quantum yield as not just a theoretical quantity, but a parameter with significant consequences for technological applications and environmental phenomena. Shrinking uncertainty about controlling quantum yields, while also finding novel ways to take advantage of light energy with ever-increasing economy and specificity, will augur even further progress in photochemistry.

Photochemical Reactions Examples

Photochemical Reactions, which are an interesting intersection between light energy and chemical conversion providing electromagnetic radiation as the catalyzing force for molecular transformation. In contrast to thermal reactions which extract energy from heat, photochemical approaches instead make use of the energy of photons to promote electrons to their respective higher energy states, allowing access to pathways that may be otherwise unavailable. Within these, the relatively unexplored photochemical domain, a vast array of reactions critical to natural processes and industrial application.

Photochemical Decomposition of Hydrogen Iodide

A classic case of the simplest photolytic process is the photochemical decomposition of hydrogen iodide (HI). Under UV light (less than 300 nm), hydrogen iodide absorbs photons resulting in homolytic bond cleavage to produce hydrogen and iodine atoms. This primary photochemical process is expressed as:

HI + hí '! H• + I•

After this first photodissociation, the highly reactive radical species engage in secondary reactions. Iodine atoms can dimerize, producing molecular iodine (I,), and hydrogen atoms can combine molecular hydrogen (H,). The general reaction might be summed up like this:

2HI + hí '! H, + I,

The reaction goes through a chain mechanism includes initiation, propagation, and termination steps. The quantum yield (the number of molecules that react per photon

absorbed) for this reaction may be greater than unity, sometimes in the hundreds under the best reaction conditions. The high quantum yield means one photon can initiate the decomposition of many HI molecules via the chain reaction.

The rate of this decomposition depends on several factors, such as light intensity, wavelength, and temperature, as well as the concentration of hydrogen iodide. Experimental studies of this reaction have thus yielded useful information on reaction kinetics, quantum yields, and radical intermediates, and have made this an important model system in photochemistry.

Photosynthesis of HBr from H, and Br,

The photochemical synthesis of hydrogen bromide from hydrogen and bromine represents another significant chain reaction initiated by light. When a mixture of hydrogen and bromine gases is exposed to visible light (particularly blue-violet light with wavelengths between 400-500 nm), a reaction occurs leading to the formation of hydrogen bromide:

H, + Br, + hí '! 2HBr

The mechanism of this photochemical process involves several distinct steps. Initially, bromine molecules absorb photons and undergo photodissociation to generate bromine atoms:

Br, + hí '! 2Br•

These bromine radicals then react with hydrogen molecules in a propagation step:

Br• + H, '! HBr + H•

The hydrogen atoms produced in this step continue the chain reaction by interacting with bromine molecules:

H• + Br, '! HBr + Br•

The cycle continues as the newly formed bromine atom participates in further reactions with hydrogen molecules. The chain is eventually terminated when radicals combine:

H• + Br• '! HBr Br• + Br• '! Br,

The photochemical synthesis showed a few interesting features. This involves chain reactions with rate-of-termination that is second-order, consistent with binary encounter

recombination of two chain radical species, and a square-root dependence of the reaction rate on the intensity of light. Moreover, the quantum yield for this reaction can be extremely high (10t –10v under idealized conditions), which results in the generation of thousands or even millions of HBr molecules from the absorption of a single photon via an autocatalytically-propagated chain reaction3,4.

Oxygen can intercept hydrogen atoms and halt the chain reaction. In a similar vein, nitric oxide can mop up bromine atoms, which also prevents the reaction from occurring. The influence of the flow or no flow state on the reaction demonstrates the use inhibition effect as a probe of the reaction mechanism and radical intermediate behavior.

Photosynthesis of HCl from H, and Cl,

The photochemical synthesis of hydrogen chloride from hydrogen and chlorine gases proceeds through a mechanism similar to the HBr synthesis but exhibits some distinctive characteristics. When a mixture of hydrogen and chlorine is exposed to ultraviolet light or even strong visible light, a rapid and sometimes explosive reaction occurs:

H, + Cl, + hí '! 2HCl

The mechanism begins with the photodissociation of chlorine molecules:

Cl, + hí '! 2Cl•

The resulting chlorine radicals react with hydrogen molecules:

Cl• + H, '! HCl + H•

The hydrogen atoms then react with chlorine molecules to continue the chain:

H• + Cl, '! HCl + Cl•

This chain propagation continues until termination occurs through radical recombination:

H• + Cl• '! HCl Cl• + Cl• '! Cl,

The photochemical HCl synthesis is much more violent than the analogous HBr synthesis, which is even reported to proceed with an explosive force given a high enough light intensity. This increased reactivity is due to the more reactive nature of Cl• radicals compared to Br• radicals and the lower activation energy for the

propagation steps. Under ideal conditions, the quantum yield for the HCl synthesis may be as high as 10v , reflecting a highly efficient chain mechanism. The sensitivity of this reaction to light makes it a colourful example of photochemistry, which was also used famously in photographic experiments and demonstrations very early on. As for the HBr synthesis, the HCl photochemical process is suppressed by a number of species capable of trapping free radicals, such as molecular oxygen, nitric oxide, and certain organic compounds. Such inhibitory effects have been well studied to understand the reaction mechanism and the behavior of the respective radical intermediates involved7,8.

Photosensitization and Quenching

Photosensitization is a complex photochemical process in which a molecule (the photosensitizer) absorbs light energy and transfers it to a second molecule, driving reactions that the second molecule would be unable to perform directly. This process effectively bypasses the need to directly excite the reactive species, enabling photochemical transformations at wavelengths not absorbable by the reactant itself.

A photosensitization process usually involves the following steps:

Sensitiser (S) absorbs a photon to become electronically excited: S + hí '! S*

Excited sensitizer transfers energy to reactive molecule (R): S* + R '! S + R*

The rousing reactive multi-atom undergoes a tempo-chemistry transformation: R* '! Products

FRET occurs via dipole-dipole coupling, while Dexter electron transfer involves electron exchange between donor and acceptor. The efficiency of sensitization is influenced by many factors: lifetime of the excited state, distance and orientation between the molecules, and spectral overlap between the emission of the sensitizer and the absorption of the acceptor. Photosensitization is used in many natural and synthetic systems. An example being photodynamic therapy where, for example, photosensitizers like porphyrins or phthalocyanines are supplied to the tissue of interest and then activate/ react to the correct wavelength of light producing reactive oxygen species (mainly singlet oxygen) which damage the components of the cell resulting in cell death. This has been beneficial in the management of some cancers and some skin diseases.

Conversely, photochemical quenching occurs when an excited molecule transfers its energy to another molecule (the quencher), resulting in deactivation without chemical change. In this process:

1. The molecule (M) absorbs a photon: M + hí '! M*
2. The excited molecule encounters a quencher (Q): M* + Q '! M + Q* or M* + Q '! M + Q

Quenching can be caused by a few different mechanisms, for example, by collisional quenching (i.e. when 2 molecules make contact, allowing energy to be released), static quenching (which occurs when a non-fluorescent complex is formed between the fluorophore and quencher), and resonance energy transfer (where energy transfer occurs without physical contact). Oxygen is a well-known quencher of both fluorescence and phosphorescence, allowing for oxygen-sensitive measurements with careful analysis of photoluminescence behavior. In the natural photosynthetic systems, quenching processes are also important for regulating energy flow and photodamage in high light.

The balance of photosensitization with quenching processes controls the efficiency of many photochemical systems and has given rise to strategies to regulate and optimize photochemistry for a variety of applications.

Photosensitized Reactions

Photosensitized reactions encompass a diverse array of chemical transformations facilitated by photosensitizers. These reactions can be broadly categorized based on the nature of the energy transfer and the subsequent chemical processes. One significant class of photosensitized reactions involves the generation of singlet oxygen (^1O,). When certain photosensitizers like methylene blue, rose bengal, or tetraphenylporphyrin absorb light, they can transfer energy to ground-state triplet oxygen (^3O,), converting it to the highly reactive singlet state:

Sens + hí '! Sens* Sens* + ^3O, '! Sens + ^1O,

Singlet oxygen is an active participant in a number of reactions such as [4+2] cyclo-additions with dienes (endoperoxides), [2+2] cyclo-additions with alkenes (dioxetanes),

and ene-type reactions where the alkene has allylic hydrogens. These transformations find applications in organic synthesis for preparing complex oxygenated compounds and in photodynamic therapy for inducing cytotoxic effects in targeted cells.

Another major class of photosensitized reactions are those that involve electron transfer processes. During these reactions, the excited state photosensitizer either transfers an electron to or receives an electron from a second molecule, forming radical ions that can participate in further reactions:

Sens + hí '! Sens* Sens* + D '! Sens•z + D•{ (reductive quenching) Sens* + A '! Sens•{ + A•z (oxidative quenching)

These photoinduced electron transfer (PET) processes are fundamental to artificial photosynthesis, photocatalysis, and photoredox catalysis. For example, transition metal complexes such as [Ru(bpy)*f*]²z and [Ir(ppy)*f*] can be used as photoredox catalysts which mediate otherwise challenging transformations that would typically require extreme conditions or toxic reagents. These catalysts have transformed organic synthesis by enabling bond formation in milder conditions and with enhanced selectivity.

Another prominent class of reactions is photosensitized isomerization. For example, the triplet sensitization of trans-stilbene can facilitate its isomerization to the cis form19.

Sens + hí '! Sens* (singlet state) Sens* '! Sens* (triplet state via intersystem crossing) Sens* (triplet) + trans-stilbene '! Sens + trans-stilbene* (triplet) trans-stilbene* (triplet) '! cis-stilbene

This approach to isomerization often offers advantages over direct photolysis, including the ability to use longer wavelengths of light and achieving different selectivity patterns.

Photosensitized cycloadditions constitute yet another important category. For instance, the [2+2] cycloaddition of enones can be efficiently promoted by triplet sensitizers like benzophenone:

Sens + hí '! Sens* Sens* + enone '! Sens + enone* (triplet) enone* (triplet) + alkene '! cyclobutane derivative

These reactions have found extensive applications in the synthesis of natural products and pharmaceuticals, offering access to structural motifs that would be challenging to construct through ground-state chemistry.

The versatility of photosensitized reactions extends to numerous other transformations, including hydrogen atom abstractions, fragmentation reactions, and rearrangements. The ability to select appropriate sensitizers and reaction conditions allows chemists to access diverse chemical pathways and achieve transformations with high efficiency and selectivity.

Photosynthesis: Nature's Masterpiece of Photochemistry

While the term "photosynthesis" has been used earlier to describe the light-induced synthesis of hydrogen halides, it is perhaps most prominently associated with the biological process occurring in plants, algae, and certain bacteria. Biological photosynthesis represents nature's most sophisticated and consequential photochemical process, converting light energy into chemical energy that sustains virtually all life on Earth.

The overall reaction of oxygenic photosynthesis can be summarized as:

6CO, + 6H, O + light energy '! C† H , O† + 6O,

This deceptively simple equation encompasses a remarkable series of photochemical and dark reactions occurring across thylakoid membranes and the stroma of chloroplasts. The process begins with the absorption of photons by chlorophyll and accessory pigments within protein complexes known as photosystems. The absorbed energy excites electrons to higher energy states, initiating electron transport chains that ultimately drive the synthesis of ATP and NADPH.

Chlorophyll molecules serve as the primary photosensitizers in this system, absorbing predominantly blue and red light while reflecting green wavelengths. When a chlorophyll molecule absorbs a photon, an electron is promoted to an excited state:

Chlorophyll + hí '! Chlorophyll*

This excited configuration triggers a cascade of electron transfers along the thylakoid membrane, establishing a proton gradient that powers ATP synthesis by a process called chemiosmosis. The electron transport chain, at the same time, reduces NADPz to NADPH, which will then be utilized as reducing agent in the following carbon fixation reactions.

Tone: Very formal and technical, academic style

The photochemical phase generates ATP and NADPH, which in the dark reactions (a.k.a. Calvin-Benson cycle, light-independent reaction) will re-reduction carbon dioxide into carbohydrates. While not directly light-driven, these reactions are related to the photochemical processes and are the final chemical process enabled by the absorbed light energy. Number of references on biomimetic approaches to artificial photosynthesis and their highlights, inspired by the efficiency and sophistication of photosynthesis to har46%0 In the past several decades, numerous biomimetic approaches to the development of artificial photosynthesis have been carried out to take advantage of solar energy for fuel and other substances. Many of these systems are inspired by both biological photosynthesis and conventional photochemistry to find efficient ways to harvest light, separate charge, and convert simple substrates into energy-rich molecules12–15.

Unit -11 Applications of Photochemical Reactions

The principles and processes of photochemistry find application across numerous fields, from industrial manufacturing to medicine and environmental remediation.

Industrial Applications

Photochemical methods are advantageous for industrial applications as they allow for mild reaction conditions, spatial and temporal control, and unique reaction pathways. Examples of large-scale photochemical synthesis include the chlorination of hydrocarbons, the manufacture of caprolactam (a nylon precursor) by the photorearrangement of cyclohexanone oxime, and the production of vitamin D by the UV irradiation of 7-dehydrocholesterol. Photopolymerization (or light-initiated chain reaction) has transformed a wide range of industries by offering rapid curing of coatings,

adhesives, and dental materials. Irradiation of photoinitiators such as benzophenone derivatives or á-hydroxyketones forms reactive species that initiate the polymerization of acrylates, methacrylates, and other functional monomers. Check out this link to read the full article on Ion Beam Induced Polymers with DBT:These processes allow for the following advantages: they are solvent-free, cure quickly and can achieve spatial control by selective irradiation.

Environmental Applications

Photochemical phenomena are important to both natural and engineered environments. In recent years, the purification of air and water based on the photodegradation of pollutants by AOPs has received attention as one of the effective approaches[7–9]. These processes generally include photochemically stimulated production of highly reactive hydroxyl radicals (•OH):

H, O, + hí '! 2•OH (direct photolysis) TiO, + hí '! e{ + hz e{ + O, '! O, •{ hz + H, O '! •OH + Hz (heterogeneous photocatalysis)

These hydroxyl radicals, in turn, can oxidize organic contaminants, eventually breaking them down to carbon dioxide, water and benign inorganic ions. Titanium dioxide-(TiO2-) and other semiconductor-based photocatalytic systems have demonstrated potential for the treatment of a wide variety of contaminants, including pharmaceutical products, pesticides, and industrial chemicals. The photochemical production of smog is an example of an environmentally unfriendly application of photochemistry. In urban areas, nitrogen oxides and volatile organic compounds react photo chemically in the presence of sunlight to form ozone, peroxyacetyl nitrate (PAN), and other secondary pollutants. Analyzing these photochemical processes is fundamental to create optimal air quality strategies.

Applications in Medicine and Biology

Photochemical principles govern a variety of medical applications, particularly photodynamic therapy (PDT). PDT involves the administration of photosensitizers (e.g., porphyrins or chlorins) to a patient, which selectively accumulate in target tissues. Afterward, irradiation with light of the appropriate wavelength induces the production of reactive oxygen species, particularly singlet oxygen, which causes cytotoxicity in a localized area. This has shown efficacy in treating a range of cancers, certain

dermatological diseases, and age-related macular degeneration. Photochemistry is also important to vision, in which the photoisomerization of 11-cis-retinal to all-trans-retinal in rhodopsin activates the signaling cascade that ultimately leads to visual perception. Triggerable by a single photon, this remarkably efficient photochemical process has served as a prized model system for understanding ultrafast photochemical reactions in biological systems. Crosslinking techniques include photochemical crosslinking in applications in corneal crosslinking (e.g., corneal collagen crosslinking for keratoconus treatment) and in photodynamic antimicrobial therapy to treat infections. These applications illustrate the precision and selectivity that photochemical approaches can provide in medical settings.

Emerging Technologies

This has led to new avenues being explored for technological breakthroughs, through photochemistry developments in recent years. Chromogenic materials, changing color upon irradiation with light of different wavelengths in a reversible fashion, have been useful in applications in smart windows, optical data storage and adaptive eyeglasses. More specifically, these materials have integrated photoswitchable moieties (e.g., azobenzenes, spiropyrans, or diarylethenes) that exhibit reversible photochemical transformations. Photoresponsive polymers/hydrogels are light-activated materials that can be applied in drug delivery systems, artificial muscles, and soft robotics. Introducing photoswitchable groups in polymeric networks allows researchers to create materials that will expand, contract or change their permeability in response to irradiation. One of the most ambitious applications of photochemistry is artificial photosynthesis, which aims to create a process that closely mimics the fundamental elements of natural photosynthesis for solar energy conversion and storage. These systems generally consist of light harvesting, charge separation, and catalytic transformation of substrates, like water or carbon dioxide, to form energy-dense products, like hydrogen or carbon-based fuels.

Understanding the theory behind photochemical reactions

The need to rely on both quantum mechanics and kinetics to interpret photochemical reactions. When a molecule absorbs a photon it transitions from its ground electronic state to an excited state as permitted by the selection rules imposed by quantum

mechanics. The energy of the incoming photon must be equal to the energy difference between these states, given by the Planck-Einstein relation:

$E = h\nu = hc/\lambda$

where h is Planck's constant, ν is the frequency, c is the speed of light, and λ is the wavelength.

The excited molecule can subsequently undergo various processes, including:

1. Photochemical reaction: The excited molecule transforms into a different chemical species
2. Radiative decay: The molecule returns to the ground state with the emission of a photon (fluorescence or phosphorescence)
3. Non-radiative decay: The energy dissipates as heat through internal conversion or intersystem crossing
4. Energy transfer: The excitation energy transfers to another molecule through various mechanisms

The quantum yield of the photochemical reaction, which is defined as the number of reactant molecules converted for every photon absorbed, can be understood as a competition between these processes. The quantum yield can only approach unity for primary photochemical steps (those directly arising from electronic excitation); it cannot exceed unity unless chain reactions or some other secondary process is taking place. Stark-Einstein law (first law of photochemistry) states that a photochemical reaction will occur only if light is absorbed by the system. The Grotthuss-Draper only the light absorbed by the system can produce a photochemical alteration (the second Law of Photochemistry).

The efficiency of a photochemical process depends on various factors, including:

1. The absorption cross-section of the molecule at the irradiation wavelength
2. The lifetime of the excited state
3. The rate constants for the various competing processes

4. Environmental factors such as temperature, solvent properties, and the presence of quenchers or sensitizers

Today, theoretical approaches to photochemistry frequently use computational methods to compute potential energy surfaces of both ground and excited states, predict reaction pathways, and simulate the dynamics of photochemical reactions. While conducted on relative small scales, TD-DFT (or time-dependent density functional theory) and multiconfigurational methods such as CASSCF (Complete Active Space Self-Consistent Field) have been particularly useful for excited states and photochemical reaction mechanisms.

Experimental Techniques in Photochemistry

Photoscientists can utilize specialized experimental methods to initiate, investigate, and characterize photochemical reactions. Ranging from conventional lamps (mercury, xenon) to lasers, light sources emit the photons necessary to excite these reactions. Wavelength selection is possible through the use of monochromators or filters, permitting wavelength-dependent studies that can illuminate mechanistic features and facilitate conditions optimization. Actinometry is an important method for measuring the photon flux in photochemical processes, through which yield measurements are made and comparative studies can be carried out. A reliable way to quantify the light intensity is by the use of a chemical actinometer such as ferrioxalate, which undergoes a well-characterized photoreduction with known quantum yield.

Time-resolved spectroscopic techniques have revolutionized the study of photochemical processes by allowing observation of short-lived intermediates and tracking reaction dynamics on timescales ranging from femtoseconds to seconds. These techniques include:

1. Transient absorption spectroscopy: Monitoring changes in absorption following excitation with a pump pulse

2. Time-resolved fluorescence: Tracking emission decay profiles to reveal excited-state dynamics

3. Flash photolysis: Using intense light pulses to generate high concentrations of intermediates for detection

4. Pump-probe techniques: Exciting the sample with one pulse and probing with another after a controlled delay

Computational methods complement experimental approaches by providing insights into electronic structures, transition states, and reaction pathways. These methods have become increasingly sophisticated, allowing simulation of excited-state dynamics and prediction of photochemical reaction outcomes.

Future Directions in Photochemistry

The field of photochemistry continues to evolve, driven by advances in both fundamental understanding and practical applications. Several emerging areas promise to shape the future landscape of photochemical research:

1. Visible light photocatalysis: Developing catalysts that operate with visible light rather than UV radiation, enhancing energy efficiency and allowing solar-driven processes

2. Flow photochemistry: Implementing continuous-flow systems for photochemical transformations, offering advantages in scale-up, reproducibility, and process intensification

3. Photoredox catalysis: Expanding the repertoire of radical-based transformations enabled by photoredox catalysts, providing access to novel chemical space for pharmaceutical and materials synthesis

4. Artificial photosynthesis: Advancing systems for solar energy conversion and storage, potentially addressing global energy challenges through sustainable fuel production

5. Two-photon and multiphoton processes: Exploring reactions triggered by the simultaneous or sequential absorption of multiple photons, enabling three-dimensional spatial control and access to high-energy intermediates using lower-energy photons

To enhance viscosity effects, we anticipate new approaches in combining photochemistry with other emerging fields, like microfluidics, nanotechnology, and machine learning, resulting in opportunities for cutting-edge approaches for fundamental studies and industrial applications. Microfluidic systems afford fine-tuning of reaction conditions and are able to provide improved light penetration, whilst nanostructured materials can act as photocatalysts with tunable properties. While the field has previously relied heavily on empirical data, returning the favor, machine learning methods are now enabling predictions of photochemical reaction outcomes and the optimization of reaction conditions, acting as a discovery accelerator in this complex area.

Photochemical reactions represent a whole class of reactions which share a basic commonality in being induced by light as the energy source for chemical change. These goes from the commutative photodissociation of hydrogen iodide to the complex machinery of biological photosynthesis, and illustrate how fundamental is the interaction of electromagnetic radiation and molecular behavior. Ferbinteanu and Zyrian (2012)—examples (again); photochemical decomposition of hydrogen iodide; photoinitiated ice-like vibrational polaron: vibrational polaron formation in photoexcited hydrogen halide or related systems; kinetics; microscopy photosensitization quenching in hydrogen halides—whispering gallery modes. These reactions function via radical chain mechanisms energy transfer electrons transferas well as the simple cleavage of chemical bonds, all of which allow new pathways for chemical conversion. Photochemistry has applications in a wide range of fields, including (but not limited to) industrial synthesis, environmental remediation, medicine, and new technologies. Concurrently, advancements in computational methods and experimental probes that enable increasingly detailed studies of photochemical processes over multiple timescales continue to enrich the theoretical landscape of the field. With continued advancements in the field, emerging catalysts, reaction mechanisms, and potential applications continue to be developed, leading to greater efficiency and selectivity and more sustainable routes to chemical synthesis and energy conversion. These photochemical transformations are even based on a reciprocity law that the principles remain true for natural systems to synthetic materials, and the fact that these two can coexist with respect to one another, exhibit, and inspire innovation in engineering designs since it

can lead directly to novel solutions.

Ideal Liquid Mixtures

Liquid-liquid blends are at the heart of many commercial processes and natural occurrences. Mixtures of liquids behave ideally if the two liquids experience from the additive molecular interactions, but generally, the behavior can be very non-ideal in case liquits interact differently. Ideal liquid mixtures are theoretical concept mixtures of fluids whose intermolecular attractors are alike, the same as those that exist between molecules of leading types. In a perfect mixture of two liquids, the interaction of molecure A with molecule B is equal to the average of an A-A interaction and a B-B interaction. This means that when different molecules meet, there is no energy cost or energy benefit compared to the pure components. This is captured in the expression for the enthalpy of mixing (ÄH_mix), which equals zero for ideal mixtures. The default assumption of ideal liquid mixtures is that the molecules of each of the components have similar size, shape, and chemical nature. As this similarity, there is an even scattering of the molecules around them, i.e., no clustering is preferred. Typical representatives for mixture of chemically close components (for example, benzene and toluene, n-hexane and n-heptane) behave closely to ideal behavior.

Ideal liquid mixtures have several important properties. First, the volume of an ideal mixture is the sum of the volumes of its pure components (no volume change on mixing). Secondly, there is no heat exchange when mixing (ÄH_mix = 0). Third, the entropy change for an ideal mixture, evaluated using statistical mechanical models, for perfect random mixing. The notion of ideality is a useful benchmark to assess from, and quantify real mixing behavior against. Ideal mixing behavior serves as a baseline for comparison and allows chemists and engineers to detect and characterize non-ideal interactions in actual systems.

Raoult's Law of Ideal Solutions

Raoult's law constitutes one of the fundamental principles governing the behavior of ideal liquid mixtures. Formulated by French chemist François-Marie Raoult in the late 19th century, this law describes the relationship between the vapor pressure of

components in a mixture and their mole fractions in the liquid phase. According to Raoult's law, for an ideal solution, the partial vapor pressure of each component equals the vapor pressure of the pure component multiplied by its mole fraction in the liquid mixture. Mathematically, this relationship is expressed as:

$P_i = P_i^\circ \times x_i$

Where:

- P_i represents the partial vapor pressure of component i in the mixture
- P_i° is the vapor pressure of pure component i at the same temperature
- x_i denotes the mole fraction of component i in the liquid phase

For a binary mixture of components A and B, the total vapor pressure follows the additive relationship:

$P_{total} = P_A + P_B = P_A^\circ \times x_A + P_B^\circ \times x_B$

According to the thermodynamic definition of an ideal solution, the chemical potential of each component is a linear function of the logarithm of its mole fraction, giving rise to Raoult's law. This relationship is true where all molecules within the solution experience identical intermolecular forces regardless of whether they are like or unlike molecules. Raoult's law can predict various colligative properties of solutions. By extending to all composition of a binary mixture, it made the vapor-liquid equilibrium diagrams on temperature function of liquid and vapor composition. Such plots (conventionally known as Pxy diagrams) are of paramount importance in designing separation processes like distillation. There are several experimental approaches to such validation of Raoult's law for a liquid mixture. This most direct approach requires measuring the vapor pressure of the mixture at different compositions and comparing it with calculated values. How these deviations from Raoult's law allow determining the molecular nature and strength of interaction in the mixture is a subject of various works.

However, we can say that in practice, Raoult's law announced above is indeed a simplification of what actually happens in a solution, and it provides incredibly good

approximations for a mixture of components that have similar chemistry and similar sizes. Ethanol and propanol, and benzene and toluene are examples of adjacent members of a homologous series from which mixtures often behave as practically ideal mixtures specifically obeying Raoult's law. Ideal mixture models like Raoult's law are generally just the beginning for a more sophisticated physical model due to non-ideality. The extent to which a real solution differs from Raoult's law is informative about the molecular interactions within and the structure of the mixture.

Deviations from Raoult's Law

Although Raoult's law is a very good approximation for ideal liquid mixtures, most real systems show some degree of non-ideality. Such deviations occur only because the intermolecular forces between unlike molecules are different from the intermolecular forces between like molecules. Positive deviations are a result of the intermolecular attractions between the unlike molecules (A-B interactions) being weaker than the intermolecular attractions present between the like molecules (A-A and B-B interactions). In these situations, molecules leave for the vapor phase more easily than suggested by Raoult's law, thus increasing vapor pressures. Typical examples are mixtures of polar and a non-polar the aromatic compounds such as ethanol–benzene in which the hydrogen bonding of ethanol network is broken by the insertion of benzene molecules. Negative deviations arise when unlike molecules attract each other more strongly than like ones. These more substantial A-B interactions make it less likely that molecules will enter the vapor phase, giving them lower vapor pressures than predicted by Raoult's law. For example, chloroform and acetone is a common example, as the strong hydrogen bonds form between the hydrogen of chloroform and oxygen of acetone creating stronger intermolecular attractions.

Typically, the width of these deviations is related to the enthalpy of mixing. Positive deviations are usually associated with endothermic mixing processes (ÄH_mix > 0), and negative deviations are more often associated with exothermic mixing (ÄH_mix < 0). Positive deviations can be huge and lead to phase separation, exhibiting partial miscibility or complete immiscibility of liquids.

To quantify these deviations, chemists use activity coefficients (ã)=, which adjust Raoult's law to account for non-ideal behavior.:

$P_i = P_i^\circ \times x_i \times \tilde{a}_i$

$\tilde{a}_i$ is defined as the activity coefficient of component i, which indicates deviation from ideal behavior. For perfect solutions $\tilde{a}_i = 1$; values > 1 denote positive and values < 1 negative deviations.

Thermodynamic models, including the Margules equations, Wilson model, NRTL (Non-Random Two-Liquid) model, and UNIQUAC (Universal Quasi-Chemical) equation, are thus developed to evaluate activity coefficients as a function of the molecular characteristics and interaction parameters of components. Such models are integral to most aspects of the design and optimization of industry separation processes.

Understanding deviations from Raoult's law has useful applications across many domains, such as pharmaceutical formulation, petrochemical processing, and modeling the environmental fate of chemicals. These deviations in their nature and magnitude provide the basis for molecular guiding principles that aids in the design of superior mixing, separation, and purification strategies.

Henry's Law and Its Applications

Henry's law, formulated by English chemist William Henry in 1803, describes the solubility of gases in liquids. While Raoult's law typically applies to the more concentrated component in a mixture, Henry's law governs the behavior of dilute components, particularly gases dissolved in liquids. According to Henry's law, at a constant temperature, the amount of a gas dissolved in a liquid is directly proportional to the partial pressure of that gas in equilibrium with the liquid. Mathematically, this relationship is expressed as:

$P_i = k_H \times x_i$

Where:

- P_i is the partial pressure of the gas above the solution
- x_i represents the mole fraction of the gas in the liquid phase
- k_H denotes the Henry's law constant, which is specific to the gas-solvent pair and temperature

For an ideal gas, the chemical potential relates to partial pressure through the logarithmic relationship:

ì_gas = ì_gas° + RT ln(P/P°)

In the liquid phase, for sufficiently dilute solutions, the chemical potential of the solute varies logarithmically with its mole fraction:

ì_solute = ì_solute° + RT ln(x)

At equilibrium, these chemical potentials must be equal, leading to the relationship:

ln(P/P°) = ln(x) + constant

This exponential form transforms into the linear relationship described by Henry's law when considering infinitely dilute solutions, where the constant term incorporates the Henry's law constant.

The theoretical basis of Henry's law connects to the fundamental principles of statistical thermodynamics. The linear relationship between concentration and pressure at infinite dilution reflects the statistical independence of solute molecules in the solution, where each molecule behaves independently without significant interaction with other solute molecules.

Modified Forms of Henry's Law

In practice, various modified forms of Henry's law are used depending on the application and the concentration units preferred. These include concentration-based forms (using molarity instead of mole fraction), mass-based forms (using mass fraction or parts per million), and dimensionless forms (using ratios of concentrations in different phases).

The concentration-based form expresses Henry's law as:

P_i = K_H × C_i

Where C_i represents the molar concentration of the solute in solution and K_H has units of pressure divided by concentration.

The dimensionless form, particularly useful in environmental applications, defines Henry's law in terms of the ratio of gas concentration in air to its concentration in water:

K_H' = C_air / C_water

This dimensionless constant facilitates the calculation of equilibrium partitioning of chemicals between environmental compartments and proves especially valuable in fate modeling of pollutants.

Limitations of Henry's Law

Henry's law gives a unique relation between the molecules in the gas and the molecules in solution, and it is an incredibly useful discussion of gas-liquid equilibria, but there are several important caveats. The first limitation is that it only applies to dilute solutions where solute-solute interactions can be ignored. At greater concentrations, these interactions lead to larger deviations. Second, the law assumes that the gas and solution phases behave ideally. In non-ideal gas systems the behavior is described using the Real (non-ideal) equation of states which accounts for the deviation of gases from ideal behavior at high pressure and real (non-ideal) solutions can have positive or negative heat of dilutions (real solution behavior). Corrections are required then for the deviations from ideality via fugacity for gas-phase systems and activity coefficients for solution-phase systems.

Third, the law presupposes that gas solubilization is purely physical, not chemically reacting with the solvent. In cases where an equilibrium between reactants and products establishes, like with dissolved carbon dioxide in water that forms carbonic acid, more complex relationships apply.

Lastly, Henry's law constants are highly dependent on temperature, usually following the van 't Hoff relation:

d(ln k_H)/d(1/T) = ÄH_soln/R

Where ÄH_soln represents the enthalpy of solution. This relationship allows the calculation of k_H at different temperatures when the enthalpy of solution is known.

Practical Applications of Henry's Law

The principles of Henry's law find application in numerous practical scenarios beyond those already mentioned. In analytical chemistry, techniques such as headspace analysis rely on Henry's law used to calculate the concentration of volatile compounds in liquid samples based on vapor concentration above the solution. Henry's law involves Gas solubility in the crude oil which helps leading gas showing a gas solubility structure in crude oil which guides in the designing of different separation processes in petroleum industry and modeling of released gas from crude oil or other hydrocarbons. In reservoir engineering, the law is a major factor in determining the behavior of gases dissolved in formation fluids.

Groundwater environmental remediation technologies like air stripping of volatile organic compounds, which utilizes these principles of Henry's law. The effectiveness of these processes is governed by the Henry's law constants of the target contaminants. In carbonated beverages, carbonation processes depend on Henry's law to model and control the levels of CO2 in products. The signature "fizz" of carbonated drinks comes from dissolved carbon dioxide escaping as pressure is reduced by opening the container. Henry's law behaviors are also observed in biological systems. This is because the transport of respiratory gases in blood obeys modified versions of Henry's law, which describe gas dissolution in solution, and the oxygen-binding characteristics of hemoglobin adds layers of complexity to the simple dissolution process.

Solution thermodynamics — which uses Michel ratio / solvent / solute ratio equations — is defined by the concepts of ideal mixtures such as Raoult's law and Henry's law, the foundation of their association by liquid-liquid and vapor-liquid systems. Although these principles describe idealized conditions, they serve as helpful benchmarks against which actual mixture behaviors can be evaluated and quantified. However, the vapor-liquid equilibrium behavior of ideal solutions is described by Raoult's law over the entire composition range (especially those of the major component of the mixture). Henry's law goes hand in hand here, describing the behavior of dilute fractions, most notably the dissolved gases. Collectively, these laws facilitate the prediction of key mixture properties and provide guidance to the design of many industrial processes, environmental models, and scientific studies. Knowing when these laws follow, and

when real systems vary from them, gives an essential knowledge of molecular connection and blending conduct. Ridley's second sense of emergence leads naturally to practical applications across disciplines as diverse as chemical engineering, environmental science, pharmaceuticals, geology and medicine. Whether it is how bubbles of gas form in carbonated drinks, or how we design and optimize distillation columns; whether it is about modeling chemical reactions in the environment, or designing a medical gas delivery system, the interrelationship between the various variables governing the behavior of liquid mixtures are the concepts provided by these laws, which continue to be the foundation upon which any theoretical understanding and innovation are built.

Nernst Distribution Law, Limitations and Applications

The Nernst distribution law (also called the partition law or distribution law) states that the ratio of the concentrations of a solute in two immiscible solvents (when the solvent is in contact with the two immiscible phases) is constant as long as the temperature is constant. This law, proposed by German chemist Walter Nernst in the late nineteenth century, serves as a cornerstone for many relevant chemical separation techniques. If two immiscible liquids contain the solute, which is distributed between both phases until equilibrium arouses. The concentrations of the solute in the two phases will achieve a constant ratio at a given temperature and regardless of the total amount of solute at equilibrium. This constant ratio is termed the partition coefficient or distribution coefficient.

Mathematically, Nernst distribution law can be expressed as:

$K = C / C$,

Where:

- K is the partition coefficient
- C is the concentration of the solute in the first solvent
- C, is the concentration of the solute in the second solvent

The partition coefficient K is a constant determining characteristic for the specific solute and the specific pair of solvents for specific temperatures. It measures the

relative solubility of the solute in both solvents. Above a value of K more solute will go to solvent 1 than to solvent 2. It is worth noting that this law is only strictly applicable if the molecular identity of the solute is identical between the two solvents. Changes in dissolved species due to association or dissociation of the solute in either solvent violate the simple form of the law, which must, therefore, be corrected for molecular changes.

The Nernst distribution law has much importance in physical chemistry and is implemented in various ways such as:

The distribution law has a thermodynamic origin that gives it its physical significance. At equilibrium the chemical potential of the solute must be equal between the two phases. It is this equality of chemical potential that results in the constant ratios of concentrations.

From the molecular viewpoint, once a solute is added to a two-phase system, the molecules exchange between the phases indefinitely. At equilibrium, molecules leaving the phase at a rate vr equals molecules entering the phase from the other phase at a rate vl. And this dynamic equilibrium leads to constant concentration ratio.

The value of the distribution coefficient depends on several factors:

1. The nature of the solute and solvents
2. Temperature
3. Pressure (though pressure effects are typically small for liquid systems)
4. The presence of other solutes that might affect solubility

Thermodynamic Derivation Background

While we won't delve into the mathematical derivation, it's worth noting that the Nernst distribution law can be derived from fundamental thermodynamic principles. At equilibrium, the chemical potential of the solute must be the same in both phases. This equality of chemical potentials leads directly to the constant ratio of concentrations expressed in the distribution law.

Limitations of Nernst Distribution Law

Despite its wide applicability, Nernst distribution law has several limitations that restrict its use in certain systems:

1. **Association of the Solute**: If the solute molecules associate to form dimers, trimers, or higher aggregates in one of the solvents, the simple form of the law breaks down. For example, benzoic acid tends to dimerize in non-polar solvents like benzene due to hydrogen bonding between carboxyl groups, while it remains predominantly monomeric in water.

   When association occurs, the effective concentration in that phase is reduced, altering the expected distribution ratio. If a solute with normal formula S exists as S, in phase 2, then the modified distribution law becomes:

   K' = C /"C,

   where C, refers to the total concentration of the solute expressed as monomers.

2. **Dissociation of the Solute**: If the solute undergoes dissociation (ionization) in one of the phases, the simple distribution coefficient no longer applies. For example, a weak acid like acetic acid may remain largely un-ionized in an organic solvent but partially dissociate in water.

   For a weak acid HA that dissociates in phase 2 to form Hz and A{ , the modified distribution law becomes:

   K' = C /(C, + Cf)

   where C, is the concentration of un-ionized solute and Cf is the concentration of ionized solute in phase 2.

3. **Chemical Reactions**: If the solute undergoes a chemical reaction with either solvent, the simple distribution law cannot be applied. The concentrations would need to account for both the original solute and its reaction products.

4. **Concentration Dependence**: The law assumes that the partition coefficient is independent of concentration. However, at high concentrations, deviations

can occur due to non-ideal behavior, molecular interactions, and changes in the properties of the solutions.

5. **Temperature Effects**: The partition coefficient is temperature-dependent. Changes in temperature can affect the solubility of the solute in both phases differently, leading to variations in the value of K. The distribution law does not explicitly account for these temperature effects.

6. **Influence of Additional Solutes**: The presence of other solutes can affect the distribution coefficient by altering the solvent properties or through specific interactions with the solute of interest.

7. **Non-Ideal Solutions**: The law assumes ideal behavior of the solute in both phases. In real systems, especially at higher concentrations, deviations from ideality can lead to variations in the distribution coefficient.

8. **Limited to Dilute Solutions**: Nernst distribution law is strictly valid only for dilute solutions where the activity coefficient approaches unity. At higher concentrations, activity coefficients must be considered instead of simple concentrations.

Unit -13 Applications of Nernst Distribution Law

Despite its limitations, Nernst distribution law finds extensive applications in various fields of chemistry and related sciences:

1. Solvent Extraction

One of the most important applications is in solvent extraction, a technique widely used for the separation and purification of compounds. The process involves transferring a solute from one liquid phase to another based on differences in solubility.

In industrial chemistry, solvent extraction is employed for:

- Purification of pharmaceutical compounds
- Recovery of metals from aqueous solutions
- Separation of aromatics from petroleum fractions
- Extraction of essential oils from plant materials

- Purification of antibiotics

The efficiency of an extraction process can be calculated using the distribution coefficient. Multiple extractions with smaller volumes of solvent are often more efficient than a single extraction with a larger volume, as predicted by the distribution law.

2. Analytical Chemistry

In analytical chemistry, liquid-liquid extraction based on Nernst distribution law is used for:

- Preconcentration of analytes
- Matrix simplification
- Interference removal
- Sample preparation prior to chromatographic or spectroscopic analysis

The distribution law helps in optimizing extraction conditions and predicting extraction efficiencies.

3. Pharmaceutical Industry

The pharmaceutical industry extensively uses the principles of Nernst distribution law for:

- Drug purification
- Determination of lipophilicity of drug molecules
- Predicting drug absorption and distribution in the body
- Development of sustained-release formulations

The partition coefficient between anol and water (log P) is a critical parameter in drug development, indicating a drug's ability to cross biological membranes.

4. Environmental Chemistry

In environmental science, distribution law helps in understanding:

- Fate and transport of pollutants in environmental compartments

- Bioaccumulation of contaminants in aquatic organisms
- Soil-water partitioning of pesticides and other contaminants
- Design of remediation strategies for contaminated sites

5. Chromatography

The theoretical foundation of various chromatographic techniques lies in Nernst distribution law. In chromatography, the stationary and mobile phases represent the two immiscible phases between which solutes distribute themselves. The retention behavior of compounds in chromatographic columns can be explained based on their distribution coefficients.

Types of chromatography based on distribution principles include:

- Liquid-liquid chromatography
- Gas-liquid chromatography
- High-performance liquid chromatography (HPLC)
- Thin-layer chromatography (TLC)

6. Study of Association and Dissociation Phenomena

The deviations from the simple form of Nernst distribution law provide valuable information about molecular association and dissociation processes. By studying how the apparent distribution coefficient varies with concentration, researchers can determine:

- Association constants for dimerization or higher-order aggregation
- Dissociation constants for weak acids and bases
- Self-association behavior of amphiphilic molecules

7. Hydrometallurgy

In hydrometallurgy, solvent extraction based on distribution principles is used for:

- Selective recovery of valuable metals from leach solutions
- Purification of metal concentrates
- Separation of rare earth elements
- Recovery of uranium and other nuclear materials

8. Food Industry

The food industry applies distribution principles for:

- Extraction of flavors and colorants
- Removal of caffeine from coffee (decaffeination)
- Purification of food additives
- Oil refining processes

9. Biological Systems and Pharmacokinetics

The distribution of drugs and xenobiotics between different body compartments follows principles similar to Nernst distribution law. Pharmacokinetic parameters such as:

- Blood-brain barrier penetration
- Placental transfer
- Milk-plasma ratio
- Tissue distribution

can be related to the partition coefficients of compounds between aqueous and lipid phases.

Case Studies Showing Application of Nernst Distribution Law

Case Study 1: Association - Benzoic Acid in Benzene and Water

Benzoic acid provides a classic example of how association affects distribution behavior. When distributed between benzene and water, benzoic acid exists

predominantly as monomers in water but dimerizes in benzene due to hydrogen bonding between carboxyl groups.

If C represents the concentration in benzene and C, the concentration in water, the simple Nernst distribution law would predict a constant ratio C /C, . However, experimental measurements show that this ratio varies with concentration.

The modified distribution coefficient accounting for dimerization is:

K' = C /"C,

where C represents the total concentration in benzene (expressed as monomers) and C, is the concentration in water.

This modification results in a more constant value of K' across different concentrations, confirming the dimerization of benzoic acid in benzene.

Case Study 2: Dissociation - Distribution of Weak Acids

Consider a weak acid HA distributing between an organic solvent (like chloroform) and water. In the organic phase, the acid remains un-ionized, while in the aqueous phase, it partially dissociates according to:

HA Ì! Hz + A{

If we denote the concentration in the organic phase as C and the total analytical concentration in the aqueous phase as C, , the simple distribution law would predict C /C, to be constant. However, because of dissociation in the aqueous phase, this ratio varies with pH.

The total concentration in the aqueous phase is the sum of the un-ionized acid [HA] and the ionized form [A{]:

C, = [HA] + [A{]

The true distribution coefficient applies only to the un-ionized form:

K = C /[HA]

From the dissociation equilibrium, we can calculate [HA] in terms of C, , pH, and the acid dissociation constant Ka:

[HA] = C, /(1 + Ka/[Hz])

This leads to the pH-dependent apparent distribution coefficient:

K' = C /C, = K/(1 + Ka/[Hz])

This equation explains why the extraction efficiency of weak acids from aqueous solutions increases at lower pH values, where dissociation is suppressed.

Case Study 3: Industrial Application - Copper Extraction

In hydrometallurgy, copper is often extracted from acidic leach solutions using organic extractants like LIX reagents (chelating agents) dissolved in kerosene. The extraction equilibrium can be represented as:

Cu²z (aq) + 2HR(org) Ì! CuR, (org) + 2Hz (aq)

where HR represents the extractant and CuR, is the copper-extractant complex.

The distribution of copper between the aqueous and organic phases depends on:

- pH of the aqueous phase
- Concentration of the extractant
- Presence of other metal ions
- Temperature

By controlling these parameters, especially pH, selective extraction of copper can be achieved. The loaded organic phase is then stripped using strong acid to recover copper in a concentrated form.

This process clearly illustrates how the principles of Nernst distribution law, modified to account for chemical reactions, guide industrial separation processes.

Modern Extensions and Modifications of Nernst Distribution Law

While the classical form of Nernst distribution law provides a solid foundation, modern approaches have extended and refined it to address its limitations:

1. **Activity-Based Formulations**: Instead of using concentrations, modern formulations often use activities to account for non-ideal behavior in concentrated solutions:

   K = a /a,

   where a and a, are the activities of the solute in phases 1 and 2, respectively.

2. **Temperature-Dependent Models**: The van't Hoff equation relates the temperature dependence of the distribution coefficient to the enthalpy change associated with the transfer of solute between phases:

   d(ln K)/d(1/T) = -ÄH°/R

   where T is the absolute temperature, ÄH° is the standard enthalpy change, and R is the gas constant.

3. **Computational Approaches**: Modern computational chemistry methods, such as molecular dynamics simulations and quantum mechanical calculations, can predict partition coefficients based on molecular structures and solvent properties.

4. **QSAR Models**: Quantitative Structure-Activity Relationship (QSAR) models correlate distribution coefficients with molecular descriptors, allowing for the prediction of partition behavior for new compounds.

5. **Multicomponent Systems**: Extensions of the basic law have been developed to handle systems with multiple solutes that may interact with each other.

Experimental Determination of Distribution Coefficients

Several methods are employed to experimentally determine distribution coefficients:

1. **Shake-Flask Method**: The traditional approach involves equilibrating the solute between two phases in a separatory funnel, separating the phases, and analyzing the concentration in each phase using appropriate analytical techniques.

2. **Slow-Stirring Method**: This method minimizes the formation of emulsions and is particularly useful for highly hydrophobic compounds.

3. **HPLC-Based Methods**: High-performance liquid chromatography can be used to rapidly determine partition coefficients between an aqueous buffer and a stationary phase that mimics a specific solvent.

4. **Potentiometric Methods**: These methods are useful for ionizable compounds and provide information about both the partition coefficient and dissociation constants.

5. **Filter-Probe Methods**: These automated systems allow for rapid determination of partition coefficients for multiple compounds.

The Nernst distribution law describes the partitioning of a solute between two immiscible phases and is a fundamental principle in physical chemistry. Although the law does not apply directly to systems containing data involving association, dissociation, or chemical reaction, it still offers an approximate theoretical background for many separation processes and analytical methods. This law is widely applicable in many areas — pharmaceutical research, environmental science, industrial separations and analytical chemistry, to name but a few — and is often used to predict the partitioning of a test compound between two phases based on its molecular structure. The distribution behavior of compounds between aqueous and non-aqueous phases is vital for the design of extraction processes, understanding environmental fate, drug delivery, and the development of analytical methods.

Multiproduct extensions, extensions to non-convex productions, imperfect batches, besides many modifications of the classical formulation soon removed most of the restrictions, making the distribution law also applicable to these types of systems but leaving the original more natural for non-multiproduct systems. With the continued development of analytical techniques and increasingly sophisticated computational approaches, the predictive power and utility of distribution-based phenomena will eventually lead to increased efficiency and selectivity of separation processes. Cases of association and dissociation, although they describe exceptions to the simple form of the law, are very informative from the point of view of molecular behavior and interaction in several solvent media. By properly modifying the fundamental relationship to account for these phenomena, the distribution law becomes useful even in complex

systems. As we move towards a more sustainable future, the Nernst distribution law remains a testament to the importance of efficient separation and purification techniques in resource recovery and environmental remediation.

SELF ASSESSMENT QUESTIONS

Multiple Choice Questions (MCQs)

1. Which of the following is a photochemical reaction?

a) Oxidation of ammonia

b) Photosynthesis

c) Rusting of iron

d) Burning of methane

2. The Jablonski diagram explains:

a) Molecular motion

b) Thermal energy transfer

c) Excited state processes

d) None of the above

3. The quantum yield of a reaction is defined as:

a) Number of molecules decomposed per photon absorbed

b) Total energy of photons absorbed

c) Total energy emitted

d) None of the above

4. The laws of photochemistry were given by:

a) Einstein

b) Grotthus-Draper

c) Kirchhoff

d) Le Chatelier

5. Photosensitization refers to:

a) Absorption of light by a molecule

b) Energy transfer from one molecule to another

c) Heat energy conversion

d) None of the above

6. Raoult's law is applicable to:

a) Gaseous mixtures

b) Non-ideal solutions

c) Ideal solutions

d) None of the above

7. Henry's law states that:

a) The solubility of a gas is inversely proportional to pressure

b) The solubility of a gas is directly proportional to pressure

c) The solubility of a gas is independent of pressure

d) None of the above

8. Nernst distribution law applies to:

a) Gas-liquid systems

b) Solid-liquid mixtures

c) Two immiscible liquids

d) None of the above

9. The main limitation of Henry's law is:

a) It applies only to ideal gases

b) It is independent of temperature

c) It applies only to ionic substances

d) It is not affected by pressure

10. Photochemical decomposition of HI occurs by:

a) Thermal activation

b) Absorption of UV light

c) Reaction with water

d) None of the above

Short Answer Questions

1. Differentiate between photochemical and thermal reactions.
2. Explain the significance of the Jablonski diagram.
3. What is quantum yield? How is it determined?
4. Write the laws of photochemistry with examples.
5. Explain the concept of photosensitization and its applications.
6. State and explain Raoult's law.
7. Describe Henry's law and give its applications.
8. What are ideal and non-ideal solutions? Give examples.
9. Explain the Nernst distribution law and its limitations.
10. How does Raoult's law explain vapor pressure in liquid mixtures?

Long Answer Questions

1. Describe the interaction of radiation with matter and its consequences.
2. Explain the laws governing photochemical reactions with examples.

3. Discuss the Jablonski diagram and various photophysical processes.
4. What are the factors affecting quantum yield? Explain with examples.
5. Explain photochemical reactions with at least three examples.
6. Discuss the principles and applications of photosensitization and quenching.
7. Derive Raoult's law and explain its significance in ideal solutions.
8. Discuss the applications and limitations of Henry's law.
9. Derive the Nernst distribution law and explain its significance.
10. Compare and contrast ideal and non-ideal solutions based on Raoult's law.

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