HALO ALKANES AND HALO ARENES

➢ Halo alkanes and Halo Arenes find wide applications in industry as well as in day-to-day life. They are used as solvents for relatively non-polar compounds and as starting materials for the synthesis of wide range of organic compounds. Chlorine containing antibiotic, *Chloramphenicol,* produced by soil microorganisms is very effective for the treatment of typhoid fever. Our body produces iodine containing hormone, *thyroxine,* the deficiency of which causes a disease called *goiter*. Synthetic halogen compounds, *viz.* Chloroquine is used for the treatment of malaria; halothane is used as an anaesthetic during surgery. Certain fully fluorinated compounds are being considered as potential blood substitutes in surgery.

➢ In halo alkanes as size of halogen increases C—X bond strength decreases hence reactivity increases.

➢ Preparation of Halo alkanes from alcohols using Thionyl chloride is preferred because the other two products are escapable gases.

➢ Preparation of Halo alkanes from alcohols using hydrogen halides, the order of reactivity of alcohols with a given halo acid is 3°>2°>1°.

➢ The above method is not applicable for the preparation of aryl halides because the carbon-oxygen bond in phenols has a partial double bond character and is difficult to break being stronger than a single bond.

➢ Iodination of Arenes with iodine is reversible in nature and requires the presence of an oxidizing agent (HNO_3, HIO_4) to oxidise the HI formed during iodination.

➢ Reactions of un saturated hydrocarbons with Bromine water yields colorless alkyl halides hence it is used as testing for un saturated hydro carbons.

➢ Markovnikov's rule: When un symmetrical alkene under goes addition with un symmetrical reagent, the major product of alkyl halide one in which, the negative part of addendum will be added to the carbon having less no. of hydrogen atoms.

➢ Anti Markovnikov's rule: (Peroxide Effect) (Kharausch Effect) When un symmetrical alkene under goes addition with un symmetrical reagent, the major product of alkyl halide one in which, the negative part of addendum will be added to the carbon having more no. of hydrogen atoms.

➢ Alkyl halides are having more boiling point as compare with hydro carbons of equal molecular mass it is due to dipole- dipole attractions present in it.

➢ For the same alkyl group, the boiling points of alkyl halides decrease in the order: RI> RBr> RCl> RF. This is because with the increase in size and mass of halogen atom, the magnitude of van der Waal forces increases.

➢ The boiling points of isomeric halo alkanes decrease with increase in branching due to decrease in spherical surface area which in turn decreases vander waal's force.

➢ Boiling points of isomeric di halo benzenes are very nearly the same. However, the *para*-isomers are high melting as compared to their *ortho* and *meta*-isomers. It is due to symmetry of *para*-isomers that fits in crystal lattice better as compared to *ortho-* and *meta*-isomers.

- *The halo alkanes are only very slightly soluble in water, Energy released during dissolution is not sufficient to break the hydrogen bond between water molecules.*
- Groups like cyanides and nitrites possess two nucleophilic centres and are called *ambident nucleophiles*.
- Halo alkanes react with KCN to form alkyl cyanides as main product while AgCN forms isocyanides as the chief product. It is because KCN is predominantly ionic and provides cyanide ions in solution. Although both carbon and nitrogen atoms are in a position to donate electron pairs, the attack takes place mainly through carbon atom and not through nitrogen atom since C—C bond is more stable than C—N bond. However, AgCN is mainly covalent in nature and nitrogen is free to donate electron pair forming isocyanide as the main product.
- Nucleophilic substitution in alkyl halides fallows two types of mechanisms, SN^1 (Substitution of Nucleophile fallows first order kinetics) & SN^2 (Substitution of Nucleophile fallows Second order kinetics).
- SN^1 reaction mechanism is followed by those alkyl halides whose carbo cation is stable like tertiary alkyl halides, Allyl halides & Benzyl halides. It forms carbo cation intermediate, which is triangular planar & SP^2 hybridized intermediate. If alkyl halide is optically active after substitution it forms racemic mixture.
- SN^2 reaction mechanism is followed by primary alkyl halide (whose carbanion is stable). It forms carbanion intermediate, which is sp^3d hybridized and pentavalent. During SN^2 mechanism optical activity is reversed this is known as optical inversion.
- Molecules which are able to rotate plane polarized light are called optically active compounds.
- Light whose waves oscillate in only one plane is known as plane polarized light.
- Non super imposable mirror images are called Enantiomers.
- Substances which rotate plane polarized light are called dextro and one which rotates towards left is known as leavo rotatory compound.
- In a molecule if Carbon atom is surrounded by four different groups called asymmetric carbon or chiral carbon which is must for optical active compound.
- 1:1 ratio of dextro and leavo mixture is known as racemic mixture.
- The process of conversion of enantiomer into a racemic mixture is known as **racemisation.**
- Secondary alkyl halides undergoes both SN^1 & SN^2 mechanism.
- If there is possibility of formation of more than one alkene due to the availability of more than one α-hydrogen atoms, usually one alkene is formed as the major product. These form part of a pattern first observed by Russian chemist, Saytzeff who in 1875 formulated a rule which can be summarized as

   "*in dehydrohalogenation reactions, the preferred product is that alkene which has the greater number of alkyl groups attached to the doubly bonded carbon atoms*."
- An alkyl halide with α-hydrogen atoms when reacted with a base or a nucleophile has two competing routes: substitution (SN1 and SN2) and elimination. Which route will be taken up depends upon the nature of alkyl halide, strength and size of base/nucleophile and reaction conditions. Thus, a bulkier nucleophile will prefer to act as a base and abstracts a proton rather than approach a tetravalent carbon atom (steric reasons) and *vice versa*.

- Aryl halides are extremely less reactive towards nucleophilic substitution reactions due to the Resonance effect (partial double bond), halogen bonded to sp^2 carbon which is more electronegative and less bond length, instability of phenyl cation & repulsion between electron rich arenas, nucleophile.
- Nucleophilic substitution on aromatic rings becomes easy in the presence of electron with drawing groups like nitro which stabilize the carbanaion. This effect is not shown when nitro group is present at meta position.
- Although chlorine is an electron withdrawing group, yet it is *ortho*-, *para*-directing in electrophilic aromatic substitution reactions. Chlorine withdraws electrons through inductive effect and releases electrons through resonance. Through inductive effect, chlorine destabilizes the intermediate carbocation formed during the electrophilic substitution. Through resonance, halogen tends to stabilize the carbocation and the effect is more pronounced at *ortho-* and *para-* positions. The inductive effect is stronger than resonance and causes net electron withdrawal and thus causes net deactivation. The resonance effect tends to oppose the inductive effect for the attack at *ortho-* and *para* positions and hence makes the deactivation less for *ortho-* and *para* attack. Reactivity is thus controlled by the stronger inductive effect and orientation is controlled by resonance effect.
- Chloroform is slowly oxidized by air in the presence of light to an extremely poisonous gas, carbonyl chloride, also known as phosgene. It is therefore stored in closed dark colored bottles completely filled so that air is kept out.

ALCOHOLS, PHENOLS & ETHERS

- The bond angle in alcohols is slightly less than the tetrahedral angle (109°-28′). It is due to the repulsion between the unshared electron pairs of oxygen.
- In phenols, the –OH group is attached to $sp2$ hybridised carbon of an aromatic ring. The carbon– oxygen bond length (136 pm) in phenol is slightly less than that in methanol. This is due to (i) partial double bond character on account of the conjugation of unshared electron pair of oxygen with the aromatic ring and (ii) $sp2$ hybridized state of carbon to which oxygen is attached.
- The bond angle is slightly greater than the tetrahedral angle due to the repulsive interaction between the two bulky (–R) groups. The C–O bond length (141 pm) is almost the same as in alcohols.
- Hydroboration-oxidation of alkenes gives addition of water to alkene as per anti Markovnikov's rule.
- The boiling points of alcohols and phenols are higher in comparison to other classes of compounds, namely hydrocarbons, ethers, haloalkanes and haloarenes of comparable molecular masses. The high boiling points of alcohols are mainly due to the presence of intermolecular hydrogen bonding in them which is lacking in ethers and hydrocarbons.
- Solubility of alcohols and phenols in water is due to their ability to form hydrogen bonds with water molecules. The solubility decreases with increase in size of alkyl/aryl (hydrophobic) groups.
- Alcohols are weak Bronstead acids i.e. they can donate proton to a stronger base.

- The acidic character of alcohols is due to the polar nature of O–H bond. An electron-releasing group (–CH_3, –C_2H_5) increases electron density on oxygen tending to decrease the polarity of O-H bond. This decreases the acid strength. Hence acidity of alcohols is $1^0 > 2^0 > 3^0$ alcohols.

- Alcohols act as Bronsted bases as well. It is due to the presence of unshared electron pairs on oxygen, which makes them proton acceptors.

- Alcohols and phenols react with Na metal gives hydrogen gas it supports the acidic nature. But Phenol even reacts with NaOH hence phenol is strong base than alcohol. It is due to the resonance stability of Phenoxide ion.

- Electron releasing groups on alcohol and phenol decrease acidity and electron withdrawing groups increase acidity. Because electron withdrawing groups stabilize the phenoxide/alkoxide ions. More K_a or Less P^K_a value indicates higher acidity.

- the relative ease of dehydration of alcohols follows the following order:
  Tertiary > Secondary > Primary it is due to stability of carbocation.

- The usual halogenation of benzene takes place in the presence of a Lewis acid, such as $FeBr_3$, which polarizes the halogen molecule. In case of phenol, the polarization of bromine molecule takes place even in the absence of Lewis acid. It is due to the highly activating effect of –OH group attached to the benzene ring.

- The commercial alcohol is made unfit for drinking by mixing in it some copper sulphate (to give it a color) and pyridine (a foul smelling liquid). It is known as denaturation of alcohol.

- The dehydration of secondary and tertiary alcohols to give corresponding ethers is unsuccessful as elimination competes over substitution and as a consequence, alkenes are easily formed.

- The weak polarity of ethers do not appreciably affect their boiling points which are comparable to those of the alkanes of comparable molecular masses but are much lower than the boiling points of alcohols. The large difference in boiling points of alcohols and ethers is due to the presence of hydrogen bonding in alcohols.

- The miscibility of ethers with water resembles those of alcohols of the same molecular mass. This is due to the fact that just like alcohols, oxygen of ether can also form hydrogen bonds with water.

- The order of reactivity of hydrogen halides is as follows: HI > HBr > HCl.

- Reaction of anisole with HI gives Phenol & methyl iodide but not other products because there is a partial double bond character between Benzene ring and Oxygen.

- Tertiary butyl methyl ether react with HI gives Methanol and tertiary butyl Iodide it is due to stability of tertiary carbocation.

- $1^0, 2^0 \& 3^0$ alcohols are distinguished by Lucas Test. Lucas reagent is HCl + $ZnCl_2$ tertiary amines react with Lucas reagent and cloudiness forms immediately, secondary amines react with Lucas reagent and cloudiness forms after 5 mts, primary amines react with Lucas reagent and cloudiness forms only by heating.

ALDEHYDES, KETONES AND CARBOXYLIC ACIDS

➢ The boiling points of aldehydes and ketones are higher than hydrocarbons and ethers of comparable molecular masses. It is due to weak molecular association in aldehydes and ketones arising out of the dipole-dipole interactions. Also, their boiling points are lower than those of alcohols of similar molecular masses due to absence of intermolecular hydrogen bonding.

➢ The lower members of aldehydes and ketones such as methanal, ethanal and propanone are miscible with water in all proportions, because they form hydrogen bond with water. However, the solubility of aldehydes and ketones decreases rapidly on increasing the length of alkyl chain.

➢ The carbon atom of the carbonyl group of benzaldehyde is less electrophilic than carbon atom of the carbonyl group present in propanal. The polarity of the carbonyl group is reduced in benzaldehyde due to resonance and hence it is less reactive than propanal.

➢ Sodium hydrogensulphite adds to aldehydes and ketoses to form the addition products by equilibrium reaction. The position of the equilibrium lies largely to the right hand side for most aldehydes and to the left for most ketones due to steric reasons. The hydrogensulphite addition compound is water soluble and can be converted back to the original carbonyl compound by treating it with dilute mineral acid or alkali. Therefore, these are useful for separation and purification of aldehydes.

➢ Addition of ammonia derivatives to the aldehydes & ketones takes place under controlled P^H because reaction takes place by acid catalyzed mechanism, if acidity is more it react with ammonia derivatives (bases).

➢ Carboxylic acids are higher boiling liquids than aldehydes, ketones and even alcohols of comparable molecular masses. This is due to more extensive association of carboxylic acid molecules through intermolecular hydrogen bonding.

➢ Characteristic reactions of aldehydes and ketones are not given by carboxylic acids in spite of having C=O it it due to resonance stabilization of carboxylic group.

➢ Aliphatic carboxylic acids having 12 to 18 carbon atoms are known as fatty acids.

➢ The solubility decreases with increasing number of carbon atoms. Higher carboxylic acids are practically insoluble in water due to the increased hydrophobic interaction of hydrocarbon part.

➢ Quantitatively acidity of carboxylic acids are compared by using K_a acid dissociation constant or P^{K}_a values. Higher K_a value or less P^{K}_a represents strong acids.

➢ Smaller the pKa, the stronger the acid (the better it is as a proton donor). Strong acids have pKa values < 1, the acids with pKa values between 1 and 5 are considered to be moderately strong acids, weak acids have pKa values between 5 and 15, and extremely weak acids have pKa values >15.

➢ Carboxylic acids are weaker acids as compare with mineral acids like HCl, $H_2SO_4.HNO_3$ but stronger acids than alcohol and phenol.

➢ Carboxylic acids are strong acids than Phenol it is due to high stability of carboxylate ion as compare to Phenoxide ion. Negative charge is distributed on

two equally electronegative atoms where as in phenol it is distributed on two un equal atoms.

➢ Electron withdrawing groups increase the acidity of carboxylic acids by stabilizing the conjugate base through delocalization of the negative charge by inductive and/or resonance effects. Conversely, electron donating groups decrease the acidity by destabilizing the conjugate base.

➢ The effect of the following groups in increasing acidity order is

$Ph < I < Br < Cl < F < CN < NO_2 < CF_3$

➢ Aromatic carboxylic acids undergo electrophilic substitution reactions in which the carboxyl group acts as a deactivating and meta-directing group. They however, do not undergo Friedel-Crafts reaction (because the carboxyl group is deactivating and the catalyst aluminum chloride (Lewis acid) gets bonded to the carboxyl group).

AMINES

➢ In nature, Amines occur among proteins, vitamins, alkaloids and hormones. Synthetic examples include polymers, dyestuffs and drugs. Two biologically active compounds, namely adrenaline and ephedrine, both containing secondary amino group, are used to increase blood pressure. Novocain, a synthetic amino compound, is used as an anesthetic in dentistry. Benadryl, a well known antihistaminic drug also contains tertiary amino group. Quaternary ammonium salts are used as surfactants. Diazonium salts are intermediates in the preparation of a variety of aromatic compounds including dyes.

➢ Ammonolysis of alkyl halides gives amines, but it has the disadvantage of yielding a mixture of primary, secondary and tertiary amines and also a quaternary ammonium salt. However, primary amine is obtained as a major product by taking large excess of ammonia. The order of reactivity of halides with amines is RI > RBr > RCl.

➢ Gabriel synthesis is used for the preparation of primary amines. Phthalimide on treatment with ethanolic potassium hydroxide forms potassium salt of phthalimide which on heating with alkyl halide followed by alkaline hydrolysis produces the corresponding primary amine. Aromatic primary amines cannot be prepared by this method because aryl halides do not undergo nucleophilic substitution with the anion formed by phthalimide.

➢ Lower aliphatic amines are soluble in water because they can form hydrogen bonds with water molecules. However, solubility decreases with increase in molar mass of amines due to increase in size of the hydrophobic alkyl part. Higher amines are essentially insoluble in water.

➢ Equal molecular masses of amines & alcohols, alcohols are more polar than amines and form stronger intermolecular hydrogen bonds than amines.

➢ This intermolecular association is more in primary amines than in secondary amines as there are two hydrogen atoms available for hydrogen bond formation in it. Tertiary amines do not have intermolecular association due to the absence of

hydrogen atom available for hydrogen bond formation. Therefore, the order of boiling points of isomeric amines is as follows:

Primary > Secondary > Tertiary

➢ Amines have an unshared pair of electrons on nitrogen atom due to which they behave as **Lewis base.** Basic character of amines can be better understood in terms of their K_b and pK_b values.

➢ Larger the value of Kb or smaller the value of pKb, stronger is the base.

➢ Basisity of amines in gaseous state increased by +ve inductive effect, but in aqueous state apart from +I effect it also depends on hydration effect & steric effect.

➢ The order of basicity of amines in the gaseous phase follows the expected order: tertiary amine > secondary amine > primary amine > NH_3.

➢ The order of basic strength in case of methyl substituted amines and ethyl substituted amines in aqueous solution is as follows:

$$(C_2H_5)_2NH > (C_2H_5)_3N > C_2H_5NH_2 > NH_3$$
$$(CH_3)_2NH > CH_3NH_2 > (CH_3)_3N > NH_3$$

➢ pK_b value of aniline is quite high than ammonia . It is because in aniline or other aryl amines, the -NH_2 group is attached directly to the benzene ring. It results in the unshared electron pair on nitrogen atom to be in conjugation with the benzene ring and thus making it less available for protonation.

➢ In case of substituted aniline, it is observed that electron releasing groups like –OCH_3, –CH_3 increase basic strength whereas electron withdrawing groups like –NO_2, –SO_3, –$COOH$, –X decrease it.

➢ Reaction of nitrous acid with different amines gives different products. Primary aliphatic amines gives alcohols, primary aromatic amines gives diazonium chloride, secondary aliphatic and aromatic amines gives N-Nitroso amines, tertiary aliphatic amines gives quaternary ammonium nitrite where as tertiary aromatic amines gives p-nitroso aniline.

➢ $1^0, 2^0$ & 3^0 amines are distinguished by Hinsberg's test i.e. primary amine react with Hinsberg's reagent (**B**enzene **S**ulphonyl **C**hloride) and resulting compound is soluble in KOH, secondary amine react with B.S.C and resulting compound is insoluble in KOH, tertiary amines do not react with B.S.C.

➢ Aniline is more reactive for electrophilic substitution due to involvement of lone pair on nitrogen makes benzene ring activated towards electrophilic substitution. This effect is minimized by adding acyl group on nitrogen. The lone pair of electrons on nitrogen of acetanilide interacts with oxygen atom due to resonance as shown below: Hence, the lone pair of electrons on nitrogen is less available for donation to benzene ring by resonance. Therefore, activating effect of –$NHCOCH_3$ group is less than that of amino group.

➢ Nitration aniline gives ortho, para & meta nitro aniline mixture of compounds. Though –NH_2 is a o-p directing it forms substantial amount of meta product also it is due to in strongly acidic medium, aniline is protonated to form the anilinium ion which is *meta* directing. That is why besides the *ortho* and *para* derivatives, significant amount of *meta* derivative is also formed.

➢ Sulphonation aniline forms sulphonilic acid which forms zwitter ion.

➢ The conversion of primary aromatic amines into diazonium salts by reacting with nitrous acid at 0-5^{0}C is known as diazotization .

➢ Benzene diazonium chloride reacts with phenol in which the phenol molecule at its para position is coupled with the diazonium salt to form *p*-hydroxyazobenzene. This type of reaction is known as coupling reaction. Similarly the reaction of diazonium salt with aniline yields *p*-amino azo benzene. This is an example of electrophilic substitution reaction.

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