Review Article

SOLUBILITY AND MOLECULAR FORCES

Satish A.Ahire[1*] and Ashwini A.Bachhav[2]

[1]Department of Chemistry, Arts, Science and Commerce College, Surgana Tal. Surgana Dist. Nashik (India)
[2]Department of Pharmaceutics, Sandip Institute of Pharmaceutical Science, Nashik- 422231(India)

A R T I C L E   I N F O

A B S T R A C T

Solubility have major importance in a large number of scientific disciplines and practical applications ranging from ore processing to the use of medicines and the transport of pollutants. Solubility is one of the characteristic property of a substance which is commonly used to describe the substance, to distinguish it from other substances and as a guide to applications of the substance. The synthesis of chemical compounds in a laboratory or in industry, need the knowledge of the relative solubility's of the desired product as well as unreacted starting materials, byproducts and side products to achieve separation. The knowledge of solubility useful in separation of mixtures. The solubility data is required in diverse field such as pharmaceuticals, agriculture, industry and environment which are related to economy and social problems such as pollution. The purpose of this review is to provide an insight to the various concepts related solubility. In this review, a relatively simple approach for understanding the concepts of solubility, the solution process, the mechanism of solution process and forces involved in the solution process. This review article will beneficial for the students, the practicing chemical engineers and scientist.

INTRODUCTION

The solubility data is required in diverse field such as agriculture, pharmaceuticals, environment and industry which are related to economy and social problems such as pollution. Solubility data have many important applications in science and technology. e.g chemical engineers planned systems for chemical separation and purification processes which depend heavily on solubility data. When selecting solvents for chemical reactions, every chemist examine both the reactant and product solubility. A number of models have been developed to predict solubility[1–3]. Those worked in the field of solution thermodynamics utilize solubility data to test the applications, predictive ability and limitations of some of these models. Solubility processes have played major role in analytical chemistry[4] A number of publications have focused on experiments involved with solubility and thermodynamics, the determination of enthalpies of solution from solubility measurements and an understanding of solubility products[5–9]

Initially, Water was used as a solvent among all known substances. Almost all chemically active liquids was considered under the name ''Divine water'' by the Greek alchemists. The word ''water'' become used to authorize everything liquid or dissolved.

Corresponding author: **Satish A.Ahire**
Department of Chemistry, Arts, Science and Commerce College, Surgana Tal. Surgana Dist. Nashik (India)

The several experiments conducted, brought about the uncovering of new reactions, new compounds and new solvents. From these experiments, the most ancient chemical rule arises so as to ''like dissolves like'' (similia similibus solvuntur). Though the words solution and dissolution involved all operations leading to a liquid product and the chemical change of a substrate occurs through dissolution. Hence, it became believed that the character of a substance lost upon dissolution. First, the Van Helmont was to strongly be in opposition to this theory. He noticed that the dissolved substance had not disappeared. It remains in the solution, although in aqueous form and could be recovered[10] . However; the dissolution of a substance in a solvent remained a mysterious method. Lomonosov stated that in the dissolution process, all solvents enter into the pores of the substance (solute) to be dissolved and gradually remove its particles. Though, there does not exist any reasonable explanation for the forces which cause this process of removal, unless one arbitrarily attributes to the solvents sharpen wedges or who understands, any other type of tools[11] Three persons; particularly the *Raoult*[12], the *Van't Hoff*[13] and the *Arrhenius*[14] were associated with the further development of modern solution theory. The effects of dissolved non-ionic substances on the freezing and boiling point of liquids was studied by Raoult. In 1886, he observed that changing the solute/solvent ratio produces precise proportional changes in the physical properties of solutions. He observed that the vapour pressure of solvent above a solution is directly proportional to the mole
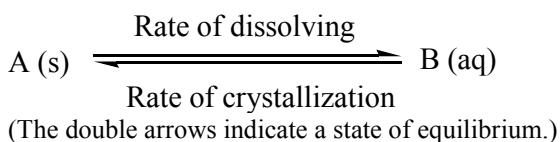
fraction of solvent in the solution, which is today known as **Raoult's law**[12] In 1884, the difficulty in justification of the effects of inorganic solutes on the physical properties of solutions led to Arrhenius' theory of incomplete and complete dissociation of ionic solutes into cations and anions in solution. From comparative results obtained by measurements of electro conductivity and osmotic pressure of dilute electrolyte solutions, Arrhenius derived his dissociation theory[14] Van't Hoff extensively studied the application of laws holding for gases to solutions replaced pressure by osmotic pressure, who made osmotic pressure measurements another important physicochemical method in studies of solutions[13]. The foundations of recent solution theory established on these three basic developments. Van't Hoff (in 1901) and Arrhenius (in 1903) were awarded with first Nobel prizes in chemistry for their work on osmotic pressure and electrolytic dissociation, respectively. The further development of solution chemistry is related with the pioneering work of Ostwald, Nernst, Lewis, Debye, E. Huckel and Bjerrum[15,16]

Understanding the concept of "solubility"

The solubility of a substance is the amount of solute that will dissolve in a specific amount of solvent at a specified temperature. Solubility is commonly expressed as a concentration, either by mass (g of solute per kg of solvent,) molarity, molality, mole fraction or other similar descriptions of concentration. The commonly used unit of solubility a substance is grams / liter at 25 °C and 1 atm. The temperature and pressure are specified because solubility can be affected by temperature and pressure.

Solubility is an example of Dynamic equilibrium

Solubility occurs under dynamic equilibrium, which means that solubility results from the simultaneous and opposing processes of dissolution and precipitation of solids. The solubility equilibrium occurs when the two processes proceed at a constant rate. For example**,** the $A_{(s)}$ - $B_{(aq)}$ system is at a state of equilibrium as follows,

$$A\ (s) \xrightleftharpoons[\text{Rate of crystallization}]{\text{Rate of dissolving}} B\ (aq)$$

(The double arrows indicate a state of equilibrium.)

Solubility is an example of Chemical equilibrium

The phenomenon of chemical equilibrium is encountered in many chemical systems and examples of equilibrium in nature are numerous. All equilibria, regardless of origin, have the following main characteristics in common:

1. The equilibrium state requires a *closed system*; i.e., a system which does not gain or lose matter.
2. The equilibrium state is a dynamic state where two or more reversible (opposing) processes are taking place at the same time and at the same rate so that no net change is apparent.

Terminology Related With Solubility

Solutions are homogeneous liquid phases consisting of more than one substance in variable ratios. For simplicity, one of the substances which is called the solvent and may itself be a mixture is treated differently from the other substances, which are called *solutes*.[17]

Normally, the component which is in greater quantity (excess) is called the *solvent* and the lesser quantity (minor) component is the *solute*. Solutes can be liquids, solids, or gases. Several terms are used to describe the degree to which a solute will dissolve in a solvent:

1.Miscible solution: When two liquids are completely soluble in each other in all proportions, they are said to be *miscible*. **E.g.** ethanol and water are miscible.

2.Immiscible solution: If the liquids do not mix, they are said to be *immiscible*. For example, Oil and water, are immiscible.

3.Unsaturated solution: It has a concentration of solute that is less than the maximum concentration. A solution that can still hold more solute is said to be *unsaturated*.

4.Saturated solution: A solution that contains the maximum amount of a solute at a given temperature is called a *saturated solution*.

If a solution has been stirred and there is still solid settling to the bottle of the container, the solution is saturated and the solute that could not dissolve will settle to the bottom.

5.Supersaturated solutions: A supersaturated solution is one that has more solute dissolved than should be possible at a given temperature. A supersaturated solution is usually made by heating a solution up so that more solute will dissolve and then letting it cool down undisturbed and sometimes the solute will stay dissolved.

6.Ideal solution

The solution is said to be a dilute solution, when the sum of the mole fractions of the solutes is small compared to unity. When solute substances have solute activity coefficients (γ) are close to unity ($\gamma = 1$) in a given solvent, this solution is treated as an ideal dilute solution.[17,18]

Over the entire composition range from pure A to pure B, Solute-solvent mixtures A + B obey Raoult's law are called **ideal solutions**. According to Raoult, the ratio of the partial pressure of component $A(p_A)$ to its vapour pressure as a pure liquid (p^*_A) is equal to the mole fraction of $A(x_A)$ in the liquid mixture, i.e. $x_A = p_A / p^*_A$. Many mixtures obey Raoult's law very well, mainly when the components have a similar molecular structure e.g. benzene and toluene.

7.Other solubility definitions[19]: Some terms are also used to describe the substance solubility in solvents are as shown in Table No.-1

Table No 1 Details showing the term used for the solute along with amount of solvent

Terminology used	Parts of solvent required for one part of solute
Very soluble	< 1
Freely soluble	1-10
Soluble	10-30
Sparingly soluble	30-100
Slightly soluble	100-1000
Very slightly soluble	1000-10000
Insoluble	>10000

The Solution Process

When a solute and a solvent are brought into contact with each other, the attractive forces of the solvent tend to break apart the structure of the solute and disperse ions or molecules from its surface. The action of the solvent is the result of the high

affinity or attractive forces between the solvent and the solute particles.

Consider the system where solute is solid and solvent is liquid. The **Solution** is formed when the ions or molecules become dislodged from the surface of the solid into the solvent. The dispersed solid which goes into a solution is described as the **solute** and the process called as **dissolution.** The ions or molecules dissolved in the solution are free to move about as a result of their kinetic energies of translation. In the solution, there is a continuous contact/return between the dissolved ions or molecules and the undissolved solid surface. When the concentration of ions or molecules becomes sufficiently high, the solution is **saturated.** A dynamic equilibrium will be established and then the solution is incapable of dissolving more solute particles. The concentration of the solute in a saturated solution is termed as the **solubility** of solute in the solvent.

Mechanism of Dissolution process

Dissolution is a process that takes place at the molecular level. When one substance dissolves in another, the particles of the solute disperse uniformly throughout the solvent. Due to interaction between the solvent and the solute molecule or ion, the solvent provide space for the solute in itself after the separation of the molecules of solvent[20]. The process of solubilization involves the breaking of inter-ionic or intermolecular bonds of the solute[21]

The ease with which a solute particle may replace a solvent molecule depends on the relative strengths of three types of interactions:

1. Solvent-Solvent interaction
2. Solute-Solute interaction
3. Solvent-Solute interaction

The solution process involves following steps (as shown in figure-1),

   Step-1: It involves the separation of solute molecules. These steps require inputs of energy to overcome attractive intermolecular forces.
   Step-2: It involves the separation of solvent molecules.
   Step-3: It involves the mixing of solute and solvent molecules; it may be exothermic or endothermic.
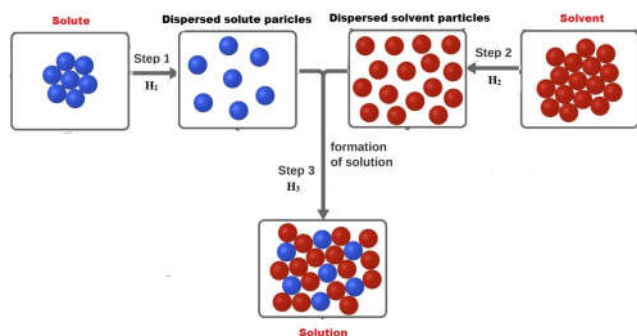

Figure1 A molecular view of the solution process

In the solution process, solute molecules and solvent molecules first being spread apart and then being mixed together. ΔH_1 is the relative strengths of forces holding solute molecules, ΔH_2 the relative strengths of forces holding solvent particles together and ΔH_3 is the relative strength of forces holding solute and solvent molecules in the solution, which have more importance in determining the solubility.

According to Hess's law, the heat of solution is given by the sum of the enthalpies of the three steps:

$$\Delta H_{soln} = \Delta H_1 + \Delta H_2 + \Delta H_3$$

1. If the solute-solvent attraction is stronger than the solvent-solvent attraction and solute-solute attraction; the solute will be soluble in the solvent and such a solution process is Exothermic.
2. If the solute-solvent interaction is weaker than the solvent-solvent and solute-solute interaction; only a relatively small amount of the solute will be dissolved and such solution process is Endothermic.

Solvation is the process in which a solute particle (an ion or molecule) is surrounded by solvent molecules due to strong solute-solvent attractive forces. When water is used as solvent, the process is called **hydration**. Generally, the solution process is assisted by an exothermic heat of solution, yet there are a number of soluble compounds with endothermic heats of solution. In addition, every substance is somewhat soluble; no matter what the value of ΔH_{soln}. It turns out that all chemical processes are governed by two factors.

Energy: The solution process either absorbs energy (endothermic) or release energy (Exothermic).

Disorder or randomness: In the pure state, the solvent and solute possess the ordered arrangement of atoms, molecules or ions in a three-dimensional crystal.

When the solute dissolves, the order in a crystal is lost and its molecules are dispersed in the solvent. The solution process is accompanied by an increase in disorder or randomness. The increase in disorder of the system favors the solubility of any substance.

Forces Involve In Solution Process (Molecular Interactions)

The arrangement of the atoms, ions or molecules of the substances and the strength of the forces of attraction between the atoms, ions or molecules explained the differences in the physical and chemical properties of substances. The two forces; the electromagnetic and gravitational forces that act between atoms and molecules (as well as between elementary particles). These forces are effective from subatomic to practically infinite distances over a much larger range and as a result these forces govern the behavior of everyday things e.g. electromagnetic forces is the source of all intermolecular interactions which determines the properties of solids; liquids and gases, the behavior of particles in solution, chemical reactions and the association of biological structures. Gravitational forces give explanation for tidal motion and many cosmological phenomena. When acts together with intermolecular forces, they determine the phenomena of the height that a liquid will rise in small capillaries and the maximum size that animals and trees can attain[22]. Therefore, Forces involved are classified according to their different physical or chemical origin. Generally, it is said that chemical forces give rise to chemical or covalent bonds while physical forces give rise to physical bonds.

Covalent or Chemical Bonding Forces: When two or more atoms come together to form a molecule, the forces that tightly bind the atoms together within the molecule are called covalent forces and the interatomic bonds formed are called covalent or chemical bonds. e.g. two hydrogen atoms and one

oxygen atom that combine to form a water molecule. Metallic bonds are closely allied to covalent bonds. In both cases, the bonds are characterized by the sharing of the electrons between the two or more atoms so that the discrete nature of the atoms is lost. Covalently bonded atoms make up molecules and crystals with well-defined structures that can not normally melt or liquify without breaking of the bonds. So they tend to vaporize, decompose or undergo a chemical reaction above some temperature rather than go through the conventional solid/liquid /gas states that are characteristic of physically bonded molecules.

Physical forces: Physical bonds usually lack the specificity, stoichiometry and strong directionality of covalent bonds. So they are the ideal for holding molecules together in liquids, as the molecules can move about and rotate while still remaining bonded to one another. Strictly, physical bonds should not be considered as bonds at all. During covalent binding, the electron charge distributions of the uniting atoms change completely and merge whereas during physical binding they are merely disturbed and the atoms remaining as distinct entities. However, physical binding forces can be as strong as covalent bonds and even the weakest is strong enough to hold together all, but the smallest atoms and molecules in solids and liquids at STP Standard Temperature and Pressure as well as in colloidal and biological assemblies. These properties coupled with the long-range nature of physical forces which make them the regulating forces in all phenomena that do not involve chemical reactions.

Forces arising from the Coulomb force between charges, are purely electrostatic in origin. The interactions among charges, ions, permanent dipoles, quadrupoles and so forth fall into this category. Electrostatic forces contain polarization interactions which arises from the dipole moments induced in atoms and molecules by the electric fields of nearby charges and permanent dipoles. All electrostatic interactions in a solvent medium involve polarization effects. The electrostatic forces between electro neutral molecules that are free to mutually orient, are generally attractive and they occur even at zero temperature (T = 0 K). Some forces have a purely entropic origin which arises from the collective behavior of molecules at finite temperatures (T > 0) and therefore can not be described in terms of force-law between two molecules. The pressure of an ideal gas is given by P = nRT/V is an example of a repulsive entropic force (P is an outward pressure) that has a purely entropic origin for molecules obeying Boltzmann statistics. Other forces like osmotic forces and various thermal fluctuation forces fall into this category. Forces which are quantum mechanical in nature give rise to covalent or chemical bonding (including van der Waals–dispersion forces, acid-base and charge-transfer interactions) and to the repulsive steric forces that balance the attractive forces at very short distances (due to the Pauli exclusion principle). Quantum systems are characterized by having discrete (quantized) energy levels. The forces of are of two types,

Intramolecular force: Atoms within a molecule are attracted to one another by the sharing of electrons.

Intermolecular Forces[23-34]

The intermolecular forces are electrostatics in nature. These forces held molecules together. In general, intermolecular forces are much weaker than the intramolecular forces. The forces which can occur between closed-shell molecules are also said to be intermolecular forces[23-34] These are also known as Van der Waals forces, as a reason for the non-ideal behavior of real gases as recognized by him. These intermolecular forces affect physical properties like melting points, boiling points, viscocity and surface tension. E.g. boiling point of liquids: if the intermolecular attractions are strong i.e. the units are more tightly are held together by strong intermolecular forces, more heat energy is needed to separate them into gases. On the other hand, if intermolecular attractions are weak, the boiling point will be low. A series of compounds with regularly varying structures and formulas also has regularly varying properties; this is the principle of homology[35]

Intermolecular forces play some role in viscosity because stronger attractions between molecules cause them to resist flow more strongly. Surface tension is also a result of intermolecular forces. Molecules at the surface of a liquid are attracted the molecules from beneath and beside, which leads to an inward force on the liquid. It generates an imbalance on the surface. This tension also causes drops of water to contract into spheres to minimize the surface area[36] There are four main types of intermolecular forces: A) ion-dipole B) dipole-dipole C) dipole-induced dipole D) Instantaneous dipole-induced dipole.

Ion-Dipole Forces[37,38]

Dipoles means an electrically asymmetrical molecule. Molecules which have dipoles are called as polar while molecules which do not have dipoles are called as non-polar molecules. e.g. Water is a polar molecule. The oxygen atom withdraws electrons from the hydrogen resulting in a charge imbalance. Dipoles are major Importance in intermolecular forces as electrical charges can attract or repel each other. Molecules having unsymmetrical charge acquire a permanent dipole moment (μ). If "q" is the magnitude of the two equal and opposite charges of this molecular dipole and "l" is distance of the separation of opposite charges, the dipole moment (μ) is given by

$$\mu = q \times l.$$

A charged ion is attracted towards the dipole of a polar molecule. The dipole will orient itself when placed in the electric field resulting from an ion, so that the attractive end will be directed toward the ion and the other repulsive end directed away. The dipole is positioned next to the ion in such a way that, the ion and the separated charges of the dipole are linearly arranged as shown in figure-2. Only molecules having permanent dipole moment should be called as *dipolar molecules*.

Figure 2 the arrangement of ion and dipole

Examples: the dissolution of salt in water; the negatively charged Cl⁻ ions will be attracted to the positive dipole near the hydrogens while the positively charged Na⁺ ions will seek the negative dipole of the oxygen atom as shown in figure-3.
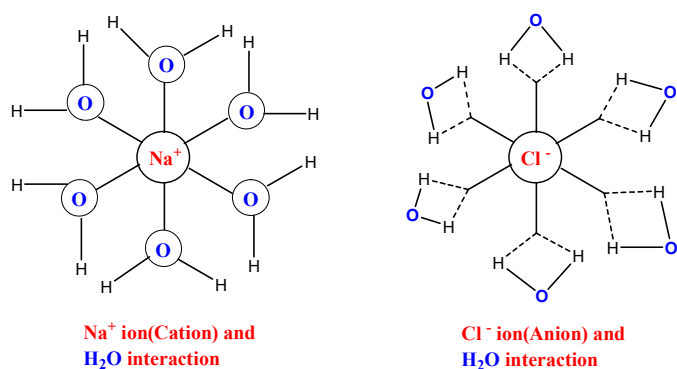
Na⁺ ion(Cation) and H₂O interaction **Cl⁻ ion(Anion) and H₂O interaction**

Figure 3 the digramatic presentation of ion-dipole forces

When salt dissolves in water, these attractions are powerful enough to break the NaCl crystal, meaning that salt dissolves. If the crystal structure is too strong to be broken by attractions between a solvent and the ionic solid, then the solid will not dissolve.

Dipole-Dipole Forces[39]

These forces depend on the electrostatic interaction between molecules and they exist in two polar molecules due to their unsymmetrical charge distribution i.e. they possess a permanent dipole moment (μ). The molecules will orientate themselves so that the opposite charges attract each other effectively. The possible arrangements of the two dipoles are as shown in figure-4. The second arrangement is the more stable one if the dipole molecules are very voluminous. The two situations exist, only when the attractive energy is larger than the thermal energies. Therefore, the thermal energy will normally prevent the dipoles from optimal orientation.
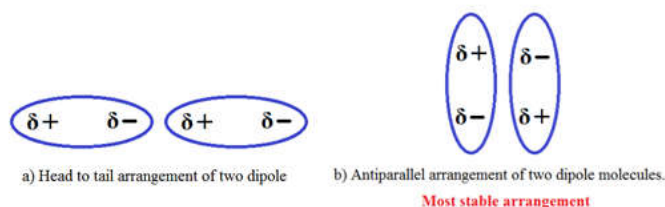

a) Head to tail arrangement of two dipole   b) Antiparallel arrangement of two dipole molecules.
Most stable arrangement

Figure 4 the arrangement of two dipoles

If all possible orientations were equally probable i.e. the dipoles correspond to freely rotating molecules, then attraction and repulsion would compensate each other. The fact that a dipole orientation which leads to attraction is statistically favored leads to a net attraction, which is strongly temperature dependent. The angle-averaged dipole-dipole interaction energy becomes less negative with the increase of temperature, until at very high temperatures all dipole orientations are equally populated and the potential energy is zero. Among other interaction forces, these dipole-dipole interactions are mainly responsible for the association of dipolar organic solvents such as dimethyl sulfoxide[40] or N,N-dimethyl formamide[41]

Example: HCl is a polar molecule and has a permanent dipole because chlorine withdraws electrons more than hydrogen which leads to a positive charge ($\delta+$) on the hydrogen and a negative charge ($\delta-$) on the chlorine. These molecules will attract each other. The dipole-dipole interaction in HCl molecule is as shown in figure-5.
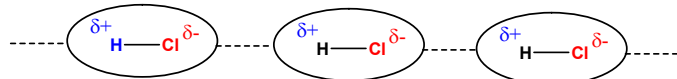

Figure-5 the dipole- dipole interaction between HCl molecule.

Dipole-Induced Dipole Forces[42]

A molecule having a permanent dipole moment (μ) i.e. polar molecule, when comes in contact with other non polar molecule where it induce a dipole moment in a non-polar molecule. The dipole of the polar molecule generates temporary dipole in the non-polar molecules. This temporary dipoles may exist for only a fraction of a second. This induced moment always lies in the direction of the inducing dipole. Thus, there is always existence of attraction between the two partners, which is independent of temperature. The larger the induced dipole moment, the larger the polarizability (α) of the non-polar molecule experiencing the induction of the permanent dipole.

Example: NH_3 is a polar having permanent dipole moment while C_6H_6 is non-polar and has zero dipole movement. The force of attraction between benzene and ammonia is the type of dipole induced dipole interaction. The general digramatic presentation of dipole-induced dipole interaction in a molecule is as shown in figure-6.
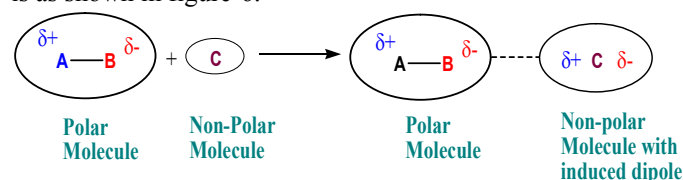

Polar Molecule **Non-Polar Molecule** **Polar Molecule** **Non-polar Molecule with induced dipole**

Figure 6 the diagrammatic representation of dipole and induced dipole forces

Instantaneous Dipole-Induced Dipole Forces[43-45]

As physical forces arise from electrostatic interactions involving charged or dipolar molecules, the various types of physical forces are quite easy to understand. But there is a another type of force that like the gravitational force acts between all atoms and molecules, even totally neutral ones such as helium, carbon dioxide and hydrocarbons. These forces have been known as dispersion forces, London forces and electro dynamic forces. It is most widely known with the name, dispersion forces. The origin of this name has to do with their relation to the dispersion of light in the visible and UV regions of the spectrum[46-47]

Generally, it is observed in atoms or molecules having no permanent dipole moment. The continuous electronic movement results in a small dipole moment (μ) at any instant, which can polarize the electrons of the neighbouring atoms or molecules. Attractions between instantaneous and induced dipoles called dispersion forces are found in all substances. A mutual attraction results from electronic movements because of this coupling. The energy of such so-called dispersion or London[43] interactions. These are universal for all atoms and molecules. These are enormously short-range in action. These are alone responsible for the aggregation of molecules which possess neither free charges nor electric dipole moments.

Strong dispersion forces exist between molecules especially with conjugated pi-electron systems due to the greater polarizability of pi-electrons e.g. aromatic hydrocarbons. As the molecular volume and the number of polarizable electrons increases, these forces also increase rapidly. Solvents with a large refractive index and hence large optical polarizability, should be capable of enjoying particularly strong dispersion forces. All aromatic compounds possess relatively high indices of refraction. For example, quinoline (*n*=1:6273), aniline (*n*=1:5863) and diphenyl ether (*n*=1:5763); of all organic solvents, carbon disulfide (*n*=1:6275) and diiodomethane

(n=1:738) have the highest indices of refraction. Due to the dispersional interactions between the solvents and the large polarizable anions like I_3^-, I^-, SCN^- or the picrate anion are significantly larger than for the smaller anions like F^-, HO^-, or R_2N^-, solvents with high polarizability are often good solvators for anions, which also possess high polarizability[48]

Dispersion forces most important contributor to the total van der Waals force between atoms and molecules. They are always present (in contrast to the other types of forces that may or may not be present, depending on the properties of the molecules) They play a role in a host of important phenomena such as adhesion; surface tension; physical adsorption; wetting; the properties of gases, liquids, and thin films; the strengths of solids; the flocculation of particles in liquids and the structures of condensed macromolecules such as proteins and polymers.

Their main features of dispersion forces may be summarized as follows:

1. They are long-range forces. Depending on the situation, they can be effective from large distances (greater than 10 nm) down to interatomic spacings (about 0.2 nm).
2. These forces may be repulsive or attractive.
3. These forces not only bring molecules together but also have a tendency to mutually align or orient them, though this orienting effect is usually weaker than with dipolar interactions.
4. Dispersion forces are not additive i.e. the force between two bodies is affected by the presence of other bodies nearby. This is called the non additivity of an interaction.

Hydrogen Bonding[49,50]

A subtype of dipole-dipole interactions is hydrogen bonding. A hydrogen bond is the attractive force between the hydrogen attached to an electronegative atom of one molecule and an electronegative atom of a different molecule. Generally, the electronegative atoms are nitrogen, oxygen or fluorine. When electronegative atom is bonded to one or more hydrogens. Each electronegative atom withdraws electrons from hydrogen, a dipole is formed. These dipoles result in strong attractions between molecules. When a hydrogen atom (H) or Liquids possessing hydroxy groups (-OH) bonded to an electronegative atom X are strongly associated and have noticeably high boiling points. The hydrogen bonding is found in water (H_2O), ammonia (NH_3), hydrogen fluoride (HF) as shown in figure-7. Hydrogen bonds are characterized by a coordinative divalency of the hydrogen atom involved. In 1919, Huggins introduced the concept of hydrogen bonding[49] Generally, hydrogen bond can be defined as when hydrogen atom covalently bound to another atom forms a new bond, this bond is referred to as a hydrogen bond[50] In 1920, Latimer and Rodebush published the first definitive paper on hydrogen bonding applied to the association of water molecules[51]
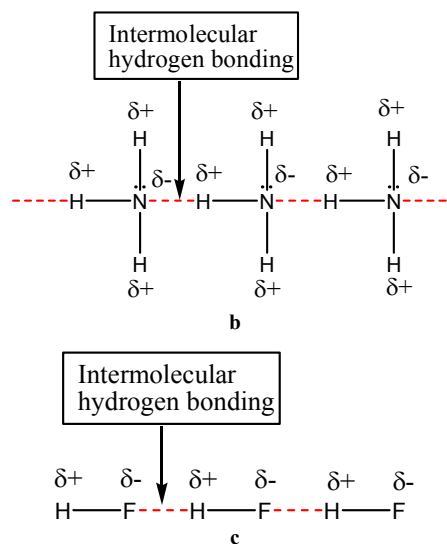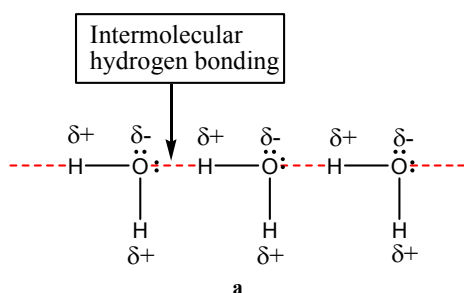
Figure 7 Hydrogen bonding in (a) Water (H_2O); (b) Ammonia (NH_3) and (c) HF

The most of the electron pair donors i.e. hydrogen bond acceptors are the oxygen atoms (O) in alcohols, ethers and carbonyl compounds as well as nitrogen atoms(N) in amines and N-heterocycles. Hydroxy(-OH), amino(NH_2), carboxyl(-COOH) and amide(-$CONH_2$) groups are the most important proton donor groups. The alkenes, alkynes and π-electron systems of aromatic compounds, can also act as weak hydrogen bond acceptors[52] The strength of hydrogen bond depends on the atoms involved in hydrogen bond formation. The strength of hydrogen bond along with their atoms involved in hydrogen bond are shown in Table No.-2

Table No 2 List showing strength of hydrogen bond and the atoms involved in hydrogen bond formation.

Strength of hydrogen bond	Atoms involved in Hydrogen bond
Strong	O-H----O
	O-H----N
	N-H----O
Weaker	N-H----N
weakest	Cl_2C-H----O
	Cl_2C-H----N

The hydrogen bonding may occur in the following types

Homo-intermolecular hydrogen bonds*:* these are formed when two or more molecules of the same type associate(as shown in Figure-8).
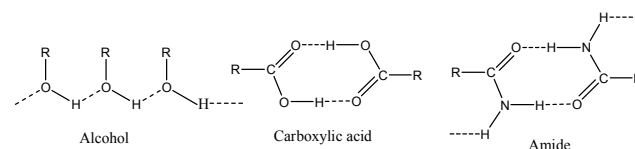
Figure 8 Homo-intermolecular hydrogen bonds

Hetero-intermolecular hydrogen bonds*:* these are formed by the association of different molecules e.g. R-O-H----NR_3. The designations homo- and hetero-molecular[53] as well as homo- and hetero-conjugated hydrogen bond are also in use.Solutions of 4-hydroxyacetophenone and 2-(2-hexyloxyethoxy) ethanol is a remarkable example of a competitive solvent dependent equilibrium between homo- and hetero-intermolecular hydrogen-bond associated species[54]

Intermolecular or Intramolecular Hydrogen bonds*:* It can be either intermolecular or intramolecular. Both types of

hydrogen bonds are found in solutions of 2-nitrophenol, depending on the Lewis basicity of the solvent[55]. The non-hydrogen bonding solvents shows the existence of intramolecular hydrogen-bonding form (e.g. tetrachloromethane, cyclohexane,). Intramolecular hydrogen bond in 2-Nitrophenol breaks its hydrogen bonding to form an intermolecular one in electron-pair donor (EPD) solvents (e.g. HMPT, anisole,).

Circular hydrogen bonds: They have been observed in the hexahydrate of α-cyclodextrin (cyclohexaamylose)[56,57] Hydration water molecules and hydroxy groups of the macromolecule cooperate to form a network-like pattern with circular O-H----O hydrogen bonds. If the O-H----O hydrogen bonds are running in the same direction, the circle is called *homodromic*(as in Figure-9) Circles with the two oppositely running chains are called *antidromic* (as in Figure-9). and circles with more randomly oriented chains are designated *heterodromic*[56,57] (as in Figure-9).
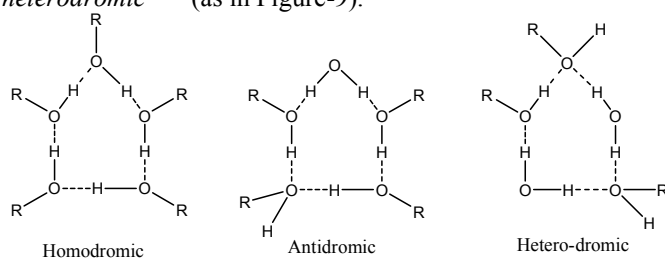

Figure 9 Three types of circular hydrogen bonds[56,57]:

The question of the exact geometry of hydrogen bonds (their distances, angles, lone pair directionality) has been reviewed[58] The bond dissociation enthalpy for normal hydrogen bonds is 13-42 kJ/mol (3-10 kcal/mol). For comparison, single covalent bonds have dissociation enthalpies of 210-420 kJ/mol (50-100 kcal/mol). Thus, hydrogen bonds are approximately ten times weaker than covalent single bonds, but also approximately ten times stronger than the non specific intermolecular interaction forces.

The hydrogen bond can be described as a dipole-dipole or resonance interaction as hydrogen bonding occurs only when the hydrogen is bound to an electronegative atom. The first assumption concerning the nature of the hydrogen bond was that it consists of a dipole-dipole interaction such as $R-X^{\delta-}-H^{\delta+}---Y^{\delta-}-R'$. This point of view is supported by the fact that the strongest hydrogen bonds are formed in pairs in which the hydrogen is bonded to the most electronegative elements (e.g. $F-H----F^-$, ΔH =155 kJ/mol). The greater strength of the hydrogen bond is due to the much smaller size of the hydrogen atom relative to any other atom, which allows it to approach another dipole more closely. This simple model accounts for the linear geometry of the hydrogen bond because such arrangement maximizes the attractive forces and minimizes the repulsion. An overlap of the orbitals of the X-H bond and the electron pair of :Y can lead to a covalent interaction when the X-Y distance is sufficiently short. Two contributing ''protomeric'' structures, which differ only in the position of the proton described this situation.

$$R-X-H----Y-R' \longleftrightarrow R-X^- ----H-Y^+-R'$$

The approximate quantum mechanical description of proton states by linear combination of these protomeric structures has been called protomerism (symbol *p*)[59,60]

Features of Hydrogen bonds

They are characterized by the following structural and spectroscopic features[61]

1. the distances between the neighbouring atoms involved in the hydrogen bond are noticeably smaller than the sum of their van der Waals radii
2. hydrogen bond formation causes its IR stretching mode to be shifted towards lower frequencies[62]
3. the dipolarity of the X-H bond increases on hydrogen bond formation
4. Hydrogen atoms are deshielded due to the reduced electron density at H-atoms involved in hydrogen bonds, resulting in substantial downfield shifts of their 1H NMR signals;
5. in hetero-molecular hydrogen bonds, increase in solvent polarity is found[63,64]

Till today there has been no general agreement as to the best explanation of the nature of the forces in the hydrogen bond[65-69]

Application of Hydrogen bonding

Classification of solvents on the basis of Hydrogen Bond: Solvents which contains proton-donor groups are designated *protic solvents*[48] or HBD solvents[70]; solvents which contains proton-acceptor groups are called HBA solvents[70] The abbreviations HBD (hydrogen-bond donor) and HBA (hydrogen-bond acceptor) refer to donation and acceptance of the proton and not to the electron pair involved in hydrogen bonding. Solvents without proton-donor groups have been designated aprotic solvents[48] However, this term is rather misleading, since, for example, solvents commonly referred to as dipolar aprotic (e.g. CH_3SOCH_3, CH_3CN, CH_3NO_2) are in fact not aprotic. In reactions, where strong bases are employed, their protic character can be recognized. Therefore, the term aprotic solvents should be replaced by non-hydroxylic or better still by non-HBD solvents[71] The nature of solvent and their examples are given in Table No.-3

Table No 3 List of nature of solvent along with their examples

Nature of Solvent	Examples
Typical protic or HBD solvents	water, ammonia, alcohols, carboxylic acids and primary amides.
Typical HBA solvents	amines, ethers, ketones and sulfoxides.
Amphiprotic solvents (can act both as HBD and as HBA solvents simultaneously)	water, alcohols, amides

Hydrogen bonding is responsible for the strong, temperature-dependent self- and hetero-association of amphiprotic solvents (e.g. water, alcohols, amides). The molecular structure of binary HBD/HBA solvent mixtures is largely determined by intermolecular hydrogen bonding between the two components, which usually leads to pronounced deviations from ideal solution behavior.[72-75]

Hydrogen bonding plays a particularly important role in the interactions between anions and HBD solvents. Hence, HBD solvents are good anion solvators. Due to the small size of the hydrogen atom, small anions like F^-, Cl^- or HO^- are more effectively solvated by such solvents than the larger ones, e.g. I_3^-, I^-, SCN^-, or the picrate ion[48] This is also one of the reasons

why the Gibbs energy of hydration, ΔG_{solv}, of the halide ions decreases in the series $F^- > Cl^- > Br^- > I^-$ [76]

Hydrogen bonding is of prime importance for the stabilization and the shape of large biological molecules in living organisms (e.g. cellulose, proteins, nucleic acids).

For example, the anaesthetic properties of some halogen-containing solvents such as chloroform, halothane (CF_3-CHClBr) and methoxyflurane (CH_3O-CF_2-$CHCl_2$) have been connected with their ability to hinder the formation of biologically important.

References

1. Liu H. , Yao X., R. Zhang, Liu M., Hu Z., Fan B., Accurate Quantitative Structure−Property Relationship Model To Predict the Solubility of C_{60} in Various Solvents Based on a Novel Approach Using a Least-Squares Support Vector Machine., *J. Phys. Chem. B*, 2005, 109 (43), 20565-20571.

2. Portier S, Rochelle C., Modelling CO_2 solubility in pure water and NaCl-type waters from 0 to 300 °C and from 1 to 300 bar: Application to the Utsira Formation at Sleipner; *Chem. Geology*, 2005, 217 (3-4), 187-199.

3. Zha S. K., Madras G., Modeling the solubilities of high molecular weight n-alkanes in supercritical carbon dioxide; *Fluid Phase Equil.*, 2004, 225 (1–2), 59-62.

4. Skoog D., West D. M., Holler F. J., Crouch S. R., Fundamentals of Analytical Chemistry, 8th ed., Thomson: Belmont, CA, 2004.

5. Silberman R. G., Solubility and Thermodynamics: An Introductory Experiment, *J. Chem. Educ.*,1996, 73(5), 426.

6. Cesaro A., Russo E., Heats of solution from solubility determinations; *J. Chem. Educ.*,1978, 55(2),133.

7. Hawkes S. J. ; What Should We Teach Beginners about Solubility and Solubility Products?, *J. Chem. Educ.*,1998, 75(9),1179.

8. Battino R.; Letcher T.M., An Introduction to the Understanding of Solubility, *J. Chem. Educ.*, 2001,78(1),103.

9. Holmes L. H. Jr., The Solubility of Gases in Liquids, *J. Chem Educ.*, 1996, 73(2),143.

10. Szabadvary F., Geschichte der Analytischen Chemie, Vieweg, Braunschweig and Akademiai Kiado, Budapest,1966, p.38.

11. Lomonosov M. V.: O Deistvii Chimicheskikh Rastvoritelei Voobshche (On the Action of Chemical Solvents in General), in S. R. Mikulinskii (ed.): M. V. Lomonosov – Izbrannye Proizvedeniya (Selected Works), Tom 1, p. 58-73; Estestvennye Naukii Filosofiya, Nauka, Moskva, 1986.

12. Van't Hoff J. H., Raoult Memorial Lecture, *J. Chem. Soc.*,1902,81,969.

13. Van't Hoff J. H., Uber die Theorie der Losungen, in F. W. Ahrens (ed.): Sammlung chemischer und chemisch-technischer Vortrage, Enke, Stuttgart, 1900, Vol. V, Heft 1; *Chem. Zentralbl.*,1900, I, 696.

14. Partington J. R., A History of Chemistry, MacMillan, London, New York,1964, Vol. 4, Chapter XX, 637

15. Laidler K. J., A Century of Solution Chemistry, *Pure Appl. Chem.*, 1990,62, 2221 and K. J. Laidler: The World of Physical Chemistry, Oxford University Press, Oxford/U.K.,1993.

16. Ohtaki H., Development of Modern Solution Chemistry: A Search of New Fields, *Coord. Chem. Rev.*, 1999,185/186, 735.

17. Whiffen D. H. (ed.), Manual of Symbols and Terminology for Physicochemical Quantities and Units, Appendix I: Solutions, *Pure Appl. Chem.*, 1979,51,1.

18. Jancso´G. and Fenby D. V., Thermodynamics of Dilute Solutions, *J. Chem. Educ.*, 1983, 60, 382.

19. Sinko P. J., Martin's physical Pharmacy & Pharmaceuitical Sciences, 5th Ed., 2006, Chapter 9, 232-244.

20. Shinde A. Solublization of poorly water soluble drugs, *Pharminfo.net* 2007, 5(6)

21. Swarbrick J. Encyclopedia of Pharmaceutical Technology, 3rd Ed. 2006, 3314-3328

22. Thompson D. W., On growth and form. New York: Cambridge University Press.,1968

23. Review on van der Waals Molecules, *Chem. Rev.*, 1988, 88(6), 813-988.

24. Israelachvili J., Intermolecular and Surface Forces, 2nd ed., Academic Press, London, 1991

25. Huyskens P. L., W. A. P. Luck, T. Zeegers-Huyskens: Intermolecular Forces, Springer, Berlin, 1991.

26. Atkins P. W., Physical Chemistry, 6th ed., Oxford University Press, Oxford/U.K., 1998, 659

27. Muller-Dethlefs K., P. Hobza, Noncovalent Interactions - A Challenge for Experiment and Theory, *Chem. Rev.*, 2000, 100, 143.

28. Schmid R., Solvent Effects on Chemical Reactivity in G. Wypych (ed.): Handbook of Solvents (+ Solvent Database on CD-ROM), ChemTec Publishing, Toronto and William Andrew Publishing, New York, 2001, Chapter 13.1, 737-777.

29. Buckingham A. D., Fowler P. W., Hutson J. M., Theoretical Studies of van der Waals Molecules and Intermolecular Forces, *Chem. Rev.*,1988, 88, 963.

30. Stone A. J., The Theory of Intermolecular Forces, Oxford University Press, Oxford/U.K., 1996.

31. Scheiner S. (ed.),Molecular Interactions–From van der Waals to Strongly Bound Complexes, Wiley-VCH, Weinheim/ Germany, 1997.

32. Tomasi J., Mennucci B., Cappelli C., Solvents and Solutions as Assemblies of Interacting Molecules, in G. Wypych (ed.): Handbook of Solvents (+ Solvent Database on CDROM), ChemTec Publishing, Toronto, and William Andrew Publishing, New York, 2001, Chapter 8.1, 419-504.

33. Maitland G. C., Rigby M., Smith E. B., Wakeham W. A., Intermolecular Forces – Their Origin and Determination, Oxford University Press, Oxford, 1987.

34. Ratajczak H., Orville W. J. -Thomas (eds.): Molecular Interactions, Wiley, New York, 1980-1982, Vols. 1-3.

35. Desiraju G.R., The C-H…O hydrogen bond in crystals: What is it?, *Accounts of Chemical Research*, 1991,24(10),290-296.

36. Brock C.P. and Dunitz J.D., Towards a grammar of crystal packing, *Chemistry of Materials*, 1994, 6(8),1118-1127.

37. Jaffe´H. H., A classical electrostatic view of chemical forces; *J. Chem. Educ.*; 1963; 40(12), 649

38. March N. H., Tosi M. P.: Coulomb Liquids, Academic Press, New York, London, 1984.

39. Keesom W. H., *Physik. Z.*,1921, 22,129, 643.

40. Amey R. L.; Extent of association in liquid dimethyl sulfoxide, *J. Phys. Chem.*;1968; 72(9), 3358-3359.

41. Rabinowitz M., Pines A., Hindered internal rotation and dimerization of N, N-dimethyl formamide in carbon tetrachlorid, *J. Am. Chem. Soc.*,1969; 91(7); 1585-1589.

42. Debye P., *Physik. Z.*, 1920, 21, 178.

43. London F., The general theory of molecular forces , *Trans. Faraday Soc.* 1937,33,8.

44. Ulbrich R., *Chemiker-Ztg.*,1975,99, 320.

45. Mahanty J. H., Ninham B. W., Dispersion Forces, Academic Press, New York, London, 1981.

46. London, F., The general theory of molecular forces, *Transactions of the Faraday Society*, 1937, 33, 8-26.

47. Israelachvili J. N., Van der Waals forces in biological systems, *Quarterly Reviews of Biophysics*, 1974, 6(4), 341-387.

48. Parker A. J., *Quart. Rev. (London)*,1962, 16, 163.

49. Huggins M. L., 50 years of hydrogen bond theory, *Angew. Chem. Int. Ed. Engl.*,1971, 10(3), 147-152.

50. Joesten M. D., Schaad L. J., Hydrogen Bonding, Dekker, New York, 1974.

51. Latimer W. M., Rodebush W. H., Polarity and ionization from the standpoint of the Lewis theory of valence, *J. Am. Chem. Soc.*,1920,42(7), 1419-1433.

52. Desiraju G., Steiner T., The Weak Hydrogen Bond in Structural Chemistry and Biology, Oxford University Press, Oxford/U.K., 1999.

53. Isenberg N., Proposed terminology for intermolecular hydrogen bonds, *J. Chem. Educ.* 1982;59(7); 547.

54. Clark J. H., Locke C. J., White M. S., Medium control in a competitive hydrogen bonding system, *Spectrochim. Acta*, Part A, 1994, 50(5), 891-896.

55. Kamlet M. J., Taft R. W., Linear solvation energy relationships: Intra- vs. intermolecular hydrogen bonding by some 2-nitroaniline and 2-nitrophenol derivatives, *J. Org. Chem.*, 1982;47(9), 1734-1738.

56. Saenger W., Circular hydrogen bonds, *Nature (London)*,1979, 279, 343.

57. Saenger W., Lindner K., OH clusters with homodromic circular arrangements of hydrogen bonds, *Angew. Chem. Int. Ed. Engl.*, 1980, 19(5), 398-399.

58. Taylor R., Kennard O., Hydrogen-Bond Geometry in Organic Crystals, *Acc. Chem. Res.*, 1984, 17, 320.

59. Zimmermann H., Protonic states in chemistry, *Angew. Chem. Int. Ed. Engl.*, 1964, 3(3), 157-164.

60. Schmidt P. P., Hydrogen bonding: the role of hydrogen delocalization in the AHB bond, *J. Phys. Chem.*, 1993, 97(17), 4249-4253.

61. Schuster P. (ed.), Hydrogen Bonds, *Top. Curr. Chem.*,1984,120, 1-113.

62. Hobza P., Havlas Z., Blue-Shifting Hydrogen Bonds, *Chem. Rev.* 2000,100(11), 4253-4264.

63. Rospenk M., Fritsch J., Zundel G., Solvent effect on the proton-transfer equilibria and thermodynamic data of the hydrogen bond in a Mannich base, *J. Phys. Chem.,*1984, 88(2),321-323.

64. Golubov N. S., Shenderovich I. G., Smirnov S. N., Denisov G. S., Limbach H-H., Nuclear Scalar Spin–Spin Coupling Reveals Novel Properties of Low-Barrier Hydrogen Bonds in a Polar Environment, *Chem. Eur. J.*, 1999; 5; 492.

65. Aakeroy C. B., K. R. Seddon, The Hydrogen Bond and Crystal Engineering, *Chem. Soc. Rev.*, 1993, 22, 397.

66. Perrin C. L., Nielson J. B., ''Strong'' Hydrogen Bonds in Chemistry and Biology, *Annu. Rev. Phys. Chem.*,1997, 48, 511.

67. Gordon M. S., Jensen J. H., Understanding the Hydrogen Bond Using Quantum Chemistry, *Acc. Chem. Res.*, 1996, 29, 536.

68. Hadzi D. (ed.): Theoretical Treatments of Hydrogen Bonding, Wiley-VCH, Weinheim/ Germany,1997.

69. Jeffrey G. A., An Introduction to Hydrogen Bonding, Oxford University Press, Oxford/U.K., 1997.

70. Kamlet M. J., Taft R. W., The solvatochromic comparison method. I. The beta.-scale of solvent hydrogen-bond acceptor (HBA) basicities, *J. Am. Chem. Soc.*, 1976, 98(2), 377-383.

71. Mashima M., McIver R. T., Taft R. W., Bordwell F. G., Olmstead W. N., Enhanced Substituent Solvation Assisted Resonance Effects in Dipolar Non-Hydrogen-Bond-Donor Solvents, *J. Am. Chem. Soc.*, 1984, 106(9), 2717-2718.

72. Dore J. C., Teixeira J. (eds.), Hydrogen-Bonded Liquids, Kluwer, Dordrecht / Netherlands, 1991.

73. Jacques P.; Synergistic effects in binary solvent mixtures: A simple approach to a special case of nonideal binary mixture behavior, *J. Chem. Educ.*, 1991, 68(4), 347.

74. Durov V. A., Shilov I. Yu., Molecular structure and physicochemical properties of acetone–chloroform mixtures , *J. Chem. Soc.*, Faraday Trans., 1996; 92, 3559-3563.

75. Daniel D. C., McHale J. L., Hydrogen Bonding in $CHCl_3$/DMSO-d_6 and $CDCl_3$/DMSO-h_6 Mixtures , *J. Phys. Chem. A*, 1997, 101(17), 3070-3077.

76. Kortum G.: Lehrbuch der Elektrochemie, 5th ed., Verlag Chemie, Weinheim, 1972.

****