CHAPTER-VIII

EXPLORATION OF INCLUSION COMPLEX FORMATION BETWEEN IONIC LIQUID AND β-CYCLODEXTRIN BY SURFACE TENSION, CONDUCTANCE AND SPECTROSCOPIC STUDY

Exploration of inclusion behaviour of a guest ionic liquid (IL) 1-methyl-3-octylimidazolium chloride ([mocimm]Cl) into the host cavity of β-cylodextrin in aqueous solution has been studied on modern research gaining far reaching effect. Surface tension and Conductivity establishe the formation of inclusion complexe while ^{1}H NMR study result confirms that 1:1 hosts-guest inclusion complex is formed and favourable with the above system. The formation and nature of the inclusion complex has been also characterized using job method by ultraviolet spectroscopy and association constants has been evaluated for the formed inclusion complex by ultraviolet spectroscopy.

VIII.1 INTRODUCTION

Ionic liquids (ILs) are a class of organic molten electrolytes whose physical and chemical properties can be tailored by judicious selection of cation, anion, and substituent. They have specific properties such as no significant vapor pressures, high ion conductivity, outstanding catalytic properties, nonflammability, and stableness at temperatures up to 300 °C or more. Therefore, ILs have attracted much attention as electrolytes and solvent media for reactions and extractions. They are popularly called “green solvents” because of their environmentally benign feature coming from nonflammability and can contribute

much in the industrial field. They are also used as heat transfer fluids for processing biomass and as electrically conductive liquids in electrochemistry (batteries and solar cells).[VIII.1-VIII.3]

Cyclodextrins are commonly used as complexing agents in biological, pharmaceutical and industrial applications since they have an effect on protein thermal and proteolytic stability, refolding yields, solubility and taste masking.

Cyclodextrins are cyclic oligosaccharides containing six (α-CD), seven (β-CD) and eight (γ-CD) glucopyranose units, which are bound by α-(1–4) linkages forming a truncated conical structure, which have a hydrophobic interior and hydrophilic rims having primary and secondary *–OH* groups.There has been an increasing interest in the use of cyclodextrins as a tool for controlled release of active compounds due to their outstanding ability to form molecular inclusion complexes with hydrophobic guest molecules. Due to their unique property that is polar hydrophilic outer shell and relatively hydrophobic/apolar inner cavity (Scheme VIII.1), they can build up host–guest complexes by inclusion[VIII.4] of suitable hydrophobic moiety of guest molecule (e.g. IL). This explains current interest for cyclodextrins having versatile applications in pharmaceuticals, pesticides, foodstuffs, toilet articles, textile processing and other industry, supramolecular and host-guest chemistry, models for studying enzyme activity, molecular recognition and molecular encapsulation, studying intermolecular interactions and chemical stabilization.[VIII.5-VIII.7] β-cyclodextrins (β-CD), because of their cavity size are a perfectly suited complexing agent for many common guest moieties.

In continuation of our earlier investigation,[VIII.8-VIII.11] here we have tried to explore the nature of the formation of inclusion complexes of IL, 1-methyl-3-octylimidazolium chloride

([mocimm]Cl) insight into the β-cyclodextrin in w_1=0.001, 0.003, 0.005 mass fraction of aq. β-cyclodextrin media by conductance, surface tension and UV-VIS spectroscopic study.

VIII.2 EXPERIMENTAL

VIII.2.1 Source and purity of samples

The studied compounds e.g., IL and β-cyclodextrin of puriss grade ware procured from Sigma-Aldrich, Germany and used as purchased. The mass fraction purity of IL and β-cyclodextrin were ≥ 0.99 and 0.98 respectively.

VIII.2.2 Apparatus and procedure

Prior to the start of the experimental work solubility of the chosen cyclodextrin in triply distilled and degassed water (with a specific conductance of 1×10^{-6}S·cm^{-1}) and title compound *viz.*, ionic liquid in aqueous cyclodextrin has been precisely checked and observed that the selected ionic liquid freely soluble in all proportion of aq. cyclodextrin. Aqueous binary solution of IL was prepared by mass (Mettler Toledo AG-285 with uncertainty ±0.0003g), and then the working solutions were obtained by mass dilution at 298.15 K. The conversion of molarity into molality was accomplished using experimental density values. All solutions were prepared afresh before use. The uncertainty in molality of the solutions is evaluated to ±0.0001 mol kg^{-3}.

The surface tension experiments were done by platinum ring detachment method using a Tensiometer (K9, KRŰSS; Germany) at the experimental temperature. The accuracy of the measurement was within ±0.1 $mN{\cdot}m^{-1}$.

The conductance measurements were carried out in a Systronics-308 conductivity bridge of accuracy ±0.01%, using a dip-type immersion conductivity cell, CD-10 having a cell constant of approximately (0.1±0.001) cm^{-1}.[VIII.12]

UV-visible spectra were recorded by JASCO V-530 UV/VIS Spectrophotometer, with an uncertainty of wavelength resolution of 2 nm. The measuring temperature was held constant by thermostat.

NMR spectra were recorded in D_2O unless otherwise stated. ^1H NMR spectra were recorded at 400 MHz and 500 MHz using Bruker ADVANCE 500 MHz and Bruker ADVANCE 400 MHz instruments respectively at 298.15K. Signals are quoted as δ values in ppm using residual protonated solvent signals as internal standard (D2O : δ 4.79 ppm). Data are reported as chemical shift.

VIII.3 RESULTS AND DISCUSSION

VIII.3.1 Surface tension:

Surface tension (γ) is an significant tool, give a valuable clue about the formation of inclusion complex in cyclodextrin.[VIII.13-VIII.14]It is observed that γ for aqueous solution of IL show remarkable change with increasing concentration of β-CD (Table VIII.1 & Fig. VIII.1). Due to the favorable structure γ value increases with increasing concentration. The fact is due to the presence of side chain hydrophobic group with the cyclodextrin. The surface tensions (γ) with corresponding concentration of IL in different mass fraction of aq. β-CD have been reported for the studied IL (Fig. VIIII.1). In each case, the trends of the curves in surface tensions (γ) against concentration (molality) are similar to that of aq. IL, but each curve clearly shows a break point in surface tension at a certain concentration, that is, the γ

values increases or decreases with corresponding concentration, reach a certain point (break point), and then become approximately steady, which obviously indicates the formation of inclusion complex. The formation of inclusion complexes is responsible for insertion of the hydrophobic (aliphatic or aromatic) group of chosen IL insight into the cavity of β-CD. The molecular structure of the studied ionic liquid is represented in Scheme VIII.2. The plausibility of the inclusion complex may have in different stoichiometries, like 1:1, 1:2, 2:1, 2:2 (Scheme VIII.3) ratios of CD and IL respectively. Since we noted that single break, double break, and so on in the curve of surface tension are indication of the 1:1, 1:2, and so on inclusion complex by cyclodextrin. In Figure VIII.1, each curve shows single break point, which further suggests that 1:1 inclusion complexe are formed. From the values of surface tension it is found that inclusion becomes feasible with increasing amount of CD in solution. This is obviously due to the fact that β-CD provides more possible feature (either size or cavity diameter and volume) for formation of feasible inclusion complex than others. The studied IL, thus, form soluble 1:1 complexes with the cyclodextrin in which we visualize the nonpolar tail group of the IL to be inserted via the wider rim, so as to make maximum contact with the cyclodextrin cavity (Scheme VIII.4), while the charged polar head residue remains in the wider rim of cyclodextrin or in bulk solution.

The binding of IL molecule within the host cyclodextrin is not fixed or permanent but rather is a dynamic equilibrium and the binding strength compatible as well the stable 'host–guest' complex fits together, on specific local interactions between surface atoms.

The stability of the formation of inclusion complexes can be described by the key factors. That is steric and depends on the relative size of the cyclodextrin to the size of the guest

molecule or certain key functional groups within the guest. Since, the IL molecule is the spot on size; it has fit properly into the cyclodextrin cavity and form stable complex.

In general, therefore, there are four energetically favourable interactions that help shift the equilibrium towards the forward (Scheme VIII.6) to form the inclusion complex:

- The release of enthalpy rich water molecules from the apolar β-cyclodextrin cavity.
- Electrostatic interaction, Vander Waals interactions, hydrophobic interaction and the hydrogen bonds formation by the primary and secondary hydroxyl (-OH) groups and rest water molecules.
- Release of the conformational strain.

VIII.3.2 Conductivity study:

Measurement of the conductivity[VIII.15] is one of the commonly used methods for studying the inclusion phenomenon, and it can be used to elucidate not only whether inclusion can occur but also the stoichiometry of the inclusion complexes (ICs) formed.[VIII.16]As discussed above, the IL is partially soluble in water. If it forms an inclusion complex with β-CD, the solution conductivity will be distinctly affected by the addition of β-CD. The conductivity of various β -CD concentrations in aqueous IL were measured at 25^0C, and the dependence of the conductivity on β-CD concentration is shown in Table VIII.2 & Figure VIII.2. The conductivity decreased remarkably with increasing β-CD concentration, indicating the inclusion-complex formation between β-CD and the hydrophobic IL. At a certain concentration in β-CD, this linear decrease of specific conductance with ionic liquid concentration halted rather abruptly to show no or little further decrease with further β-CD additions. A discernible break in the conductivity curve occurred at a concentration of

about 3.0 mmolL_1 β-CD, suggesting that the stoichiometry of the β-CD–IL ionic compound is equimolar. [VIII.17] This indicates that the chief inclusion complex of β-CD with IL in this range is 1:1 which indicates that the IL has been almost totally complex. This conclusion is the same as that deduced from the surface tension curves above.

VIII.3.3 UV-Visible Spectroscopy:

UV-Vis spectroscopy detects the complexation by a change in the absorption spectrum of the guest molecule. The modification in peak intensity are assumed to result from changes in the solvent microenvironment upon inclusion of the guest [VIII.18]. The 1:1 stoichiometry of the complex is confirmed by the continuous variation method [VIII.19]. Figure VIII.3 presents the Job plot for the complex formed between IL and β-CD. In this curve, the position of the maximum is at R = [β-CD]/[IL] + [β-CD]) = 0.5, corresponding to a complex with 1:1 stoichiometry.

The evaluation of stability constants by direct spectroscopic methods relies on analytical differences between the free and complexed guest [VIII.20]. Changes in the absorption intensity of IL at 212 nm were monitored as a function of β-CD concentration to measure the binding constant. To conveniently calculate the stability constant (K_b) we needed to rearrange the Benesi-Hildebrand equation [VIII.21] into a straight line form:

$$1/\Delta A = 1/K_b \,.\, 1/[\beta\text{-CD}] + \Delta\varepsilon[G] \qquad (1)$$

where ΔA is the difference in absorbance of IL in the presence and absence of β-CD, K_b is the stability constant, [β-CD] and [G] are the concentrations of β-CD and IL, respectively and Δε is the difference in the molar absorptivities between free and complexed IL.

Therefore, a plot of 1/A *versus* 1/[β-CD] (Figure VIII.4), gives a straight line with slope $1/K_b$. The K_b calculated value is 2914.9 M−1.

VIII.3.4 ^{1}H NMR Study

Insertion of a guest molecule into the hydrophobic cavity of α and β-CD results in the chemical shift of the protons of the cyclodextrin molecule in the ^{1}H NMR spectra, which is due to the interaction of the host cyclodextrin with the guest molecule.[VIII.22] In the structure of cyclodextrin the H3 and H5 hydrogens are located inside the conical cavity, particularly, the H3 are placed near the wider rim while H5 are placed near the narrower rim of cyclodextrin molecule. The other H1, H2 and H4 hydrogens are situated at the exterior of the cyclodextrin molecule (Scheme VIII.5).[VIII.23] Thus when a guest molecule enters into the cavity of cyclodextrin it interacts with the H3 and H5 protons, resulting in the upfield chemical shift of these protons. As the H3 is located near the wider rim of cyclodextrin, through which usually the guest enters, the shift is higher for it than that for the H5 proton which is situated near the narrower rim at the interior of cyclodextrin. The other H1, H2 and H4 hydrogens also show upfield chemical shift, but it is less compared to that of the interior protons.[VIII.24]

In this work the molecular interactions of studied IL with β-cyclodextrin has been studied by ^{1}H NMR spectra by taking 1:1 molar ratio of the IL and β- cyclodextrin in D_2O at 298.15K. It has been found that there are considerable upfield shifts ($\Delta\delta$) of interior H3 and H5 protons, little shifts of exterior H1, H2 and H4 protons of cyclodextrin, as well as that of the interacting protons of the IL (Figure VIII.5). This establishes that inclusion phenomenon has occurred between the chosen host and guest molecules. Upon inclusion the upfield chemical shift values ($\Delta\delta$) of the H3 and H5 protons of α and β-cyclodextrin

have been listed in Table VIII.3, which show that the interaction of the guest amino acids with H3 is more than that with H5, suggesting the inclusion has taken place through the wider rim of *β*-cyclodextrin.

3. 5 ^{1}H NMR data

***β*-CD:** ^{1}H NMR (400 MHz, D_2O): δ = 3.49-3.54 (6H, t, J = 9.2 Hz), 3.57-3.60 (6H, dd, J = 9.6, 3.2 Hz), 3.79-3.84 (18H, m), 3.87-3.92 (6H, t, J = 9.2 Hz), 5.00-5.01 (6H, d, J = 3.6 Hz).

***β*-CD+IL:** ^{1}H NMR (400 MHz, D_2O): δ = 0.95-0.98 (3H, t, J = 6.0 Hz), 1.23-1.26 (12H, m), 1.71-1.73 (2H, m), 3.21 (3H, s), 3.44-3.49 (6H, t, J = 9.2 Hz), 3.53-3.56 (6H, dd, J = 9.6, 3.2 Hz), 3.69-3.74 (6H, t, J = 9.2 Hz), 3.75-3.80 (18H, m), 5.00-5.01 (6H, d, J = 3.6 Hz), 7.42-7.49 (2H, m), 8.63 (1H, s).

VIII.3.6 Structural effect of the β-CD:

The structure is a novel packing of β -CD monomers that is less compact (2300 Å^3 per β-CD) than known monomeric (≈1500-1750 Å^3) or dimeric (≈1800 Å^3) structures.

In the first X-ray crystal structure, which was determined on a crystal in contact with mother liquor, about seven disordered water molecules may be located in each β-CD cavity, and five more water molecules in interstitial sites between the β-CD macrocycles resulting in an overall composition β-CD (12 of 0.5)H_2O^6 (16 wt % H_2O). In the neutron diffraction study [VIII.25](in which not all of the weakly populated water sites were located), at room temperature, most water molecules and hydroxyl groups of β-CD are orientationally disordered and alternately form hydrogen bonds with different neighbors. This disorder is highly dynamic, i.e. associated with rapid flips of O-H groups between discrete alternative orientations (“flip-flop” bonds).

Inclusion complexes are in fact energy favourable, since water molecules from the cavity are displaced by hydrophobic long chain guest molecules to obtain an apolar-apolar interaction and decrease the cyclodextrin ring strain, thereby leading to a more stable lower energy state. The complexation strength depends on the factors such as the size of the guest molecule, the van der Waals interactions, the release of water molecules, hydrogen bonding, charge transfer interactions, hydrophobic interactions, and the release of conformational strain, etc. [VIII.26] With considering the above factors, β-CD are proposed in such a way that the inclusion is favorable with the studied ionic liquid.

The insertion of the guest IL molecule is expected from the wider rim of the cyclodextrin molecule, so as to make maximum contact of the alkyl groups with the cyclodextrin cavity (Scheme 4), which is also supported by NMR data.

VIII.4 CONCLUSION

The exceptional inclusion behaviour of β-CD and considered IL in aqueous solution has been explored by surface tension, conductance and spectroscopic measurements. The results point out that β-CD and IL finally form stable inclusion complexes (ICs) with a 1:1 stoichiometry. They both are promoting to each other due to hydrophilic and hydrophobic interactions among them. NMR study confirms the Inclusion Phenomenon through the wider of the β-CD.

Tables:

Table VIII.1. Values of surface tension at the break point (γ) with corresponding concentration of IL in different mass fraction of aqueous β-cyclodextrin at 298.15K[a]

mass fraction (*w*)	conc (*m*).10^4	γ /mNm^{-1}
	IL	
w_1=0.001	5.473	64.60
w_1=0.003	5.105	66.61
w_1=0.005	4.227	67.89

[a]Standard uncertainties *u* are: *u*(*T*) =0.01K

Table VIII.2. Values of Specific conductance at the break point (κ) with corresponding concentration of ILin different mass fraction of aqueous β-cyclodextrin at 298.15K[a]

mass fraction (*w*)	conc (*m*).10^4	κ /$S.m^{-1}$
	IL	
w_1=0.001	5.706	2.17
w_1=0.003	5.342	1.89
w_1=0.005	5.099	1.70

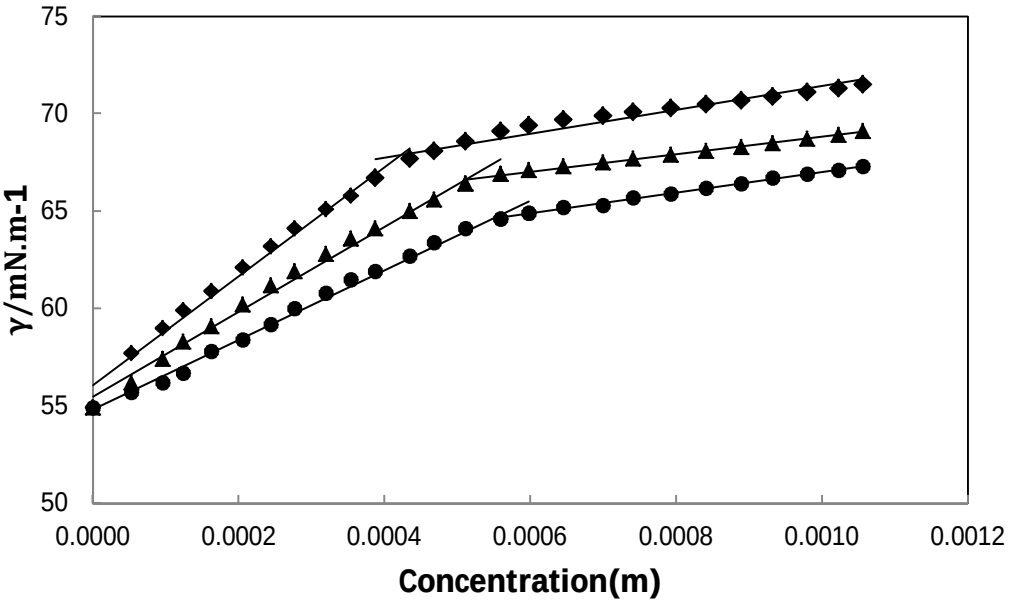
[a]Standard uncertainties *u* are: *u*(*T*) =0.01K

Table VIII.3. Change in chemical shifts (ppm) of the H3 and H5 protons of cyclodextrin host molecules when complexed with amino acid guest molecules in D_2O at 298.15K*a*

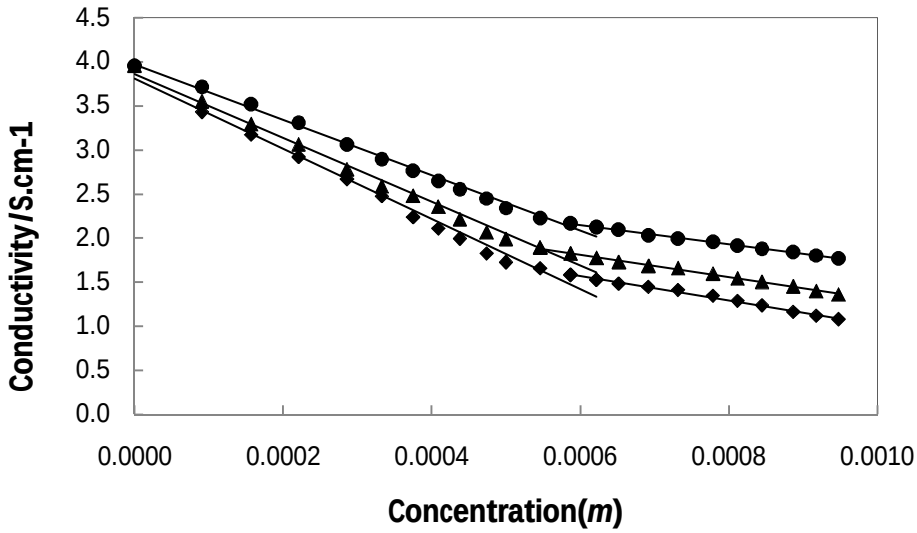
	Δδ	
Protons	H3	H5
β-cyclodextrin	0.181	0.095

a Standard uncertainties in temperature *u* are: *u*(T) = 0.01 K.

Figures:



FigureVIII.1. Plot of surface tension of ionic liquid corresponding to the added conc of aq. β-cyclodextrin



FigureVIII.2. **Plot of conductance of ionic liquid corresponding to the added conc of aq. β-cyclodextrin**

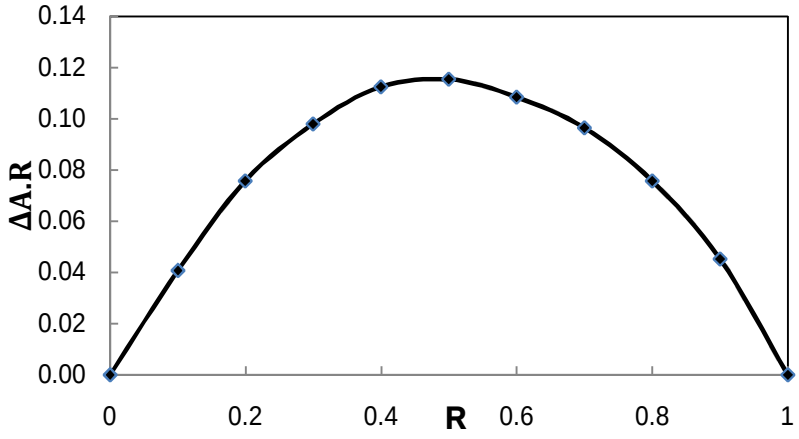


Figure VIII.3: Job plot for the complex IL:β-CD (λ = 212 nm).

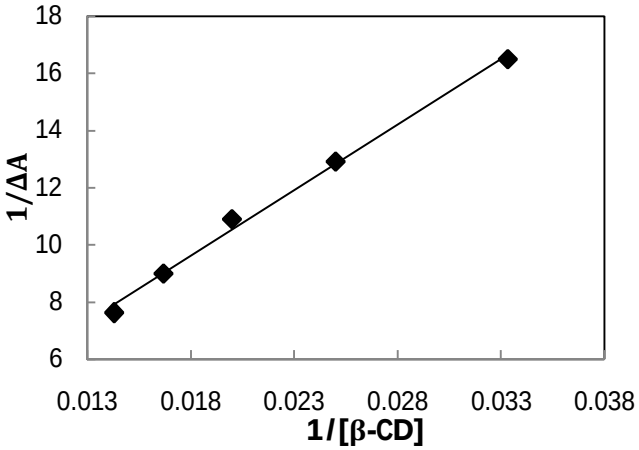


Figure VIII.4. Dependence of IL absorbance from β-CD concentration (λ = 212 nm).

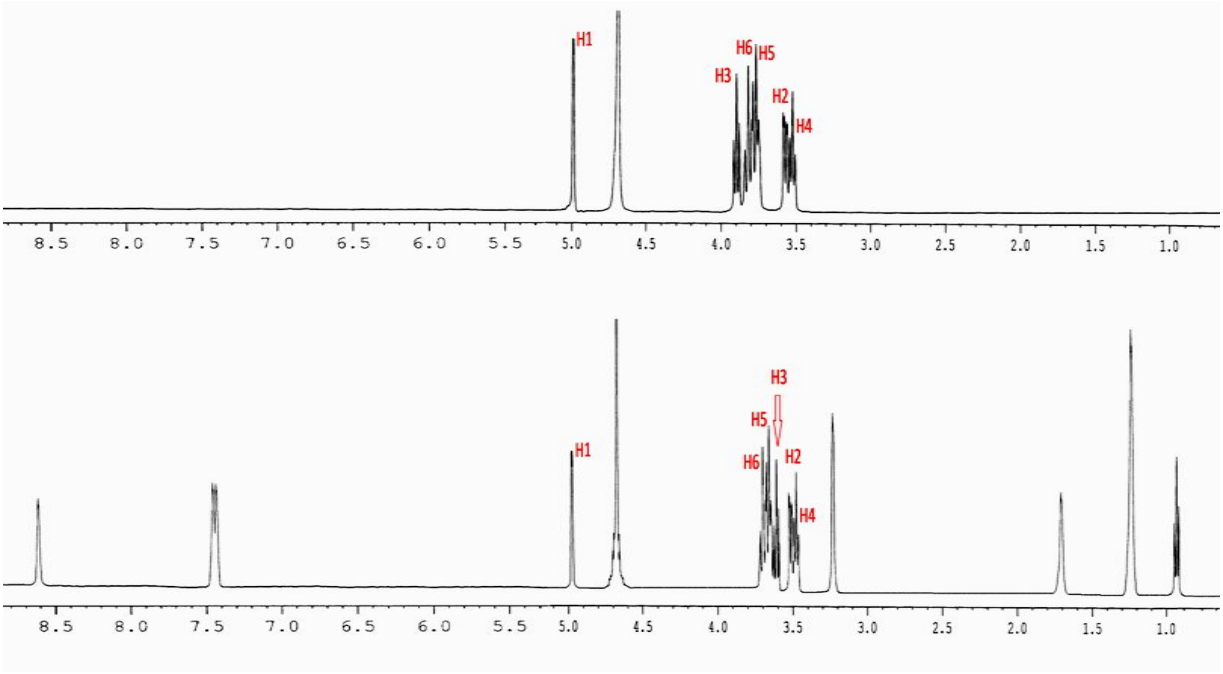
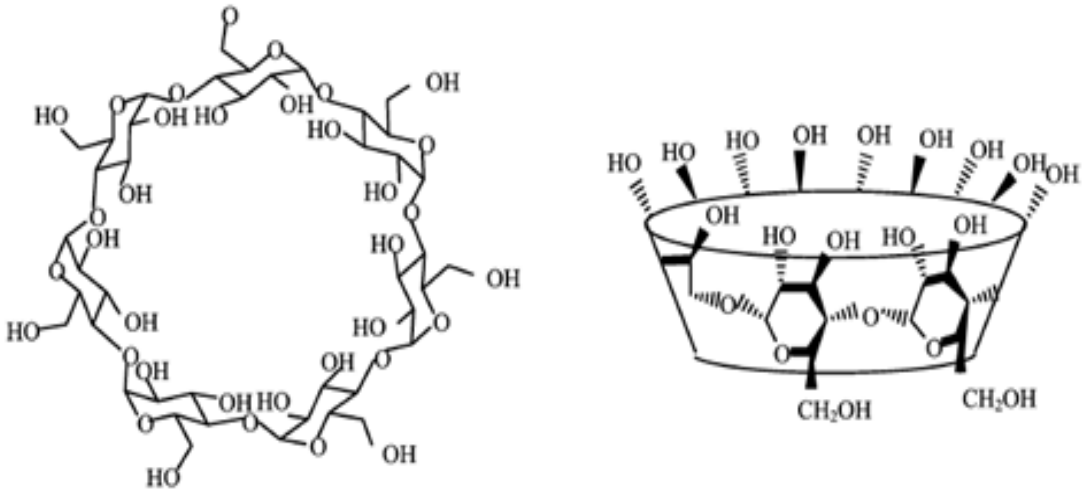


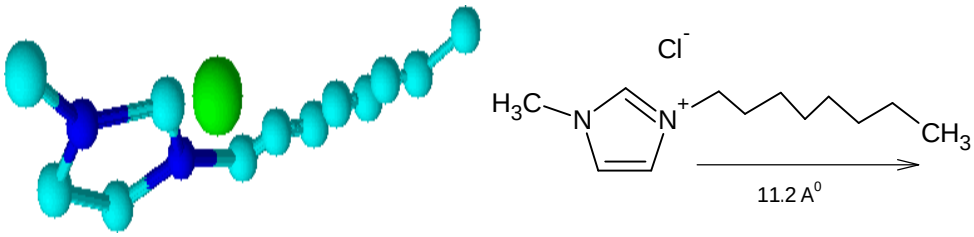
Figure VIII.5. The ^{1}H NMR spectra of β-CD and β-CD+IL mixture in 1:1 molar ratio.

Schemes:

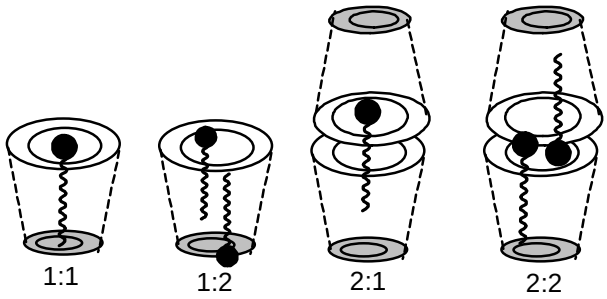


Top view **Side view**

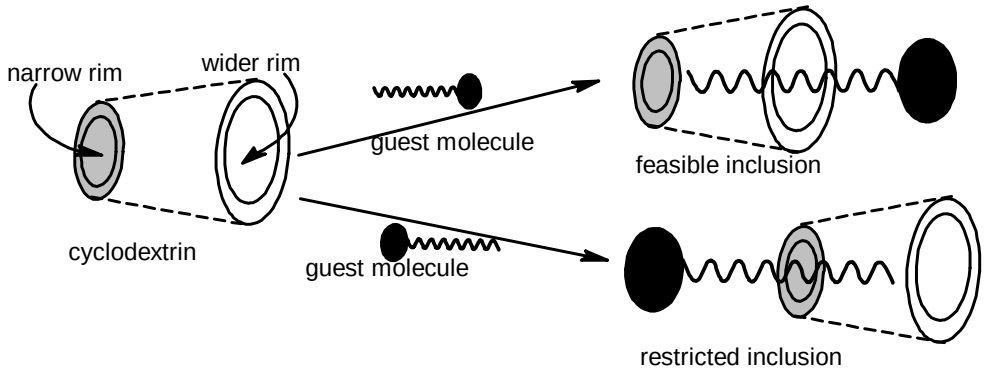
Scheme 1: The molecular structure of β-CD.



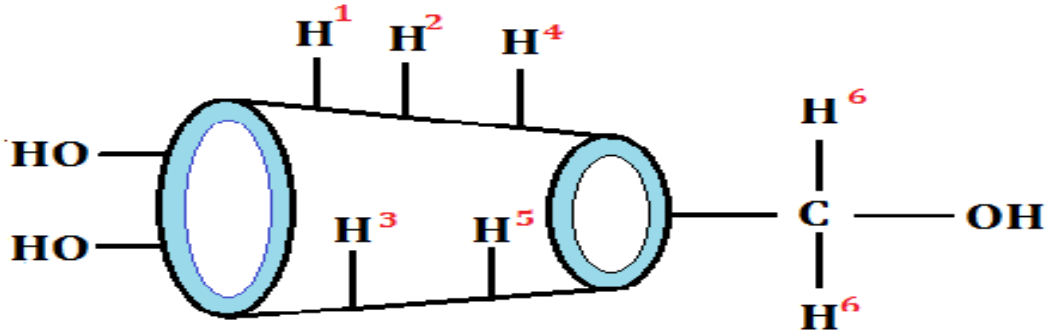
Scheme 2: The molecular structure of 1-methyl-3-octylimidazolium chloride



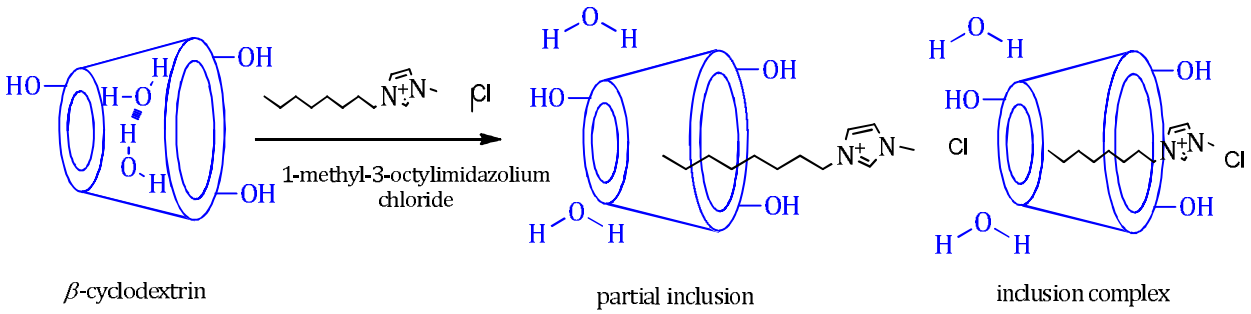
Scheme 3:The plausible stoichiometries inclusion ratio of host:guest molecule



Scheme VIII.4: The feasible and restricted inclusion of host:guest molecule



Scheme VIII.5: Truncated conical structure of β-Cyclodextrin.



Scheme VIII.6: Schematic representation of convincing mechanism of 1 : 1 inclusion complexes' insight into *β*-cyclodextrin with the titled ionic liquid.