

CHAPTER IX

INVESTIGATION OF INCLUSION COMPLEX FORMED BY IONIC LIQUID AND β -CYCLODEXTRIN THROUGH HYDROPHILIC AND HYDROPHOBIC INTERACTIONS

9.1. INTRODUCTION

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 1), they can build up host–guest complexes by inclusion¹ 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.²⁻⁴

Ionic liquids (ILs) are very attractive because of their unique properties, such as large liquid range, high thermal stability, negligible vapor pressure, ability of dissolving a variety of chemicals, miscibility with common molecular liquids, large electrochemical window and their potential as “designer solvents” and “green” replacements, i.e., alternative solvents to volatile organic solvents⁵⁻⁷ used in reactions involving inorganic compounds as well as bio-catalysts. They are also used as heat transfer fluids for processing biomass and as electrically conductive liquids in electrochemistry (batteries and solar cells).⁸⁻¹⁰

In view of the above and in continuation of our study,¹¹⁻¹⁴ we have attempt to ascertain the nature of formation of inclusion complexes of IL insight into the β -cyclodextrin in

$w_1=0.001, 0.003, 0.005$ mass fraction of aq. β -cyclodextrin media as a literature survey reveals that no work has been carried out in the present ternary systems.

9.2. Experimental Section:

9.2.1. Materials

The studied compounds e.g., IL and β -cyclodextrin of puriss grade were 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.

9.2.2 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 $1 \times 10^{-6} \text{ S} \cdot \text{cm}^{-1}$) 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 $\pm 0.0003\text{g}$), 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 $\pm 0.0001 \text{ mol kg}^{-3}$.

The surface tension experiments were completed by platinum ring detachment method using a Tensiometer (K9, KRÜSS; Germany) at the experimental temperature. The precision of the measurement was within $\pm 0.1 \text{ mN} \cdot \text{m}^{-1}$. Temperature of the system has been preserved by circulating auto-thermostated water (within $\pm 0.01\text{K}$) through a double-wall glass vessel holding the solution.

The densities (ρ) of the solvents were measured by means of vibrating u-tube Anton Paar digital density meter (DMA 4500M) with a accuracy of $\pm 0.00005\text{g cm}^{-3}$ maintained at $\pm 0.01\text{K}$ of the desired temperature. It was calibrated by passing deionized, doubly distilled, degassed water and dry air.

The viscosities (η) were measured using a Brookfield DV-III Ultra Programmable Rheometer with fitted spindle size-42. The detail explanation has already been described earlier.¹⁵ The temperature was maintained to within ± 0.01 K. The viscosities were measured with an accuracy of ± 1 %. Each measurement reported herein is an average of triplicate reading with a precision of 0.3 %.

Refractive index was measured with the help of a Digital Refractometer Mettler Toledo at 298.15 K and the temperature has been controlled by Digital Temperature Controller (± 0.01 K). The light source was LED, $\lambda=589.3$ nm. The refractometer was calibrated twice using distilled water and calibration was checked after every few measurements. The uncertainty of refractive index measurement was ± 0.0002 unit.

9.3. Results and Discussions

9.3.1. Surface tension:

Surface tension (γ) is an important tool, provided a valuable clue about the formation of inclusion complex in cyclodextrin.¹⁶⁻¹⁷ It is observed that γ for aqueous solution of IL show remarkable change with increasing concentration of β -CD (Fig. 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 titled IL (Fig. 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 2. The plausibility of the inclusion complex may have in different stoichiometries, like 1:1, 1:2, 2:1, 2:2 (Scheme 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 Fig. 1, each curve shows single break point, which further suggests that 1:1 inclusion complexes are formed. From the values of surface tension it is found that inclusion becomes feasible with increasing amount of CD in solution. 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, make more contact with the cyclodextrin cavity (Scheme 4). The hydrophobic cavity of β -CD from the wider rim which is geometrically allowed can easily encounter suitable guest molecule. The hydrophilic part of the IL remains outside and can make H-bonds with the hydrophilic rim of cyclodextrin and also surrounded by water molecules. This is also in correlation with the data from density and viscosity measurements, discussing underway, undoubtedly establish that β -CD has the favourable structure for the formation of inclusion complexes with the above selected IL.

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 5) to form the inclusion complex:

- The displacement of exits polar water molecules from the apolar cavity of β -cyclodextrin.
- The formation of extended hydrogen bonds by the primary and secondary hydroxyl (-OH) groups and rest water molecules that open a face for entering the guest molecule.

- A reduction of the repulsive interactions between the hydrophobic guest and the aqueous environment.
- An increase in the hydrophobic interactions as the guest inserts itself into the apolar cyclodextrin cavity.

9.3.2 Conductivity study:

Measurement of the conductivity¹⁸ 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.¹⁹As discussed above, the IL is freely 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°C, and the dependence of the conductivity on β -CD concentration is shown in Figure 2. When the hydrophobic part of the IL enters into the hydrophobic inner cavity of β CD then the movement of the free ions gets arrested by the β -CD and the free ions per unit volume gets decreased, as a result the conductivity decreases. 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–moimBF₄ ionic compound is equimolar.²⁰This 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.

9.3.3 Apparent molar volume and viscosity *B*-coefficient

The remarkable behavior of interaction or inclusion of chosen ionic liquid into β -CD has also been obtained from apparent molar volume and viscosity *B*-coefficient. Both the

valuable parameter signifies the solute-solvent interactions in the IL+aq. β -CD ternary solution systems. The limiting molar volume (ϕ_{v^0}) and viscosity B -coefficient have been obtained from appropriate equation¹⁴ using the experimental values of density (ρ) and viscosity (η) respectively and are presented in Table S2-S3 (supporting information) and Fig 3 and 4. The scrutiny of Fig 3, 4 shows that the limiting molar volume (ϕ_{v^0}) and viscosity B -coefficient both raise regularly with increasing temperature, and these values are higher in $w=0.003$ than 0.001, which in turn higher in 0.005 mass fraction of aq. β -CD.

The trend shrugs the interactions between the ionic liquid and β -CD molecules are enhanced with increasing temperature and also with mass fraction of aq. β -CD. This is due to the fact that β -CD shows favorable interaction with IL. The facts support the data and results observed from surface tension and conductance that have been discussed earlier.

9.3.4 Limiting Molar Refraction:

The remarkable behavior of interaction or inclusion of chosen ionic liquid into β -CD has also been obtained from limiting molar refraction values. This valuable parameter also signifies the solute-solvent interactions in the IL +aq. β -CD ternary solution systems. The limiting molar refraction (R_M^0) has been obtained from appropriate equation²¹ using the experimental values of refractive index (n_D) and are presented in Table S4 (supporting information) and Fig 5.

The trend indicates the interfaces between the ionic liquid and β -CD molecules are enhanced with mass fraction of aq. β -CD. This is due to the circumstance that β -CD shows satisfactory interface with selected IL. This is also in good agreement with the results obtained from surface tension and conductance that have been discussed earlier.

9.3.5. Structural effect of the β -CD:

The structure is a novel packing of β -CD monomers that is less compact (2300 \AA^3 per β -CD) than known monomeric ($\approx 1500\text{-}1750 \text{ \AA}^3$) or dimeric ($\approx 1800 \text{ \AA}^3$) 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)H₂O (16 wt % H₂O). In the neutron diffraction study²²(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). Very similar disorders of solvent molecules and hydroxyl groups were described for the complex β -CD-ethanol octahydrate.

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.²³ With considering the above factors, β -CD are proposed in such a way that the inclusion is favorable with the studied ionic liquid.

9.3.6. Other Thermodynamic Properties

According to Eyring and co-workers²⁴ the free energy of activation of viscous flow per mole of solvent, $\Delta\mu_1^{0\#}$, can be calculated using the equation:

$$\eta_0 = (hN_A / \bar{V}_1^0) \exp(\Delta\mu_1^{0\#} / RT) \quad (25)$$

where h , N_A , and $\bar{V}_1^0 (= \phi_1^0)$ are the Planck constant, Avogadro number and partial molar volumes of the solvent, respectively. Feakins and co-workers²⁵ applied the transition state treatment of relative viscosity to solutions and exhibited that the B-coefficient is given as:

$$B = (\bar{V}_1^0 - \bar{V}_2^0) / 1000 + \bar{V}_2^0 [(\Delta\mu_2^{0\#} - \Delta\mu_1^{0\#}) / RT] / 1000 \quad (26)$$

where $\bar{V}_2^0 (= \phi_V^0)$ is the partial molar volume of the solute (IL) and $\Delta\mu_2^{0\#}$ is the contribution per mole of the solute to the free energy of activation of viscous flow of the solution. On rearranging eqs. (25) and (26), the values of $\Delta\mu_2^{0\#}$ and $\Delta\mu_1^{0\#}$ are obtained as:

$$\Delta\mu_1^{0\#} = RT \ln(\eta_0 \bar{V}_1^0 / hN_A) \quad (27)$$

$$\Delta\mu_2^{0\#} = \Delta\mu_1^{0\#} + (RT / \bar{V}_1^0)[1000B - (\bar{V}_1^0 - \bar{V}_2^0)] \quad (28)$$

The values $\Delta\mu_2^{0\#}$ and $\Delta\mu_1^{0\#}$ for the IL in aqueous β -CD at 298.15, 303.15 and 308.15K are listed in Table 3. The total free energy of activation of viscous flow of the solution, $\Delta\mu^{0\#}$, was calculated from the relation:

$$\Delta\mu^{0\#} = n_1 \Delta\mu_1^{0\#} + n_2 \Delta\mu_2^{0\#} \quad (29)$$

where n_1 and n_2 are the number of moles of mixed solvent and solute, respectively. The values of $\Delta\mu^{0\#}$, are also presented in Table 3. The thermodynamic data, ΔH^* and ΔS^* of the IL in aqueous β -CD were calculated using the following equation and are listed in Table 3:

$$\Delta\mu^{0\#} = \Delta H^* - T\Delta S^* \quad (30)$$

The ΔH^* and ΔS^* values were attained from the intercepts and slopes of the plots of $\Delta\mu^{0\#}$ versus T . ΔH^* and ΔS^* values have proved useful in yielding structural information about solute species and about solute-solvent interactions.

It is evident from the data in Table 3 that $\Delta\mu_1^{0\#}$ and $\Delta\mu_2^{0\#}$ values are positive and almost same, for all the solvent composition. This may be due to the fact that IL-cosolute interactions in the ground state are almost in the transition state. In other words, the solvation of IL in the transition state is also favourable in terms of free energy. As $\Delta\mu_2^{0\#} \cong \Delta\mu_1^{0\#}$ then according to the Feakins model²⁵, the solutes (IL) behave as structure-makers. This again supports the behavior of dB/dT for these solutes in aqueous β -CD. This indicates that the solvation of the IL in the ground state becomes increasingly favorable as the hydrophobicity (number of carbon atoms) of the side chain is very long.

The values of the activation enthalpy, ΔH^* and entropy, ΔS^* , calculated using eq. (30) of the IL + aqueous β -CD mixtures are listed in Table 3. The data reveal that the ΔH^* values of the ternary mixtures are positive, thereby, suggesting that the formation of activated species for viscous flow becomes difficult as the amount of IL in the mixtures increases. The negative values of $T\Delta S^*$, which increase with increasing temperature of the solution, for all the studied mixtures, suggest that the net order of the system decreases as the temperature in the mixture increases. Thus, the behavior of $T\Delta S^*$ supports that of ΔH^* . The ΔH^* and ΔS^* quantities contain contributions from the following processes:

- (i) formation of the solute-cosolute interaction due to non-covalent interactions (H-binding, van der Waals forces, hydrophobic and electrostatic interactions and steric effects)
- (ii) dehydration of the cosolutes during the molecular interactions
- (iii) hydration of the complex and
- (iv) conformation changes

The predominance of items (i) to (iii) during these processes determines the negative values for the entropy of interaction. The contribution from process (iv) can be not considerable because the β -cyclodextrin molecule is not flexible and can't change conformation upon binding with a guest molecule, it itself retain the same conformation before and after the interaction with IL.

9.4. Conclusion

The exceptional inclusion behaviour of β -CD and studied IL in aqueous solution has been studied by surface tension and conductance 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. The experimental values obtained from the volumetric, viscometric and refractometric studies also support the data and results observed from surface tension and conductance measurements.

TABLES:**Table 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)	γ /mNm ⁻¹
IL		
^b $w_1=0.001$	0.0311	56.60
^b $w_1=0.003$	0.0297	57.21
^b $w_1=0.005$	0.0289	58.22

^a Standard uncertainties u are: $u(T) = 0.01\text{K}$ ^b w_1 is the mass fractions of β -cyclodextrin in aqueous mixture.**Table 2. Values of Specific conductance at the break point (κ) with corresponding concentration of IL in different mass fraction of aqueous β -cyclodextrin at 298.15K^a**

mass fraction (w)	conc (m)	κ /S.m ⁻¹
IL		
$w_1=0.001$	0.042	1.21
$w_1=0.003$	0.038	1.15
$w_1=0.005$	0.033	1.10

^a Standard uncertainties u are: $u(T) = 0.01\text{K}$

Table 3. Values of ϕ_1^0 , ϕ_V^0 (aqueous), $\mu^{0\#}$, $T\Delta S^\#$, $\Delta H^\#$, for IL in different mass fraction of aqueous β -CD (w_1) at 298.15 to 308.15K respectively

Parameters	$\phi_1^0 \cdot 10^6 / m$ 3·mol ⁻¹	$\Delta\mu_1^{0\#} /$ kJ·mol ⁻¹	$\Delta\mu_2^{0\#} /$ kJ·mol ⁻¹	$\Delta\mu^{0\#} /$ kJ	$T\Delta S^\# /$ kJ	$\Delta H^\# /$ kJ
$w_1 = 0.001$						
Temp/K						
298.15	18.016	62.97	62.98	62.97	-22.65	
303.15	18.062	62.45	62.45	62.45	-23.03	85.58
308.15	18.084	62.21	62.20	62.21	-23.41	
$w_1 = 0.003$						
Temp/K						
298.15	18.016	62.98	62.98	62.98	-22.65	
303.15	18.062	62.45	62.45	62.45	-23.03	85.58
308.15	18.084	62.22	62.22	62.22	-23.41	
$w_1 = 0.005$						
Temp/K						
298.15	18.016	62.98	62.98	62.98	-22.65	
303.15	18.062	62.46	62.46	62.46	-23.03	85.59
308.15	18.084	62.22	62.22	62.22	-23.41	

FIGURES:

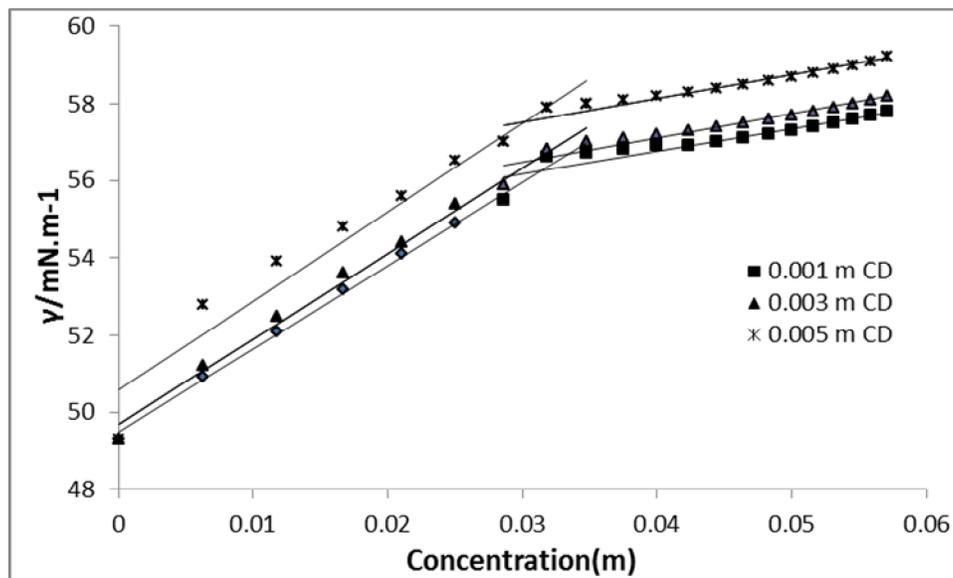


Figure1. Plot of surface tension of ionic liquid corresponding to the added conc. of aq. β -cyclodextrin

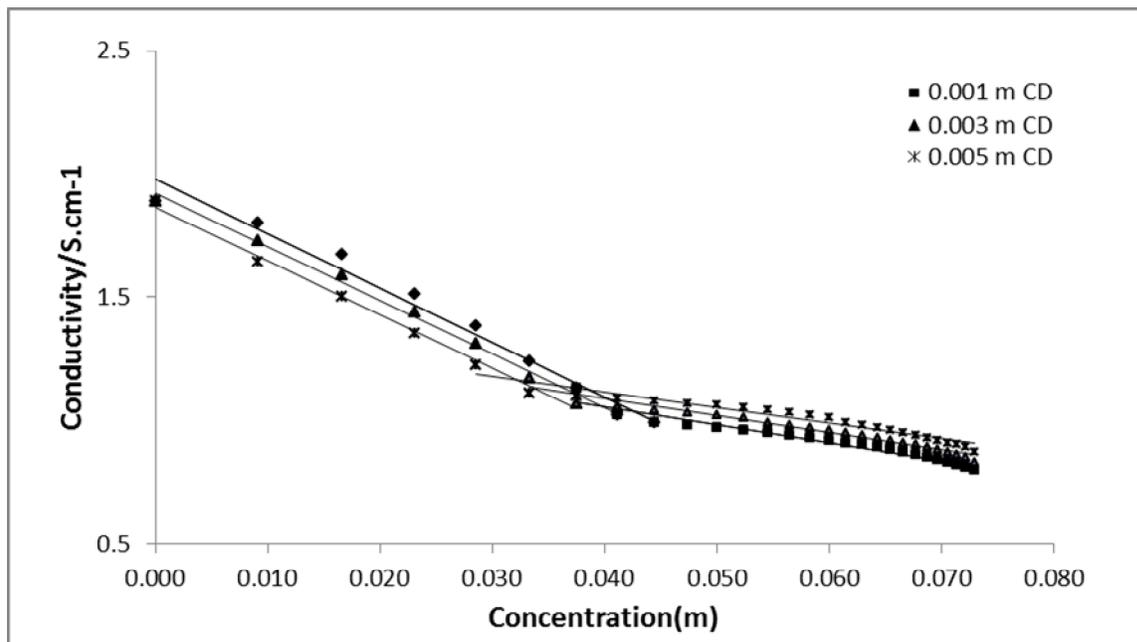
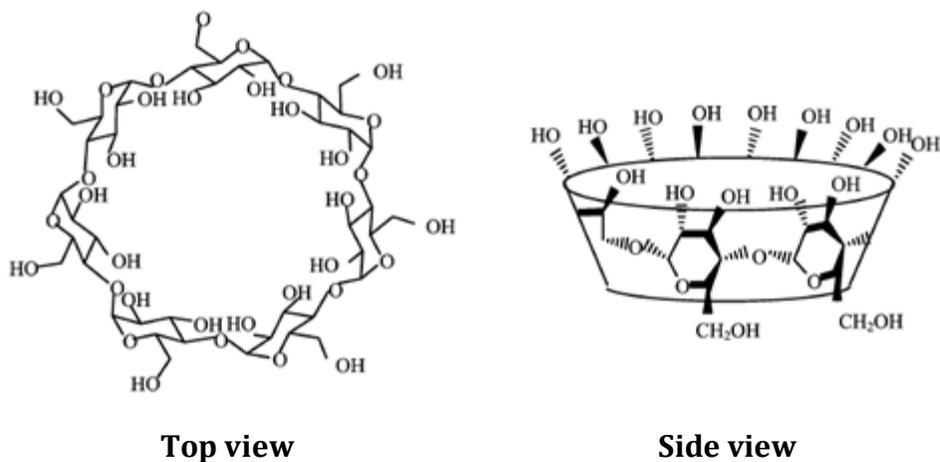
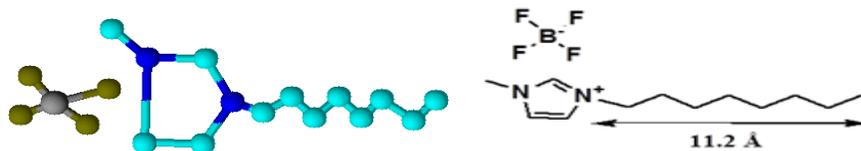
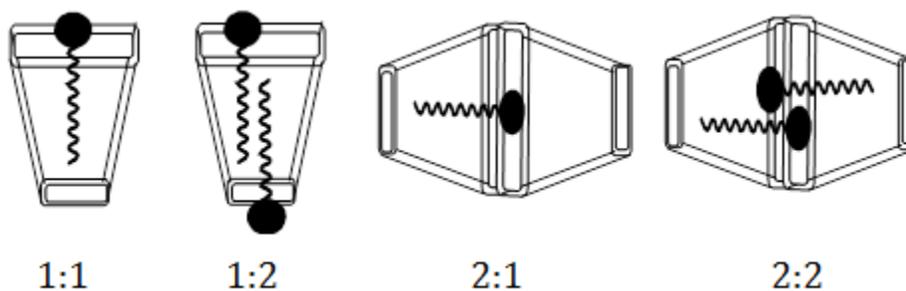
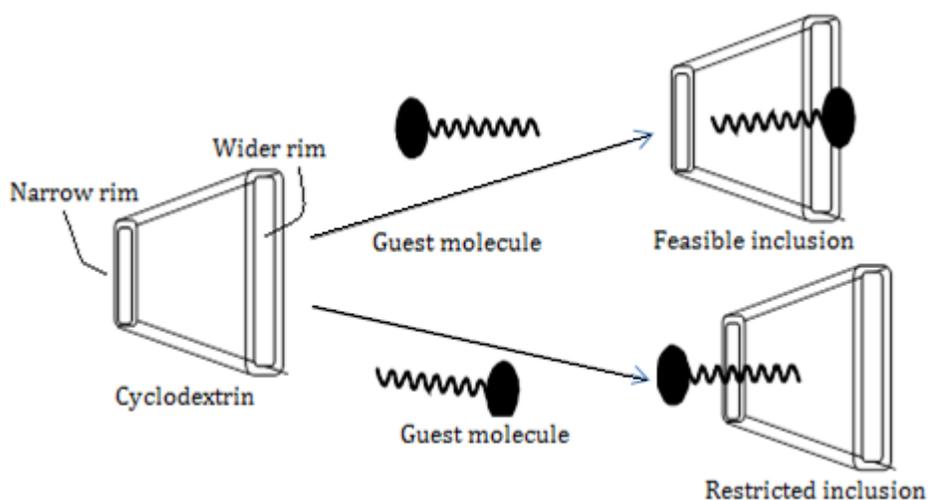
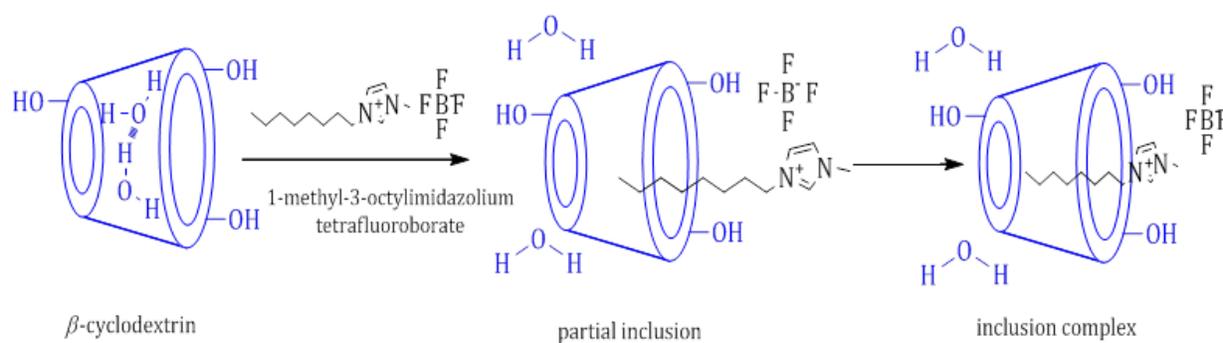


Figure2. Plot of conductance of ionic liquid corresponding to the added conc of aq. β -cyclodextrin

SCHEMES:**Scheme 1: The molecular structure of β -CD.****Scheme 2: The molecular structure of 1-methyl-3-octylimidazolium tetrafluoroborate****Scheme 3: The plausible stoichiometries inclusion ratio of host:guest molecule**



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



Scheme 5: Schematic representation of convincing mechanism of 1:1 inclusion complexes' insight into β -cyclodextrin with the titled ionic liquid.