International Journal of Innovation Engineering and Science Research

Open Access

Subsistence of Host Guest Inclusion Complexes ofBiologically Active Moleculeswith Ionic Liquid Probed by Physicochemical Exploration

KalipadaSarkar[$], Niloy Roy[#],Raja Ghosh[#], MahendraNath Roy*

[$] *Assistant Professor, Department of Chemistry, Islampur College, Islampur, Uttar Dinajpur, India,*
[#]*Department of Chemistry, University of North Bengal, Darjeeling*
* *Professor and Corresponding Author, Department of Chemistry, University of North Bengal, Darjeeling, India*

ABSTRACT

In this present work we studied the supramolecular interaction of 1-hexyl-3-methylimidazolium hexaflurophosphate(HMIm)$PF_6$with α-cyclodextrin (α-CD) and β-cyclodextrin (β-CD) using various physicochemical method and spectroscopic technique. The formation of inclusion complex of any ionic liquid inside the cyclodextrin affects the physicalchemical properties like solubility, conductivity, surface tension, etc. So from the discrepancy of physicochemical andspectral properties we can confirm the formation inclusion complex. The stoichiometry of host - guest of the inclusion complexes was evaluated from conductivity, surface tensionstudy and Job's plot from UV-visible spectroscopy. We also calculated the association/binding constant from conductivity, surface tension measurements and Benesi-Hildebrand equation. The infra-red (IR) and ^{1}H NMR spectroscopy also affirm the formation of inclusion complexes however the plausible mode of inclusion was described from ^{1}H NMR and 2D ROESY NMR spectroscopies.

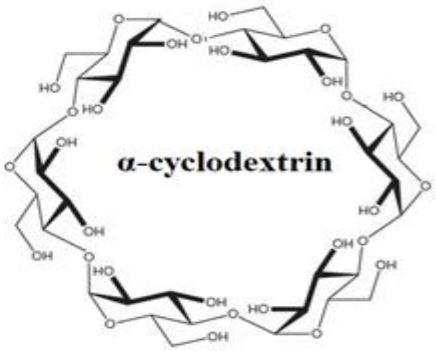
Key words: Inclusion complex, cyclodextrins, Benesi-Hildebrand equation, 1-hexyl-3-methylimidazolium hexaflurophosphate,

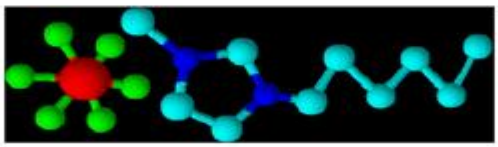
I. Introduction

The cyclodextrins(CDs) are the truncated shaped cyclic oligosaccharides having n glucopyranose units. The three kinds of cyclodextrins namely α -cyclodextrin (α-CD), β -cyclodextrin(-CD) and γ-cyclodextrin(γ-CD) contain 6, 7 and 8 glucopyranose units respectively which are attached together by α-(1–4) linkages [1,2].The structure of cyclodextrins are shown in **Scheme1** and **2**. The inner cavity of cyclodextrin is hydrophobic in nature whereas exterior part is hydrophilic in nature. This kind of unique features make cyclodextrin suitable for complexion with different kind of molecules like vitamins, amino acids, ionic liquids, hormones, polymers,dyes etc. [3-7]. The hydrophobic parts of the ionic liquid become encapsulated inside the hydrophobic cavity of cyclodextrins and thus forming a stable inclusion complex [8].

The formation of inclusion complexes increase the solubility, stability against heat, light, oxidation and bioavailability andreduce volatility of the guest moleculeswithout disturbing the structure of host molecules.

3D View of cyclodextrin

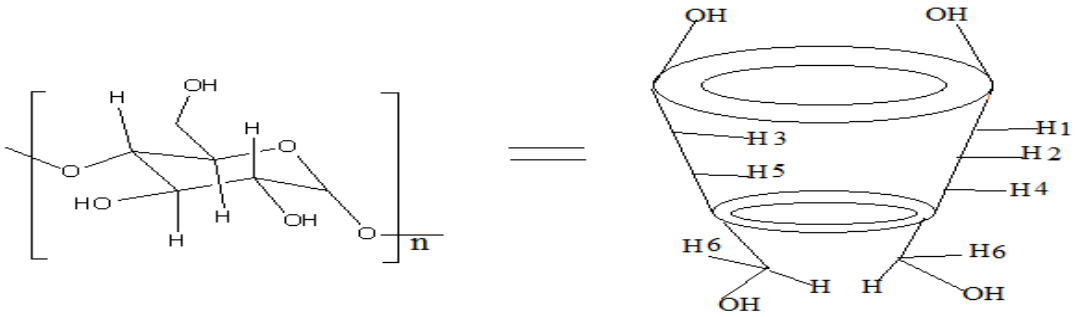




1-hexyl-3-methylimidazolium hexaflurophosphate

Scheme 1: Structure of cyclodextrin and 1-hexyl-3-methylimidazolium hexaflurophosphate

Ionic liquids (ILs) have some special properties such as non-flammability, chemical and thermal stability, high polarity, non-volatility and non-hazardous character [9, 10]. Ionic liquids (ILs) are extensively used in variousarenas of chemistry like electrochemistry, supramolecular chemistry, nuclear chemistry, industrial chemistry etc. [11, 12]. It is also used in processing of cellulose, chemical syntheses, recycling of waste materials, electrophoresis and high-performance liquid chromatography[13, 14]. Due to the non-hazardous feature, ionic liquids are considered as green solvents in various organic and inorganic reactions.



Scheme-2: Structure of cyclodextrin

The studied ionic liquid, 1-hexyl-3-methylimidazolium hexaflurophosphate(HMIm)PF_6acts as a cationic surfactant and forms inclusion complex with cyclodextrins. In this article we studied the formation of self-assembly inclusion complex of this ionic liquid inside the cavity of α- and β- cyclodextrins. Various physicochemical and spectrometric methods were used to examine the inclusion phenomenon. The inclusion complexes so formed may be applied in agriculture textile, detergent, food, the drug or pharmaceutical and cosmetics as antistatic, corrosion inhibitory, antibacterial, emulsifying, dispersants, solubilizing agents etc.

II. Experimental Section

2.1. Materials

The IL, 1-hexyl-3-methylimidazolium hexaflurophosphate(HMIm)PF_6 was procured from TCI Chemicals (Japan) Pvt. Ltd and α -and β- cyclodextrins were procured from Sigma-Aldrich, Germany. All these chemicals were used as purchased as their mass fraction purity were >0.98.

2.2 Apparatus and procedure

Triply distilled water was taken to prepare the solutions. The weight was taken on an electronic balance, Mettler AG-285 accuracy of which was ±0.0003 x 10-3 kg.

The surface tensions (γ) of the solutions of the studied IL with varying concentration of cyclodextrins were measured with tensiometer (K9, KRUSS; Germany). Carefully washed platinum plate was used for measuring the surface tension after calibrating the tensiometerwith Millipore water [15]

The conductances of ionic liquid solutions in presence of varying concentrations of cyclodextrins were taken with Systronic-308 conductivity meter comprised with dip-type conductivity cell. The cell constant was calibrated with aqueous KCl (0.01M and 0.1M) solution [16]. The cell constant is approximately 0.1 ± 0.001 cm^{-1}. The solution of CDs was added with micro-pipette keeping the solution in a thermostat. The conductance was recorded when the solution reached in the equilibrium temperature.

UV-vis absorption spectra of varying concentration of ionic liquid and CDs were taken at 298.15 K by JASCO V-530 UV-VIS Spectrophotometer. Since the studied ionic liquid does not absorb in the UV and VIS range, we used methyl orange (MO) as a probe.

The FT-IR spectra of the solutions were takenfrom Perkin Elmer FT-IR spectrometer after preparing the KBr disk of IL, CDs and inclusion complexes. The KBr disk wasprepared by mixing 100 mg of the KBr and 1 mg of the compound thoroughly.

^{1}H NMR, NMR-ROSEY spectra was taken at 298 K in D_2O by BrukerAvance400 MHz spectrometer.

III. Result and discussion

3.1. Surface tension study

The surface tension study provides an important clue about the formation of inclusion complexes of cyclodextrins with any guest molecule [17, 18]. No any notable variation of surface tension occurs on addition CDs in water which indicates thatα-and β- cyclodextrins are surface inactive compounds [19]. But when we measured the surface tension of ionic liquid solution with successive addition of cyclodextrin solution, wewitnessed that the surface tension values increase with the increasing concentration of the cyclodextrin up to a certain level after which the surface tension values diminish gradually**(Fig.1).**The values of surface tension corresponding to the end-point of different mixtures are reported in **Table.1**. This trend may be regarded as the development of bigger micelle and the process goes on up to a certain concentration of CD which may be described on the basis of the formation of inclusion complexes (**Scheme 3**). The alkyl part of the ionic liquid becomes encapsulated into the cavity of CDs due to the existence of hydrophobic –hydrophobic interaction and the ionic part of the ionic liquid left outside the cavity of CD. It is also observed in the plot of surface tension vs. molarity of CDs that there is asingle break point which specifies that the stoichiometry of inclusion complex is 1:1. More break points will indicate 1:2 or 2:1stoichiometry (**Scheme 4**)

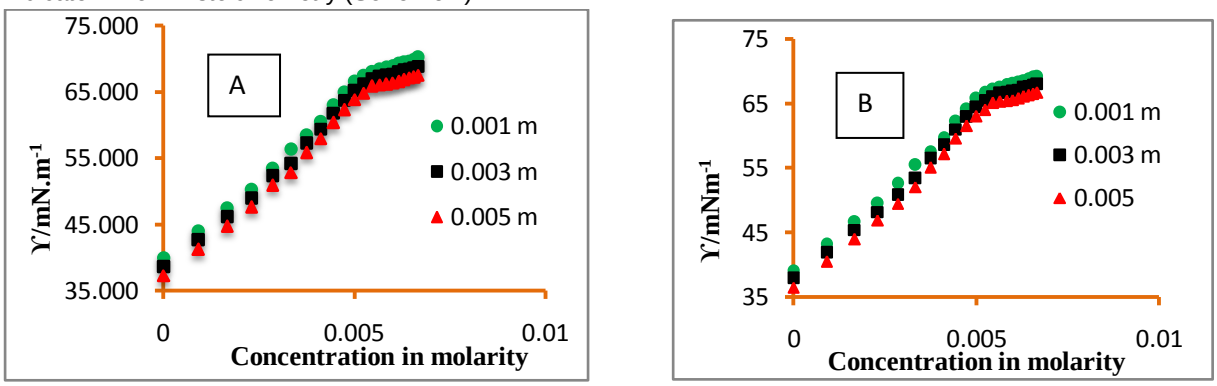


Fig.1. Variation of surface tension of (HMIm)PF_6 with the added conc. of aq
(A) α -cyclodextrin and (B) β-cyclodextrin.

Table 1.

Surface tension valuesat the break point in different mass fractions of aqueous cyclodextrins at 298.15 K

Molarity of IL	Surface tension at break point for β-CD **Ɣ/mN.m^{-1}**	Surface tension at break point for α-CD **Ɣ/mN.m^{-1}**
0.001 m	63.83	63.05
0.003 m	65.25	64.46
0.005 m	66.6	65.85

Association constants of 1:1 inclusion complexes (ICs) may be derived from the surface tension measurements using the following equation.

We can also derive the association constants for 1:1 inclusion complexes from surface tension measurements using the following quantitative relation [20].

CD + S = CDS (1)

$K_a = \frac{[CDS]}{[CD][S]}$ (2)

$CD_0 = [CD] + [CDS]$ (3)

$S_0 = [S] + [CDS]$ (4)

Where K_a = association constant, S = ionic liquid, CDS = inclusion complex, CD_0= total concentration of cyclodextrin and S_0=total concentration of IL.

$K_a = \frac{S_0 - [S]}{(CD_0 - S_0 + [S])[S]}$ (5)

$\frac{1}{K_a} = \frac{(CD_0 - S_0 + [S])[S]}{S_0 - [S]} = \frac{(CD_0 - S_0 + [S])}{\frac{S_0}{[S]} - 1}$ (6)

$S_0 - [S] = -\frac{1}{K_a}\left(\frac{S_0}{[S]} - 1\right) + CD_0$ (7)

The (S_0 – [S]) varies linearly with ($\frac{S_0}{[S]} - 1$). If we draw a plot of (S_0 – [S]) vs. ($\frac{S_0}{[S]} - 1$), we will get a straight line with the slope 1/K_a and intercept CD_0 **(Fig.2**). So association constant of formation of inclusion complexes = 1/slope. The association constants calculated in this method for OMImBr/ α-CD system is 1.23x103M^{-1}and for OMImBr/ β-CD system is1.34x103M^{-1}.

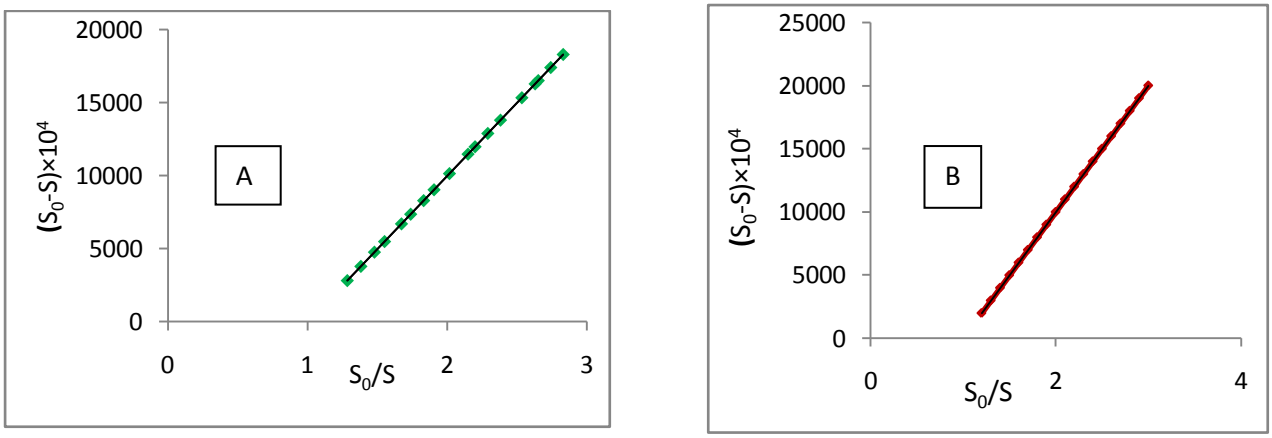


Fig.2. Plot of (S_0– [S]) against (S_0/[S]-1) for (A) $(HMIm)PF_6$ / α-cyclodextrin system (B) $(HMIm)PF_6$ /β-cyclodextrin system

3.2 Conductivity study

Theformation of inclusion complexescan also be described by conductivity study with more precision[21, 22]. The conductivities of the ionic liquid solutionswere measured with successive addition of CD solutions at 298.15 K.

The variations of conductance with molarity of α- and β-cyclodextrins are shown in **Fig.3**. It is seen that the values of conductance decrease gradually with molarities of CDs up to a certain point after which the conductance become steady. The molar conductance values corresponding to the end-point of different mixtures are given in **Table 2.**This incidence can be explained on the basis of formation ofhost and guest inclusion complexes. The hydrophobic alkyl part of (HMIm)PF_6enters into the cavity of α- and β-cyclodextrins and forminclusion complexes. The mobility of the IL decreases due to penetration of the IL inside the cavity of CDs as a result the conductance values decrease gradually with the concentration of CDs. The concentration of (HMIm)$PF_6$and cyclodextrin at the break point of the conductance vs. [CD] graph which suggests the formation 1:1 stoichiometric inclusion complexes[23, 24].

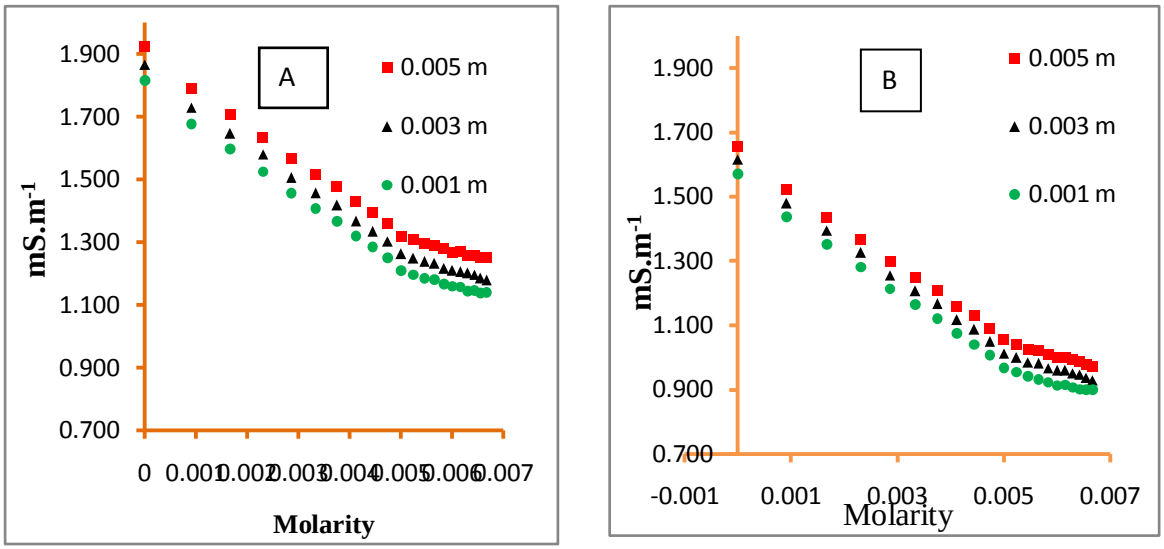


Fig.3. Variation of conductance of (HMIm)PF_6 with the added concentration of aqueous (A) α-cyclodextrin and (B) β-cyclodextrin

Table 2.

Values of conductance at the break point in different mass fractions of aqueous cyclodextrins at 298.15 K

Molarity of IL	Conductance at break point for β-CD **mS.m^{-1}**	Conductance at break point for α-CD **mS.m^{-1}**
0.001 m	1.21	0.968
0.003 m	1.263	1.013
0.005 m	1.32	1.055

The association constant of the 1:1 inclusion complexes of ionic liquid/cyclodextrin system can be evaluated by the non-linear programme at varying temperatures as follows[25, 26].

$IL_f + CD_f = IC$ (8)

The association constant (K_a) of inclusion complex may be expressed as

$$K_a=\frac{[IC]}{[IL]_f\times[CD]_f} \quad (9)$$

where, [IC] is the concentration of inclusion complex, $[IL]_f$ is the concentration of free ionic liquids and and $[CD]_f$is the concentration offree cyclodextrin respectively. As per the binding isotherm, the association constant (K_a) of the formation of inclusion complex may be written as

$$K_a = \frac{(K_{obs}-K_0)}{(K-K_{obs})\times[CD]_f} \quad (10)$$

$$[CD]_f = [CD]_{ad} - \frac{[IL]_{ad}-(K_{obs}-K_0)}{K-K_0} \quad (11)$$

Here, K_o, K_{obs} and K symbolize the conductance of (IL + CD) mixtures at initial, during the addition of CD and final state respectively.
Here, Ko, Kobs and K are the conductance of IL + CD mixture at starting, during the addition of CD and final state respectively and $[IL]_{ad}$ and $[CD]_{ad}$symbolize the concentrations of the added IL and added CD respectively. We can deriveK_a from the above equations (10) and (11) using the value of $[CD]_f$.The larger K_a value for β-CD than α-CD signifies that the former fits better than the later.
The thermodynamic parameters like enthalpy, entropy and free energy for the formation of the inclusion complex of $(HMIm)PF_6$into cyclodextrins can be evaluated as follows.

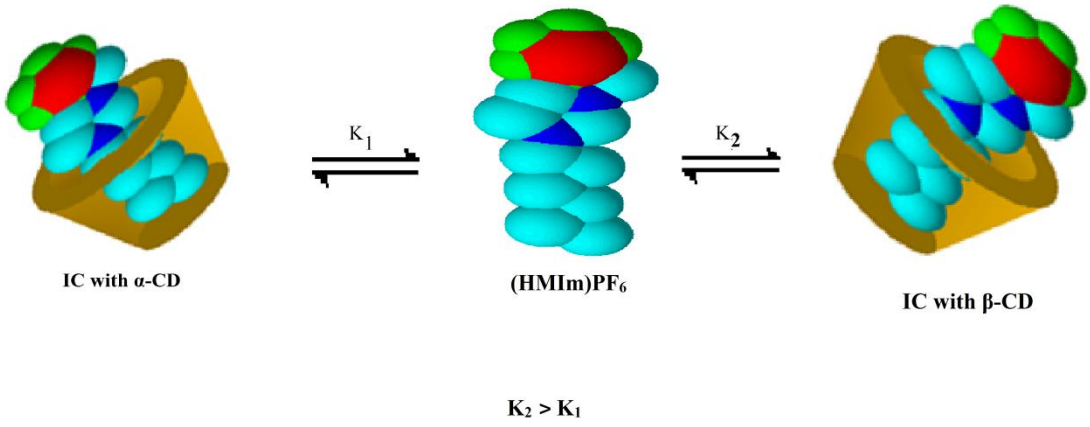
$$2.303\log Ka = -\frac{\Delta H_0}{RT} + \frac{\Delta S_0}{R} \qquad (12)$$

The plot of $\log K_a$against 1/T gives a straight line with an intercept $\Delta S_0/2.303R$ and a slope of $\Delta H_0/2.303R$. So from the value of intercept and slope we can easily calculate ΔS_0 and ΔH_0 and also ΔG of the formation of the inclusion complexes (reported in the **Table 1**). The negativeΔGvalues signify the spontaneityof the process[27, 28].

Table 1.

Association constants (K_a), Gibb's free energy, enthalpy and entropy of ionic liquid/cyclodextrin systems

IL and CD system	logKa (M^{-1})			ΔG (kJ mol^{-1})	ΔH (kJ mol^{-1})	ΔS (J mol-1) K^{-1}
	293.15 K	303.15 K	313.15 K			
OMImBR and α-CD	3.078	2.93	2.81	-29.882	-23.570	-21.53
OMImBR and β-CD	3.187	3.023	2.94	-25.545	-21.674	-13.2058



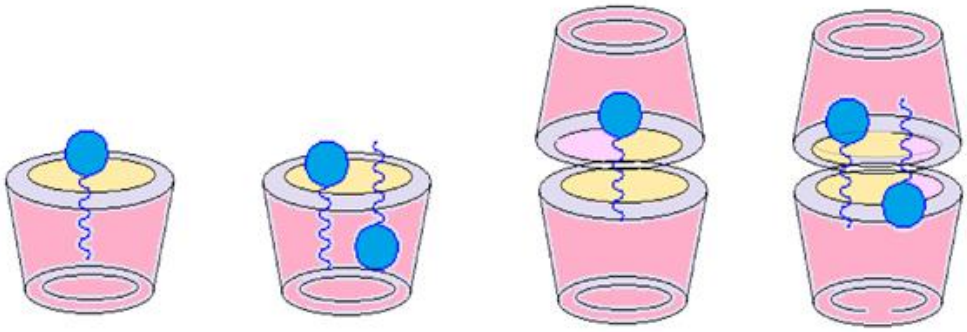
Scheme 3: Formation of inclusion complex with α-and β-CD

Scheme 3: Formation of inclusion complex

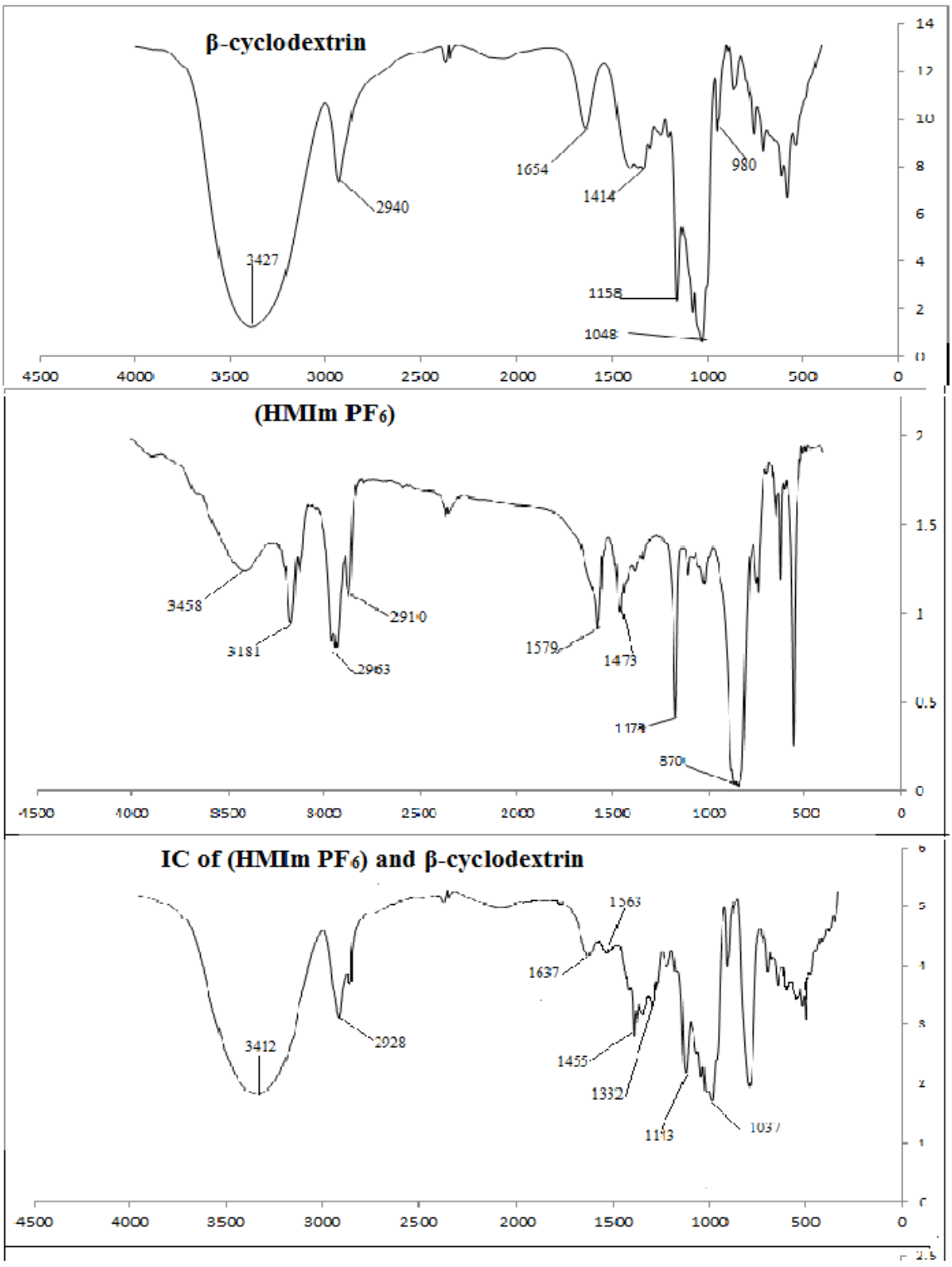
3.3. FT-IR spectroscopy

The FT-IR study is another trustworthy technique to probe the inclusion phenomena [29-31]. The FT-IR spectra of pure $(HMIm)PF_6$, cyclodextrins and their inclusion complexes are shown in **Fig.4.** Some characteristic frequencies of the ionic liquid are 2963 cm^{-1}, 3458 cm^{-1}, 1634.5 cm^{-1}, 1173 cm^{-1} and 1589 cm^{-1}probably for the groups of -C-H, =C-H, –C=N, -C-N and –C=C groups respectively and 3434.10 cm^{-1} and 3327 cm^{-1} for–OH group of α- and β-CD .(Fig.3).The frequencies for–O-H group of both the α- and β-CD shifted to the lower frequencies which may be considered due to the presence of hydrophilic-hydrophilic interaction between -OH groups of the CDs and the immidazolium part of ionic liquid. Thepeaks position for–C=N and –C-N groups

remained unchanged because these groups are situated outside the cavity of CD. The -C-H stretching frequency for alkyl group of ionic liquid is absent due to encapsulation of alkyl group into the cavity of CD.



Scheme 4. Plausible host guest stoichiometry of inclusion complex**.**


β-cyclodextrin
3427
2940
1654
1414
1158
1048
980
(HMIm PF6)
3458
3181
2963
2910
1579
1473
1178
870
IC of (HMIm PF6) and β-cyclodextrin
3412
2928
1637
1455
1332
1113
1363
4500
4000
3500
3000
2500
2000
1500
1000
500
0

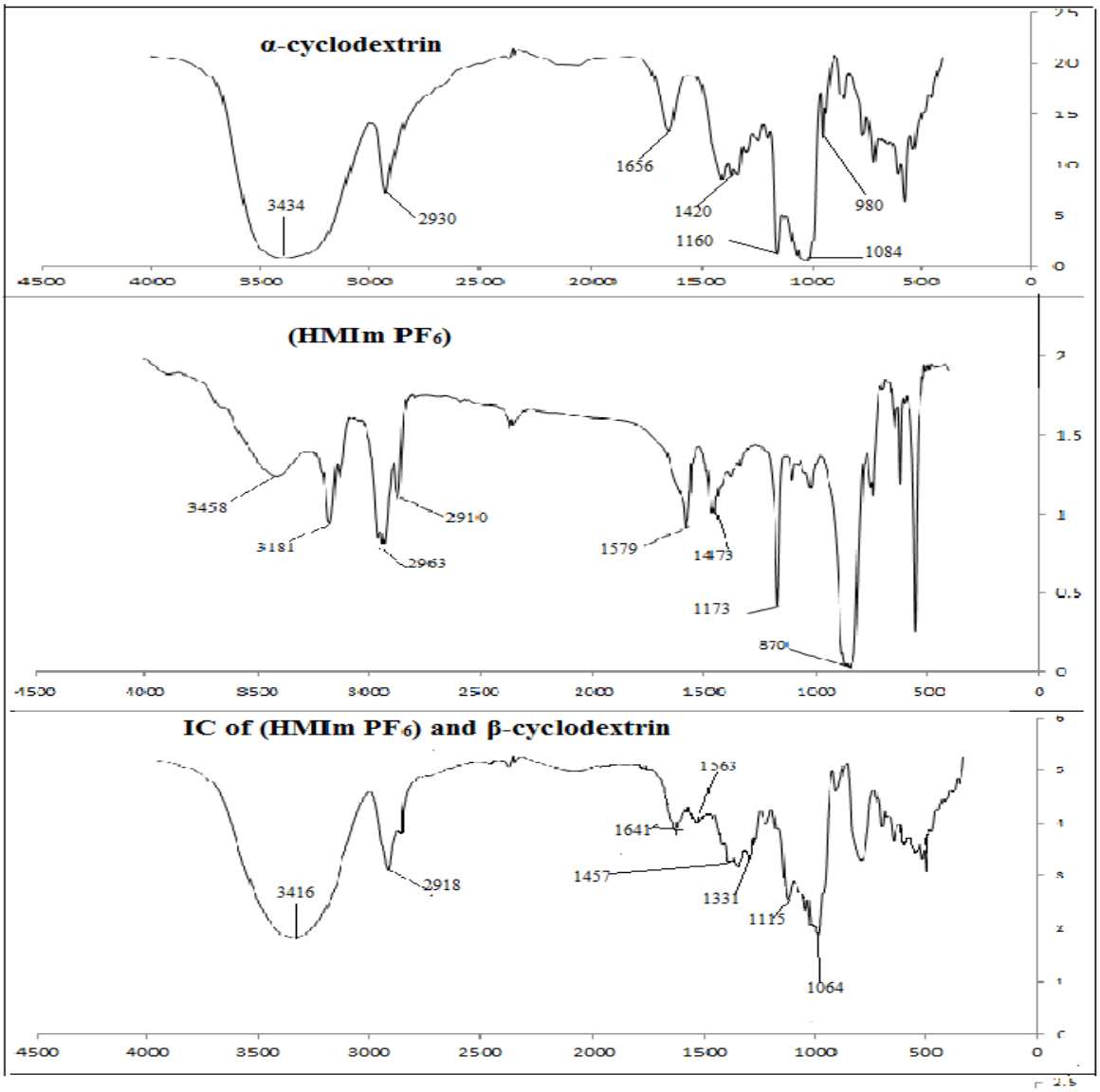


Fig.4. FTIR spectra of (HMIm)PF_6 and inclusion complexes of it in α-and β-CD at 298.15 K

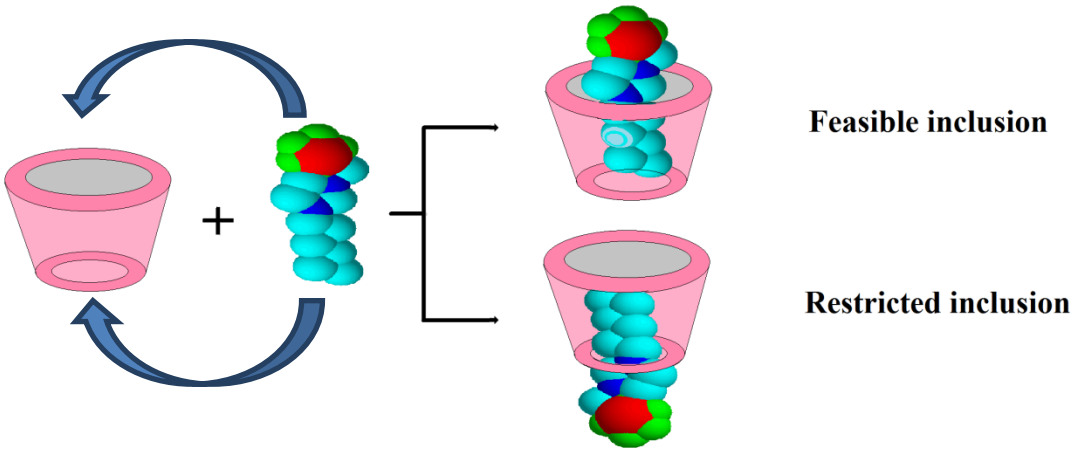
The frequencies of different groups are as follows:
(HMIm)PF_6:3458 cm^{-1}(=C-H), 2963 cm^{-1}(-C-H), 1634 cm^{-1}(-C=N), 1589 cm^{-1}(C=C), 1473 cm^{-1}(Bending –CH2), 1406 cm^{-1}(Bending-CH2), 1173 cm^{-1}(-C-N)

α –Cyclodextrin:3434 cm^{-1}(Stetching of O-H), 2930 cm^{-1}(Stretching of –CH from –CH2), 1420 cm^{-1}(Bending –CH), 1160 cm^{-1}(Bending of C-O-C), 1080 cm^{-1}(stretching of C-C-O), 956 cm^{-1}(Vibration α-1,4 linkage)

β- Cyclodextrin:3327 cm^{-1}(Stetching of O-H), 2944 cm^{-1}(Stretching of –CH from –CH2), 1430 cm^{-1}(Bending –CH), 1158 cm^{-1}(Bending of C-O-C), 1030 cm^{-1}(stretching of C-C-O), 953 cm^{-1}(Vibration α-1,4 linkage)

(HMIm)PF_6/ α -CD inclusion complex:3316 cm^{-1}(Strtching of O-H of B-CD), 2918 cm^{-1}(Strtching of –C-H), 1457 cm^{-1}(Bending of –C-H), 1115 cm^{-1}(Bending of C-O-C), 1064 cm^{-1}(Stetching of C-C-O)

(HMIm)PF_6/ β -CD inclusion complex:3427 cm^{-1}(Strtching of O-H of B-CD), 2940 cm^{-1}(Strtching of –C-H), 1654 cm^{-1}(Stretching of –C=N), 1414 cm^{-1}(Bending of –C-H), 1158 cm^{-1}(Bending of C-O-C)



Scheme 5. Feasible and restricted inclusion complex formation of host-guest molecule

3.4. UV-Vis Spectroscopy Investigation

UV-Vis spectroscopy study also gives the clear indication of formation of host-guest inclusion complex [32]. In our present study we used methyl orange as a probe since the cyclodextrins and the $(HMIm)PF_6$do not absorb in the UV-Vis range.

Here the absorption spectra of methyl orange in presence of ionic liquid were measured at varying molarities of CDs**(Fig.5)**. It is found that absorbance increases increasing concentration of cyclodextrins when the concentration of the IL was kept unchanged.

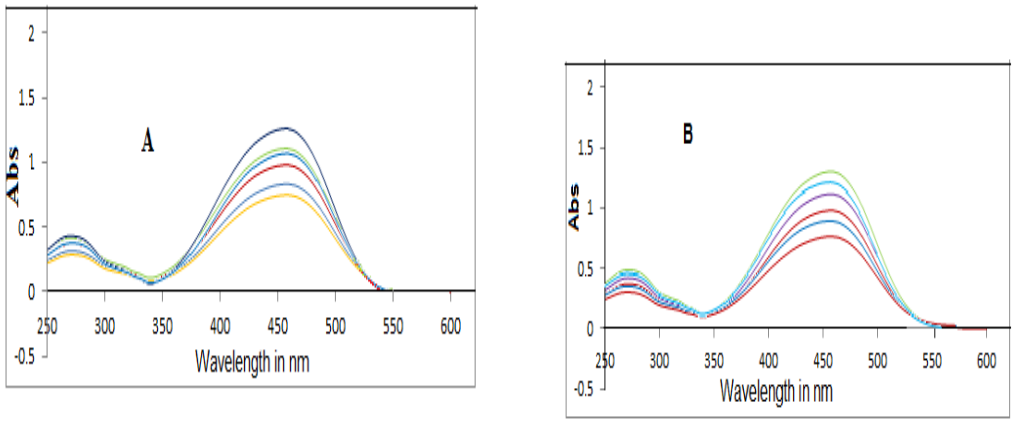


Fig.5. UV-vis spectra of methyl orange (MO) containing different concentration of (A) β-CD in $(HMIm)PF_6$ (B) α-CD in $(HMIm)PF_6$

The host-guest stoichiometry of inclusion complex may be evaluated by Job's plot calculated from UV-visible spectroscopy. The spectra were taken of ionic liquid and cyclodextrins mixture different concentration keeping the total concentration constant and shown in **Fig.6**.

Concentration ratio of ionic liquid, R = [IL]/([IL] + [CD])

The stoichiometry of host and guest of inclusion complex may be obtained by plotting the graph of ΔA×R vs. R [33-35].

Where, ΔA represents the absorbance of the studied IL without and with cyclodextrin at 298.15 K.

R = 0.5, 0.33 and 0.66 at the maxima of the graph signify the 1:1, 1:2 and 2:1 host-guest stoichiometry of the inclusion complexes. The R values in case of our studiedionic liquid, $(HMIm)PF_6$, is 0.5 which signify the 1:1 stoichiometry.

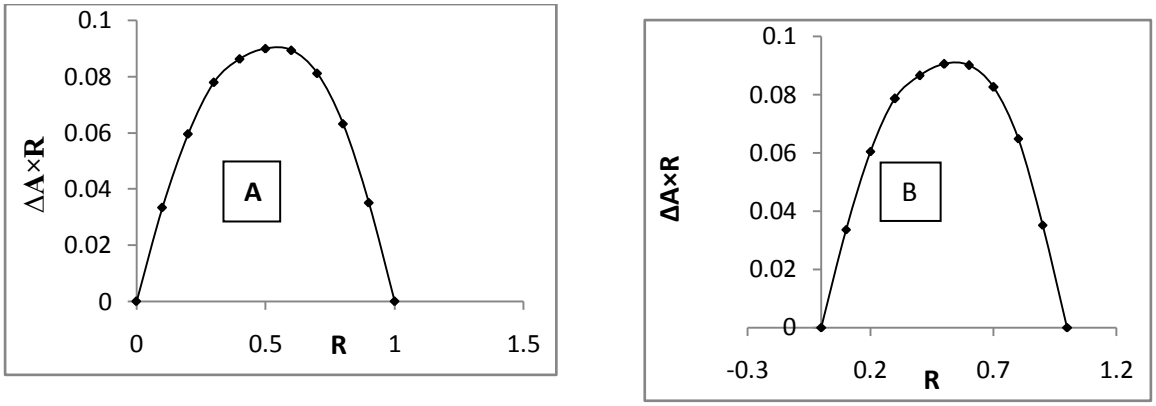


Fig.6. UV-vis spectra of methyl orange (MO) containing different concentration of (A) β-CD in $(HMIm)PF_6$ (B) α-CD in $(HMIm)PF_6$

The association constant of the inclusion complex for the cyclodextrin-ionic liquid system, $K_a$may be evaluated from the values of molar absorptivity of UV-Visible spectra. Here the spectra of the ionic liquid at constant molarity were taken with varying concentration of cyclodextrin in presence of the probe (methyl orange). We used the famous Benesi-Hildebrand equation to calculate the association constants (K_a) of I:I inclusion complex [36].

$$\frac{1}{\Delta A} = \frac{1}{\Delta\varepsilon K[Guest]} \times \frac{1}{[Host]} + \frac{1}{\Delta\varepsilon}$$

Where, ΔA denotes the absorbance difference of the ionic liquid in the presence and absence of CDs, Δε denotes the molar absorption co-efficient difference of IL in the presence and absence of CDs, [Guest] and [Host] represent the concentration of ionic liquid and cyclodextrin respectively.A plot of 1/ΔA versus 1/[CDs] (shown in **Fig.7)** gives a straight line with an intercept 1/Δε and a slope of $\frac{1}{\Delta\varepsilon K[Guest]}$. The association constant, K_a may be obtained by dividing the intercept with the slope of the double reciprocal plot at a certain concentration of ionic liquid. The K_a calculated from above equation for OMImBr/ α-CD system is $3.145 \times 10^3 M^{-1}$ and for OMImBr/ β-CD system is $3.192 \times 10^3 M^{-1}$.

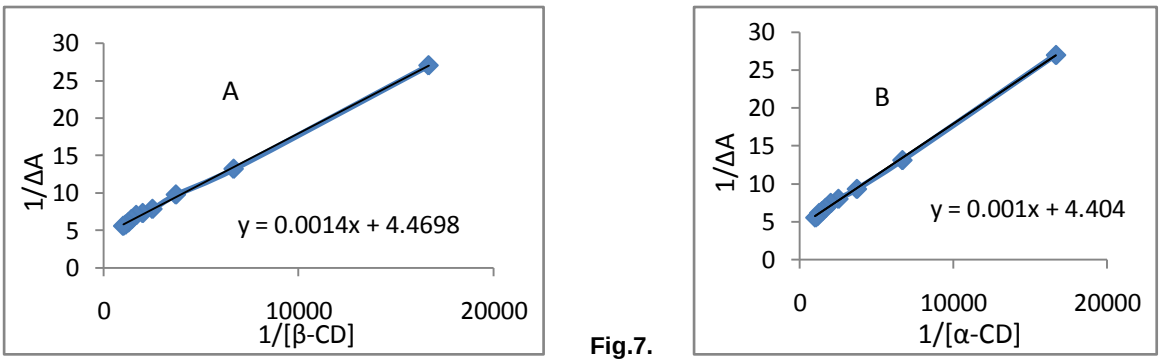


Fig.7. (A) Plot of 1/ΔA against 1/[β-CD]for examining stoichiometry of inclusion complexes .(B) Plot of 1/ΔA against 1/[α-CD] for examining stoichiometry of inclusion complexes.

3.5 ^{1}H NMR study

^{1}H NMR study also reveals the formation of host-guest inclusion complex of an ionic liquid into the cavity of cyclodextrins[37]. The ^{1}H NMR spectra of ionic liquid, cyclodextrins and their IC were carried out in D_2Oat 298 K and shown in **Fig.8**. Chemical shift of some protons of theinclusion complexes from CDs and IL may be regarded as the penetration of the alkyl part of IL inside the cavity of the CD molecule. We are aware that H3 and H5 protons of both cyclodextrins are situated inside the cavity whereas the H1, H2 and H4 protons are situated outside the cavity [38, 39]. In addition to that, H3 proton is located near the wider rim and H5 proton is situated near the narrower rim of the CDs. Due to the insertion of the alkyl part of the ionic liquid into the cavity of CDs, there was a significant up field chemical shift of the H3 and H5 protons of cyclodextrins and down field chemical shift of protons of alkyl part of the ionic liquid [40]. It is also seen that the chemical shift for H3 of IC is higher than

that of H5 protons which indicates that the hydrophobic alkyl part of IL enters into the hydrophobic cavity of CD through the wider rim of CD (**Scheme 5**). The significant chemical shift of the protons of N-methyl group may be regarded as presence of hydrophilic-hydrophilic interaction between the imidazolium part of the ionic liquid and the peripheral –OH group of nearby cyclodextrin molecules.

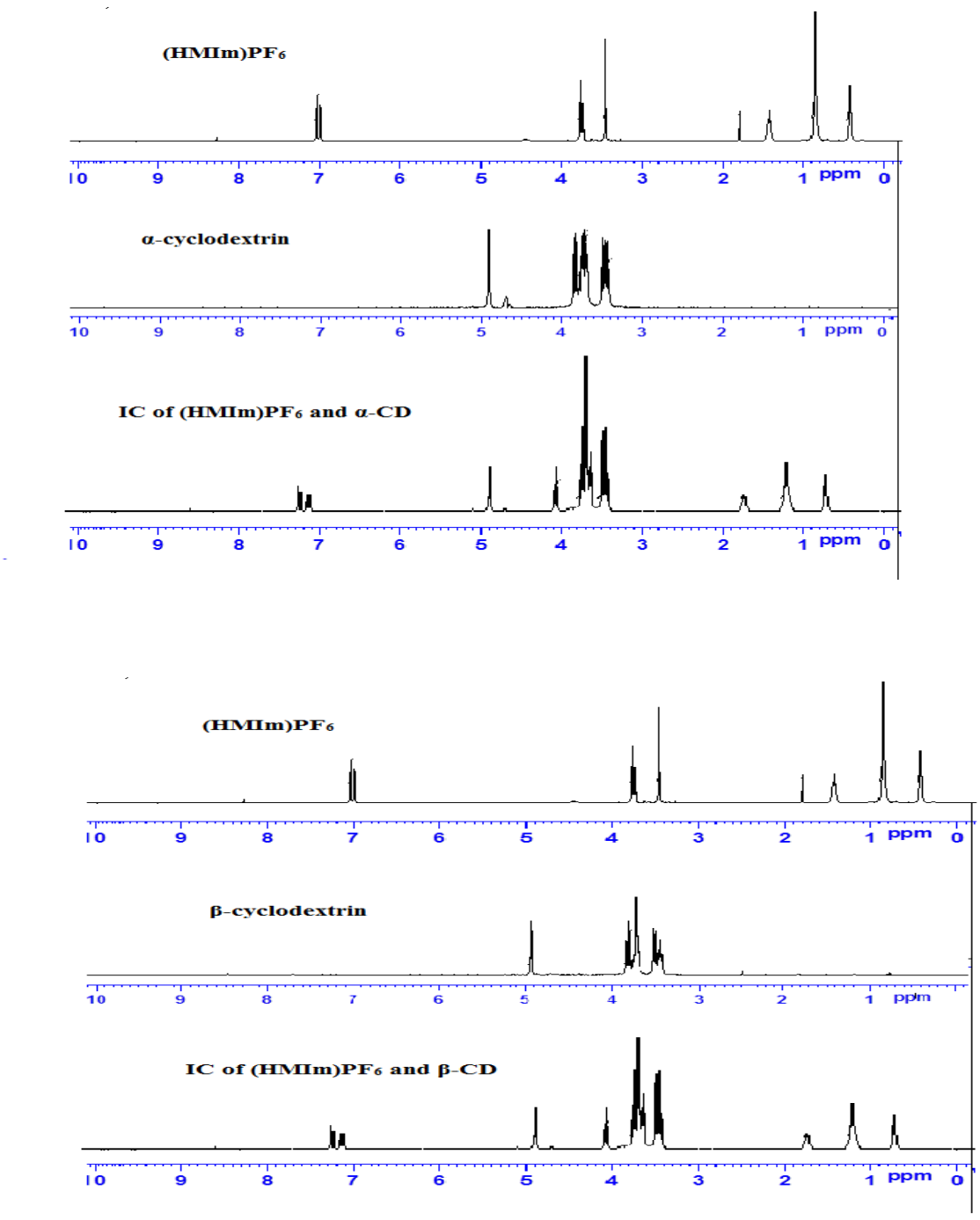


Fig.8. ^{1}H NMR spectra of $(HMIm)PF_6$ and inclusion complexes of it with α-and β-CD in D_2O at 299.15 K.

^{1}H NMR data:

(HMIm)PF6: [1H NMR (300 MHz, D2O)]: δ 0.409-0.443 (3H,m), 0.867(6H,m), 1.416-1.468 (2H, m), 1.803 (1H, S), 3.454 (3H, s), 3.733-3.774 (3H,m), 6.989-7.036 (1H,d)

α –Cyclodextrin:[^{1}H NMR (300 MHz, D_2O)]: δ 3.42-3.43 (6H, j=9.00Hz), 3.51-3.52 (6H, j=10Hz), 3.74-3.83 (18H, m), 3.87-3.91(6H, J=9Hz) 4.96-4.97 (6H, J=3Hz)

β –Cyclodextrin: [^{1}H NMR (300 MHz, D_2O)]: δ 3.41-3.42 (6H, j=9.00Hz), 3.53-3.56 (6H, j=10Hz), 3.75-3.77 (18H, m), 3.82-3.83(6H, J=9Hz) 4.97-4.98 (6H, J=3Hz)

(HMIm)PF6/ β –CD: [^{1}H NMR (300 MHz, D_2O)]: δ 0.72-0.754(3H,m), 1.209 (6H, s), 1.231-1.783 (2H, m), 3.425-3.498 (6H, m), 3.625-3.736(18H,m), 3.753-4.873(6H, m), 3.86-3.84(2H, s), 4.885 (2H, d), 7.245-7.256(1H,d),7.329-7.333(1H,d)

(HMIm)PF6/ α-CD: [^{1}H NMR (300 MHz, D_2O)]: δ 0.718-0.751(3H,m), 1.207 (6H, s), 1.228-1.779 (2H, m), 3.422-3.497 (6H, m), 3.622-3.733(18H,m), 3.757-4.874(6H, m), 3.81-3.80(2H, s), 4.883 (2H, d), 7.24-7.25(1H,d),7.324-7.328(1H,d)

3.6. 2D ROESY NMR

2D ROESY NMR study is a sophisticate technique to probe the formation of inclusion complexes [41, 42]. We know that two neighboring protons situated within a distance of 0.4 nm can exert a nuclear overhauser eff ect which may be ascertained by 2D ROESY NMR (rotating-frame NOE spectroscopy). The ROESY NMR spectra of inclusion complexes of (HMIm)PF_6withboth the cyclodextrins are displayed in **Fig.9**. The H3 and H5 protons of CDs which are located inside the cavity exert nuclear overhauser eff ect with the protons attached with the alkyl part of IL. As a result cross-peakscorresponding to the H3 and H5 protons are found in the ROESY NMR spectra inclusion complexes of (HMIm)PF_6 and cyclodextrins.

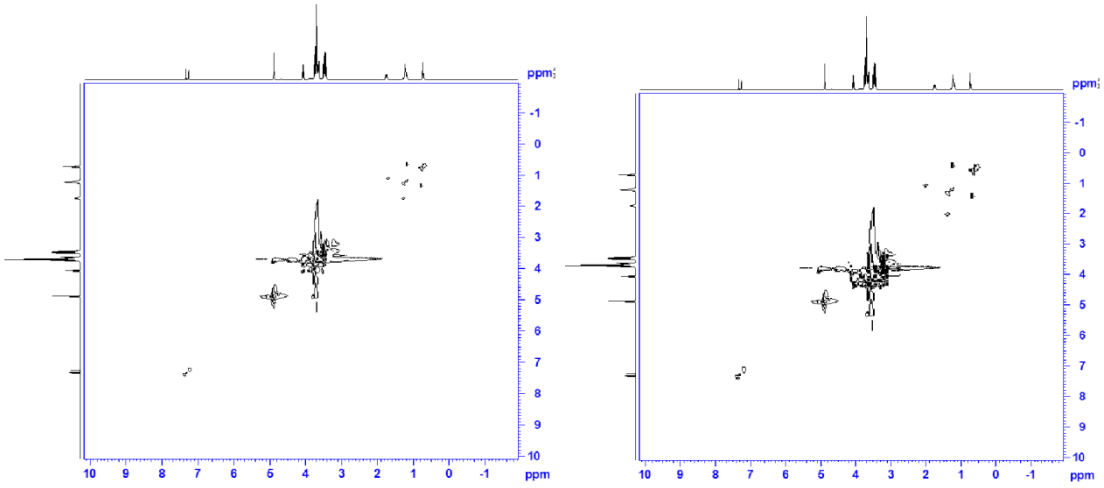


Fig.9. NMR ROSEY spectra of inclusion complexes of (A) (HMIm)PF_6 and α-CD (B) (HMIm)PF_6 and β-CD

IV. Conclusion

The size of the non-polar part of the guest molecule and the diameter of the cavity of cyclodextrins are the main determining factor of the formation of inclusion complex. The diameters of cavity of α- and β-CD are 4.7–5.3 Å and 6.0–6.5 Å respectively. We also discussed earlier that the both cyclodextrins have hydrophobic inside and hydrophilic outside. This kind of special characteristic provides a suitable environment for the non-polar part of guest ionic liquid to be encapsulated inside the cavity of cyclodextrin. The alkyl part of an ionic liquid is held inside the cavity of CD through hydrophobic- hydrophobic interaction without forming or breaking any bond. The imidazolium part of ionic liquid is located outside the wider rim of CD and form H-bonds with the –OH groups present at the periphery of another CD molecule. Overall studies reveal that the complexation between (HMIm)$PF_6$and cyclodextrins is of 1:1 stoichiometry and(HMIm)PF_6fits better in the cavity of β –CD than α-CD.

V. Acknowledgement

We convey our heartfelt gratitude to UGC, New Delhi, India (No. 540/27/DRS/2007, SAP-DSR) and UGC-RGNF India (No.F117.1/201617/RGNF201517SCWES1846 and F.1/2012-13/RGNF- 2012-13-SC-WES-17229) for funding the project. Prof. M.N. Roy is indebted to the UGC, New Delhi, India for giving him one-time

Grant-in-Aid [No.F4-10/2010 (BSR)] todevelop research facilities for the scholars. We express our gratefulness to the SAIF, North Eastern Hill University, Shillong, India for performing the NMR analysis.

References

[1.] E. Leyva, E. Moctezuma, J. Strouse, M. A. Garcla-Garibay, Journal of Inclusion Phenomena and Macrocyclic Chemistry. 39 (2001) 41-46.

[2.] Y. Kawaguchi, T. Nishiyama, M. Okada, M. Kamachi, A. Harada, Complex Formation of poly (ε-caprolactone) with cyclodextrins, Macromolecules, 33 (2000) 4472-4477.

[3.] M.E. Brewster, T. Loftsson, Cyclodextrins as pharmaceutical solubilizers, Adv Drug Deliv Rev. 59 (2007) 645-666.

[4.] A. Harada, T. Nishiyama, Y. Kawaguchi, M. Okada, M. Kamachi, Preparation and Characterization of Inclusion Complexes of Aliphatic Polyesters with Cyclodextrins, Macromolecules, 30 (1997) 7115-7118.

[5.] S. S. Satav, R. N. Karmalkar, M. G. Kulkarni, N. Mulpuri and G. N. Sastry, Formation of linear polymers with pendant vinyl groups via inclusion complex mediated polymerization of divinyl monomers, J. Am. Chem. Soc. 128 (2006) 7752-7753.

[6.] S. H. Cho, S. Y. Kim, S. I. Lee, Y. M. Lee, Hydroxypropyl-3-cyclodextrin inclusion complexes for transdermal delivery: preparation, inclusion properties, stability and release behaviour, J. Ind. Eng. Chem. 12 (2006) 50-59.

[7.] X. Zhu, J. Sun, J. Wu, Spectrofluorimetric determination of trace Co(II) in aqueous samples with quinalizarin-β-cyclodextrin inclusion complex, Talanta. 72 (2007) 237–242.

[8.] H. Jiao, S. Goh, S. Valiyaveettil, Inclusion Complexes of Poly(4-vinylpyridine)−Dodecylbenezenesulfonic Acid Complex and Cyclodextrins, Macromolecules 35 (2002) 3997-4002

[9.] N.L. Strutt, R.S. Forgan, J.M. Spruell, Y.Y. Botros, J.F. Stoddart, , Monofunctionalized pillar [5] arene as a host for alkanediamines, J. Am. Chem. Soc.133 (2011) 5668-5671.

[10.] X. Chi, M. Xue, Y. Yao, F. Huang, Redox-responsive complexation between a pillar [5] arene with mono (ethylene oxide) substituents and paraquat, Org. Lett, 15 (2013) 4722-4725.

[11.] T.F. A. Azemi, M. Vinodh, F.H. Alipour, and A.A. Mohamod, Constitutional Isomers of Pentahydroxy-Functionalized Pillar[5]arenes: Synthesis, Characterization, and Crystal Structures, J. of Org. Chem., 82 (20), (2017) 10945-10952

[12.] X. Chi, M. Xue, Y. Yao, F. Huang, Formation of a Cyclic Dimer Containing Two Mirror Image Monomers in the Solid State Controlled by van der Waals Forces, Org. Lett. 15 (2013) 4722-4725.

[13.] T. Welton, Room-Temperature Ionic Liquids. Solvents for Synthesis and Catalysis, Chem. Rev. 99 (1999) 2071-2083.

[14.] K. Huang, X. Zhang, D.W. Armstrong, Ionic cyclodextrins in ionic liquid matrices as chiral stationary phases for gas chromatography,J. Chromatogr. A 1217 (2010) 5261-5273.

[15.] K. A. Connors, The stability of cyclodextrin complexes in solution, chem. Rev. 97(1997) 1325–1357.

[16.] R. Gopal , M.A. Siddique, A study of ion-solvent interactions of some tetra alkyl- ammonium and common ions in N-methyl acetamide from apparent molar volume data, J. of Phy. Chem. 72 (1969) 1814–1817.

[17.] H.M. Zerth, N.M. Leonard, R.S. Mohan, Synthesis of Homoallyl Ethers via Allylation of Acetals in Ionic Liquids Catalyzed by TrimethylsilylTrifluoromethanesulfonate, Org. Lett. 5 (2003) 55–57.

[18.] M. N. Roy, D. Ekka, S. Saha and M. C. Roy, Host–guest inclusion complexes of α and β-cyclodextrins with α-amino acids, RSC Adv. 4 (2014) 42383–42390.

[19.] A. Pineiro, X. Banquy, S. Perez-Casas, E. Tovar, A. Garcia, A. Villa, A. Amigo, A. E. Mark and M. Costas, On the Characterization of Host-Guest Complexes: Surface Tension, Calorimetry, and Molecular Dynamics of Cyclodextrins with a Non-ionic Surfactant, J. Phys. Chem. B. 111 (2007) 4383–4392.

[20.] S.D. Qi, S.Y. Cui, X.G. Chen, Z.D. Hu, Rapid and sensitive determin- ation of anthraquinones in Chinese herb using 1-butyl-3- methylimidazolium-based ionic liquid with beta-cyclodextrin as modifier in capillary zone electrophoresis, J. Chromatogr. A. 1059 (2004) 191–198.

[21.] R. Lu, J. Hao, H. Wang, and L. Tong, Determination of Association Constants for Cyclodextrin–Surfactant Inclusion Complexes: A Numerical Method Based on Surface Tension Measurements, J. of Col. and Int. S. 192 (1997) 37–42.

[22.] Y.A. Gao, Z.H. Li, J.M. Du, G.Y. Zhang, Preparation and Characterization of Inclusion Complexes of β-Cyclodextrin with Ionic Liquid, Chem. Eur. J. 11 (2005) 5875-5880.

[23.] R.Palepu, J.E. Richardson, V.C. Reinsborough, Binding constants of. beta. -Cyclodextrin/Surfactant Inclusion by Conductivity Measurements, Langmuir. 5 (1989) 218-221

[24.] A. Apelblat, E. Manzurola and Z. Orekhova, Electrical Conductance Studies in Aqueous Solutions with Glutamic Ions, J. Solution Chem. 36 (2007) 891–900.
[25.] G. Law, P.R. Watson, Surface Tension Measurements of N-Alkylimidazolium Ionic Liquids, Langmuir. 17 (2001) 6138–6141.
[26.] D. Evans, S. Wellington, J. Nadis, E. Cussler, The conductance of cyclic polyether-cation complexes, J. Solut. Chem.1 (1972) 499-506.
[27.] G. Khayatian, S. Shariati, M. Shamsipur, Conductance study of the thermodynamics of binding of some macrocyclicpolyethers with Tlþ ion in dimethylformamide-acetonitrile mixtures, J. Inclusion Phenom. Macrocycl. Chem. 45 (2003) 117-121.
[28.] S. Barman, M.N. Roy, Hollow circular compound-based inclusion complexes of an ionic liquid, RSC Adv. 6 (2016) 76381-76389.
[29.] S. Saha, A. Roy, M.N. Roy, Mechanistic investigation of inclusion complexes of a sulfa drug with a- and b-cyclodextrins, Ind. Eng. Chem. Res. 56 (2017) 11672–11683
[30.] W. Zhang, X. Gong, Y. Cai, C. Zhang, X. Yu, J. Fan and G. Diao, Investigation of water-soluble inclusion complex of hypericin with β-cyclodextrin polymer, Carbohydr. Polym. 95 (2013) 366–370.
[31.] S. Milovanovic, D. Markovic, K. Aksentijevic, D. B. Stojanovic, J. Ivanovic, I. Zizovic, Application of cellulose acetate for controlled release of thymol, Carbohydr. Polym, 147 (2016) 344–353.
[32.] J. S. Negi, S. Singh, Spectroscopic investigation on the inclusion complex formation between amisulpride and γ-cyclodextrin, Carbohydr. Polym. 92 (2013) 1835–1843.
[33.] Y. Sueishi, T. Ide, Inclusion complexation of methyl orange with β-cyclodextrin in a roomtemperature ionic liquid, Z. Phys. Chem., 218 (2004) 829-835.
[34.] P. Job, Formation and stability of inorganic complexes in solution, Annali di ChimicaApplicata 9 (1928) 113–203.
[35.] J.S. Renny, L.L. Tomasevich, E.H. Tallmadge, D. B. Collum, Angew, Method of continuous variations: applications of job plots to the study of molecular associations in organometallic chemistry, Chem. Int. Ed. 52 (2013) 11998–12013.
[36.] Caso, L. Russo, M. Palmieri, G. Malgieri, S. Galdiero, A. falanga, C. Isernia, R. Iacovino, Investigating the inclusion properties of aromatic amino acids complexing beta-cyclodextrins in model peptides, Amino Acids 47 (2015) 2215–2227.
[37.] H.A. Benesi, J.H. Hildebrand, A Spectrophotometric Investigation of the Interaction of Iodine with Aromatic Hydrocarbons, J. Am. Chem. Soc. 71 (1949) 2703-2707.
[38.] J. V. Caso, L. Russo, M. Palmieri, G. Malgieri, S. Galdiero, A. Falanga, C. Isernia and R. Iacovino, Investigating the inclusion properties of aromatic amino acids complexing beta-cyclodextrins in model peptides, Amino Acids. 47 (2015) 2215–2227
[39.] V. Sindelar, M. A. Cejas, F. M. Raymo, W. Chen, S. E. Parker and A. E. Kaifer, Supramolecular assembly of 2,7-dimethyldiazapyrenium and cucurbit[8]uril: A new fluorescent host for detection of catechol and dopamine, Chem. Eur. J. 11 (2005) 7054–7059.
[40.] T. Wang, M. D. Wang, C. Ding and J. Fu, Mono-benzimidazole functionalized β-cyclodextrins as supramolecularnanovalves for pH-triggered release of p-coumaric acid, Chem. Commun. 50 (2014) 12469–12472.
[41.] J. V. Caso, L. Russo, M. Palmieri, G. Malgieri, S. Galdiero, A. Falanga, C. Isernia, R. Iacovino, Investigating the Inclusion Properties of Aromatic Amino Acids Complexing beta-Cyclodextrins in Model Peptides, Amino Acids 47 (2015) 2215-2227.
[42.] E. Bednarek, W. Bocian, J. Pozna´nski, J. Sitkowski, N. S. Sosnowska and L. Kozerski, Complexation of steroid hormones: prednisolone, ethinyloestradiol and estriol with ß- cyclodextrin. An aqueous 1 H NMR study, J. Chem. Soc. Perkin Trans. 2, (2002) 999–1004.
[43.] T. Stalin, K. Srinivasan, K. Sivakumar and S. Radhakrishnan, Preparation and characterizations of solid/aqueous phases inclusion complex of 2,4-dinitroaniline with β-cyclodextrin, Carbohydr. Polym., 107 (2014) 72–84.