

Further understanding of the multiple equilibria interaction pattern between ionic liquid and β -cyclodextrin

Jingjing Zhang · Jianfeng Shi · Xinghai Shen

Received: 20 May 2013 / Accepted: 20 July 2013 / Published online: 31 July 2013
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Abstract The interactions of the ionic liquids 1-alkyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide ($C_n\text{mimTf}_2\text{N}$, $n = 2, 4, 6, 8, 10, 12$) with β -cyclodextrin (β -CD) in aqueous solutions are investigated in this work. The stoichiometry and apparent association constants are obtained by competitive fluorescence method and isothermal titration calorimetry (ITC). The results show that $C_2\text{mimTf}_2\text{N}$, $C_4\text{mimTf}_2\text{N}$, and $C_6\text{mimTf}_2\text{N}$ mainly form 1:1 (guest:host) inclusion complexes with β -CD, whereas $C_8\text{mimTf}_2\text{N}$, $C_{10}\text{mimTf}_2\text{N}$, and $C_{12}\text{mimTf}_2\text{N}$ form both 1:1 and 1:2 inclusion complexes, the latter of which are mainly attributed to the formation of the $C_n\text{mim}^+-2\beta$ -CD complexes. Besides, Tf_2N^- only forms the 1:1 complex with β -CD owing to a charge resonance structure that breaks the symmetry of the structure of Tf_2N^- , which is proved by Fourier transform infrared spectra. The thermodynamic parameters obtained by ITC reveal that the formation of the inclusion complexes are enthalpy-controlled for $C_2\text{mimTf}_2\text{N}$, $C_4\text{mimTf}_2\text{N}$, and $C_6\text{mimTf}_2\text{N}$, while for the $C_8\text{mimTf}_2\text{N}/\beta$ -CD system, the process becomes entropy and enthalpy driven. Based on high-resolution mass spectrometry used with electrospray ionization results, the interaction between $C_n\text{mimTf}_2\text{N}$ and β -CD is found to follow the multiple equilibria interaction pattern which was suggested in our previous work.

Introduction

Cyclodextrins (CDs) are a series of macrocyclic oligosaccharides composed of 6, 7, and 8 D-(+)-glucose units named α -, β -, and γ -CD, respectively, which can encapsulate a number of organic and inorganic guest molecules in their hydrophobic cavity to form inclusion complexes [1–3]. They are commercially available, nontoxic and water soluble, making them widely used in the pharmaceutical and life science in supramolecular chemistry and industry, foodstuffs and so on [4, 5]. Ionic liquids (ILs) consist of organic cations and appropriate anions, and have been regarded as a good alternative to the conventional and environmentally detrimental volatile solvents. They have intriguing properties such as negligible vapor pressure, nonflammability, tunable physico-chemical properties, high electrical conductivity, and wide electrochemical window, attracting considerable attention in the fields of chemical reactions, separations and electrochemistry [6–11]. Furthermore, ILs are becoming more and more important in the field of supramolecular chemistry, as they can either directly participate in the assembly of supramolecular[(-9.8([rgcan]77.6izationsy,51-4.(r,5150.70001(nf

Keywords Cyclodextrin · Ionic liquid · Tf_2N^- · Inclusion complex · Multiple equilibria

J. Zhang · J. Shi · X. Shen (✉)
Beijing National Laboratory for Molecular Sciences (BNLMS),
Radiochemistry and Radiation Chemistry Key Laboratory
of Fundamental Science, College of Chemistry and Molecular
Engineering, Peking University, Beijing 100871, China
e-mail: xshen@pku.edu.cn

ILs 1-alkyl-3-methylimidazolium hexafluorophosphate ($C_n\text{mimPF}_6$, $n = 2, 4, 6, 8$) for examples [27]. This interaction pattern successfully demonstrates the existence of contact ion pairs and the dissociated ions of ILs, and indicates how they interact with β -CD respectively. ILs mainly exist as the dissociated ions with a minor percentage of ion pairs in aqueous solutions. The cation or the anion part of the ion pair first interacts with β -CD depending on which part of the ion pair interacts more strongly with β -CD. If both the cation and the anion can interact strongly, the 1:2 (β -CD-cation)·(anion- β -CD) inclusion complex will form and thereupon dissociate into β -CD-cation and anion- β -CD complexes, of which the cation with long chain will further interact with β -CD to form the 1:2 complexes cation-2 β -CD. On the other hand, the dissociated cations and anions of the ILs interact with β -CD randomly to form two kinds of 1:1 inclusion complexes, of which the cation with long chain will also be included in another β -CD [27].

Here we try to further investigate the above interaction pattern by using the ILs 1-alkyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide ($C_n\text{mimTf}_2\text{N}$, $n = 2, 4, 6, 8, 10, 12$, illustrated in Scheme 1) instead of $C_n\text{mimPF}_6$. With the symmetrical structure and two SO_2CF_3 groups, Tf_2N^- should be able to form the 1:2 inclusion complex with β -CD, which would expand our multiple equilibria interaction pattern. Ritter and co-workers [14] considered that Tf_2N^- and β -CD form 1:1 inclusion complex, which led to the generation of separated ion pair from the contact ion pair. In our previous work, we suggested that both the cation and the anion part of $C_{12}\text{mimTf}_2\text{N}$ would interact with β -CD by using ^1H - ^1H 2D ROESY and ^{19}F NMR [26], and it was supposed that Tf_2N^- interacts with only one β -CD despite two CF_3SO_2 groups exists, which may be due to the steric hindrance coming from the separated ion pair (β -CD- $C_n\text{mim}^+$)·(Tf_2N^- - β -CD) [26]. On the basis of the multiple equilibria interaction pattern [27], we further suggested that the (β -CD- $C_n\text{mim}^+$)·(Tf_2N^- - β -CD) ion pair will dissociate into separated β -CD- $C_n\text{mim}^+$ and Tf_2N^- - β -CD, which breaks the steric hindrance. However, the detailed

interaction mechanism between $C_n\text{mimTf}_2\text{N}$ and β -CD has not been ascertained yet. So we need to pay more attention to the interaction pattern between $C_n\text{mimTf}_2\text{N}$ and β -CD, for which we use fluorescence spectra, isothermal titration calorimetry (ITC) and high-resolution mass spectrometry (HRMS) to study the $C_n\text{mimTf}_2\text{N}/\beta$ -CD systems. We will try to not only validate our multiple equilibria interaction pattern in the $C_n\text{mimTf}_2\text{N}/\beta$ -CD systems, but also unearth how Tf_2N^- interacts with β -CD. This work will help predict interaction patterns between other ILs and β -CD.

Experimental section

Materials

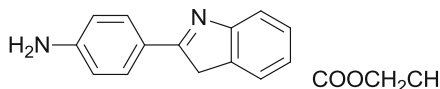
β -CD (Beijing Aoboxing, China) was recrystallized twice using tridistilled water and dried under vacuum for 24 h. LiTf_2N (>99 % purity) was purchased from Lanzhou Institute of Chemical Physics, China. The ILs $C_n\text{mimTf}_2\text{N}$ were synthesized via a metathetical reaction as previously reported [29]. The synthesis and purification of the fluorescent probe 2-(*p*-aminophenyl)-3,3-dimethyl-5-carboethoxy-3*H*-indole (**1**, Scheme 1) were done according to [30, 31]. Spectrographic grade reagent methanol was used as received. Tridistilled water was used throughout the experiments.

Instruments

Fluorescence spectra were measured on an FL-4500 (Hitachi, Japan) spectrophotometer. The temperature was controlled by placing the sample in a cell compartment whose walls were accessible to water circulation and the final temperature (298.0 ± 0.1 K) of the sample was obtained by a thermocouple (Check-temp, Hanna, Italy). Fourier transform infrared (FTIR) spectra were recorded on a NICOLET iN10 MX spectrometer. The HRMS used with electrospray ionization (ESI) was performed on a Fourier Transform Ion Cyclotron Resonance. ITC was carried out on a Nano ITC 2G.



$C_n\text{mim}^+$, ($n = 2, 4, 6, 8, 10, 12$)



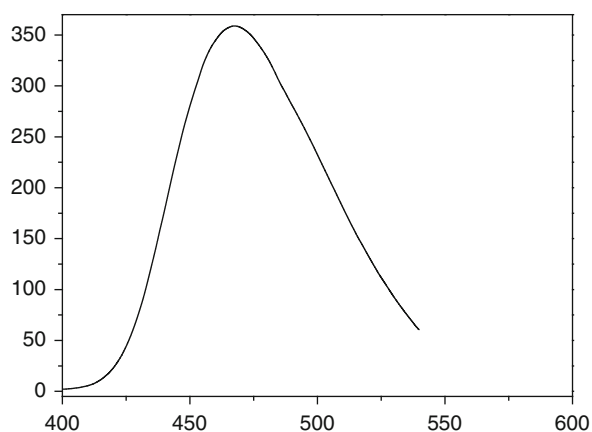


Table 1 Stoichiometry and association constants of LiTf_2N , $\text{C}_n\text{mimTf}_2\text{N}$ ($n = 2, 4$) with $\beta\text{-CD}$ in water by competitive fluorescence method

	Stoichiometry	$K_1 \text{ (M}^{-1}\text{)}$
LiTf_2N	1:1	2490 ± 42
$\text{C}_2\text{mimTf}_2\text{N}$	1:1	3255 ± 172
$\text{C}_4\text{mimTf}_2\text{N}$	1:1	4374 ± 303

Methods

Competitive fluorescence measurement

Stock solution of **1** was prepared in methanol and 50 μL aliquots of this stock solution were added into 5 mL volumetric flasks to maintain a final concentration of 10^{-6} M for fluorescence measurements. The pH values of all the solutions with **1** as a probe in this study were adjusted to 9.5 by adding NaOH and no buffer was used [32, 33].

Isothermal titration calorimetry

In the experimental process of ITC, the IL solution in the syringe was injected over 28 drops with a respective volume of 8 μL into the measuring cell, which was filled with the aqueous solution of $\beta\text{-CD}$. The temperature was kept at 298.0 K and the stirrer rotational speed was 250 min^{-1} . The

equilibrium time between two injections was long enough for the signal to return to the baseline. The dilution heat was determined in a separate measurement by injecting the corresponding IL solutions into water and it was subtracted from the determined heat flow. The net reaction heat in each run was analyzed by using the “ligand binding analysis” within the software Digitam 4.1 to simultaneously compute the association constant K and molar reaction enthalpy (ΔH°), and the standard deviation from the titration curve. Other thermodynamic parameters, i.e., the standard Gibbs free energy of binding (ΔG°) and entropy change (ΔS°) can be obtained by the following equations:

$$\Delta G^\circ = -RT \ln K, \quad (1)$$

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ, \quad (2)$$

where R is the gas constant and T is the absolute temperature.

Results

Competitive fluorescence method

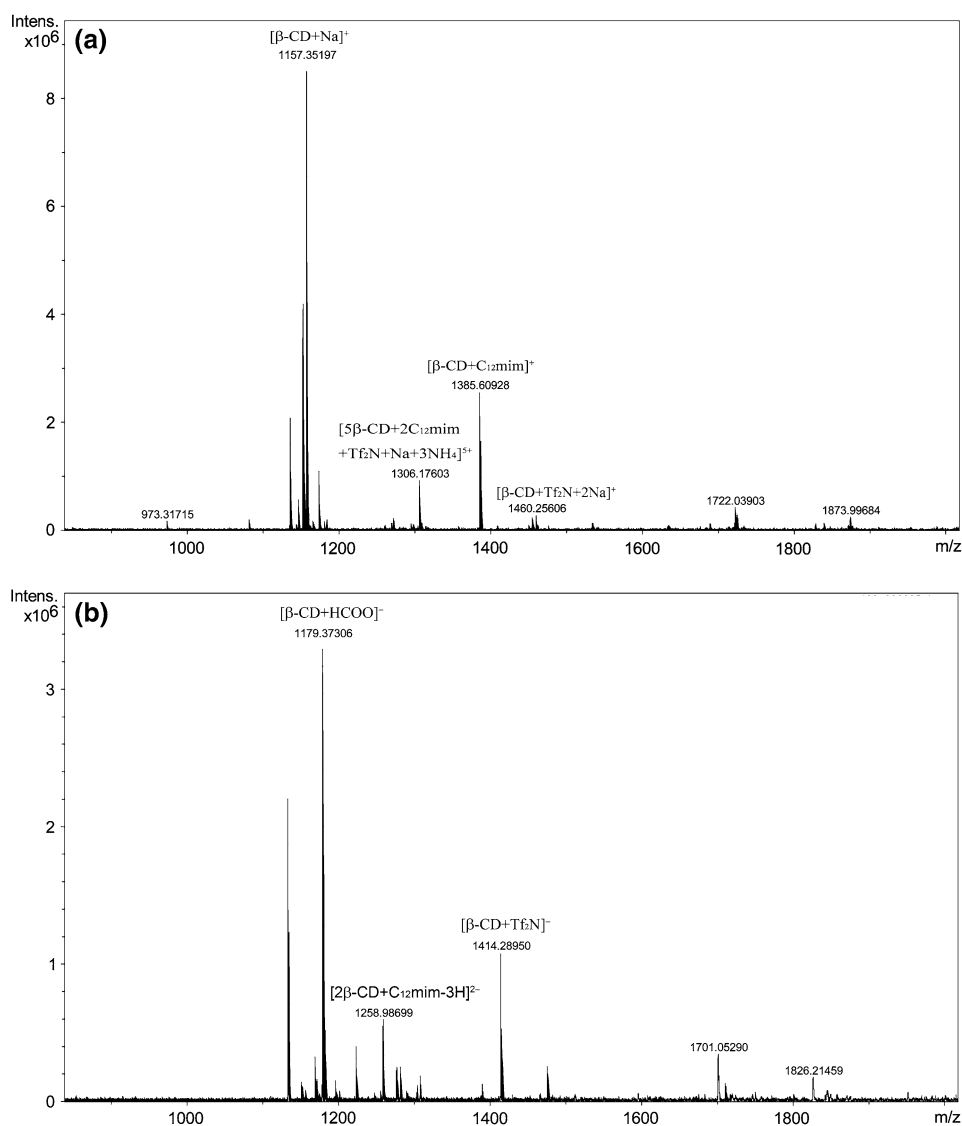
The competitive fluorescence method is suitable for the systems of weak interactions between ILs and $\beta\text{-CD}$ with molecule **1** as fluorescent probe [26, 27]. Here we use it in $\text{LiTf}_2\text{N}/\beta\text{-CD}$ and $\text{C}_n\text{mimTf}_2\text{N}/\beta\text{-CD}$ ($n = 2, 4$) systems.

Table 2 IR spectra peaks and the corresponding vibrational modes of LiTf₂N

Groups	Wavenumber (cm ⁻¹)	Corresponding vibrational modes
O=S=O	1330	ν_{as}
	1141	ν_s
O=S-O ⁻	1200	ν_{as}
	1055	ν_s
S-N-S	646	ν_{as}
	595	ν_s
S-N=S	797	ν_{as}
	741	ν_s
Two kinds of S-CF ₃	575	ν_{as} and ν_s of -S-CF ₃
	516	ν_{as} and ν_s of =S-CF ₃

Other C_nmimTf₂N ($n = 6, 8, 10, 12$) ILs were not studied due to their poor solubility in water. According to the previous report [32], at low fluorescence probe concentrations, the total fluorescence intensity of **1** in 1/β-CD solutions can be expressed by Eq. 3 with different initial concentrations of β-CD ([CD]₀), and the K'_1 , K'_2 , I_1/I_0 , and I_2/I_0 values (K'_1 and K'_2 are the association constants for 1:1 and 1:2 complexes between **1** and β-CD, respectively, and I_0 , I_1 , and I_2 stand for the fluorescence intensity of **1** in pure water, in the 1:1 complex, and in the 1:2 complex, respectively) can be estimated by nonlinear regression analysis.

$$I = \frac{(I_0 + I_1 K'_1 [CD]_0 + I_2 K'_1 K'_2 [CD]_0^2)}{1 + K_1 [CD]_0 + K_1 K_2 [CD]_0^2} \quad (3)$$

Fig. 3 The positive (a) and negative (b) ESI spectra of equal mole of C₁₂mimTf₂N and β-CD

After that, the fluorescence spectra of **1** in the LiTf₂N/ β -CD, C₂mimTf₂N/ β -CD, and C₄mimTf₂N/ β -CD systems were measured and that in the C₄mimTf₂N/ β -CD system is shown in Fig. 1a as an example. Within the range of the ILs concentration studied in this paper, the fluorescence intensity decreases noticeably with the increase of the initial concentration of ILs. The equilibrium concentrations of β -CD, i.e., [CD], at different [C_{*n*}mimTf₂N]₀ (the initial concentration of C_{*n*}mimTf₂N) can be calculated using the K'_1 , K'_2 , I_1/I_0 , and I_2/I_0 values according to Eq. 3 [34]. The concentration of β -CD binding with ILs can be obtained from [CD]₀ to [CD]. Thus by analyzing the variation of [C_{*n*}mimTf₂N]₀ as a function of [CD] with Eq. 4 for 1:1 inclusion complexes [25, 27

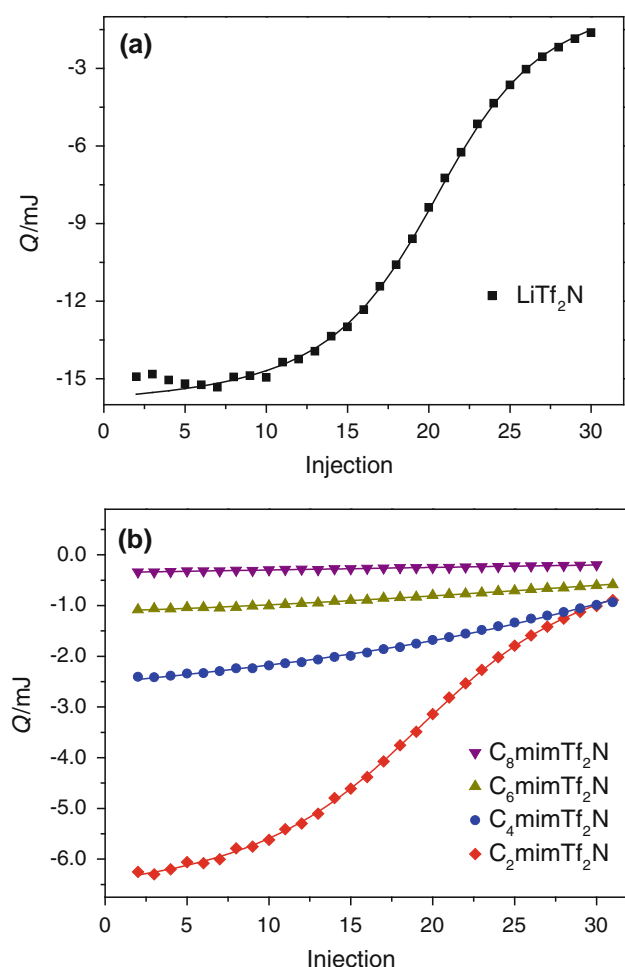


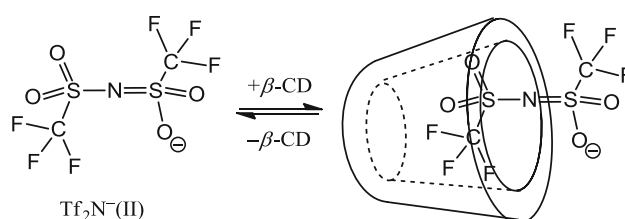
Fig. 4 The heat caused by the host–guest interaction versus the injection number of LiTf₂N (a) and C_nmimTf₂N (*n* = 2, 4, 6, 8) (b) into β-CD. The points are obtained from the experiment and the solid lines are the results by regression analysis

(S-3) will dissociate into two kinds of 1:1 complexes (S-4 and S-5).

Isothermal titration calorimetry

ITC, which is accurate for the determination of thermodynamic parameters, i.e., ΔG , ΔH and ΔS [14, 27, 35–37], can also be used here to study the interaction between C_nmimTf₂N and β-CD in aqueous solutions. The fitting curves to obtain the thermodynamic parameters of the formation of LiTf₂N/β-CD and C_nmimTf₂N/β-CD complexes are shown in Fig. 4, and Table 4 shows the results of the complexation (C₁₀mimTf₂N and C₁₂mimTf₂N are not investigated because of their poor solubility in water, leading to weak complex heat).

The negative ΔG values for all the systems indicate that the inclusion processes of LiTf₂N/β-CD and C_nmimTf₂N/β-CD are spontaneous. In the case of LiTf₂N, C₂mimTf₂N, C₄mimTf₂N, and C₆mimTf₂N, the negative ΔH and



Scheme 2 The supposed charge resonance hybrids of Tf₂N[−] and the inclusion equilibrium of Tf₂N[−] (II) with β-CD

ΔS values mean that the inclusion complexations are exothermic and enthalpy-controlled, but not entropy driven. While for C₈mimTf₂N/β-CD system, the ΔS value of the inclusion complexation becomes positive, indicating that the process turns entropy and enthalpy driven.

Discussion

The inclusion pattern of Tf₂N[−]/β-CD

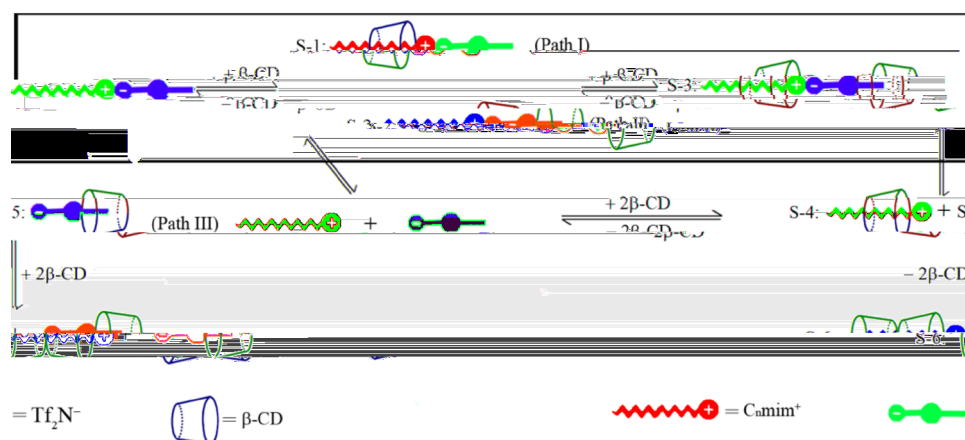
The competitive fluorescence method is the most sensitive method for the systems of weak interactions between ILs and β-CD. According to the results, Tf₂N[−] only forms 1:1 complex with β-CD despite its symmetrical structure and two SO₂CF₃ groups. As regards ESI/HRMS results of equal mole of ILs and β-CD in Table 4, no signals corresponding to the 1:2 inclusion complexes between Tf₂N[−] and β-CD occur, while those corresponding to the Tf₂N[−]–β-CD, C_nmim⁺–β-CD, and C_nmim⁺–2β-CD (when *n* = 8, 10, 12) inclusion complexes can be seen. Even in LiTf₂N/β-CD system where there is little steric hindrance between the cation Li⁺ and Tf₂N[−], no Tf₂N[−]–2β-CD inclusion complexes are detected. This also confirms that Tf₂N[−] only forms the 1:1 complex with β-CD.

One of the reasons for this phenomenon shall be the steric hindrance between β-CD molecules. Moreover, considering the structure of Tf₂N[−], we suggest to explain the phenomenon with a charge resonance structure according to the FTIR results which indicate the coexistence of the resonance hybrids of Tf₂N[−] (I and II, shown in Scheme 1). The resonance tautomer Tf₂N[−] (II) loses the structural symmetry, so when another β-CD molecule gets close to the 1:1 Tf₂N[−] (II)–β-CD complex, both the poor symmetry of Tf₂N[−] (II) and the steric hindrance will obstruct the resonance tautomer from further forming the 1:2 complex (Scheme 2).

This supposed resonance equilibrium can get support from the similar mechanism mentioned in a previous study about imidodisulfuryl fluoride ion (SO₂F)₂N[−] [38]. The inductive effect of the SO₂F group will greatly reduce the electron density on the nitrogen in (SO₂F)₂N[−], thus forming the (SO₂F)N–S(=O)(F)O[−] structure with a

Table 4 Thermodynamic parameters ΔG , ΔH , ΔS and association constant K for the complex formed by LiTf_2N , $\text{C}_n\text{mimTf}_2\text{N}$ and $\beta\text{-CD}$ in aqueous solution

ILs	Stoichiometry	K (M^{-1})	ΔH (kJ mol^{-1})	ΔG (kJ mol^{-1})	ΔS ($\text{J mol}^{-1} \text{K}^{-1}$)
LiTf_2N	1:1	2836 ± 116	-30.0 ± 1.3	-19.7	-34.5
$\text{C}_2\text{mimTf}_2\text{N}$	1:1	2740 ± 92	-31.1 ± 1.6	-19.6	-38.6
$\text{C}_4\text{mimTf}_2\text{N}$	1:1	2921 ± 119	-31.2 ± 0.4	-19.8	-38.2
$\text{C}_6\text{mimTf}_2\text{N}$	1:1	9808 ± 595	-28.8 ± 0.2	-22.8	-20.1
$\text{C}_8\text{mimTf}_2\text{N}$	1:1	12069 ± 1088	-20.5 ± 0.3	-23.3	9.39

Scheme 3 The multiple equilibria interaction pattern between $\text{C}_n\text{mimTf}_2\text{N}$ and $\beta\text{-CD}$ in aqueous solution

sulfur–nitrogen π bonding [38]. This phenomenon has also been considered by Cruickshank [39], who concluded that it occurs to an appreciable extent in sulfamates and other relative derivatives. X-ray data of the imidodisulfonate ion, $\text{HN}(\text{SO}_3)_2^{2-}$, also indicates that appreciable sulfur–nitrogen π bonding occurs in this kind of species indeed [40].

The interaction pattern involved multiple equilibria

Based on the results above, when the interaction pattern between $\text{C}_n\text{mimTf}_2\text{N}$ and $\beta\text{-CD}$ in aqueous solutions is discussed, both the dissociation equilibrium of $\text{C}_n\text{mim}^+\cdot\text{Tf}_2\text{N}^-$ ion pairs and the complexation of the dissociated ions by $\beta\text{-CD}$ should be considered. From the competitive fluorescence method and ESI/HRMS results, the C_nmim^+ forms the 1:1 or 1:2 complexes due to different length of alkyl side chains. That is, C_2mim^+ , C_4mim^+ , and C_6mim^+ form the 1:1 complexes with $\beta\text{-CD}$, while C_8mim^+ , $\text{C}_{10}\text{mim}^+$, and $\text{C}_{12}\text{mim}^+$ form the 1:2 complexes. In addition, the signals of 1:2 complexes in HRMS mainly correspond to $\text{C}_n\text{mim}^+-2\beta\text{-CD}$ ($n = 8, 10, 12$), which indicates that the intermediate 1:2 complex ($\beta\text{-CD}-\text{C}_n\text{mim}^+$)-($\text{Tf}_2\text{N}^--\beta\text{-CD}$) will dissociate into $\text{C}_n\text{mim}^+-\beta\text{-CD}$ and $\text{Tf}_2\text{N}^--\beta\text{-CD}$. With regard to the anion moiety, Tf_2N^- forms the 1:1 complex with $\beta\text{-CD}$. The interaction pattern between $\text{C}_n\text{mimTf}_2\text{N}$ and $\beta\text{-CD}$ successfully validates our multiple equilibria interaction pattern (Scheme 3), and the association constants K_1 of

$\text{C}_n\text{mimTf}_2\text{N}/\beta\text{-CD}$ complexes should be attributed to the weighting average of the association constants of 1:1 $\text{C}_n\text{mim}^+\cdot\text{Tf}_2\text{N}^--\beta\text{-CD}$ (S-1 or S-2), 1:1 $\text{C}_n\text{mim}^+-\beta\text{-CD}$ (S-4), and 1:1 $\text{Tf}_2\text{N}^--\beta\text{-CD}$ (S-5) complexes, while K_2 of $\text{C}_n\text{mimTf}_2\text{N}/\beta\text{-CD}$ complexes originates from that of $\text{C}_n\text{mim}^+-2\beta\text{-CD}$ (S-6).

Thermodynamic parameters of the inclusion complexes

When the ILs are $\text{C}_2\text{mimTf}_2\text{N}$ and $\text{C}_4\text{mimTf}_2\text{N}$, both the association constants (by competitive fluorescence method and ITC method) and the thermodynamic parameters (by ITC method) are close to those of $\text{LiTf}_2\text{N}/\beta\text{-CD}$ (Tables 1, 3). This conforms to the strength order of C_2mim^+ , C_4mim^+ , and Tf_2N^- interacting with $\beta\text{-CD}$, that is, $\text{Tf}_2\text{N}^- > \text{C}_4\text{mim}^+ > \text{C}_2\text{mim}^+$, which we previously suggested [26]. For $\text{C}_6\text{mimTf}_2\text{N}$ and $\text{C}_8\text{mimTf}_2\text{N}$, the association constants in Table 3 are bigger than that of $\text{LiTf}_2\text{N}/\beta\text{-CD}$, indicating that the C_6mim^+ and C_8mim^+ interact much more strongly with $\beta\text{-CD}$.

The processes of the inclusion complexation of LiTf_2N , $\text{C}_2\text{mimTf}_2\text{N}$, $\text{C}_4\text{mimTf}_2\text{N}$, and $\text{C}_6\text{mimTf}_2\text{N}$ with $\beta\text{-CD}$ are exothermic and enthalpy-controlled, but not entropy driven. The unfavorable effect of the negative ΔS values can be overcome by the more negative values of ΔH , leading to energetically favorable values. This is the common situation concerning the formation of inclusion complexes

between CDs and various guest molecules, similar to C_n mimPF₆/β-CD systems [27].

However, for C_8 mimTf₂N/β-CD system, the ΔS value of the inclusion complexation becomes positive, that is, the process is entropy and enthalpy driven. Before association, both the host CD and guest are highly solvated, and the solvent molecules around the host and the guest are highly ordered. During the association, the solvation shells of both the host and the guest undergo reorganization accompanied by the loss of some solvent molecules. This process creates disorder in the system and thus leads to a favorable entropic gain [41], and the positive ΔS of the C_8 mimTf₂N/β-CD system is just the combined result.

Conclusions

We have investigated the interactions between C_n mimTf₂N and β-CD in aqueous solutions. The competitive fluorescence measurement, ITC and ESI/HRMS results show that the interaction between C_n mimTf

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