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Temperature dependence of the inclusion–dissociation behavior of the inclusion complexes between cationic substituted 3H-indoles and β-cyclodextrin
Design of a novel type of semi-rotaxane

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Abstract

We report herein the syntheses of cationic surface-active molecular probes having long oligo(ethylene glycol) chains as spacers between the cationic nitrogen and the amino nitrogen, named [2-(*p*-oligoethyloxyethylene amino phenyl)-3,3-dimethyl-5-ethoxycarbonyl-3H-indole] methyl dihexadecyl ammonium iodide (molecules **1**a, **1**b and **1**c), and their interactions with β-cyclodextrin (β-CD) investigated by spectral and photophysical characterizations. It was found that the inclusion–dissociation behavior occurs for the inclusion complexes of molecules **1**a and **1**b with β-CD, that is, the 1:3 (guest:host) inclusion complex can be formed at lower temperatures and with increasing temperature, the 1:2 inclusion complex can be found. Molecule **1**c can only form the 1:1 inclusion complex in the range of temperatures studied, even though it possesses a longer spacer than **1**a and **1**b. This phenomenon can be interpreted in terms of that the solvation energy of **1**c is much larger than that of **1**a and **1**b, which is unfavorable to form a complex of higher stoichiometry. The association constants of the three types of inclusion complexes at different temperatures were estimated, from which the thermodynamic parameters were also calculated. The negative entropies and enthalpies show that the inclusion complexation is an entropically unfavorable and enthalpy-driven process.

Keywords: β-Cyclodextrin; Substituted 3H-indole; Temperature effect; Inclusion–dissociation interaction; Solvation effect

1. Introduction

Cyclodextrins (CDs) are a well-known class of water-soluble hosts that can form stable inclusion complexes with a variety of substrates, particularly those possessing hydrophobic subunits of appropriate size. 1:1 and 1:2 (guest:host) inclusion complexes are the most common type existing either in aqueous and nonaqueous solutions [1–9]. And also the thermodynamic parameters of the 1:1 type were investigated extensively, thus the compensatory enthalpy–entropy relationship has been suggested to analyze the extrathermodynamic relationship between ΔH (change of enthalpy) and ΔS (change of entropy) [5–9], which was first proposed as an empirical rule by Leffer [10]. The global trends of the relationship between the thermodynamic quantities (ΔG (change of free energy), ΔH and ΔS) for 1:1 complexation, and structural and electronic features of the guest molecules can be rationalized in terms of hydrophobicity, the shape-matching and steric effects upon host–guest interaction, the hydrogen bonding ability of an aromatic hydroxyl group, the position of a substituent in aromatic or aliphatic guests, and the flexibility of the guest molecules [5]. The complexation process, which has been proposed by many chemists and physicists [11], is driven by enthalpy in most situations, typically exhibiting large and negative enthalpic changes as well as small and also negative entropic changes. Theoretically, the negative enthalpic change results from van der waals interaction and hydrogen bonding between guests and the cavities of cyclodextrins, while the negative entropic change

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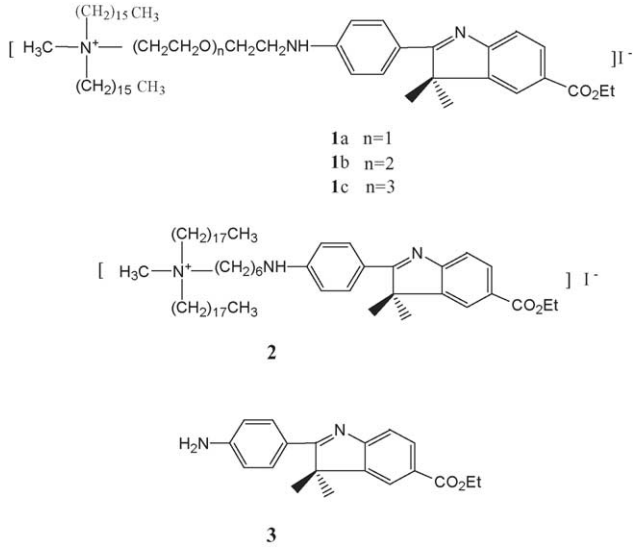
is due to the steric barrier caused by molecular geometrical shape and the limit of β-CD cavity to the freedom of shift and rotation of guest molecules. According to the relationship $\Delta G = \Delta H - T\Delta S$, the negative enthalpic and entropic changes may lead to the temperature dependence of the inclusion–dissociation behavior. Zarzycki and his co-worker reported an experiment demonstrating qualitatively the temperature effect of the inclusion complex between phenolphthalein and β-CD [12]. Also, Saito and Okumura investigated the temperature dependence of inclusion–dissociation behavior between cyclodextrin nanotube and a linear polymer [13]. On the basis of the Flory–Huggins lattice model and the induced circular dichroism results, they proposed theoretically and experimentally the formation of inclusion complex at lower temperatures and dissociation at higher temperatures. Recently, our research group started a project about the formation of nanotubes between small molecules and β-CD [14]. Preliminary results show that the formation of the nanotube greatly depends on temperature, that is, the nanotube is dissociated at higher temperature [14a,b].

^{1}H NMR experiments indicate that inclusion complexes of cyclodextrins are not static species [15]. Rather, it has been reported that guest molecules can have different orientations about the axis parallel to the cavity and/or be rapidly spinning about this axis within the cavity [3]. Guest molecules also exchange rapidly between free and bound forms. The recombination and dissociation rate constants have been determined to be on the order of 10^7–10^9 and 10^4–10^7 $M^{-1}s^{-1}$ by using temperature-jump [16] and ultrasonic relaxation [17] techniques, respectively.

To the best of our knowledge, the 1:3 inclusion complexes reported in the literature are very scarce [14a,18,19]. Consequently, the thermodynamic parameters and the temperature dependence of the inclusion–dissociation behaviors of the 1:3 inclusion complex were seldom reported quantitatively. Recently, it was found that 1:3 rotaxane-like inclusion complexes could be formed between β-CD and [2-(*p*-hexylamino)phenyl-3,3-dimethyl-5-ethoxycarbonyl-3H-indole] methyldioctadecyl ammonium iodide [18], which has a hexyl group as a spacer between the cationic nitrogen and the amino nitrogen (see Scheme 1, molecule **2**). We think that increasing the length of the spacer [20] or introducing a partial hydrophilic or amphoteric spacer may be very useful to investigate the mechanism of the inclusion complexation, including the solvation effect. Thus, in the present paper, diethylene glycol (DEG), triethylene glycol (TEG) and tetraethylene glycol (TTEG) were used to synthesize the molecule series **1**a, **1**b and **1**c (Schemes 1 and 2). It is speculated that the inclusion complexes between these molecules and β-CD may be more susceptible to temperature. If this is true, we will have opportunity to study the thermodynamic parameters of the inclusion complexation from which the compensatory enthalpy–entropy relationship can be obtained. On the other hand, we will also explore how the length of the spacer in molecules **1**a, **1**b and **1**c affects the inclusion process. Could the 1:4 inclusion complex be formed



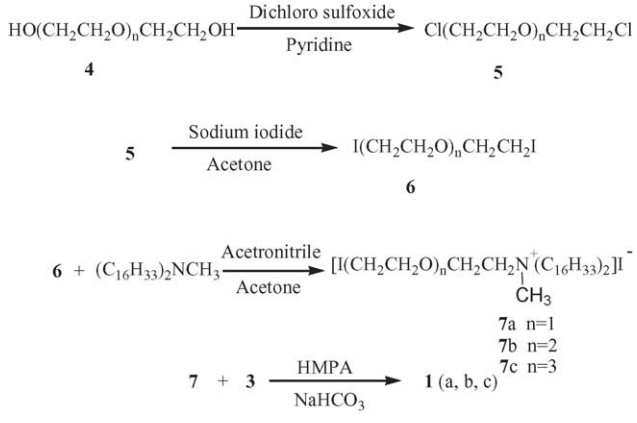
Scheme 1. Molecular structures of **1** (a, b, c), **2** and **3**.

with increasing the length of the spacer from **1**a to **1**c? Or, on the contrary, will the solvation of the long spacer in **1**c be strong enough to prevent the **1**c/β-CD inclusion complexes of higher stoichiometries to be formed? Finally, we hope that the present work will provide insight into the formation of rotaxane, an attractive architecture in supramolecular chemistry.

2. Experimental section

2.1. Materials

The syntheses of molecules **1***a*, ***1***b and ***1***c: The synthesis and purification for compound **3** have been carried out according to the methods of Skrabal [21] and Popowycz [22], while those for compound **6** according to literature [23]. Certain amounts of diiodides **6** and amine in dry acetonitrile (50 ml) were mixed and heated at reflux under an atmosphere of nitrogen for 24 h with a mechanical stir. The cooled solvent was removed in vacuum. The residual solid was purified by



Scheme 2. Synthesis route of molecule **1** (a, b, c).

column chromatography (dichloromethane:methanol = 20:1) to give a white product, which was then recrystallized three times from acetone to give the product **7**.

Compound **3** was dissolved in 30 ml of dry HMPA (hexamethylphosphoramide, caution: cancer suspect agent, handle with care) under an atmosphere of nitrogen. An excess of sodium bicarbonate was added. After agitation of 10 min, the ammonium **7** dissolved in 20 ml HMPA was added dropwise. The stirring was continued for 36 h at 80 °C. After cooling, the solvent was removed by distillation under reduced pressure. The residue was redissolved in 1.5 L hexane and 100 ml ethyl acetate and then washed with water (20×100 ml). After removal of the organic solvent, the crude product was dealt with column chromatography (dichloromethane:methanol = 40:1). Further purification was performed by recrystallization with acetone. The products were identified by means of ^{1}H NMR, IR, MS and elemental analysis [24].

Analytical grade reagents sodium hydroxide, sulfuric acid, dichloromethane, acetone and methanol were used as received. β-CD (AP, Fine Chemical Products of Nankai Univ.) was recrystallized twice using deionized and tridistilled water and dried under vacuum. Tridistilled water was used throughout the experiments.

2.2. Instruments

The FT-IR spectra were recorded using Bruker Vector22 FT-IR Spectrometer. The ^{1}H NMR spectra of all compounds in $CDCl_3$ were recorded on a Varian (300 MHz) with TMS as internal standard. Mass spectra were recorded with Bruker Proflex III mass spectrometer. Elemental analyses were carried out at the Flash EA 1112. The column chromatography was performed using silica gel (100–200 mesh). Absorption spectra were recorded on an U-3010 (Hitachi, Japan) spectrophotometer using 1 cm-path quartz cells. The slit width was 5 nm. Fluorescence spectra were measured on a FL-4500 (Hitachi, Japan) spectrofluorimeter. The temperature control was achieved with the sample placed in a cell compartment whose walls were accessible to water circulation. Water from a thermostated bath was allowed to circulate through the walls of the sample compartment. The final temperature of the sample was measured by means of a thermocouple (Checktemp, Hanna, Italy) immersed in the solution (±0.1 °C). Each solution was excited near the absorption wavelength maximum using 1 cm-path quartz cells. Both the excitation and emission band passes were 10 nm for molecules **1**a, **1**b and **1**c.

2.3. Methods

Fresh sample solutions were used in the absorption and fluorescence measurements. A stock solution of β-CD was prepared with tridistilled water, and dilutions were made from this stock solution to get the different desired concentrations. In preparing these cyclodextrin solutions, the pH was maintained by adding NaOH and no buffers were used [18]. Stock solutions of **1**a, **1**b and **1**c were prepared in methanol, and 50 μl aliquots of these stock solutions were added to 5 ml of cyclodextrin solutions to maintain a final concentration of 2×10^{-6} M for fluorescence measurements and 5×10^{-5} M for absorption measurements.

3. Results and discussion

3.1. Spectral characteristics and the temperature effect on the fluorescence intensity

Similar to other substituted 3H-indoles studied before [18–23,25], molecules **1**a, **1**b and **1**c belong to the unique 3H-indolic molecules which are not rigid and whose phenyl ring can liberate within the *kT* energy barrier. This torsional movement is responsible for the geometric changes taking place in the ground and excited states and provides an important deactivation pathway for the S_1 state. This main nonradiative decay pathway can be ascribed to the formation of a nonemissive twisted intramolecular charge transfer (TICT) state originating in the amino group [26,27].

When the concentration of β-CD is slowly increased at pH 9.5 for molecule **1**a, the absorption spectra are almost unchanged [28], while the fluorescence spectra show an obvious blue shift and a large increase in the fluorescence intensity (Fig. 1). Similar phenomenon occurs for molecules **1**b and **1**c (figures not shown). Thus, one can infer that the fluorophores of molecules **1**a, **1**b and **1**c move to the hydrophobic cavity of β-CD, which prevents water from interacting with the electron lone-pair of the indolic nitrogen that can cause the reduced conjugation of the phenyl ring with the indolic moiety [26,27]. This indicates that molecules **1**a, **1**b and **1**c transfer from a polar environment to a less polar environment [18,25].

The fluorescence intensity and quantum yield of aqueous solutions are greatly influenced by temperature. Generally, both the fluorescence intensity and quantum yield increase with reducing temperature, while the absorbance remains almost unchanged. Three different mechanisms have been proposed to explain the temperature effect [29,30]. The first is the solvent interaction mechanism, in which the fluorescence quantum yield is related to the relative radiative rate and nonradiative rate in the absence of quencher in the system. The relative radiative rate is usually considered not to correlate with temperature. Therefore, only the nonradiative rate affects the fluorescence quantum yield. The viscosity of the medium is usually reduced by increasing the temperature, which results in enhancement of the chance of collision quenching between the fluorescent molecules and the solvent molecules. The second is an intramolecular energy translation mechanism, whereby the potential energy curves of the ground and excited states of the poly-atom molecules may have a tangent or intersectant point, where the excimer might translate to the potential energy curve of ground state from the potential energy curve of excited state when they

obtain extra-heat energy, and then lose the energy through oscillation relaxation. The third is an inclusion–dissociation mechanism, in which the inclusion process is entropically unfavorable and the inclusion complex may dissociate by increasing temperature, which reflects on the reduction of the fluorescence intensity and quantum yield. In order to investigate the temperature dependence in the systems of molecules **1**a, **1**b and **1**c with β-CD, the absorption and fluorescence spectra were recorded at different temperatures (see Fig. 1 for **1**a). The plot of fluorescence intensity of molecule **1**a versus temperature is shown in Fig. 2, both in the presence and absence of β-CD. It can be seen that in the presence of β-CD the fluorescence intensity is increased remarkably and the absorbance is unchanged by the reduction in temperature. However, both the fluorescence intensity and the absorbance are changed very slightly in the absence of β-CD. The first and second mechanisms apply not only in the presence but also in the absence of β-CD. So the above results suggest that the third mechanism, i.e., the inclusion–dissociation mechanism, plays a key role on the temperature dependence of inclusion complexes between molecules **1**a, **1**b and **1**c and β-CD. Further experimental evidences will be given in the following sections.

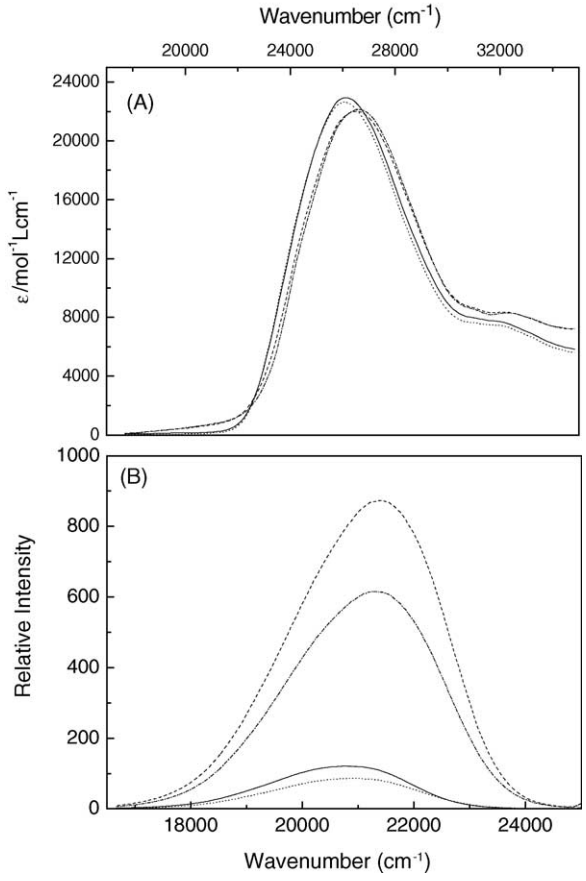


Fig. 1. Absorption (A) and fluorescence (B) spectra of **1**a in: water (solid), aqueous solution of 0.0128 M β-CD (dash) at $T = 278$ K; water (dot), aqueous solution of 0.0128 M β-CD (dash dot) at $T = 323$ K.

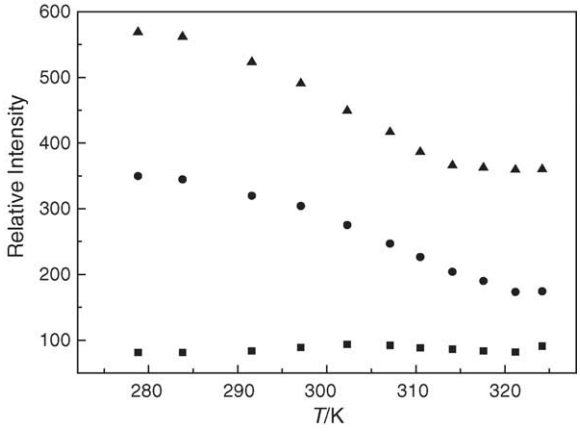


Fig. 2. Plot of the relative fluorescence intensity vs. temperature for **1**a in: water (■); aqueous solution of 0.0064 M β-CD (●); aqueous solution of 0.0128 M β-CD (▲) at pH 9.5.

3.2. Stoichiometries and association constants

In the literature, different types of inclusion complexes between β-CD and various guest molecules were well investigated using microcalorimeter, fluorescence, NMR, room-temperature phosphorescence and rayleigh light scattering [5–9,18,25,31,32]. Since the structures of molecules **1**a, **1**b and **1**c are similar to that of molecule **2**, we consider the following stepwise equilibria according to the literature [18]:

$$S + CD \overset{K_1}{\rightleftharpoons} SCD \tag{1}$$

$$SCD + CD \overset{K_2}{\rightleftharpoons} S(CD)_2 \tag{2}$$

$$S(CD)_2 + CD \overset{K_3}{\rightleftharpoons} S(CD)_3 \tag{3}$$

where S, S(CD), $S(CD)_2$ and $S(CD)_3$ represent the free fluorescent substrate, 1:1, 1:2, 1:3 inclusion complexes, respectively, while K_1, K_2 and K_3 denote the stepwise association constants.

At low concentration of fluorescence probe, the following equations concerning the fluorescence intensity in various cases have been obtained [18,26]:

Case 1. only the 1:1 complex is formed:

$$I = \frac{I_0 + I_1 K_1 [CD]_0}{1 + K_1 [CD]_0} \tag{4}$$

Case 2. the 1:1 and 1:2 complexes coexist:

$$I = \frac{I_0 + I_1 K_1 [CD]_0 + I_2 K_1 K_2 [CD]_0^2}{1 + K_1 [CD]_0 + K_1 K_2 [CD]_0^2} \tag{5}$$

Case 3. only the 1:2 complex is formed:

$$I = \frac{I_0 + I_2 K_2' [CD]_0^2}{1 + K_2' [CD]_0^2} \tag{6}$$

Case 4. only the 1:3 complex is formed:

$$I = \frac{I_0 + I_3 K'_3 [\mathrm{CD}]_0^3}{1 + K'_3 [\mathrm{CD}]_0^3} \quad (7)$$

where I_0, I_1, I_2 and I_3 denote the fluorescence intensity in pure water, in 1:1, 1:2 and 1:3 inclusion complexes, respectively, and $K'_2 = K_1 K_2$, $K'_3 = K_1 K_2 K_3$.

Fig. 3 illustrates the fluorescence intensity versus $[\mathrm{CD}]_0$ for molecules **1**a, **1**b and **1**c complexed with β-CD. All the experimental data were analyzed by Eqs. (4–7). Reasonable results (values of variables, standard errors, 95% confidence intervals, correlation coefficient and absolute sum of squares) can be obtained only when a certain equation among Eqs. (4–7) applies. And also, the Benesi–Hildebrand type double reciprocal plots should be obtained [33], i.e., $1/(I - I_0)$ versus $[\mathrm{CD}]_0{}^{-1}$, $[\mathrm{CD}]_0{}^{-2}$ and $[\mathrm{CD}]_0{}^{-3}$ should exhibit straight lines for the 1:1, 1:2 and 1:3 inclusion complexes, respectively.

As concerning with molecules **1**a and **1**b, the experimental data obtained at lower temperatures were reasonably analyzed by NLR method only when using Eq. (7) (correlation coefficients $r^2 \geq 0.995$) and $1/(I - I_0)$ versus $[\mathrm{CD}]_0{}^{-3}$ gave straight lines ($r \geq 0.995$). This implies that the 1:3 inclusion complexes are formed between **1**a, **1**b and β-CD at lower temperatures. The data obtained at higher temperatures were tested by NLR analysis according to the 1:2 inclusion complex model (Eq. (6)) and by $1/(I - I_0)$ versus $[\mathrm{CD}]_0{}^{-2}$, which gave the correlation coefficients (r^2) larger than 0.995 for the former and the correlation coefficients (r) at about 0.999 for the latter. Double reciprocal plots were illustrated in Figs. 4 and 5 for molecules **1**a and **1**b. For safety, we have considered some other cases: (1) 1:2 and 1:3 complexes coexisting in the solution; (2) 1:3 and 1:4 complexes coexisting in the solution; (3) only the 1:4 complex. However, no

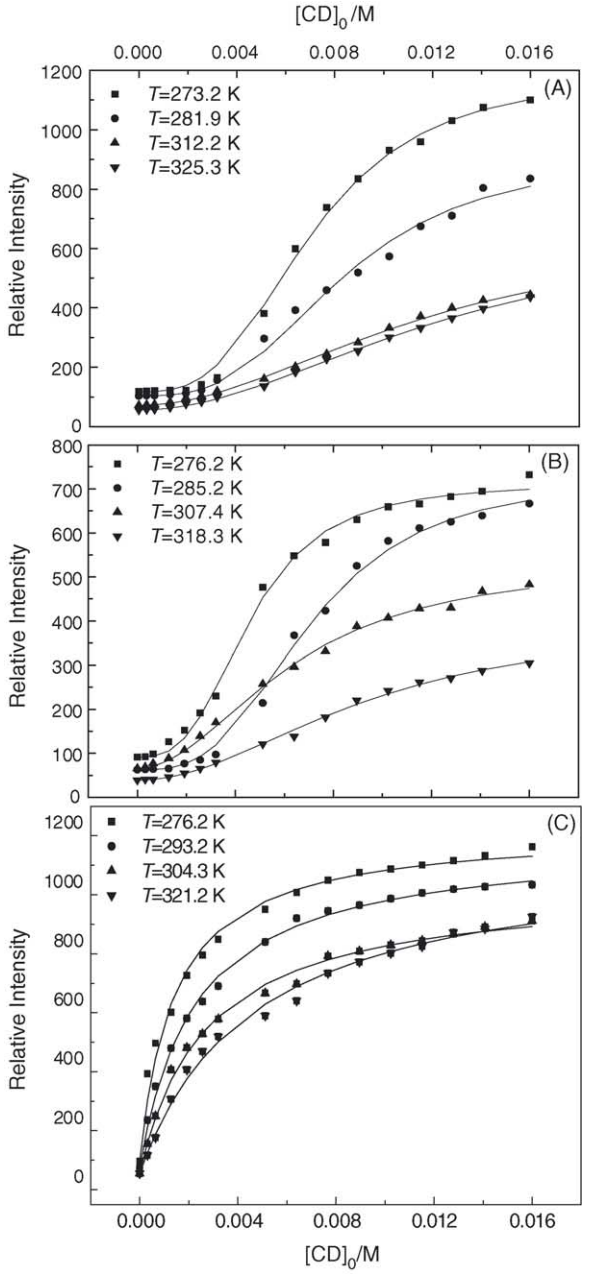


Fig. 3. Plot of the relative fluorescence intensity vs. $[\mathrm{CD}]_0$ for **1**a (A), **1**b (B) and **1**c (C) complexed with β-CD. The full line is the nonlinear regression fit to the experimental data points at different temperatures.

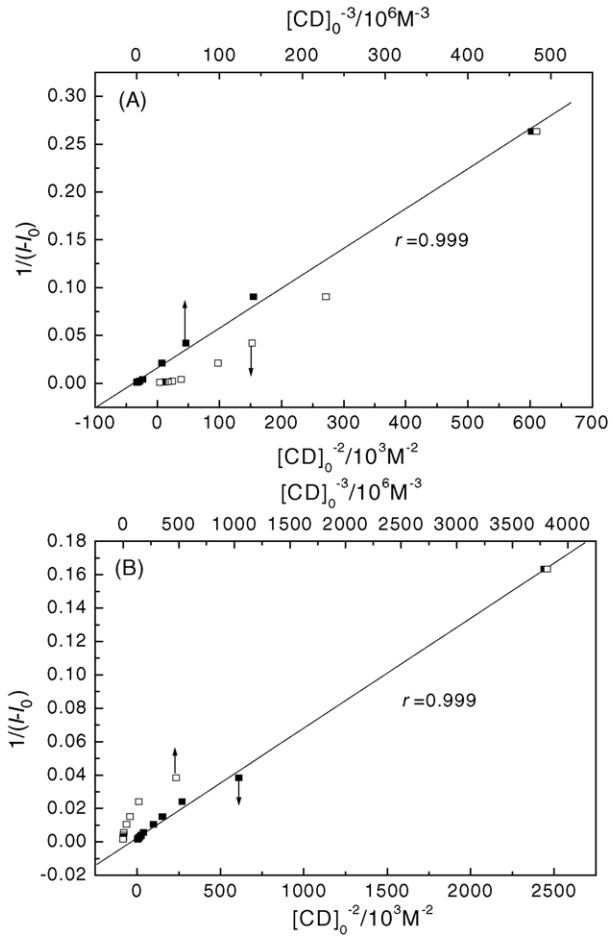


Fig. 4. $1/(I - I_0)$ as a function of $[\mathrm{CD}]_0{}^{-2}$ and $[\mathrm{CD}]_0{}^{-3}$ at different temperatures for molecule **1**a: $T = 273.2$ K (A) and $T = 312.2$ K (B), respectively.

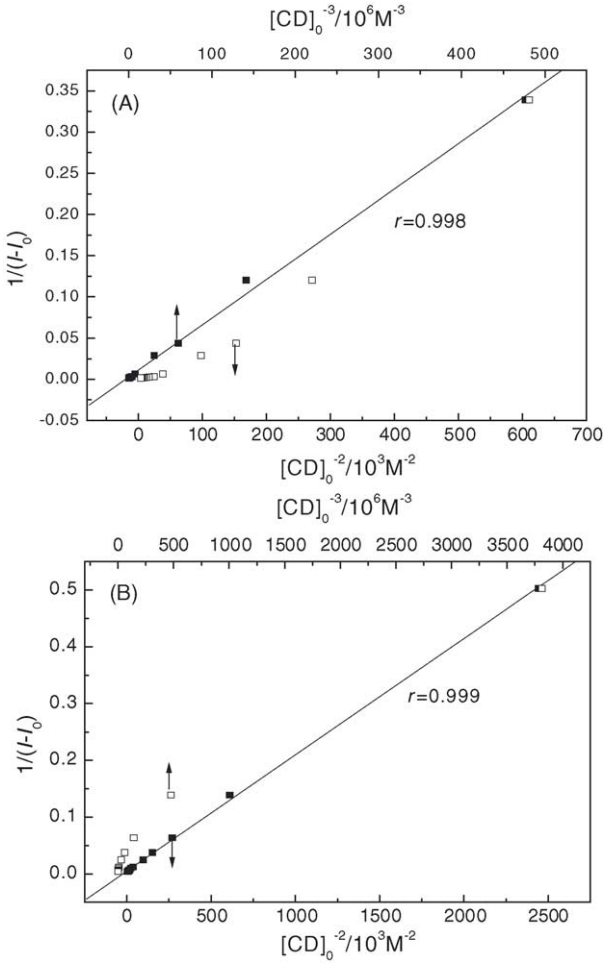


Fig. 5. $1/(I - I_0)$ as a function of $[CD]_0{}^{-2}$ and $[CD]_0{}^{-3}$ at different temperatures for molecule **1**b: $T = 285.2$ K (A) and $T = 318.3$ K (B), respectively.

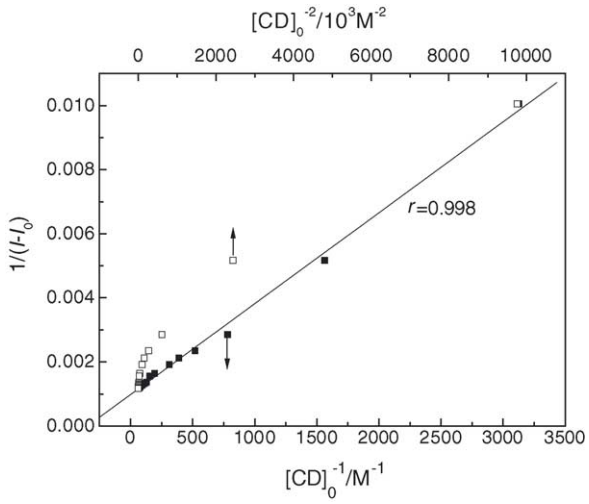


Fig. 6. $1/(I - I_0)$ as a function of $[CD]_0{}^{-1}$ and $[CD]_0{}^{-2}$ for molecule **1**c at $T = 304.3$ K.

reasonable results were obtained. All the about facts lead us to conclude that molecules **1**a and **1**b can only form the 1:3 inclusion complex at lower temperatures and that increasing temperature may result in its dissociation to the 1:2 inclusion complex.

Now, a very interesting question is raised, that is, what happened for the inclusion complexation of **1**a and **1**b at an intermediate temperature between two extreme temperatures? Actually, We have studied the inclusion behaviors for **1**a between 292.7 and 304.7 K; however, the fit according to the 1:2 and 1:3 coexisting model as well as other models did not give very reasonable results. The values of variables, standard errors, 95% confidence intervals, correlation coefficient and absolute sum of squares are not satisfied. Similar phenomenon for **1**b occurs. At the present time, we do not know the exact reason. Nevertheless, we think it should be possible for the 1:2 and 1:3 inclusion complexes to coexist at intermediate temperatures. However, it seems not easy to judge the possibility that there is a critical temperature at which all the 1:3 type changes to the 1:2 type. It should be pointed out that the "lower" and "higher" temperatures reported here are quite safe scopes for the formation of 1:3 and 1:2 inclusion complexes, respectively.

When it comes to the molecule **1**c, within the measured range of temperatures, the experimental data were well fitted only when Eq. (4) applies (Fig. 3C) and $1/(I - I_0)$ versus $[CD]_0{}^{-1}$ exhibited a straight line (Fig. 6). This indicated that the 1:1 type inclusion complex was formed between **1**c and β-CD, even though the spacer of **1**c is longer than those of **1**a and **1**b. It should be mentioned that other types of inclusion complexation model have also been analyzed carefully for molecule **1**c; however, the results were obviously not satisfied.

The association constants between molecules **1**a, **1**b and **1**c and β-CD are listed in Table 1. It can be seen that the values of K_3' and K_2' decrease when the temperature is increased, and the change extent of K_3' is much greater than that of K_2'. For molecule **1**c, the K_1 value is also reduced by the increasing of temperature and its change extent is much smaller than those of K_2' and K_3'. This reflects that the inclusion complex with higher stoichiometry is more susceptible to the temperature change. In addition, one can find that the K_2' and K_3' values of molecule **1**b are larger than the corresponding values of **1**a at similar temperatures, which seems to suggest that the longer the spacer, the easier the formation of the inclusion complex could be. Furthermore, it can be found that the K_3' values of molecules **1**a and **1**b are larger than those of molecule **2** at similar temperatures [18]. This phenomenon can be rationalized by the fact that hydrogen bonding exists between the ether oxygen in the spacers of **1**a or **1**b, and the hydrogen in the hydroxy group of β-CD.

Now, we will discuss the inclusion phenomenon of **1**c with β-CD. A question arises first, that is, why can molecule **1**c with a longer spacer only form the 1:1 inclusion complex, which is obviously contrary to the trend from **1**a to **1**b regarding the formation of inclusion complexes? The striking

Table 1
Association constants K_1, K_2' and K_3' of molecules **1**a, **1**b and **1**c with β-CD at various temperatures

Molecule	T (K)	$K_1/10^2$ M^{-1}	$K_2'/10^3$ M^{-2}	$K_3'/10^6$ M^{-3}
1a	273.2			2.80
	277.7			2.21
	281.9			1.71
	285.5			1.32
	289.7			1.09
	292.7			0.82
	304.7		9.61	
	308.3		8.50	
	312.2		7.31	
	318.2		6.42	
	325.3		5.08	
1b	276.2			12.3
	281.2			7.61
	285.2			4.79
	289.2			3.01
	293.2			2.02
	303.2		27.1	
	307.4		24.0	
	312.4		18.2	
	318.3		11.9	
	323.2		9.69	
1c	276.2	7.04		
	282.2	6.23		
	293.2	4.42		
	304.3	3.71		
	310.2	2.84		
	321.2	2.16		

feature of DEG, TEG and TTEG is that their concentrated aqueous solutions can be easily prepared. Many chemists appended variety of molecules to cylcodextrins [34] and polymer chains [35], using PEG (poly(ethylene glycol)) as a spacer to increase the hydrophilicity. The strong hydration is mainly induced by topological effect: within the helicoidal configuration of PEG, the distance between the ether oxygens (2.88 Å) in the PEG chain is almost coincident with that of the oxygens of water (2.85 Å) in a tetrahedral water lattice [36]. Cross-links among H_2O and PEG molecules are energetically favorable and each chain can fit within the H_2O structure without undergoing strong distortions [37,38]. The hydrophilic ether oxygens play a role as an acceptor in the hydrogen bond formation with the aqueous interface, whereas the apolar ethylene units are thought to reside in the interstitial cavities of the highly structured liquid water. Thus, unlike the hydrophobic interaction and the hydrogen bonding effect, the solvation energy effect is unfavorable to the formation of inclusion complexes of molecules **1**a, **1**b and **1**c with β-CD. Since the solvation energy is increased with increasing number of CH_2CH_2O unit, the hydration energy of TTEG is much higher than those of DEG and TEG [38]. This should be the reason that **1**a and **1**b can form 1:3 inclusion complexes, whereas **1**c can only form the 1:1 inclusion complex with β-CD.

3.3. Thermodynamic parameters of the inclusion complexation

On the basis of the association constants listed in Table 1, one can easily find that linear relationships between ln K and $1/T$ exist (figures not shown), where K can be K_1, K_2' or K_3'. According to the van't Hoff equation:

$$\ln K = -\frac{\Delta H}{RT} + \frac{\Delta S}{R} \tag{8}$$

Thermodynamic parameters ΔH, ΔS of the inclusion complexation and then ΔG have been obtained (see Table 2).

Negative ΔG values strongly suggest that the inclusion processes proceed spontaneously, while negative ΔH and ΔS values mean that the inclusion complexation is exothermic and enthalpy-controlled, but not entropy-driven. This is the common situation concerning the formation of inclusion complexes between cyclodextrins and various guest molecules. It is widely accepted that the negative entropy change is due to the steric barrier caused by molecular geometrical shape and the limit of β-CD cavity to the freedom of shift and rotation of guest molecules. It should also be pointed out here that the replacement of one or more water molecules existing in the cyclodextrin cavity by a certain guest molecule will cause positive ΔS; however, this effect is usually not predominant. For the interactions between molecules **1**a, **1**b, **1**c and β-CD, the negative ΔS values are unfavorable to the formation of the inclusion complexes. Fortunately, this unfavorable effect is overcome by the more negative values of ΔH leading to energetically favorable values, i.e., negative values of ΔG. To our knowledge, the compensatory phenomenon between ΔH and ΔS for the 1:1 inclusion complex of cyclodextrin has been well investigated in the past [5–9]; however, that for the 1:3 inclusion complex was seldom reported before.

The analysis on the ΔH, ΔS and ΔG values compiled in Table 2 will help understanding the different interaction pattern of **1**c with β-CD from those of **1**a, **1**b with β-CD. For the 1:2 inclusion complexes from **1**a to **1**b, $\Delta(\Delta H) = -19.5\,\text{kJ mol}^{-1}$, $\Delta(\Delta S) = -55.3\,\text{J mol}^{-1}\,\text{K}^{-1}$. The large difference of ΔH ($\Delta(\Delta H)$) is compensated by the large difference of ΔS ($\Delta(\Delta S)$), leading to the similar ΔG values ($\Delta(\Delta G) = -3.0\,\text{kJ mol}^{-1}$) within experimental error. For the 1:3 inclusion complexes from **1**a to **1**b, $\Delta(\Delta H) = -31.6\,\text{kJ mol}^{-1}$, $\Delta(\Delta S) = -100.2\,\text{J mol}^{-1}\,\text{K}^{-1}$, $\Delta(\Delta G) = -1.8\,\text{kJ mol}^{-1}$. It can be seen that the above compensatory effect for the 1:3 inclusion complexes from **1**a to **1**b is more remarkable than that for 1:2 inclusion complexes from **1**a to **1**b. In other words, for both of the 1:2 and the 1:3 inclusion complexes, the compensatory effect of ΔS on ΔH concerning **1**b is larger than that concerning **1**a. Now, it should be reasonable to assume that the compensatory effect of ΔS on ΔH concerning **1**c would be too large for the 1:2 or 1:3 inclusion complexes to be formed. This is the reason why only the 1:1 inclusion complex between **1**c and β-CD can be formed.

Table 2
ΔH, ΔS and ΔG (298 K) values for the 1:1, 1:2 and 1:3 inclusion complexes of molecules **1**a, **1**b and **1**c with β-CD

Molecule	Complex type	ΔH (kJ mol^{-1})	ΔS (J mol^{-1} K^{-1})	ΔG (kJ mol^{-1})
1a	1:2	−24.9	−5.7	−23.2
	1:3	−41.1	−26.8	−33.1
1b	1:2	−44.4	−61.0	−26.2
	1:3	−72.7	−127	−34.9
1c	1:1	−19.3	−15.0	−14.8

3.4. The structure characteristic of the inclusion complexes

It was found that neutral substituted 3H-indole, e.g., molecule **3**, can form 1:2 inclusion complexes with β-CD [25,26a,26b]. In the 1:2 inclusion complex, a substituted 3H-indole molecule is totally entrapped in the cavities of β-CD except for the junction of the two cyclodextrins, in which the indolic nitrogen of the 3H-indole is close to the "alcoholic" secondary rims of two macrocycles [25a]. According to our previous study [18], there is no different absorption and fluorescence behaviors between molecule **2** and it homologue [2-(*p*-hexylamino)phenyl-3,3-dimethyl-5-ethoxycarbonyl-3H-indole] trimethylammonium iodide (**8**) and these two cationic substituted 3H-indoles can form the 1:3 inclusion complexes with β-CD. Since the stopper groups exist in the left side of molecule **2** (see Scheme 1), three β-CD molecules should accommodate molecule **2** from its right side. Besides the two β-CD molecules residing in similar locations to those in the 1:2 inclusion complex between the neutral substituted 3H-indole molecule **3** and β-CD, the β-CD molecule accommodating molecule **2** first should be located in the linear part between the cationic nitrogen and the amino nitrogen. In this case, the 1:3 inclusion complex is actually a semi-rotaxane. For molecules **1**a, **1**b and **8** with β-CD, the 1:3 inclusion complexes are also believed to exhibit the structure of a semi-rotaxane. However, there are no direct evidences confirming the structure of the 1:2 inclusion complexes between **1**a, **1**b and β-CD and of the 1:1 inclusion complex between **1**c and β-CD. Here, we suppose that in the 1:2 inclusion complexes of **1**a and **1**b, the two β-CD molecules residing in similar locations to those in the 1:2 inclusion complex of **8**, while the linear ethyloxyethylene chain is in the aqueous environment. We also suppose that in the 1:1 inclusion complex of **1**c, the unique β-CD molecule resides in the part from the indolic nitrogen to the right side of molecule **1**c.

4. Concluding remarks

Molecules **1**a, **1**b and **1**c, which possess different lengths of oligo(ethylene glycol) chains as spacers, were synthesized and characterized. The investigation by absorption and fluorescence measurements showed that molecules **1**a and **1**b can form 1:3 inclusion complexes with β-CD at lower temperatures and increasing temperatures may lead to gradually dissociating to 1:2 inclusion complexes. Since hydration energy is increased with increasing the number of CH_3CH_2O unit, molecule **1**c with a longer spacer can only form the 1:1 inclusion complex. The association constants of molecules **1**a, **1**b and **1**c with β-CD at different temperatures showed that an inclusion complex with higher stoichiometry is more susceptible to the temperature change. The thermodynamic parameters were calculated according to van't Hoff equation. The negative entropy and enthalpy changes indicated that the formation of above inclusion complexes is entropically unfavorable and enthalpy-driven. From the viewpoint of thermodynamics, the compensatory effect of $T\Delta S$ on ΔH causes the temperature-dependent inclusion–dissociation behavior of the inclusion complexes of **1**a, **1**b with β-CD. When **1**c interacting β-CD, the compensatory effect is too large for the 1:2 and 1:3 inclusion complexes to be formed.

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References

[1] S. Li, W.C. Purdy, Chem. Rev. 92 (1992) 1457.
[2] J. Szejtli, Cyclodextrin Technology, Kluwer Academic Publishers, Dordrecht, The Netherlands, 1988.
[3] M.L. Bender, M. Komiyama, Cyclodextrin Chemistry, Springer-Verlag, Berlin, 1978.
[4] A.F. Danil de Namor, R. Traboulssi, D.F.V. Lewis, J. Am. Chem. Soc. 112 (1990) 8442.
[5] M.V. Rekharsky, Y. Inoue, Chem. Rev. 98 (1998) 1875.
[6] Y. Inoue, T. Hakushi, Y. Liu, L. Tong, B. Shen, D. Jin, J. Am. Chem. Soc. 115 (1993) 475.
[7] Y. Inoue, Y. Liu, L. Tong, B. Shen, D. Jin, J. Am. Chem. Soc. 115 (1993) 10637.
[8] M.V. Rekharsky, M.P. Mayhew, R.N. Goldberg, P.D. Ross, Y. Yamashoji, Y. Inoue, J. Phys. Chem. B 101 (1997) 87.
[9] M.V. Rekharsky, R.N. Goldberg, F.P. Schwarz, Y.B. Tewari, P.D. Ross, Y. Yamashoji, Y. Inoue, J. Am. Chem. Soc. 117 (1995) 8830.
[10] J.E. Leffler, J. Org. Chem. 20 (1955) 1202.
[11] I. Tabushi, Y. Kiyosuke, T. Sugimoto, K. Yamamura, J. Am. Chem. Soc. 100 (1978) 916.

[12] P.K. Zarzycki, H. Lamparczyk, J. Chem. Educ. 73 (1996) 459.
[13] (a) M. Saito, T. Shimomura, Y. Okumura, K. Ito, J. Chem. Phys. 114 (2001) 1;
(b) Y. Okumura, K. Ito, R. Hayakawa, Phys. Rev. Lett. 80 (1998) 5003.
[14] (a) C. Zhang, Ph.D. Thesis, Peking University, Beijing, 2002;
(b) C. Zhang, X. Shen, H. Gao, Spectrosc. Spect. Anal. 23 (2003) 217;
(c) C. Zhang, X. Shen, H. Gao, Chem. Phys. Lett. 363 (2002) 515.
[15] P.V. Demarco, A.L. Thakkar, Chem. Commun. (1970) 2.
[16] F. Cramer, W. Saenger, H. Spatz, J. Am. Chem. Soc. 89 (1967) 14.
[17] R.P. Rohrbach, L.J. Rodriguez, E.M. Eyring, J.F. Wojcik, J. Phys. Chem. 81 (1977) 944.
[18] (a) X. Shen, M. Belletête, G. Durocher, J. Phys. Chem. B 102 (1998) 1877;
(b) X. Shen, M. Belletête, G. Durocher, Chem. Phys. Lett. 301 (1999) 193.
[19] (a) H. Asanuma, M. Kakazu, M. Shibata, T. Hishiya, M. Komiyama, Chem. Commun. (1997) 1971;
(b) P. Claudy, J.M. Letoffe, P. Germain, J.P. Bastide, A. Bayol, S. Blasquez, R.C. Rao, B. Gonzalez, J. Thermal Anal. 37 (1991) 2497.
[20] T. Xu, X. Shen, H. Gao, Chinese Chem. Lett. 15 (2004) 26.
[21] P. Skrabal, J. Steiger, H. Zellinger, Helv. Chim. Acta 58 (1975) 800.
[22] A. Popowycz, M.Sc. Thesis, University of Montreal, Montreal, 1991.
[23] J. Martin, D. Johannes, Acta Chem. Scand. Serb. B 36 (1982) 241.
[24] Notes: **7**a ($n=1$, 61.1%): IR (KBr, ν/cm^{-1}): 3454, 2919, 2850, 1638, 1469, 1311, 1125, 777. ^{1}H NMR (300 MHz, $CDCl_3$) δ/ppm: 0.88 (t, 6H, –CH_3), 1.26–1.90 (m, 56H, –CH_2–, –CH_3), 3.25–4.30 (m, 15H, –CH_2O–, –CH_2N–, CH_3N–). MS *m*/*z*: 679 (M^+-I+1). **7**b ($n=2$, 56.4%): IR (KBr, ν/cm^{-1}): 3451, 2919, 2851, 1636, 1470, 1351, 1310, 1110, 777. ^{1}H NMR (300 MHz, $CDCl_3$) δ/ppm: 0.88 (t, 6H, –CH_3), 1.25–1.70 (m, 56H, –CH_2–, –CH_3), 3.27–4.02 (m, 19H, –CH_2O–, –CH_2N–, CH_3N–). MS *m*/*z*: 723 (M^+-I+1). **7**c ($n=3$, 57.3%): IR (KBr, ν/cm^{-1}): 3453, 2918, 2851, 1639, 1470, 1311, 778. ^{1}H NMR (300 MHz, $CDCl_3$) δ/ppm: 0.86 (t, 6H, –CH_3), 1.26–2.00 (m, 56H, –CH_2–, –CH_3), 3.27 (t, 2H, –CH_2N–), 3.34 (s, 4H, CH_3N–), 3.48 (t, 4H, –CH_2N–), 3.64–3.76 (m, 14H, –CH_2O–). MS *m*/*z*: 767 (M^+-I+1). **1**a (32.9%): IR (KBr, ν/cm^{-1}): 3301, 2923, 2852, 1717, 1606, 1463, 1343, 1283, 1231, 1105, 780. ^{1}H NMR (300 MHz, $CDCl_3$) δ/ppm: 0.88 (t, 6H, –CH_3), 1.21–1.67 (m, 65H, –CH_2–, –CH_3), 3.32–4.10 (m, 17H, –CH_2O–), 4.38 (q, 2H, –CH_2O–), 6.81 (d, ^{1}H, Ar-H), 7.61–7.90 (d, 2H, Ar-H), 8.04 (m, 3H, Ar-H), 8.36 (s, ^{1}H, Ar-H). MS *m*/*z*: 859 (M^+-I+1). Anal. Calcd. (%) for $C_{56}H_{96}N_3O_3I{\cdot}2H_2O$: C, 65.82; H, 9.79; N, 4.11. Found: C, 65.91; H, 9.86; N, 3.81. **1**b (23.9%): IR (KBr, ν/cm^{-1}): 3474, 2923, 2852, 1717, 1607, 1463, 1341, 1284, 1232, 1105, 781. ^{1}H NMR (300 MHz, $CDCl_3$) δ/ppm: 0.87 (t, 6H, –CH_3), 1.24–1.65 (m, 65H, –CH_2–, –CH_3), 3.25–4.03 (m, 22H, –CH_2O–), 4.39 (q, 2H, –CH_2O–), 6.80 (d, ^{1}H, Ar-H), 7.60–7.79 (d, 2H, Ar-H), 8.06 (m, 2H, Ar-H), 8.35 (2H, s, Ar-H). MS *m*/*z*: 903 (M^+-I+1). Anal. Calcd. (%) for $C_{58}H_{100}N_3O_4I{\cdot}3H_2O$: C, 64.27; H, 9.79; N, 3.88. Found: C, 64.10; H, 9.85; N, 3.52. **1**c (20.5%): IR (KBr, ν/cm^{-1}): 3411, 2927, 2852, 1714, 1605, 1529, 1462, 1348, 1284, 1231, 1107, 781, 750. ^{1}H NMR (300 MHz, $CDCl_3$) δ/ppm: 0.88 (t, 6H, –CH_3), 1.13–1.66 (m, 65H, –CH_2–, –CH_3), 3.32–4.00 (m, 26H, –CH_2O–), 4.38 (q, 2H, –CH_2O–), 6.76 (d, ^{1}H, Ar-H), 7.50–7.80 (d, 2H, Ar-H), 8.05 (m, 2H, Ar-H), 8.36 (s, 2H, Ar-H). MS *m*/*z*: 946 (M^+-I+1). Anal. Calcd. (%) for $C_{60}H_{104}N_3O_5I{\cdot}3H_2O$: C, 63.89; H, 9.76; N, 3.73. Found: C, 63.60; H, 9.63; N, 3.65.
[25] (a) S. Nigam, G. Durocher, J. Phys. Chem. 100 (1996) 7135;
(b) S. Nigam, G. Durocher, J. Photochem. Photobiol. A: Chem. 103 (1997) 143.
[26] (a) X. Shen, M. Belletête, G. Durocher, J. Phys. Chem. B 101 (1997) 8212;
(b) X. Shen, M. Belletête, G. Durocher, Langmuir 13 (1997) 5830;
(c) X. Shen, M. Belletête, G. Durocher, Chem. Phys. Lett. 298 (1998) 201.
[27] M. Belletête, R.S. Sarpal, G. Durocher, Can. J. Chem. 72 (1994) 2239.
[28] The absorbance values are with some errors due to the scattering in the absorption spectra resulting from the large size of the 1:3 inclusion complexes (see Ref. 18a and see also: J.F. Rabeh, Experimental Methods in Polymer Chemistry, J. Wiley & Sons, New York, 1980, pp. 191).
[29] G.G. Guilbault, Practical Fluorescence, Marcel Dekker, New York, 1973.
[30] C.A. Parker, Photoluminescence of Solution, Elsevier, Amsterdam, 1968.
[31] (a) R. Yang, K. Li, K. Wang, F. Liu, N. Li, F. Zhao, Spectrochim. Acta A 59 (2003) 153;
(b) S. Hamai, J. Phys. Chem. B 103 (1999) 293;
(c) S. Hamai, J. Phys. Chem. B 101 (1997) 1707;
(d) D.R. Alston, T.H. Lilley, J.F. Stoddart, J. Chem. Soc., Chem. Commun. (1985) 1600;
(e) J. Li, Y. Wei, L. Ding, C. Dong, Spectrochim. Acta A 59 (2003) 2759.
[32] (a) H. Gharibi, S. Jalili, T. Rajabi, Colloids Surf. A 175 (2000) 361;
(b) J. Peeters, P. Neeskens, J. Adriaensen, M. Brewster, J. Incl. Phenom. Macro. 44 (2002) 75.
[33] H.A. Benesi, J.H. Hildebrand, J. Am. Chem. Soc. 71 (1949) 2703.
[34] H.F.M. Nelissen, F. Venema, R.M. Uittenbogaard, M.C. Feiters, R.J.M. Nolte, J. Chem. Soc. Perkin Trans. 2 (1997) 2045.
[35] A. Benrebouh, Y.H. Zhang, X.X. Zhu, Maromol. Rapid Commun. 21 (2000) 685.
[36] T.W.N. Bieze, A.C. Barnes, C.J.M. Huige, J.E. Enderby, J.C. Leyte, J. Phys. Chem. 98 (1994) 6568.
[37] K.J. Liu, J.L. Parsons, Macromolecules 2 (1969) 529.
[38] D. Rudan-Tasic, C. Klofutar, J. Mol. Liquid 103/104 (2003) 187.