Study of inclusion complex of β-cyclodextrin and nitrobenzene

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Abstract

β-cyclodextrin can react with nitrobenzene to form an inclusion complex which is characterized by ^{1}H NMR and powder X-ray diffractometry. The ratio of β-CD to NB in inclusion complex is determined as 1:1. At 25 °C, the dissociated constant, K_D, of the inclusion complex is measured as 6.5×10^{-3} M in neutral solution (pH = 7.0), but in alkali (pH = 13.5), K_D is 3.2×10^{-2} M which is much larger than that measured in neutral.
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1. Introduction

Cyclodextrins (CDs) are cyclic oligosaccharides made up of six to twelve α-D-glucopyranose monomers connected at 1 and 4 carbon atoms. CDs with 6–8 α-D-glucopyranose units are denoted α-, β-, and γ-CDs, respectively. They have the property of forming inclusion complex with various guest molecules with suitable polarity and dimension because of their special molecular structure—hydrophobic internal cavity and hydrophilic external surface (Connors, 1997; Szejtli, 1998). It has been demonstrated that several weak forces, including van der Waals, hydrophobic, dipole–dipole, and hydrogen bonding interactions, cooperatively determine the inclusion complex behavior of the cyclodextrin host (Inoue et al., 1993a,b). Thus CDs have been widely used in pharmaceutical industry (Tavornvipas et al., 2002),

foodstuff (Padukka et al., 2000; Szente and Szejtli, 2004), separate technique (Schneiderman and Stalcup, 2000; Perrin et al., 2003), and environmental protection (Morillo et al., 2001; Jozefaciuk et al., 2003), and so on.

Nitrobenzene is often used to produce intermediate of dye, pesticide, and detonator. However, it is also one of serious organic contaminations. Environmental Protection Agency (EPA) regulates that nitrobenzene, 2,4-dinitromethylbenzene and 2,6-dinitromethylbenzene are prior for detection. However, it is usually difficult to treat industrial waste and living sewage. In most cases, the complicated equipments are needed and cost much for the treatment of contaminations. To solve the problem, environmental scientists are striving their way to work out effective and economic methods to treat the pollutions. Cyclodextrins can increase the solubility of some contaminations (Boving and Brusseau, 2000; Manolikar and Sawant, 2003), reduce their toxicity, and catalyze their decomposition (Bardi et al., 2000; Kamiya et al., 2001). In this article, the writers focus on the interaction between β-cyclodextrin and nitrobenzene at different conditions. The results showed that

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β-cyclodextrin and nitrobenzene can form an inclusion complex, which makes the solubility of nitrobenzene in water increase. The dissociated constant of the inclusion complex at different acidity shows the inclusion complex becomes unstable at alkali.

2. Experimental

2.1. Reagents

β-Cyclodextrin (β-CD, Shanghai Chemical Reagents Company) was purified by twice recrystallization before using. Nitrobenzene (NB, Shanghai Chemical Reagents Company) and other chemical reagents were of analytical reagent grade and used as commercial. Double distilled and sterilized water was used to prepare all solution.

2.2. Apparatus

Powder X-ray diffraction spectrum was taken by M03XFH (MAC Science) diffractometer. ^1H NMR spectrum was taken with Bruker AV 600 MHz spectrometer. The UV–vis spectrum was recorded on a UV-2550 (Shimazu, Japan) double-beam spectra photometer equipped with a stoppered quartz cell with 1.0 cm optical path length.

Eletrochemical experiments were performed with CHI660a electrochemical work station (Shanghai Chenhua, China) equipped with a three-electrode jacked cell. Platinum disc electrode (diameter: 1 mm) is served as a working electrode. Reference and counter electrodes were saturated calomel electrode (SCE) and platinum wire electrode, respectively. All experiments were carried out at 25 ± 0.1 °C. The working electrode was polished to a mirror with 0.05 μm alumina aqueous slurry, and rinsed with double distilled and sterilized water before each experiment. The supporting electrolyte was 0.1 M KNO_3.

2.3. Synthesis of inclusion complex

1.00 g β-CD and 0.108 g NB were dissolved by 60 ml double distilled water and 1 ml CH_3OH, respectively. Then NB-CH_3OH solution was slowly dropped into β-CD aqueous solution with sufficiently stirring. The stirring operation was kept for at least 24 h at room temperature. At the end of the reaction, a great deal of white crystal precipitate, inclusion complex of NB and β-CD, was obtained by filtrating. The product was washed with methanol and water for three times in turn, respectively, to clean the residual guest and host monomers. Then it was dried in a vacuum oven at 50 °C for 48 h.

The product was confirmed by powder X-ray diffractometry and ^1H NMR spectra.

2.4. Solubility experiment

The excess NB was put into different concentration of β-CD aqueous solution and shaken intensively with a laboratory vibrator (180 rpm) for 24 h at 25 °C. Then the solution was centrifuged and superstratum liquid was removed and diluted with 1:1 CH_3OH aqueous solution. In the solution, whole the inclusion complex decomposed according to Cao et al. (2002). Then the concentration of NB was determined by UV–vis spectrum.

3. Results and discussion

3.1. Powder X-ray diffraction spectrum

The formation of the inclusion complex can be confirmed by X-ray diffractometry (Pralhad and Rajendrakumar, 2004; Scalia et al., 2004). Fig. 1 is the powder X-ray diffraction spectrum of β-CD monomer and inclusion complex. The X-ray spectrum of the inclusion complex shown in Fig. 1b was evidently different from that of β-CD monomer itself shown in Fig. 1a. The difference between both spectra of β-CD and inclusion complex is due to the interaction of β-CD with NB and formed a new crystal structure.

3.2. ^1H NMR spectrum

Direct evidence for the formation of inclusion complex can be obtained from ^1H NMR (Schneider et al., 1998) and ^{13}C NMR (O'Brien and Moyna, 2004) spectra. In addition, from ^1H NMR and ^{13}C NMR, the information of the stoichiometry, stability, and structure
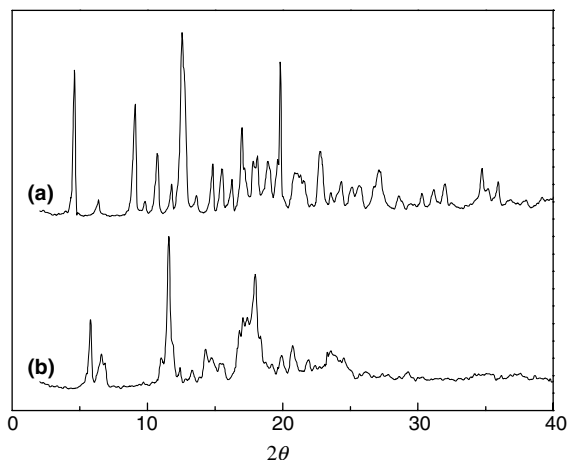

Fig. 1. Powder X-ray diffraction spectra of β-CD (a) and the inclusion complex (b).

of CD complexes can be obtained (Schneider et al., 1998; Wimmer et al., 2002; Cao et al., 2003). Fig. 2 showed the typical ^{1}H NMR spectra of NB in CD$_3$OD, β-CD and the inclusion complex of NB with β-CD in D$_2$O. The significant distinguish for these ^{1}H NMR spectra strongly confirmed that the inclusion complex formed. The values of chemical shifts, δ for different protons in β-CD, NB and NB-β-CD inclusion complex were listed in Tables 1 and 2.

It can be seen from the ^{1}H NMR that in inclusion complex, a great upfield shift was occurred for H3 and H5, which locate in the cavity of β-CD (Fig. 3). In addition, the signal of H5 was split into doublets (Fig. 4b). The changes of chemical shift (Δδ) of H3 and H5 suggested that the NB monomer completely entered into the hydro-

phobic cavity of β-CD. The phenyl ring of NB made the signals of protons (H3 and H5), upfield shift. On the contrary, the chemical shifts of H1, H2, H4, and H6ab, which are on the outer surface of β-CD and the narrow opening of β-CD as shown as in Fig. 3, were only slightly affected by the guest molecule. Similarly, the chemical shifts of Ha, Hb and Hc of NB locate in the hydrophobic cavity of β-CD was also moved in upfield significantly because the interaction between NB and β-CD. On the other hand, as shown as in Fig. 4d, when NB monomer entered into the hydrophobic cavity of β-CD, the change of the micro-environment of NB protons leaded the phenyl ring proton signals split.

The ratio of NB to β-CD in inclusion complex can be determined by the peak area of proton of NB and β-CD

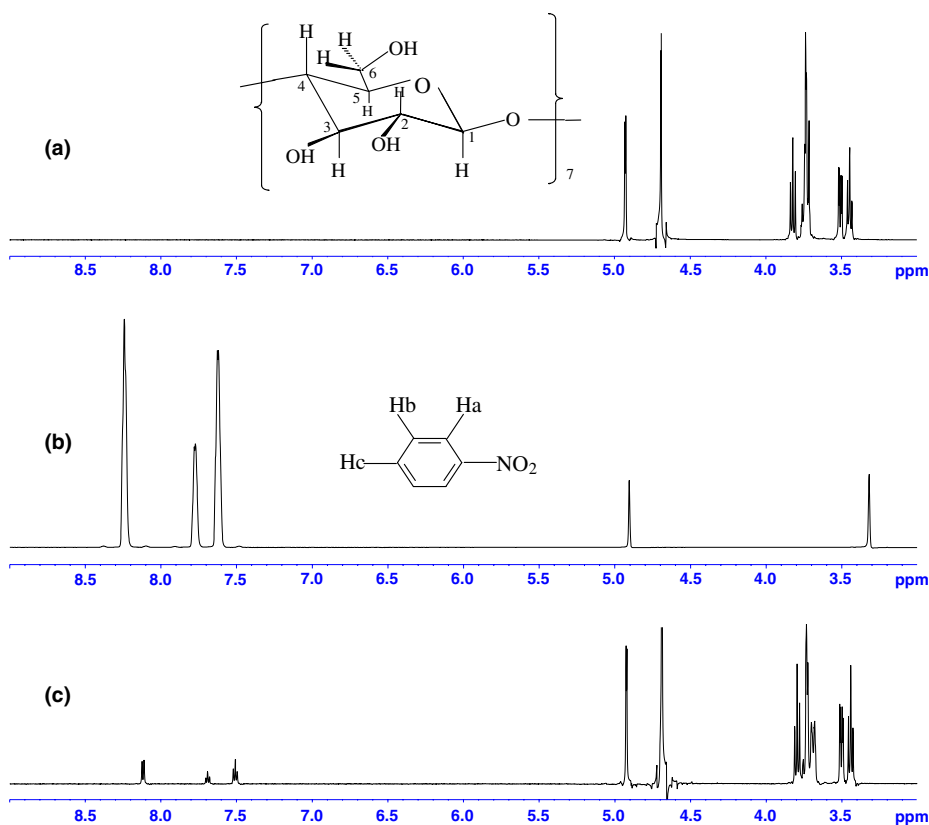Fig. 2. ^{1}H NMR spectra of (a) β-CD, (b) NB, and (c) the inclusion complex.

Table 1
Chemical shift δ and Δδ of protons of β-CD in free host and inclusion complex

	H1[a]	H2	H3	H4	H5	H6ab
β-CD	4.9296	3.5085	3.8376	3.4461	3.7152	3.7318
NB–β-CD	4.9242	3.5037	3.7959	3.4418	3.6798	3.7252
Δδ	−0.0054	−0.0048	−0.0417	−0.0043	−0.0454	−0.0066

[a] The hydrogen atom was labeled in Fig. 2a.

Table 2
Chemical shift δ and $\Delta\delta$ of protons of NB in free guest and inclusion complex

	Ha[a]	Hb	Hc
NB	8.2431	7.6235	7.7761
NB–β-CD	8.1193	7.5094	7.6924
$\Delta\delta$	−0.1238	−0.1141	−0.0837

[a] The hydrogen atom was labeled in Fig. 2b.

in inclusion complex, respectively. The number of the proton located at different position was measured and tabulated in Table 3. The theoretical value is also listed in Table 3 assuming 1:1 ratio of NB to β-CD in inclusion complex. The experimental results were closed to the theoretical value, which confirms that the ratio of NB to β-CD in inclusion complex is 1:1. The experimental value of protons in β-CD (H1–H6) is 20% higher than

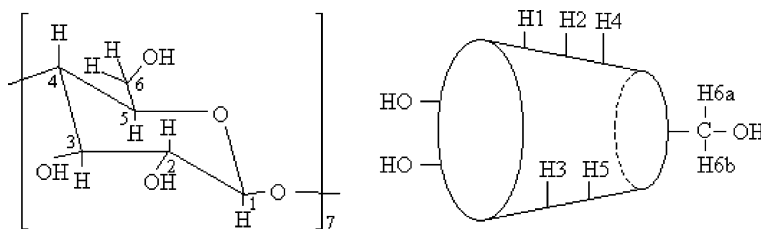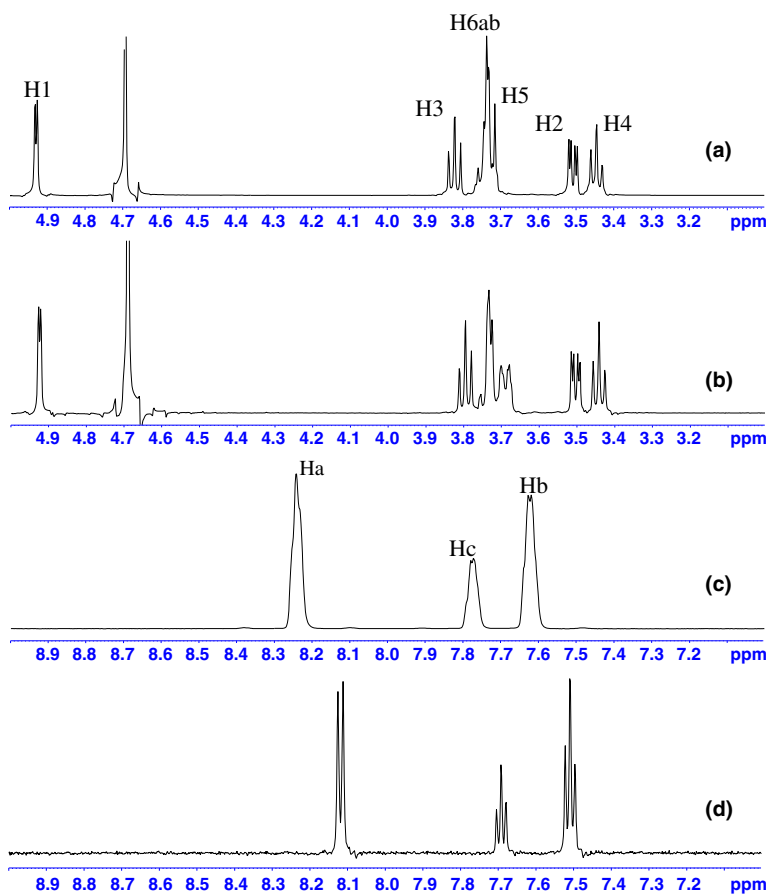Fig. 3. The scheme of stereo-configuration, truncated-cone of β-CD.

Fig. 4. ¹H NMR spectra of (a) β-CD and (b) the inclusion complex (chemical shift from 3 to 5 ppm); (c) NB and (d) the inclusion complex (chemical shift from 7 to 9 ppm).

Table 3
The number of the protons determined by ^{1}H NMR

	Ha	Hb	Hc	H1	H2	H3	H4	H5 + H6ab
Experiment	2.06	2.17	1.00	8.39	8.29	8.51	8.79	25.89
Theoretical[a]	2	2	1	7	7	7	7	21

[a] Assuming 1:1 ratio of β-CD and NB in inclusion complex.

the theoretical value, which maybe owe to the residual of β-CD monomer existed in inclusion complex.

3.3. Dissociated constant of inclusion complex

The formation of the inclusion complex of NB and β-CD in neutral solution (pH = 7.0) can be confirmed by UV–vis spectrum shown in Fig. 5. The peak position was independent of the addition of β-CD. However, the peak intensity increased with β-CD, which showed that the molar absorption coefficient of the inclusion complex was larger than that of NB itself. Assuming the ratio of NB to β-CD in inclusion complex is 1:1, then the formation of the inclusion complex can be described as follows:

$$H + G = HG \qquad (1)$$

where H represents the host, β-CD, G the guest, NB, and HG the inclusion complex. If the initial concentrations of H and G are $[H]_0$ and $[G]_0$, respectively, and $[H]_0 \gg [G]_0$, the concentration of HG at equilibrium is x, then
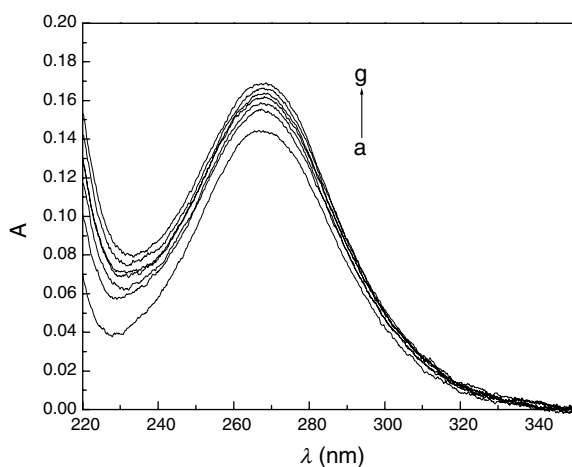
$$K_D = \frac{([G]_0 - x)([H]_0 - x)}{x} \qquad (2)$$

Fig. 5. At 25 °C, UV–vis spectra of 19.5 µM NB aqueous solution (pH = 7.0) with different concentrations of β-CD. $c_{\beta-CD}$ (mM): (a) 0; (b) 2.01; (c) 2.98; (d) 3.88; (e) 4.88; (f) 5.89; (g) 6.83.

where K_D is the dissociated constant of the inclusion complex. Taking account of the optical path length, $l = 1.0$ cm, the UV–vis absorbance at a given wavelength can be described as follows:

$$A = \varepsilon_H([H]_0 - x) + \varepsilon_G([G]_0 - x) + \varepsilon_{HG}x \qquad (3)$$

where ε_H, ε_G and ε_{HG} are molar absorption coefficients of H, G and HG, respectively.

Because $[H]_0 \gg [G]_0$, therefore, $[H]_0 \gg x$. Combining Eq. (2) with Eq. (3), we have

$$\frac{A - \varepsilon_H[H]_0 - \varepsilon_G[G]_0}{\varepsilon_{HG} - \varepsilon_G} = \frac{[H]_0[G]_0}{K_D + [H]_0} \qquad (4)$$

There is almost no absorbance when wavelength ranges from 220 to 350 nm for β-CD, ε_H can be negligible comparing to ε_G and ε_{HG}. Let $\Delta A = A - \varepsilon_G[G]_0$, $\Delta \varepsilon = \varepsilon_{HG} - \varepsilon_G$, Eq. (4) can be rearranged as

$$\frac{[H]_0[G]_0}{\Delta A} = \frac{[H]_0}{\Delta \varepsilon} + \frac{K_D}{\Delta \varepsilon} \qquad (5)$$

Plotting $[H]_0[G]_0/\Delta A$ versus $[H]_0$, a straight line can be obtained. The experimental result was shown in Fig. 6. The linear relationship between $[H]_0[G]_0/\Delta A$ and $[H]_0$ showed that the assumption of 1:1 ratio of NB to β-CD in inclusion complex was correct. According to the slope and the intercept of the line, the dissociated constant, K_D, of the inclusion complex was evaluated as 6.8 mM and $\Delta \varepsilon$ is 2.5 mM^{-1} cm^{-1}. Taking account of the molar absorption coefficient of NB (7.0 mM^{-1} cm^{-1}), the molar
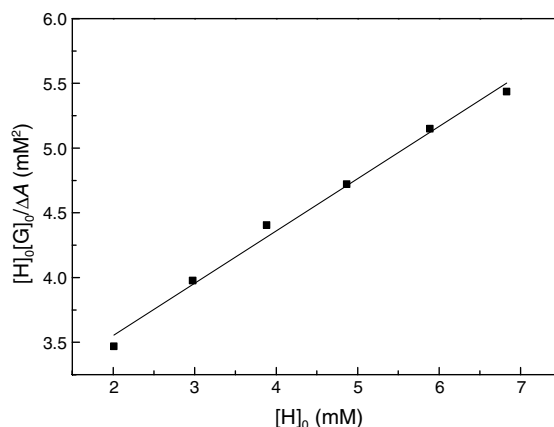

Fig. 6. The plot of $[H]_0[G]_0/\Delta A$ versus $[H]_0$.

absorption of inclusion complex can be calculated as $9.5\,\mathrm{mM^{-1}\,cm^{-1}}$.

The formation of inclusion complex of NB and β-CD was also confirmed by electrochemical method. The electrochemical behavior of NB has been widely researched (Vassiliev et al., 1981; Rubinstein, 1985). If β-CD interacted with NB, different electrochemical properties would be observed. The effect of β-CD on the electrochemical reaction of NB would be discussed next paragraph.

First, some β-CD was put into NB neutral aqueous solution (pH = 7.0) with sufficiently stirring. Then the cyclic voltammograms were recorded after the solution kept static for at least 24 h and shown in Fig. 7. The cathodic peak current, i_{cp}, decreased slightly with β-CD increasing. The cathodic peak potential, E_{cp}, shifted in negative direction when β-CD increased. The result showed that the inclusion complex between β-CD and NB was formed when β-CD was added into NB aqueous solution. The diffusion coefficient of the inclusion complex was smaller than that of the NB monomer itself, which leaded the current decrease. On the other hand, because NB monomer entered into the hydrophobic cavity of β-CD, it was reasonable for that the electrochemical reduction of the inclusion complex was more difficult than that of NB monomer itself, which would lead the cathodic peak potential shift in negative direction and also higher activation energy would be observed.

Assuming β-CD wrapped NB and formed 1:1 inclusion complex. Taraszewska et al. suggested that the apparent diffusion coefficient, D can be expressed as follows (Taraszewska and Piasecki, 1987):

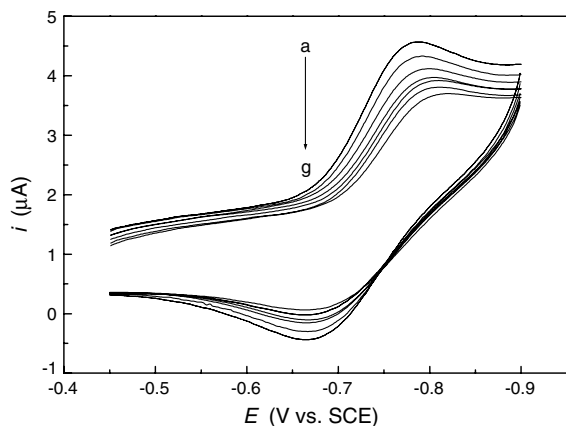$$D = \frac{D_G + D_{HG}K}{1 + K} \qquad (6)$$

where D_G is the diffusion coefficient of the free guest, D_{HG} the diffusion coefficient of the inclusion complex

$$K = [H]_0/K_D \qquad (7)$$

where K_D is the dissociated constant of the inclusion complex, $[H]_0$ initial or total concentration of β-CD in aqueous solution.

For a quasireversible electrochemical reaction, at low potential scan rate, the peak current i_{cp} is proportional to $D_O^{1/2}$ (Wang et al., 2001). Therefore, by substituting D with i_{cp}^2, Eq. (6) can be converted as follows:

$$i_{cp}^2 = \frac{K_D}{[H]_0}(i_{cp,G}^2 - i_{cp}^2) + i_{cp,HG}^2 \qquad (8)$$

The plot of i_{cp}^2 versus $(i_{cp,G}^2 - i_{cp}^2)/[H]_0$ should be a straight line. Fig. 8 showed the experimental result. From the slope of the straight line, the value of K_D was evaluated as 6.5 mM, which is almost same to that measured by UV.

The cyclic voltammetry of NB + β-CD in NaOH (pH = 13.5) was shown in Fig. 9. Similarly, the dissociated constant, K_D, was determined as 32 mM. The value of K_D in alkali is much larger than that in neutral solution. The reasons may be due to the losing protons of hydroxy groups in β-CD in alkaline which weakened the hydrophobic capability of the internal cavity in β-CD (Bertrand et al., 1989). At acidic condition, β-CD will be hydrolyzed, so the experiment was not performed in acidic condition.

3.4. Effect of β-CD to the solubility of NB

At 25 °C, the solubility, S_t of NB in water was measured as 9.8 mM which is near to that reported in the reference (Gao et al., 2000). As previously described that β-CD can increase the solubility of organic compound in
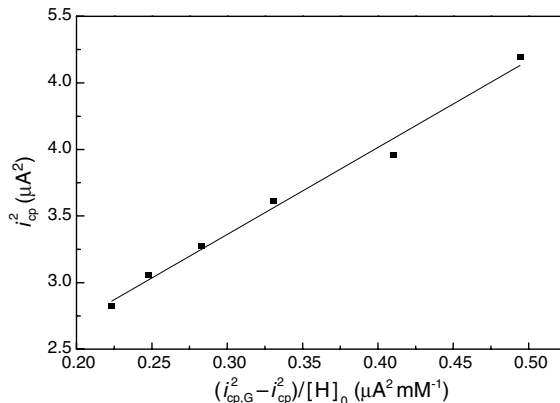

Fig. 7. At 25 °C, pH = 7.0 and 100 mV s⁻¹, the cyclic voltammograms of 1.1 mM NB + β-CD. $c_{\beta\text{-CD}}$ (mM): (a) 0; (b) 2.2; (c) 4.4; (d) 6.6; (e) 8.8; (f) 11.0; (g) 13.2.

Fig. 8. The plot of i_{cp}^2 versus $(i_{cp,G}^2 - i_{cp}^2)/[H]_0$.
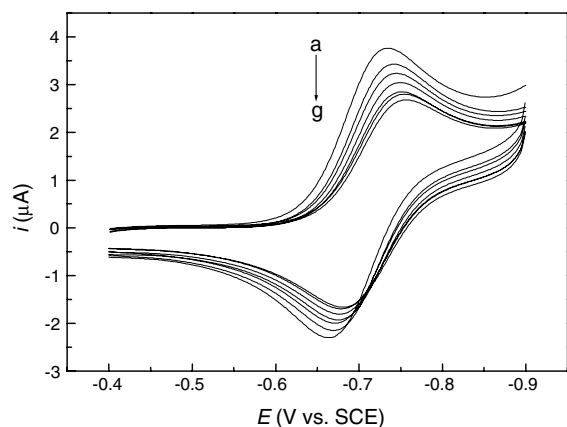
Fig. 9. At 25 °C, pH = 13.5 and 100 mV s^{-1}, the cyclic voltammograms of 2.1 mM NB + β-CD. $c_{\beta-CD}$ (mM): (a) 0; (b) 4.2; (c) 8.4; (d) 12.6; (e) 16.8; (f) 21.0; (g) 25.1.

water (Boving and Brusseau, 2000; Manolikar and Sawant, 2003) because of the formation of inclusion complex. Therefore, if β-CD is put into a solution with excess NB, the absorbency will increase due to solubility of NB increasing. The relation between the solubility of NB and the concentration of β-CD can be measured according to Cao's method (Cao et al., 2002). The experimental result was shown in Fig. 10. Liu et al. reported that the solubility of β-CD in water is 16.3 mM at 25 °C (Liu et al., 2001). From Fig. 10, when the concentration of β-CD is less than 5 mM, the solubility of NB increases linearly with the concentration, $[H]_0$ of β-CD. However, with the increasing of the concentration of β-CD, due to analogously homology ion effect, β-CD restrained the dissolution of inclusion complex which lead to the solubility of NB decreased shown as in Fig. 10 (Gao et al., 2000).
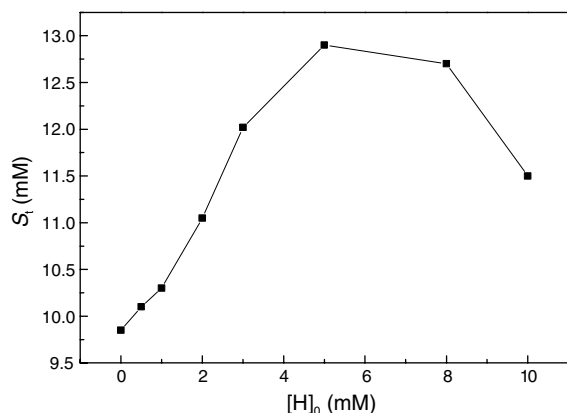

Fig. 10. At 25 °C and pH = 7.0, the plot of S_t versus $[H]_0$.

4. Conclusions

Between NB and β-CD an inclusion complex is formed. The ratio of NB to β-CD in inclusion complex is 1:1. NB entered into the hydrophobic cavity of β-CD completely, which makes the solubility of NB in water increase. The dissociated constant of the inclusion complex is measured as 6.5×10^{-3} M in neutral solution (pH = 7.0), and 3.2×10^{-2} M in alkali (pH = 13.5) which is very important to the environmental scientists. At neutral condition, a stable inclusion complex can be formed between NB and β-CD which will make NB absorbed on the material, for example, soil desorb easier. However, at alkali the NB can be released from β-CD.

Acknowledgements

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