

## Raman Spectra of Nitrophenol Molecules Included in Cyclodextrin Polymers Cross-linked with Epichlorohydrine

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(Received Oct. 15, 2003, Accepted Nov. 10, 2003)

**Abstract** : Inclusion complexes of the *p*-nitrophenol with  $\beta$ -cyclodextrin (CD), sulfated  $\beta$ -CD, and  $\beta$ -CD polymer cross-linked with epichlorohydrine (EP) were prepared and characterized by Raman spectroscopy. The intensity of vibration peaks of the C-O and C-N at 1284 and 856  $\text{cm}^{-1}$  of the *p*-nitrophenol in the presence of EP-linked CD polymer was remarkably increased, respectively. The vibration modes at 1284 and 856  $\text{cm}^{-1}$  are assigned to the out-of phase C-C-O stretching mode and the C-N stretching mode, respectively. The vibration peaks at 1284 and 856  $\text{cm}^{-1}$  increased with increasing the content of EP-linked CD polymers, while decreased with increasing the *p*-nitrophenol content. Furthermore, the vibration mode of the  $\text{NO}_2$  symmetric stretch at 1344  $\text{cm}^{-1}$  enhanced with increasing the content of *p*-nitrophenol.

**Key words** : Cyclodextrin polymer, Epichlorohydrine, Raman Spectra, *p*-Nitrophenol, Inclusion complexes

### 1. Introduction

$\beta$ -Cyclodextrine ( $\beta$ -CD) is a cyclic natural oligomer containing seven glucose units connected via  $\alpha$ -(1,4)-linkage. Schematically, the shape of  $\beta$ -CD can be presented as a truncated cone with seven primary hydroxyl groups attached to the smaller opening of the cone while the remaining fourteen secondary hydroxyl groups are located on the larger opening of the cone. Both unfunctionalized and functionalized  $\beta$ -CDs, chemically bonded to silica, have been reported to separate a variety of analytes by HPLC under reversed-phase condition.<sup>1-4</sup> The separation mechanism has often been claimed to depend on the formation of inclusion complexes where guest molecule enters the

relatively hydrophobic interior of the cone from larger side of the opening of the cone. This has traditionally resulted in  $\beta$ -CD being chemically bonded to support particles via the primary hydroxyl groups situated on the smaller opening of the cone.

As a consequence of these structure, CDs are capable of forming inclusion complexes, even with molecules significantly larger than their cavity, as long as at least some part of the guest can penetrate into the cavity.<sup>5,6</sup> CDs are known to be good models for enzyme action, combining the cage effects with the conformational control of the guest molecule. Their stereoselectivities, especially of  $\alpha$  and  $\beta$ -CDs, offer new possibilities in particular for pharmaceutical applications, e.g. enhancement of the bioavailability of certain drug.<sup>7-10</sup> However, CDs also present several advantages in other areas, such as food and cosmetics industrials and agrochemistry,<sup>11,12</sup> especially owing to

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their capacity to protect the guest molecules against oxidation, light-induced reactions and loss by evaporation. Additionally, they usually enhance the solubility of slightly soluble or even insoluble compound. Several studies concerning the effects of CDs on the acyl transfer reactions and photochemical reactions have been published recently.<sup>13,14</sup>

Phenol is widely used in chemical industry as raw material and, therefore, often present in waste waters. Phenol and a number of its chloro and nitro derivatives appear as the most highly toxic and commonly occurring pollutants. In a previous paper,<sup>15</sup> we reported that the geometrical isomers of substituted phenols was successfully separated by HPLC using dynamically coated  $\beta$ -CDs station. The separation mechanism has often been claimed to depend on the formation of inclusion complexes where guest molecule enters the relative hydrophobic interior of the cone from larger side of the opening. However, the inclusion formation of geometrical isomers of substituted phenols was not studied in an aqueous solution. On the other hand, the nitrophenol was good compound as a model compound to characterize inclusion formation by Raman spectroscopy, because the stretch from the nitro group is easily characterized in aqueous solution.

In this study, the inclusion complexes of *m*- and *p*-nitrophenol with  $\beta$ -CD, sulfated  $\beta$ -CD, and  $\beta$ -CD polymer cross-linked with epichlorohydrine were prepared and characterized by Raman spectroscopy.

## 2. Experimental

### 2.1. Materials

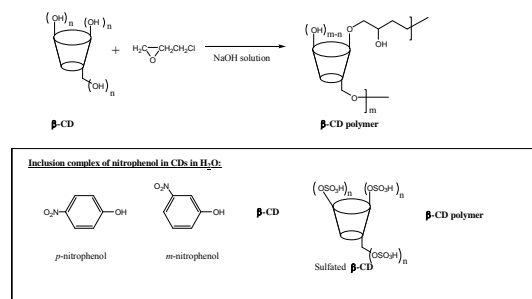
$\beta$ -cyclodextrin (CD), epichlorohydrine (EP), sulfated  $\beta$ -CD and *m*- and *p*-nitrophenol were obtained from Aldrich Co.. The chemical reagents were used without further purification.

### 2.2. Preparation of CD polymers and inclusion complexes

The CD cross-linked with EP polymers were prepared by the following method (Scheme I): 4.0

mmol CD was dissolved in 0.05 mol/mL NaOH solution. 60.0 mmol EP was added slowly dropwise at 60 °C under stirring. After 60 minutes the reaction was stopped by the addition of acetone/methanol (1/1, vol-%), and then washed with MeOH until the MeOH solution reached pH=7.0. The obtained polymer was dried in vacuo at 50 °C for 3 hrs. Inclusion complexes were prepared as below: The  $\beta$ -CD, sulfated  $\beta$ -CD, and  $\beta$ -CD polymer was dissolved in H<sub>2</sub>O (14 mL), and then the *m*- and *p*-nitrophenol (7.0 mg) was added.

Scheme I. Preparation of Cyclodextrin(CD) Polymer Cross-linked with Epichlorohydrine in NaOH Solution.



Scheme I. Preparation of CD polymer cross-linked with epichlorohydrine in NaOH solution.

### 2.3. Characterizations

In order to determine the structure of  $\beta$ -CD polymers, one-dimensional <sup>1</sup>H NMR (400 MHz for <sup>1</sup>H) spectra were taken on a Bruker, Avance Digital 400 in D<sub>2</sub>O. IR spectra were recorded using a Mattson Instruments, Inc., Galaxy 7020A. The differential scanning calorimetry (DSC) of the CD polymers with epichlorohydrine were measured on DSC220C (Seiko, SSC5200H Disk) with a heating rate of 10 °C/min in the temperature range of 50-300 °C. Thermogravimetric analysis (TGA) of the CD polymers were made on the TA instruments, TA4000 /Auto DSC 2910 system with a heating rate of 10 °C/min in the temperature range of 50-700 °C.

For determination of inclusion formation, the Raman spectra of the liquid samples in the range of 50-4000 cm<sup>-1</sup> were obtained with a Coherent, Innova 90-5/Spex, 1403 0.85 m double spectrometer. Samples were in Kimax glass capillary tubes of i.d. 0.8 mm.

### 3. Results and discussion

#### 3.1. Properties of CD polymer cross-linked epichlorohydrine

There has been considerable interest in the preparation, properties and application of EP linked CD polymer. Crini et al.<sup>16</sup> was reported that the structure of the insoluble EP linked CD polymer by solid state NMR spectroscopy. However, it has been reported little information on thermal properties and application of the EP linked CD polymer.

Table 1 shows the results of the different polymerization of  $\beta$ -CD using EP, which contains two reactive functional groups, in NaOH aqueous solution. The  $\beta$ -CD contents were ranged from 20 to 80% (wt-%) by NMR. The polymer obtained with EP was soluble in only water. The possible structure of the  $\beta$ -CD polymer is shown in scheme II. This entity is a polymeric mixture containing CD units joined by repeating glyceryl linker. However, in this study, the structure of the EP linked  $\beta$ -CD polymer was not studied because the Crini et al.<sup>16</sup> was clearly reported the structure of the  $\beta$ -CD polymer by solid NMR technique.

Table 1. Polymerization of  $\beta$ -CD using Epichlorohydrin in NaOH solution<sup>a)</sup>

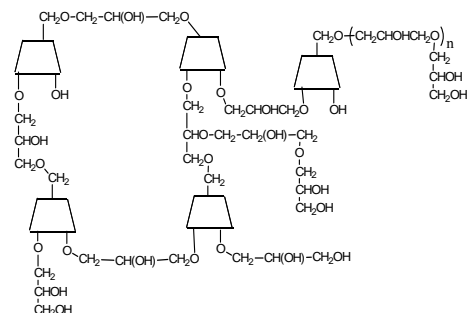
Run	$\beta$ -CD (mmol)	Epichlorohydrin (mmol)	Temperature (°C)	Time (hrs)	Yield <sup>b)</sup> (%)
1	1.76	3.52	50	24	~100
2	1.76	35.2	50	24	~100
3	1.76	88.0	50	24	~100
4	1.76	35.2	70	24	~100
5	1.76	88.0	70	24	~100
6	1.76	88.0	70	48	~100

<sup>a)</sup>The ratio of NaOH/H<sub>2</sub>O is 30%(wt).

<sup>b)</sup>Aceton/methanol mixture (1/1, vol-%) insoluble part.

Fig. 1 shows the TGA (a) and DSC (b) curves of the  $\beta$ -CD (1), and  $\beta$ -CD polymer cross-linked with EP (2, 3) (run 1, 2 in Table 1). The considerable change in the thermal behavior of the EP linked  $\beta$ -CD polymer was observed. In Fig. 1(a) of  $\beta$ -CD (1), the first weight loss around 100 °C can be explained as the

Scheme II. Possible Structure of the  $\beta$ -CD Polymer Cross-linked with Epichlorohydrin.



Scheme II Possible structure of the  $\beta$ -CD polymer cross-linked with epichlorohydrin.

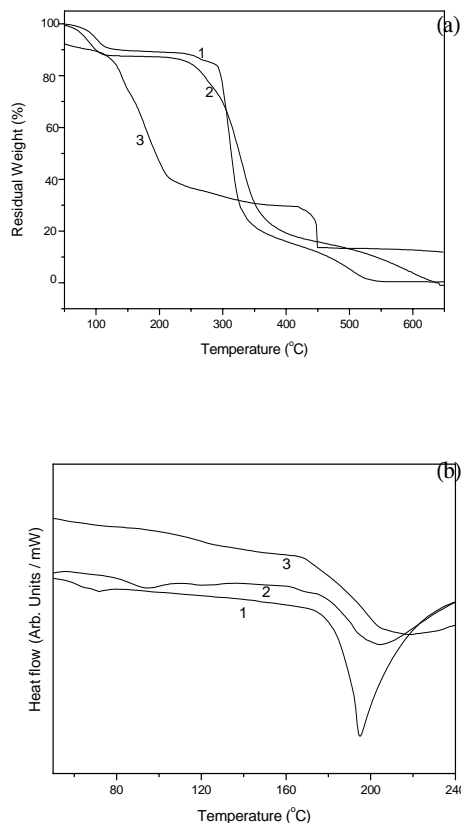


Fig. 1. TGA (a) and DSC (b) curves of the  $\beta$ -CD and  $\beta$ -CD polymer with epichlorohydrine. 1:  $\beta$ -CD, 2:  $\beta$ -CD polymer (run 1 in Table 1), 3:  $\beta$ -CD polymer (run 2 in Table 1).

moisture, and the second weight loss around 300 °C can be due to dehydration of the CD compound, and third weight loss at 350 °C due to decomposition of cyclodextrin. In Fig. 1(a)  $\beta$ -CD polymer (3), the first weight loss from 100 to 200 °C can be explained as the dehydration of the CD polymers, second weight loss due to the decomposition of the cross-linked glyceryl linker, and the third weight loss at 400 °C can be due to decomposition of cyclodextrin. In Fig. 1 (b), the  $\beta$ -CD (1) melting peak at 180 °C and the EP linked  $\beta$ -CD polymer (2, 3) melting peak at 200 °C were observed. This phenomena may be attributed to the loss of water. The presence on the DSC curves of a thermal rise near 300 °C is generally attributed to the beginning of decomposition of the cyclodextrin.

### 3.2. Inclusion formation of *p*-nitrophenol onto $\beta$ -CDs in H<sub>2</sub>O

CD cavity can include another organic compound with suitable geometric and polarity. Indeed, long alkyl chains and aromatic compounds form inclusion complex with cyclodextrin in water. However, the characterization of inclusion complex was very difficult because solvent is water. Raman spectroscopy is a good method for measurement of inclusion complex because water gives no Raman signal. The inclusion formation of organic guests such as nitrophenol derivatives insides CDs was not studied by Raman spectroscopy in H<sub>2</sub>O yet.

Fig. 2 shows the Raman spectra of the *p*-nitrophenol of (a) pure solid and (b) in H<sub>2</sub>O, for 800-1800 cm<sup>-1</sup> regions, at room temperature. The symmetric,  $\nu_s(\text{NO}_2)$ , and asymmetric,  $\nu_{as}(\text{NO}_2)$ , stretching vibration were appeared at 1328 and 1588 cm<sup>-1</sup> in solid state, respectively, while at 1344 and 1592 cm<sup>-1</sup> in H<sub>2</sub>O. The vibration of the C-N stretch was also shown at 872 cm<sup>-1</sup>. On the other hand, the symmetric,  $\nu_s(\text{C-O})$ , stretching vibration was shown at 1284 cm<sup>-1</sup> in solid state, while at 1288 cm<sup>-1</sup> in H<sub>2</sub>O. In Fig. 2(a), the other stretching vibration peaks at 1112, 1172, 1220, 1520, and 1612 cm<sup>-1</sup> in solid state are assigned to the combination mode of the  $\nu_{\text{CN}} + \nu_{\text{CC}}$  stretching,  $\nu_{\text{CH}}$  stretching,  $\nu_{\text{CN}} + \nu_{\text{OH}}$  stretching,  $\nu_{\text{CC}}$  stretching, and  $\nu_{\text{CC}}$

stretching, respectively. Furthermore, the stretching peaks of the *p*-nitrophenol in H<sub>2</sub>O were blue shifted.

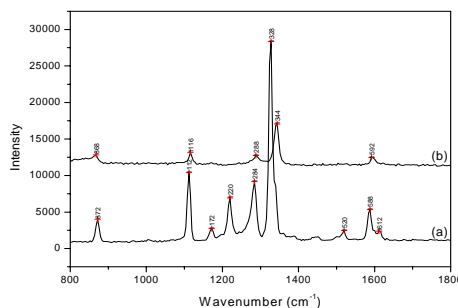


Fig. 2. Raman spectra of *p*-nitrophenol, for the 800-1800 cm<sup>-1</sup> regions, at room temperature: (a) pure solid and (b) in H<sub>2</sub>O (14 mg/mL).

Fig. 3 shows the Raman spectra of the *p*-nitrophenol (7 mg) in H<sub>2</sub>O at room temperature: (a) without CDs, (b) in the presence of CD polymers, (c) in the presence of sulfated CD, and (d) in the presence of CD (100 mg). In Fig. 3(b),  $\nu_{\text{CC}}$  stretching bands at 1172, 1472 of the, and 1524 cm<sup>-1</sup> band were observed in the presence of CD polymer. At the same time, the intensity of bands at 856 cm<sup>-1</sup> and 1288 cm<sup>-1</sup> was increased in the presence of  $\beta$ -CD polymer cross-linked EP. The peak at 1288 cm<sup>-1</sup>, which is referred to as C-O stretching,<sup>17</sup> is assigned to the out-of phase C-C-O stretching mode. Colthup *et al.*<sup>18</sup> described that the this vibration also give rise to a medium to strong intensity Raman peak. The in-phase C-C-O stretching occur at the frequencies lower than the corresponding out-of-phase vibration mode. The vibration peak at 856 cm<sup>-1</sup> may be assigned to the C-N stretching. Lin-Vien *et al.*<sup>19</sup> also described that Raman bands appeared in the 863-847 cm<sup>-1</sup>, in the group of -NO<sub>2</sub> containing compounds. From the results, the *p*-nitrophenol was incused in  $\beta$ -CD polymers, which was modified by the strong hydrophilic glyceryl linker.

Fig. 4 shows the Raman spectra of *p*-nitrophenol of 7.0 mg in the presence of EP-linked  $\beta$ -CD polymer of (a) 50, (b) 75, (c) 95, and (d) 150 mg/mL. The vibration peaks of the C-O at 1284 cm<sup>-1</sup> and the C-N at

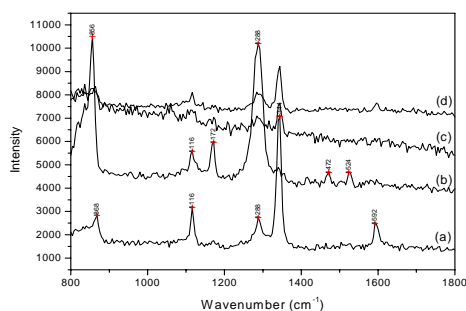


Fig. 3. Raman spectra of *p*-nitrophenol of 7 mg in H<sub>2</sub>O at room temperature: (a) without β-CD derivatives, (b) in the presence of β-CD polymer (100 mg/mL), (c) in the presence of sulfated β-CD (100 mg/mL), and (d) in the presence of β-CD (100 mg/mL).

856 cm<sup>-1</sup> increased with the content of EP-linked β-CD polymers, respectively. Fig. 5 shows the Raman spectra of *p*-nitrophenol of (a) 7.0, (b) 7.2, (c) 9.0, and (d) 11.0 mg in the presence of EP-contained CD polymer. The vibration peaks of C-O at 1284 cm<sup>-1</sup> and the C-N at 856 cm<sup>-1</sup> decreased with increase of the *p*-nitrophenol content, respectively, while the vibration peak of NO<sub>2</sub> group at 1344 cm<sup>-1</sup>,  $\nu_s(\text{NO}_2)$ , increased. From the results, the inclusion complex structure, which is the NO<sub>2</sub> group inserted in hydrophobic cavity is proposed as shown scheme III.

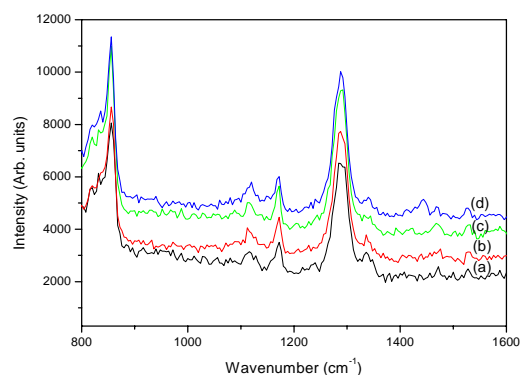
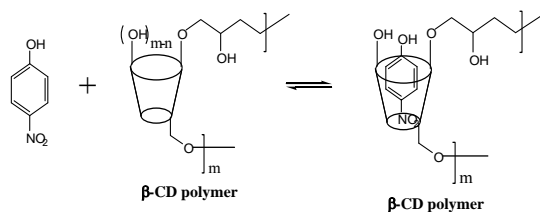


Fig. 4. Raman spectra of *p*-nitrophenol of 7.0 mg in the presence of β-CD polymer of (a) 50, (b) 75, (c) 95, and (d) 150 mg/mL.



Scheme III. Inclusion complex of the *p*-nitrophenol in aqueous solution.

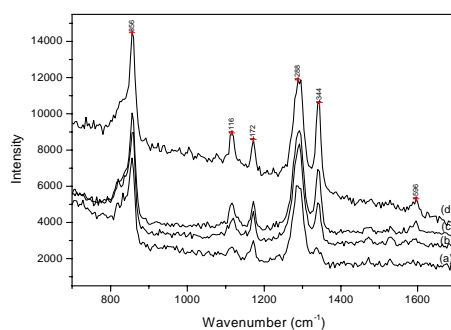


Fig. 5. Raman spectra of *p*-nitrophenol of (a) 7.0, (b) 7.2, (c) 9.0, (d) 11.0 mg in the presence of β-CD polymer (150 mg/mL).

Fig. 6 shows the Raman spectra of spectra of *p*-nitrophenol of (a) 7.0, (b) 9.0, and (c) 11.0 mg in the presence of CD of 150 mg/mL, respectively. The vibration peaks of the both  $\nu_s(\text{C-O})$  at 1284 and the

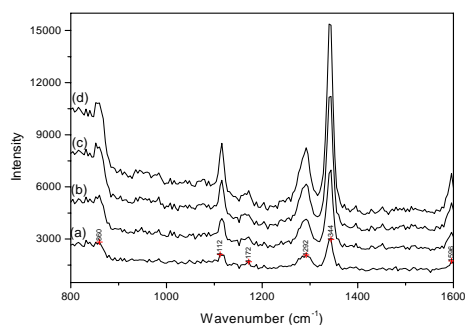


Fig. 6. Raman spectra of *p*-nitrophenol of (a) 5.0, (b) 7.0, (c) 9.0, and (d) 11.0 mg in the presence of β-CD (150 mg/mL) in H<sub>2</sub>O.

$\nu_s(\text{NO}_2)$  at  $1344\text{ cm}^{-1}$  increased with increase of the *p*-nitrophenol content. The Raman spectra of the *p*-nitrophenol of 7.0 mg in the presence of EP-contained CD polymer of (a) 50, (b) 75, (c) 95, and (d) 150 mg/mL as shown Fig. 7. The vibration peaks of the both  $\nu_s(\text{C-O})$  and the  $\nu_s(\text{NO}_2)$  werenot appeared.

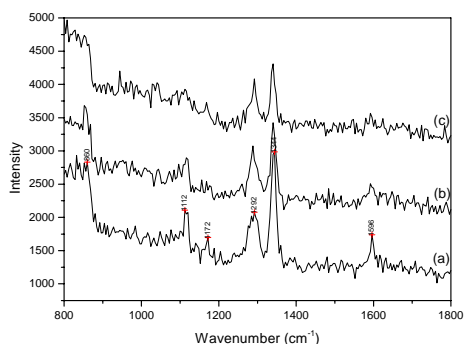


Fig. 7. Raman spectra of *p*-nitrophenol of 7.0 mg in the presence of  $\beta$ -CD of (a) 75, (b) 95, and (c) 150 mg/mL in  $\text{H}_2\text{O}$ .

#### 4. Conclusions

Inclusion complexes of *p*-nitrophenol with  $\beta$ -CD, sulfated  $\beta$ -CD, and  $\beta$ -CD polymer cross-linked with EP were prepared in  $\text{H}_2\text{O}$  and characterized by Raman spectroscopy.

- (1) The inclusion complex was successfully characterized by Raman spectroscopy.
- (2) The intensity of vibration peaks of the C-O at  $1284\text{ cm}^{-1}$  and the C-N at  $856\text{ cm}^{-1}$  of the *p*-nitrophenol in the presence of EP-linked CD polymer was remarkable increased.
- (3) The intensity of the vibration peak,  $\nu_s(\text{NO}_2)$ , of the *p*-nitrophenol was increased, while the intensity of  $\nu_s(\text{C-O})$  decreased, with increasing *p*-nitrophenol content.

#### Acknowledgement

This work was supported by Korea Research

Foundation Grant (KRF-2002-KRF-2002-005-C00012).

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