

Oxidative polymerization of hydroquinone using deoxycholic acid supramolecular template

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Polyhydroquinone (PHQ) is a redox-active polymer with quinone/hydroquinone redox active units in the main chain and may have potential applications as a mediator in biosensors and biofuel cells. By the oxidative polymerization of hydroquinone (HQ), PHQ can be easily synthesized, but the reaction lacks control over the structure of the product. Deoxycholic acid (DCA) was introduced as a supramolecular template to control the reaction. The reaction rate is 14 times of that in deionized water and twice of that in buffer. The DCA template increases not only the reaction rate, but also the molecular weight of the polymer obtained. The template effect of DCA was attributed to the supramolecular assemblies of DCA formed in the solution. Cyclic voltammetry study indicated the resulting PHQ was redox-active. While the supramolecular assemblies of DCA provided a template for the oxidative polymerization of HQ, the protons released as a by-product of the oxidative polymerization of HQ in turn enhanced the self-assembly of DCA. As a result, DCA microfibers form and separate out of the solution.

polyhydroquinone, deoxycholic acid, self-assembly, oxidative polymerization

1 Introduction

Redox-active polymers [1, 2] have found a wide range of applications such as antioxidants and inhibitors of corrosion or degradation reactions. Particularly, they play a critical role in the development of transducers for biosensors and biofuel cells. Polyhydroquinone (PHQ) is a main-chain type redox polymer. Its redox active units, quinone and hydroquinone (HQ), are among the simplest ones. Its redox potential is low, and it can undergo direct two-electron oxidation and reduction [3]. However, this polymer received much less attention than other redox polymers, such as polyaniline and polythiophene. The main reason may be the difficulty in its preparation [4].

Up to now, there are four methods for PHQ synthesis in the literature: chemical oxidative polymerization [5, 6],

electrooxidative polymerization [7], chemoenzymatic polymerization [3], and dehalogenative organometallic polycondensation [8]. Among them, chemical oxidative polymerization is the simplest. PHQ can be obtained by one-pot oxidative polymerization of HQ or p-benzoquinone in alkali solutions. Unfortunately, this method lacks control over the structure of the products. In contrast, PHQ with a well-defined structure can be synthesized by chemoenzymatic polymerization or organometallic polycondensation, however, both methods involve several steps of reaction and also expensive reagents.

Recently we found that oxidative polymerization of HQ can take place in acidic solutions using chitosan as template [9]. Because of the presence of the template, the reaction rate increases significantly. It is well-known that template polymerization may increase the reaction rate and help in the control of the molecular weight and the structure of the resultant polymer [10]. Our previous results suggest it is

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possible to control the oxidative polymerization of HQ by the use of a template. To further exploit this possibility, deoxycholic acid (DCA) supramolecular assemblies [11–13] were used as the template. The oxidative polymerization of HQ was carried out in the presence of DCA and its template effects were studied.

2 Experimental

2.1 Materials

HQ and DCA were purchased from Alfa Aesar. Other reagents were all purchased from Tianjin Chemical Reagent Company. All chemicals were of analytical grade and were used as received without further purification.

2.2 Preparation of PHQ

2.2.1 Polymerization of HQ in the presence of DCA

DCA (1.179 g, 3 mmol) was dissolved in 15 mL of 0.3 M NaOH solution in an open conical flask, to which 6 mL of deionized water and 3.5 mL of 0.1 M HCl were added to adjust the pH close to neutral for the formation of DCA supramolecular assembly. 3 mL of 1.0 M HQ was then added into the DCA solution and mixed thoroughly. The pH of the mixture was adjusted with dilute HCl solution to a desired value (close to neutral) and the final volume of the mixture was kept at 30 mL by adding water. The reaction was allowed to proceed at 47 °C for 7 days. The resulting mixture was centrifuged to remove DCA fibers formed during the reaction. Then it was acidified with HCl and centrifuged again. The black sediments were washed two times with deionized water and dried under vacuum for 24 h at 50 °C. About 50 mg of PHQ was obtained (yield 15.2%).

As a control experiment, the polymerization of HQ in an atmosphere of nitrogen was carried out similarly except that nitrogen was bubbled through the mixture. In this case, the reaction mixture remains transparent. No color change was observed.

2.2.2 Polymerization of HQ in water, alkaline and buffer solutions

HQ (0.330 g, 3 mmol) was dissolved in 30 mL of deionized water. The pH of the solution was adjusted with NaOH and HCl solution to the desired value in an open conical flask. The polymerization proceeded under the same conditions as described above. The resulting mixture was acidified with HCl, but no product was obtained by precipitation in water.

Similarly, the same amount of HQ was dissolved in 30 mL of 0.1 M NaOH, or in 30 mL of 0.1 M phosphate buffer or 0.1 M phosphate-citric acid (about 0.09 M and 0.01 M, respectively) buffer in an open conical flask, followed by polymerization under the same conditions. About 8 mg of PHQ was obtained (yield 2.4%) upon acidifying the reac-

tion mixtures in buffer.

2.3 Characterizations

pH was measured with a Leici PHS-2F pH meter. UV-visible spectra were recorded on a Cary 100 (Varian) spectrometer. Fourier transform infrared (FTIR) spectra were obtained on a Bruker Tensor-27 spectrometer. ¹H NMR spectra were recorded on a Varian UNITY-plus 400 NMR spectrometer. GPC was carried out on Waters 1525 with a UV detector ($\lambda = 289$ nm) at 35 °C using THF as eluent with a flow rate of 1.0 mL/min. The system was calibrated with polystyrene standards. Cyclic voltammetry (CV) measurements were performed on an electrochemical workstation (Lanlike, LK2005A) using a glassy carbon electrode as the working electrode, a platinum as the counter electrode, and an Ag/AgCl electrode as the reference electrode. The sample was prepared by dissolving 1 mg of PHQ in 20 mL of 0.2 M PBS (pH 7.4) containing 0.1 M KCl.

3 Results and discussion

3.1 Oxidative polymerization of HQ in the presence of DCA

DCA is one of the natural bile acids found in the human body [14] (Figure 1). It has long been observed that an aqueous solution of DCA provide a gel when its pH is adjusted to be ~7. Later it was revealed that helical microfibrils was formed as a result of the spontaneous association of DCA molecules [11–13]. Here these supramolecular assemblies were used as template for oxidative polymerization of HQ. It is noteworthy that commonly used templates are synthetic or natural polymers, in which the repeated units are connected covalently [9]. In contrast, the DCA supramolecular template used here is a “polymer” whose repeated units are linked by non-covalent interactions.

The supramolecular template was prepared by adjusting the pH of DCA solution to ~7.5 according to a published procedure [15]. The monomer HQ was then added. After reaction for three days, a dark solution was obtained (Figure 2(c)). The dramatic color change suggests the formation of PHQ in the solution. As a control, an aqueous solution of HQ with the same initial pH was prepared using deionized

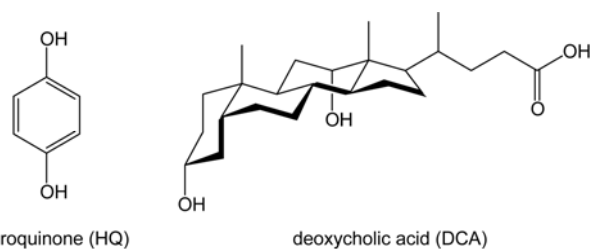


Figure 1 The chemical structures of HQ and DCA.

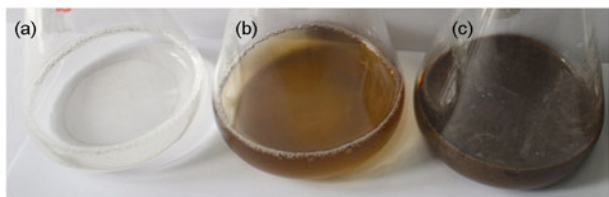


Figure 2 Photographic images of the mixture of HQ and DCA after three days at 47 °C in air. (a) 0.1 M DCA, no HQ; (b) 0.1 M HQ in water; (c) 0.1 M HQ in 0.1 M DCA. The initial pH values are all at 7.5.

water. After reaction under the same conditions, the solution turned to be brown (Figure 2(b)). From the different extent in color change, one can tell that much more PHQ formed in the presence of DCA. It was well-known that the atmosphere oxygen acts as oxidant in the oxidative polymerization of HQ. In another control, oxygen was removed by bubbling with nitrogen. In this case, the color of the reaction mixture remains almost unchanged, indicating that little PHQ forms even in the presence of DCA supramolecular template. From these results, one can conclude that atmosphere oxygen also acts as an oxidant in the template polymerization of HQ.

The preliminary results shown above indicate that DCA enhances the oxidative polymerization of HQ, however, one should be careful when attributing the increased reaction rate to template effect of the DCA supramolecular assemblies. It is known that an alkali environment is favorable for the oxidative polymerization of HQ. To study the effect of pH, we first monitored the pH variations in different systems. As shown in Figure 3, the pH of a pure DCA solution remains unchanged during the experiment. For the reaction mixtures of DCA/HQ, a small pH drop was observed in the first 10 min. Afterwards, the pH remained at ca. 6.8 regardless the initial pH value of the mixture. In contrast, for the control experiment containing HQ only, the pH dropped dramatically from 8.0 to ca. 4 in the first 24 h (Figure 3), since protons are known to be released as a by-product of the oxidative polymerization of HQ [6]. The small initial drop in pH of the DCA/HQ mixtures should also be attributed to the released protons. However, these protons neutralized by the sodium salt DCA (the pK_a of DCA is 6.58), therefore only a small decrease in pH was observed. It is known that higher pH is favorable for the oxidative polymerization of HQ so that the increased reaction rate in the presence of DCA should be partially attributed to the higher pH (indicated in Figure 3) of the medium containing DCA. To study if DCA really acts as a template, the reaction rate of the oxidative polymerization was measured under various conditions. As shown in Figure 4(a), as the reaction proceeds, the absorption of the DCA/HQ reaction mixture in the range from 350 to 600 nm increases gradually, because of the formation of larger conjugated structures of the phenolic rings. Figure 4(b) plots the absorbance at 500 nm as a function of time. A linear relationship between the ab-

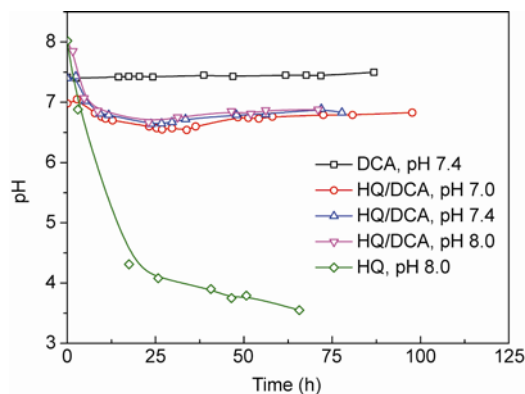


Figure 3 The variation of pH with time in the different reaction mixtures at 47 °C. [HQ] = [DCA] = 0.1 M. The initial pH values are indicated in the Figure.

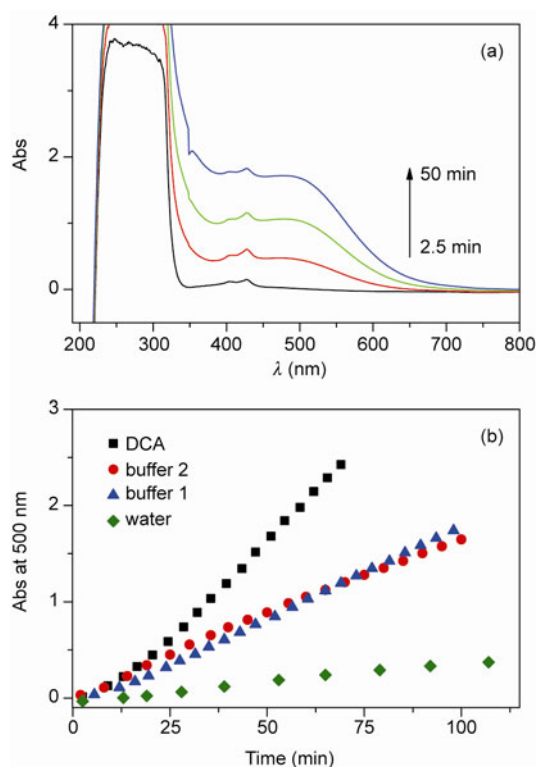


Figure 4 (a) UV-visible spectra of the mixture of HQ and DCA supramolecular assemblies at different reaction times (2.5, 20, 35, and 50 min, from bottom to top) at 47 °C. The initial pH was at 7.6. Concentrations of HQ and DCA were both at 0.1 M; (b) absorbance of various reactive mixtures at 500 nm as a function of reaction time. The initial pH, the concentrations of HQ and reactant are same as in (a). Buffer 1: 0.1 M $\text{Na}_2\text{HPO}_4\text{-NaH}_2\text{PO}_4$; Buffer 2: 0.1 M $\text{Na}_2\text{HPO}_4\text{-citric acid}$.

sorbance and time was found, suggesting the reaction rate can be easily represented by the slope of the absorbance-time plot.

From Figure 4(b), the reaction rate in the presence of DCA is 14 times of that in deionized water, confirming the previous observation in Figure 2. To study the effect of pH, the reaction rates of the polymerization in two buffer solu-

tions (both the phosphate and phosphate-citric acid buffers) were also measured. From Figure 4(b), the reaction rates are almost the same; they are 7 times of that in deionized water. These results reveal that pH does significantly influence the oxidative polymerization of HQ. Meanwhile the effect of the buffer composition seems negligible, since the reaction rates in the two buffers are the same.

Compared with the reaction rate in the buffers, the reaction rate in the presence of DCA is faster (twice of that in buffers). Therefore the DCA solution acts not only as a buffer (keeping the pH at ca. 6.8), but also as a template for the oxidative polymerization. Two factors should contribute to the template effect of DCA. One is the ability of DCA to self-assemble to form nanofibers in the solution [11, 12]. These supramolecular assemblies, like commonly used polymer templates, allow the growing chains to propagate along the template. Another factor is that HQ and PHQ can bind to the DCA assemblies through hydrogen bonds. Because the template effect of DCA, the reaction rate is faster than that in simple buffers.

We have compared the yields of PHQ under various reaction conditions after 7 days. The yield in water was very low and no precipitation appeared when the reaction mixture was acidified. The yields of PHQ in phosphate buffer and DCA solution were calculated to be 2.4% and 15.2%, respectively. The result indicates that PHQ yield is the highest in a DCA solution.

3.2 Structure and molecular weight of PHQ prepared in the presence of DCA

Previously Ragimov *et al.* [6] studied the structure of PHQ prepared by oxidative polymerization of HQ in alkali solutions. They concluded that PHQ obtained is a sequence of phenyl rings linked at the *ortho* or *para* position. However other author claimed that the phenyl rings are connected mainly at the *ortho* position [16]. Generally, the degree of polymerization is low (in the range of 2–10) with a molecular weight of only a few hundreds.

Figure 5 compares the FT-IR spectra of PHQ prepared under different conditions. The spectra of the samples prepared in a phosphate buffer and NaOH are almost the same, suggesting their structure is the same. The PHQ sample prepared in the presence of DCA also presents bands of DCA, indicating DCA was not removed completely. Except for the bands assigned to DCA, other bands can all be found in the spectra of the other two samples, suggesting their structure is the same. Particularly, the strong absorption band between 3600 and 3100 cm^{-1} confirms the presence of abundant OH groups. The band at 1625 cm^{-1} is assigned to C=O stretching vibration, indicating the presence of quinones. The bands at 1590, 1512 and 1460 cm^{-1} are assigned to the phenyl rings. The band at 1200–1250 cm^{-1} is attributed to C–O stretching vibration, confirming the existence of phenols. Importantly, they all present a band at 824 cm^{-1}

which is assigned to the out-of-plane C–H bending or wagging of the phenyl ring, indicating that the phenyl rings are linked at the same position.

GPC was used to characterize the molecular weight of PHQ. As PHQ absorbs strongly at 289 nm while DCA does not, UV detector was used for the GPC (wavelength of detection at 289 nm). From Figure 5, PHQ samples prepared under various conditions contain three main components. The elution times of 29.3, 28.3 and 27.6 min correspond to molecular weights of 200, 400 and 860, respectively. PHQ prepared in alkali solution contains only one main component, i.e. the one with an elution time of 29.3 min, while the sample obtained in buffer contains two main components with elution times at 28.3 and 29.3 min, respectively. In contrast, all three main components were found in the PHQ sample synthesized in the presence of DCA. From these results, the molecular weights of all three samples are still low. Compared with the PHQ prepared in alkali solution and buffers, the molecular weight of the PHQ prepared in the presence of DCA is higher ($M_n = 860$). The higher molecular weight of PHQ may be attributed to the template effect of DCA. This template not only accelerates the rate of

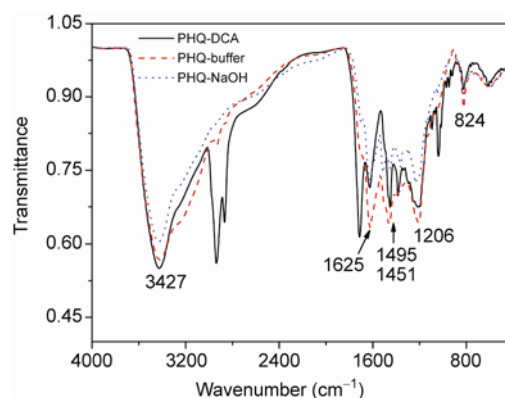


Figure 5 The FT-IR spectra of PHQ prepared in various polymerization systems showing the PHQ has similar structures.

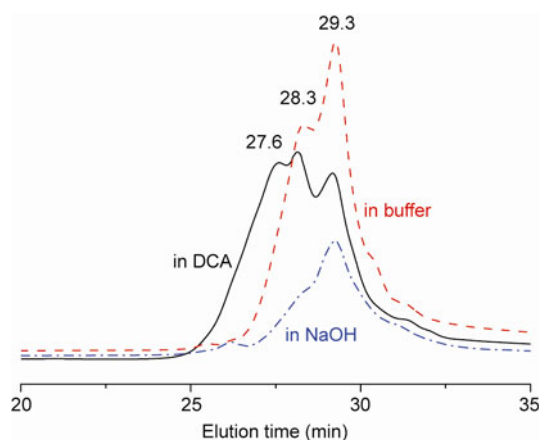


Figure 6 GPC curves of PHQ prepared in alkali solution, in buffer, and in the presence of DCA.

the polymerization, but also increases the molecular weight of the resultant polymer.

3.3 Electrochemical behaviors of PHQ prepared in the presence of DCA

The electrochemical properties of PHQ were studied by cyclic voltammetry [17]. As shown in Figure 7(a), PHQ presents an oxidation peak at 0.025 V and a reduction peak at -0.150 V, indicating it is redox-active as expected. Compared with that of HQ, the reduction peak of the polymer does not shift significantly, but the oxidative potential

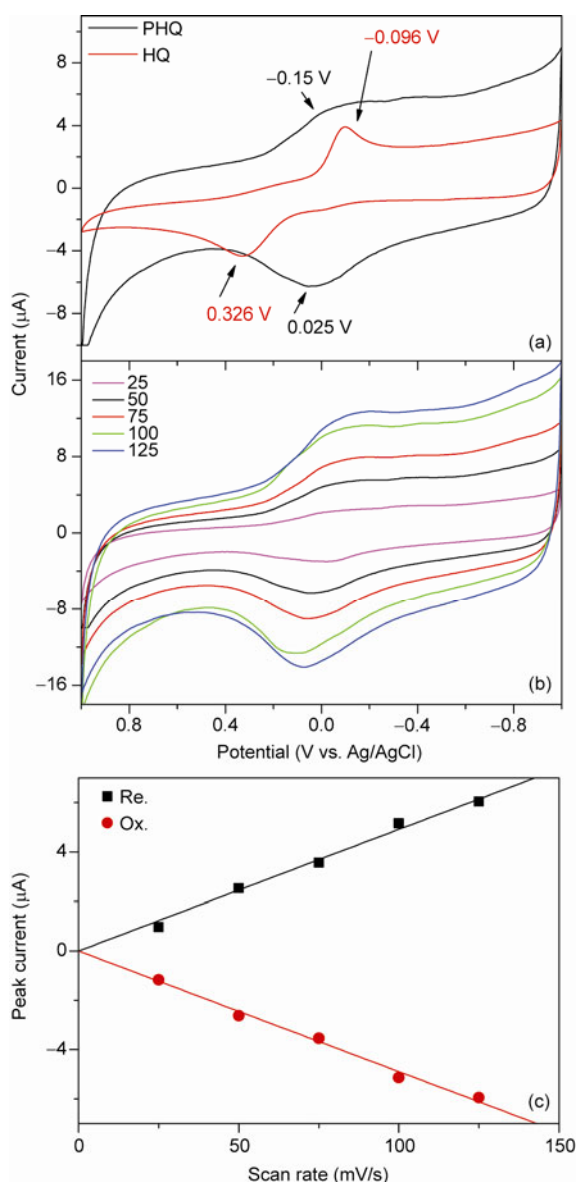


Figure 7 (a) Cyclic voltammograms of HQ and PHQ synthesized in the presence of DCA. The electrolyte is 0.2 M in PBS at pH 7.4 containing 0.1 M KCl. Scan rate is 50 mV/s; (b) cyclic voltammograms of PHQ measured at various scanning rates. [PHQ] = 0.8 wt%. The electrolyte is 0.2 M in PBS at pH 7.4 containing 0.1 M KCl; (c) linear relationships between peak currents and scan rate for the PHQ prepared in the presence of DCA.

of the polymer is decreased by 301 mV. Figure 7(b) shows the cyclic voltammograms of PHQ measured in various scanning rates. In Figure 7(c), both the oxidative peak current and the reductive peak current increase linearly with increasing scan rate. Peak current reflects the transfer rate of electrons. The linear relationship between the peak current and the scan rate suggests that the electrode reaction is a surface process [18].

3.4 Promotion of the self-assembly of DCA by oxidative polymerization of HQ

The freshly prepared DCA/HQ solution is homogeneous. With the process of the oxidative polymerization, the solution gradually becomes viscous. Fibrous crystals form and separate out from the solution [11]. Figure 8 shows the micrograph of the fibers obtained after a 6-day reaction. These fibers are birefringent when observed under cross-polarized light by polarizing microscopy (Figure 8). Although the as-prepared samples are brown in color, white fibers were obtained after washing with water. The ^1H NMR spectra of the white fibers show only absorptions from 0 to 4.5 ppm, which can be assigned to DCA (Data not shown), while no phenyl peaks were found between 6 and 8 ppm. These results suggest the fibers contain only DCA.

The formation of DCA fibers confirms that DCA self-assemble into supramolecular aggregates in the solution, which were used as template for the oxidative polymerization of HQ. The continuous formation of DCA fibers during the reaction suggest the oxidative polymerization of HQ in turn enhances the self-assembly of DCA. As mentioned before, the self-assembly of DCA was usually achieved by adding an acid [11]. In this case, protons were released automatically as a by-product of the oxidative polymerization of HQ. As a result, more and more DCA fibers form as the polymerization proceeds.

4 Conclusions

The oxidative polymerization of HQ was studied in the presence of DCA. Atmosphere oxygen acts as oxidant in this reaction. DCA shows template effect in two aspects. On one hand, the reaction is accelerated as compared with the

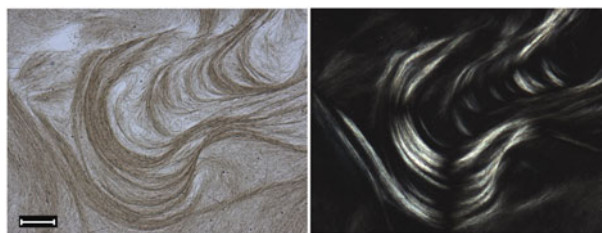


Figure 8 Photographs of the DCA fibers obtained after reacting for 6 days. The image on the right is the same as the left but observed under a cross-polarized light. Bar length is 150 μm .

reaction rate in water and in buffers of the same pH value. On the other hand, the molecular weight of the resulting polymer is higher. DCA can act as template because DCA can self-assemble into supramolecular structures. The DCA accelerates the oxidative polymerization of HQ, which releases protons into the system. The acidity of the protons released in turn promotes the self-assembly of DCA and leads to the formation of more DCA fibers.

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