สำนักงานวิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

CHAPTER III

MOLECULAR IMPRINTING OF BISPHENOL A-BASED POLYBENZOXAZINES VIA STRUCTURE SPECIFIC DESIGN

Abstract

An approach to create the recognition site in bisphenol A-based polybenzoxazines via molecular imprinting has been developed. Benzoate bisphenol A is applied as a phenol source in curing of bisphenol A-based benzoxazine monomer. Benzoyl group is excluded from the polymer network by acid hydrolysis to have polybenzoxazines with an imprinting structure of benzoyl group. The effectiveness of MIP polybenzoxazine network is demonstrated by rebinding with a series of template-like molecules, which are carboxylic acids, pyridine, and carbamate.

Introduction

For the past few years, molecular imprinting (MIP), a phenomenon under the concept of host–guest compounds, has received much expectation for practical applications via a molecular recognition at nano level through the simple network of polymeric material.[1-3] In general, the recognition ability through the network is achieved by imprinting a model molecule, so-called a template, on functional monomers to form a complex via covalent linkages[4-5] or non-covalent interaction.[6] When the templates are removed, the polymer network will retain a specific cavity with the spatial features of the template molecule. The free polymer framework or networks obtained with specific cavities and specific binding sites, so-called imprinting polymer, can rebind with the template or template-like molecules via secondary forces, such as, hydrogen bond, dipole-dipole interaction, and ionic bond. This leads to advance separation technique, especially for racemic[7], dyes[8], drugs[9], steroids[10-11], and pesticides.[12]

The polybenzoxazine was proposed by Ishida et al.[13] to be a novel phenolic resin with superb physical and mechanical properties. Recently, our group has focused on the development of benzoxazine derivatives and clarified a series of pseudo-cyclic structures by simple reactions.[14-15] The unique structure of polybenzoxazines consisting of phenolic groups and aza-methylene linkages (Scheme I), was previously reported for inclusion properties, especially the interaction with metal ions.[14]

Kirsch et al.[16] reported that divinylbenzene (DVB) polymer performs molecular imprinting to selectively bind with heterocyclics, such as, pyridine, quinoline, and acridine[16] via hydrogen bonding between phenol ring. The imprinting network of DVB was achieved by co-curing with template molecules. It is important to note that phenol units of polybenzoxazines may interact with neutral molecules by hydrogen bonding similar to that of DVB polymer. Thus, the present work is focused on the possibility to design polybenzoxazines for molecular imprinting polymer. The strategy of the work is to modify polybenzoxazines by co-curing the monomer and esterified bisphenol A. The molecular imprinting network is achieved after removing the ester group out of the network. The success of MIP network will

be evaluated from the rebinding with template-like molecules, which are benzoic acid, cholic acid, deoxycholic acid, chloramphenicol, carbaryl, and pyridine.

Experimental

Materials. Bisphenol A was purchased from Aldrich Chemical Company, Inc. Anhydrous sodium sulfate, benzoic acid, benzoyl chloride, and chloramphenicol were purchased from Fluka Chemicals (Buchs, Switzerland). Dichloromethane, isopropanol, and pyridine were the products from Lab-scan (Thailand). Methanol was purchased from J.T. Baker (USA.). Aniline and sodium hydroxide were obtained from Ajax Chemicals (Australia). Paraformaldehyde was from E. Merck (Germany). Cholic acid was purchased from TCI group (Japan). Deoxycholic acid was purchased from Nacalai Tesque (Japan). A commercial grade of 1-naphthyl methylcarbamate or carbaryl was received from AG-GRO (THAILAND) Co., Ltd. and recrystallized in acetone before use. The other chemicals were used without further purification.

Procedures. Fourier transform infrared spectra were measured at a resolution of 4 cm^{-1} by using a Bruker Equinox55/S spectrophotometer equipped with deuterated triglycine (DTGS) detector under the constant purge with dry air. Differential scanning calorimeter (DSC) used was Perkin-Elmer DSC7 using N_2 as a purge gas. For DSC, the sample (10 mg) was sealed in a closed aluminum sample pan and heated from 30°C to 350°C at a rate of 10°C/min. The template binding ability was analyzed by a Perkin-Elmer Lamda-10 ultraviolet-visible spectrophotometer (UV-vis).

Preparation of Bis(3,4-dihydro-2H-3-phenyl-1,3-benzoxazinyl)iso-propane, 1. Bisphenol A-based benzoxazine monomer, **1** was prepared to obtain a white powder as a product according to Ning and Ishida.[13]

Compound **1**: mp = 86.3°C; FTIR (KBr, cm^{-1}): 1500 (m, trisubstituted benzene), 1257 (m, C-N).

Preparation of Bisphenol A with Benzoyl Chloride, 2. Bisphenol A (2.28 g, 10 mmol), benzoyl chloride (1.15 mL, 10 mmol), and NaOH (0.40 g, 10 mmol) were stirred in the mixture of dichloromethane/water (3:1) at room temperature. After 12 h, the organic phase was collected, washed by water and dried over anhydrous sodium sulfate. Dichloromethane was removed by vacuum distillation to obtain the white solid as a product. The product was recrystallized in isoproponal to obtain a clear colorless crystal.

Compound **2**: FTIR (KBr, cm^{-1}): 3463(m, OH), 1713 (s, C=O).

Preparation of Molecular Imprinting Polybenzoxazines. Compound **1** (9.68 g, 20.95 mmol) was mixed with **2** (0.48 g, 1.38 mmol) and heated in vacuum oven at 190°C (0.01 torr) for 8 h. The polymer film was ground and hydrolyzed by suspending in 5N NaOH solution at room temperature for 24 h. The polymer was collected, washed by water and dried at 60°C for 3 h.

Template Rebinding Procedures. The molecular imprinting polybenzoxazines (50 mg) was immersed in solution of 10 mM benzoic acid (10 mL). The rebinding procedures were done in three different solution conditions, which are (i) immersing at room temperature overnight, (ii) heating at 40°C overnight, and (iii) sonication for 15 min and kept it afterward overnight. The polymer was filtered and the concentration of the template molecule remained in the solution was determined by UV-vis. Other template molecules, such as, cholic acid, deoxycholic acid, carbaryl, chloramphenicol, and pyridine, were studied with the similar procedures.

Results and Discussion

Monomer Preparation and Optimum Curing Conditions. FTIR spectrum of **1** confirms the successful preparation of **1** as clarifying from the band at 1499 cm^{-1} for tri-substituted benzene ring.

By curing at various temperatures from 130 to 190°C, the samples obtained appeared to be yellow rigid sheet. However, Figure 1 shows that the product cured at 190°C gives significant peaks at 3200 cm^{-1} and 1481 cm^{-1} due to hydroxyl group and tetrasubstituted benzene, respectively. This supports that the ring opening polymerization is accomplished from the curing process at 190°C for 8 h *in vacuo*. It should be noted that the curing condition at 170°C might bring a complete curing product similar to the one at 190°C as observed from FTIR (Figure 1(c) and 1(d)).

To clarify the optimal condition of **1**, all curing products were studied by DSC. As shown in Figure 2, the products prepared at lower temperature than 190°C show the polymerization exotherm around 230°C while the curing product obtained at 190°C does not show the significant exothermic peak. This supports that nearly complete polymerization has been achieved at 190°C for 8 h.

Template Preparation. Compound **2** includes a template molecule connected by esterification to bisphenol A as shown in Scheme II. Through this approach the template is covalently bonded to the network via an ester group. In order to incorporate benzoyl group into the polybenzoxazine framework, benzoate bisphenol A was prepared by using stoichiometrically unbalanced benzoyl chloride. Here, bisphenol A was expected to esterify either one side or both OH groups of bisphenol A. Scheme II shows a possibility where stoichiometric ratio reaction occurs at single OH group of bisphenol A. The esterified bisphenol A would be not only a part of MIP but also giving a binding site when the ring opening polymerization occurred as shown in Scheme III. After the reaction, the crude product was recrystallized in isopropanol to obtain a clear crystal. Figure 3 shows that the product obtained gives not only a strong carbonyl peak at 1730 cm^{-1} belonging to ester functional group but also a broad band at 3500 cm^{-1} referred to hydroxyl group remained in bisphenol A after esterification. By confirming an existence of OH group, we conclude that our purified **2** might be a mono-substituted

product. Although there should be some di-substituted products mixed in **2**, the curing process of **1** will selectively react with **2**, which OH group can be provided to crosslink (see the next session).

Polybenzoxazine Framework Formation and Template Removal. After **1** and **2** were mixed and cured under the optimal condition at 190°C for 8 h, a yellow-brownish sheet was obtained. FTIR was applied to qualitative analysis the template formation and removal. Figure 4(a) and 4(b) show the IR spectra of the polybenzoxazine without the template molecule and product from co-curing of **1** and **2**. The product obtained shows a broad band at 3400 cm^{-1} due to the hydroxyl group of the polybenzoxazine and at 1730 cm^{-1} due to the carbonyl group of the ester. This indicates that **1** and **2** was cured while the ester species belonging to **2** still remained in the network after curing.

Since the binding site is bonded with framework by covalent bond, the chemical reaction is needed to remove the template. Hydrolysis in basic condition was thus used to eliminate benzoyl group from the polybenzoxaine framework. The product suspended in NaOH was changed from yellow-brownish color to red color indicating the reaction proceeded. Figure 4(b) and 4(c) show FTIR spectra of the polybenzoxazine framework before and after the template removal. The product after the template removal does not exhibit the carbonyl peak at 1730 cm^{-1}. This implies that the polybenzoxazine framework without template was successfully prepared. In addition, the disubstituted benzoate bisphenol A was completely eliminated.

Rebinding of Template and Template-like Molecules. The MIP property of the polybenzoxazine framework was demonstrated by rebinding with template, which is benzoic acid and other template-like molecules, such as, cholic acid, deoxycholic acid, carbaryl, chloramphenicol, and pyridine. Figure 5 summarizes the rebinding property of MIP with a series of templates. Benzoic acid shows the highest percentage of rebinding (~ 45%) as compared with other template-like molecules. This might be related to the fact that the structure and the binding site in the polybenzoxazine framework were originated from benzoyl group. This imprinting network is, thus, able to form hydrogen bond through the established network. Although cholic acid and deoxycholic acid have similar carboxylic

functional group to benzoic acid, the percentage rebinding is rather low. It suggests that the cavity size might not be appropriate for cholic acid and deoxycholic acid despite the potential for forming hydrogen bonding. Carbaryl also gives percentage rebinding up to 15%. Considering the chemical structure and the molecular size of carbaryl, it is possible that the size and the structure for molecular interaction are somewhat effective for binding in the network. Chloramphenicol and Pyridine did not give significant rebinding property to the framework.

Effect of External Stimuli Conditions. To enhance the MIP property, the external stimuli conditions, such as, heating at 40°C and shaking in a sonicator, were applied. It was expected that by heat or external forces from vibration, the framework might be expanded to trap more template molecules inside structure. As shown in Figure 6, it was found that the external stimuli conditions could not enhance the rebinding property. At room temperature, the polybenzoxazine framework gives the maximum rebinding property as compared to other conditions. This might be due to the destruction of MIP interaction by thermal or ultrasonic energy. Although all percentage rebinding at the external stimuli conditions decreased, MIP still interacted selectively with its template, which is benzoic acid.

Conclusions

The present work shows another approach to develop polybenzoxazine structure as a molecular imprinting polymer via structure specific design process and ring opening reaction. By esterifying bisphenol A with benzoyl chloride and curing with benzoxazine monomer, a polybenzoxazine framework with a benzoyl group can be obtained. Benzoyl group was eliminated using acid hydrolysis. The molecular imprinting polymer obtained was demonstrated to be sensitive to benzoic acid, which was used as the covalently attached template molecule.

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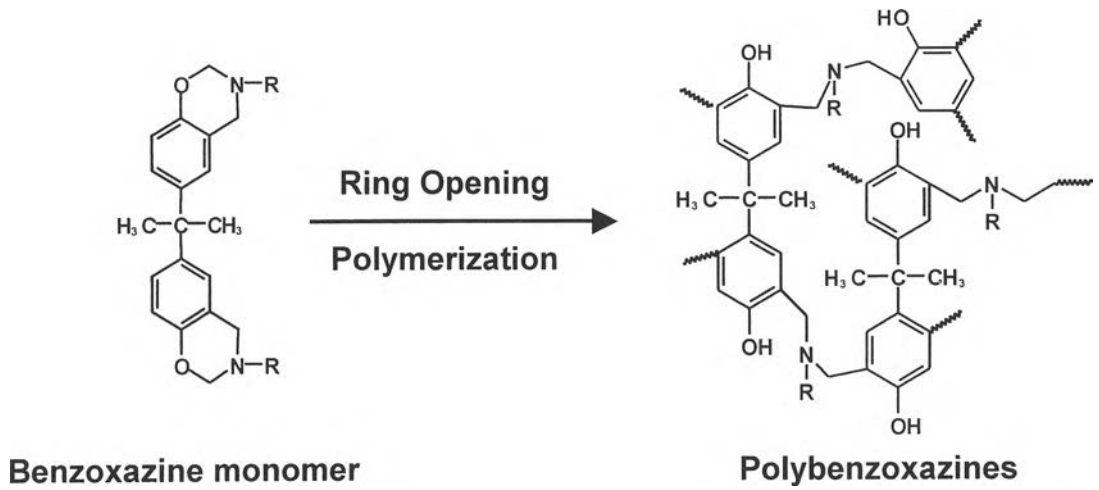
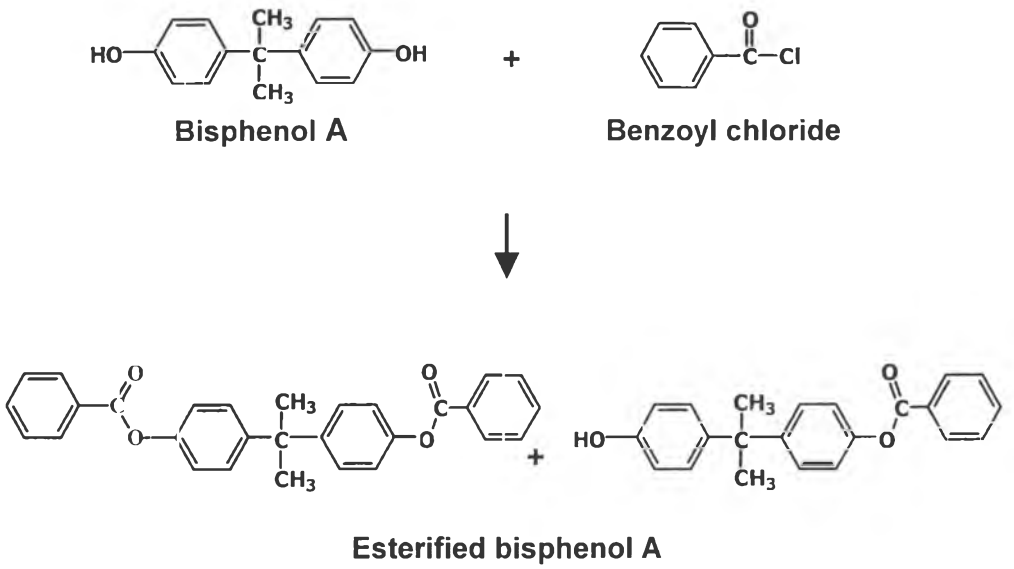
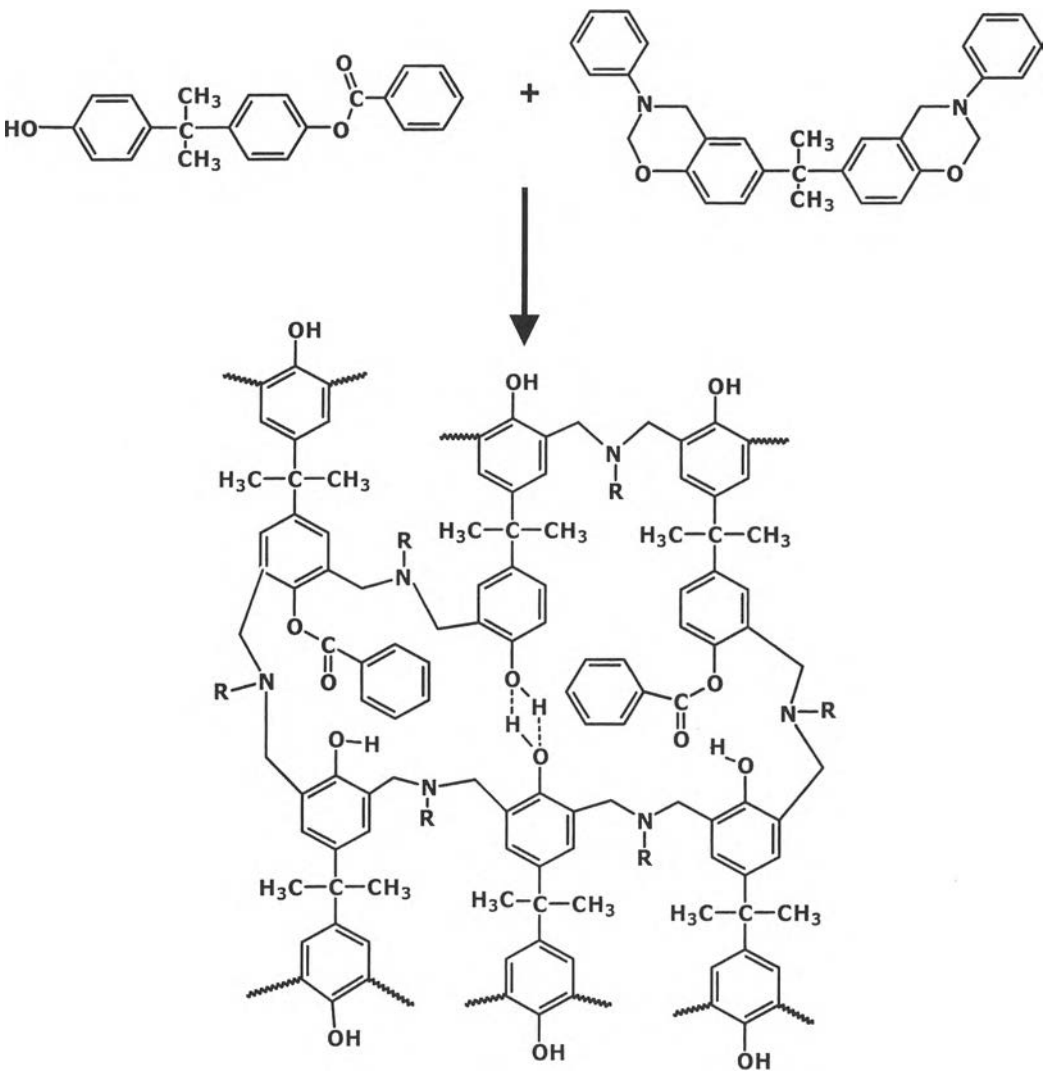


Scheme I (Chatchai et al.)



Scheme II (Chatchai et al.)



Scheme III (Chatchai et al.)

Figure Captions

Figure 1. FTIR spectra of, (a) **1**; and **1** after curing at, (b) 130; (c) 150; (d) 170; and (e) 190°C.

Figure 2. DSC thermograms of **1** after curing at, (a) 130; (b) 150; (c) 170; and (d) 190°C.

Figure 3. FTIR spectra of, (a) bisphenol A; and (b) esterified bisphenol A.

Figure 4. FTIR spectra of curing product of **1**, (a) before modification; (b) after modification with benzoyl chloride without hydrolysis; and (c) after modification with benzoyl chloride after hydrolysis in NaOH.

Figure 5. Rebinding percentage of template molecules by polybenzoxazines.

Figure 6. Effect of external stimuli conditions to rebinding percentage of template molecules by MIP polybenzoxazines.

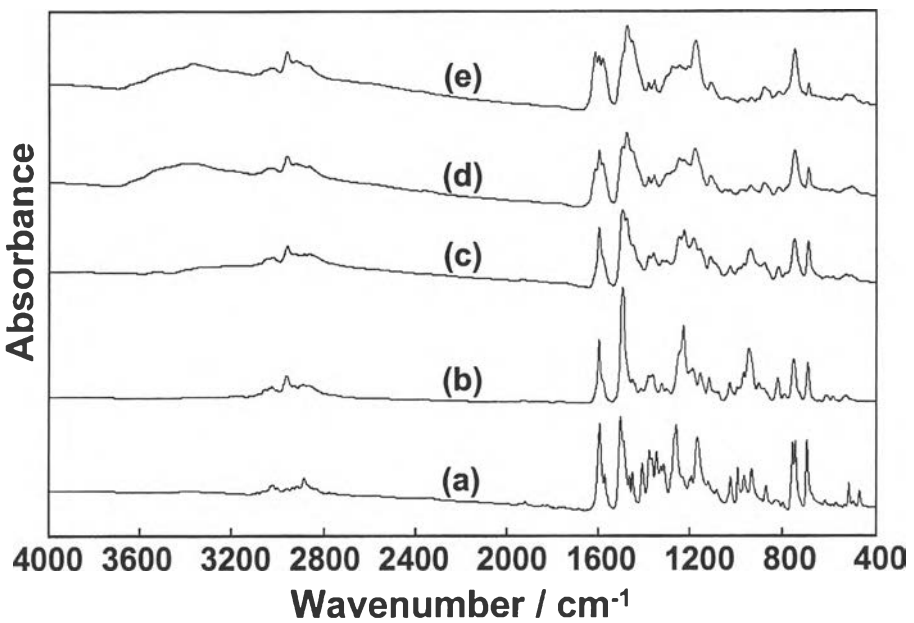


Figure 1. (Chatchai et al.)

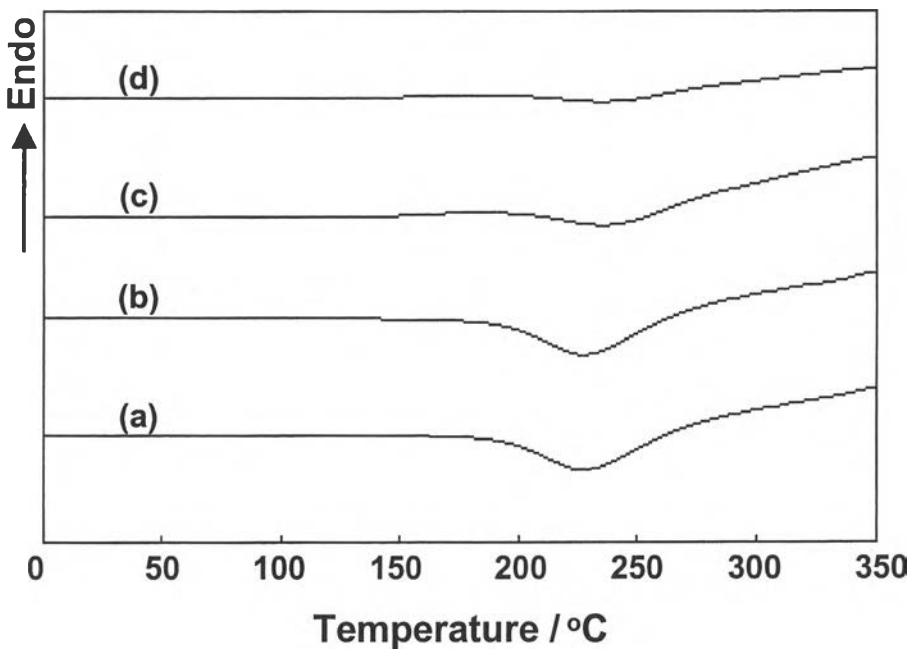


Figure 2. (Chatchai et al.)

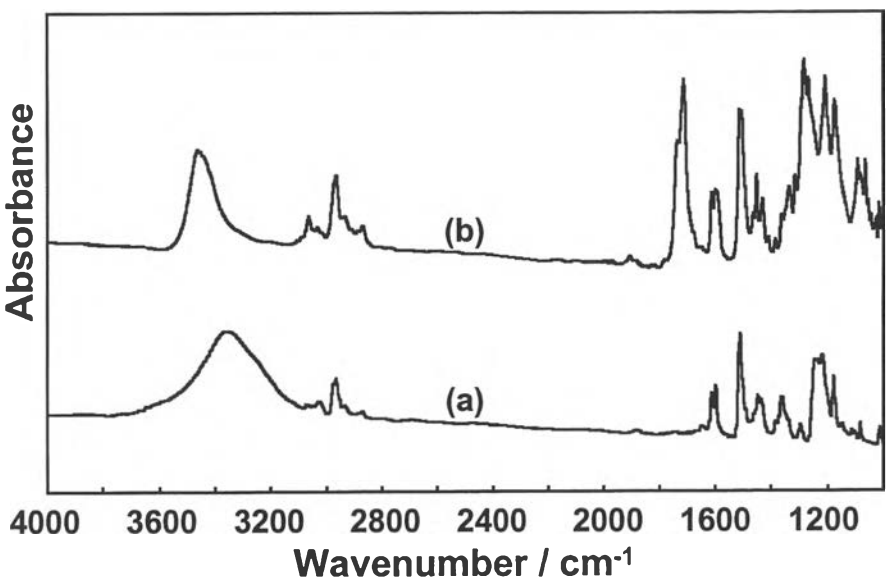


Figure 3. (Chatchai et al.)

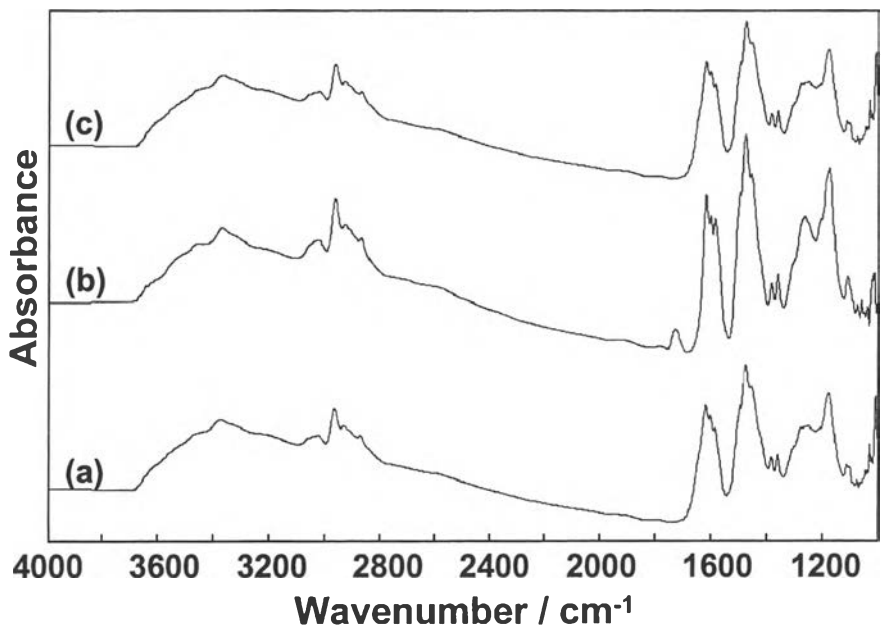


Figure 4. (Chatchai et al.)

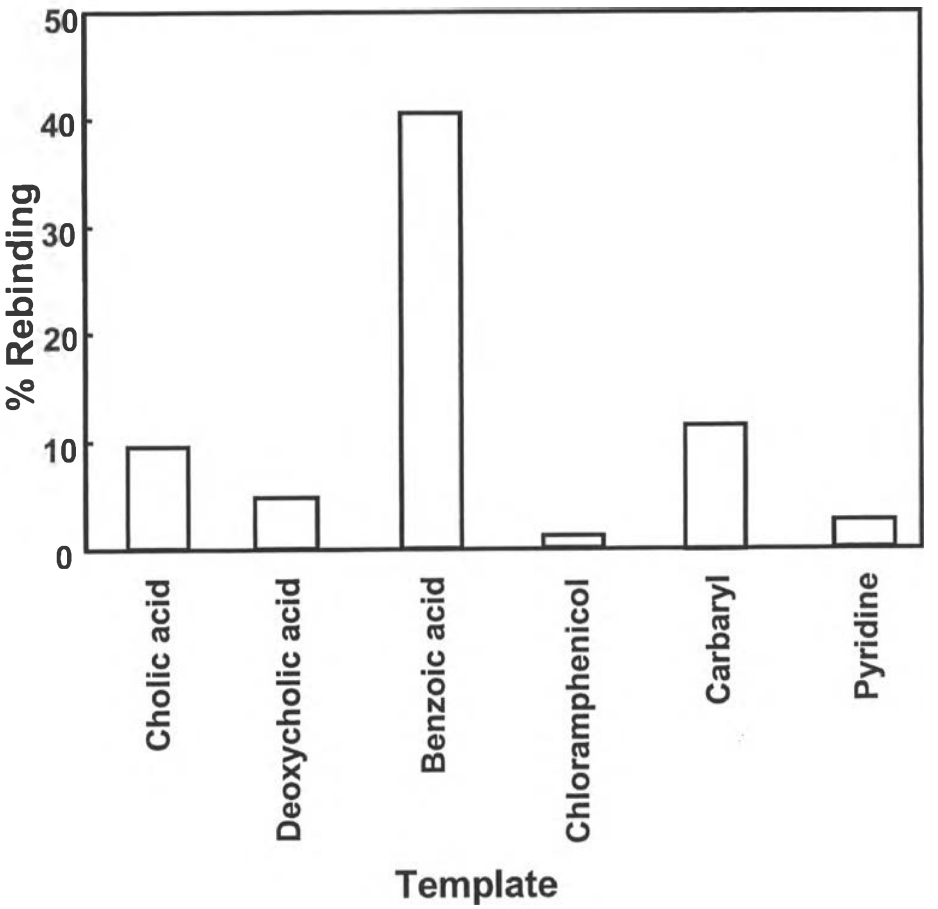


Figure 5. (Chatchai et al.)

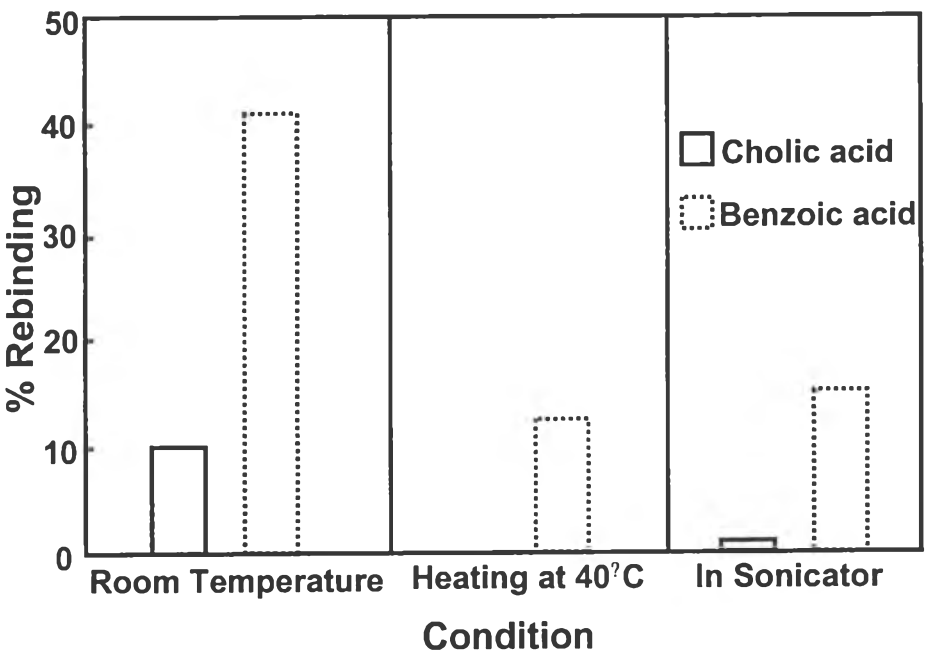


Figure 6. (Chatchai et al.)