

Full Research Paper

Molecularly Imprinted Polymers: Thermodynamic and Kinetic Considerations on the Specific Sorption and Molecular Recognition

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Received: 5 November 2007 / Accepted: 25 February 2008 / Published: 23 April 2008

Abstract: This article presents a work aiming at thermodynamically and kinetically interpreting the specific sorption and recognition by a molecularly imprinted polymer. Using Boc-L-Phe-OH as a template, the imprinted material was prepared. The result indicates that the prepared polymer can well discriminate the imprint species from its analogue (Boc-D-Phe-OH), so as to adsorb more for the former but less for the latter. Kinetic analysis indicates that this specific sorption, in nature, can be a result of a preferential promotion. The imprint within the polymer causes a larger adsorption rate for the template than for the analogue. Thermodynamic study also implies that the molecular induction from the specific imprint to the template is larger than to the analogue, which thus makes the polymer capable of preferentially alluring the template to bind.

Keywords: Molecular imprinting; polymers; molecular recognition; thermodynamics; kinetics

1. Introduction

There is considerable interest in molecular imprinting due to its importance in a broad range of applications [1,2]. Described as a ‘from-key-to-lock’ process, this methodology presents usually an important pathway for the straightforward preparation of antibody-like polymers. To fabricate a ‘from-

key-to-lock' complement, the molecular imprinting uses usually molecular self-assemblies to position the groups of functional monomers around an inducible template [3,4]. A polymerization in the presence of a crosslinker is subsequently performed to fix this organized architecture. The imprinted template is then removed from the polymer, leaving behind binding sites complementary to this template in terms of the structure and function. The recognition of the binding framework constitutes an induced molecular memory, which makes the polymer capable of specifically recognizing the imprint species. Thus, being comparable to interactions generated from some natural biomolecules to their substrates, such as antibody-antigen, receptor-ligand and enzyme-substrate etc, molecularly imprinted materials can specific recognize their templates basing on the same principle [5,6].

Since the molecular recognition by imprinted materials is mainly based on a 'from-lock-to-key' principle, the architecture of imprints plays usually a crucial role on steering the specificity. It is generally accepted that the specific sorption and molecular recognition, in essence, is a result of complementary conformations. The regularized arrangement of functional groups within the imprint delivers a binding framework, which makes the polymer capable of selectively binding the template [7,8]. The shape of the imprint may play partially a molecular sieve role, permitting the molecule as the identical as, or smaller than, the template to enter the interior [9,10]. This guidable theory, though in principle, presents logical interpretations to some general applications [11,12], the conclusions drawn are usually in a qualitative, modal or theoretical form. Almost no specific work has been performed to quantitatively evaluate the practical function. As a matter of fact, there is actually a certain limitation in some special cases, such as glucoside- and chloramphenicol-imprinted polymers- in which [13,14], the recognition behavior does not seem to depend completely on the specific imprint. Thus, the presentation of more parsing particularly additional considerations on such a process is essentially necessary.

Herein we present specially thermodynamic and kinetic considerations on such a process. Thermodynamics and kinetics were used as both of them display not only a merit of quantification but also the general insight into the probable essence of molecular recognition. The Boc-L-Phe-OH-imprinted polymer was prepared as the template is easily available in a highly purified form and has an ideal analogue Boc-D-Phe-OH (enantiomer), as the control, for contrastive studies. After polymerizing and releasing template from the precursor (Scheme 1), the binding framework is left behind and used as a cognitive element (MIP). For the sake of contrasting, a blank polymer (Blank) was also prepared via the same procedures but without the template. The main aim of this study is to present a guidable explanation to the general comprehension on the molecular recognition by imprinted polymers.

2. Results and Discussion

2.1 SEM and Infrared spectrum

Figure 1 presents the SEM images of prepared materials. The blank polymer displays a relatively smooth surface. There are definitely some speckles and cavities appearing in the MIP. Correlating to the preparation process (Scheme 1), these can be a consequence of imprinting. The imprinting embeds the framework of template within the polymer, thereby leaving behind these tracks. Figure 2 presents the infrared spectra of prepared materials. To highlight the trail of imprinting, we also include the MIP

precursor and the template in these spectra. There are three main absorption bands (3200-3600, 2900-3100 and ~ 1750 cm^{-1}) and some overlapped peaks appearing in these spectra. These main absorption bands, as already displayed [15,16], can be related to the stretching of amido/hydroxyl, C-H and carbonyl. These overlapped peaks may be responsible for the vibrations of C-N and C-C bonds. As noted, there is similarity existing in both the spectra of template and the precursor, and which is particularly evidenced in the vibrating areas of C-N and C-C bonds (500-1600 cm^{-1}). After washing, the spectrum of the MIP becomes comparable to that of the blank polymer. This indicates that almost all templates are removed from the precursor, which therefore presents an advantage for the study of binding behaviors.

Figure 1. SEM images of prepared materials (a: Blank; b: MIP).

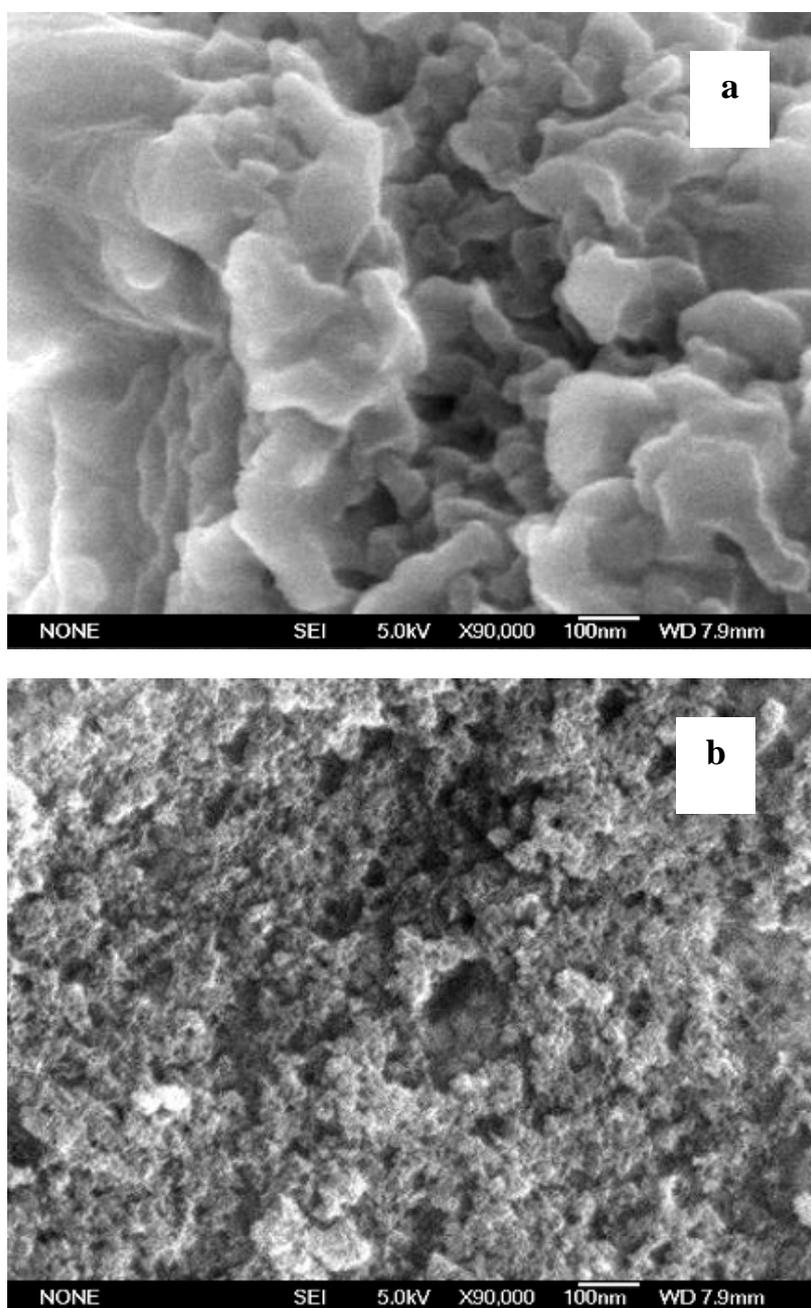
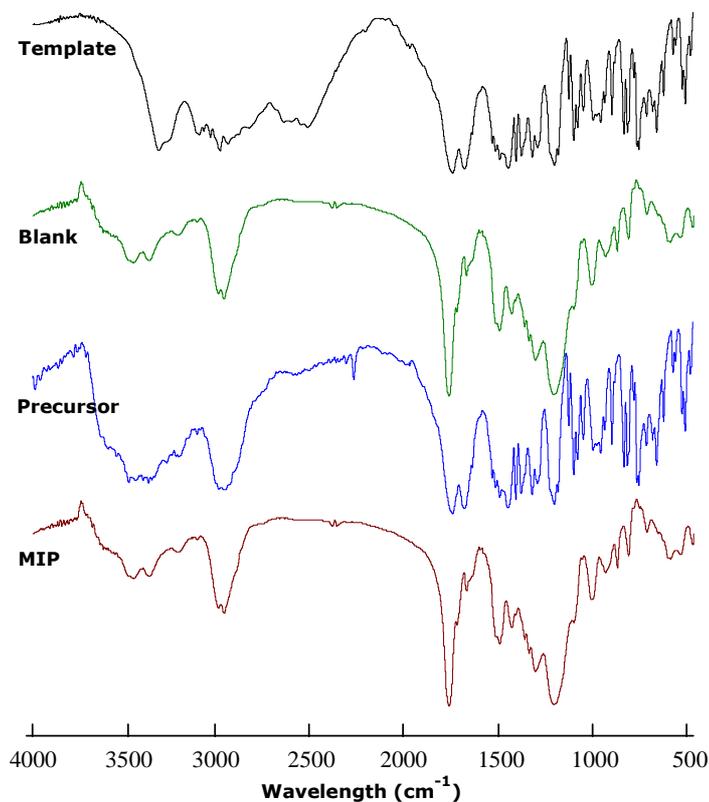


Figure 2. IR spectra of prepared materials.

2.2 Interaction of MIP-substrate and its specificity

Figure 3 shows the TPD profiles. At *ca.* 142 °C, a main desorption for the Boc-D-Phe-OH adsorbed by MIP is observed. However, the main desorption of the template is raised up to 164 °C. The MIP displays a stronger remaining-behavior to the template than to its analogue. To clarify such a resolution, we also show the desorption profiles held by the Blank in Figure 3. As noted, both the desorptions of the template and its analogue from the Blank are at *ca.* 132 °C. The blank polymer displays no notable resolution. These thus reveal that there is a highly specific interaction existing between the MIP and the template. Correlating to the observation in Section 2.1, this can be a consequence of the specific imprint. Since the specific sorption and recognition by imprinted materials is essentially due to a ‘from-lock-to-key’ induction, the specific interaction is expected.

2.3 Specific sorption and molecular recognition

Figures 4 and 5 present the sorptions of prepared materials. An increase in adsorption time or temperature results in a higher-level adsorption. In the case of the Blank, there is no notable difference from the template to its analogue available in the adsorption curves. However, using the MIP, the adsorbed Boc-L-Phe-OH is more than its analogue. The MIP shows a specific sorption for the template. The specific imprint within the MIP plays obviously a role on steering the specificity. As already mentioned, molecular recognition by the imprinted materials, in essence, is due to a conformational complement between template and the imprint. Since the Boc-L-Phe-OH presents a

structural match to the binding framework, the specific adsorption is shown. Further information from kinetic studies indicates that the specific sorption can be internally due to a larger promotion from the binding framework. The adsorption rate for the template can be 1.58 times as much as that for the analogue. Thermodynamic analysis also implies that the induction interaction from the specific imprint to the template is larger than to the analogue. Thus, the increasing adsorption-rate and the larger induction, in principle, may be responsible for the specific sorption. More information is shown below.

Figure 3. TPD profiles of prepared materials.

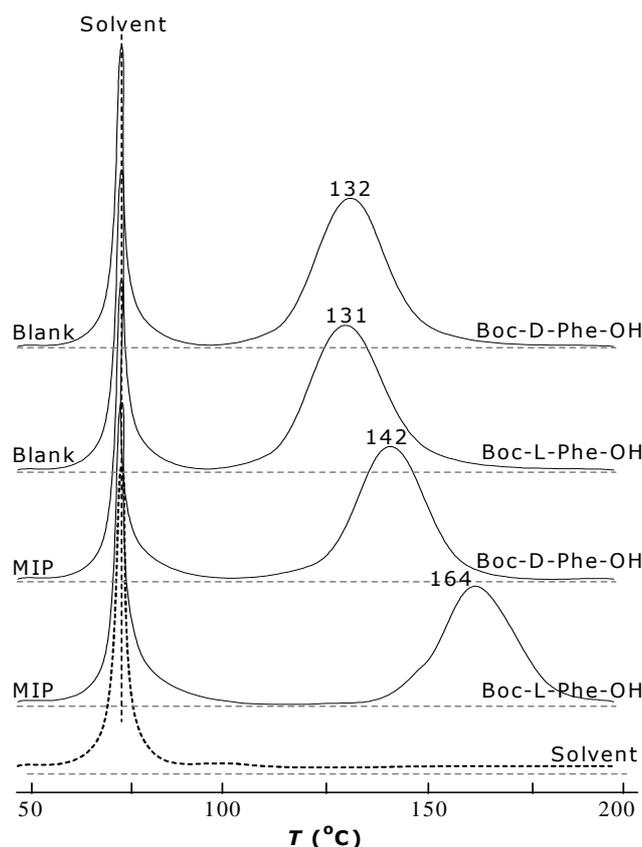


Figure 4. Adsorption curves with time (20 oC).

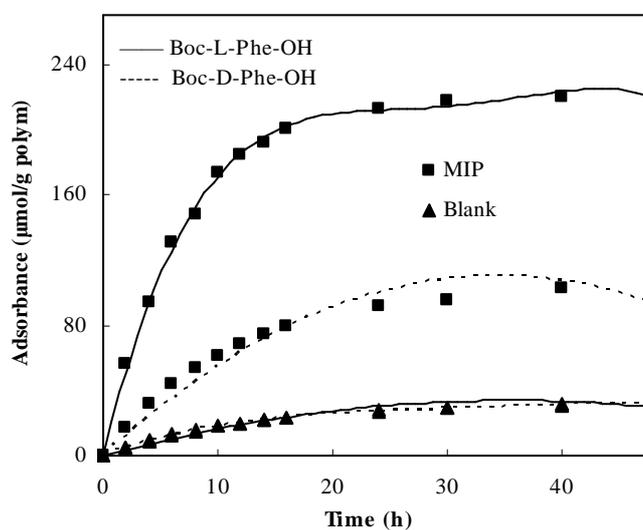
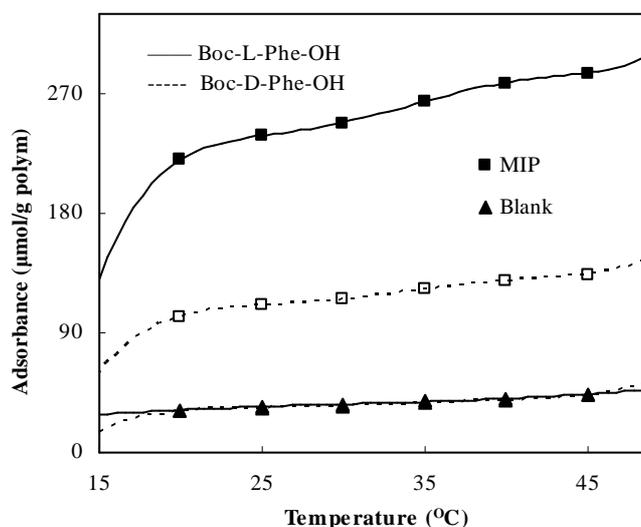


Figure 5. Adsorption curves with temperature (48h).

2.4 Kinetic consideration

To track or simulate sorption, first-order kinetics is presently in common use [17,18]. This may be due to the fact that such a process shows usually a rapid initiation and then a slow approach to a limiting value, as is apparent in this case. In generalization, the first-order kinetics is also tentatively used herein:

$$-\frac{dC}{dt} = kC$$

or

$$-\frac{d(1-\theta)}{dt} = k(1-\theta) \quad (1)$$

Here C and θ are the free concentration of substrate and the coverage degree, respectively, and $1-\theta$ represents the uncovered portion of sorbent. Correlating this relationship in the template with in the analogue would present the relative sorption of a polymer:

$$\left. \frac{d(1-\theta_i)}{1-\theta_i} \right|_T = \frac{k_T}{k_A} \cdot \left. \frac{d(1-\theta_i)}{1-\theta_i} \right|_A \quad (2)$$

Here the subscripts ' T ' and ' A ' are related to the template and the analogue, respectively. Defining a constant A_r that reflects the relative adsorption-rate of Boc-L-Phe-OH and Boc-D-Phe-OH will change Eqn (2) into

$$\ln(1-\theta_i)_T = A_r \cdot \ln(1-\theta_i)_A \quad (3)$$

in which,

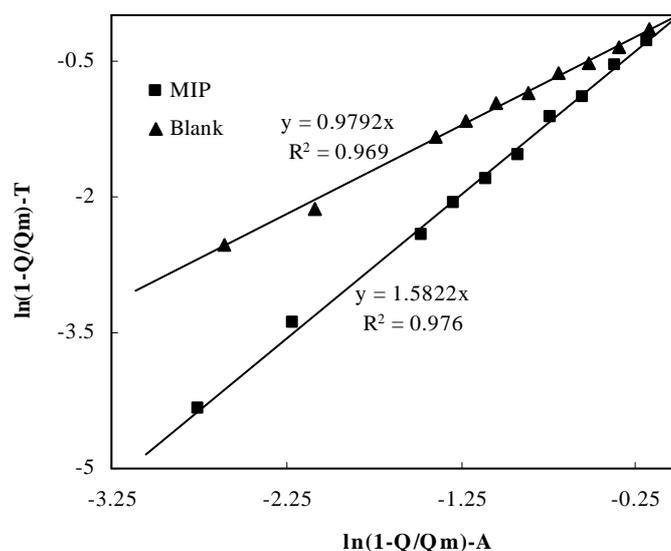
$$A_r \equiv \frac{k_T}{k_A}$$

Solving Eqn (3) would further present:

$$\ln\left(1 - \frac{Q_t}{Q_m}\right)_T = A_r \cdot \ln\left(1 - \frac{Q_t}{Q_m}\right)_A \quad (4)$$

Here Q_t and Q_m are the actual and the maximal adsorbances. Now, based on this Eqn, the relative sorption of a polymer for the template and its analogue can be correlated. Plotting $\ln(1 - Q_t/Q_m)_T$ versus $\ln(1 - Q_t/Q_m)_A$ (as in Figure 4) is normally expected a straight-line (Figure 6). From the slope (i.e. A_r -value), the specificity of prepared materials can be displayed. As noted in the case of the blank polymer, the A_r -value is approximately 1- revealing a typical nonspecific sorption. However, using the MIP, the result shows obviously a preferential promotion. The adsorption rate for the template can be 1.58 times as much as that for the analogue. This thus indicates that the higher sorption of the MIP for the template can be internally a result from the larger promotion.

Figure 6. Kinetic simulations for the specific sorption.



2.5 Thermodynamic analysis

As already known, the extent to a chemical process can be closely associated with a changing chemical-potential [19,20]:

$$\mu = \mu^\phi + RT \ln \frac{C}{C^\phi} \quad (5)$$

Here μ and μ^ϕ are the actual and the standard chemical-potentials, and C and C^ϕ are the corresponding concentrations. With the adsorption in progress, a change in solute concentrations would cause a corresponding change in chemical potentials:

$$d\mu = RT \frac{dC}{C} \quad (6)$$

Integrating the relationship from the initiation to a final equilibrium can present:

$$\begin{aligned} \Delta\mu &= RT \ln \frac{C_1}{C_0} = RT \ln \frac{n_1}{n_0} \\ &= RT \ln \frac{n_0 - (n_0 - n_1)}{n_0} \\ &= RT \ln \left(1 - \frac{n_0 - n_1}{n_0} \right) = RT \ln \left(1 - \frac{Q \cdot w}{n_0} \right) \end{aligned} \quad (7)$$

Here the subscripts '0' and '1' are related to the initial and the terminative states, n the molar number of substrate, w the mass of polymer and Q the adsorbance. Now, according to thermodynamic theory, one can know:

$$\Delta\mu = \Delta\bar{H}_{ad} - T \cdot \Delta\bar{S}_{ad} \quad (8)$$

Combining Eqns (7) with (8) will present:

$$\ln\left(1 - \frac{Q \cdot w}{n_0}\right) = \frac{\Delta\bar{H}_{ad}}{RT} - \frac{\Delta\bar{S}_{ad}}{R} \quad (9)$$

Correlating this relationship in the template with in the analogue would present the relative sorption:

$$\Delta\ln\left(1 - \frac{Q \cdot w}{n_0}\right) = \frac{\Delta(\Delta\bar{H}_{ad})}{RT} - \frac{\Delta(\Delta\bar{S}_{ad})}{R} \quad (10)$$

Here $\Delta\bar{H}_{ad}$ and $\Delta\bar{S}_{ad}$ are the adsorption enthalpy and the entropy, respectively. As commonly known, the adsorption enthalpy is usually a result of changing internal-energy, large or small depending on the interaction of sorbent-substrate. Since the adsorption by imprinted materials, in nature, is a result of the induced molecular memory. Thus, the change of adsorption enthalpies can be indirectly related to the induced interaction between the MIP and substrates. The adsorption entropy, however, is a measurement of disorders before-and-after adsorption, which reflects the change of molecular motions from the free space to a two-dimensional surface. Hence, basing on the changes of adsorption enthalpies and entropies, one can expect to learn about the interaction process. According to Eqn (10), plotting $\ln(1-Q \cdot w/n_0)$ versus $1/T$ (as in Figure 5) is normally expected to be a straight-line (Figure 7). From the slope and the intercept, the specificity of a sorption can be shown. As noted in the Blank, there is only a minor change in the enthalpy and the entropy (which reveals a minor difference on the adsorption behavior of template and analogue). However, using the MIP, the adsorption behavior of the template differs significantly from that of the analogue. Relative to the analogue, the adsorption enthalpy of the template is obviously larger. These thus indicate that the induced interaction from the MIP to the template is much larger than to the analogue. Regarding the smaller adsorption-entropy, as already mentioned, this can be the result of a larger restriction on molecular motions due to the binding. Correlating to previous discussions, the larger induced interaction, in logic, plays a role on preferentially alluring the template to bind.

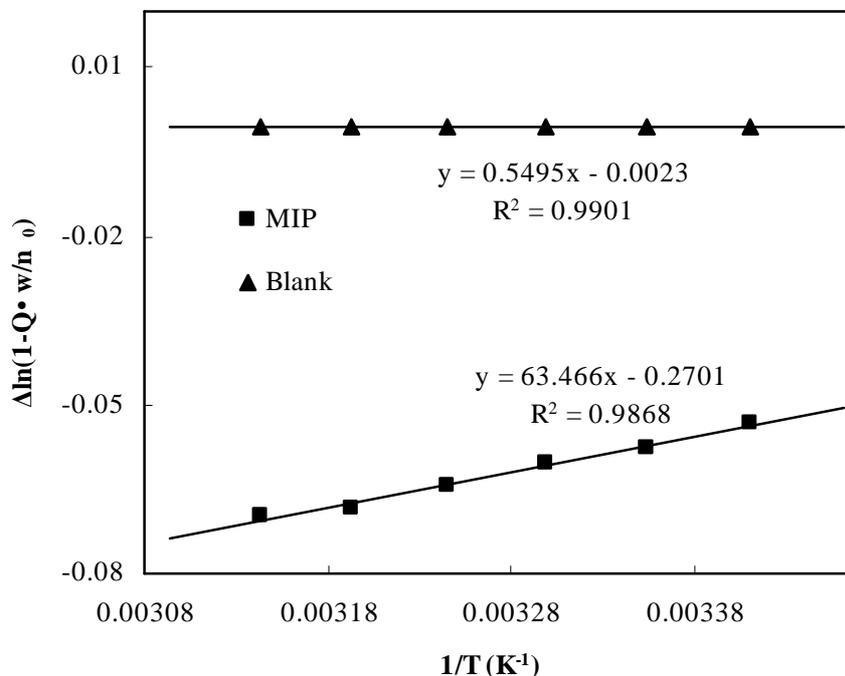
3. Experimental Section

3.1 Preparation of imprinted materials

The preparation of imprinted materials was followed with classic procedures of molecular imprinting (Scheme 1). Solvents and chemicals were commercially available products of reagent grade and used as received. Boc-L-Phe-OH (0.761g; 2.88mmol), acrylamide (0.711g; 10mmol), ethylene glycol dimethacrylate (EGDMA) (9.5ml; 48.5mmol) and 2,2'-azobis(isobutyronitrile) (AIBN) (0.1g; 0.61mmol) were dissolved in acetonitrile (15ml). After fully dispersing and deoxygenating with sonication and nitrogen, the system was irradiated by ultraviolet light (365nm) at 4 °C until all monomers were polymerized. The resulting polymer (precursor) was roughly crushed and subsequently washed by a mixture of methanol and acetic acid (vol: vol= 9:1) to remove the imprinted

template. The final imprinted polymer (MIP) was dried in a vacuum vessel (20 °C) and then ground into a size of 40-50 mesh for further studies.

Figure 7. Thermodynamic fittings on the specific sorption.

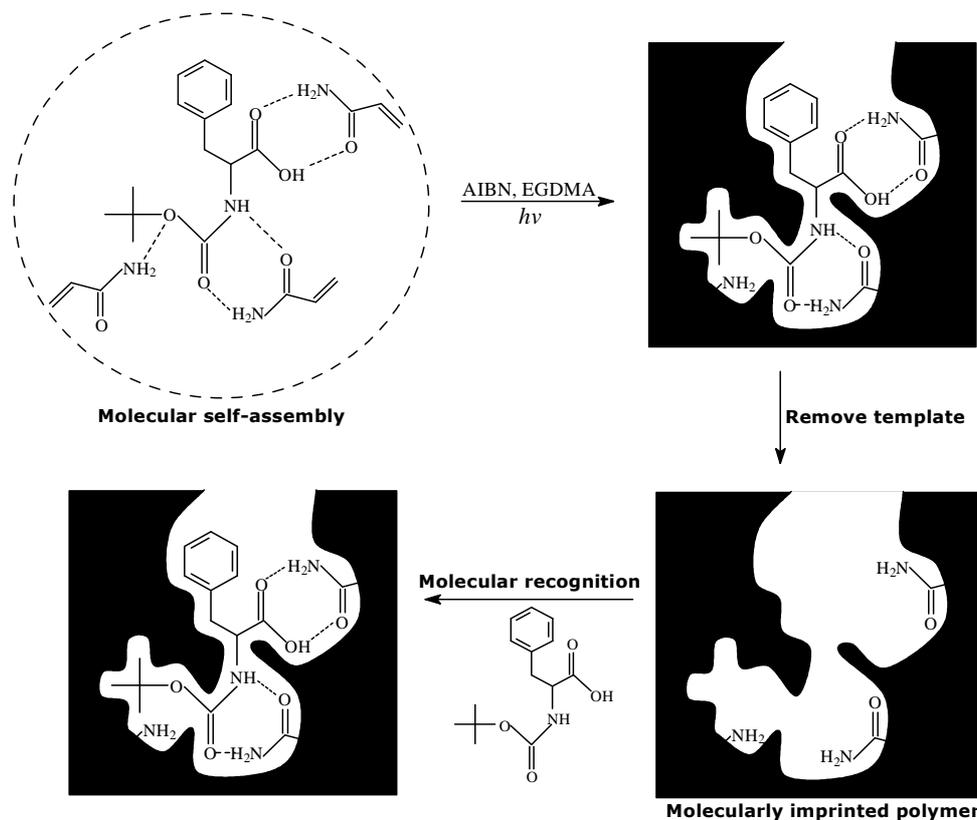


3.2 Sorption test

In a batched format, the sorption test of prepared materials was performed at a thermostatic apparatus [21]. The substrate Boc-L-Phe-OH was dissolved in acetonitrile (initial concentration, 0.48 μmol/ml). The solid content of polymer was 2.0 mg/ml in each operation. The extent of adsorption was determined with a regularized time and the change of solute concentrations was monitored spectrophotometrically at 258nm. The adsorption amount per gram polymer was obtained from the mass balance of substrate, and finally the average value of identical quadruple runs was presented. To learn about the recognition behavior, adsorbing Boc-D-Phe-OH, as the control, was also carried out under comparable conditions.

3.3 Temperature-programmed desorption

The temperature-programmed desorption (TPD) experiments were carried out to evaluate the interaction of imprinted materials and related substrates [22]. Using the apparatus consisting of a gas chromatography (TCD detector) and a data processing system, 0.2g polymer was placed into an online quartz U-shaped tube (4mm I.D.). After being pre-adsorbing 10 μl substrate (0.48 μmol/ml-acetonitrile), the system was heated under a flow of nitrogen (40ml/min; 0.2MPa) from room temperature to 200 °C with a rate of 10 °C/min. The signal for substrate desorption was recorded simultaneously by the data processing system.

Scheme 1. Technical outline for the preparation of imprinted materials.

Acknowledgements

The authors want to thank the National Science Foundation of China (Grant No. 20603010) and the Natural Science Foundation of Hubei Province (Grant Nos. 2007ABA339 and 2007ABA381) for presenting financial supports to carry out this research.

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