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Rationally Designing Molecularly Imprinted Polymer Toward a High Specific Adsorbent by Using Metal as Assembled Pivot

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This article presents an original work aimed at rationally designing molecularly imprinted polymer (MIP) toward a high specific adsorbent. Assembling with cobalt as the pivot, the MIP was prepared by coordinating polymerizable monomers around an inducible template. The use of pivot obviously plays a positive role on increasing the specificity of MIP, so as to adsorb more for the template and less for its analogue. Related studies indicate that these may be a result of increasing specific interaction, which makes the MIP capable of recognizing the imprint species. Further information from thermodynamic analysis reveals that the increasing specific interaction, in logic, can be due to a higher fidelity of imprint, which specifically allures the template to bind.

Keywords: molecularly imprinted polymer; adsorption; metal; assembled pivot

1 Introduction

There is considerable interest in molecular imprinting because of its importance in a broad range of applications (1–4). It has been known that this technique is quite a straightforward method for the preparation of polymer with predetermined selectivity. Normally, based on the molecular self-assembly, the imprint is achieved by arranging polymerizable monomers around an inducible template (i.e. the imprint molecule). Subsequently, a photo- or thermal- polymerization in the presence of crosslinker is performed to fix this organized architecture. The imprint molecule is then removed from the polymer, leaving behind binding sites complementary to the imprint species in terms of the shape and position. The recognition of the imprinted cavity constitutes an induced molecular memory, making the polymer capable of exactly recognizing the imprint species. Thus, comparable to some natural biomolecules (such as antibody, enzyme and receptor, etc.), the MIP can be a kind of 'artificial antibody' (5, 6). However, relative to these natural biomolecules, the significant advantages offered by MIP include physical robustness, high strength, resistance to elevated temperature and pressure, and inertia usually to acid, base, metal ion and organic solvent as well. Owing to these features, the MIP can be used not only partially as the substitute of natural biomolecules, but also as substrate-selective or separation materials under harsh conditions (7–9).

As commonly known, the selective adsorption and molecular recognition by MIP, in essence, is a result of shape- and structural-complement between the arrangement of functional groups (binding sites) and template. Thus, relatively a higher fidelity of imprint can deliver a better molecular recognition. To achieve a high fidelity of imprint, one feasible pathway is to appropriately stabilize the self-organized architecture (10–12). The reason for this can be related to the fact that the stabilization makes the relative thermo-and mechanical motion of monomer-or oligomer-template become less possible in the fabrication process, which thus favors the form of higher fidelity. Perceived from these weak interactions of monomer-template as commonly used, such as hydrogen bond, van den Waals or Coulomb force, etc. (Pathway **a**; Scheme 1), one would normally expect to achieve a relatively better MIP if using metal as the assembled pivot (Pathway **b**; Scheme 1). This may be due to the fact that the coordination bond is usually stronger than the hydrogen bond, van den Waals or Coulomb force as commonly used. Assembling with metal as the pivot, monomers are regularly positioned around the template via coordinative bridge, which largely restrains the relative motion of monomer- or oligomer-template. As a

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result, a high specific MIP can be anticipated. In tune with this idea, we have made an endeavor in this topic. In the literature, as noted, some researchers have tentatively mentioned this promising prospect (13–17). However, most are limited only to the theoretical, formal or preliminary level. Almost no organizational work has been dedicated to the specialized design of MIP with metal as the assembled pivot.

To the best of our knowledge, this article is the first work that specially contributes to the rational design of MIP. Cobalt (cobalt nitrate) is chosen, as it is soluble in some general solvents, and usually forms a coordination bond with many polymerizable monomers (such as methacrylic acid, etc.). Assembling with cobalt as the pivot, the MIP was prepared by coordinating methacrylic acid around the template Boc-L-Phe-OH (Scheme 1). For a contrasting presentation, the general MIP and blank polymer (prepared without cobalt or cobalt and template) were selected as the controls. The aim is to present complementary research to the general design of imprinted polymers.

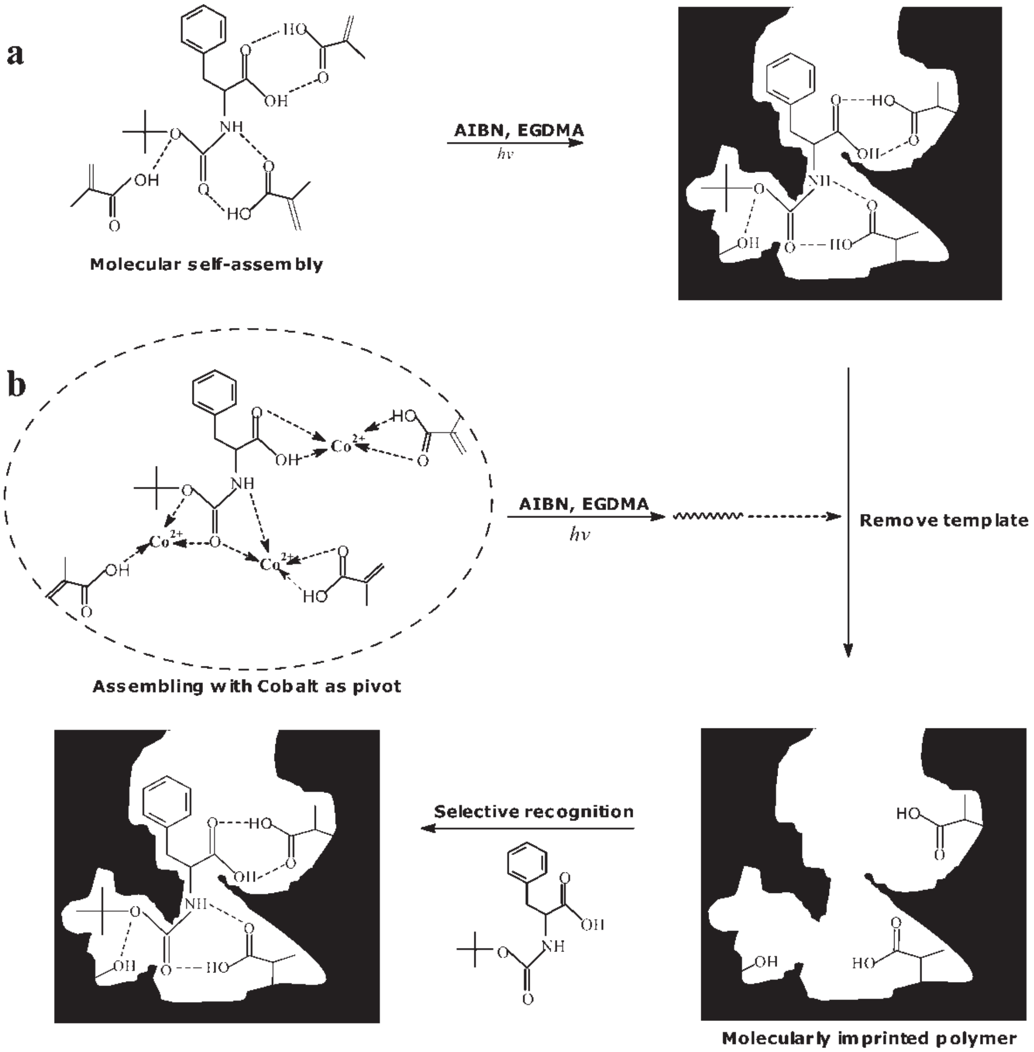
2 Experimental

2.1 Materials

Boc-L-Phe-OH and Boc-D-Phe-OH were purchased from Dongfeng Biotechnology Co. (China). Ethylene glycol dimethacrylate (EGDMA) was obtained from Acros Organics (Belgium). Methacrylic acid (MAA) and 2,2′-azobis (isobutyronitrile) (AIBN) were purchased from Peking Chemical Reagent Plant (China). All other chemicals used are commercially available products of reagent grade.

2.2. Preparation of MIP

Scheme 1 presents a technical outline for the preparation of MIP. 0.617 gram (2.34 mmol) of Boc-L-Phe-OH, 9.5 ml (48.58 mmol) of EGDMA, 0.1 gram (0.61 mmol) of AIBN and a certain amount of MAA and cobalt nitrate (stated additionally in the text) were dissolved in acetonitrile



Sch. 1. Schematic presentation of the preparation and recognition of MIP.

(14.65 ml). After deoxygenation with sonification and nitrogen, the system was irradiated by ultraviolet light (365 nm) at 0°C for 72 h. The resulting polymer (MIP precursor) was roughly crushed and subsequently washed by hydrochloric acid (0.1 mol/l) and methanol-acetic acid (in a volume ratio of 9:1) with numerous cycles to remove the imprinted template and cobalt. The final polymer (i.e., MIP) was dried in a vacuum vessel (20°C) and then ground into 40–50 mesh for further study. For a contrasting study, both mentioned controls (i.e., the general MIP and blank polymer) were also prepared under comparable conditions, but without cobalt or cobalt and template (Pathway **a**). For a suitable presentation, the polymers prepared in the presence and absence of cobalt are mentioned, respectively as 'Co-MIP' and 'MIP', and the blank polymer as 'NIP'.

2.3 *Adsorption*

In a batch format, the adsorption experiment was performed under room temperature (except for additional statement) (18, 19). The substrate Boc-L-Phe-OH was dissolved in acetonitrile (with an initial concentration of 0.48 μmol/ml). The solid content of Co-MIP was 2 mg/ml in each operation. The sample solutions (in identical quadruple) were stirred for a regular time (2, 4 and 6 h, etc.). The change of substrate concentration before and after adsorption was spectrophotometrically monitored at 258 nm. The adsorption amount per gram polymer was obtained from the mass balance of substrate, and finally, the average value of quadruple samples was presented. For a comparative study, the adsorption by both controls, along with the adsorption of enantiomer Boc-D-Phe-OH, were also carried out under comparable conditions.

2.4 *Temperature-Programmed Desorption*

Temperature-programmed desorption (TPD) experiments were carried out to evaluate the interaction of MIP and related substrates (20, 21). In an apparatus including gas chromatography, TCD detector and data processing system, 0.2 gram of MIP was placed into an online quartz U-shaped tube (4 mm I.D.). After pre-adsorbed with 10 μl of substrate (0.48 μmol/ml-acetonitrile), the MIP was heated in a nitrogen flow (40 ml/min; 0.2 MPa) from room temperature to 360°C with a rate of 10°C/min. The signal for substrate desorption was simultaneously recorded by the data processing system.

3 Results and Discussion

3.1 *Template-Monomer Interaction and Intervention of Metal*

As already mentioned, the molecular self-assembly between monomer and template is a premise for the fabrication of imprint. Normally, depending on this monomer-template interaction, the imprint is achieved by arranging functional monomers around the template. Assembling with metal as the pivot, monomers are linked to the template via coordinative bridge. Figures 1–3 present the titration of MAA or template to Boc-L-Phe-OH and cobalt nitrate under the

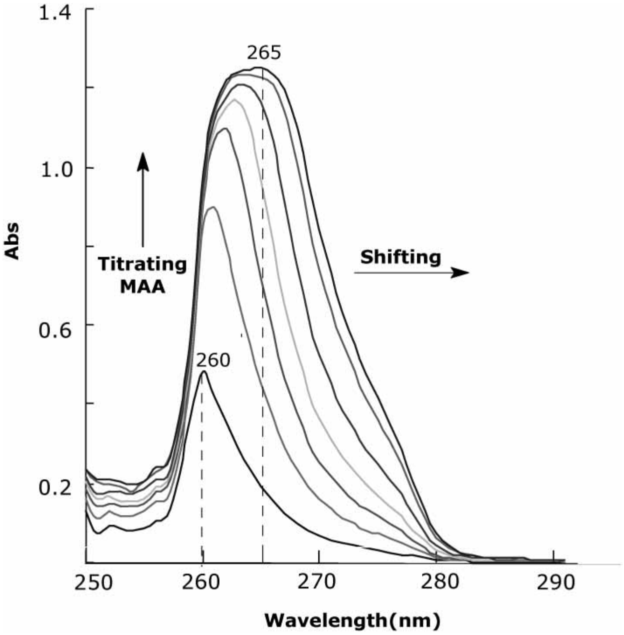


Fig. 1. The curve of titrating MAA to Boc-L-Phe-OH under the monitoring of UV spectrum.

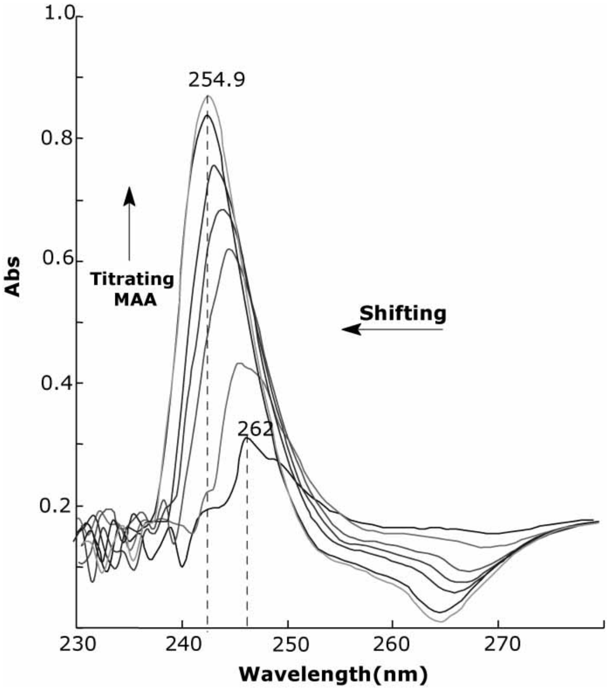


Fig. 2. The curve of titrating MAA to cobalt nitrate under the monitoring of UV spectrum.

monitoring of UV spectrum. With the proportional recipe as the control and titration basis (Section 2.2), the monomer and template are titrated. A titration of monomer and template results in a shift of UV absorption-bands. The shift is evidenced by an increase in the titration amount. The shift in the absorption bands achieves a maximum when the titrated monomer and template reach a critical value (corresponding to 3.2 mol/mol of monomer-template, 3.16 mol/mol of monomer-metal and 1.33 mol/mol of template-metal ratios). Beyond the critical value, no additional shift in the absorption bands is observed except for an increasing absorbency. This strongly indicates that there are interactions existing bilaterally in the monomer-template, monomer-metal and template-metal, and that these interactions are subsequently saturated by adding a stoichiometric amount of monomer and template. As perceived from the general mechanism of MIP (Scheme 1), an excessively high amount of assembled monomer will render the imprinted cavity with spatial and steric mismatch to the template, due to an over abundance of functional groups that distribute randomly throughout the polymer. Too low an amount of assembled monomer will deliver the polymer with an insufficient quantity of functional groups to achieve a complete self-assembly. Thus, for the rational design of MIP, the use of stoichiometric monomer is essentially necessary. According to the basic recipe (Section 2.2), 7.49 mmol of MAA is thus used to synthesize these MIPs. Based on the connection of coordinative bridge, 4.13 mmol of metal is therefore required to achieve a complete extent of self-assembly (i.e., the sum of (monomer/3.16) and (template/1.33)). Now, with this recipe in hand, one can easily prepare the MIP with a complete extent of metal-mediated self-assembly, which thus presents a convenience for the contrasting study in the presence and absence of metallic pivot.

Regarding the shift direction of UV absorption-bands, it is necessary to mention the general principle. As commonly known, the UV spectrum can be related to the transition of valent electron from ground-state to a higher energy-level. The electron tied tighter would need more energy to excite this transition than the one tied looser. In the self-assembly process, the groups of functional monomer are regularly positioned around templates due to the mutual induction. The electron-releasing performance from the induced template would result in an easier transition, which thereby presents a 'red shift' in the absorption band of monomer. Otherwise, a 'blue shift' can be observed, as is apparent in the presence of cobalt.

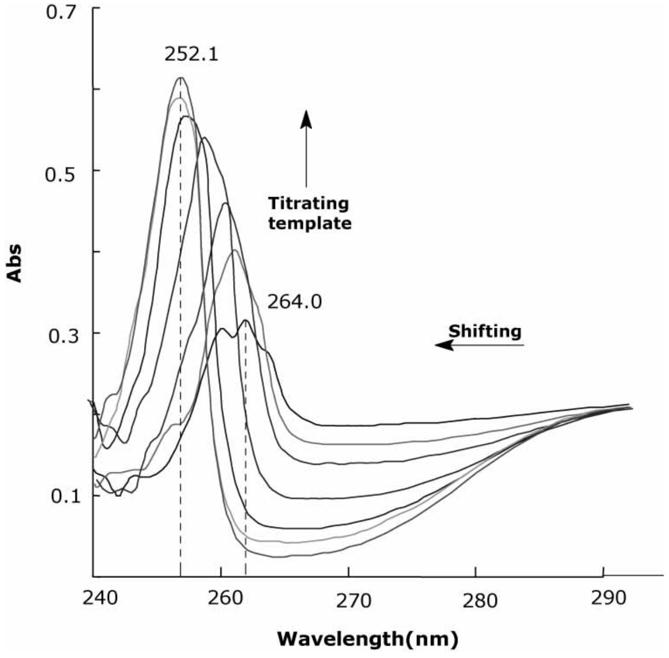


Fig. 3. The curve of titrating Boc-L-Phe-OH to cobalt nitrate under the monitoring of UV spectrum.

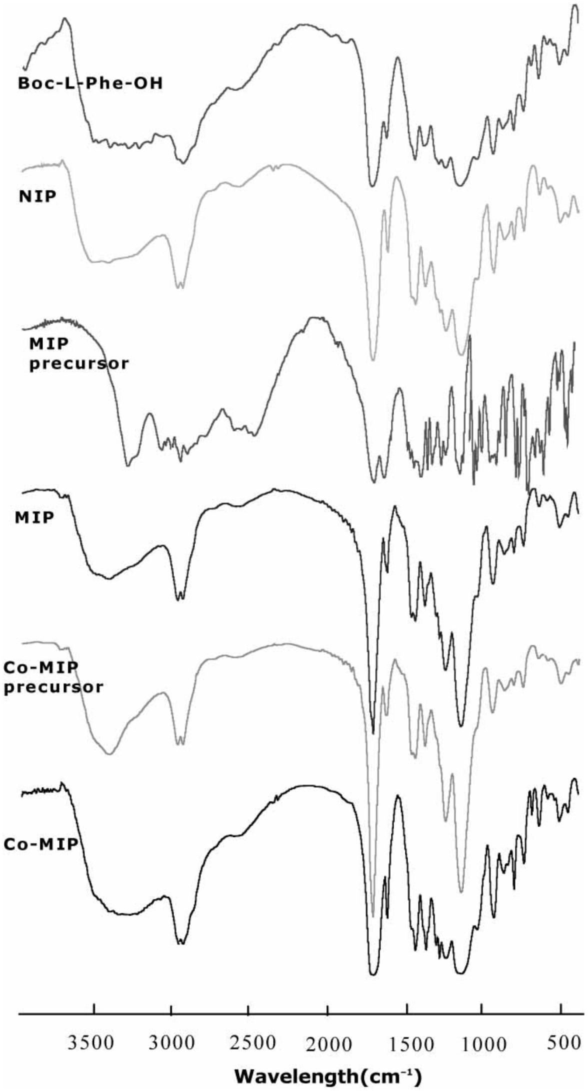
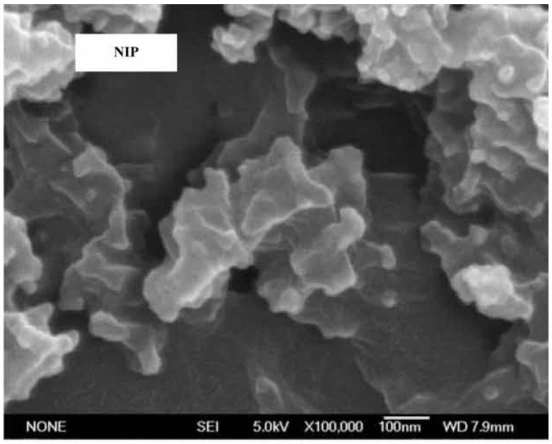


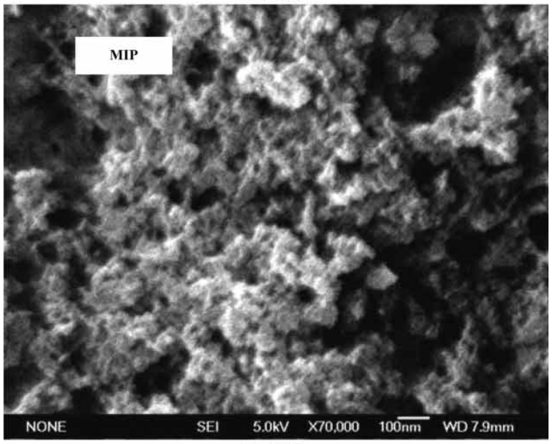
Fig. 4. IR spectra of polymers prepared.

3.2 Revelation of Imprint

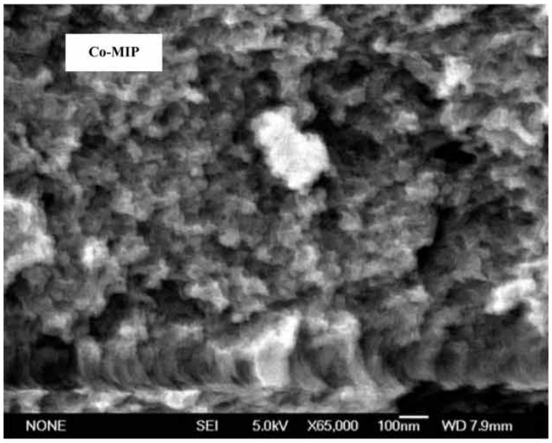
Figure 4 presents the infrared spectrum of Co-MIP prepared. Beyond the fingerprint area, there are two main absorption bands existing in the spectrum, distributing, respectively within 2800–3100 and 3300–3700 cm^{-1}. In basic conditions, as already displayed (22, 23), the absorption band ranged from 2800 to 3100 cm^{-1} can be related to the stretching of hydroxyl (containing carboxyl group). The peak within 3300–3700 cm^{-1} may be responsible for the stretching of C-H. For clarification purpose, we also enclose the spectra of both controls and Boc-L-Phe-OH in Figure 4. As observed, there is similarity existing among the Co-MIP precursor, MIP precursor and Boc-L-Phe-OH. After washing, the spectra of Co-MIP and MIP are almost the same as that of NIP. Figure 5 presents the morphological difference of Co-MIP, MIP and NIP the NIP shows a slippery surface. However, there are obviously some holes existing within the Co-MIP and MIP. These strongly indicate that a template imprint is formed within the Co-MIP and MIP. Regarding the difference of both imprinted polymers, it is important to mention the general role cobalt played in the preparation of Co-MIP. Assembling with metal as the pivot, as already explained, monomers are regularly positioned around the templates via a coordinating bridge. Since the coordination bond is stronger than the hydrogen bond used



a: NIP



b: MIP



c: Co-MIP

Fig. 5. SEM profiles of polymers prepared.

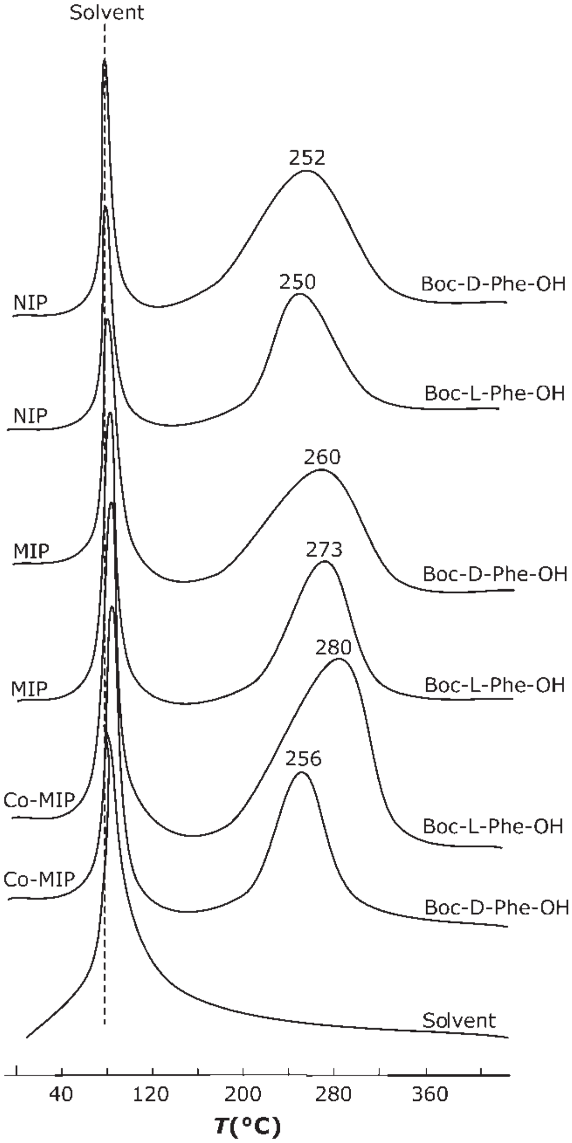


Fig. 6. TPD profiles of polymers prepared.

in MIP, the relative motion of monomer-template is largely restricted. After polymerization and removed template, the imprint with a relative higher fidelity is thus left behind. As a result, the prepared Co-MIP, in logic, can be expected to show a better recognition toward the imprint molecule. Further information would be discussed below.

3.3 Interaction of Imprint-Substrate and Specificity

Figure 6 presents the TPD profiles of Co-MIP. At *ca.*256°C, the main desorption of Boc-D-Phe-OH occurred. However, the main desorption of Boc-L-Phe-OH is raised up to 280°C. The remaining temperature of the template is higher than that of its enantiomer. For contrasting clarification, the TPD profiles of MIP and NIP are also enclosed in Figure 6. As noted, using the NIP as adsorbent, no actual discrimination for Boc-L-Phe-OH and Boc-D-Phe-OH is shown. Although the MIP shows similar remaining behavior toward the template, the relative remaining-value between both enantiomers (13°C) is much lower than that in the case of Co-MIP (24°C). These indicate that there is a high specific interaction existing between the Co-MIP and Boc-L-Phe-OH, and that the imprint obviously plays a role on determining this specificity. As already explained, the molecular recognition by imprinted polymer, is, in essence, a result of shape-and structural-complement between imprint and template. Since the assembly with coordination bond can present higher imprint dependability, the larger remaining-value is expected.

3.4 Preferential Adsorption and Molecular Recognition

Figures 7 and 8 present the adsorption curves of Co-MIP. An increase in adsorption time or temperature results in a higher level of adsorption. Relative to Boc-D-Phe-OH, the Co-MIP shows preferential adsorption for Boc-L-Phe-OH. This reveals that adsorption by the Co-MIP can be a substrate-discriminated process. For the purpose of clarification, we also enclose the adsorption curves of both controls in Figures 7 and 8. With the NIP as adsorbent, no actual difference existing between both enantiomers is presented. Although the MIP shows a trend to adsorb more for the template, the specificity is much lower than that in the case of Co-MIP (Figure 9; Q_L/Q_D is the ratio of adsorbance). Clearly, the high specific interaction between the Co-MIP and Boc-L-Phe-OH plays a crucial role on steering this preferential adsorption. As previously mentioned, the molecular recognition by imprinted polymer, in nature, is due to the induced molecular memory. Since the Co-MIP can present the highest specific interaction toward the imprint species (Section 3.3), the best recognition is shown. Associated with the previous discussion, this highest specific interaction within Co-MIP, in logic, is a result of high fidelity of imprint, which arose by the stabilization of self-assembled architecture.

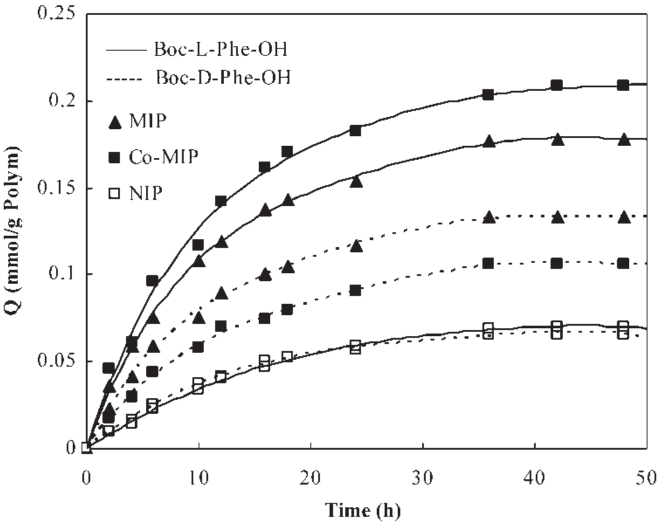


Fig. 7. Adsorption curves of polymers prepared (room temperature).

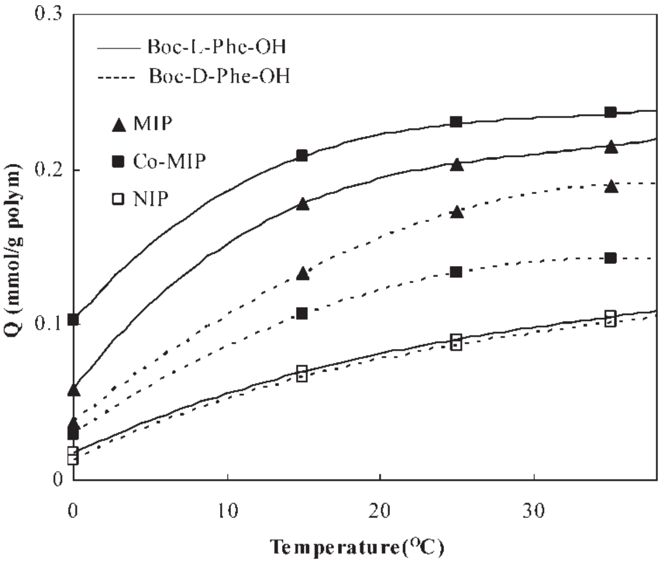


Fig. 8. Adsorption curves of polymers prepared (72 h).

3.5 Thermodynamic Consideration

As commonly known, thermodynamics is efficient in many complicated processes. Based on the initial and terminative states, thermodynamics can present some valuable information insightful to the probable essence. It is known that the extent to a reaction can be correlated to the changing chemical-potential. According to thermodynamic theory, the basic relationship of chemical potential is:

$$\mu = \mu^{\varphi} + RT\ln\frac{C}{C^{\varphi}} \tag{1}$$

Here μ and μ^{φ} are the actual and standard chemical-potentials and C and C^{φ} are the corresponding concentrations. In the adsorption, a minor change of substrate

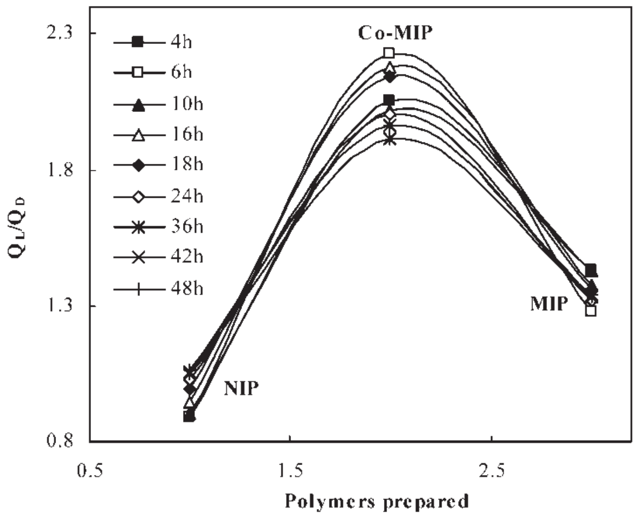


Fig. 9. The specificity of adsorption from polymers prepared.

concentration would result in a corresponding change of chemical potential:

$$d\mu = RT\frac{dC}{C} \tag{2}$$

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

$$\begin{aligned}\Delta\mu &= RT\ln\frac{C_1}{C_0} = RT\ln\frac{n_1}{n_0}\\ &= RT\ln\frac{n_0-(n_0-n_1)}{n_0}\\ &= RT\ln\left(1-\frac{n_0-n_1}{n_0}\right) = RT\ln\left(1-\frac{Q\cdot w}{n_0}\right)\end{aligned} \tag{3}$$

Here the subscripts '0' and '1' are related to the initial and terminative states, n the molar number of substrate, w the mass of MIP and Q is the adsorption amount. Now, basing on thermodynamics, one can see:

$$\Delta\mu = \Delta\bar{H}_{ad} - T\cdot\Delta\bar{S}_{ad} \tag{4}$$

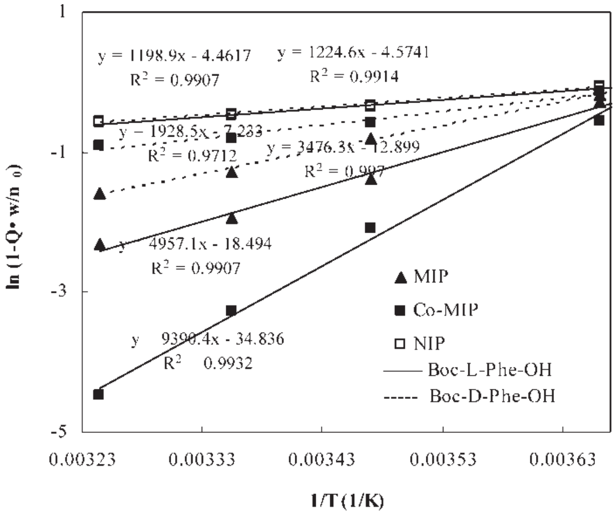


Fig. 10. Thermodynamic analysis for the adsorption by polymers prepared.

Combining Equations (3) with (4) will present:

$$\ln\left(1-\frac{Q\cdot w}{n_0}\right) = \frac{\Delta\bar{H}_{ad}}{RT} - \frac{\Delta\bar{S}_{ad}}{R} \tag{5}$$

Here, $\Delta\bar{H}_{ad}$ and $\Delta\bar{S}_{ad}$ are the adsorption enthalpy and entropy, respectively. As commonly known, the adsorption enthalpy is usually a result of changing internal-energy, large or small depending on the specific interaction of adsorbent-substrate. Since the adsorption by imprinted polymer, in nature, is a result of induced molecular memory. Thus, the change of adsorption enthalpy can be indirectly related to the induced interaction between MIP and substrate. The adsorption entropy is, however, a measurement of disorder before-and-after adsorption, which reflects the change of particles from the free space to a two-dimensional surface. Hence, based on the change of enthalpy and entropy, one can expect to learn the adsorption process. According to Equation (6), the diagram (plotting ln ($1\text{-}Q\cdot w/n_0$) vs. $1/T$) is normally expected to be a straight-line (Figure 10). From the slope and intercept, the difference on the adsorption process can be obtained. With the NIP as adsorbent, almost no thermodynamic difference between both enantiomers is presented, thereby revealing a similar interaction between NIP and both substrates. However, using the Co-MIP as support, the adsorption of Boc-L-Phe-OH appears to significantly differ from Boc-L-Phe-OH. Relative to the enantiomer, the adsorption enthalpy in the case of template is obviously larger. This indicates that the induced interaction of Co-MIP toward the template is larger than that toward its enantiomer. Regarding the smaller adsorption-entropy, as already mentioned, this can be a result of the larger restriction on molecular motion due to the high specific imprint. As also noted, relative to the general MIP, the difference between both enantiomers over Co-MIP is larger. The adsorption by Co-MIP leads to a larger change in the adsorption enthalpy and entropy. These indicate that the specific induction within Co-MIP is larger than that in the case of MIP. Correlated to the previous discussion, the larger specific induction within Co-MIP, in logic, may be responsible for the high specific imprint, which makes the polymer capable of preferentially alluring the template to bind.

4 Conclusions

This article presents an original work aimed at rationally designing molecularly imprinted polymer (MIP) toward high specific sorption. Assembling with cobalt as the pivot, the MIP was prepared by coordinating polymerizable monomers (methacrylic acid) around the template Boc-L-Phe-OH. For a contrasting study, the general MIP and blank polymer were also prepared under comparable conditions. The use of pivot obviously plays a positive role on increasing the specificity of MIP, so as to adsorb more for the template and less for its analogue. Related studies from TPD and adsorption indicate that these may be a result of increasing specific interaction, which makes the MIP capable of recognizing the imprint species. Thermodynamic analysis reveals that the increasing specific interaction, in logic, can be due to the higher fidelity of imprint, which preferentially allures the template to bind. In content, this work presents a complementary study to the general design of imprinted polymers. It is also necessary to point out that these results are preliminary and that further work is necessary regarding a clearer understanding.

5 Acknowledgments

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