

Recognition Interactions of Metal-complexing Imprinted Polymer

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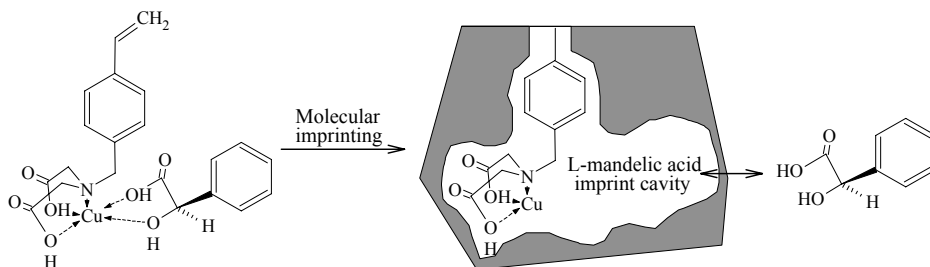
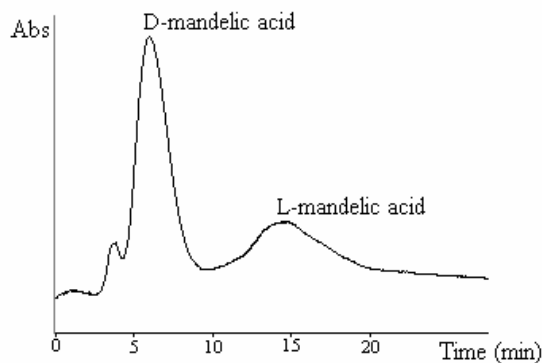
Abstract: Molecularly imprinted polymer, exhibiting considerable enantioselectivity for L-mandelic acid, was prepared using metal coordination-chelation interaction. By evaluating the recognition characteristics in the chromatographic mode, the recognition interactions were proposed: specific and nonspecific metal coordination-chelation interaction and hydrophobic interaction were responsible for substrate binding on metal-complexing imprinted polymer; while the selective recognition only came from specific metal coordination-chelation interaction and specific hydrophobic interaction.

Keywords: Molecularly imprinted polymer, metal coordination-chelation interaction, recognition interaction, enantioseparation.

Molecularly imprinted polymer is a tailor-made synthetic polymer that possesses highly selective recognition properties¹. To date, molecularly imprinted polymers were mostly prepared using non-covalent interactions (such as electrostatic interactions, hydrogen bonding, hydrophobic interactions, van der Waals forces, and so on) as the binding force between the template molecule and the functional monomer. Although above-mentioned non-covalent interactions provide polymers faster rebinding kinetics, the recognition capability is limited by the weak nature of individual interactions^{2,3}. Metal coordination-chelation interaction is well-suited to molecular recognition, because it offers important advantages over other interactions for molecular imprinting: 1) it is generally stronger than hydrogen bonding and van der Waals forces⁴, and therefore can significantly reduce the random incorporation of functional monomers; 2) this force is usually steady in water-alcohol system; 3) Metal coordination-chelation interaction has oriented property; 4) it belongs to non-covalent force.

Some metal-complexing imprinted polymers exhibiting various recognition properties have been made in recent years²⁻⁷. However, no specific discussion has been dealt with regarding recognition interactions of metal-complexing imprinted polymer up to now. Understanding recognition interactions is essential to develop metal-complexing imprinted polymers with enhanced selectivity. In this study, metal-complexing imprinted polymer with high enantioselectivity was prepared using L-mandelic acid as the template molecule and possible recognition interactions were discussed.

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Figure 1 Schematic representation of metal-complexing imprinted polymer for L-mandelic acid**Figure 2** Enantioseparation of D,L-mandelic acid on metal-complexing imprinted polymer MIP1

Conditions: 6/4 (v/v) MeOH/30 mmol/L sodium phosphate buffer (pH 8.0), 0.5 mL/min, 254 nm.

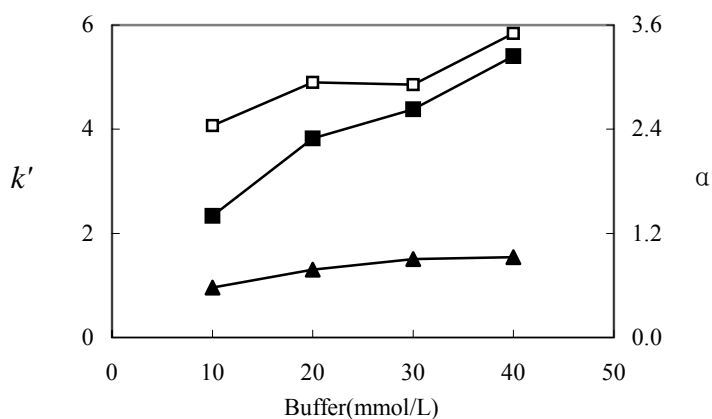
Cu^{II} -N-(4-vinyl)benzyliminodiacetic acid (Cu^{II} -VBIDA) was prepared as the method described by Arnold⁴. Metal-complexing imprinted polymer MIP1 was prepared using L-mandelic acid (1 mmol) as the template molecule, Cu^{II} -VBIDA (1 mmol) as the functional monomer, trimethylolpropane trimethacrylate (TRIM) (7 mmol) as crosslinker, methanol (10 mL) as porogen and azobis(isobutyronitrile) (AIBN) as initiator at 60 °C for 48 h (**Figure 1**). Resultant polymer was ground and sieved (20~43 μm), and then washed exhaustively with acidified 50% aqueous methanol (pH 1), distilled water, aqueous CuCl_2 (0.5 mol/L) and distilled water, sequentially. The imprinted polymer MIP2 and the reference polymer were prepared similarly as above, only in the absence of the treatment with $\text{Cu}(\text{II})$ (MIP2) or the addition of the template molecule during the polymerization process (the reference polymer).

The performance of the imprinted polymer MIP1 was compared chromatographically with the reference polymer using the polymers as stationary phases. MIP1 demonstrated considerable enantioselectivity to the template molecule L-mandelic acid, while the reference polymer exhibited essentially no selectivity, as shown in **Figure 2** and **Table 1**. The result suggested that enantioseparation of the template molecule on the imprinted polymer was induced by imprint effect, that is, complementary arrangement of functional monomers and production of template-modeled cavities.

Table 1 Effect of pH of the mobile phase on retention and enantioselectivity of D,L-mandelic acid on metal-complexing imprinted polymers.

pH*	MIP1			MIP2			Reference polymer		
	k'_L	k'_D	α	k'_L	k'_D	α	k'_L	k'_D	α
3.0	3.65	3.49	1.05	2.17	2.17	1.00	2.51	2.49	1.01
5.0	2.64	2.17	1.22	0.97	0.97	1.00	1.94	1.91	1.01
6.0	2.37	1.43	1.65	0.97	0.97	1.00	1.54	1.54	1.00
7.0	2.81	1.25	2.25	0.84	0.84	1.00	1.47	1.48	0.99
9.0	9.47	5.34	1.77	0.85	0.86	0.99	1.56	1.57	0.99

* MeOH/30 mmol/L sodium phosphate buffer (6/4, v/v) at different pH values of the buffer.

Figure 3 Effect of buffer concentration in the mobile phase on retention and enantioselectivity of D,L-mandelic acid on MIP1.

Solid squares: k'_L ; solid triangles: k'_D ; open squares: α . Mobile phase: MeOH/sodium phosphate buffer (6/4, v/v) at different buffer concentrations.

In order to gain insight into recognition interactions of metal-complexing imprinted polymer, the dependences of the recognition and selective abilities for D,L-mandelic acid on pH and buffer concentration of the mobile phase were examined for the imprinted polymers (**Table 1** and **Figure 3**).

MIP2, which was prepared similarly as MIP1 except for the exclusion of the treatment with Cu(II), displayed weakly retention and essentially no enantioselectivity (**Table 1**). It proved that metal coordination-chelation interaction presumably played an important role when metal-complexing imprinted polymer recognized the template molecule. In addition, it was found that retention and enantiomeric recognition of D,L-mandelic acid on MIP1 depended very much upon pH of the mobile phase. As shown in **Table 1**, when pH of the mobile phase was increased from 3.0 to 7.0, the capacity factors for both isomers decreased, while the enantioseparation factor increased; by contraries, when pH of the mobile phase was successively increased from 7.0 to 9.0, the capacity factors for both isomers increased and the enantioseparation factor decreased. We considered that the metal coordination-chelation interaction probably was more important one of several binding forces, and there seemed to be other interactions during recognition process that were unfavorable to enantiomeric recognition. Since pH of the

mobile phase could significantly influence the ionization of the carboxyl group and the hydroxyl group of mandelic acid and therefore the hydrophobicity, we speculated that nonspecific hydrophobic interaction between substrates and the imprinted polymer might be an important binding force too. The decrease of nonspecific hydrophobic interactions resulted in the enantioseparation improvement in acidic mobile phase. Furthermore, it should be pointed out that metal coordination-chelation interactions consist of two parts: the specific metal coordination-chelation interactions between the substrate and the imprint cavity, which were produced by imprint effect, and the nonspecific metal coordination-chelation interactions. The nonspecific metal coordination-chelation interactions were not contributed to the selective recognition and could only enhance the retention of substrate, it was the enhancement of which that resulted in the decrease of the enantioseparation factor in basic mobile phase.

However, unexpected results were presented when examining the effect of buffer concentration of the mobile phase on retention and enantioselectivity for D,L-mandelic acid on MIP1 (**Figure 3**). We found that with increased buffer concentration of the mobile phase, the retention of D, L-mandelic acid on MIP1 became much more strong indeed due to the enhancement of hydrophobic interactions between the substrates and the imprinted polymer, but the recognition selectivity of MIP1 was simultaneously improved greatly. This can be explained by the fact hydrophobic interactions also consist of two parts — specific hydrophobic interactions and nonspecific hydrophobic interactions. The specific hydrophobic interactions conceivably resulted from complementarity in shape and size between the template molecule and the imprint cavity and favored to selective recognition. Furthermore, only when specific hydrophobic interaction is coupled with specific metal coordination-chelation interaction, the contribution of the former for recognition was just demonstrated. The results in **Table 1** could be explained reasonably too.

In conclusion, the recognition of metal-complexing imprinted polymer to substrates mainly depended upon specific metal coordination-chelation interactions and specific hydrophobic interactions between substrates and imprint cavities, which were produced by imprint effect. And nonspecific metal coordination-chelation interactions and nonspecific hydrophobic interactions could only enhance the substrates retention on metal-complexing imprinted polymer.

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