

Application of High Performance Liquid Chromatography to Separation of Novel Chiral Tetrahedral Heterometal Clusters

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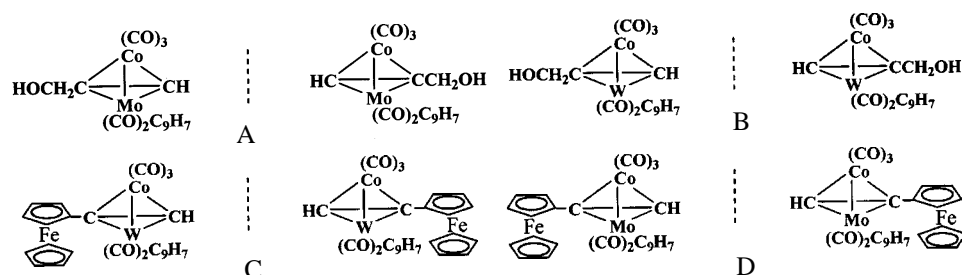
Abstract: A series of novel chiral tetrahedral heterometal clusters have firstly been separated on cellulose tris-(3,5-dimethylphenylcarbamate) stationary phase by high performance liquid chromatography, using hexane as the mobile phase with various alcohols as modifiers.

Keywords: Chiral stationary phase, cellulose tris-(3,5-dimethylphenylcarbamate), mobile-phase composition, chiral tetrahedral clusters, enantioseparation.

Chiral tetrahedral heterometal clusters have aroused growing interest because of their potential application as asymmetric reaction catalysts¹. Using a framework chirality cluster as the catalyst, it would not only bring a new concept in the asymmetric catalysis, in which the most asymmetric induction originates from the central or planar chirality of P or N ligand, but also extend the methodology in the designs of new chiral catalysts. Although a number of chiral tetrahedral transition metal clusters have been synthesized^{2,3}, enantioseparation of the chiral clusters was still a major problem. The traditional method of chiral separation was to convert the chiral clusters into diastereoisomers first and then to separate the diastereoisomers. This method was not only troublesome but also inefficient. Furthermore, it was found that after separation of the diastereoisomers the auxiliary optically active group could not be removed without the destruction of the cluster or loss of the optical activity⁴. If the chiral clusters can be separated without derivatization by HPLC on a chiral stationary phase, the above problems would be solved.

In this paper, four pairs of chiral tetrahedral clusters were separated on the cellulose tris-(3,5-dimethylphenylcarbamate) chiral stationary phase (CDMPC-CSP).

In our experiment, the HPLC system consisted of a Waters 515 HPLC pump (Waters, USA), a Waters 2487 double absorbance detector (Waters, USA) and the chromatograms were acquired and processed by a Millennium³² chromatography manager software. CDMPC was prepared as described in reference⁵. CDMPC was coated on aminopropylated silica gel with a coating amount of 15% (w/w). The CSP was packed into a stainless steel column (25 cm × 4.6 mm) by the conventional high pressure slurry-packing procedure. The mobile phases were composed of various mixtures of hexane and alcohol. The flow-rate was maintained at 1.5 mL/min, and UV

Figure 1 The structures of chiral tetrahedral clusters

detector was at 254 nm. The column temperature was ambient temperature.

From the structures of the tetrahedral cluster enantiomers (shown in **Figure 1**), it could be found that the chirality of the tetrahedral heterometal clusters is different from the classical chiral organic molecules. There is no chiral atom, the chirality is due to the general asymmetry of the tetrahedral framework.

It has been assumed that the separation of enantiomers on the cellulose-based CSPs was due to the formation of solute-CSP complexes, when the solute entered the chiral cavities in the higher order structures of the CSPs. Chiral discrimination between the enantiomers was due to the differences in their steric fit in the chiral cavities of the CSP⁶. The alcohol modifier not only competes for the binding sites with the solute, but also can alter the steric environment of the chiral cavities on the CSP by binding to achiral sites at or near the chiral cavities. Therefore, not only the structure and concentration of alcohol in mobile phase, but also the structural variation of the solute has a large effect on their enantioseparation.

Table 1 Effect of structure of alcohol modifiers on the chiral separation of clusters

Solute		ethanol	1-propanol	2-propanol	1-butanol	2-butanol	tertbutanol	2-pentanol
A	k_1'	2.95	4.57	6.00	4.26	4.98	6.85	10.38
	α	1.23	1.17	1.11	1.16	1.10	1.00	1.12
	R_s	1.07	0.82	0.47	0.75	0.36	0.00	0.53
B	k_1'	3.70	3.14	6.99	6.14	6.83	1.56	6.38
	α	1.24	1.18	1.11	1.16	1.11	1.00	1.14
	R_s	1.19	0.76	0.54	0.76	0.44	0.00	0.61
C	k_1'	1.40	1.51	2.48	0.42	1.58	2.86	1.12
	α	1.11	1.11	1.18	1.00	1.17	1.23	1.00
	R_s	0.48	0.23	0.71	0.00	0.58	1.04	0.00
D	k_1'	2.78	1.67	4.51	1.70	2.68	5.27	1.86
	α	1.12	1.00	1.12	1.00	1.13	1.20	1.00
	R_s	0.39	0.00	0.78	0.00	0.40	0.80	0.00

Mobile phase: *n*-hexane/alcohol = 95/5, *v/v*, flow rate: 1.5 mL/min, column temperature: 25 °C, λ = 254 nm.

Table 2 Effect of concentration of alcohol modifiers on the chiral separation of clusters

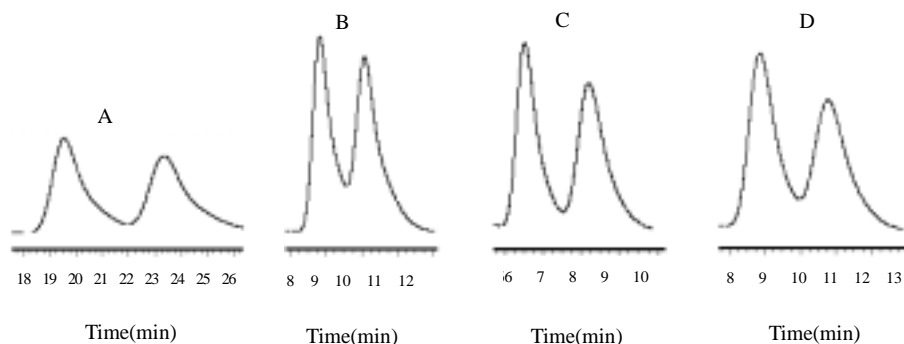
Solute		2%	5%	10%	20%
A	k_1'	7.89	2.95	1.51	0.88
	α	1.22	1.23	1.22	1.23
	R_s	1.30	1.07	0.94	0.74
B	k_1'	10.61	3.70	2.30	0.97
	α	1.25	1.24	1.25	1.24
	R_s	1.15	1.19	1.14	0.72

Mobile phase: n-hexane/ethanol, v/v, flow rate: 1.5 mL/min, column temperature: 25°C, $\lambda = 254$ nm.

In this paper, the effect of the structure of the alcohol on enantioseparation was investigated using a series of alcohols as mobile phase modifiers(MPM), the results were presented in **Table 1**. For clusters A and B, the optimal MPM was ethanol, and for clusters C and D, the most effective MPM was tert butyl alcohol.

The data in **Table 2** showed that increase in the concentration of alcohol resulted decrease in k' . The resolution remarkably increased as the concentration of alcohol decreased, whereas too low concentration of alcohol may result in band broadening in some cases.

Under the optimal conditions, four pairs of tetrahedral cluster enantiomers were separated satisfactorily. **Figure 2** shows their typical chromatograms.

Figure 2 Optimal chromatograms of chiral clusters

Chromatographic conditions: flow-rate: 1.5 mL/min; column temperature: 25°C; UV detector: 254 nm; mobile phase: A B, hexane:ethanol(98:2,v/v), C D, hexane: tert butyl alcohol(98:2, v/v).

The separation of chiral tetrahedral heterometal clusters was successfully achieved on CDMPC-CSP by HPLC. The results showed that the structure and the concentration of the alcohol modifiers in the mobile phase had a large effect on the chiral separation. Both the element in the metal core of the tetrahedral framework and the substitute group of the cluster had significant effects on their separation.

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