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Insoluble β -cyclodextrin polymer for capillary gas chromatographic separation of enantiomers and isomers

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Abstract

An insoluble β -cyclodextrin polymer cross-linked with identified epichlorohydrin has been prepared; its structure was identified by means of infrared and ^{13}C NMR spectra. Three capillary columns have been coated with the polymer treated by ultrasonication by three coating methods. Chromatographic characteristics such as column efficiency, thermal stability and polarity, have been studied, and two kinds of disubstituted benzene isomers and eight pairs of enantiomers have been separated on the three capillary columns. The results show that the β -cyclodextrin polymer is suitable for use as a capillary gas chromatographic stationary phase, and that the column, prepared by loading β -cyclodextrin polymer stationary phase with 50% methyl–50% phenylsilicone (OV-17), shows good chromatographic properties in separating enantiomers and positional isomers. © 2000 Published by Elsevier Science B.V.

Keywords: Stationary phases, GC; Enantiomer separation; Positional isomers; Cyclodextrin stationary phases

1. Introduction

As β -cyclodextrin (β -CD) has many chiral carbon atoms and a special cavity structure, it cannot only separate aromatic compounds, but also enantiomers. Since 1988, the use of cyclodextrins (CDs) and their derivatives for the separation of enantiomers has been developed and the use of these materials as stationary phases in capillary gas chromatography has become increasingly popular. The tremendous potential of cyclodextrins and their derivatives for enantiomeric separation was described in reviews by Schurig and Nowotny [1,2]. Because of the high melting points and the bad film forming abilities of CDs, CD derivatives are used in capillary gas chromatography (GC), instead of using CDs directly.

Up to the present, many CD derivatives have been synthesized and some of them have been proved to be versatile GC stationary phases. With regard to the application of a β -CD polymeric stationary phase for the separation of enantiomers and isomers, β -CD polymer bonded phases have been reported in liquid chromatography [3–12], and there has been a report on the use of the water-soluble polymer in packing gas chromatography by Liu et al. [13]. But the packed column is of low column efficiency; its high selectivity is not used enough. It only separated alkanes, low-boiling-point alcohols, benzene and some substituted benzenes rather than enantiomers. However, as far as we know, there is no report on the use of β -CD polymer as a stationary phase in capillary gas chromatography.

In this work, we synthesized an insoluble β -cyclodextrin polymer cross-linked with epichlorohydrin by

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a modified literature method [14]. The structure of the β -CD polymer was proved with infrared and ^{13}C NMR spectra. The colloid stationary liquid was prepared with the β -CD polymer in the mixed solvent (10 ml) of diisopropyl ether, methylene dichloride and benzene treated by ultrasonication, and fused silica capillary columns were coated with the β -CD polymer stationary liquid by three coating methods. The chromatographic performance of these columns was investigated, and some disubstituted benzene isomers and enantiomers were separated on them. It was found that the column modified with 50% methyl–50% phenylsilicone (OV-17) was excellent for separating positional isomers and enantiomers.

2. Experimental

2.1. Apparatus and chemicals

The gas chromatograph was an American HP-S 890A with a hydrogen flame ionization detector. The fused silica capillary columns (30 m \times 0.25 mm I.D.) were purchased from the Hebei Yongnian optical fiber plant in China. The infrared spectrometer was a Shimadzu IR-460. β -Cyclodextrin, methylene dichloride, benzene, epichlorohydrin, diisopropyl ether and 50% methyl–50% phenylsilicone (OV-17) were purchased from the Beijing Chemical Agent Corporation.

2.2. Synthesis and characterization of insoluble β -cyclodextrin polymer

The insoluble β -CD polymer was prepared using a modified method of Harada et al. [14]. Into a mixture of a solution of 12.0 g of β -CD in 150 ml of water and 40 ml of 20% NaOH, 11.8 g of epichlorohydrin was added dropwise at 60°C over 45 min. After the reaction mixture was kept at 65°C for 48 h, it was neutralized with 2 mol/l HCl, dialyzed with distilled water for several days and freeze-dried. A total of 8.0 g of gray product was obtained. The product consisted of insoluble polymers rather than water-soluble ones. But the use of lower amounts of epichlorohydrin resulted in water-soluble polymers.

Infrared and ^{13}C NMR spectra were used for the

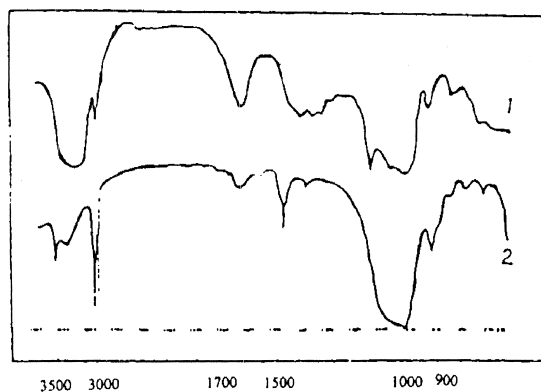


Fig. 1. Infrared spectra of (1) β -CD and (2) β -CD polymer. x-Axis: cm^{-1} .

characterization of the insoluble β -CD polymer. From the infrared spectra of β -CD and β -CD polymer (Fig. 1) we found that the amount of methylene groups increased, and the amount and degree of adsorption of hydroxy groups decreased. From ^{13}C NMR spectra, the peaks at 102, 81.8, 73.4, 73, 71 and 61 ppm, indicate carbon atoms of C-1, C-4, C-2, C-3, C-5 and C-6, respectively, which were nearly equal to those of the unmodified β -CD. The ^{13}C NMR spectra also present some more useful information about the positions of substitution. The peak at 63.3 ppm shows the terminal carbon of the glyceryl tail. The peaks at 47.8 and 51.7 ppm show the existence of the glycidyl groups which are responsible for gelation of the polymer in the presence of larger amounts of epichlorohydrin than that in the synthesis of the water-insoluble β -CD polymer. The relatively strong peak at 70 ppm is indicative of the C-6 substitution; some information (the relatively weak peaks at 100.5 and 78.5 ppm), may show the C-2 and C-3 substitution. There is no positive evidence that only the hydroxyl groups in the 6-position react with epichlorohydrin rather than those in the 2- and 3-position, but in view of the higher reactivity of the 6-OH groups than that of the 2-OH or 3-OH groups, larger amounts of 6-OH groups can be assumed to be substituted than those of 2-OH and 3-OH groups. We can be sure that the β -CD polymer retained the cavity structure of β -CD. A more careful structural analysis is needed and is presently under investigation.

2.3. Preparation of fused silica capillary columns

2.3.1. Preparation of stationary liquid

The 2.6% (w/v) colloid stationary liquid I was prepared by mixing the mixed solvent (10 ml) of diisopropyl ether, methylene dichloride and benzene with a volume ratio 2:1:2, β -CD polymer (0.26 g) and two drops of Tween-80 and then treating the reaction mixture for 0.5 h by ultrasonication. The 2.6% (w/v) diluted colloid stationary liquid II was prepared by adding OV-17 (0.26 g) to stationary liquid I with a mass ratio β -cyclodextrin polymer:OV-17 of 1:1.

2.3.2. Preparation of capillary columns

2.3.2.1. Column 1

At first, a fused silica capillary column was heated at 250°C with nitrogen for 4 h. It was coated with the stationary liquid I by superdynamic coating method under the pressure of 1 MPa at room temperature. After evaporation of the solvent, the column was conditioned, for 1 h at 60°C, heated to 200°C by temperature programming at 2°C/min and for 8 h at 200°C.

2.3.2.2. Column 2

The preparation of column 2 coated with stationary liquid II was the same as described for column 1.

2.3.2.3. Column 3

At first, column 3 was coated with 1.6% OV-17 by superdynamic coating under 0.8 MPa. After evaporation of the solvent for 1 h at 60°C, the column was conditioned by programming to 160°C and left for 2 h. Then, column 3 was coated with stationary liquid I under the pressure of 1 MPa, and it was aged by the same method as column 1.

3. Results and discussion

3.1. Evaluation of the capillary columns

We evaluated the performance of the three capillary columns with non-polar *n*-dodecane, semi-polar naphthalene and polar *n*-nonanol under the conditions of column temperature at 140°C, carrier gas of N₂ and precolumn pressure of 40 kPa. Table 1 lists the performance of the three columns. The efficiency of the three columns with the β -CD polymer stationary liquid treated by ultrasonication is all above 2500 plates. The tailing factors of them approach 1, which shows that the inertness of the three columns is good. At the same time, from Table 1, we can see that the efficiency of columns 2 and 3 are much higher than that of column 1. After column 3 is modified with OV-17, the film-forming ability of the β -CD polymer is improved greatly and the column efficiency increases. On the other hand, the column efficiency can be increased by diluting the β -CD polymer with polysiloxane [15].

According to the literature [16], we evaluated the relative polarity of the three columns by measuring the retention indices of benzene, butanol, 2-pentanone, nitropropane and pyridine. If the total of the retention indices of the five compounds on the column is less than 3000, the relative polarity of the column is non-polar. If it is beyond 5000, it is strongly polar. If it is between 3000 and 5000, it is moderately polar. From Table 2, we know that the polarity of the three columns is moderate and the polarity of the columns decreases with introduction of OV-17; as we expected.

We investigated the thermal stability of the three columns by the degree of the baseline drift by temperature programming. We found that there was no baseline drift when the column temperature

Table 1
Performance of the three columns

Column	Capacity ratio <i>k</i>			Column efficiency (n/m)			Coating efficiency (%)			Peak asymmetry
	<i>n</i> -Dodecane	Naphthalene	<i>n</i> -Nonanol	<i>n</i> -Dodecane	Naphthalene	<i>n</i> -Nonanol	<i>n</i> -Dodecane	Naphthalene	<i>n</i> -Nonanol	
1	2.23	2.64	2.49	2715	2580	2537	70	65	63	0.98
2	2.39	2.66	2.48	3102	2986	3027	76	77	70	1.01
3	2.42	2.87	2.68	3118	3054	2935	78	76	71	1.10

Table 2
Kováts retention indices of five compounds on the three columns

Column	Retention index					
	Benzene	Butanol	2-Pentanone	Nitropropane	Pyridine	Total
1	822	887	844	893	946	4292
2	807	838	816	876	882	4219
3	810	840	817	875	893	4235

reached 200°C. We measured the retention of naphthalene, *n*-octane and *n*-dodecane several times, and we found that the difference of the retention on the same column was very small. From the experimental facts, we can see that the stability of the three columns is good.

3.2. Separation of disubstituted benzene isomers and enantiomers on the three capillary columns

Only a small amount of substituents are introduced to the side of the β -CD cavity, and the geometrical shape does not change greatly, which does not affect the enantioselectivity of the chiral field of force and inclusion. The β -CD polymer used as the stationary phase in capillary gas chromatograph is of very good selectivity. Table 3 lists the separation of disubstituted benzene isomers and eight pairs of enantiomers

on the three capillary columns. From Table 3, we find that the three columns cannot only separate disubstituted benzene isomers, but also many enantiomers. At the same time, we can see that the separation ability of column 3 is much stronger than that of columns 1 and 2. After column 3 was modified with OV-17, the film-forming ability of the β -CD polymer loaded by OV-17 was improved greatly, which did not only retain the strong selectivity of the β -CD polymer, but also raised the column efficiency and enhanced the chromatographic separation ability. As column 1 was directly coated with β -CD polymer of bad film-forming ability, its column efficiency was low and its selectivity was not high. Column 2 was of high column efficiency, but its selectivity was lost to some extent owing to the introduction of OV-17 used as the diluent of β -CD polymer, a dilution reported previously [15]. Figs.

Table 3
The separation of disubstituted benzene isomers and enantiomers on the three capillary columns^a

Compound	Column temperature (°C)	Column											
		1			2			3					
		k_1	α	R_s	k_1	α	R_s	k_1	α	R_s			
Xylene	50	4.21	p/m	1.008	1.83	4.30	p/m	1.009	1.72	428	p/m	1.113	2.89
			m/o	1.124	2.28		m/o	1.113	2.17		m/o	1.286	5.64
Dichlorobenzene	120	5.22	p/m	1.006	1.58	5.19	p/m	1.009	1.94	5.14	p/m	1.110	2.62
			m/o	1.125	2.67		m/o	1.127	2.82		m/o	1.428	9.75
α -Pinene	90	1.64		1.143	2.97	1.75		1.102	2.31	1.76		1.172	3.74
β -Pinene	90	1.68		1.127	2.03	1.78		1.101	2.27	1.81		1.153	3.02
Ethyl lactate	120	2.72		1.201	4.36	2.84		1.214	5.12	2.93		1.232	7.05
α -Phenylethanol	150	4.07		1.312	8.63	4.31		1.128	2.95	4.26		1.516	12.42
1,2-Propanediol	100	3.02		1.323	8.72	2.98		1.327	8.96	3.12		1.470	9.46
α -Lonone	150	3.48		1.285	7.95	3.60		1.196	3.86	3.65		1.528	12.7
Methyl α -chloro-propionate	90	1.41		1.116	2.46	1.39		1.092	2.01	1.58		1.112	2.84
γ -Valerolactone	140	3.83		1.218	5.04	3.94		1.208	4.08	3.98		1.336	8.82

^a k_1 = Capacity factor of the first eluted compounds; α = separation factor, R_s = resolution.

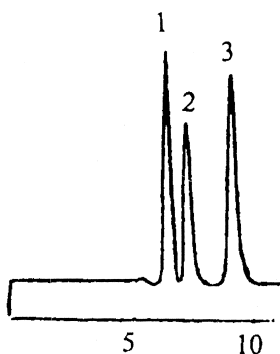


Fig. 2. Chromatographic separation of xylenes; 1=*p*, 2 *m*, 3=*o*. Column temperature=50°C. Time scale in min.

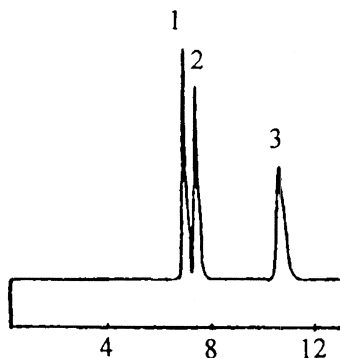


Fig. 3. Chromatographic separation of dichlorobenzenes; 1=*p*, 2=*m*, 3=*o*. Column temperature=120°C. Time scale in min.



Fig. 4. Chromatographic separation of α -phenylethanol. Column temperature=150°C. Time scale in min.

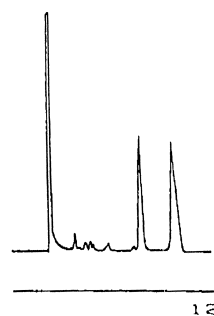


Fig. 5. Chromatographic separation of 1,2-propanediol, Column temperature=100°C. Time scale in min.

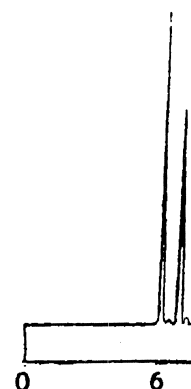


Fig. 6. Chromatographic separation of α -, β -pinene. Column temperature=90°C. Time scale in min.

2–9 show good baseline separation of two kinds of disubstituted benzene isomers and seven pairs of enantiomers in Table 3 on column 3.

4. Conclusion

This work reports the properties of insoluble β -CD polymer as capillary gas chromatographic stationary phases. In the key step of the preparation of the stationary liquid, mixed solvent and ultrasonic treatment are adopted. The data obtained from experiments show that the capillary column (column 3), which is prepared by loading β -CD polymer treated by ultrasonication with OV-17, does not only retain the strong selectivity of the β -CD polymer, but also is of higher column efficiency and stronger chro-



Fig. 7. Chromatographic separation of ethyl lactate. Column temperature=120°C. Time scale in min.

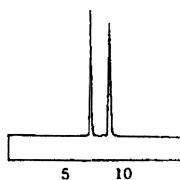


Fig. 8. Chromatographic separation of γ -valerolactone. Column temperature=140°C. Time scale in min.



Fig. 9. Chromatographic separation of methyl α -chloropropionate. Column temperature=90°C. Time scale in min.

matographic separation ability. By this way, the difficult problem of the column efficiency of the capillary column with β -CD polymer as a stationary

phase being low, is easily solved. The column does not only separate aromatic isomers, but also separates chiral compounds. It is a capillary column of strong selectivity with a vast range of prospects for application.

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