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A chiral porous organic cage for molecular recognition using gas chromatography

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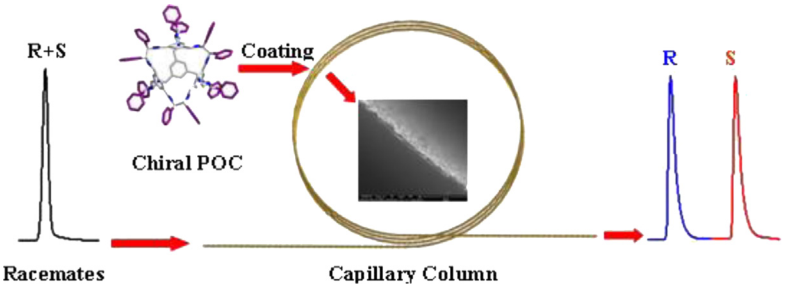
HIGHLIGHTS

- A novel capillary column was fabricated using chiral porous organic cage (CC9) as stationary phase in GC.
- The capillary column exhibited excellent enantioseparation for various racemates.
- The capillary column has good complementarity to β-DEX 120 column and CC3-R column for enantioseparation.
- Positional isomers were also efficiently separated on the capillary column.

GRAPHICAL ABSTRACT



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ABSTRACT

Molecular organic cages as shape-persistent organic molecules with permanent and accessible cavities have attracted a lot of interest because of their importance as host-guest systems. Herein, we report a chiral porous organic cage (POC) CC9 diluted with a polysiloxane OV-1701 to fabricate a CC9-coated capillary column, which was used for the high-resolution gas chromatographic separation of organic compounds, including positional isomers and racemates. On the CC9-coated capillary column, a large number of racemic compounds such as chiral alcohols, esters, ethers and epoxides can be resolved without derivatization. By comparing the chiral recognition ability of the CC9-coated column with the commercially available β-DEX 120 column and the POC CC3-R coated column recently reported by our group, the CC9-coated column offered good resolution during the separation of some racemates, that were not separated using the β-DEX 120 column or POC CC3-R coated column. Therefore, the CC9-coated column can be complementary to the β-DEX 120 column and CC3-R coated column. The results indicated that the CC9-coated column exhibited great potential for application in the separation of positional isomers and enantiomers with great selectivity, high resolution and good reproducibility.

1. Introduction

Enantiomers have identical physical and chemical properties except for optical rotation as well as exhibiting different biological and pharmacological properties [1]. So chiral discrimination has

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become more and more important in various fields, such as the pharmaceutical industry, stereospecific synthesis, food industry and in environmental studies. However, the separation of enantiomers remains a challenge due to their identical physical and chemical properties in an achiral environment [2]. GC using a column coated with a chiral stationary phase (CSP) is an effective choice for enantiomeric separation due to its high efficiency, short analysis time and low sample consumption. In enantioselective GC, there are three major types of chiral stationary phase, including cyclodextrin and its derivatives [3], chiral amino acid derivatives [4] and chiral metal coordination compounds [5]. Cyclodextrin-based CSPs are currently the most widely used stationary phase used in GC and show a broad enantioselectivity towards a large number of racemates. Over the past few decades, many efforts have been devoted to the development and application of new homochiral materials as CSPs with higher and broader selectivity for enantioseparation.

Microporous crystalline materials with pore sizes smaller than 2 nm have been of intense scientific and technological interest because of their potential applications in gas storage, heterogeneous catalysis and molecular separation. Most microporous solids are made up of extended networks, such as zeolites [6], metal-organic frameworks (MOFs) [7–10], covalent-organic frameworks [11,12] or organic polymer networks [13]. Recently, these porous materials, especially MOFs [14–21], have been widely used as separation media owing to their unusual properties such as high surface area, versatile framework topologies and uniform structured cavities, as well as their good chemical and thermal stability. Unlike extended networks, porous molecular solids (discrete molecules) can be soluble in organic solvents [22]. The solubility of porous organic molecules offers some advantages in comparison to insoluble network materials: Porous molecules are miscible in solution, which can allow the properties of the material to be adjusted; an exhaustive post-functionalization process using chemical reactions in the inner cavities of the cage [23,24]. Hence, porous organic molecules are very suitable as separation material in gas chromatography.

The Cooper research group have synthesized a new class of porous organic cages (POCs) with permanent and accessible cavities formed via the condensation reaction of 1,3,5-triformylbenzene or tris(4-formylphenyl)amine and various diamines [23,25–30]. In 2014, Cooper and co-workers first reported the use of POC (CC3-R) towards chiral separation [31]. Subsequently, they utilized CC3-R as a chromatographic stationary phase during the GC separation of various mixtures including aromatic compounds, racemates and alkanes [32]. The CC3-R coated column exhibited excellent resolution abilities, especially for some 2-substituted linear alcohols such as 2-butanol, 2-pentanol, 2-hexanol and 2-heptanol. However, it showed a narrow range of chiral enantioselectivity and poor chromatographic peaks for some compounds owing to the large CC3-R crystal particles. Fortunately, a variety of non-chiral hydrocarbons including xylene isomers, benzene and mesitylene, and five hexane isomers were separated with comparatively sharper peaks on the another capillary column coated using *rac*-CC3 nanoparticles when compared to the CC3-R coated column. Another homochiral POC, CC9, not only possessed intrinsic porosity, but also additional extrinsic porosity between the cage units that enhanced the pore volume. This cage was synthesized via the cycloimination of 1,3,5-triformylbenzene with (1*R*,2*R*)-1,2-diphenylethylenediamine in dichloromethane using trifluoroacetic acid as the catalyst [28]. Herein, we have prepared a CC9-coated capillary column using CC9 as the stationary phase via a static method, which was used for molecular recognition using gas chromatography. The CC9-coated column show excellent selectivity and recognition ability towards a range of organic molecules, especially for racemates. By comparing the CC9-coated column to the commercially available β-DEX 120 column and POC CC3-R coated column previously reported by our group [33], the results revealed that the CC9-coated column can be complementary to the CC3-R coated column and β-DEX 120 column, and can promote the commercial application prospects of homochiral POCs used as the CSP in GC.

2. Experimental

2.1. Apparatus and reagents

The apparatus used for column evaluation was a Shimadzu GC-2014C system (Japan) equipped with a FID, split injection port and capillary control unit. A N-2000 chromatography data system (Zhida Information Engineering Co. Ltd., Zhejiang University, China) was used for data acquisition. The carrier gas was nitrogen (99.999%). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX 500 NMR ultrashield spectrometer (Germany). Powder X-ray diffraction data (PXRD) were collected on a Rigaku D/max-3B diffractometer (Japan) using Cu K_α radiation. SEM images were obtained using a FEI Quanta FEG 650 scanning electron microscope (USA). Thermogravimetric analysis (TGA) was performed on a ZRY-1P simultaneous thermal analyzer (China) from room temperature to 700 °C at a ramp rate of 10 °C min^{-1}.

All chemicals were at least of analytical grade and used without further purification. All racemates were purchased from Sigma–Aldrich (USA), Adamas-beta (China) or TCI (Japan). The dibromobenzenes and nitrotoluenes were purchased from Aladdin Chemistry Co. Ltd. (China). (1*R*,2*R*)-1,2-Diphenylethylenediamine and 1,3,5-triformylbenzene obtained from Acros (Belgium) were used for the synthesis of CC9. The fused-silica capillary column (0.25 mm inner diameter) was purchased from Yongnian Optical Fiber Factory (China). Ultrapure water (18.2 MΩ cm) was produced from an ELGA LabWater water purification system (UK).

2.2. Synthesis of CC9

CC9 was synthesized according to a literature procedure [28] (Scheme S1). Typically, trifluoroacetic acid (26.9 mg, 0.236 mmol) was added to a mixture of the (1*R*,2*R*)-1,2-diphenylethylenediamine (1.50 g, 7.06 mmol) and 1,3,5-triformylbenzene (0.764 g, 4.71 mmol) in dichloromethane (60 mL) and the mixture was stirred at 15 °C for 50 h. The reaction was quenched upon the addition of excess $NaHCO_3$. The suspension was diluted using dichloromethane (60 mL) and filtered. The reaction vessel was rinsed with dichloromethane (60 mL) and the rinse added to the filter cake. The filtrate was concentrated to 40 mL using a rotatory evaporator, acetone (50 mL) was added and the suspension filtered. Finally, the filter cake was washed with acetone (50 mL) and dried under suction to afford a white solid. ^{1}H NMR ($CDCl_3$) $\delta = 8.48$ (s, $(R)_3$-Ar-*H*, 12H), 8.24 (s, C*H*=N, 12H), 7.18–7.08 (m, Ar–H, 60H), 4.79 (s, $(R)_2$-C*H*N, 12H) ppm. ^{13}C NMR ($CDCl_3$) δ = 159.90, 141.30, 136.67, 130.37, 128.08, 127.86, 126.91, 82.38 ppm.

2.3. Preparation of the CC9-coated capillary column

A fused-silica capillary column (30 m long × 0.25 mm i.d.) was pretreated according to the following method: The column was sequentially rinsed with 1.0 M NaOH for 3 h, ultrapure water for 1 h, 0.1 M HCl for 1 h and ultrapure water again until the outflow was pH neutral. Finally, the capillary was dried using a nitrogen purge for 6 h at 120 °C.

The high thermal stability and favorable diffusion characteristics of polysiloxane diluting agents have provided significant