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Permethylated β-cyclodextrin in liquid poly(oxyethylene) as a stationary phase for capillary gas chromatography

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ABSTRACT

This paper reports the study of poly(oxyethylene) as a solvent for heptakis(2,3,6-tri-*O*-methyl)-β-cyclodextrin (PM-β-CD) and the potential of these mixtures for constructing enantioselective gas chromatography columns. Enantioseparations of volatile racemic mixtures using capillaries coated with 10–50% PM-β-CD diluted in Carbowax 20M were evaluated. The influence of the polymer type on retention, separation and reproducibility over a period of time is critically discussed. The poly(oxyethylene)-based columns were also compared to columns prepared by dilution of PM-β-CD in two polysiloxanes, SE-30 and SE-54, at several temperatures. Finally, we evaluated a new stationary phase prepared by crosslinking the chiral selector to the poly(oxyethylene) matrix.

1. Introduction

Capillary columns based on cyclodextrin derivatives (CDs) are widely used for enantioselective separations by high-resolution gas chromatography (HRGC). These chiral selectors were first introduced by Koscielsky et al. [1] for use in packed columns. Since then, several other authors have systematically investigated the performance of chiral capillary columns coated with a large number of modified CDs [2–12]. Most of these stationary phases, derived from α-, β- or γ-CDs, were prepared by diluting the CD derivative in a polysiloxane to obtain selective enantioseparations at relatively low temperatures [3]. A few stationary phases derived from β-CD were prepared by chemically bonding permethylated alkenyl-β-CD to a polysiloxane backbone, leading to columns characterized by good chiral recognition abilities when used in capillary GC and in supercritical fluid chromatography [13,14]. Since then, a wide variety of derivatives have been used to coat capillary columns. A review of the reported results shows that the enantioseparation ability of a given CD derivative is not limited to certain class of compounds; their chiral recognition abilities are observed toward an extremely wide variety of chemical families [3,11,15].

The dilution of cyclodextrin derivatives in a polysiloxane stationary phase has proven to have several advantages. First, the thermodynamic data that characterize the enantioselectivity can be obtained from the retention data of the two enantiomers being separated in columns containing different concentrations of the chiral selector. The second reason for diluting the chiral selector is a wider range of the column temperature; that is, it is possible to work at temperatures below the usually high melting points of the pure derivatives. Finally, improved column efficiencies can be achieved due to the favorable coating properties of polysiloxanes. For these phases, the amount of chiral selector in the polymeric stationary phase has a large influence on enantioselectivity. As expected, Schmarr et al. reported that low cyclodextrin concentrations reduce enantioresolution [16]. Hardt and Konig [17] also reported a significant increase in selectivity as the amount of octakis(3-*O*-butyryl-2,6-di-*O*-pentyl)-γ-cyclodextrin in OV-1701 increased, but the separation factor leveled off when the concentration of the chiral selector neared 50% (w/w). Bicchi et al. achieved separation of 1,8-epoxy-9-(3-methyl-6-buten-1-yl)-p-methane using 30% permethylated β-CD in OV-1701 but failed when the permethylated β-CD was at a concentration of 10% (w/w)[10]. Jung et al. demonstrated both theoretically and experimentally that different solutes exhibited different behaviors; that is, the apparent enantioselectivity factor for each racemate reached a plateau at different amounts of chiral selector [18]. In general, however, it is expected that the highest possible concentration of the CD derivative compatible with its solubility in the polymeric solvent should be used to achieve the highest enantioresolution factor for most solutes. On the other hand, several experiments conducted by using the same concentration of chiral CD diluted in different polymeric stationary phases demonstrated the significant influence of the polysiloxane chosen as the solvent on the enantioresolution. As a general rule,

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it has been stated that less polar polymers lead to enhanced enantioselectivity. However, the conclusions of those experiments do not seem to be conclusive. Thus, the main dilemma is that the solubility of the most polar CD derivatives in weakly or moderately polar polysiloxanes is rather limited at relatively low temperatures, while low elution temperatures are required to enhance the molecular interactions that lead to enantioseparation. Therefore, conditions that favor low chromatographic temperatures should be selected to improve the resolution of enantiomers. The maximum solubility that allows gas–liquid chromatographic separations at low temperatures has to be critically studied for each mixture of the specific cyclodextrin derivative and the achiral stationary phase in which it is diluted.

Heptakis(2,3,6-tri-*O*-methyl)-β-cyclodextrin (PM-β-CD) is one of the CD derivatives most often used as the chiral phase in GC [8,19]. PM-β-CD is most commonly diluted in moderately polar polysiloxanes such as OV-1701 [3]. These chiral columns have given very good results, and this type of chiral stationary phase has been shown to be highly universal [15]. The solubility of PM-β-CD in moderately polar OV-1701 is, however, limited to about 10–14% (w/w) (∼0.11 molal). To increase the relative amount of the chiral selector to 0.17 molal, Schurig chemically immobilized mono-6-*O*-octamethylenepermethyl-β-cyclodextrin on poly(dimethylpolysiloxane) [20]. Chiral GC columns using this stationary phase are under the trade name of Chirasil-DEX.

Capillary columns based on Carbowax 20M, the more common name for poly(oxyethylene) [21], are used for the retention of compounds of medium and high polarities. These phases exhibit good selectivity toward alcohols, diols and aromatic isomeric molecules. The structure of the polymer, H-(OCH2CH2)$_n$–OH, makes it especially interesting as a solvent for relatively polar molecules, such as cyclodextrin derivatives. Despite the potential usefulness of Carbowax, their use as a solvent of PM-β-CD has been very scarce [22,23].

This paper aims to study the use of poly(oxyethylene) (Carbowax 20M) as the diluting polymer for PM-β-CD. We have evaluated the selector solubility, chromatographic performance and enantioselective ability of the capillary columns constructed with these systems. The physical properties of this polymer do not allow the column temperature to drop below its melting point (about 60 °C) [24]. Below this temperature, adsorption, and no partition, does occur. We have also crosslinked the poly(oxyethylene) after coating the inner wall of the capillary with the phase solution to allow lower chromatographic temperatures. Different relative amounts of crosslinking reagents were tested with the aim of optimizing the capillary column performance.

2. Experimental

2.1. Materials

Permethyl-β-cyclodextrin was obtained from Cyclolab (Budapest, Hungary). Fused-silica capillaries were obtained from Microquartz Electronics (Münich, Germany). Poly(oxyethylene) (Carbowax 20M) was purchased from Alltech (Deerfield, IL, USA). SE-30, SE-54 and OV-1701 were obtained from Supelco (Bellefonte, PA, USA). Benzoyl peroxide, poly[oxy(methyl-1,2-ethanediyl)] (PPGDA, CAS number 25322-694) and all other materials including the racemic mixtures were obtained from Aldrich (Milwaukee, WI, USA), Sigma (St. Louis, MO, USA) or Fluka (Ronkonkoma, NJ, USA). All solvents used in the construction of the capillary columns were spectroscopic grade and were obtained from Merck (Darmstadt, Germany). A 25 m Hydrodex β-PM column (250 μm I.D.) was purchased from Macherey-Nagel (Macherey-Nagel GmbH & Co. KG, Düren, Germany).

2.2. Capillary gas chromatography

Chromatographic runs were carried out on a HP6890 chromatograph with flame ionization detection and manual injection. The solutes were injected in the vapor phase by applying the "wet-needle" technique, using split ratios greater than 100:1. The instrument was connected to a computer, and data acquisition was done through Clarity software (DataApex, Czech Republic). Chromatographic grade dinitrogen was used as the carrier gas, and the flow was controlled by keeping the pressure constant at the column inlet. Injector and detector temperatures were 220 and 250 °C, respectively. All chromatographic measurements were isothermal, ranging from 25 to 100 °C.

2.3. Preparation of the coated capillary columns

Silica capillary tubes of about 20 m in length with an internal diameter of 250 μm were heated to 200 °C in a slow stream of dinitrogen for several hours and then statically coated with the stationary phases. In all experimental procedures, great care was taken to avoid introducing dioxygen into the capillary columns.

A fast static evaporation method at a high temperature was used. We designed a special oven for this purpose. The static method has the advantage of reducing the evaporation time required compared to the time needed for the usual vacuum procedure. This method has been successfully applied to the preparation of several capillary columns in our laboratory [25,26]. Thus, mixtures of PM-β-CD and Carbowax 20M were prepared and then dissolved in dichloromethane. The columns filled with these solutions were heated to allow evaporation of the solvent. After complete solvent evaporation, the columns were conditioned by raising the temperature to 150 °C. The columns were left overnight at 120 °C under a dinitrogen stream, then were cooled and transferred to the HP6890 gas chromatograph. The film thickness was kept at approximately 0.1 μm. The columns constructed are described in Table 1.

Poly(oxyethylene) and poly(oxypropylene) diacrylate (PPGDA) were crosslinked during the coating of some columns (see Table 1).

Table 1
Columns[a] and stationary phases.

Denomination	Column length (m) and film thickness (μm)	Stationary phase
WX	20 × 0.2	Carbowax 20M (C20M)
βPWX10	23 × 0.1	10% Permethyl-β-CD/C20M
βPWX20	36 × 0.1	20% Permethyl-β-CD/C20M
βPWX30	20 × 0.1	30% Permethyl-β-CD/C20M
βPWX50	20 × 0.2	50% Permethyl-β-CD/C20M
βPXL10-10	20 × 0.1	10% Permethyl-β-CD/C20M/10% PPG DA
βPXL20-10	20 × 0.1	20% Permethyl-β-CD/C20M/10% PPG DA
βPXL10-20	20 × 0.2	10% Permethyl-β-CD/C20M/20% PPG DA
βPXL10-30	20 × 0.25	10% Permethyl-β-CD/C20M/30% PPG DA
βPXL30-50	20 × 0.17	30% Permethyl-β-CD/C20M/50% PPG DA
βPXL30-10	20 × 0.14	30% Permethyl-β-CD/C20M/10% PPG DA
βPSE54-30	20 × 0.1	30% Permethyl-β-CD/SE54
βPSE30-30	17 × 0.1	30% Permethyl-β-CD/SE30

[a] Capillary diameter was 250 μm id for all columns.