Journal of Chromatography A, 666 (1994) 147–159
Elsevier Science B.V., Amsterdam

CHROM. 25 733

Examination of the enantioselectivity of wall-immobilized cyclodextrin copolymers in capillary gas chromatography

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ABSTRACT

Approximately 90 chiral compounds were resolved by capillary GC on three different cyclodextrin-based, wall-immobilized capillary columns. Despite similarities in their structure and make-up, these stationary phases often displayed different enantioselectivities. Also their selectivities were different from wall-coated varieties of neat alkyl or alkyl–acyl derivatives of cyclodextrin. It is apparent that the immobilization chemistry affects selectivity as well as stability and efficiency. While the variety of different cyclodextrin-based capillary columns may be disconcerting to many, the practical result is a net increase in the number and types of compounds that can be resolved as well as their expanded usefulness in other capillary techniques.

INTRODUCTION

The development of gas chromatographic (GC) capillary columns sometimes seems to follow a natural progression from coated varieties to analogous wall-immobilized types. Chiral stationary phase (CSP) development for GC is following this trend. The first commercial GC CSP was a polysiloxane-L-valine-*tert.*-butylamide copolymer that was coated on glass capillaries and is known as *Chirasil-Val* [1,2]. This and analogous stationary phases proved to be effective for a variety of enantiomeric separations [3–7]. Benecke and Schomburg [8] first immobilized an alkylpolysiloxane-L-valine-(*S*)-α-phenethylamide polymer in a capillary using free radical generating agents. Lai *et al.* [9] subsequently produced an immobilized version of Chirasil-Val.

Cyclodextrin-based CSPs for wall-coated GC capillaries were introduced in a variety of forms. König and co-workers [10,11] reported neat alkylated derivatives of β-cyclodextrin. These were later expanded to a variety of different derivatives [12–17]. We first described the heterogenity of these derivatives [16]. Schurig and co-workers [18–20] first dissolved methylated cyclodextrins in silicon oil to produce effective CSPs. Lee and co-workers [21,22] described a linear copolymer of methylated cyclodextrin in which the two pendant arms contain aryl, dimethyloligosiloxane and alkane moieties. Schurig *et al.* [23] made a polymer of permethyl-β-cyclodextrin and dimethylpolysiloxane. The cyclodextrin moieties are attached through a single linkage to form a "necklace"-type polymer in which the chiral moieties are spaced along the siloxane polymer like "pendants" (Fig. 1A). Chirasil-Val has a similar structure [1–5]. Subsequently, this polymer was thermally immobilized [24]. This CSP is known as *Chirasil-Dex* and was shown to be useful in GC, supercritical fluid chromatography (SFC) and capillary electrophoresis (CE) [24–27]. We produced a branched or "star" oligomer of cyclodextrin and a short-chain, hydrogen terminated methyloligosiloxane [28]. When attached to the wall of fused-silica capillary and cross-linked it produces a stable

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0021-9673/94/$07.00
SSDI 0021-9673(93)E1198-9

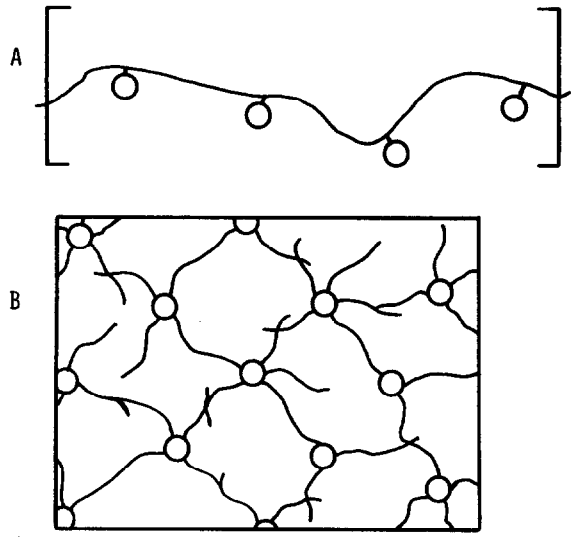


Fig. 1. Over simplified schematic showing two possible approaches for immobilizing multifunctional chiral selectors using organosilanes. The circle (○) represents the chiral selector attached to polymeric or oligomeric organosilanes. (A) Linear or "necklace"-type polymer where the chiral selectors are linked, through a single attachment, along the length of an organosilane polymer [8,9,22–25]. Note that this polymer is subsequently immobilized on the capillary wall. (B) Branched or "star-oligomer" approach where several organosilane oligomers are attached to the chiral selectors and these are subsequently crosslinked and bonded [26]. Note that the copolymer is not formed until the cross-linking procedure occurs in the capillary.

three-dimensional network (Fig. 1B). This also has been shown to be useful in GC, SFC and CE [28]. Yi *et al.* [29] also reported on an immobilized polysiloxane polymer containing singly attached cyclodextrins.

Immobilized chiral stationary phases often are more rugged and stable than coated analogues. This provides obvious benefits in regards to column lifetimes, temperature limits in GC and their use with supercritical fluids or solvent-based techniques such as liquid chromatography and CE [9,24–29]. Often it is not understood by the casual users of these technologies that immobilization chemistries frequently change the selectivities of these CSPs. Each different cyclodextrin-based CSP (whether coated or bonded) has different selectivities. Some of these differences are small or relate to a few compounds while other show pronounced differences. Even in cases where two different cyclodextrin columns seem to resolve the same enantiomers, a closer examination often reveals that the retention order can be reversed [30]. The purpose of the present work is narrowly focused and straight-forward. We examined the GC enantioseparation of a larger number of chiral compounds on three different wall immobilized cyclodextrin-based capillary columns. The enantioselective retention data is listed and examined to determine similarities and differences, advantages and disadvantages to some coated neat alkyl–acyl-derivatized cyclodextrin CSPs.

EXPERIMENTAL

Materials

Native β-CD was obtained from Astec (Whippany, NJ, USA). Commercially polar pretreated capillaries were purchased from Restek (Bellefonte, PA, USA). Azo-*tert.*-butane was purchased from Lancaster (Windham, NH, USA) and M_r 400 hydrogen-terminated polydimethylsiloxane (PS537) was obtained from Hüls (Bristal, PA, USA). All standard racemates and other materials were obtained from Aldrich (Milwaukee, WI, USA), Sigma (St. Louis, MO, USA) or Fluka (Ronkonkoma, NY, USA).

Methods

The stationary phases were synthesized as described previously [28]. The native β-cyclodextrin was first converted into an alkene derivative and then permethylated. The latter was allowed to couple with organo–hydrosiloxane oligomer in different ratios. In this way, a yellowish, viscous oil was produced [28]. Columns for GC use were prepared as follows: a diethyl ether solution containing 0.4% (w/v) synthesized stationary phase was filtered and coated on a commercially polar pretreated column (10 m × 0.250 mm I.D.) by the static method. The film thickness was about 0.4 μm. This coated column was flushed with dry nitrogen gas for about 30 min. The column was then conditioned from 35 to 150°C at the rate of 2°C/min. After conditioning for 8–10 h, column efficiency was tested with naphthalene at 90°C. Chiral selectivity was examined by α-ionone at 120°C or 1,5,8-trimethyltetraline at 100°C. Only

those columns with a height equivalent to a theoretical plate of 0.25 mm or better were selected for further cross-linking as described previously [28]. After cross-linking the changes in column efficiency and chiral selectivity were usually negligible (see ref. 28 for more details).

Racemic amines and amino alcohols were derivatized with trifluoroacetic anhydride (TFA). In a 3-ml glass vial, about 1 mg of the analyte was dissolved in 0.2 ml of diethyl ether and 0.1 ml of TFA was added. After 5–10 min, the excess of anhydride reagent was removed by flushing the vial with dry nitrogen gas. The derivatized amine was then dissolved in about 1.0 ml diethyl ether. Other standards were directly dissolved in diethyl ether. The sample concentration was about 0.1% (w/v).

A Varian Model 3700 gas chromatograph equipped with a flame ionization detector was used for all separations. Approximately 0.1 μl sample was injected with a split ratio of 1/100. The injection port and detector temperature were set at 250°C. Nitrogen was used as the carrier gas with a linear velocity of 10 cm/s at gas inlet pressure of *ca.* 2.8 p.s.i. (1 p.s.i. = 6894.76 Pa).

RESULTS AND DISCUSSION

Three different cyclodextrin (CD)-based chiral stationary phases were synthesized. Based on the type of derivatized β-cyclodextrin used and the proportion of hydrogen-terminated polydimethylsiloxane present, these stationary phases are classified as: (A) 1:6 (w/w) ratio of allyl-permethylated β-CD to PS537 (APβCD I), (B) 1:4 (w/w) ratio of allyl-permethylated β-CD to PS537 (APβCD II) and (C) 1:6 (w/w) ratio of 5-pent-1-enyl-permethylated β-CD to PS537 (PPβCD I). Since all of these CSPs utilize derivatized β-CD as the chiral selector, host–guest interaction via complex formation and/or loose, external, multiple associations via dipole–dipole, Van der Waals forces and/or hydrogen bonding are thought to be responsible for chiral selectivities [31]. One question to be considered involves the degree to which the introduction of the oligosiloxane and the crosslinking procedure affects the enantioselectivity of the CSPs when used in GC (as well as other techniques).

Approximately 90 compounds were successfully resolved on these immobilized CSPs. The results are summarized in Tables I and II. Table I lists racemates that contain single stereogenic centers, while Table II lists those having multiple stereogenic centers. Racemic compounds examined include alcohols, amines, amino alcohols, bicyclic compounds, diols, esters and lactones, epoxide and glycidol derivatives, furan and pyran derivatives, hydrocarbons and ketones. It is apparent from these data that despite the similarities in these three immobilized CSPs, there can be significant differences in their enantioselectivities. The last columns of Tables I and II lists the type of columns used for the separation. If a column was not listed, then the separation could not be achieved on that CSP. Clearly a large amount of data such as this provides information that cannot be obtained from looking at a specific separation or a few separations. The allyl-derivatized cyclodextrins (columns A and B) were more generally selective and useful than was the pentenyl derivative (column C). Also, the degree of substitution and amount of siloxane oligomer affects enantioselectivity (Tables I and II). There are specific cases (1-octen-3-ol or 1-methylbutylamine in Table I, for example) where there appears to be little difference between the columns. More often, however, one or another of the columns is superior (see many of the esters and the first two bicyclic compounds in Table I).

The weight ratio of the oligosiloxane (PS537) to cyclodextrin (column A *vs.* Column B) not only affects the selectivity in some cases but also the overall efficiency. Usually stationary phases containing a greater amount of PS537 (column A) were more efficient. However, too great a proportion of the oligosiloxane can dilute the cyclodextrin to the point that chiral selectivity is reduced. For some compounds there seems to be an inverse relationship between selectivity and efficiency as controlled by the ratio of cyclodextrin to oligosiloxane. However there are many exceptions to this [*i.e.*, where the more diluted cyclodextrin stationary phase (A) seems to have greater enantioselectivity]. Currently it is

TABLE I

ENANTIOMERIC SEPARATIONS OF SEVERAL GROUPS OF RACEMIC COMPOUNDS ON IMMOBILIZED β-CD-BASED STATIONARY PHASES

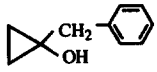
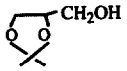
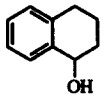
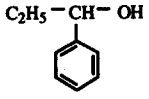
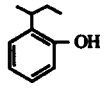
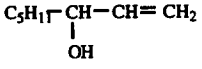
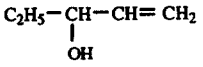
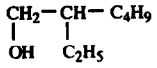
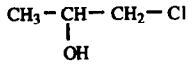
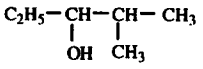
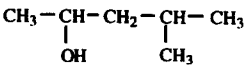
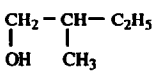
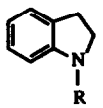
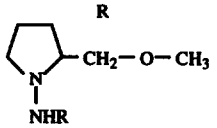
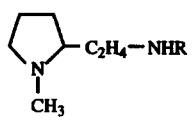
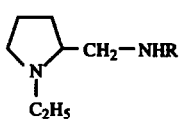
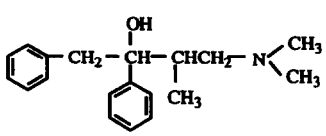
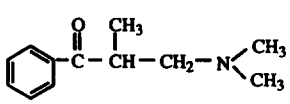
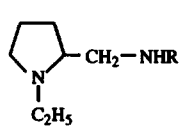
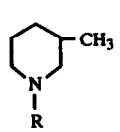
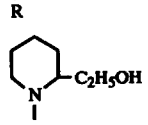
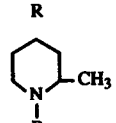
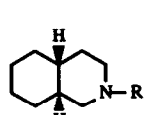
Racemic compound	Structure[a]	k'[b]	α[c]	Column temperature (°C)	CSP[d]
Alcohols					
α-Cyclopropyl-benzylalcohol		18.9	1.02	110	A
		17.3	1.03	110	B
Solketal		15.3	1.03	70	A
		13.2	1.08	100	B
1,2,3,4-Tetrahydro-1-naphthol		3.74	1.02	150	A
		10.3	1.03	120	B
1-Phenyl-1-propanol		2.52	1.04	135	A
		12.4	1.04	100	B
2-*sec*-Butylphenol		19.2	1.02	110	A
		26.1	1.01	90°C + 1°C[e]	B
sec-Phenethyl-alcohol		10.3	1.03	90	A
		17.2	1.02	80	B
1-Octen-3-ol		17.7	1.02	65	A
		19.6	1.03	65	B
		12.5	1.02	65	C
1-Penten-3-ol		7.72	1.02	30	A
		5.70	1.01	30	B
2-Ethyl-1-hexanol		15.2	1.01	75	A
1-Chloro-2-propanol		7.29	1.03	35	A
		7.44	1.01	50	B
2-Methyl-3-pentanol		11.7	1.03	40	A
		16.3	1.02	40	B
		7.16	1.04	40	C
4-Methyl-2-pentanol		12.9	1.02	40	A
2-Methyl-1-butanol		14.9	1.02	35	A

TABLE I *(continued)*

Racemic compound	Structure[a]	k'^{b}	α^{c}	Column temperature (°C)	CSP[d]
Amines					
1-Aminoindan		13.6	1.11	120	A
		11.8	1.07	120	B
		9.80	1.06	120	C
1-Amino-2-(methoxymethyl)-pyrrolidine		14.2	1.02	80	A
		11.7	1.06	100	B
		12.5	1.05	80	C
2-(Aminoethyl)-1-methylpyrrolidine		25.7	1.03	30°C + 3°C[e]	A
2-(Aminomethyl)-1-ethylpyrrolidine		34.6	1.04	40°C + 2°C[e]	A
Oxyphene[f]		34.6	1.08	170	A
		22.9	1.07	190	B
		32.8	1.10	170	C
3-DAP		8.50	1.01	130	A
		10.4	1.04	140	B
2-(aminomethyl)-1-ethylpyrrolidine		34.6	1.04	40°C + 2°C[e]	A
3-Methylpiperidine		8.66	1.04	85	A
		9.60	1.02	80	B
		6.07	1.04	85	C
2-Piperidineethanol		6.32	1.02	135	A
		14.3	1.02	110	B
		12.9	1.03	110	C
2-Methylpiperidine		9.21	1.06	85	A
		10.3	1.10	80	B
		6.53	1.05	85	C
trans-Perhydroisoquinoline		6.00	1.03	150	A
		16.1	1.02	110°C + 1°C[e]	B
		15.1	1.03	130	C

(Continued on p. 152)

TABLE I *(continued)*

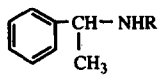
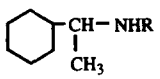
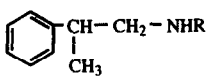
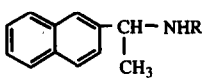
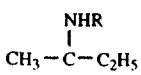
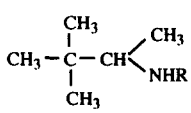
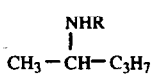
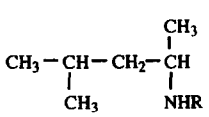
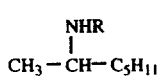
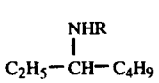
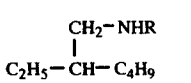
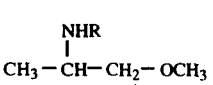
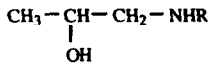
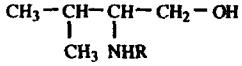
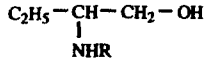
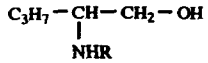
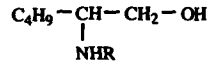
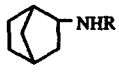
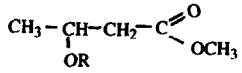
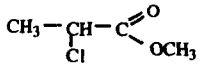
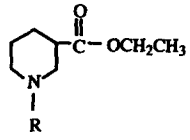
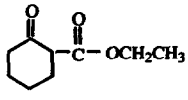
Racemic compound	Structure[a]	k'[b]	α[c]	Column temperature (°C)	CSP[d]
α-Methylbenzyl-amine		13.4	1.05	100	A
		34.7	1.01	40°C + 3°C[e]	B
1-Cyclohexyl-ethylamine		10.2	1.06	110	A
		14.8	1.07	100	B
		14.9	1.04	95	C
β-Methylphen-ethylamine		8.08	1.02	130	A
		13.0	1.01	110°C + 1°C[e]	B
1-(1-Naphthyl)-ethylamine		35.6	1.01	35°C + 3°C[e]	A
1-sec-Butylamine		9.94	1.01	45	A
2-Amino-3,3-di-methylbutane		9.76	1.07	55	A
		3.90	1.04	70	B
		7.26	1.06	55	C
1-Methyl-butyl amine		5.60	1.05	65	A
		7.90	1.04	60	B
		4.75	1.04	60	C
1,3-Dimethyl-butylamine		5.45	1.12	75	A
		5.70	1.10	75	B
		4.09	1.08	75	C
2-Amino-heptane		7.81	1.05	90	A
3-Amino-heptane		11.2	1.03	75	A
2-Ethylhexylamine		13.8	1.03	100	A
		34.7	1.01	40°C + 3°C[e]	B
		15.1	1.04	90	C
2-Amino-1-methoxy propane		7.33	1.03	55	A
		10.3	1.01	55	B
		11.8	1.02	45	C

TABLE I *(continued)*

Racemic compound	Structure[a]	k'[b]	α[c]	Column temperature (°C)	CSP[d]
Amino alcohols					
1-Amino-2-propanol		20.7	1.04	65	A
		13.0	1.01	90	B
		9.10	1.05	70	C
2-Amino-3-methyl-1-butanol		13.6	1.03	80°C + 2°C[e]	A
		8.30	1.05	110	B
		11.6	1.03	80°C + 2°C[e]	C
2-Amino-1-butanol		13.7	1.03	95	A
		10.0	1.04	120	B
2-Amino-1-pentanol		14.6	1.02	80°C + 2°C[e]	A
		10.0	1.03	110	B
2-Amino-1-hexanol		17.8	1.02	90	A
		8.25	1.05	120	B
		8.58	1.03	120	C
Bicyclic compounds					
exo-2-Chloronorbornane		26.6	1.02	60	A
exo-2-Bromonorbornane		30.0	1.02	70	A
exo-2-Aminonorbornane		19.8	1.06	100	A
		17.4	1.07	100	B
		13.6	1.05	100	C
Esters and lactones					
Ethyl-3-hydroxybutyrate		26.8	1.02	40	A
		15.8	1.01	65	B
Methyl 2-chloropropionate		12.2	1.06	R.T.[f]	A
		15.2	1.04	40	B
Ethylnipecoate		24.0	1.02	110	A
Ethyl 2-cyclohexanonecarboxylate		24.4	1.01	70°C + 1°C[e]	A

(Continued on p. 154)

TABLE I *(continued)*

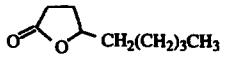
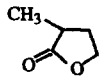
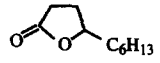
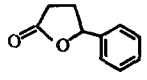
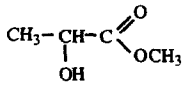
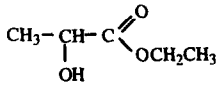
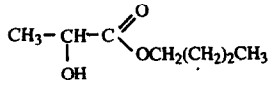
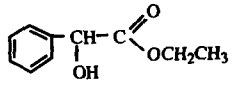
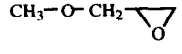
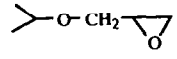
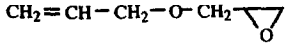
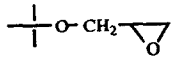
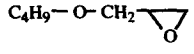
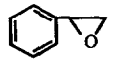
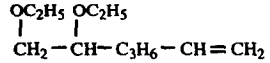
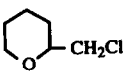
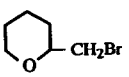
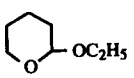
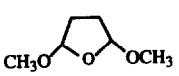
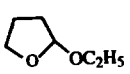
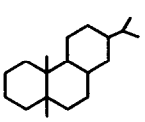
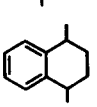
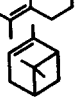
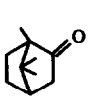
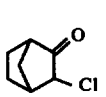
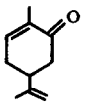
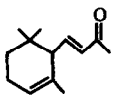
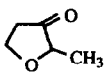
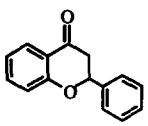
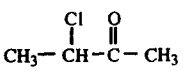
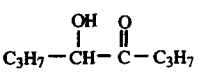
Racemic compound	Structure[a]	k'[b]	α[c]	Column temperature (°C)	CSP[d]
γ-Nonanoic lactone		13.8	1.03	120	A
		11.8	1.02	150	B
α-Methyl-γ-butyro lactone		20.0	1.03	55	A
γ-Decanolactone		20.1	1.02	130	A
		16.6	1.01	130	B
γ-Phenyl-γ-butyro lactone		10.6	1.02	150	A
		15.1	1.03	140	B
Methyl lactate		8.07	1.02	30°C + 1°C[e]	A
Ethyl lactate		11.6	1.03	40	A
Butyl lactate		16.2	1.02	65	A
Mandelic acid ethyl ester		17.1	1.01	110	A
Epoxide and glycidole derivatives					
Glycidyl-methylether		4.03	1.03	R.T.[g]	A
Glycidyl-isopropylether		5.58	1.04	50	A
		8.43	1.02	60	B
Allylgycidylether		7.71	1.03	50	A
		19.3	1.01	40	B
tert.-Butylglycidyl-ether		16.5	1.05	50	A
		22.0	1.06	50	B
		11.2	1.01	50	C
Butylglycidyl-ether		18.3	1.01	50	A
Styrene oxide		18.8	1.02	60	A
		37.8	1.02	70	B
1,2-Epoxy-7-octene		25.1	1.01	45	A

TABLE I *(continued)*

Racemic compound	Structure[a]	k'^{b}	α^{c}	Column temperature (°C)	CSP[d]
2-Chloromethyltetra-hydro-2H-pyran		6.48 4.60	1.04 1.04	85 85	A B
2-Bromomethyltetra-hydro-2H-pyran		12.3 10.1	1.02 1.03	85 80	A C
3,4-Dihydro-2--ethoxy-2H-pyran		21.7	1.01	35°C + 2°C[e]	A
2,5-Dimethoxytetra-hydrofuran, data for *trans* only		5.35 5.29 7.31	1.06 1.03 1.03	55 55 40	A B C
2-Ethoxytetra-hydrofuran		11.1	1.02	30	A
Hydrocarbons					
Fichtelite		54.9	1.01 1.01	150	A
1,4-Dimethyltetraline, data for *trans* only		6.26 18.6 6.58	1.05 1.10 1.03	110 100 100	A B C
1,8-Dimethyltetraline		19.5 15.7 24.0	1.03 1.03 1.02	90 100 110	A B C
1,5,8-Trimethyltetraline		25.5 24.0	1.04 1.05	100 110	A B
α-Pinene		18.7	1.03	60	B
Ketones					
Camphor		21.2 36.9	1.02 1.03	80 90	A B
3-Chloro-2--norbornanone		23.9	1.01	40°C + 2°C[e]	A

(Continued on p. 156)

TABLE I *(continued)*

Racemic compound	Structure[a]	k'[b]	α[c]	Column temperature (°C)	CSP[d]
Carvone		16.6	1.02	100	A
		12.5	1.02	100	B
		18.9	1.03	90	C
α-Ionone		13.7	1.04	120	A
		29.5	1.05	120	B
		10.2	1.03	120	C
2-Methyl-tetra-hydrofuran-3-one		12.9	1.01	35	A
Flavanone		22.8	1.02	170	A
3-Chloro-2-butanone		7.44	1.03	R.T.[g]	A
		9.85	1.02	40	B
Butyroin		4.69	1.02	100	A

[a] R group in the structure is the trifluoroacetyl group.
[b] k' = Capacity factor for the first eluted enantiomer.
[c] α = Ratio of the capacity factor of the second eluted enantiomer to that of the first eluted enantiomer. Compounds with α values of 1.01 were not baseline resolved on a 10 *M* column. Usually they had resolution values between 0.7 and 1.1.
[d] A, B, and C stand for different stationary phases. A is APβCD I; B is APβCD II; and C is PPβCD I (see Results and discussion).
[e] This expression designates that a temperature program was used. The program started at the initial temperature indicated by the first number and increased at the rate (per minute) indicated by the second number of the expression.
[f] The data are for the separation of an enantiomeric mixture of the (2*S*,3*R*) and (2*R*,3*S*) isomers.
[g] R.T. means the separation was done at room temperature (*i.e.*, 22°C).

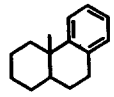
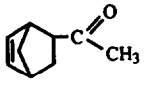
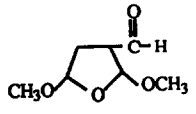
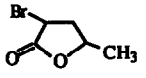
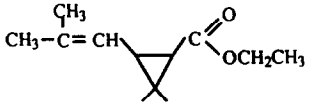
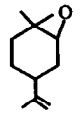
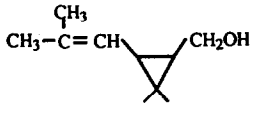
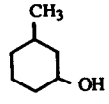
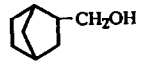
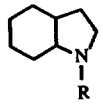
difficult to make any generalizations in this area with the exception that significant dilution of the cyclodextrin selector eventually negates the enantiomeric separation.

The immobilized cyclodextrin-based capillary columns often are not directly comparable (in terms of selectivity) to other wall coated columns that we have worked with (*i.e.*, neat alkyl, alkyl–acyl and hydroxypropyl derivatives [15–17]). Some compounds that could not be separated on the wall-coated GC columns were resolved on immobilized-CD stationary phases. Examples include flavanone, oxyphene and 3-dimethylaminopropiophenone (3-DAP). Fig. 2 shows the separation of one pair enantiomers of α-oxyphene and its precursor 3-DAP. Fig. 3 shows the enantiomeric separation of ethyl chrysanthemumate and 2,5-dimethoxy-3-tetrahydrofurancarboxaldehyde, which contain two and three stereogenic centers, respectively. Also the immobilized-CD stationary phases effectively resolve underivatized chiral alcohols and diols at higher temperatures. When using the neat wall coated CD-derivative columns, lower separation temperatures and trifluoroacetylation often were preferred. Finally, amine-containing compounds

TABLE II

RETENTION AND SELECTIVITY OF CHIRAL COMPOUNDS CONTAINING MULTIPLE STEREOGENIC CENTERS ON IMMOBILIZED β-CD-BASED STATIONARY PHASES

All definitions for symbols as in Table I.

Racemic compound	Structure	Stationary phase								
		A			B			C		
		k'	α	Column temperature (°C)	k'	α	Column temperature (°C)	k'	α	Column temperature (°C)
4a-Methyl-1,2,3,4,4a,9,10,10a-octahydrophenathrene		31.0 39.6	1.01 1.04	120	41.9 57.3	1.01 1.03	130			
2-Acetyl-5-Norbornene, mixture of *endo*- and *exo*		28.3 42.3	1.01 1.03	70 + 2	15.0 22.8	1.00 1.06	80	31.9 20.5	1.00 1.04	80
2,5-Dimethoxy--3-tetrahydrofurancarboxaldehyde		8.37 9.09 10.4 11.1	1.03 1.05 1.06 1.03	85	10.4 12.0 13.1 17.6	1.04 1.06 1.10 1.03	80			
α-Bromo-γ--valero lactone, mixture of *cis*- and *trans*-		26.3 29.2	1.10 1.01	40 + 2	12.2 18.7	1.04 1.00	40 + 2			
Ethyl chrysanthemumate		26.2 28.4	1.01 1.01	35 + 2	7.60 9.20	1.03 1.01	80 + 2	24.1 26.8	1.01 1.01	35 + 2
Limonene oxide, mixture of *cis*- and *trans*-		19.1 19.7	1.03 10.3	80	21.0 22.0	1.10 1.02	80			
Chrysanthemyl alcohol, mixture of *cis*- and *trans*-		8.10 9.18	1.00 1.04	100	18.1 20.4	1.01 1.02	100	10.5 12.5	1.00 1.02	90
3-Methylcyclohexanol, mixture of *cis*- and *trans*-		10.5 11.4	1.03 1.03	75						
2-Norbornanemethanol, mixture of *endo*- and *exo*-		15.4 15.7	1.01 1.02	80 + 2	17.0 17.4	1.01 1.01	100	14.0 14.2	1.01 1.01	75 + 2
Perhydroindole, mixture of *cis*- and *trans*-		6.60 10.1	1.05 1.09	130	3.30 4.90	1.05 1.10	140	4.89 7.69	1.04 1.06	130

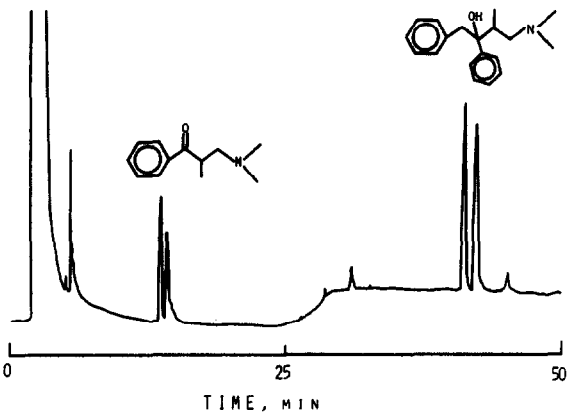


Fig. 2. GC resolution of enantiomers of α-oxyphene and its precursor 3-dimethylaminopropiophenone ($t_R \approx 13$ min). Note that the oxyphene has two stereogenic centers. This separation is of the (2*S*,3*R*) and (2*R*,3*S*) enantiomers. A 10 *M* column "B" (Table I) was used with nitrogen carrier gas. The column was held at 140°C for 25 min then the temperature was increased to 200°C at 15°C/min.

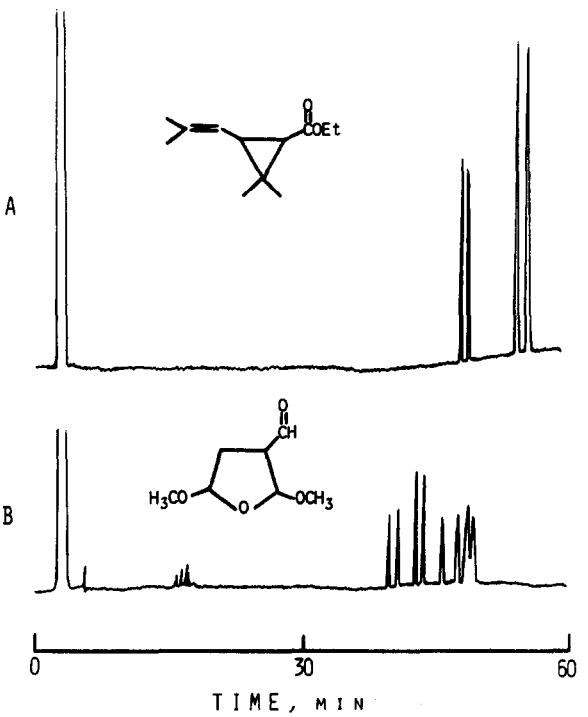


Fig. 3. GC resolution of compounds containing multiple stereogenic centers on a 10-m column "A" (Table I). (A) Ethyl chrysanthemumate (two pairs of enantiomers). (B) 2,5-Dimethoxy-3-tetrahydrofurancarboxaldehyde (four pairs of enantiomers). The temperature program began at 35°C and increased at 2°C/min until the peaks were eluted. See Experimental for further details.

seem to be resolved more easily on the immobilized CD stationary phases than on coated varieties (Tables I and II). Conversely, these immobilized-CD stationary phases were often less effective in resolving the smaller, more volatile chiral compounds such as halocarbons, certain hydrocarbons, etc.

In summary, although immobilization of cyclodextrin on capillary walls results in a more stable stationary phase, it also affects the enantioselectivity and sometimes efficiency. Even closely related immobilized phases such as those in this study can have different selectivities for some compounds. In general the immobilized CD columns appeared to be more useful in resolving the larger, more bulky chiral compounds as well higher boiling compounds with good hydrogen bonding groups (such as the diols). When comparing the selectivity of the immobilized CSPs to the neat, wall-coated varieties they were most similar to the alkyl-CD derivatives and most dissimilar to the acyl and hydroxypropyl derivatized CDs.

ACKNOWLEDGEMENT

Support of this work by the Department of Energy, Office of Basic Sciences (grant DE FG 02 88ER13819) and The Petroleum Research Fund are gratefully acknowledged.

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