Separation of Positional Isomers on a Calix[4]arene-methylsiloxane Polymer as Stationary Phase in Capillary GC

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Poly(*p-tert*-butyltrimethoxymonopropyloxycalix[4]arene-methylsiloxane) (TBCX-MS) has been prepared and used as a stationary phase in isothermal capillary gas chromatographic separation of some positional isomers. Retention factors (k) and separation factors (α) for the isomers were measured and compared with those on poly(*p-tert*-butyl-dimethoxydipropyloxycalix[4]arene-tetramethyldisiloxane) (TBCX-TMDS), poly(dimethoxy-dipropyloxycalix[4]arenetetramethyl-disiloxane) (CX-TMDS). Most of the isomers investigated are well resolved on TBCX-MS. Retention of all the compounds decreases on the three phases in the order, TBCX-TMDS ≥ TBCX-MS > CX-TMDS. Similar retention values on TBCX-TMDS and TBCX-MS seem to indicate that retention property of the two phases is not significantly affected by the spatial position of the calixarene moiety.

Keywords : Positional isomers separation, Calix[4]arene-methylsiloxane polymer, Stationary phase, Capillary GC.

Introduction

Calixarenes are cavity-shaped cyclic molecules made up of phenol units linked *via* alkylidene groups.[1] They represent receptor molecules of widely varying size for metal cations and organic molecules. Since they possess a cylindrical architecture similar to cyclodextrins, they are expected to form inclusion complexes. Cyclodextrins (CDs) have been extensively employed in liquid chromatographic separations[2-9] because of their ready accessibility and rather unique properties as compared to micellar inclusion.[10]

Ready accessibility also accounts for the increasing attention that calixarenes have received during the past decade.[1,11,12] Recently, calixarenes have been utilized in gas chromatography (GC), liquid chromatography (LC) and capillary electrophoresis. Mangia *et al.*[13] reported separation of alcohols, chlorinated hydrocarbons and aromatic compounds by GSC with *p-tert*-butylcalix[8]arene absorbed on Chromosorb. Mnuk *et al.* studied the inclusion properties of *p-tert*-butylcalix[n]arenes (n = 4-8) by GC.[14,15] Glennon and coworkers prepared silica bonded calix[4]arene tetraester stationary phases to separate alkali metal ions and amino acid esters.[16-19] They recently reported enantioseparation of 1-phenyl-2,2,2-trifluoroethanol racemate on L-(−)-ephedrine-calix[4]arene-bonded silica in reversed-phase LC.[20] Krauss *et al.* used of *p-tert*-butylcalix[n]arene-bonded silica materials in LC separation of some regioisomers and proline-containing dipeptides.[21-24] Park *et al.* used water-soluble calix[6]arene-*p*-sulfonate (CAPS)[25] as the mobile phase additive in RPLC separation of some mono-substituted phenols.[26] They also used CAPS-bonded silica for the RPLC separation of a number of positional isomers.[27] CAPS has also been used as the mobile phase additive in capillary electrophoresis.[28] Park *et al.* recently reported isothermal capillary GC separation of a number of positional and geometric isomers on two calix[4]-arene-siloxane polymers, poly(*p-tert*-butyl-dimethoxydipropyl-oxycalix[4]arene-tetramethyldisiloxane) (TBCX-TMDS) and poly(dimethoxydipropyloxycalix[4]arene-tetramethyldisiloxane (CX-TMDS).[29] Schurig and coworkers used *p*-(2`-methyl-tridecyl-2')calix[8]arene-containing polysiloxane as the stationary phase in capillary GC separation of positional isomers of disubstituted benzenes.[30] They also reported chiral separation of amino acid derivatives on a polymeric chiral resorc[4]arene in capillary GC.[31] Wu and coworkers reported the use of crown ether-containing calixarenes in capillary GC separation of various structural isomers.[32-34]

In the present work poly(*p-tert*-butyltrimethoxymono-propyloxycalix[4]arene-methylsiloxne) (TBCX-MS) has been prepared and used as stationary phases in isothermal capillary gas chromatographic separation of a number of positional isomers. Retention (k) and separation factors (α) for the isomers were measured and compared with values on TBCX-TMDS and CX-TMDS. In TBCX-MS calixarene moieties are tethered to the polylsiloxane chain while in TBCX-TMDS and CX-TMDS they are incorporated into the polylsiloxane chain. We thought it is of interest to see if the spatial position of the calixarene moiety affects retention and selectivity properties of the calixarene-polysiloxane phases.

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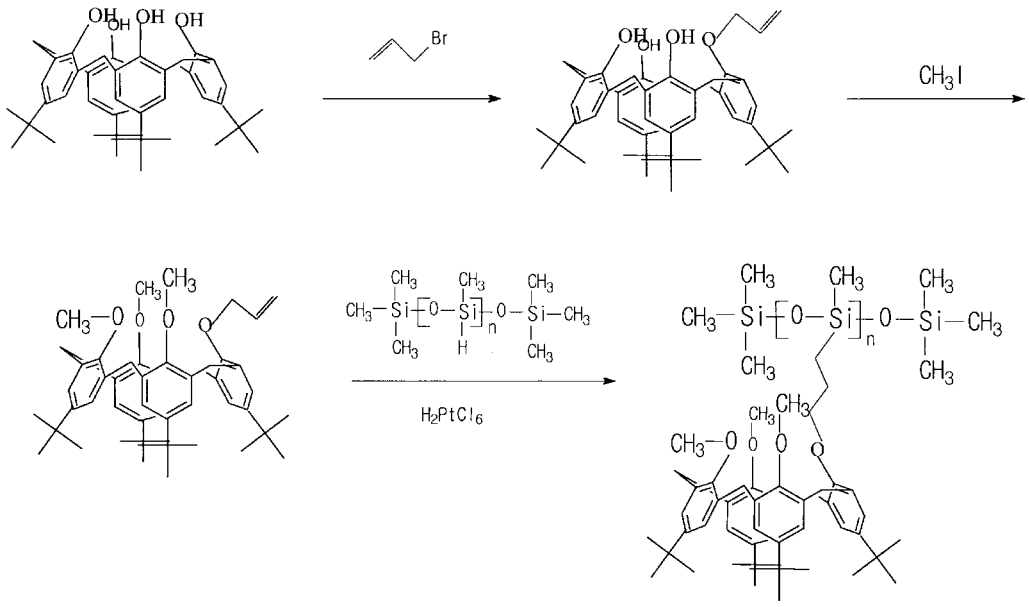

Scheme 1. Preparation of TBCX-MS.

Experimental Section

Preparation of poly(*p-tert*-butyltrimethoxymonopropyloxycalix[4]arene-methylsiloxne). Poly(*p-tert*-butyltrimethoxymonopropyloxycalix[4]arene-methylsiloxne) was prepared according to the procedure described in the literature (see Scheme 1). *p-tert*-Butylcalix[4]arene was synthesized by the reaction of *p-tert*-butylphenol, potassium hydroxide, formaldehyde and $AlCl_3$ by the reported procedure.[35,36] *p-tert*-Butyl-allyloxycalix[4]arene was prepared by the reaction of *p-tert*-butylcalix[4]arene with allyl bromide in the presence of K_2CO_3 in acetonitrile by the reported procedure.[37] Reaction of *p-tert*-butylallyloxycalix[4]arene with methyl iodide in the presence of sodium hydride in refluxing tetrahydrofuran/*N,N*-dimethylformamide gave *p-tert*-butyltrimethoxyallyloxycalix[4]arene after recrystallization from chloroform-methanol[38] (yield 87%; mp 188-190 °C; IR (KBr, cm^{-1}) 1620 (C=C) 1020 ($ArOCH_3$); ^1H NMR ($CDCl_3$, δ) 7.2-6.8 (m, 8H ArH) 6.2-4.5 (m, 3H, C-CH=CH_2) 4.5-2.8 (m, 15H, CH_2-C=C, OCH_3, $ArCH_2Ar$) 1.23 (d, 36H, *t*-Bu)). TBCX-MS was prepared by the reaction of *p-tert*-butyltrimethoxyallyloxycalix[4]arene with polymethylhydrosiloxane in the presence of H_2PtCl_6 in THF and purified by column chromatography (silica, ethyl acetate/*n*-hexane) (^1H MNR ($CDCl_3$, δ) 7.2-6.8 (m, ArH) 3.5-4.4 ($ArCH_2Ar$, OCH_3) 2.9-3.4 ($ArOCH_2$) 1.0-1.7 (Si-C-CH_2O, *t*-Bu) 0.7-0.9 (Si-CH); ^{13}C NMR $CDCl_3$, δ) 143.9, 135.6, 133.1, 132.4, 125.2 (Ar), 59.9 (OCH_3), 34.1 (OCH_2), 31.4, 31.5 (*t*-Bu), 31.7 ($ArCH_2Ar$), 12.4 ($OCCH_2$), 1.6 (Si-CH_2), 1.1 (Si-CH_3)).

Preparation of fused silica capillary column. Deactivated empty fused silica capillaries were purchased from Alltech Associates (Deerfield, IL 60015, USA). Fused silica columns (30 m × 0.25 mm I.D.) were statically coated with 0.2-μm film of 25% (w/w) of the calixarene-siloxane polymers dissolved in the polysiloxane OV-1701.[39] Coating was performed with 0.33% solutions of the stationary phase in pentane/dichloromethane (1 : 1, v/v).[40-42]

Capillary Gas Chromatography. GC analyses were performed on a Donam 6200 Gas Chromatograph (Seoul, Korea) equipped with a split injector (250 °C) and a FID detector (300 °C). Helium at a pressure of 25 psi was used as carrier gas. One μL of 1% solution in dichloromethane was injected with a split ratio of 1/100. The column dead time was determined from retention times of three successive *n*-alkane homologues by using the equation by Guardino *et al.*[43]

Results and Discussion

Tables 1 and 2 list retention (k) and separation factors (α) of a number of positional isomers of monosubstituted phenols and other aromatic compounds separated on TBCX-MS along with those obtained on CX-TMDS and TBCX-TMDS as the stationary phases.[29] Most of the positional isomers are well resolved on TBCX-MS except *m*- and *p*-isomers of chlorophenol and xylene. In particular, very closely boiling *m*- and *p*-isomers of methoxyphenol (Δb.p. = 1.3 °C) and cresol (Δb.p. = 0.3 °C) are baseline-resolved.

Elution orders for all the isomers of the compounds studied follow their boiling points except aminophenols and nitrophenols. The higher boiling *o*-nitrophenol (b.p. 214.6 °C) elutes earlier than the lower boiling *m*-nitrophenol (b.p. 194.0 °C). The elution order for aminophenol isomers is the same as that for nitrophenol isomers. It is likely that the stronger intramolecular hydrogen bonding interactions between the nitro (or amino) and hydroxyl group on the *o*-isomers of these phenols predominate over the weaker orientation and induction interactions between the polar groups on the phenol and the stationary phase. This will reduce retention of *o*-isomers significantly compared to *m*- or *p*-isomers where both the hydroxyl and the polar substituent group are

Table 1. Retention (k) and Separation Factors (α) for Monosubstituted Phenols on Calix[4]arene-Siloxane Polymer Phases

Compounds	b.p. (°C)	Temp. (°C)	CX-TMDS[a]		TBCX-TMDS[b]		TBCX-MS[c]	
			k[d]	α[e]	k	α	k	α
o-Aminophenol	153.0[g]	150	1.93	1.00	2.43	1.00	2.49	1.00
m-Aminophenol	164.0		3.24	1.22	4.03	1.21	4.13	1.23
p-Aminophenol	284.0		2.66	1.38	3.33	1.37	3.35	1.35
o-Nitrophenol	214.6	160	0.50	1.00	0.73	1.00	0.69	1.00
m-Nitrophenol	194.0		7.85	15.8	10.86	14.9	10.88	15.77
p-Nitrophenol	279.0		12.30	1.57	16.85	1.55	17.04	1.57
o-Cresol	191.0	130	1.17	1.00	1.60	1.00	1.45	1.00
m-Cresol	202.2		1.50	1.04	2.00	1.05	1.84	1.04
p-Cresol	201.9		1.44	1.23	1.90	1.19	1.76	1.21
o-Chlorophenol	174.9	130	0.64	1.00	0.91	1.00	0.82	1.00
m-Chlorophenol	214.0		3.69	5.78	5.10	5.59	4.93	1.00
p-Chlorophenol	219.8		3.73	1.01	5.13	1.01	4.92	6.01
o-Methoxyphenol	205.1	130	1.15	1.00	1.57	1.00	1.35	1.00
m-Methoxyphenol	244.3		4.43	1.26	6.06	1.24	5.42	1.21
p-Methoxyphenol	243.0		3.53	3.06	4.88	3.08	4.47	3.30

[a]Poly(dimethoxydipropyloxycalix[4]arene-tetramethyldisiloxane). The k and α values are from ref. 29. [b]Poly(*p-tert*-butyldimethoxydipropyloxycalix[4]arene-tetramethyldisiloxane). The k and α values are from ref. 29. [c]Poly(*p-tert*-butyltrimethoxymonopropyloxycalix[4]arene-methylsiloxane). [d]$k = (t_R-t_0)/t_0$. [e]The α value of unity was assigned to the first-eluting isomer and computed for closely eluted isomer pairs using the relationship. $\alpha = k_2/k_1$. [g]Sublimation temperature at 11 torr.

Table 2. Retention (k) and Separation Factors (a) for Other Aromatic Compounds on Calix[4]arene-Siloxane Polymer Phases*

Compounds	b.p. (°C)	Temp. (°C)	CX-TMDS[a]		TBCX-TMDS[b]		TBCX-MS[c]	
			k[d]	α[e]	k	α	k	α
1-Bromo-4-nitrobenzene	256.0	130	3.92	1.00	6.20	1.00	5.18	1.00
1-Bromo-2-nitrobenzene	258.0		4.58	1.17	6.91	1.11	5.89	1.14
o-Nitroaniline	284.0	180	1.52	1.00	2.03	1.00	2.03	1.00
m-Nitroaniline	305.0		2.51	1.55	3.36	1.65	3.36	1.66
p-Nitroaniline	332.0		5.15	2.05	6.82	2.03	6.86	2.04
o-Nitrotoluene	221.7	100	5.49	1.00	7.57	1.00	6.86	1.00
m-Nitrotoluene	232.6		6.36	1.16	9.18	1.21	8.56	1.25
p-Nitrotoluene	238.3		7.09	1.12	10.14	1.10	9.86	1.15
o-Fluorotoluene	114.4	50	1.10	1.00	2.05	1.00	1.67	1.00
m-Fluorotoluene	116.5		1.17	1.06	2.12	1.03	1.74	1.04
p-Fluorotoluene	116.6		1.19	1.02	2.17	1.03	1.76	1.02
o-Xylene	144.4	50	3.92	1.25	5.42	1.24	4.54	1.26
m-Xylene	139.1		3.12	1.00	4.38	1.02	3.61	1.04
p-Xylene	138.3		3.13	1.00	4.31	1.00	3.46	1.00
1,3-Dichlorobenzene	173.0	100	1.33	1.06	1.91	1.04	1.76	1.03
1,4-Dichlorobenzene	174.0		1.25	1.00	1.84	1.00	1.71	1.00
cis-1,2-Dimethylcyclohexane	129.7	50	1.52	1.36	2.13	1.32	2.04	1.33
trans-1,2-Dimethylcyclohexane	123.4		1.11	1.00	1.61	1.00	1.54	1.00
cis-Decahydronaphthalene	195.8	100	1.77	1.37	2.54	1.33	2.39	1.34
trans-Decahydronaphthalene	187.3		1.29	1.00	1.91	1.00	1.78	1.00

*See footnotes in Table 1.

available for interactions with the stationary phase. Isomers of other compounds whose substituent group is not capable of strong intramolecular hydrogen bonding interactions with the hydroxyl group are eluted in the order of their increasing boiling points.

Retention of all the compounds decreases on the three phases in the order. TBCX-TMDS ≥ TBCX-MS > CX-TMDS. Similar retention factors observed for the solutes on TBCX-

TMDS and TBCX-MS seem to indicate that retention property of the two phases is not appreciably affected by the spatial position of the calixarene moiety, whether it is inserted into or tethered to the polysiloxane chain. The longer retention on TBCX-MS and TBCX-TMDS is likely due to increased dispersive interactions by the *tert*-butyl moiety on the phases with the solute in the gas phase. While retention of all the compounds is longer on TBCX-MS and TBCX-TMDS than on CX-TMDS separation factors are similar on the two phases. This seems to indicate either that the *tert*-butyl moieties do not play a role in discriminating the isomer molecules in coming into the cavity of the calixarene if the solute is retained by the inclusion processes or that the solutes are retained by non-inclusion processes on these phases.

Conclusions

The positional isomers investigated are well resolved on TBCX-MS. Retention of all the compounds decreases on the three phases in the order. TBCX-TMDS ≥ TBCX-MS > CX-TMDS. Similar retention values for the solutes on TBCX-TMDS and TBCX-MS seem to indicate that retention property of the two phases is not appreciably affected by the spatial position of the calixarene moiety, whether it is inserted into or tethered to the polysiloxane chain.

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