Separation of Positional Isomers on Polymeric Calix[4]arene–Siloxane Stationary Phases in Capillary GC

H. J. Lim[1] / H. S. Lee[1] / I. W. Kim[2] / S. H. Chang[3] / S. C. Moon[3] / B. E. Kim[4] / J. H. Park[1]*

[1]Department of Chemistry, Yeungnam University, Kyongsan 712–749, Korea
[2]Department of Chemical Education, Taegu University, Kyongsan 712–714, Korea
[3]Department of Chemistry, Taegu University, Kyongsan 712–714, Korea
[4]Research Institute of Industrial Science and Technology, Pohang 790–330, Korea

Key Words

Gas chromatography
Calix[4]arene–tetramethyldisiloxane stationary phases
Geometric and positional isomer separations

Summary

Poly(*p-tert*-butyldimethoxydipropyloxycalix[4]arene--tetramethyldisiloxane) (TBCX-TMDS) and poly(dimethoxydipropyloxycalix[4]arene-tetramethyldisiloxane) (CX-TMDS), have been prepared and used as stationary phases for isothermal capillary gas chromatographic separations of positional isomers. Retention factors and separation factors for the isomers were measured. The isomers investigated were well-resolved on the two phases. Retention of all the solutes investigated is greater on TBCX-TMDS than on CX-TMDS, probably because of extra dispersive interactions of the solutes with the *tert*-butyl groups of the phase. Separation factors for closely-eluting isomer pairs are similar on the two phases. This seems to indicate either that the solutes are retained by non-inclusion processes or that if the isomer molecules do enter the cavity of the calixarene, i.e. the solute is retained by inclusion, the *tert*-butyl groups do not play a role in discriminating between the isomers.

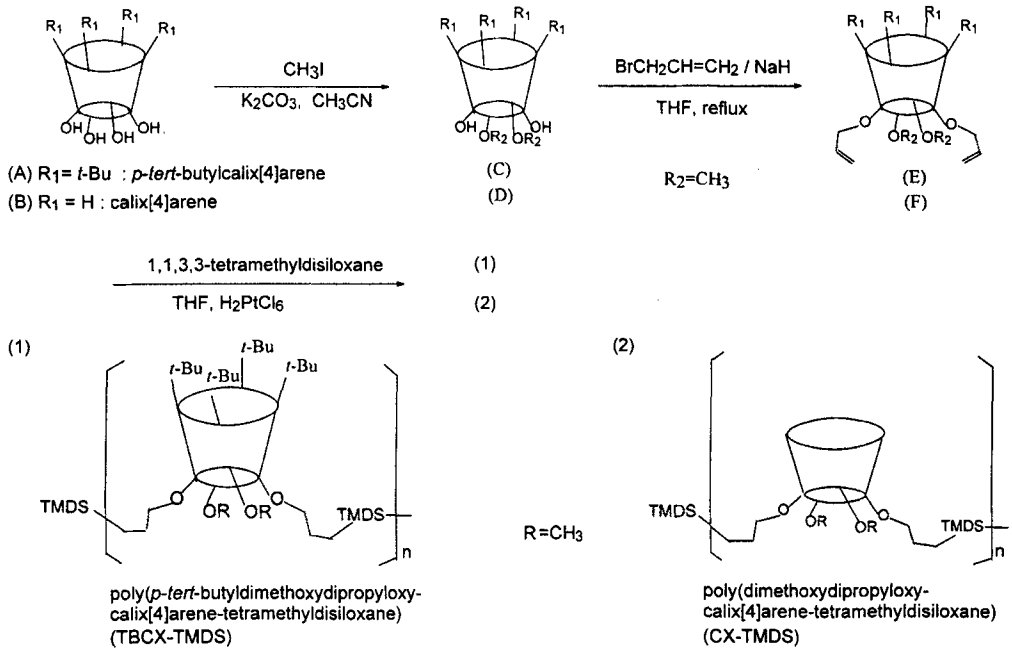
Introduction

Calixarenes are cavity-shaped cyclic molecules, comprising phenol units linked by alkylidene groups, which act as receptor molecules of widely varying size for metal cations and organic molecules [1]. Because they have cylindrical architecture similar to that of 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 in comparison with micellar inclusion [10].

Ready accessibility also accounts for the increasing attention that calixarenes have received during the past decade [1, 11, 12]. Calixarenes have recently been used in gas chromatography, liquid chromatography and capillary electrophoresis. Mangia et al. [13] reported separation of alcohols, chlorinated hydrocarbons and aromatic compounds by gas–solid chromatography 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 gas chromatography [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]. Freibe et al. reported the use of *p-tert*-butylcalix[4]arene-bonded silica material for the liquid-chromatographic separation of nitroaniline regioisomers, nucleosides and three proline-containing dipeptides [20]. Park et al. used water-soluble calix[6]arene-*p*-sulfonate (CAPS) [21] as mobile-phase additive in the reversed-phase liquid-chromatographic (RPLC) separation of some monosubstituted phenols [22]. They also used a CAPS-bonded silica for the RPLC separation of several positional isomers [23]. CAPS has also been used as the mobile-phase additive in capillary electrophoresis [24].

In this work we report the preparation of two calix[4]arene-siloxane polymers, poly(*p-tert*-butyldimethoxydipropyloxycalix[4]arene-tetramethyldisiloxane) and poly(dimethoxydipropyloxycalix[4]arene-tetramethyldisiloxane) and their use as stationary phases for the isothermal capillary gas-chromatographic separation of positional and geometric isomers.

0009-5893/98/09 422-05 $ 03.00/0 © 1998 Friedr. Vieweg & Sohn Verlagsgesellschaft mbH



Scheme 1
Preparation of calix[4]arene-TMDS polymers.

Experimental

Preparation of Calixarene-Tetramethyldisiloxane polymers

Poly(*p-tert*-butyldimethoxydipropyloxycalix[4]arene-tetramethyldisiloxane) (TBCX-TMDS) and Poly(dimethoxydipropyloxycalix[4]arene-tetamethyldisiloxane) (CX- TMDS) were prepared according to the procedure shown in Scheme 1.

p-tert-Butylcalix[4]arene (**A**) and calix[4]arene (**B**) were synthesized by the reaction of *p-tert*-butylphenol, potassium hydroxide, formaldehyde and $AlCl_3$ using a procedure reported elsewhere [25, 26]. *P-tert*-Butyl-25,27-dimethoxycalix[4]arene (**C**) and 25,27-dimethoxycalix[4]arene (**D**) were prepared by the reaction of compounds **A** and **B**, respectively, with methyl iodide in the presence of K_2CO_3 in acetonitrile using a procedure reported elsewhere [27]. Reaction of **C** with allyl bromide in the presence of sodium hydride under reflux in tetrahydrofuran gave *p-tert*-butyl-25,27-dimethoxy-26,28-diallyloxycalix[4]arene (**E**) after recrystallization from chloroform-methanol [28]. Yield 8 7%; 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, 6H, C–CH=CH_2), 4.5–2.8 (m, 18H, CH_2–C=C, OCH_3, $ArCH_2Ar$), 1.23 (d, 36H, *t*-Bu). By following the procedure used for the preparation of **E**, 25,27-dimethoxy-26,28-diallyloxycalix[4]arene (**F**) was obtained from **D**. Yield 90%; mp 157–158 °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, 6H, C–CH=CH_2), 4.5–2.8 (m, 18H, CH_2–C=C, OCH_3, $ArCH_2Ar$), 1.23 (d, 36H, *t*-Bu).

TBCX-TMDS was prepared by reaction of **E** with 1,1,3,3-tetramethyldisiloxane in the presence of H_2PtCl_6 in THF and purified by column chromatography (silica, ethyl acetate–*n*-hexane). ^1H NMR ($CDCl_3$, 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)). CX-TMDS was prepared from **F** by following the procedure described for TBCX-TMDS. ^1H NMR ($CDCl_3$, δ) 7.2–6.8 (ArH), 3.8–4.5 ($ArOCH_2$), 3.0 and 3.6 ($ArCH_2Ar$), 3.8–4.0 (m, 6H, OCH_3), 0.8–1.6 (Si–C–CH_2), 0.05 (Si–CH); ^{13}C NMR ($CDCl_3$, δ) 156.6, 136.9, 132.7, 127.0, 121.8 (Ar), 60.5 (OCH_3), 36.4 (OCH_2), 30.8 ($ArCH_2Ar$), 11.0 ($OCCH_2$), 1.12 (Si–CH_2), 1.06 (Si–CH_3)).

Preparation of Fused-Silica Capillary Columns

Deactivated empty fused silica capillary tubing was 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 films of solutions (25 %, *w/w*) of the calixarene-siloxane polymers in the polysiloxane OV-1701 [29]. Coating was performed with 0.33 % solutions of the stationary phase mixture in pentane-dichloromethane (1:1, *v/v*) [30–32].

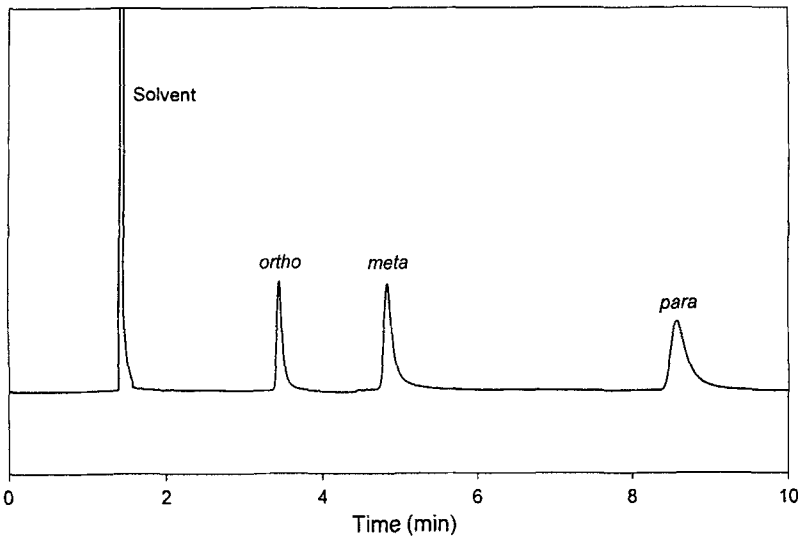


Figure 1
Separation of nitroanilines on poly(dimethoxydipropyloxycalix[4]arene–tetramethyldisiloxane).

Capillary Gas Chromatography

Gas chromatographic analysis was performed with a Hewlett–Packard (Wilmington, DE 19808, USA) 5890 Series II chromatograph equipped with split injection (250 °C) and an FID detector (300 °C). Helium at a pressure of 25 psig was used as carrier gas. Solutions (1 %) in dichloromethane (1 µL) were injected with a split ratio of 1:100. The column dead-time was determined from retention times of three successive *n*-alkane homologues by use of the equation of Guardino et al. [33].

Results and Discussion

Tables I and II list capacity factors (k) and separation factors (α) of positional isomers of monosubstituted phenols and other aromatic compounds separated on TBCX-TMDS and CX-TMDS. Figure 1 shows a typical chromatogram of the separation of nitroanilines on CX-TMDS. Most of the positional isomers are well resolved on the two phases; exceptions are the *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.

The orders of elution of the isomers of the compounds studied follow their boiling points except for 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 order of elution of the 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 groups on the *ortho* 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 *ortho* isomers significantly compared with the *meta* and *para* isomers for which both the hydroxyl and the polar substituent group are available for interactions with the stationary phase. Isomers of other compounds with substituent groups 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 are greater on TBCX-TMDS than on CX-TMDS. The greater retention on TBCX-TMDS is probably because of stronger dispersive interactions between the *tert*-butyl group on the phase with the solutes in the gas phase. Although retention of all the compounds is greater on TBCX-TMDS than on CX-TMDS, separation factors are similar on the two phases. This seems to indicate either that the *tert*-butyl groups are not involved in discrimination between isomer molecules entering the cavity of the calixarene (if the solute is retained by inclusion) or that the solutes are retained by non-inclusion processes on these phases.

Conclusions

The positional isomers investigated are well-resolved on the two phases. Retention of all the solutes investigated is greater on TBCX-TMDS than on CX-TMDS, probably because of stronger dispersive interactions of the solute with the *tert*-butyl groups on the phase. Separation factors for closely-eluting isomer pairs are similar on the two phases. This seems to indicate either that the *tert*-butyl groups do not discriminate between isomer molecules entering the cavity of the calixarene (if the solute is retained by inclusion) or that the solutes are re-

Table I. Capacity factors (k) and separation factors () of monosubstituted phenols on calix[4]arene-TMDS polymer phases.

Compound	b.p. (°C)	Separation temp. (°C)	CX-TMDS[a]		TBCX-TMDS[b]	
			k[c]	α[d]	k	α
o-Aminophenol	153.0[e]	150	1.93	1.00	2.43	1.00
m-Aminophenol	164.0		3.24	1.22	4.03	1.21
p-Aminophenol	284.0		2.66	1.38	3.33	1.37
o-Nitrophenol	214.6	160	0.50	1.00	0.73	1.00
m-Nitrophenol	194.0		7.85	15.77	10.86	14.87
p-Nitrophenol	279.0		12.30	1.57	16.85	1.55
o-Cresol	191.0	130	1.17	1.00	1.60	1.00
m-Cresol	202.2		1.50	1.04	2.00	1.05
p-Cresol	201.9		1.44	1.23	1.90	1.19
o-Chlorophenol	174.9	130	0.64	1.00	0.91	1.00
m-Chlorophenol	214.0		3.69	5.78	5.10	5.59
p-Chlorophenol	219.8		3.73	1.01	5.13	1.01
o-Methoxyphenol	205.1	130	1.15	1.00	1.57	1.00
m-Methoxyphenol	244.3		4.43	1.26	6.06	1.24
p-Methoxyphenol	243.0		3.53	3.06	4.88	3.08

[a]Poly(dimethoxydipropyloxycalix[4]arene-tetramethyldisiloxane).
[b]Poly(*p-tert*-butyldimethoxydipropyloxycalix[4]arene-tetramethyldisiloxane).
[c]$k = (t_R - t_0)/t_0$.
[d]An α value of unity was assigned to the first-eluting isomer and computed for closely-eluting isomer pairs by use of the relationship $\alpha = k_2 / k_1$.
[e]Sublimation temperature at 11 torr.

Table II. Capacity factors (k) and separation factors (α) for other aromatic compounds on calix[4]arene-TMDS polymer phases.

Compound	b.p. (°C)	Separation temp. (°C)	CX-TMDS[a]		TBCX-TMDS[b]	
			k[c]	α[d]	k	α
1-Bromo-2-nitrobenzene	258.0	130	4.58	1.17	6.91	1.11
1-Bromo-4-nitrobenzene	256.0		3.92	1.00	6.20	1.00
o-Nitroaniline	284.0	180	1.52	1.00	2.03	1.00
m-Nitroaniline	305.0		2.51	1.55	3.36	1.65
p-Nitroaniline	332.0		5.15	2.05	6.82	2.03
o-Nitrotoluene	221.7	100	5.49	1.00	7.57	1.00
m-Nitrotoluene	232.6		6.36	1.16	9.18	1.21
p-Nitrotoluene	238.3		7.09	1.12	10.14	1.10
o-Fluorotoluene	114.4	50	1.10	1.00	2.05	1.00
m-Fluorotoluene	116.5		1.17	1.06	2.12	1.03
p-Fluorotoluene	116.6		1.19	1.02	2.17	1.03
o-Xylene	144.4	50	3.92	1.25	5.42	1.24
m-Xylene	139.1		3.12	1.00	4.38	1.02
p-Xylene	138.3		3.13	1.00	4.31	1.00
1,3-Dichlorobenzene	173.0	100	1.33	1.06	1.91	1.04
1,4-Dichlorobenzene	174.0		1.25	1.00	1.84	1.00
cis-1,2-Dimethylcyclohexane	129.7	50	1.52	1.36	2.13	1.32
trans-1,2-Dimethylcyclohexane	123.4		1.11	1.00	1.61	1.00
cis-Decahydronaphthalene	195.8	100	1.77	1.37	2.54	1.33
trans-Decahydronaphthalene	187.3		1.29	1.00	1.91	1.00

[a]Poly(dimethoxydipropyloxycalix[4]arene-tetramethyldisiloxane).
[b]Poly(*p-tert*-butyldimethoxydipropyloxycalix[4]arene-tetramethyldisiloxane).
[c]$k = (t_R - t_0) / t_0$.
[d]An α value of unity was assigned to the first-eluting isomer and computed for closely-eluting isomer pairs by use of the relationship $\alpha = k_2 / k_1$.

tained by non-inclusion processes on these phases. Preparation of other potentially more efficient calixarene stationary phases for the separation of positional and geometrical isomers is being attempted by introducing different substituents on to the calixarene rim.

Acknowledgement

This work was supported by a grant (No. 96-0501-07-01-3) from the Korea Science and Engineering Foundation.

References

[1] *J. Vicens, V. Bohmer*, Calixarenes: A Versatile Class of Macrocyclic Compounds, Kluwer, Dordrecht (1991).
[2] *W. Saenger*, Angew. Chem. Int. Ed. Engl. **19**, 344 (1980).
[3] *W. L. Hinze*, Sep. Purif. Methods **10**, 159 (1981).
[4] *Y. Nobuhara, S. Hirano, Y. Nakanishi*, J. Chromatogr. **258**, 276 (1983).
[5] *D. W. Armstrong, A. Alak, K. Bui, W. DeMond, T. Ward, T. E. Riehl, W. L. Hinze*, J. Inclusion Phenom. **2**, 533 (1984).
[6] *D. W. Armstrong, W. DeMond*, J. Chromatogr. Sci. **22**, 411 (1984).
[7] *W. L. Hinze, T. E. Riehl, D. W. Armstrong, W. DeMond, A. Alak, T. Ward*, Anal. Chem. **57**, 237 (1985).
[8] *R. M. Mohseni, R. J. Hurtubise*, J. Chromatogr. **499**, 395 (1990).
[9] *J. H. Park, M. D. Jang, M. J. Shin*, J. Chromatogr. **595**, 45 (1992).
[10] *K. W. Street, Jr*, J. Liq. Chromatogr. **10**, 655 (1987).
[11] *C. D. Gutsche, B. Dhawan, K. H. No, R. Muthukrishnan*, J. Am. Chem. Soc. **103**, 3782 (1981).
[12] *B. Dhawan, S.-I. Chen, C. D. Gutsche*, Makromol. Chem. **188**, 921 (1987).
[13] *A. Mangia, A. Pochini, R. Ungaro, G. D. Andreetti*, Anal. Lett. **16**, 1027 (1983).
[14] *P. Mnuk, L. Feltl*, J. Chromatogr. A **696**, 101 (1995).
[15] *P. Mnuk, L. Feltl, V. Schurig*, J. Chromatogr. A **732**, 63 (1996).
[16] *J. D. Glennon, E. Horne, S. Srijaranai, K. Manley, S. J. Harris, M. A. McKervey*, Anal. Lett. **26**, 153 (1993).
[17] *J. D. Glennon, E. Horne, K. O'Connor, G. A. Kearney, S. J. Harris, M. A. McKervey*, Anal. Proc. **31**, 33 (1994).
[18] *R. Brindle, K. Albert, S. J. Harris, C. Troltzsch, E. Horne, J. D. Glennon*, J. Chromatogr. A **731**, 41 (1996).
[19] *J. D. Glennon, E. Horne, K. Hall, D. Cocker, A. Kuhn, S. J. Harris, M. A. McKervey*, J. Chromatogr. A **731**, 47 (1996).
[20] *S. Freibe, S. Gebauer, G. J. Krauss, G. Goermar, J. Krueger*, J. Chromatogr. Sci. **33**, 281 (1995).
[21] *S. Shinkai, S. Mori, H. Koreishi, T. Tsubaki, O. Manabe*, J. Am. Chem. Soc. **108**, 2409 (1986).
[22] *J. H. Park, Y. K. Lee, N. Y. Cheong, M. D. Jang*, Chromatographia **37**, 221 (1993).
[23] *Y. K. Lee, Y. K. Ryu, J. W. Ryu, B. E. Kim, J. H. Park*, Chromatographia **46**, 507 (1997).
[24] *D. Shohat, E. Grushka*, Anal. Chem. **66**, 747 (1994).
[25] *C. D. Gutsche, M. Iqbal, D. J. Stewart*, J. Org. Chem. **51**, 742 (1986).
[26] *C. D. Gutsche, L. G. Lin*, Tetrahedron **42**, 1633 (1986).
[27] *J.-D. V. Loon, A. Arduini, L. Coppi, W. Verboom, A. Pochini, R. Ungaro, S. Harkema, D. N. Reinhoudt*, J. Org. Chem. **55**, 5639 (1990).
[28] *J.-D. V. Loon, A. Arduini, W. Verboom, R. Ungaro, G. J. Hummel, S. Harkema, D. N. Reinhoudt*, Tetrahedron Lett. **30**, 2681 (1989).
[29] *J. Bouche, M. Verzele*, J. Gas Chromatogr. **6**, 501 (1968)..
[30] *B. E. Kim, S. H. Lee, K.-P. Lee, K.-S. Park, J. H. Park*, J. High Resol. Chromatogr. **20**, 208 (1997).
[31] *B. E. Kim, K.-P. Lee, K.-S. Park, S. H. Lee, J. H. Park*, J. High Resol. Chromatogr. **20**, 437 (1997).
[32] *B. E. Kim, K.-P. Lee, K.-S. Park, S. H. Lee, J. H. Park*, Chromatographia **46**, 145 (1997).
[33] *X. Guardino, J. Albaiges, G. Firpo, R. V. Rodriguez, M. Gassiot*, J. Chromatogr. **118**, 13 (1976).

Received: Jan 28, 1998
Revised manuscript
received: Mar 31, 1998
Accepted: Apr 24, 1998