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TOTAL MOLECULAR SURFACE AREAS AS A PREDICTOR FOR REVERSED-PHASE HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY IN VARIOUS ORGANOTIN SYSTEMS

IMPORTANCE AND APPLICATIONS OF CARBON HYBRIDIZATION SUMMARIES*

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SUMMARY

Various organotin compounds were separated using a C₁₈ reversed-phase column with methanol–water (93:7) as mobile phase. Both holistic total molecular surface area (TSA) calculations and molecular TSAs assembled from additions of “mean functional groups and atom” TSA values were employed in this study. A significant linear correlation was obtained between the natural logarithms of the capacity factors and the TSA values for both fluxional and rigid organotin system as defined by summed carbon hybridization. The two systems were intercorrelated by taking into account the carbon hybridization. Tie-lines could be drawn between the two systems and the use of these column-dependent tie-lines allows the prediction of unreported compounds incorporating mixed ligands. In addition, the data suggest that the quantitative hybridization summary determines the fluxionality of the organic moieties and consequent solvophobic properties.

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INTRODUCTION

It has been known and recognized for many years that a correlation exists between the logarithms of partition coefficients ($\log P$) and the logarithms of aqueous solubilities ($\log S$) with various molecular surface areas¹. Both the partitioning and the dissolution processes have been associated with free energy changes^{1,2}. Since chromatographic separations are also proportional to free energy changes², it is not surprising to find high correlations between chromatographic parameters such as the logarithms of the capacity factor, $\log k'$ values, and molecular surface areas. Recently, Funasaki *et al.*³ showed a linear relationship between the $\log k'$ values and the molecular cavity surface areas for a series of alcohols and ethers. Other organic systems that correlate well with molecular surface areas include alkylbenzenes⁴, polycyclic aromatic hydrocarbons⁴, and amino acids⁵. Recently Möckel *et al.*⁶⁻⁹, using a fragment approach to calculate the total surface areas (TSA) for several classes of compounds, demonstrated an excellent correlation between their TSA values and $\ln k'$ data. Brinkman and co-workers¹⁰⁻¹² earlier extended to organometallic systems the concept of the TSA as a predictor, and demonstrated very high linear correlations between the natural logarithms of the capacity factor and the TSA for two series of mixed tetraorganotin^{10,11} as well as for a series of Group VA triphenyl derivatives¹³. Two distinct solvophobic patterns were observed for the organotin. The more rigid phenyl substituents, which have limited rotation exhibited a shorter retention time on the C₁₈ reversed-phase column than did more flexible molecules such as the alkyltins^{10,11}. However, these two classes of organotin were not intercorrelated. Thus, it was of interest to expand the initial work to include: additional molecules with flexibility or fluxionality (alkyltins), molecules that can act as rigid rotors (phenyl- and allyltins), and molecules with partial rigidity (alkylaryl/allyltins) to determine whether the various classes of organotin can be intercorrelated. Furthermore, the established use of TSA values as a predictor of organophysical properties may be utilized not only to estimate the chromatographic retention times of specific compounds, but also to correlate experimentally determined retention times with possible structures of unknown compounds as defined by their carbon hybridization number.

EXPERIMENTAL*

Chemicals and materials

n-Butyltriphenyltin (BuPh₃Sn), di-*n*-butyldiphenyltin (Bu₂Ph₂Sn), tri-*n*-butylphenyltin (Bu₃PhSn), *n*-propyltriphenyltin (nPrPh₃Sn), di-*n*-propyldiphenyltin (nPr₂Ph₂Sn), tri-*n*-propylphenyltin (nPr₃PhSn), were synthesized by a redistribution reaction between tetraphenyltin (Ph₄Sn) and either tetra-*n*-butyltin (Bu₄Sn) or tetra-*n*-propyltin (nPr₄Sn), as described by Calengaert *et al.*¹⁴. The remaining organotin were obtained from Alpha Products (Danvers, MA, U.S.A.) and Strem Chemicals (Newburyport, MA, U.S.A.). The compounds obtained commercially were used without further purification. The water used in this study was purified using a Cul-

* Certain commercial products or equipment are mentioned in order to describe adequately experimental procedures. In no case does such identification imply endorsement by the National Bureau of Standards, nor does it imply that the material is necessarily the best available for the purpose.

ligan exchange resin system (Northbrook, IL, U.S.A.) to obtain $18 \Omega \cdot \text{cm}$ resistivity. Spectrophotometric-grade methanol was obtained from Fisher Scientific (Fair Lawn, NJ, U.S.A.). Stock solutions of the organotin compounds containing either 40 ppm as tin or 10 ppm (for the less soluble compounds) were prepared with methanol. These stock solutions were then diluted to 0.5–2.0 ppm with methanol on a daily basis prior to chromatographic runs.

Instrumentation and procedures

An Altex (Deerfield, IL, U.S.A.) Model 100 high-performance liquid chromatograph equipped with two dual-piston solvent pumps was coupled with a Perkin-Elmer (Norwalk, CT, U.S.A.) graphite furnace atomic absorption spectrometer and an Altex analytical UV detector (254 nm). The complete system with auto sampling interface and digital read-out peripherals has been described in detail^{15,16}. The chromatographic separation of the organotin compounds was carried out isocratically on a Scientific Glass Engineering (Austin, TX, U.S.A.) C_{18} (octadecylsilane) reversed-phase column (5 μm particle size; 250 mm \times 4 mm) using a flow-rate of 1.0 ml/min. The mobile phase was methanol–water (93:7, v/v). A minimum of three replicate measurements were made for each substance to calculate the capacity factor.

Topological calculations

The SAREA program¹⁷, suitably modified for the National Bureau of Standards main frame computer (VAX 11/785), was employed to calculate total surface areas (in \AA^2). The details of our procedures have been described previously^{13,18–20}. The input data necessary for the TSA calculations, including conventional bond distances, bond angles, and Van der Waal's radii, were all obtained from the literature. Both holistic molecular calculations¹³ and an assembly of molecular TSAs from the addition of mean functional groups and atom TSA values¹⁰ were employed in this study.

RESULTS AND DISCUSSION

A typical UV–graphite furnace atomic absorption (GFAA) chromatogram (Fig. 1) shows the separation of a mixture of allyltriphenyltin, allyltributyltin and tetraallyltin, along with examples of element-specific detection for the alkyltins. The $\ln k'$ values for the alkyl- and aryltins are listed in Table I, as well as standard deviations calculated from a minimum of three chromatographic measurements. Also included in Table I are the TSA values for the various compounds calculated by summing fragment values¹⁰ or from total molecular calculations¹³. Table II summarizes the natural logarithms of the capacity factors for the allyltins along with TSA values calculated using a holistic-TSA approach. The term "holistic" refers to a particular fixed conformation for the complete molecule and does not necessarily imply that the TSA value for the whole molecule is greater than the sum of its parts.

Horváth and co-workers^{2,21,22} presented a model of solvophobic chromatographic separations based on thermodynamic principles. According to this solvophobic theory, parameters such as the TSA of a molecule could be correlated with the time of retention in reversed-phase liquid chromatography. Plots of the $\ln k'$ values *versus* TSA are shown in Fig. 2 for the various alkyl- and aryltin compounds.

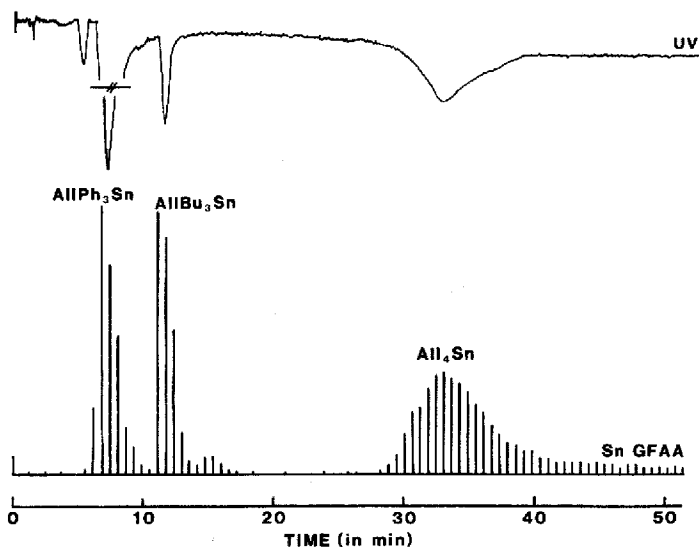


Fig. 1. Dual chromatograms of the separation of allyltriphenyltin (AllPh_3Sn), allyltributyltin (AllBu_3Sn), and tetraallyltin (All_4Sn) compared in element-specific GFAA Sn (bottom) and conventional UV (top) modes. Chromatographic conditions: column, C_{18} bonded-phase (250 mm \times 4 mm I.D., 5 μm); mobile phase, methanol-water (93:7, v/v); isocratic flow, 1.0 ml/min; detection at 254 nm, a.u.f.s. = 0.04; chart speed, 5 mm/min. GFAA conditions: furnace program: dry at 80°C for 13 s, char at 700°C for 5 s, atomize at 2700°C for 7 s; Ar at 200 ml/min stopped flow; 20 μl sample volume; Sn λ , 224.6 nm; slit width, 0.7 mm.

The alkyltins show an excellent correlation ($r^2 = 0.995$). As shown in the plot, the organotin compounds containing larger alkyl groups exhibit larger retention times, since these large fluxional molecules tend to experience greater interaction with the hydrophobic stationary phase.

Phenyltins can be considered to be a rigid rotor type of molecule, since their only allowable conformational changes involve rotations around the Sn-C bonds. These compounds, however, also show an excellent correlation between the calculated TSA values and their $\ln k'$ values (Fig. 2). For the aryltin series, on the other hand, three distinct correlations are observed, depending upon the mixed alkyl-phenyl system studied.

The addition of the rigid phenyl moiety decreases the retentivity of the organotin molecule on the C_{18} column substrate owing to the loss of the alkyl, as observed for both the propyl- and the butylphenyltin series. For example, as the number of phenyl groups increases in the series $\text{Bu}_n\text{Ph}_{4-n}\text{Sn}$, where $n = 0-4$, the $\ln k'$ values decrease from 2.579 (Bu_4Sn) to 0.690 (Ph_4Sn). It is apparent (Fig. 2) that the decrease in retention time in the butylphenyltin series is a function of the number of phenyl groups attached to the tin atom and displaces the butyl groups, since the phenyl group experiences less interaction with the stationary phase than the butyl group. Methylphenyltins, however, show a reverse trend, owing to the smaller size of the methyl substituents compared to the butyl ligands. This series of methylphenyltins also demonstrates that hydrophobic interactions between the column and/or phenyl

TABLE I
CAPACITY FACTORS AND TSA VALUES FOR ORGANOTIN COMPOUNDS

Compound	$\ln k'_{exp}$	Std. dev.	TSA (\AA^2) _{frag}	$\ln k'_{calc}$
<i>Alkyls</i>				
Me ₄ Sn	-0.228	0.085	148.5	-0.192
Me ₂ Et ₂ Sn	0.325	0.091	193.9	0.343
Et ₄ Sn	0.922	0.031	239.3	0.877
Et ₃ BuSn	1.373	0.144	279.3	1.347
Me ₃ OctSn	1.613	0.016	294.8	1.530
iPr ₄ Sn	1.796	0.034	320.1	1.827
nPr ₄ Sn	1.800	0.352	315.3	1.771
Et ₂ Bu ₂ Sn	1.826	0.016	319.3	1.818
EtBu ₃ Sn	2.241	0.034	359.3	2.289
Bu ₄ Sn	2.579	0.051	399.3	2.759
Pr ₃ OctSn	3.010	0.044	419.9	3.002
Me ₂ Oct ₂ Sn	3.365	0.012	441.1	3.251
<i>Aryls</i>				
Me ₂ Ph ₂ Sn	0.447	0.012	267.7	0.314
MePh ₃ Sn	0.664	0.051	327.3	0.570
nPr ₃ PhSn	1.330	0.009	333.2	1.385
nPr ₂ Ph ₂ Sn	0.970	0.010	351.1	1.102
nPrPh ₃ Sn	0.720	0.010	369.0	0.819
Bu ₃ PhSn	1.919	0.051	396.2	1.987
Bu ₂ Ph ₂ Sn	1.397	0.034	393.1	1.517
BuPh ₃ Sn	0.999	0.049	390.0	1.047
Ph ₄ Sn	0.690	0.043	386.9	0.577

groups also affect the retention mechanism. The importance of alkyl chain length is evident (Fig. 2) as well in the very high correlation of TSA and capacity factors for a series of linear alkyltins.

The fact that tie-lines can be drawn between systems is a highly significant observation, since these tie-lines can be used to predict $\ln k'$ values of new or unreported compounds. For example, it could be possible to calculate TSA values for compounds in series such as ethylphenyl- or octylphenyltins and then determine their $\ln k'$ values from the tie-lines drawn between R₄Sn and Ph₄Sn.

TABLE II
CAPACITY FACTORS AND TSA VALUES FOR ALLYL TIN COMPOUNDS

Compound	$\ln k'_{exp}$	Std. dev.	TSA (\AA^2) _{hols}	$\ln k'_{calc}$
All ₄ Sn	0.186	0.010	293.5	—
AllPh ₃ Sn	0.541	0.054	367.4	0.567
AllBu ₃ Sn	1.908	0.445	369.5	1.906

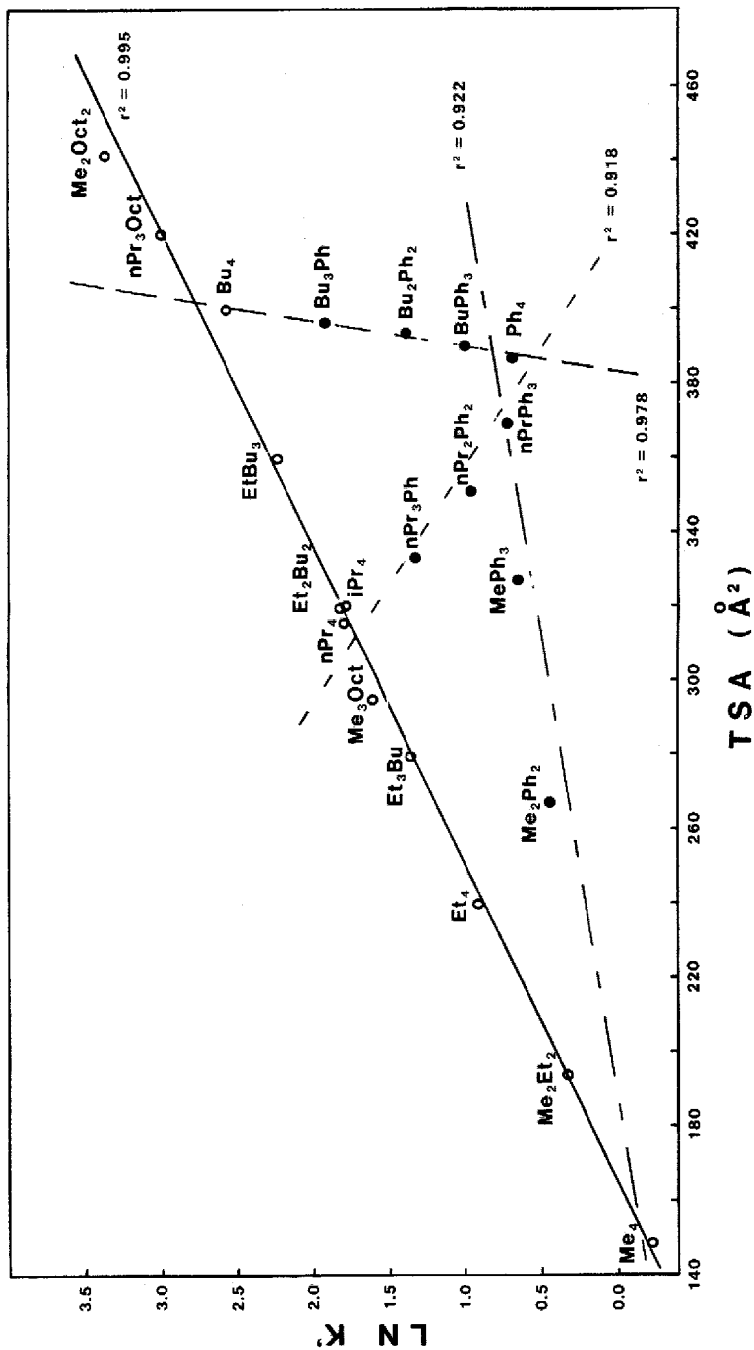


Fig. 2. Correlations between computed TSAs and $\ln k'$ for alkyl-, aryl-, and alkylaryl compounds.

Another system that can be considered as a rigid rotor contains allyl groups such as the compound tetraallyltin (All_4Sn), since these molecules also have restricted rotations. Fig. 3 shows that as the number of allyl groups increase, there is a decrease in the $\ln k'$ values, indicating that these rigid molecules also have limited interaction with the stationary phase as do the phenyl compounds. Steric effects have been shown to play a major role in the retentivity of a solute²³. A comparison of the $\ln k'$ values shows that there is nearly a ten-fold decrease from $n\text{-Pr}_4\text{Sn}$ to All_4Sn despite the fact that the number of carbon atoms is identical in both compounds and their TSA values are similar. This perhaps implies that steric effects are governing the retentivity.

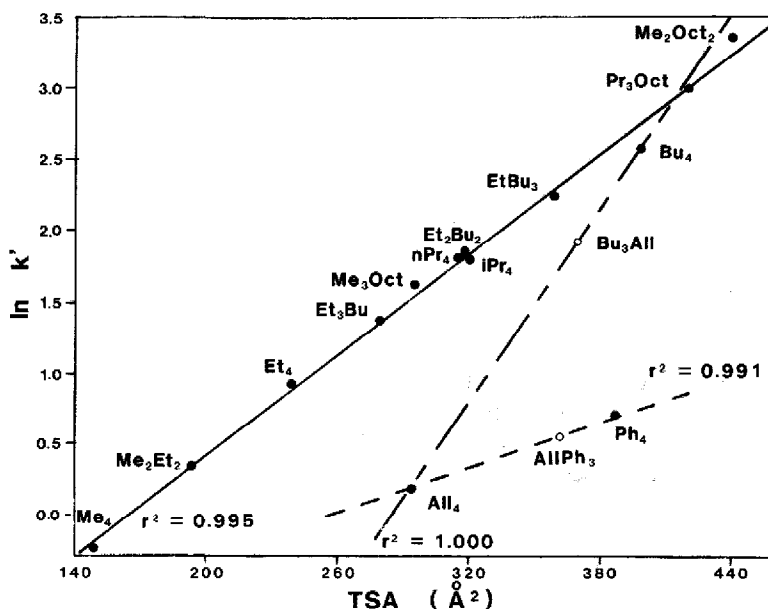


Fig. 3. Correlations between computed TSAs and $\ln k'$ for alkyltin and allyltin compounds. The experimental $\ln k'$ values as well as the $\ln k'$ values calculated from the tie-lines for AllPh_3Sn and AllBu_3Sn are included as indicated by the open circles.

The use of the tie-lines drawn between All_4Sn and Bu_4Sn , as well as between All_4Sn and Ph_4Sn , allowed prediction of the $\ln k'$ values for AllBu_3Sn and AllPh_3Sn designated by open circles. The $\ln k'$ values obtained from the plotted tie-lines for AllBu_3Sn and AllPh_3Sn were 1.906 and 0.567, respectively. These compared well with the experimental values of 1.908 and 0.541.

The number of carbon atoms present in a molecule has been a useful quantity for the characterization of a compound in gas chromatographic analysis²⁴. A plot of the number of sp^3 hybridized carbons versus $\ln k'$ for the alkyltin compounds (eqn. 1), showed a very high linear correlation ($r^2 = 0.994$):

$$\ln k' = 0.243 (\text{No. of } \text{sp}^3 \text{ carbons}) - 1.15 \quad (1)$$

However, if the organotins containing sp^2 hybridized carbons are included, no significant correlation is found, and the r^2 value is 0.034. It is evident that the consideration of carbon hybridization is important and that carbon number is an accurate predictor only for a series of homologous compounds. A multiple linear regression analysis was performed in which carbon hybridization was factored in by weighing the contributions of both the sp^3 and the sp^2 carbons in each compound. For the resulting equation (eqn. 2), the high correlation of $r^2 = 0.971$ was obtained:

$$\ln k' = 0.231 (\text{No. of } sp^3 \text{ carbons}) + 0.065 (\text{No. of } sp^2 \text{ carbons}) - 1.031 \quad (2)$$

Although the statistical fit of the line for eqn. 2 is quite good, the reader should be cautioned that this modification for the use of carbon number still represents a fragmentation of the molecule into discrete moieties and does not take the entire molecular conformation into consideration. The compound is broken into segments according to the hybridization of individual carbon atoms. For example, compounds which may not fit the correlation are trimethylphenyltin and trivinyl-*n*-propyltin. Both compounds have six sp^2 carbons and three sp^3 carbons. According to eqn. 2, one would expect these structures to have the same capacity factor. However, although both the vinyl (Vi) and the phenyl groups are rigid molecules, the single phenyl substituent of the Me_3PhSn rotates around only one Sn-C bond, whereas the vinyl groups rotate around three Sn-C bonds. There will be less interaction between Me_3PhSn and the C_{18} column than for $\text{Vi}_3n\text{-PrSn}$, resulting in a smaller capacity factor for Me_3PhSn .

The expansion of carbon number to include hybridization as a predictor can be very useful. However, as with any method which does not utilize the entire conformational and structural information of a molecule, care must be taken for its application to unstudied compounds.

CONCLUSION

Several conclusions emerge from this work. Very good correlations between TSA and $\ln k'$ values exist for both fluxional and rigid organotin systems, both separately and in mixed derivatives. The introduction of a rigid or stiff moiety such as a phenyl or allyl group dramatically decreases the $\ln k'$ values within the $\text{R}_n\text{R}'_{4-n}\text{Sn}$ system. This is attributed to the reduced interaction of the solute with the stationary phase. A tie-line effect is observed for these $\text{R}_n\text{R}'_{4-n}\text{Sn}$ systems and, as a result, the relative retentivity can be accurately predicted for a molecule in the $\text{R}_n\text{R}'_{4-n}\text{Sn}$ system or homologous series if the TSA is known by means of an independent method, such as HPLC performed on a well-behaved column substrate such as C_{18} . Carbon hybridization may be factored into eqn. 1 (which uses carbon number as a predictor). It is then possible to diagnose, from experimental capacity factor data, the amount of carbon hybridization for an unknown compound involving any central or metallic element.

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REFERENCES

- 1 R. S. Pearlman, in W. J. Dunn III, J. H. Block and R. S. Pearlman (Editors), *Partition Coefficient Determination and Estimation*, Pergamon Press, New York, 1986, pp. 3–20.
- 2 Cs. Horváth, W. Melander and I. Molnár, *J. Chromatogr.*, 125 (1976) 129.
- 3 N. Funasaki, S. Hada and S. Neya, *J. Chromatogr.*, 361 (1986) 33.
- 4 K. Jinno and K. Kawasaki, *J. Chromatogr.*, 316 (1984) 1.
- 5 Cs. Horváth, W. Melander and I. Molnár, *Anal. Chem.*, 49 (1977) 142.
- 6 H. J. Möckel, G. Welter and H. Melzer, *J. Chromatogr.*, 388 (1987) 255.
- 7 H. J. Möckel, F. Höfler and H. Melzer, *J. Chromatogr.*, 388 (1987) 267.
- 8 H. J. Möckel, F. Höfler and H. Melzer, *J. Chromatogr.*, 388 (1987) 275.
- 9 H. J. Möckel, F. Höfler and H. Melzer, *J. Chromatogr.*, 388 (1987) 285.
- 10 P. J. Craig and F. E. Brinckman, in P. J. Craig (Editor), *Organometallic Compounds in the Environment*, Wiley, New York, 1986, pp. 1–64.
- 11 K. J. Irgolic and F. E. Brinckman, in M. Bernhard, F. E. Brinckman and P. J. Sadler (Editors), *The Importance of Chemical "Speciation" in Environmental Processes*, Springer, Berlin, Heidelberg, 1987, pp. 667–684.
- 12 C. S. Weiss, K. L. Jewett, F. E. Brinckman and R. H. Fish, in F. E. Brinckman and R. H. Fish (Editors), *Proc. DOE/NBS Workshop on Environment, Speciation and Monitoring Needs, NBS Spec. Publ. 618*, National Bureau of Standards, Washington, DC, 1981, pp. 197–216.
- 13 G. Eng, R. B. Johannesen, E. J. Tierney, J. M. Bellama and F. E. Brinckman, *J. Chromatogr.*, 403 (1987) 1.
- 14 G. Calingaert, H. Soroos and H. Shapiro, *J. Am. Chem. Soc.*, 62 (1940) 1104.
- 15 F. E. Brinckman, W. R. Blair, K. L. Jewett and W. P. Iverson, *J. Chromatogr. Sci.*, 15 (1977) 493.
- 16 K. L. Jewett and F. E. Brinckman, *J. Chromatogr. Sci.*, 19 (1981) 583.
- 17 R. S. Pearlman, *QCPE, Bulletin 1, Program No. 413*, Indiana University, Bloomington, IN, 1981.
- 18 R. B. Laughlin, Jr., W. French, R. B. Johannesen, H. E. Guard and F. E. Brinckman, *Chemosphere*, 13 (1984) 575.
- 19 R. B. Laughlin, Jr., R. B. Johannesen, W. French, H. E. Guard and F. E. Brinckman, *Environ. Toxicol. Chem.*, 4 (1985) 343.
- 20 F. E. Brinckman, G. J. Olson, W. R. Blair and E. J. Parks, in W. J. Adams, G. A. Chapman and W. G. Laudis (Editors), *Proc. Aquatic Toxicology and Hazard Assessment: 10th Vol., ASTM Publ. STP 971*, American Society for Testing and Materials, Philadelphia, PA, 1987, pp. 219–232.
- 21 Cs. Horváth and W. Melander, *Am. Lab. (Fairfield, Conn.)*, 10 (1978) 17.
- 22 W. Melander, J. Stoveken and Cs. Horváth, *J. Chromatogr.*, 199 (1980) 35.
- 23 K. Jinno and K. Kawasaki, *Chromatographia*, 17 (1983) 337.
- 24 C. S. G. Phillips and P. L. Timms, *Anal. Chem.*, 35 (1963) 505.