ELSEVIER

Journal of Chromatography A, 930 (2001) 145–154

JOURNAL OF CHROMATOGRAPHY A

www.elsevier.com/locate/chroma

Determination of octanol–water partition coefficients of pesticides by microemulsion electrokinetic chromatography

W.L. Klotz[a,b,*], M.R. Schure[b,c], J.P. Foley[d]

[a]*Department of Chemistry, Villanova University, Villanova, PA 19085, USA*
[b]*Analytical and Computational Technology Center, Rohm and Haas Company, Spring House, PA 19477-0904, USA*
[c]*Theoretical Separation Science Laboratory, Rohm and Haas Company, Spring House, PA 19477-0904, USA*
[d]*Department of Chemistry, Drexel University, Philadelphia, PA 19104, USA*

Received 23 March 2001; received in revised form 25 July 2001; accepted 31 July 2001

Abstract

Microemulsion electrokinetic chromatography (MEEKC) was evaluated as a screening tool for the indirect measurement of octanol–water partition coefficients (log $P_{o/w}$) of pesticide compounds. Over 80 pesticide compounds representing a variety of structural characteristics were studied, and good correlation of log $P_{o/w}$ with the logarithm of the retention factor was found. The microemulsion system studied allowed the separation of compounds in the log $P_{o/w}$ range of -1 to 7. In addition, a smaller set of simple organic molecules that vary in structural features was evaluated and compared to the pesticide log $P_{o/w}$ calibration. The pesticide and simple organic molecule log $P_{o/w}$ calibration lines were statistically similar. This suggests that a universal set of standard compounds may be employed for the log $P_{o/w}$ calibration to provide measurements for a variety of compounds with good accuracy.

Keywords: Partition coefficients; Microemulsion electrokinetic chromatography; Octanol–water partition coefficient; Pesticides

1. Introduction

The logarithm of the partition coefficient between octanol and water (log $P_{o/w}$) has been used as an indicator of the physicochemical and biological behavior of many classes of organic compounds. The hydrophobic character of organic molecules can be used to predict biomembrane transport [1–3], bioaccumulation in plants and animals [4,5], and soil adsorption [6]. Log $P_{o/w}$ values are also used in quantitative structure–activity relationship analysis [7,8] and new drug compound design [9].

Reversed-phase liquid chromatography (RPLC) has been widely explored as an alternative to the direct measurement of log $P_{o/w}$ through a linear relationship of the capacity factor and log $P_{o/w}$ [4,10–14]. This approach is advantageous over the traditional direct measurement method, providing faster analysis times, improved reproducibility, and requiring less amounts of sample for testing.

Other alternative methods have been pursued for the estimation of log $P_{o/w}$. Micellar liquid chromatography was successfully used for the correlation of

*Corresponding author: Rohm and Haas Company, 727 Norristown Road, Spring House, PA 19477-0904, USA. Tel.: +1-215-641-7438; fax: +1-215-641-7254.

E-mail address: wklotz@rohmhaas.com (W.L. Klotz).

0021-9673/01/$ – see front matter
PII: S0021-9673(01)01171-2

retention with hydrophobicity for a number of aromatic compounds [15–21]. Several studies have been conducted to evaluate micellar electrokinetic chromatography (MEKC) for the indirect measurement of hydrophobicity by the correlation of the logarithm of the retention factor to log $P_{o/w}$. A variety of molecules have been evaluated, including aromatics, polyaromatic hydrocarbons, pharmaceuticals, and pesticides [22–29].

Microemulsion electrokinetic chromatography (MEEKC) has been applied to the separation of molecules such as naphthalene derivatives, ketones and diketones [30,31], hop acids [32,33], vitamins [34], steroids [35,36], pharmaceuticals [37–40], and pesticides [41]. The oil-in-water type of microemulsion has mainly been used for separations in EKC. These microemulsions are clear liquids that consist of a surfactant, sometimes a cosurfactant that is generally an alcohol of intermediate chain length, and an oil component in aqueous solutions. Microemulsions form spontaneously and are stable for long periods of time.

MEEKC offers some advantages over MEKC separations [42]. The microemulsion formations are generally larger in size than micelles, giving them a higher capacity for the solubilization of hydrophobic molecules and a greater potential for separating very hydrophobic solutes in EKC separations. In microemulsions, the larger size of the structure in addition to the oil core component provides a higher solubilization capacity of molecules over micellar structures. Solutes may more easily penetrate and partition into the core oil of the microemulsion, allowing more hydrophobic compounds to be distinguished in separations. MEEKC can provide a larger elution range and higher peak efficiency, compensating for the potential loss of resolution due to the higher solute retention of MEKC. Increasing the surfactant portion of a microemulsion composition can readily increase the migration window, because the electrophoretic mobility of the microemulsion is increased.

There have also been efforts made to use MEEKC for the indirect measurement of hydrophobicity of a variety of small neutral organic molecules [43], anionic and cationic species in the charged state at pH 7 [44–46], and at the extreme pH values of 1.19 and 12 [47]. The test solutes evaluated in the studies have ranged from hydrophilic (log $P_{o/w}=-0.4$) to moderately hydrophobic (log $P_{o/w}=4.5$).

A linear solvation energy relationship (LSER) analysis was conducted using the data generated for the study in Ref. 43 [48]. It was found that the coefficients in the LSER evaluation of the retention data were very similar to the resulting coefficients obtained via LSER evaluation of the octanol–water system. This suggests that the results obtained with the above SDS/butanol/heptane microemulsion system may be a close model of octanol–water partitioning.

The type of compounds used in the above study (Ref. 43) were small organic molecules with simple functional character. Compounds such as pesticides tend to be larger in shape and size and contain more complex functionality than many of the compounds used in the evaluation described in Ref. 43. For example, in addition to the phosphorous group, the organophosphorous classification of insecticide compounds may contain a combination of one or more rings, chlorine, bromine, sulfur, nitrogen, carbonyl, ether, ester, or alkyl groups.

The purpose of the study reported here was to evaluate the use of MEEKC as a method for the indirect measurement of log $P_{o/w}$ of a variety of pesticide compound types, covering a variety of chemistries and functional groups and a wide range of hydrophobicity. Over 80 pesticides from very hydrophilic to very hydrophobic were evaluated using the MEEKC technique for their retention behavior and correlation to their log $P_{o/w}$ values. The results of the pesticide log $P_{o/w}$ calibration will be compared to the calibration of some small organic compounds to determine whether MEEKC is a reliable, universal model of octanol–water partitioning useful for log $P_{o/w}$ measurements for compounds other than small organics.

2. Experimental

2.1. Instrumental

A Waters Quanta 4000 (Waters Corporation, Milford, MA, USA) capillary electrophoresis instrument equipped with fixed-wavelength UV detection at 254 nm was employed for all separations. Electrokinetic separations on the Waters Quanta 4000 were performed using a 37.5 cm length fused-silica capillary with a 50 μm internal diameter (375 μm outer

diameter) (Polymicro Technologies, Tucson, AZ, USA). Injections were made electrokinetically for 10 s at 5 kV unless otherwise indicated. The applied voltage for the studies was 7.5 kV. The operating current for the microemulsion solution run under the analysis conditions was typically 35–36 μA (approximately 0.7 W/m). The data were collected at a rate of 10 Hz and processed on a PC using ChemStation software (Hewlett-Packard, Wilmington, DE, USA). All experiments were performed at ambient temperature (≈25°C).

2.2. Materials

The organic test solutes, heptane, and 1-butanol were purchased from Aldrich (Milwaukee, WI, USA). The pesticide compounds were purchased from Chem Service (West Chester, PA, USA). Sodium phosphate, sodium tetraborate and sodium dodecyl sulfate (SDS) were obtained from J.T. Baker (Phillipsburg, NJ, USA). The water used for the preparation of the buffer solutions was obtained from a Milli-Q purification system (Millipore Corp., Milford, MA, USA).

Stock buffer solutions were prepared with sodium dihydrogen phosphate at a concentration of 0.05 *M* in Milli-Q water and adjusted to pH 7.0 with 0.1 *M* sodium tetraborate. The oil-in-water type of microemulsion chosen for this study contained heptane as the oil component, SDS as the surfactant, and 1-butanol as the cosurfactant. This is the same type of microemulsion used in the analysis of the simple organic molecules for log $P_{o/w}$ that proved to be a similar model of octanol–water partitioning, discussed in Ref. 43. The microemulsion solutions were prepared by weighing appropriate amounts of heptane, butanol, SDS, and buffer solution and mixing by ultrasonication for 30 min. The microemulsion solutions were allowed to equilibrate at ambient temperature for 1 h prior to use in electrokinetic separations. The solutions are transparent and may be stable for several months at room temperature storage [49,50]. The microemulsion solutions were filtered through 0.45 μm GHP Acrodisc filters (Pall Gelman, Ann Arbor, MI, USA) prior to use.

The test solutes were dissolved in the microemulsion solution for injection onto the capillary. Samples dissolved in solvent, buffer solution, or microemulsion modified with higher levels of solvent may provide shifts in retention that lead to inaccurate measurements of k'. The solubilization of very hydrophobic molecules into the microemulsion system can be facilitated by dissolving the neat compound with a very small (ca. 1–2 μl) amount of organic solvent prior to dilution with the microemulsion solution. The solute concentrations ranged from 0.2–0.5 mg/ml.

2.3. Methods

The capillary was treated by purging with 1.0 *M* NaOH for 15 min, followed by a purge of 0.1 *M* NaOH for 15 min. The capillary was then rinsed with water for 15 min, followed by the microemulsion solution for 10 min. Purges with 0.1 *M* NaOH and water were performed periodically to remove contaminants from the capillary wall.

2.4. Calculations

The retention factor, k', is defined by the ratio of n_{me}/n_{aq}, where n_{me} is the total number of moles of solute in the microemulsion phase and n_{aq} is the total number of moles of solute in the aqueous phase. The retention factor in MEEKC can be calculated using the equation [51]:

$$k' = \frac{t_r - t_0}{t_0(1 - t_r/t_{me})} \quad (1)$$

where t_r, t_o, and t_{me} are the migration time of the solute, the void time due to electroosmotic flow, and the migration time of the microemulsion, respectively. The electroosmotic flow time was measured using the response of 1-butanol, contained in the microemulsion solution. The migration time of the microemulsion through the capillary, t_{me}, was measured for each separation using the migration time of dodecylbenzene as a tracer. The relationship between retention factor and octanol–water partitioning may be expressed using the functional form [10,11]:

$$\log P_{o/w} = a \log k' + b \quad (2)$$

where a and b are constants that represent the slope and intercept of a linear calibration line.

3. Results and discussion

Fig. 1 shows the effect of increasing the concentration of the SDS component of the microemulsion system to increase the migration window of separation for a set of alkylphenone compounds. The chromatograms demonstrate that increasing the SDS concentration increases the migration times of the solutes, enhancing the resolution by increasing the electrophoretic mobility of the microemulsion toward the anode or inlet end of the capillary. A microemulsion composed of 2.16% SDS (w/w), 0.82% heptane (w/w), 6.49% 1-butanol (w/w) in 0.05 *M* sodium phosphate–0.1 *M* borate at pH 7.0 was chosen as the model system for study in these investigations. It was selected because this composition provided a reasonably wide migration window to facilitate the separation of very hydrophobic and very hydrophilic compounds without excessively long analysis times. The buffer system used in the experiments was the same as in Ref. 43 for the purpose of comparing results.

Table 1 lists the pesticide and organic standard compounds investigated along with their corresponding log $P_{o/w}$ values. Fig. 2a and b show the separation of some representative pesticide and organic standard compounds. The resulting peaks remain narrow throughout the chromatograms.

The partitioning relationship between retention and octanol–water partitioning was evaluated by plotting log $P_{o/w}$ versus log k' for all of the pesticide and organic standard compounds. Linear regression analysis of the pesticides yielded the following equation:

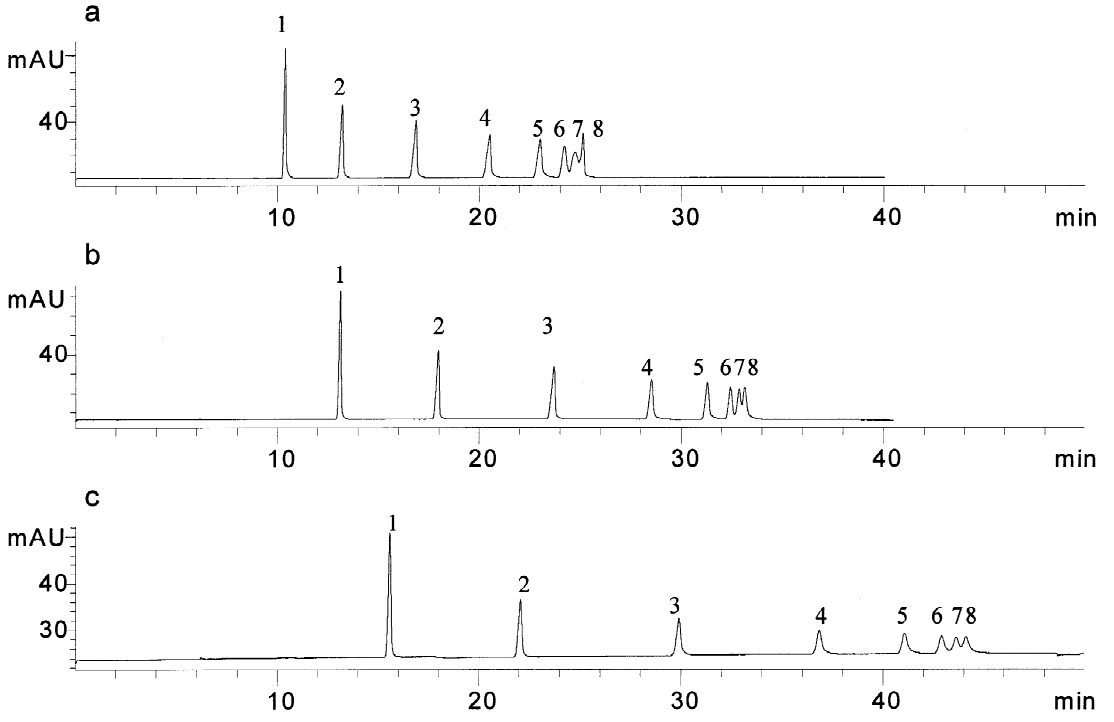

Fig. 1. Effect of the SDS surfactant concentration on the migration window and resolution in MEEKC. Separation of (1) acetophenone, (2) propiophenone, (3) butyrophenone, (4) valerophenone, (5) hexanophenone, (6) heptanophenone, (7) octanophenone, and (8) decanophenone using a microemulsion composed of (a) 1.44%, (b) 2.16%, or (c) 2.88% SDS (w/w), 0.82% heptane (w/w), 6.49% 1-butanol (w/w) in 0.05 *M* sodium phosphate–0.1 *M* borate at pH 7. The resulting migration windows (equal to t_{me}/t_o) were (a) 4.0, (b) 5.4, (c) 7.1. Capillary dimensions: 37.5 cm×50 μm I.D. The injection was electrokinetic at 5 kV for 5 s, and the operating voltage was 7.5 kV with detection at 254 nm.

Table 1
Test solutes and their literature log $P_{o/w}$ values

Pesticide compounds Compound	log $P_{o/w}$ [52,53]	Compound	log $P_{o/w}$ [52,53]
Aldicarb	1.13	Kelthane	4.28
Aldrin	5.52	Leptophos	5.88
Aminocarb	1.73	Linuron	3.20
Atrazine	2.66	Malathion	1.02
Banol	2.30	Metalaxyl	1.65
Benfluralin	5.29	Methiocarb	3.34
Bensulide	4.20	Metribuzin	1.70
Bifenthrin	6.00	Napropamide	3.30
Bromophos ethyl	5.68	Omite	3.72
Bromophos methyl	4.88	Oxadiazon	4.09
Buprofezin	4.30	Oxyfluorfen	4.47
Captafol	3.83	Paclobutrazol	3.20
Captan	2.78	Paraoxon	1.98
Carbaryl	2.34	Parathion	3.83
Carbofuran	1.52	p-dichlorobenzene	3.44
Carbophenothion	4.82	Pendimethalin	5.18
Chlordane	6.00	Pentachloroanisole	5.70
Chlorpyrifos	5.27	Pentachloronitrobenzene	5.40
Chlortoluron	2.50	Pentachlorophenol	5.13
Coumaphos	4.13	Permethrin	6.60
Cycloheximide	0.55	Phenothiazine	4.15
Cypermethrin	4.47	Phosalone	4.30
p,p′-DDD	6.22	Pirimicarb	1.70
p,p′-DDE	6.09	Pirimiphos-ethyl	4.85
p,p′-DDT	6.38	Pirimiphos-methyl	4.20
Dicapthon	3.44	Profenfos	4.44
Dichlofenthion	5.14	Profluralin	5.58
Dimethoate	0.704	Propanil	3.07
Dipropetryn	3.81	Propoxur	1.56
Dithiopyr	4.39	Propyzamide	3.09
Diuron	2.80	Pyrazon	1.14
Endrin	5.16	Simazine	2.11
EPN	5.02	Simetryn	2.66
Fenchlorphos	5.07	Sonar	3.16
Fenobucarb	2.79	Systhane	2.94
Fensulfothion	2.33	Tebufenozide	4.25
Fenuron	0.96	Tetrachlorvinphos	3.53
Fluorodifen	4.40	Tetramethrin	4.70
Heptachlor	5.40	Thiazopyr	3.89
Heptachlor epoxide	5.45	Tolylfluanid	3.90
Hexachlorobenzene	5.47	Toxaphene	5.50
Imazapyr	0.11	Trichloronate	5.23
Imazaquin	0.34	Tricyclazole	1.40
Iprodione	3.00	Trietazine	3.35
Isofenphos	4.04	Trifluralin	5.34
Isoprocarb	2.30		

Table 1. Continued

Organic standard compounds Compound	log $P_{o/w}$ [1,7]	Compound	log $P_{o/w}$ [1,7]
2-aminopyrimidine	−0.22	naphthalene	3.37
anisole	2.11	2-naphthol	2.84
benzaldehyde	1.48	nitrobenzene	1.86
benzopenone	3.18	2-nitrotoluene	2.30
bibenzyl	4.60	1,2-phenylenediamine	0.15
1-bromonaphthalene	5.29	propyl benzene	3.69
6-bromo-2-naphthol	4.80	4-propylphenol	3.00
butyl benzene	4.38	pyrimidine	−0.40
1,3-chloronitrobenzene	2.46	quinoxaline	1.30
m-cresol	1.96	resorcinol	0.80
4-cyanophenol	1.63	sulfanilamide	−1.05
4,6-dimethylpyrimidine	0.62	1,2,4,5-tetrabromobenzene	5.10
hexyl benzene	5.52	1,2,3,4-tetrachlorobenzene	4.50
hydroquinone	0.55	theophylline	−0.02
methyl-2-fuorate	1.00	1,2,4-trichlorobenzene	3.98
1-methylindole	2.64	uracil	−1.07
2-methylpyrazine	0.21	o-xylene	3.12
4-methylpyrimidine	0.16		

$$\log P_{o/w} = (1.995 \pm 0.047) \log k' + 0.977 \pm 0.075$$
$$r^2 = 0.952,\ n = 91,\ SE = 0.350 \quad (3)$$

where r^2 is the correlation coefficient, n is the number of data, and SE is the standard error.

The log $P_{o/w}$ values for the pesticides group ranged from 0.11 to 6.6. Five outliers were identified by inspection of a graph of the residuals (not shown). Three of the compounds, Imazapyr, Imazaquin, and cycloheximide are located at the lower end of the hydrophobicity range of compounds chosen for study and exhibit stronger retention than their log $P_{o/w}$ values would indicate. Imazapyr and Imazaquin are imidazolinone compounds and contain imide functional groups as well as an acid group on each molecule. Both functional groups may contribute to the molecules being more highly retained by interacting with the microemulsion structure. The two compounds may also be partially ionized at the pH used in the investigations. Cycloheximide also contains an imide functional group that may be causing this molecule to be more retained by the microemulsion.

Cypermethrin and Carbophenothion were also outliers in the data set. Both compounds exhibit a greater amount of retention with the microemulsion system than is predicted by their log $P_{o/w}$ values. The structures of both compounds contain both hydrogen bonding and non-hydrogen bonding groups and are also relatively large in size. These factors may be contributing to the stronger interactions with the microemulsion structure, perhaps through interaction with 1-butanol. Removal of the outliers provided the following linear correlation relationship for the pesticides group:

$$\log P_{o/w} = (1.956 \pm 0.042) \log k' + 1.080 \pm 0.067$$
$$r^2 = 0.962,\ n = 86,\ SE = 0.293 \quad (4)$$

The correlation coefficient and the standard error were slightly improved with the removal of the outliers from the data set.

Linear regression analysis of the organic standard compounds yielded the following equation:

$$\log P_{o/w} = (1.916 \pm 0.064) \log k' + 1.181 \pm 0.070$$
$$r^2 = 0.964,\ n = 35,\ SE = 0.364 \quad (5)$$

The log $P_{o/w}$ values in the simple organic molecule set ranged from −1.07 to 5.52. Upon investigating the regression data, two outliers were identified in this compound set by inspection of a graph of the residuals (not shown). Uracil and sulfanilamide contain amine groups and may possibly have interaction with the charged portion of the SDS component of the microemulsion. If both of these outliers are removed from the data set, the following linear

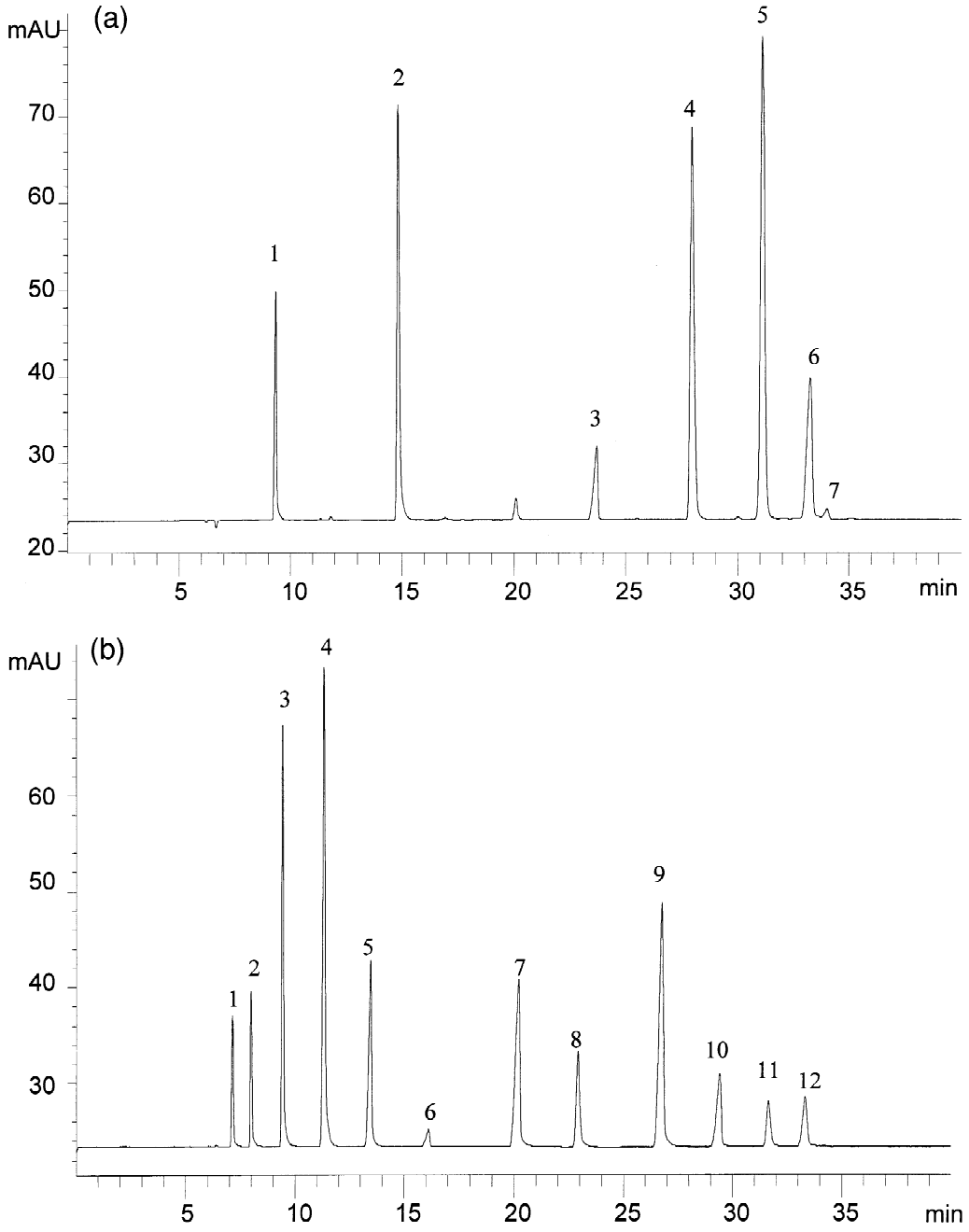

Fig. 2. (a) Separation of seven representative pesticide compounds by MEEKC: (1) Fenuron, (2) Pirimicarb, (3) Fensulfothion, (4) Propanil, (5) Phenothiazine, (6) Pendimethalin, and (7) p,p′-DDT. The microemulsion was composed of 2.16% SDS (w/w), 0.82% heptane (w/w), 6.49% 1-butanol (w/w) in 0.05 *M* sodium phosphate–0.1 *M* borate at pH 7. Capillary dimensions: 37.5 cm×50 μm I.D. The injection was electrokinetic at 5 kV for 8 s, and the operating voltage was 7.5 kV with detection at 254 nm. (b) Separation of 12 representative standard organic compounds by MEEKC: (1) pyrimidine, (2) 4,6-dimethylpyrimidine, (3) methyl-2-fuorate, (4) 4-cyanophenol, (5) nitrobenzene, (6) anisole, (7) 1,3-chloronitrobenzene, (8) 2-naphthol, (9) benzophenone, (10) naphthalene, (11) 6-bromo-2-naphthol, and (12) 1-bromo-naphthalene. Conditions are as in Fig. 2a.

relationship is established for the organic standard compounds:

$$\log P_{o/w} = (1.850 \pm 0.061) \log k' + 1.261 \pm 0.067$$
$$r^2 = 0.968, n = 33, SE = 0.324 \quad (6)$$

Fig. 3 includes the log $P_{o/w}$ versus log k' data for the pesticides and organic standard compounds. From the linear regression analyses that yielded Eqs. 4 and 6, the pesticide and simple organic sets of compounds appear to be similar in linearity and standard error. The two calibration lines also appear to be similar in slope and intercept. If the calibration data of both groups are similar, it may be acceptable to use a general set of standard compounds to calibrate for the indirect measurement of log $P_{o/w}$ for a wide variety of organic molecules.

The calibration curves were compared statistically to determine whether a single, general set of data may be used for a universal calibration to determine the hydrophobicity of any test solute with acceptable accuracy. SAS JMP (SAS Institute Inc., Cary, NC, USA) statistical software is capable of evaluating more than one set of data by a contrast test to determine differences and similarities between sets of data. The program was used to compare the two compound group calibration curves and determine whether they are statistically similar or different from one another. If the observed probability (*P* value) of the *F*-test in the comparison test for differences among calibration lines is less than 0.05, then there is a 95% probability that there is at least one pair of calibration lines that are statistically different. In testing for differences between the calibration lines in slope and intercept, if the observed probability (*P* value) of the *t*-test is less than 0.05, then there is evidence that there is a statistically significant difference at 95% confidence. The calibration lines of the pesticide and simple organic standard compound calibration lines were contrasted, tested for differences, and were found to be statistically similar. Therefore, in the case of the compounds evaluated in this work, it may be feasible to use a universal set of compounds to form a valid calibration for the determination of hydrophobicity of a variety of compound types. If the pesticide and standard organic compound data are pooled to provide a single calibration, the following equation results:

$$\log P_{o/w} = (1.899 \pm 0.031) \log k' + 1.180 \pm 0.047$$
$$r^2 = 0.968, n = 119, SE = 0.304 \quad (7)$$

The practical range of analysis was approximately

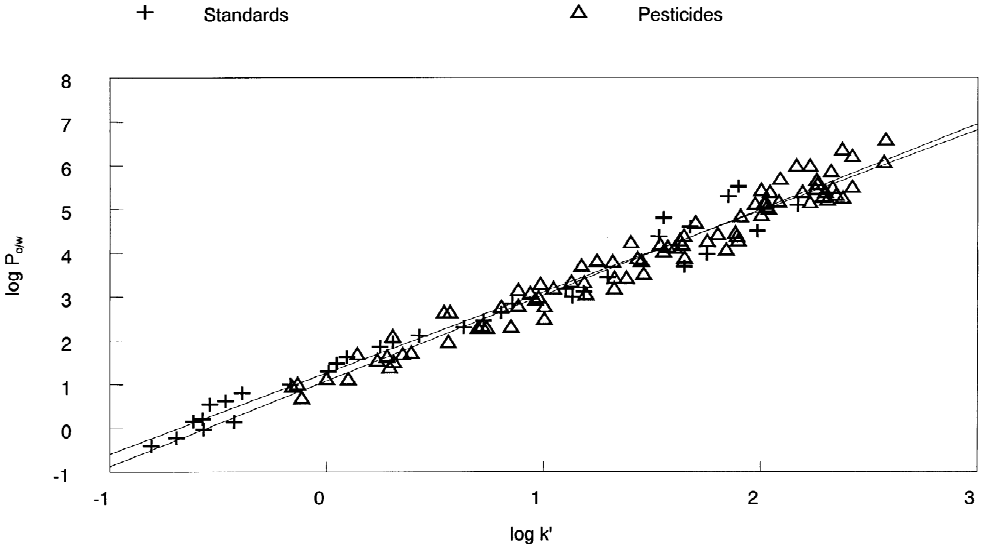

Fig. 3. Plot of log $P_{o/w}$ versus log k' of the pesticide and organic standard compound linear regression data. The injection was electrokinetic at 5 kV for 10 s. Other conditions are as in Fig. 2a.

$-1 < \log P_{o/w} < 7$ for the microemulsion system and run conditions chosen for this study. The migration window and analysis time may be further optimized by adjusting the conditions of the analysis to accommodate a broader or narrower range of compounds for separation. The elution window may be extended or decreased by adjusting the composition of the microemulsion. The most effective adjustment of the microemulsion to optimize the migration window is the optimization of the surfactant component concentration.

4. Conclusion

MEEKC using a microemulsion composed of heptane as the oil component, SDS as the surfactant, and 1-butanol as the cosurfactant has been successful for the indirect measurement of hydrophobicity of pesticide compounds based on the octanol–water partition coefficient. Good correlation of log k' to log $P_{o/w}$ resulted for over 80 pesticide compounds with various functional groups, shapes and sizes. The linear regression of the pesticide calibration data was compared to that of a smaller set of organic standard compounds. The correlation data for both sets of calibrations were statistically similar. It may therefore be acceptable to use a universal set of compounds to form a valid calibration for the indirect measurement of log $P_{o/w}$ of a variety of compound types.

References

[1] A. Leo, C. Hansch, D. Elkins, Chem. Rev. 71 (1971) 525.
[2] C. Hansch, T. Fujita, J. Am. Chem. Soc. 86 (1964) 1616.
[3] R.D. Schoenwald, H.S. Huang, J. Pharm. Sci. 72 (1983) 1266.
[4] T. Braumann, J. Chromatogr. 373 (1986) 191.
[5] M.G. Barron, Environ. Sci. Technol. 24 (1990) 1612.
[6] D.S. Brown, E.W. Flagg, J. Environ. Qual. 10 (1981) 382.
[7] C. Hansch, A. Leo (Eds.), Exploring QSAR, Vol. 1, American Chemical Society, Washington, DC, 1995.
[8] R. Kaliszan, Quantitative Structure–Chromatographic Retention Relationships, John Wiley and Sons, New York, 1987.
[9] C. Hansch (Ed.), Drug Design, Vol. 1, Academic Press, New York, 1971.
[10] R. Collander, Acta Chem. Scand. 4 (1950) 1085.
[11] R. Collander, Acta Chem. Scand. 5 (1951) 774.
[12] R. Kaliszan, J. Chromatogr. A 656 (1993) 417.
[13] J.G. Dorsey, M.G. Khaledi, J. Chromatogr. A 656 (1993) 485.
[14] W.J. Lambert, J. Chromatogr. A 656 (1993) 469.
[15] J.L. Collet, L. Koo, J. Pharm. Sci. 64 (1975) 1253.
[16] C. Treiner, Can. J. Chem. 59 (1981) 2518.
[17] C. Treiner, J. Colloid Interface Sci. 93 (1983) 33.
[18] C. Treiner, A.K. Chattopadhyay, J. Colloid Interface Sci. 109 (1986) 101.
[19] F. Gago, J. Alvarez-Builla, J. Elguero, J.C. Díez-Masa, Anal. Chem. 59 (1987) 921.
[20] M.G. Khaledi, E.D. Breyer, Anal. Chem. 61 (1989) 1040.
[21] E.D. Breyer, J.K. Strasters, M.G. Khaledi, Anal. Chem. 63 (1991) 828.
[22] S. Takeda, S. Wakida, M. Yamane, A. Kawahara, K. Higashi, Anal. Chem. 65 (1993) 2489.
[23] N. Chen, Y.K. Zhang, S. Terabe, T. Nakagawa, J. Chromatogr. A 678 (1994) 327.
[24] Y. Ishihama, Y. Oda, K. Uchikawa, N. Asakawa, Chem. Pharm. Bull. 42 (1994) 1525.
[25] B.J. Herbert, J.G. Dorsey, Anal. Chem. 67 (1995) 744.
[26] M.A. García, J.C. Díez-Masa, M.L. Marina, J. Chromatogr. A 742 (1996) 251.
[27] J.T. Smith, D.V. Vinjamoori, J. Chromatogr. B 669 (1995) 59.
[28] G. Dinelli, R. Mallegni, A. Vicari, Electrophoresis 18 (1997) 214.
[29] Y.S. Wu, H.K. Lee, S.F.Y. Li, Electrophoresis 19 (1998) 1719.
[30] H. Watarai, Chem. Lett. (1991) 391.
[31] H. Watari, Anal. Sci. (Suppl.) 7 (1991) 245.
[32] R. Szücs, J. Vindevogel, E. Everaert, L.D. Cooman, P. Sandra, D.D. Keukeleire, J. Inst. Brew. 100 (1994) 293.
[33] R. Szücs, E.V. Hove, P. Sandra, J. High Resolut. Chromatogr. 19 (1996) 189.
[34] R.L. Boso, M.S. Bellini, I. Míkšík, Z. Deyl, J. Chromatogr. A 709 (1995) 11.
[35] S.T. Cartas, M.C.G. Alvarez-Coque, R.M.V. Camañas, Anal. Chim. Acta 302 (1995) 163.
[36] L. Vomastová, I. Míkšík, Z. Deyl, J. Chromatogr. B 681 (1996) 107.
[37] X. Fu, J. Lu, A. Zhu, J. Chromatogr. A 735 (1996) 353.
[38] L. Debusschère, C. Demesmay, J.L. Rocca, G. Lachatre, H. Lofti, J. Chromatogr. A 779 (1997) 227.
[39] M.F. Miola, M.J. Snowden, K.D. Altria, J. Pharm. Biomed. Anal. 18 (1998) 785.
[40] K.D. Altria, J. Chromatogr. A 844 (1999) 371.
[41] L. Song, Q. Ou, W. Yu, G. Li, J. Chromatogr. A 699 (1995) 371.
[42] S. Terabe, N. Matsubara, Y. Ishihama, Y. Okada, J. Chromatogr. 608 (1992) 23.
[43] Y. Ishihama, Y. Oda, K. Uchikawa, N. Asakawa, Anal. Chem. 67 (1995) 1588.
[44] Y. Ishihama, Y. Oda, N. Asakawa, Anal. Chem. 68 (1996) 1028.
[45] Y. Ishihama, Y. Oda, N. Asakawa, Anal. Chem. 68 (1996) 4281.

[46] Y. Mrestani, R.H.H. Neubert, A. Krause, Pharm. Res. 15 (1998) 799.
[47] S.J. Gluck, M.H. Benkö, R.K. Hallberg, K.P. Steele, J. Chromatogr. A 744 (1996) 141.
[48] M.H. Abraham, C. Treiner, M. Roses, C. Rafols, Y. Ishihama, J. Chromatogr. A 752 (1996) 243.
[49] R.J. Hunter, Foundations of Colloid Science, Oxford University Press, New York, 1986.
[50] D. Myers, Surfaces, Interfaces and Colloids: Principles and Applications, Wiley-VCH, New York, 1999.
[51] S. Terabe, K. Otsuka, T. Ando, Anal. Chem. 57 (1985) 834.
[52] C. Tomlin (Ed.), The Pesticide Manual, British Crop Protection Council and The Royal Society of Chemistry, Cambridge, UK, 1994.
[53] A. Noble, J. Chromatogr. 642 (1993) 3.