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Measurements and predictions of hexadecane/air partition coefficients for 387 environmentally relevant compounds

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ABSTRACT

The logarithm of the hexadecane/air partition coefficient L is a common descriptor for non-specific interaction properties of solutes and is used in poly-parameter linear free energy relationships (pp-LFERs) to predict other partition coefficients. However, the L value data set available for complex and multifunctional substances is rather small. This limits the applicability of the pp-LFER equation. Hence, we experimentally determined L values for 387 complex compounds using GC-retention time measurements on a non-polar column (SPB^{TM} Octyl). The target substances include environmentally relevant compounds such as pesticides, flame retardants and hormones. We determined L values that span a large range of 4.28–15.92. In addition to these experimental measurements several prediction tools (connectivity indices, SPARC, ABSOLV, COSMOthermX) for the L value were evaluated. The root mean squared errors (rmse) were 1.55 (connectivity indices), 1.28 (SPARC), 0.99 (ABSOLV) and 0.94 (COSMOthermX). The number of outliers (prediction error > 3) was 18 (connectivity indices), 12 (SPARC), 2 (ABSOLV) and 0 (COSMOthermX). Based on these results the best prediction accuracy in this evaluation is reached by ABSOLV and COSMOthermX, whose results are comparable.

1. Introduction

The hexadecane/air partition coefficient $K_{hexadecane/air}$ [$L_{air}/L_{hexadecane}$] is a useful descriptor to characterize the non-specific intermolecular interactions of organic chemicals in other partition processes. Hence, this coefficient, in its logarithmic form $\log K_{hexadecane/air} = L$, is used as a basic substance descriptor in poly-parameter linear free energy relationships (pp-LFERs) that describe partition coefficients between two phases. For example, the pp-LFER from Goss [1] appears:

$$\log K = l \cdot L + s \cdot S + a \cdot A + b \cdot B + v \cdot V + c \quad (1)$$

K is a partition coefficient between two arbitrary phases. S is the dipolarity/polarizability descriptor. A indicates the H-bond donor properties of the substance and B the H-bond acceptor properties. V is the molar volume. The small letters represent the complementary system properties. This relationship is based on the linear solvation energy relationship (LSER) equations developed by Abraham [2–4]. The capital letters on the right hand side of Eq. (1) represent the intermolecular interaction properties of the substances of interest. The L and V terms represent the non-specific interactions: van der Waals interactions and interactions related to cavity formation. The remaining compound descriptors S, A and B describe the specific interactions. It has been repeatedly shown that pp-LFER models of this type can accurately describe biphasic partitioning processes of neutral organic chemicals.

To describe nonspecific interactions, only the V and L terms are necessary. Because V is calculated from the molecular structure using an increment method (McGowan approach [5]), only L needs to be experimentally determined. L values have been determined for a number of compounds [6,7]. However, only a limited number of L values is available so far for complex, polar and multifunctional compounds. The availability of L values for environmentally relevant substances is also severely limited, which hampers applications of pp-LFER models for estimating environmental partitioning behavior of pollutants. The first objective of this study is, thus, to measure the L values for a large data set (all in all 387 compounds) using a GC method. The target substances include pesticides, organosilicon compounds, flame retardants, hormones, pharmaceuticals and phthalates. These compounds are highly diverse in molecular structure and are of current environmental interest. No L values have been reported so far for 2/3 of the compounds in this data set.

The second key aspect of this work is the evaluation of different prediction methods for the L value. Prediction methods are necessary for compounds for which no experimental values are available.

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Significance of prediction should be stressed due to the high and constantly growing number of chemical substances. A large fraction of these substances cannot be measured experimentally or the effort for this measurement is unreasonably large. Therefore, it is desirable to have accurate prediction methods that can compensate for missing experimental values. Since the L value is the log of a partition coefficient, prediction tools that calculate partition coefficients can also be used for prediction of L. In this study, connectivity indices, SPARC, ABSOLV, and COSMOthermX are evaluated by comparing the predictions obtained from these tools to the experimental values measured in this study. The evaluation is rigorous and should delineate the applicability domains of these tools, as it is based on a large data set of multifunctional compounds.

2. Materials and methods

2.1. Chemicals

Chemicals were purchased from ABCR GmbH & Co. KG (Karlsruhe, Germany), Sigma–Aldrich Chemie GmbH (Steinheim, Germany), TCI Europe N.V. (Zwijndrecht, Belgium), Accu Standard Inc. (New Haven, USA), Dr. Ehrenstorfer GmbH (Augsburg, Germany) and Alfa Aesar GmbH & Co. KG (Karlsruhe, Germany). Solvents (dichloromethane, methanol and iso-hexane; SupraSolv quality) were purchased from Merck KGaA (Darmstadt, Germany).

2.2. Experimental determination of the L value

In an isothermal gas chromatographic system the net retention time of organic substances is proportional to the stationary phase-gas partition coefficient; thus, the retention can be described using a pp-LFER equation:

$$\log t_{net} = l \cdot L + s \cdot S + a \cdot A + b \cdot B + v \cdot V + c \quad (2)$$

where t_{net} is the net retention time. If the system descriptors a, b and s are zero or at least insignificant, Eq. (2) can be reduced to:

$$\log t_{net} = l \cdot L + v \cdot V + c \quad (3)$$

The remaining coefficients l, v und c can be determined through a calibration and V is known through the McGowan approach. Eq. (3) can be solved for L and used to determine L based on measured values of t_{net}. Because a, b and s represent the polar interactions, a stationary phase suited for the determination of L needs to be non-polar. Thus, the phase should not undergo any of the polar interactions mentioned above. Previous studies have shown that the SPB™ Octyl column (Supelco, Taufkirchen, Germany) fulfils the necessary conditions [8,9]. The stationary phase of this column consists of poly(50% n-octyl, 50% methyl)siloxane. This phase is even less polar than the most frequently used nonpolar phase, pure poly(dimethylsiloxane), because of the n-octyl fraction. In addition, the SPB™ Octyl column has a high thermal stability, allowing measurements at high temperatures that are needed for compounds with low volatility.

The calibration of Eq. (3) was done by measuring the retention times of different classes of compounds (including polar and non-polar, and aliphatic and aromatic compounds; see Table S1 for a list of the calibration compounds used). L values of the calibration set span over a wide range (4.62–15.79). Regressing the known substance descriptors against measured $\log t_{net}$ through Eq. (3) provided the calibration equation, which was used to determine the L values of the target compounds.

The target compounds consist of 284 pesticides, 53 flame retardants (mostly brominated), 15 organosilicon compounds, 15 hormones and pharmaceuticals, and others (see Table 1). To possibly improve the values of 13 calibration compounds they were also included in the target compound set. In total, 387 compounds were investigated (detected isomers are considered as individual compounds).

The retention time measurements were performed using a gas chromatograph (7890A GC System) coupled to a mass spectrometer (5975C inert MSD, both from Agilent Technologies Deutschland GmbH, Böblingen, Germany). The GC–MS was equipped with an autosampler (MPS 2XL, Gerstel GmbH & Co. KG, Mühlheim an der Ruhr, Germany). The software MSD ChemStation (version E.02.00.493; Agilent Technologies) in combination with Gerstel Maestro 1 (version 1.3.7.69/3.5; Gerstel GmbH) was used for instrument control and data recording. The measurements were performed at an oven temperature of 180 °C and 250 °C in order to detect compounds of varying volatility. Fourteen flame retardants were measurable at both temperatures. The L values were calculated separately in these cases and the average out of both L values are given in Table 1. The differences between the two L values were small (average difference: 0.06). The remaining target substances were analysed either at 180 °C or at 250 °C. At both temperatures, nitrogen gas was measured to obtain the column dead time. Solutions of the target compounds (≈50 mg/l) were prepared in dichloromethane. Methanol or iso-hexane was used for compounds that did not dissolve well in dichloromethane. Up to 5 compounds were mixed in one solution. A split injection (1:5) was performed unless the desired peak could not be detected. In this case a splitless injection was carried out. The injection mode (i.e., split or splitless) did not have a significant influence on the retention time except for very early eluting compounds, for which only the split injection was performed. The mass spectra were recorded using a broad scan range (m/z 50–1050) to detect compounds in a broad size range in one run. The SIM mode was used for the brominated diphenyl ether (BDE) 183 (m/z 564 and 722) to achieve high sensitivity that was necessary for this large and late eluting compound. Further method details are described in Table 2. Typically, there appeared only one distinct peak for each compound, but in some cases more than one peak was found in the chromatogram. Peak identification was done in comparison to reference mass spectra stored in the NIST-Database (NIST 08) using the NIST MS Search 2.0 software (both from the National Institute of Standards and Technology, USA). If no NIST spectra were available, peaks were identified by manually checking the mass spectra of the most intensive peaks. The identification was accepted if the majority of high abundant mass peaks could be explained by probable fragmentation reactions. Substances having no clear identification were removed from consideration.

A subset of 22 (180 °C) or 19 (250 °C) substances was chosen to examine the reproducibility of the retention times. These compounds were injected three times and the standard deviation (SD) of the $\log t_{net}$ was calculated. The largest standard deviation was found to be 0.0024 for 180 °C and 0.0026 for 250 °C. This magnitude of variability is far smaller than general fitting errors generated by Eq. (3) (see Table 3). Hence, single injections were used in the entire work.

2.3. Evaluated prediction models

The experimentally determined L values were compared to different predicted L values. The following prediction tools were used:

(a) Connectivity indices (CI) calculated with "E-Dragon" (version 1.0, http://146.107.217.178/lab/edragon/) [10]. These indices are numerical values that directly represent the molecular structure. The simplest first order CI is the reciprocal square-root product of the number of neighbouring carbon atoms of each substructure fragment. The CI will be given by the sum over all substructure fragment values. The higher order CI's take

Table 1
Experimentally determined and predicted *L* values.

CAS	Compound	Exp.	CI(1)[a]	CI(2)[b]	SPARC	COSMO	ABSOLV
26530-20-1	2-Octyl-4-isothiazoline-3-one	7.89	7.30	7.31	7.85	8.12	8.18
2581-34-2	3-Methyl-4-nitrophenol	6.06	5.80	5.63	6.16	5.71	5.73
158076-64-3	4′-Hydroxy-2,2′,3,3′,4,5,5′-heptachlorobiphenyl	11.60	12.61	12.37		10.95	11.45
59512-50-4	4-Hydroxy-2,2′,4′,5,5′-pentachlorobiphenyl	9.94	11.00	10.75		9.56	10.10
158076-63-2	4-Hydroxy-2′,3,3′,5,5′,6′-hexachlorobiphenyl	10.76	11.80	11.56		10.53	10.88
	4-Hydroxy-2′,3,4′,5,6′-pentachlorobiphenyl	9.95	10.84	10.90		9.96	10.15
189578-00-5	4-Hydroxy-2′,3,4′,6′-tetrachlorobiphenyl	9.17	10.08	10.10		8.76	9.57
30560-19-1	Acephate	5.65	5.34	5.63	3.69	5.22	6.49
74070-46-5	Aclonifen	9.43	10.30	9.82	10.04	8.80	9.84
15972-60-8	Alachlor	8.36	9.84	9.52	9.25	7.76	9.36
309-00-2	Aldrin	8.77	9.59	10.80	8.17	9.07	9.48
834-12-8	Ametryn	8.25	8.03	7.93	8.41	8.97	8.72
101-05-3	Anilazine	9.12	9.68	9.42	9.32	8.32	8.96
1912-24-9	Atrazine	7.44	7.50	7.34	7.75	8.59	7.57
35575-96-3	Azamethiphos	9.57	11.01	11.03	8.34	9.70	11.08
2642-71-9	Azinphos-ethyl	11.04	11.44	11.96	12.93	11.84	11.79
86-50-0	Azinphos-methyl	10.51	10.75	10.88	11.96	10.70	10.80
103-33-3	Azobenzene	7.12	7.89	7.53	7.21	6.90	6.31
131860-33-8	Azoxystrobin	12.77	17.44	16.29	14.51	15.40	14.49
71626-11-4	Benalaxyl	10.27	12.83	12.32	11.59	10.23	12.01
82560-54-1	Benfuracarb	11.72	14.75	14.26	12.63	12.11	13.94
82657-04-3	Bifenthrin	11.18	13.59	13.27	11.5	12.25	11.89
485-31-4	Binapacryl	9.69	12.25	11.54	10.08	9.98	10.68
92-52-4	Biphenyl	6.07	6.53	6.41	5.94	5.77	6.30
55179-31-2	Bitertanol 1	11.58	13.43	12.84	12.21	11.71	13.00
55179-31-2	Bitertanol 2	11.61	13.43	12.84	12.21	11.71	13.00
314-40-9	Bromacil	8.01	7.50	7.45	7.88	8.05	8.10
1715-40-8	Bromocyclen 1	8.26	8.81	9.68	8.39	8.42	8.48
1715-40-8	Bromocyclen 2	8.41	8.81	9.68	8.39	8.42	8.48
2104-96-3	Bromophos	8.81	10.02	9.97	8.98	8.74	9.34
4824-78-6	Bromophos-ethyl	9.35	10.73	11.03	10.07	10.22	10.32
18181-80-1	Bromopropylate	10.87	12.64	12.21	11.27	11.39	11.34
1689-84-5	Bromoxynil	7.06	6.84	6.83	7.58	6.54	7.42
116255-48-2	Bromuconazole 1	10.43	11.59	11.62	11.93	11.19	11.00
116255-48-2	Bromuconazole 2	10.58	11.59	11.62	11.93	11.19	11.00
41483-43-6	Bupirimate	9.55	11.36	10.96	10.6	10.82	11.08
69327-76-0	Buprofezin	9.73	10.65	10.78	12.38	10.05	11.29
2939-80-2	Captafol	9.98	10.35	10.30	9.71	9.76	11.76
133-06-2	Captan	8.69	8.90	9.05	8.94	8.47	10.33
63-25-2	Carbaryl	7.90	8.28	7.98	7.95	7.66	8.20
90-15-3	1-Naphthol	6.23	5.87	5.86	6.11	5.56	6.15
1563-66-2	Carbofuran	7.23	8.24	8.09	7.69	8.13	8.21
786-19-6	Carbophenothion	10.21	9.99	10.79	11.7	10.90	11.11
55285-14-8	Carbosulfan	11.20	13.49	13.22	12.46	13.13	13.44
5103-71-9	*cis*-Chlordane	9.39	10.12	11.19	8.81	10.02	9.76
27304-13-8	Oxy-chlordane	9.07	10.62	11.76	9.56	9.89	10.09
470-90-6	Chlorfenvinfos 1	8.98	11.95	11.87	7.66	10.04	10.46
470-90-6	Chlorfenvinfos 2	9.04	11.95	11.87	7.66	10.04	10.46
106-47-8	4-Chloroaniline	4.82	4.44	4.33	4.77	4.88	4.68
510-15-6	Chlorobenzilate	9.82	11.91	11.41	10.05	9.58	9.85
57-15-8	Chlorobutanol	4.07	4.20	3.87	4.32	3.81	3.89
1897-45-6	Chlorothalonil	7.76	8.69	8.66	8.01	6.85	7.91
101-21-3	Chlorpropham	7.00	7.60	7.35	7.04	7.46	7.26
2921-88-2	Chlorpyrifos	8.76	10.62	10.83	9.44	9.56	9.88
5598-13-0	Chlorpyrifos-methyl	8.18	9.91	9.77	8.36	8.69	8.89
1861-32-1	Chlorthal-dimethyl	8.54	10.86	10.64	9.41	8.69	8.51
60238-56-4	Chlorthiophos 1	9.82	11.01	11.43	11.32	10.58	10.88
60238-56-4	Chlorthiophos 2	9.91	11.01	11.43	11.32	10.58	10.88
60238-56-4	Chlorthiophos 3	9.97	11.01	11.43	11.32	10.58	10.88
72391-46-9	Chlozolinate	8.88	11.68	11.47	10.12	9.45	10.27
81777-89-1	Clomazone	7.57	8.50	8.31	8.15	8.35	9.12
56-72-4	Coumaphos	11.34	12.22	12.41	11.69	12.65	11.12
21725-46-2	Cyanazine	8.23	8.71	8.34	8.92	9.10	8.56
2636-26-2	Cyanophos	7.40	8.72	8.51	7.62	7.89	8.25
68359-37-5	β-Cyfluthrin	12.20	15.68	14.96	12.14	13.84	13.56
68359-37-5	β-Cyfluthrin	12.23	15.68	14.96	12.14	13.84	13.56
91465-08-6	λ-Cyhalothrin	11.47	15.13	14.53	12.36	13.74	12.70
91465-08-6	λ-Cyhalothrin	11.54	15.13	14.53	12.36	13.74	12.70
57966-95-7	Cymoxanil	6.46	7.92	7.32	6.66	6.95	7.42
67375-30-8	α-Cypermethrin	12.34	15.75	15.00	13.08	13.62	13.51
52315-07-8	ζ-Cypermethrin	12.28	15.75	15.00	13.08	13.29	13.51
52315-07-8	ζ-Cypermethrin	12.34	15.75	15.00	13.08	13.29	13.51
52315-07-8	ζ-Cypermethrin	12.37	15.75	15.00	13.08	13.29	13.51
94361-06-5	Cyproconazole	9.63	10.75	10.48	10.58	8.67	10.61
53-19-0	2,4′-DDD	9.62	10.66	10.44	10.02	9.83	9.45
72-54-8	4,4′-DDD	9.88	10.67	10.39	10.3	10.02	9.45

Table 1 (*Continued*)

CAS	Compound	Exp.	CI(1)[a]	CI(2)[b]	SPARC	COSMO	ABSOLV
72-56-0	DDD, -ethyl	10.06	10.86	10.70	10.46	10.35	10.12
3424-82-6	2,4′-DDE	9.27	10.87	10.56	10.29	9.45	9.38
72-55-9	4,4′-DDE	9.54	10.88	10.51	10.36	9.45	9.38
789-02-6	2,4′-DDT	10.03	11.19	10.96	10.25	10.01	9.88
50-29-3	4,4′-DDT	10.30	11.19	10.91	10.6	10.25	9.88
298-03-3	Demeton-O	7.04	7.58	7.94	7.14	8.61	8.03
126-75-0	Demeton-S	7.45	7.39	7.98	5.15	8.92	8.68
919-86-8	Demeton-S-methyl	6.80	6.65	6.94	4.33	7.08	7.69
1014-69-3	Desmetryn	7.95	7.58	7.46	7.94	8.43	8.23
1596-84-5	Diaminozid	5.49	5.69	5.33	5.71	5.84	6.06
1194-65-6	Dichlobenil	5.58	5.90	5.88	5.52	5.62	5.37
97-17-6	Dichlofenthion	8.28	9.73	10.03	8.54	9.91	9.20
1085-98-9	Dichlofluanid	8.43	10.11	10.06	7.77	8.99	9.80
120-36-5	Dichlorprop	7.16	8.01	7.65	7.09	7.79	6.98
62-73-7	Dichlorvos	4.95	7.01	6.60	2.53	5.75	5.78
99-30-9	Dicloran	7.17	6.99	6.72	7.35	6.64	6.96
10606-46-9	2,4-Dicofol	10.64	11.70	11.42	10.83	10.23	10.52
115-32-2	4,4-Dicofol	10.77	11.73	11.35	11.22	10.15	10.52
90-98-2	4,4′-Dichlorobenzophenone	8.63	9.30	8.90	8.78	8.34	8.57
60-57-1	Dieldrin	9.41	10.05	11.34	9.06	9.60	9.92
87130-20-9	Diethofencarb	8.56	10.04	9.62	9.02	10.63	9.62
119446-68-3	Difenoconazol 1	12.58	15.37	14.91	14.09	14.22	13.60
119446-68-3	Difenoconazol 2	12.61	15.37	14.91	14.09	14.22	13.60
83164-33-4	Diflufenican	10.34	12.54	12.08	11.35	10.72	11.70
50563-36-5	Dimethachlor	8.13	9.32	8.97	9.16	8.16	8.87
87674-68-8	Dimethenamid	8.20	9.32	9.25	7.63	8.43	9.03
60-51-5	Dimethoate	7.10	6.64	6.81	6.74	7.38	8.00
83657-24-3	Diniconazole	9.96	11.54	11.13	12.25	9.58	10.82
122-39-4	Diphenylamine	6.96	7.16	6.94	6.89	6.31	7.33
298-04-4	Disulfoton	7.96	7.27	8.12	8.26	9.08	8.88
5131-24-8	Ditalimfos	9.12	10.11	10.75	9.79	9.67	10.42
33213-66-0	α-Endosulfan	9.33	11.22	12.00	9.16	9.91	11.33
33213-65-9	β-Endosulfan	9.67	11.22	12.00	9.16	9.92	11.33
1031-07-8	Endosulfan sulfate	10.00	11.67	12.44	9.51	9.99	10.18
72-20-8	Endrin	9.61	10.05	11.34	9.06	9.30	9.92
133855-98-8	Epoxiconazole	10.24	12.37	12.07	11.87	11.16	11.37
66230-04-4	Esfenvalerate	13.06	16.79	15.99	14.32	13.86	14.71
29973-13-5	Ethiofencarb	7.79	8.31	8.04	7.77	8.03	8.52
563-12-2	Ethion	10.14	9.76	11.47	12.03	11.74	12.09
26225-79-6	Ethofumesate	8.27	10.00	10.01	8.88	9.36	8.70
13194-48-4	Ethoprophos	7.12	6.30	7.23	4.87	8.60	8.30
38260-54-7	Etrimfos	7.93	10.09	9.92	8.7	8.99	9.27
22224-92-6	Fenamiphos	9.39	10.13	10.42	6.12	10.04	10.20
31972-44-8	Fenamiphos, -sulfone	10.28	11.08	11.44	7.17	10.97	10.38
31972-43-7	Fenamiphos, -sulfoxide	10.28	10.69	11.00	6.05		11.61
60168-88-9	Fenarimol	11.07	12.68	12.29	11.53	10.77	11.60
120928-09-8	Fenazaquin	11.08	12.16	11.78	11.73	10.75	11.51
114369-43-6	Fenbuconazole	11.61	13.61	12.98	12.68	11.86	12.60
299-84-3	Fenchlorphos	8.36	9.83	9.72	8.46	8.60	8.78
122-14-5	Fenitrothion	8.22	9.59	9.41	8.4	8.59	8.96
2255-17-6	Fenitrothion, -oxon	6.62	9.67	9.31	5.28	7.44	8.76
72490-01-8	Fenoxycarb	10.42	12.37	11.60	10.87	11.36	11.03
39515-41-8	Fenpropathrin	11.00	13.62	13.19	11.9	12.00	12.13
67306-00-7	Fenpropidin	9.06	9.51	9.49	9.28	9.28	9.58
67306-03-0	Fenpropimorph	9.37	10.44	10.42	9.68	10.65	10.22
115-90-2	Fensulfothion	9.53	10.06	10.39	9.68	10.68	11.02
55-38-9	Fenthion	8.55	9.12	9.20	9.01	9.02	9.09
3254-63-5	Fenthion, -oxon	8.02	8.85	8.66	4.65	8.17	8.42
14086-35-2	Fenthion, -oxon-sulfone	8.96	10.15	10.12	6.13	9.93	9.06
6552-13-2	Fenthion, -oxon-sulfoxid	8.98	9.76	9.68	5.95	9.48	10.30
3761-42-0	Fenthion, -sulfone	9.41	10.07	10.23	9.61	10.96	9.27
3761-41-9	Fenthion, -sulfoxide	9.42	9.68	9.79	8.96	9.98	10.50
79622-59-6	Fluazinam	10.09	12.70	12.32	10.98	10.68	11.21
70124-77-5	Flucythrinate 1	12.62	16.99	16.21	14.25	14.74	14.60
70124-77-5	Flucythrinate 2	12.70	16.99	16.21	14.25	14.74	14.60
131341-86-1	Fludioxonil	8.35	8.85	8.75	7.25	8.73	8.77
62924-70-3	Flumetralin	9.59	13.04	12.53	11.06	9.52	11.55
103361-09-7	Flumioxazin	11.88	13.42	13.28	12.24	12.40	13.64
136426-54-5	Fluquinconazole	11.30	13.91	13.62	13.44	11.53	12.86
85509-19-9	Flusilazole	9.50	10.10	10.65	9.91	8.88	9.67
102851-06-9	Fluvalinate 1	13.28	17.61	16.81	15.25	15.67	15.71
102851-06-9	Fluvalinate 2	13.33	17.61	16.81	15.25	15.67	15.71
133-07-3	Folpet	8.75	9.24	9.25	9.68	8.70	9.09
944-22-9	Fonofos	7.82	7.10	7.90	9.00	8.17	8.48
65907-30-4	Furathiocarb	11.15	13.90	13.39	12.56	11.50	13.60
319-84-6	α-HCH	7.51	7.21	7.50	7.28	7.99	7.00
319-85-7	β-HCH	7.69	7.21	7.50	7.28	8.21	7.00

Table 1 (*Continued*)

CAS	Compound	Exp.	CI(1)[a]	CI(2)[b]	SPARC	COSMO	ABSOLV
319-86-8	δ-HCH	7.80	7.21	7.50	7.28	8.17	7.00
76-44-8	Heptachlor	8.45	9.50	10.55	8.02	9.38	8.96
1024-57-3	Trans-heptachloroepoxide	8.96	9.94	11.11	9.18	9.57	9.41
23560-59-0	Heptenophos	6.55	8.51	8.59	2.35	7.70	7.81
118-74-1	Hexachlorobenzene	7.66	7.84	7.86	7.71	6.28	6.55
79983-71-4	Hexaconazole	9.55	11.05	10.86	10.8	9.65	10.59
35554-44-0	Imazalil	9.35	10.99	10.61	9.42	10.12	9.73
18181-70-9	Iodfenphos	9.39	10.28	10.27	9.98	9.60	9.93
1689-83-4	Ioxynil	8.25	7.34	7.46	8.39	7.87	8.61
36734-19-7	Iprodione	10.29	11.57	11.39	11.33	10.30	12.26
465-73-6	Isodrin	9.00	9.59	10.80	8.17	9.19	9.48
25311-71-1	Isofenphos	9.27	11.43	11.71	9.54	11.39	11.21
31120-85-1	Isofenphos-oxon	8.86	11.57	11.55			10.57
143390-89-0	Kresoxim-methyl	9.64	12.94	12.18	9.79	10.49	10.35
2164-08-1	Lenacil	9.56	8.45	8.70	8.67	9.35	9.45
58-89-9	Lindane	7.75	7.21	7.50	7.28	8.01	7.00
1634-78-2	Malaoxon	8.00	10.41	10.30	4.82	9.76	9.55
121-75-5	Malathion	8.48	10.32	10.41	8.06	10.23	9.76
55814-41-0	Mepronil	9.79	10.61	10.24	10.62	10.28	10.55
57837-19-1	Metalaxyl	8.33	10.63	10.17	9.29	8.50	9.70
41394-05-2	Metamitron	8.86	8.22	7.92	7.17	8.26	7.50
67129-08-2	Metazachlor	8.87	10.56	10.20	10.48	8.92	10.54
125116-23-6	Metconazol	10.87	11.51	11.30	11.49	11.20	11.37
30864-28-9	Methacrifos	6.19	8.07	7.68	5.3	7.92	6.78
10265-92-6	Methamidophos	4.58	3.90	3.98	1.85	4.60	4.57
950-37-8	Methidathion	8.82	9.22	9.51	8.36	9.25	9.99
2032-65-7	Methiocarb	8.20	8.07	8.00	8.17	8.02	8.38
2179-25-1	Methiocarb sulfone	8.00	8.98	9.06	9.35	9.29	8.56
2635-10-1	Methiocarb sulfoxide	7.93	8.61	8.61	9.11	9.05	9.79
16752-77-5	Methomyl	6.17	5.71	5.33	5.23	5.93	5.33
13749-94-5	Methomyl oxime	3.81	3.35	3.27	3.56	3.51	3.28
841-06-5	Methoprotryne	9.55	9.85	9.52	9.82	10.74	10.09
72-43-5	Methoxychlor	10.68	11.93	11.54	10.7	10.96	10.32
51218-45-2	Metolachlor	8.75	10.19	9.90	9.75	8.19	9.74
21087-64-9	Metribuzin	7.88	7.23	7.24	6.29	7.45	7.20
7786-34-7	Mevinphos	5.74	8.04	7.63	3.1	7.77	6.58
6923-22-4	Trans-monocrotophos	6.69	7.95	7.58	4.12	6.64	7.79
81-14-1	Musk ketone	8.66	10.44	10.28	10.13	8.08	10.16
81-15-2	Musk xylene	8.22	10.67	10.41	9.79	7.05	9.97
88671-89-0	Myclobutanil	9.42	11.08	10.65	10.89	10.02	10.42
300-76-5	Naled	7.04	8.38	8.15	3.95	6.98	8.30
15299-99-7	Napropamide	9.41	10.52	10.26	9.87	9.12	10.50
54-11-5	Nicotin	5.87	6.10	6.17	6.09	6.07	6.10
100-17-4	4-Nitroanisol	5.69	6.07	5.75	5.58	5.66	5.29
1836-75-5	Nitrofen	9.42	10.54	10.06	9.82	9.30	9.16
63284-71-9	Nuarimol	10.17	11.82	11.53	10.68	9.97	10.90
1113-02-6	Omethoate	6.49	6.72	6.71	4.4	8.20	7.80
34622-58-7	Orbencarb	8.51	8.82	8.73	8.62	8.10	9.23
77732-09-3	Oxadixyl	9.40	10.73	10.42	10.5	9.43	10.55
301-12-2	Oxydemeton-methyl	7.78	7.30	7.54	4.71	9.69	9.10
311-45-5	Paraoxon-ethyl	8.06	10.08	9.88	5.7	9.13	9.28
950-35-6	Paraoxon-methyl	7.40	9.32	8.86	4.79	8.36	8.29
56-38-2	Parathion	8.53	9.95	10.03	8.95	9.84	9.48
298-00-0	Parathion-methyl	7.92	9.24	8.97	7.87	8.36	8.49
2051-60-7	PCB 1	6.58	7.30	7.20	6.72	6.55	6.93
37680-73-2	PCB 101	9.35	10.45	10.24	10	9.34	9.30
35065-28-2	PCB 138	10.22	11.26	11.05	11.09	9.98	10.10
2050-68-2	PCB 15	7.85	8.13	7.86	7.83	7.47	7.56
35065-27-1	PCB 153	10.08	11.23	11.03	11	9.92	9.95
35065-29-3	PCB 180	10.89	12.04	11.83	11.94	10.38	10.61
2051-61-8	PCB 2	6.93	7.30	7.16	6.85	6.63	6.93
7012-37-5	PCB 28	8.28	8.85	8.70	8.56	8.06	8.10
15862-07-4	PCB 29	8.19	8.87	8.72	8.62	7.69	8.13
2051-62-9	PCB 3	6.96	7.33	7.13	6.89	6.63	6.93
13029-08-8	PCB 4	7.10	8.09	7.98	7.41	7.27	7.56
35693-99-3	PCB 52	8.56	9.67	9.45	9.03	8.69	8.64
34883-39-1	PCB 9	7.36	8.10	7.93	7.53	7.24	7.47
66246-88-6	Penconazole	8.95	10.09	9.92	9.78	9.07	9.47
40487-42-1	Pendimethalin	8.95	10.37	9.98	9.83	8.18	10.24
87-86-5	Pentachlorophenol	7.58	7.62	7.58	7.42	6.55	6.71
1825-21-4	Pentachloroanisol	7.61	8.19	8.20	7.84	6.71	6.80
52645-53-1	Permethrin 1	11.83	14.50	13.86	12.15	12.83	12.41
52645-53-1	Permethrin 2	11.88	14.50	13.86	12.15	12.83	12.41
298-02-2	Phorate	7.44	6.71	7.72	7.68	8.38	8.39
2588-05-8	Phorate sulfoxide	8.27	7.51	8.13	6.12	7.46	9.60
2588-04-7	Phorate, -sulfone	8.36	7.84	8.70	8.32	9.22	8.56
2310-17-0	Phosalone	10.83	11.54	12.15	12.66	11.60	12.24

Table 1 (*Continued*)

CAS	Compound	Exp.	CI(1)[a]	CI(2)[b]	SPARC	COSMO	ABSOLV
732-11-6	Phosmet	10.14	10.54	10.82	11.11	10.24	11.15
13171-21-6	Phosphamidon 1	7.65	10.14	9.75	5.71	8.41	9.44
13171-21-6	Phosphamidon 2	7.90	10.14	9.75	5.71	8.41	9.44
51-03-6	Piperonyl butoxide	10.70	12.93	12.36	11.42	12.55	11.57
23103-98-2	Pirimicarb	7.86	8.86	8.35	8.85	8.16	8.42
67747-09-5	Prochloraz	11.59	13.26	12.92	13.36	11.68	12.55
32809-16-8	Procymidone	8.89	9.46	9.67	9.69	9.57	11.49
41198-08-7	Profenofos	9.52	10.27	10.74	6.8	10.37	10.90
7287-19-6	Prometryn	8.39	8.36	8.26	8.71	9.28	9.10
1918-16-7	Propachlor	6.90	7.57	7.39	7.42	6.96	7.44
2312-35-8	Propargite	10.69	13.06	12.63	11.04	11.53	12.69
139-40-2	Propazine	7.60	7.83	7.68	8.06	9.08	7.95
122-42-9	Propham	6.12	6.84	6.59	6.3	6.02	6.72
23950-58-5	Propyzamide	7.83	8.82	8.54	8.24	8.28	8.42
34643-46-4	Prothiofos	9.53	10.25	10.47	10.24	10.03	9.69
13457-18-6	Pyrazophos	11.16	13.10	13.22	10.79	12.74	11.91
96489-71-3	Pyridaben	12.04	12.37	12.24	12.24	12.70	12.13
119-12-0	Pyridaphenthion	10.36	12.26	12.31	11.34	11.61	11.71
53112-28-0	Pyrimethanil	7.76	8.02	7.83	8.66	7.88	8.19
124495-18-7	Quinoxyfen	9.98	10.92	10.81	10.71	9.65	9.89
82-68-8	Quintozene	7.73	8.76	8.74	8.03	6.47	7.48
527-20-8	Pentachloroaniline	7.98	7.58	7.55	8.07	6.80	7.13
7286-69-3	Sebuthylazine	7.89	8.05	7.84	8.24	8.90	8.06
122-34-9	Simazine	7.37	7.17	7.01	7.43	8.02	7.19
122836-35-5	Sulfentrazone	10.21	11.80	11.71	12.43	11.15	11.91
3689-24-5	Sulfotep	7.40	8.97	10.16	8.95	7.78	9.52
112410-23-8	Tebufenozide	11.64	13.28	12.83	12.91	12.99	13.95
35256-85-0	Tebutam	7.59	8.27	8.02	7.69	7.81	8.41
117-18-0	Tecnazene	6.94	7.98	7.92	7.17	6.16	6.84
107-49-3	Tetraethyl pyrophosphate	6.54	9.30	9.79	0.96	9.14	9.11
13071-79-9	Terbufos	7.95	7.27	8.31	8.23	9.65	9.04
5915-41-3	Terbuthylazine	7.65	7.77	7.62	8.07	8.39	7.84
886-50-0	Terbutryn	8.46	8.30	8.21	8.72	8.97	9.00
22248-79-9	Tetrachlorvinphos	9.13	12.02	11.60	7.84	9.65	10.13
116-29-0	Tetradifon	10.66	11.54	11.58	10.54	10.25	9.84
2227-13-6	Tetrasul	9.98	10.45	10.32	9.75	9.72	9.66
148-79-8	Thiabendazole	8.55	8.02	8.08	9.99	8.09	8.83
117718-60-2	Thiazopyr	8.74	10.56	10.77	10.16	10.15	9.39
31895-21-3	Thiocyclam	6.60	4.95	5.68	6.56	5.56	6.49
640-15-3	Thiometon	7.40	6.58	7.05	7.18	8.01	7.89
137-26-8	Thiram	7.84	7.05	7.00	9.84	8.56	7.80
57018-04-9	Tolclofos-methyl	8.25	9.34	9.44	8.34	8.14	8.83
731-27-1	Tolylfluanid	8.94	10.49	10.42	8.31	9.70	10.27
43121-43-3	Triadimefon	8.70	10.92	10.37	9.85	9.32	10.08
55219-65-3	Triadimenol 1	9.08	10.84	10.33	9.7	9.43	10.20
55219-65-3	Triadimenol 2	9.12	10.84	10.33	9.7	9.43	10.20
2303-17-5	Triallate	8.22	8.92	8.77	8.45	8.08	8.85
24017-47-8	Triazophos	9.65	11.18	11.32	10.59	11.95	11.08
52-68-6	Trichlorfon	6.14	6.95	6.97	3.68	6.38	6.62
1582-09-8	Trifluralin	7.51	10.28	9.95	9.03	8.04	9.39
50471-44-8	Vinclozolin	8.18	10.02	9.92	9.39	8.82	9.10
78-38-6	Diethyl ethyl phosphonate	4.28	5.02	5.25	3.22	5.14	5.24
2781-11-5	Diethyl N,N-bis(2-hydroxyethyl)amino methyl phosphonate	7.18	8.48	8.52	5.19	9.71	8.97
35948-25-5	Dihydrooxaphospha phenanthrene oxide	8.85	8.34	8.62	7.62		8.82
78-40-0	Triethyl phosphate	4.37	5.83	6.01	2.35	6.38	5.61
1330-78-5	Tricresyl phosphate 1	11.55	14.42	14.18	8.99	12.56	13.58
1330-78-5	Tricresyl phosphate 2	11.67				12.56	13.58
1330-78-5	Tricresyl phosphate 3	11.77				12.56	13.58
1330-78-5	Tricresyl phosphate 4	11.84				12.56	13.58
115-86-6	Triphenyl phosphate	10.27	13.24	12.98	8.04	10.83	12.16
13674-87-8	Tris(1,3-dichloro-2-propyl)phosphate	10.13	12.91	12.79	7.09	11.82	10.66
126-72-7	Tris(2,3-dibromo-propyl) phosphate	12.96	14.07	13.51	10.64	15.81	14.77
115-96-8	Tris(2-chloro-ethyl)phosphate	7.22	8.93	8.64	5.13	7.95	7.57
636-28-2	1,2,4,5-Tetrabromobenzene	7.78	7.01	7.23	7.67	6.68	7.59
615-54-3	1,2,4-Tribromobenzene	6.53	6.06	6.17	6.45	5.86	6.46
3194-55-6	1,2,5,6,9,10-Hexabromocyclo dodecane	13.37	11.35	11.34	12.93	12.51	13.32
37853-59-1	1,2-Bis(2,4,6-tribromophenoxy) ethane	14.32	14.37	15.09	15.5	13.51	14.87
59080-40-9	2,2′,4,4′,5,5′-Hexabromobiphenyl	12.61	12.33	12.55	13.7	11.70	13.30
3296-90-0	2,2-Bis (bromomethyl)-1,3-propanediol	6.33	5.55	5.75	5.56	5.26	6.00
23488-38-2	2,3,5,6-Tetrabromo-p-xylene	9.16	7.78	8.13		7.16	8.53
35109-60-5	2,3-Dibromopropyl-2,4,6-tribromophenyl ether	10.63	10.16	10.45	11.05	9.70	10.87
118-79-6	2,4,6-Tribromophenol	7.15	6.45	6.84	6.82	6.49	7.23
615-58-7	2,4-Dibromophenol	5.79	5.61	5.68	5.83	5.05	6.05
183658-27-7	2-Ethyl-1-hexyl 2,3,4,5-tetrabromobenzoate	12.41	12.69	12.63		11.49	12.60
79-94-7	3,3′,5,5′-Tetrabromo bisphenol A	12.82	12.69	12.71	13.53	12.67	13.69
60044-26-0	3,3′,4,4′,5,5′-Hexabromobiphenyl	13.66	12.38	12.50	14.21	11.83	13.60
626-41-5	3,5-Dibromophenol	6.26	5.46	5.78	5.95	5.89	5.92

Table 1 (*Continued*)

CAS	Compound	Exp.	CI(1)[a]	CI(2)[b]	SPARC	COSMO	ABSOLV
–	3-OH BDE47	11.49					
2039-82-9	4-Bromostyrene	5.09	5.25	5.14	5.26	4.75	5.05
79755-43-4	6-OH BDE47	11.21	11.49	11.70	12.47	10.46	11.71
3278-89-5	Allyl-2,4,6-tribromophenylether	7.94	8.18	8.54	8.25	7.56	8.25
189084-64-8	BDE 100	11.71	11.83	12.30	12.70	11.27	12.30
68631-49-2	BDE 153	12.95	13.05	13.09	14.26	12.21	13.38
207122-15-4	BDE 154	12.64	12.84	13.29	14.29	11.71	13.43
207122-16-5	BDE 183	13.83	13.92	14.26	15.59	12.85	14.64
41318-75-6	BDE 28	9.79	10.12	10.00		9.57	9.92
5436-43-1	BDE 47	10.84	11.01	11.11	11.29	10.54	11.10
60348-60-9	BDE 99	11.90	12.03	12.10	12.75	11.30	12.23
26040-51-7	Bis(2-ethyl-1-hexyl)tetrabromo phtalate	15.92	18.33	18.09	18.11	15.73	17.53
4162-45-2	Bis(2-hydroxyethyl ether) TBBPA	15.11	16.15	16.10	16.67		16.73
115-28-6	Chlorendic acid	8.57	10.64	11.29	9.08	9.49	9.86
115-27-5	Chlorendic anhydride	8.41	10.04	10.94	8.75	8.68	10.19
87-82-1	Hexabromobenzene	10.57	8.86	9.47		8.03	9.90
51939-55-1	Hexachlorocyclo pentenyl-dibromocyclooctane	12.29	11.80	12.48			12.39
59447-55-1	Pentabromobenzyl acrylate	11.45	11.44	11.56	11.84	9.88	11.30
38521-51-6	Pentabromobenzyl bromide	11.05	9.37	10.17	11.27	8.80	10.47
85-22-3	Pentabromoethyl benzene	10.18	8.76	9.38		8.00	9.75
608-71-9	Pentabromophenol	9.88	8.49	8.90	9.7	7.93	9.50
87-83-2	Pentabromotoluene	9.90	8.32	8.80		7.67	9.26
3322-93-8	Tetrabromoethyl cyclohexane 1	8.86	7.55	7.74	8.53	8.33	8.90
3322-93-8	Tetrabromoethyl cyclohexane 2	8.90				8.33	8.90
632-79-1	Tetrabromphthalic anhydrid	10.16	9.74	10.18	11.03	8.49	9.92
79-95-8	Tetrachlorobisphenol A	11.28	11.98	11.67	11.72	11.41	11.46
1522-92-5	Tribromoneopentyl alcohol	6.82	5.91	6.40	6.23	5.36	6.37
57-63-6	17α-Ethynylestradiol	11.42	10.71	11.07	11.75	10.71	11.81
80-05-7	Bisphenol A	8.97	8.83	8.55	8.75	8.71	8.89
298-46-4	Carbamazepine	9.62	9.83	9.66		9.27	10.79
64-85-7	Deoxycorticosterone	12.85	11.37	11.85	12.29	12.46	12.24
50-28-2	17β-Estradiol	11.05	9.57	10.02	10.93	10.15	11.17
50-27-1	Estriol	11.66	10.16	10.54	10.92	10.71	11.83
53-16-7	Estrone	10.91	9.66	10.07	10.92	10.21	11.15
485-72-3	Formononetin	11.08	11.10	10.72	10.28	10.59	10.37
3380-34-5	Irgasan (triclosan)	9.06	10.09	9.78	9.62	8.88	8.90
137-58-6	Lidocaine	8.31	8.65	8.40	9.25	8.20	9.09
61337-67-5	Mirtazapine	9.97	10.49	10.56	11.67	7.77	10.63
50-33-9	Phenylbutazone	10.36	12.36	12.10	12.77	10.65	14.10
57-83-0	Progesterone	12.12	10.59	11.22	11.57	11.82	12.04
61413-54-5	Rolipram	10.49	10.45	10.32	10.28	11.27	11.94
72-14-0	Sulfathiazole	10.19	9.35	9.42	9.59	10.11	10.15
58-22-0	Testosterone	11.38	9.64	10.23	11.13	10.91	11.18
117-81-7	Bis(2-ethylhexyl) phthalate	11.79	14.52	13.83	12.93	13.17	12.81
85-69-8	Butyl 2-ethylhexylphthalate	10.22	12.60	12.00	11.10	11.18	10.95
84-61-7	Dicyclohexyl phthalate	11.00	12.48	12.24	11.49		11.41
84-75-3	Di-n-hexyl phthalate	10.52	12.69	12.04	11.35	11.76	11.06
84-74-2	Di-n-butyl phthalate	8.59	10.69	10.16	9.28	9.92	9.09
84-66-2	Di-n-ethyl phthalate	6.75	8.66	8.30	7.33	7.87	7.11
131-18-0	Di-n-pentyl phthalate	9.55	11.69	11.10	10.31	10.70	10.07
131-16-8	Di-n-propyl phthalate	7.67	9.69	9.21	8.29	8.90	8.10
92-67-1	4-Aminobiphenyl	7.40	7.04	6.85	7.31	7.10	7.48
486-25-9	9-Fluorenon	7.47	7.49	7.58	7.37	6.77	7.74
86-74-8	Carbazol	7.68	6.96	7.05	7.57	6.69	7.87
91-22-5	Quinoline	5.28	5.41	5.39	5.58	4.86	5.45
120-72-9	Indol	5.16	4.77	4.84	4.92	4.82	5.50
119-65-3	Isoquinoline	5.37	5.41	5.40	5.62	4.80	5.45
92-83-1	Xanthene	7.23	7.54	7.53	7.62	6.60	7.22
86-57-7	1-Nitronaphthalene	6.80	7.09	6.94	7.18	5.99	6.81
5522-43-0	1-Nitropyrene	10.67	10.28	10.30	10.42	8.61	10.59
118-96-7	2,4,6-TNT	7.01	8.82	8.27	7.46	6.40	7.87
121-14-2	2,4-DNT	6.28	7.05	6.67	6.24	5.62	6.39
91-23-6	2-Nitroanisole	5.38	6.06	5.81	5.20	5.56	5.29
555-03-3	3-Nitroanisole	5.42	6.07	5.76	5.62	5.26	5.29
602-60-8	9-Nitroanthracene	9.03	9.28	9.16	9.80	7.75	9.19
2474-02-4	1,7-Dichloro-octamethyltetra siloxane	5.61	5.44	8.81		5.13	4.99
16106-81-3	1,11-Dichloro-dodecamethylhexa siloxane	7.80	7.98	12.96			7.14
1009-93-4	2,2,4,4,6,6-Hexamethylcyclotri silazane	4.77	2.83	5.91	5.55	3.20	4.42
42292-18-2	3-Aminopropyl methylbis(trimethyl siloxy)silane	5.73	5.09	7.40		5.54	5.50
919-30-2	3-Aminopropyltri ethoxysilane	5.38	6.87	7.25	5.47	6.89	5.95
541-02-6	Decamethylcyclo pentasiloxane (D5)	5.45	5.88	10.36	6.61	5.74	5.42
540-97-6	Dodecamethylcyclo hexasiloxane (D6)	6.63	7.16	12.44	7.65	5.54	6.50
2530-83-8	Glycidoxypropyltri methoxysilane	6.09	7.97	7.90	5.43	7.13	5.97
24801-88-5	Isocyanatopropyltri ethoxysilane	5.86	8.28	8.43	6.09	6.85	6.35
2530-85-0	Methacryloxypropyl trimethoxysilane	6.11	8.47	8.25	5.51	6.18	5.96
–	1,9-Divinyldeca methylpentasiloxane	5.86	7.74	11.34			6.62
–	1,11-Divinyldodeca methylhexasiloxane	7.02	9.02	13.42			7.69

Table 1 (*Continued*)

CAS	Compound	Exp.	CI(1)[a]	CI(2)[b]	SPARC	COSMO	ABSOLV
–	1,13-Divinyltetradeca methylheptasiloxane	8.15	10.29	15.49			8.77
–	1,15-Divinylhexadeca methyloctasiloxane	9.24	11.56	17.57			9.84
–	1,17-Divinyloctadeca methylnonasiloxane	10.26	12.83	19.65			10.91
37589-57-4	Perfluoreicosane	6.59	7.79	8.26	−1.41		3.10

The numbers after the compound name indicate isomers that appeared in the chromatogram.
[a] CI(1): Connectivity indices: calibration using first data set (experimental compounds).
[b] CI(2): Connectivity indices: calibration using second data set (experimental + literature compounds).

Table 2
GC–MS method parameters for the experimental determination of the *L* value.

Column (SPB™ Octyl, Supelco)	Length [m]	30
	ID [mm]	0.25
	Phase thickness [μm]	0.25
	Maximum temperature [°C]	280
GC	Carrier gas	Helium
	Flow rate [ml/min]	1.5
	Injection	Split mode (split ratio, 1:5); if necessary, splitless mode (splitless time, 0.2 min)
	Injection volume [μl]	1.0
	Temperature program	Isothermal
	Oven temperature [°C]	180 or 250
	Auxiliary heater temperature [°C]	180 or 250
	Injector temperature [°C]	210 or 250
MS	Ion source temperature [°C]	230
	Quadrupole temperature [°C]	150
	Gain factor	1.0
	Acquisition mode	Scan (*m*/*z* 50–1050)

more complicated structures into account, e.g. by integrating the number of valence electrons to account for heteroatoms. This empirical approach was first presented by Randic [11] and developed by Kier et al. [12–14]. The CI's can simply be calculated from molecular structure, but the CI's, per se, do not represent any physical properties or intermolecular forces. Thus, for prediction of *L*, the CI's have to be correlated with experimental values of *L*.

(b) The "SPARC online calculator" ("properties" function), version 4.5, release w4.5.1522-s4.5.1522 September 2009 (http://archemcalc.com/sparc/). SPARC expresses a physical property using a summation over all intermolecular interaction energies (i.e., dispersion, induction, dipole and H-bond interactions) [15]. The individual interaction energies are calculated from molecular descriptors such as polarizability and H-bond parameters, which are directly estimated from the molecular structure. Additionally, non-interaction processes such as excess entropy changes are taken into account.

(c) ABSOLV (module in ADME Boxes version 5.0, Pharma Algorithms Inc., Toronto, Canada). ABSOLV estimates the solute descriptors involved in Eq. (2) by summing up all molecular fragment contributions [16]. ABSOLV determines matching fragments for the compound of interest based on a SMILES string input. The fragment values have been derived by a linear regression against many experimental descriptors determined by Abraham et al. (>4200 molecules, according to [16]).

(d) COSMOthermX (version C21_0111, from COSMOlogic GmbH & Co. KG, Leverkusen, Germany). COSMOthermX is a program for the quantitative calculation of solvation mixture thermodynamics based on quantum-chemical calculations [17,18]. The underlying algorithm uses a dielectric continuum solvation model to approximate the electrostatic interaction of a solvent with the solute. The molecules are regarded as embedded in a virtual conductor ("COSMO" refers to a conductor-like screening model) and interaction energies are calculated. Partition coefficients and other properties are then calculated according to statistical thermodynamics. In contrast to the other tools mentioned above, COSMOthermX can account for the conformation of molecules. In this work, possible conformers were created using COSMOconf (version 2.1).

3. Results and discussion

3.1. Experimentally determined L values and literature comparison

The calibration equations together with the statistics are shown in Table 3. The standard deviation of the fitted $\log t_{net}$ is 0.08 for 180 °C and 0.06 for 250 °C. The fitted *L* value of the calibration substances plotted against the literature experimental values are presented in Fig. 1. The polar calibration substances fit very well into the calibration equations, although the equations do not take polar interactions into account. This confirms the lack of polar sorption sites on the SPB™ Octyl column.

The experimentally determined *L* values of the target compounds cover a large range of 4.28–15.92. Table 1 indicates the experimentally determined as well as the predicted *L* values. Estimated errors for the experimentally determined *L* values are given by the quotient SD/*l* = 0.17 (180 °C) and 0.15 (250 °C). These errors are much smaller than the errors for the predicted *L* values, as shown in Table 4 and explained below.

There are literature values for 104 compounds measured in this work. A comparison with these values [7,9,19–30] resulted in an rmse (root mean square error) of 0.25. For all substances the deviation is within ±1.0, and for about 80% it is within ±0.3. The largest deviation is shown by dieldrin; the literature value is 0.92 smaller than the experimental value. A comparison only with the values determined by Bronner et al., who used the same column and the same method, results in an rmse of 0.12, and the comparison only with the remaining literature values (without those from Bronner et al.) gives an rmse of 0.31. Note that the determination methods

Table 3
Calibration equations and statistics for the experimental determination of the *L* value.[a]

GC oven temperature	Equation	r^2	SD	*n*
180 °C	$\log t_{net} = -0.336(\pm0.024)V + 0.465(\pm0.009)L - 2.207(\pm0.051)$	0.983	0.081	62
250 °C	$\log t_{net} = -0.413(\pm0.015)V + 0.375(\pm0.005)L - 2.253(\pm0.030)$	0.992	0.055	61

[a] Values in parentheses: standard error of coefficients.

Table 4
Comparison of rmse-values for the used prediction tools.

	rmse	*n*	Number of outliers (> 3 log units)
COSMOthermX	0.94	374	0
ABSOLV	0.99	387	2
SPARC	1.28	365	12
CI(1)[a]	1.55	387	18
CI(2)[b]	1.69	387	16

[a] CI(1): Connectivity indices: calibration using first data set (experimental compounds).
[b] CI(2): Connectivity indices: calibration using second data set (experimental + literature compounds).

for many of the cited *L* values are not clearly specified. The values could also be from extrapolation and not based on experimental determination. The advantage of the *L* values determined in this work is that one method was used for a large number of compounds. This provides a consistent data set.

3.2. Evaluation of the prediction tools for the L value

3.2.1. Connectivity indices

Ghavami and Faham demonstrated that a linear combination of three selected connectivity indices (^1X_v, $^1X_{sol}$, $^4X_{sol}$) provides the best correlation with Kováts retention index, a standardized retention time [31], on 4 nonpolar and 8 polar stationary phases. In analogy to this procedure a linear combination of the three connectivity indices was tested in this study to predict the *L* value. Because the *L* value correlates with the retention time, it is anticipated that the connectivity indices can describe the *L* value as well according to Eq. (4):

$$L = {}^1x_v \cdot {}^1X_v + {}^1x_{sol} \cdot {}^1X_{sol} + {}^4x_{sol} \cdot {}^4X_{sol} + c \quad (4)$$

where ^1x_v, $^1x_{sol}$, and $^4x_{sol}$ are fitting coefficients. A calibration of these coefficients with substances with known *L* values is necessary to predict *L* values using connectivity indices. Two different calibration data sets were used here to examine influences of calibration data on the prediction results:

- the first data set consisting of 74 compounds, which were also used for the calibration of Eq. (2) for the experimental determination of the *L* values, and
- the second data set of 1488 compounds, including the 74 calibration compounds of the first set, for which *L* values can be obtained from different literature sources [7,9,19–30].

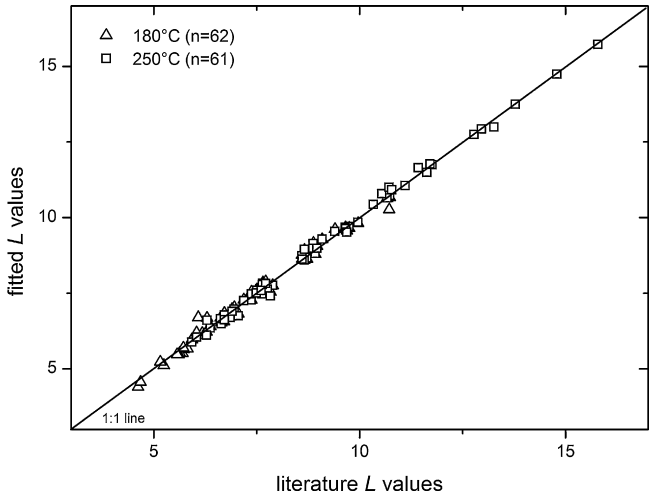

Fig. 1. Comparison of the fitted *L* values obtained by the calibration equations (*y*-axis) with the literature *L* values (*x*-axis). Data plotted are for the calibration compounds.

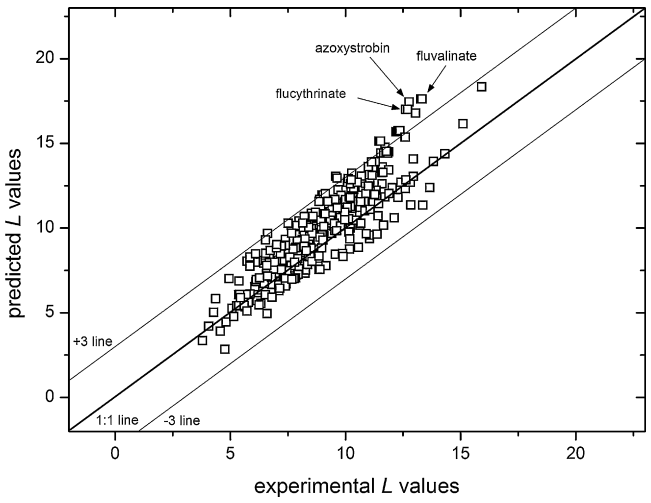

Fig. 2. Comparison of the predicted *L* values using connectivity indices (*y*-axis) with the experimentally measured *L* values (*x*-axis). Calibration for connectivity indices was done using the first calibration data set (i.e., 74 calibration compounds used in this study).

The resulting calibration equations are shown in Table S2, and the predictions based on these equations are listed in Table 1. The deviation of predicted *L* values from the experimentally determined *L* values are quite large (rmse = 1.55, maximum deviation > 4, Fig. 2) if the first calibration data set is used. Examples for extreme outliers are: flucythrinate (predicted – experimental = +4.29), fluvalinate (+4.28) and azoxystrobin (+4.67). Smaller deviations for these outliers were obtained using the second calibration data set (Fig. 3): flucythrinate (+3.50), fluvalinate (+3.48) and azoxystrobin (+3.52). However, the overall rmse became even higher (rmse = 1.69) using the second data set. One reason for the higher rmse values are the organosilicon compounds, which occur as strong outliers in the predictions based on the second data set (+4.91 to +9.39; Fig. 3). This indicates that the predictions obtained through connectivity indices strongly depend on the calibration data set.

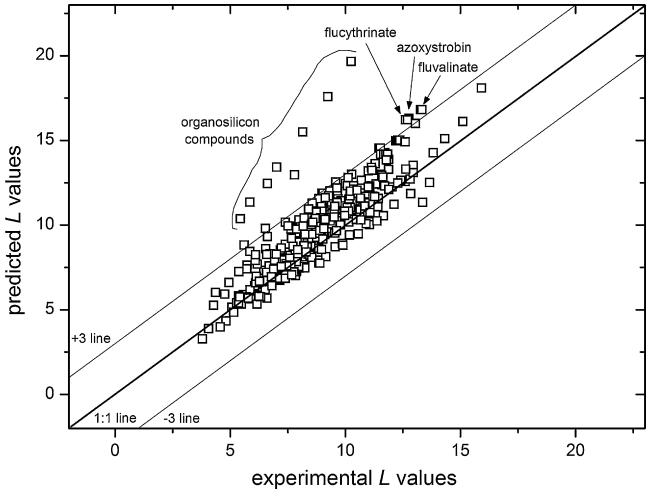

Fig. 3. Comparison of the predicted *L* values using connectivity indices (*y*-axis) with the experimentally measured *L* values (*x*-axis). Calibration for connectivity indices was done using the second calibration data set (i.e., 1488 compounds for which *L* values are available in the literature).

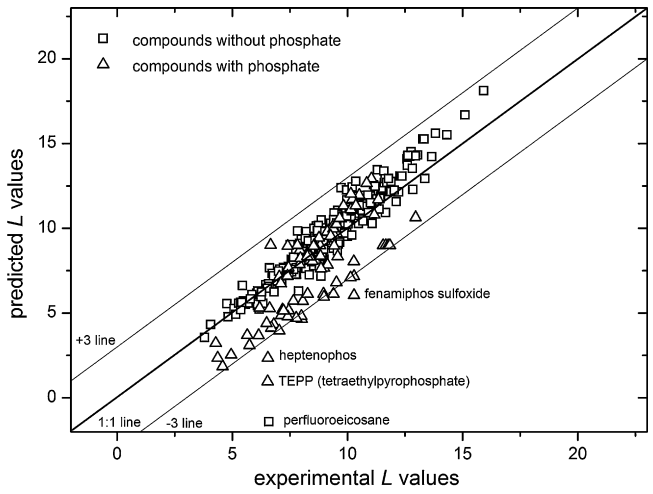

Fig. 4. Comparison of the predicted L values using SPARC (y-axis) with the experimentally measured L values (x-axis).

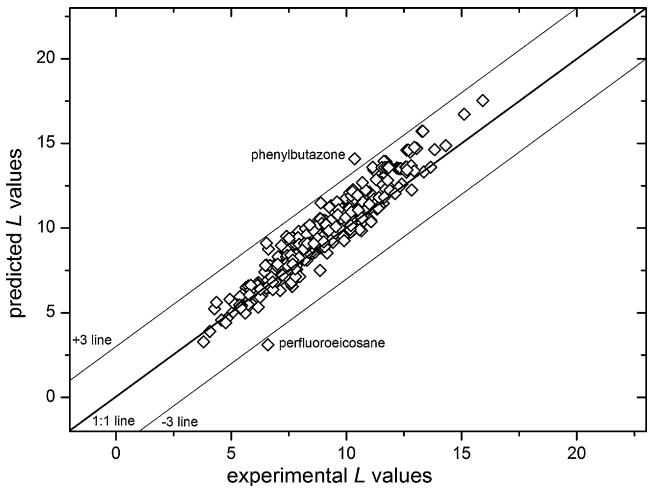

Fig. 5. Comparison of the predicted L values using ABSOLV (y-axis) with the experimentally measured L values (x-axis).

3.2.2. SPARC

Previously, Hilal et al. reported that SPARC predicts the L value for a variety of compounds with an accuracy of rmse = 0.19 [15]. However, the compounds analysed by Hilal et al. were rather simple (i.e., usually only one functional group). The predictions for our compound set show a much larger error (rmse = 1.28) compared to Hilal et al., most likely because our target compounds are mainly multifunctional. Nevertheless, the SPARC predictions for our compounds are significantly better than the predictions based on the connectivity indices (see Table 1 for all predicted values). The compounds that were outliers using connectivity indices do not occur as outliers using SPARC. However, there is a large systematic underestimation of the L values of highly fluorinated compounds and many phosphates (Fig. 4). Examples of these substances are perfluoroeicosane (−8.00), heptenophos (−4.20), fenamiphos sulfoxide (−4.23) and tetraethyl pyrophosphate (−5.58). Note that the deviations for some phosphates are rather small. Examples are bromophos methyl (+0.17) and chlorpyriphos methyl (+0.18). The fact that highly fluorinated compounds and many phosphates are underestimated in the used version of SPARC (v4.5) has been reported before [9]. Since this problem did not appear in an earlier version, it was speculated that the underlying calibration in version 4.5 is not optimal [9]. It is also noted that SPARC calculations did not give results for all substances. Particularly the calculations for highly brominated substances, like hexabromobenzene and tetrabromo-*p*-xylene, resulted in error messages. Overall, 22 compounds are missing in the comparison between SPARC-predicted and experimental L values.

On the course of this study, a new version of SPARC became available (version 4.6, release w4.6.1691-s4.6.1687 October 2011). We tested this version for predicting our data set and found that the rmse value becomes smaller when this version is used (rmse = 0.97). The major improvement occurred in the predictions of the phosphates. Examples are tetraethyl pyrophosphate (version 4.6: L = 6.75, version 4.5: L = 0.96, measured: L = 6.54) and heptenophos (version 4.6: L = 4.02, version 4.5: L = 2.35, measured: L = 6.55). In contrast, the value for perfluoroeicosane did not change. As this comparison shows, predictions by SPARC depend on the version, sometimes to a great extent. As stated above the phosphates had been well predicted with an older SPARC version already. It is a disadvantage of SPARC that only the latest version can be used and that the changes made are not communicated.

3.2.3. ABSOLV

The ABSOLV predictions were generally more accurate than the predictions using SPARC (v4.5) or connectivity indices; the rmse was smaller (rmse = 0.99, predicted values are shown in Table 1), and the number of outliers (deviation >3) was lower. There were 2 outliers with ABSOLV, compared to 12 with SPARC and 16 or 18 with the connectivity indices (see Table 4). The outliers include one substantially underestimated compound (perfluoroeicosane, −3.49, Fig. 5) and one substantially overestimated compound (phenylbutazone, +3.74). Phenylbutazone also occurred as a strong outlier (+3.91) in a previous study [9]. The reason for these large deviations is unknown. However, there were no systematic deviations for specific compound classes, in contrast to the SPARC (v4.5) calculations in which phosphates were strong outliers.

As an additional feature ABSOLV includes a database of experimental substance descriptors. For our target compounds we found 82 matching values in the database. These database values were compared to our experimentally determined values. The comparison resulted in an rmse of 0.61. This error is larger than the error obtained through the comparison to the literature data collected by ourselves (rmse = 0.25 if all literature values are included, see Section 3.1). Moreover, the number of outliers (deviation >1) is also higher when using the ABSOLV database (outliers: 6 (ABSOLV database), 0 (our database)). Even if the comparison is limited to the 56 compounds for which there are experimental L values both in our and ABSOLV databases, the values measured in this study agree better with the literature data compiled by ourselves.

3.2.4. COSMOthermX

The rmse of the COSMOthermX predictions was the smallest of all compared methods (rmse = 0.94). Moreover the predictions contained no outlier (deviation >3, see Tables 1 and 4 for individual values). Nevertheless the deviation of some predictions from the experimental value is still rather high (Fig. 6).

All in all we conclude that the accuracy of the tested predictive methods is not satisfying because a higher accuracy is typically desired to use the L value as a descriptor for the prediction of other partitioning processes. The large prediction errors found here are apparently in contradiction to the results in a previous report [32]. Goss [32] performed COSMOthermX calculations for partitioning processes between various polymers and air or water. The results suggested that COSMOthermX can provide good predictions for most polymers within rmse < 0.3 log units of partition coefficients. However, in Goss 2011, only relatively simple compounds (not more than one functional group in most cases) were used as a test

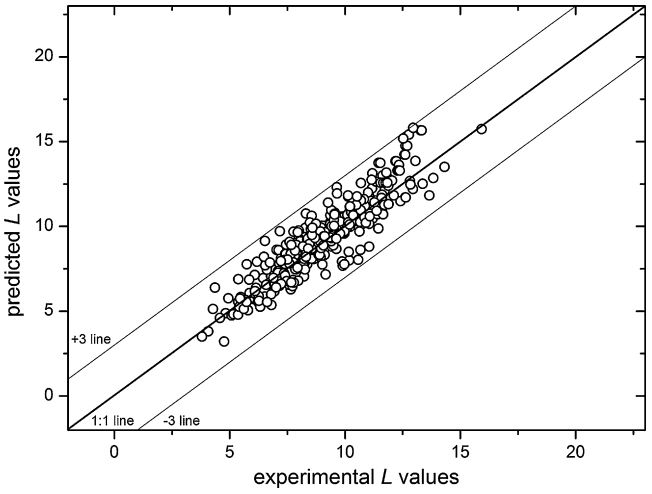

Fig. 6. Comparison of the predicted *L* values using COSMOthermX (*y*-axis) with the experimentally measured *L* values (*x*-axis).

compound set. To test whether the complexity of the compound influences the accuracy of COSMOthermX prediction, COSMOthermX values for *L* were calculated in this work for 385 selected simple compounds, for which literature *L* values were available. The calculations resulted in a much smaller deviation (rmse = 0.50) than for the compounds measured in this study. The prediction of complex multifunctional compounds seems to provide less accurate results, although the underlying fundamental approach of COSMOthermX does not necessarily differentiate simple and complex compounds. It should also be noted that COSMOthermX values are not available for all compounds in this work. Especially for large compounds such as Dechlorane Plus, dicyclohexylphthalate and tetrabromobisphenol A diallyl ether, the computational time that the COSMOconf software needs for structure optimization was too long to obtain the result in our computers.

4. Conclusions

Several prediction methods for nonspecific interactions were evaluated in this work. The connectivity indices are not well suited to characterize non-polar interactions. If SPARC values are available the reliability of these values is higher than the reliability of the predictions using connectivity indices, as judged from the rmse (exceptions for SPARC v4.5 are highly fluorinated compounds and some phosphates). The commercial prediction tools ABSOLV and COSMOthermX perform better than both SPARC (v4.5) and the connectivity indices. They have rmse-values lower than 1 and show no extreme outliers. Nevertheless the error for the analysed multifunctional compounds is still too large to achieve reliable predictions that could replace the experimental determination. Therefore, experimental *L* values are still necessary for partition coefficient estimations through pp-LFER models. Developing more accurate prediction methods remains to be a future challenge. The data presented here include a number of compounds with multifunctional, complex molecular structure and thus may serve as a basis to establish empirical and theoretical prediction methods for nonspecific interactions.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.chroma.2011.11.053.

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