HYDROGEN BONDING. 38. EFFECT OF SOLUTE STRUCTURE AND MOBILE PHASE COMPOSITION ON REVERSED-PHASE HIGH-PERFORMANCE LIQUID CHROMATOGRAPHIC CAPACITY FACTORS

MICHAEL H. ABRAHAM

Department of Chemistry, University College London, 20 Gordon Street, London WC1H 0AJ, UK

AND

MARTÍ ROSÉS

Department de Quimica Analítica, Universitat de Barcelona, Avda. Diagonal 647, 08028 Barcelona, Spain

Reversed-phase HPLC capacity factors, as log k', have been correlated through the LFER equation:

$$\log k' = c + rR_2 + s\pi_2^H + a\Sigma a_2^H + b\Sigma\beta_2^0 + vV_x$$

where k' is the capacity factor for a series of solutes in a given stationary phase–mobile phase system, and the explanatory variables are the solute descriptors: R_2 an excess molar refraction, π_2^H the dipolarity/polarizability, Σa_2^H the overall hydrogen-bond acidity, $\Sigma\beta_2^0$ the overall hydrogen-bond basicity and V_x the McGowan volume. This equation was applied to various C_{18} stationary phases with methanol–water, acetonitrile–water and tetrahydrofuran–water buffered mobile phases. The solute and mobile phase factors that influence log k' values are set out, and a comparison is made between log k' values and water–octanol partition coefficients.

INTRODUCTION

There are a number of physical and chemical factors that influence retention in reversed-phase high-performance liquid chromatography (HPLC). Of the chemical factors, the most important are the nature of the solute, the composition of the mobile phase and the nature of the stationary phase itself.[1] In this paper we consider the first two factors, and will examine the effect of the stationary phase subsequently.

Apart from methods based on linear free energy relationships (LFERs), there have been few attempts to set up schemes that can be used for the prediction of retention data of solutes in a fixed mobile phase–stationary phase system, at least for a varied set of solutes. Smith and Burr[2] have devised a group contribution scheme for the prediction of retention indices, but extension from simple aliphatic and aromatic solutes to disubstituted aromatic compounds required the incorporation of terms related to interaction between the substituents.[3] As Smith and Burr[3] noted, the more complicated the solute structure, the more involved becomes any group contribution scheme.

A more general method for the analysis of HPLC capacity factors, k', or HPLC retention indices is the LFER pioneered by Kamlet et al.[4] These workers, and others including Carr and co-workers, have shown[5–12] that it is possible to construct LFERs that include various solute descriptors and which yield excellent correlations of log k' values for a series of solutes in a given HPLC system. The one difficulty with the system of Kamlet et al.[4] is that there is no general protocol for the determination of several of the descriptors. Hickey and Passino-Reader[13] have attempted to remedy this by setting out estimation rules, but it is significant that the most recent work in this area[12] includes only solute descriptors dating from 1988. We do not detail the LFERs based on the Kamlet system, because in principle the methodology is the same as that which we use for our own LFERs.

The effect of the mobile phase on HPLC capacity factors has also been examined by Kamlet et al.,[10] albeit for a restricted set of 27 aromatic solutes. Nevertheless, such an analysis provides a more fundamental approach than do solvent selectivity schemes,[14] even though the latter are very useful as a practical aid to chromatographers.[15]

Our LFER is based on the general solvation equation

$$\log SP = c + rR_2 + s\pi_2^H + a\Sigma\alpha_2^H + b\Sigma\beta_2^H + vV_x \quad (1)$$

where SP is some property of a series of solutes in a given system and the explanatory variables, or descriptors, are solute properties as follows.[16,17] R_2 is an excess molar refraction that can be determined simply from a knowledge of the compound refractive index, or easily estimated. Since R_2 is almost an additive property, it is straightforward to deduce values of compounds from molecular structure. π_2^H is the solute dipolarity/polarizability, it being impossible to devise descriptors for these properties separately. This descriptor was first obtained experimentally from gas–liquid chromatographic (GLC) data, but can now be obtained through use of water–solvent partition coefficients.[18] $\Sigma\alpha_2^H$ is the solute overall or effective hydrogen-bond acidity. For mono-acids, this descriptor was originally[19] based on the α_2^H parameter, obtained from 1:1 hydrogen-bond complexation constants. Now that the acid scale is established, further values of $\Sigma\alpha_2^H$ can be obtained from water–solvent partition coefficients.[18] $\Sigma\beta_2^H$ is the solute overall or effective hydrogen-bond basicity. For mono-bases, this was also first obtained from 1:1 hydrogen-bond complexation constants,[20] as β_2^H, and subsequently modified and developed through water–solvent partition coefficients as the $\Sigma\beta_2^H$ scale.[18] Leahy et al.[21] examined partitioning in four water–solvent systems using an LFER equation that resembles equation (1), but with different descriptors. They showed that for a number of solutes it was not possible to assign a constant hydrogen-bond basicity. In other words, for these solutes, the relative hydrogen-bond basicity varies with the solvent system. Abraham[18] later showed that this was also the case for the LFER equation (1). For a number of solutes, including anilines and alkylpyridines, an alternative descriptor $\Sigma\beta_2^0$ had to be used in partitions between water and solvents that were fairly miscible with water. It must be noted that this alternative descriptor is used only for specific solutes; for all the other solutes, $\Sigma\beta_2^H$ can be used in all the water–solvent partitions. V_x is the McGowan characteristic volume that can be calculated for any solute simply from molecular structure, using a table of atomic constants.[22]

The coefficients, or constants, in equation (1) are found by the method of multiple linear regression analysis (MLRA) and serve to characterize the phase in question as follows. The r constant is a measure of the propensity of the phase to interact with solute π- and n-electron pairs, the s constant measures the phase dipolarity/polarizability, the a constant is a measure of the phase hydrogen-bond basicity (because an acidic solute will interact with a basic phase) and the b constant is a measure of the phase acidity. The v constant is a measure of the phase hydrophobicity. Of course, if equation (1) is applied to distribution between

two phases, the constants will then refer to differences between the phases concerned.

Thus water–octanol partition coefficients, as $\log P_{OCT}$, were shown to follow equation (2); in this equation, only solutes with a constant hydrogen-bond basicity descriptor ($\Sigma\beta_2^H$) were included:

$$\log P_{OCT} = 0\cdot088 + 0\cdot562R_2 - 1\cdot054\pi_2^H + 0\cdot034\Sigma\alpha_2^H$$
$$- 3\cdot460\Sigma\beta_2^H + 3\cdot814V_x \quad (2)$$

$$n = 613, \; \rho = 0\cdot9974, \; \text{s.d.} = 0\cdot116, \; F = 23\,161\cdot6$$

where n is the number of data points, ρ is the correlation coefficient, s.d. is the regression standard deviation and F is the Fisher F-statistic. The characteristic constants in equation (2) show that the main factors influencing water–octanol partitioning are solute excess molar refraction (weakly) and solute volume (strongly), which favour octanol, and solute dipolarity and hydrogen-bond basicity (strongly), which favour water. Conversely, it can be deduced that water is more dipolar and more acidic than octanol, but is less polarizable and much less hydrophobic than octanol. Interestingly, equation (2) shows that water and octanol (more correctly, wet octanol) have the same hydrogen-bond basicity, since solute hydrogen-bond acidity plays no part.[23]

Equation (1) has already been applied to HPLC $\log k'$ values by Miller and Poole[24] and by ourselves,[25] although with a limited number of solutes in each case. The aim of this work was to apply equation (1) to the very wide range of solutes studied by Smith and Burr[2,3,26–29] and by Smith and Wang[30] using the same Spherisorb ODS-2 stationary phase, and various methanol–water, acetonitrile–water, and tetrahydrofuran (THF)–water mobile phases buffered at pH 7 in all cases. This work of Smith and co-workers represents by far the most extensive set of solutes and mobile phases studied with the same stationary phase, and hence allows the effects of variations of solute and mobile phase on $\log k'$ values to be investigated in some detail.

RESULTS AND DISCUSSION

The solutes studied by Smith and co-workers[2,3,26–30] are listed in Table 1, together with their descriptors, as in equation (1). Most of the descriptors were taken from our previous compilations,[16,18,31,32] and the rest were obtained as we have described.[18] Of course, not all the solutes were examined with all the mobile phases, but even so the list of solutes shows how comprehensive is the work of Smith and co-workers. The only compounds for which $\Sigma\beta_2^H$ and $\Sigma\beta_2^0$ differ are the anilines. We found that the use of the alternative descriptor $\Sigma\beta_2^0$ for the anilines resulted in slightly better regression equations, and so we used the following amended

Table 1. Solutes and their descriptors used in the regression equations

Solute	R_2	π_2^H	$\Sigma\alpha_2^H$	$\Sigma\beta_2^H$	$\Sigma\beta_2^O$	V_x
Benzene	0·610	0·52	0·00	0·14	0·14	0·7164
Toluene	0·601	0·52	0·00	0·14	0·14	0·8573
Ethylbenzene	0·613	0·51	0·00	0·15	0·15	0·9982
o-Xylene	0·663	0·56	0·00	0·16	0·16	0·9982
m-Xylene	0·623	0·52	0·00	0·16	0·16	0·9982
p-Xylene	0·613	0·52	0·00	0·16	0·16	0·9982
n-Propylbenzene	0·604	0·50	0·00	0·15	0·15	1·1391
Isopropylbenzene	0·602	0·49	0·00	0·16	0·16	1·1391
n-Butylbenzene	0·600	0·51	0·00	0·15	0·15	1·2800
Isobutylbenzene	0·580	0·47	0·00	0·15	0·15	1·2800
s-Butylbenzene	0·603	0·48	0·00	0·16	0·16	1·2800
t-Butylbenzene	0·619	0·49	0·00	0·16	0·16	1·2800
trans-β-Methylstyrene	0·913	0·72	0·00	0·18	0·18	1·0961
Allylbenzene	0·717	0·60	0·00	0·22	0·22	1·0961
Biphenyl	1·360	0·99	0·00	0·22	0·22	1·3242
2-Methylbiphenyl	1·331	0·88	0·00	0·23	0·23	1·4650
3-Methylbiphenyl	1·371	0·95	0·00	0·23	0·23	1·4650
4-Methylbiphenyl	1·380	0·98	0·00	0·23	0·23	1·4650
Naphthalene	1·340	0·92	0·00	0·20	0·20	1·0854
Fluorobenzene	0·477	0·57	0·00	0·10	0·10	0·7341
Chlorobenzene	0·718	0·65	0·00	0·07	0·07	0·8388
2-Chlorotoluene	0·762	0·65	0·00	0·07	0·07	0·9797
3-Chlorotoluene	0·736	0·67	0·00	0·07	0·07	0·9797
4-Chlorotoluene	0·705	0·67	0·00	0·07	0·07	0·9797
Benzyl chloride	0·821	0·82	0·00	0·33	0·33	0·9797
2-Chloroethylbenzene	0·801	0·90	0·00	0·25	0·25	1·1206
1-Chloro-3-phenylpropane	0·794	0·90	0·00	0·24	0·24	1·2615
Bromobenzene	0·882	0·73	0·00	0·09	0·09	0·8914
2-Bromotoluene	0·923	0·72	0·00	0·09	0·09	1·0320
3-Bromotoluene	0·896	0·75	0·00	0·09	0·09	1·0320
4-Bromotoluene	0·879	0·74	0·00	0·09	0·09	1·0320
Benzyl bromide	1·014	0·98	0·00	0·20	0·20	1·0320
2-Bromo-1-phenylethane	0·974	0·94	0·00	0·30	0·30	1·1732
1-Bromo-3-phenylpropane	1·078	1·00	0·00	0·27	0·27	1·3030
Methyl phenyl ether	0·708	0·75	0·00	0·29	0·29	0·9160
2-Methylanisole	0·725	0·75	0·00	0·30	0·30	1·0569
3-Methylanisole	0·709	0·78	0·00	0·30	0·30	1·0569
Benzaldehyde	0·820	1·00	0·00	0·39	0·39	0·8730
2-Methylbenzaldehyde	0·870	0·96	0·00	0·40	0·40	1·0140
3-Methylbenzaldehyde	0·840	0·97	0·00	0·42	0·42	1·0140
4-Methylbenzaldehyde	0·862	1·00	0·00	0·42	0·42	1·0140
Acetophenone	0·818	1·01	0·00	0·48	0·48	1·0139
3-Methylacetophenone	0·806	1·00	0·00	0·49	0·49	1·1550
4-Methylacetophenone	0·842	1·00	0·00	0·51	0·51	1·1550
Ethylphenylketone	0·804	0·95	0·00	0·51	0·51	1·1550
n-Propyl phenyl ketone	0·797	0·95	0·00	0·50	0·50	1·2960
n-Butyl phenyl ketone	0·795	0·95	0·00	0·50	0·50	1·4370
n-Pentyl phenyl ketone	0·719	0·95	0·00	0·50	0·50	1·5780
n-Hexyl phenyl ketone	0·720	0·95	0·00	0·50	0·50	1·7190
Methyl benzoate	0·733	0·85	0·00	0·46	0·46	1·0726
Ethyl benzoate	0·689	0·85	0·00	0·46	0·46	1·2135
Methyl 2-methylbenzoate	0·772	0·87	0·00	0·43	0·43	1·2135
Methyl 3-methylbenzoate	0·754	0·88	0·00	0·47	0·47	1·2135
Methyl 4-methylbenzoate	0·730	0·88	0·00	0·47	0·47	1·2135
Phenyl acetate	0·661	1·13	0·00	0·54	0·54	1·0730
Benzyl acetate	0·798	1·06	0·00	0·65	0·65	1·2135
Methyl phenylacetate	0·703	1·13	0·00	0·58	0·58	1·2135
Ethyl phenylacetate	0·660	1·01	0·00	0·57	0·57	1·3544
Methyl 3-phenylpropanoate	0·687	1·21	0·00	0·59	0·59	1·3544
Ethyl 3-phenylpropanoate	0·654	1·20	0·00	0·62	0·62	1·4953
Methyl 4-phenylbutanoate	0·693	1·29	0·00	0·59	0·59	1·4953
Dimethyl phthalate	0·780	1·41	0·00	0·88	0·88	1·4288
Benzonitrile	0·742	1·11	0·00	0·33	0·33	0·8711
2-Methylbenzonitrile	0·780	1·06	0·00	0·31	0·31	1·0120
3-Methylbenzonitrile	0·762	1·08	0·00	0·34	0·34	1·0120
4-Methylbenzonitrile	0·740	1·10	0·00	0·34	0·34	1·0120
Phenylacetonitrile	0·751	1·15	0·00	0·45	0·45	1·0120
3-Phenylpropanonitrile	0·771	1·35	0·00	0·51	0·51	1·1529
4-Phenylbutanonitrile	0·759	1·38	0·00	0·51	0·51	1·2938
Aniline	0·955	0·96	0·26	0·41	0·50	0·8162
o-Toluidine	0·966	0·92	0·23	0·45	0·59	0·9570
m-Toludine	0·946	0·95	0·23	0·45	0·55	0·9570

continued

Table 1. *continued*

Solute	R_2	π_2^H	$\Sigma\alpha_2^H$	$\Sigma\beta_2^H$	$\Sigma\beta_2^0$	V_x
p-Toludine	0·923	0·95	0·23	0·45	0·52	0·9570
2-Bromoaniline	1·070	0·98	0·31	0·31	0·39	0·9910
3-Bromoaniline	1·128	1·19	0·31	0·30	0·34	0·9910
2-Nitroaniline	1·180	1·37	0·30	0·36	0·36	0·9910
3-Nitroaniline	1·200	1·71	0·40	0·35	0·35	0·9910
4-Nitroaniline	1·220	1·91	0·42	0·38	0·38	0·9910
N-Ethylaniline	0·945	0·85	0·17	0·43	0·51	1·0980
Nitrobenzene	0·871	1·11	0·00	0·28	0·28	0·8910
2-Nitrotoluene	0·866	1·11	0·00	0·27	0·27	1·0320
3-Nitrotoluene	0·874	1·10	0·00	0·25	0·25	1·0320
4-Nitrotoluene	0·870	1·11	0·00	0·28	0·28	1·0320
Benzamide	0·990	1·50	0·49	0·67	0·67	0·9728
3-Methylbenzamide	0·990	1·50	0·49	0·63	0·63	1·1137
N-Methylbenzamide	0·950	1·44	0·35	0·73	0·73	1·1137
N,N-Dimethylbenzamide	0·950	1·40	0·00	0·98	0·98	1·2546
Phenylacetamide	0·950	1·60	0·52	0·79	0·79	1·1137
3-Phenylpropanamide	0·940	1·65	0·52	0·80	0·80	1·2546
Acetanilide	0·870	1·40	0·50	0·67	0·67	1·1133
Phenol	0·805	0·89	0·60	0·30	0·30	0·7751
o-Cresol	0·840	0·86	0·52	0·30	0·30	0·9160
m-Cresol	0·822	0·88	0·57	0·34	0·34	0·9160
p-Cresol	0·820	0·87	0·57	0·31	0·31	0·9160
2,4-Dimethylphenol	0·843	0·80	0·53	0·39	0·39	1·0569
2,5-Dimethylphenol	0·840	0·79	0·54	0·37	0·37	1·0569
4-*t*-Butylphenol	0·810	0·89	0·56	0·41	0·41	1·3387
2-Isopropyl-5-methylphenol	0·822	0·79	0·52	0·44	0·44	1·3387
2-Phenylphenol	1·550	1·40	0·56	0·49	0·49	1·3829
3-Phenylphenol	1·560	1·41	0·59	0·45	0·45	1·3829
4-Phenylphenol	1·560	1·41	0·59	0·45	0·45	1·3829
2-Chlorophenol	0·853	0·88	0·32	0·31	0·31	0·8975
3-Chlorophenol	0·909	1·06	0·69	0·15	0·15	0·8975
4-Chlorophenol	0·915	1·08	0·67	0·20	0·20	0·8975
2-Bromophenol	1·037	0·90	0·35	0·31	0·31	0·9501
3-Bromophenol	1·060	1·15	0·70	0·16	0·16	0·9501
4-Bromophenol	1·080	1·17	0·67	0·20	0·20	0·9501
2-Bromo-4-methylphenol	1·040	0·90	0·35	0·31	0·31	1·0910
2-Methoxyphenol	0·837	0·91	0·22	0·52	0·52	0·9747
3-Methoxyphenol	0·879	1·17	0·59	0·39	0·39	0·9747
4-Methoxyphenol	0·900	1·17	0·57	0·48	0·48	0·9747
2-Hydroxybenzaldehyde	0·962	1·15	0·11	0·31	0·31	0·9317
3--Hydroxybenzaldehyde	0·990	1·38	0·74	0·40	0·40	0·9317
4-Hydroxybenzaldehyde	1·010	1·01	0·77	0·44	0·44	0·9317
2-Cyanophenol	0·920	1·33	0·74	0·33	0·33	0·9298
3-Cyanophenol	0·930	1·55	0·77	0·28	0·28	0·9298
4-Cyanophenol	0·940	1·63	0·79	0·29	0·29	0·9298
2-Aminophenol	1·110	1·10	0·60	0·66	0·66	0·8749
3-Aminophenol	1·130	1·15	0·65	0·79	0·79	0·8749
4-Aminophenol	1·150	1·20	0·65	0·83	0·83	0·8749
2-Nitrophenol	1·015	1·05	0·05	0·37	0·37	0·9493
3-Nitrophenol	1·050	1·57	0·79	0·23	0·23	0·9493
4-Nitrophenol	1·070	1·72	0·82	0·26	0·26	0·9493
Catechol	0·970	1·07	0·85	0·52	0·52	0·8340
Resorcinol	0·980	1·00	1·10	0·58	0·58	0·8340
Hydroquinone	1·000	1·00	1·16	0·60	0·60	0·8340
Methylparaben	0·900	1·37	0·69	0·45	0·45	1·1313
n-Propylparaben	0·860	1·35	0·69	0·45	0·45	1·4131
Methyl 3-hydroxybenzoate	0·905	1·40	0·66	0·45	0·45	1·1313
2-Hydroxybenzamide	1·140	1·50	0·59	0·52	0·52	1·0315
Benzyl alcohol	0·803	0·87	0·33	0·56	0·56	0·9160
3-Nitrobenzyl alcohol	1·064	1·35	0·44	0·64	0·64	1·0902
4-Nitrobenzyl alcohol	1·064	1·39	0·44	0·62	0·62	1·0902
2-Phenylethanol	0·811	0·91	0·30	0·64	0·64	1·0569
3-Phenylpropanol	0·821	0·90	0·30	0·67	0·67	1·1978
2-Phenylpropan-2-ol	0·848	0·85	0·32	0·65	0·65	1·1978
4-Phenylbutanol	0·811	0·90	0·33	0·70	0·70	1·3387
5-Phenylpentanol	0·804	0·90	0·33	0·72	0·72	1·4796
1-Phenylpropan-1-ol	0·775	0·83	0·30	0·66	0·66	1·1978
2-Phenylpropan-1-ol	0·810	0·90	0·30	0·64	0·64	1·1978
1-Phenylpropan-2-ol	0·787	0·90	0·30	0·72	0·72	1·1978
Benzenesulphonamide	1·130	1·55	0·55	0·80	0·80	1·0971

equation throughout:

$$\log SP = c + rR_2 + s\pi_2^H + a\sum \alpha_2^H + b\sum \beta_2^0 + vV_x \quad (3)$$

A summary of the regression equations obtained for the log k' values with methanol–water, acetonitrile–water and THF–water mobile phases is given in Table 2. The percentage of organic cosolvent is given in v/v before mixing. For the first two systems the number of solutes is around 120 in most cases, but for the THF–water system, the equations refer to only 30 solutes, except for 20% THF, where 17 solutes were studied.

The regression equations obtained are all good, with the correlation coefficient ranging from 0·997 to 0·985 for all the mobile phases except that for 90% acetonitrile, where the k' values are too small for accurate results. Standard deviations in log k' average about 0·06 log units. That for 60% methanol, 0·072 may be compared with the results of the detailed study by Smith and Burr,[27] who showed that the reproducibility of log k' values on three columns was 0·03 for a solute of average retention (pentanophenone), and that errors in the calculated void volume could amount to another 0·03 log units. If the average reproducibility in log k' for different columns of Spherisorb ODS-2 at different times is perhaps 0·04 log units, then our s.d. values of 0·06 log units are not far from the average experimental error. It is not possible to compare our regression equations as predictors of further log k' values with the group contribution scheme of Smith and Burr,[2] other than by use of a test set of compounds that have not been used to set up the predictive schemes. Since we used all the available data, including the test set of Smith and Burr,[2] a comparative analysis is not possible.

One advantage of the LFER method over any group contribution scheme is that the LFER equations can be used to estimate log k' values for compounds with groups that have not been examined by HPLC. Thus Smith and Burr[2] recorded no log k' values for any sulphone, sulphoxide or sulphonamide derivative so that these groups do not appear in the group contribution scheme. However, descriptors in equation (3) are available[16,18] for such derivatives, and can be used to estimate log k' values, as shown in Table 3 for 70% methanol as an example.*

Rosés and Bosch[33] have also set out a scheme for the prediction of log k' values for phenols using an LFER approach that is, in principle, similar to ours, but based on the old Kamlet[4] solute descriptors. Again, comparison with the present scheme is difficult, because we deal with a much wider range of solutes.

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* R. M. Smith and Y. Wang (personal communication from Dr Smith) have recently obtained capacity factors for benzensulphonamide. Their measured log k' value in buffered 70% methanol is −0·64, compared with our predicted value of −0·70 (Table 3).

Table 2. Regression equations[a] for log k' from results of Smith and co-workers[2,3,26-30]

Mobile phase	Organic component (%)	r	s	a	b	v	c	ρ	s.d.	n	F
Methanol–water	40	0·367 (0·050)	−0·828 (0·036)	−0·488 (0·031)	−2·069 (0·043)	2·701 (0·045)	−0·360 (0·051)	0·995	0·069	112	2069
	50	0·253 (0·047)	−0·693 (0·038)	−0·463 (0·033)	−1·842 (0·047)	2·139 (0·045)	−0·236 (0·052)	0·993	0·077	114	1551
	60	0·252 (0·043)	−0·651 (0·032)	−0·429 (0·030)	−1·529 (0·042)	1·773 (0·040)	−0·322 (0·047)	0·992	0·072	126	1408
	70	0·277 (0·037)	−0·583 (0·027)	−0·443 (0·025)	−1·231 (0·036)	1·349 (0·034)	−0·361 (0·041)	0·991	0·062	126	1337
	80	0·276 (0·036)	−0·547 (0·027)	−0·398 (0·025)	−0·897 (0·035)	1·025 (0·034)	−0·451 (0·040)	0·987	0·061	126	919
	90	0·194 (0·078)	−0·397 (0·047)	−0·384 (0·036)	−0·778 (0·050)	0·719 (0·026)	−0·507 (0·054)	0·998	0·020	16	391
Acetonitrile–water	30	0·384 (0·062)	−0·627 (0·042)	−0·630 (0·038)	−2·097 (0·053)	2·267 (0·054)	−0·106 (0·063)	0·993	0·083	103	1320
	40	0·293 (0·049)	−0·530 (0·038)	−0·542 (0·034)	−1·653 (0·047)	1·722 (0·047)	−0·076 (0·053)	0·991	0·079	112	1155
	50	0·221 (0·039)	−0·437 (0·029)	−0·522 (0·026)	−1·335 (0·037)	1·326 (0·037)	−0·105 (0·043)	0·990	0·065	127	1222
	60	0·177 (0·033)	−0·397 (0·024)	−0·456 (0·022)	−1·089 (0·031)	1·098 (0·031)	−0·207 (0·036)	0·990	0·055	127	1259
	70	0·152 (0·032)	−0·370 (0·024)	−0·431 (0·021)	−0·872 (0·030)	0·892 (0·030)	−0·289 (0·035)	0·988	0·053	127	993
	80	0·119 (0·031)	−0·335 (0·024)	−0·365 (0·021)	−0·760 (0·030)	0·782 (0·030)	−0·411 (0·035)	0·985	0·053	127	771
	90	0·202 (0·165)	−0·310 (0·104)	−0·208 (0·094)	−0·481 (0·134)	0·686 (0·069)	−0·760 (0·120)	0·970	0·057	20	45
Tetrahydrofuran–water	20	0·229 (0·223)	−0·510 (0·146)	−0·065 (0·094)	−2·965 (0·156)	2·577 (0·121)	0·123 (0·127)	0·977	0·057	17	350
	30	−0·071 (0·072)	−0·328 (0·079)	−0·117 (0·076)	−2·375 (0·098)	1·952 (0·055)	0·191 (0·066)	0·996	0·059	30	604
	40	−0·105 (0·060)	−0·258 (0·066)	−0·185 (0·063)	−1·752 (0·082)	1·370 (0·046)	0·138 (0·056)	0·995	0·049	30	481
	50	−0·105 (0·048)	−0·205 (0·053)	−0·199 (0·051)	−1·297 (0·066)	0·962 (0·037)	0·027 (0·044)	0·994	0·040	30	425
	60	−0·088 (0·043)	−0·201 (0·048)	−0·255 (0·046)	−0·984 (0·059)	0·688 (0·033)	−0·091 (0·040)	0·993	0·036	30	343

[a] Standard deviations are given for each coefficient following the main value.

Table 3. Descriptors for some compounds not studied by Smith and co-workers and estimates of log k' values in 70% methanol

Solute	R_2	π_2^H	$\Sigma\alpha_2^H$	$\Sigma\beta_2^0$	V_x	Log k'(calc.)[a]
Phenyl methyl sulphone	1·080	1·85	0·00	0·76	1·1382	−0·54
Phenyl methyl sulphoxide	1·104	1·80	0·00	0·75[b]	1·0795	−0·57
Benzenesulphonamide	1·130	1·55	0·55	0·80	1·0971	−0·70[c]

[a] Using equation (3) with the coefficients in Table 2.
[b] $\Sigma\beta_2^H = 0·91$.
[c] A recently measured value by R. M. Smith and Y. Wang (personal communication from Dr R. M. Smith) is −0·64 units.

The equations summarized in Table 2 show exactly the solute factors that influence log k' values. For most of the mobile phases used, the r coefficient is positive, so that the solute excess molar refraction leads to an increase in log k', i.e. the stationary phase is favoured. The dipolarity/polarizability s coefficient is always negative so that solute dipolarity favours the mobile phase and leads to a decrease in log k'. The influence of solute hydrogen-bond acidity is not very large, but the a coefficient is always negative so that an increase in acidity leads to a decrease in log k'. Solute hydrogen-bond basicity favours the mobile phase very greatly, again leading to a decrease in log k', whereas solute size has a large, and opposite, effect.

However, in order to assess the relative effect of the various solute properties, it is not enough merely to examine the coefficients in the LFER equations, because the descriptors themselves cover different ranges of values. A term-by-term analysis of log k' values with 70% methanol mobile phase is given in Table 4 as an illustration. Although the s coefficient is much smaller than the b coefficient in this case (−0·58 as against −1·23), the $s\pi_2^H$ term often contributes more than the $b\Sigma\beta_2^0$ term, because for many solutes π_2^H is much larger than $\Sigma\beta_2^0$. Thus, even for the fairly strong hydrogen-bond base benzamide, the $s\pi_2^H$ term is larger than the $b\Sigma\beta_2^0$ term (Table 4), because π_2^H is over twice as large as $\Sigma\beta_2^0$ (1·50 as against 0·67). Similar analyses can be carried out for any set of solutes in any of the systems listed in Table 2.

As set out in the Introduction, the coefficients in the LSER equation (3), when applied to HPLC log k' values, reflect the difference in properties of the mobile

phase and the stationary phase. Of course, it must be recognized that the stationary phase will be saturated with the mobile phase, possibly preferentially with one or other component, so that the stationary phase properties are not constant along a set of different mobile phases. With this in mind, we can still interpret the LFER coefficients as follows. The generally positive r coefficient and the negative s coefficient indicate that the stationary phase is more polarizable but less dipolar than the mobile phases. The negative a, coefficient shows that the mobile phases are more basic in the hydrogen-bond sense than the stationary phase, and the large negative b coefficient indicates that the mobile phases are much more acidic than the stationary phase. Finally, the positive v coefficient shows that the stationary phase is much more hydrophobic than the mobile phases. All this seems reasonable in terms of the chemical nature of the mobile and stationary phases.

The variation of the LFER coefficients (Table 2) with mobile phase composition is of interest, and plots of the coefficients against mobile phase composition are in Figures 1–5. Reasonably smooth curves are obtained in all cases. Since the coefficients should reflect to some extent the mobile phase properties, we give in Table 5 the Kamlet–Taft solvatochromic solvent properties[34,35] π_1^*, α_1 and β_1 and the Hildebrand cohesive energy density[34] δ_H^2. We note that the original[34] β_1 value of 0·18 for water seems far too low, and a value of over 0·40 is more reasonable.[36]

Not much can be deduced from the plots of the r coefficient against percentage of organic solvent, except that the three curves could all reach the same value at 0% organic solvent, as required. The plots of the s

Table 4. Effect of solute properties on log k' values with 70% methanol mobile phase

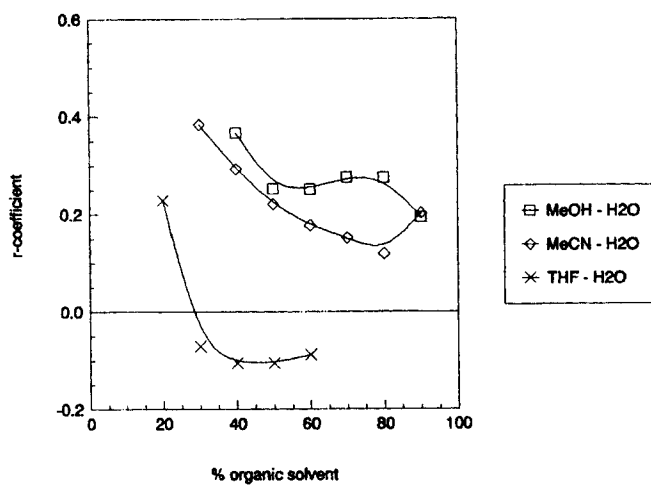| Solute	c	rR_2	$s\pi_2^H$	$a\Sigma\alpha_2^H$	$b\Sigma\beta_2^0$	vV_x	Calc.	Obs.
Toluene	−0·36	0·17	−0·30	0·00	−0·17	1·16	0·50	0·53
Butylbenzene	−0·36	0·17	−0·30	0·00	−0·18	1·73	1·07	1·13
Phenol	−0·36	0·22	−0·52	−0·27	−0·37	1·04	−0·26	−0·31
Benzamide	−0·36	0·58	−0·87	−0·22	−0·82	1·31	−0·38	−0·48

Figure 1. Plots of the *r* coefficients vs mobile phase composition for the equations in Table 2.

Figure 2. Plots of the *s* coefficients vs mobile phase composition for the equations in Table 2.

Figure 3. Plots of the *a* coefficients vs mobile phase composition for the equations in Table 2.
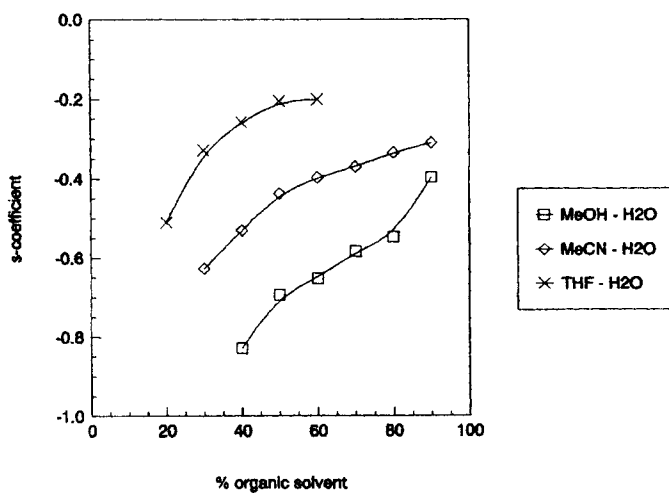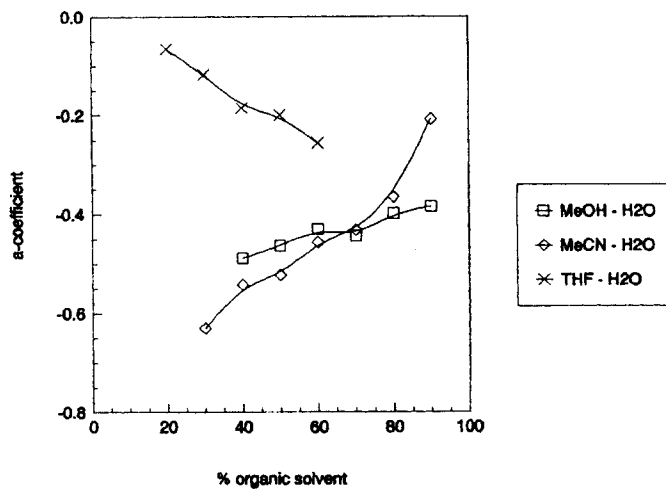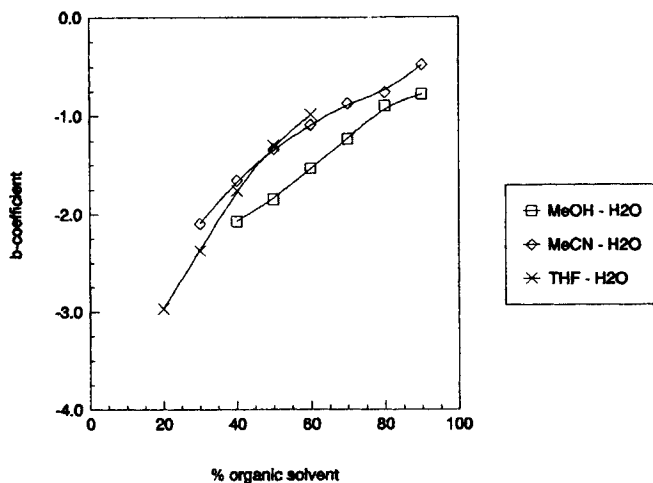
Figure 4. Plots of the b coefficients vs mobile phase composition for the equations in Table 2.
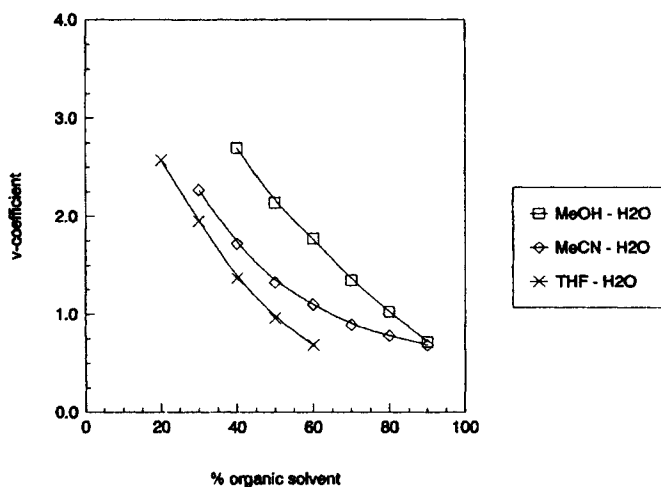

Figure 5. Plots of the v coefficients vs mobile phase composition for the equations in Table 2.

Table 5. Kamlet–Taft solvatochromic parameters and cohsive energy densities for some solvents[a]

Solute	π_1^*	α_1	β_1	δ_H^2	R^b
Water	1·09	1·17	0·43[c]	549	0·000
Methanol	0·60	0·93	0·62	205	0·278
Acetonitrile	0·75	0·19	0·37	138	0·237
Tetrahydrofuran	0·58	0·00	0·55	86	0·289
Hexadecane	0·08	0·00	0·00	64	0·000

[a] Refs 34 and 35.
[b] Excess molar refraction.[16]
[c] Ref. 36, using 4-nitroaniline as the indicator.

coefficients (Figure 2) are more informative. Again, all three plots could intersect at 0% organic solvent, and all could reach nearly the same value at 100% organic solvent, again reasonable, since all three organic components have similar π_1^* values. The a coefficients shown in Figure 3 reflect the difference in hydrogen-bond basicity of the mobile and stationary phase. Since β_1 for water is about 0·43, and the water-saturated mobile phase probably has some basicity, all three curves might be expected to intersect at 0% organic solvent with a small negative a coefficient. To reach this, the a coefficients for the methanol–water and acetonitrile–water mixtures will have to alter

appreciably in the 0–30% region. Towards the 100% region, where the basicities of methanol and THF are about the same, the methanol and THF curves should nearly intersect, with the a coefficient for acetonitrile being less negative; this indeed might be the case, as can be seen from the results given in Table 8. The b coefficients in Figure 4 must reflect changes in mobile phase hydrogen-bond acidity and should all reach a large negative value at 0% organic phase. A limit of $-5 \cdot 0$ for the b coefficient at 0% organic solvent can be set from water–alkane partitioning.[18,23] Since the stationary phase at 0% organic solvent might have some acidity due to absorbed water, in practice the limiting value of the b coefficient will not be as negative as $-5 \cdot 0$ units. At 100% organic solvent there should be a division between methanol ($a_1 = 0 \cdot 93$) and acetonitrile and THF ($a_1 = 0 \cdot 19$ and $0 \cdot 00$), with the b coefficient still being considerably negative for methanol and nearly zero for acetonitrile and THF. Finally, the v coefficients (see Figure 5) must all approach a limiting value at 0% organic solvent that must not be more than $4 \cdot 5$ (the value of the v coefficient for water–alkane partitioning).[18,23] This could probably be the case. At the other composition end, the v coefficient should become small; judging from the cohesive energy densities, those for methanol and acetonitrile are expected to be similar, with that for THF being smaller.

By and large, the signs and magnitudes of the mobile phase coefficients make reasonable chemical sense. We have not presented plots of, e.g., the variation of coefficients with solvatochromic parameters as a function of mobile phase composition, partly because of difficulties in assigning the solvatochromic parameters, and partly because of the inherent problem of selective solvation of the stationary phase by the mobile phase.

RESULTS FROM OTHER C_{18} COLUMNS

We shall examine the variation of log k' values with stationary phase in detail in a subsequent publication, but thought it useful to compare a few other C_{18} columns with that of Smith and co-workers. In Table 6 are given details of C_{18} columns in cases where mobile phase compositions have been varied. Application of the

LFER, equation (3) to the results of Smith and Finn,[37] Kaibara et al.[38] and Hafkensheid[39] with methanol–water mobile phases are given in Table 7, together with details of the equations of Miller and Poole,[24] also based on equation (3). The general trend in coefficients with methanol percentage is the same in all five sets of equations, but there is some difference in the coefficients of the sets. In part this will be due to the very varied solute sets used, especially as the number of solutes in the regression equations is often small, but in part this also reflects differences in the columns used.

A similar result is found for acetonitrile mobile phases, from log k' values recorded by Smith and Finn[37] and by Hanai and Hubert.[40,41] Details are given in Table 8. Again, the general trend of constants with percentage of organic solvent is similar to that between data sets, but there are also differences in the absolute values of the coefficients.

The results in Tables 7 and 8 show, as expected, that data on different C_{18} columns with the same mobile phase cannot be combined (note that the temperature often varies from one system to another). However, the general trends in the variations of coefficients with percentage of organic solvent are similar from one C_{18} column to another, and the absolute magnitudes of the coefficients do not vary greatly from one C_{18} column to another. Hence the general conclusions as to the effect of solute structure and mobile phase compositions on log k' values reached by examination of log k' values on one particular C_{18} column will still be valid for other C_{18} columns.

COMPARISON WITH WATER–OCTANOL PARTITION COEFFICIENTS

The relationship between log P_{OCT} and log k' for HPLC measurements using a C_{18} stationary phase and methanol–water mobile phases has been examined by Kamlet et al.[10] and Abraham et al.,[25] albeit using a limited data set in each case ($n = 27$ and 43, respectively). Both sets of workers concluded that correlations between log P_{OCT} and log k' in a given system would be valid only within a restricted (similar) set of solutes.

For a plot of log P_{OCT} against log k' to hold over a

Table 6. Various C_{18} columns used in HPLC work

Authors	Column	Length $\times$ i.d.	Ref.
Smith and co-workers (SMI)	Spherisorb ODS-2	$100 \times 5 \cdot 0$	2, 3, 26–29
Smith and Finn (SF)	Hypersil ODS	$100 \times 5 \cdot 0$	37
Kaibara et al. (KHN)	Nucleosil 5-C_{18}	$150 \times 4 \cdot 6$	38
Hafkensheid (HAF)	Hypersil ODS	$100 \times 3 \cdot 0$	39
Hanai and Hubert (HH1)	ERC-1000 (ODS)	$150 \times 6 \cdot 0$	40
Hanai and Hubert (HH3)	Unisil C_{18}	$150 \times 4 \cdot 1$	41
Miller and Poole (MP)	Bakerbond C_{18}	$250 \times 4 \cdot 6$	24

Table 7. Regression equations for log k' with methanol–water mobile phases[a]

Authors[b]	MeOH (%)	r	(sd)	s	(sd)	a	(sd)	b	(sd)	v	(sd)	c	(sd)	s.d.	ρ	n	F
SMI	40	0·367	0·050	−0·828	0·036	−0·488	0·031	−2·069	0·043	2·701	0·045	−0·360	0·051	0·069	0·995	112	2069
	50	0·253	0·047	−0·693	0·038	−0·463	0·033	−1·842	0·047	2·139	0·045	−0·236	0·052	0·077	0·993	114	1551
	60	0·252	0·043	−0·651	0·032	−0·429	0·030	−1·529	0·042	1·773	0·040	−0·322	0·047	0·072	0·992	126	1408
	70	0·277	0·037	−0·583	0·027	−0·443	0·025	−1·231	0·036	1·349	0·034	−0·361	0·041	0·062	0·991	126	1337
	80	0·276	0·036	−0·547	0·027	−0·398	0·025	−0·897	0·035	1·025	0·034	−0·451	0·040	0·061	0·987	126	919
	90	0·194	0·078	−0·397	0·047	−0·384	0·036	−0·788	0·050	0·719	0·026	−0·507	0·054	0·020	0·998	16	391
SF	20	0·205	0·049	−0·741	0·084	−0·331	0·090	−2·101	0·094	3·239	0·058	−0·344	0·088	0·048	0·998	19	801
	30	0·200	0·044	−0·720	0·079	−0·333	0·085	−2·089	0·089	2·859	0·045	−0·277	0·081	0·046	0·999	21	1010
	40	0·179	0·049	−0·696	0·088	−0·342	0·094	−1·923	0·099	2·409	0·050	−0·186	0·090	0·051	0·997	21	582
	50	0·163	0·047	−0·670	0·084	−0·342	0·091	−1·704	0·095	1·969	0·051	−0·147	0·088	0·049	0·996	20	366
KHN	45	0·198	0·049	−0·558	0·046	−0·435	0·034	−1·764	0·071	2·022	0·088	0·105	0·063	0·046	0·992	31	304
	50	0·194	0·041	−0·512	0·040	−0·441	0·030	−1·615	0·061	1·779	0·073	0·119	0·053	0·042	0·994	34	502
	55	0·223	0·038	−0·478	0·041	−0·427	0·031	−1·477	0·062	1·552	0·074	0·106	0·053	0·043	0·994	35	523
	60	0·201	0·037	−0·424	0·039	−0·404	0·029	−1·309	0·059	1·341	0·071	0·101	0·051	0·041	0·994	35	455
	65	0·195	0·036	−0·338	0·039	−0·369	0·029	−1·131	0·059	1·101	0·071	0·134	0·051	0·041	0·992	35	351
	70	0·158	0·031	−0·322	0·033	−0·326	0·025	−0·957	0·051	0·945	0·061	0·091	0·044	0·035	0·992	35	343
	75	0·154	0·029	−0·281	0·030	−0·293	0·023	−0·771	0·048	0·759	0·055	0·087	0·039	0·031	0·991	32	299
	80	0·118	0·026	−0·234	0·028	−0·245	0·022	−0·649	0·042	0·622	0·051	0·085	0·037	0·029	0·989	33	235
HAF	30	0·243	0·104	−0·704	0·063	−0·131	0·054	−2·646	0·111	3·217	0·128	−0·553	0·115	0·057	0·996	23	382
	45	0·224	0·062	−0·612	0·054	−0·205	0·055	−2·354	0·113	2·530	0·124	−0·530	0·090	0·059	0·996	23	519
	60	0·155	0·053	−0·543	0·060	−0·264	0·062	−1·947	0·127	2·087	0·103	−0·718	0·084	0·067	0·996	29	543
	75	0·120	0·050	−0·463	0·056	−0·280	0·058	−1·603	0·119	1·629	0·096	−0·894	0·078	0·062	0·994	29	407
	90	0·105	0·043	−0·415	0·048	−0·295	0·050	−1·238	0·103	1·229	0·084	−1·117	0·068	0·054	0·994	29	354
MP[24]	30	0·44	0·15	−0·58	0·14	−0·43	0·11	−2·52	0·18	3·34	0·26	−0·32	0·21	0·07	0·995	19	241
	50	0·34	0·18	−0·74	0·15	−0·31	0·15	−2·00	0·26	2·75	0·34	−0·41	0·30	0·11	0·988	19	103
	70	0·16	0·13	−0·44	0·11	−0·32	0·11	−1·59	0·18	2·12	0·23	−0·71	0·21	0·08	0·990	19	124
	100	0·01	0·13	−0·19	0·11	−0·03	0·11	−0·62	0·19	1·22	0·24	−0·98	0·21	0·08	0·932	19	17

[a] Standard derivations for each coefficient are given after each main value.
[b] See Table 6.

Table 8. Regression equations for log k' with acetonitrile–water mobile phases[a]

Author[b]	MeCN (%)	r	s	a	b	v	c	ρ	s.d.	n	F
SMI	30	0.384 (0.062)	−0.627 (0.042)	−0.630 (0.038)	−2.097 (0.053)	2.267 (0.054)	−0.106 (0.063)	0.993	0.083	103	1320
	40	0.293 (0.049)	−0.530 (0.038)	−0.542 (0.034)	−1.653 (0.047)	1.722 (0.047)	−0.076 (0.053)	0.991	0.079	112	1155
	50	0.221 (0.039)	−0.437 (0.029)	−0.522 (0.026)	−1.335 (0.037)	1.326 (0.037)	−0.105 (0.043)	0.990	0.065	127	1222
	60	0.177 (0.033)	−0.397 (0.024)	−0.456 (0.022)	−1.089 (0.031)	1.098 (0.031)	−0.207 (0.036)	0.990	0.055	127	1259
	70	0.152 (0.032)	−0.370 (0.024)	−0.431 (0.021)	−0.872 (0.030)	0.892 (0.030)	−0.289 (0.035)	0.998	0.053	127	933
	80	0.119 (0.031)	−0.335 (0.024)	−0.365 (0.021)	−0.760 (0.030)	0.782 (0.030)	−0.411 (0.035)	0.985	0.053	127	771
	90	0.202 (0.165)	−0.310 (0.104)	−0.208 (0.094)	−0.481 (0.134)	0.686 (0.069)	−0.760 (0.120)	0.970	0.057	20	45
SF	10	0.085 (0.074)	−0.177 (0.175)	−0.267 (0.094)	−2.251 (0.158)	3.358 (0.057)	−0.652 (0.192)	0.999	0.038	16	892
	20	0.095 (0.063)	−0.337 (0.113)	−0.525 (0.122)	−2.641 (0.128)	2.755 (0.068)	−0.111 (0.118)	0.996	0.065	20	388
	30	0.061 (0.082)	−0.242 (0.136)	−0.586 (0.144)	−2.334 (0.150)	2.156 (0.099)	−0.072 (0.139)	0.992	0.076	18	151
HH1	50	0.016 (0.039)	−0.179 (0.045)	−0.580 (0.032)	−1.497 (0.046)	1.600 (0.038)	−0.200 (0.045)	0.995	0.035	44	766
	60	−0.018 (0.032)	−0.172 (0.043)	−0.524 (0.029)	−1.338 (0.038)	1.372 (0.031)	−0.257 (0.036)	0.996	0.034	51	1278
	70	−0.014 (0.027)	−0.178 (0.044)	−0.499 (0.031)	−1.190 (0.035)	1.241 (0.023)	−0.392 (0.028)	0.997	0.035	57	1623
	80	−0.008 (0.030)	−0.191 (0.051)	−0.466 (0.036)	−1.016 (0.040)	1.097 (0.020)	−0.518 (0.029)	0.996	0.041	60	1294
	90	0.011 (0.038)	−0.216 (0.065)	−0.393 (0.046)	−0.795 (0.051)	0.915 (0.022)	−0.617 (0.037)	0.992	0.053	62	717
HH3	20	0.239 (0.163)	−0.393 (0.083)	−0.285 (0.062)	−2.112 (0.117)	2.812 (0.153)	−0.261 (0.210)	0.994	0.050	21	268
	30	0.213 (0.123)	−0.300 (0.059)	−0.310 (0.042)	−1.532 (0.060)	2.148 (0.075)	−0.243 (0.130)	0.994	0.041	34	475
	40	0.282 (0.118)	−0.264 (0.056)	−0.260 (0.040)	−1.184 (0.056)	1.665 (0.060)	−0.323 (0.117)	0.992	0.041	37	362
	50	0.282 (0.103)	−0.237 (0.049)	−0.219 (0.035)	−0.902 (0.049)	1.274 (0.053)	−0.333 (0.103)	0.989	0.036	37	279
	60	0.277 (0.090)	−0.208 (0.043)	−0.178 (0.030)	−0.689 (0.043)	0.999 (0.046)	−0.365 (0.089)	0.987	0.031	37	228
	70	0.236 (0.081)	−0.192 (0.038)	−0.128 (0.027)	−0.527 (0.038)	0.778 (0.041)	−0.340 (0.080)	0.982	0.028	37	167
	80	0.206 (0.067)	−0.152 (0.032)	−0.104 (0.023)	−0.377 (0.032)	0.596 (0.034)	−0.351 (0.067)	0.978	0.024	37	138
	90	0.172 (0.049)	−0.129 (0.023)	−0.064 (0.017)	−0.275 (0.023)	0.410 (0.025)	−0.296 (0.049)	0.976	0.017	37	126

[a] Standard deviations for each coefficient are given after each main value.
[b] See Table 6.

Table 9. Adjusted LFER coefficients for the log k' regression equations in Table 2

Solvent	Concentration (%)	r'	s'	a'	b	v'
MeOH	40	0·52	−1·17	−0·69	−2·92	3·81
	50	0·45	−1·24	−0·83	−3·28	3·81
	60	0·54	−1·40	−0·92	−3·29	3·81
	70	0·78	−1·65	−1·25	−3·48	3·81
	80	1·03	−2·04	−1·48	−3·34	3·81
	90	1·03	−2·11	−2·04	−4·13	3·81
MeCN	30	0·65	−1·05	−1·06	−3·53	3·81
	40	0·65	−1·17	−1·20	−3·66	3·81
	50	0·64	−1·26	−1·50	−3·84	3·81
	60	0·61	−1·38	−1·58	−3·78	3·81
	70	0·65	−1·58	−1·84	−3·73	3·81
	80	0·58	−1·63	−1·78	−3·71	3·81
	90	1·12	−1·72	−1·16	−2·67	3·81
THF	20	0·34	−0·75	−0·10	−4·39	3·81
	30	−0·14	−0·64	−0·23	−4·64	3·81
	40	−0·29	−0·72	−0·52	−4·88	3·81
	50	−0·42	−0·81	−0·79	−5·14	3·81
	60	−0·49	−1·11	−1·41	−5·45	3·81
Log P_{Oct}		0·56	−1·05	0·03	−3·46	3·81

wide series of solutes, it is not necessary for the coefficients in the log P_{OCT} equation (2) to match those for the log k' regression equation. All that is required is that the relative magnitude of the coefficients should be the same in the log P_{OCT} and the log k' equations. We can proceed by multiplying the coefficients in any given log k' regression equation by a factor so as to make the v coefficient correspond to that for the log P_{OCT} equation, i.e. 3·814 units. Then the magnitude of the other coefficients (after multiplication by the factor) can be compared with the log P_{OCT} coefficients. Results are given in Table 9, using the regression equations summarized in Table 2. There is no log k' equation that exactly matches the log P_{OCT} equation, even when adjusted as above. The nearest equations are those for 70% methanol and 30% acetonitrile mobile phases. The former matches the log P_{OCT} equation in the terms $b\Sigma\beta_2^0$ and vV_x, but has too negative an adjusted s coefficient and a much too negative adjusted a coefficient. Hence if 70% methanol is used as the mobile phase for the HPLC determination of log P_{OCT}, great care must be taken to ensure that the solutes in the training set and in the test set all have about the same hydrogen-bond acidity. Even then, large variations in solute dipolarity/polarizability will lead to incorrect estimations of log P_{OCT}. The equation for 30% acetonitrile mobile phase is interesting, in that the adjusted coefficients are very well matched to the log P_{OCT} equation, with the single exception of the a coefficient. Hence for solutes that have no hydrogen-bond acidity, or for which Σa_2^H is the same, we suggest that the HPLC method with 30% acetonitrile will lead to good estimates of log P_{OCT}. Of course, this only applies to the

HPLC system of Smith and co-workers. We have already seen that different C_{18} columns with the same mobile phase give rise to a different set of coefficients in the LFER equation (3), and so an adjusted set will also be different. Thus, for the data of Hanai and Hubert[41] using a C_{18} Unisil column with 30% acetonitrile [see Table 8 (HH3)], adjusted coefficients of $r' = 0·38$, $s' = -0·53$, $a' = -0·55$, $b' = -2·72$ and $v' = 3·81$ are different to those for log P_{OCT} (compare Table 9). Each C_{18}–mobile phase system must therefore be treated individually. Because Smith and co-workers' C_{18}–30% acetonitrile system seems to be useful for the estimation of log P_{OCT} values, this does not mean that any other C_{18}–30% acetonitrile system will be equally useful.

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