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SOLVENT STRENGTH OF MULTICOMPONENT MOBILE PHASES IN LIQUID–SOLID CHROMATOGRAPHY

FURTHER STUDY OF DIFFERENT MOBILE PHASES AND SILICA AS AD-SORBENT

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SUMMARY

A previous model for the understanding and prediction of solvent strength as a function of mobile phase composition has been applied to recent data from the literature and further tested in terms of data reported here. On the basis of this study, we can now predict solvent strength (silica as adsorbent) for a broader range of mobile phase mixtures than previously, and the accuracy of the model has been further improved by recognition of two kinds of solvent delocalization: (a) restricted-access delocalization and (b) site-competition delocalization. Mixtures of alcohols behave normally so that the strength of such mobile phases can be predicted with adequate accuracy. This was not the case for alumina as adsorbent. This and other differences between silica and alumina as regards mobile phase effects can be rationalized in terms of differences in their surface structures.

INTRODUCTION

A general model has been developed[1-5] which describes solvent strength in liquid–solid chromatography (LSC) as a function of mobile phase composition. Soc-zewinski and co-workers[6-8] have further developed a special case of this model, for more polar mobile phases composed of two solvents, which simplifies its experimental application in some systems. More recently, Hara and co-workers[9-11] have reported extensive experimental data on solvent strength for a wide range of binary solvent mobile phases and silica as adsorbent. Hara and co-workers interpreted their data in terms of the Soczewinski equation[6]:

$$\log k' = c' - n \log X_s \tag{1}$$

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where k' is a solute capacity factor value for a given LSC system and X_s is the molar fraction of the more polar solvent B in a binary solvent mobile phase A–B; c' and n are constants for the system, defined by the solute and two solvents.

The data of Hara and co-workers provide a further test of the more fundamental and comprehensive model of refs. 1–5, and this paper describes the re-interpretation of these data in terms of that model. This re-examination of the data of Hara and co-workers also provides values of certain solvent parameters (ε^0) that were not known previously or were based on fragmentary data. This, in turn, allows the prediction of solvent strength data for more complex mobile phases (ternary and quaternary solvent systems) than is possible in terms of the Soczewinski model[5].

The data of Hara and co-workers also include results for binary solvent mobile phases that include the alcohols as solvents. For alumina as adsorbent, it was shown[4] that the model of refs. 1–5 does not accurately describe the solvent strength of alcohol-containing mobile phases. We shall see here, in terms of the data of Hara and co-workers, that this is not the case for alcohols and silica as adsorbent. That is, such LSC systems are accurately described by the model of refs. 1–5. This means that the full range of mobile phase compositions can now be handled in terms of the latter model for silica as adsorbent; predictions of solvent strength are now possible for any mobile phase composition (any number of constituent solvents, any kind of solvent).

Finally, the data of Hara and co-workers show that the model described in refs. 4 and 5 is inaccurate in one respect: its failure to recognize a phenomenon we call *site-competition solvent delocalization*. Previous data[1] provide a reasonable approach to incorporating this effect into the overall model of refs. 1–5, as described here. The final result is a comprehensive and accurate model of mobile phase effects in LSC so far as solvent strength is concerned. A latter paper[12] will use this model to calculate solvent strength as a function of composition for "optimum" quaternary solvent systems in LSC with silica as adsorbent.

EXPERIMENTAL

Retention data were obtained for several solutes and mobile phases for Zorbax-SIL (silica) as adsorbent, as described earlier[5]. All mobile phases were 50% water-saturated. These data are summarized in Table I.

THEORY

The model of refs. 1–5 as regards solvent strength in LSC can be summarized as follows. The retention of a solute molecule X onto an adsorbent from a mobile phase M can be regarded as a competition or displacement process:

$$X_n + n\,M_a \rightleftharpoons X_a + n\,M_n \qquad (2)$$

where a molecule of X in the non-sorbed phase (X_n) displaces some number n of pre-adsorbed mobile phase molecules M_a to yield an adsorbed solute molecule X_a and n molecules of desorbed mobile phase M_n. The net free energy of adsorption ($\Delta G^0/2.3RT$) (dimensionless) can be represented by E_{xm} and this is related to the free energy of adsorption from the gas phase of X (E_x) and M (E_m):

$$E_{xm} = E_x - n\,E_m \qquad (3)$$

TABLE I

RETENTION DATA FOR SEVERAL SOLUTES AND VARIOUS HEXANE–METHYLENE CHLORIDE–MTBE MOBILE PHASES; DERIVED SOLVENT STRENGTH VALUES

MTBE = Methyl *tert.*-butyl ether. N_A, N_B and N_C are the mole fractions of hexane, methylene chloride and MTBE, respectively.

Solute	$\alpha' A_s^*$	A'^{**}	k' $(\varepsilon^0)^{***}$			
			1	2	3	4
			$N_A = 0.000$	0.100	0.300	0.500
			$N_B = 0.985$	0.880	0.675	0.462
			$N_C = 0.015$	0.020	0.025	0.038
1-Acetonaphthalene	9.86	2.86	0.49	0.59	0.67	0.88
			(0.321)	(0.313)	(0.308)	(0.296)
2-Acetonaphthalene	9.86	2.99	0.72	0.70	0.85	1.12
			(0.318)	(0.319)	(0.310)	(0.298)
N,N-Dimethyl-1-naphthamide	10.89	4.50	8.42	9.22	16.3	24.7
			(0.328)	(0.325)	(0.302)	(0.285)
Methyl 1-naphthyl sulfone	9.75	3.30	1.03	1.29	2.30	4.20
			(0.337)	(0.327)	(0.301)	(0.275)
1,4-Diacetylbenzene	15.2	5.12	1.59	1.84	3.18	5.07
			(0.325)	(0.320)	(0.305)	(0.291)
Average ε^0			0.326	0.321	0.305	0.289

* A_s calculated as in ref. 5, from ref. 1; $\alpha' = 0.57$.

** A' defined by eqn. 12a; A' for first two solutes calculated from data in ref. 5; A' for other solutes best fit of eqn. 12a to these data (including first two solutes).

*** Values of k' (experimental) and ε^0 (calculated from eqn. 12a).

Eqn. 3 ignores all solution-interaction terms, which are believed effectively to cancel in most LSC systems. Eqn. 3 then leads to the relationship

$$\log (k_2/k_1) = \alpha' A_s (\varepsilon_1 - \varepsilon_2) \tag{4}$$

Here, k' refers to the capacity factor of a given solute in two different mobile phases, 1 and 2, respectively. α' is a surface activity parameter which we can regard as constant (equal to 0.57) for present chromatographic silicas. A_s is the molecular cross-sectional area of the solute X, and ε_1 and ε_2 are the solvent strength parameters ε^0 for mobile phases 1 and 2.

The model assumed in eqns. 3 and 4 is further illustrated in Fig. 1a for adsorption of molecules X and M within a surface monolayer. Although discrete surface adsorption sites are assumed to exist for polar adsorbents, such as silica and alumina (shown in Fig. 1 by asterisks), here individual molecules of X and M do not localize on to an individual site. Rather, they interact as shown by the dashed lines in Fig. 1a. Thus, one position on the surface is regarded as equivalent to another. This model provides good agreement for experimental retention data with alumina or silica as adsorbent for solute and solvent molecules which are non-polar or of intermediate polarity (class N compounds, as defined in ref. 3).

For more polar molecules of the solute and solvent, localized adsorption as in Fig. 1b occurs. Here, molecules of X and M are centered over adsorption sites (*) with strong interaction (solid line) between the localized adsorbate and the adsorp-
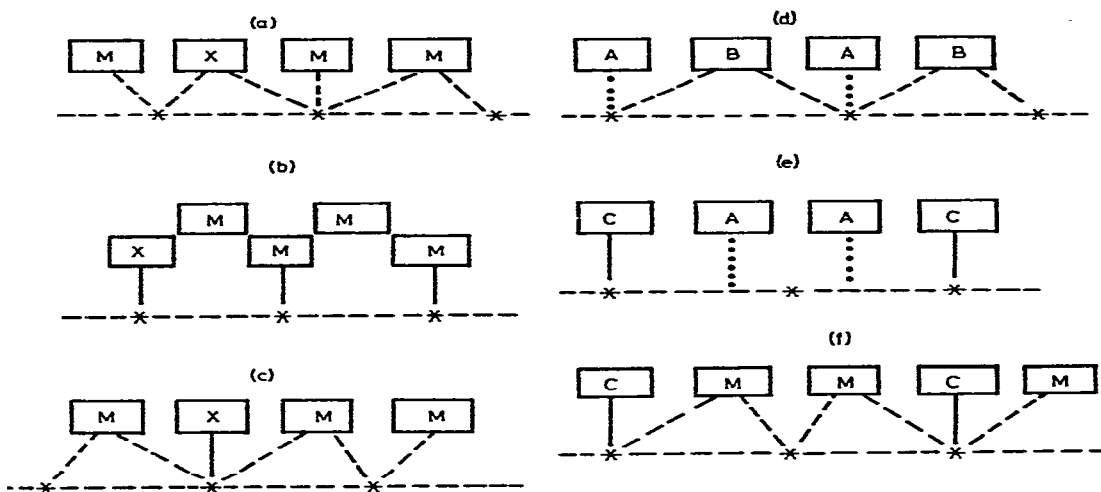
Fig. 1. Localized adsorption of solvent and solute molecules in the surface monolayer. X and M refer to molecules of solute and mobile phase, A is a non-polar, non-localizing solvent, B is a polar, non-localizing solvent and C is a more polar, localizing solvent. ————, Localizing interaction; ——, polar, non-localizing interaction; · · · ·, dispersion interaction. See text.

tion site. Not all molecules in the adsorbed monolayer can localized, and these molecules are shown in Fig. 1b as slightly displaced from the surface (although this may not actually be the case). We shall refer to the latter effect as *restricted-access delocalization*. These delocalized molecules in the surface monolayer are more weakly held (their values of E_x or E_m are smaller). LSC systems in which localized adsorption exists as in Fig. 1b are accurately described by the Soczewinski equation (eqn. 1). Here, the value of n indicates the number of surface sites that interact with the solute molecule (localized adsorption on to each site), and it is assumed that each solvent molecule M interacts with a single site.

Fig. 1c shows an intermediate situation, where solute molecules X localize but mobile phase molecules M do not. In the case of moderately polar, non-localizing molecules M (benzene, CH_2Cl_2, $CHCl_3$, RCl, etc.), these can interact laterally with sites upon which a solute molecule X is localized. This added competition for the site by both X and M weakens the net interaction of X with the surface (lower value of E_x) so that an increasing polarity of M (and a greater solvent strength ε^0 of pure M) results in a greater decrease in k' with ε^0 than is predicted by eqn. 2. We shall refer to this lowering of E_x as the *site-competition delocalization* of X. This effect, which is observed for silica but not alumina (ref. 1, Fig. 8.6), can be quantitatively accounted for by assuming a larger value of A_s than is calculated from the molecular dimensions of X[1]. The increase in A_s (ΔA_s) with respect to the actual molecular size of X correlates closely with increasing values of E_x and the relative localization of X.

Values of ε^0 for various pure solvents can be measured experimentally using eqn. 4 as described in ref. 1. However, most LSC mobile phases will be mixtures of two or more solvents, and it is useful to relate the ε^0 values of such mixtures to the ε^0 values of the pure solvents. We can begin by assuming an equilibrium between adsorbed and non-sorbed molecules A and B for a binary solvent A–B (B is the more

polar solvent, with a larger ε^0 value for pure B). This equilibrium will be essentially similar to that of eqn. 2 except that we shall assume that the molecules A and B are of similar size (so that $n = 1$):

$$B_n + A_a \rightleftharpoons B_a + A_n \tag{5}$$

The solvent strength ε^0 of the binary A–B can now be calculated as summarized earlier[5]:

$$\varepsilon^0 = \varepsilon_A + [\log(N_A/\theta_A)]/\alpha' \, n_b \tag{6}$$

or (binary solvents only)

$$\varepsilon^0 = \varepsilon_A + \frac{\log (N_B \, 10^{\alpha' n_b \, (\varepsilon_2 - \varepsilon_1)} + 1 - N_B)}{\alpha' n_b} \tag{6a}$$

Here, ε_A and ε_B are ε^0 values of pure solvents A and B, N_A is the mole fraction of A in the mobile phase, θ_A is the mole fraction of A in the surface monolayer and n_b is the A_s value of solvent B. The quantity θ_A is in turn a function of all of these parameters (ε_A, ε_B, N_A, α' and n_b); θ_A can be calculated as in ref. 5.

For mobile phases that contain additional solvents C, D, ..., we must consider the further equilibria (as in eqn. 5):

$$C_n + B_a \rightleftharpoons C_a + B_n \tag{5a}$$

$$D_n + C_a \rightleftharpoons D_a + C_a \tag{5b}$$

If the n_b value is taken as the average of A_s values for solvents B, C and D (non-polar solvents A are not considered in this average), then the ε^0 value for the multi-component solvent is given by the same relationship (eqn. 6) as for binary solvents. However, θ_A is now also a function of the mole fractions (N_C, N_D) and ε^0 values (ε_C, ε_D) of additional solvents in the mobile phase mixture (see ref. 5).

So far, our treatment of solvent strength effects in LSC has been limited to the case of solvents A, B, C, ..., that do not localize. This is illustrated in Fig. 1d for a binary A–B. For binaries A–C, where solvent C is polar enough to undergo localization, the situation becomes more complex. For low concentrations of C in the mobile phase, as illustrated by Fig. 1e, all molecules of C in the surface monolayer are localized, and the solvent strength ε_C of C is constant. However, with further increase in the surface concentration of C (roughly, up to $\theta_C = 0.75$), a maximum number of localized molecules C is approached. Beyond this point, additional molecules of C adsorb without localization (restricted-access delocalization); for example, the two molecules of M in Fig. 1b (no lines from M to ⋆ in 1b). In this region ($\theta_C \approx 0.75$), the adsorption of energy of C (E_c) decreases sharply with increase in θ_C, and the average value of ε_C derivable from eqn. 6a ($\equiv \varepsilon_B$) decreases with θ_C. Thus, for mobile phase systems where one or more solvents localize, the ε^0 values of these solvents become a function of their surface coverage θ. Specifically, for the case of a binary A–C, the value of ε_C for this binary is given by

$$\varepsilon_C = \varepsilon_C'' + \%_{1c} (\varepsilon_C' - \varepsilon_C'') \tag{7}$$

The quantity ε_C'' is the solvent strength of C for pure C. The quantity ε_C' is the apparent solvent strength of C in dilute mixtures of C in A. The quantity $\%_{01_C}$ is the fractional localization of C in the binary A–C, and varies from 1.0 for $\theta_C = 0.00$ to 0.0 for $\theta_C = 1.0$. Values of $\%_{01_C}$ as a function of θ are given in ref. 4, allowing the calculation of ε_C for any mixture of C and other solvents (when values of ε_C'' and ε_C' are known).

As the solvent strength of C (ε_C) in dilute solutions of C in A is governed by the equilibrium

$$C_n + A_a \rightleftharpoons C_a + A_n$$
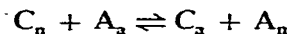
which is of the same form as eqn. 2 for the adsorption of solute X, the value of ε_C' should be given as

$$\varepsilon_C' = E_c/A_c \tag{8}$$

where E_c is the adsorption energy of C from the gas phase and A_c is the A_s value of C. We have previously assumed[4,5] that values of ε_C' will be independent of other solvents in a multi-solvent mobile phase that includes C. However, we now know that this is not correct. Just as the E_x value of a localized solute X is lowered by adjacent molecules of more polar solvents M (Fig. 1c, site-competition delocalization), for the same reason the quantity E_c must be reduced by an increase in the solvent strength of the remainder of the mobile phase exclusive of C. This means that ε_C' must decrease with increase in the solvent strength of pure A (ε_A) in mixtures of C with A as the mobile phase.

A quantitative model for site-competition delocalization of solute and solvent molecules in LSC

First consider the effect for solute molecules, which leads to anomalously large values of A_s in eqn. 4 for localizing solutes. Assume a mobile phase M which is a solvent mixture A–B where A is non-polar ($\varepsilon_A = 0$) and B is polar ($\varepsilon_B > 0$) but non-localizing. Let the solute adsorption energy E_x be given as E_x^0 for the case where $\varepsilon_M = 0$ (pure A as mobile phase). Now consider how E_x changes with change in the solvent strength ε_M of the mobile phase M (composed of mixtures A–B). From Fig. 1c, it is seen that both mobile phase molecules M and localizing-solute molecules X compete for the same adsorption site. C competes by direct (covalent) interaction, while M competes indirectly by lateral (non-covalent) interactions as shown. It is intuitively reasonable that the interaction of X with a site is decreased in proportion to both the strength of the interactions between M and the site and the relative localization of X (when X is non-localizing, E_x is independent of ε_M). The strength of interactions between all surrounding molecules M and the site occupied by localized X will be proportional to the adsorption energy of M per unit area or ε_M. Similarly, the relative localization of X can be described by a localization function $f_i(X)$, which should increase with E_x^0 or the adsorption energy of a localizing group k within the molecule X. Thus,

$$E_x = E_x^0 - f_i(X)\,\varepsilon_M \tag{9}$$

Eqn. 3 can be combined with eqn. 9 to give

$$E_x = E_x^0 - f_1(X) \varepsilon_M - n E_m \qquad (9a)$$

which, as in the derivation of eqn. 4, can be written as

$$E_x = E_x^0 - f_1(X) \varepsilon_M - A_s \varepsilon_M$$
$$= E_x^0 - [A_s + f_1(X)] \varepsilon_M \qquad (9b)$$

Values of k' are proportional to K and $10^{E_{x}}$ so that $\log(k_1/k_2)$ for mobile phases 1 and 2 (cf., eqn. 4) is

$$\log(k_1/k_2) = E_{x1} - E_{x2}$$

where E_{x1} and E_{x2} refer to values of E_x for mobile phases 1 and 2, respectively. Therefore,

$$\log(k_1/k_2) = [A_s + f_1(X)](\varepsilon_2 - \varepsilon_1)$$
$$= (A_s)_{expt.} (\varepsilon_2 - \varepsilon_1) \qquad (10)$$

Comparing eqn. 10 with eqn. 4, we see that the two are identical if the calculated value of A_s in eqn. 4 is replaced by the experimental quantity $(A_s)_{expt.} = [A_s + f_1(X)]$ in eqn. 10. That is, when localizing solutes X are subjected to site-competition delocalization, the apparent value of A_s, equal $(A_s)_{expt.}$, is larger than that estimated from the molecular dimensions of X. The quantity $f_1(X)$ was referred to as Δa_i in ref. 1 for monofunctional solutes (one localizing group i in the molecule).

Site-competition delocalization of solutes X has been observed for adsorption of localizing solutes X on to silica and amino-bonded-phase packings but not for alumina[1,14]. The requirement for site-competition delocalization of the solute would appear to be an adsorption site which allows both (a) the localization of a solute molecule X and (b) the lateral interaction by the same site with an adjacent mobile phase molecule M, as in Fig. 1c. The presence of this phenomenon for some LSC systems and not others implies a fundamental difference in the relative accessibility of the adsorbent sites to both solvent and solute molecules. We shall comment on this elsewhere.

Consider next how site-competition delocalization affects ε^0 for the mobile phase. When a binary solvent mobile phase B–C is used, where C is localizing and B is not, the value of E_c^0 for the localized solvent C (analogous to E_x^0 for localized solute X, eqn. 9a) will vary with ε_B, just as for site-competition delocalization of the solute. As in eqn. 9,

$$E_c = E_c^0 - f_1(C) \varepsilon_B \qquad (11)$$

Combining this with eqn. 8 then yields

$$\varepsilon_c' = E_c^0/A_c - [f_1(C)/A_c] \varepsilon_B$$

or

$$\varepsilon_c' = (\varepsilon_c')^0 - [f_1(C)/A_c] \, \varepsilon_B$$
$$= a - b \, \varepsilon_B \tag{12}$$

The quantity $(\varepsilon_c')^0$ is the value of ε_c' for a mixture B–C, where $\varepsilon_B = 0$. However, the delocalization of C as a result of site competition only proceeds up to the point where C is completely delocalized: ε_C cannot decrease below the value ε_C''. We shall see that derived values of ε_C' for various solvents C capable of localization obey this general relationship (which yields the general curves in Fig. 2).

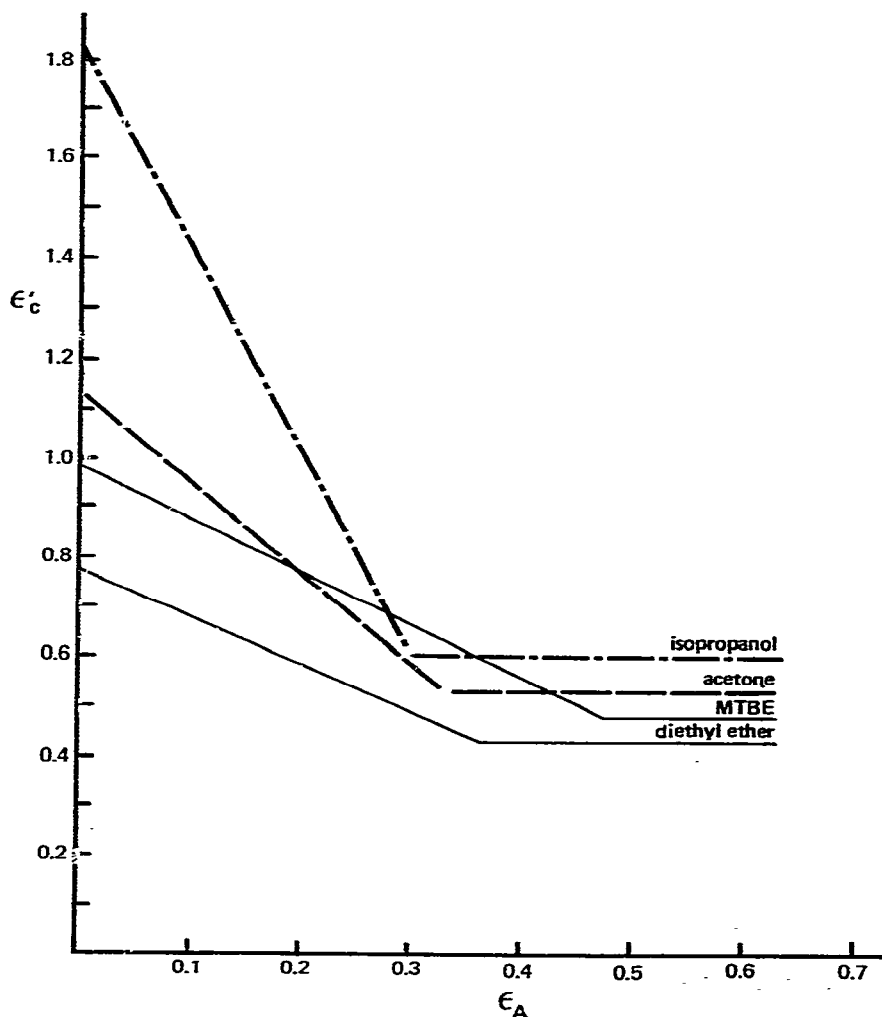Fig. 2. Examples of the variation of ε_C with the solvent strength of the A solvent in A–C mixtures. Solvent C is localized in these examples (see Table III).

RESULTS

Prediction of solvent strength for binary solvent mixtures

Hara and co-workers[9-11] published a large and systematic data base relating to the solvent strength of numerous binary solvent mixtures and silica as adsorbent. These experimental k' values for various steroids and peptides were determined by high-performance liquid chromatography (HPLC) and are, therefore, free of the usual limitations of corresponding thin-layer chromatographic (TLC) data. The solvent compositions studied also span a wide and theoretically interesting range of solvent strengths ($0.18 \leqslant \varepsilon^0 \leqslant 0.53$) and comprise most of the commonly used HPLC solvents of moderate or strong polarity.

It is possible to derive experimental ε^0 values from the data of Hara and co-workers as follows. Their experimental values of k' are fitted to eqn. 1, with values of C and n reported in refs. 9–11. The apparent fit of these data to eqn. 1 (plots of log k' vs. X_s are shown in refs. 9 and 11) appears excellent over the range of X_s values studied for various solvent pairs and solutes. We have, therefore, recalculated experimental values of log k' for selected solutes from values of C and n reported in refs. 9–11, confining X_s values to (roughly) the range used for determining k' values in a given system. Thus, we believe that the smoothing of original experimental data in this manner increases the reliability of final k' values so determined. We then chose selected solutes from the large number used in the studies of Hara and co-workers: solutes b, c, g and n from ref. 9 and solutes 1, 4 and 7 from ref. 11.

For an individual solute, eqn. 4 can be rewritten (see ref. 1) as

$$\log k' = A' - x' A_s \varepsilon^0$$
$$= A' - B' \varepsilon^0 \tag{12a}$$

A' and B' are a function of the solute, but not of the mobile phase; thus, for a given solute, A' and B' are constants. For mobile phases consisting of the binaries benzene–hexane, diethyl ether–hexane and ethyl acetate–hexane, it was possible to calculate ε^0 vs. mobile phase composition on the basis of previously reported values of ε'_B and ε''_B (ref. 4). Plots of log k' from the study of ref. 9 against these calculated values of ε^0 for each mobile phase reported in ref. 9 then yielded values of A' and B' for the selected solutes. The resulting equations based on eqn. 12a for each solute could be solved for ε^0 as a function of log k':

solute a or b, ref. 9:

$$\varepsilon^0 = (2.11 - \log k')/9.5 \tag{13}$$

solute g, ref. 9:

$$\varepsilon^0 = (4.18 - \log k')/12.9 \tag{13a}$$

solute n, ref. 9:

$$\varepsilon^0 = (3.76 - \log k')/8.6 \tag{13b}$$

The above equations were then used to derive experimental values of ε^0 from the data of ref. 9 as summarized in Table II.

Once calculated values of ε^0 for acetone–hexane mixtures were available (based on ε_B' and ε_B'' values derived from the data of ref. 9), it became possible to apply a similar approach to the experimental data of ref. 11 using ethyl acetate–hexane and acetone–hexane as reference mobile phases with known ε^0 values. The resulting equations, analogous to eqns. 13–13b, for the data of ref. 11 are then as follows:

TABLE II

EXPERIMENTAL SOLVENT STRENGTH DATA (ε^0)[9,11] *VERSUS* VALUES CALCULATED ACCORDING TO REF. 4, WITH SILICA AS ADSORBENT

For each solvent pair, the upper ε^0 value is experimental and the lower value is calculated (see text).

Solvent pair	ε^0									S.D.*	ε_B'	ε_B''	ref.**
	$X_s = 0.005$	0.010	0.020	0.050	0.100	0.20	0.40	0.70	1.00				
Diethyl ether–hexane***				0.222	0.248	0.279	0.308	0.353	0.407				
				0.207	0.243	0.277	0.316	0.379	0.430	0.017	0.78	0.43	9
Diethyl ether–benzene			0.216	0.289	0.326	0.351	0.387	0.409	0.421				
			0.267	0.289	0.319	0.358	0.391	0.404	0.430	0.022	0.54	0.43	9
Ethyl acetate–hexane***			0.185	0.231	0.267	0.318	0.360	0.444	0.498				
			0.204	0.239	0.268	0.302	0.357	0.433	0.480	0.014	0.94	0.48	9
Ethyl acetate–benzene		0.234	0.259	0.294	0.318	0.356	0.405	0.447	0.472				
		0.259	0.267	0.290	0.319	0.361	0.404	0.444	0.480	0.008	0.53	0.48	9
Benzene–hexane***						0.144	0.219	0.266					
						0.158	0.212	0.250		0.016	0.25[§]	0.25	9
Acetone–hexane		0.209	0.238	0.283	0.319	0.332	0.405	0.477					
		0.209	0.242	0.282	0.313	0.346	0.394	0.475		0.008	1.14	0.53	9
Acetone–benzene		0.275	0.300	0.326	0.362	0.415	0.463						
		0.273	0.292	0.337	0.380	0.421	0.476			0.012	0.68	0.53	9
Tetrahydrofuran–hexane						0.330	0.400	0.480	0.514				
						0.331	0.402	0.483	0.530	0.009	1.00[§§]	0.53	11
Tetrahydrofuran–benzene			0.339	0.385	0.429	0.452	0.471	0.499					
			0.340	0.377	0.417	0.457	0.492	0.518		0.014	0.68	0.53	11
Dioxane–hexane					0.304	0.340	0.385	0.477	0.515				
					0.277	0.324	0.402	0.471	0.510	0.018	1.0[§§]	0.51	11
Dioxane–benzene				0.355	0.392	0.445	0.473	0.498					
				0.373	0.403	0.428	0.448	0.473		0.021	0.74	0.51	11
Acetonitrile–benzene					0.350	0.373	0.416	0.488					
					0.337	0.388	0.436	0.477		0.017	0.60	0.52	11
Isopropanol–hexane	0.271	0.291	0.312	0.331	0.364	0.412	0.458						
	0.271	0.290	0.310	0.339	0.364	0.395	0.477			0.011	1.83	0.60	9
Isopropanol–benzene			0.302	0.351	0.414	0.463							
			0.300	0.334	0.390	0.430				0.019	0.80	0.60	9
Ethanol–benzene	0.295	0.332	0.354	0.409	0.463								
	0.288	0.318	0.360	0.423	0.468					0.011	0.89	0.69	9

* Standard deviation between experimental and calculated ε^0 values.
** Reference for experimental data of Hara and co-workers.
*** These solvent pairs were used to determine eqns. 13–14b.
§ Benzene does not localize, so $\varepsilon_B' = \varepsilon_B''$.
§§ Approximate values.

solute 1, ref. 11:

$$\varepsilon^0 = (8.30 - \log k')/22.5 \tag{14}$$

solute 4, ref. 11:

$$\varepsilon^0 = (4.98 - \log k')/11.6 \tag{14a}$$

solute 7, ref. 11:

$$\varepsilon^0 = (9.4 - \log k')/19.2 \tag{14b}$$

Application of these data to log k' values from ref. 11 yielded the additional experimental ε^0 values in Table II.

The calculated values for ε^0 in Table II were determined as described in ref. 4, using best-fit values of ε_B'' and ε_B' as determined from these experimental data. This is the same procedure used to derive values of these parameters in ref. 4 for various solvent pairs. As theory predicts that ε_B'' should be constant for different A solvents (hexane *vs.* benzene), the derivation of values of ε_B'' was subjected to this requirement.

We should first note the good agreement between experimental and calculated values of ε^0, as shown in Table II. The overall standard deviation for 15 binary systems and about 85 individual mobile phases is ± 0.016 in ε^0, which is virtually the same as found previously for 93 binary solvent mobile phases and both alumina and silica as adsorbents (standard deviation = 0.017). This agreement further confirms our ability to predict values of ε^0 using the approach of ref. 4. It also strengthens confidence in the model in refs. 1–5 upon which this predictive scheme is based. Finally, we should note that the quality of the data reported in refs. 9–11 is also substantiated by this correlation.

We had previously noted that alcohols as B-solvents and alumina as adsorbent result in ε^0 values that do not correlate with eqn. 6. This was attributed to a change in the retention mechanism as described by eqns. 2 and 5 (or some other complication not recognized in the present model). However, this exception to eqn. 6 is not found for the alcohols as B-solvents and silica as adsorbent. Thus, the overall agreement between calculated and experimental values of ε^0 for alcohol-containing mobile phases in refs. 9–11 is ± 0.014, which is slightly better than the figure for all solvents in Table II (± 0.016).

Some data reported by Hara and co-workers were omitted from further consideration in our study. These include data for mobile phases containing either methylene chloride or methanol. In the case of methylene chloride, the data of ref. 9 suggest that this solvent is weaker than benzene ($\varepsilon^0 < 0.25$), whereas all previous studies of which we are aware show that methylene chloride is significantly stronger than benzene ($\varepsilon^0 = 0.25$, benzene; 0.30, methylene chloride; see ref. 4). Until this discrepancy is resolved, we feel that data reported in refs. 9–11 for methylene chloride as co-solvent must be regarded as atypical. Similarly, the data in ref. 11 suggest that methanol is weaker than ethanol, which again contradicts prior experience.

TABLE III

SUMMARY OF SOLVENT PROPERTIES DERIVED FROM DATA OF TABLE II AND REFS. 1 AND 4

B-solvent	n_b	ε'_B		ε''_B	E^0_c*	b**	$f_1(C)$***
		Hexane	Benzene				
Diethyl ether	4.5	0.78	0.54	0.43	3.5	0.96	4.3
MTBE [§]	4.5	1.01	—	0.48	4.5	1.12	5.0
Ethyl acetate	5.2	0.94	0.53	0.48	4.9	1.64	8.5
Tetrahydrofuran	5.0	1.0	0.68	0.53	5.0	1.28	6.4
Dioxane [§§]	6.0	1.0	0.74	0.51	6.0	1.04	6.2
					(3.0)		
Acetone	4.2	1.14	0.68	0.53	4.2	1.28	5.4
Acetonitrile	3.1	1.0	0.60	0.52	3.1	1.60	5.0
Isopropanol	4.4	1.83	0.80	0.60	8.1	4.12	18.1

   * Equal to n_b times ε'_B for hexane as solvent.

   ** Difference in ε'_B for hexane vs. benzene, divided by difference in ε^0 values for latter two solvents (0.25); eqn. 12.

   *** Equal to b times n_b ($n_b = A_c$); see eqn. 12.

   [§] See Fig. 4.

   [§§] E^0_c is equal to half of n_b ε'_B, because the solvent molecule has two equivalent functional groups.

Variation of ε'_B with ε^0 for the A solvent

Values of ε'_B for several B solvents, with both hexane and benzene as A solvent, are listed in Table III. All of these B solvents localize upon adsorption (i.e., $\varepsilon'_B \neq \varepsilon''_B$), and it is seen that values of ε'_B are invariably lower for benzene than hexane as A solvent. This is predicted by eqn. 12 and the related discussion under Theory. Values of the parameters E^0_c, b and $f_1(C)$ can also be calculated for each B solvent. Thus, E^0_c is given by

$$E^0_c = n_b (\varepsilon'_B)_{hexane} \qquad (15)$$

from the definition of ε^0 for a pure solvent: $\varepsilon^0 = E_m/A_s$ (where $A_s = n_b$ for the B solvent). Similarly, b is defined by eqn. 12 so that b is equal to the change in ε'_B for benzene vs. hexane as A solvent, divided by the difference in ε^0 values for these two A solvents (0.25 − 0.00 = 0.25). Finally, $f_1(C)$ is given as b n_b, from eqn. 12.

According to the discussion of Fig. 1f and eqn. 10, $f_1(C)$ is expected to increase with increasing polarity of the solvent C or with increase in E^0_c. This has already been seen (ref. 1, Fig. 8.6) for the related dependence of solute $f_i(X)$ values (equal Δa_i) for various solute substituents i on the polarity or retention of i. In ref. 1, Δa_i is found to increase with the adsorption energy of i (Q^0_i), which is analogous to an increase in $f_1(C)$ with increase in E^0_c and ε'_c. As $f_1(X)$ and $f_1(C)$ are in fact the same functions, according to the theory so far derived we should be able to plot $f_1(X)$ vs. Q^0_i and $f_1(C)$ vs. E^0_c, and observe a single curve through both sets of data. Such a plot is shown in Fig. 3, and it is seen that this is approximately the case. That is, values of $f_1(X)$ or $f_1(C)$ are predictable from the relative adsorption strength of the adsorbate, whether solute or solvent. Thus, we now have a consistent model with derived, quan-
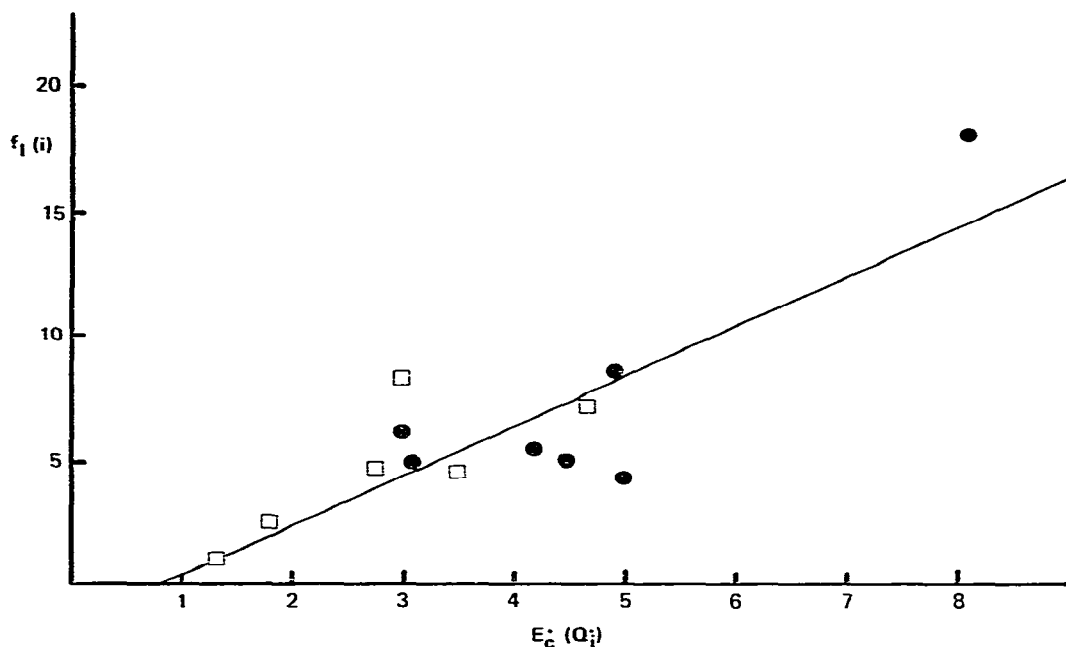
Fig. 3. Similarity of mobile phase effects in adsorption of localized solutes and solvents. Plots of $f_1(C)$ *vs.* E_c^0 (●) for solvents and $f_1(\times)$ *vs.* Q_i^0 (□) for solutes.

titative relationships for treating solvent-related delocalization effects of either solvent or solute in exactly the same way. This provides further support for the underlying model on which these predictions are based.

Ternary and quaternary solvent mobile phases

The analysis of multi-solvent mobile phases in terms of solvent strength was reported in refs. 5 and 13, together with experimental data on the strength of such mixtures. A constant value of ε' for each localizing solvent (MTBE or acetonitrile) was assumed there, which we have seen is not correct. Therefore, we have re-analyzed these data in terms of the present treatment. Table IV summarizes this re-examination of the data in refs. 5 and 13.

Column 7 in Table IV gives values of ε for the localizing solvent D (MTBE) or E (acetonitrile). These can be derived from the model of ref. 5, and correspond to the value required to give the experimentally observed value of ε^0 for the mobile phase in question. At the same time, a value of θ for the localizing solvent is obtained, which defines the value of $\%_{1\varepsilon}$ (column 8) as described in ref. 4. The value of ε'' is known for these two solvents (D, E), as given in Table III. Therefore, eqn. 7 can be used to calculate a value of ε' (column 9) for the localizing solvent and mobile phase in question. The solvent strength of the mobile phase exclusive of D or E, $\varepsilon(-D, E)$, is also required, and this can be calculated as in ref. 5 (column 10). Finally, experimental and calculated values of ε^0 for the multi-solvent mobile phase are listed in columns 11 and 12. The latter is calculated using a value of ε_D' or ε_E', as determined from eqn. 12 and the data in Table III.

TABLE IV

ANALYSIS AND CORRELATION OF SOLVENT STRENGTH DATA FOR BINARY, TERNARY AND QUATERNARY SOLVENT MOBILE PHASES WHICH CONTAIN THE LOCALIZING SOLVENTS MTBE AND/OR ACETONITRILE

Data from refs. 5 and 13 and this study.

Mobile phase No.	Composition*					$\varepsilon_D, \varepsilon_E$**	%olc	$\varepsilon'_D, \varepsilon'_E$	$\varepsilon(-D,E)$	ε^0	
	N_A	N_B	N_C	N_D	N_E					Expt.	Calc.
3[5]	0.956	0.000	0.000	0.044	0.000	0.736	0.482	1.01	0.000	0.241	0.249
4[5]	0.7165	0.000	0.270	0.0135	0.000	0.839	0.956	0.86	0.138	0.248	0.232
5[5]	0.5875	0.399	0.000	0.0135	0.000	0.816	0.943	0.84	0.155	0.240	0.251
7[5]	0.502	0.286	0.204	0.008	0.000	0.794	0.982	0.80	0.188	0.252	0.231
8[5]	0.574	0.244	0.176	0.0064	0.000	0.813	0.982	0.82	0.171	0.225	0.214
9[5]	0.474	0.053	0.470	0.0017	0.000	0.771	0.997	0.772	0.212	0.225	0.215
11[5]	0.542	0.053	0.402	0.0033	0.000	0.789	0.994	0.791	0.195	0.221	0.206
12[5]	0.841	0.071	0.048	0.038	0.000	0.773	0.649	0.93	0.069	0.250	0.278
13[5]	0.978	0.000	0.000	0.022	0.000	0.812	0.626	1.01	0.000	0.219	0.219
14[5]	0.913	0.000	0.000	0.087	0.000	0.659	0.337	1.01	0.000	0.273	0.278
A (Table I)	0.000	0.000	0.985	0.015	0.000	0.672	0.991	0.674	0.300	0.326	0.319
B (Table I)	0.100	0.000	0.880	0.020	0.000	0.690	0.988	0.692	0.284	0.321	0.311
C (Table I)	0.300	0.000	0.675	0.025	0.000	0.728	0.978	0.733	0.247	0.305	0.298
D (Table I)	0.500	0.000	0.462	0.038	0.000	0.766	0.934	0.786	0.200	0.289	0.313
17[13]	0.958	0.000	0.000	0.042	0.000	0.741	0.493	1.01	0.000	0.226	0.247
25[13]	0.7675	0.000	0.220	0.0125	0.000	0.856	0.948	0.88	0.119	0.225	0.223
14[13]	0.881	0.000	0.096	0.000	0.023	0.878	0.939	0.90	0.062	0.218	0.195
15[13]	0.849	0.000	0.094	0.000	0.057	0.833	0.824	0.90	0.063	0.242	0.273
16[13]	0.818	0.000	0.092	0.000	0.090	0.792	0.718	0.90	0.063	0.254	0.312
18[13]	0.870	0.000	0.100	0.000	0.030	0.867	0.918	0.90	0.064	0.227	0.217
19[13]	0.686	0.000	0.300	0.000	0.014	0.757	0.981	0.762	0.149	0.224	0.195
20[13]	0.565	0.000	0.4305	0.000	0.0045	0.699	0.995	0.700	0.187	0.227	0.198
21[13]	0.555	0.000	0.442	0.000	0.003	0.695	0.997	0.696	0.190	0.220	0.198
22[13]	0.553	0.000	0.440	0.000	0.007	0.695	0.994	0.696	0.190	0.224	0.207
24[13]	0.710	0.000	0.280	0.000	0.010	0.770	0.985	0.774	0.141	0.229	0.179
23[13]	0.680	0.000	0.310	0.006	0.005	0.832, 0.753	0.978	0.84, 0.76	0.152	0.225	0.208
26[13]	0.920	0.000	0.048	0.0016	0.0016	0.855, 0.844	0.761	0.97 0.95	0.034	0.221	0.246

* Molar fractions of hexane (A), $CHCl_3$ (B), CH_2Cl_2 (C), MBTE (D) and acetonitrile (E).

** Value of ε for localizing solvent (either D or E), derived from ε^0 (expt.).

Consider first the variation of values of ε' with values of $\varepsilon(-D, E)$. The theory discussed in connection with eqn. 12 suggests that plots as in Fig. 2 should result. This is tested in Fig. 4, for the data in Table IV*. These plots in Fig. 4 show that the ε'

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* Fig. 4 requires explanation. When all ε' data for a given localizing solvent were plotted, significant scatter of the data was observed because of the imprecision of these values of ε' (Table IV). The latter are imprecise because the experimental ε^0 values are solute dependent (see below), and small changes in ε^0 can have a large effect on derived values of ε'. To improve the precision of these ε' values, therefore, we

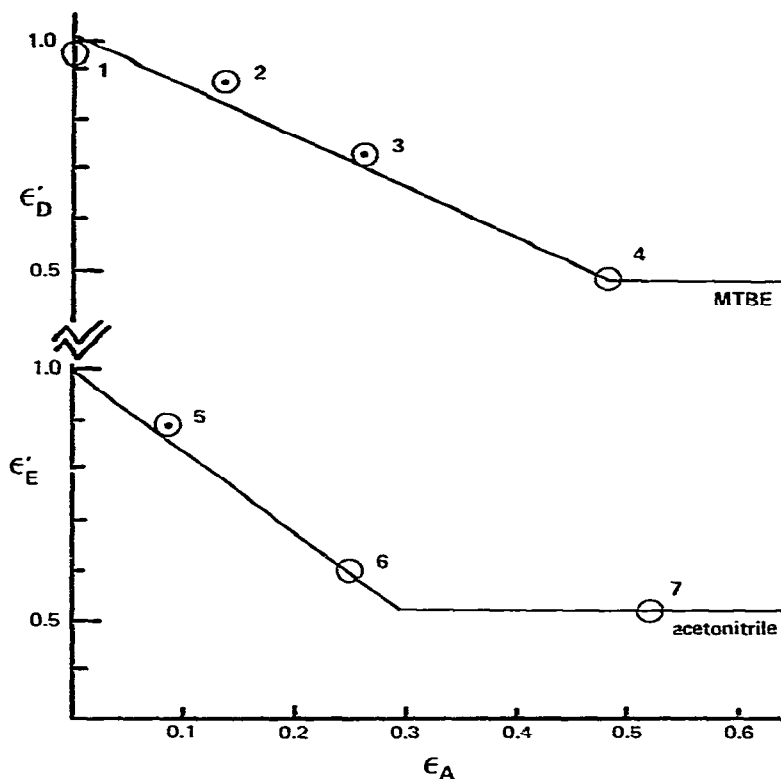Fig. 4. Variation of ε' for localizing solvents D (MTBE) and E (acetonitrile) with change in strength of remaining mobile phase exclusive of D or E (ε_A). 1. Average of MTBE data for A–D mixtures; 2, average of MTBE data in ref. 5, exclusive of A–D mixtures; 3, average of MTBE data of Table I; 4, value of ε''; 5, average of A–C–E mixtures of ref. 12; 6, acetonitrile–hexane mixtures (Table II). A, hexane; B, CHCl$_3$; C, CH$_2$Cl$_2$.

value of the localizing solvent is affected by the composition of the mobile phase exclusive of the concentration of localizing solvent. Moreover, this relationship is given quantitatively by eqn. 12. When the plots in Fig. 4 are used to calculate ε^0 values for the multi-solvent mobile phases in Table IV, the values shown in the last column in Table IV result. These show excellent agreement with experimental values (1 S.D. of 0.015 in ε^0) for the first group of mobile phases (ref. 5, Table I, and Nos. 17 and 25 from ref. 12), which contain MTBE as localizing solvent (D). Agreement is poorer for the acetonitrile-containing mobile phases in the second group of Table IV: ±0.043. The poorer agreement of the latter correlation is surprising, and we are studying it further. However, the overall agreement (all mobile phases) of experimental and

averaged values for several mobile phases of similar composition and value of $\varepsilon(-D, E)$. For example, point 1 in Fig. 4 consists of all MTBE-containing mobile phases of the type A–D, i.e., containing only hexane and MTBE and all having an $\varepsilon(-D, E)$ value of 0.00. Similarly, point 2 in Fig. 4 is the average value for all mobile phases containing MTBE reported in refs. 5 and 13, exclusive of A–D mobile phases [with average value of $\varepsilon(-D, E)$ of 0.13]. Point 3 refers to the data in Table I where the value of $\varepsilon(-D, E)$ is significantly larger. The origin of the other points in Fig. 4 is explained in the caption.

calculated ε^0 values from Table IV is about ± 0.03, which is adequate for purposes of predicting solvent strength in multi-solvent LSC systems with silica as adsorbent. It must be remembered that large solvent selectivity effects occur in these LSC systems, and for a limited group of test solutes used to measure ε^0 this means a corresponding uncertainty in ε^0. Hara *et al.*[11] have reported similar variations in solvent strength for different groups of solutes (steroids *vs.* peptides in ref. 10).

CONCLUSIONS

This study has clarified the origin of certain puzzling effects previously encountered in correlating LSC k' values with solvent strength. Thus, the phenomenon of site-competition delocalization accounts quantitatively for the need to increase solute A_s values in the case of silica as adsorbent when the solute is a localizing compound. Site-competition delocalization also explains the variation of ε' values for localizing solvents as the mobile phase composition and strength are varied. It is further necessary to differentiate site-competition from restricted-access delocalization; the latter occurs for both alumina and silica as adsorbents, whereas the former is found only for silica. The reason for these differences between alumina and silica is believed to arise from the difference in the nature and positioning of adsorption sites. Surface silanols in the case of silica are readily accessible to lateral interactions (as by molecules M in Fig. 1f), as well as direct interactions (as by C in Fig. 1f), because the silanols protrude from the silica surface. The surface hydroxyls present on alumina are inactive as adsorption sites, and the cationic sites responsible for polar interactions between alumina and adsorbing molecules are buried within the underlying alumina matrix[1]. Thus, site-competition delocalization and its concomitant effects are associated only with adsorbents where the adsorption sites are freely exposed to both overhead and lateral interactions. For related discussion of site-competition delocalization in the case of amino-phase columns, see ref. 14. A full review of these and other localization-related effects will be provided elsewhere.

All solvents so far studied as mobile phase constituents for LSC on silica fit the present retention model. Therefore, the quantitative relationships developed here and previously plus solvent strength parameters as summarized in Table III allow the calculation of the solvent strength of a wide range of multi-solvent mixtures. We are at present engaged in reducing this large mass of data for convenient nomogram calculations of solvent strength for use in retention optimization strategies as in ref. 15. These results will be published elsewhere[12].

SYMBOLS

a, b	coefficients in eqn. 12;
a, n	subscripts where a refers to a molecule in the adsorbed phase and n to a non-adsorbed molecule:
A, B, C, D, ...	individual (pure) solvents whose ε^0 values increase from A to D;
A_a, A_n, B_a, B_n	molecules of A or B in adsorbed phase (a) or non-sorbed phase (n);
A_s, A_a, A_c	molecular cross-sectional areas of a molecule of solute (s), solvent A (a) and solvent C (c);

A', B'	coefficients in eqn. 12a;
c'	coefficient in eqn. 1;
E_a, E_c, E_m, E_x	dimensionless free energies of adsorption of solvent A, solvent C, a molecule of mobile phase (M) and solute (X), respectively;
E_c^0	value of E_c for hexane or other non-polar solvent ($\varepsilon^0 = 0.00$) as mobile phase;
k'	solute capacity factor;
k_1, k_2	values of k' for a solute with mobile phases 1 and 2;
M, M_a, M_n	a molecule of mobile phase, in adsorbed (a) or non-sorbed (n) phases;
n	the number of solvent molecules displaced from the adsorbent surface by an adsorbing solute molecule (eqns. 1 and 2);
n_b	the A_x value of a polar solvent molecule; for a mobile phase A–B, A_x for solvent B;
Q_i^0	dimensionless free energy of adsorption of a solute substituent i;
X_a, X_n	molecule of a solute X in the adsorbed (a) or non-sorbed (n) phase;
X_s	mole fraction of B-solvent in a binary solvent mobile phase A–B; eqn. 1;
$\%_{o1c}$	a localization function that describes the variation in ε^0 for a localizing solvent C as a function of θ_C (eqn. 7) (restricted-access delocalization);
α'	adsorbent activity function, equal to 0.57 for chromatographic silicas;
ΔA_s	the apparent increase in a calculated value of A_x (based on molecular dimensions) required to make eqn. 4 valid for the retention of polar solute molecules on silica; see Fig. 3;
Δa_i	the value of ΔA_s for a solute with a single polar substituent i; for polysubstituted solute molecules, ΔA_s is the sum of Δa_i values for each group i in the solute molecule;
ε^0	solvent strength parameter for a mobile phase; equal to E_m/A_m for a mobile phase M;
ε_A, ε_B, ε_C, ...	value of ε^0 for solvents A, B, C, etc.;
ε_1, ε_2	value of ε^0 for mobile phases 1 and 2 (eqn. 4);
ε', ε_C'	for a localizing solvent C, the value of ε_C as θ_C approaches zero; E_c/A_c for the localized molecule C;
ε'', ε_C''	for a localizing solvent C, the value of ε_C as θ_C approaches unity; E_c/A_c for the fully delocalized molecule C;
$\varepsilon(-D, E)$	for a mobile phase A–B–C–D–E as in Table IV, the value of ε^0 for the mobile phase which results if localizing solvents D and E are removed from the mixture;
θ_A, θ_B, θ_C, ...	molar fractions of solvents A, B, C, ..., in the adsorbed monolayer.

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