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MOBILE PHASE EFFECTS IN LIQUID-SOLID CHROMATOGRAPHY

IMPORTANCE OF ADSORPTION-SITE GEOMETRY, ADSORBATE DELOCALIZATION AND HYDROGEN BONDING

L. R. SNYDER

Lloyd R. Snyder, Inc., 2281 William Court, Yorktown Heights, NY 10598 (U.S.A.)

SUMMARY

A comprehensive and detailed physicochemical model is presented for sample retention in liquid-solid chromatography, using either classical adsorbents such as silica or alumina, or polar-bonded-phase packings such as aminoalkyl, diol, etc. Application of the model to a large mass of data for wide variation of adsorbent, mobile phase and solute shows good agreement between theory and experiment. The model is based upon displacement and localization phenomena as primary contributions to retention. Localization phenomena can be sub-classified into at least four distinct effects, and these latter effects can be correlated with the geometry of adsorption sites in various adsorbents. A preliminary model of solute-solvent hydrogen bonding in these liquid-solid chromatographic systems is presented and compared with limited experimental data. The latter effect can be significant in these systems.

INTRODUCTION

The mobile phase in liquid-solid chromatography (LSC) is an incredibly versatile tool for adjusting sample retention to enhance the overall separation (*e.g.*, refs. 1-3). So far the primary emphasis on understanding the basis of mobile phase optimization in LSC has been for classical adsorbents such as alumina and silica (*e.g.*, refs. 2-5). However, there is increasing practical and theoretical interest in the various polar-bonded-phase packings, such as aminoalkyl, cyanoalkyl, diol, etc. (*e.g.*, see refs. 6-8 for aminoalkyl columns). There is every indication that a single retention model, one based on *displacement* of adsorbed mobile phase molecules by adsorbing solute molecules, provides an adequate physical basis to describe both classical and bonded-phase adsorbents^{2-6,8}. In addition to displacement effects, the *localization* of adsorbing solute and solvent molecules can play an important role in determining the retention of polar solutes, and the solvent strength of mobile phases containing polar solvents. These localization effects show interesting differences among the various adsorbents so far studied, and previous work^{8,9} suggests that these differences correlate with the nature of adsorption sites for the different packings used in high-performance liquid chromatography (HPLC).

Other work (e.g., refs. 4, 10, 11) suggests that hydrogen bonding between sample and solute molecules can also play an important role in affecting sample retention and solvent selectivity. However, polar compounds capable of hydrogen bonding will generally also exhibit localized adsorption. The combination of these two effects makes it difficult to sort out their individual contributions to retention in typical LSC systems. Furthermore, hydrogen bonding interactions between solvent and sample (where possible) can occur in both the mobile and adsorbed phases. Consequently, a general theoretical description of such effects will be somewhat complex, and their experimental unraveling represents a considerable challenge.

In the present paper an attempt will be made to fill in some of the gaps in our present understanding of retention in LSC. First, recent data will be used to further test the ability of the displacement model to predict solvent strength and selectivity. Second, retention data plus the displacement model also allow prediction of the adsorption isotherm for binary-solvent mobile phases, and a few comparisons will be shown of such calculated isotherms with experimental data. Third, experimental differences in localization for various adsorbents will be correlated with the known geometry of their adsorption sites. Finally, an initial model of hydrogen-bonding effects in LSC will be presented, particularly as these affect solvent selectivity. The overall emphasis will be on the further development of a comprehensive and detailed model of retention for all polar-phase separations.

THEORY

The following review of earlier work on a retention model for LSC is brief, and descriptive comment is held to a minimum. For a complete summary see refs. 3-5, 8 and 9 and a review¹².

Displacement model without localization

The displacement model assumes that retention of a solute molecule X occurs by displacement of previously adsorbed mobile phase molecules M:



Subscripts n and a refer to molecules in the non-sorbed and adsorbed phases, respectively. The value of n is determined by the area on the adsorbent surface that is required by a molecule of solute, A_s , or mobile phase, A_m :

$$n = A_s/A_m \quad (1a)$$

The displacement model further assumes that interaction energies for X and M with the mobile phase are cancelled by corresponding stationary phase interactions, and by the similarity of these interactions for X and M in either phase; see ref. 12 for a more complete justification. The dimensionless free energy of adsorption, ΔE_{xm} , is then given as:

$$\begin{aligned} \Delta E_{xm} &= \Delta G^0/2.3RT \\ &= E_x - n E_m \end{aligned} \quad (1b)$$

Here, E_x is the interaction energy of X with the adsorbent surface, and E_m is the corresponding energy for M. Eqn. 1b then leads to a general expression for the variation of solute k' values with mobile phase composition:

$$\log(k_1/k_2) = \alpha' A_s (\varepsilon_2 - \varepsilon_1) \quad (2)$$

Here, k_1 and k_2 refer to k' values for a solute X, using mobile phases 1 and 2. The adsorbent activity parameter, α' , is characteristic of a particular lot of adsorbent, and ε_1 and ε_2 refer to solvent strength values (ε^0) for mobile phases 1 and 2, respectively. Solvents 1 and 2 can be pure solvents, or mixtures of two or more solvents.

For the case of mobile phases which are mixtures of two or more solvents, the displacement model allows the calculation of their solvent strength, ε^0 , as a function of the chromatographic properties of the individual solvents. Thus, for a mobile phase A + B, where solvent B is more polar than solvent A, and therefore $\varepsilon_B > \varepsilon_A$,

$$\varepsilon^0 = \varepsilon_A + \frac{\log(N_B K + 1 - N_B)}{\alpha' n_b} \quad (3)$$

where K (the equilibrium constant corresponding to eqn. 1 for displacement of adsorbed molecules A by adsorbing molecules B) is given as:

$$K = 10^{\alpha' n_b (\varepsilon_B - \varepsilon_A)} \quad (3a)$$

Here, N_B is the mole fraction of solvent B in the mobile phase, and n_b is equal to A_m (the cross-sectional area of a molecule B).

Eqn. 3, which predicts the ε^0 value of a binary-solvent mobile phase A + B, can be generalized for the case of mobile phases which contain any number (two, three, four, ...) of component solvents¹³:

$$\varepsilon^0 = \varepsilon_A + \log(N_A/\theta_A)/\alpha' n_b \quad (3b)$$

Here, N_A refers to the mole fraction of the weakest solvent A in the mixture (smallest ε^0 value), and θ_A is the fraction of the surface covered by molecules A. For a binary-solvent mobile phase, $N_A = (1 - N_B)$, and $\theta_A = (1 - \theta_B)$, where θ_B is the fraction of the surface covered by molecules B. The fractional surface coverage by B is

$$\theta_B = N_B K / (N_A + N_B K) \quad (4)$$

where K is given by eqn. 3a. Eqn. 4 applies only to binary-solvent mobile phases. Values of θ_A (for use in eqn. 3b with mobile phases containing three or more solvents) can also be calculated¹³.

Restricted-access delocalization

On the basis of observations summarized in refs. 2-5, 9, 12 and 13 it appears that polar molecules of solute or solvent are subject to adsorbate localization. That is, these molecules (or polar functional groups within the molecule) tend to become fixed at positions on the adsorbent surface where adsorption sites are located; there is then

a strong close-range interaction of the polar adsorbate molecule with a specific adsorption site on the surface of the packing. In the case of mobile-phase mixtures A + B, where B is a polar, localizing solvent, B will adsorb with localization — when the concentration of B in the mobile phase is small; the effective solvent strength, ϵ'_B , under these conditions will be large. However, with increasing coverage of the adsorbent surface by B (up to $\theta_B \approx 0.75$), a point is reached where preadsorbed molecules of B interfere with the localized adsorption of further molecules of B. Further adsorption of B ($0.75 < \theta_B \leq 1.00$) then occurs without localization. This is referred to as restricted-access delocalization of the solvent, meaning that later molecules of B adsorb in a delocalized (*i.e.*, non-localized) state. The effective solvent strength of B for large values of θ_B (ϵ''_B for delocalized B) is correspondingly smaller: $\epsilon''_B < \epsilon'_B$.

It is found experimentally that the effective solvent strength of B in mixtures A + B is given as:

$$\epsilon_B = \epsilon'_B + \%_{\text{olc}} (\epsilon'_B - \epsilon''_B) \quad (5)$$

Here, the function $\%_{\text{olc}}$ is a measure of the relative overall localization of B on the surface; it varies from 1.00 for small values of θ_B (localized B) to 0.00 for large values of θ_B (delocalized B). The localization parameter, $\%_{\text{olc}}$, can be described by the empirical function:

$$\%_{\text{olc}} = (1 - \theta_B) \{ [1/(1 - 0.94\theta_B)] - 14.5 \theta_B^2 \} \quad (5a)$$

As expected, the value of $\%_{\text{olc}}$ changes rapidly in the region of $\theta_B \approx 0.75$, where the transition occurs from localized B to delocalized B.

Site-competition delocalization

The localization of a molecule of solute X or solvent B on the adsorbent surface results in a certain energy of interaction with the surface, E_x or E_b . This interaction energy is larger as a result of localization, and will be decreased if localization is disturbed (as in the above case of restricted-access delocalization). It appears that the adsorption of mobile phase molecules M adjacent to a localized molecule X or B can interfere with the localization of X or B, when the molecule M is polar. Competing interactions between M and the adsorption site are apparently possible, although other reasons exist for this reduction of E_x or E_b as a result of increasing polarity of the mobile phase M. In any case, where site-competition delocalization is possible, it would be expected that the decrease in E_x or E_b will be proportional to the polarity of M or to its solvent strength, ϵ_M . For a solute X, this means that:

$$E_x = E_x^0 - f_1(X) \epsilon_M \quad (6)$$

Here, E_x^0 is the value of E_x when $\epsilon_M = 0$, and $f_1(X)$ is a localization function (different from $\%_{\text{olc}}$) that increases with increasing localization of X. Since the localization of X is a function of the adsorption energy of X for a monofunctional compound, or of the most polar substituent group k in the molecule X, $f_1(X)$ will be a function of this adsorption energy. Substitution of eqn. 6 into eqn. 1b in the derivation of eqn. 2 then leads to an analogous relationship which now includes site-competition delocalization:

$$\begin{aligned}\log(k_1/k_2) &= \alpha' [A_s + f_1(X)] (\varepsilon_2 - \varepsilon_1) \\ &= \alpha' (A_s)_{\text{exptl}} (\varepsilon_2 - \varepsilon_1)\end{aligned}\quad (7)$$

According to eqn. 7, LSC systems where site-competition occurs can exhibit apparent A_s values, equal to $(A_s)_{\text{exptl}}$, that are larger than the values (A_s) calculated from the dimensions of the localizing molecule X.

Site-competition delocalization is also possible for polar solvents B in mixtures A + B, whenever B is capable of localization. Thus, the adsorption energy E_b for B is completely analogous to its adsorption energy as a solute. Therefore, as in eqn. 6:

$$E_b = E_b^0 - f_1(B) \varepsilon_A \quad (8)$$

The solvent strength, ε^0 , of B is given as $E_b/A_b \equiv E_b/n_b$, so for localized B

$$\begin{aligned}\varepsilon'_B &= E_b/A_b \\ &= E_b^0/n_b - [f_1(B)/n_b] \varepsilon_A\end{aligned}$$

where $\varepsilon'_B \geq \varepsilon''_B$. That is, site-competition delocalization reaches a limit at $\varepsilon'_B = \varepsilon''_B$, corresponding to fully delocalized B. The latter relationship can then be written as:

$$\begin{aligned}\varepsilon'_B &= (\varepsilon_B^0)^0 - [f_1(B)/n_b] \varepsilon_A \\ &= a - b \varepsilon_A\end{aligned}\quad (8a)$$

According to eqn. 8a, the localized solvent strength of B in mixtures A + B varies with the value of ε_A . The localization function, $f_1(B)$, is the same function of adsorbate interaction energy, E_b^0 , as the function $f_1(X)$.

Values of $f_1(X)$ or $f_1(B)$ as a function of adsorbate adsorption energy, E_x^0 or E_b^0 , are given in Fig. 3 of ref. 9. Note that for all values of ε_A , $\varepsilon' \leq \varepsilon''$.

The function $f_1(X)$ is referred to in ref. 4 as Δa_i , or the apparent increase in A_s as a result of the localization of some solute group i . Hammers and co-workers^{6,14} have studied the variation of values of $f_1(X)$ for different adsorbents, and have defined the value of $f_1(X)$ relative to silica as standard adsorbent:

$$\gamma = f_1(X)/[f_1(X)]_{\text{sil}} \quad (9)$$

Thus, the experimental parameter γ is larger for a given adsorbent type, when site-competition delocalization is more important for that adsorbent. For silica, $\gamma = 1$.

Limited experimental data for alumina (reviewed in ref. 12) suggest that site-competition delocalization of the solvent does not occur for alumina as adsorbent. Thus, the ε'_B value for the localizing solvent dioxane in ternary-solvent mixtures¹² is independent of the ε^0 value of the remainder of the mobile phase exclusive of dioxane.

Intramolecular delocalization

This phenomenon is not related to mobile phase effects, being strictly a function of the solute X. However, it is included here to complete our discussion of localization effects. For a non-localizing solute molecule X, the interaction energy of

X will usually be the sum of interaction energies of constituent groups i in the molecule X:

$$E_x = \sum^m E_i \quad (10)$$

Here the summation is over the m groups i in the solute molecule, each contributing E_i to the interaction energy E_x . Eqn. 10 leads to the Martin equation¹⁵:

$$R_M = \log k' = \sum^m \Delta R_M \quad (10a)$$

Thus, k' for a multifunctional solute can be related to group contributions to k' : ΔR_M . In LSC systems, eqn. 10a can fail for reasons discussed in ref. 4. One cause of failure is intramolecular delocalization, where the localization of some polar group k in the solute molecule leads to delocalization of remaining groups i in the molecule. That is, once the group k is localized, the adsorbate molecule is "anchored" onto the surface, and remaining groups in the adsorbate molecule cannot achieve an optimum configuration on the surface. This effect can be stated as:

$$E_x = \sum^m E_i - f(Q_k^0) \sum^{m \neq k} E_i \quad (10b)$$

The localization function, $f(Q_k^0)$, increases with the adsorption energy, Q_k^0 , of the group k , and differs from other localization functions so far defined [$\%_{\text{orc}}$ and $f_1(X)$]. The effect of intramolecular delocalization as expressed in eqn. 10b is to lower the value of ΔR_M (eqn. 10a) for a given group i , as a result of the delocalization of i . Hammers *et al.*^{6,14} have studied the variation of this effect for different adsorbents, and have defined a parameter β which expresses the relative importance of intramolecular delocalization for a given adsorbent (*cf.*, eqn. 9):

$$\beta = f(Q_k^0)/[f(Q_k^0)]_{\text{alum}} \quad (10c)$$

The value of β is taken as unity for the adsorbent alumina (alum).

Solvent selectivity

There are three major contributions to solvent selectivity: (a) solvent strength, (b) solvent-solute localization and (c) solvent-solute hydrogen bonding. Solvent-solute localization can be further subdivided according to the basicity of the solvent B. We can discuss these various contributions to solvent selectivity in terms of two mobile phases, A + B and A + C, and two solutes X and Y. If the solute k' values are k_{xb} and k_{xc} for solute X in mobile phases A + B and A + C, respectively, and k_{yb} and k_{yc} for solute Y in mobile phases A + B and A + C, then the separation factors for each mobile phase can be defined as

$$\alpha_b = k_{xb}/k_{yb} \quad (\text{mobile phase A + B}) \quad (11)$$

and

$$\alpha_c = k_{xc}/k_{yc} \quad (\text{mobile phase A + C}) \quad (11a)$$

Solvent selectivity differences for the two mobile phases then result in $\alpha_b \neq \alpha_c$.

Solvent-strength selectivity. If the A_s values of solute X, A_x , and solute Y, A_y , differ, and if the solvent strengths of mobile phase A + B, ε_b , and A + C, ε_c , are not the same, this results in differences in α_b vs. α_c (from eqn. 2):

$$\alpha_c/\alpha_b = \alpha'(A_x - A_y)(\varepsilon_b - \varepsilon_c) \quad (12)$$

A change in solvent strength is usually of limited value in altering α values, because hard-to-separate solutes will generally be similar in their physical and chemical properties, which means that A_x and A_y will also be similar. Therefore, it is recommended to vary ε^0 only for controlling the sample k' range, not for optimizing α . For a further discussion, see ref. 16.

Solvent-solute localization. This effect arises from the competition of localizing solute and solvent molecules for the same adsorption site. As a result, a localizing solvent C will preferentially reduce the retention of a localizing solute X, and the value of α_c (vs. the case of non-localizing solute Y and non-localizing solvent B). This effect can be described (see ref. 3) as:

$$\log(\alpha_c/\alpha_b) = C_1 + C_2 (m_c - m_b) \quad (13)$$

Here, C_1 and C_2 are first-approximation constants for a particular adsorbent and pair of solutes (X and Y). The parameters m_b and m_c are the solvent-selectivity values, m , of the mobile phases A + B and A + C, respectively. The value of m for a mobile phase defines the effect of mobile phase localization on the retention of localizing solute molecules, as in eqn. 13. Increasing values of the solvent parameter m mean increasing mobile phase localization. The value of m for a given mobile phase can be calculated from:

$$m_c = m_c^0 f(\theta_c) \quad (13a)$$

Here, for a mobile phase A + C, m_c^0 is characteristic of the polar, localizing solvent C (increasing with greater localization of C). The localization function, $f(\theta_c)$, varies from zero for $\theta_c = 0$ to one for $\theta_c = 1$.

While eqn. 13 accounts for the major contribution of solvent-solute localization to solvent selectivity, a lesser effect has been noted: solvent-specific solvent-solute localization. The latter effect manifests itself as a variability of the constant C_2 in eqn. 13, which is correlated with the basicity of solvent C as measured by its classification within the "selectivity triangle" of ref. 17. Thus, whereas eqn. 13 predicts similar solvent selectivity for mobile phases of similar m value, solvent-specific selectivity predicts a further effect, according to the basicity of the localizing solvent C in the mobile phase. This is discussed in detail in ref. 3.

Solvent-solute hydrogen bonding. Assume a proton-donor solute X-H and a proton-acceptor solvent C, such that hydrogen bonding in either phase is possible



to give the complex XH-C. We can then define equilibrium constants K^{cx} (mobile phase) and K^{cx*} (adsorbed phase):

$$K^{cx} = (\text{XH-C})_n / (\text{XH})_n N_C \quad (14a)$$

$$K^{cx*} = (\text{XH-C})_a / (\text{XH})_a \theta_C \quad (14b)$$

The capacity factor of X with A + C as mobile phase is then

$$k_{xc} = (V_a/V_n) \left[\frac{(\text{XH})_a + (\text{XHC})_a}{(\text{XH})_n + (\text{XHC})_n} \right] \quad (14c)$$

where (V_a/V_n) is the phase ratio, and $(i)_j$ refers to the concentration of i in the adsorbed (a) or non-sorbed (n) phase. Eqns. 14a-c then yield:

$$k_{xc} = (V_a/V_n) K_{xc} \left(\frac{1 + K^{cx*} \theta_C}{1 + K^{cx} N_C} \right) \quad (14d)$$

Here, the quantity $K_{xc} = (\text{X})_a / (\text{X})_n$; it is the distribution constant in the absence of hydrogen bonding.

The values of k_{xb} , k_{yc} and k_{yb} are given as $(V_a/V_n)K_{xb}$, $(V_a/V_n)K_{yc}$ and $(V_a/V_n)K_{yb}$, because hydrogen bonding of solute and solvent does not occur for these combinations (only XH and C hydrogen bond, by definition). These relationships can be combined with eqn. 14d to yield:

$$\alpha_c/\alpha_b = \left(\frac{1 + K^{cx*} \theta_C}{1 + K^{cx} N_C} \right) \quad (14e)$$

Eqn. 14e gives the effect of hydrogen bonding between XH and C, apart from other solvent-selectivity effects; *i.e.*, it is assumed that $\epsilon_b = \epsilon_c$ and $m_b = m_c$. If the latter selectivity effects (eqns. 12, 13) are included, overall solvent selectivity is given as:

$$\begin{aligned} \log(\alpha_c/\alpha_b) &= C_1 + \alpha'(A_x - A_y) (\epsilon_b - \epsilon_c) + C_2 (m_c - m_b) \\ &+ \log \left(\frac{1 + K^{cx*} \theta_C}{1 + K^{cx} N_C} \right) \end{aligned} \quad (15)$$

Considering hydrogen-bonding selectivity only (eqn. 14b), it can be assumed that the binding constants K^{xc} and K^{cx*} will in general differ, because hydrogen bonding in the stationary phase will often involve localized molecules of XH and C. Localization must have an effect on the acidity and basicity of adsorbate molecules, since a strong interaction between adsorbate molecule and surface site is involved (*e.g.*, hydrogen bonding between silica silanols and localized molecules). Likewise, a basic solvent molecule C will be preferentially adsorbed from the mobile phase in most cases, which means that usually $\theta_C \gg N_C$. We will explore the consequences of these relationships in the following section.

RESULTS AND DISCUSSION

Solvent strength

Consider first the experimental verification of eqn. 2 for various adsorbents. The linearity of plots of $\log k'$ vs. ϵ^0 has been demonstrated in many studies referenced in ref. 4 for alumina and silica. Similar plots have been shown for an aminoalkyl packing⁸. The slopes of these $\log k'$ vs. ϵ^0 plots are equal to $\alpha' A_s$, from which values of $(A_s)_{\text{exptl}}$ can be derived and compared with values calculated from solute geometry and dimensions. For alumina as adsorbent, $(A_s)_{\text{exptl}} = A_s$ in almost every case. Thus, in one study¹⁸ 52 solutes were studied, using different pairs of pure solvents as mobile phases: pentane-carbon tetrachloride, carbon tetrachloride-benzene and benzene-methylene chloride. An overall average A_s value was found of 10.3 (exptl.), vs. a value of 10.1 (calc.). Calculated A_s values ranged from 5 to 21, and experimental values agreed with these latter values within ± 1.5 units (1 S.D.). In the case of silica and various bonded-phase adsorbents^{4,6,8,14}, values of $(A_s)_{\text{exptl}}$ agree closely with calculated values A_s , as long as the solute molecule is weakly polar and therefore non-localizing. Fig. 1 for several aromatic hydrocarbons and polyethoxylated nonyl phenols with an amino-phase packing shows good agreement (± 1.8 units for $8 \leq A_s \leq 46$) between experimental and calculated values of A_s .

For more polar, localizing solute molecules, several studies have shown that $(A_s)_{\text{exptl}}$ is greater than A_s , and the difference ΔA_s [equal to $f_1(X)$ for monofunctional solutes] correlates closely with the relative retention of polar, localizing groups k

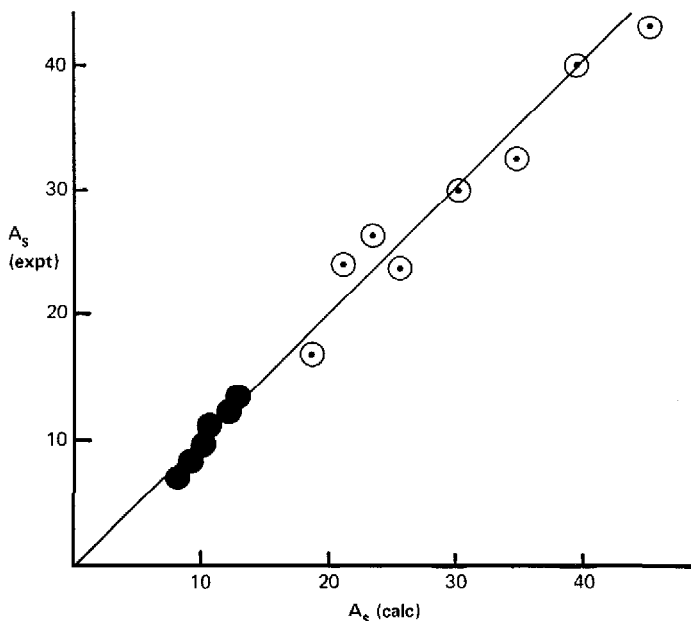


Fig. 1. Experimental A_s values (eqn. 2 or 7) for aromatic hydrocarbons (●) and polyethoxyphenols (○) as solutes, and an amino-phase adsorbent (data of ref. 8) plotted against values calculated from solute cross-sectional area (as in ref. 4).

within the solute molecule: silica⁴, partially silanized silica¹⁴, and amino-alkyl silica^{6,8}. This agrees with our model for site-competition delocalization.

ϵ_B values for mobile phases *A + B*. Previous papers^{9,13,19} have summarized about 200 experimental ϵ^0 values for various binary-solvent mobile phases *A + B* and alumina or silica as adsorbent. When various localization phenomena are taken into account (eqns. 5 and 8a), it is possible to calculate values of ϵ^0 via eqn. 3 with an overall precision of ± 0.016 units, for a range in ϵ^0 of 0.02–0.66. A similar precision is found for ternary- and quaternary-solvent mobile phases (alumina and silica), using eqn. 3b^{9,13}.

Correction for restricted-access delocalization (eqn. 5) is required for alumina and silica¹⁹, but not for amino-phase columns⁸. The effect for silica and alumina is best seen in plots of experimental ϵ_B values vs. calculated values of θ_B . Thus, eqns. 3 and 3a can be solved for the apparent value of ϵ_B as a function of an experimental ϵ^0 value for the mobile phase, plus known values of ϵ_B of the other parameters. Fig. 2 shows resulting plots of ϵ_B vs. θ_B for different mobile phases *A + B* and either silica or alumina as adsorbent. Values of θ_B were determined from derived values of ϵ_B and eqn. 4.

For the case of less polar, non-localizing solvents *B*, the data of Fig. 2a show that the *B*-solvent adsorption energy, ϵ_B , is essentially constant as N_B and θ_B are varied. With increasing polarity and greater localization of solvent *B* (Fig. 2b; calculated plots from eqn. 5a), ϵ_B becomes a function of θ_B , increasing as θ_B decreases. This reflects restricted-access delocalization of *B* at higher values of θ_B . The ability of eqn. 5 to correlate values of ϵ_B as in Fig. 2b is shown in Fig. 3. The curves in each case are from eqn. 5a, which was derived from earlier studies of alumina¹⁹. The data points are from refs. 20 and 21 for silica, as reviewed in ref. 9. In Fig. 3a, for mixtures of various polar solvents *B* with hexane, it is seen that the data fall on top of the earlier curve for alumina. The plot for isopropanol as solvent *B* is displaced to the right, to better show its equally good correlation with eqn. 5a. Similar plots are shown in Fig. 3b for various solvents *B* in admixture with benzene as solvent *A*. For various reasons the determination of ϵ_B is less precise in these cases; the uncertainty lines through each point assume an error in the original mobile phase ϵ^0 value of ± 0.005 units (which is a reasonable estimate). The various plots of Fig. 3 confirm the existence of restricted-access delocalization for alumina and silica as adsorbents. The fact that %_{olc} vs. θ_B plots are described by the same function (eqn. 5a) is expected, in view of the essentially geometrical origin of this effect, with completion of a localized monolayer of *B* at $\theta_B \approx 0.75$. These data also confirm that accurate predictions of ϵ_B and ϵ^0 should be possible.

Fig. 4 shows a similar plot of ϵ_C vs. θ_C (data of refs. 20 and 21) for the polar solvent-*C* acetone in admixture with hexane (open circles) or benzene (closed circles) as solvent *A*. It is clear that the limiting value of ϵ_B at low values of θ_B (equal to ϵ'_B) is greater for hexane as solvent *A* than for benzene. This reflects site-competition delocalization of the solvent *B* in the presence of the more polar solvent-*A* benzene (eqn. 8a). Values of ϵ'_B derived as in Fig. 4 (via eqn. 5) can be correlated with ϵ'_B for hexane as solvent *A*, using eqn. 8a⁹. The function $f_1(B)$ as a function of E_B^0 was shown in ref. 9 to be the same as $f_1(X)$ in eqns. 6 and 7 — as predicted by theory.

Solvent selectivity

Non-hydrogen-bonding systems. Consider first the case where solute and solvent

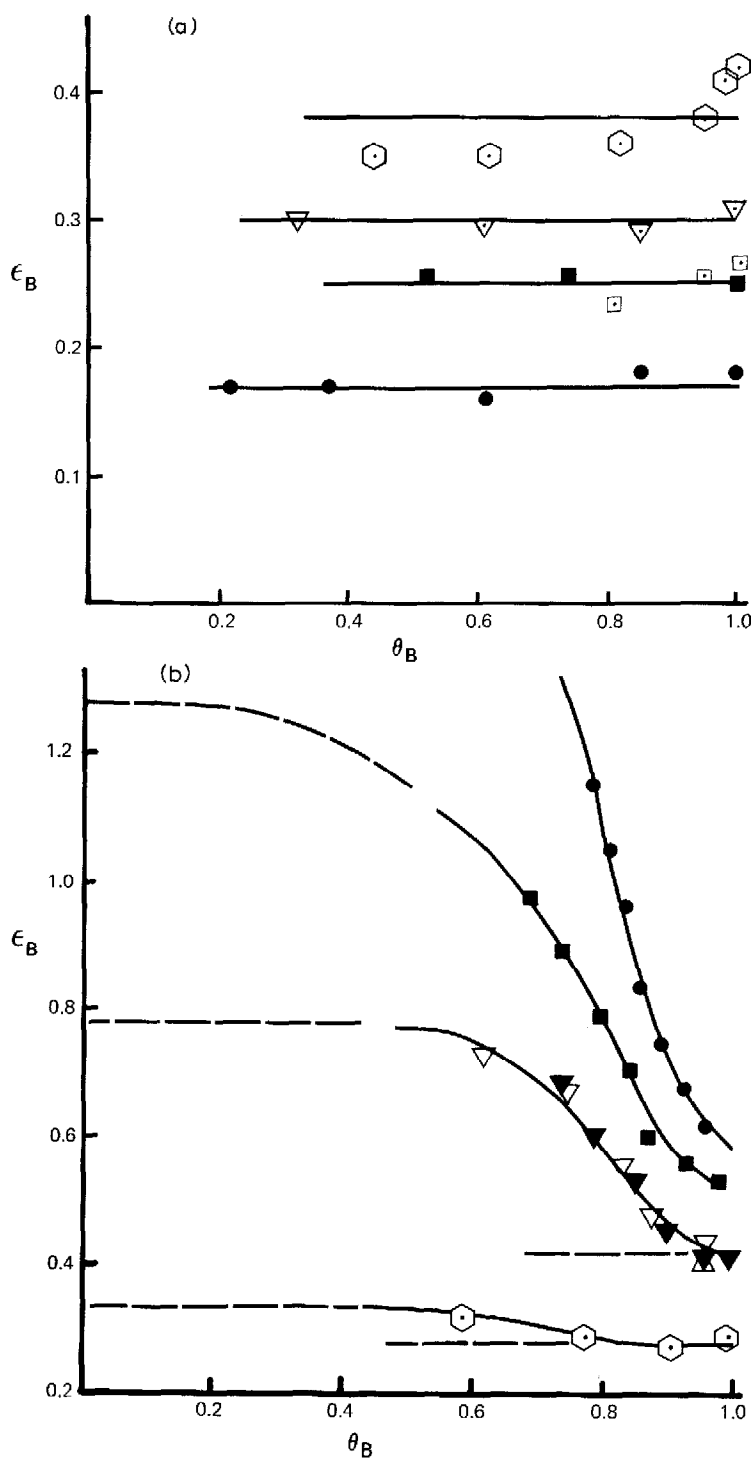


Fig. 2. Experimental values of ϵ_B (from eqn. 3 and data summarized in ref. 9) versus calculated values of θ_B . (a) Non-localizing solvents B: ●, carbon tetrachloride + pentane/alumina; ■, benzene + pentane/silica; □, benzene + hexane/silica; ▽, methylene chloride + pentane/silica; ⊕, methylene chloride + pentane/silica, (b) Localizing solvents B (curves are best fit of eqns. 5 and 5a to data); ⊕, diisopropyl ether + pentane/alumina; ▼, diethyl ether + pentane/silica; ▽, diethyl ether + hexane/silica; ■, acetone + hexane/silica; ●, isopropanol + hexane/silica.

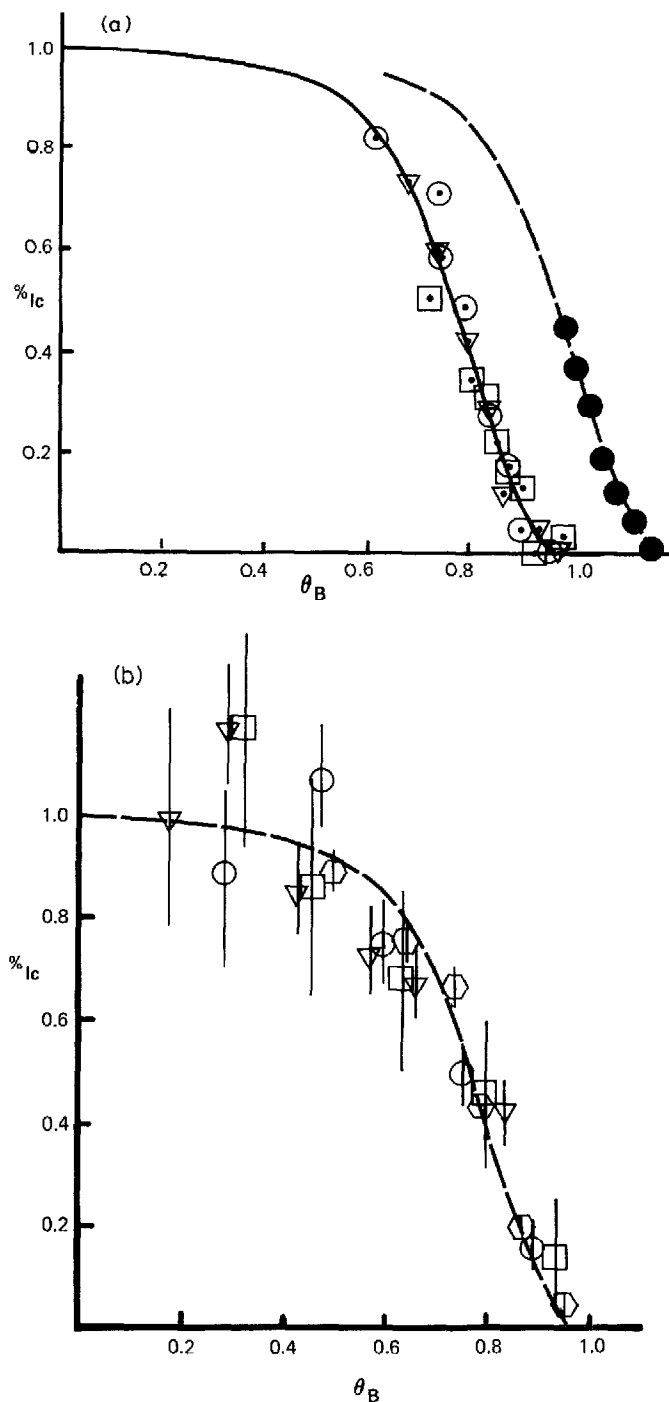


Fig. 3. Experimental values of localization function, $\%lc$, for various localizing solvents B, as a function of surface coverage, θ_B (from data of ref. 9), for silica as adsorbent. (a) Solvent A is hexane; data for isopropanol (●) displaced to right by 0.2 units in θ_B ; (b) solvent A is benzene. For identification of individual solvents B, see ref. 12.

cannot hydrogen bond to each other, because of the absence of proton-donor groups in either molecule. The localization of polar solute molecules on all of the polar-phase adsorbents can be inferred from the various delocalization effects discussed in the Theoretical section and confirmed in various experimental studies (*e.g.*, see above). This in turn suggests that solvent-solute delocalization and eqn. 13 will apply for localizing solutes and each of the polar-phase adsorbents (both classical and bonded-phase). This has been confirmed experimentally for about 70 different solutes, 20 different solvents B, 80 different mobile phases (including binary-, ternary- and quaternary-solvent mixtures) and both alumina and silica as adsorbent^{2,3,22}. In each of these cases, eqn. 13 provides a reasonable correlation of experimental k' values or separation factors, α , and resulting experimental m values can be correlated with eqn. 13a. The function $f(\theta_c)$ of eqn. 13a varies with θ_c as described in ref. 3, and this relationship correlates well with the model proposed for solvent-solute localization and solvent selectivity. The coefficient C_2 of eqn. 13 can be rationalized with differences in solute localization as reflected by solute Q_k^0 values (Fig. 3 of ref. 2). Several-hundred-fold variations in α as a result of changes in mobile phase composition (and localization m) are possible for a solute pair of quite different functionality². Interestingly, closely similar compounds such as diastereomers can also exhibit up to three-fold change in α as a result of change in the mobile-phase m value²².

Hydrogen-bonding systems. Eqn. 15 gives the expected effect of solvent-solute hydrogen bonding on solvent selectivity. However, this expression includes contri-

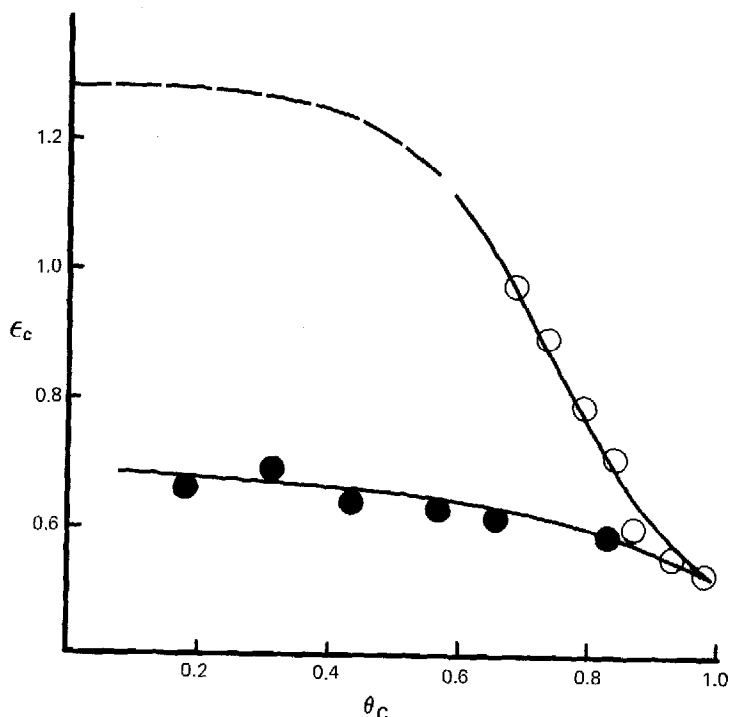


Fig. 4. Experimental values of ϵ_c (as in Fig. 2) versus calculated values of θ_c , for acetone as solvent C. Solvent A is hexane (O) or benzene (●). Mobile phases A + C.

TABLE I

EFFECT OF HYDROGEN BONDING ON SOLVENT SELECTIVITY

Variation of α for 1-naphthol/1-acetonaphthalene in LSC system of refs. 3 and 13. Mobile phases are mixtures of hexane, chloroform and methylene chloride with methyl *tert.*-butyl ether (MTBE) or acetonitrile.

| Mobile phase* | N_D^{**} | θ_D^{***} | N_E^{**} | θ_E^{***} | m^\S | $\epsilon^0{}^{\S\S}$ | $(\log \alpha)_{corr}{}^{\S\S\S}$ |
|---------------|------------|------------------|------------|------------------|--------|-----------------------|-----------------------------------|
| 1 | 0.000 | 0.00 | 0.000 | 0.00 | 0.09 | 0.223 | 0.067 |
| 2 | 0.000 | 0.00 | 0.000 | 0.00 | 0.05 | 0.222 | 0.054 |
| 3 | 0.044 | 0.78 | 0.000 | 0.00 | 0.81 | 0.241 | 0.261 |
| 4 | 0.013 | 0.41 | 0.000 | 0.00 | 0.44 | 0.248 | 0.219 |
| 5 | 0.013 | 0.46 | 0.000 | 0.00 | 0.32 | 0.240 | 0.306 |
| 6 | 0.000 | 0.00 | 0.000 | 0.00 | 0.16 | 0.236 | 0.149 |
| 7 | 0.008 | 0.23 | 0.000 | 0.00 | 0.24 | 0.252 | 0.249 |
| 8 | 0.006 | 0.23 | 0.000 | 0.00 | 0.24 | 0.234 | 0.224 |
| 9 | 0.002 | 0.04 | 0.000 | 0.00 | 0.15 | 0.225 | 0.051 |
| 10 | 0.003 | 0.08 | 0.000 | 0.00 | 0.20 | 0.233 | 0.148 |
| 11 | 0.039 | 0.72 | 0.000 | 0.00 | 0.60 | 0.250 | 0.238 |
| 12 | 0.022 | 0.73 | 0.000 | 0.00 | 0.71 | 0.219 | 0.327 |
| 13 | 0.087 | 0.82 | 0.000 | 0.00 | 0.66 | 0.273 | 0.131 |
| 14 | 0.000 | 0.00 | 0.023 | 0.47 | 0.75 | 0.218 | 0.504 |
| 15 | 0.000 | 0.00 | 0.057 | 0.63 | 0.85 | 0.242 | 0.523 |
| 16 | 0.000 | 0.00 | 0.090 | 0.69 | 0.83 | 0.254 | 0.493 |
| 17 | 0.042 | 0.78 | 0.000 | 0.00 | 0.68 | 0.226 | 0.284 |
| 18 | 0.000 | 0.00 | 0.030 | 0.52 | 0.68 | 0.227 | 0.508 |
| 19 | 0.000 | 0.00 | 0.014 | 0.23 | 0.43 | 0.224 | 0.273 |
| 20 | 0.000 | 0.00 | 0.004 | 0.06 | 0.17 | 0.227 | 0.119 |
| 21 | 0.000 | 0.00 | 0.003 | 0.04 | 0.16 | 0.220 | 0.088 |
| 22 | 0.000 | 0.00 | 0.007 | 0.09 | 0.21 | 0.224 | 0.128 |
| 23 | 0.006 | 0.17 | 0.005 | 0.09 | 0.34 | 0.225 | 0.330 |
| 24 | 0.000 | 0.00 | 0.010 | 0.19 | 0.33 | 0.229 | 0.215 |
| 25 | 0.012 | 0.44 | 0.000 | 0.00 | 0.37 | 0.225 | 0.238 |
| 26 | 0.016 | 0.34 | 0.016 | 0.33 | 0.69 | 0.221 | 0.357 |

* Numbering system of refs. 3 and 13 (Tables IV and II, respectively; Nos. 10–13 of ref. 13 were originally labeled Nos. 11–14).

** Mole fractions of MTBE (D) and acetonitrile (E) in mobile phase.

*** Surface coverage of MTBE (D) or acetonitrile (E); eqn. 4 plus experimental values of ϵ^0 .

§ Value of m for mobile phase, from Table V of ref. 3.

§§ Experimental ϵ^0 values for mobile phase.

§§§ Value of α corrected to $\epsilon^0 = 0.237$, using eqn. 12.

butions from solvent-strength selectivity (eqn. 12) and solvent-solute localization selectivity (eqn. 13). Consider the application of eqn. 15 to some appropriate experimental data where solvent-solute hydrogen bonding is expected. Glajch and co-workers^{3,13} have reported retention data on silica for 1-naphthol (XH) and 1-acetonaphthalene (Y), using various mobile phases; the latter comprise binary-, ternary- and quaternary-solvent mixtures, including basic solvents such as methyl *tert.*-

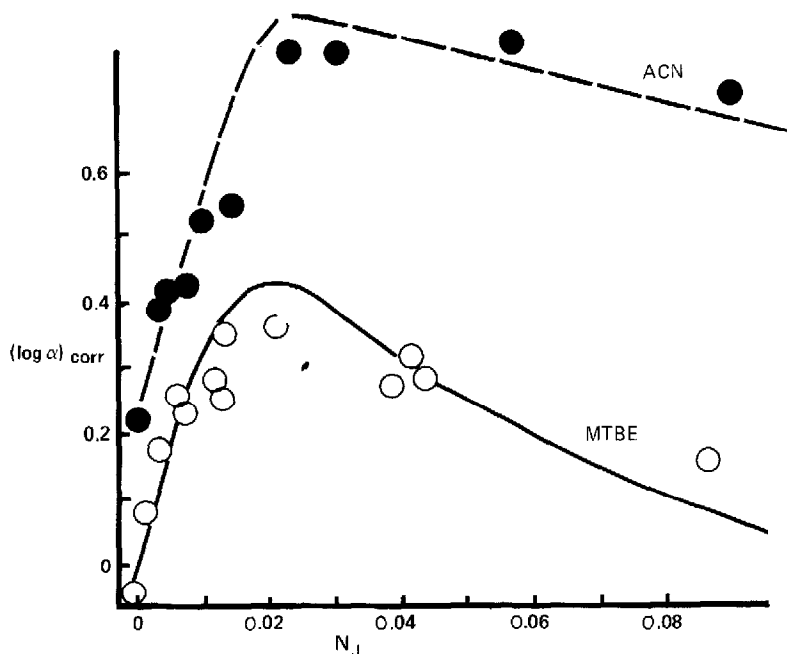


Fig. 5. Hydrogen-bonding effects in LSC of 1-naphthol and 1-acetonaphthalene on silica (data of Table I). Corrected separation factors vs. basic-solvent (MTBE or ACN) mole fraction, N_j . ACN curve (top) displaced vertically by +0.2 log units.

butyl ether (MTBE) (D) and acetonitrile (E) in admixture with the non-basic solvents hexane, chloroform and methylene chloride. Where a single basic solvent (either MTBE or acetonitrile) is included in the mobile phase, eqn. 15 should apply for the solutes in question. Table I summarizes these data, including derived values of N_j and θ_j for localizing (basic) solvents J in the mobile phase mixture. One potential problem in evaluating eqn. 15 and hydrogen-bonding effects is avoided here, that due to large variations in ϵ^0 for the mobile phase. Thus, the exclusive use of binary-solvent mobile phases A + J restricts the range of N_j values for which convenient k' values can be obtained, and likewise increases the contribution of the second term of eqn. 15. Each of these effects introduces experimental error in the evaluation of the fourth term of eqn. 15 (the hydrogen-bonding term). In Table I the use of ternary- and quaternary-solvent mobile phases, where the proportions of hexane, methylene chloride and chloroform can be varied, allows ϵ^0 to be held roughly constant while N_j (*i.e.*, N_D , N_E in Table I) is varied over wide limits. Residual small differences in ϵ^0 can be accurately estimated from eqn. 12, yielding (from eqn. 15):

$$\begin{aligned} \log (\alpha_c / \alpha_b)_{\text{corr}} &= \log (\alpha_c / \alpha_b) - \alpha' (A_x - A_y) (\epsilon_b - \epsilon_c) \\ &= C_1 + C_2 (m_c - m_b) + \log \left(\frac{1 + K^{\text{ex}} \theta_c}{1 + K^{\text{ex}} N_c} \right) \end{aligned} \quad (16)$$

In order to test the present hydrogen-bonding model, the data of Table I are plotted in Fig. 5 as separate curves for the basic solvents MTBE (open circles) and acetonitrile (closed circles). Regression analysis can be used to provide a best fit of these data to eqn. 16, however at this point it is not clear that the data are sufficiently precise to differentiate the effects of C_2 and $K^{\text{cx}*}$ on α . Further analysis of these and other data will be reported elsewhere. The plots of Fig. 5 do show an initial increase in values of $(\log \alpha)_{\text{corr}}$ vs. N_J as a result of increase in m and/or θ_J , *cf.*, eqn. 16. At higher concentrations of J , mobile-phase hydrogen bonding becomes more important, with a resulting decrease in α . Analysis of these data in terms of eqn. 16 does indicate that values of $K^{\text{cx}*}$ are significantly smaller than are values of K^{cx} , which could have been expected.

For mobile phases containing two basic solvents, D and E, in the case of solutions 23 and 26 of Table I, eqn. 16 can be expanded to:

$$\log (\alpha_{\text{de}}/\alpha_{\text{b}}) = C_1 + C_2 (m_{\text{de}} - m_{\text{b}}) + \log \left(\frac{1 + K^{\text{dx}*}\theta_{\text{D}} + K^{\text{cx}*}\theta_{\text{E}}}{1 + K^{\text{dx}}N_{\text{D}} + K^{\text{ex}}N_{\text{E}}} \right) \quad (16a)$$

Here, α_{de} refers to the value of α for the mobile phase containing D + E, m_{de} is the m value for this mobile phase and $K^{\text{cx}*}$ and K^{ex} refer to hydrogen-bonding constants analogous to $K^{\text{cx}*}$ and K^{cx} , for the basic solvent E.

Delocalization effects and the structure of adsorption sites for different adsorbents

Preceding sections have presented a theoretical analysis of the various delocalization-related effects that involve the mobile phase and/or solute. Experimental data for different adsorbents show when each of these delocalization effects arises for a given polar-phase packing, as summarized in Table II.

Five different localization/delocalization phenomena are listed in Table II; their relative importance in retention on four different LSC adsorbents is described on the basis of data reviewed in preceding sections. The four adsorbents are alumina, a partly silanized C_{18} -silica, silica and aminoalkyl silica ("amino-silica"). Before we examine these data as a function of adsorbent type, consider what is known concerning the structure of adsorption sites on these various packings. This is graphically summarized in Fig. 6, where in each case the adsorption site is circled.

For alumina, it is known⁴ that the surface is covered with oxide and hydroxyl groups as shown in Fig. 6, but these groups do not interact strongly with typical solvents and solutes. Rather, the primary sites are cationic or acidic in nature²³, and are believed to be aluminum ions in the second layer (or possibly defect sites of similar character). Thus, these sites are buried within the adsorbent, rather than being exposed for covalent interactions at the surface, and are rigidly positioned with respect to the surface.

In the case of silica, it is known that the sites are surface silanols^{4,5}. These extend above the adsorbent surface, so are fully accessible for covalent bonding — and such silanol-adsorbate interactions have been observed spectroscopically. The positions of silanol groups are fixed on the silica surface.

A partially silanized silica, such as the C_{18} -silica studied by Hammers *et al.*¹⁴, is similar to silica in its retention properties and in the nature of the surface sites. These are silanols, the only difference being their partial shielding by surrounding alkyl

TABLE II
LOCALIZATION/DELOCALIZATION EFFECTS FOR DIFFERENT ADSORBENTS

The nature of adsorption sites in each case.

| <i>Delocalization effect</i> | <i>Alumina</i> | <i>C₁₈-silica</i> | <i>Silica</i> | <i>Amino-silica</i> |
|--------------------------------------|----------------|------------------------------|---------------|---------------------|
| Intramolecular solute (β) | 1.0 | 0.5 | 0.4 | 0.3 |
| Site-competition solute (γ) | 0.0 | 0.6 | 1.0 | 1.0-1.1 |
| solvent | 0.0 | ? | 1.0 | ? |
| Restricted-access | Yes | ? | Yes | No |
| Solvent-solute selectivity | Yes | ? | Yes | Yes |
| <i>Nature of sites</i> | | | | |
| Positions fixed on surface? | Yes | Yes | Yes | No |
| Sites exposed above surface? | No | Partial | Yes | Yes |

groups, which means that they are partially exposed to (or "partially hidden" from) adsorbing molecules.

Amino-silicas are bonded with alkylamino groups; the adsorption site is believed to be the amino group, which is attached by a flexible propyl or butyl chain to the surface^{7,8}. Therefore, these sites are fully exposed for covalent interaction with the adsorbate, but their precise position on the surface is not fixed within narrow limits, as for the other adsorbents of Table II.

The localization of polar adsorbates on the packing surface should be affected by the geometry of the adsorption site, as we will shortly see. Localization can also be affected by the surface concentration of these sites, when a monolayer of adsorbate molecules must compete for a more limited number of sites. However, the concentration of sites for the adsorbents of Table II is generally in the range of 2 $\mu\text{moles}/\text{m}^2$ or larger (*e.g.*, refs. 4 and 8), which means that more sites are available than are required for one-to-one interaction between site and adsorbate molecule. Therefore, the varying concentration of adsorption sites for the packings of Table II should be less important in affecting localization and delocalization.

Consider first intramolecular delocalization of the solute, as summarized in Table II. According to the value of β (eqn. 10c), this effect is most important for alumina ($\beta = 1$) and least important for aminoalkylsilica ($\beta = 0.3$), with C_{18} -silica and silica falling in-between. Theoretically we expect that intramolecular delocalization should be greater for rigidly positioned sites, and less important for more exposed sites. The reason is that intramolecular delocalization arises as a result of the inability of two or more groups within the solute molecule to overlap two adjacent sites on the adsorbent surface. As the distance between sites becomes "adjustable", and/or the sites become more accessible for a variety of interaction positions, it should become easier for localization of several solute groups to occur simultaneously—with a decrease in intramolecular delocalization. In terms of the known geometry of the adsorbents of Table II and of their surface sites, we can say the following: alumina exhibits fixed sites that are inaccessible for covalent interaction; C_{18} -silica sites are fixed, but partly exposed; silica sites are fixed and fully exposed and amino-silica sites

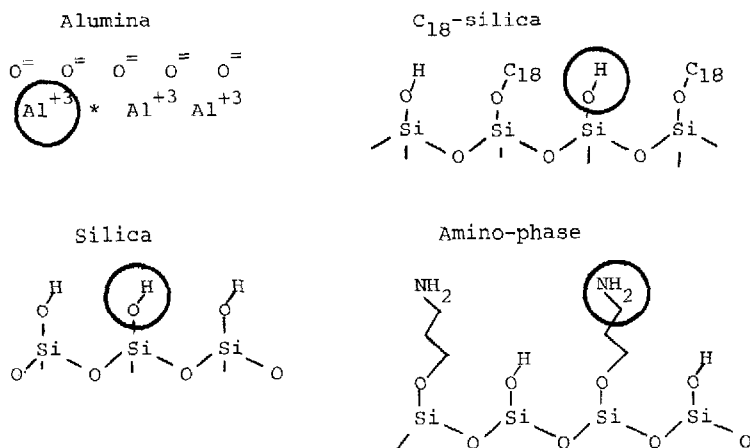
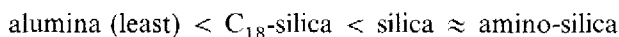


Fig. 6. Adsorption sites (circled) for various LSC packings: * refers to "vacancy" or "defect" site.

are not fixed and are fully exposed. Thus the sequence of β values in Table II is predictable.

Turning next to site-competition delocalization of solute and solvent (Table II), we see for the solute that the effect is least important for alumina ($\gamma = 0.0$, eqn. 9) and most important for amino-silica ($\gamma = 1.0$ – 1.1), with C_{18} -silica and silica intermediate. The same order should be observed for the solvent, and this is the case for alumina (no effect) and silica (effect observed, equal to that for solute). What does theory predict, in terms of the known properties of these adsorbent sites? The effect should be more important as the accessibility of the site increases, and we have already noted that accessibility is in the order:



Thus, the nature of these sites again explains the relative importance of site-competition delocalization for the various adsorbents.

There is one interesting exception to the observation that alumina is free from site-competition-delocalization effects. The A_s values of the various benzopyrrole derivatives (where the polar localizing group is $=NH$) are about 2.6 units smaller than values of $(A_s)_{\text{exptl}}$, suggesting delocalization of the solute molecule⁴. Acidic compounds such as the pyrroles are preferentially retained on alumina vs. silica, and this has been attributed to interaction of the $=N-H$ group with surface oxide sites (an acid-base interaction). Since the surface oxide sites on alumina are fully exposed, it could have been predicted that localizing, acidic solutes would indeed exhibit larger $(A_s)_{\text{exptl}}$ values for alumina. It would be further expected that methylation of the pyrrole ring, to form the N-methylpyrrole derivative, would lead to values of $(A_s)_{\text{exptl}}$ that are equal to calculated A_s values, and this also is observed⁴.

Restricted-access delocalization is simply a function of whether the sites are fixed on the surface, and we therefore predict that alumina, C_{18} -silica and silica will each exhibit this effect, while amino-silica will not. This is observed.

Finally, solvent-solute selectivity reflects the ability of adsorbates to adsorb

with localization. Localization effects are observed for all four of the adsorbents of Table II, so solvent-solute localization selectivity would be predicted for each adsorbent. This is in agreement with experimental data, as summarized in Table II.

Binary-solvent isotherm data

Adsorption isotherm data for several chromatographically useful binary-solvent mobile phases A + B have been reported for silica as adsorbent^{5,24}. It is interesting to see how well eqn. 4 with parameters determined from retention data is able to predict experimental isotherms for binary-solvent mobile phases and dry silica samples. The conversion of θ_B values into grams of B per gram of silica requires that we know the surface area of the silica and the maximum g/m² of adsorbed solvent B (w^0). For the silica described in the isotherm studies of refs. 5 and 24, this information is known and has been tabulated (Table III of ref. 5). Fig. 7 (solid curves) shows the resulting calculated isotherms for five different binary-solvent systems, based on eqn. 4 and retention data from refs. 9 and 19 and summarized in ref. 12.

The resulting correlations of experimental and calculated isotherm data shown in Fig. 7 show rather good agreement. In view of the approximations involved, and differences in the experimental isotherm and retention systems that yield these plots* it is probably a mistake to attempt a detailed examination of the deviations of experimental points from the calculated curves (but see ref. 12 for such a comparison). In Fig. 7e for isopropanol-heptane, the deviation of data points at large values of N_B could correspond to pore filling or other multi-layer adsorption processes for this very polar solvent B.

CONCLUSIONS

The present study and review of earlier work has led to a detailed and comprehensive formulation of the displacement-localization model of retention in LSC with polar-phase adsorbents. One set of derived equations, based on this model, is able to provide quantitative agreement with experimental retention data for a wide range of experimental conditions, involving major changes in adsorbent, mobile phase and solutes. There is no need to invoke arbitrary differences in the way retention is treated for different adsorbents, although various adsorbents show major differences in retention. Rather, these retention differences are seen to be the natural consequence of the geometry of the adsorption sites in different LSC packings. A knowledge of site geometry in turn allows us to predict observed differences in separation on different adsorbents.

The model can be critically tested by comparing the values of certain secondary retention parameters with values predicted by the model. Thus, the apparent solvent strength of the more polar solvent in a mobile phase A + B shows a variety of dependencies on the concentration of that solvent in the mobile phase. These effects

* The studies of refs. 5 and 24 furnish isotherm data for water-free adsorbent and mobile phase, while most prior studies of LSC retention on silica have used water-deactivated adsorbent. Furthermore, the adsorbent samples used in the retention studies have generally differed in terms of surface area and pore dimensions from the samples used in the isotherm studies. On the other hand, it has been argued⁴ that the surfaces involved in these two cases (which generally have smaller pores where water deactivation was used) show similar adsorption of polar molecules.

can be completely rationalized in terms of the physicochemical processes upon which the present model is based. This in turn leads to accurate predictive relationships for solvent strength as a function of mobile phase composition, regardless of the complexity of the mobile phase.

The model can also be tested by comparing experimental isotherm data for

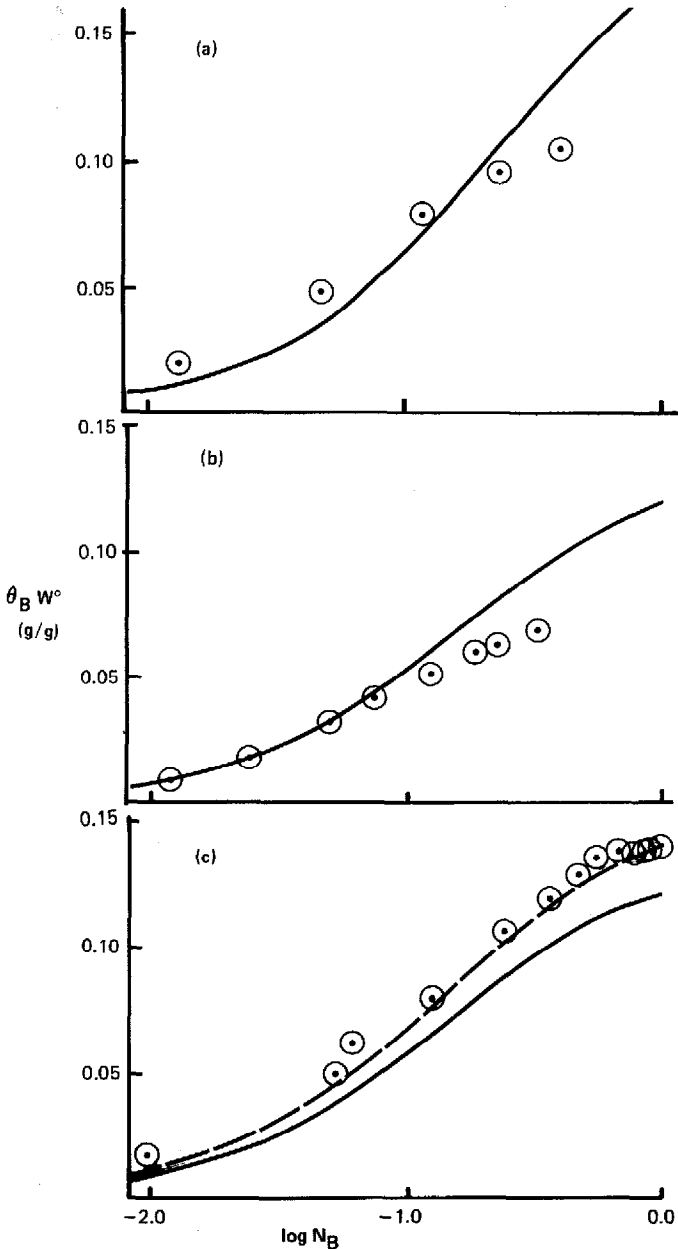


Fig. 7.

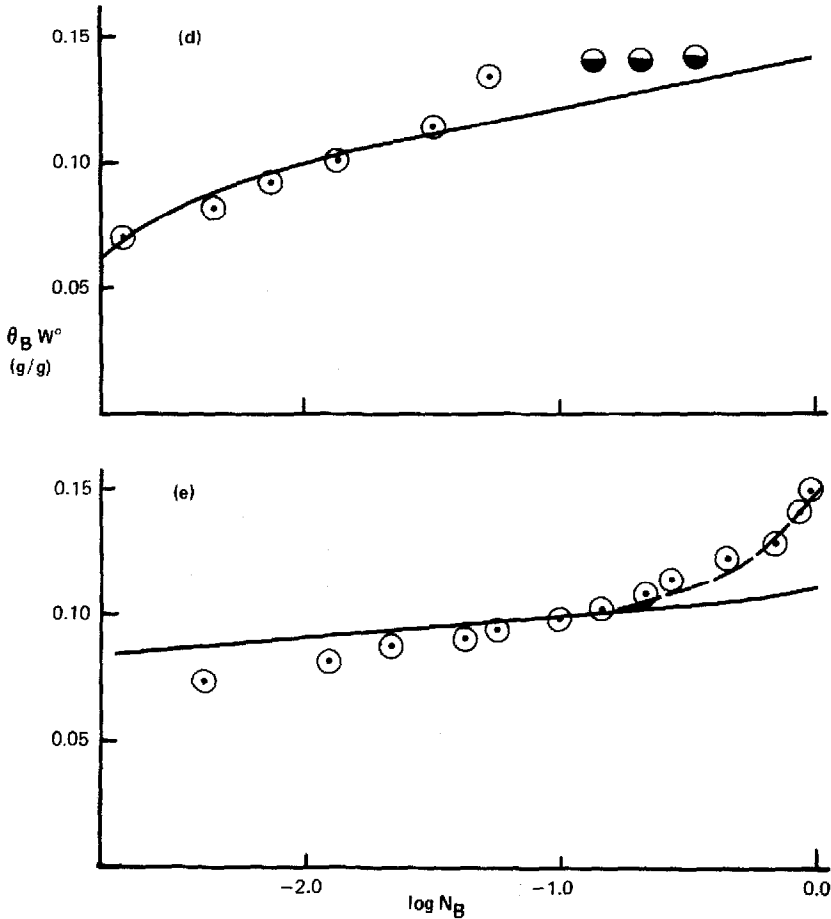


Fig. 7. Experimental and calculated isotherms for various LSC binary-solvent mobile phases and silica as adsorbent. Solid curves are calculated from the present model with parameters of Table I (based on retention data only); points are experimental values from refs. 5 and 24. (a) Chloroform + hexane; (b) benzene + hexane; (c) toluene + hexane; (d) ethyl acetate + hexane; (e) isopropanol + hexane.

binary-solvent mobile phases with calculated isotherms based on the model and data for *solute retention* (i.e., totally independent measurements). Resulting correlations of experimental and calculated isotherm data are surprisingly good, especially since the adsorbents (silica) compared differ in significant respects.

Finally, a beginning has been made on including solute-solvent hydrogen-bonding effects in the displacement-localization model. It appears that these effects can be rather substantial in some cases, and much more experimental and theoretical work will be required to adequately understand and optimally use these effects in the design of practical LSC separations.

SYMBOLS

A, B, C, D, various pure solvents; A is normally non-polar, and sol-

| | |
|-----------------------------------|--|
| $A_a, A_n, B_a, B_n, \text{etc.}$ | vents B–D are polar; C and D are normally localizing solvents, and B is usually (but not always) non-localizing a molecule (A, B, ...) in the adsorbed (a) or non-sorbed (n) phase |
| $A_m, A_s, A_x, A_y, A_1, A_2$ | molecular cross-sectional area (1 unit = 0.085 nm ²) of mobile phase (m), solute (s), solutes X and Y or mobile phases 1 or 2 |
| $(A_s)_{\text{exptl}}$ | the apparent value of A_s for a solute molecule, inferred from the application of eqn. 2 to experimental data for the solute; see eqn. 7 |
| ACN | acetonitrile |
| C_1, C_2 | constants (eqn. 13) for an LSC system with a given adsorbent and a given pair of solutes |
| E_m, E_x | dimensionless free energy of interaction of a molecule of mobile phase M or solute X with the adsorbed phase |
| E_{x1} | for a localized solute X, the value of E_x when ε^0 for the mobile phase is zero (eqn. 6) |
| $f_1(B), f_1(X), f_1(k)$ | a localization function (Fig. 3, ref. 9) for localizing molecules C, X or functional group k (eqns. 7, 8a); recognizes site-competition delocalization |
| $f(\theta_C)$ | a localization function (eqn. 13a) which recognizes the effect of restricted-access delocalization on the value of m_c for a localizing solvent C in a mixture of C and non-localizing solvents (A + C, A + B + C) |
| k' | solvent capacity factor |
| k_x, k_y | k' values of solutes X and Y |
| $k_{xb}, k_{xc}, k_{yb}, k_{yc}$ | k' values of solute X and Y in mobile phases containing B and C, respectively |
| k_1, k_2 | solute k' value for mobile phases 1 and 2 (eqn. 2) |
| K | adsorption equilibrium constant (eqn. 3a) |
| $K_{xb}, K_{xc}, K_{yb}, K_{yc}$ | values of K for solutes X and Y and mobile phases containing B or C |
| $K^{\text{cx}}, K^{\text{cx}*}$ | hydrogen-bonding equilibrium constants in mobile phase and adsorbed (*) phase, respectively (eqns. 14a, b); for reactions of eqn. 14 |
| m | mobile phase localization-selectivity function (eqns. 13, 13a) |
| m^0 | value of m for pure solvent (eqn. 13a) |
| MTBE | methyl <i>tert.</i> -butyl ether |
| m_b, m_c, m_i | values of m for mobile phase containing B, C or i (eqn. 13) |
| M_a, M_n | molecules M in adsorbed (a) or non-adsorbed (n) phase |
| n | stoichiometry of adsorption equilibrium (eqn. 1) |
| n_b | value of A_m for the mobile phase (see eqn. 3a) |
| $N_A, N_B, N_C, \dots N_i$ | mole fractions of solvent components A, B, C, ... i in mobile phase |
| Q_j^0 | adsorption energy of functional group k (localizing) in solute or solvent molecule |

| | |
|--|---|
| R | gas constant |
| R_M | retention factor, equal to $\log k'$ |
| T | absolute temperature, °K |
| V_a, V_n | volumes of adsorbed and non-sorbed phases, per gram of adsorbent |
| X_a, X_n | molecule of solute X in adsorbed or non-sorbed phases |
| $(X)_a, (X)_n$ | concentration of X in adsorbed or non-sorbed phase |
| XH | a proton-donor solute |
| $(XH)_a, (XH)_n$ | concentrations of XH in adsorbed and non-sorbed phases |
| XHC | complex of solute XH and proton-acceptor solvent C |
| $(XHC)_a, (XHC)_n$ | concentrations of XHC in adsorbed and non-sorbed phases |
| α | separation factor for compounds X and Y; equal k_x/k_y |
| α_b | value of α for mobile phase containing solvent B |
| α_c | value of α for mobile phase containing solvent C |
| $(\alpha_c)_{\text{corr}}$ | value of α for different mobile phases, corrected to a constant ε^0 value (eqn. 16) |
| α' | adsorbent activity function, proportional to adsorbent surface energy |
| β | parameter which measures relative effect of intramolecular delocalization (eqn. 10c) |
| γ | parameter which measures relative effect of site-competition delocalization (eqn. 9) |
| Δa_i | increase in A_s due to localization of a solute group i ; equal $f_1(X)$ |
| ΔE_{xm} | dimensionless free energy of adsorption of solute X from mobile phase M (eqn. 1b) |
| ΔG^0 | standard free energy for reaction of eqn. 1 |
| ΔR_M | increase in R_M as a result of substituting a functional group i into the solute molecule; equal to $\log k_{xi} - \log k_x$, where k_{xi} is for the solute substituted by i and k_x for the solute substituted by -H |
| ε^0 | solvent strength parameter, equal E_m/A_m for solvent M |
| $\varepsilon_b, \varepsilon_c$ | values of ε^0 for mobile phases containing solvents B and C (eqn. 12) |
| $\varepsilon_A, \varepsilon_B, \varepsilon_C, \dots$ | values of ε^0 for pure solvents A, B, C, ... |
| ε_M | value of ε^0 for a mixture A + B (mobile phase M) |
| $\varepsilon_1, \varepsilon_2$ | value of ε^0 for mobile phases 1 and 2 (eqn. 2) |
| $\varepsilon', \varepsilon''$ | values of ε^0 for the pure solvent (localizing) in mobile phase mixtures; ε' is for $\theta_B = 0$ and ε'' is for $\theta_B = 1.0$ |
| $\varepsilon'_B, \varepsilon'_C, \varepsilon''_B, \varepsilon''_C$ | values of ε' and ε'' for solvents B and C |
| $\theta_A, \theta_B, \theta_C, \dots, \theta_i$ | mole fraction of solvents A, B, C, ... i in adsorbed phase |

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