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Modelling retention in reversed-phase liquid chromatography as a function of pH and solvent composition

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ABSTRACT

Models describing the concomitant effects of pH and organic modifier concentration on retention in reversed-phase liquid chromatography are established. Two different octadecyl-modified silica columns were used. The retention behaviour of several acidic, basic and neutral solutes were studied, using methanol as the organic modifier. The suggested models accurately describe retention as a function of pH and composition. A unified formalism for retention modelling that is applicable to all ionogenic solutes is also established. This formalism is tested with the modelling of retention for several weak bases. The resulting (general) model describes retention accurately and is applicable to all solutes studied.

INTRODUCTION

Optimizing chromatographic selectivity (relative retention) in liquid chromatography (LC) is a difficult task. Many procedures have been developed, most of them specifically designed for reversed-phase liquid chromatography (RPLC), owing to the major role of this technique in modern chromatography. It is now generally accepted that the interpretive approach, in which the chromatogram is interpreted as the sum of a number of individual peaks, is the most efficient [1,2].

The problem of optimizing concentration(s) of organic modifier(s) in the mobile phase has been tackled with considerable success [1,3]. The inclusion of pH as one of the optimization parameters presents great potential advantages [4], but also raises several problems. Some of these are specific to the interpretive procedures that we strive to use, others are connected with the chemistry of the problem:

(1) Generally, we cannot use pH as the only parameter in selectivity optimization procedures, because absolute retention also varies with the acidity of the mobile phase. To keep capacity factors in the optimum range, it is necessary to vary another parameter concomitantly (modifier concentration is the logical choice) [4].

(2) If one has a quaternary mobile phase (water plus three organic modifiers), the four apparent variable parameters are interconnected (their percentages add up to 100%). Using the concept of isoeluotropic mixtures, we can reduce the parameter space by including only two optimization parameters [1]. When considering pH as one of the optimization parameters, the parameter space acquires an additional dimension and, most important, a different and more complex structure (in comparison with solvent optimization). To work with the same dimensionality as quaternary solvent optimization, only the concentration of one organic modifier can be considered along with pH. Even then, the structure of the parameter space is different, as is illustrated in Fig. 1. Therefore, the direct application of experimental designs and optimiza-

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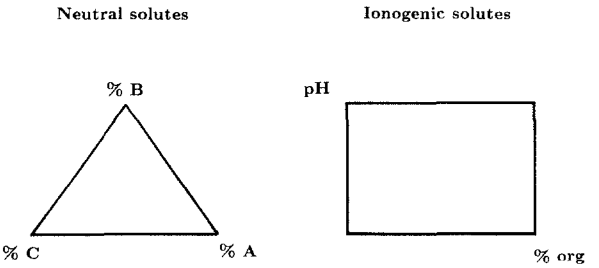

Fig. 1. Compared structure of the parameter space for organic modifier (quaternary mixtures) and for simultaneous pH and organic modifier optimization (binary mixtures).

tion routines already in use for solvent optimization is not possible.

(3) Defining and measuring pH in aqueous–organic mixtures gives rise to some theoretical and practical complications. We shall discuss this later.

(4) In addition to retention and selectivity, there are other characteristics of the peaks of ionogenic solutes that are variable with pH. Peak shape is highly dependent on this factor, as has been shown in a previous paper [4]. This implies that we cannot rely solely on selectivity or retention criteria to assess the quality of a chromatogram.

(5) Peak tracking is essential for interpretive procedures [1]. The peak tracking procedures developed for solvent optimization, based on the spectra of the solutes [5–7], cannot be directly transferred to pH optimization, because the spectra of ionogenic solutes vary with pH.

(6) Owing to the characteristics of interpretive procedures, it is necessary to develop (new) models for the peak characteristics (plate counts, asymmetry factors) as functions of two variables (simultaneously): pH and organic content.

It was the aim of this work to develop and compare models that accurately describe retention as a function of pH and solvent composition throughout a large parameter space. We also aimed to establish an experimental design that allows the coefficients of the above models to be derived from a limited number of experiments. Ultimately, our intention is to use the models and experimental design for the simultaneous interpretive optimization of pH and composition.

THEORY

Our aim is a function to describe the capacity factor k:

$$k = \frac{t_{r,i} - t_0}{t_0} \tag{1}$$

as a function of pH and concentration of organic modifier:

$$k = F([\mathrm{H}^+], \varphi) \tag{2}$$

where $t_{r,i}$ is the retention time of the solute i and t_0 the hold-up time of the column (proportional to the retention volume and the void volume, respectively), $[\mathrm{H}^+]$ is the concentration of "hydrogen ions" and φ the fraction of organic modifier in the mobile phase.

To obtain a grasp of the kinds of functions that can be used, we first searched the literature for functions that adequately model the variation of k with each of the parameters separately. The variation of retention as a function of the solvent composition (keeping other relevant factors constant) has been extensively studied. Several functions have been proposed. Among others, these include a logarithmic model [8]:

$$\log k = A + B\varphi + C \log (1 + D\varphi) \tag{3}$$

a reciprocal model [9]:

$$\frac{1}{k} = A + B\varphi + C\varphi^2 \tag{4}$$

and quadratic and linear exponential models [10]:

$$\log k = A + B\varphi + C\varphi^2 \tag{5}$$

$$\log k = A + B\varphi \tag{6}$$

Of these, the quadratic exponential model (eqn. 5) works most satisfactorily. Because of its accuracy, simplicity and good numerical behaviour, we judged it to be the best available. The linear exponential model (eqn. 6) fits data very well for most solutes over moderately large ranges, as has been observed by several workers (see, *e.g.*, refs. 10 and 11).

The variation of k with pH (with other factors constant) has also been investigated by several workers (see, *e.g.*, refs. 11–17). Let us consider the case of a weak monoprotic acid HA. If we assume a simple reversible retention mechanism to hold (Fig. 2), several equilibria can be thought to influ-

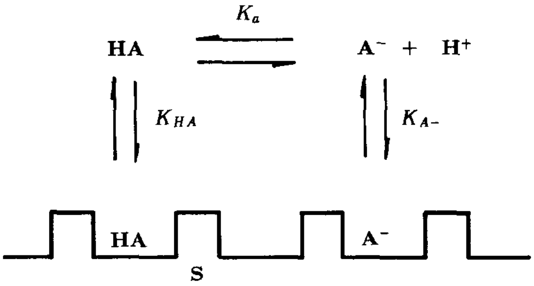

Fig. 2. Model describing the equilibria involved in the retention of a weak monoprotic acid HA.

ence the concentration of the acid in its various forms (S represents the stationary phase):

$$HA + S \overset{K_{HA}}{\rightleftharpoons} HA(S) \tag{7}$$

$$A^- + S \overset{K_{A^-}}{\rightleftharpoons} A(S)^- \tag{8}$$

$$HA \overset{K_a}{\rightleftharpoons} A^- + H^+ \tag{9}$$

The corresponding equilibrium constants are given by

$$K_{HA} = \frac{[HA(S)]}{\{[S]_0 - [HA(S)] - [A(S)^-]\}[HA]} \tag{10}$$

$$K_{A^-} = \frac{[A(S)^-]}{\{[S]_0 - [HA(S)] - [A(S)^-]\}[A^-]} \tag{11}$$

$$K_a = \frac{[H^+][A^-]}{[HA]} \tag{12}$$

where $[S]_0$ is the total "concentration" of substrate (free and occupied sites). This approach is very similar to that recently described by Armstrong *et al.* [16]. One may note that we are implicitly assuming that the number of available sites is the same for all forms of the solute and independent of pH and φ. This may not always be true [4].

If the capacity of the stationary phase is kept significantly above the total concentration of solutes, one may assume that the number of available sites remains constant, simplifying the equilibrium expressions. In fact, if $[S]_0 \gg [HA(S)] + [A(S)^-]$, eqn. 10 reduces to $K_{HA} = [HA(S)]/[HA][S_0]$ and the capacity factor of the protonated species, $k_0 = \beta[HA(S)]/[HA]$, where β is the ratio of stationary and mobile phase volumes ($\beta = V_s/V_m$), can be written as

$$k_0 = \beta[S_0]K_{HA} \tag{13}$$

and analogously for k_{-1}:

$$k_{-1} = \beta[S_0]K_{A^-} \tag{14}$$

From this, we obtain

$$k = \frac{k_0 + k_{-1}K_a/[H^+]}{1 + K_a/[H^+]} \tag{15}$$

The same result is obtained by assuming from the start that the observed capacity factor is a weighted average of the capacity factors of the individual species [1,4]:

$$k = k_0\left(\frac{[HA]}{[HA] + [A^-]}\right) + k_{-1}\left(\frac{[A^-]}{[HA] + [A^-]}\right) \tag{16}$$

For a weak monoprotic base, a similar equation can be obtained [14]:

$$k = \frac{k_0 + k_1[H^+]/K_a}{1 + [H^+]/K_a} \tag{17}$$

where K_a is defined in terms of the basicity constant K_b and the ionic product of water, K_w ($= [H_3O^+][OH^-]$), as

$$K_a = K_w/K_b \tag{18}$$

and k_0 and k_1 are the capacity factors of B and HB^+, respectively.

For diprotic acids, zwitterions, etc., the principle for the derivation of analogous equations is the same (see, *e.g.*, ref. 14).

It is possible to derive a single equation applicable to all cases by using some ideas taken from complexometric and acid–base studies. To our knowledge, this has not been done before. In the paragraphs that follow, we omit electric charges for the sake of simplicity.

Suppose a completely deprotonated solute A, which establishes the following general equilibria in solution:

$$mH + nA \rightleftharpoons H_mA_n;\ m,n = 0,1,2,\ldots;\ n \neq 0 \tag{19}$$

For each of the H_mA_n species we can write a global stoichiometric formation constant

$$\kappa_{m,n} = \frac{[H_mA_n]}{[H]^m[A]^n} \tag{20}$$

Basic species of general formula $A_n(OH)_m$ can be formally accounted for in this set of equations by writing the corresponding equilibrium equations in terms of H^+ instead of OH^- and by redefining the resulting global formation constants. For example, for A(OH), we have

$$A + OH \rightleftharpoons A(OH) \tag{21}$$

or, adding H to both sides,

$$A + H_2O \rightleftharpoons A(OH) + H \tag{22}$$

The equilibrium constant for this equation is given by $[A(OH)]/[A][H]^{-1}$, which can be conventionally assigned to a "compound" with the formula AH_{-1} and with a formation constant $\kappa_{-1,1} = K_w/K_a$.

The observed global capacity factor, k, is given by an averaged sum of the capacity factors $k_{m,n}$ of each H_mA_n species:

$$k = \sum_m \sum_n k_{m,n} \frac{[H_mA_n]}{C_A} \tag{23}$$

where m may be zero (completely deprotonated solute), n is at least unity and C_A is the analytical concentration of A (sum of the concentrations of A in all its possible forms).

Developing the above equation leads to

$$k = \frac{\sum\limits_{m,n} k_{m,n}\kappa_{m,n}[H^m][A^{n-1}]}{\sum\limits_{m,n} \kappa_{m,n}[H^m][A^{n-1}]} \tag{24}$$

Note that, in the above equation, $\kappa_{0,1}$ ("formation constant" of the deprotonated solute) is implicitly equal to 1 (eqn. 20).

This systematization, although more complex, unifies all expressions derived from phenomenological approaches to the elution of the various types of ionogenic compounds separable by RPLC (diprotic acids, bases, zwitterions, etc.). It is also potentially useful for developing formalized optimization procedures, because it allows the use of one equation for all kinds of compounds.

There are few reports in the literature in which the capacity factor is studied as a combined function of pH and concentration of organic modifier in the mobile phase. Haddad *et al.* [18] studied the simultaneous optimization of pH and organic modifier concentration for some aromatic acids, using planar surfaces to represent ln k as a function of the two variables. This approach is not sufficiently precise for the purpose of determining modelling functions that are accurate over (moderately) large ranges of the variables. Otto and Wegscheider [19] investigated modelling functions, including the ionic strength of the mobile phase, for the separation of several diprotic acids. The general model derived by these authors included thirteen parameters. Assuming the ionic strength to be constant, this number is reduced to eleven. Grushka *et al.* [20] studied the combined effects of pH and methanol concentration on the capacity factor and on the selectivity of some deoxyribonucleotides, but only from a descriptional point of view. Modelling functions were not derived.

In the remainder of this section we shall refer to methanol–water mixtures. Most of the discussion should also be applicable to other binary systems. Consider eqn. 15 (valid for weak monoprotic acids). At each methanol concentration, this equation describes a sigmoidal function. The curves are different for different methanol concentrations (φ values), because k_0, k_{-1} and K_a vary with φ, but the general form of the equation is maintained. Establishing functions for the variation of these three parameters with φ and substituting them into eqn. 15, or substituting related functions into eqn. 24, should give us a modelling function for k as a function of both [H] and φ.

The complementary approach is also conceivable. At constant pH, the curves follow eqn. 5. Determining A, B and C functions of [H] and substituting these into eqn. 5 should also produce retention-modelling functions.

The two approaches are not equivalent, because all the functions (eqns. 5 and 15, in addition to equations for the coefficients therein) are approximate.

Considering eqn. 15 first, we observe that k_0 is the capacity factor of the protonated form of the acid, HA. Its variation with φ should logically follow eqn. 5:

$$\ln k_0 = \ln k_0^0 + S_0\varphi + T_0\varphi^2 \tag{25}$$

and analogously for k_{-1},

$$\ln k_{-1} = \ln k_{-1}^0 + S_{-1}\varphi + T_{-1}\varphi^2 \tag{26}$$

It is well known that the acidity constant K_a cannot be assumed to be independent of φ. The works of Paabo *et al.* [21] and Rorabacher *et al.* [22] seem to indicate that a cubical expression is needed to model K_a against φ:

$$\ln K_a = \ln K_a^0 + Q_1\varphi + Q_2\varphi^2 + Q_3\varphi^3 \qquad (27)$$

Substituting eqns. 25–27 (or similar ones) into eqn. 15 and introducing an additional parameter (δ) to account for any constant shift in the observed retention, we obtain a modelling class of functions of the general form

$$k = \delta + \frac{k_0(\varphi) + k_{-1}(\varphi)K_a(\varphi)/[H^+]}{1 + K_a(\varphi)/[H^+]} \qquad (28)$$

Modelling functions belonging to this class will be called "class 1 functions".

The second approach starts with $\ln k = A + B\varphi + C\varphi^2$. We observe that A represents the logarithm of the observed capacity factor for 0% methanol, which should be a sigmoidal function of [H], so that

$$A = \ln\left[\frac{k_0^w + k_{-1}^w K_a^w/[H^+]}{1 + K_a^w/[H^+]}\right] \qquad (29)$$

In this equation, k_0^w represents the capacity factor of HA, k_{-1}^w the capacity factor of A^- and K_a^w the acidity constant of HA (all in pure water). There are no literature reports about the variation of B or C with pH.

We can gain some insight into the expected variation of B with pH if we assume that the linear relation $\ln k = \ln k_0 - S\varphi$ holds. Measuring the capacity factor k at a fixed pH and two different percentages (φ_α and φ_β) of methanol, we can estimate the value of S as the slope of the straight line defined by the two measurements:

$$S \approx \frac{1}{\varphi_\alpha - \varphi_\beta}(\ln k_\beta - \ln k_\alpha) \qquad (30)$$

As the pH varies, the capacity factors at φ_α and φ_β% methanol, k_α and k_β vary according to sigmoidal relationships. This results in the following type of expression for S:

$$S([H]) = \frac{1}{\varphi_\alpha - \varphi_\beta}\left[\ln\left(\frac{k_{0,\beta} - k_{-1,\beta}K_{a,\beta}/[H]}{1 + K_{a,\beta}/[H]}\right) - \ln\left(\frac{k_{0,\alpha} - k_{-1,\alpha}K_{a,\alpha}/[H]}{1 + K_{a,\alpha}/[H]}\right)\right] \qquad (31)$$

It appears that the variation of S with [H] follows a difference of log-sigmoidals. If K_a is constant over the pH range studied, the above equation simplifies to a single log-sigmoidal. After some manipulations we find

$$S([H]) = \frac{1}{\varphi_\alpha - \varphi_\beta}\ln\left(\frac{k_{0,\beta} - k_{-1,\beta}K_a/[H]}{k_{0,\alpha} - k_{-1,\alpha}K_a/[H]}\right) \qquad (32)$$

Modelling functions derived using this approach will be called "class 2 functions" and have the general form

$$k = \delta + k^w([H])\exp(B([H])\varphi + C([H])\varphi^2) \qquad (33)$$

pH MEASUREMENTS

There is no general consensus on how to measure and report, or even use, the pH values of mixed eluents in the chromatographic literature. The pH is sometimes reported as a pragmatic pH (pH^P), measured before mixing the buffer with the organic modifier, sometimes as an operational pH after mixing, and sometimes as a "true" (thermodynamic) pH. This lack of uniformity is due to two main reasons, one theoretical and the other practical. It is not simple to assess the "true" pH in aqueous–organic media [23] and measurements before mixing can be much more conveniently implemented in a routine method-development procedure [3].

In methanol–water mixtures, the pH^T (thermodynamic pH) is determined by

$$pH^T = pH^O + \zeta \qquad (34)$$

where pH^O (operational pH) is the value measured with a glass electrode calibrated with standard aqueous buffers and ζ is a correction term, which is a function of the methanol content of the solution [22]. Because ζ is tabulated, the difficulties involved in reporting pH^T and pH^O are essentially the same. Using pH^T we may write

$$[H] = 10^{-pH^T} \qquad (35)$$

However, it is much more practical to report and use pH^P. In an automated system, it is technically difficult to measure the pH of the eluent after mixing (pH^O in our nomenclature) and it is experimentally inconvenient to prepare a different eluent for each desired composition in order to measure pH^T before pumping. If one wants a formalized and simple optimization procedure, one has to simplify this process.

Measuring pH before mixing reduces the required number of measurements, because pH only has to be measured once for each different buffer. We believe that pH^P measurements are adequate, in the sense that they enable us to fit the data accurately with physically meaningful models. We have not studied the relationship between pH^P and pH^T, but our models show no signs of problems that may be attributable to this factor. Of course, physically meaningful parameters, such as K_a, cannot be derived reliably from the model.

EXPERIMENTAL

Retention data for all solutes were taken from a previous paper [4]. The main experimental conditions are given below. The experiments were carried out on an HP 1090 liquid chromatograph (Hewlett-Packard, Palo Alto, CA, USA). The data acquisition was performed using a Waters (Milford, MA, USA) Maxima 820 data station.

Two ODS (octadecyl-modified silica) columns were used: a 5-μm ChromSpher C_{18} glass cartridge (10 cm × 3 mm I.D.) from Chrompack (Middelburg, Netherlands) and a 10-μm μBondapak-C_{18} stainless-steel column (30 cm × 3.9 mm I.D.) from Waters. Buffers were 1:2 stoichiometric mixtures of citrate and phosphate, with a total ionic strength of 0.05 *M*. The organic modifier was high-performance liquid chromatographic-grade methanol.

Samples either were obtained as gifts from Organon (Oss, Netherlands) or were of analytical-reagent grade purchased from Merck (Darmstadt, Germany). All solutes and their structures are listed in ref. 4.

For acidic solutes, methanol concentrations of 30, 40 and 50% were used, and for basic solutes 50, 60 and 70%. For each composition, a number of pH values were studied, ranging from 2.6 to 7.03. The pH values are reported as the pH of the aqueous solution, before mixing with methanol.

Solutes and buffers were filtered before use. Solutes were injected individually to avoid mutual interferences. The flow-rate was 0.5 ml/min for the ChromSpher column and 1.25 ml/min for the μBondapak column. The columns were thermostated at 40°C. For more details, see ref. 4.

Hold-up times for both columns were estimated using replicate injections of saturatad $NaNO_3$, according to ref. 24, as being 2.17 min (75.6% porosity) for the μBondapak column and 0.86 min (60.8% porosity) for the ChromSpher column. These values are slightly different from those given in ref. 4, which were either determined gravimetrically [24] or estimated assuming $\varepsilon = 0.625$.

For one of the data sets described in ref. 4 we noted a significant degradation of the column and subsequently a lack of reproducibility is the observed retention times. In this paper, these data were excluded. For all data considered here the experimental uncertainty is much smaller than the modelling errors.

The evaluation of peak characteristics was performed by feeding the "raw" files created by the Maxima data station into a computer program written by the authors.

All model-fitting calculations were performed on a VAX 11/780 computer (Digital Equipment, Maynard, MA, USA) with a program (written by the authors) based on non-linear least squares. The numerical algorithms were adapted from ref. 25.

RESULTS

Retention modelling

We tried nine different class 1 models, by assigning several functions to k_0, k_{-1}, K_a and δ (eqn. 28). These models are listed in Table I. The results obtained for each acidic and neutral solute that was studied are listed in Tables II–XI.

For class 2, eight different models were tested, using different functions for k_0, B, C and δ (eqn. 33). These are listed in Table XII.

In models 2.A–2.D, we assumed ln k to vary linearly with φ and we tentatively assigned polynomial functions to the slope $S([H])$ (see eqns. 5 and 32), with or without a constant shift parameter (δ) embedded in the models.

In models 2.E and 2.F, ln k was assumed to be a quadratic function of φ. To the quadratic term we assigned a first-degree polynomial and to the linear term a second-degree polynomial for describing the effect of [H].

Models 2.G and 2.H are based on the approximate analysis of the kind of variation expected for S (eqn. 33). We considered ln k to vary linearly with φ, and assigned a sigmoidal function to S.

TABLE I

CLASS 1 MODELS: MODEL k AS A FUNCTION OF pH AND ASSUME THE COEFFICIENTS TO DEPEND ON COMPOSITION

Model No.	Model eqn.	No. of parameters	Comments	Eqn. No.
1.A	$k = \dfrac{k_0^0\exp(S_0\varphi)[\mathrm{H}] + k_{-1}^0 K_\mathrm{a}^0\exp[(Q_1 + S_{-1})\varphi + Q_2\varphi^2]}{[\mathrm{H}] + K_\mathrm{a}^0\exp(Q_1\varphi + Q_2\varphi^2)}$	7	Ln k_0 linear with φ, ln k_{-1} linear, ln K_a quadratic, $\delta = 0$	36
1.B	$k = \dfrac{k_0^0\exp(S_0\varphi)[\mathrm{H}] + k_{-1}^0 K_\mathrm{a}^0\exp[(Q_1 + S_{-1})\varphi + Q_2\varphi^2 + Q_3\varphi^3]}{[\mathrm{H}] + K_\mathrm{a}^0\exp(Q_1\varphi + Q_2\varphi^2 + Q_3\varphi^3)}$	8	Ln k_0 linear, ln k_{-1} linear, ln K_a cubic, $\delta = 0$	37
1.C	$k = \dfrac{k_0^0\exp(S_0\varphi + T_0\varphi^2)[\mathrm{H}] + k_{-1}^0 K_\mathrm{a}^0\exp[(Q_1 + S_{-1})\varphi + (Q_2 + T_{-1})\varphi^2]}{[\mathrm{H}] + K_\mathrm{a}^0\exp(Q_1\varphi + Q_2\varphi^2)}$	9	Ln k_0 quadratic, ln k_{-1} quadratic, ln K_a quadratic, $\delta = 0$	38
1.D	$k = \dfrac{k_0^0\exp(S_0\varphi)[\mathrm{H}] + k_{-1}^0 K_\mathrm{a}^0\exp[(Q_1 + S_{-1})\varphi + (Q_2 + T_{-1})\varphi^2]}{[\mathrm{H}] + K_\mathrm{a}^0\exp(Q_1\varphi + Q_2\varphi^2)}$	8	Ln k_0 linear, ln k_{-1} quadratic, ln K_a quadratic, $\delta = 0$	39
1.E	$k = \delta + \dfrac{k_0^0\exp(S_0\varphi)[\mathrm{H}] + k_{-1}^0 K_\mathrm{a}^0\exp[(Q_1 + S_{-1})\varphi + Q_2\varphi^2]}{[\mathrm{H}] + K_\mathrm{a}^0\exp(Q_1\varphi + Q_2\varphi^2)}$	8	Like model 1.A, except $\delta \neq 0$	40
1.F	$k = \delta + \dfrac{k_0^0\exp(S_0\varphi)[\mathrm{H}] + k_{-1}^0 K_\mathrm{a}^0\exp[(Q_1 + S_{-1})\varphi + (Q_2 + T_{-1})\varphi^2]}{[\mathrm{H}] + K_\mathrm{a}^0\exp(Q_1\varphi + Q_2\varphi^2)}$	9	Like model 1.D, except $\delta \neq 0$	41
1.G	$k = \delta + \dfrac{k_0^0\exp(S_0\varphi + T_0\varphi^2)[\mathrm{H}] + k_{-1}^0 K_\mathrm{a}^0\exp[(Q_1 + S_{-1})\varphi]}{[\mathrm{H}] + K_\mathrm{a}^0\exp(Q_1\varphi)}$	8	Ln k_0 quadratic, ln k_{-1} linear, ln K_a linear, $\delta \neq 0$	42
1.H	$k = \delta + \dfrac{k_0^0\exp(S_0\varphi)[\mathrm{H}] + k_{-1}^0 K_\mathrm{a}^0\exp[(Q_1 + S_{-1})\varphi]}{[\mathrm{H}] + K_\mathrm{a}^0\exp(Q_1\varphi)}$	7	Ln k_0 linear, ln k_{-1} linear, ln K_a linear, $\delta \neq 0$	43
1.I	$k = \delta + \dfrac{k_0^0\exp(S_0\varphi + T_0\varphi^2)[\mathrm{H}] + k_{-1}^0 K_\mathrm{a}^0\exp[(Q_1 + S_{-1})\varphi + Q_2\varphi^2]}{[\mathrm{H}] + K_\mathrm{a}^0\exp(Q_1\varphi + Q_2\varphi^2)}$	9	Ln k_0 quadratic, ln k_{-1} linear, ln K_a quadratic, $\delta \neq 0$	44

TABLE II

FITTED PARAMETERS FOR CLASS 1 MODELS

Solute caffeine.

Model	k_0^0	S_0	T_0	k_{-1}^0	S_{-1}	T_{-1}	K_a^0	Q_1	Q_2	Q_3	δ	SSQ^a
ChromSpher												
1.A	6.88	−6.13	–	6.88	−6.2	–	−0.119	−78.7	129	–	–	0.0223
1.B	7.18	−6.26	–	6.55	−6	–	$-0.135 \cdot 10^{-2}$	−51.9	65.9	155	–	0.0208
1.C	23.8	−12.9	8.82	24.2	−13	8.9	$-0.180 \cdot 10^{-2}$	−48.6	73.3	–	–	0.00409
1.D	5.95	−5.49	–	22.9	−13	9	$0.322 \cdot 10^{-16}$	161	−192	–	–	0.00218
1.E	13.4	−8.98	–	13.6	−9	–	$-0.267 \cdot 10^{-4}$	−36.9	81.1	–	0.194	0.00383
1.F	13.4	−8.96	–	13.8	−9.1	0.2	$-0.257 \cdot 10^{-2}$	−50.8	76.6	–	0.191	0.00406
1.G	10.8	−7.65	−2.11	25.2	−10.4	–	$-0.195 \cdot 10^{-10}$	18.0	–	–	0.204	0.00454
1.H	13.0	−8.85	–	20.3	−9.69	–	$-0.215 \cdot 10^{-10}$	17.7	–	–	0.187	0.00455
1.I	10.7	−7.62	−2.18	29.6	−11.2	–	$-0.161 \cdot 10^{-10}$	18.8	−0.807	–	0.205	0.00454
μBondapak												
1.A	12.1	−6.78	–	27.1	−8.35	–	$-0.273 \cdot 10^{-7}$	−0.883	8.55	–	–	0.00982
1.B	12.1	−6.77	–	$-0.164 \cdot 10^{9}$	−35.1	–	$0.170 \cdot 10^{-14}$	40.5	−10.2	−14.1	–	0.0101
1.C	29.9	−11.8	6.61	42.6	−12.7	6.8	$-0.394 \cdot 10^{-7}$	2.56	2.12	–	–	0.000769
1.D	12.1	−6.78	–	21.6	0.52	−0.68	$-0.342 \cdot 10^{-7}$	−0.893	7.19	–	–	0.00983
1.E	18.4	−8.57	–	84.1	−12.3	–	$-0.207 \cdot 10^{-6}$	−18.5	44.4	–	0.180	0.000738
1.F	18.5	−8.57	–	736	−22.1	11.0	$-0.116 \cdot 10^{-8}$	6.01	15.5	–	0.180	0.000740
1.G	15.6	−7.50	−1.94	87.8	−12.5	–	$-0.115 \cdot 10^{-8}$	12.2	–	–	0.209	0.000762
1.H	18.6	−8.61	–	20.7	−8.83	–	$-0.962 \cdot 10^{-7}$	1.16	–	–	0.184	0.000772
1.I	29.0	−11.6	6.77	64.8	−14.4	–	$-0.301 \cdot 10^{-7}$	3.57	−13.6	–	−0.0372	0.00421

[a] SSQ = Sum of squares of the residuals (in all tables).

TABLE III

FITTED PARAMETERS FOR CLASS 1 MODELS

Solute benzoic acid.

Model	k_0^0	S_0	T_0	k_{-1}^0	S_{-1}	T_{-1}	K_a^0	Q_1	Q_2	Q_3	δ	SSQ
ChromSpher												
1.A	46.2	−7.07	–	3.92	−2.96	–	$0.869 \cdot 10^{-4}$	−0.936	−2.03	–	–	0.0572
1.B	46.2	−7.07	–	3.92	9.25	–	$0.869 \cdot 10^{-4}$	−0.954	−1.95	−0.0995	–	0.0572
1.C	55.7	−8.08	1.32	2.86	−7.50	−2.55	$0.167 \cdot 10^{-3}$	−4.50	2.65	–	–	0.0544
1.D	46.2	−7.07	–	2.59	−8.77	−3.15	$0.864 \cdot 10^{-4}$	−0.906	−2.07	–	–	0.0572
1.E	46.9	−7.13	–	7.37	−11.8	–	$0.973 \cdot 10^{-4}$	−1.58	−1.17	–	0.0244	0.0567
1.F	47.2	−7.16	–	0.00319	33.6	−65.7	$0.108 \cdot 10^{-3}$	−2.13	−0.434	–	0.0368	0.0558
1.G	54.4	−7.95	1.18	3.35	−8.59	–	$0.116 \cdot 10^{-3}$	−2.51	–	–	−0.00881	0.0547
1.H	47.0	−7.14	–	8.65	−12.3	–	$0.115 \cdot 10^{-3}$	−2.47	–	–	0.0278	0.0566
1.I	55.5	−8.06	1.27	3.16	−7.75	–	$0.178 \cdot 10^{-3}$	−4.85	3.12	–	0.00735	0.0544
μBondapak												
1.A	38.6	−6.78	–	16.4	−18.8	–	$0.352 \cdot 10^{-3}$	−7.52	7.30	–	–	0.104
1.B	38.6	−6.78	–	15.1	−12.8	–	$0.169 \cdot 10^{-3}$	−7.39	−1.76	12.2	–	0.104
1.C	40.2	−7.00	0.300	$0.277 \cdot 10^{-6}$	78.4	−125	$0.263 \cdot 10^{-3}$	−5.98	5.40	–	–	0.103
1.D	38.6	−6.78	–	$0.925 \cdot 10^{-7}$	85.0	−135	$0.255 \cdot 10^{-3}$	−5.81	5.16	–	–	0.103
1.E	36.4	−6.50	–	0.750	−4.37	–	$0.160 \cdot 10^{-3}$	−2.85	0.535	–	−0.131	0.0947
1.F	37.0	−6.57	–	$0.118 \cdot 10^{-4}$	57.1	−85.0	$0.710 \cdot 10^{-4}$	1.61	−5.34	–	−0.0969	0.0878
1.G	51.3	−8.25	5.72	2.47	−0.32	–	$0.156 \cdot 10^{-3}$	−2.57	–	–	−2.18	0.0901
1.H	36.3	−6.49	–	0.738	−4.23	–	$0.149 \cdot 10^{-3}$	−2.45	–	–	−0.137	0.0947
1.I	53.4	−8.49	5.96	1.93	0.77	–	$0.182 \cdot 10^{-3}$	−3.52	1.37	–	−2.09	0.0872

TABLE IV

FITTED PARAMETERS FOR CLASS 1 MODELS

Solute phenol.

Model	k_0^0	S_0	T_0	k_{-1}^0	S_{-1}	T_{-1}	K_a^0	Q_1	Q_2	Q_3	δ	SSQ
ChromSpher												
1.A	12.0	−5.27	–	13.1	−5.43	–	$0.812 \cdot 10^{-4}$	−0.820	41.2	–	–	0.0167
1.B	11.2	−5.05	–	13.1	−5.44	–	$0.581 \cdot 10^{-5}$	−3.71	151	−232	–	0.0162
1.C	9.57	−4.21	−1.06	14.1	−5.84	0.5	$0.162 \cdot 10^{-3}$	3.69	17.9	–	–	0.0163
1.D	10.8	−4.92	–	14.1	−5.85	0.5	$0.676 \cdot 10^{-4}$	4.69	24.0	–	–	0.0163
1.E	11.2	−5.11	–	13.6	−5.63	–	$0.756 \cdot 10^{-4}$	−7.95	40.1	–	0.0530	0.0163
1.F	13.2	−6.10	–	8.21	−2.63	−5.7	$0.218 \cdot 10^{-3}$	1.61	21.2	–	0.341	0.0160
1.G	10.3	−4.67	−0.604	13.6	−5.6	–	$0.190 \cdot 10^{-4}$	16.1	–	–	0.0516	0.0163
1.H	11.2	−5.11	–	13.6	−5.56	–	$0.669 \cdot 10^{-4}$	11.9	–	–	0.0470	0.0163
1.I	7.49	−2.52	−5.25	8.94	−3.153	–	$0.633 \cdot 10^{-3}$	0.993	4.76	–	0.305	0.0161
µBondapak												
1.A	11.3	−5.27	–	7.06	−5.0	–	$0.389 \cdot 10^{6}$	−129	159	–	–	0.130
1.B	11.3	−5.29	–	7.24	−4.92	–	0.185	8.24	−255	398	–	0.127
1.C	11.3	−5.28	0.0366	0.877	6.5	−14.6	0.163	−50.0	59.5	–	–	0.113
1.D	11.2	−5.25	–	0.878	6.5	−14.6	0.147	−49.5	58.8	–	–	0.113
1.E	10.6	−4.93	–	6.70	−5.0	–	$0.537 \cdot 10^{8}$	−155	192	–	−0.103	0.127
1.F	11.3	−5.27	–	0.864	6.5	−14.8	0.169	−50.2	59.8	–	0.00456	0.113
1.G	19.3	−1.61	1.26	14.5	−0.44	–	$0.353 \cdot 10^{-4}$	−3.93	–	–	−11.1	0.118
1.H	8.79	−3.63	–	5.65	−2.96	–	$0.421 \cdot 10^{-4}$	−4.61	–	–	−0.647	0.141
1.I	13.4	−5.32	3.28	3.26	0.86	–	$0.892 \cdot 10^{-4}$	−8.32	3.91	–	−1.32	0.115

TABLE V

FITTED PARAMETERS FOR CLASS 1 MODELS

Solute *o*-nitrophenol.

Model	k_0^0	S_0	T_0	k_{-1}^0	S_{-1}	T_{-1}	K_a^0	Q_1	Q_2	Q_3	δ	SSQ
ChromSpher												
1.A	42.0	−6.03	–	10.4	−7.74	–	$0.196 \cdot 10^{-6}$	1.28	−1.31	–	–	0.0949
1.B	42.0	−6.03	–	10.4	−7.74	–	$0.234 \cdot 10^{-6}$	−0.109	2.23	−2.95	–	0.0949
1.C	43.9	−6.27	0.311	17.2	−10.5	3.64	$0.263 \cdot 10^{-6}$	−0.310	0.765	–	–	0.0942
1.D	42.0	−6.03	–	10.6	−7.83	0.12	$0.198 \cdot 10^{-6}$	1.24	−1.26	–	–	0.0949
1.E	42.8	−6.13	–	13.5	−8.80	–	$0.271 \cdot 10^{-6}$	−0.484	0.994	–	0.0601	0.0942
1.F	42.8	−6.12	–	6.96	−5.13	−4.87	$0.227 \cdot 10^{-6}$	0.490	−0.289	–	0.0591	0.0942
1.G	43.4	−6.21	0.178	11.5	−8.13	–	$0.236 \cdot 10^{-6}$	0.274	–	–	0.0242	0.0942
1.H	42.7	−6.11	–	12.4	−8.50	–	$0.234 \cdot 10^{-6}$	0.301	–	–	0.0501	0.0943
1.I	49.7	−5.52	4.20	26.3	−5.39	–	$0.407 \cdot 10^{-6}$	0.888	−5.40	–	−6.93	0.165
µBondapak												
1.A	36.3	−5.95	–	20.9	−8.8	–	$0.421 \cdot 10^{-2}$	−38.4	45.9	–	–	1.06
1.B	36.4	−5.96	–	22.5	−9.06	–	$0.528 \cdot 10^{-4}$	−2.34	−50.5	83.8	–	1.05
1.C	36.8	−6.02	0.0768	0.0350	27.5	−50.0	$0.563 \cdot 10^{-3}$	−27.0	30.5	–	–	1.04
1.D	36.4	−5.96	–	0.0114	33.8	−58.7	$0.293 \cdot 10^{-3}$	−23.5	25.9	–	–	1.04
1.E	35.2	−5.79	–	17.2	−7.9	–	$0.365 \cdot 10^{-2}$	−37.4	44.3	–	−0.104	1.05
1.F	36.4	−5.95	–	0.0277	28.7	−51.4	$0.382 \cdot 10^{-3}$	−25.0	27.9	–	−0.00236	1.04
1.G	40.7	−5.78	3.82	8.66	−1.49	–	$0.875 \cdot 10^{-5}$	−4.05	–	–	−4.04	1.07
1.H	30.3	−5.00	–	8.74	−4.63	–	$0.780 \cdot 10^{-5}$	−3.73	–	–	−0.685	1.11
1.I	41.4	−6.68	2.25	1.69	4.55	–	$0.504 \cdot 10^{-4}$	−13.5	12.3	–	−0.735	1.05

TABLE VI

FITTED PARAMETERS FOR CLASS 1 MODELS

Solute *p*-nitrophenol.

Model	k_0^0	S_0	T_0	k_{-1}^0	S_{-1}	T_{-1}	K_a^0	Q_1	Q_2	Q_3	δ	*SSQ*
ChromSpher												
1.A	23.4	−6.18	–	31.7	−16.2	–	$0.356 \cdot 10^{-6}$	−0.862	1.3	–	–	0.0296
1.B	23.4	−6.18	–	31.6	−16.3	–	$0.302 \cdot 10^{-6}$	0.427	−2.01	2.77	–	0.0296
1.C	25.2	−6.59	0.541	0.376	9.32	−35.8	$0.404 \cdot 10^{-6}$	−1.53	2.12	–	–	0.0289
1.D	23.4	−6.18	–	0.0193	25.3	−56.4	$0.274 \cdot 10^{-6}$	0.554	−0.532	–	–	0.0294
1.E	23.6	−6.22	–	66.0	−18.9	–	$0.420 \cdot 10^{-6}$	−1.83	2.68	–	0.0148	0.0295
1.F	23.6	−6.22	–	0.352	10.33	−39.2	$0.369 \cdot 10^{-6}$	−1.11	1.73	–	0.0131	0.0294
1.G	26.3	−6.85	1.11	7.22	−10.5	–	$0.324 \cdot 10^{-6}$	−1.38	–	–	−0.0615	0.0287
1.H	23.5	−6.20	–	22.5	−15.2	–	$0.286 \cdot 10^{-6}$	0.244	–	–	0.00588	0.0296
1.I	26.7	−6.93	1.32	5.48	−9.77	–	$0.259 \cdot 10^{-6}$	1.08	−1.60	–	−0.0903	0.0287
µBondapak												
1.A	25.9	−6.22	–	42.2	−14.0	–	$0.341 \cdot 10^{-2}$	−38.7	46.9	–	–	0.451
1.B	25.9	−6.22	–	49.0	−14.4	–	$0.435 \cdot 10^{-4}$	−3.58	−45.1	78.6	–	0.451
1.C	37.3	−8.20	2.61	$0.527 \cdot 10^{-5}$	77.7	−129	$0.600 \cdot 10^{-2}$	−41.6	50.6	–	–	0.437
1.D	25.9	−6.21	–	$0.646 \cdot 10^{-5}$	75.7	−125	$0.130 \cdot 10^{-2}$	−33.3	39.9	–	–	0.446
1.E	25.6	−6.16	–	31.7	−12.9	–	$0.257 \cdot 10^{-2}$	−37.1	44.8	–	−0.0227	0.451
1.F	25.8	−6.18	–	$0.109 \cdot 10^{-4}$	72.8	−120	$0.135 \cdot 10^{-2}$	−33.5	39.9	–	−0.0123	0.446
1.G	29.5	−4.67	3.78	8.21	−0.62	–	$0.665 \cdot 10^{-5}$	−3.82	–	–	−6.18	0.456
1.H	22.6	−5.53	–	6.03	−6.27	–	$0.544 \cdot 10^{-5}$	−3.26	–	–	−0.285	0.489
1.I	35.6	−7.96	4.42	1.15	3.63	–	$0.250 \cdot 10^{-4}$	−11.0	9.41	–	−0.845	0.445

TABLE VII

FITTED PARAMETERS FOR CLASS 1 MODELS

Solute dinitrophenol (first of two peaks observed for this solute [4]).

Model	k_0^0	S_0	T_0	k_{-1}^0	S_{-1}	T_{-1}	K_a^0	Q_1	Q_2	Q_3	δ	*SSQ*
ChromSpher												
1.A	14.1	−5.12	–	4.79	−5.86	–	$0.118 \cdot 10^{-4}$	14.8	−12.7	–	–	0.0261
1.B	14.1	−5.13	–	4.79	−5.88	–	$0.689 \cdot 10^{-4}$	1.22	21.5	−28.0	–	0.0260
1.C	7.17	−1.46	−4.70	0.518	6.1	−15.4	$0.133 \cdot 10^{-6}$	39.1	−43.8	–	–	0.0237
1.D	13.9	−5.08	–	1.50	0.4	−8	$0.458 \cdot 10^{-5}$	19.8	−18.8	–	–	0.0253
1.E	11.5	−3.88	–	3.10	−2.6	–	$0.494 \cdot 10^{-6}$	31.9	−34.5	–	−0.583	0.0245
1.F	11.5	−3.87	–	2.40	−1.3	−1.7	$0.298 \cdot 10^{-6}$	34.6	−37.8	–	−0.583	0.0242
1.G	19.0	−6.76	2.03	5.37	−6.40	–	$0.719 \cdot 10^{-4}$	5.03	–	–	0.0363	0.0276
1.H	15.3	−5.52	–	7.96	−8.07	–	$0.800 \cdot 10^{-4}$	4.66	–	–	0.115	0.0281
1.I	18.2	−6.42	2.69	6.91	−7.48	–	$0.359 \cdot 10^{-4}$	8.87	−5.14	–	−0.339	0.0270
µBondapak												
1.A	17.2	−5.39	–	7.11	−6.23	–	$0.395 \cdot 10^{-4}$	8.81	−6.54	–	–	0.241
1.B	17.2	−5.39	–	7.13	−6.24	–	$0.209 \cdot 10^{-4}$	13.8	−19.3	10.6	–	0.241
1.C	22.6	−6.91	2.07	25.7	−13.3	9.6	$0.416 \cdot 10^{-3}$	−4.26	11.0	–	–	0.236
1.D	17.1	−5.36	–	24.1	−13.0	9.03	$0.157 \cdot 10^{-3}$	1.16	3.77	–	–	0.237
1.E	19.3	−5.97	–	14.9	−9.42	–	$0.475 \cdot 10^{-3}$	−4.88	11.7	–	0.219	0.236
1.F	19.9	−6.12	–	6.78	−4.45	−8.41	$0.614 \cdot 10^{-3}$	−6.25	13.5	–	0.264	0.236
1.G	14.7	−4.49	−1.82	12.4	−8.69	–	$0.918 \cdot 10^{-4}$	4.07	–	–	0.186	0.237
1.H	18.3	−5.75	–	11.0	−8.17	–	$0.875 \cdot 10^{-4}$	4.20	–	–	0.158	0.237
1.I	17.1	−5.29	−1.02	7.13	−5.02	–	$0.247 \cdot 10^{-3}$	−1.21	6.74	–	0.242	0.236

TABLE VIII

FITTED PARAMETERS FOR CLASS 1 MODELS

Solute dinitrophenol (second peak).

Model	k_0^0	S_0	T_0	k_{-1}^0	S_{-1}	T_{-1}	K_a^0	Q_1	Q_2	Q_3	δ	SSQ
ChromSpher												
1.A	28.0	-5.94	–	4.01	-6.36	–	$0.531 \cdot 10^{-4}$	6.47	-6.26	–	–	0.0657
1.B	28.1	-5.96	–	4.01	-6.40	–	$0.320 \cdot 10^{-1}$	-43.5	121	-106	–	0.0650
1.C	25.6	-5.47	-6.19	5.72	-8.31	2.57	$0.428 \cdot 10^{-4}$	7.62	-7.74	–	–	0.0652
1.D	27.9	-5.94	–	6.57	-9.06	3.57	$0.650 \cdot 10^{-4}$	5.35	-4.78	–	–	0.0654
1.E	28.4	-6.02	–	4.72	-7.08	–	$0.701 \cdot 10^{-4}$	4.95	-4.27	–	0.0347	0.0655
1.F	27.3	-5.84	–	6.61	-9.17	4.71	$0.505 \cdot 10^{-4}$	6.71	-6.55	–	-0.0469	0.0653
1.G	28.3	-5.78	-0.138	6.11	-8.18	–	$0.126 \cdot 10^{-3}$	1.72	–	–	0.0745	0.0660
1.H	28.9	-6.10	–	5.94	-8.05	–	$0.126 \cdot 10^{-3}$	1.72	–	–	0.0704	0.0660
1.I	27.0	-6.00	-0.717	7.88	-9.75	–	$0.547 \cdot 10^{-4}$	6.27	-5.97	–	-0.0481	0.0654
µBondapak												
1.A	29.7	-5.96	–	6.19	-6.85	–	$0.114 \cdot 10^{-3}$	0.330	1.96	–	–	0.764
1.B	29.7	-5.96	–	6.20	-6.85	–	$0.115 \cdot 10^{-3}$	0.382	1.56	0.544	–	0.764
1.C	25.4	-5.08	-1.21	0.507	7.12	-18.8	$0.207 \cdot 10^{-4}$	9.88	-11.0	–	–	0.753
1.D	30.0	-5.99	–	0.462	7.67	-19.6	$0.299 \cdot 10^{-4}$	7.83	-8.25	–	–	0.754
1.E	25.4	-5.11	–	3.49	-3.3	–	$0.868 \cdot 10^{-5}$	14.7	-17.4	–	-0.510	0.753
1.F	27.0	-5.44	–	2.22	-1.2	-3.9	$0.115 \cdot 10^{-4}$	13.1	-15.3	–	-0.302	0.752
1.G	37.3	-7.23	2.66	3.52	-3.52	–	$0.930 \cdot 10^{-4}$	1.60	–	–	-0.442	0.755
1.H	27.9	-5.64	–	4.31	-4.96	–	$0.929 \cdot 10^{-4}$	1.61	–	–	-0.181	0.759
1.I	37.7	-7.22	3.68	4.34	-3.37	–	$0.707 \cdot 10^{-4}$	2.99	-1.64	–	-1.05	0.755

We also tried other models, using functions for $S([\mathrm{H}])$ that were equivalent (or similar) to a difference of log-sigmoidals, but when fitting these models severe numerical problems occurred.

The obtained results for class 2 models are listed in Tables XIII–XXII.

Experimental design

On determining a model to fit experimental retention data with the final objective of using it in a systematic method-development procedure, it is important to consider the number of experimental data points (chromatograms) required in order to

TABLE IX

FITTED PARAMETERS FOR CLASS 1 MODELS

Solute org-9935.

Model	k_0^0	S_0	T_0	k_{-1}^0	S_{-1}	T_{-1}	K_a^0	Q_1	Q_2	Q_3	δ	SSQ
ChromSpher												
1.A	528	-10.6	–	$0.127 \cdot 10^{4}$	-13.4	–	$0.195 \cdot 10^{-8}$	5.38	132	–	–	2.96
1.B	309	-10.2	–	$0.136 \cdot 10^{4}$	-13.6	–	$0.187 \cdot 10^{-8}$	5.87	467	-995	–	1.35
1.C	547	-10.6	-0.305	$0.620 \cdot 10^{4}$	-22.3	13	$0.400 \cdot 10^{-9}$	7.64	140	–	–	1.40
1.D	540	-10.6	–	$0.620 \cdot 10^{4}$	-22.3	13	$0.400 \cdot 10^{-9}$	7.64	140	–	–	1.40
1.E	522	-10.6	–	$0.183 \cdot 10^{4}$	-14.7	–	$0.161 \cdot 10^{-8}$	6.03	130	–	0.692	1.41
1.F	625	-11.1	–	$0.513 \cdot 10^{4}$	-21.2	10	$0.462 \cdot 10^{-9}$	6.96	141	–	0.156	1.40
1.G	951	-10.9	-5.80	$0.170 \cdot 10^{6}$	-28.4	–	$-0.814 \cdot 10^{-10}$	8.28	–	–	0.882	1.67
1.H	1790	-14.6	–	$0.181 \cdot 10^{4}$	-14.7	–	$-0.416 \cdot 10^{-9}$	14.6	–	–	0.678	1.65
1.I	966	-10.8	-6.02	$0.123 \cdot 10^{4}$	-12.6	–	$0.114 \cdot 10^{-7}$	5.70	3.04	–	0.859	1.66

TABLE X

FITTED PARAMETERS FOR CLASS 1 MODELS

Solute 2,3,4-trihydroxybenzophenone.

Model	k_0^0	S_0	T_0	k_{-1}^0	S_{-1}	T_{-1}	K_a^0	Q_1	Q_2	Q_3	δ	SSQ
ChromSpher												
1.A	527	−10.7	–	143	−12.6	–	$0.590 \cdot 10^{-7}$	8.23	−11.2	–	–	2.78
1.B	526	−10.7	–	109	−11.7	–	$0.115 \cdot 10^{-6}$	1.05	12.7	−24.3	–	2.77
1.C	1090	−14.8	5.55	228	−15.6	5.08	$0.315 \cdot 10^{-6}$	−1.28	2.11	–	–	2.22
1.D	526	−10.7	–	4.78	6.2	−24.8	$0.120 \cdot 10^{-7}$	17.0	−22.7	–	–	2.77
1.E	645	−11.5	–	2160	−22.2	–	$0.310 \cdot 10^{-5}$	−14.4	20.3	–	0.593	2.27
1.F	638	−11.4	–	6.03	8.93	−38.6	$0.867 \cdot 10^{-6}$	−7.44	11.3	–	0.568	2.27
1.G	1130	−15.0	5.95	107	−11.5	–	$0.242 \cdot 10^{-6}$	0.223	–	–	−0.0570	2.22
1.H	623	−11.3	–	351	−16.2	–	$0.192 \cdot 10^{-6}$	0.957	–	–	0.503	2.31
1.I	697	−12.0	0.991	218	−12	–	$0.650 \cdot 10^{-6}$	−5.50	8.08	–	0.455	2.26
μBondapak												
1.A	342	−9.62	–	196	−12.3	–	$0.139 \cdot 10^{-7}$	24.8	−30.4	–	–	0.919
1.B	341	−9.61	–	163	−11.8	–	$0.682 \cdot 10^{-7}$	7.08	−24.6	−51.8	–	0.919
1.C	365	−9.92	0.338	597	−17.7	6.54	$0.397 \cdot 10^{-6}$	9.48	−13.1	–	–	0.919
1.D	341	−9.61	–	666	−18.3	7.24	$0.494 \cdot 10^{-6}$	8.46	−11.9	–	–	0.919
1.E	371	−9.86	–	332	−13.8	–	$0.877 \cdot 10^{-6}$	5.92	−9.16	–	0.107	0.919
1.F	352	−9.71	–	504	−16.5	4.46	$0.560 \cdot 10^{-6}$	7.94	−11.4	–	0.0421	0.919
1.G	16800	−11.0	−23.8	−0.101	6.13	–	$0.548 \cdot 10^{-5}$	−2.33	–	–	2.60	0.919
1.H	$0.217 \cdot 10^6$	−26.8	–	−0.0800	6.44	–	$0.434 \cdot 10^{-5}$	−1.79	–	–	2.46	0.920
1.I	68.8	−2.29	−8.38	635	−16.9	–	$0.260 \cdot 10^{-5}$	1.01	−3.69	–	0.0954	0.919

obtain reliable results, *i.e.*, to reproduce to a good approximation the real retention surface.

To assess the behaviour of the models when limited sets of data are available, we selected two prospective experimental designs with 9 and 12 points (3 × 3 and 4 × 3, respectively). These are shown in Fig. 3. Next, we refitted all the models using only the set of points defined by each of the

TABLE XI

FITTED PARAMETERS FOR CLASS 1 MODELS

Solute N-vinylpyrrolidone.

Model	k_0^0	S_0	T_0	k_{-1}^0	S_{-1}	T_{-1}	K_a^0	Q_1	Q_2	Q_3	δ	SSQ
ChromSpher												
1.A	9.07	−5.97	–	5.87	−4.8	–	$0.884 \cdot 10^{-17}$	−46.1	316	–	–	0.00398
1.B	8.77	−5.86	–	5.91	−4.8	–	$0.868 \cdot 10^{-17}$	−46.1	573	−660	–	0.00396
1.C	9.06	−5.97	0.00259	25.7	−11.4	7	$0.389 \cdot 10^{-17}$	−42.9	312	–	–	0.00330
1.D	9.06	−5.96	–	25.9	−11.4	8	$0.544 \cdot 10^{-17}$	−43.1	310	–	–	0.00330
1.E	11.9	−7.46	–	13.0	−7.6	–	$0.596 \cdot 10^{-17}$	−44.7	309	–	0.245	0.00335
1.F	9.54	−6.28	–	27.2	−11.6	7	$0.350 \cdot 10^{-17}$	−43.0	312	–	0.0639	0.00330
1.G[a]	–	–	–	–	–	–	–	–	–	–	–	–
1.H[a]	–	–	–	–	–	–	–	–	–	–	–	–
1.I[a]	–	–	–	–	–	–	–	–	–	–	–	–

[a] Values not calculated, owing to numerical problems.

TABLE XII

CLASS 2 MODELS: MODEL k AS A FUNCTION OF COMPOSITION AND ASSUME THE COEFFICIENTS TO DEPEND ON pH

Model No.	Model eqn.	No. of parameters	Comments	Eqn. No.
2.A	$k = \frac{k_0^w[\mathrm{H}] + k_{-1}^w K_a^w}{[\mathrm{H}] + K_a^w} \exp\{\varphi(S_0 + S_1[\mathrm{H}] + S_2[\mathrm{H}]^2)\}$	6	k^w sigmoidal, B quadratic, $C = 0, \delta = 0$	45
2.B	$k = \delta + \frac{k_0^w[\mathrm{H}] + k_{-1}^w K_a^w}{[\mathrm{H}] + K_a^w} \exp\{\varphi(S_0 + S_1[\mathrm{H}] + S_2[\mathrm{H}]^2)\}$	7	Like model 2.A, except $\delta \neq 0$	46
2.C	$k = \frac{k_0^w[\mathrm{H}] + k_{-1}^w K_a^w}{[\mathrm{H}] + K_a^w} \exp\{\varphi(S_0 + S_1[\mathrm{H}] + S_2[\mathrm{H}]^2 + S_3[\mathrm{H}]^3)\}$	7	k^w sigmoidal, B cubic, $C = 0, \delta \neq 0$	47
2.D	$k = \delta + \frac{k_0^w[\mathrm{H}] + k_{-1}^w K_a^w}{[\mathrm{H}] + K_a^w} \exp\{\varphi(S_0 + S_1[\mathrm{H}] + S_2[\mathrm{H}]^2 + S_3[\mathrm{H}]^3)\}$	8	Like model 2.C, except $\delta \neq 0$	48
2.E	$k = \frac{k_0^w[\mathrm{H}] + k_{-1}^w K_a^w}{[\mathrm{H}] + K_a^w} \exp\{\varphi(S_0 + S_1[\mathrm{H}] + S_2[\mathrm{H}]^2) + \varphi^2(T_0 + T_1[\mathrm{H}])\}$	8	k^w sigmoidal, B quadratic, C linear, $\delta = 0$	49
2.F	$k = \delta + \frac{k_0^w[\mathrm{H}] + k_{-1}^w K_a^w}{[\mathrm{H}] + K_a^w} \exp\{\varphi(S_0 + S_1[\mathrm{H}] + S_2[\mathrm{H}]^2) + \varphi^2(T_0 + T_1[\mathrm{H}])\}$	9	Like model 2.E, except $\delta \neq 0$	50
2.G	$k = \frac{k_0^w[\mathrm{H}] + k_{-1}^w K_a^w}{[\mathrm{H}] + K_a^w} \exp\left(\frac{S_0 + S_1[\mathrm{H}]}{S_2 + [\mathrm{H}]}\right)$	6	k^w sigmoidal, B sigmoidal, $C = 0, \delta = 0$	51
2.H	$k = \delta + \frac{k_0^w[\mathrm{H}] + k_{-1}^w K_a^w}{[\mathrm{H}] + K_a^w} \exp\left(\frac{S_0 + S_1[\mathrm{H}]}{S_2 + [\mathrm{H}]}\right)$	7	Like model 2.G, except $\delta \neq 0$	52

TABLE XIII

FITTED PARAMETERS FOR CLASS 2 MODELS

Solute caffeine.

Model	k_0^w	k_{-1}^w	K_a^w	S_0	S_1	S_2	S_3	T_0	T_1	δ	SSQ
ChromSpher											
2.A	$-0.920 \cdot 10^6$	6.98	5290	−6.21	226	$-0.515 \cdot 10^5$	–	–	–	–	0.0201
2.B	1.92	13.6	0.136	−9.07	225	$-0.659 \cdot 10^5$	–	–	–	0.194	0.00165
2.C	$-0.920 \cdot 10^6$	6.98	5300	−6.21	269	$-0.114 \cdot 10^6$	$0.187 \cdot 10^8$	–	–	–	0.0209
2.D	11.7	13.6	0.0221	−9.08	289	$-0.161 \cdot 10^6$	$0.284 \cdot 10^8$	–	–	0.194	0.00162
2.E	234	14.2	0.0250	−10.2	−2300	$0.188 \cdot 10^6$	–	5.38	2370	–	0.00431
2.F	79.0	5.41	0.0996	−3.45	−501	$-0.492 \cdot 10^5$	–	−9.09	936	0.239	0.00181
2.G	6.89	35.9	$-0.372 \cdot 10^{-10}$	−4.37	−0.320	0.0519	–	–	–	–	0.0223
2.H	13.6	225	$-0.143 \cdot 10^{-10}$	−6.67	−0.387	0.0427	–	–	–	0.194	0.00269
μBondapak											
2.A	11.8	9.64	$0.110 \cdot 10^{-4}$	−6.57	−259	$0.838 \cdot 10^5$	–	–	–	–	0.0353
2.B	15.9	12.7	$0.765 \cdot 10^{-5}$	−7.89	−210	$0.682 \cdot 10^5$	–	–	–	0.139	0.0290
2.C	12.1	9.44	$0.160 \cdot 10^{-4}$	−6.51	−1290	$0.160 \cdot 10^7$	$-0.450 \cdot 10^9$	–	–	–	0.0319
2.D	16.4	12.7	$0.944 \cdot 10^{-5}$	−7.91	−973	$0.124 \cdot 10^7$	$-0.351 \cdot 10^9$	–	–	0.145	0.0263
2.E	16.5	13.4	$0.148 \cdot 10^{-4}$	−8.41	−245	$0.997 \cdot 10^5$	–	2.51	−186	–	0.0311
2.F	16.6	13.2	$0.931 \cdot 10^{-5}$	−8.08	−186	$0.821 \cdot 10^5$	–	0.121	−195	0.151	0.0281
2.G	11.1	11.0	$-0.337 \cdot 10^{-4}$	−312	22.2	−3.31	–	–	–	–	0.112
2.H	16.3	13.2	$0.817 \cdot 10^{-5}$	$-0.133 \cdot 10^5$	$-0.318 \cdot 10^4$	396	–	–	–	0.149	0.0306

TABLE XIV

FITTED PARAMETERS FOR CLASS 2 MODELS

Solute benzoic acid.

Model	k_0^w	k_{-1}^w	K_a^w	S_0	S_1	S_2	S_3	T_0	T_1	δ	SSQ
ChromSpher											
2.A	43.3	1.76	$0.566 \cdot 10^{-4}$	−6.71	−316	$0.111 \cdot 10^6$	–	–	–	–	0.0844
2.B	43.9	1.59	$0.564 \cdot 10^{-4}$	−6.78	−311	$0.110 \cdot 10^6$	–	–	–	0.0213	0.0832
2.C	44.4	1.70	$0.677 \cdot 10^{-4}$	−6.47	−1450	$0.125 \cdot 10^7$	$-0.301 \cdot 10^9$	–	–	–	0.0615
2.D	44.5	1.67	$0.676 \cdot 10^{-4}$	−6.48	−1440	$0.125 \cdot 10^7$	$-0.299 \cdot 10^9$	–	–	0.00327	0.0615
2.E	52.2	2.14	$0.538 \cdot 10^{-4}$	−8.03	−59.0	$0.924 \cdot 10^5$	–	2.01	−526	–	0.0599
2.F	52.5	2.23	$0.539 \cdot 10^{-4}$	−8.07	−58.2	$0.928 \cdot 10^5$	–	2.09	−533	−0.00690	0.0598
2.G	42.4	1.74	$0.491 \cdot 10^{-4}$	−5.47	−0.395	0.0576	–	–	–	–	0.112
2.H	43.4	1.46	$0.490 \cdot 10^{-4}$	−5.64	−0.350	0.0504	–	–	–	0.0324	0.109
μBondapak											
2.A	34.6	0.129	$0.564 \cdot 10^{-4}$	−6.66	236	$-0.520 \cdot 10^5$	–	–	–	–	0.104
2.B	34.8	0.0309	$0.563 \cdot 10^{-4}$	−6.69	244	$-0.544 \cdot 10^5$	–	–	–	0.00933	0.104
2.C	35.8	0.209	$0.717 \cdot 10^{-4}$	−6.28	−1550	$0.198 \cdot 10^7$	$-0.557 \cdot 10^9$	–	–	–	0.0912
2.D	35.4	0.385	$0.738 \cdot 10^{-4}$	−6.18	−1710	$0.216 \cdot 10^7$	$-0.603 \cdot 10^9$	–	–	−0.0191	0.0905
2.E	31.6	0.0637	$0.531 \cdot 10^{-4}$	−6.54	602	$-0.876 \cdot 10^5$	–	0.190	−701	–	0.0785
2.F	33.0	0.233	$0.532 \cdot 10^{-4}$	−6.80	600	$-0.849 \cdot 10^5$	–	0.611	−724	−0.0161	0.0781
2.G	39.3	−0.0602	$0.115 \cdot 10^{-3}$	−6.78	$-0.166 \cdot 10^{-3}$	$0.380 \cdot 10^{-4}$	–	–	–	–	0.0687
2.H	36.5	6.16	$0.140 \cdot 10^{-3}$	−6.39	$-0.169 \cdot 10^{-3}$	$0.495 \cdot 10^{-4}$	–	–	–	−0.188	0.0469

TABLE XV

FITTED PARAMETERS FOR CLASS 2 MODELS

Solute phenol.

Model	k_0^w	k_{-1}^w	K_a^w	S_0	S_1	S_2	S_3	T_0	T_1	δ	SSQ
ChromSpher											
2.A	13.0	12.7	$0.587 \cdot 10^{-5}$	−5.37	−162	$0.580 \cdot 10^5$	–	–	–	–	0.0103
2.B	13.4	13.1	$0.621 \cdot 10^{-5}$	−5.52	−167	$0.598 \cdot 10^5$	–	–	–	0.0412	0.00994
2.C	13.1	12.7	$0.632 \cdot 10^{-5}$	−5.37	−182	$0.846 \cdot 10^5$	$-0.768 \cdot 10^7$	–	–	–	0.0103
2.D	13.4	13.1	$0.660 \cdot 10^{-5}$	−5.52	−186	$0.853 \cdot 10^5$	$-0.737 \cdot 10^7$	–	–	0.0416	0.00993
2.E	13.3	12.9	$0.102 \cdot 10^{-4}$	−5.43	−253	$0.610 \cdot 10^5$	–	0.0256	213	–	0.00766
2.F	13.1	12.7	$0.584 \cdot 10^{-5}$	−5.33	−244	$0.588 \cdot 10^5$	–	−0.265	208	0.0342	0.00767
2.G	12.9	12.9	$-0.875 \cdot 10^{-4}$	−6.23	−0.559	0.104	–	–	–	–	0.0130
2.H	11.4	13.3	$0.266 \cdot 10^{-2}$	1.96	−0.565	0.103	–	–	–	0.0172	0.0151
μBondapak											
2.A	10.4	7.63	$0.127 \cdot 10^{-4}$	−4.96	−248	$0.933 \cdot 10^5$	–	–	–	–	0.172
2.B	9.52	7.17	$0.145 \cdot 10^{-4}$	−4.43	−261	$0.958 \cdot 10^5$	–	–	–	−0.162	0.168
2.C	10.8	7.37	$0.186 \cdot 10^{-4}$	−4.86	−1730	$0.227 \cdot 10^7$	$-0.643 \cdot 10^9$	–	–	–	0.155
2.D	9.12	6.93	$0.176 \cdot 10^{-4}$	−4.09	−528	$0.477 \cdot 10^6$	$-0.112 \cdot 10^9$	–	–	−0.276	0.161
2.E	7.73	5.72	$0.858 \cdot 10^{-5}$	−3.48	−19.3	$0.587 \cdot 10^5$	–	−1.89	−323	–	0.159
2.F	7.53	5.66	$0.106 \cdot 10^{-4}$	−3.29	−74.8	$0.741 \cdot 10^5$	–	−1.71	−310	−0.0889	0.155
2.G	10.3	7.75	$0.973 \cdot 10^{-5}$	−4.49	−0.217	0.0433	–	–	–	–	0.180
2.H	8.86	6.99	$0.958 \cdot 10^{-5}$	−3.65	−0.197	0.0476	–	–	–	−0.279	0.175

TABLE XVI

FITTED PARAMETERS FOR CLASS 2 MODELS

Solute *o*-nitrophenol.

Model	k_0^w	k_{-1}^w	K_a^w	S_0	S_1	S_2	S_3	T_0	T_1	δ	SSQ
ChromSpher											
2.A	42.5	6.42	$0.274 \cdot 10^{-6}$	−6.04	−88.8	$0.308 \cdot 10^6$	–	–	–	–	0.0912
2.B	40.8	6.88	$0.272 \cdot 10^{-6}$	−5.85	−87.4	$0.301 \cdot 10^6$	–	–	–	−0.118	0.0832
2.C	42.5	6.38	$0.271 \cdot 10^{-6}$	−6.05	−33.8	$-0.454 \cdot 10^6$	$0.225 \cdot 10^8$	–	–	–	0.0904
2.D	40.8	6.81	$0.270 \cdot 10^{-6}$	−5.86	−38.6	$-0.375 \cdot 10^6$	$0.200 \cdot 10^8$	–	–	−0.117	0.0826
2.E	43.3	6.58	$0.275 \cdot 10^{-6}$	−6.10	−151	$0.295 \cdot 10^6$	–	0.0184	176	–	0.0808
2.F	46.7	8.73	$0.275 \cdot 10^{-6}$	−6.59	−131	$0.295 \cdot 10^6$	–	1.13	121	−0.225	0.0651
2.G	42.4	6.19	$0.266 \cdot 10^{-6}$	−6.71	−0.264	0.0437	–	–	–	–	0.105
2.H	40.7	6.71	$0.266 \cdot 10^{-6}$	−6.55	−0.260	0.0443	–	–	–	−0.116	0.0969
μBondapak											
2.A	34.7	7.70	$0.196 \cdot 10^{-5}$	−5.86	26.0	$0.131 \cdot 10^6$	–	–	–	–	1.15
2.B	32.4	8.23	$0.198 \cdot 10^{-5}$	−5.52	16.6	$0.152 \cdot 10^5$	–	–	–	−0.191	1.14
2.C	34.8	7.79	$0.208 \cdot 10^{-5}$	−5.83	−380	$0.663 \cdot 10^6$	$-0.197 \cdot 10^9$	–	–	–	1.14
2.D	32.3	8.34	$0.211 \cdot 10^{-5}$	−5.47	−400	$0.682 \cdot 10^6$	$-0.202 \cdot 10^9$	–	–	−0.207	1.12
2.E	24.7	5.44	$0.195 \cdot 10^{-5}$	−4.05	99.0	$0.115 \cdot 10^5$	–	−2.32	−189	–	1.12
2.F	25.5	6.13	$0.194 \cdot 10^{-5}$	−4.26	114	$0.115 \cdot 10^5$	–	−1.74	−235	−0.125	1.11
2.G	34.6	7.64	$0.193 \cdot 10^{-5}$	11.7	−1.67	0.285	–	–	–	–	1.15
2.H	32.3	8.17	$0.192 \cdot 10^{-5}$	14.3	−1.90	0.342	–	–	–	−0.188	1.14

TABLE XVII

FITTED PARAMETERS FOR CLASS 2 MODELS

Solute *p*-nitrophenol.

Model	k_0^w	k_{-1}^w	K_a^w	S_0	S_1	S_2	S_3	T_0	T_1	δ	SSQ
ChromSpher											
2.A	23.7	1.35	$0.315 \cdot 10^{-6}$	−6.21	−56.6	$0.231 \cdot 10^5$	–	–	–	–	0.0373
2.B	22.5	1.80	$0.313 \cdot 10^{-6}$	−5.97	−56.1	$0.225 \cdot 10^5$	–	–	–	−0.0763	0.0330
2.C	23.7	1.27	$0.309 \cdot 10^{-6}$	−6.22	78.9	$-0.164 \cdot 10^6$	$0.553 \cdot 10^8$	–	–	–	0.0360
2.D	22.5	1.72	$0.308 \cdot 10^{-6}$	−5.99	68.1	$-0.149 \cdot 10^6$	$0.507 \cdot 10^8$	–	–	−0.0745	0.0318
2.E	24.9	1.42	$0.316 \cdot 10^{-6}$	−6.44	−120	$0.218 \cdot 10^5$	–	0.233	179	–	0.0339
2.F	27.1	2.72	$0.316 \cdot 10^{-6}$	−6.98	−95.9	$0.224 \cdot 10^5$	–	1.50	107	−0.135	0.0255
2.G	23.7	1.26	$0.309 \cdot 10^{-6}$	−6.24	−0.266	0.0428	–	–	–	–	0.0395
2.H	22.5	1.76	$0.309 \cdot 10^{-6}$	−6.06	−0.261	0.0436	–	–	–	−0.0754	0.0352
μBondapak											
2.A	25.0	3.26	$0.173 \cdot 10^{-5}$	−6.12	−73.8	$0.475 \cdot 10^5$	–	–	–	–	0.499
2.B	23.1	3.87	$0.173 \cdot 10^{-5}$	−5.76	−75.0	$0.468 \cdot 10^5$	–	–	–	−0.131	0.489
2.C	25.1	3.49	$0.197 \cdot 10^{-5}$	−6.05	−1190	$0.184 \cdot 10^7$	$-0.544 \cdot 10^9$	–	–	–	0.454
2.D	23.0	4.55	$0.198 \cdot 10^{-5}$	−5.63	−1150	$0.178 \cdot 10^7$	$-0.526 \cdot 10^9$	–	–	−0.153	0.442
2.E	22.5	2.93	$0.173 \cdot 10^{-5}$	−5.56	−39.1	$0.473 \cdot 10^5$	–	−0.708	−95.9	–	0.497
2.F	24.4	4.35	$0.172 \cdot 10^{-5}$	−6.12	−5.47	$0.462 \cdot 10^5$	–	0.656	−190	−0.166	0.487
2.G	24.9	3.16	$0.165 \cdot 10^{-5}$	−3.59	−0.289	0.0471	–	–	–	–	0.506
2.H	23.1	3.76	$0.164 \cdot 10^{-5}$	3.65	−1.11	0.192	–	–	–	−0.125	0.497

TABLE XVIII

FITTED PARAMETERS FOR CLASS 2 MODELS

Solute dinitrophenol (first of two peaks observed for this solute [4]).

Model	k_0^w	k_{-1}^w	K_a^w	S_0	S_1	S_2	S_3	T_0	T_1	δ	SSQ
ChromSpher											
2.A	17.6	6.19	$0.168 \cdot 10^{-3}$	−6.82	643	$-0.116 \cdot 10^6$	–	–	–	–	0.0102
2.B	17.5	6.21	$0.169 \cdot 10^{-3}$	−6.77	623	$-0.111 \cdot 10^6$	–	–	–	−0.00658	0.0102
2.C	17.0	6.95	$0.130 \cdot 10^{-3}$	−7.18	1850	$-0.121 \cdot 10^7$	$0.276 \cdot 10^9$	–	–	–	0.00714
2.D	17.9	7.86	$0.964 \cdot 10^{-4}$	−7.87	2830	$-0.198 \cdot 10^7$	$0.458 \cdot 10^9$	–	–	0.0609	0.00565
2.E	22.2	7.41	$0.189 \cdot 10^{-3}$	−7.73	398	$-0.736 \cdot 10^5$	–	1.12	244	–	0.00748
2.F	23.2	7.92	$0.192 \cdot 10^{-3}$	−8.02	387	$-0.592 \cdot 10^5$	–	1.87	118	−0.0368	0.00720
2.G	18.3	5.81	$0.211 \cdot 10^{-3}$	10.2	−0.438	0.0664	–	–	–	–	0.0132
2.H	17.6	5.73	$0.213 \cdot 10^{-3}$	9.81	−0.434	0.0680	–	–	–	−0.0367	0.0124
μBondapak											
2.A	17.0	5.91	$0.153 \cdot 10^{-4}$	−7.33	1960	$-0.499 \cdot 10^6$	–	–	–	–	0.0756
2.B	21.6	2.68	$0.801 \cdot 10^{-5}$	−8.74	2630	$-0.692 \cdot 10^6$	–	–	–	0.192	0.0530
2.C	16.9	5.82	$0.137 \cdot 10^{-4}$	−7.39	2320	$-0.958 \cdot 10^6$	$0.131 \cdot 10^9$	–	–	–	0.0752
2.D	22.5	−5.35	$0.325 \cdot 10^{-5}$	−9.30	4660	$-0.331 \cdot 10^7$	$0.745 \cdot 10^9$	–	–	0.225	0.0512
2.E	327	5.07	0.0122	−4.21	−4760	$0.624 \cdot 10^6$	–	−2.44	4280	–	0.309
2.F	297	5.41	0.0111	−4.44	−4820	$0.698 \cdot 10^6$	–	−0.620	3790	−0.203	0.302
2.G	16.8	5.88	$0.115 \cdot 10^{-4}$	−5.02	−0.00473	$0.629 \cdot 10^{-3}$	–	–	–	–	0.0834
2.H	21.9	2.22	$0.608 \cdot 10^{-5}$	−6.05	−0.00455	$0.499 \cdot 10^{-3}$	–	–	–	0.207	0.0500

TABLE XIX

FITTED PARAMETERS FOR CLASS 2 MODELS

Solute dinitrophenol (second peak).

Model	k_0^w	k_{-1}^w	K_a^w	S_0	S_1	S_2	S_3	T_0	T_1	δ	SSQ
ChromSpher											
2.A	30.0	4.14	$0.173 \cdot 10^{-3}$	−6.53	242	$-0.372 \cdot 10^5$	–	–	–	–	0.0500
2.B	29.9	4.17	$0.174 \cdot 10^{-3}$	−6.50	226	$-0.329 \cdot 10^5$	–	–	–	−0.00526	0.0499
2.C	28.9	4.65	$0.142 \cdot 10^{-3}$	−6.89	1440	$-0.111 \cdot 10^7$	$0.272 \cdot 10^9$	–	–	–	0.0420
2.D	29.4	4.85	$0.117 \cdot 10^{-3}$	−7.35	2250	$-0.177 \cdot 10^7$	$0.428 \cdot 10^9$	–	–	0.0456	0.0383
2.E	34.1	4.49	$0.190 \cdot 10^{-3}$	−6.88	−23.4	6160	–	0.342	294	–	0.0450
2.F	34.0	4.48	$0.189 \cdot 10^{-3}$	−6.86	−21.7	5100	–	0.308	300	0.00199	0.0450
2.G	30.3	4.07	$0.182 \cdot 10^{-3}$	3.47	−0.536	0.0829	–	–	–	–	0.0508
2.H	30.0	4.12	$0.183 \cdot 10^{-3}$	−1.80	−0.242	0.0376	–	–	–	−0.0111	0.0504
μBondapak											
2.A	27.6	5.68	$0.271 \cdot 10^{-4}$	−7.53	2180	$-0.588 \cdot 10^6$	–	–	–	–	0.257
2.B	29.2	5.27	$0.258 \cdot 10^{-4}$	−7.83	2320	$-0.628 \cdot 10^6$	–	–	–	0.0642	0.247
2.C	26.8	6.09	$0.149 \cdot 10^{-4}$	−8.02	4820	$-0.379 \cdot 10^7$	$0.894 \cdot 10^9$	–	–	–	0.224
2.D	29.4	5.24	$0.138 \cdot 10^{-4}$	−8.58	5470	$-0.447 \cdot 10^7$	$0.107 \cdot 10^{10}$	–	–	0.106	0.193
2.E	22.3	4.63	$0.240 \cdot 10^{-4}$	−6.75	2540	$-0.623 \cdot 10^6$	–	−0.643	−664	–	0.233
2.F	21.8	4.18	$0.238 \cdot 10^{-4}$	−6.55	2550	$-0.640 \cdot 10^6$	–	−1.20	−548	0.0362	0.231
2.G	30.4	5.10	$0.767 \cdot 10^{-4}$	12.9	−0.423	0.0631	–	–	–	–	0.452
2.H	29.4	5.28	$0.785 \cdot 10^{-4}$	−104	2.26	−0.345	–	–	–	−0.0465	0.452

experimental designs, for benzoic acid (ChromSpher column only). From the new calculated parameters, we evaluated the difference between the observed and the predicted retention values, both for the design points and for all the data set. This enabled us to obtain a rough idea of the precision of each model (that is, the degree of approximation for predictions made). The results are given in Tables XXIII and XXIV.

Basic solutes

The general function that we developed (eqn. 24) embodies models for mono-, di- and polyprotic acids and bases and amphoteric compounds. All

TABLE XX

FITTED PARAMETERS FOR CLASS 2 MODELS

Solute org-9935.

Model	k_0^w	k_{-1}^w	K_a^w	S_0	S_1	S_2	S_3	T_0	T_1	δ	SSQ
ChromSpher											
2.A	1270	1230	$0.124 \cdot 10^{-4}$	−13.3	−277	$0.970 \cdot 10^5$	–	–	–	–	2.08
2.B	1840	1770	$0.876 \cdot 10^{-5}$	−14.6	−275	$0.936 \cdot 10^5$	–	–	–	0.701	0.528
2.C	1290	1220	$0.295 \cdot 10^{-4}$	−13.3	−594	$0.461 \cdot 10^6$	$-0.101 \cdot 10^9$	–	–	–	2.03
2.D	1840	1770	$0.893 \cdot 10^{-5}$	−14.6	−434	$0.304 \cdot 10^6$	$-0.615 \cdot 10^8$	–	–	0.700	0.497
2.E	2240	2170	$0.512 \cdot 10^{-5}$	−16.5	−352	$0.879 \cdot 10^5$	–	4.42	324	–	1.15
2.F	1530	1470	$0.224 \cdot 10^{-5}$	−13.6	−206	$0.811 \cdot 10^5$	–	−1.68	−98.7	0.765	0.634
2.G	1160	1300	$0.219 \cdot 10^{-3}$	−13.2	$-0.897 \cdot 10^{-3}$	$0.665 \cdot 10^{-4}$	–	–	–	–	2.41
2.H	1670	1850	$0.273 \cdot 10^{-3}$	−14.5	$-0.103 \cdot 10^{-2}$	$0.698 \cdot 10^{-4}$	–	–	–	0.690	0.902

TABLE XXI

FITTED PARAMETERS FOR CLASS 2 MODELS

Solute N-vinylpyrrolidone.

Model	k_0^w	k_{-1}^w	K_a^w	S_0	S_1	S_2	S_3	T_0	T_1	δ	SSQ
ChromSpher											
2.A	−161	7.40	0.754	−5.29	−1.58	$0.318 \cdot 10^5$	–	–	–	–	0.0124
2.B	−2.45	10.2	0.224	−6.83	−92.1	$0.365 \cdot 10^5$	–	–	–	0.210	0.00239
2.C	4.60	7.41	0.0103	−5.29	−16.3	$0.665 \cdot 10^5$	$-0.121 \cdot 10^8$	–	–	–	0.0124
2.D	−2.24	10.2	0.218	−6.83	−127	$0.886 \cdot 10^5$	$-0.157 \cdot 10^8$	–	–	0.210	0.00237
2.E	13.2	13.2	$0.547 \cdot 10^{-3}$	−8.46	−97.3	$0.264 \cdot 10^5$	–	4.15	60.2	–	0.00246
2.F	10.7	10.7	$0.433 \cdot 10^{-3}$	−7.14	−140	$0.399 \cdot 10^5$	–	0.671	55.2	0.190	0.00238
2.G	6.44	7.42	$0.200 \cdot 10^{-2}$	2.92	−0.574	0.108	–	–	–	–	0.0125
2.H	9.71	10.2	$0.709 \cdot 10^{-3}$	−4.84	−0.649	0.0951	–	–	–	0.207	0.00253

that is required is the substitution of the appropriate functions in eqn. 24. The model was tested by applying a derived model (described below) to the solutes from the database that showed basic behaviour (see ref. 4). The model was designed taking into account the results obtained for the class 1 model. There, we showed that the best model was obtained by assigning parabolic functions of the organic modifier concentration to the logarithms of the capacity factors of the individual species and to the pK_a of the solute (*cf.*, eqns. 25–27 and 38).

When we write eqn. 24 applied to a weak base HB^+, we obtain

$$k = \frac{k_{0,1} + k_{1,1}\kappa_{1,1}[H]}{1 + \kappa_{1,1}[H]} \tag{53}$$

where $k_{0,1}$ and $k_{1,1}$ are the capacity factors of B and HB^+, respectively, and $\kappa_{1,1}$ is the global stoichio-

TABLE XXII

FITTED PARAMETERS FOR CLASS 2 MODELS

Solute 2,3,4-trihydroxybenzophenone.

Model	k_0^w	k_{-1}^w	K_a^w	S_0	S_1	S_2	S_3	T_0	T_1	δ	SSQ
ChromSpher											
2.A	530	94.8	$0.305 \cdot 10^{-6}$	−10.6	−291	$0.983 \cdot 10^6$	–	–	–	–	1.07
2.B	592	100	$0.310 \cdot 10^{-6}$	−11.0	−299	$0.102 \cdot 10^6$	–	–	–	0.302	0.845
2.C	530	95.8	$0.307 \cdot 10^{-6}$	−10.6	−354	$0.187 \cdot 10^6$	$-0.262 \cdot 10^8$	–	–	–	1.07
2.D	593	99.0	$0.309 \cdot 10^{-6}$	−11.0	−357	$0.184 \cdot 10^6$	$-0.243 \cdot 10^8$	–	–	0.311	0.838
2.E	986	173	$0.301 \cdot 10^{-6}$	−14.1	−367	$0.988 \cdot 10^5$	–	4.60	238	–	0.501
2.F	977	177	$0.302 \cdot 10^{-6}$	−14.1	−362	$0.981 \cdot 10^5$	–	4.83	229	−0.110	0.486
2.G	526	87.6	$0.281 \cdot 10^{-6}$	−13.1	−0.446	0.0419	–	–	–	–	1.96
2.H	584	88.7	$0.280 \cdot 10^{-6}$	−13.4	−0.453	0.0410	–	–	–	0.292	1.74
μBondapak											
2.A	366	102	$0.296 \cdot 10^{-5}$	−9.75	−142	$0.643 \cdot 10^5$	–	–	–	–	1.06
2.B	290	87.8	$0.279 \cdot 10^{-5}$	−9.09	−120	$0.565 \cdot 10^5$	–	–	–	−0.284	1.04
2.C	366	101	$0.337 \cdot 10^{-5}$	−9.68	−972	$0.138 \cdot 10^7$	$-0.397 \cdot 10^9$	–	–	–	0.969
2.D	287	86.4	$0.317 \cdot 10^{-5}$	−8.99	−864	$0.124 \cdot 10^7$	$-0.356 \cdot 10^9$	–	–	−0.301	0.944
2.E	878	216	$0.247 \cdot 10^{-5}$	−13.8	−140	$0.484 \cdot 10^5$	–	4.55	115	–	0.942
2.F	784	211	$0.230 \cdot 10^{-5}$	−13.8	−56.8	$0.427 \cdot 10^5$	–	5.42	−49.9	−0.330	0.911
2.G	366	102	$0.271 \cdot 10^{-5}$	−8.59	−0.374	0.0382	–	–	–	–	1.11
2.H	291	88.3	$0.265 \cdot 10^{-5}$	−7.95	−0.362	0.0396	–	–	–	−0.275	1.09

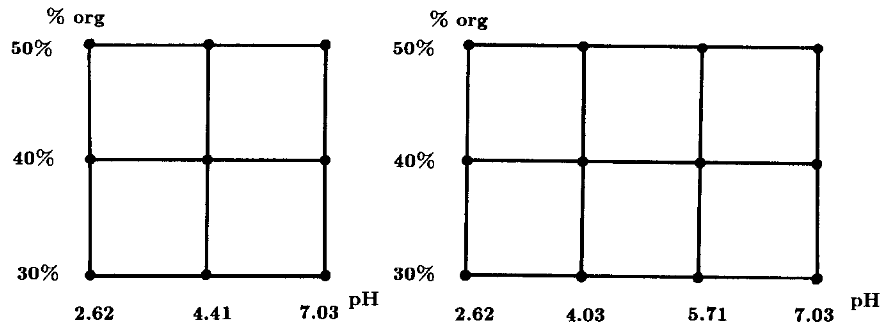

Fig. 3. 3 × 3 and 4 × 3 experimental designs used in the study of the behaviour of the models over limited sets of data.

metric formation constant of HB^+.

Assigning a parabolic function of the organic-modifier concentration to each of these three parameters results in a nine-parameter model that is essentially equivalent to model 1.C, but this time applied to basic compounds:

$$k = \frac{\left\{\begin{matrix} k^0_{0,1}\exp(S_0\varphi + T_0\varphi^2) + k^0_{1,1}\kappa^0_{1,1}\exp[(Q_1 + \\ S_1)\varphi + (Q_2 + T_1)\varphi^2][\mathrm{H}] \end{matrix}\right\}}{1 + \kappa^0_{1,1}\exp(Q_1\varphi + Q_2\varphi^2)[\mathrm{H}]} \tag{54}$$

The results are shown in Table XXV.

TABLE XXIII

RESULTS OBTAINED BY FITTING CLASS 1 MODELS TO LIMITED FRACTIONS OF THE DATA SET (3 × 3 AND 3 × 4 EXPERIMENTAL DESIGNS)

Solute, benzoic acid; column, ChromSpher ODS.

Model	NP[a]	SSQ_M[b]	SSQ_T[c]	MD[d]
1.A	9	$0.110 \cdot 10^{-3}$	0.105	0.136
	12	$0.509 \cdot 10^{-2}$	0.101	0.141
1.B	9	$0.110 \cdot 10^{-3}$	0.105	0.136
	12	$0.509 \cdot 10^{-2}$	0.101	0.141
1.C	9	$0.853 \cdot 10^{-10}$	0.106	0.138
	12	$0.508 \cdot 10^{-2}$	0.101	0.141
1.D	9	$0.677 \cdot 10^{-5}$	0.105	0.136
	12	$0.508 \cdot 10^{-2}$	0.101	0.141
1.E	9	$0.510 \cdot 10^{-4}$	0.104	0.134
	12	$0.508 \cdot 10^{-2}$	0.101	0.141
1.F	9	$0.751 \cdot 10^{-2}$	0.094	0.106
	12	$0.508 \cdot 10^{-2}$	0.101	0.141
1.G	9	$0.121 \cdot 10^{-3}$	0.105	0.136
	12	$0.508 \cdot 10^{-2}$	0.102	0.142
1.H	9	$0.138 \cdot 10^{-3}$	0.104	0.133
	12	$0.509 \cdot 10^{-2}$	0.101	0.141
1.I	9	$0.158 \cdot 10^{-5}$	0.115	0.146
	12	$0.508 \cdot 10^{-2}$	0.101	0.141

[a] NP = Number of points in the experimental design.
[b] SSQ_M = Sum of squares of the residuals, model points.
[c] SSQ_T = Sum of squares of the residuals, all points.
[d] MD = Maximum deviation between predicted and observed capacity factors.

TABLE XXIV

RESULTS OBTAINED BY FITTING CLASS 2 MODELS TO LIMITED FRACTIONS OF THE DATA SET (3 × 3 AND 3 × 4 EXPERIMENTAL DESIGNS)

Solute, benzoic acid; column, ChromSpher ODS.

Model	NP[a]	SSQ_M[b]	SSQ_T[c]	MD[d]
2.A	9	$0.317 \cdot 10^{-3}$	—[e]	—[f]
	12	$0.129 \cdot 10^{-1}$	34.2	4.01
2.B	9	$0.169 \cdot 10^{-3}$	—[e]	—[f]
	12	$0.445 \cdot 10^{-2}$	61.2	5.08
2.C	9	$0.317 \cdot 10^{-3}$	—[e]	—[f]
	12	$0.104 \cdot 10^{-2}$	—[e]	—[f]
2.D	9	$0.169 \cdot 10^{-3}$	—[e]	—[f]
	12	$0.441 \cdot 10^{-2}$	63.7	5.19
2.E	9	$0.932 \cdot 10^{-4}$	—[e]	—[f]
	12	$0.208 \cdot 10^{-2}$	—[e]	—[f]
2.F	9	$0.279 \cdot 10^{-3}$	0.638	0.389
	12	$0.215 \cdot 10^{-2}$	0.879	0.559
2.G	9	$0.139 \cdot 10^{-2}$	5.58	1.27
	12	$0.145 \cdot 10^{-1}$	1.01	0.535
2.H	9	$0.746 \cdot 10^{-3}$	6.49	1.36
	12	$0.104 \cdot 10^{-1}$	1.40	0.627

[a–d] See Table XXIII.
[e] Higher than 10^2.
[f] Higher than 6.

TABLE XXV

RESULTS OBTAINED BY FITTING THE RETENTION DATA FOR BASIC SOLUTES WITH A MODEL DERIVED BY THE APPLICATION OF A GENERAL EQUATION TO THE PARTICULAR CASE OF A WEAK BASE HB^+ (*cf.*, EQNS. 24 AND 54)

Solute	$k^0_{0.1}$	S_0	T_0	$k^0_{1.1}$	S_1	T_1	$\kappa^0_{1.1}$	Q_1	Q_2	SSQ	MD[a]	RMD[b]
Org-20494	$0.502 \cdot 10^7$	−3.98	−22.7	0.341	12.2	−88.0	$0.534 \cdot 10^{10}$	9.96	−33.2	0.0563	0.141	3.4%
Org-3770	$0.602 \cdot 10^9$	−46.2	26.8	36.4	−7.7	−0.7	$0.393 \cdot 10^{11}$	−27.1	11.4	0.0678	0.154	6.2%
Org-5222	$0.151 \cdot 10^{14}$	−49.9	14.0	53.8	−2.1	−7.6	$0.126 \cdot 10^{14}$	−16.8	−12.5	1.073	0.635	31%
Org-5730	$0.118 \cdot 10^{11}$	−41.8	33.8	$0.302 \cdot 10^6$	−23.3	8.6	$0.844 \cdot 10^{10}$	−15.0	18.3	0.101	0.222	4.5%
Org-gb94	$0.101 \cdot 10^6$	−12.4	−2.06	13.5	0	−8.3	$0.281 \cdot 10^5$	21.7	−28.9	0.473	0.451	8.5%

[a] MD = Maximum deviation between observed and calculated capacity factors.

[b] RMD = Relative MD for observed capacity factors higher than 1.

DISCUSSION

Neutral solutes

Solutes with predominantly neutral behaviour in the pH zone of interest (phenol, caffeine, org-9935, N-vinylpyrrolidone) were included in the fitting calculations for acidic compounds. There were two reasons to do so: first, to assess the behaviour of the models for these compounds; second, if the models fit the data for neutral solutes without problems, it will not be necessary to establish a rigorous threshold to distinguish between "almost acidic" and "almost neutral" solutes.

We conclude that the models do fit the data with good accuracy, as can be seen from Tables I, III, VIII and IX (class 1 models) and Tables XIII, XV, XX and XXI (class 2 models).

The fitted parameters show a peculiar but understandable behaviour. As the capacity factors of neutral solutes are almost constant (the variations are mainly due to experimental error), some of the calculated parameters have no physical meaning and are just circumstantial. Other parameters will compensate the retention behaviour within the model. For example, the calculated k_0 and k_{-1} values may be very different (Table I, model 1.D) if the acidity constant has a very high or low value, so that only one of the species is predicted to be present. In some instances, such as phenol in Table XV (model 2.G, ChromSpher data), the calculated K_a is negative. In this instance, k_0 and k_{-1} have the same value, so that retention will be essentially independent of the value assigned to K_a.

Stationary phases

From the results obtained for class 2 models (Tables XIII–XXII), it seems that the observed acidity constant of the solutes, equal to the [H] at which both forms of the acidic solute are present in equal concentrations, is higher on the μBondapak than on the ChromSpher column for some solutes, and lower for others. This is most apparent for phenol. This solute shows a decrease in retention for pH > 5 on the μBondapak column, like a typical acidic solute, whereas on the ChromSpher column it appears to be neutral in the pH range considered. The calculated K_a for several models illustrates this behaviour. 2,3,4-Trihydroxybenzophenone (Table XXII), *o*-nitrophenol (Table XVI) and *p*-nitrophenol (Table XVII) appear to be more acidic on the μBondapak column, whereas peaks 1 and 2 of dinitrophenol, a solute that turned out to be impure [4], (Tables XVIII and XIX) are apparently more basic on that column.

Similar comparisons could be made for class 1 models, but as the acidity constant K_a^0 evaluated using these models corresponds to an extrapolation for 0% methanol, it would be more hazardous to make such comparisons.

Class 1 models

The nine models tested give, in general, similar results. Apart from some exceptions, the quality of fit is comparable. This is mainly due to the fact that class 1 models are not very flexible, *i.e.*, they cannot adapt to irregularities in the retention surfaces. The addition of new parameters to a base model undoubtedly improves this flexibility, but within a restricted range of values.

When determining the "best" model, one must take into account the practicality in addition to the accuracy. Too many parameters are undesirable, because many chromatograms are required to determine their values. A small number of parameters requires a small number of chromatograms, but usually implies a less accurate description of the retention surface. We fixed a maximum number of nine parameters for all models tested.

Comparing models 1.E and 1.F with their analogues 1.A and 1.D, we see that, in the models in which a constant shift parameter δ is added (1.E and 1.F), the resulting sum of squares of the residuals (*SSQ*) is for all solutes at least equal and in two cases significantly lower (2,3,4-trihydroxybenzophenone, caffeine). However, the results for benzoic acid are, in our opinion, a warning. Although showing a good fit, models 1.G and 1.I (μBondapak) give δ values of about -2, which (in absolute terms) is very high in comparison with the values of about 0.1 for the other models. The introduction of this type of parameter increases the probability of the model converging to a false minimum, because as k_0^0 and k_{-1}^0 are asymptotic values, variations in both may be compensated by changing the δ value accordingly. In this way, the particular model obtained for a given solute, with a constant shift parameter added, may somehow be circumstantial.

The cubic factor in the ln K_a expression (*cf.*, eqn. 27; parameter Q_3 in Tables I–X) is not important in the range of methanol percentages used in this work. The improvement from model 1.A to model 1.B is very small, except for the neutral solute org-9935 on the ChromSpher column.

Comparing model 1.A with models 1.C and 1.D, we can conclude that the inclusion of quadratic terms in the capacity factor expressions for the individual species (*cf.*, eqns. 25–26; coefficients T_0 and T_{-1} in Tables I–X) is beneficial, especially for the k_0 factor; see, for example, Tables II, VI and X (ChromSpher data) and Table V (μBondapak data). It is possible to compare the beneficial effects of both parameters separately, by comparing the *SSQ* of models 1.G and 1.H, for T_0, and models 1.E and 1.F, for T_{-1}. The improvements found by including T_0 in the models are, understandably, more important, because for acidic solutes the neutral species has a greater capacity factor than the negative species so that k_0 accounts for a greater part of the observed capacity factor than k_{-1}.

From the discussion above about each of the parameters, it seems that models 1.C, 1.F, 1.G and 1.I are the most useful. The smaller *SSQ* values are in most instances obtained for models 1.C and 1.I. Choosing one between them is mostly a matter of common sense. If we are to use the model in relatively large parameter species, it seems logical to use parabolical expressions for ln k_0, ln k_{-1} and ln K_a (model 1.C, with nine parameters). A constant shift parameter may be excluded, for two reasons. First, as was explained above, this reduces the danger of having a model converging to a false minimum. Second, model 1.C is as good as any other model tested with the inclusion of a δ parameter. A model "1.C + δ" would require ten parameters. The difficulty in fitting the model increases noticeably with increase in the number of parameters, and so does the need for good initial estimates. Model 1.C is, in our opinion, the best compromise between precision and practicality.

Class 2 models

In this class of models, the inclusion of a δ term gives much greater improvements than for class 1 models (*cf.*, results for N-vinylpyrrolidone and 2,3,4-trihydroxybenzophenone, Tables XX and XXII). Comparing models 2.B and 2.D, which differ by the cubic factor S_3, shows model 2.D to be significantly better for some solutes. Going from model 2.D to 2.F, that is, removing the cubic term and assuming ln k to be a quadratic function of φ, gives mixed results: nine lower and nine higher values for *SSQ*. Some of the variations are fairly large. This indicates that a blending of both models, that is,

$$k = \delta + \frac{k_0[\mathrm{H}] + k_{-1}K_a}{[\mathrm{H}] + K_a} \exp\{\varphi(S_0 + S_1[\mathrm{H}] + S_2[\mathrm{H}]^2 + S_3[\mathrm{H}]^3) + \varphi^2(T_0 + T_1[\mathrm{H}])\} \qquad (55)$$

might perform better. However, this model contains ten parameters, which we believe is too many.

Models 2.G and 2.H did not live up to our expectations, giving results that were worse than most of the other models. Their advantage is that they have a small number of parameters (six and seven, respectively).

Comparison of class 1 and class 2 models

We show in Fig. 4 representative retention surfaces for one model from each class. They are almost identical within the parameter space covered by the experiments.

In general, models from class 2 give marginally better *SSQ* values. However, any slight extrapolation for the class 2 models (Fig. 5) results in the prediction of very high retention values towards lower pH. This indicates why class 2 models fit the data better. They are more "curvable", in other words, they have a potentially higher number of inflections, which enables them to adjust better to deviations in the data.

If we use a relatively large number of data points (at least twenty), we can describe the data with high precision by using any model from 1.C, 2.D or 2.F (nine parameters at most). Models with ten parameters, which would probably do better, are model 1.C with a constant shift term added, or eqn. 53. However, nine parameters are adequate for practical purposes.

Experimental design

The results were surprising. Although models from class 2 perform "better" (lower *SSQ* values) when using the whole data set for calculating the model parameters, reducing the number of design points led them to "explode", oscillating violently

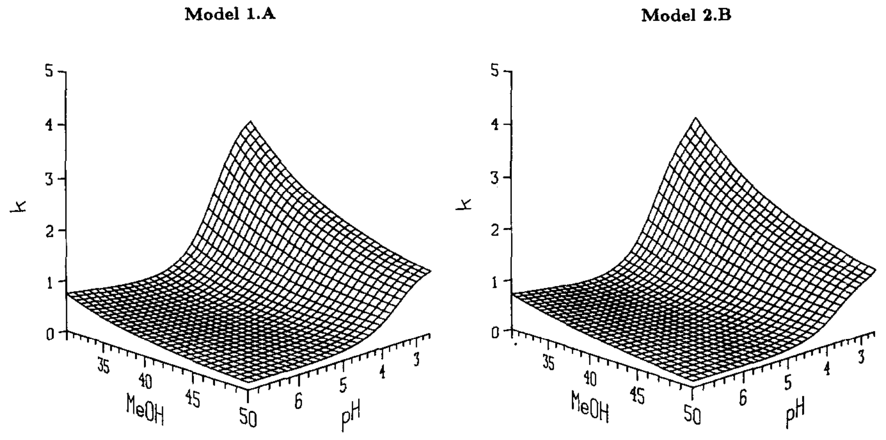

Fig. 4. Calculated retention surfaces for a class 1 and a class 2 model (1.A and 2.B, respectively) over the parameter space covered by the experimental data available. Solute, dinitrophenol (peak 2); column, ChromSpher ODS. MeOH = Methanol.

between points of the experimental design and therefore resulting in grossly inaccurate predictions for intermediate control points.

In contrast, all class 1 models give very good (and similar) results. Their precision is good. In absolute terms, the greatest deviation between the predicted and observed capacity factors is about 0.15. The relative deviations at certain combinations of pH and organic modifier concentration, where the capacity factors are small, can be high. For capacity factors higher than 1.0, the maximum relative deviation was about 6% and for capacity factors between 0.5 and 1.0 it was 12%.

Judging from the results (Tables XXIII and XXIV), nine points may suffice but twelve are preferable. The latter reduces the probability of having one bad experimental run ruining the optimization.

Basic solutes

The results in Table XXV show that eqn. 54 provides a good representation of the retention

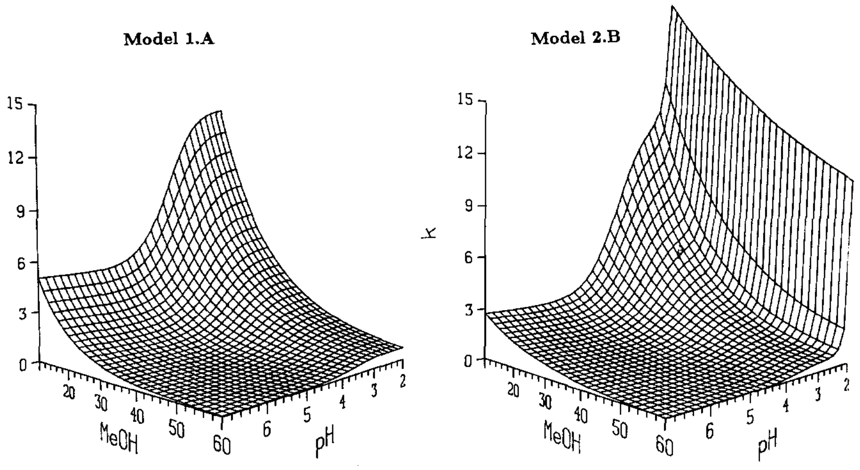

Fig. 5. Extrapolation of the calculated retention surfaces for a class 1 and a class 2 model (1.A and 2.B, respectively). Note expansion of the scale in comparison with Fig. 4. Solute, dinitrophenol (peak 2); column, ChromSpher ODS.

surface of the basic solutes studied. The major discrepancies that are apparent in Table XXV concern the relative deviations between the observed and calculated capacity factors, which for capacity factors around 1 can be as high as 30%, and for smaller capacity factors (not shown) they can be much higher (we observed a deviation of 60% for org-20494). There is a major reason why these values should be considered "normal". It is convenient to employ an absolute minimization criterion (sum of squares of deviations) to perform the model calculations, because if we were to use a relative criterion (*e.g.*, sum of squares of relative deviations) then we would have disproportionated contributions for that sum around zero. In this way, relative deviations are not minimized and it is natural that high (and seemingly unacceptable) values are obtained for small capacity factors. Another factor that may be included in the data and contributing in some extent to the deviations between observed and calculated values is column degradation between successive experiments. The effect of column degradation has been discussed elsewhere [4].

CONCLUSIONS

We can describe capacity factors for monoprotic acids with good accuracy using models derived from two distinct approaches. When a limited number of data points is available, models derived by first describing the capacity factor as a function of pH and then assuming the coefficients in this equation to be a function of composition are to be preferred over models derived the other way around. In the latter instance the numerical curve-fitting approach may give rise to anomalous results. Using an experimental design of twelve points, it is possible to predict capacity factors accurately using several of the models derived from eqn. 15. From these results, taking into account the modelling work done with larger data sets, we conclude that of the models studied the best one is

$$k = \frac{\left\{ \begin{array}{l} k_0^0 \exp(S_0\varphi + T_0\varphi^2)[\mathrm{H}] + k_{-1}^0 K_a^0 \exp[(Q_1 \\ + S_{-1})\varphi + (Q_2 + T_{-1})\varphi^2] \end{array} \right\}}{[\mathrm{H}] + K_a^0 \exp(Q_1\varphi + Q_2\varphi^2)} \tag{56}$$

(referred to in the text as model 1.C).

Assigning a parabolic function of the organic modifier concentration to the logarithm of each parameter figuring in

$$k = \frac{\sum_{m,n} k_{m,n}\kappa_{m,n}[\mathrm{H}^m][\mathrm{A}^{n-1}]}{\sum_{m,n} \kappa_{m,n}[\mathrm{H}^m][\mathrm{A}^{n-1}]}$$

results in a general model that is applicable with good results to the modelling of retention as a simultaneous function of pH and organic modifier concentration for weak acids and bases, as well as for neutral compounds.

The extension of this model to polyprotic compounds is not straightforward, because each new parameter in the equation above means three more parameters in the model. Two solutions seem apparent: either an experimental design with more points is developed, or linear instead of parabolic functions may be used for describing the logarithm of the capacity factor. This will be the object of future work.

Our ultimate aim is not to describe retention functions, but to optimize separations. We have incorporated model 1.C into selectivity optimization procedures and are currently studying their applicability in this context.

SYMBOLS

β	ratio between stationary and mobile phase volumes
C_A	sum of the concentrations of a solute A in all its possible forms
δ	constant shift parameter included in some retention models
k	observed capacity factor
k_0	capacity factor of neutral species
k_0^w	capacity factor of neutral species in pure water
k_{-1}	capacity factor of negatively charged species
k_{-1}^w	capacity factor of negatively charged species in pure water
k_1	capacity factor of positively charged species
k_α	observed capacity factor of a solute at α% of organic modifier
$k_{i,\alpha}$	capacity factor of a solute with charge i at α% of organic modifier

k_i^0	$\ln k_i^0$ is the first coefficient of a polynomial model for $\ln k_i$ as a function of the fraction of organic modifier (constant pH)
$k_{m,n}$	capacity factor of H_mA_n
k^w	observed capacity factor of a solute in water
K_a	acidity constant of a monoprotic acid HA
K_a^0	$\ln K_a^0$ is the first coefficient of a polynomial model for $\ln K_a$ as a function of the fraction of organic modifier (constant pH)
K_a^w	acidity constant of a monoprotic acid HA in pure water
K_A	equilibrium constant for the partition of A^- between mobile and stationary phases
K_{HA}	equilibrium constant for the partition of HA between mobile and stationary phases
$\kappa_{m,n}$	stoichiometric formation constant of H_mA_n
pH^O	pH of a mixed eluent as measured with a glass electrode calibrated with aqueous buffers (operational pH)
pH^P	pH of a mixed eluent as measured before mixing the buffer with the organic modifier (pragmatic pH)
pH^T	thermodynamic pH
φ	fraction of organic modifier in the mobile phase
Q_1, Q_2, Q_3	second, third and fourth coefficients, respectively, of a polynomial model for $\ln K_a$ as a function of the fraction of organic modifier (constant pH)
S	slope of a linear model for $\ln k$ as a function of the fraction of organic modifier (constant pH)
$S([H])$	variation of the slope S with the acidity of the mobile phase
S_n	second coefficient of a polynomial model for $\ln k_n$ as a function of the fraction of organic modifier (constant pH), or the n-degree coefficient of a polynomial model for minus S as a function of pH (constant φ)
SSQ	sum of squares of the differences between calculated and observed values
t_0	hold-up time
T_n	third coefficient of a polynomial model for $\ln k_n$ as a function of the fraction of organic modifier (constant pH), or the n-degree coefficient of a polynomial model for the variation of T in the model describing $\ln k$ as a function of the organic modifier concentration: $\ln k = \ln k_0 - S\varphi + T\varphi^2$
$t_{r,i}$	retention time of solute i

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