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Correlation analysis in liquid chromatography of metal chelates

II. One-dimensional retention–mobile phase composition (physicochemical property) models in reversed-phase liquid chromatography

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ABSTRACT

The applicability of linear correlation models for describing the effect of mobile phase composition and properties on the retention of metal chelates in reversed-phase liquid chromatography is demonstrated. The macroscopic (dielectric constant, surface tension, viscosity, concentration of organic modifier, distribution constant in an *n*-octanol–water system, etc.) and microscopic (characteristics of donor and acceptor ability) parameters of binary water–organic mixtures are used as variables. Although each of the studied parameters alone is somewhat limited in application, together they allow retention values to be estimated and the chromatographic behaviour of metal chelates to be predicted. The dominant influence of mobile phase composition and proton-donating ability on chelate retention in reversed-phase liquid chromatography is confirmed.

INTRODUCTION

The complex polyfunctional structure of metal chelates requires an extensive application of mathematical modelling to describe their liquid chromatographic behaviour at the quantitative level [1–4]. In a previous paper [1] we confirmed the necessity for the development of multiparametric correlation models based both on the structural parameters of chelates and on the parameters of a chromatographic system. This paper deals with the effect of mobile phase composition and physicochemical properties on metal chelate retention in reversed-phase liquid chromatography (RPLC) and is the next stage in developing such models.

EXPERIMENTAL

The synthesis of metal chelates (dialkyldithiocarbamates and dialkyldithiophosphates) and the conditions of the chromatographic experiments are described in

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ref. 1. Parameters for organic solvents and the corresponding binary water–organic mixtures were taken from refs. 5–11.

RESULTS AND DISCUSSION

Correlation dependences of the general type:

$$\log k' = a + bx \qquad (1)$$

where k' is the capacity factor and x is the eluent parameter (or its logarithmic function), are widely used in RPLC of organic compounds to describe the effect of the mobile phase and to optimize its composition. There is every reason to believe that one-dimensional models of the type in eqn. 1 may be used to estimate retention parameters of the sulphur-containing chelates under consideration. Firstly, owing to the covalent character of metal–ligand bonds and the small effective charge of the metal atom, the major contribution to the intermolecular interactions within a chromatographic system is made by the organic part of the molecule. Secondly, most chelates of a given type are relatively stable in a chromatographic process, *i.e.* the interphase distribution may be considered to be the main type of physico-chemical equilibrium. Moreover, as was shown in ref. 12, the behaviour of sulphur-containing chelates in RPLC is well described in terms of the solvophobic theory [13]. Therefore the effect of the mobile phase may be evaluated by such parameters as surface tension, dielectric constant, characteristics of donor–acceptor ability, etc.

The mobile phase parameters as well as structural parameters of chelates [1] should not be selected formally. For example, determination of the parameters most closely connected to retention values provides additional information for the theoretical understanding of the retention mechanism. On the other hand, the readily accessible x parameters affect the selection, since the main purpose of the correlation analysis is a practical one —to obtain the means of predicting relative changes of retention and to optimize separation. One final task of this study was to confirm that the principles of liquid chromatography of organic compounds may be applied to metal chelates.

All studied parameters x may be conditionally divided into two groups: macroscopic parameters characterize the properties of the mobile phase as a continuous medium, and molecular parameters reflect the ability of the mobile phase to participate in intermolecular interactions of different types. The former comprise such physical–chemical properties of solvents as surface tension, viscosity, dielectric permeability, hydrophobicity, etc., and the latter parameters of electron- and proton-donating ability.

Macroscopic parameters of mobile phase

Concentration of organic modifier. The concentration of the organic component (the simplest characteristic of mobile phase composition) was experimentally shown to be indicative of eluent strength in RPLC with regard to compounds of the most diverse nature, including metal chelates [14,15].

According to the theoretical calculations of free energies of intermolecular interactions of metal chelates in RPLC systems determined by the mathematical treatment of solvophobic theory [16] (for more details see ref. 12), the dependence of log k'

values on the volume ratio of the organic solvent is almost linear (Fig. 1; the model system is mercury diethyldithiophosphate–octadecylsilanized silica gel–dioxane–water) over a wide range of compositions (from 40 to 100% in the case under consideration). The experimental dependences of capacity factors *vs.* composition of mobile phases modified by various organic solvents (Fig. 2a) are fairly well described by the model:

$$\log k' = a - bc \tag{2}$$

($r = 0.973$–0.998; $s = 0.06$–0.08). A mobile phase of water–isopropanol is the only exception. In this case another approach is necessary, based on the replacement model developed by Snyder [17]. According to this model, at high concentrations of the organic modifier the following linear correlation applies:

$$\log k' = a - b\log C \tag{3}$$

where C is molar concentration of the organic solvent. In the above example, changing the coordinates system from eqn. 2 to eqn. 3 results in better linear correlation (Fig. 2b). This shows that solvation processes are most marked when mobile phases are modified by isopropanol. This is consistent with the fact that isopropanol is the most hydrophobic of all solvents studied.

Hydrophobicity. According to both the solvophobic theory and the concept of competitive adsorption (the basis of our study of the behaviour of metal chelates in

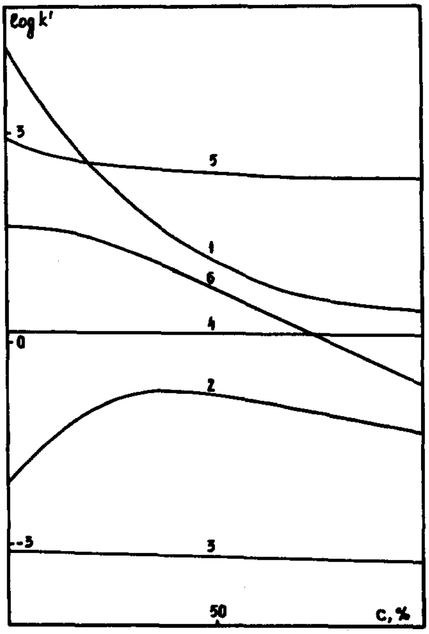

Fig. 1. Energetic contributons of the various parameters to log k' values at different mobile phase compositions. 1,2 = Formation of cavity in mobile phase [$\Delta A\gamma N$ and $(k^e\text{-}1)A_S\gamma N$, respectively], 3 = Van der Waals interactions; 4 = dipole–dipole interactions; 5 = changes of mobile phase free volume; 6 = total dependence. A and A_s are the surface area of the cavity and a solvent molecule, respectively; γ is the surface tension value; N is Avogadro's number and k^e is the dimensionless value.

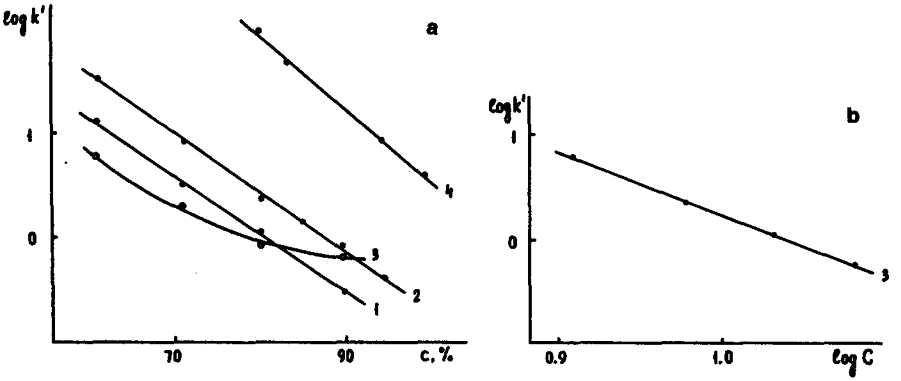

Fig. 2. Dependence of the retention parameters of cobalt (1, 2) and mercury (3, 4) diethyldithiocarbamates on (a) volume and (b) molar concentration of organic modifier in mobile phase. 1 = Dioxane; 2 = acetonitrile; 3 = isopropanol; 4 = methanol. Stationary phase: octadecylsilanized silica gel.

RPLC) chelate retention should depend on the hydrophobic properties of the mobile phase. The hydrophobicity of eluent was evaluated by measuring the same parameter as was used for the sorbate [1] – the distribution constant in an *n*-octanol–water system (P_S) [18]. The dependence of $\log k'$ of metal diethyldithiocarbamates on the P_S values of water–methanol and water–acetonitrile mixtures (Fig. 3) is well described by the equation:

$$\log k' = a - b \log P_S \tag{4}$$

but only for large contents of organic component, *i.e.* at weak eluent structuring. The non-linearity region for water–methanol mobile phases is extended, apparently because methanol molecules are capable of entering the hydrated structures of the associated mobile phase without destroying them.

Methylene selectivity. Another parameter which affects mobile phase relative hydrophobicity is methylene selectivity, $\log \alpha_{CH_2}$, defined as the difference in retention

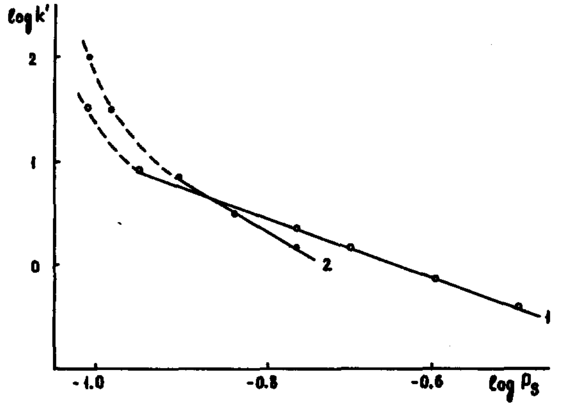

Fig. 3. Effect of mobile phase hydrophobicity on retention of mercury diethyldithiocarbamate. 1 = Methanol–water; 2 = acetonitrile–water.

of two adjacent alkyl homologues. It is a convenient measure of the influence of mobile phase composition on metal chelates with various alkyl substituents. The calculated log α_{CH_2} values agree well with the data calculated from retention parameters of various classes of organic compounds (Table I). The effect of the methylene selectivity of a dioxane–water mobile phase on the retention of metal dithiocarbamates is described by the equation:

$$\log k' = a + b \log \alpha_{CH_2} \qquad (5)$$

with good correlation (r = 0.990–0.997; s = 0.04–0.06).

Surface tension. The solvophobic theory of RPLC established the linear correlation between retention parameters and the surface tension of the mobile phase [19]. For mixtures of water and aprotic solvents (acetonitrile, dioxane) the log k' *vs.* γ dependences (Fig. 4) take the shape of a linear function (r = 0.991–0.998; s = 0.04–0.08). Deviations from linearity are observed for water–alcoholic eluents; these are less pronounced for methanol than for isopropanol. Nevertheless, the importance of γ as a measure of mobile phase eluting strength in relation to metal chelates is beyond doubt.

Viscosity. The molecular properties affecting viscosity are volume, polarizability, dipole moment, molecular weight, etc. Most of these properties determine simultaneously the specific interactions of sorbate within the mobile phase. Thus, the relation between log k' and viscosity (η) must also reflect the intermolecular interactions of metal chelate with eluent components. However, the majority of dependences are non-linear (Fig. 5). This may be attributed to the fact that changes in viscosity with changing water–organic solution composition are non-monotonous [5]. The peak dependence is determined by the concentration of the organic component and by its hydrophobicity. Therefore the heuristic properties of η values apply only over a limited range of component ratios that correspond to the region of monotonous viscosity changes (as a rule, the range in which the organic component does not exceed 60%).

Dielectric constant (ε). The experimental data show the increase in chelate retention with increasing dielectric permeability of the mobile phase (Fig. 6). In general the obtained dependences have a high degree of correlation (r = 0.998–0.999; s = 0.01–0.04) regardless of the type of mobile phase. This may be interpreted as a prevalence of solvophobic over specific interactions for the metal chelates studied. Conversely, owing to the growth in specific solvation with increasing eluent polarity (proportional to ε values) the log k' values were assumed to decrease.

TABLE I

ELUTION ABILITY OF ACETONITRILE–WATER MOBILE PHASE IN TERMS OF METHYLENE SELECTIVITY VALUES

Composition acetonitrile–water (v/v)	Log α_{CH_2}		
	Alkylbenzenes [8]	Nitroalkanes [8]	Copper dialkyldithiocarbamates
65:35	0.167	0.165	0.165
80:20	0.133	0.129	0.130

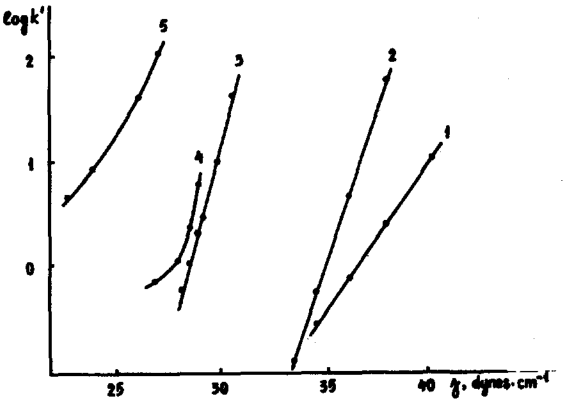

Fig. 4. Dependence of the capacity factors of copper (1, 3) and mercury (4, 5) diethyldithiocarbamates and copper di-*n*-butyldithiophosphate (2) on the surface tension of mobile phase. 1, 2 = Dioxane–water; 3 = acetonitrile–water; 4 = isopropanol–water; 5 = methanol–water.

Molecular parameters

The chromatographic behaviour of metal chelates in RPLC is affected by specific interemolecular interactions with components of the mobile phase (mostly hydrogen bonds and donor–acceptor interactions [20]). However, it is difficult to describe in terms of macroscopic parameters how the solvation processes affect chelate retention. Therefore we turned to a large class of empiric parameters that characterize the proton- and electron-donating ability of solvents and that are widely used to evaluate the elution strength of the mobile phase in RPLC [9–11].

All parameters studied (Kamlet–Taft basicity parameter π^*, Dimroth–Reichardt acceptor strength parameter E_T, Kosower and Brounstein's parameters z and S) are more or less able to predict chelate retention in terms of one-dimensional

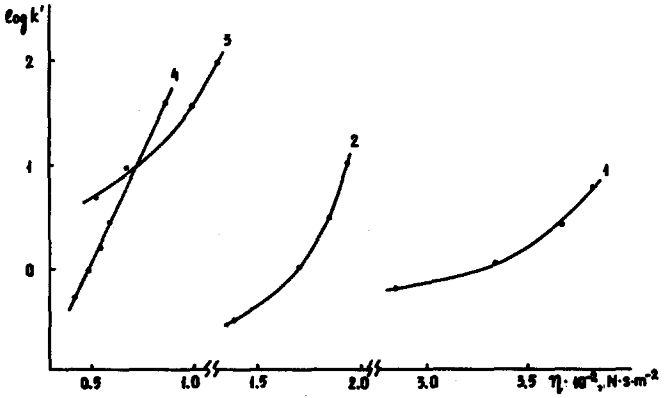

Fig. 5. Plots of log k' and dynamic viscosity coefficient of mobile phase for mercury (1, 3), copper (2) and cobalt (4) diethyldithiocarbamates. 1 = Isopropanol–water; 2 = dioxane–water; 3 = methanol–water; 4 = acetonitrile–water.

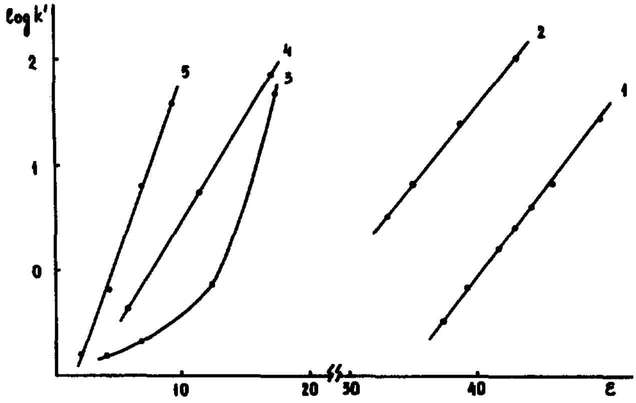

Fig. 6. Log k' values of mercury (1) and cobalt (2) diethyldithiocarbamates and mercury diethyl (3), dibutyl (4) and dioctyl (5) dithiophosphates *vs.* dielectric constants. Mobile phase: 1 = methanol–water; 2 = acetonitrile–water; 3–5 = dioxane–water.

linear models. However, as one would expect, no one of them is universal. Thus, the dependence of log k' on π^* values is linear only when mobile phases are modified by aprotic solvents (Fig. 7), because π^* parameters fail to reflect the solvent's ability to form hydrogen bonds. On the other hand, the E_T parameter is sensitive to the proton-donating properties of the mobile phase. Therefore, it is linearly correlated with log k' values only for water–alcoholic eluents. The z and S parameters, which characterize the solvation capacity of a solvent as a proton donor, exhibit linear correlation only for mobile phases containing aprotic solvents (Fig. 8). This may be due to the fact that the proton-donating ability of such mixtures decreases proportionally to the increase in the organic component, while for water–alcoholic eluents (both components are proton donors of different strength) there is no such proportional relationship.

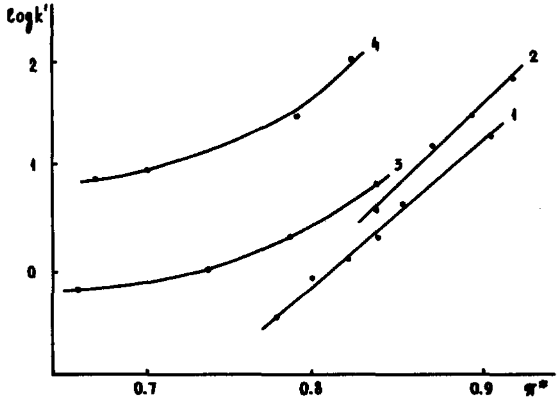

Fig. 7. Dependence of log k' values of lead (1) and mercury (2–4) diethyldithiocarbamates on the basicity parameter of the mobile phase. 1 = Acetonitrile–water; 2 = tetrahydrofuran–water; 3 = isopropanol–water; 4 = methanol–water.

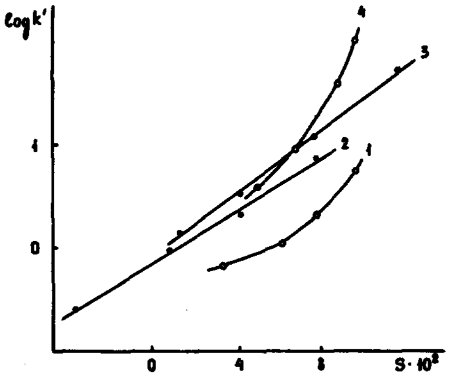

Fig. 8. Dependence of retention on mobile phase electron-accepting ability (by Kosower) for mercury (1, 3, 4) and antimony (2) diethyldithiocarbamates. 1 = isopropanol–water; 2,3 = dioxane–water 4 = methanol–water.

It must be stressed that as the mobile phase solvation capacity increases as measured by the above-mentioned parameters, the retention does not decrease (as it would if specific sorbate–eluent interactions mostly contributed to retention) but increases. This can be explained if the ability of mobile phase to form hydrogen bonds is considered as a reason for its association or, in other words, its solvophobic effect.

Other possible parameters used to estimate the elution strength of mobile phase in RPLC, like Snyder's P' parameter [21] of solvent polarity or Hildebrand's δ_T parameter [22], proved to be ineffective in evaluating metal chelate retention. They may only be applied for rather ideal solutions. However, this condition is rarely observed for polar water–organic eluents, especially when sorbates (like metal chelates) undergo specific intermolecular interactions with components of these mobile phases.

The above retention models can be applied to the optimization of metal chelate separation by the interpretive strategy approach. We use the single-parametric opti-

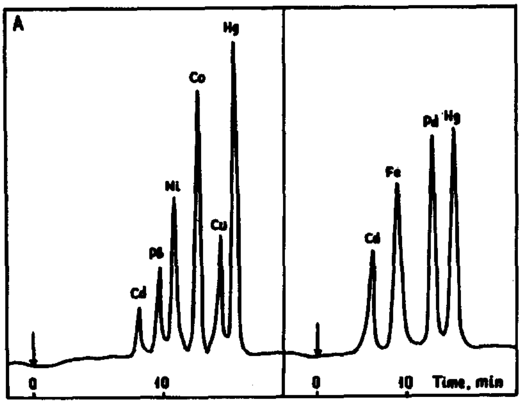

Fig. 9. Optimized separation of metal diethyldithiocarbamates by RP-HPLC. Column: 64 × 2 mm. Stationary phase: Separon C_{18} (5 μm). Mobile phase: acetonitrile–water (70:30, v/v) containing 2% chloroform. Flow-rate: 50 μl/min. UV-detection (280 nm).

mization procedure based on the analysis of window diagrams and α_{min} as an optimization criterion [23]. The selected optimal eluent was applied to separation of metal diethyldithiocarbamates under high-performance liquid chromatography (HPLC) conditions. Fig. 9 depicts two chromatograms obtained with the predicted mobile phase composition and indicates that the optimization was rather successful.

CONCLUSIONS

Thus, one-dimensional models based on the principle of free energy linear relations may be widely applied for the *a priori* estimation of retention parameters and the prediction of chromatographic retention behaviour of metal chelates, especially when the macroscopic parameters of the mobile phase are used as variables. As a rule, the molecular parameters are only limited to certain types of solvent or certain component ratios since such eluent properties as proton- or electron-donating ability characterize specific interactions of only one type. It is obvious that the analysis of retention–mobile phase composition (or physico-chemical property) models also provides valuable data for establishing the nature of intermolecular interactions and understanding the retention mechanism of metal chelates.

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