Journal of Chromatography A, 656 (1993) 537–547
Elsevier Science Publishers B.V., Amsterdam

CHROM. 25 426

Review

Solvatochromically based solvent-selectivity triangle

L.R. Snyder
LC Resources, 26 Silverwood Court, Orinda, CA 94563 (USA)

P.W. Carr*
Department of Chemistry, University of Minnesota, Minneapolis, MN 55455 (USA)

S.C. Rutan
Department of Chemistry, Virginia Commonwealth University, Richmond, VA 23284 (USA)

ABSTRACT

A classification of common solvents according to their dipolarity and hydrogen-bonding acidity and basicity has been developed, based on the Kamlet–Taft solvatochromic parameter scheme. This approach has been compared with the Snyder–Rohrschneider solvent-selectivity triangle (SST). The two solvent-classification schemes are found to be generally similar. Both SST-based schemes are also compared to an analysis of solvent selectivity based on linear solvation energy relationships. While there are considerable similarities, important practical differences, especially in the case of reversed-phase liquid chromatography, are evident.

CONTENTS

1. INTRODUCTION

A problem of continuing interest and importance in high-performance liquid chromatography (HPLC) is the selection of the "best" mobile phase composition for a given sample [1–3]. The usual goal is to optimize solvent strength and selectivity [4], so as to provide convenient sample retention and an even spacing of bands within the chromatogram. This in turn

* Corresponding author.

0021-9673/93/$24.00

requires knowledge of the relevant chromatographic properties of different solvents that might be used for the mobile phase. In this context, solvent "selectivity" —the ability of the solvent to affect relative retention and band spacing— is of considerable interest. In contrast, the term solvent "strength" means the ability to adjust overall retention without alterations in relative band spacing.

Several different procedures have been proposed for the classification of solvent selectivity [5–9]. A basic assumption in this work and other schemes for sorting out solvent selectivity is that one can separate solvent strength and selectivity. Most such schemes begin with the forces of attraction between solvent and solute molecules, with emphasis on dipolar and hydrogen-bonding interactions. This in turn leads to a description of different solvents in terms of their relative hydrogen-bond acidity, basicity and dipolarity. One widely cited classification of this type is the so-called *solvent-selectivity triangle* (SST) [8]. It is based on gas–liquid distribution constants originally reported by Rohrschneider [10]. Since its introduction in 1974, the SST has been widely used in the development of optimization schemes for both HPLC [11–13] and gas chromatography [14]. The SST approach was subsequently modified in various ways [15,16] that have not significantly affected the classification of different solvents in terms of acidity, basicity and dipolarity. The most significant concept offered by the SST approach is that mobile phase optimization is more likely to be successful if one uses solvents that incorporate major differences in those chemical interactions that influence the separation selectivity.

The SST classification scheme is based on the relative interaction between different solvents and test solutes classified as acidic (ethanol), basic (dioxane) and dipolar (nitromethane). It has been appreciated for some time that these compounds are each capable of more than one kind of interaction. For example, ethanol is clearly dipolar, protic and a good proton acceptor, in turn raising questions concerning the reliability of solvent classification by means of the SST. More recently [16], a comparison was carried out of solvent acidity, basicity and dipolarity as measured by the SST [8,15] and the solvatochromic approach developed by Kamlet *et al.* [9]. This study confirmed that the SST procedure is, indeed, based on test compounds that have multiple interactions. The solvatochromic approach, on the other hand, in inherently free of the problem; *i.e.*, selectivity coefficients that purport to measure acidity, basicity and dipolarity/polarizability do so very closely. Furthermore, the spectroscopic methodologies used to measure solvent dipolarity, hydrogen bond (HB) acidity and HB basicity are essentially independent of any models or assumptions used to cancel or minimize cavity formation energetics and dispersive (London) interactions between the probe solutes and the solvent (see below).

In view of the latter findings, it seems worthwhile to reconstruct the SST on the basis of "pure" selectivity coefficients from the solvatochromic method. In this paper, we provide such a reconstruction and examine some of its practical implications.

2. THEORY AND BACKGROUND

2.1. Solvent-selectivity triangle

The original SST classification was based on apportioning the various polar interactions of which a solvent is capable: acidic (x_d), basic (x_e) and dipolar (x_n). Values of x_d measure the interaction of the solvent with the test-solute dioxane, x_e measures interactions with ethanol, and x_n measures interactions with nitromethane; $x_d + x_e + x_n = 1$. These interaction coefficients x_i (i = d, e or n) are corrected for non-polar (dispersive) interactions and are normalized to the total polarity of the solvent. As a result, values of x_i sum to one. It is tacitly assumed that this "polarity normalization" results in a separation of solvent strength from solvent selectivity.

A plot using triangular coordinates to display values of x_i for different solvents results in the solvent-selectivity triangle shown in Fig. 1. Solvents falling near the corners of the plot of Fig. 1 are assumed to exhibit primarily one kind of selectivity (acidic, basic or dipolar), while sol-

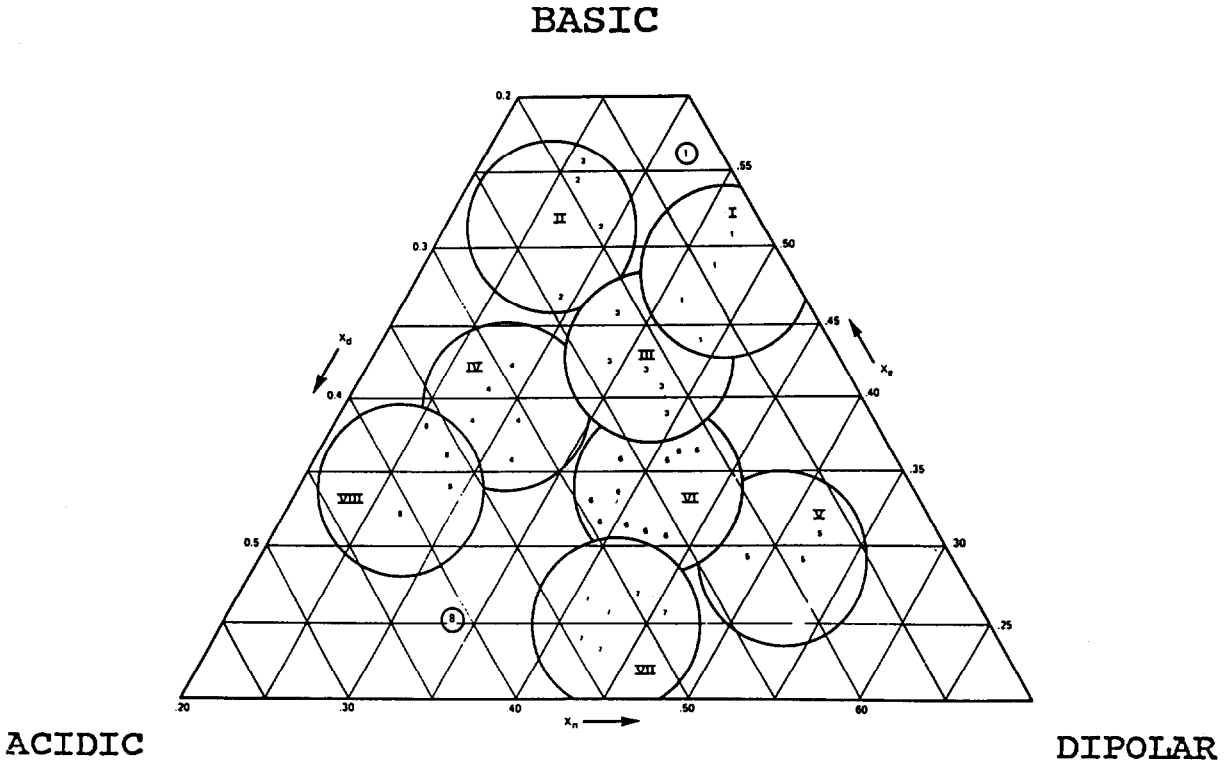

Fig. 1. Solvent-selectivity triangle of ref. 15. Numbers in figure refer to individual solvents: solvents of similar selectivity are circled.

vents within the triangle are capable of all three interactions.

Classification of solvents by the SST is in principle useful for two reasons:

Selecting a solvent of different selectivity, in order to separate two sample bands that overlap with an initial solvent;

Selecting some minimum number of solvents for a systematic approach to selectivity optimization; three such solvents (each close to one of the corners of the SST) should provide a broad range of solvent selectivity in either reversed-phase (RP) [12] or normal-phase (NP) [13] HPLC; blends of these three solvents in various proportions should then allow the continuous variation of solvent selectivity over the widest possible limits.

In addition, the SST classification provides a rational basis for interpreting experimental results when the mobile-phase solvents are varied.

2.2. Solvatochromic model

The solvatochromic approach to classifying solvent selectivity is qualitatively similar to the phase equilibrium based data used to develop the SST [9]. A set of three solvent parameters, similar to x_e, x_d and x_n, has been devised to describe solvent hydrogen bond acidity (α), basicity (β) and dipolarity/polarizability (π^*). However, values for these parameters for different solvents are derived from spectroscopic (hence the name solvatochromic) and other measurements, that were specifically designed so as to measure only a single interaction. Furthermore, values of these parameters are averages over results obtained with several probe solutes for each parameter, in contrast to the SST parameters, each of which is based on the thermodynamic property of a single solute. The solvatochromic parameters have been used to

correlate literally hundreds of chemically distinct processes [17]. It can therefore be argued that α, β, and π^* are inherently better measures of solvent acidity, basicity and dipolarity than are values of x_i.

The solvatochromic parameters were developed within the context of linear solvation energy relationships (LSERs). For the case of gas–liquid partition equilibria (the basis for the derivation of the SST parameters), the usual LSER for a solvent study, (fixed solute, varying solvent) is written as:

$$\log k' = SP_0 + m\delta_H^2 + s(\pi^* - d\delta_{KT}) + a\alpha + b\beta \quad (1)$$

In this equation k' is a chromatographic capacity factor, SP_0 is a solute-dependent intercept, δ_H is the Hildebrand solubility parameter used to represent the endoergic process of forming a cavity in the solvent large enough to accomodate the solute, π^* encodes the solvent's ability to interact with a solute by dipolar and polarization factors, α represents the solvent's ability to act as a hydrogen bond donor towards a basic (HB acceptor) solute and β denotes the solvent's ability to act as a hydrogen bond acceptor towards a protic (HB donor) solute. The term $d\delta_{KT}$ is a polarizability correction factor. The coefficients m, s, a and b are related to the test solute size, dipolarity/polarizability, HB basicity and HB acidity, respectively.

Recalling that the SST parameters are derived by appropriately normalizing the behavior of the test solute to a reference alkane solute of the same size, the LSER for a ratio of capacity factors should be written as:

$$\log k'/k'_{alkane} = SP_0 + s(\pi^* - d\delta_{KT}) + a\alpha + b\beta \quad (2)$$

It is assumed that by taking the ratio of the capacity factor for the test solute relative to the capacity factor of an equivalently sized alkane, the solvent cavity formation energy term ($m\delta_H^2$) can be neglected in eqn. 2. It is now evident within the solvatochromic LSER formalism that a solvent can be represented in terms of three primary parameters (π^*, α and β) and a correction factor ($d\delta_{KT}$). This correction factor is small for processes that do not involve significant solute–dipole, solvent-induced dipole interactions.

It is possible to predict accurate values for x_i from the corresponding solvatochromic parameters, by assuming that values of x_d, x_e and x_n are each some function of solvent acidity, basicity and dipolarity [16]. (Note that the SST and solvatochromic scales of solvent selectivity are each derived from completely different sets of experimental data.)

In addition, the solvatochromic model has been used to correlate retention for a number of reversed-phase HPLC systems, with generally good results [18,19]. In this case, a series of solutes were studied and the mobile and stationary phase were held constant. Studies of RP-HPLC by use of solvatochromic LSERs have very clearly shown that there are two dominant solute variables: size and hydrogen bond basicity. Solute dipolarity and hydrogen bond donor strength are much less important.

2.3. Failures in the application of the SST

Several studies have evaluated the reliability of the SST for predictions of solvent selectivity in reversed-phase HPLC. Although the SST has been successfully applied in a wide variety of systems, it was found to be a poor predictor of selectivity for the separation of stereoisomers of polystyrene [20] and various steroid derivatives [21,22]. More recent work [23] with another series of sample compounds found that selectivity differences *do* correlate with predictions from the SST; the authors attributed the opposite conclusions of earlier workers [20–22] to a failure to distinguish large and small selectivity effects. That is, the SST appears to be a somewhat imprecise measure of solvent selectivity in reversed-phase HPLC (for reasons given below), so that *minor* changes in relative retention cannot be predicted accurately.

It is nevertheless intriguing to consider whether these past "failures" of the SST are related to the use of test compounds of "mixed" selectivity character. For this and other reasons, it seemed interesting to develop an alternative SST based on the solvatochromic parameters α,

β and π^* and to examine the resulting changes (if any) in the relative positions of different solvents within this SST. The most straightforward approach was deemed to be the simple replacement of values of x_i with the corresponding values of α, β and π^* —after the latter values are normalized so as to sum to unity. A similar approach has recently been reported by Li *et al.* [24] for the classification of liquids used as gas chromatographic stationary phases.

3. RESULTS AND DISCUSSION

Values of α, β and π^* for various solvents that were examined in this study are from refs. 18 and 25 (in turn taken mainly from ref. 9). The

TABLE 1

CLASSIFICATION OF SOLVENTS ACCORDING TO NORMALIZED SELECTIVITY

Solvent	Normalized selectivity factors[a]			Solvent	Normalized selectivity factors[a]		
	π^*/Σ	α/Σ	β/Σ		π^*/Σ	α/Σ	β/Σ
Aromatics				*Amines*			
Benzene	0.86	0.00	0.14	Triethylamine	0.16	0.00	0.84
Toluene	0.83	0.00	0.17	Tributylamine	0.20	0.00	0.80
p-Xylene	0.81	0.00	0.19	*Carboxylic acids*			
Fluorobenzene	0.90	0.00	0.10	Acetic acid	0.31	0.54	0.15
Chlorobenzene	0.91	0.00	0.09	*Esters*			
Bromobenzene	0.93	0.00	0.07	Methyl acetate	0.55	0.05	0.40
Iodobenzene	1.00	0.00	0.00	Ethyl acetate	0.55	0.00	0.45
Phenyl oxide	0.84	0.00	0.16	γ-Butyrolactone	0.64	0.00	0.36
Anisole	0.77	0.00	0.23	Ethylacetoacetate	0.60	0.00	0.40
Nitrobenzene	0.72	0.00	0.28	*Ethers*			
Benzonitrile	0.69	0.00	0.31	Diethyl	0.36	0.00	0.64
Dibenzylether	0.66	0.00	0.34	Diisopropyl	0.36	0.00	0.64
Acetophenone	0.65	0.00	0.35	Dibutyl	0.34	0.00	0.66
Quinoline	0.58	0.00	0.42	Tetrahydrofuran	0.51	0.00	0.49
Pyridine	0.58	0.00	0.42	1,2-Dimethoxyethane	0.54	0.00	0.46
2,6-Lutidine	0.51	0.00	0.49	*p*-Dioxane	0.60	0.00	0.40
Benzyl alcohol	0.45	0.32	0.22	*Ketones*			
Alcohols				Acetone	0.56	0.06	0.38
Methanol	0.28	0.43	0.29	2-Butanone	0.55	0.05	0.40
Ethanol	0.25	0.39	0.36	Cyclohexanone	0.59	0.00	0.41
Propanol	0.24	0.36	0.40	*Nitriles*			
Butanol	0.22	0.37	0.41	Actonitrile	0.60	0.15	0.25
Isopropanol	0.22	0.35	0.43	*Nitro-compounds*			
tert.-Butanol	0.19	0.33	0.48	Nitromethane	0.64	0.17	0.19
Glycol	0.39	0.38	0.23	*X-miscellaneous*			
Hexachloro-2-propanol	0.25	0.75	0.00	Methylenechloride	0.73	0.27	0.00
Trifluorethanol	0.32	0.68	0.00	Chloroform	0.57	0.43	0.00
Amides				Ethylenechloride	1.00	0.00	0.00
Formamide	0.46	0.33	0.21	Dimethylsulfoxide	0.57	0.00	0.43
N,N-Dimethylformamide	0.56	0.00	0.44	Sulfolane	0.83	0.00	0.17
N,N-Dimethylacetamide	0.54	0.00	0.46	Water[b]	0.45	0.43	0.18
Hexamethylphosphoramide	0.46	0.00	0.54				
Tetramethylurea	0.51	0.00	0.49				
N-methylpyrrolidinone	0.57	0.00	0.43				

[a] See eqns.

[b] The β value used for water was 0.48 which is based on more recent estimates (ref. 26).

sole exception is the β value for water which is now taken as 0.48 [26]. These values of α, β and π^* for each solvent were first normalized by summing values of α, β and π^* ($=\Sigma$), then expressing solvent acidity, basicity and dipolarity as the fractional interaction coefficients α/Σ (acidity), β/Σ (basicity) and π^*/Σ (dipolarity). The resulting normalized interaction coefficients are summarized in Table 1. It must be understood that the solvatochromic parameters are only relative measures of the strength of intermolecular interactions. They will properly rank a set of solvents in terms of their strength. However, the absolute values of these parameters cannot be assigned any additional meaning. One can make only very rough cross comparisons of the strength between the different scales. Thus the strength of a dipolar interaction should not be directly compared to the strength of a hydrogen bonding interaction. For example, a π^* value of 0.5 does not correspond to the same amount of Gibbs energy as does an α of 0.5; however, the overall magnitude of the scales is such that normalization gives a triangle plot with a reasonable distribution of solvent points.

Plots of these solvatochromic measures of solvent acidity, basicity and dipolarity were next displayed in a format similar to that used for the original SST (Fig. 1). However, the resulting display was somewhat confusing due to the fact that more than half of the solvents of Table 1 have values of $\alpha \approx 0.0$. This tends to bunch most solvents along one axis of the SST. The data of Table 1 also do not include any information on solvent polarizability, which is known to be important in determining the interaction of a solute with aliphatic *vs.* aromatic solvents (see the discussion of the δ_{KT} term in eqn. 2).

Inasmuch as aliphatic solvents are of primary interest in HPLC (because of their lower viscosities and more convenient use with UV detectors), we will limit further discussion to the aliphatic solvents of Table 1. Fig. 2 is a triangular plot of the data of Table 1 for aliphatic

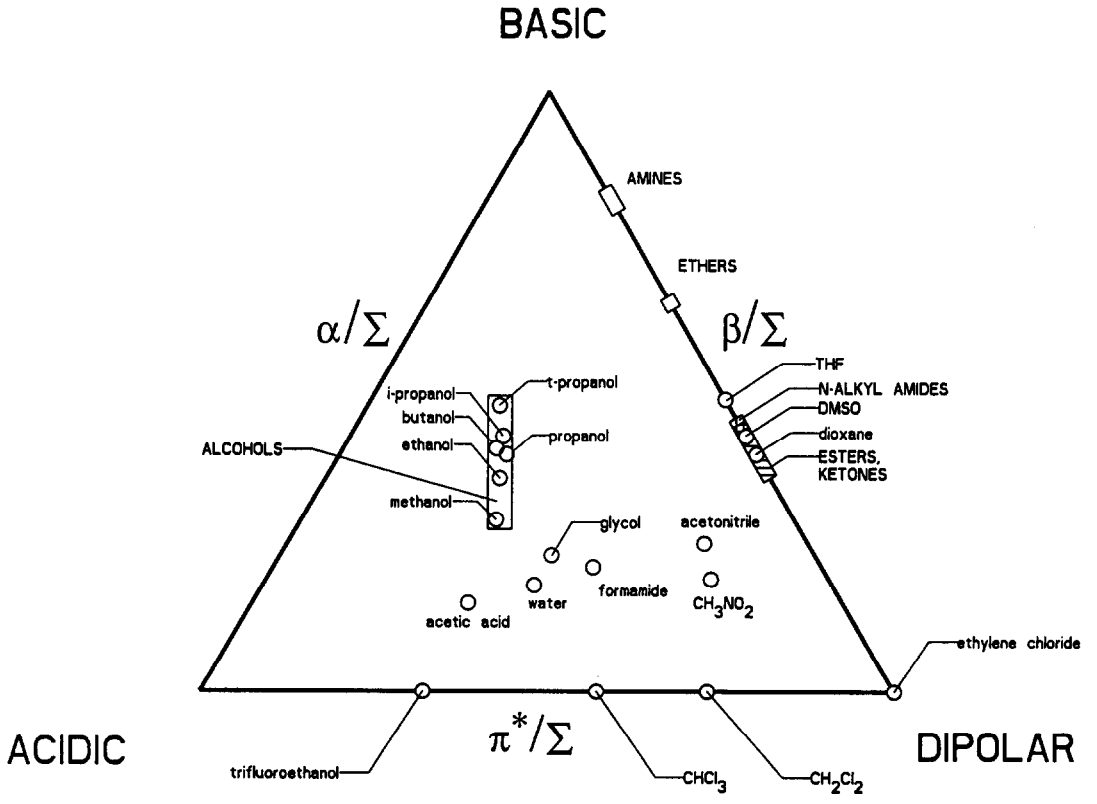

Fig. 2. Solvent-selectivity triangle based on solvatochromic data of Table 1. Aliphatic solvents.

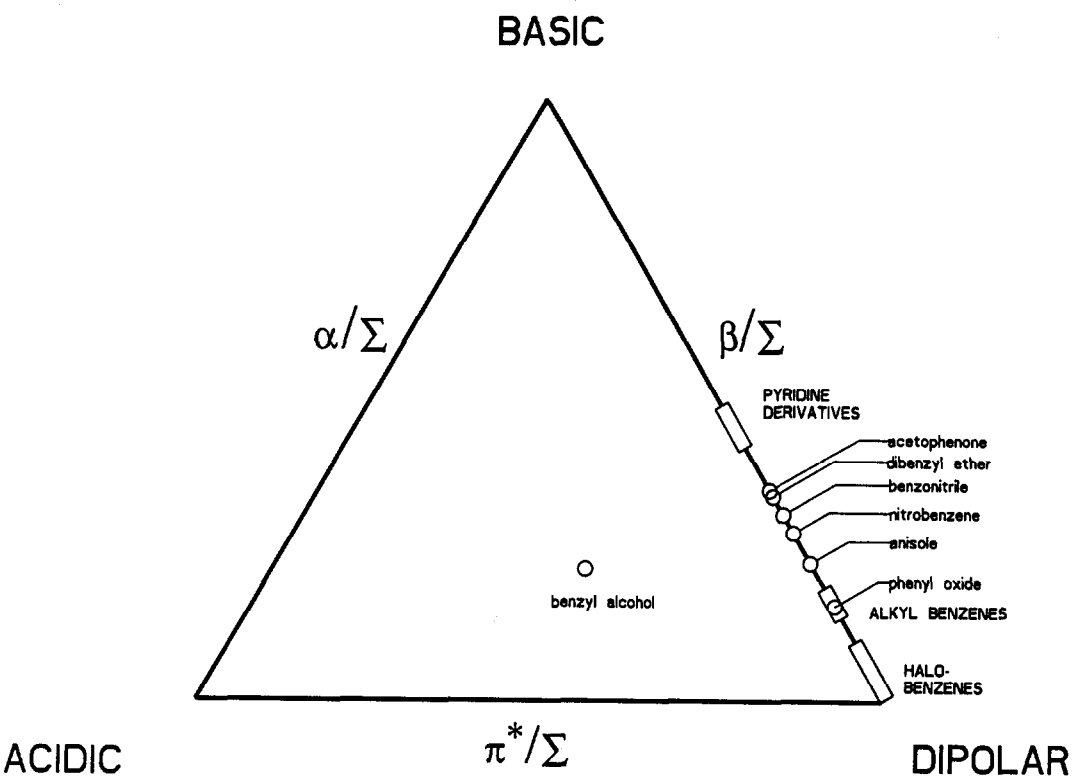

Fig. 3. Solvent-selectivity triangle based on solvatochromic data of Table I. Aromatic solvents.

solvents; Fig. 3 shows the corresponding plot for aromatic solvents. The positioning of different solvents or solvent types in Figs. 2 and 3 is very much as expected. For example, fluoroalcohols are very powerful HB donors and very weak acceptors, and thus are located on the acidic-dipolar axis (see Fig. 2). Use of the revised value of 0.48 for water's basicity places water near formamide and glycols, both of which resemble water in that they are hydrogen bond network forming solvents. Due to the almost complete absence of any aromatic hydrogen bond donor solvents among the aromatic solvents shown in Fig. 3, the data for aromatic liquids can really be represented, except for benzyl alcohol, as a line joining the basic and dipolar apices of the triangle.

3.1. Differences between Figs. 1 and 2

It has been argued that the approach to solvent-selectivity classification shown in Fig. 2 should in principle be better than that of Fig. 1. We will next compare these two schemes and see if this is reasonable in terms of what we know about solvent interactions. A direct comparison of Figs. 1 and 2 is not possible, in view of the inclusion of both aliphatic and aromatic solvents in Fig. 1. We therefore replotted the data for aliphatic solvents and solvent types in Fig. 1 as shown in Fig. 4. This plot is further simplified by

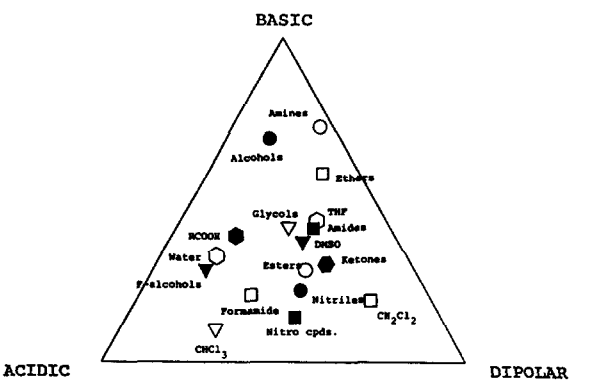

Fig. 4. Replot of Fig. 1 for indicated *aliphatic* solvents and solvent types.

averaging values of x_i for solvents of a given type (amines, alcohols, etc.), which was shown to be justified in ref. 16. A similar approach applied to the data of Fig. 2 gives Fig. 5. We will next compare Figs. 4 and 5.

It will be seen that the relative positioning of different solvents in Figs. 4 and 5 is similar, in that solvents which are more basic, acidic or dipolar in Fig. 4 are also more basic, acidic or dipolar in Fig. 5. A further examination of Figs. 4 and 5, however, shows that solvents of similar acidity or basicity are better grouped in the solvatochromic approach of Fig. 5. Thus, amines and ethers show up as distinctly basic, as compared to the alcohols in Fig. 5. The alcohols, glycols, formamide, carboxylic acids, water and chloroform show up as acidic solvents in Fig. 5. The acidity of these latter solvents seems inadequately expressed in Fig. 4.

The placement of acetonitrile and nitromethane *vs.* esters and ketones in Fig. 5 also seems more logical than in Fig. 4. Infrared studies [27] clearly show that acetonitrile and nitromethane are relatively poor bases compared to esters and ketones. These problems in the original solvent-selectivity triangle (Figs. 1 and 4) probably arise from the fact that the test solutes used to construct the SST of Table 2 are not "pure" measures of acidity, basicity and dipolarity. This is verified in Table 2, which gives solute solvatochromic parameters (determined by chromatographic methods) for the acidity

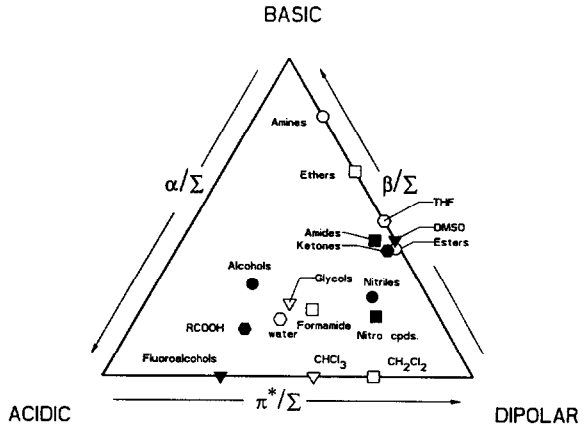

Fig. 5. Replot of Fig. 2 for same (aliphatic) solvents and solvent types of Fig. 4.

TABLE 2

SOLVATOCHROMIC SOLUTE PARAMETERS FOR TEST-COMPOUNDS USED IN FIG. 1

π_2^*, α_2 and β_2 measure, respectively, solute dipolarity/polarizability, acidity and basicity (determined by chromatographic methods).

Solute	π_2^{*c}	α_2^c	β_2^c
Dioxane (base)	0.45	0.00	0.79
Ethanol (acid)	0.29	0.29	0.52
Nitromethane (dipolar)	0.67	0.06	0.16

(α_2), basicity (β_2) and dipolarity (π_2^*) of the three polar compounds used as test-solutes in the scheme of Fig. 1. While nitromethane interacts mainly by dipolar forces ($\pi^* \gg \beta > \alpha$), ethanol (intended as an *acidic* probe) appears more basic than acidic ($\beta > \alpha = \pi^*$), and dioxane (the basic probe) has significant dipolar character ($\pi^* = 0.45$). These results make it clear that the choice of probes used in many previous studies of solvent strength has been far from optimum. Many solutes are available whose polarity arises almost exclusively from acidity, basicity, or dipolarity. For example, trifluoroethanol is a very strong acid but only a very weak base; triethylamine is quite basic but only slightly dipolar and not at all acidic.

3.2. Solvent-selectivity in RP-HPLC

We have referred to criticisms [20–22] of the original solvent-selectivity triangle as a basis for predictions of solvent selectivity in RP-HPLC. Other studies, however, suggest that the acidity, basicity and dipolarity of the organic modifiers used in RP-HPLC are only partly responsible for mobile phase selectivity. Thus changes in the mobile-phase *concentration* of the organic modifier often lead to significant changes in separation selectivity [28]. This is an effect which is not predicted by the solvent-selectivity triangle. As originally developed, the SST approach assumes that solvent strength can be varied (by varying the % water in RP-HPLC) without changing selectivity. However, in RP-HPLC the most common diluent is water. This

solvent is far from inert. Furthermore, direct spectroscopic studies of solvatochromism in mixtures of water with the four more common organic modifiers used in RP-HPLC show very considerable variations in their dipolarity (π^*), HB acidity (α) and HB basicity (β) as the volume fraction of organic modifier is varied [29,30]. These criticisms imply that the SST approach to adjusting solvent strength and selectivity in RP-HPLC is overly simplified.

As so far described, the original SST and the solvatochromic parameter approach are qualitatively similar in that they group solvents into similarly related classes and mandate the use of multi-parameter scales of solvent selectivity. We turn now to a more formal comparison of the two approaches. The sole purpose of this more formal analysis (see eqns. 3 and 4 below) is to clarify the similarities and point out the differences between the SST and the solvatochromic parameter approaches in more detail; however, we caution that neither method is as yet capable of making quantitative predictions of relative retention (selectivity).

We mentioned above that solvatochromically based LSERs have been used to study retention in RP-HPLC. These studies involve correlating the retention of a series of solutes (almost exclusively aromatic) in a fixed mobile and stationary phase. In RP-HPLC, the appropriate *solute* LSER is written as:

$$\log k' = SP_0 + mV_2 + s(\pi_2^* - d\delta_{KT}) + a\alpha_2 + b\beta_2 \quad (3)$$

where V_2 is some measure of solute size, such as its molar volume, and the subscript 2 denotes a solute property. The solute dependent term, V_2, complements the Hildebrand solubility parameter term which appears in the *solvent* LSER (see eqn. 1). It is needed to describe the endoergic (unfavorable) composite cavity and dispersive interactions of the solute with the mobile and stationary phase. For the most part, the other solute parameters in eqn. 3 are now derived from gas chromatographic measurements [31,32].

The coefficients (m, s, d, a, and b) in eqn. 3 depend on the mobile phase composition and the nature of the stationary phase. Experimental work [18,19] shows that the most important terms in eqn. 3 are m and b, while s, and a are smaller in that order. Because the test solutes are almost always aromatic, we can make no comment about the importance of the d coefficient.

The issue of solute selectivity (relative retention) is chromatographically more important than is absolute retention. Dropping the term in α_2, which is usually negligible, leads to an equation for the selectivity of two solutes (denoted i and ii):

$$\log[k'(\mathrm{i})/k'(\mathrm{ii})] = m(V_{2,\mathrm{i}} - V_{2,\mathrm{ii}}) + s(\pi^*_{2,\mathrm{i}} - \pi^*_{2,\mathrm{ii}}) + b(\beta_{2,\mathrm{i}} - \beta_{2,\mathrm{ii}}) \quad (4)$$

In accord with the SST approach to solvent selectivity, three mobile phase dependent coefficients are required to define selectivity in RP-HPLC. Note that as the volume fraction of organic modifier in the mobile phase is changed, all three coefficients (m, s, and b) in eqn. 4 will vary, as will selectivity. Eqns. 3 and 4 further show that as the solute size increases, k' will depend more strongly on the mobile phase composition. This is in good agreement with the fact that the slope of plots of log k' *vs.* volume fraction becomes larger as solute size increases [33].

In a homologous series of solutes, the solute π_2^*, α_2 and β_2 parameters are essentially constant [31,32]. Consequently, all variations in retention from solute to solute are due to the solute size, which is directly proportional to the number of methylene units in the solute. Therefore, the m coefficient is directly related to the "hydrophobic" selectivity of RP-HPLC.

At this point, we run into a definite contradiction between the SST approach, regardless of whether it is based on Rohrschneider's partition coefficients or Kamlet and Taft's parameters, and the LSER approach. First, LSER analysis of RP-HPLC data strongly supports the view that solvent basicity is not very important in RP-HPLC, and thus that it should not be included in a solvent triangle for RP-HPLC. Second, the LSER approach reveals that some measure of solvent cohesitivity is a very important parame-

ter. This is in good agreement with solvophobic theory in which the mobile phase surface tension is used as a measure of solvent cohesivity [34]. This suggests that a surface tension or solubility parameter, which can be roughly correlated with surface tension, ought to be used in the triangle. We have not *explicitly* included any term related to cohesivity in the SSTs displayed here.

These seeming contradictions are easily rationalized in view of the fact that a solvent's Hildebrand parameter (δ_H), must be related to its dipolarity, HB acidity and HB basicity. Indeed, multi-component solubility parameter schemes [35,36] are founded on this concept.

Thus, based on solvatochromic LSER correlations of retention in RP-HPLC, we probably only need three solvent parameters to describe retention in RP-HPLC. However, it is not clear that the three factors can or ought to be separated, as we have done here. It might, in fact, be more appropriate, at least in the case of RP-HPLC, to use some measure of solvent cohesivity as one of the apices of the triangle, and solvent dipolarity and HB donor strength as the others. We base this comment on the fact that cohesivity depends on the complex interplay of acidity and basicity. For example, hexafluoroisopropanol, a very acidic but weakly basic solvent, and triethylamine, a very basic but weakly acidic solvent, and triethylamine, a very basic but weakly acidic solvent, are certainly not very cohesive. Thus, a solvent triangle for RP-HPLC based on these concepts will not have the same pattern as either the classical SST or the Kamlet–Taft based SST. Despite the differences in the two approaches, it is still quite reasonable to use the overall SST approach in a *qualitative* manner. The essential concept of the SST approach is to use mixtures of solvents with maximal differences in their properties to explore the full range of available mobile phase induced selectivity and to optimize a separation.

The above discussion presents a tentative rationale as to why considerable variations in selectivity in RP-HPLC are observed when the volume fraction of organic modifier is changed. It is all but impossible to vary the mobile phase strength via a change in the water content without also varying some other significant solvent-selectivity property (mainly solvent cohesivity and acidity). As a final complication, we must admit that the bonded phase in RP-HPLC sorbs considerable amounts of organic modifier and thereby influences retention and selectivity, so that no SST scheme can be used for quantitative prediction of selectivity.

3.3. Solvent-selectivity in NP-HPLC

The original solvent-classification scheme was found to provide a basis for interpreting and predicting solvent selectivity in NP-HPLC [13]. Specifically, for non-protic solvents it was found that selectivity varied with solvent basicity, x_e. Reexamination of the data of ref. 13 in the light of Fig. 5 shows a similar correlation of solvent selectivity with position in the new solvent-selectivity triangle. Nine solvents can be grouped cleanly into two selectivity groups on the basis of chromatographic studies: (I, less basic) nitromethane, acetonitrile, acetone, ethyl acetate, dimethyl sulfoxide (DMSO) and (II, more basic) triethylamine, tetrahydrofuran (THF), ethyl ether, pyridine. Figs. 2 and 5 show a distinct separation of these two groups of solvents within the triangle, group I being more basic and group II being more dipolar.

4. CONCLUSIONS

A solvent-selectivity triangle derived by Snyder from data reported by Rohrschneider has been used widely as a basis for solvent selection in HPLC method development. The test solutes employed by Rohrschneider were intended as "pure" examples of dipolarity, acidity and basicity, but in fact, all of these compounds exhibit mixed-interaction tendencies to some extent. This in turn casts doubt on the validity of the original Snyder–Rohrschneider approach.

An alternative solvent-selectivity triangle (SST) based on the Kamlet–Taft solvatochromic classification of common solvents is described here. It can be argued that the latter approach is less affected by mixed-interaction effects. A comparison of these two solvent-selectivity triangles for aliphatic solvents shows that they are in general similar, with little difference in the

relative assignment of different solvents according to their dipolarity, acidity and basicity. The solvatochromic SST appears to provide a better *qualitative* classification of solvent selectivity. Although application of the alternative Kamlet–Taft based SST should not be used to make quantitative predictions of selectivity (especially for RP-HPLC), this SST appears to provide a better qualitative classification of solvent selectivity.

REFERENCES

1 P.J. Schoenmakers, *Optimization of Chromatographic Selectivity*, Elsevier, Amsterdam, 1986.
2 Sz. Nyiredy (Editor), *J. Liq. Chromatogr.*, 12, Nos. 1 and 2 (1989).
3 L.R. Snyder, J.L. Glajch and J.J. Kirkland, *Practical HPLC Method Development*, Wiley-Interscience, New York, 1988.
4 L.R. Snyder and J.J. Kirkland, *Introduction to Modern Liquid Chromatography*, Wiley-Interscience, New York, 2nd ed., 1979.
5 L. Rohrschneider, *Adv. Chromatogr.*, 4 (1967) 333.
6 R.A. Keller, B.L. Karger and L.R. Snyder, in R. Stock (Editor), *Gas Chromatography 1970*, Institute of Petroleum, London, 1971, p. 125.
7 L.R. Snyder, *J. Chromatogr.*, 92 (1974) 223.
8 M. Chastrette, M. Rajzmann, M. Chanon and K.F. Purcell, *J. Am. Chem. Soc.*, 107 (1985) 1.
9 M.J. Kamlet, J.-L.M. Abboud, M.H. Abraham and R.W. Taft, *J. Org. Chem.*, 48 (1983) 2877.
10 L. Rohrschneider, *Anal. Chem.*, 45 (1973) 1241.
11 L.R. Snyder, in A. Weissberger and E.S. Perry (Editors), *Techniques of Chemistry*, Vol. III, Part I, Wiley-Interscience, New York, 2nd ed., 1978, Ch. 2.
12 J.L. Glajch, J.J. Kirkland, K.M. Squire and J.M. Minor, *J. Chromatogr.*, 199 (1980) 57.
13 L.R. Snyder, J.L. Glajch and J.J. Kirkland, *J. Chromatogr.*, 218 (1981) 299.
14 M.L. Klee, M.A. Kaiser and K.B. Laughlin, *J. Chromatogr.*, 279 (1983) 681.
15 L.R. Snyder, *J. Chromatogr. Sci.*, 16 (1978) 223.
16 S.C. Rutan, P.W. Carr, W.J. Cheong, J.H. Park and L.R. Snyder, *J. Chromatogr.*, 463 (1989) 21.
17 M.J. Kamlet and R.W. Taft, *Acta Chem. Scand. B*, 39 (1985) 611.
18 P.C. Sadek, P.W. Carr, R.M. Doherty, M.J. Kamlet, R.W. Taft and M.H. Abraham, *Anal. Chem.*, 57 (1985) 2971.
19 J.H. Park, P.W. Carr, M.H. Abraham, R.W. Taft, R.M. Doherty and M.J. Kamlet, *Chromatographia*, 25 (1988) 373.
20 R.J. Lewis, L.B. Rogers and R.E. Pauls, *J. Chromatogr.*, 264 (1983) 339.
21 S.D. West, *J. Chromatogr. Sci.*, 25 (1987) 122.
22 S.D. West, *J. Chromatogr. Sci.*, 27 (1989) 2.
23 B. Starcevic, presented at the *15th International Symposium on Column Liquid Chromatography, Basel, June 3–7, 1991*, poster P175/2.
24 J. Li, Y. Zhang and P.W. Carr, *Anal. Chem.*, 64 (1992) 210.
25 D.C. Luehrs, D.S. Chesney and K.A. Godbole, *J. Chromatogr. Sci.*, 29 (1991) 463.
26 R.W. Taft, personal communication.
27 G.C. Pimentel and A.L. McClellan, *The Hydrogen Bond*, Reinhold, New York, 1960.
28 L.R. Snyder, M.A. Quarry and J.L. Glajch, *Chromatographia*, 24 (1987) 33.
29 W.J. Cheong and P.W. Carr, *Anal. Chem.*, 60 (1988) 820.
30 J.H. Park, M.D. Jang, D.S. Kim and P.W. Carr, *J. Chromatogr.*, 513 (1990) 107.
31 J. Li, Y. Zhang, A.J. Dallas and P.W. Carr, *J. Chromatogr.*, 550 (1991) 101.
32 M.H. Abraham, G.S. Whiting, R.M. Doherty and W.J. Schuely, *J. Chem. Soc., Perkin Trans.*, 2 (1990) 1451.
33 P. Jandera, *J. Chromatogr.*, 314 (1984) 13.
34 C. Horváth, W. Melander, and I. Molnár, *J. Chromatogr.*, 125 (1976) 129.
35 B.L. Karger, L.R. Snyder and C. Eon, *J. Chromatogr.*, 125 (1976) 71.
36 E.R. Thomas and C.A. Eckert, *Ind. Eng. Chem. Process Des. and Dev.*, 23 (1984) 194.