Molecular-microscopic characterization of 10 binary solvent mixtures based on solvatochromic reference solutes: a comparison of multiparametric empirical solvent scales

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ABSTRACT: The main objective of this work was the comparison of molecular-microscopic solvent descriptors measured from different solvatochromic reference probes. The π^*, β and α (Kamlet, Abboud and Taft) and SPP, SB and SA (Catalán and co-workers) multiparametric approaches were selected for this analysis. Attention was focused on the comparison of paired measurements corresponding to different types of binary solvent mixtures in which the pure solvents are able to form molecular associates by specific intermolecular interactions. The linear correlation between paired parameters measured using both scales was analyzed in order to investigate the strength of the relationship between them. Taking into account that the correlation coefficient says nothing about the magnitude of the differences between paired solvent descriptors, the Bland and Altman method was applied in order to establish the degree of agreement between different scales which measure the same solvent molecular-microscopic property. Although both multiparametric approaches are fairly powerful tools to quantify the molecular-microscopic solvent properties of pure and mixed solvents, the unequivocally correct measurements remain unknown. It can be considered that the mean of paired values is the best estimate available. Copyright © 2005 John Wiley & Sons, Ltd.

KEYWORDS: molecular-microscopic solvent properties; solvatochromic parameters; binary mixtures; multiparametric approaches; linear correlation

INTRODUCTION

The active role of solvents in chemical processes has long been recognized. From the combination of pure solvents in binary mixtures, both the availability and diversity of reaction media have strongly increased. Different empirical scales have been proposed for describing the solvation interactions at a molecular level.[1] Among them, one of the most extensively used method is that based on the use of solvatochromic reference probes reflecting the specific and non-specific solute–solvent interactions and their influence on the UV–visible spectral band shifts. The multiparametric approaches particularly associate each kind of solute–solvent interaction with a separate parameter. All parameters are necessary to reflect the overall solvation power of the solvent. In this direction, π^*, β and

α scales have been developed by Kamlet, Abboud and Taft (KAT)[2] with the purpose of quantifying the dipolarity/polarizability, hydrogen-bond basicity and hydrogen-bond acidity of the solvent, respectively. More recently, Catalán and co-workers[3] (Catalán) have defined analogously the SPP dipolarity/polarizability, SB basicity and SA acidity scales. It should be remarked that both the KAT and Catalán approaches are based on the application of the solvatochromic comparison method,[2] the reference solutes proposed to construct each scale being different.

The chemical characteristics of mixed solvents are customarily determined by the same techniques as are applied to pure solvents. However, solute–solvent interactions are more complex in mixed solvents than in pure solvents owing to the intermolecular solvent–solvent interactions and to the preferential solvation phenomenon.[4] A recent investigation showed that binary mixtures can be characterized with the same accuracy as pure solvents in terms of SPP, SB and SA scales, although the preferential solvation is influenced by features of the solute such as its shape, charge, properties and size.[5] Our previous studies[6] included the determination of the empirical parameters π^*, β and α for binary solvent

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mixtures formed mainly by aprotic solvents, in which specific intersolvent interactions are involved. We have analyzed (a) the preferential solvation effects for the reference solutes used in the quantification of the KAT parameters through the application of preferential solvation models; (b) the response patterns of the solvent mixtures to the chemical properties of the probes; (c) the correlation between the solvent parameters and the data corresponding to other solvent-dependent processes (kinetic results of aromatic nucleophilic substitution reactions); and (d) the convergence for KAT parameter values obtained from comparable solutes.

We have recently determined[7] the molecular-microscopic solvent parameters SPP, SB and SA for binary mixtures of ethyl acetate with chloroform or acetonitrile or methanol, which are of the type cited above. The results were related to the solvent's π^* dipolarity/polarizability, β basicity and α acidity, evaluating the agreement between the values corresponding to different scales by the application of the Bland–Altman method.

In a first instance, the shortcoming of this type of approach (which are based on reference solutes) is that the solute–solvent interactions are unique to the probe used to develop each scale. At this point, our attention was drawn to comparable molecular-microscopic solvent descriptors measured from different reference probes. In this direction, we selected the KAT and Catalán multiparametric approaches, focusing on the comparison of paired measurements. The aim of this work was twofold: (a) to analyze the relationship between paired parameters measured using both scales in order to investigate the strength in the relation between them; and (b) to analyze the values of the difference between paired measurements in order to establish the degree of agreement between them. It is expected that the results will contribute to the evaluation of the adequacy of multiparametric approaches to describe the solvent features and to the discussion of the concept of an intrinsic, solute-independent property of a solvent mixture.

RESULTS AND DISCUSSION

The solvent systems selected for this analysis are considered representative of different types of binary mixtures in which the pure components are able to form complexes or cross-associated species via hydrogen bonding between them. Moreover, the molecular associates are believed to be relevant to the behavior of the mixtures.[6d,8]

The properties of the pure solvents constituting the selected mixtures are as follows: ethyl acetate (EtOAc), $\pi^* = 0.55$, $\alpha = 0$, $\beta = 0.45$, SPP = 0.795, SA = 0, SB = 0.542); dimethyl sulfoxide (DMSO), $\pi^* = 1$, $\alpha = 0$, $\beta = 0.76$, SPP = 0.795, SA = 0, SB = 0.542); acetonitrile (AN), $\pi^* = 0.75$, $\alpha = 0.19$, $\beta = 0.40$, SPP = 0.895, SA = 0.044, SB = 0.286); trichloromethane, $\pi^* = 0.58$, $\alpha = 0$

(it should be pointed out that this value is different from that measured in dilute solutions of CCl_4, as a monomer), $\beta = 0.10$, SPP = 0.786, SA = 0.047, SB = 0.071; dichloromethane, $\pi^* = 0.78$, $\alpha = 0.13$, $\beta = 0.65$, SPP = 0.898, SA = 0.040, SB = 0.178; and methanol (MeOH), $\pi^* = 0.71$, $\alpha = 0.98$, $\beta = 0.57$, SPP = 0.857, SA = 0.605, SB = 0.545).[2,3,5b]

The solvent systems investigated were [EtOAc + cosolvent $CHCl_3$ or AN or MeOH], [DMSO + cosolvent cosolvent $CHCl_3$ or CH_2Cl_2 or AN or MeOH],[AN + cosolvent $CHCl_3$ or MeOH] and [$CHCl_3$ + MeOH]. For the proposed mixtures, the π^*, α and β empirical parameters are available at nine molar fractions of cosolvent.[6] The SPP, SB and SA molecular-microscopic properties were reported previously for the mixtures with EtOAc and DMSO.[7,9] Catalán's parameters for [AN + $CHCl_3$ or MeOH] and [$CHCl_3$ + MeOH] mixtures were determined in this work.

Determination of SPP, SB and SA parameters

The SPP dipolarity/polarizability was determined from the solvatochromic shifts undergone by the longest-wavelength UV–visible absorption band of two indicators, 2-(dimethylamino)-7-nitrofluorene (DMANF) and 2-fluoro-7-nitrofluorene (FNF). The SB and SA scales are based on the probe–homomorph pairs 5-nitroindoline (NI)–1-methyl-5-nitroindoline (MNI) and o-tert-butylstilbazolium (TBSB)–o,o'-di-tert-butylstilbazolium (DTBSB) betaine dyes, respectively. The parameters were calculated from the experimental wavenumbers of the absorption maxima of the solvatochromic solutes according to the following equations:[3]

$$\text{SPP} = \Delta\tilde{\nu} \text{ (solvent)} - 4692/2119$$
$$\Delta\tilde{\nu} \text{ (cm}^{-1}) = \tilde{\nu}_{\text{FNF}} - \tilde{\nu}_{\text{DMANF}} \tag{1}$$

$$\text{SB} = (\Delta\tilde{\nu} - 1570)/1735$$
$$\Delta\tilde{\nu} \text{ (cm}^{-1}) = \tilde{\nu}_{\text{NI}} - \tilde{\nu}_{\text{MNI}} \tag{2}$$

$$\text{SA} = (\Delta\tilde{\nu}/1299.8) \times 0.4$$
$$\Delta\tilde{\nu} \text{ (cm}^{-1}) = \tilde{\nu}_{\text{TBSB}} - (1.4099\tilde{\nu}_{\text{DTBSB}} - 6288.7) \tag{3}$$

Deconvolution of the experimental spectra was applied for the calculation of SA values using the PeakFit v4.11 program.[10] The results are presented in Table 1.

Figure 1 shows the property versus mixture composition plots. The shape of the curves reflects the response patterns of the explored mixtures to the chemical properties of the probes being analyzed according to their deviation from ideality.

Table 1. Solvatochromic parameters SPP, SB and SA for binary (acetonitrile + trichloromethane or methanol) and (trichloromethane + methanol) solvents mixtures, measured at 25 °C[a]

Parameter	x (cosolvent)								
	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
	Acetonitrile + trichloromethane								
SPP	0.847	0.870	0.900	0.858	0.824	0.825	0.818	0.799	0.771
SB	0.361	0.348	0.341	0.347	0.318	0.312	0.304	0.229	0.203
SA	0.055	0.078	0.100	0.108	0.106	0.102	0.086	0.055	0.057
	Acetonitrile + methanol								
SPP	0.828	0.830	0.856	0.860	0.875	0.873	0.855	0.881	0.899
SB	0.369	0.394	0.397	0.405	0.426	0.454	0.489	0.533	0.560
SA	0.290	0.323	0.317	0.331	0.380	0.391	0.401	0.454	0.512
	Trichloromethane + methanol								
SPP	0.752	0.755	0.728	0.761	0.798	0.784	0.791	0.819	0.854
SB	0.191	0.271	0.332	0.418	0.453	0.517	0.561	0.558	0.550
SA	0.056	0.087	0.131	0.160	0.208	0.263	0.313	0.394	0.476

The dipolarity/polarizability of the mixtures varies in a special way according to those reported previously for the cases in which the pure components have almost the same SPP values.[7,9] The basicity is always higher than the ideal value, the departure being minimal for the [AN+MeOH] mixture. Moreover, synergistic effects for the property are observed [excluding AN+MeOH]. The acidity of [AN+CHCl₃] mixtures (in which the SA values of the pure components are similar) exhibits a synergetic effect on the property throughout the cosolvent mole fraction. The mixtures with MeOH as cosolvent (in which the difference between the acidity of the pure components is ≥ 0.558) show increments in SA from the low values corresponding to AN or CHCl₃ to the high value corresponding to MeOH, exhibiting negative deviations from the ideal behavior with the exception of the AN-rich zone in which the acidity increases rapidly. All these results can be related to the formation of hydrogen-bonded complexes within the solvation shell of the reference probes.

Comparison between the multiparametric scales of KAT and Catalán

Correlation analysis: SPP, SA and SB vs π*, α and β solvent parameters.

The comparison between the solvent scales was performed by analyzing the linear correlation between paired parameters. The data calculated by the expression Catalán parameter $= A + B \times$ KAT parameter are presented in Table 2. The correlations were assessed by the evaluation of the correlation coefficient (r) and the standard deviation (SD).

SPP vs π*.

The data clearly demonstrate that the two parameters are not linearly related except for the mixtures with DMSO (a solvent that exhibits the highest dipolarity/polarizability values on both scales), which exhibit a fairly good linear correlation.

The contamination of the π* scale with effects other than those inherent in non-specific contributions (particularly
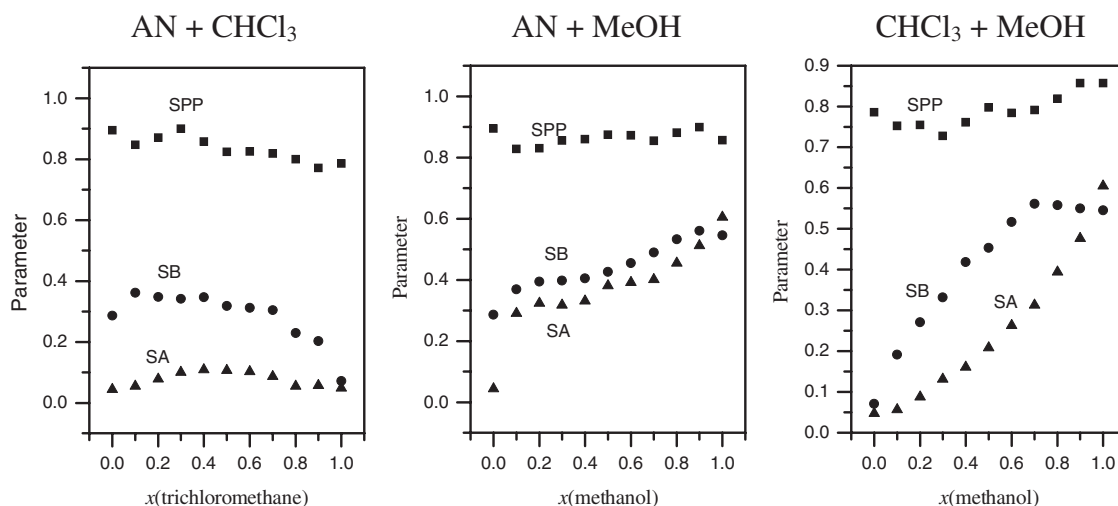
Figure 1. Plots of SPP, SB and SA parameters against cosolvent mole fraction

Table 2. Correlation coefficient (r) and standard deviation (SD) corresponding to the linear correlation of Catalán vs KAT parameters

Solvent system	SPP vs π^*	SB vs β	SA vs α	N^a
			r (SD)	
AN+CHCl$_3^b$	0.190 (0.074)	0.946 (0.035)	0.449 (0.114)	11
AN+MeOH^b	−0.300 (0.020)	0.886 (0.032)	0.831 (0.140)	11
CHCl$_3$+MeOH^b	−0.057 (0.090)	0.987 (0.033)	0.977 (0.065)	11
EtOAc+CHCl$_3^c$	0.317 (0.049)	0.900 (0.044)	0.263 (0.081)	11
EtOAc+AN^c	0.317 (0.049)	0.762 (0.023)	0.328 (0.102)	11
EtOAc+MeOH^c	0.751 (0.045)	0.364 (0.062)	0.811 (0.178)	11
DMSO+CHCl$_3^d$	0.975 (0.026)	0.948 (0.065)	0.519 (0.075)	11
DMSO+CH$_2$Cl$_2^d$	0.930 (0.028)	0.696 (0.044)	−0.269 (0.032)	11
DMSO+AN^d	0.953 (0.028)	0.899 (0.045)	−0.777 (0.054)	11
DMSO+MeOH^d	0.912 (0.021)	0.747 (0.039)	0.957 (0.097)	11
All mixtures and pure solvents	0.701 (0.051)	0.845 (0.074)	0.877 (0.078)	96

[a] N: number of data points.
[b] KAT parameters, Ref. 6(e); Catalán parameters, determined in this work.
[c] Solvent parameters from Refs 6a and 7.
[d] Solvent parameters from Refs 6a, b, d, e and 9.

with specific effects such as acidity) was examined.[6d,11] For this reason, the SPP scale was proposed on the basis of a probe–homomorph (DMANF–FNF) pair in order to offset the contribution of these spurious effects. In connection with this, different empirical scales as descriptors of non-specific solvent effects were compared: the ET(30), π^*, SPP, P_y (Dong–Winnick) and S (Drago) scales were correlated with E_{pNA} (Matyushow scale).[12]

Bearing in mind what has been said above, the results obtained can be connected with our previous studies[6d] in which we demonstrated that the π^* values of mixtures with DMSO are dictated by non-specific interactions, the contamination being minimized by specific effects.

SB vs β. The results suggest that, to a greater or lesser extent, the two parameters are proportional to each other (excluding the [EtOAc+MeOH] system). Moreover, the best linear correlations ($r \geq 0.9$) are observed for the mixtures that contain CHCl$_3$. The results can be connected with reported studies in which the SB values are linearly related with β values for 98 pure solvents ($r = 0.928$).[3c]

SA vs α. The highest values of r correspond to mixtures with the protic solvent MeOH (which exhibits the highest acidity values on both scales).

Agreement of SPP, SA and SB with the empirical parameters π^*, α and β: application of the Bland and Altman method

The use of correlations is often inappropriate in order to evaluate the agreement between measurements obtained by two different methods. In a first instance, the correla-

tion coefficient (r) measures the relation between the two properties, not the agreement between them. In addition to the linear correlation analysis between paired parameters, the comparison between the solvent scales was performed applying the Bland–Altman (B–A) method, which focuses on the magnitude of the differences between paired measurements exclusively. The general features of the B–A plot have been well described.[13] The B–A approach was applied to each of the selected binary solvent systems. The data treatment was carried out using the GraphPad Prism Version 4.0 program. The results are summarized in Table 3. The B–A plots are presented in Fig. 2 for each of the investigated solvent systems. Additionally, the agreement was analyzed including all the solvent systems together.

Agreement between the SPP and π^* scale. The results obtained show that (a) the differences between paired values in most cases are higher than zero, revealing that SPP values tend to be higher than π^* values; (b) the differences do not vary in a systematic way with the average values, excluding the mixtures with DMSO in which the differences tend to become smaller as the average increases, reflecting a relationship between the differences and the averages (a case of a proportional error); (c) the bias values (which must be interpreted considering whether the discrepancy is large enough to be important from the point of view of the quantified property) are relatively small ($\leq |0.1|$) except for the mixtures with EtOAc and the [AN+MeOH] mixture; and (d) the differences, in general, do not exceed the limits of agreement (mean $\pm$ 1.96SD). It should be pointed out that the SDs of the bias are high (therefore, the agreement limits are also high) for [AN+CHCl$_3$ or MeOH], [CHCl$_3$+MeOH] and [DMSO+CH$_2$Cl$_2$] mixtures.

Table 3. Bland–Altman results

Solvent system	Parameter	Bias[a]	SD[b]	95% limits of agreement	N[c]
AN+CHCl$_3$[d]	SPP vs π^*	0.049	0.076	−0.100/0.198	11
	SB vs β	−0.099	0.035	−0.167/−0.032	11
	SA vs α	−0.125	0.112	−0.344/0.094	11
AN+MeOH[d]	SPP vs π^*	0.024	0.048	0.029/0.219	11
	SB vs β	−0.122	0.040	−0.200/−0.044	11
	SA vs α	−0.507	0.144	−0.789/−0.224	11
CHCl$_3$+MeOH[d]	SPP vs π^*	0.001	0.099	−0.193/0.195	11
	SB vs β	−0.038	0.043	−0.122/0.047	11
	SA vs α	−0.266	0.151	−0.562/0.029	11
EtOAc+CHCl$_3$[e]	SPP vs π^*	0.176	0.056	0.066/0.285	11
	SB vs β	0.079	0.09	−0.097/0.254	11
	SA vs α	−0.097	0.077	−0.247/0.054	11
EtOAc+AN[e]	SPP vs π^*	0.197	0.043	0.112/0.281	11
	SB vs β	−0.010	0.072	−0.151/0.131	11
	SA vs α	−0.219	0.098	−0.410/0.027	11
EtOAc+MeOH[e]	SPP vs π^*	0.214	0.024	0.167/0.261	11
	SB vs β	−0.027	0.060	−0.154/0.091	11
	SA vs α	−0.479	0.173	−0.818/−0.141	11
DMSO+CHCl$_3$[f]	SPP vs π^*	0.100	0.060	−0.017/0.217	11
	SB vs β	−0.062	0.062	−0.184/0.060	11
	SA vs α	−0.070	0.074	−0.215/0.074	11
DMSO+CH$_2$Cl$_2$[f]	SPP vs π^*	0.024	0.041	−0.056/0.104	11
	SB vs β	−0.134	0.119	−0.367/0.099	11
	SA vs α	−0.005	0.041	−0.086/0.076	11
DMSO+AN[f]	SPP vs π^*	+0.051	0.061	−0.068/0.171	11
	SB vs β	−0.102	0.048	−0.196/−0.008	11
	SA vs α	−0.052	0.090	−0.228/0.124	11
DMSO+MeOH[f]	SPP vs π^*	+0.065	0.065	−0.063/0.193	11
	SB vs β	−0.113	0.037	−0.185/−0.04	11
	SA vs α	−0.168	0.183	−0.527/0.190	11
All mixtures and pure solvents	SPP vs π^*	0.094	0.092	−0.086/0.274	96
	SB vs β	−0.060	0.086	−0.227/0.108	96
	SA vs α	−0.213	0.202	−0.608/0.183	96

[a] Bias: average of the differences between Catalán and KAT parameter values.
[b] SD: standard deviation of the differences.
[c] N: number of data points.
[d] KAT parameters, Ref. 6e; Catalán parameters, determined in this work.
[e] Solvent parameters from Refs 6a and 7.
[f] Solvent parameters from Refs 5a, b, d, e and 9.

These observations indicate that the SPP and π^* scales do not produce, in general, the same or at least similar dipolarity/polarizability values, excluding [AN+CHCl$_3$] and [CHCl$_3$+MeOH] mixtures (for which the SPP dipolarity/polarizability compares closely enough with the π^* dipolarity/polarizability).

Agreement between the SB and β scale. The results reveal that the differences between paired values: (i) exhibit a random distribution between the limits of agreement; (ii) are not centered around zero for the [AN+MeOH] system and the mixtures with DMSO; and (iii) in most cases do not exceed the limits of agreement. The average of the differences is $\leq |0.1|$ except for [AN+MeOH] and [DMSO+CH$_2$Cl$_2$ or AN or MeOH] mixtures. The SDs of the bias are high for [EtOAc+CHCl$_3$ or AN or MeOH] and [CHCl$_3$+ MeOH] mixtures.

These results reveal that there is acceptable agreement between the basicity values measured through both scales for [AN + CHCl$_3$], [CHCl$_3$+MeOH] and all mixtures with EtOAc.

Agreement between the SA and α scale. The results reveal that the differences between paired values, in most cases: (i) vary in a systematic way over the range of measurement indicating the existence of a relationship between the differences and the averages (except [DMSO+CHCl$_3$ or CH$_2$Cl$_2$]); and (ii) are not centered around zero because SA values clearly tend to be lower than α values. The bias values are high ($>|0.1|$) except for the [DMSO+CH$_2$Cl$_2$] system.

These results allow us to consider that for each of the solvent systems explored there is no acceptable agreement between the acidity values quantified according to the Catalán and KAT scales, except for the [DMSO+CH$_2$Cl$_2$] mixtures.
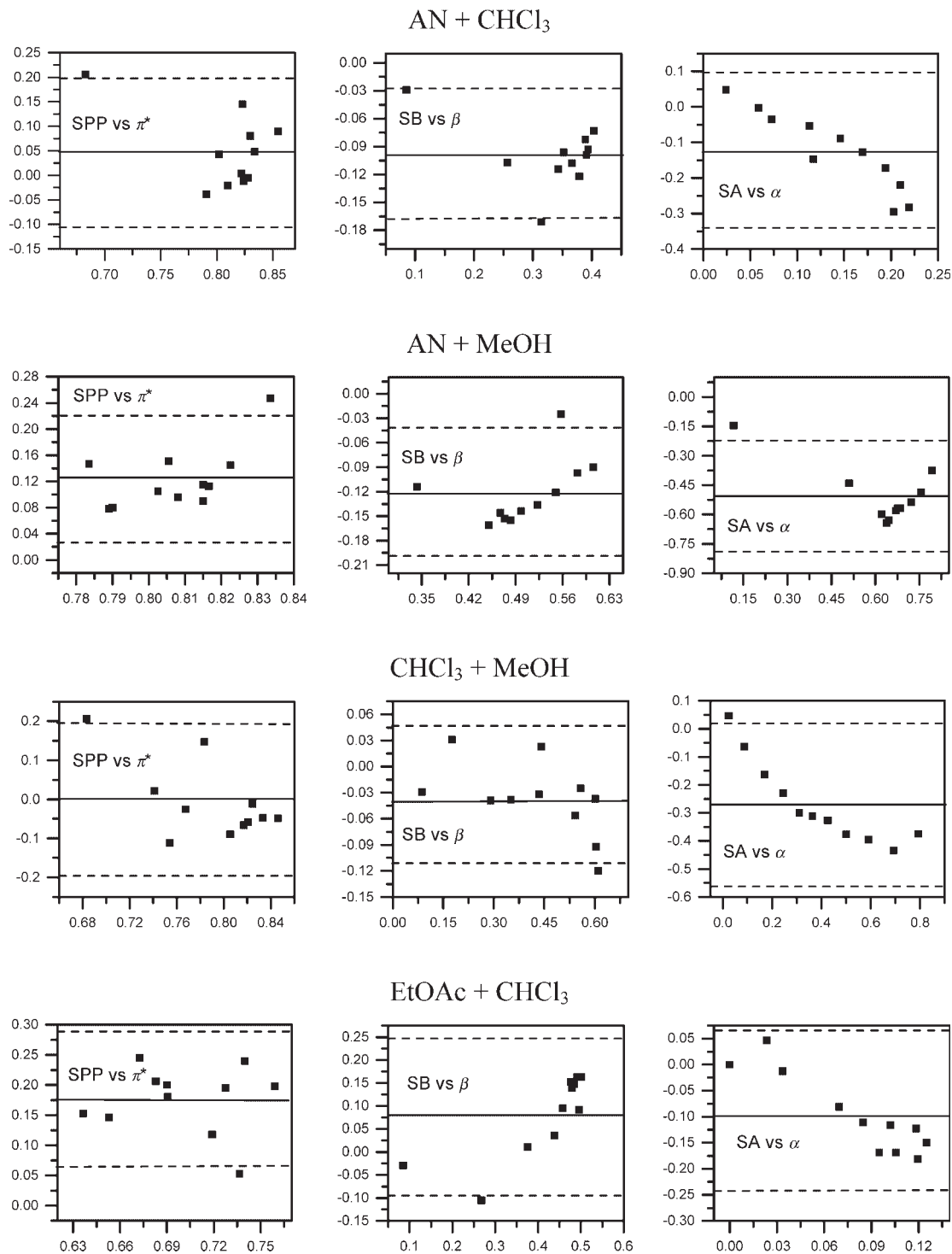
Figure 2. Bland–Altman plots of the differences between the Catalán and KAT parameters against average values (solid line, bias; dashed line, limits of agreement)

Comparison between the scales of KAT and Catalán: main results

The correlation coefficient measures the linear relation between two variables, which, however, says nothing about the magnitude of the differences between paired measurements. The B–A approach is useful in analyzing whether two different methods of measurement agree close enough.

The results presented in this work allow us to make the following observations:

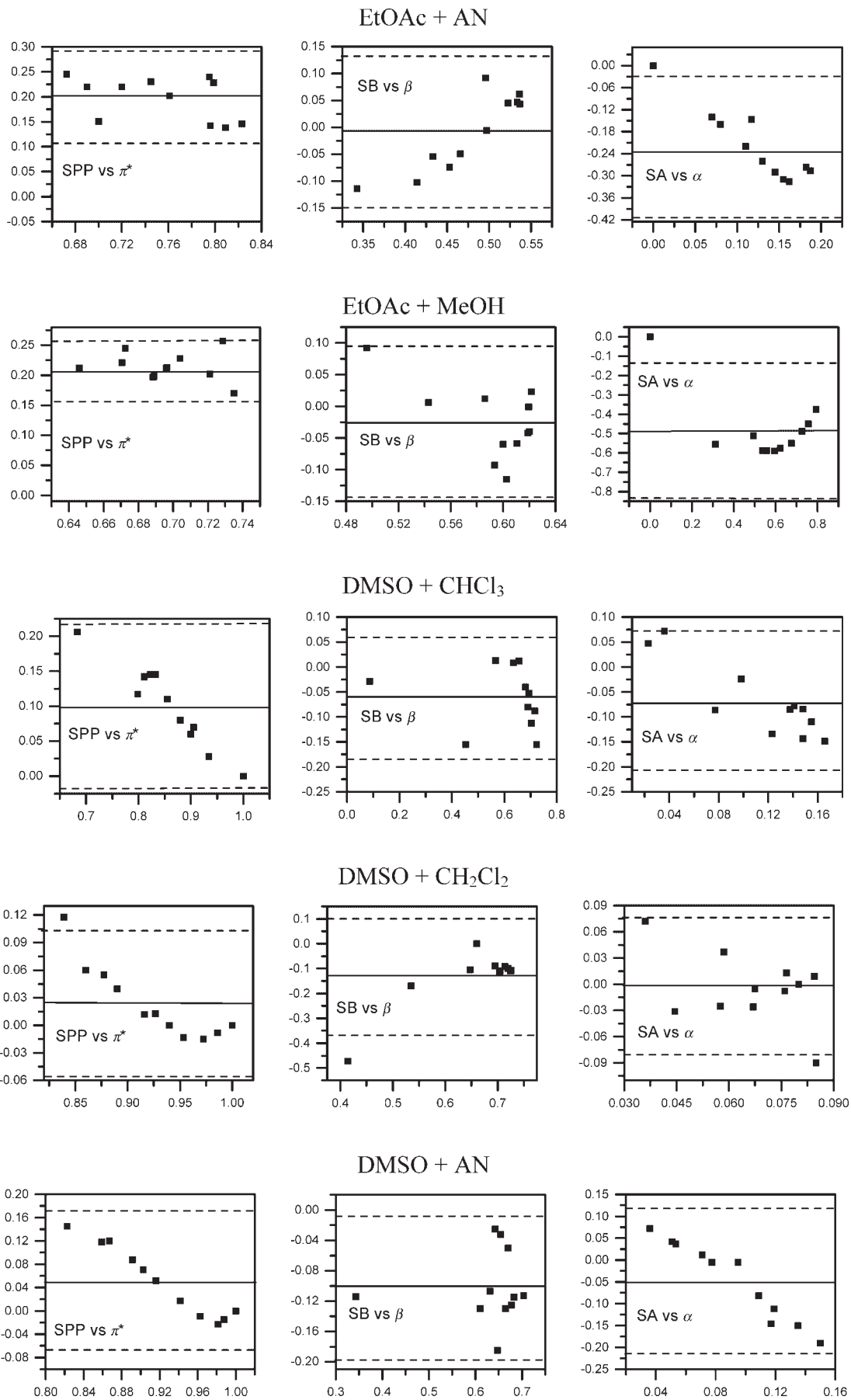- The correlation analysis shows that the SPP and π^* scales are linearly related for mixtures with the

Figure 2. Continued

DMSO + MeOH
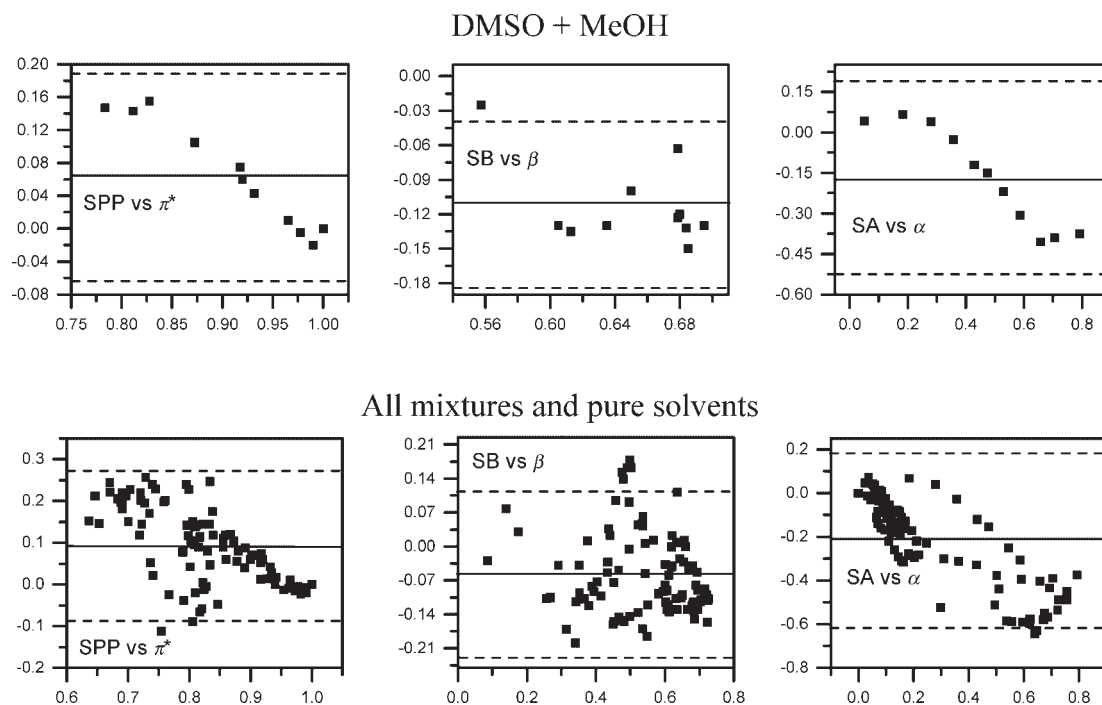

All mixtures and pure solvents

Figure 2. Continued

highly dipolar solvent DMSO. For these mixtures, the B–A analysis reveals that there is no agreement between paired values.

- The results show that, to a greater or lesser extent, a linear correlation exists between the solvent basicity scales SB and β (except for the [EtOAc+MeOH] system). A very good linear relation was particularly detected for the mixtures containing $CHCl_3$. The B–A analysis reveals that SB and β values agree closely for [AN+$CHCl_3$], [$CHCl_3$+MeOH] and the mixtures with EtOAc. It can be pointed out that there is agreement and linear correlation between both basicity parameters when the mixtures contain $CHCl_3$ (except for the [$CHCl_3$+DMSO] system).
- The correlation analysis shows that SA and α scales are linearly related for the solvent systems that contain the protic solvent MeOH. The B–A analysis reveals that, in all systems, there is bad agreement between paired acidity values (with the exception of [DMSO+CH_2Cl_2]).
- When all the mixtures and the pure solvents are simultaneously included in the analysis, the results presented in Table 2 and Fig. 3 show that: (i) there is a poor linear correlation ($r < 0.800$) and an acceptable degree of agreement between the SPP and π^* scale; (ii) there is a fair linear correlation ($r = 0.845$) and agreement between the SB and β scale; and (iii) in contrast, there is a moderately good linear correlation ($r = 0.877$) but no agreement between the SA and α scale.

CONCLUSIONS

The solvatochromic reference probes used by KAT to establish the solvent's π^*, β and α values and those used by Catalán to establish the solvent's SPP, SA and SB values in the framework of the so-called 'solvatochromic comparison method' are chemically different compounds. Therefore, the composition of the solvation shell of the respective solvatochromic probe molecules, dissolved in the same binary solvent mixture, should be different because of the different intermolecular probe–solvent interactions.

The results presented here are good evidence of the fact that the scales involved in this analysis are dependent on the type of probe and method used to develop each scale.

The experimental data demonstrate that, for the analyzed binary solvent mixtures, the Catalán multiparametric approach overestimates the dipolarity/polarizability and underestimates the acidity with respect to the KAT approach.

If there is agreement between the two scales designed to measure the same quantity, one parameter can be replaced by the other. In this situation we could think, in a first instance, about a solute-independent, intrinsic molecular-microscopic solvent property. Although both multiparametric approaches are fairly powerful tools to quantify the molecular-microscopic solvent properties of pure and mixed solvents, the unequivocally correct measurements remain unknown. It can be considered that the mean of paired values is the best estimate available. This means that, in the first instance, solute-independent

intrinsic parameters could not be experimentally determined in this way, using solvatochromic probe molecules of different molecular structure.

EXPERIMENTAL

The solvatochromic indicators were prepared and/or purified as described elswhere.[3] The solvents used were purified as reported previously and were kept over molecular sieves.[4] The binary mixtures and the indicator solutions were prepared prior to use.

The spectroscopic data were obtained with a Perkin-Elmer Lambda 40 UV–visible spectrophotometer equipped with a thermostatic cell holder. For each system explored, the property values were systematically determined throughout the total solvent composition range (at nine mixed solvent compositions) at 25 °C.

Acknowledgements

REFERENCES

1. Reichardt C. *Solvents and Solvent Effects in Organic Chemistry* (3rd edn). Wiley-VCH: Weinheim, 2003.
2. (a) Kamlet MJ, Taft RW. *J. Am. Chem. Soc.* 1976; **98**: 377–383; (b) Taft RW, Kamlet MJ. *J. Am. Chem. Soc.* 1976; **98**: 2886–2894; (c) Kamlet MJ, Abboud J-LM, Taft RW. *J. Am. Chem. Soc.* 1977; **99**: 6027–6038.
3. (a) Catalán J, López V, Pérez P, Martín-Villamil R, Rodríguez J-G. *Liebigs Ann. Chem.* 1995; 241–252; (b) Catalán J, López V, Pérez P. *Liebigs Ann. Chem.* 1995; 793–795; (c) Catalán J, Díaz C, López V, Pérez P, Paz J-L de; Rodríguez JG. *Liebigs Ann. Chem.* 1996; 1785–1794; (d) Catalán J, Palomar J, Díaz C, de Paz J-L. *J. Phys. Chem. A* 1997; **101**: 5183–5189; (e) Catalán J, Díaz C. *Liebigs Ann. Chem.* 1997; 1941–1949.
4. Marcus Y. *J. Chem. Soc., Perkin Trans. 2* 1994; 1015.
5. Catalán J, Díaz C, García-Blanco F. *J. Org. Chem.* 2000; **65**: 9226–9229.
6. (a) Mancini PM, Terenzani A, Adam C, Pérez A, Vottero LR. *J. Phys. Org. Chem.* 1999; **12**: 207–220; (b) Mancini PM, Terenzani A, Adam C, Pérez A, Vottero LR. *J. Phys. Org. Chem.* 1999; **12**: 713–724; (c) Mancini PM, Adam C, Pérez A, Vottero LR. *J. Phys. Org. Chem.* 2000; **13**: 221–231; (d) Mancini PM, Pérez A del C, Vottero LR. *J. Solution Chem.* 2001; **30**: 695–707; (e) Mancini PM, Pérez A del C, Vottero LR. *Phys. Chem. Liq.* 2003; **41**: 45–54.
7. Mancini PM, Bock A, Adam C, Pérez A del C, Vottero LR. *Arkivoc* 2003; **10**: 373–381.
8. (a) Dohnal V, Costas M. *J. Solution Chem.* 1996; **25**: 635–655; (b) Tkadlecová M, Dohnal V, Costas M. *Phys. Chem. Chem. Phys.* 1999; **1**: 1479–1486; (c) Daniel CD, McHale JL. *J. Phys. Chem.* 1997; **101**: 3070–3077; (d) Reimers JR, Hall LE. *J. Am. Chem. Soc.* 1999; **121**: 3730–3744; (e) Durov VA, Tereshrin OG, Shilov IY. *J. Mol. Liq.* 2004; **110**: 69–79.
9. Catalán J, Díaz C, García-Blanco F. *J. Org. Chem.* 2001; **66**: 5846–5852.
10. (a) Catalán J, Mena W, Meutermans W, Elguero J. *J. Phys Chem.* 1992; **96**: 3615–3621; (b) Catalán J, Pérez P, Elguero J, Meutermans W. *Chem. Ber.* 1993; **126**: 2445–2448.
11. (a) Drago RS. *J. Chem. Soc., Perkin Trans. 2* 1992; 1827–1838; (b) Drago RS. *J. Org. Chem.* 1992; **57**: 6547–6552; (c) Catalán J. *J. Org. Chem.* 1995; **60**: 8315–8317; (d) Effenberger F, Würthner F, Steybe F. *J. Org. Chem.* 1995; **60**: 2082–2091; (e) Laurence C, Nicolet P, Dalati MT, Abboud J-LM, Notario R. *J. Phys. Chem.* 1994; **98**: 5807–5816; (f) Abboud J-LM, Notario R. *J. Phys. Chem.* 1994; **98**: 5807–5816; (g) Abboud J-LM, Notario R. *Pure Appl. Chem.* 1999; **71**: 645–718.
12. Catalán J. *J. Org. Chem.* 1997; **62**: 8231–8234.
13. (a) Altman DG, Bland JM. *Statistician* 1983; **32**: 307–317; (b) Bland JM, Altman DG. *Lancet* 1986; **i**: 307–310.