

Determination of Solvation Descriptors for Ionic Species: Hydrogen Bond Acidity and Basicity

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Literature values of Gibbs energies of transfer of ions from water to other solvents have been used in conjunction with our solvation equation to obtain descriptors for univalent ions. It is suggested that descriptors used for nonelectrolytes are not adequate to describe transfers of single ions, and that two specific ionic descriptors (J^+ and J^-) for cations and anions, respectively, are required. The ions studied include the alkali metal and tetraalkylammonium cations, halide and other anions, and the tetraphenylarsonium, tetraphenylphosphonium, and tetraphenylborate ions. It is shown that simple cations such as Na^+ act as very strong hydrogen bond acids and that the R_4N^+ ions are only weak hydrogen bond acids. The halide anions are very strong hydrogen bond bases, as is also the acetate anion. Other anions, such as azide, cyanide, and nitrate, are again very strong hydrogen bond bases. The tetraphenylarsonium, tetraphenylphosphonium, and tetraphenylborate ions have no hydrogen bond acidity but are quite strong hydrogen bond bases. It is suggested that this is due to the basic properties of the phenyl groups.

Introduction

The transfer of nonelectrolytes from water to organic and other solvents has been extensively studied. Numerous methods have been designed to predict partition coefficients of nonelectrolytes, especially in the water–octanol system,¹ and various properties or “descriptors” of nonelectrolytes have been put forward to explain and to predict partition. However, many drugs and candidate drug molecules are ionized or partly ionized at the relevant pH. For example, the pH of the human intestinal tract is about 6.5, and so any strong base with a pK_a of more than 8.5 will be 99% ionized under such conditions.^{2,3} This does not prevent strong bases from being readily absorbed. Morphine ($pK_a = 7.9$), nicotine ($pK_a = 8.2$), propranolol ($pK_a = 9.6$), and pindolol ($pK_a = 9.7$) are examples of strong bases that are readily absorbed (>90%) by the human intestinal tract.^{2,3} Austin et al.⁴ have studied the partition of ionizable compounds between water and dimyristoylphosphatidylcholine (DMPC) unilamellar vesicles. They observed that the charged forms of some compounds were able to partition into DMPC, particularly protonated amines. The ion-pair partition of compounds, studied in some detail by the Swedish group,^{5–7} has recently been reexamined in

connection with solubilization of drugs and proteins⁸ and enhanced membrane permeability.⁹ Takács-Novák and Szász¹⁰ and Lengsfeld et al.¹¹ have determined the effect of various anionic counterions on the partition of protonated bases.

In view of the current interest in the effect of ions on partitioning and transport, it would be of some interest to obtain properties or “descriptors” of ions that influence their partition and transport. Furthermore, it would be useful to compare these properties with those that influence the partition and transport of nonelectrolytes, especially properties such as hydrogen bonding. This is the aim of the present work.

Comparatively little work has been done on properties of ions that might be relevant to transport and partitioning. The 1:1 complexation of anions (as ion pairs with quaternary ammonium cations) with various hydrogen bond acids, eq 1, has been studied a few times.



Singh and Rao¹² obtained equilibrium constants, K , for eq 1 with heptyl $_4N^+I^-$ against a number of alcohols in tetrachloromethane. These K values can be treated¹³ through eq 2, where α^{H_2} is the 1:1 hydrogen bond acidity

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TABLE 1. Values of 1:1 Hydrogen Bond Basicities of Tetraalkylammonium Ion Pairs, $R_4N^+X^-$: Comparison with Nonelectrolytes

X^- in ion pair, or nonelectrolyte	β^{H_2}
Cl^-	1.17, ¹⁵ 1.04 ¹⁶
Br^-	0.98, ¹⁵ 0.93 ¹⁶
I^-	0.90, ¹⁴ 0.82, ¹⁵ 0.78 ¹⁶
picrate ⁻	0.76 ¹⁶
HMPA	1.00
Ph_3PO	0.92
$(EtO)_3PO$	0.79
triethylamine	0.67
acetonitrile	0.44
alkanes	0.00

of the acid, HA, and β^{H_2} is the 1:1 hydrogen bond basicity of the base in eq 2.

$$\log K = 7.354 * \alpha^H_2 * \beta^{H_2} - 1.094 \quad (2)$$

Knowing α^H_2 for the various alcohols,¹⁴ we can deduce a value of 0.90 ± 0.06 for the 1:1 hydrogen bond basicity of heptyl $_4N^+I^-$. Equilibrium constants for eq 1 have also been obtained for a number of tetraalkylammonium ion pairs containing halide and picrate anions against phenol in dichloromethane¹⁵ and against trichloromethane in tetrachloromethane.¹⁶ Values of β^{H_2} that we have calculated from these results are in Table 1, together with 1:1 hydrogen bond basicities of some nonelectrolytes.¹⁷ Even though the basicities are for ion pairs and not the free anions, those for the anions are still quite large compared to strong hydrogen bond bases such as triphenylphosphine oxide or hexamethylphosphoric triamide, HMPA.

Raevsky et al.^{18,19} have listed descriptors for the overall hydrogen bond acidity, ΣCd , and hydrogen bond basicity, ΣCa , of drugs and other compounds, but give no indication as to how these descriptors were obtained. They do, however, list some average values of ΣCd and ΣCa , so that comparison with other compounds^{20,21} can be made; see Table 2. Carboxylate anions are as strongly basic as HMPA, and the substituted ammonium cations are as, or more than, acidic than trichloroacetic acid, depending on the degree of substitution.

Nearly 20 years ago, Taft et al.²² correlated the Gibbs energies of transfer of ion pairs, $R_4N^+X^-$, and pairs of ions, $R_4N^+ + X^-$, from water to other solvents with properties of the solvents. They did not calculate any

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TABLE 2. Hydrogen Bond Acidity, ΣCd , and Basicity, ΣCa , of Some Ionic and Neutral Species, after Raevsky et al.^{18–21}

solute or group	ΣCd	ΣCa
RCO_2^-	0.00	3.00 to 5.00
RNH_3^+	–6.00 to –7.50	0.00
$R_2NH_2^+$	–4.00 to –6.00	0.00
R_3NH^+	–3.50 to –4.50	0.00
pentachlorobenzene	0.00	
trichloromethane	–0.80	
methanol	–1.35	1.93
pyrrole	–1.67	1.32
phenol	–2.49	1.37
4-nitrophenol	–3.65	2.43
trichloroacetic acid	–4.78	
triethylamine		2.21
tributylamine		3.65
$(EtO)_3PO$		3.16
Ph_3PO		3.63
HMPA		4.00

properties of ion pairs or of pairs of ions, but the work did indicate that correlations could be set up for ions and ion pairs that were similar in nature to those for nonelectrolytes. Marcus et al.²³ used a method similar to that of Taft et al.²² They started from Gibbs energies of transfer of ions from water to various solvents, with data in kJ mol^{-1} at 298 K on the molar scale. The single-ion-transfer properties were based on the extra-thermodynamic assumption that the contribution of Ph_4As^+ and Ph_4B^- is the same; this is the well-known Ph_4As^+/Ph_4B^- (or TATB) assumption.²⁴ Marcus et al. also carried out an analysis in terms of enthalpies of transfer, but we comment only on the work on Gibbs energies.

In the method of Marcus et al.,²³ values of ΔG°_{tr} for transfer of a given ion, X, to a number of solvents is correlated with properties of the solvents, in a multiple linear regression, MLR, equation. The properties considered were as follows:^{25,26} π^* the Kamlet–Taft solvatochromic dipolarity/polarizability, α the solvent hydrogen bond acidity, β the solvent hydrogen bond basicity, δ^2 the Hildebrand cohesive energy density, and $V/100$ where V is the solvent molar volume. The MLR equation was then formulated as

$$\Delta G^\circ_{tr}(X) = Ai(\pi^*)\Delta\pi^* + Ai(\alpha)\Delta\alpha + Ai(\beta)\Delta\beta + Ai(\delta)\Delta\delta^2 + Ai(V)\Delta V/100 \quad (3)$$

The solvent-dependent variables, denoted as $\Delta\pi^*$, $\Delta\alpha$, $\Delta\beta$, $\Delta\delta^2$, and ΔV , are the values of the solvent property less that of water. The coefficients $Ai(\pi^*)$, $Ai(\alpha)$, $Ai(\beta)$, $Ai(\delta)$, and $Ai(V)$ reflect the corresponding properties of the ions. Marcus et al.²³ list properties of numerous ions but unfortunately not on any scale that can be used to compare them with nonelectrolytes.

In a subsequent paper, Marcus²⁷ carried out a similar analysis, but this time in terms of $\log P$ for partition. No details of calculations for ions were given, but Marcus tabulates values of α and β for ions, on the same scale

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TABLE 3. Properties of Ions from Marcus²⁷

ion	α	β	solute	α	β
Li ⁺	2.07		formic acid	1.05	
Na ⁺	0.83		4-nitrophenol	0.93	
K ⁺	0.85		benzoic acid	0.75	
Rb ⁺	0.49		phenol	0.61	
Cs ⁺	0.47		methanol	0.33	
F ⁻		2.95	HMPA		1.00
Cl ⁻		1.00	Ph ₃ PO		0.94
Br ⁻		0.67	(EtO) ₃ PO		0.77
I ⁻		0.30	triethylamine		0.60
CN ⁻		1.37	ethyl acetate		0.45
SCN ⁻		0.33	acetonitrile		0.31
N ₃ ⁻		0.80	benzene		0.10
NO ₃ ⁻		0.09	alkanes		0.00
ClO ₄ ⁻		0.08			
MeCO ₂ ⁻		1.49			

as for nonelectrolytes. Some values are given in Table 3. Rather extraordinarily, no values for tetraalkylammonium ions were given by Marcus,²⁷ even though they were listed before.²³

There is disagreement as regard to the values collected in Tables 1–3. The hydrogen bond basicities of the halide ions given by Marcus are much less than the 1:1 hydrogen bond basicities in Table 1. On the calculations of Marcus,²⁷ the bromide ion has about the same basicity as triethylamine, and the iodide ion about the same as acetonitrile, but the 1:1 basicities of the bromide ion and the iodide ion are very much greater than these—the basicity of the iodide ion (Table 1) is almost the same as that of triphenylphosphine oxide. On the other hand, the basicity of the acetate ion according to Marcus is far larger than that for HMPA, whereas Raevsky ranks carboxylate ions about the same as HMPA. Clearly, further work is needed to elucidate the properties of the simple univalent anions and cations.

In a long series of papers, Drago et al.^{28–30} used a four-parameter equation to correlate enthalpies of 1:1 adduct formation between two neutral molecules, in either the gas phase or in a poorly solvating medium. Kroeger and Drago³¹ then extended their studies to include 1:1 adduct formation between two ions and between an ion and a neutral molecule. But in order to include ions, Kroeger and Drago had to abandon their four parameter equation and had to replace it by a completely new six-parameter equation, in which the original “acid” and “base” descriptors for neutral molecules were replaced by a new set of “acid”, “base”, and “electron transfer” descriptors. We did not wish to follow this route, but hoped to be able to retain the hydrogen bond acidity and hydrogen bond basicity descriptors that we had already worked out for several thousand neutral molecules.

Methodology

We use essentially the same data as Marcus,^{23,24,26} that is Gibbs energies of transfer of ions from water to various

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TABLE 4. Coefficients in eq 4 for Water/Solvent Partitions

solvent	<i>c</i>	<i>e</i>	<i>s</i>	<i>a</i>	<i>b</i>	<i>v</i>
dichloromethane	0.314	0.001	0.022	-3.238	-4.137	4.259
1,2-dichloroethane	0.227	0.278	-0.167	-2.816	-4.324	4.205
methanol	0.329	0.299	-0.671	0.080	-3.389	3.512
ethanol	0.208	0.409	-0.959	0.186	-3.645	3.928
propan-1-ol	0.148	0.436	-1.098	0.389	-3.893	4.036
butan-1-ol	0.152	0.438	-1.177	0.096	-3.919	4.122
DMF	0.136	0.305	0.431	0.469	-4.833	3.735
acetonitrile	0.413	0.077	0.326	-1.566	-4.391	3.364
DMSO	-0.221	0.226	0.878	1.312	-4.604	3.403
acetone	0.335	0.349	-0.231	-0.411	-4.793	3.963

solvents at 298 K on the molar scale, with single-ion transfer energies based on the Ph₄As⁺/Ph₄B⁻ extra-thermodynamic assumption.^{32–34} These single ion transfer energies were converted into partition coefficients through $\Delta G_{tr}^{\circ} = -RT \ln P$.

Taft et al.²² and Marcus et al.^{23,27} correlated ΔG_{tr}° or log *P* values for a given ion against various properties of the relevant solvents. In our method, we use the solvation equation of Abraham, eq 4, in which log *P* values for a series of solutes in a given system are correlated against properties of the solutes.^{35–37}

$$SP = c + e.E + s.S + a.A + b.B + v.V \quad (4)$$

Here, the dependent variable, SP (in the present case log *P*), is a property of a series of solutes in a given system. The independent variables, or solute descriptors, are as follows:³⁷ **E** is an excess molar refraction in units of (cm³ mol⁻¹)/10, **S** is the dipolarity/polarizability, **A** and **B** are the overall hydrogen bond acidity and basicity respectively, and **V** is the McGowan characteristic volume in units of (cm³ mol⁻¹)/100. The equation coefficients, *c*, *e*, *s*, *a*, *b*, and *v*, are obtained by multiple linear regression.

To apply eq 4 to any solute, be it a nonelectrolyte or an ion, the equation coefficients must be known for the particular processes under consideration. Values of these coefficients for the systems we shall consider are in Table 4.^{37–39} Note that many of the water/solvent systems are “hypothetical” in that the components are miscible. This does not preclude such systems from our analysis at all.

The general method of analysis has been set out in considerable detail already.^{37,40,41} In brief, values of log *P* for a given solute in various systems are matched with the corresponding system coefficients. Sets of values are assigned to the missing solute descriptors, log *P* values

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TABLE 5. Partition Coefficients of Ions (log *P*) in Different Water/Solvent Systems^a

ion	DCM	DCE	MeOH	EtOH	PrOH	BuOH	DMF	MeCN	DMSO	Me ₂ CO
Li ⁺	-5.78	-4.73	-0.88	-1.93	-1.98		1.75	-4.38	2.63	-0.88
Na ⁺	-4.03	-4.38	-1.40	-2.45	-2.95	-3.47	1.75	-2.63	2.28	-1.58
K ⁺	-3.68	-4.56	-1.75	-2.80	-3.11	-3.47	1.75	-1.40	2.28	-0.70
Rb ⁺	-3.15	-4.38	-1.75	-2.80	-3.39	-3.97	1.75	-1.05	1.75	-0.70
Cs ⁺	-2.80	-4.21	-1.58	-2.63	-3.06	-3.25	1.93	-1.05	2.28	-0.70
NH ₄ ⁺	-3.51	-3.68	-0.88	-1.23	-1.25	-2.05	0.53	-0.70	0.00	-0.35
NMe ₄ ⁺	-3.33	-2.63	-1.05	-1.93	-1.86	-2.13	0.88	-0.53	0.35	-0.53
NEt ₄ ⁺	-0.70	-0.88	-0.18	-1.05	-0.85	-1.28	1.40	1.23	1.58	1.93
NPr ₄ ⁺	1.58	1.58	0.88	1.05	1.12	1.18	2.98	2.28	3.33	3.51
NBu ₄ ⁺	3.86	3.15	3.68	1.40	2.96	2.06	5.08	5.43	6.48	6.66
Ph ₄ P ⁺	7.54	5.78	4.21	3.68	4.25	3.78	6.84	5.78	6.48	5.78
Ph ₄ As ⁺	7.54	5.78	4.21	3.68	4.42	3.53	6.84	5.78	6.48	5.78
F ⁻	-10.34	-10.52	-2.80	-4.73			-8.94	-8.76	-7.71	-10.52
Cl ⁻	-8.24	-9.46	-2.28	-3.51	-4.47	-5.12	-8.41	-7.36	-7.01	-9.99
Br ⁻	-6.84	-6.84	-1.93	-3.15	-3.84	-4.15	-6.31	-5.43	-4.73	-7.36
I ⁻	-4.73	-4.38	-1.23	-2.28	-3.37	-3.87	-3.51	-2.98	-1.75	-4.38
ClO ₄ ⁻	-3.68	-2.98	-1.05	-1.75	-3.04	-3.78	-0.70	-0.35	1.05	-1.75
CN ⁻	-5.26	-6.66	-1.58	-3.51			-7.01	-6.13	-6.13	-8.41
NO ₃ ⁻	-6.31	-5.96	-1.05	-2.45	-3.32		-7.36	-3.68	-6.13	-6.31
SCN ⁻	-4.21	-4.21	-1.05	-2.28			-3.15	-2.45	-1.75	-5.26
N ₃ ⁻	-5.96	-5.96	-1.58	-2.98			-6.31	-6.48	-4.56	-7.54
Ac ⁻	-7.71	-7.89	-2.80	-6.48			-11.39	-10.69	-8.76	-9.29
Pic ⁻	-1.23	-1.23	1.05	-0.18			1.23	0.70	-2.45	-2.45
Ph ₄ B ⁻	7.54	5.78	4.21	3.68	4.42	3.53	6.84	5.61	6.48	5.78

^a Abbreviations as follows: DCM, dichloromethane; 12DCE, 1,2-dichloroethane; MeOH, methanol; EtOH, ethanol; PrOH, propanol; BuOH, butanol; DMF, *N,N*-dimethylformamide; MeCN, acetonitrile; DMSO, dimethyl sulfoxide; Me₂CO, acetone; Ac⁻, acetate; Pic⁻, picrate.

are calculated from the solute descriptors and the system coefficients, and the set of solute descriptors that best reproduces the log *P* values is taken as the “best” set. As a criterion of the best set, we use the standard deviation between the observed and calculated log *P* values.

In principle, five solute descriptors are needed in eq 4, so that for any “new” solute, all five descriptors need to be determined. However, the McGowan volume (**V**) for nonelectrolytes is easily calculated, and we have recently shown that the McGowan volume (**V**) for ions can also be calculated.⁴² The excess molar refraction, **E**, for nonelectrolytes that are liquid at room temperature can be obtained from the refractive (MR_x) index at 293 K together with the McGowan volume. **E** for ions can be obtained from ionic molar refractions.^{23,43–45} The calculation is rather cumbersome, and so is set out in detail as Supporting Information. Knowing values of **E** and **V** for ions reduces the descriptors that have to be calculated to **S**, **A**, and **B**. In Table 5 are listed the single ion log *P* values that we used, and in Table 6 are given values of **E** and **V** for the ions that we have studied.

Results and Discussion

For the various ions listed in Table 5, there are between 8 and 10 log *P* values. Since we have the **E** and **V** descriptors to hand, the 8–10 log *P* values must be reproduced by chosen values of the three descriptors **S**, **A**, and **B**. This was carried out either by using the “Solver” add-on feature in Excel or our program “Descfit” exactly as described before.^{40,41} Results are in Table 6, together with *N*, the number of systems studied, and SD,

TABLE 6. Calculated Values of *E* and *V*, and the Obtained Descriptors *S*, *A*, and *B* for Ions

ion	<i>E</i>	<i>S</i>	<i>A</i>	<i>B</i>	<i>V</i>	<i>N</i>	SD
Li ⁺	-0.02	1.62	1.74	0.16	0.014	9	0.81
Na ⁺	-0.02	2.38	1.24	0.21	0.033	10	0.50
K ⁺	0.00	2.70	1.16	0.22	0.092	10	0.44
Rb ⁺	0.02	2.81	0.98	0.28	0.130	10	0.55
Cs ⁺	0.10	2.77	1.02	0.27	0.177	10	0.47
NH ₄ ⁺	0.06	1.06	0.87	0.30	0.127	10	0.54
NMe ₄ ⁺	-0.20	1.94	0.83	0.85	0.814	10	0.62
NEt ₄ ⁺	-0.52	2.37	0.59	1.04	1.406	10	0.82
NPr ₄ ⁺	-0.07	2.33	0.52	1.12	1.920	10	0.69
NBu ₄ ⁺	-0.10	3.37	0.62	1.05	2.484	10	1.15
Ph ₄ P ⁺	2.22	3.32	-0.01	1.24	2.766	10	0.43
Ph ₄ As ⁺	2.22	3.37	-0.01	1.28	2.811	10	0.46
F ⁻	-0.05	-1.40	1.11	1.87	0.105	8	1.08
Cl ⁻	0.10	-1.09	0.82	1.82	0.228	10	1.16
Br ⁻	0.17	-0.30	0.71	1.49	0.307	10	0.79
I ⁻	0.38	0.95	0.61	1.09	0.408	10	0.62
ClO ₄ ⁻	-0.16	2.20	0.75	0.69	0.493	10	0.62
CN ⁻	0.07	-0.92	0.32	1.54	0.231	8	1.16
NO ₃ ⁻	0.17	-1.16	0.36	1.48	0.320	9	1.13
SCN ⁻	0.40	0.74	0.55	1.02	0.365	8	0.89
N ₃ ⁻	0.16	-0.71	0.61	1.44	0.282	8	1.02
Ac ⁻	0.01	-1.38	0.27	2.33	0.443	8	1.35
Pic ⁻	-0.73	0.49	0.36	1.21	1.276	8	1.33
Ph ₄ B ⁻	1.95	3.23	0.00	1.17	2.700	10	0.44

the standard deviation between the observed log *P* values and the log *P* values calculated from the obtained descriptors. For some of the ions, the SD values are reasonably small, around 0.40 log units for some of the small cations. However, for many of the anions, very large values of SD are obtained.

In regard to the obtained descriptors, Table 6, it is expected that the dipolarity/polarizability descriptor, **S**, should be very large for both the anions and the cations. This is the case for most, but not all, of the ions; five of the anions have negative values of **S**. The **A** descriptor should be large for the smaller cations, but not so large for the larger cations, again as observed. However, **A**

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(43) Seeliger, B. R. *Phys. Z.* **1925**, *26*, 526–556.

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TABLE 7. Observed and Calculated log P Values for Cl⁻ from the Descriptors Given in Table 6 and Table 10

solvent	obsd	calcd from Table 6	residue	calcd from Table 10	residue
dichloromethane	-8.24	-8.90	0.67	-7.97	-0.26
1,2-dichloroethane	-9.46	-8.76	-0.70	-9.08	-0.38
methanol	-2.28	-4.19	1.92	-2.10	-0.18
ethanol	-3.51	-4.27	0.77	-3.63	0.13
propan-1-ol	-4.47	-4.44	-0.04	-4.68	0.20
butan-1-ol	-5.12	-4.61	-0.50	-4.97	-0.15
DMF	-8.41	-7.84	-0.57	-8.47	0.06
acetonitrile	-7.36	-8.42	1.06	-7.65	0.29
DMSO	-7.01	-7.67	0.66	-6.94	-0.07
acetone	-9.99	-7.51	-2.48	-10.29	0.30
		SD = 1.16		SD = 0.23	

should be small or 0 for the anions, but this is not the case. We stress that the **A** descriptor is notionally a hydrogen bond acidity, but in practice it will include the tendency of a species to act as a Lewis acid as well. For example,⁴⁶ **A** is quite large (0.29) for sulfur dioxide even though this solute has no hydrogen atom at all. In a similar vein, **B** should be small or zero for the cations and large for the anions. It is certainly large for the anions, but it is not negligible for the cations. Thus, the descriptors in Table 6 are not entirely chemically reasonable, and the SD values for a number of ions are too large for the analysis to be regarded as successful.

We attempted to obtain descriptors that were more chemically meaningful by setting **A** = 0 for anions and **B** = 0 for cations, but results were completely useless. Not only did the SD value increase considerably, but the other descriptors took on chemically meaningless values. For example, when **A** was fixed at 0 for Cl⁻ the SD value rose from 1.16 (Table 6) to 1.62, and the **S** descriptor became negative (-1.19)! When **B** was fixed at 0 for Na⁺ the SD value rose from 0.50 to 0.94, and again the **S** descriptor became negative.

It seems clear from this work that log *P* values for ions cannot satisfactorily be correlated using only descriptors that are the same in kind as those for nonelectrolytes. This is probably why Marcus et al.²³ find chemically unreasonable values for ionic descriptors. For example, they found that the partition of cations, small or large, did not depend on their volume, yet the partition of anions depended positively or negatively on their volume, seemingly at random.²³

As an example of the analysis of log *P* values, we give in Table 7 the output for the chloride ion as a typical example. The overall standard deviation, SD, between observed and calculated values is 1.16 log units, rather too high for the analysis to be regarded as successful. The largest differences in observed and calculated log *P* values mostly arise for transfer of anions to the alcohol solvents. For example, the observed log *P* value for transfer of the chloride ion from water to methanol is -2.28 but the calculated log *P* is -4.19 there being a difference of nearly two log units. Similar discrepancies are observed for the other halide ions.

A number of studies in which solvent refractive index, η , and dielectric constant, ϵ , are used to calculate the dipole moment, μ , of the solvent⁴⁷⁻⁵⁰ have shown that

alcohols and water have anomalous properties. All calculations yield reasonable values for the dipole moment for aprotic solvents, but for associated solvents the calculated values of μ for the bulk solvents are always much larger than the observed dipole moments for the gaseous molecules. For the calculation of μ , the method of Böttcher⁵⁰ is the most rigorous and leads to eq 5.

$$\mu^2 = (9kTM/4\pi Nd)(\epsilon - \eta^2)(2\epsilon + \eta^2)/\epsilon(\eta^2 + 2)^2 \quad (5)$$

In eq 5, *k* is Boltzmann's constant, *T* is the temperature in K, *M* is the solvent molecular weight, *N* is Avogadro's constant, and *d* is the solvent density. Results of calculations using eq 5 are in Table 8. Solvents that are associated through hydrogen bonding all have significant positive values of $\mu(\text{calcd} - \text{obsd})$. Now since the enhanced dipole in the bulk solvent is a response to an applied electric field, we reasoned that alcohols could be similarly anomalous in response to the electric field of an ion. This seemed to be justification for introducing an extra term, $f^- \cdot \mathbf{J}^-$, into the general eq 4; f^- is a system coefficient that is 0 except for alcohols, where $f^- = 3.0$ (this value is used only to provide a convenient scale). The solute descriptor, \mathbf{J}^- , takes a 0 value for cations and nonelectrolytes, and whatever value is determined in the analysis by "Solver" for anions.

Another difficulty rests with the tetraalkylammonium ions that are also not well correlated through eq 4. Heat capacities in water for the tetraalkylammonium ions indicate that as the alkyl groups become larger, these ions become more and more hydrophobic structure-making ions.^{26,51,52} Such behavior cannot be accounted for by the descriptors used for nonelectrolytes, eq 4, and so we introduce another term, $f^+ \cdot \mathbf{J}^+$ in the equation, specifically to take the tetraalkylammonium ions into account. For this term, we fix the system coefficient, f^+ as -3, and the solute descriptor, \mathbf{J}^+ , is then defined such that it is 0 for anions and nonelectrolytes and takes whatever value is found by the trial-and-error "Solver" procedure for all cations (not just the tetraalkylammonium cations).

The final equation for nonelectrolytes, univalent anions, and univalent cations is then given as eq 6, where $\text{SP} = \log P$ in the present case.

$$\text{SP} = c + e \cdot \mathbf{E} + s \cdot \mathbf{S} + a \cdot \mathbf{A} + b \cdot \mathbf{B} + v \cdot \mathbf{V} + f^+ \cdot \mathbf{J}^+ + f^- \cdot \mathbf{J}^- \quad (6)$$

Note that the two new descriptors are not included in eq 6 at the same time. \mathbf{J}^+ is used when a cation is the solute, \mathbf{J}^- when an anion is the solute, and neither is used when a nonelectrolyte is the solute. It is very important that the new ionic descriptors are used together with the descriptors originally chosen for nonelectrolytes. This ensures that values of **S**, **A** and **B** for ions are on the same scale as those for nonelectrolytes.

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TABLE 8. Calculated and Observed Solvent Dipole Moments^a at 298 K Using the Equation of Bottcher⁵⁰

solvent	μ (calcd-obsd)	solvent	μ (calcd-obsd)
tetrachloromethane	0.31	γ -butyrolactone	0.03
trichloromethane	0.23	dimethyl sulfoxide	0.30
toluene	-0.06	<i>N,N</i> -dimethylformamide	0.25
1,2-dichloroethane	-0.87	water	1.25
dioxane	0.38	methanol	1.29
tetrahydrofuran	0.16	ethanol	1.33
chlorobenzene	-0.23	propan-1-ol	1.37
bromobenzene	-0.31	butan-1-ol	1.42
nitrobenzene	-0.05	pentan-1-ol	1.23
acetonitrile	-0.39	hexan-1-ol	1.40
propionitrile	-0.42	octan-1-ol	1.29
nitromethane	0.02	ethan-1,2-diol	1.20

^a Dipole moments are in debye units; 1 D = 3.336×10^{-30} C-m.

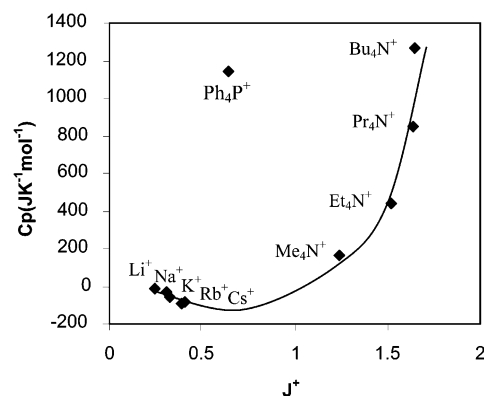
TABLE 9. Ionic System Coefficients for Water–Solvent Partition Systems

solvent	J^+	J^-
dichloromethane	-3	0
1,2-dichloroethane	-3	0
methanol	-3	3
ethanol	-3	3
propan-1-ol	-3	3
butan-1-ol	-3	3
DMF	-3	0
acetonitrile	-3	0
DMSO	-3	0
acetone	-3	0

TABLE 10. Revised Descriptors for Ions, with the Additional Descriptors

ion	<i>E</i>	<i>S</i>	<i>A</i>	<i>B</i>	<i>V</i>	J^+	J^-	SD	AAE
Li ⁺	-0.02	1.52	1.73	0	0.014	0.24	0	0.80	0.60
Na ⁺	-0.02	2.27	1.25	0	0.033	0.31	0	0.50	0.39
K ⁺	0.00	2.58	1.15	0	0.092	0.33	0	0.41	0.35
Rb ⁺	0.02	2.66	0.97	0	0.130	0.41	0	0.53	0.45
Cs ⁺	0.10	2.62	1.01	0	0.177	0.39	0	0.45	0.38
NH ₄ ⁺	0.06	0.90	0.87	0	0.127	0.44	0	0.51	0.43
NMe ₄ ⁺	-0.20	1.48	0.82	0	0.814	1.24	0	0.52	0.44
NEt ₄ ⁺	-0.52	1.81	0.57	0	1.406	1.52	0	0.67	0.57
NPr ₄ ⁺	-0.07	1.72	0.49	0	1.920	1.64	0	0.44	0.33
NBu ₄ ⁺	-0.10	1.90	0.40	0	2.484	1.65	0	1.24	1.11
Ph ₄ P ⁺	2.22	3.09	-0.02	0.80	2.766	0.64	0	0.41	0.34
Ph ₄ As ⁺	2.22	3.15	-0.02	0.85	2.811	0.63	0	0.44	0.39
F ⁻	-0.05	3.56	0	2.39	0.105	0	2.29	0.63	0.45
Cl ⁻	0.10	3.27	0	2.26	0.228	0	2.19	0.23	0.20
Br ⁻	0.17	2.99	0	1.83	0.307	0	1.66	0.36	0.24
I ⁻	0.38	3.46	0	1.37	0.408	0	1.27	0.50	0.32
ClO ₄ ⁻	-0.16	4.36	0	0.96	0.493	0	1.11	0.91	0.61
CN ⁻	0.07	2.01	0	1.80	0.231	0	1.43	0.45	0.37
NO ₃ ⁻	0.17	4.00	0	1.83	0.320	0	2.17	1.24	0.99
SCN ⁻	0.40	3.76	0	1.32	0.365	0	1.43	0.31	0.20
N ₃ ⁻	0.16	2.63	0	1.77	0.282	0	1.57	0.46	0.34
Ac ⁻	0.01	0.40	0	2.50	0.443	0	0.85	1.22	1.14
Pic ⁻	-0.73	2.14	0	1.39	1.276	0	0.77	1.38	1.28
Ph ₄ B ⁻	1.95	2.82	0.07	1.13	2.700	0	-0.21	0.43	0.36

In Table 9 are given the two additional system coefficients of the general solvation equations for ions, and in Table 10 are collected the revised descriptors for ions based on the full eq 6. Also included in Table 10 are the SD values between observed $\log P$ and $\log P$ calculated from the full eq 6, as well as the absolute average error (AAE). The SD values for the anions are now very much less than before; compare Table 10 with Table 6, and especially see Table 7 for calculations on the chloride ion. The new descriptors, Table 10, are chemically much more reasonable than those we calculated before. The hydrogen bond acidity, *A*, is 0 for all anions. We would expect *A* to

**FIGURE 1.** Partial molar heat capacities of cations in water⁵² as a function of J^+ .

be 0 for the tetraalkylammonium cations, but, although small, it is not 0. The hydrogen bond basicity, *B*, is 0 for all cations, as expected. The two cations Ph₄As⁺ and Ph₄B⁻ are exceptions, and we shall consider these ions later. In general, our procedure can correlate the $\log P$ values for single ions to around 0.5 log units, with a few exceptions; this corresponds to SD values of about 3 kJ mol⁻¹ for single-ion Gibbs energies of transfer. This is probably all that can be expected. Gritzner,⁵³ in his survey of single ion transfers, suggested that there was a variation of about 5 kJ mol⁻¹ per ion depending on the particular assumption used to assign anion and cation contributions.

The two additional descriptors, J^+ and J^- , are needed to represent partition properties of ions. The J^+ descriptor for cations seems to be related to structural effects of the ions. A plot of partial molal heat capacities in water⁵² against J^+ shows that as structural effects such as hydrophobic hydration increase for the tetraalkylammonium ions,⁵¹ so does J^+ increase, Figure 1. Shin et al.⁵¹ showed that a plot of partial molar heat capacities in water against cation radius was similar in shape to that in Figure 1, so that it is no surprise to find that J^+ itself correlates with ionic radius (Figure 2); this might be useful in assigning values of J^+ for other cations. The tetraphenyl cations are anomalous, and we consider these later. The J^- descriptor deals with specific interactions between anions and hydroxylic solvents. For the halide series of anions, J^- follows the hydrogen bond basicity,

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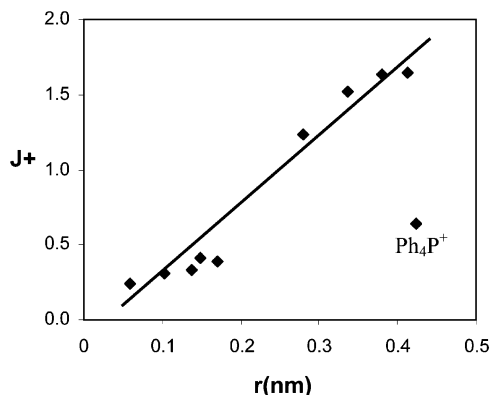


FIGURE 2. Plot of J^+ against radii of cations.

TABLE 11. Determination of Descriptors for the Chloride Ion Using the “Leave-One-Out” Procedure

descriptor	total ^a	leave-one-out			AAE
		mean	SD	AE	
<i>S</i>	3.27	3.28	0.11	0.00	0.08
<i>A</i>	0.00	0.00	0.00	0.00	0.00
<i>B</i>	2.26	2.26	0.01	0.00	0.01
<i>J⁻</i>	2.19	2.20	0.05	0.00	0.04

^a Results using all 10 systems, see Table 10.

rather as expected, but this correlation does not extend over the whole series of anions.

A reviewer has kindly suggested that the coefficients listed in Table 9 could be altered solvent by solvent in order to improve the fit of observed and experimental $\log P$ values. The two solvents that lead to the largest numerical absolute average errors, AAE, are acetone with $AE = 0.70$ for cations and 0.66 for anions and dichloromethane with $AAE = 0.57$ for cations and 0.44 for anions. These can be compared with AAE values for other aprotic solvents such as dimethylformamide (0.50 and 0.56) and DMSO (0.47 and 0.58). Alteration by trial-and-error of the coefficients for dichloromethane and acetone is thus not likely to reduce the numerical values of AAE by more than about 0.2 log unit. We suggest that until experimental $\log P$ values for ions are obtained with much greater accuracy than at present, there is little to be gained by trial-and-error alteration of the solvent coefficients.

It is not easy to assign errors to the descriptors that we have obtained by the “Solver” procedure in which three unknowns are obtained from 8 to 10 equations. Note that if two unknowns are obtained from two equations, as in the simultaneous equation method, the error in the two unknowns is apparently zero; this is because the errors in the equation coefficients have not been taken into account. One method that at least investigates the internal self-consistency of the analysis is the “leave-one-out” procedure. We illustrate this with reference to the determination of descriptors for the chloride ion.

For this ion, there are 10 $\log P$ values, Table 5, and 10 corresponding equations of the form of eq 6. If all 10 values are used, then the descriptors given in Table 10 and in Table 11 (second column) are obtained. We exclude the first $\log P$ value, and the corresponding first equation, and carry out an analysis on the remaining nine systems

to obtain a set of descriptors. We then exclude the second system and repeat the analysis, and continue until we have 10 separate sets of descriptors. From the 10 sets we can calculate the standard deviation, SD, the average error, AE, that shows any positive or negative bias, and the average absolute error, AAE, that is another measure of the ‘goodness – of – fit’. Results are in Table 11. The AAE values, we suggest, are a reasonable measure of the error in the calculated descriptors. For the chloride ion, the J^- descriptor is only relevant for the alcohols, and so we calculate the error in the four terms of eq 6 for partition to ethanol, corresponding to the descriptors in Table 11, using the coefficients in Table 4 and the AAE values in Table 11. The errors are *s.S* (0.25), *a.A* (0.000), *b.B* (-0.10) and *j.J⁻* (0.26). When summed statistically, these lead to an overall error in the calculated $\log P$ of 0.37 log units, as compared to that in the full “Solver” analysis of 0.13 log unit. Although the calculated error by the summation of terms is higher than the “Solver” error in the particular case given, it is reasonable as regards the general error; see Table 10.

The (Ph₄As⁺, Ph₄P⁺)/Ph₄B⁻ Assumption. There have been a number of assumptions that have been used to obtain free energies of transfer of single ions. Several workers have compared assumptions and have concluded that the (Ph₄As⁺, Ph₄P⁺)/Ph₄B⁻ assumption yields realistic single ion free energies of transfer.^{53–61} The rationale behind this assumption is that the four phenyl groups effectively shield the central ionic entity from direct interaction with the solvent. The value of ΔG_{tr}° for (Ph₄As⁺, Ph₄P⁺) or for Ph₄B⁻ is mainly due to the “neutral” part, together with an electrostatic ion–dipole part. Both of these depend on the solute radius which is very nearly the same for the cations and anion. Kim and Gomaa⁵⁸ have analyzed the ion–solvent interactions in detail, and have concluded that for transfer from water to a number of solvents, $\Delta G_{tr}^\circ(\text{Ph}_4\text{As}^+)/\Delta G_{tr}^\circ(\text{Ph}_4\text{B}^-) = 1.10$ rather than unity. Kim⁵⁹ later suggested a value of 1.08 . These unsymmetrical divisions will hold only for transfers from water. As regards the present work, use of $\Delta G_{tr}^\circ(\text{Ph}_4\text{As}^+)/\Delta G_{tr}^\circ(\text{Ph}_4\text{B}^-) = 1.10$ would alter the $\log P$ values we have used by no more than around 0.2 or 0.3 log units, too trivial a difference to take into account.

We did, however, investigate what the effect would be if a larger nonsymmetrical division was used. We found that addition of one log unit to the $\log P$ values in Table 3 for cations, and subtraction of one log unit for anions led to slightly more reasonable descriptors, but the difference was small, and the SD values remained the same. We did not pursue this approach further.

Comparison of Descriptors. The ionic descriptors that we have obtained can now be compared to those for nonelectrolytes and to those obtained by Raevsky^{19–21} and by Marcus.²⁷ Some comparisons found in this work between ions and nonelectrolytes are in Table 12. The

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TABLE 12. Comparison of Descriptors for Ions and Nonelectrolytes

ion	A	B	solute	A	B
Li ⁺	1.59	0.00	formic acid	0.76	0.33
Na ⁺	1.16	0.00	4-nitrophenol	0.82	0.26
K ⁺	1.07	0.00	benzoic acid	0.59	0.40
Rb ⁺	0.94	0.00	phenol	0.60	0.30
Cs ⁺	0.96	0.00	methanol	0.43	0.47
NH ₄ ⁺	0.82	0.00			
NMe ₄ ⁺	0.76	0.00			
NEt ₄ ⁺	0.52	0.00			
NPr ₄ ⁺	0.44	0.00			
Ph ₄ As ⁺	0.00	1.04			
F ⁻	0.00	2.66	HMPA	0.00	1.84
Cl ⁻	0.00	2.53	Ph ₃ PO	0.00	1.50
Br ⁻	0.00	2.12	(EtO) ₃ PO	0.00	1.06
I ⁻	0.00	1.63	triethylamine	0.00	0.79
CN ⁻	0.00	2.08	ethyl acetate	0.00	0.45
SCN ⁻	0.00	1.60	acetonitrile	0.07	0.32
N ₃ ⁻	0.00	2.04	benzene	0.00	0.14
NO ₃ ⁻	0.00	1.92	alkanes	0.00	0.00
ClO ₄ ⁻	0.00	1.23			
MeCO ₂ ⁻	0.00	2.77			
Ph ₄ B ⁻	0.00	1.47			

hydrogen bond acidity descriptor, **A**, is very large for the small cations and steadily decreases with size. One might consider species such as M⁺(OH)₂_n or M(OH)₂_{n-1}(OH₃)⁺ as able to donate a hydrogen bond. Relative to the corresponding nonelectrolytes, the hydrogen bond acidities of the small cations found by Marcus are smaller than those we find; see Table 3. There are more comparisons to be made for anions, and their various hydrogen bond basicities can be summarized as

1:1 (Table 1): Cl⁻ > HMPA, Br⁻ ~
Ph₃PO, I⁻ ~ (EtO)₃PO

Marcus (Table 3): Cl⁻ ~ HMPA, Br⁻ ~
Ph₃PO/(EtO)₃PO, I⁻ = MeCN

this work: Cl⁻ > HMPA, Br⁻ >
HMPA, I⁻ ~ Ph₃PO/(EtO)₃PO

Our hydrogen bond basicities for the halide anions are all rather larger than the 1:1 hydrogen bond basicities, Table 1. This is as expected, because first the halide anions in the ion pairs used in the 1:1 experiments will partly be shielded from the solvent, and second the **B** values are for overall basicities so that several molecules of the solvent may be involved. The hydrogen bond basicities found by Marcus,²⁷ Table 3, fall off greatly with increase in the size of the anions, until the iodide ion has the same hydrogen bond basicity as the weakly basic acetonitrile molecule. We find a much less severe progression, with the iodide ion being as strong a hydrogen bond base as triphenylphosphine or triethyl phosphate. All workers^{18-21,27} agree that the acetate ion (or general carboxylate ions) are very strong hydrogen bond bases.

The tetraphenylarsonium, tetraphenylphosphonium, and tetraphenylborate ions are special cases. Marcus,²⁷ in his 1991 paper, gives no values for these ions, but Marcus et al.²³ previously took the hydrogen bond acidity and basicity of these ions as zero. On our calculations, the three ions have substantial hydrogen bond basicity,

TABLE 13. Factors that Influence the Partition of Solutes, as log P, between Water and Acetonitrile^a

solute	e.E	s.S	a.A	b.B	v.V	j ⁺ .J ⁺	j ⁻ .J ⁻	calcd	obsd
Rb ⁺	0.00	0.87	-1.52	0	0.44	-1.23	0.00	-1.03	-1.05
Br ⁻	0.01	0.97	0.00	-8.04	1.03	0.00	0.00	-5.62	-5.43
HFIP	-0.02	0.18	-1.21	-0.44	2.34	0.00	0.00	1.26	
butanone	0.01	0.23	0.00	-2.24	2.31	0.00	0.00	-0.72	-0.78

^a The calculated and observed log P values include 0.41 as the constant term.

that for Ph₄B⁻ (1.13) being rather larger than those for the tetraphenyl anions, Ph₄P⁺ (0.80) and Ph₄As⁺ (0.85). The difference between the values for the anion and cations arises from the unsymmetric nature of the j⁺.J⁺ and j⁻.J⁻ terms.

As mentioned above in discussions on single ion transfers, it is considered that the transfer energy for the tetraphenyl ions is due to a "neutral" part and an "electrostatic" part, the latter being mainly ion-dipole with some ion-quadrupole character.⁵¹⁻⁵³ It has never been considered that the presence of the aromatic rings can lead to an effect such as hydrogen bond basicity. Even if the central ion is shielded from the solvent, this does not apply to the four phenyl groups. From Table 9, it appears that Ph₄B⁻ is a somewhat stronger base than Ph₄P⁺ or Ph₄As⁺. This seems reasonable, because the effect of the negatively charged central ion will be to increase the electron density in the phenyl rings and enhance basicity, whereas the positively charged central ions will reduce the electron density and reduce basicity. In any case, the hydrogen bond basicity of the tetraphenyl compounds per phenyl group is compatible with that for benzene (0.15) or diphenylmethane (0.33).

Finally, for the first time, it is possible to compare the factors that influence the partition of nonelectrolytes and ions, term by term in the general eq 6. This is shown in Table 13 for transfer from water to acetonitrile for the ions Rb⁺ and Br⁻ and the nonelectrolytes HFIP and butanone. The nonelectrolytes are chosen as examples of a typical hydrogen bond acid (to compare with Rb⁺) and a typical hydrogen bond base (to compare with Br⁻). Hexafluoropropan-2-ol, HFIP, is one of the few hydrogen bond acids that have little hydrogen bond basicity.

The volume term always favors acetonitrile, as it does for all nonaqueous solvents. The hydrogen bond terms all favor water: Rb⁺ and HFIP are both hydrogen bond acids and the large hydrogen bond basicity of water results in the negative a.A term. Br⁻ and butanone are hydrogen bond bases, hence the large negative b.B term due to the very strong hydrogen bond acidity of water.

We point out very strongly that other models will dissect the overall log P values, or the overall Gibbs energies of transfer, in quite different ways. This is no reflection on how "good" a model is, but simply indicates that various models each have their own particular uses. The partition of an ion between water and a solvent, as we have shown, can be related to the Gibbs energy of solvation in water and the solvent. Hence, models of ionic solvation will also be models of ionic partition. One of the most successful models of the solvation of ions is the continuum solvent model, as discussed by Ehrenson,⁶² particularly those in which the solvent is considered to

(62) Ehrenson, S. J. *Phys. Chem.* **1987**, *91*, 1868-1873.

form regions of different dielectric constants as “shells” surrounding an ion. It is quite pointless to try to interpret our model on the basis of a continuum model, or vice versa, because the dissection of the overall energies is completely different. One of the models discussed by Ehrenson⁶² is the one-layer model of Abraham and Liszi.⁶³ These workers set out a breakdown of solvation energies,⁶⁴ from which it is possible to deduce the corresponding breakdown of Gibbs energies of partition. For the Rb⁺ ion, interactions with the local solvent layer next to the ion greatly favor a non aqueous solvent, such as acetonitrile, and interactions with the bulk solvent layer greatly favor water. The latter predominates, and hence log P is negative. Clearly, there is no way that the interactions outlined in Table 12 can be related to interactions in a continuum model. The former relate to particular solute–solvent interactions, and the latter to general solute–solvent interactions in particular regions of space.

Conclusions

Data on Gibbs energies of transfer of ions from water to other solvents can be used to determine descriptors

(63) Abraham, M. H.; Liszi, J. *J. Chem. Soc., Faraday Trans. 1* **1978**, *74*, 1604–1614.

(64) Abraham, M. H.; Liszi, J. *J. Chem. Soc., Faraday Trans. 1* **1980**, *76*, 1219–1231.

for ions, on the same scales as descriptors for nonelectrolytes. However, this cannot be achieved using just the descriptors for nonelectrolytes. Two additional ionic descriptors (J^+ and J^-) are required in order to obtain chemically reasonable values for all the descriptors. Although we have dealt only with a restricted set of univalent cations and anions, there is no reason why the method should not be extended to other univalent ions. We are currently analyzing the partition of some 600 univalent ions from water to (wet) octanol and hope to report on this later. In principle, divalent or trivalent ions could be examined, but in order to do this, it would be necessary to determine if the same system coefficients, (j^+ and j^-), could be used for the specific ionic descriptors (J^+ and J^-).

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Supporting Information Available: The calculated values of excess molar refraction (E) for ions and neutral species and the method of calculation. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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