A Quantitative Measure of Solvent Solvophobic Effect

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Gibbs energies of transfer of argon, alkanes, and alkane-like compounds from water to numerous aqueous–organic mixtures and to pure solvents are tabulated. It is shown that these ΔG_t° values can be correlated through a set of equations, where ΔG_t° refers to transfer of a series of solutes from water to a

$$\Delta G_t^\circ \text{ (to solvent)} = MR_T + D$$

given solvent, R_T is a solute parameter, and M and D characterise the solvent. For 20 solutes in 51 solvent systems, 375 ΔG_t° values are thus correlated with a standard deviation of 0.078 kcal mol^{-1}. The M values in the above equation are then used to define a solvent solvophobic effect so that Sp values are scaled

$$Sp = 1 - M/M \text{ (hexadecane)}$$

from unity (water) to zero (hexadecane). The Sp values so obtained agree with the qualitative series reported by Sinanoglu and Abdulnur for pure solvents, and are shown to be quantitatively related to h.p.l.c. capacity factors.

Although there is still considerable discussion and calculation on the microscopical origin of the hydrophobic effect,[1–8] the experimental nature of the effect, at least in terms of equilibria or Gibbs free energies, is well established.[9] The hydrophobic effect can then simply be regarded as the phenomenon of the relative insolubility in water or aqueous solutions of certain organic solutes, by comparison to their solubility in non-aqueous solvents.† Some years ago,[10,11] one of us attempted a quantitative evaluation of the hydrophobic effect of water on a number of alkanes or alkane-like solutes. It was shown that the Gibbs energy of solution of inert gaseous solutes in all non-aqueous solvents for which results were available could be correlated through a set of equations,

$$\Delta G_s^\circ \text{ (in solvent)} = lR_G + d \qquad (1)$$

In equation (1), ΔG_s° refers to the solution of a series of solutes in a given solvent, R_G is a parameter characteristic of the solute and related to solute size, and l and d are then parameters characteristic of the solvent. Solutes covered by equation (1) included the rare gases, inorganic gases (H_2, N_2, CO, and O_2), alkanes, cycloalkanes, and the alkane-like solutes R_4M where M = Si, Ge, Sn, and Pb. The set of non-aqueous solvents, 32 in all, covered most of the general types of solvent, sufficient to establish the generality of equation (1), and the resulting equations correlated[11] 489 ΔG_s° values to within 0.08 kcal mol^{-1}. When applied to water as a solvent, equation (1) held only for the rare gases and the inorganic gases, see Figure 1, and the deviation of the observed ΔG_s° value in water from that calculated from the 'rare gas line' was taken as a quantitative measure of the hydrophobic effect for that particular solute in water. In principle, the same method of analysis could be used for a series of inert solutes in an aqueous–organic solvent, the deviation from the rare gas line being expected to be rather less than that observed for water itself. It would then be possible to derive a set of deviations that could then be used to describe the propensity of the solvent to provoke a hydrophobic effect on a given solute. If this hydrophobic tendency were scaled as 1 for water, all non-aqueous solvents would be set as 0, and various aqueous–organic solvents would have a hydrophobic tendency between 1 and 0. Unfortunately, the quantity of data required to carry out such analyses for any extended list of aqueous–organic solvents is so large that it seems very unlikely to be obtained in the near future. We have, therefore, resorted to another method of analysis that yields values for solvents that are related to the hydrophobic tendency, above, although not identical to it.

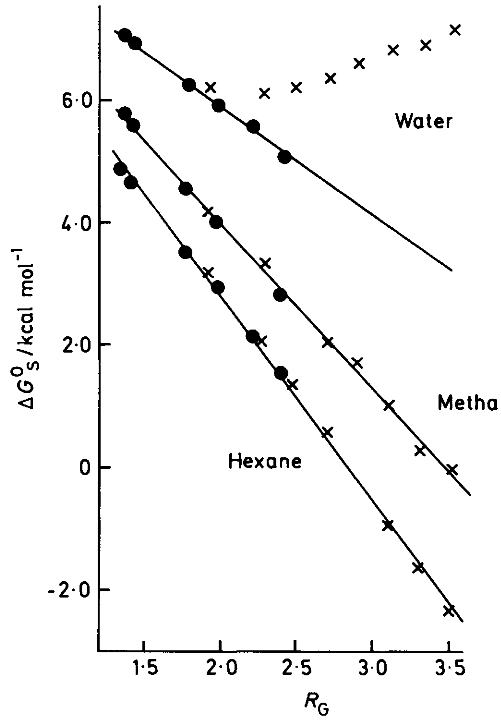

Figure 1. Plots of ΔG_s° for rare gases (●) and for n-alkanes (×) against the solute parameter R_G

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† This effect should carefully be distinguished from the hydrophobic interaction, which refers to the effect of water or aqueous solutions on the interaction between two solute particles in solution. The hydrophobic effect concerns only the interaction between the solvent and one solute particle in solution.

Table 1. Values of ΔG_t° for transfer from water, in kcal mol^{-1} on the molar scale at 298 K

Solvent (vol %)	Ar	CH_4	C_2H_6	C_3H_8	C_4H_{10}	Iso-C_4H_{10}	C_5H_{12}	C_6H_{14}	C_7H_{16}	C_8H_{18}	c-C_5H_{10}	c-C_6H_{12}	c-C_6H_{11}Me	Me_4C	Me_4Si	Me_4Ge	Me_4Sn	Et_4C	Et_4Si	Et_4Sn
10% Methanol	−0.075													−0.25	−0.33	−0.34	−0.33	−0.40	−0.47	−0.59
20% Methanol	−0.116													−0.59	−0.71	−0.76	−0.71	−0.86	−1.01	−1.13
30% Methanol	−0.155													−0.96	−1.14	−1.21	−1.14	−1.37	−1.59	−1.80
40% Methanol	−0.218													−1.34	−1.61	−1.70	−1.60	−1.91	−2.26	−2.56
50% Methanol	−0.317													−1.74	−2.10	−2.24	−2.13	−2.59	−3.10	−3.42
60% Methanol	−0.455													−2.23	−2.73	−2.92	−2.77	−3.41	−4.02	−4.35
70% Methanol	−0.623													−2.78	−3.39	−3.57	−3.43	−4.32	−4.80	−5.20
80% Methanol	−0.810													−3.34	−3.99	−4.17	−4.04	−5.18	−5.64	−6.15
90% Methanol	−1.017													−3.92	−4.57	−4.73	−4.59	−5.85	−6.56	−7.00
Methanol	−1.223	−1.618	−2.337	−3.09	−3.81	−3.78	−4.42	−5.34	−6.11	−6.69	−3.82	−4.54		−4.42	−5.05	−5.13	−5.12	−6.52	−7.27	−7.80
10% Ethanol	−0.017	−0.060	−0.096											−0.31				−0.51	−0.66	
20% Ethanol	−0.040	−0.087	−0.160											−0.68				−1.07	−1.42	
30% Ethanol	−0.073	−0.130	−0.275											−1.06				−1.76	−2.38	
40% Ethanol	−0.134	−0.268	−0.810											−1.55				−2.59	−3.45	
50% Ethanol	−0.250	−0.498	−1.050											−2.22				−3.63	−4.55	
60% Ethanol	−0.412	−0.730	−1.300											−2.88				−4.60	−5.38	
70% Ethanol	−0.587	−0.948	−1.568											−3.42				−5.26	−5.99	
80% Ethanol	−0.762	−1.170	−1.850											−3.91				−5.87	−6.58	
90% Ethanol	−0.975	−1.395	−2.125											−4.34				−6.46	−7.16	
Ethanol	−1.206	−1.615	−2.423	−3.20	−4.00	−3.96	−4.76	−5.60	−6.33	−7.12	−3.99	−4.71		−4.70			−5.32	−6.99	−7.71	−8.11
10% Dioxane	−0.012	−0.038	−0.092											−0.36				−0.46		
20% Dioxane	−0.023	−0.090	−0.220											−0.74				−0.95		
30% Dioxane	−0.045	−0.168	−0.378											−1.15				−1.55		
40% Dioxane	−0.088	−0.270	−0.595											−1.57				−2.31		
50% Dioxane	−0.175	−0.417	−0.850											−2.03				−3.24		
60% Dioxane	−0.300	−0.585	−1.140											−2.57				−4.22		
70% Dioxane	−0.435	−0.790	−1.450											−3.19				−5.30		
80% Dioxane	−0.605	−1.035	−1.760											−3.78				−6.15		
90% Dioxane	−0.780	−1.245	−2.060											−4.30				−6.80		
Dioxane	−0.941	−1.439	−2.300											−4.66			−5.53		−8.07	−8.58
10% Acetone														−0.49				−0.57	−0.64	
20% Acetone														−0.94				−1.23	−1.39	
30% Acetone														−1.37				−1.96	−2.21	
40% Acetone														−1.81				−2.86	−3.23	
50% Acetone														−2.31				−3.73	−4.32	
60% Acetone														−2.83				−4.53	−5.11	
70% Acetone														−3.35				−5.28	−5.86	
80% Acetone														−3.81				−5.84	−6.57	
90% Acetone														−4.24				−6.41	−7.29	
Acetone	−1.288	−1.698	−2.511	−3.34			−5.02	−5.83		−7.25		−4.86		−4.74			−5.56	−7.08	−8.00	−8.37
Dimethyl sulphoxide	−0.258	−0.850	−1.770	−2.32	−3.07	−2.85	−3.59	−4.34	−4.91	−5.73		−3.65					−4.37			−6.95
Hexane	−1.550	−1.960	−2.870	−3.75	−4.62	−4.65	−5.63	−6.60	−7.38	−8.34	−4.90	−5.65		−5.40	−6.21		−6.34	−8.11	−9.10	−9.49
Hexadecane	−1.063	−1.553	−2.494	−3.39	−4.28	−4.24	−5.29	−6.19	−6.96	−7.90	−4.55	−5.20	−6.06							
Formamide	0.047							−3.08	−3.53	−4.16		−2.58	−3.07							
Ethylene glycol	−0.040	−0.480	−0.980	−2.00	−2.37	−2.25		−3.32	−3.79	−4.44		−2.77	−3.29				−3.32			
Dimethylformamide	−0.830	−1.270	−2.120	−2.76			−4.39	−5.22	−5.90	−6.72		−4.38	−5.22				−5.15			
N-Methylpyrrolidinone	−0.660	−1.190	−2.160	−2.84	−3.63	−3.52	−4.45	−5.28	−5.90	−6.68		−4.44	−5.24				−5.22			
Acetonitrile	−1.220				−3.59		−4.43	−5.22	−5.84	−6.46	−3.73	−4.19					−5.03			
Propan-2-ol	−1.190	−1.540		−3.28	−4.08	−4.03			−6.43	−7.29		−5.05					−5.54			
Propan-1-ol	−1.190	−1.610	−2.450					−5.75	−6.50	−7.28							−5.52			
Butan-1-ol	−1.160	−1.590	−2.460	−3.31			−5.05	−5.85	−6.63	−7.34		−4.97					−5.60			

Table 2. Constants in the regression equation (5) derived from the primary ΔG°_t values in Table 1

Solvent (vol. %)	*M*	*R*	S.d.	*r*	*n*
10% Methanol	−0.2452	0.4194	0.0300	−0.9830	8
20% Methanol	−0.5019	0.8356	0.0146	−0.9990	8
30% Methanol	−0.8067	1.3548	0.0355	−0.9980	8
40% Methanol	−1.1474	1.9424	0.0476	−0.9980	8
50% Methanol	−1.5500	2.6480	0.0305	−0.9996	8
60% Methanol	−1.9728	3.3155	0.0275	−0.9998	8
70% Methanol	−2.3284	3.7752	0.0783	−0.9987	8
80% Methanol	−2.7133	4.3295	0.1113	−0.9981	8
90% Methanol	−3.0557	4.7866	0.0982	−0.9988	8
Methanol	−3.3626	5.1920	0.1039	−0.9984	19
10% Ethanol	−0.3478	0.6587	0.0241	−0.9967	6
20% Ethanol	−0.7583	1.4606	0.0639	−0.9951	6
30% Ethanol	−1.2592	2.4361	0.1213	−0.9936	6
40% Ethanol	−1.7442	3.2180	0.1692	−0.9935	6
50% Ethanol	−2.3133	4.1809	0.1239	−0.9980	6
60% Ethanol	−2.7532	4.8451	0.0458	−0.9998	6
70% Ethanol	−3.0262	5.1665	0.0572	−0.9998	6
80% Ethanol	−3.2735	5.4361	0.0973	−0.9994	6
90% Ethanol	−3.4992	5.6567	0.1240	−0.9991	6
Ethanol	−3.5971	5.6285	0.1228	−0.9983	17
10% Dioxane	−0.3170	0.5941	0.0383	−0.9867	5
20% Dioxane	−0.6465	1.1995	0.0724	−0.9885	5
30% Dioxane	−1.0305	1.8986	0.0865	−0.9935	5
40% Dioxane	−1.4860	2.7205	0.0546	−0.9987	5
50% Dioxane	−2.0146	3.6562	0.0200	−0.9999	5
60% Dioxane	−2.5648	4.6006	0.0688	−0.9993	5
70% Dioxane	−3.1733	5.6405	0.1136	−0.9988	5
80% Dioxane	−3.6176	6.3097	0.1148	−0.9991	5
90% Dioxane	−3.9400	6.7386	0.0900	−0.9995	5
Dioxane	−3.8686	6.3660	0.0728	−0.9998	7
10% Acetone	−0.1665	−0.0137	0.0158	−0.9889	3
20% Acetone	−0.5116	0.5125	0.0073	−0.9997	3
30% Acetone	−0.9668	1.3641	0.0255	−0.9991	3
40% Acetone	−1.6470	2.8367	0.0853	−0.9966	3
50% Acetone	−2.3153	4.2362	0.0676	−0.9989	3
60% Acetone	−2.6479	4.6374	0.1482	−0.9961	3
70% Acetone	−2.9292	4.8982	0.2101	−0.9936	3
80% Acetone	−3.1986	5.2164	0.1571	−0.9970	3
90% Acetone	−3.5170	5.7004	0.1148	−0.9987	3
Acetone	−3.6701	5.6801	0.1055	−0.9990	13
Dimethyl sulphoxide	−3.2492	5.7280	0.1200	−0.9982	13
Hexane	−4.1642	6.4232	0.1233	−0.9986	18
Hexadecane	−4.2024	6.9232	0.0542	−0.9997	13
Formamide	−2.5791	4.9429	0.0508	−0.9995	6
Ethylene glycol	−2.6212	4.7830	0.1322	−0.9957	12
Dimethylformamide	−3.6202	6.0538	0.0632	−0.9995	11
N-Methylpyrrolidinone	−3.6897	6.2424	0.0849	−0.9990	13
Acetonitrile	−3.2917	5.1321	0.0971	−0.9982	9
Propan-2-ol	−3.7844	6.0451	0.0729	−0.9995	9
Propan-1-ol	−3.7503	5.9495	0.0431	−0.9999	7
Butan-1-ol	−3.8413	6.1422	0.0558	−0.9997	10

Sinanoglu and Abdulnur[12] investigated the effect of solvents in stabilising the double helix of DNA with respect to the two separate coils. They invented the term 'solvophobic effect' to describe the tendency of a solvent to stabilise the double helix, and expressed the order of decreasing solvophobic effect as,

water > glycerol, formamide > ethylene glycol > methanol, ethanol, propan-1-ol, butan-1-ol > t-butyl alcohol (2)

In a later paper, Sinanoglu,[13] using a cavity theory of solution, deduced an expression for the Gibbs energy of solution of a solute gas into a solvent, based on the use of the solvent macroscopic surface tension, γ_1, as a measure of the energy required to make a cavity in the solvent [equation (3)].

$$\Delta G^\circ_s \simeq a - b\mu_2^2/\bar{V}_2 + c\bar{V}_2^{2/3}\gamma_1 + RT\ln kT/\bar{V}_1 \quad (3)$$

In equation (3), μ_2 and $\bar{V}_2$ are the solute dipole moment and molar volume, γ_1 and $\bar{V}_1$ are the solvent surface tension and molar volume, and *a*, *b*, and *c* are constants that can be evaluated or estimated. Sinanoglu[13] pointed out that for non-polar solutes the term $V_2^{2/3}\gamma_1$ dominates, and gives rise to the solvophobic effect in general, or hydrophobic effect in the particular case of water as the solvent. Although equation (3) and an analogous equation for the association of solutes in solution could be applied to pure solvents, Sinanoglu[13] concluded that it was difficult to predict the solvophobic sequence of mixed solvents.

The general ideas of Sinanoglu were later applied by Horvath *et al.*[14,15] to characterise the eluant strength of mixed solvents in reversed-phase liquid chromatography, in terms of solvophobic power. In particular, for a given solute under constant experimental conditions, the capacity factor is related

$$\ln K = A + B\left[\frac{2(\varepsilon - 1)}{2\varepsilon + 1}\right] + C\gamma_1 + D(K_1^{e} - 1)\bar{V}_1^{2/3}\gamma_1 \quad (4)$$

to change in solvent composition through equation (4), where A, B, C, and D are constants, ε is the solvent dielectric constant, and K_1^{e} is a solvent constant that itself depends on γ_1 as well as on ΔH_v, the enthalpy of vaporisation of the solvent.[14] Horvath *et al.* showed that ln K values for a particular solute were, indeed, dependent on the γ_1 value of the mixed solvent used as the eluate, for aqueous methanol and aqueous acetonitrile mixtures, although no numerical values for solvent solvophobic effects were actually reported.

Since the solvophobic effect is certainly very important in areas such as reversed-phase chromatography,[14,15] adsorption on charcoal,[16] *etc.*, we set out to obtain a scale of solvophobic power that would apply both to pure solvents, and especially to aqueous–organic mixed solvents.

Inspection of Figure 1 suggests that a measure of the solvophobic effect could be the difference ΔG_s° (in solvent) − ΔG_s° (in water), in other words, the standard Gibbs energy of transfer of a given solute from water to another solvent. Indeed, since the n-alkanes, ethane to octane, together with krypton, form almost a straight-line plot against R_G, transfers of these solutes from water to another solvent would also yield a straight line when plotted against R_G. As usual, lack of data (this time on krypton and also on some of the alkanes) prevents application of these equations, but argon and the alkanes, as well as larger inert solutes such as cycloalkanes and R_4M compounds, form a suitable series. In this case, a modified R_G parameter must be used, and so we set up equations of similar form to equation (1), in terms of Gibbs energies of transfer from water,

$$\Delta G_t^\circ(\text{to solvent}) = MR_T + D \qquad (5)$$

Since we deal especially with mixed solvents, it is more convenient to express ΔG_t° on the molar concentration scale, rather than on the mole fraction scale (as for ΔG_s°), but this does not affect the form of the equations at all.

The data we have used relate mostly to transfers from water to aqueous organic systems. Most of the values are from the work of de Ligny and van der Veen,[17] together with our own values for transfers in the aqueous methanol system.[18] Values for argon and ethane were from the Solubility Data Project Series,[19] and those for methane and ethane in aqueous ethanol and aqueous dioxane from Ben-Naim and co-workers.[20] In all cases, ΔG_t° values at rounded-off volume % before mixing compositions were obtained either from large-scale plots or by polynomial curve fits. For the pure solvents, values of ΔG_s° listed before[10,11] were combined with ΔG_s° in water[10,11,21] to yield mole fraction transfer parameters which were then converted into molar ΔG_t° values. In the case of hexadecane, an updated set of ΔG_s° values[22] were used. For a number of pure solvents, previous results[11] were supplemented by data obtained *via* gas chromatography: these solvents were formamide,[23] ethylene glycol (EG),[24] dimethylformamide (DMF),[25] and *N*-methylpyrrolidin-2-one (NMP).[25] The entire set of ΔG_t° values used in correlations through equation (5) is in Table 1. We refer to this set of 375 data points as primary values. A computer program was devised to enable equation (5) to be applied to all the solvent systems and all the solutes in an iterative procedure that

Table 3. Values of the solute parameter R_T

Solute	R_T	S.d.	n
Primary values			
Argon	1.906	0.032	42
Methane	2.019	0.014	31
Ethane	2.228	0.038	30
Propane	2.469	0.041	11
n-Butane	2.679	0.025	9
Isobutane	2.660	0.013	8
n-Pentane	2.893	0.019	10
n-Hexane	3.120	0.014	13
n-Heptane	3.308	0.025	13
n-Octane	3.526	0.011	14
Cyclopentane	2.699	0.024	5
Cyclohexane	2.888	0.024	13
Methylcyclohexane	3.100	0.015	5
Me_4C	2.835	0.056	41
Me_4Si	3.067	0.019	11
Me_4Ge	3.142	0.037	10
Me_4Sn	3.078	0.017	22
Et_4C	3.417	0.056	40
Et_4Si	3.711	0.048	32
Et_4Sn	3.889	0.072	15
Secondary values[a]			
n-Nonane	3.769	0.014	5
2,2,4-Trimethylpentane	3.339	0.016	4
Methylcyclopentane	2.938	0.018	13
Ethylcyclohexane	3.434	0.008	4

[a] These include R_T values derived from some additional ΔG_t° values to those given in Table 4; n-nonane (−4.82 to formamide, −5.10 to EG); iso-octane (−3.73 to formamide, −3.94 to EG); methylcyclopentane (−4.58 to DMF, −4.58 to NMP), and ethylcyclohexane (−3.93 to formamide, −4.19 to EG).

Table 4. Values of ΔG_t° used in the secondary calculations

Solvent[a]	Ar	C_6H_{14}	C_7H_{16}	C_8H_{18}	C_9H_{20}	Iso-C_8H_{18}	Methylcyclopentane	Cyclohexane	Methylcyclohexane	Ethylcyclohexane
50% DMF	−0.04	−2.68	−3.07	−3.70			−2.16	−2.06	−2.53	
75% DMF	−0.30	−3.76	−4.21	−4.87			−3.30	−3.18	−3.68	
85% DMF	−0.48	−4.33	−4.84	−5.57			−3.77	−3.62	−4.24	
90% DMF	−0.60	−4.63	−5.20	−5.97			−4.04	−3.90	−4.54	
95% DMF	−0.71	−4.81	−5.42	−6.21			−4.20	−4.04	−4.74	
60% EG	0.18	−2.25	−2.53	−3.01			−1.81	−1.70	−2.01	
75% EG	0.14	−2.55	−2.90	−3.43			−2.12	−2.01	−2.39	
85% EG	0.08	−2.81	−3.19	−3.77			−2.37	−2.27	−2.68	
90% EG	0.03	−2.96	−3.37	−3.95			−2.53	−2.42	−2.85	
95% EG	−0.02	−3.12	−3.53	−4.15			−2.68	−2.57	−3.02	
Diethylene glycol		−3.95	−4.58	−5.38	−5.99	−4.69	−3.32	−3.33	−3.98	−4.99
Triethylene glycol		−4.10	−4.66	−5.40	−6.14	−4.78		−3.49	−4.12	−5.12
Glycerol		−2.61	−3.22	−4.05	−4.89			−1.66	−2.29	

[a] DMF dimethylformamide; EG ethylene glycol.

Table 5. Constants in the regression equation (5) derived from ΔG_t° values in Table 4

Secondary values	*M*	*R*	S.d.	*r*	*n*
50% DMF	−2.2179	4.2659	0.0988	−0.9969	7
75% DMF	−2.8084	5.0109	0.0589	−0.9993	7
85% DMF	−3.1328	5.4669	0.0374	−0.9998	7
90% DMF	−3.3012	5.6771	0.0306	−0.9999	7
95% DMF	−3.3810	5.7355	0.0178	−0.9999	7
60% EG	−1.9526	3.9223	0.0693	−0.9980	7
75% EG	−2.1874	4.3152	0.0425	−0.9994	7
85% EG	−2.3568	4.5684	0.0386	−0.9996	7
90% EG	−2.4414	4.6709	0.0357	−0.9997	7
95% EG	−2.5298	4.7848	0.0409	−0.9996	7
Diethylene glycol	−3.1665	5.8840	0.0682	−0.9975	9
Triethylene glycol	−3.0328	5.3138	0.0433	−0.9989	8

is repeated until constant values of *M*, *D* and R_T are obtained. The final equations for the 51 solvent systems are in Table 2, and the calculated R_T values are in Table 3. These equations and R_T values yield ΔG_t° (calc) values for 375 points with a standard deviation (s.d.) of 0.078 kcal mol^{-1}; s.d. is defined as $\{[\Delta G_t^\circ(\text{calc}) - \Delta G_t^\circ(\text{obs})]^2/(n-1)\}^{\frac{1}{2}}$. It is therefore now possible to predict ΔG_t° values for all the missing entries in the 51 × 20 matrix with an error not very different to the experimental. As expected, the R_T values listed in Table 3 are quite close to the R_G values used before, especially for the C(3)—C(8) n-alkanes.

In addition to the primary data given in Table 1, ΔG_t° for a number of solutes can be obtained from gas chromatographic data on the interesting solvents, diethylene glycol,[25,26] triethylene glycol,[26] and glycerol[27] (see Table 4). Unfortunately, values for the smaller solutes are not available and so we have not used these solvents in our primary set. Popescu *et al.*[28] have reported gas chromatographic data on several aqueous–organic solvents from which ΔG_t° values can be derived. Solvent compositions are given[28] as a percentage without, however, detailing whether the percentage refers to volumes before mixing, weight percentage, or mole fraction percentage. We have repeated some of the quoted experiments and have confirmed that the percentages must be either volumes before mixing, or weight percentages. For most of the solvents used by Popescu *et al.*,[28] densities are very close to unity, and it was impossible for us to decide between volume or weight percentage. On the assumption that volume compositions are volumes before mixing, we have calculated the ΔG_t° values given in Table 4 for hydrocarbons.* Also in Table 4 are values of ΔG_t° for argon obtained from Krestov *et al.*,[29] who also gave results from which ΔG_t° values to pure formamide and pure DMF were obtained (see Table 1). We regard the ΔG_t° values in Table 4 as secondary values, and list the obtained set of equations of the type of equation (5) in Table 5, and the secondary set of R_T parameters in Table 3. Although derived from our secondary set of ΔG_t° values, the results in Table 5 are quite reasonable, with the exception of solvent glycerol. In this case, the *M* and *R* values seem anomalous, and we have not used results for glycerol any further.

Values of *M*, the slopes of the lines in equation (5), are automatically referred to water as a standard, since *M* = 0 by definition for water. We can construct a scale of solvophobic power by defining another fixed point, for example the *M* value for the most hydrophobic solvent n-hexadecane. If the solvophobic power of water and hexadecane are arbitrarily defined as unity and zero respectively, then a solvophobic power, *Sp*, can be calculated through equation (6) or equation (7).

Table 6. Values of the solvent solvophobic parameter, *Sp*

Solvent	*Sp*	Solvent	*Sp*
Primary values			
10% Methanol	0.9417	10% Dioxane	0.9246
20% Methanol	0.8806	20% Dioxane	0.8462
30% Methanol	0.8080	30% Dioxane	0.7548
40% Methanol	0.7270	40% Dioxane	0.6464
50% Methanol	0.6312	50% Dioxane	0.5206
60% Methanol	0.5306	60% Dioxane	0.3899
70% Methanol	0.4459	70% Dioxane	0.2449
80% Methanol	0.3543	80% Dioxane	0.1392
90% Methanol	0.2729	90% Dioxane	0.0624
Methanol	0.1998	Dioxane	0.0794
10% Ethanol	0.9172	10% Acetone	0.9604
20% Ethanol	0.8196	20% Acetone	0.8783
30% Ethanol	0.7004	30% Acetone	0.7699
40% Ethanol	0.5850	40% Acetone	0.6081
50% Ethanol	0.4495	50% Acetone	0.4491
60% Ethanol	0.3449	60% Acetone	0.3699
70% Ethanol	0.2799	70% Acetone	0.3030
80% Ethanol	0.2210	80% Acetone	0.2389
90% Ethanol	0.1673	90% Acetone	0.1631
Ethanol	0.1440	Acetone	0.1267
Ethylene glycol	0.3763	DMSO	0.2268
Formamide	0.3863	Acetonitrile	0.2167
Propan-1-ol	0.1076	DMF	0.1384
Propan-2-ol	0.0995	NMP	0.1220
Butan-1-ol	0.0859	n-Hexane	0.0091
Water	1	n-Hexadecane	0
Secondary values			
50% DMF	0.4703	60% EG	0.5337
75% DMF	0.3293	75% EG	0.4776
85% DMF	0.2519	85% EG	0.4372
90% DMF	0.2116	90% EG	0.4170
95% DMF	0.1926	95% EG	0.3959
Diethylene glycol	0.2438		
Triethylene glycol	0.2757		

$$Sp = 1 - M/M\,(\text{hexadecane}) \tag{6}$$

$$Sp = 1 + M/4.2024 \tag{7}$$

Calculated *Sp* values for both the primary and secondary data sets of solvents are in Table 6. These *Sp* values provide a simple quantitative measure of the solvophobic effect, relative to the two fixed solvents water and n-hexadecane at 298 K. As mentioned in the Introduction, these *Sp* values are not the same as any hydrophobic effects obtained by the rare gas method, see Figure 1, for reasons there outlined.

For pure solvents, the order of decreasing solvophobic power is:

water > formamide > ethylene glycol > methanol >
ethanol > propan-1-ol > propan-2-ol > butan-1-ol (8)

Sequence (8) is virtually identical to sequence (2) obtained by Sinanoglu and Abdulnur,[12] suggesting that our method of analysis does indeed lead to the effect introduced by these workers. The non-polar term in equation (3), $c\bar{V}_2^{2/3}\gamma_1$, reduces simply to an expression in γ_1 for a given solute, and following Sinanoglu and Abdulnur,[12] it might be expected that *Sp* would be linearly related to γ_1. However, for 13 pure solvents there is only a poor correlation between *Sp* and γ_1 (*r* = 0.885), and for aqueous–organic solvents plots of γ_1 against *Sp* are markedly

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* Required parameters for solution in water were from refs. 11, 21, and 30.

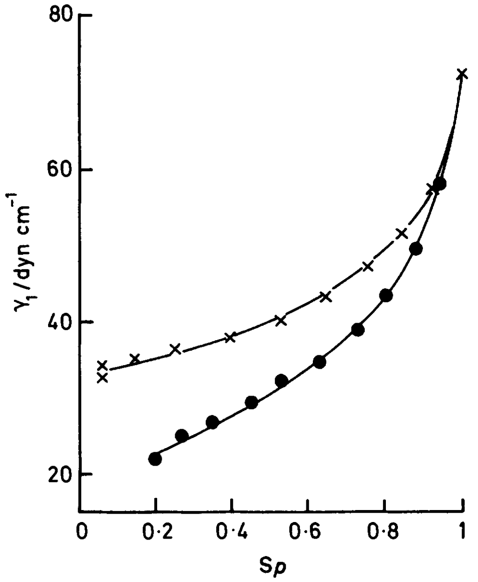

Figure 2. Plots of surface tension γ_1 against the solvophobic parameter *Sp* for aqueous methanol mixtures (●) and aqueous dioxane mixtures (×)

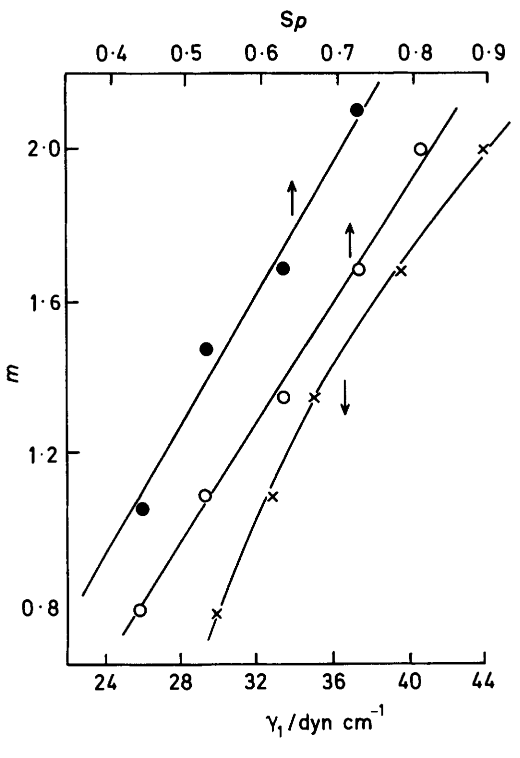

Figure 3. Plots of *m* in equation (9) for the decyl column (●) and for the heptadecafluorodecyl column (○) against *Sp*, and for the heptadecafluorodecyl column against γ_1 (×)

curved (see Figure 2). Horvath *et al.*[14,15] used the solvophobic theory to account for various effects in reversed-phase liquid chromatography. Following our derivation of *Sp*, capacity factors for a given solute, as log *k′* values, should be related to *Sp* as the mobile phase is altered. Unfortunately, no numerical values of log *k′* were given by Horvath *et al.*,[14,15] so it is not possible to analyse his data using *Sp* values. However, Carr *et al.*[31] have correlated log *k′* values for numerous aromatic molecules on a decyl column and on a heptadecafluorodecyl column using aqueous–methanol mobile phases through equation (9). This equation relates log *k′* for a series of solutes

$$\log k' = c + m\bar{V}_2/100 + s\pi^*_2 + b\beta_2 \qquad (9)$$

on a given bonded phase with a given mobile phase to parameters ($\bar{V}_2$, π^*_2, and β_2) characteristic of the solute, where $\bar{V}_2$ is the solute molar volume, π^*_2 is the solute dipolarity and β_2 is the solute hydrogen bond basicity;[31] *c*, *m*, *s*, and *b* are constants found by the method of multiple linear regression analysis, The value of *m* in equation (9) then represents the effect of the change in mobile phase on log *k′* due to the size of the solute. Since this is a non-polar effect, *m* should certainly be related to *Sp* or, following Horvath *et al.*,[14,15] to γ_1. Plots of *m* for the decyl column and for the heptadecafluorodecyl column against *Sp* are shown in Figure 3, resulting in good straight lines (r = 0.989 and 0.998 respectively). Corresponding plots of *m* against γ_1 are definitely curved, see the example in Figure 3, so that for the aqueous methanol mobile phase *Sp* is a more useful solvent parameter than γ_1.

There is little point in attempting to relate *Sp* values to most of the general 'solvent polarity' parameters, because the former is not designed to represent any such parameter. It is useful, however, to compare *Sp* to parameters that have been suggested as relevant to processes, like liquid chromatography, in which solvophobic power may be important. Snyder[32] has devised a solvent polarity scale, *P′*, for use in liquid chromatography and in gas–liquid chromatography, but limited to pure solvents. There is a general connection, though not linear, between *P′* and *Sp*, but clearly *P′* and *Sp* define rather different solvent properties. The rank order of solvents in the *Sp* series is also similar to those with respect to the 'solvent strength' *S* values of Snyder *et al.*,[33] and to the eluotropic solvent series in reversed-phase chromatography,[34] although neither of these series are quantitatively well established.

The eluotropic series of Colin and co-workers[35] is better defined, and in Table 7 are compared eluotropic strengths of solvents as given by Snyder *et al.*,[23] Karch *et al.*,[34] and Colin *et al.*,[35] with our own *Sp* values. In order to show the comparison more clearly, we have rescaled our *Sp* values to give eluotropic strengths of water as 0.00 and methanol as 3.00; these rescaled values match these of Colin *et al.*,[35] particularly well.

Although we have discussed briefly the connection between solvophobic effects and liquid chromatography, it has not been our intention in the present work to apply the *Sp* scale to

Table 7. Some measures of solvent eluotropic strengths

		Eluotropic strength			
Solvent	*Sp*	*a*	35	33	34
Water	1	0	0	0	0
Methanol	0.1998	3.00	2.95	3.0	1.0
Ethanol	0.1440	3.21	3.14	3.6	3.1
Propan-1-ol	0.1076	3.35	—	—	10.1
Propan-2-ol	0.0995	3.38	—	4.2	8.3
DMSO	0.2268	2.90	—	—	—
Acetonitrile	0.2167	2.94	2.87	3.1	3.1
DMF	0.1384	3.23	—	—	7.6
Acetone	0.1267	3.27	3.19	3.4	8.8
Dioxane	0.0794	3.45	—	3.5	11.7
Ethyl acetate	0.0635	3.51	3.48	—	—
Tetrahydrofuran	—	—	3.52	4.4	—
Hexane	0.0091	3.71	—	—	—
Hexadecane	0	3.75	—	—	—

[a] This work, obtained by scaling the *Sp* values from 0 (water) to 3.00 (methanol); the value of *Sp* for ethyl acetate was obtained in a similar way to the secondary values in Table 4.

various phenomena. Schneider and Sangwan[36] have correlated rates of Diels–Alder reactions with the *Sp* solvent scale, and we hope to investigate the general applicability of the *Sp* scale in a later publication.

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