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Partition of compounds from water and from air into the wet and dry monohalobenzenes†

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Values of the partition coefficient from the gas phase (K_s) and from water (P_s) to the monohalobenzene solvents have been collected for fluorobenzene (21 solutes), chlorobenzene (212 solutes), bromobenzene (126 solutes) and iodobenzene (65 solutes). It is shown that for the wide range of solutes studied, partitions into the dry and wet (water-saturated) solvents are essentially the same, and that equations can be constructed that include data on both dry and wet solvents. Using the Abraham equations, that contain a maximum of five descriptors, statistically satisfactory equations are obtained for log K_s and log P_s with estimated predictive standard deviations of around 0.20 log units. The coefficients in the Abraham equations for the four halobenzene solvents are surprisingly similar and except for the s-coefficient, which reflects the solvent dipolarity/polarisability, are also similar to the coefficients for partition into toluene.

Introduction

The halobenzenes, especially chlorobenzene and to a lesser extent bromobenzene, are important extraction agents and have been used particularly for the extraction of ligands and ligand–cationic complexes.[1–6] In spite of their importance, there has been comparatively little work on the factors that influence partition from water to the halobenzenes. Of the general studies of partitioning from water to organic solvents,[7–13] that of Marcus[7] deals with 36 compounds into chlorobenzene and 28 into bromobenzene, Meyer and Maurer[9] use only 20 compounds into chlorobenzene, 15 into bromobenzene and 12 into iodobenzene. Cramer *et al.*[13] list gas to solvent data for 5 compounds in fluorobenzene, 36 compounds in chlorobenzene, 24 compounds in bromobenzene and 19 compounds in iodobenzene, but Torrens *et al.*[11,12] do not deal with the halobenzenes at all. Kolář *et al.*[14] suggest a method for solvent selection for pharmaceuticals, but do not include any of the halobenzene solvents in their examples. We have shown that for a number of aliphatic organic solvents the solvation of a compound in the wet solvent (that is the solvent saturated with water as in 'practical' partition experiments) will not necessarily be the same as solvation in the dry solvent, as we have demonstrated for the solvents ethers,[15,16] alcohols[17,18] acetates,[19] and ketones.[20] However for solvents that take up very little water when in equilibrium with water, solvation in the wet and dry solvents may be almost the same. This is the case for olive oil and hexadecane solvents[21] and might be so for the halobenzenes. We therefore consider two different data sets. First, we use data on practical partitioning from water to the water-saturated halobenzenes,[22] and second we use data on partitioning from the gas phase to the dry halobenzenes. The aims of the present work are twofold. We shall attempt to ascertain if the data on partitioning into water-saturated (wet) and dry halobenzenes can be combined, and then we shall attempt to identify the factors that influence solvation in the halobenzenes and to compare effects on the four halobenzene solvents.

Methodology

The experimental data for partitioning from water into the wet halobenzenes are observed partition coefficients, P_s, as listed in the Medicinal Chemistry Project database,[22] and also as obtained by Takeda *et al.*,[1–6] who have studied a number of crown ethers. These water to wet halobenzene partition coefficients can be converted into air to wet halobenzene partition coefficients, K_s, through eqn (1), where K_w is the air to water partition coefficient. All partition coefficients that we use refer to 298 K.

$$\log P_s = \log K_s - \log K_w \qquad (1)$$

The air to water partition coefficient has no units when defined through eqn (2); air to solvent partition coefficients are similarly defined.

$$K_w = (\text{conc. of solute in water, mol L}^{-1})/(\text{conc. of solute in gas phase, mol L}^{-1}) \qquad (2)$$

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† Electronic supplementary information (ESI) available: Tables S1-S4, including details of all the values of log Ks and log Ps that have been used, together with the corresponding compound descriptors. See DOI: 10.1039/b823403e

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Air to dry halobenzene partition coefficients for gaseous solutes can be obtained by direct measurements. One of the most useful sets of measurements is that of Saylor and Battino[23] who obtained Ostwald solubility coefficients, equivalent to air to solvent partition coefficients as defined through eqn (2), for the rare gases in all four halobenzenes. Values of K_s can also be obtained from experimentally determined Henry's law constants and the experimentally known solute vapour pressure. They can also be obtained from the solute activity coefficient at infinite dilution in the halobenzene, together with the solute vapour pressure. For less volatile solutes, water to dry halobenzene partition coefficients can be obtained from the ratio of the solute solubility in water and in the dry halobenzene, with a number of provisos: there should be no hydrate or solvate formation, and the secondary medium activity coefficient of the solute in water and in the dry halobenzene should not deviate substantially from unity. The obtained values of K_s can be converted to P_s through eqn (1).

Two linear free energy equations are used to correlate the obtained partition coefficients as shown in eqn (3) and (4).

$$\log K_s = c + eE + sS + aA + bB + lL \tag{3}$$

$$\log P_s = c + eE + sS + aA + bB + vV \tag{4}$$

The independent variables in eqn (3) and (4) are solute descriptors as follows.[24,25] E is the solute excess molar refraction in units of $(\text{cm}^3\ \text{mol}^{-1})/10$, S is the solute dipolarity/polarisability, A and B are the overall or summation solute hydrogen bond acidity and basicity, V is the McGowan characteristic volume[26] in units of $(\text{cm}^3\ \text{mol}^{-1})/100$, and L is the logarithm of the gas to hexadecane partition coefficient at 298 K.

Results

Fluorobenzene

For dry fluorobenzene, values of log K_s were available for the rare gases,[23] oxygen[27] and a few solutes studied by Park *et al.*,[28] as given in Table S1 (ESI†). These values of log K_s can be transformed into log P_s through eqn (3), as shown also in Table S1 (ESI†). The required values of log K_w were taken from the literature.[29–33] We also determined the solubility of a number of solutes in dry fluorobenzene and combination with their solubility in water yield values of log P_s for transfer from water to dry fluorobenzene. We then had a total of 17 values of log K_s and log P_s for transfer from water to dry fluorobenzene. There was only one solute in the MedChem database for which the water to wet fluorobenzene partition coefficient was available. In view of our assessment of solubilities in dry and wet chlorobenzene, below, we included this single data point to give a total of 18 solutes for transfer to dry and wet fluorobenzene. Although this is far too small a number of data points for a five parameter equation, we applied eqn (3) and (4) to yield the LFERs, eqn (5) and (6); in eqn (5) the term in bB was not significant and was omitted.

$$\log K_s\ (\text{fluorobenzene, dry and wet}) = 0.181(0.031) - 0.621(0.062)E + 1.432(0.093)S + 0.647(0.092)A + 0.986(0.018)L \tag{5}$$

$N = 21$, $R^2 = 0.999$, SD $= 0.091$, $F = 10\,136$, $Q^2 = 0.999$, PRESS $= 0.28488$, PSD $= 0.133$.

$$\log P_s\ (\text{fluorobenzene, dry and wet}) = 0.139(0.048) + 0.152(0.090)E - 0.374(0.147)S - 3.030(0.117)A - 4.601(0.210)B + 4.540(0.095)V \tag{6}$$

$N = 21$, $R^2 = 0.998$, SD $= 0.108$, $F = 1971$, $Q^2 = 0.994$, PRESS $= 0.73513$, PSD $= 0.221$.

In eqn (5) and (6), N is the number of data points (the number of compounds), R is the correlation coefficient, SD is the regression standard deviation, and F is the F-statistic. The leave-one-out statistics are Q^2, PRESS, and PSD the 'predictive' standard deviation. The model is fitted without the ith observation, and this fitted model is then used to predict the response, $\hat{y}_{(i)}$ at x_i. The PRESS residuals are defined as $e_{(i)} = y_i - \hat{y}_{(i)}$, and PRESS is given as PRESS $= \sum e^2_{(i)}$. $Q^2 = 1 - (\text{PRESS}/\text{SST})$ where SST is the total sum of squares. Although Q^2, PRESS, and PSD are calculated from the entire data set and hence cannot be truly predictive, Hawkins[34] has suggested that for data sets that are too small to divide into substantial training sets and test sets, PSD is very useful in assessment of predictive capability. PSD is defined similarly to SD; the latter is given by SD $= \sqrt{[\text{SSE}/(N - 1 - v)]}$ where SSE is the sum of squares of errors and v is the number of independent variables, and PSD $= \sqrt{[\text{PRESS}/(N - 1 - v)]}$.

In the event, although the number of data points is very small, the PSD values suggest that eqn (5) and (6) could be used to predict further values with standard deviations of 0.133 and 0.221 log units, respectively.

Chlorobenzene

For solubility in dry chlorobenzene, data were available on the rare gases,[23,35–37] and quite a large number of other solutes,[38–54] see Table S2 (ESI†), and another set of 11 values could be obtained from solubilities in dry chlorobenzene and water,[55–63] see also Table S2 (ESI†), making a total of 80 compounds. The equations for log K_s and log P_s in dry chlorobenzene are given as eqn (7) and (8). Both of these equations are statistically very good, with SD values of only 0.090 and 0.132 log units, respectively. There are hardly enough data points to construct large enough training sets and test sets (Hawkins[34] suggests that test sets should contain at least 50 data points), but the PSD values of 0.101 and 0.144 log units provide an estimate of the predictive capability of eqn (7) and (8), respectively.

$$\log K_s\ (\text{chlorobenzene, dry}) = 0.068(0.015) - 0.390(0.049)E + 0.918(0.060)S + 0.650(0.071)A + 0.155(0.076)B + 1.055(0.008)L \tag{7}$$

$N = 80$, $R^2 = 0.999$, SD $= 0.090$, $F = 16\,426$, $Q^2 = 0.999$, PRESS $= 0.76071$, PSD $= 0.101$

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$$\log P_s\ (\text{chlorobenzene, dry}) = 0.009(0.031) + 0.275(0.068)E - 0.553(0.090)S - 2.863(0.104)A - 4.796(0.112)B + 4.743(0.044)V \quad (8)$$

$$N = 80,\ R^2 = 0.996,\ \text{SD} = 0.132,\ F = 4092,\ Q^2 = 0.996,\ \text{PRESS} = 1.54571,\ \text{PSD} = 0.144$$

For transfer from water to wet chlorobenzene, there were available partition coefficients for 133 compounds, mostly taken from the MedChem database,[22] but also including partition coefficients for mercury,[64] methylmercury(II) chloride,[65] phenylmercury(II) chloride,[65] a number of arylbenzohydroxamic acids,[66] and diethyl ether and tetrahydrofuran.[67] We did not use partition coefficients given in the MedChem database for salts, such as the propylsulfonyl salt of malachite green, because we deal only with neutral species. Equations for log K_s and log P_s into wet chlorobenzene were as follows:

$$\log K_s\ (\text{chlorobenzene, wet}) = 0.059(0.046) - 0.348(0.052)E + 1.199(0.047)S + 0.267(0.076)A + 0.245(0.081)B + 1.010(0.016)L \quad (9)$$

$$N = 132,\ R^2 = 0.997,\ \text{SD} = 0.201,\ F = 9062,\ Q^2 = 0.997,\ \text{PRESS} = 5.51900,\ \text{PSD} = 0.209$$

$$\log P_s\ (\text{chlorobenzene, wet}) = 0.091(0.039) + 0.420(0.035)E - 0.507(0.036)S - 3.240(0.061)A - 4.624(0.065)B + 4.524(0.051)V \quad (10)$$

$$N = 132,\ R^2 = 0.990,\ \text{SD} = 0.165,\ F = 2435,\ Q^2 = 0.989,\ \text{PRESS} = 3.72794,\ \text{PSD} = 0.172$$

We omitted crotonic acid which was a large outlier, log P_s (obs.) = 0.44, log P_s (calc.) = −1.06 log units. By comparison to methacrylic acid [log P_s (obs.) = −0.52, log P_s (calc.) = −0.79] the experimental value for crotonic acid seems much too high. Both eqn (9) and (10) are statistically quite good, and there are enough data points to divide into a training set and a test set in order to assess their predictive capability.

The training equation for log K_s is given as eqn (11);

$$\log K_s\ (\text{chlorobenzene, wet}) = 0.057(0.061) - 0.290(0.079)E + 1.211(0.059)S + 0.308(0.096)A + 0.340(0.113)B + 0.987(0.022)L \quad (11)$$

$$N = 66,\ R^2 = 0.998,\ \text{SD} = 0.199,\ F = 5158,\ Q^2 = 0.997,\ \text{PRESS} = 2.80143,\ \text{PSD} = 0.216$$

Eqn (11) was then used to predict log K_s for the 66 compounds in the test set, with AE = −0.018, AAE = 0.152, RMSE = 0.207 and SD = 0.209. Here, AE is the average error, a measure of any bias in the predictions, AAE is the absolute average error, RMSE is the root mean square error and SD is the standard deviation. Interestingly, the latter value (0.209) is exactly the same as the estimated prediction error, PSD, from the full eqn (9).

For log P_s the training equation is

$$\log P_s\ (\text{chlorobenzene, wet}) = 0.098(0.054) + 0.447(0.055)E - 0.507(0.049)S - 3.201(0.081)A - 4.542(0.099)B + 4.450(0.078)V \quad (12)$$

$$N = 66,\ R^2 = 0.990,\ \text{SD} = 0.171,\ F = 1218,\ Q^2 = 0.988,\ \text{PRESS} = 2.09285,\ \text{PSD} = 0.187$$

and the 66 values of log P_s in the test set were predicted with AE = −0.010, AAE = 0.119, RMSE = 0.164 and SD = 0.165, the latter being close to PSD = 0.172 in the full eqn (10). We conclude that the full equations for log K_s and log P_s can be used to predict further values in wet chlorobenzene with almost no bias and with expected errors of around 0.21 and 0.17 log units, respectively.

We can now combine the data for dry and wet chlorobenzene to give 212 values of log K_s and log P_s. The regression equation for log K_s is given as eqn (13), and that for log P_s as eqn (14).

$$\log K_s\ (\text{chlorobenzene, dry plus wet}) = 0.064(0.022) - 0.399(0.039)E + 1.151(0.036)S + 0.313(0.051)A + 0.171(0.048)B + 1.032(0.009)L \quad (13)$$

$$N = 212,\ R^2 = 0.998,\ \text{SD} = 0.175,\ F = 21\,889,\ Q^2 = 0.998,\ \text{PRESS} = 6.70261,\ \text{PSD} = 0.180$$

$$\log P_s\ (\text{chlorobenzene, dry plus wet}) = 0.065(0.024) + 0.381(0.030)E - 0.521(0.033)S - 3.183(0.046)A - 4.700(0.043)B + 4.614(0.033)V \quad (14)$$

$$N = 212,\ R^2 = 0.993,\ \text{SD} = 0.160,\ F = 5546,\ Q^2 = 0.992,\ \text{PRESS} = 5.57112\ \text{PSD} = 0.164$$

Both eqn (13) and (14) are statistically good, with estimated predictive standard deviations, PSD of 0.180 and 0.164 log units, respectively. It is then of considerable interest to attempt to ascertain if these equations for 'dry plus wet' data are equivalent to those for 'dry' or 'wet' data separately. Comparison of the equations in log K_s, eqn (7) and (9), shows that differences in the *c*-, *e*-, *b*- and *l*- coefficients are within the errors of the coefficients, but that differences in the *s*- and *a*-coefficients are somewhat larger (although the terms in *sS* and *aA* are relatively unimportant). For the equations in log P_s, eqn (8) and (10), the *a*-coefficient and the *v*-coefficient differ by more than the errors in the coefficients. Of course, all these differences could be due to the different data sets used in the 'dry' and 'wet' regression equations.

In terms of the practical use of the equations, the important feature is how well can further values of log K_s and log P_s be predicted. We therefore divide the 212 data points in the 'wet plus dry' equations into a training set of 106 compounds

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and a test set of 106 compounds. The training equations are given as eqn (15) and (16).

$$\log K_s \text{ (chlorobenzene, dry plus wet)} = 0.067(0.030) - 0.361(0.058)E + 1.167(0.048)S + 0.325(0.070)A + 0.193(0.069)B + 1.020(0.014)L \quad (15)$$

$N = 106$, $R^2 = 0.998$, SD $= 0.175$, $F = 11\,931$, $Q^2 = 0.998$, PRESS $= 3.55820$ PSD $= 0.189$

$$\log P_s \text{ (chlorobenzene, dry plus wet)} = 0.077(0.033) + 0.406(0.045)E - 0.515(0.043)S - 3.171(0.064)A - 4.683(0.062)B + 4.573(0.050)V \quad (16)$$

$N = 106$, $R^2 = 0.993$, SD $= 0.160$, $F = 2701$, $Q^2 = 0.992$, PRESS $= 2.92761$ PSD $= 0.171$

These equations can then be used to predict values for the 106 compounds (with dry or wet partition) in the test set, as shown in Table 1. As we have seen before, predictions *via* the method of training and test set equations yield SD values almost exactly the same as PSD for the full equation. Values for $\log K_s$ are 0.180 from eqn (13) and 0.177 in Table 1, from applying eqn (15) to the test set; values for $\log P_s$ are 0.164 from eqn (14) and 0.161 in Table 1, from applying eqn (16) to the test set.

However, there is enough data to be able to determine how well the equations predict $\log K_s$ and $\log P_s$ for partition into dry chlorobenzene or wet chlorobenzene separately; details are presented in Table 1. Very strikingly, predictions of $\log K_s$(wet) from the combined (dry plus wet) eqn (15) with an SD of 0.205 are just as good as predictions of $\log K_s$(wet) from the simple (wet) eqn (11) with an SD of 0.209 log units. The combined (dry plus wet) eqn (16) yields predictions of $\log P_s$(wet) with essentially the same SD as predictions from the simple (wet) eqn (12), *viz.* 0.162 and 0.165, respectively. All this suggests that data on solvation into dry and wet chlorobenzene can be combined, at least for the quite extensive range of solutes that we have studied.

Bromobenzene

Data were available for solubility of 43 gases into dry bromobenzene,[23,28,36–38,41,42,46,50,51,53,68,69] and for the solubility of 2-naphthol,[59] 4-nitrobenzyl chloride,[70] anthracene[71] and pyrene[71] into dry bromobenzene, giving a total of 47 compounds as shown in Table S3 (ESI†). Application of eqn (1) then yielded 47 values of $\log K_s$ and $\log P_s$ for transfer from the gas phase and from water to dry bromobenzene. In the equation for $\log K_s$ the b-coefficient was statistically not significant and was omitted to leave:

$$\log K_s \text{ (bromobenzene, dry)} = -0.067(0.027) - 0.425(0.072)E + 1.218(0.115)S + 0.922(0.125)A + 1.042(0.017)L \quad (17)$$

$N = 47$, $R^2 = 0.998$, SD $= 0.127$, $F = 4951$, $Q^2 = 0.997$, PRESS $= 1.0929$, PSD $= 0.161$

The corresponding equation for $\log P_s$ was:

$$\log P_s \text{ (bromobenzene, dry)} = -0.122(0.046) + 0.317(0.101)E - 0.281(0.155)S - 2.811(0.161)A - 4.704(0.164)B + 4.629(0.091)V \quad (18)$$

$N = 47$, $R^2 = 0.994$, SD $= 0.144$, $F = 1295$, $Q^2 = 0.991$, PRESS $= 1.2864$, PSD $= 0.177$

For transfer from water to wet bromobenzene, $\log P_s$ values for 79 solutes were available, mostly from the MedChem database,[22] together with values for diethyl ether and tetrahydrofuran,[67] crown ethers,[1–6,72] mercury,[64] methylmercury(II) chloride,[65] and phenylmercury(II) chloride.[65] Eqn (19) and (20) were obtained for $\log K_s$ and $\log P_s$. Both equations are statistically reasonable, and the values of PSD afford an indication of their predictive capability, with PSD values of 0.221 and 0.182 log units, respectively.

$$\log K_s \text{ (bromobenzene, wet)} = -0.066(0.062) - 0.248(0.114)E + 1.339(0.101)S + 0.227(0.112)A + 0.326(0.115)B + 0.973(0.030)L \quad (19)$$

$N = 79$, $R^2 = 0.996$, SD $= 0.205$, $F = 3960$, $Q^2 = 0.996$, PRESS $= 3.56047$, PSD $= 0.221$

$$\log P_s \text{ (bromobenzene, wet)} = 0.029(0.056) + 0.416(0.083)E - 0.362(0.081)S - 3.241(0.090)A - 4.557(0.094)B + 4.366(0.088)V \quad (20)$$

$N = 79$, $R^2 = 0.984$, SD $= 0.167$, $F = 926$, $Q^2 = 0.982$, PRESS $= 2.4245$, PSD $= 0.182$

If the data for dry and wet bromobenzene are combined, there are 126 values of $\log K_s$ and $\log P_s$; equations are given as eqn (21) and (22).

$$\log K_s \text{ (bromobenzene, dry plus wet)} = -0.064(0.030) - 0.326(0.072)E + 1.261(0.080)S + 0.323(0.076)A + 0.292(0.084)B + 1.002(0.019)L \quad (21)$$

Table 1 Predictions of $\log K_s$ and $\log P_s$ for partition into dry or wet chlorobenzene

Training equation	Prediction	AE	AAE	RMSE	SD
(15) $\log K_s$ (dry + wet)	All, 106	−0.002	0.123	0.176	0.177
	Dry, 40	0.011	0.089	0.118	0.120
	Wet, 66	−0.012	0.144	0.203	0.205
(11) $\log K_s$ (wet)	Wet, 66	−0.018	0.152	0.207	0.209
(16) $\log P_s$ (dry + wet)	All, 106	0.001	0.115	0.160	0.161
	Dry, 40	0.013	0.125	0.161	0.163
	Wet, 66	−0.006	0.109	0.161	0.162
(12) $\log P_s$ (wet)	Wet, 66	−0.010	0.119	0.164	0.165

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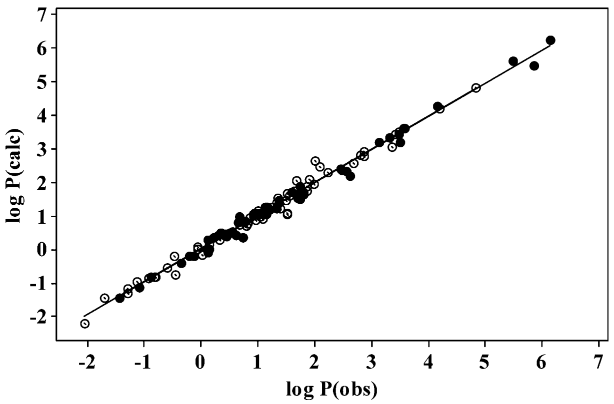

Fig. 1 A plot of calculated log P values in eqn (22) against observed values of log P for partition from water to bromobenzene: ● dry data, ○ wet data.

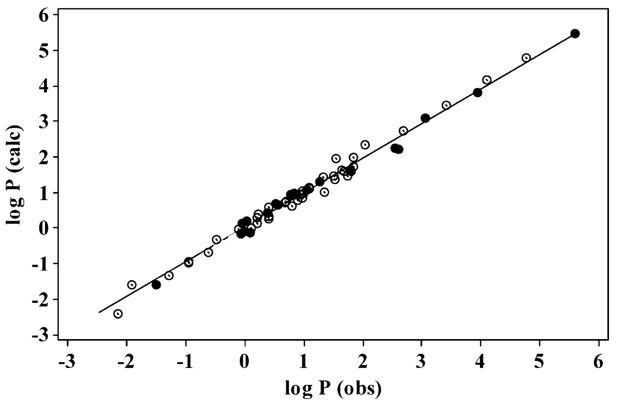

Fig. 2 A plot of calculated log P_s values in eqn (24) against observed values of log P for partition from water to iodobenzene: ● dry data, ○ wet data.

$$N = 126,\ R^2 = 0.997,\ \mathrm{SD} = 0.188,\ F = 9515,\ Q^2 = 0.997,\ \mathrm{PRESS} = 4.78502,\ \mathrm{PSD} = 0.200$$

$$\log P_\mathrm{s}\ (\text{bromobenzene, dry plus wet}) = -0.017(0.034) + 0.436(0.057)E - 0.424(0.065)S - 3.174(0.066)A - 4.558(0.075)B + 4.445(0.065)V \qquad (22)$$

$$N = 126,\ R^2 = 0.988,\ \mathrm{SD} = 0.166,\ F = 1937,\ Q^2 = 0.986,\ \mathrm{PRESS} = 3.68574,\ \mathrm{PSD} = 0.175$$

Inspection of eqn (17) and (19) shows that the two sets of coefficients differ statistically only for the *a*- and *b*-coefficient; neither of the terms *aA* or *bB* makes a significant contribution. Coefficients in eqn (18) and (19) are also essentially the same, except for the *a*-coefficient and possibly also the *v*-coefficient. In view of the more detailed analysis of solvation in dry and wet chlorobenzene, we conclude that solvation in dry and wet bromobenzene can be taken to be the same, and that eqn (21) and (22) can be used for both the dry and wet solvent. Estimated errors in prediction, as given by PSD, are 0.200 and 0.175 log units for log K_s and log P_s, respectively. Although we cannot carry out as extensive an analysis as for chlorobenzene, inspection of Fig. 1 does indicate that data for solvation in dry bromobenzene and wet bromobenzene can be combined.

Iodobenzene

Values of log K_s were available for 20 gaseous solutes[23,28,37,46,50,69] into dry iodobenzene and of log P_s for partition of 45 solutes between water and wet iodobenzene,[22] as given in Table S4 (ESI†). There are too few data points to carry out regressions separately, and so equations were constructed for all 65 solutes, eqn (23) and (24).

$$\log K_\mathrm{s}\ (\text{iodobenzene, dry plus wet}) = -0.171(0.049) - 0.192(0.138)E + 1.197(0.119)S + 0.245(0.110)A + 0.245(0.134)B + 1.002(0.027)L \qquad (23)$$

$$N = 65,\ R^2 = 0.996,\ \mathrm{SD} = 0.191,\ F = 2826,\ Q^2 = 0.995,\ \mathrm{PRESS} = 2.66857,\ \mathrm{PSD} = 0.213$$

$$\log P_\mathrm{s}\ (\text{iodobenzene, dry plus wet}) = -0.192(0.054) + 0.298(0.108)E - 0.308(0.101)S - 3.213(0.093)A - 4.653(0.113)B + 4.588(0.091)V \qquad (24)$$

$$N = 65,\ R^2 = 0.988,\ \mathrm{SD} = 0.163,\ F = 983,\ Q^2 = 0.985,\ \mathrm{PRESS} = 1.95764,\ \mathrm{PSD} = 0.182$$

Both equations are statistically quite good, with estimated predictive ability of 0.213 and 0.182 log units, as shown by the values of PSD. In Fig. 2 is shown a plot of calculated values of log P_s against observed values. There is random scatter about the line of best fit, both for data for dry iodobenzene and wet iodobenzene, so that it seems the two sets of data can indeed be treated together.

Discussion

The equations for partition into dry chlorobenzene and wet chlorobenzene are very similar as regards the coefficients. Predictions of log K_s and log P_s for partition into dry or wet chlorobenzene are essentially the same, no matter if the defining equation is based on data for dry chlorobenzene, data for wet chlorobenzene or on data for dry and wet chlorobenzene combined, see Table 1. In a similar vein, equations for partition into dry bromobenzene and wet bromobenzene are very similar. The calculated log P_s values from an equation based on both dry and wet data, eqn (22) when plotted against the observed values, show no sign of separation into two classes, see Fig. 1. Finally, the very good statistics for partition into iodobenzene, taking both dry and wet data together, again suggests that there must be very little difference in solvation of solutes in dry and wet iodobenzene, eqn (23) and (24), see also Fig. 2. We conclude that for the solutes we have studied, solvation in dry monohalobenzenes and wet monohalobenzenes is so similar that data pertaining to the dry and wet solvents may be combined. The equations that include data on both dry and wet solvents have an advantage over those that refer to just dry solvents or just wet solvents, in that they cover a much wider range of solutes. The solutes range from the rare gases, other inorganic gases (hydrogen and oxygen) to organometallic compounds

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(tetramethyltin, methylmercury(II) chloride) and a wide range of organic compounds (methanol and methylamine to phenols and crown ethers). They include quite hydrophilic compounds such as propanone, proprionic acid, methanol, ammonia and methylamine. However, it is possible that for even more hydrophilic solutes, the quantity of water in the water-saturated solvent may influence solvation appreciably.

We can calculate the effect of water in chlorobenzene as follows. In dilute solution in an inert solvent, a hydrogen bond acid and a hydrogen bond base will interact as in eqn (25) with an equilibrium constant K_{ab}.

$$\text{A–H} + \text{:B} \rightarrow \text{A–H}\cdots\text{:B} \qquad (25)$$

Many years ago we showed[73] that in the solvent tetrachloromethane, the equilibrium constant could be expressed as eqn (26) where α_2^H is the 1 : 1 hydrogen bond acidity of the acid and β_2^H is the 1 : 1 hydrogen bond acidity of the base. A similar equation has now been found to obtain in solvent chlorobenzene,[74] eqn (27). We know values of α_2^H for water, 0.35, and for hydrogen bond acids[75] such as 4-nitrophenol (ArOH), 0.82, and values of β_2^H for water, 0.38, and for hydrogen bond bases[76] such as dimethylformamide (DMF), 0.66, and can then use eqn (27) to calculate K_{ab} for the complexation reactions eqn (28) and (29).

$$\log K_{ab}\ (\text{in } CCl_4) = (7.354 \times \alpha_2^H \times \beta_2^H) - 1.094 \qquad (26)$$

$$\log K_{ab}\ (\text{in PhCl}) = (6.822 \times \alpha_2^H \times \beta_2^H) - 1.086 \qquad (27)$$

$$\text{HO–H} + \text{:DMF} \rightarrow \text{HO–H}\cdots\text{:DMF} \qquad (28)$$

$$\text{ArO–H} + \text{:OH}_2 \rightarrow \text{ArO–H}\cdots\text{:OH}_2 \qquad (29)$$

Taking values of α_2^H for water as 0.35, and β_2^H for the quite strong hydrogen bond base, DMF, we find that K_{ab} in chlorobenzene for eqn (28) is 3.09; a similar calculation gives K_{ab} as 10.96 for association of water with the strong hydrogen bond acid, 4-nitrophenol in chlorobenzene, eqn (29). Now the concentration of water in water-saturated chlorobenzene is 0.024 mol dm^{-3},[77] and at this concentration must largely be in the monomeric form, so that we can apply eqn (28) and (29) to the complexation of acids and bases with water in water-saturated chlorobenzene. If the concentration of the solute is much less than 0.024 mol dm^{-3}, as is the case with partition experiments, we can calculate that DMF is 93% uncomplexed and 4-nitrophenol is 80% uncomplexed by water in water-saturated chlorobenzene.

Of course, an even stronger hydrogen bond base than DMF or an even stronger hydrogen bond acid than 4-nitrophenol will be more complexed by the water, and so our finding that dry chlorobenzene and water-saturated chlorobenzene have very similar solvation properties may then not apply. The results for bromobenzene and iodobenzene suggest, again, that for the solutes that we have assembled, solvation into the dry and wet solvents is so similar that the two data sets can be combined. It therefore seems that many dry and wet aprotic solvents have very similar solvation properties, as we have also shown for 1,2-dichloroethane.[78]

The coefficients in eqn (3) and (4) are not just fitting coefficients, but encode information about the chemical nature of the solvent phase. A summary of the equations for dry and wet data taken together is presented in Table 3. We had thought that the coefficients for the four monohalobenzenes would vary quite considerably, but as shown in Table 2, there is remarkably little variation in the coefficients. The equations in log K_s are easier to interpret. For all four solvents, it is the terms in sS and lL that make the most contributions. The former refers to the effect of solvent dipolarity/polarisability, and the latter to the hydrophobicity of the solvent. All four solvents are dipolar/polarisable, and all four are strongly hydrophobic, but the differences between the four solvents are quite small; note that the monohalobenzenes all have similar dipole moments.

Included in Table 2 are coefficients for partition into toluene for comparison. As might be expected from the very small dipole moment of toluene, the s-coefficient in the equation for log K_s is smaller than for the monohalobenzenes, but the other coefficients do not differ very much. The effect of the halogen substituent on partition properties is surprisingly small.

Conclusion

We have shown that data for partition into dry and wet monohalobenzenes are essentially the same, so that equations for partition from the gas phase or from water to the monohalobenzenes can be constructed using both sets of data. This results in equations that cover a wide range of solute (except for fluorobenzene solvent) and which can be used to predict

Table 2 A summary of the regression equations for dry and wet data taken together

System	*c*	*e*	*s*	*a*	*b*	*v*/*l*
log K_s PhF	0.181	−0.621	1.432	0.647	0.000	0.986
log K_s PhCl	0.064	−0.399	1.151	0.313	0.171	1.032
log K_s PhBr	−0.064	−0.326	1.261	0.323	0.292	1.002
log K_s PhI	−0.171	−0.192	1.197	0.245	0.245	1.002
log K_s PhMe	0.121	−0.222	0.938	0.467	0.099	1.012
log P_s PhF	0.139	0.152	−0.374	−3.030	−4.601	4.540
log P_s PhCl	0.065	0.381	−0.521	−3.183	−4.700	4.614
log P_s PhBr	−0.017	0.436	−0.424	−3.174	−4.558	4.445
log P_s PhI	−0.192	0.298	−0.308	−3.213	−4.653	4.588
log P_s PhMe	0.143	0.527	−0.720	−3.010	−4.824	4.545

Table 3 Values of the predicted standard deviation, PSED, for partition from the gas phase and water to the halobenzenes

Solvent	*N*[a]	log K_s	log P_s
Fluorobenzene	21	0.133	0.221
Chlorobenzene	212	0.180 (0.177)[b]	0.164 (0.161)[b]
Bromobenzene	126	0.200	0.175
Iodobenzene	65	0.213	0.182

[a] Number of solutes studied. [b] SD value for predictions of the test set.

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further partition coefficients to around 0.20 log units. The predictive standard deviations are shown in Table 3, together with the SD value found for the test set in the case of chlorobenzene solvent. As we have found previously,[20] the PSD values from the full equations are very close indeed to the SD values for the predictions for the test sets. The number of solutes studied in this work is far greater than in any previous work,[7–13] and so the equations that we have set out should provide a much more reliable procedure for the prediction of further values.

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