Prediction of Partition Coefficients of Fluorous and Nonfluorous Solutes in Fluorous Biphasic Solvent Systems by Mobile Order and Disorder Theory

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The universal model for predicting lipophilicity based on the mobile order and disorder (MOD) solution thermodynamics was used for the successful prediction of the partition coefficient of 88 fluorous and nonfluorous chemicals in fluorous biphasic PFMCH/toluene and FC-72/benzene binary solvent systems at 25 °C. A general thermodynamic expression aimed to calculate the distribution of substances in any fluorous biphasic system at any temperature is presented. Interestingly, the predictive expression requires the knowledge of only the molar volume and the nonspecific cohesion parameter of the solute allowing valuable estimation of log *P* of nonexisting fluorous molecules. The present partition model predicts that grafting more and/or longer perfluoroalkyl tails on a given substance does not automatically result in higher partition coefficients.

Introduction

The successful application of fluorous biphasic separation techniques for the recycling of homogeneous catalysts requires the design of fluorous ligands with optimal partition coefficients.[1] In the absence of any suitable structure−property relationships, this process has so far been a time-consuming trial-and-error activity, requiring extensive synthetic effort. To speed up the ligand design process, a model that even crudely estimates a fluorous ligand's log *P* on the basis of its basic topology or physical properties, would be highly desirable.[2] It would allow one to select the most interesting candidates out of a hypothetical pool of possible ligands already before their actual synthesis.

In drug design and environmental studies, linear relationships between values of log *P* in octanol/water biphasic mixtures and the molar volume of the solute have proven to be highly successful.[3] For the prediction of log *P* of fluorous compounds in fluorous biphasic systems, several qualitative trends are described, i.e., longer tails, more tails, or a higher weight percentage of fluorine all lead to higher partition coefficients. Recently, Kiss et al.[4] in an attempt to derive a similar quantitative relationship for fluorous biphasic solvent systems developed an *empirical* relationship (eq 1) containing the Hildebrand solubility parameter (δ) of the solute and the molar volumes of the fluorous solute (V_b) and solvent (V_F) along with two empirical coefficients (A and B).

$$\ln P = \frac{V_b}{V_F}(A + B\delta) \qquad (1)$$

The method is highly useful for optimizations within a class of closely related compounds. Not withstanding the fact that this approach is a major step forward, the applicability of eq 1 remains limited, because *A* and *B* have to be determined for different classes of compounds, requiring the synthesis of a basis set of molecules for each class of compounds. More recently, Huque et al. have used Abraham's general solvation equation that is also based on a *empirically* fitted relation between log *P* and a number of solute descriptors to predict fluorophilicity.[5] A sixth descriptor *F*, being the wt % of fluorine, had to be introduced to obtain good correlations and was found to be the most important descriptor.

In this work, a general relationship aimed at predicting the partition coefficients of solutes in fluorous biphasic systems has been derived from the universal log *P* model[6] based on the mobile order and disorder (MOD) theory.[7] Following a strictly thermodynamic approach, a predictive relationship is derived that is totally free from empirical constants that do not bear a direct physical meaning. In practice, the thermodynamic properties of a particular solute can be either obtained experimentally or successfully estimated by group incremental methods.

Results and Discussion

Application of MOD Theory to Partitioning of Solutes in Fluorous Biphasic Systems. According to the MOD universal log *P* model,[6] the partition coefficient of a solute in any immiscible two-phase liquid system can be described by five terms (eq 2)

$$\log P = \Delta B + \Delta D + \Delta F + \Delta O + \Delta OH \qquad (2)$$

$$\Delta B = \frac{1}{\ln 10}\left[0.5V_b\left(\frac{1}{V_F} - \frac{1}{V_O}\right) + 0.5\ln\frac{V_O}{V_F}\right] \qquad (3)$$

$$\Delta D = \frac{1}{\ln 10}\left[\frac{V_b}{RT}((\delta'_O - \delta'_b)^2 - (\delta'_F - \delta'_b)^2)\right] \qquad (4)$$

where V_b is the molar volume of the solute (cm^3/mol), V_F is the molar volume of the fluorous solvent (cm^3/mol), V_O is the molar volume of the organic solvent (cm^3/mol), δ'_b is the modified

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nonspecific cohesion parameter of the solute ($\mathrm{MPa}^{1/2}$), δ'_{F} is the modified nonspecific cohesion parameter of the fluorous solvent ($\mathrm{MPa}^{1/2}$), δ'_{O} is the modified nonspecific cohesion parameter of the organic solvent ($\mathrm{MPa}^{1/2}$), R is the universal gas constant (J/mol K), and T is the working temperature (K). For aprotic fluorous biphasic systems, the ΔF, ΔO, and ΔOH terms can be neglected because these terms describe the influence of hydrogen-bonded chains of the solvent, the effects of hydrogen bond acceptance and donation between the solute and the solvent, respectively. Practically, because in most fluorous biphasic systems the organic phase does not contain proton-donor or -acceptor sites, only the ΔB and ΔD terms are considered to be important. The first term represents the correction factor for the entropy of mixing between the solute and the solvent molecules (eq 3), and the second term describes the enthalpic change in the solute−solute, solvent−solvent, and solute−solvent nonspecific cohesion forces upon mixing (eq 4).

Application of the expressions for ΔB and ΔD terms in eq 2 results in a general predictive equation (eq 5) for log P of solutes in any fluorous biphasic system the organic solvent phase of which does not contain proton-donor or -acceptor sites.

$$\log P = 0.2171 \ln \frac{V_{\mathrm{O}}}{V_{\mathrm{F}}} - 0.2171 V_{\mathrm{b}}\left(\frac{1}{V_{\mathrm{O}}} - \frac{1}{V_{\mathrm{F}}}\right) + 0.0522 \frac{V_{\mathrm{b}}}{T}({\delta'_{\mathrm{O}}}^{2} - {\delta'_{\mathrm{F}}}^{2}) - 0.1045 \frac{V_{\mathrm{b}}\delta'_{\mathrm{b}}}{T}(\delta'_{\mathrm{O}} - \delta'_{\mathrm{F}}) \quad (5)$$

Although eq 5 depends directly on the temperature (as evidenced from the last two terms), it should be kept in mind that also the molar volumes and the modified nonspecific cohesion parameters of the solute and solvents are temperature dependent. Furthermore, it is important to note that the modified nonspecific cohesion parameter δ' used in the present model differs from the cohesion or Hildebrand solubility parameter δ previously used by Kiss et al.[3] Whereas the Hildebrand solubility parameter involves three types of contributions (dispersive, polar, and hydrogen bonding) arising from different interactions between molecules in the liquid state and may be obtained directly from experimentally determined parameters, the modified nonspecific cohesion parameter accounts for the nonspecific forces only exhibited between molecules in liquids. As a result, the modified nonspecific cohesion parameter of a given compound can only be derived theoretically or calculated from experimental data like solubility or partition coefficient by applying the MOD theory.[7]

TABLE 1: Solvent Parameters of Fluorous Solvents at 25 °C

	PFMCH	FC-72
$\Phi_{\text{fluorous solvent in toluene}}{}^{a}$	0.03^{b}	
$\Phi_{\text{benzene in fluorous solvent}}{}^{a}$		0.027^{c}
$\Phi_{\text{toluene in fluorous solvent}}{}^{a}$	0.09^{b}	0.03^{c}
V_{F} (cm^3/mol)	196.0	205.0
δ'_{F} (MPa$^{1/2}$)^{d}	10.66	9.61

[a] Volume fraction solubility. [b] Extrapolated from data in ref 9. [c] This work, determined by gravimetric methods. [d] Back-calculated from the experimental volume fraction solubility. (Properties of toluene: $V = 106.9$ cm^3/mol; $\delta' = 18.1$ MPa$^{1/2}$; Properties of benzene: $V = 89.4$ cm^3/mol; $\delta' = 18.9$ MPa$^{1/2}$).

TABLE 2: Comparison between the Experimental Molar Volumes of Fluorous Liquid Compounds and the Values Calculated Using Fedors' and Lawson's Group Increments at 25 °C

compound	V_{exp} (cm^3/mol)	V_{cal} (cm^3/mol)
$C_6F_{13}I$	216.4	201.8
$C_8F_{17}I$	265.6	248.0
CF_3CH_2OH	72.3	80.9
$C_6F_{13}CH_2CH_2OH$	216.7	212.5
$C_7F_{15}CH_2NMe_2$	276.9	267.5
CF_3Ph	122.0	126.2
$C_8F_{17}CH{=}CH_2$	265.5	258.5

From inspection of eq 5, it becomes immediately apparent that the only parameters required for the prediction of log P are the modified nonspecific cohesion parameters and the molar volumes of the solutes and solvent phases. Dealing in particular with fluorous biphasic systems, the fluorous and organic solvent phases can be chosen by filling in the corresponding solvent properties. Although these properties have been reported for a wide variety of organic solvents,[7] the δ'_{F} values of fluorous solvents were yet unknown. For that reason, the δ'_{F} values of the fluorous phases used in this work, i.e., FC-72 (mixture of C_6F_{14} isomers) and PFMCH (c-$C_6F_{11}CF_3$), were determined from the MOD solubility model[8] using their experimental mutual solubilities in toluene and/or benzene. The results are presented in Table 1.Through insertion of the data of Table 1 into eq 5, the general log P equation for fluorous biphasic systems gives rise to two simplified predictive expressions (eqs 6a and 6b) for the partition coefficient in PFMCH/toluene and FC-72/benzene at 25 °C, respectively.

$$\log P(\text{PFMCH/toluene}) = -0.132 + V_{\mathrm{b}}(0.0365 - 0.00261\delta'_{\mathrm{b}}) \quad (6a)$$

$$\log P(\text{FC-72/benzene}) = -0.141 + V_{\mathrm{b}}(0.0413 - 0.00289\delta'_{\mathrm{b}}) \quad (6b)$$

Although eqs 6a and 6b are different from eq 1 in that the former implicitly include constants that are dependent on the organic phase, both eq 1 and eqs 6a,b show similar dependencies of log P on V_{b} and $V_{\mathrm{b}}\delta_{\mathrm{b}}$ or $V_{\mathrm{b}}\delta'_{\mathrm{b}}$, respectively. However, it is also immediately apparent that, once the required properties of the partitioning system are known, eqs 6a and 6b offer the possibility of calculating the partition coefficient of all solutes from the knowledge of their molar volume and modified nonspecific cohesion parameter only, hence allowing the prediction of log P of nonexisting fluorous molecules if reasonable estimates of V_{b} and δ'_{b} can be made.

Prediction of Partition Coefficients in Fluorous Biphasic Systems. Although the V_{O} and δ'_{O} properties are known and tabulated for a lot of organic solvents, the corresponding experimental values of fluorous compounds are often not available. Nevertheless, these properties can be easily obtained from group contribution incremental methods. So V_{b} and V_{F} may quite easily be calculated by summation of the relevant molar volume increments reported by Fedors[10] for most organic groups and by Lawson[11] for the CF_2 and CF_3 fluoro groups. A comparison between the calculated molar volumes of several fluorous compounds and the values experimentally determined from liquid density measurements (Table 2) demonstrates that reasonable accuracy can be achieved following this procedure.

Similarly to the above method for obtaining molar volumes, and in analogy with the classical approach[12] to estimate the Hildebrand solubility parameter from molar volume and vaporization energy group contributions, the δ'_{b} modified

TABLE 3: Group Contributions to the Molar Nonspecific Vaporization Energy $(\Delta E'_v)_i$ and Molar Volume V_i at 25 °C

group	$(\Delta E'_v)_i$ [a]	V_i [b]	group	$(\Delta E'_v)_i$ [a]	V_i [b]
CH_3 in alkyl	7.82	33.5	P to arom ring	0.73	35[c]
CH_3 to heteroatom	3.93	33.5	Cl to arom ring	5.71	24.0
CH_2	4.47	16.1	Br to arom ring	9.15	30.0
$CH{=}CH_2$	11.65	42.0	I	12.34	31.5
CF_2	3.02	23.1	S	9.48	12
CF_3 in perfluoroalkyl	4.64	54.8	C=O (carbonyl)	7.32	10.8
CF_3 benzylic	9.12	54.8	−C(O)O−	6.44	18.0
Ph	23.82	71.4	−OH	11.02	10.0
C_6H_4[d]	23.54	52.4	Si	5.93	−1.5[c]
C_6H_3[e]	19.67	33.4	Si−H	11.19	13.8[c]
NH_2 (primary amine)	8.53	19.2	Sn−H	18.19	16.0[c]
NH (secondary amine)	8.53	4.5	−NHC(O)−(amide)	15.85	9.5
N (tertiary amine)	8.53	−9.0	−NMeC(O)−(amide)	19.78	25.8
P-alkyl	11.97	−1.0			

[a] Increment values for the nonspecific part of the evaporation energy (kJ/mol). [b] Increment values for the molar volume in cm^3/mol, obtained from ref 8, unless noted otherwise. [c] Volume increment calculated from densities of existing compounds containing the relevant functional group (PPh_3, P(p-Tol)$_3$, Et_4Si, Bu_4Si, Et_3SiH, Pr_3SiH, Bu_3SiH, Et_3SnH, Pr_3SnH, Bu_3SnH). [d] Subtract 5.10 kJ/mol if CF_2-substituents are directly attached to the aromatic ring. [e] Subtract 5.12 or 12.27 kJ/mol when 2 or 3 CF_2 substituents are directly attached to the aromatic ring, respectively.

TABLE 4: log *P* Values of Nonfluorous Compounds in PFMCH/Toluene at 27 °C

compound	V_b (cm^3/mol)	δ'_b (MPa$^{1/2}$)	log P_{exp} [a]	log P_{cal}	diff
decane*	195.8	16.20	**−1.244**	−1.241	0.003
undecane*	211.9	16.24	**−1.356**	−1.352	0.004
dodecane*	228	16.27	**−1.456**	−1.462	−0.006
tridecane	244.1	16.29	**−1.602**	−1.573	0.029
tetradecane	260.2	16.32	**−1.721**	−1.683	0.038
hexadecane	292.4	16.36	**−1.959**	−1.904	0.055
1-decene*	188.2	16.42	**−1.301**	−1.306	−0.005
1-undecene*	204.3	16.44	**−1.420**	−1.416	0.004
1-dodecene	220.4	16.46	**−1.585**	−1.526	0.059
1-tridecene	236.5	16.47	**−1.721**	−1.637	0.084
1-tetradecene	252.6	16.48	**−1.796**	−1.747	0.049
1-hexadecene	284.8	16.50	**−2.045**	−1.968	0.077
benzene	89.4	18.95	**−1.199**	−1.275	−0.076

[a] Data obtained from ref 13. Modified nonspecific cohesion parameter (MPa$^{1/2}$) and molar volume (cm^3/mol) calculated from increments at 25 °C. Experimental log *P* values taken from refs 4, 13, and 14. Compounds marked with an asterisk were used for the determination of the molar nonspecific vaporization energy increments.

nonspecific cohesion parameters of the fluorous solutes at 25 °C can be obtained according to eq 7.

$$\delta'_b = \sqrt{\frac{\Delta E'_v}{V_b}} = \sqrt{\frac{\Sigma(\Delta E'_v)_i}{\Sigma(V_i)}} \qquad (7)$$

In this equation, V_i represent the various volume group contributions to the molar volume V of the compound, and $(\Delta E'_v)_i$ are the corresponding group energy contributions to the nonspecific component of the molar vaporization energy $\Delta E'_v$. However, the use of δ'_b values, estimated in a first stage from the original Fedors' and Lawson's molar volume and vaporization energy group increments, to calculate the log *P* by eq 5 led to large deviations with respect to the experimental partition coefficients. The observed deviations undoubtedly had to be attributed to the fact that, in such a procedure, the $(\Delta E_v)_i$ molar vaporization energy group increments were used to calculate the δ'_b value instead of using group increments specifically designed to model the nonspecific part of the vaporization energy $\Delta E'_v$. Accordingly, a new set of $(\Delta E'_v)_i$ values was determined for a large variety of functional groups from the experimental partition coefficients of a small subset of compounds (indicated with an asterisk in Tables 4−8). Table 3 lists the obtained values of the new group contributions to the nonspecific component of the vaporization energy along with the corresponding molar volume increments. Note that some volume increments (SnH, Si, SiH, and P) have been added or adjusted with respect to the values earlier reported, because they either did not exist in Fedors' list or were unrealistic in comparison with the experimental liquid molar volumes of compounds bearing these groups.

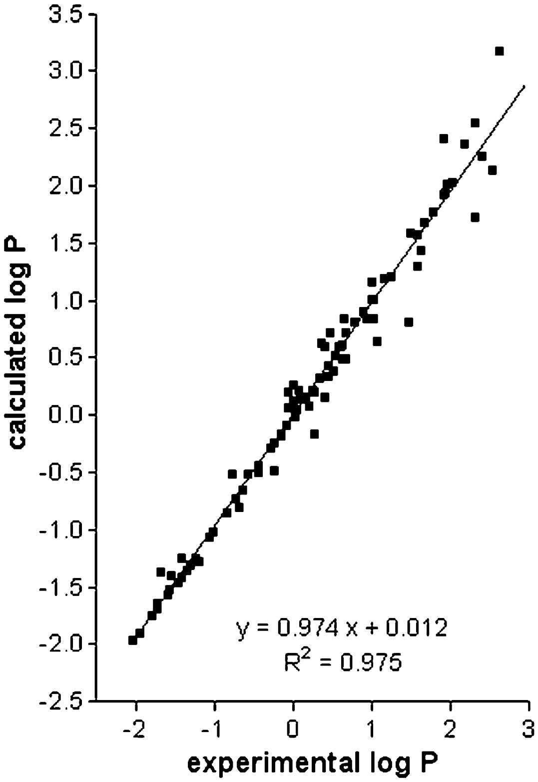

Figure 1. Experimental vs predicted values of log *P* for the complete data set of substances reported in Tables 4−8.

Using the data of Table 3, the molar volume and the modified nonspecific cohesion parameter of 88 different solutes were calculated, allowing the subsequent estimation of their partition coefficients. Tables 4−6 present the PFMCH/toluene log *P* values obtained using eq 6a at 25−27 °C for nonfluorous molecules (Table 4), fluorous haloarenes, amines, sulfides, esters, alcohols, amides (Table 5), and silanes (Table 6), respectively. The estimated partition coefficients of fluorous tin compounds in FC-72/benzene at 27 °C using eq 6b are reported in Table 7. Finally, the log *P* values of large fluorous phosphines in PFMCH/toluene at 25 °C using eq 6a are reported in Table 8. As can be observed from the comparison between the calculated and experimental log *P* values given in these tables,

TABLE 5: log *P* Values of Fluorous Molecules in PFMCH/Toluene at 25−27 °C[a]

compound	V_b (cm^3/mol)	δ'_b ($MPa^{1/2}$)	log P_{exp}	log P_{cal}	diff
Rf_6I*	201.8	12.61	**0.569**	0.593	0.024
Rf_8I*	248	12.40	**0.886**	0.895	0.009
$Rf_{10}I$*	294.2	12.25	**1.233**	1.199	−0.034
CF_3Ph*	126.2	16.16	**−0.847**	−0.847	0.000
Rf_6Ph*	241.7	13.42	**0.235**	0.221	−0.014
Rf_8Ph*	287.9	13.13	**0.539**	0.514	−0.025
$Rf_{10}Ph$*	334.1	12.90	**0.769**	0.810	0.041
o-$Rf_8C_6H_4CF_3$*	323.7	12.84	**0.651**	0.838	0.187
m-$Rf_8C_6H_4CF_3$*	323.7	12.84	**1.029**	0.838	−0.191
p-$Rf_8C_6H_4CF_3$	323.7	12.84	**0.925**	0.838	−0.087
(p-$CF_3C_6H_4(CF_2)_4)_2$*	399.2	14.09	**−0.243**	−0.244	−0.001
p-$Rf_8C_6H_4Rf_8$	485.4	12.01	**2.163**	2.371	0.208
p-$BrC_6H_4C_6F_{13}$[b]	252.7	13.69	**−0.072**	0.065	0.137
1,3,5-$BrC_6H_3(C_6F_{13})_2$[b]	404.1	12.50	**1.616**	1.430	−0.186
1,3,5-$Rf_8C_6H_3(CF_3)_2$*[b]	359.5	11.96	**1.768**	1.768	0.000
$Rf_8CH{=}CH_2$	258.5	12.03	**1.159**	1.185	0.026
$Rf_8(CH_2)_3Ph$	336.2	13.69	**−0.009**	0.127	0.136
o-$(Rf_6(CH_2)_3)_2{-}C_6H_4$*	489.6	13.55	**0.447**	0.428	−0.019
o-$(Rf_8(CH_2)_3)_2{-}C_6H_4$	582	13.23	**1.017**	1.009	−0.008
m-$(Rf_8(CH_2)_3)_2{-}C_6H_4$*	582	13.23	**0.991**	1.009	0.018
p-$Rf_6(CH_2)_2C_6H_4Cl$*	278.9	14.41	**−0.443**	−0.443	0.000
p-$Rf_8(CH_2)_2C_6H_4Cl$	325.1	14.03	**−0.161**	−0.168	−0.007
p-$Rf_6(CH_2)_2C_6H_4Br$*	284.9	14.68	**−0.647**	−0.647	0.000
$N((CH_2)_5Rf_8)_3$	881.1	13.17	**2.300**	1.732	−0.568
$N((CH_2)_4Rf_8)_3$	832.8	12.94	**2.520**	2.132	−0.388
$N((CH_2)_3Rf_8)_3$	784.5	12.68	**2.302**	2.543	0.241
$Rf_8CH_2CH_2CH_2NMe_2$*	322.8	13.12	**0.595**	0.595	0.000
$(Rf_8CH_2CH_2CH_2)_2NMe$*	554.1	12.80	**1.576**	1.576	0.000
Rf_7CH_2NHMe	247.5	12.66	**0.465**	0.721	0.256
$Rf_7CH_2NMe_2$	267.5	12.77	**0.664**	0.716	0.052
$Rf_8CH_2CH_2CH_2NH_2$	284	12.96	**0.343**	0.626	0.283
$(Rf_8CH_2CH_2CH_2)_2NH$	534.1	12.76	**1.478**	1.580	0.102
$Rf_8CH_2CH_2CH_2NHMe$	302.8	13.06	**0.387**	0.598	0.211
CF_3SPh*	138.2	16.57	**−1.064**	−1.064	0.000
m-$CF_3SC_6H_4CF_3$	174	15.48	**−0.686**	−0.810	−0.124
Rf_8SPh	299.9	14.04	**0.256**	−0.172	−0.428
$Rf_6SCH_2CH_2CO_2Et$*	282.1	14.20	**−0.291**	−0.291	0.000
$Rf_8SCH_2CH_2CO_2Et$	328.3	13.85	**0.017**	−0.012	−0.029
p-$Rf_8C_6H_4CO_2Me$	320.4	13.51	**−0.004**	0.265	0.269
Rf_7CO_2Ph	282.8	13.69	**0.208**	0.084	−0.124
1,3,5-$(Rf_8)_2C_6H_3CO_2Me$	517.9	12.46	**1.933**	1.933	0.000
$Rf_6CH_2CH_2OH$*	212.5	13.67	**0.043**	0.043	0.000
CF_3CH_2OH	80.9	15.77	**−0.769**	−0.510	0.259
$Rf_8CH_2CH_2OH$	258.7	13.30	**0.443**	0.332	−0.111
$Rf_6CH_2CH_2CH_2OH$	228.6	13.90	**−0.100**	−0.082	0.018
$Rf_8CH_2CH_2CH_2OH$	274.8	13.52	**0.256**	0.203	−0.053
$Rf_{10}CH_2CH_2CH_2OH$	321	13.24	**0.617**	0.494	−0.123
1,3,5-$(Rf_8)_2C_6H_3CH_2OH$	492.5	12.87	**1.581**	1.298	−0.283
$Rf_7C(O)SMe$	249.7	13.20	**0.504**	0.381	−0.123
$Rf_7C(O)NHMe$	236.4	13.41	**0.065**	0.220	0.155
$Rf_7C(O)NMe_2$*	252.7	13.56	**0.148**	0.148	0.000

[a] Modified nonspecific cohesion parameter ($MPa^{1/2}$) and molar volume (cm^3/mol) calculated from increments at 25 °C. Experimental log *P* values taken from refs 4, 13, and 14. Rf_x denotes a C_xF_{2x+1} group. Compounds marked with an asterisk were used for the determination of the molar nonspecific vaporization energy increments. [b] Data from this work.

the partition coefficient of fluorous and nonfluorous solutes can be predicted with reliable accuracy in both fluorous binary solvent systems. The fair correlation between the whole set of predicted and experimental log *P* values presented in Tables 4−8 is also clearly demonstrated from the log P_{calc} vs log P_{exp} plot (Figure 1) characterized by a slope close to 1 and an intercept value near 0.

To further check the accuracy of the group contribution method to obtain the modified nonspecific cohesion parameters, the δ'_b value of a large fluorous compound, i.e., $P[p\text{-}C_6H_4SiMe_2CH_2CH_2C_6F_{13}]_3$, was determined in two different ways: from the volume and nonspecific evaporation energy increments on one hand, and from its experimental solubilities in toluene and PFMCH using the MOD solubility model on the other hand. For the latter method, the melting enthalpy and liquid partial molar volume of the substance, needed for the calculation, were experimentally determined by DSC and densitometric measurements, respectively. Both methods led to comparable δ'_b values, i.e., 14.13 and 14.01 $MPa^{1/2}$, bringing therefore some confidence to the whole procedure followed along this work. Such a confidence was furthermore strengthened from the agreement observed between the two log *P* values calculated by combining the δ'_b results with the estimated (996.2 cm^3/mol) or experimental (1070 cm^3/mol) molar volume of the substance, and from the agreement of these values with the experimental partition coefficient determined at 25 °C.

Predicted Trends. From a general point of view, eq 5 shows the theoretical linear dependency of log *P* on the V_b molar volume and δ'_b modified nonspecific cohesion parameter of the solute. However, because δ'_b also depends on the molar

TABLE 6: log *P* Values of Silanes in PFMCH/Toluene at 25 °C[a]

compound	V_b (cm^3/mol)	δ'_b (MPa$^{1/2}$)	log P_{exp}[b]	log P_{cal}	diff
m-$BrC_6H_4SiMe_3$	181.4	16.67	**−1.557**	−1.403	0.154
p-$BrC_6H_4-SiMe_2CH_2CH_2Rf_6$*	350.4	14.65	**−0.737**	−0.737	0.000
p-$BrC_6H_4-SiMe_2CH_2CH_2CF_3$	234.9	15.99	**−1.692**	−1.362	0.330
p-$BrC_6H_4Si(CH_2CH_2Rf_6)_3$	688.4	13.46	**1.456**	0.816	−0.640
1,3,5-$Br_2C_6H_3(SiMe_2CH_2CH_2Rf_6)$*	361.5	14.92	**−1.012**	−1.012	0.000
1,3,5-$BrC_6H_3(SiMe_2CH_2CH_2Rf_6)_2$	599.5	13.78	**−0.065**	0.196	0.261
$HSiMe_2Ph$	152.2	16.78	**−1.430**[c]	−1.244	0.186
$HSiMe_2CH_2CH_2Rf_6$*	283.3	12.98	**0.611**	0.611	0.000
$HSiMe(CH_2CH_2Rf_8)_2$	544.7	12.46	**2.013**	2.036	0.023
$HSi(CH_2CH_2Rf_8)_3$	759.9	12.32	**2.610**	3.168	0.558
$HSi(CH_2CH_2Rf_6)_3$	621.3	12.51	**2.393**	2.260	−0.133

[a] Modified nonspecific cohesion parameter (MPa$^{1/2}$) and molar volume (cm^3/mol) calculated from increments at 25 °C. Experimental log *P* values taken from refs 4, 13, and 14. Rf_x denotes a C_xF_{2x+1} group. Compounds marked with an asterisk were used for the determination of the molar nonspecific vaporization energy increments. [b] Data from this work, unless noted otherwise. [c] From ref 15.

TABLE 7: log *P* Values of Fluorous Tin Compounds in FC-72/Benzene at 27 °C[a]

compound	V_b (cm^3/mol)	δ'_b (MPa$^{1/2}$)	log P_{exp}[b]	log P_{cal}	diff
$(Rf_4(CH_2)_2)_3SnH$	484.9	13.33	**1.071**	0.640	−0.431
$(Rf_6(CH_2)_2)_3SnH$*	623.5	12.93	**1.653**	1.678	0.025
$(Rf_4(CH_2)_3)_3SnH$	533.2	13.66	**0.079**	0.139	0.060
$(Rf_6(CH_2)_3)_3SnH$	671.8	13.23	**1.000**	1.159	0.159
$Rf_6(CH_2)_2SnMe_2H$*	285.5	13.85	**−0.155**	−0.179	−0.024
$Rf_8(CH_2)_2SnMe_2H$	331.7	13.54	**0.398**	0.155	−0.243
$Rf_{10}(CH_2)_2SnMe_2H$	377.9	13.30	**0.672**	0.495	−0.177

[a] Modified nonspecific cohesion parameter (MPa$^{1/2}$) and molar volume (cm^3/mol) calculated from increments at 25 °C. Experimental log *P* values taken from refs 4, 13, and 14. Rf_x denotes a C_xF_{2x+1} group. Compounds marked with an asterisk were used for the determination of the molar nonspecific vaporization energy increments. [b] Data from ref 16.

TABLE 8: log *P* Values of Large Fluorous Phosphines in PFMCH/Toluene at 25 °C

compound	V_b (cm^3/mol)	δ'_b(MPa$^{1/2}$)	log P_{exp}[a]	log P_{cal}	diff
$P(CH_2CH_2Rf_6)_3$*	606.5	12.71	**1.915**	1.915	0.000
$P(CH_2CH_2CH_2Rf_8)_3$	793.4	12.78	**1.915**	2.411	0.496
$P(CH_2CH_2CH_2CH_2Rf_8)_3$	841.7	13.03	**1.954**	2.012	0.058
$P(p$-$C_6H_4CH_2CH_2CH_2Rf_6)_3$	848.0	14.19	**−0.569**	−0.520	0.049
$P(p$-$C_6H_4CH_2CH_2CH_2Rf_8)_3$*	986.6	13.84	**0.322**	0.322	0.000
$P[p$-$C_6H_4SiMe_2CH_2CH_2Rf_6]_3$	996.2	14.13	**−0.439**[b]	−0.497	−0.058
	1070[c]	14.01[d]	**−0.439**[b]	−0.203	0.236
$[CH_2P\{p$-$C_6H_4SiMe_2CH_2CH_2Rf_6\}_2]_2$[b]	1383.8	14.08	**−0.245**[b]	−0.486	−0.241

[a] Data obtained from ref 13, unless noted otherwise. Modified nonspecific cohesion parameter (MPa$^{1/2}$) and molar volume (cm^3/mol) calculated from increments at 25 °C. Experimental log *P* values taken from refs 4, 13, and 14. Rf_x denotes a C_xF_{2x+1} group. Compounds marked with an asterisk were used for the determination of the molar nonspecific vaporization energy increments. [b] This work. [c] Molar volume experimentally determined by densitometry. [d] Modified nonspecific cohesion parameter determined from the experimental solubilities of this compound in PFMCH and toluene (74 g/L in PFMCH and 175 g/L in toluene; $\Delta H_{melt} = 17.4$ kJ/mol at 84 °C, determined by DSC).[8]

volume according to eq 7, a nonlinear dependency of log *P* on the molar volume has rather to be expected. Although eq 5 exhibits a linear dependency of log *P* on the reverse of the temperature, it should be noted that, apart from the terms containing the temperature itself, all molar volumes and modified nonspecific cohesion parameters are temperature dependent as well. Therefore, a general temperature effect on log *P* is quite difficult to assess. In the following, let us then focus essentially on the log *P* variations with respect to the relative values of the solute and solvent phase properties at 25 °C.

As, for most practical combinations of fluorous and organic solvent, $V_F > V_O$ and $\delta'_F < \delta'_O$, the ΔB term, describing the correction of the entropy of mixing from ideality, will be always negative. In other words, the entropy factor always results in a smaller affinity of the solute for the fluorous solvent, hence preferentially choosing the organic phase. From the enthalpic point of view, the ΔD term may be either positive or negative. From eq 4, the enthalpic term becomes positive only if the δ'_b value adheres to the following inequality:

$$\delta'_b < \frac{1}{2}(\delta'_O + \delta'_F) \qquad (8)$$

The ΔD term is positive only when the solute δ'_b value is sufficiently small, i.e., when the solute molecule is largely fluorinated and resembles more the fluorous than the organic solvent in terms of the nonspecific cohesive energy density. In short, eq 8 could then be regarded as a quantitative description of the well-known like-dissolves-like principle. Nevertheless, for the solute to exhibit a greater affinity for the fluorous phase leading to positive log *P* values, the ΔD term must not only be positive but also overcome the ΔB term. With respect to the solute δ'_b value, the combined conditions imply that

$$\delta'_b < \frac{1}{2}(\delta'_O + \delta'_F) - 2.078T\frac{\frac{1}{V_F} - \frac{1}{V_O}}{\delta'_F - \delta'_O} - 2.078\frac{T}{V_b}\frac{\ln\left(\frac{V_O}{V_F}\right)}{\delta'_F - \delta'_O} \qquad (9)$$

Practically, when the requirement of eq 9 is met, the log *P* value of the solute will be positive, and any increase in the molar volume will lead to an increase in its partition coefficient. In contrast, the log *P* value of a solute in a given fluorous biphasic system will always be ≤0 if eq 9 is not satisfied. In this case, any increase in the molar volume of the solute will result in a decrease of its log *P*. It is furthermore clear from inspection of eq 9 that the δ'_b value below which log *P* of a given solute can

TABLE 9: Upper Limit δ'_b Values of a Solute To Obtain Positive log *P* Values at 25 °C in Several Binary Partitioning Systems Involving PFMCH as the Fluorous Phase

organic solvent	V_O (cm^3/mol)[a]	δ'_O (MPa$^{1/2}$)[a]	δ'_b (MPa$^{1/2}$)
n-decane	195.9	15.14	$12.90-0.071/V_b$
toluene	106.9	18.10	$14.02-50.48/V_b$
$CHCl_3$	80.7	18.77	$14.16-67.79/V_b$
benzene	89.4	18.90	$14.32-59.02/V_b$
THF	81.4	19.30	$14.46-63.01/V_b$

[a] Data obtained from ref 5.

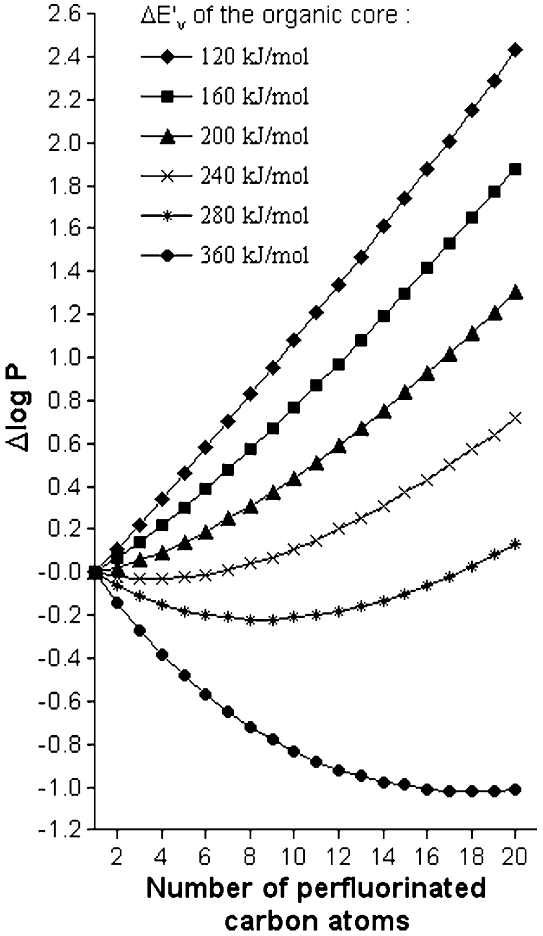

Figure 2. Effect of the elongation of the perfluoroalkyl tail on log *P* in the PFMCH/toluene system at 25 °C (Δ log *P* = log *P*(higher homologous compound) − log *P*(parent compound)).

become positive depends on the fluorous biphasic solvent system considered. Selecting, for instance, various biphasic partitioning systems containing PFMCH as fluorous phase, the last column of Table 9 lists the critical values of δ'_b below which the solute will preferentially flow to the fluorous phase for reasonable values of V_b. The analysis of these results reveals that the critical δ'_b value decreases with the lowering of the δ'_O, the modified nonspecific cohesion parameter of the organic solvent phase. This observation demonstrates that a lower δ'_b value is required for a solute to preferentially dissolve into the fluorous phase of a biphasic fluorous solvent system of which the organic phase is more apolar in character. From a chemical point of view, this requirement may be achieved only by grafting more perfluoroalkyl chains and/or by lengthening the size of the perfluoroalkyl tails of a parent fluorous compound.

As stated in the Introduction, it is generally assumed that both elongation of the perfluoroalkyl tails and/or increasing the number of tails of a given substance result in higher partition coefficients. Can the MOD theory justify and confirm this kind of empirical behavior?

To study first the effect of elongation of a perfluoroalkyl tail on the partition coefficient, let us calculate the log *P* of some hypothetical substances: Consider a set of different molecules all sharing an organic core bearing only one CF_3 group. The cores of all these molecules have the same molar volume, i.e., 400 cm^3/mol (close to the size of the organic core of the triarylphosphines listed in Table 8), but differ from one another by their nonspecific vaporization energy $\Delta E'_v$ within the range 120−360 kJ/mol. On each of these molecules, one inserts successively up to 19 $-CF_2$ units between the organic core and the CF_3 group. Then, the PFMCH/toluene partition coefficient of each homologous series of molecules is calculated using eq 6a with V_b and δ'_b values estimated from the group contribution technique. The results are presented in Figure 2. Inspection of this figure reveals that, for homologous series of molecules based on parent compounds with small $\Delta E'_v$ values (120−240 kJ/mol), the log *P* increases with the number of added CF_2 groups. Nevertheless, it is also observed that the increase in log *P* diminishes with the rise in $\Delta E'_v$. When the $\Delta E'_v$ value of the parent compounds amounts or exceeds ca. 280 kJ/mol, the addition of additional CF_2 units does not significantly affect the partition coefficient. The log *P* of the homologous molecules in this series remains close to the value of the parent compound. Finally, if the $\Delta E'_v$ value of the parent compound is further increased up to 360 kJ/mol, the log *P* starts to decrease upon increasing the number of perfluorinated carbon atoms. This reasoning shows that, for fluorous molecules containing an organic part characterized by high values of their nonspecific vaporization energy, elongation of the perfluoroalkyl tail(s) does not necessarily result in a rise of the partition coefficient. This is in contrast to the commonly accepted idea that addition of more perfluoroalkyl groups or elongation thereof increases a compound's fluorophilicity.

Let us now study the effect of enlarging the number of perfluoroalkyl tails on the log *P*. With that aim, consider, as we did previously, a set of different nonfluorous organic molecules sharing the same volume, i.e., 400 cm^3/mol, but differing by the $\Delta E'_v$ values of their nonspecific vaporization energies ranging from 120 to 360 kJ/mol. On each of these molecules, up to 10 perfluorohexyl ($-C_6F_{13}$) tails were grafted and its log *P* was subsequently calculated. The results are shown in Figure 3. Here again, a linear dependency of log *P* on the number of tails is observed for the homologous series of molecules with low $\Delta E'_v$ values of the parent compounds. The larger the $\Delta E'_v$ values, the lower the log *P* increase. When the $\Delta E'_v$ value is maximal (360 kJ/mol), the log *P* of the homologous series of molecules decreases upon addition of the first C_6F_{13} groups until a minimum value is reached. Beyond this minimum, the log *P* of the molecules increases again with respect to the number of perfluorohexyl groups added. This last behavior once again demonstrates that increasing the number of perfluoroalkyl tails can have either a positive or a negative effect on the partition coefficient of solutes in fluorous biphasic systems.

As a whole, all the results presented in Figures 2 and 3 can be understood and discussed in terms of the relative changes in the Δ*B* entropic and Δ*D* enthalpic contributions to log *P* through the variations of the V_b and δ'_b properties of the hypothetical molecules associated to either the elongation of the perfluoroalkyl tails or to the addition of an increasing number of perfluorohexyl tails. Whatever the chemical modification introduced on a given compound, its molar volume is generally

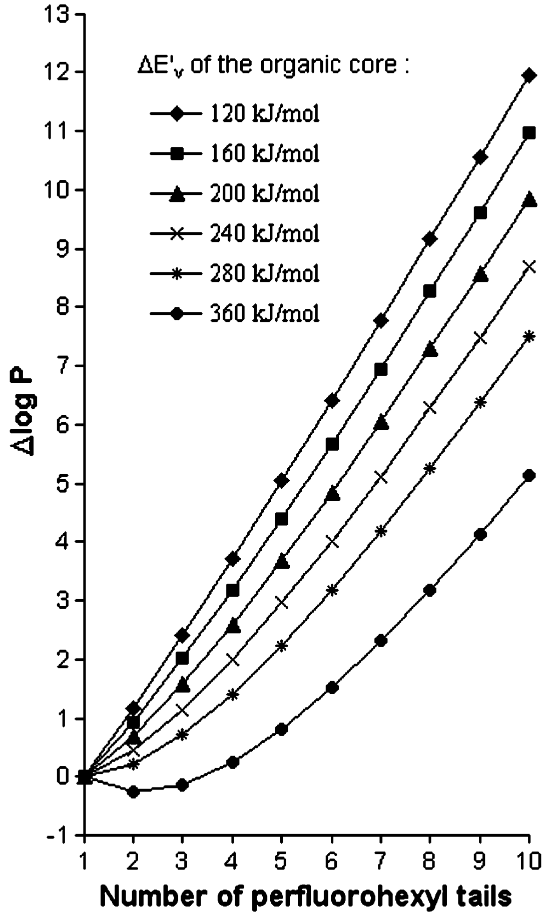

Figure 3. Effect of adding perfluorohexyl tails on log *P* in the PFMCH/toluene system at 25 °C (Δ log *P* = log *P*(higher homologous compound) − log *P*(parent compound)).

enlarged, and consequently the negative entropic Δ*B* term will be more negative. Simultaneously, the corresponding enthalpic Δ*D* term will be either decreased or increased depending essentially on the relative δ'_b magnitude of the compound with respect to the δ'_F and δ'_O values of the fluorous and organic solvent phases, respectively. Because for most theoretical cases studied, the increase in the Δ*D* term more or less overcomes the decrease in Δ*B* term, the resulting log *P* is accordingly raised within each homologous series of molecules. As can be observed from Figures 2 and 3, the reverse evolution may, however, theoretically occur. Such a change in the log *P* values would in fact be observed for molecules of which the nonfluorous organic core is characterized by an exceptionally high value of its nonspecific vaporization energy ($\Delta E'_v$ greater than 240 kJ/mol for a corresponding volume close to 400 cm^3/mol).

Given the above analysis, it can now be understood easily why, in the case of the real molecules (Tables 4-8) studied in the course of this work, elongation and/or addition of perfluoroalkyl tails result in higher partition coefficients. In fact the majority of these molecules exhibit a relatively small nonfluorous organic core characterized by a low nonspecific vaporization energy. An opposite partition behavior has nevertheless been observed[18,20] for the silyl-substituted phosphines $P[p\text{-}C_6H_4\text{-}SiMe_{3-b}(CH_2CH_2C_xF_{2x+1})_b]_3$ and $P[3,5\text{-}C_6H_3\{SiMe_{3-b}(CH_2\text{-}CH_2C_xF_{2x+1})_b\}_2]_3$ ($b = 1, 2, 3$; $x = 6, 8$) in the PFMCH/toluene biphasic system at 0 °C. Within these particular homologous series of fluorous molecules, the lengthening of the perfluoroalkyl tails from 5 to 7 CF_2 groups and/or the substitution of more methyl groups with fluorous tails on the Si atom most often yield to lower partition coefficients. Can this reverse partition behavior be fully accounted for by the MOD thermodynamic model of partitioning, hence still be regarded as normal? Although the log *P* at 0 °C can at the present time only be roughly estimated because of the absence of accurate molar volume and nonspecific vaporization energy increment values at this temperature, it follows from the above discussion that such a reverse partition behavior should originate from especially high values of the nonspecific vaporization energy associated with the organic core of the parent compounds. However, a closer look into this last property in the case of the incriminated fluorous phosphines shows that the nonspecific vaporization energies of their organic cores are far below the values necessary to account for the trend observed. The partition behavior of these compounds can thus not be explained by the MOD model and must therefore be considered “anomalous”. This is further substantiated by the isomeric structures $P[m\text{-}C_6H_4SiMe_{3-b}(CH_2CH_2C_xF_{2x+1})_b]_3$ that display the usual and theoretically expected partition behaviors.[17] These results and observations call then for great caution and, in the case of the silyl-substituted fluorous phosphines, need further investigations into the nature of the actual chemical species that are involved in the partitioning process to precisely identify the cause of the anomalous partition behavior.

Conclusions

The partition coefficient of 88 nonfluorous and fluorous compounds in either PFMCH/toluene or FC-72/benzene binary solvent systems was successfully predicted at 25 °C using the universal lipophilicity model based on the mobile order and disorder (MOD) solution theory. A predictive expression for the fluorophilicity based on thermodynamic concepts has been derived for calculating the distribution of solutes between organic and fluorous solvents at any temperature. According to this expression, the log *P* is estimated from the knowledge of the molar volume and modified nonspecific cohesion parameter of the solute. These properties are in turn easily obtained from new group increment contributions derived in this work.

From a general point of view, the actual partition model predicts that grafting and elongation of perfluoroalkyl tails do not necessarily yield higher partition coefficients. In fact, the model shows that, for fluorous substances containing an organic core characterized by an especially high value of its nonspecific vaporization energy, addition of CF_2 groups and/or perfluorohexyl tails may result in lower partition constants. Although the Huque empirical model also contains a volume-dependent term that reduces partitioning with respect to the molar volume of the chemical solute, the present MOD theory-derived partition model for the first time reveals the underlying thermodynamic principles for this unusual partition behavior in terms of both the enthalpic and entropic effects through the molar volume and nonspecific cohesion parameter of the solute.

The accuracy of the proposed model should be fair enough for synthetic studies aimed at optimization of fluorophilicity. However, in the present stage of their development, the predictive log *P* equations used in this work do not yet specifically account for the differences in shape of strongly related and/or isomeric solutes on one hand, and for possible amphiphilic behavior of some solutes on the other hand. Such features could be responsible for discrepancies between predicted and experimental log *P* values, particularly in the case where the fluorous solute molecule is able to form aggregates in solution.

Experimental Section

General Procedures. All reactions were performed under dry N_2 atmosphere using standard Schlenk techniques. Tetrahydrofuran, diethyl ether, and hexane were distilled from sodium benzophenone ketyl. Chlorodimethyl(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)silane,[18] bromotris(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)silane,[18] *p*-bromo(dimethyl(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)silyl)benzene,[18] 1-bromo-3,5-bis(perfluorohexyl)benzene,[19] $(C_xF_{2x+1}CH_2CH_2)_b$-$SiMe_{3-b}H$ ($x = 6, 8$; $b = 2, 3$),[18] $P[C_6H_4(SiMe_2CH_2CH_2C_6F_{13})$-$4]_3$,[18] and $[CH_2P\{C_6H_4(SiMe_2CH_2CH_2C_6F_{13})\text{-}4\}_2]_2$[20] were synthesized according to literature procedures. All other chemicals were used as received. Elemental analyses were carried out by H. Kolbe, Mikroanalytisches Laboratorium, Mülheim an der Ruhr. The melting enthalpy of $P[C_6H_4(SiMe_2CH_2CH_2C_6F_{13})$-$4]_3$ was determined using a Mettler DSC 12E calorimeter and its molar volume using a Anton Paar DMA 5000 densitometer following the usual techniques.[21] GC analyses were performed on a Perkin-Elmer AutoSystem XL gas chromatograph.

Determination of Partition Coefficients. The silane or phosphine (10−100 μmol) was dissolved in toluene (2 mL) and PFMCH (2 mL), and the solution was stirred for 30 min and equilibrated until two clear phases appeared. The partition coefficients were determined by analysis of equal volumes of both phases by GC (silanes) or gravimetrically after removal of all volatiles (phosphines).

Determination of Group Increments for Molar Nonspecific Evaporation Energy. From the partitioning data of carefully selected compounds (indicated with asterisks in Tables 4−8), containing a large variety of functional groups, the modified nonspecific cohesion parameter and subsequently the molar nonspecific evaporation energy were determined by back-calculation from eq 5. Molar volumes were calculated using the increments in Table 3. From this set of nonspecific evaporation energies, the increments were calculated using linear regression.

General Procedure for the Synthesis of Bromo((1*H*,1*H*,2*H*,2*H*-perfluoroalkyl)silyl)benzenes.[18] To a solution of a bromobenzene in ether was slowly added 1 equiv of a solution of *n*-BuLi in pentane at room temperature (1,4-$C_6H_4Br_2$) or −60 °C (1,3,5-$C_6H_3Br_3$). The solution was subsequently cooled to −78 °C and 1 equiv of halosilane was added. The mixture was stirred for 2 h and allowed to warm to room temperature. The resulting suspension was poured into H_2O and extracted with Et_2O, the combined organic layers were dried over $MgSO_4$ and all volatiles were removed in vacuo.

***p*-Bromo(dimethyl(3,3,3-trifluoropropyl)silyl)benzene.** 1,4-Dibromobenzene (6.25 g, 26.5 mmol), *n*-BuLi (17.2 mL, 1.54 M in hexanes, 26.5 mmol), and chlorodimethyl(3,3,3-trifluoropropyl)silane (4.55 mL, 26.5 mmol) yielded 7.07 g (86% yield) of a colorless oil. ^{1}H NMR ($CDCl_3$, 300.1 MHz): δ 7.54 (d, ${}^3J_{HH} = 10.2$ Hz, 8H), 7.37 (d, ${}^3J_{HH} = 10.2$ Hz, 8H), 2.00 (m, 2H), 0.98 (m, 2H), 0.34 (s, 36H). ${}^{13}C\{{}^1H\}$ NMR ($CDCl_3$, 75.5 MHz): δ 136.5 (s), 135.4 (s), 131.5 (s), 129.8 (m), 124.5 (s), 28.0 (q, ${}^2J_{CF} = 29.9$ Hz), 7.2 (s), −3.4 (s). Anal. Calcd for $C_{11}H_{14}BrF_3Si$: C, 42.45; H, 4.53; F, 18.31. Found: C, 42.22; H, 4.65; Si, 18.18.

***p*-Bromo(tris(1H,1H,2H,2H-perfluorooctyl)silyl)benzene.** 1,4-Dibromobenzene (1.72 g, 7.30 mmol), *n*-BuLi (4.5 mL, 1.6 M in hexanes, 7.2 mmol), and bromotris(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)silane (8.92 g, 7.38 mmol) yielded 7.28 g (81% yield) of yellow oil. ^{1}H NMR ($CDCl_3$, 300.1 MHz): δ 7.61 (d, ${}^3J_{HH} = 8.1$ Hz, 2H), 7.31 (d, ${}^3J_{HH} = 8.1$ Hz, 2H), 2.03 (m, 6H), 1.14 (m, 6H). ${}^{13}C\{{}^1H\}$ NMR ($CDCl_3$, 75.5 MHz): δ 135.2 (s), 132.3 (s), 130.2 (s), 126.0 (s), 121.4 (m) 118.8 (m), 115.4 (m), 114.8 (m), 110.4 (m), 107.5 (m), 25.5 (t, ${}^2J_{CF} = 23.9$ Hz), 1.5 (s). Anal. Calcd for $C_{30}H_{16}BrF_{39}Si$: C, 29.41; H, 1.32; F, 60.46. Found: C, 29.24; H, 1.24; F, 60.75.

1,3-Dibromo-5-(dimethyl(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)silyl)benzene. 1,3,5-Tribromobenzene (1.36 g, 4.32 mmol), *n*-BuLi (3.42 mL, 1.6 M in hexanes, 4.32 mmol), and chlorodimethyl(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)silane (1.9 g, 4.32 mmol) yielded 2.57 g (93% yield) of a white solid. ^{1}H NMR ($CDCl_3$, 300.1 MHz): δ 7.71 (s, 1H), 7.53 (s, 2H), 2.03 (m, 2H), 1.00 (m, 2H), 0.34 (s, 6H). ${}^{13}C\{{}^1H\}$ NMR ($CDCl_3$, 75.5 MHz): δ 143.1 (s), 135.2 (s), 134.8 (s), 124.1 (s), 122.0 (m), 118.8 (m), 115.3 (m), 111.6 (m), 110.6 (m), 108.7 (m), 25.7 (t, ${}^2J_{CF} = 24.1$ Hz), 5.2 (s), −3.6 (s). Anal. Calcd for $C_{16}H_{13}Br_2F_{13}Si$: C, 30.02; H, 2.05; F, 38.58. Found: C, 29.87; H, 1.95; F, 38.75.

1-Bromo-3,5-bis(dimethyl(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)silyl)benzene. 1,3-Dibromo-5-(dimethyl(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)silyl)benzene (11.38 g, 17.76 mmol), *n*-BuLi (11.45 mL, 1.55 M in hexanes, 17.75 mmol), and chlorodimethyl(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)silane (7.84 g, 17.76 mmol) yielded 15.58 g (91% yield) of a white solid. ^{1}H NMR ($CDCl_3$, 300.1 MHz): δ 7.68 (s, 2H), 7.55 (s, 1H), 2.03 (m, 4H), 1.05 (m, 4H), 0.38 (s, 12H). ${}^{13}C\{{}^1H\}$ NMR ($CDCl_3$, 75.5 MHz): δ 140.6 (s), 137.4 (s), 135.2 (s), 124.1 (s), 122.0 (m), 118.9 (m), 116.1 (m), 111.9 (m), 110.9 (m), 109.3 (m), 25.7 (t, ${}^2J_{CF} = 24.1$ Hz), 5.2 (s), −3.6 (s). Anal. Calcd for $C_{26}H_{23}BrF_{26}Si_2$: C, 32.34; H, 2.40; F, 51.16. Found: C, 32.55; H, 2.34; F, 51.12.

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(2) Log $P \equiv \log(c_F/c_O)$, where c_F and c_O are the concentrations (in mol/L or g/L) of the solute in the fluorous phase and the organic phase, respectively.

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(8) According to the MOD Theory, the solubility ($\ln \Phi_b$) can be obtained from

$$\ln \Phi_b = A + B + D + F + O + OH$$

where the terms *F*, *O*, and *OH* are not relevant for fluorous biphasic systems and

$$A = (\Delta H_m/R)(1/T - 1/T_m) + (\Delta H_{trans}/R)(1/T - 1/T_{trans})$$
$$B = 0.5\Phi_S(V_b/V_S - 1) + 0.5\ln(\Phi_b + \Phi_S V_b/V_S)$$
$$D = (\Phi_S{}^2 V_b/RT)(\delta'_b - \delta'_S)$$

Here, Φ_b and Φ_S are the volume fractions of the solute and the solvent, respectively, ΔH_m and ΔH_{trans} are the enthalpies of melting or other phase transitions, and T_m and T_{trans} are the corresponding melting or phase transition temperatures

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