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Prediction of Soil Sorption Coefficients for Organic Nonelectrolytes from Solvatochromic Parameters

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The fate of an organic chemical introduced into the environment depends on a variety of physical, chemical and biological processes. The soil (or sediment)-water sorption coefficient, which is often expressed on the basis of organic carbon (K_{oc}) or organic matter (K_{om}), is one of the key input parameters in models to estimate the mobility and fate of contaminants. This parameter provides an indication of the extent to which a chemical partitions between the solid and solution phases in soil or between water and sediment in aquatic ecosystems, and indicates whether a chemical is likely to leach through soil or be immobile. Since the experimental determination of K_{oc} is difficult and expensive, a number of estimation methods for K_{oc} , most of which are regression equations with water solubility, octanol-water partition coefficient or bioconcentration factor, have been developed.¹²

However, these models suffer from several shortcomings such as (1) low precision of water solubility, octanol-water partition coefficient and BCF data and (2) limited range of applicability of the models so developed.³ Recently, molecular connectivity indices have been successfully used to predict K_{oc} for nonpolar compounds.³⁻⁶ However, extension of the model to polar compounds has been problematic. Accuracy and range of applicability of molecular connectivity models are superior to the other correlational models based on above-mentioned empirical parameters. However, as we have pointed out elsewhere⁷ these models are not able to give a quantitative information on the solute-target system interactions which determine the property of interest.

In this paper we report the use of the Kamlet-Taft solvatochromic parameters⁸ in the linear solvation energy relationship (LSER)^{9,10} to correlate and predict K_{oc} . It has been demonstrated that many disparate physicochemical, biochemical, toxicological, pharmacological properties of organic nonelectrolytes that depend on solute/solvent interactions and aqueous solubilities in a variety of media can be correlated, rationalized, and predicted by the application of this methodology. Examples include octanol-water¹¹⁻¹³ and triolein-water partition coefficients,¹⁴ gas-blood partition coefficients,¹⁵ aqueous solubilities,¹⁶ inhibition of bioluminescence in *Photobacterium phosphoreum* (the Microtox test),¹⁷ toxicities to the Golden Orfe Fish¹⁸ and binding to bovine serum albumin,¹⁴ binding into the β -cyclodextrin cavity,¹⁹ bioconcentration factors in fish²⁰ and retention behavior of solutes in gas and liquid chromatography.²¹⁻²⁹

The LSER for a property of solutes (SP) that depends on solute-solvent interactions is given by eq. 1, which specifically identifies and evaluates the individual solute-solvent interactions that contribute to the SP.

$$SP = SP_0 + mV_I/100 + sn^* + d\delta + b\beta_m + a\alpha_m \quad (1)$$

The coefficients m , s , d , b and a are obtained by multiple linear regression of SP vs. the solute parameters. The $mV_I/100$ term measures the endoergic process of separating the solvent molecules to provide a suitably sized cavity for the solute. V_I is computer-calculated intrinsic molecular volume of the solute.³⁰ V_I is scaled by 1/100 so that it should cover roughly the same range as the other independent variables. The sn^* and $d\delta$ term together measure exoergic solute-solvent dipole-dipole and dipole-induced dipole interactions; n^* is the solvatochromic parameter which measures the ability of a molecule to stabilize a neighboring charge or dipole, and to induce a dipole in a neighboring nondipolar molecule. The δ term in eq. 1 is a polarizability correction parameter, equal to 0.0 for non-polyhalogenated aliphatic compounds, 0.5 for polyhalogenated aliphatics, and 1.0 for single-ring aromatic compounds. For some multiple-ring aromatic compounds δ has values of 2.0.¹³ Exoergic effects of hydrogen bonding interactions are measured by $b\beta_m$ and $a\alpha_m$ terms; β and α are the solvatochromic parameters that measure hydrogen bond acceptor (HBA) basicity and hydrogen bond donor (HBD) acidity, respectively. The subscript m indicates that for compounds capable of self-association, the parameter applies to the non-self-associated "monomer" solute, rather than the self-associated "oligomer" solvent. For non-self-associating compounds, $\alpha_m = \alpha$, $\beta_m = \beta$. The solvatochromic parameters of over 500 compounds available at present were

Table 1. Data Used for Correlation of Sorption Coefficients (K_{oc}) for Soils and Sediments

No.	Compound	$V_f/100^a$	π^{*a}	δ^a	β^a	α^a	log K_{oc}		
							Exptl.	eq. 3	Diff. ^b
1	3-methylaniline	0.660	0.69	1	0.51	0.13	1.65	1.91	0.26
2	anisole	0.630	0.73	1	0.32	0	1.54	1.96	0.41
3	acetophenone	0.690	0.90	1	0.49	0.03	1.63	1.97	0.34
4	nitrobenzene	0.631	1.01	1	0.30	0	1.94	1.85	-0.09
5	1-naphthol	0.798	0.82	1	0.33	0.61	2.64	2.72	0.08
6	phenol	0.536	0.72	1	0.33	0.61	1.43	1.50	0.07
7	4-bromophenol	0.669	0.79	1	0.23	0.69	2.41	2.22	-0.19
8	4-bromonitrobenzene	0.764	1.16	1	0.26	0	2.42	2.46	0.04
9	n-butylbenzene	0.883	0.49	1	0.12	0	3.39	3.53	0.14
10	1,4-dimethylbenzene	0.671	0.51	1	0.12	0	2.52	2.49	-0.03
11	1,3,5-trimethylbenzene	0.769	0.47	1	0.13	0	2.82	2.97	0.15
12	1,2,3-trimethylbenzene	0.769	0.47	1	0.13	0	2.80	2.97	0.17
13	naphthalene	0.753	0.70	1	0.15	0	3.11	2.76	-0.35
14	2-methylnaphthalene	0.851	0.66	1	0.16	0	3.93	3.24	-0.69
15	anthracene	1.015	0.80	1	0.20	0	4.42	3.92	-0.50
16	phenanthrene	1.015	0.80	1	0.20	0	4.36	3.92	-0.44
17	tetracene	1.277	0.90	1	0.25	0	5.81	5.09	-0.72
18	pyrene	1.156	0.90	1	0.25	0	4.92	4.50	-0.42
19	7,12-dimethylbenzanthracene	1.473	0.82	1	0.27	0	5.37	6.05	0.68
20	1,2,5,6-dibenzanthracene	1.539	1.00	1	0.30	0	6.31	6.25	-0.06
21	chlorobenzene	0.581	0.71	1	0.07	0	2.41	2.01	-0.40
22	1,2-dichlorobenzene	0.671	0.80	1	0.03	0	2.50	2.44	-0.06
23	1,3-dichlorobenzene	0.671	0.75	1	0.03	0	2.47	2.47	0.00
24	1,4-dichlorobenzene	0.671	0.70	1	0.03	0	2.44	2.50	0.06
25	1,2,4-trichlorobenzene	0.761	0.75	1	0	0	2.94	2.94	0.00
26	1,3,5-trichlorobenzene	0.761	0.70	1	0	0	2.85	2.96	0.11
27	1,2,3,4-tetrachlorobenzene	0.851	0.80	1	0	0	3.84	3.35	-0.49
28	1,2,3,5-tetrachlorobenzene	0.851	0.80	1	0	0	3.20	3.35	0.15
29	pentachlorobenzene	0.941	0.75	1	0	0	3.50	3.81	0.31
30	hexachlorobenzene	1.031	0.70	1	0	0	3.59	4.27	0.68
31	dichloromethane	0.336	0.82	0.5	0.10	0.25	1.44	1.03	-0.41
32	trichloromethane	0.427	0.58	0.5	0.10	0.35	1.65	1.59	-0.06
33	tetrachloromethane	0.514	0.28	0.5	0.10	0	1.85	2.17	0.31
34	1,1,1-trichloroethane	0.519	0.49	0.5	0.10	0	2.26	2.08	-0.18
35	1,1,2-trichloroethane	0.492	0.53	0.5	0	0	2.00	1.99	-0.01
36	1,1,2,2-tetrachloroethane	0.617	0.95	0.5	0.10	0	1.90	2.33	0.43
37	1,2-dibromoethane	0.528	0.75	0.5	0.05	0	1.64	2.05	0.41
38	2,5,2',5'-PCB	1.280	1.35	2	0.06	0	4.91	4.49	-0.42
39	2,3,4,2',5'-PCB	1.370	1.50	2	0.03	0	4.54	4.88	0.34
40	2,4,5,2',5'-PCB	1.370	1.45	2	0.03	0	4.63	4.91	0.28
41	2,3,4,2',3',4'-PCB	1.460	1.70	2	0	0	5.05	5.25	0.20
42	2,3,4,5,6,2',5'-PCB	1.550	1.40	2	0.03	0	5.95	5.80	-0.15

^aSolute parameters are either from refs. 12 and 13 or estimated by parameter estimation rules.¹³ ^bCalculated minus experimental.

either measured⁸ or can be estimated by parameter estimation rules.^{12,13} Any one or combination of terms in eq. 1 may drop out if not applicable to the property studied. We applied the LSER of eq. 1 in order to correlate and predict K_{oc} and also to obtain quantitative information on the factors affecting it.

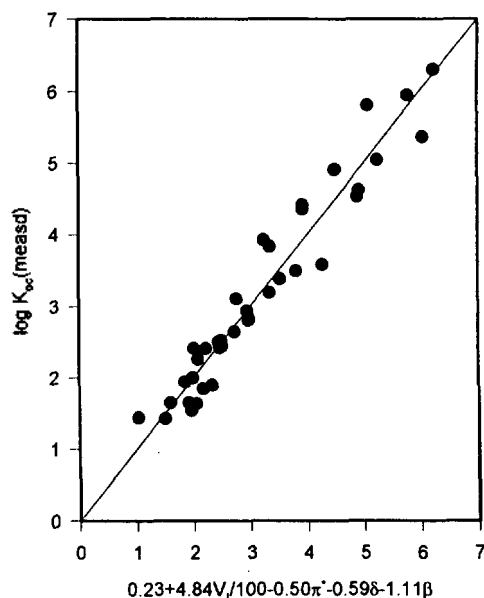
Results and Discussion

The K_{oc} data, taken from a compilation of Bahnick *et al.*⁵ are assembled in Table 1 for the 42 (of 106) compounds whose solvatochromic parameters are known or could be estimated using the parameter estimation rules.^{11,12} The multi-

Table 2. Comparison of Estimated Log K_{oc} Values to Experimental Values for Compounds Not Used in Developing the LSER Equation

Compound	$V_i/100$	π^*	δ	β	eq. 3	Exptl.	diff.	Lit. ^a
tetrachloroethene	0.578	0.28	0.5	0.05	2.52	2.56	-0.04	31
1,2-dichloroethane	0.442	0.80	0.5	0.10	1.54	1.52	0.02	31
benzene	0.491	0.59	1	0.10	1.60	1.92	-0.32	32
toluene	0.592	0.55	1	0.11	2.09	2.39	-0.30	33
1,3-dimethylbenzene	0.671	0.51	1	0.12	2.48	2.26	0.22	34
1,2,4,5-tetramethylbenzene	0.867	0.43	1	0.15	3.43	3.12	0.31	35
9-methylanthracene	1.113	0.76	1	0.21	4.38	4.81	-0.43	32
1,2,3-trichlorobenzene	0.761	0.85	1	0	2.88	3.37	-0.49	33
1,2,4,5-tetrachlorobenzene	0.851	0.70	1	0	3.38	3.86	-0.48	33
2,4'-PCB	1.100	1.42	2	0.14	3.38	4.14	-0.66	31
2,4,5,2',4',5'-PCB	1.460	1.50	2	0	5.32	6.08	-0.75	31

^aThe K_{oc} values given in the literature were converted to K_{oc} values by multiplying K_{oc} values by 1.724.

**Figure 1.** Plot of measured vs. calculated log K_{oc} .

ple linear regression equation for 42 compounds of Table 1 is given by eq. 2.

$$\log K_{oc} = 0.22(\pm 0.19) + 4.87(\pm 0.29)V_i/100 - 0.51(\pm 0.33)\pi^* - 0.60(\pm 0.27)\delta - 1.17(\pm 0.46)\beta + 0.12(\pm 0.37)\alpha \quad (2)$$

$n=42$, $r=0.968$, $s.d.=0.36$

The coefficient for the α term is statistically zero and subsequently removed in the correlation. The resulting LSER equation is given by eq. 3.

$$\log K_{oc} = 0.23(\pm 0.19) + 4.84(\pm 0.27)V_i/100 - 0.50(\pm 0.33)\pi^* - 0.59(\pm 0.27)\delta - 1.11(\pm 0.42)\beta \quad (3)$$

$n=42$, $r=0.968$, $s.d.=0.36$

Important requirements that need to be met for an LSER to correctly represent the property studied are a high correlation coefficient (r) and a low standard deviation ($s.d.$). An equally important and more rigorous test is that the equation be 'robust', i.e., the intercept and the coefficients for the

independent variables should be reasonably similar for different subsets of the data. To test robustness of eq. 3 we performed a jackknife test similarly to the one performed for log BCF values²⁰ and found that the equation is quite 'robust' (results not shown). Quality of the fit by eq. 3 is demonstrated in Figure 1.

As expected *a priori* based on the previous correlation with eq. 1, increasing V_i leads to decreasing solubility in water and thereby increasing adsorption to soil/sediment organics. Increasing dipolarity and polarizability lead to increasing water solubility, which in turn decrease adsorption to the soil or sediment. Increasing HBA basicity of compound favors solubility in water over the soil organics and should lead to decreased adsorption.

Accuracy of the LSER predictions is comparable to that of a molecular connectivity model (correlation coefficient, 0.968 (LSER model) vs. 0.969²¹). Range of applicability of LSER model is lower than molecular connectivity models due to limited applicability of present parameter estimation rules. However, as has been demonstrated in the case of BCF,²⁰ the LSER model is useful to analyze quantitatively solute-soil interactions which determines K_{oc} , which are seldom obtainable by molecular connectivity models. The LSER model (eq. 3) was tested by choosing a different subset of organic chemical compounds and their corresponding log K_{oc} values from the literature. Calculated log K_{oc} values are compared with the experimental values in Table 2. The average difference for 11 compounds is 0.36 log units which is the same as the standard error of estimate (0.36) obtained from the LSER model. This result demonstrates the applicability of eq. 3 to the types of organic compounds used to develop the model.

In conclusion, sorption coefficients on soils and sediments (K_{oc}) of organic nonelectrolytes are well correlated by linear solvation energy relationship of eq. 3. Accuracy of predicted values for K_{oc} by the LSER model is comparable to, but range of applicability is lower than molecular connectivity models. However, the LSER model can provide information on the nature and relative strength of solute-target system interactions affecting the property of interest, which can hardly be obtained from molecular connectivity models.

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Boron Trifluoride Etherate on Alumina-A Modified Lewis Acid Reagent(V) A Convenient Single-step Synthesis of Cannabinoids

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Since the early 1960s, when the structures of cannabinoid analogs were elucidated,¹ cannabinoid research has maintained sustained progress resulting in the synthesis of a large number of analogs with a varied degree of resemblance to the natural substances. Although accurate correlation between the structure and function for the several hundred cannabinoid analogs is complicated by uncertainties about the enantiomeric purity of the different analogs and by the large variability of the testing procedures, some general features associated with pharmacological activity can be identified from the existing literature.^{2a}

Recently, several syntheses of delta-9-tetrahydrocannabinol (Δ^9 -THC) metabolites have been reported. Tius *et al.*^{2b} reported a novel syntheses of (\pm)-11-hydroxy- Δ^9 -THC which does not address the double-bond isomerization difficulties. A new approach to 11-nor-9-carboxy- Δ^9 -THC by Huffman *et al.*^{2c} avoided both of these problems but gave racemic product as well as a cis/trans mixture which had to be separated. The same group solved the problem of racemization subsequently.²ⁱ Siegel *et al.*^{2e} described in detail their efforts to circumvent these problems in the synthesis of optically active Δ^9 -THC metabolites.

We have reported that when BF_3 -diethyl ether on alumina was used as a condensing reagent, the reaction of (+)-*p*-mentha-2,8-dien-1-ol with olivetol on 0.8 mmole scale led to cannabidiol (CBD) as the major product in 55% yield as chromatographically pure oil or 41% yield as crystalline material.^{2b} In previous paper we reported a much more efficient