



## RELATIONSHIPS BETWEEN MOLECULAR PROPERTIES AND LOG *P* AND SOIL SORPTION ( $K_{oc}$ ) OF SUBSTITUTED PHENYLUREAS: QSAR MODELS

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### ABSTRACT

Molecular modeling techniques were used to establish relationships between the molecular properties of 45 substituted phenylureas and their octanol/water partition coefficient ( $\log P$ ) and soil sorption normalized to organic carbon ( $K_{oc}$ ).  $\log P$  and  $K_{oc}$  values were obtained from the literature. The molecular properties were calculated using MOPAC-MNDO molecular orbital methods. The QSAR models based on van der Waals volume, dipole moment, and energy of lowest unoccupied molecular orbital produced estimates of  $\log P$  and  $K_{oc}$  that correlate well with experimental values. The QSAR models appear to be specific to structurally similar chemicals.

### KEYWORDS

Herbicides,  $\log K_{ow}$ , octanol/water partition coefficient, molecular modelling.

### INTRODUCTION

The octanol/water partition coefficient is defined as the ratio of chemical concentration in the octanol phase to its concentration in the aqueous phase and is expressed as the logarithm of partition coefficient ( $\log P$ ).  $\log P$  is a measure of solute hydrophobicity or lipophilicity. The soil sorption coefficient ( $K_{oc}$ ) is the ratio between the concentrations of a chemical sorbed by the soil and dissolved in the soil water normalized to soil organic carbon.  $\log P$  and  $K_{oc}$  are among the several fate constants used to assess the transformation and transport potential of a chemical.<sup>1</sup> The United States Federal Drug Administration requires  $\log P$  values for a drug to be registered and the United States Environmental Protection Agency (EPA) uses  $\log P$  values to estimate the environmental fate and bioaccumulation of pesticides and other chemicals released to the environment. Fate constants may not be needed for all of the millions of chemicals listed in the Chemical Abstract Services Registry, but many of the 70,000 manufactured chemicals on the EPA's inventory will be evaluated for their potential environmental impact in the near future.<sup>1</sup> The experimental determination of  $\log P$  and  $K_{oc}$  values of all organic pollutants is often time consuming and/or cost prohibitive. On the other hand,

chemical industries are faced with higher costs of experimentation and the costs associated with disposal of unwanted materials synthesized during the product development. Consequently, the chemical industries are increasingly relying on predictive models to estimate  $\log P$  and other solution properties of chemicals as a pre-screening tool. By pre-screening hundreds or even thousands of compounds, valuable time and resources are saved.

Mathematical models that relate some physical, chemical, biological, or environmental activity to some quantitative structural descriptors or physicochemical properties are collectively known as quantitative structure activity relationship (QSAR) models. The basic assumption is that the variations in the activity within a series of similar structures can be correlated with changes in parameters which reflect molecular properties. The QSAR models are usually developed for a group of compounds with similar structure. The primary objective of QSAR modeling is to predict the activities of untested, structurally similar compounds. The statistical procedure used to derive QSAR models is linear regression analysis. This procedure can be univariate or multivariate, depending on the number of structural descriptors used in a particular analysis.<sup>2</sup> The QSAR models have been used to study the mechanism of action of pesticides,<sup>3-6</sup> as well as to design and develop new compounds.<sup>7</sup>

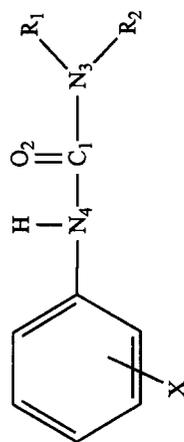
Several models based on molecular properties such as molecular volume, dipole moment, hydrogen bond acceptor basicity, hydrogen bond donor acidity,<sup>8-11</sup> molecular surface areas and volumes,<sup>12,13</sup> solvent accessible surface area,<sup>14</sup> and molar polarizability<sup>15</sup> have been reported to predict  $\log P$  of several chemical classes. Water solubility and  $\log P$  of chemicals have been used as parameters for describing and predicting soil sorption coefficients.<sup>16,17</sup> Several workers believe that water solubility and  $\log P$  are not accurate predictors of  $K_{oc}$ .<sup>18-20</sup> Molecular connectivity models which are based on chemical structure have been shown to outperform traditional empirical models based on water solubility and  $\log P$  in predicting  $K_{oc}$ .<sup>18,20-24</sup> Recently, there was one study which examined models based on molecular properties (molar volume and self-polarizability) to predict  $K_{oc}$  of 50 carboxylic acids, esters, amines, and amides.<sup>25</sup> However, information on QSAR models based on molecular properties calculated by molecular orbital methods to predict  $K_{oc}$  is limited. In this paper we describe and discuss QSAR modeling techniques to predict  $\log P$  as well as  $K_{oc}$  based on molecular properties of 45 substituted phenylureas.

## MATERIALS AND METHODS

### 1. Molecular Properties

Chem-X (Chemical Design Limited, Oxford, United Kingdom) molecular modeling software was used to build 3-dimensional chemical structures and to compute various molecular properties (descriptors) of phenylurea and its analogues. The method of computation of molecular properties has been published recently by Nandihalli et al.<sup>4-6</sup> A brief description of methods used to compute molecular descriptors in this study is given. The 3-dimensional structure of phenylurea (Table 1) was built using urea and benzene fragments available in the molecule fragment library of the Chem-X software. The structures of other analogues (Table 1) were built on phenylurea structure using the standard atoms, functional groups, and fragments. The structures were subjected to full geometry optimization via MOPAC (Quantum Chemistry Exchange Program 560, version 6.0,

Table 1. Structures, observed  $\log P$  and  $\log K_{oc}$  values, and the molecular descriptors of substituted phenylureas<sup>ab</sup>.



Abbreviation/ common name	X	R <sub>1</sub>	R <sub>2</sub>	Log P	Log K <sub>oc</sub>	Descriptors		
						VDW <sub>V</sub>	μ	ε <sub>LUMO</sub>
						(Å <sup>3</sup> )	(D)	(eV)
Phenylureas								
PU	H	H	H	0.80	1.35	93.3	3.328	0.002
2FPU	2-F	H	H	0.88	1.32	106.1	4.127	-0.427
2CLPU	2-Cl	H	H	1.27	1.61	119.0	4.334	-0.505
3FPU	3-F	H	H	1.29	1.77	100.3	1.657	-0.366
3CLPU	3-Cl	H	H	1.82	2.01	119.0	1.771	-0.398
3BRPU	3-Br	H	H	2.08	2.06	129.5	2.064	-0.361
3MPU	3-CH <sub>3</sub>	H	H	1.29	1.56	116.6	3.403	-0.077
3FMPU	3-CF <sub>3</sub>	H	H	2.31	1.96	129.5	3.627	-0.987
4FPU	4-F	H	H	1.04	1.52	99.1	1.657	-0.382
4BRPU	4-Br	H	H	1.98	2.12	122.5	1.973	-0.348
4POXPU	4-OC <sub>6</sub> H <sub>5</sub>	H	H	2.80	2.56	179.6	4.000	-0.301

Table 1. (cont'd)

Abbreviation/ common name	X	R <sub>1</sub>	R <sub>2</sub>	Log P	Log K <sub>oc</sub>	VDW <sub>V</sub>	Descriptors		
							μ	(D)	ε <sub>LUMO</sub>
34DCLPU	3,4-Cl <sub>2</sub>	H	H	2.64	2.49	137.6	0.270	-0.741	
3CL4MOPU	3-Cl, 4-OCH <sub>3</sub>	H	H	1.37	2.00	140.0	2.431	-0.604	
3M4FPU	3-CH <sub>3</sub> , 4-F	H	H	1.59	1.78	109.7	1.840	-0.440	
3M4BRPU	3-CH <sub>3</sub> , 4-Br	H	H	2.49	2.37	134.1	2.106	-0.388	
Phenyl-1-cycloalkylureas									
PCYPROU	H	H	C <sub>3</sub> H <sub>5</sub>	1.65	1.72	142.3	3.915	-0.108	
PCYPENU	H	H	C <sub>3</sub> H <sub>9</sub>	2.65	1.93	169.1	4.125	-0.146	
PCYHEXU	H	H	C <sub>6</sub> H <sub>11</sub>	2.77	2.07	178.5	4.240	-0.141	
PCYHEPU	H	H	C <sub>7</sub> H <sub>13</sub>	2.95	2.37	198.3	4.049	-0.117	
SIDURON	H	H	C <sub>6</sub> H <sub>10</sub> CH <sub>3</sub>	-	2.62	196.0	4.146	-0.131	
Phenyl-1-methylureas									
PMU	H	H	CH <sub>3</sub>	1.17	1.29	124.8	3.004	0.043	
3CLPMU	3-Cl	H	CH <sub>3</sub>	2.18	1.93	142.3	2.684	-0.412	
34DCLPMU	3,4-Cl <sub>2</sub>	H	CH <sub>3</sub>	2.94	2.46	158.6	1.208	-0.743	
3CLAMPMU	3-Cl, 4-CH <sub>3</sub>	H	CH <sub>3</sub>	2.61	2.10	162.1	2.560	-0.466	
3CL4MOPMU	3-Cl, 4-OCH <sub>3</sub>	H	CH <sub>3</sub>	1.76	1.84	163.3	3.560	-0.561	
Phenyl-1,1-dimethylureas									
FENURON	H	CH <sub>3</sub>	CH <sub>3</sub>	0.96	1.12	127.1	2.710	-0.005	
3CLPDMU	3-Cl	CH <sub>3</sub>	CH <sub>3</sub>	2.01	1.79	158.6	1.864	-0.380	

Table 1. (cont'd)

Abbreviation/ common name	X	R <sub>1</sub>	R <sub>2</sub>	Log <i>P</i>	Log <i>K</i> <sub>oc</sub>	VDW <sub>v</sub> (Å <sup>3</sup> )	Descriptors		
							μ	(D)	<i>e</i> <sub>LUMO</sub> (eV)
3MOPDMU	3-OCH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	1.73	1.72	154.0	2.600	-0.089	
3FPDMU	3-F	CH <sub>3</sub>	CH <sub>3</sub>	1.37	1.73	140.0	1.853	-0.343	
FLUOMETURON	3-CF <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	2.42	1.82	164.5	2.442	-0.786	
4FPDMU	4-F	CH <sub>3</sub>	CH <sub>3</sub>	1.13	1.43	143.5	0.955	-0.387	
MONURON	4-Cl	CH <sub>3</sub>	CH <sub>3</sub>	1.98	1.70	155.1	1.154	-0.384	
4MPDMU	4-CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	1.33	1.51	154.0	2.335	-0.070	
4MOPDMU	4-OCH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	0.83	1.40	154.0	2.887	-0.189	
METOXURON	3-Cl, 4-OCH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	1.64	1.74	176.1	2.525	-0.494	
CHLORTOLURON	3-Cl, 4-CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	2.41	2.02	170.3	1.381	-0.397	
35DMPPDMU	3,5-(CH <sub>3</sub> ) <sub>2</sub>	CH <sub>3</sub>	CH <sub>3</sub>	1.90	1.73	166.8	2.141	0.014	
35DM4BRPDMU	3,5-(CH <sub>3</sub> ) <sub>2</sub> , 4-Br	CH <sub>3</sub>	CH <sub>3</sub>	2.92	2.53	187.8	1.253	-0.354	
DIURON	3,4-Cl <sub>2</sub>	CH <sub>3</sub>	CH <sub>3</sub>	2.68	2.21	170.3	1.286	-0.686	
KARBUTILATE	3-OCONHC(CH <sub>3</sub> ) <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	1.60	-	222.8	3.137	-0.287	
CHLOROXURON	4-OC <sub>6</sub> H <sub>4</sub> Cl	CH <sub>3</sub>	CH <sub>3</sub>	3.20	3.48	222.8	0.903	-0.518	
Phenyl-1-methyl-1-methoxyureas									
MONOLINURON	4-Cl	OCH <sub>3</sub>	CH <sub>3</sub>	2.30	1.84	162.1	2.124	-0.579	
METOBROMURON	4-Br	OCH <sub>3</sub>	CH <sub>3</sub>	2.38	2.02	163.3	2.427	-0.525	
LINURON	3,4-Cl <sub>2</sub>	OCH <sub>3</sub>	CH <sub>3</sub>	2.76	2.43	176.1	1.413	-0.853	
CHLORBROMURON	3-Cl, 4-Br	OCH <sub>3</sub>	CH <sub>3</sub>	3.09	2.58	172.6	1.722	-0.793	

<sup>a</sup>Log *P* and log *K*<sub>oc</sub> data were collected from the literature.<sup>16,26,27</sup>

<sup>b</sup>For abbreviated descriptor terms refer to Table 2.

Department of Chemistry, Indiana University, Bloomington, Indiana) using MNDO (modified neglect of diatomic overlap) parameterization. Ground electronic states were obtained as closed-shell molecular orbital wave functions in the restricted Hartree-Fock framework.

The van der Waals molecular volume ( $VDW_V$ ) and surface area maps depict the overall size and shape of the molecule. The  $VDW_V$  maps were calculated using Chem-X, which displays the surface of the molecule at the VDW radius. The surface is based on the radius of the various atom types stored in the Chem-X energy parameters. To calculate the map, Chem-X uses a continuous function, instead of a step function to describe the transition across the molecular surface.

The molecular electrostatic potential (MEP) is the interaction energy of a point positive unit charge with the atoms of the structure. There are two contributions to the value of the electrostatic potential at any point: a nuclear contribution and a contribution from the electrons within their molecular orbitals. Chem-X treats the charge on each atom in a molecule as a point charge positioned at the center of the atom. For calculating MEP, positive unit charge equivalent to that of a proton is placed at each grid point, and the electrostatic interaction between the atoms of the structure and the unit charge is then calculated. When calculations are completed, a map showing positive and negative isopotential contour lines is drawn. The levels of potential energy as defined by contour levels were +10 and -10 kcal mol<sup>-1</sup> for positive and negative energy potentials, respectively.

The superdelocalizability (S) of an atom is a measure of its available electron density. It is the ratio of orbital density to orbital energy summed over all orbitals. The S of highest occupied molecular orbital ( $S_{HOMO}$ ) and lowest unoccupied molecular orbital ( $S_{LUMO}$ ) along with the orbital energy of HOMO ( $\epsilon_{HOMO}$ ) and LUMO ( $\epsilon_{LUMO}$ ) were computed. The electrophilic S ( $S_E$ ) and nucleophilic S ( $S_N$ ) based on occupied and unoccupied orbitals, respectively, were also computed.

## 2. Log *P* and log $K_{oc}$

Octanol-water partition coefficient (log *P*) and soil sorption normalized for organic carbon ( $K_{oc}$ ) values for substituted phenylureas were collected from the literature (Table 1). The majority of data quoted is from the comprehensive study of Briggs.<sup>16</sup> The soil sorption normalized for organic matter ( $K_{om}$ ) in the Briggs study was converted to  $K_{oc}$  using the relationship  $K_{oc} = 1.724 K_{om}$ . The log *P* values for karbutilate and chloroxuron were from the Pesticide Manual<sup>26</sup> and  $K_{oc}$  values for siduron and chloroxuron were from a database reported by Wauchope et al.<sup>27</sup>

## 3. QSAR Analysis

The quantum mechanical calculations generated several molecular properties (Table 2) representing bulk, steric, and electronic descriptors. Molecular properties were considered as independent variables and log *P* and  $K_{oc}$  as two dependent variables. Pearson correlation matrix was performed for molecular descriptors using SAS software (SAS Institute Inc., Cary, NC). The descriptors which showed significant correlations ( $P \leq 0.05$ ) with log *P* or  $K_{oc}$  were used to build the QSAR models. Siduron was excluded in log *P* models and karbutilate excluded in log  $K_{oc}$  models for lack of experimental values.

**Table 2.** Molecular properties used in QSAR models.

Type	Descriptors
Whole molecule properties:	
Bulk descriptors	van der Waals molecular volume ( $VDW_V$ ) van der Waals molecular area ( $VDW_A$ )
Electronic descriptors	Total dipole moment ( $\mu$ ) Molecular electrostatic potentials: + and - volumes and areas ( $+MEP_V$ , $-MEP_V$ , $+MEP_A$ , and $-MEP_A$ ) Superdelocalizability (S): $S_{HOMO}$ and $S_{LUMO}$ Electrophilic S ( $S_E$ ) Nucleophilic S ( $S_N$ )
Energy descriptors	energy ( $\epsilon$ ) of HOMO ( $\epsilon_{HOMO}$ ) and of LUMO ( $\epsilon_{LUMO}$ ) MOPAC energies: Total ( $\epsilon_T$ ), Electronic ( $\epsilon_E$ ), and Nuclear ( $\epsilon_N$ )
Atom centered properties:	
Electronic	Atomic charges, $S_E$ and $S_N$ for atoms C1, O2, N3, N4, and 6 carbon atoms of phenyl ring attached to N4.

Note: HOMO, highest occupied molecular orbital; LUMO, lowest unoccupied molecular orbital.

## RESULTS AND DISCUSSION

Pearson correlation analysis of 51 molecular descriptors of substituted phenylureas revealed that van der Waals molecular volume ( $VDW_V$ ) was most significantly correlated with  $\log P$  ( $r = 0.65$ ) and  $\log K_{oc}$  ( $r = 0.66$ ). The van der Waals surface area was the second most significantly correlated descriptor with  $\log P$  ( $r = 0.61$ ) and  $\log K_{oc}$  ( $r = 0.63$ ). Since molecular volumes and surface areas calculated on van der Waals radius are highly inter-correlated ( $r = 0.98$ ), only the molecular volume was used to build regression models. The simple regression equations based on  $VDW_V$  did not account for variation (differences between observed and predicted) greater than 42% in  $\log P$  and 45% in  $\log K_{oc}$ . Thus, multiple regression analysis was performed to study the potential contribution to the model from other molecular properties. For both  $\log P$  and  $K_{oc}$ , the most significant model was that involving the three descriptors,  $VDW_V$ , total dipole moment ( $\mu$ ), and  $e_{LUMO}$  (Table 1). The other molecular properties such as various superdelocalizabilities, energy of the highest occupied molecular orbitals, electrostatic potentials, and partial atomic charges (Table 2) did not contribute significantly to regression models. The relevant multiple regression equations for  $\log P$  and  $K_{oc}$  are given below.

$$\log P = 0.2859 + 0.0134 (VDW_V) - 0.5816 (\mu) + 0.10569 (\mu)^2 - 0.8928 (e_{LUMO})$$

$$r^2 = 0.59; \quad n = 44; \quad F = 14.0 \quad [1]$$

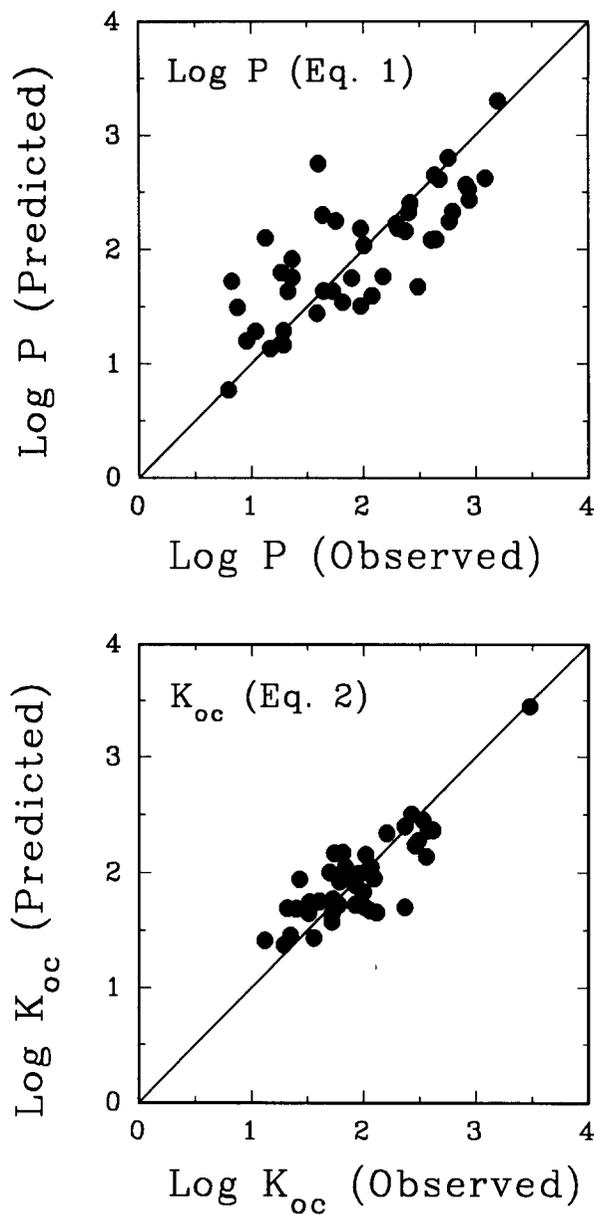
$$\log K_{oc} = 3.6424 - 0.0306 (VDW_V) + 0.00013 (VDW_V)^2 - 0.3116 (\mu) + 0.05009 (\mu)^2 - 0.5716 (e_{LUMO})$$

$$r^2 = 0.70; \quad n = 44; \quad F = 17.4 \quad [2]$$

Graphical representation of  $\log P$  predicted from equation 1 as a function of  $\log P$  observed and  $\log K_{oc}$  predicted from equation 2 as a function of  $\log K_{oc}$  observed are shown in Figure 1. The equation predicting  $\log K_{oc}$  ( $r^2 = 0.70$ ) values explained more of the variability than the equation for  $\log P$  ( $r^2 = 0.59$ ). The moderate relationships shown by these regression equations could be due to narrow range of experimental data (0.80 to 3.48 logarithmic units) and/or structural differences among substituted phenylureas in terms of substitution on atom N3 (Table 1).

The substituted phenylureas can be divided into five general classes based on substitution on atom N3 as: phenylureas, phenyl-1-methylureas, phenyl-1,1-dimethylureas, phenyl-1-methyl-1-methoxyureas, and phenyl-1-cycloalkylureas. The multiple regression analysis within each of these five chemical classes gave equations with  $r^2$  from 0.70 to 1.00 (Table 3). The same three molecular properties,  $VDW_V$ ,  $\mu$ , and  $e_{LUMO}$  appeared to be determinants of  $\log P$  and  $\log K_{oc}$  in the five chemical classes.  $\log P$  and  $\log K_{oc}$  predicted from equations 3 to 10 as a function of  $\log P$  and  $\log K_{oc}$  observed are shown in Figure 2. Equations for  $\log K_{oc}$  had a higher  $r^2$  than  $\log P$ . For phenyl-1-cycloalkylureas equation 11 based on three molecular properties,  $VDW_V$ ,  $\mu$ , and  $e_{LUMO}$  explained 100% variation in  $\log P$  (Table 3). However, only  $VDW_V$  produced a significant model (equation 12) which explained 86% variation in  $\log K_{oc}$  (Table 3).

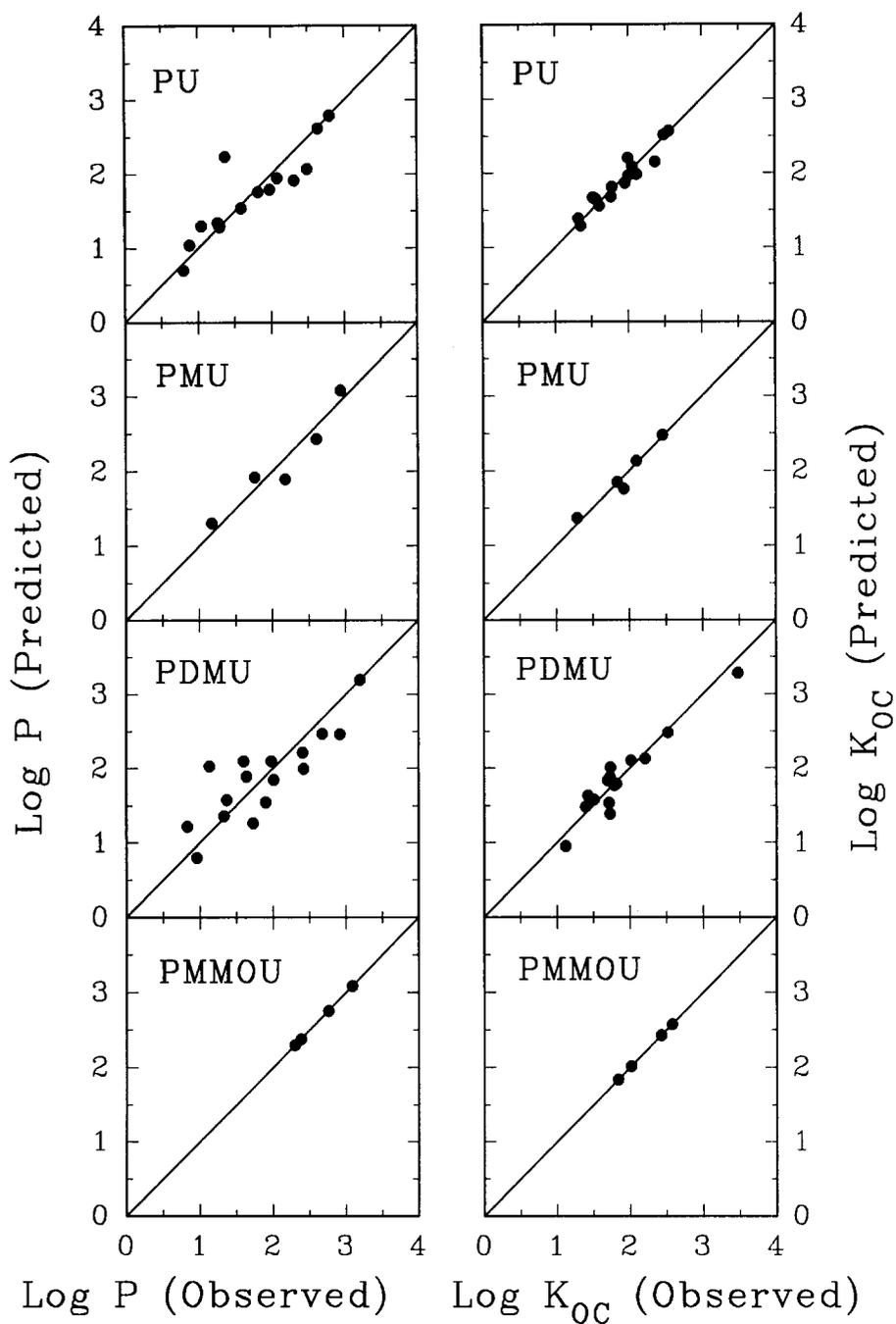
The molecular properties such as molecular cavity, molecular polarity, hydrogen bond acceptor basicity, and hydrogen bond donor acidity are known to affect octanol/water partition process.<sup>8-10</sup> The molecular cavity, represented by molar volume<sup>8</sup> (molecular weight divided by density at 25 C), could be replaced by an intrinsic



**Figure 1.** Predicted  $\log P$  (Eq. 1) and  $K_{oc}$  (Eq. 2) plotted as a function of observed  $\log P$  and  $K_{oc}$  of substituted phenylureas.

Table 3. Regression equations for predicting log  $P$  and  $K_{oc}$  of different chemical classes of phenylureas.

Regression equations	n	r <sup>2</sup>	F	Equation
<b>Phenylureas</b>				
$\log P$	15	0.79	13.6	3
				$= -0.9598 + 0.0242 (VDW_V) - 0.1798 (\mu) - 0.3898 (e_{LUMO})$
$\log K_{oc}$	15	0.92	42.7	4
				$= 0.3376 + 0.0158 (VDW_V) - 0.1591 (\mu) - 0.0524 (e_{LUMO})$
<b>Phenyl-1-methylureas</b>				
$\log P$	5	0.91	10.0	5
				$= -0.0409 + 0.0238 (VDW_V) - 0.5391 (\mu)$
$\log K_{oc}$	5	0.95	19.0	6
				$= 0.1723 + 0.0168 (VDW_V) - 0.3007 (\mu)$
<b>Phenyl-1,1-dimethylureas</b>				
$\log P$	16	0.70	9.3	7
				$= 0.2436 + 0.0131 (VDW_V) - 0.4115 (\mu) - 0.7537 (e_{LUMO})$
$\log K_{oc}$	15	0.91	36.4	8
				$= -1.1505 + 0.0206 (VDW_V) - 0.1879 (\mu) - 0.0215 (e_{LUMO})$
<b>Phenyl-1-methyl-1-methoxyureas</b>				
$\log P$	4	1.00	-	9
				$= 0.4729 - 0.0653 (VDW_V) + 2.6244 (\mu) - 11.8284 (e_{LUMO})$
$\log K_{oc}$	4	1.00	-	10
				$= -6.0038 - 0.00007 (VDW_V) + 1.8209 (\mu) - 6.8824 (e_{LUMO})$
<b>phenyl-1-cycloalkylureas</b>				
$\log P$	4	1.00	-	11
				$= -1.9734 + 0.0217 (VDW_V) - 0.1977 (\mu) - 12.0519 (e_{LUMO})$
$\log K_{oc}$	5	0.86	18.0	12
				$= -0.4183 + 0.0144 (VDW_V)$



**Figure 2.** Predicted  $\log P$  and  $K_{oc}$  plotted as a function of observed  $\log P$  and  $K_{oc}$  for phenylureas (PU) from Eq. 3 and 4, phenyl-1-methylureas (PMU) from Eq. 5 and 6, phenyl-1,1-dimethylureas (PDMU) from Eq. 7 and 8, and phenyl-1-methyl-1-methoxyureas (PMMOU) from Eq. 9 and 10.

molecular volume represented by van der Waals volume<sup>9,10</sup> as a measure of the cavity term in linear solvation energy relationships. The  $VDW_V$ ,  $\mu$ , and  $e_{LUMO}$  in our models represent molecular bulk, molecular polarity, and reactivity (hydrogen bond donor acidity). Recently, models based on  $VDW_V$ ,  $\mu$ , and  $e_{HOMO}$  derived from MOPAC-MNDO molecular orbital calculations have been reported to predict  $\log P$ .<sup>11</sup> The  $e_{HOMO}$  represents the electron donating power of the molecule and is thus related to hydrogen bond acceptor basicity<sup>8,11</sup> while, the  $e_{LUMO}$  in our equations represents the electron accepting power of the molecule and thus related to hydrogen bond donor acidity.<sup>8</sup>

A molecule with a larger  $VDW_V$  and a smaller  $\mu$  and  $e_{LUMO}$  could encounter greater hydrophobic interactions resulting in higher  $\log P$  and  $\log K_{oc}$ . The repulsive interactions of a molecule with the water present in the solution would drive the molecule away from water to a non-polar organic phase such as octanol ( $\log P$ ) or organic carbon ( $K_{oc}$ ).

### CONCLUSIONS

The QSAR models based on three molecular properties, van der Waals volume, dipole moment, and energy of lowest unoccupied molecular orbital together accounted for 59 and 70% of the variation in  $\log P$  and  $K_{oc}$ , respectively. When phenylureas were broadly divided into five chemical classes based upon the substitution on atom N3 of phenylurea, the same three molecular properties explained 70 to 100% of the variation in  $\log P$  and  $K_{oc}$  within these chemical classes. The present models based on molecular properties produce estimates that correlate well with experimental values. These models can accurately predict not only  $K_{oc}$  but also  $\log P$ . Moreover, these models do not require measured or estimated  $\log P$  values to predict  $K_{oc}$ , unlike several existing models. The above analysis supports the basic assumption of QSAR model that the variations in  $\log P$  and  $\log K_{oc}$  within a series of structurally similar compounds can be correlated with changes in parameters which reflect molecular properties. The models presented here are not necessarily an alternative to currently available models for predicting either  $\log P$  or  $K_{oc}$ . Nevertheless, these models can provide a useful starting point for predicting the potential environmental contamination of new compounds even before they are synthesized. Furthermore, these models can be used to create priority lists for testing, so that time, money, and effort can be focused on the potentially most hazardous chemicals.

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### REFERENCES

1. Donaldson, W. T., *Environ. Toxicol. Chem.*, **11** (1992) 887-891.
2. Sabljic, A. & Piver, W. T., *Environ. Toxicol. Chem.*, **11** (1992) 961-972.
3. Camilleri, P., Bowyer, J. R., Gilkerson, T., Odell, B. & Weaver, R. C., *J. Agric. Food Chem.*, **35** (1987) 479-483.

4. Nandihalli, U. B. & Rebeiz, C. A., *Pestic. Biochem. Physiol.*, **40** (1991) 27-46.
5. Nandihalli, U. B., Duke, M. V. & Duke, S. O., *Pestic. Biochem. Physiol.*, **43** (1992) 193-211.
6. Nandihalli, U. B., Duke, M. V. & Duke, S. O., *J. Agric. Food Chem.*, **40** (1992) 1993-2000.
7. Simmons, K. A., Dixson, J. A., Halling, B. P., Plummer, E. L., Plummer, M. J., Tymonko, J. M., Schmidt, R. J., Wyle, M. J., Webster, C. A., Baver, W. A., Witkowski, D. A., Peters, G. R. & Gravelle, W. D., *J. Agric. Food Chem.*, **40** (1992) 297-305.
8. Taft, R. W., Abraham, M. H., Famini, G. R., Doherty, R. M., Abboud, J. M. & Kamlet, M. J., *J. Pharmaceut. Sci.*, **74** (1985) 807-814.
9. Leahy, D. E., *J. Pharmaceut. Sci.*, **75** (1986) 629-636.
10. Hickey, J. P. & Passino-Reader, D. R., *Environ. Sci. Technol.*, **25** (1991) 1753-1760.
11. Nandihalli, U. B., Duke, M. V. & Duke, S. O., *J. Agric. Food Chem.*, **41** (1993) 582-587.
12. Doucette, W. J. & Andren, A. W., *Environ. Sci. Technol.*, **21** (1987) 821-824.
13. De Bruijn, J. & Hermens, J., *Quant. Struct.-Act. Relat.*, **9** (1990) 11-21.
14. Dunn, W. J., III, Koehler, M. G. & Grigoras, S., *J. Med. Chem.*, **30** (1987) 1121-1126.
15. Lewis, D. F. V., *J. Comput. Chem.* **10** (1989) 145-151.
16. Briggs, G. G., *J. Agric. Food Chem.*, **29** (1981) 1050-1059.
17. Lyman, W. J., Reehl, W. F. & Rosenblatt, D. H., *Handbook of Chemical Property Estimation Methods*, 2nd edition, American Chemical Society, Washington, DC. (1990).
18. Sabljic, A., *J. Agric. Food Chem.*, **32** (1984) 243-246.
19. Gustafson, D. I., *Environ. Toxicol. Chem.*, **8** (1989) 339-357.
20. Meylan, W., Howard, P. H. & Boethling, R. S., *Environ. Sci. Technol.*, **26** (1992) 1560-1567.
21. Sabljic, A. & Protic, M., *Bull. Environ. Contam. Toxicol.*, **28** (1982) 162-165.
22. Sabljic, A., *Bull. Environ. Contam. Toxicol.*, **30** (1983) 80-83.
23. Sabljic, A., *Environ. Sci. Technol.*, **21** (1987) 358-366.
24. Domine, D., Devillers, J., Chastrette, M. & Karcher, W., *Pestic. Sci.*, **35** (1992) 73-82.
25. von Oepen, B., Kordel, W., Klein, W. & Schuurmann, G., *Sci. Total Environ.*, **109/110** (1991) 343-354.
26. Worthing, C. R. & Hance, R. J., *The Pesticide Manual, A World Compendium*. 9th edition. The British Crop Protection Council. Surrey, United Kingdom. 1991.
27. Wauchope, R. D., Buttler, T. M., Hornsby, A. G., Augustijn-Beckers, P. W. M. & Burt, J. P., *Rev. Environ. Contam. Toxicol.*, **123** (1992) 1-164.