The Octanol–Water Partition Coefficient of Aromatic Solutes: the Effect of Electronic Interactions, Alkyl Chains, Hydrogen Bonds, and *ortho*-Substitution

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The calculation from structure of the hydrophobic parameter, log *P* (octanol–water), involves the addition of fragment values (or of π constants to parent log *P*) plus correction factors for interactions not present in the standard state from which the *f* or π values were determined. In this paper the important correction factors for multply substituted aromatic solutes are classified as: electronic, negative *ortho*, hydrogen bonding, and alkyl–aryl. The electronic factor F_σ is best treated as a continuous function in a manner similar to Hammett's ρσ product. Both field and resonance components appear to be present in the electronic effect. σ and ρ values for 50 substituents are reported in a generalized structural form which makes possible estimation of many others. While the other factors F_o, F_{HB}, and $F_{\alpha\varphi}$ are probably continuous functions also, they are conveniently treated as ' quantized '. Calculated in this way, the standard deviation for nearly 400 solutes amounts to less than twice the estimated error in their measurement, and thus a more precise estimation of these effects is unwarranted at this time. The overall equation is: observed log *P* = additive log *P* + $\rho\sigma - 0.29F_o + 0.63F_{HB} - 0.15F_{\alpha\varphi}$.

The measurement of the distribution of various solutes between two immiscible liquids has a long history in physical and biological chemistry beginning with Nernst [1] who defined the constant $K_P = (C_{org})/(C_{polar})$. The polar liquid was most often water, and the expression held as long as the solute concentration measured in each phase was that of the same species. The theory, and methods for calculation of this parameter from structure, have been the subject matter for a review article [2] and several books.[3–5] Applications of the hydrophobic parameter are being reported at such a rapid rate that a bibliography is nearly outdated by the time it reaches print, but the following references will serve to lead the reader to some of the primary areas: drug and pesticide design,[6a,b] pharmacokinetics,[6c] anaesthesiology,[6d] environmental transport and soil binding,[6e,f] toxicology,[6g] bioaccumulation,[6h] protein folding,[6i] enzyme binding,[6j,k] enzymic reactions in non-aqueous solvents,[6l] and host–guest complexation.[6m] There exist files of organic structures numbered in the hundreds of thousands for which hydrophobic parameters are desired. Measurement is out of the question for the majority of them. Calculation by computer is the only feasible way of meeting the need in a reasonable time.

In the present paper, octanol–water partition coefficients, in the free energy-based form of log *P*,[7] are analysed in order to quantify the effect of substituent types and their position on an aromatic ring. The purpose of the analysis is two-fold: first, to predict log *P* values more accurately from structure, and second, to understand better the nature of the solvation–desolvation forces as a small solute passes from an aqueous phase to a lipid-like phase. As a basis for solvation theory, this analysis can only be suggestive, because the basic forces which determine ' hydrophobicity ' (that is, the preference for a lipid phase over water) are still the subject of an intense debate.[8]

Hansch and his co-workers were the first to appreciate how the linear free energy approach of Hammett [9] could be applied to partitioning phenomena. In the first successful effort to place log *P* (octanol–water assumed hereafter, unless otherwise specified) on an additive-constitutive basis, Fujita *et al.*[10] discussed the electronic effect in disubstituted benzenes in terms of the change in the sum of π constants compared to the sum of the individual π constants from monosubstituted benzene, the standard state for π, that is, equations (1)—(3).

$$\Pi_{X(std.)} = \log P_{C_6H_5\text{-}X} - \log P_{C_6H_5} \quad (1)$$

$$\Pi_{X(\text{aniline solute syst.})} = \log P_{H_2NC_6H_4X} - \log P_{C_6H_5NH_2} \quad (2)$$

$$\Delta\Pi_X = \Pi_{X(\text{aniline})} - \Pi_{X(std.)} \quad (3)$$

These authors related ΔΠ to the Hammett σ constant [9] by expression (4). For *meta*- and *para*-derivatives in the aniline

$$\Delta\Pi_X = f\sigma_X + c \quad (4)$$

solute system, the coefficient and intercepts are *f* 0.90 and *c* 0.016. The respective values for the phenol solute system are 0.82 and 0.61. *ortho*-Derivatives were not treated.

Instead of developing a set of ΔΠ values for the aniline analogues, another for phenols, a third for phenoxyacetic acids, *etc.*, a more generalized approach is to consider one of the substituents, X, acting on the other, Y, in a way which changes the sum of their Π values. Equation (2) expresses this if we consider Y = NH_2 and X is any substituent with strong electron-withdrawing power, such as NO_2, CN, *etc.* The latter groups will hereafter be referred to as ' inducers ' (I) which act upon ' responders ' (R) of which NH_2 is the most potent example. In general terms the most useful form of the expression is (5). The first three terms on the right-hand side can be considered as the ' simple additive ' log *P* (ALP) and

$$\log P_{XC_6H_4Y} = \log P_{C_6H_6} + \Pi_X + \Pi_Y + \Delta\Pi_{X\leftrightarrow Y} \quad (5)$$

the last term the interactive factor(s) which for electronic effects is designated F_σ.

In the early paper defining the π constant, Fujita *et al.*[10] theorized that ΔΠ was positive in value, at least when Y = OH or NH_2, because in the octanol–water solvent system the superior hydrogen bond-accepting properties of octanol were favoured when an electron-attracting second substituent increased the acidity of the OH or NH_2 group. Since that early work, Fujita has expanded this concept [11,12] to consider the interaction to be bidirectional, that is each substituent can be assigned both a σ value as an inducer and a ρ value as a responder. It is not difficult to imagine how a substituent, such as $CONH_2$ (σ_p 0.36), can act as an inducer when it is on a ring with NH_2. On the other hand, if it is present with NO_2

(σ_p 0.78), the hydrogen-bonding properties of the carboxy- and amino-portions of the carboxamide should be quite different than they were on an electron-rich ring, and it may be considered a responder in this situation. For a group to act simultaneously as an inducer–responder (I/R) is more difficult to rationalize mechanistically, but this possibility will be taken up in the Discussion section.

If the two substituents on an aromatic ring system are in *ortho-* or *peri*-positions, effects other than electronic (field and/or resonance) may well be evidenced by $\Delta\Pi$. For example, an adjacent bulky group might twist the heteroatom attaching a polar group to the ring, decoupling its lone pair(s) from the π bonding system. This explanation was invoked earlier for the observed lowering of $\Sigma\Pi$ for 1,2,3-trimethoxybenzene.[13] This negative *ortho*-effect is referred to in this paper as F_o.

Adjacent substituents having hydrogen-bond donor and acceptor capability and possessing appropriate geometry can also form an intramolecular hydrogen bond. Since this would reduce the solvation potential in water, one would predict, for such substituent pairs, a higher partition coefficient in the *ortho-* than in the *meta-* or *para*-isomers. This is invariably the case for the hydrocarbon–water, $CHCl_3$–water, and CCl_4–water solvent systems. The observed log *P* values are over 3.0 log units higher for the *ortho*-isomers in the most favourable cases, such as *o*-nitrophenol. However, in the octanol–water solvent system both phases lose solvating power when intramolecular hydrogen-bonding occurs and $\Delta\Pi_{HB}^{oct}$ for *o*-nitrophenol appears slightly negative. The structural requirements and the levels of significant positive hydrogen-bond effects are covered in the Discussion section. It will be referred to subsequently as F_{HB}.

The data available to early investigators of this field appeared to support the view that the hydrophobicity of alkanes is essentially unchanged by attachment to an aromatic ring.[14] Since most alkyl substituents on aromatic rings are limited to a single methyl group, reasonable calculations can be made using the same π-CH_3 as was developed for purely alkane chains, namely 0.54. However, consistent positive calculation errors arise when two or more alkyl carbon atoms are attached to one aromatic ring. This is consistent with an earlier finding [15] that there is a different slope in plots of log *P versus* molecular volume for alkyl–aryl hybrids compared with either pure alkyl or aryl solutes. This negative correction factor will be referred to as $F_{\alpha\varphi}$.

Methods

In order to perform a proper multi-variate analysis of data cast in the form of equation (5), considering that F_σ, F_o, F_{HB}, and $F_{\alpha\varphi}$ will each require its own $\Delta\Pi$ term, a sizable file of suitable partition coefficients must be available. One of the primary purposes of the Pomona College Medicinal Chemistry Project [16] is to measure such values, conduct a literature search for others, and act as a clearing house for unpublished determinations. The Project data base, sorted by structure *via* WLN,[17] provided the material for Table 5.

The limits of experimental error were not available for many of the literature values, and so a valid reliability estimate of the factors determined in this paper is not possible. Another source of variance arises from the failure of most investigators to maintain a constant temperature of measurement or to report it in any event. Even though for the aromatic solutes in this study the temperature coefficient ($\Delta\log P/T$) is of the order of only 0.002, this could be significant in evaluating the smaller effects such as $F_{\alpha\varphi}$.

When more than one log *P* value was reported for a given solute, the choice for inclusion in Table 5 was made after considering the following: (a) limits of error, if given; (b) need to suppress ionization; (c) probable precision of analytical method; (d) agreement with a third determination. It should be noted that sometimes a choice was not warranted and an average value was taken. F_σ and $F_{\alpha\varphi}$, can each operate in a solute independently of the others, and so appropriate subsets of Table 5 were selected to analyse these effects first. F_o and F_{HB} are most often superimposed on F_σ or $F_{\alpha\varphi}$, and were analysed later.

Since one of the objectives of this study was to improve the computerized calculation of the hydrophobic parameter, log *P*,[18] it was of high priority to keep F_σ as simple as possible. It was apparent that a procedure based on Fujita's method [11] of separately accounting for σ_m and σ_p as well as allowing each substituent to act bi-directionally would result in calculations having a high precision. Offsetting this would be some formidable programming problems plus the necessity of determining a great number of ρ values for each substituent acting as a responder. The three important simplifications developed in this paper are: (1) use of a single constant (slightly different from Hammett's) for *ortho-*, *meta-*, and *para*-interactions; (2) limiting bi-directionality (I/R) to about one-third the total substituents; (3) use of 'generalized' substituent structures wherever possible to greatly reduce the number of ρ and σ values needed for calculation.

At first it appeared possible to treat F_σ as if it occurred at discrete levels. The highest level would apply where the X of the solute in equation (5) was of the strongly electron-attracting type: NO_2, CN, or N= (*i.e.*, pyridine, following the Jaffé convention of treating the fused nitrogen as a substituent) characterized by a large σ and low ρ, while Y was of the electron-releasing type: O, NH_2. Using equation (5) and regression analysis with $\Delta\Pi_{XY}$ represented by an indicator variable taking the value of 2,1, or 0, an equation was obtained for 250 solutes which reduced the standard deviation approximately three-fold. Treated in this 'quantum level' fashion, F_σ could be either +0.29 or 2(+0.29) with no distinction made between *ortho-*, *meta-*, and *para*-interactions. This procedure presented no serious problem in designing a computer algorithm and, interestingly enough, seemed to show the effect to be a multiple of Rekker's 'Magic Constant'.[5] Some serious limitations of this 'quantized' approach appeared when a wider selection of data was studied, and it became apparent that F_σ could be more effectively treated as a continuous variable, *i.e.* as the product $\rho\sigma$. To obtain ρ values appropriate to their hydrophobic effect, the partioning data were used and a simple program for successive approximations [19] was applied to equation (5) rewritten as (6).

$$\mathrm{OLP} = \mathrm{ALP} + \rho_Y\sigma_X \qquad (6)$$

where OLP = observed log *P* of X-C_6H_4-Y

ALP = additive log *P* = log $P_{C_6H_6}$ + Π_X + Π_Y

$$\rho_Y\sigma_X = \Delta\Pi_{XY}$$

92 Solutes from Table 5, which included only those whose exclusive role as I or R was evident, served as the determinant set. Since an earlier relationship based on the Hammett constant had already been established, the average of σ_m and σ_p was entered as the first approximation on which the first-level ρ values would be estimated. The successive approximations proceeded until the change was < 0.01 in either parameter. As input, both inductive, σ_I,[16] and field effects, $\mathcal{F}$,[16] were also tried, but the final sets of σ/ρ values were essentially identical. They appear in Table 1 together with specific examples of the generalized structures of substituents for which the calculations can be applied. Using the 'training-set' results in a

regression analysis of a larger subset of Table 5, it was determined that the simplifications discussed above were statistically justified, and in addition, it was possible to treat the halogens as a single class.

The partition coefficient appears to follow other physical chemical parameters in respect to the difficulty of separating and evaluating polar and steric effects for *ortho*-substituents.[20,21] Ogino *et al.*[22] developed an equation using σ_p, E_s, and $\mathscr{F}$ to explain the $\Delta\Pi$ observed in 2- and/or 6-substituted guanamines where bulky groups keep the two rings from being planar. To account for the electronic effect, σ_p was used (because of the lack of reliable σ_o values) and $\mathscr{F}$ added as a correction term.

It is reasonable to suppose that, like ring twisting, substituent twisting could lead to the lowering of log *P*, an effect frequently seen in *ortho*-substitution. However, since E_s values were not available for many of the substituents studied, and a calculated E_s[23] did not significantly reduce the variance over a simple 'quantized' correction, the latter, simpler procedure was pursued. For all 1,2-disubstituted solutes, where intramolecular hydrogen-bonding would not affect log *P* (see below), the difference of log P_{ortho} − average log $P_{meta\,+\,para}$ was tabulated. Where a value for only the *meta*- or *para*-isomer was available, it was used in place of the average. In the cases where the difference (a negative number) was significantly different from zero (*i.e.*, lower than <0.1), both members of the pair were entered into F_o (Table 3). With two exceptions it was possible to use the same generalized substituent structures used in Table 1 for F_σ. The average for all the low-level differences (*e.g.* where Y = O or OH) was −0.28. This substituent class was taken as the lowest level for F_o, and as an indicator variable in the regression equation, each member was given a value of 1. On this scale the highest factor assigned (for benzene-1,2-dicarboxamide) was 5.* Other F_o values were assigned the nearest multiple of the difference, *ortho* − average of (*meta* + *para*), for the substituents qualifying for any given generalized structure.

The inner square in Table 3 indicates the interaction of 1,2-substituents where intramolecular hydrogen-bonding greatly *increases* log *P*. These are given an indicator variable value of 1.0 in appropriate regression equations. This includes the F_o described above, and thus both indicator variables are never called for with a 1,2-disubstituted aromatic compound. With one possible exception, F_{HB} does not appear to be a continuous function in the compounds studied, nor was more than one level needed to account for it.

Results and Discussion

Electronic Effect.—The first subset of Table 5 selected for analysis (1—196) comprises those solutes which should only show a single, uni-directional effect, *i.e.*, $F_\sigma = \rho_1\sigma_1$. No *ortho* or alkyl substituents are present in this set of 196 solutes. Using the ρ and σ constants in Table 1 (see Methods section), equation (7a) was derived by regression.

$$\text{OLP} = 0.993(\pm0.018)\text{ALP} + 0.921(\pm0.075)\rho_1\sigma_1 \quad (7a)$$
$$+0.007(\pm0.044)$$
$$n = 187;\ s = 0.0976;\ r^2 = 0.986$$

It is apparent that equation (7a) meets the requirements that the coefficients of the (ALP) and (ρσ) terms be close to 1.0 and the intercept close to 0.0. In this and all regression equations which follow, *n* = the number of data points in the regression, *s* = the standard deviation from the regression, r^2 = the square of the coefficient of regression (also = fraction of the variance 'explained' by the equation), and the numbers in parentheses are the 95% confidence limits on each coefficient.

A reasonable estimate of average experimental error for the partition coefficients used is ±0.05 (in log units), and so any simplified calculation method which results in a standard deviation less than twice this amount is worthwhile, especially since its incorporation into a computer algorithm becomes entirely feasible. The simplifications which were used in this and the following equations which include F_σ are four: (1) use of a single electronic parameter for *ortho*-, *meta*-, and *para*-interactions; (2) assignment of most substituents either to an I or an R class; (3) use of generalized substituent structures, each member of a class being assigned the same ρ or σ value; (4) treating the halogens as a single class (except for the F_o of fluorine as noted in Table 3).

Equation (7a) can be compared to (7b) which has no F_σ term. Solute 163 in equations (7a and b) was dropped from

$$\text{OLP} = 0.888(\pm0.032)\text{ALP} + 0.464(\pm0.045) \quad (7b)$$
$$n = 187;\ s = 0.20;\ r^2 = 0.942$$

the regression because it was out of line with the higher homologues 164—167. Solute 58 probably requires a special effect for alkoxy adjacent to a fused nitrogen, as do 382 and 383 in a later subset. Solute 112, a phosphate ester, probably requires a small bond correction for alkyl chains beyond methyl. There is no apparent reason to consider the other data points dropped (11, 60, 87, 96, 128, 154) as representative of effects as yet unaccounted for until repeat measurements confirm data reliability. Even when all the data points are retained, as in equation (7c), the interpretation remains the same as in equation (7a).

$$\text{OLP} = 0.975(\pm0.021)\text{ALP} + 0.849(\pm0.088)\rho_1\sigma_1 \quad (7c)$$
$$+0.054(\pm0.051)$$
$$n = 196;\ s = 0.118;\ r^2 = 0.979$$

The use of generalized substituent structures (Table 1) has some important implications for solvation theory as well as being advantageous because of its simplicity. As noted above, hydrogen-bond donating ability appears to be an important criterion for a substituent's responsiveness to electronic enhancement of hydrophobicity. The substituents with the highest ρ values (NH, 1.08; OH, 1.06) have this parameter reduced by one-half if the hydrogen(s) on the heteroatom is replaced. In the case of NH, the hydrogen-donating can be 'insulated' from the ring by an electronegative group and still retain a relatively high ρ value, as shown by SO_2NH = 0.88 and C(=O)NH = 0.72. This is not true for OH since CO_2H becomes much like C(=O) (ρ 0.35 and 0.27, respectively). It is also worthy of note that with its remaining bond, NH can be attached to an electron-releasing group such as CH_3 or NH_2, or to an electron-attracting group such as carbonyl or SO_2CF_3, and the same ρ value persists. It would seem that the presence of the donatable hydrogen atom is important rather than its acidity. Even when it has no attached hydrogen atoms to act as donors, the nitrogen atom (as compared to oxygen) appears to promote ρ values for the groups which contain it: $-N\lesssim$ = 0.61 *versus.* $^-O^-$ = 0.50; $^-C(=O)N\lesssim$ = 0.6 *versus* $^-C(=O)O^-$ = 0.27.

Optimization of Hammett σ constants to the data one has

* For example: log *P* of benzene-1,2-dicarboxamide = −1.73; for the 1,3-analogue, log *P* = −0.21; Δlog *P* = −1.52; −1.52/−0.28 = 5.

Table 1. σ and ρ constants

No.	σ	ρ	Generalized structure	Examples
1	0.84	0.00	−N=	pyridine, quinoline [a]
2	0.71	0.00	$-SO_2F$	
3	0.65 *	0.00	$-SO_2-X$	X = alk, $N(Me)_2$
4	0.65	0.00	−CN	
5	0.60	0.00	$-NO_2$	
6	0.49	0.00	$-CF_3$	
7	0.28	0.00	Halogens	F, Cl, Br, I
8	0.58	0.44 *	−CHO	
9	0.51	0.27	−C(=O)−X	X = alk, OCH_3, C_6H_5, $N(Me)_2$
10	0.32	0.35 *	$-CO_2H$	
11	0.32	0.72	−CONH−X	X = H, NH_2, C_6H_5, alk
12	0.17 *	0.50 [b]	−O−X	X = alk, $CONHCH_3$, $CON(Me)_2$, CH_2CO_2H, $PO(O\text{-alk})_2$, $COCH_3$
13	0.50 [c]	0.88 [c]	$-SO_2NH-X$	X = H, C_6H_5
14	0.00 [d]	0.50 [d]	−S−X	X = H, alk
15	0.00	0.61	−N<	$-N(Me)_2$, $-N{=}NN(Me)_2$
16	0.00	1.06	−OH	
17	0.00	1.08	−NH−X	X = COMe, $CON(Me)_2$, CHO, alk, $CONHC_6H_5$, C_6H_5, SO_2CF_3, H

* Not determined by successive approximation program.

[a] Effect cut in half for responders on non-hetero-ring. [b] With original training set of 90 solutes, 0.51 was obtained. With the set enlarged with bi-directional solutes, 0.50 gave coefficients for the F_σ term closer to unity. [c] Acts *either* as I or R but not both at the same time, *i.e.* it is not truly bi-directional; exception is solute 208 in Table 5. [d] Not well characterized; should be considered tentative.

at hand has been previously proposed,[24,25] but there is an understandable resistance to the undue proliferation of special sets.[26] Unlike the usual Hammett model, however, where the substituent is at some distance from the reaction centre, the partitioning process is a solvation equilibrium where each substituent is a reaction centre. Other evidence that the relative solvation energy between octanol and water may, indeed, call for a modified σ parameter comes from the Hammett treatment of pK_a values in mixed solvent systems.[27] The usual Hammett σ values are excellent parameters for prediction up to 80—85% organic solvent, at which point the standard deviation rises markedly. In water-saturated octanol (2% water) the electronic influence on solvation may not exactly follow the usual Hammett model systems. If equation (7a) is recalculated with accepted σ_m and σ_p values, the standard deviation is increased by 10% (to 0.1084). This is deemed sufficient reason to use the optimized set in the computer program. A qualitative comparison of the partitioning-optimized σ values with the classical Hammett values discloses no obvious trends. Those which remain essentially unchanged are CF_3, CO_2H, CONH, and the halogens. Those which are lower for F_σ are NO_2 and SO_2^- (F, Alk, or N<). Those which are higher are CN, N=, C(=O), and CHO.

As is seen in Table 1, six of the common substituents have significant values of both ρ and σ and thus must be classed I–R. The solutes in Table 5 showing this I–R effect (197—223) have a second σ entered in column 9 and ρ in 10. When these 26 are added to the 187 solutes in the simple F_σ set of equation (7), the regression equations (8a and b) are obtained. The

$$OLP = 0.971(\pm 0.018)ALP + 0.854(\pm 0.078)\rho_1\sigma_1 \quad (8a)$$

$$+0.666(\pm 0.042)$$
$$n = 213;\ s = 0.108;\ r^2 = 0.983$$

$$OLP = 0.991(\pm 0.017)ALP + 0.925(\pm 0.074)\rho_1\sigma_1 \quad (8b)$$

$$+1.144(\pm 0.334)\rho_2\sigma_2 + 0.006(\pm 0.042)$$
$$n = 213;\ s = 0.0976;\ r^2 = 0.986;\ F_{1\,210} = 39.5$$

larger 95% confidence limits on the ' reverse ' electronic term, $\rho_2\sigma_2$, in equation (8b) clearly indicate that the available data do not characterize it as well as they do the ' forward ' term, but its significance is well established by the *F* test, and the coefficient does not differ significantly from unity.

The attenuation of electronic effects on an adjacent fused ring depends a great deal upon the relative contribution of field and resonance components. All but one of the examples currently in hand are limited to N= as the inducer, as seen in Table 2. For the R substituents NH_2, $NHCOCH_3$, OCH_3, and $COCH_3$ it seems appropriate to reduce the ρ value by one-half. An exception is the dimethylamino-substituent which apparently responds unattenuated. Further studies on these and the di-substituted naphthalenes are under way.

Alkyl–Aryl Effect.—The third subset from Table 5 to be analysed (224—293) contains 70 solutes, each with the aromatic–aliphatic factor $F_{a\varphi}$. The regression equation, dropping but one of these, is (9a). The $F_{a\varphi}$ term is entered as an indicator

$$OLP = 1.029(\pm 0.018)ALP - 0.110(\pm 0.03)F_{a\varphi} \quad (9a)$$

$$-0.077(\pm 0.042)$$
$$n = 69;\ s = 0.062;\ r^2 = 0.996$$

variable which takes the value $(n - 1)$, where n is of the number of alkyl carbon atoms * present on the ring system. Methyl groups *ortho* to each other (285) or to Cl (224) need no F_o and are included in equation (9a), but those adjacent to CO_2H or CONHX (327 and 352) do require it and are treated later.

ortho-*Effects.*—As discussed in the Methods section, the total effect of *ortho*-substitution can be composed of three components: (1) an electronic effect, F_σ, considered as equal to that of *meta* or *para*; (2) a negative effect, which may in part stem from decoupling *via* twisting, and in part to a reversal of the field effect if two polar substituents are in close proximity; (3) a positive effect when certain types of intramolecular hydrogen-bonds can occur, *i.e.*, F_{HB}. It is convenient to apply the F_σ in any case, but whenever F_{HB} is called for, it should include *all* the remaining *ortho*-effect.

Hydrogen Bonding.—When 15 solutes (294—308) containing an octanol-sensitive intramolecular hydrogen-bonds are added to the original F_σ subset, the regression equation (10) is obtained.

$$OLP = 0.994(\pm 0.017)ALP + 0.930(\pm 0.071)\rho_1\sigma_1 \quad (10)$$

$$+0.63(\pm 0.055)F_{HB} + 0.003(\pm 0.04)$$
$$n = 201;\ s = 0.098;\ r^2 = 0.987$$

Except for one solute (303), F_{HB} appears restricted to a carbonyl moiety functioning as hydrogen-acceptor and either OH or NH acting as hydrogen-donor. Both ' halves ' must be attached directly to the ring, but the NH, as noted for F_σ, may be followed either by a strongly electronegative moiety, such

* Either as chains or rings (227, Table 5), but not CH_2X. Solutes 227 and 286 indicate that an upper limit for this indicator variable may be 3.

Table 2. Attenuation of electronic effect, F_σ, in adjacent fused ring

Compound	Obs. log *P*	Add. log *P*	σ	½ρ *	Calc. log *P*	Deviation
1 5-Aminoquinoline	1.16	0.80	0.84	0.54	1.25	+0.09
2 6-Aminoquinoline	1.28	0.80	0.84	0.54	1.25	−0.03
3 6-Acetylaminoquinoline	1.55	1.06	0.84	0.54	1.51	−0.04
4 6-Methoxyquinoline	2.20	2.01	0.84	0.26	2.23	+0.03
5 7-Methoxyquinoline	2.37	2.01	0.84	0.26	2.23	−0.14
6 6-Acetylquinoline	1.58	1.48	0.84	0.13	1.59	+0.01
7 1-Aminoacridine	2.47	2.17	0.84	0.54	2.62	+0.15
8 7-Dimethylaminoquinoline	2.71	2.21	0.84	0.25	2.42	−0.29
				(0.50)	(2.63)	(−0.08)
9 1-Dimethylamino-5-sulphonamidonaphthalene	2.01	1.66	0.50	0.25	1.79	−0.22
				(0.50)	(1.91)	(−0.10)

* Examples of 2-, 3-, and 4-substituted quinolines with full ρ values can be found in Table 5. Values in parentheses for dimethylamino-analogues have full ρ values.

Table 3. *ortho*-Factor levels

	1. CN	2. NO_2	3. CF_3	4. I	5. Br	6. Cl	7. F	8. SO_2NH–(V)	9. C(O)–(W)	10. CHO	11. CO_2H	12. CONH–(X)	13. O–(Y)	14. SCH_3	15. SH	16. OH	17. NH–(Z_1)	18. NH–(Z_2)	19. NH_2	20. CH_3	21. Pr^i	22. Bu^t	
1. CN													0			0							1.
2. NO_2	0					1		1	1	0	1	3	1			0		2	0	(0)		1	2.
3. CF_3																0							3.
4. I								*2*	*1*		2	*3*	1			1	*2*						4.
5. Br			(1)					*2*	*1*		2	3	1			1	*2*						5.
6. Cl				0				2	1		2	*3*	1			1	2	3	0	0			6.
7. F					*0*			*1*	0		1	1	0			1	1						7.
8. SO_2NH–(V)																				0			8.
9. C(O)–(W)								3			3		1			intra-				0			9.
10. CHO																molecular				0			10.
11. CO_2H											4		1*		0	hydrogen				1			11.
12. CONH–(X)												5	0†			bonds				2			12.
13. O–(Y)													0			(1)				0		1	13.
14. SCH_3																			1				14.
15. SH																	0						15.
16. OH															0					0(0)	(0)		16.
17. NH–(Z_1)																			0	0			17.
18. NH–(Z_2)																				0			18.
19. NH_2																							19.
20. CH_3																							20.
21. Pr^i																							21.
22. Bu^t																							22.

V = H
W = OMe, Me, $N(Me)_2$
X = H, NH_2
Y = CONHMe, COMe, Me, $CON(Me)_2$, OCH_2CO_2H
Z_1 = $CONH_2$
Z_2 = COMe
*This level becomes 5 if Y = C_6H_5
( ) = borderline effect
Within submatrix, 'hydrogen bonds', $F_0 = 0$; $F_{HB} = 1$.
† = anomalous; see text
italicized numbers are interpolated.

as carbonyl, or an electron-releasing group such as methyl or amino. The one outlier, *o*-hydroxybenzamide (306), needs an even larger correction (*i.e.*, 0.63 + 0.34), indicating that a continuous function for F_{HB} may eventually be required as a greater variety of *ortho*-substituents are included in the data set.

If F_{HB} is the actual source of the +ΔΠ in *o*-nitroaniline (303), it would appear that both hydrogens on the nitrogen are necessary, because *N*-methyl-*o*-nitroaniline (343) and *o*-nitroacetanilide (342) do not show this ΔΠ. And the fact that *o*-nitrophenol (391) also does not need correction raises the question of whether a nitro-group *can* participate in an intramolecular hydrogen-bond which is solvated differently by octanol and water. However, there is evidence that thiocarbonyl, as well as carbonyl, can act as an octanol-sensitive hydrogen-acceptor. Assuming the σ of the thioamide group in *o*-aminothiobenzamide (log *P* 0.99) to be slightly lower than the oxygen analogue (307), this would still leave a factor of *ca.* +0.45 to be accounted for by something like F_{HB}.

Negative ortho-*Effect*.—There is no compelling reason to believe that non-hydrogen-bonding *ortho*-effects should be 'quantized' rather than being better represented by a continuous function. (However, for arguments favouring quantized effects in hydrophobicity, see ref. 5.) Nevertheless, for ease of computer calculation it was decided to approximate it as a multiple of a fixed lowest level since attempts to rationalize it in terms of size (E_s) and field effect ($\mathscr{F}$) were no improvement (see Methods section). In Table 3 the appropriate interaction levels between the substituents are displayed in matrix format. The regression equation for the 59 solutes (309—369) in the non-hydrogen-bonding subset is (11a). Merging this set with the subset containing just F_σ effects [equation (8b)], the four-variable equation becomes (11b).

$$\text{OLP} = 0.979(\pm0.036)\text{ALP} + 1.052(\pm0.196)\rho_1\sigma_1 \quad (11a)$$

$$+1.646(\pm0.73)\rho_2\sigma_2 - 0.300(\pm0.031)F_\sigma - 0.008(\pm0.105)$$
$$n = 59;\ s = 0.085;\ r^2 = 0.990$$

$$\text{OLP} = 0.988(\pm0.016)\text{ALP} + 0.943(\pm0.068)\rho_1\sigma_1 \quad (11b)$$

$$+1.228(\pm0.298)\rho_2\sigma_1 - 0.289(\pm0.017)F_\sigma + 0.002(\pm0.04)$$
$$n = 272;\ s = 0.0958;\ r^2 = 0.986$$

Although far from complete, Table 3 contains a great deal of useful information. For instance, substituents can be placed in an approximate order of their ability to cause an F_o: CONH, $NHCOCH_3 > CO_2H$, SO_2NH, $NHCONH_2 > CO_2 >$ I, Br, Cl > F, $NO_2 >$ O, OH > NH_2. Of course these distinctions may not apply in all pairings. For instance, Cl > NO_2, when paired with SO_2NH, CO_2 H, OH, and $NHCOCH_3$, but Cl = NO_2 for CO and O. The most glaring anomaly is the alkoxy-amido pairing (solute 209). It requires no F_o although, from a comparison with the carboxy-, carbonyl-, and halogen-alkoxy-pairings, one would be expected. Since 2-methoxybenzoylhydrazine behaves as expected (354; $F_o = 1$), it is possible that the substituent CONHX cannot be generalized in a way that X = either H or NH_2. There are insufficient data to characterize an *ortho*-$N(CH_3)_2$, but the fact that no factor is required with methyl adjacency is surprising (280).

An effort is under way to fill in the blank spaces in Table 3 and to characterize the effect of 2,6-disubstitution. In the meantime, it is likely that calculations of log *P* using interpolated values (in italics in Table 3) would be more accurate

Table 4. Multiple electronic effects

	Solute	OLP	ALP	F_σ	Calc.	Deviation
1	2,3-Dichloroaniline	2.78	2.32	0.75 (0.28 + 0.28) (1.08)	2.77	+0.01
2	3,4-Dichloroaniline	2.78	2.32	0.75 (0.28 + 0.28) (1.08)	2.77	+0.01
3	2,4-Dichlorophenol	3.08	2.88	0.75(2) (0.28) (1.06) − 0.28 *	3.05	+0.03
4	3,5-Dichlorophenol	3.44	2.88	0.75(2) (0.28) (1.06)	3.33	+0.11
5	2,4-Dibromophenol	3.22	3.18	0.75(2) (0.28) (1.06) − 0.28 *	3.34	−0.12
6	3,5-Dinitrobenzamide	0.83	0.12	0.75(2) (0.6) (0.72)	0.77	+0.06
7	2-Aminopyrimidine	−0.22	−1.63	0.75(2) (0.84) (1.08)	−0.27	+0.05
8	2-Aminopyrazine	−0.07	−1.45	0.75(2) (0.84) (1.08)	−0.09	+0.02
9	2,6-Dinitro-4-trifluoromethyl-aniline	2.29	1.26	0.6 (0.60 + 0.60 + 0.49) (1.08)	2.35	−0.06
10	2-Iodo-4-aminobenzoic acid	1.65	1.99	0.75 (0.28 + 0.32) (1.08 + 0.35) ÷2 − 2 (0.28) *	1.75	−0.10
11	2-Bromo-4-aminobenzoic acid	1.49	1.73	(as 10)	1.49	0.0
12	2-Chloro-4-aminobenzoic acid	1.33	1.58	(as 10)	1.34	−0.01
13	2-Fluoro-4-aminobenzoic acid	1.29?	1.01	0.75 (0.28 + 0.32) (1.08 + 0.35) ÷2 − 0.28 *	1.05	−0.24
14	2,3,4,6-Tetrachlorophenol	4.10	4.30	0.35(4) (0.28) (1.06) − 2 (0.28) *	4.16	−0.06

* F_o; see text and Table 3. ? = double value.

than calculations ignoring this effect altogether. Interpolation was done keeping in mind the likelihood that both E_s and $\mathscr{F}$ play a role.[22] Thus, in the halogen series, where the field effects remain nearly constant, but the size varies from fluorine up to iodine, the remainder of the series can be estimated when the effect of only one member is known. The methyl group lacks a positive field effect, but is the same size as a bromide. Thus one expects it to have a lower effect, as is noted when each is paired with CO_2H.

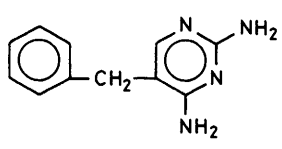
It should be noted that the range of measured solutes represented by the generalized structures shown in Table 3 is not as great as in Table 1. Note also that in Table 3 $NHCONH_2$ must be separated from $NHCOCH_3$. However, since the E_s parameter depends greatly on the bulk close to the attachment atom,[28] and the field effect may in this case operate only over very short distances, it is a reasonable expectation that much of the generality implied in Table 3 will be supported, and the symbols V, Z_1, and Z_2 will then represent more than one substituent each.

Multiple I and R Effects.—In the above treatment of disubstituted aromatic solutes, the correction factors F_σ, F_o, F_{HB}, and $F_{\alpha\varphi}$ combine to reduce the deviation between the observed log P and the ' simple additive ' log P by a factor of 3 or better. For many applications this improvement could be vital. But an even greater need for correction arises when the solute contains multiple I or R groups. In many cases, as will be seen below, $\Delta\Pi$ is >2 log units, and *uncorrected calculations would be entirely misleading*. The problem is complicated by the fact that, for calculating hydrophobicity, the σ parameters are not truly additive as they are in the ideal Hammett application. Furthermore, the classic Hammett applications do not envisage the use of more than one ρ in any given expression. From an examination of just the multichlorinated aromatics it would seem that the electronic effect upon a polar substituent by a second chlorine was only half as great as the first, and all further chlorines could be added without considering an electronic effect at all. On the other hand, the ρ values of multiple R substituents might best be either added or averaged, depending upon the particular inducer present.

To study the effect when two or more inducers are present with a single responder, the ideal solutes would appear to be anilines or phenols substituted in the 3-, 4-, and/or 5-positions with NO_2, CF_3, SO_2F, or the halogens. Substitution in the 2-position can be accepted to enlarge the set since allowance can be made for F_o. Unfortunately, there are no data for the di-CF_3, the di-SO_2F compounds, or the dinitroanilines. The di- and tri-nitrophenols are anomalous when partitioned in 0.1N-HCl to suppress ionization [log P (picric acid) = 0.89]. Quite a few multi-halogenated phenoxyacetic acids have been measured, but they are not considered suitable for analysis of this effect for two reasons: the value for the O-X substituent is low, making the system rather insensitive, and also there was no effort to suppress ionization in these measurements. There is no way of making sure that the electronic effect on pK_a (*i.e.* the ratio of neutral to ionized solute) is *not interfering with the desired observation of purely hydrophobic effects.*

This leaves a rather limited set of halogenophenols, halogenoanilines, halogenobenzamides, and halogenoanthranilic acids which appear in Table 4. From this set can be drawn the tentative conclusion that the effect diminishes with the number of I groups so that the coefficient for the Σσ follows the series: 1.0; 0.75; 0.60; 0.35. It will be noted that in solutes 10—13 in Table 4, where an R and I–R substituent appear together, the ρ values are averaged. Other examples of averaging ρ values for multiple occurrence of R groups are 315, 361, 382, 383, and 385—389 in Table 5.

In contrast to the examples just cited, an aromatic nitrogen (N=) appears to affect multiple responders on its ring at ' full strength ', *i.e.*, their ρ values are added, not averaged. As multiple I groups, however, the attenuation of σ for N= follows the same series illustrated in Table 4. The only examples in the present data base are those where the multiple R groups are amino and the multiple I groups are N=, *i.e.*, amino-substituted pyrimidines and *sym*-triazines. The following calculations would indicate that there may be a maximum value for F_σ of 2.8:



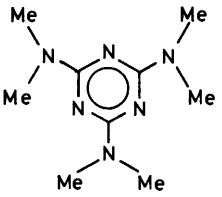
$$\text{ALP} = \log P(\text{pyrimidine}) + 2\,\Pi_{NH_2} + \Pi_{CH_2C_6H_5} \quad \text{(C-1)}$$

$$0.40 + 2(-1.23) + 2.01 = -0.85 +$$

$$F_\sigma = (n = 2)\text{coef.} \quad \Sigma\sigma \quad \Sigma\rho$$

$$(0.75) \times (0.84 + 0.84) \times (1.08 + 1.08) = 2.72$$

obs. = 1.58 calc. = 1.87



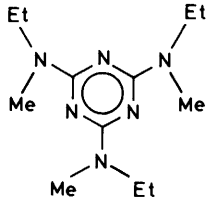
ALP = log *P*(triazine) + 3 $\Pi_{N(Me)_2}$ (C-2)

$-0.73 + 3(0.18) = -0.19 +$

F_σ = (n = 3)coef. $\Sigma\sigma$ $\Sigma\rho$

$(0.6) \times 3(0.84) \times 3(0.61) = 2.77$

obs. = 2.73 calc. = 2.58

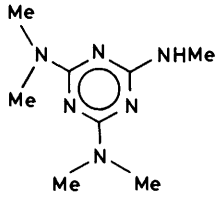


ALP = log *P*(triazine) + 3$\Pi_{N(Me)Et}$ (C-3)

$-0.73 + 3(0.64) = 1.19 +$

F_σ = as C-2 = 2.77

obs. = 3.90 calc. = 3.96



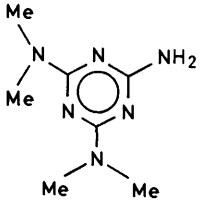
ALP = log *P*(triazine) + 2 $\Pi_{N(Me)_2}$ + Π_{NHMe} (C-4)

$-0.73 + 2(0.18) + (-0.47) = -0.84 +$

$F_\sigma = 0.6(3)(0.84)(1.08 + 0.61 + 0.61) = (3.48)$

take max F_σ = 2.80

obs. = 1.83 calc. = 1.96



ALP = log *P*(triazine) + 2 $\Pi_{N(Me)_2}$ + Π_{NH_2} (C-5)

$-0.73 + 2(0.18) + (-1.23) = -1.60 +$

F_σ = as C-4 = 3.48; take max F_σ = 2.80

obs. = 1.20 calc. = 1.20

Groups on Insulating Side-chains.—There is a positive $\Delta\Pi$ for an I–R interaction even when the responding substituent is not directly attached to the ring but is instead on a benzyl carbon atom. This lower but significant F_σ indicates that the field effect [29] must play an important role. The data now in hand are insufficient to determine whether the attenuation is equal for all groups listed in Table 1. A factor of 0.6 has been applied to the ρ values of solutes 393—397 and 401 with reasonably satisfactory results. The reverse interaction, where the I substituent is on the benzyl carbon and the R is attached to the ring, appears to need no correction factor. Thus, log *P* for *m*- and *p*-hydroxyphenylacetic acid is 0.85 and 0.75, respectively. The 'simple additive' log *P* is 0.74, and so it would appear that no more than 15% of the 'directly attached' effect was transmitted. In the case of *m*- and *p*-methoxyphenylacetic acid, both groups are I–R and the 'simple additive' log *P* is only 0.1 lower than the observed values, which are 1.50 and 1.48, respectively.

If the role of resonance in the electronic enhancement of log *P* were dominant, one would predict that substituents on the styryl carbon atom would interact strongly with others on the ring. This appears to be the case for an NO_2 group on the styryl carbon, as the following examples indicate:

	OLP	ALP	ρ σ	
3-methoxy-β-nitrostyrene	2.37	2.09	(0.5) × (0.6) = 2.39	(C-6)
4-methoxy-β-nitrostyrene	2.20	2.09	(0.5) × (0.6) = 2.39	(C-7)
3-hydroxy-β-nitrostyrene	2.07	1.44	(1.06) × (0.6) = 2.08	(C-8)
4-hydroxy-β-nitrostyrene	2.12	1.44	(1.06) × (0.6) = 2.08	(C-9)

The data for substituted cinnamic acids, on the other hand, cannot be interpreted directly in this fashion. The 4-hydroxy- and 3,4-dimethoxy-cinnamic acids (log *P* = 1.79 and 2.34, respectively) need no F_σ to correct the 'simple additive' log *P*, while the ρσ values from Table 1 seem to apply well for the 4-methoxy- and the 4-hydroxy-3-methoxy-analogues (log *P* = 2.68 and 1.87, respectively).

The final subset in Table 5, solutes 369—401, include examples of mixed and multiple factors. The ρ and σ values from Table 1 were used with adjustments appropriate to the methods discussed above. The overall regression equation, dropping 15 data points for reasons discussed above, is (12a). If

$$\text{OLP} = 0.987(\pm0.012)\text{ALP} + 0.924(\pm0.054)\rho_1\sigma_1 \quad (12a)$$

$$+1.036(\pm0.22)\rho_2\sigma_2 - 0.286(\pm0.016)F_o + 0.624(\pm0.053)F_{HB}$$

$$-0.153(\pm0.022)F_{a\varphi} + 0.018(\pm0.029)$$

$$n = 386;\ s = 0.0950;\ r^2 = 0.990$$

all the data points are used, the statistics are affected, but there is no significant change in the values for the factors which are derived, as is seen in equation (12b). If no correction

$$\text{OLP} = 0.972(\pm0.013)\text{ALP} + 0.907(\pm0.06)\rho_1\sigma_1 + \quad (12b)$$

$$0.910(\pm0.25)\rho_2\sigma_2 - 0.282(\pm0.019)F_o + 0.640(\pm0.059)F_{HB}$$

$$-0.137(\pm0.025)F_{a\varphi} + 0.042(\pm0.034)$$

$$n = 401;\ s = 0.111;\ r^2 = 0.986$$

factors are employed, the observed log *P* and 'simple additive' log *P* are related as in equation (12c).

$$\text{OLP} = 0.812(\pm0.03)\text{ALP} + 0.465(\pm0.054) \quad (12c)$$

$$n = 386;\ s = 0.323;\ r^2 = 0.881$$

Comparing equations (12a and c), we can judge the significance of the five correction terms (four, if $\rho_1\sigma_1$ and $\rho_2\sigma_2$ are combined as F_σ) by an *F* test: $F_{5\ 379} = 810$.

Giving more weight to the earlier equations from the subsets dealing with the least variety of factors, the preferred values are: $F_\sigma = \rho_1\sigma_1 + \rho_2\sigma_2$ with ρ and σ values taken from Table 1, $F_o = -0.15$, $F_{HB} = +0.63$, and $F_{a\varphi} = -0.29$.

Table 5. Observed partition coefficients and parameters for aromatic solutes

	Solute	OLP†	ALP ‡	σ_1	ρ_1	*a* ORTH *b* HBND *c* ALPH *a b c*	σ_2	ρ_2	p_{red}	Deviation
1	Br-C_6H_4-3-OCONHCH$_3$	2.25	2.07	0.28	0.50	0 0 0	0.00	0.00	2.19	0.06
2	Br-C_6H_4-4-NHCOCH$_3$	2.29	2.02	0.28	1.08	0 0 0	0.00	0.00	2.29	0.00
3	Br-C_6H_4-4-OCONHCH$_3$	2.17	2.07	0.28	0.50	0 0 0	0.00	0.00	2.19	−0.02
4	Br-C_6H_4-4-COCH$_3$	2.43	2.40	0.28	0.27	0 0 0	0.00	0.00	2.45	−0.02
5	F-C_6H_4-3-OCONHCH$_3$	1.48	1.35	0.28	0.50	0 0 0	0.00	0.00	1.48	0.00
6	F-C_6H_4-4-NHCOCH$_3$	1.47	1.30	0.28	1.08	0 0 0	0.00	0.00	1.58	−0.11
7	F-C_6H_4-4-OCONHCH$_3$	1.28	1.35	0.28	0.50	0 0 0	0.00	0.00	1.48	−0.20
8	F-C_6H_4-4-OCOCH$_3$	1.74	1.63	0.28	0.50	0 0 0	0.00	0.00	1.75	−0.01
9	F-C_6H_4-4-COCH$_3$	1.72	1.72	0.28	0.27	0 0 0	0.00	0.00	1.78	−0.06
10	CF_3-C_6H_4-3-NHCONMe$_2$	2.36	1.86	0.49	1.08	0 0 0	0.00	0.00	2.34	0.02
11 *	CF_3-C_6H_4-3-NHCOCH$_3$	2.20	2.04	0.49	1.08	0 0 0	0.00	0.00	2.52	−0.32
12	CF_3-C_6H_4-3-OCONHCH$_3$	2.37	2.09	0.49	0.50	0 0 0	0.00	0.00	2.30	0.07
13	CF_3-C_6H_4-3-OCOCH$_3$	2.63	2.37	0.49	0.50	0 0 0	0.00	0.00	2.58	0.05
14	Cl-C_6H_4-3-COCH$_3$	2.51	2.29	0.28	0.27	0 0 0	0.00	0.00	2.34	0.17
15	Cl-C_6H_4-4-NHCOCH$_3$	2.05	1.87	0.28	1.08	0 0 0	0.00	0.00	2.14	−0.09
16	Cl-C_6H_4-4-OCOCH$_3$	2.01	1.92	0.28	0.50	0 0 0	0.00	0.00	2.04	−0.03
17	NC-C_6H_4-3-OCONHCH$_3$	0.97	0.64	0.65	0.50	0 0 0	0.00	0.00	0.95	0.02
18	NC-C_6H_4-3-COCH$_3$	1.16	1.01	0.65	0.27	0 0 0	0.00	0.00	1.18	−0.02
19	NC-C_6H_4-4-OCONHCH$_3$	0.95	0.64	0.65	0.50	0 0 0	0.00	0.00	0.95	−0.00
20	NC-C_6H_4-4-COCH$_3$	1.22	1.01	0.65	0.27	0 0 0	0.00	0.00	1.18	0.04
21	HO-C_6H_4-3-CN	1.70	0.89	0.65	1.06	0 0 0	0.00	0.00	1.54	0.16
22	HO-C_6H_4-3-Br	2.63	2.32	0.28	1.06	0 0 0	0.00	0.00	2.58	0.05
23	HO-C_6H_4-3-F	1.93	1.60	0.28	1.06	0 0 0	0.00	0.00	1.87	0.06
24	HO-C_6H_4-3-Cl	2.48	2.17	0.28	1.06	0 0 0	0.00	0.00	2.43	0.05
25	HO-C_6H_4-3-I	2.93	2.58	0.28	1.06	0 0 0	0.00	0.00	2.83	0.10
26	HO-C_6H_4-3-CO_2CH_3	1.89	1.44	0.51	1.06	0 0 0	0.00	0.00	1.94	−0.05
27	HO-C_6H_4-3-COCH$_3$	1.39	0.91	0.51	1.06	0 0 0	0.00	0.00	1.42	−0.03
28	HO-C_6H_4-3-CF_3	2.95	2.34	0.49	1.06	0 0 0	0.00	0.00	2.80	0.15
29	HO-C_6H_4-4-CN	1.60	0.89	0.65	1.06	0 0 0	0.00	0.00	1.54	0.06
30	HO-C_6H_4-4-Br	2.65	2.32	0.28	1.06	0 0 0	0.00	0.00	2.58	0.07
31	HO-C_6H_4-4-F	1.79	1.60	0.28	1.06	0 0 0	0.00	0.00	1.87	−0.08
32	HO-C_6H_4-4-Cl	2.40	2.17	0.28	1.06	0 0 0	0.00	0.00	2.43	−0.03
33	HO-C_6H_4-4-I	2.92	2.58	0.28	1.06	0 0 0	0.00	0.00	2.83	0.09
34	HO-C_6H_4-4-OCH$_3$	1.39	1.39	0.17	1.06	0 0 0	0.00	0.00	1.56	−0.17
35	HO-C_6H_4-4-CO_2CH_3	1.96	1.44	0.51	1.06	0 0 0	0.00	0.00	1.94	0.02
36	HO-C_6H_4-4-COCH$_3$	1.30	0.91	0.51	1.06	0 0 0	0.00	0.00	1.42	−0.12
37	HO-C_6H_4-4-COEt	2.03	1.45	0.51	1.06	0 0 0	0.00	0.00	1.95	0.08
38	CO_2H-C_6H_4-3-CN	1.48	1.30	0.65	0.35	0 0 0	0.00	0.00	1.51	−0.03
39	CO_2H-C_6H_4-3-Br	2.87	2.73	0.28	0.35	0 0 0	0.00	0.00	2.79	0.08
40	CO_2H-C_6H_4-3-F	2.15	2.01	0.28	0.35	0 0 0	0.00	0.00	2.09	0.06
41	CO_2H-C_6H_4-3-Cl	2.68	2.58	0.28	0.35	0 0 0	0.00	0.00	2.65	0.03
42	CO_2H-C_6H_4-3-I	3.13	2.99	0.28	0.35	0 0 0	0.00	0.00	3.05	0.08
43	CO_2H-C_6H_4-3-OH	1.50	1.20	0.32	1.06	0 0 0	0.00	0.00	1.52	−0.02
44	CO_2H-C_6H_4-3-CF_3	2.95	2.75	0.49	0.35	0 0 0	0.00	0.00	2.88	0.07
45	CO_2H-C_6H_4-4-CN	1.56	1.30	0.65	0.35	0 0 0	0.00	0.00	1.51	0.05
46	CO_2H-C_6H_4-4-Br	2.86	2.73	0.28	0.35	0 0 0	0.00	0.00	2.79	0.07
47	CO_2H-C_6H_4-4-F	2.08	2.01	0.28	0.35	0 0 0	0.00	0.00	2.09	−0.01
48	CO_2H-C_6H_4-4-Cl	2.65	2.58	0.28	0.35	0 0 0	0.00	0.00	2.65	0.00
49	CO_2H-C_6H_4-4-I	3.02	2.99	0.28	0.35	0 0 0	0.00	0.00	3.05	−0.03
50	CO_2H-C_6H_4-4-NHCOCH$_3$	1.31	0.90	0.32	1.08	0 0 0	0.00	0.00	1.23	0.08
51	CO_2H-C_6H_4-4-OH	1.58	1.20	0.32	1.06	0 0 0	0.00	0.00	1.52	0.06
52	HO_2CCH_2O-C_6H_4-3-CN	0.93	0.77	0.65	0.50	0 0 0	0.00	0.00	1.08	−0.15
53	HO_2CCH_2O-C_6H_4-3-CO_2H	1.11	1.08	0.32	0.50	0 0 0	0.00	0.00	1.23	−0.12
54	HO_2CCH_2O-C_6H_4-4-CN	0.95	0.77	0.65	0.50	0 0 0	0.00	0.00	1.08	−0.13
55	HS-C_6H_4-2-CO_2H	2.39	2.26	0.32	0.50	0 0 0	0.00	0.00	2.39	−0.00
56	Acridine-9-NH_2	2.74	2.17	0.84	1.08	0 0 0	0.00	0.00	2.99	−0.25
57	Pyr-2-NHCOCH$_3$	0.61	−0.32	0.84	1.08	0 0 0	0.00	0.00	0.55	0.06
58 *	Pyr-2-OCH$_3$	1.37	0.58	0.84	0.50	0 0 0	0.00	0.00	0.98	0.39
59	Pyr-3-NHCOCH$_3$	0.41	−0.32	0.84	1.08	0 0 0	0.00	0.00	0.55	−0.14
60 *	Pyr-3-OH	0.48	−0.02	0.84	1.06	0 0 0	0.00	0.00	0.83	−0.35
61	Pyr-3-CONHC_6H_5	1.73	1.14	0.84	0.72	0 0 0	0.00	0.00	1.70	0.03
62	Pyr-3-CONHPr^i	0.59	0.24	0.84	0.72	0 0 0	0.00	0.00	0.82	−0.23
63	Pyr-3-CONHCH$_3$	0.00	−0.62	0.84	0.72	0 0 0	0.00	0.00	−0.02	0.02
64	Pyr-3-CO_2CH_3	0.82	0.63	0.84	0.27	0 0 0	0.00	0.00	0.85	−0.03
65	Pyr-3-CO_2Et	1.34	1.17	0.84	0.27	0 0 0	0.00	0.00	1.38	−0.04
66	Pyr-3-COC_6H_5	1.88	1.70	0.84	0.27	0 0 0	0.00	0.00	1.90	−0.02
67	Pyr-3-CONH$_2$	−0.37	−0.84	0.84	0.72	0 0 0	0.00	0.00	−0.24	−0.13
68	Pyr-3-COCH$_3$	0.43	0.10	0.84	0.27	0 0 0	0.00	0.00	0.33	0.10

Table 5 (*continued*)

	Solute	OLP†	ALP ‡	σ_1	ρ_1	*a* ORTH *b* HBND *c* ALPH *a b c*	σ_2	ρ_2	p_{red}	Deviation
69	Pyr-3-NH_2	0.15	−0.58	0.84	1.08	0 0 0	0.00	0.00	0.29	−0.14
70	Pyr-4-$NHCOCH_3$	0.59	−0.32	0.84	1.08	0 0 0	0.00	0.00	0.55	0.04
71	Pyr-4-NMe_2	1.34	0.87	0.84	0.61	0 0 0	0.00	0.00	1.35	−0.01
72	Pyr-4-OCH_3	1.00	0.58	0.84	0.50	0 0 0	0.00	0.00	0.98	0.02
73	Pyr-4-CHO	0.43	0.00	0.84	0.44	0 0 0	0.00	0.00	0.37	0.06
74	Pyr-4-$CONHNH_2$	−0.50	−1.27	0.84	0.72	0 0 0	0.00	0.00	−0.66	0.16
75	Pyr-4-CO_2CH_3	0.87	0.63	0.84	0.27	0 0 0	0.00	0.00	0.85	0.02
76	Pyr-4-CO_2Et	1.43	1.14	0.84	0.27	0 0 0	0.00	0.00	1.35	0.08
77	Pyr-4-COC_6H_5	1.98	1.70	0.84	0.27	0 0 0	0.00	0.00	1.90	0.08
78	Pyr-4-$COCH_3$	0.54	0.10	0.84	0.27	0 0 0	0.00	0.00	0.33	0.21
79	Pyr-4-NH_2	0.26	−0.58	0.84	1.08	0 0 0	0.00	0.00	0.29	−0.03
80	Quin-4-$NHCOCH_3$	1.92	1.06	0.84	1.08	0 0 0	0.00	0.00	1.90	0.02
81	Quin-4-NH_2	1.63	0.80	0.84	1.08	0 0 0	0.00	0.00	1.65	−0.02
82	Quin-5-NH_2	1.63	0.80	0.84	1.08	0 0 0	0.00	0.00	1.65	−0.02
83	Quin-6-NH_2	1.16	0.80	0.84	0.54	0 0 0	0.00	0.00	1.23	−0.07
84	Quin-7-$NHCOCH_3$	1.55	1.06	0.84	0.54	0 0 0	0.00	0.00	1.48	0.07
85	Quin-7-NH_2	1.28	0.80	0.84	0.54	0 0 0	0.00	0.00	1.23	0.05
86	NC-C_6H_4-4-NHCHO	1.08	0.58	0.65	1.08	0 0 0	0.00	0.00	1.24	−0.16
87 *	CH_3CO-C_6H_4-4-NHCHO	0.94	0.71	0.51	1.08	0 0 0	0.00	0.00	1.23	−0.29
88	CHO-C_6H_4-3-OH	1.38	0.81	0.58	1.06	0 0 0	0.00	0.00	1.39	−0.01
89	CHO-C_6H_4-3-CF_3	2.47	2.36	0.49	0.44	0 0 0	0.00	0.44	2.54	−0.07
90	CHO-C_6H_4-4-NMe_2	1.81	1.71	0.58	0.50	0 0 0	0.00	0.00	1.97	−0.16
91	CHO-C_6H_4-4-OH	1.35	0.81	0.58	1.06	0 0 0	0.00	0.00	1.39	−0.04
92	NO_2-C_6H_4-3-NHCHO	1.40	0.89	0.60	1.08	0 0 0	0.00	0.00	1.50	−0.10
93	NO_2-C_6H_4-3-$NHCOCH_3$	1.47	0.90	0.60	1.08	0 0 0	0.00	0.00	1.51	−0.04
94	NO_2-C_6H_4-3-NO_2	1.49	1.61	0.60	0.00	0 0 0	0.00	0.00	1.60	−0.11
95	NO_2-C_6H_4-3-$OCONHCH_3$	1.39	0.95	0.60	0.50	0 0 0	0.00	0.00	1.23	0.16
96 *	NO_2-C_6H_4-3-$OCOCH_3$	1.82	1.23	0.60	0.50	0 0 0	0.00	0.00	1.51	0.31
97	NO_2-C_6H_4-3-OCH_3	2.16	1.80	0.60	0.50	0 0 0	0.00	0.00	2.07	0.09
98	NO_2-C_6H_4-3-OCH_2CO_2H	1.37	1.08	0.60	0.50	0 0 0	0.00	0.00	1.36	0.01
99	NO_2-C_6H_4-3-OH	2.00	1.20	0.60	1.06	0 0 0	0.00	0.00	1.79	0.21
100	NO_2-C_6H_4-3-CHO	1.47	1.22	0.60	0.44	0 0 0	0.00	0.00	1.47	0.00
101	NO_2-C_6H_4-3-CO_2Et	2.35	2.39	0.60	0.27	0 0 0	0.00	0.00	2.52	−0.17
102	NO_2-C_6H_4-3-CO_2H	1.83	1.61	0.60	0.35	0 0 0	0.00	0.00	1.80	0.03
103	NO_2-C_6H_4-3-$COCH_3$	1.42	1.32	0.60	0.27	0 0 0	0.00	0.00	1.47	−0.05
104	NO_2-C_6H_4-3-CF_3	2.62	2.75	0.60	0.00	0 0 0	0.00	0.00	2.72	−0.10
105	NO_2-C_6H_4-4-NHCHO	1.43	0.89	0.60	1.08	0 0 0	0.00	0.00	1.50	−0.07
106	NO_2-C_6H_4-4-$NHCONMe_2$	1.51	0.89	0.60	1.08	0 0 0	0.00	0.00	1.50	0.01
107	NO_2-C_6H_4-4-$NHCOCH_3$	1.66	0.90	0.60	1.08	0 0 0	0.00	0.00	1.51	0.15
108	NO_2-C_6H_4-4-$NHCH_3$	2.04	1.38	0.60	1.08	0 0 0	0.00	0.00	1.98	0.06
109	NO_2-C_6H_4-4-NO_2	1.49	1.61	0.60	0.00	0 0 0	0.00	0.00	1.60	−0.11
110	NO_2-C_6H_4-4-NMe_2	2.27	2.09	0.60	0.61	0 0 0	0.00	0.00	2.41	−0.14
111	NO_2-C_6H_4-4-$OPO(OMe)_2$	1.30	0.96	0.60	0.50	0 0 0	0.00	0.00	1.24	0.06
112 *	NO_2-C_6H_4-4-$OPO(OEt)_2$	1.69	1.66	0.60	0.50	0 0 0	0.00	0.00	1.93	−0.24
113	NO_2-C_6H_4-4-$OCONHCH_3$	1.43	0.95	0.60	0.50	0 0 0	0.00	0.00	1.23	0.20
114	NO_2-C_6H_4-4-$OCONMe_2$	1.50	1.35	0.60	0.50	0 0 0	0.00	0.00	1.63	−0.13
115	NO_2-C_6H_4-$OCOCH_3$	1.49	1.23	0.60	0.50	0 0 0	0.00	0.00	1.51	−0.02
116	NO_2-C_6H_4-4-OCH_3	2.03	1.80	0.60	0.50	0 0 0	0.00	0.00	2.07	−0.04
117	NO_2-C_6H_4-4-OCH_2CO_2H	1.48	1.08	0.60	0.50	0 0 0	0.00	0.00	1.36	0.12
118	NO_2-C_6H_4-4-OH	1.91	1.20	0.60	1.06	0 0 0	0.00	0.00	1.79	0.12
119	NO_2-C_6H_4-4-CHO	1.56	1.22	0.60	0.44	0 0 0	0.00	0.00	1.47	0.09
120	NO_2-C_6H_4-4-CO_2Et	2.33	2.39	0.60	0.27	0 0 0	0.00	0.00	2.52	−0.19
121	NO_2-C_6H_4-4-CO_2H	1.89	1.61	0.60	0.35	0 0 0	0.00	0.00	1.80	0.09
122	NO_2-C_6H_4-4-$COCH_3$	1.48	1.32	0.60	0.27	0 0 0	0.00	0.00	1.47	0.01
123	FSO_2-C_6H_4-4-$NHCOCH_3$	2.17	1.32	0.71	1.08	0 0 0	0.00	0.00	2.03	0.14
124	FSO_2-C_6H_4-4-OCH_2CO_2H	1.82	1.50	0.71	0.50	0 0 0	0.00	0.00	1.82	−0.00
125	CH_3SO_2-C_6H_4-3-$NHSO_2CF_3$	1.85	1.42	0.65	1.08	0 0 0	0.00	0.00	2.07	−0.22
126	CH_3SO_2-C_6H_4-3-OCH_3	0.86	0.49	0.65	0.50	0 0 0	0.00	0.00	0.81	0.05
127	CH_3SO_2-C_6H_4-4-$NHSO_2CF_3$	1.99	1.42	0.65	1.08	0 0 0	0.00	0.00	2.07	−0.08
128 *	CH_3SO_2-C_6H_4-4-$OCONHCH_3$	0.34	−0.42	0.65	0.50	0 0 0	0.00	0.00	−0.09	0.43
129	CH_3SO_2-C_6H_4-4-CO_2H	0.67	0.24	0.65	0.35	0 0 0	0.00	0.00	0.47	0.20
130	Br-C_6H_4-3-$CONHNH_2$	1.26	1.05	0.28	0.72	0 0 0	0.00	0.00	1.24	0.02
131	Cl-C_6H_4-3-$CONHNH_2$	1.18	0.90	0.28	0.72	0 0 0	0.00	0.00	1.09	0.09
132	I-C_6H_4-3-$CONHNH_2$	1.53	1.31	0.28	0.72	0 0 0	0.00	0.00	1.50	0.03
133	NO_2-C_6H_4-3-$CONHNH_2$	0.23	−0.05	0.62	0.72	0 0 0	0.00	0.00	0.39	−0.16
134	HO-C_6H_4-3-$CONHNH_2$	−0.08	−0.46	0.32	1.06	0 0 0	0.00	0.00	−0.11	0.03
135	H_2N-C_6H_4-3-$CONHNH_2$	−0.86	−1.02	0.32	1.08	0 0 0	0.00	0.00	−0.66	−0.20
136	Br-C_6H_4-4-$CONHNH_2$	1.28	1.05	0.28	0.72	0 0 0	0.00	0.00	1.24	0.04

Table 5 (*continued*)

	Solute	OLP †	ALP ‡	σ_1	ρ_1	*a* ORTH *b* HBND *c* ALPH *a b c*	σ_2	ρ_2	p_{red}	Deviation
137	Cl-C_6H_4-4-$CONHNH_2$	1.12	0.90	0.28	0.72	0 0 0	0.00	0.00	1.09	0.03
138	I-C_6H_4-4-$CONHNH_2$	1.55	1.31	0.28	0.72	0 0 0	0.00	0.00	1.50	0.05
139	NO_2-C_6H_4-4-$CONHNH_2$	0.35	−0.05	0.60	0.72	0 0 0	0.00	0.00	0.38	−0.03
140	HO-C_6H_4-4-$CONHNH_2$	−0.33	−0.46	0.32	1.06	0 0 0	0.00	0.00	−0.11	−0.22
141	H_2N-C_6H_4-4-$CONHNH_2$	−0.75	−1.02	0.32	1.08	0 0 0	0.00	0.00	−0.66	−0.09
142	H_2N-C_6H_4-3-CN	1.07	0.33	0.65	1.08	0 0 0	0.00	0.00	1.00	0.07
143	H_2N-C_6H_4-3-Cl	1.88	1.61	0.28	1.08	0 0 0	0.00	0.00	1.88	−0 00
144	H_2N-C_6H_4-3-NO_2	1.37	0.64	0.60	1.08	0 0 0	0.00	0.00	1.25	0.12
145	H_2N-C_6H_4-3-OCH_3	0.93	0.83	0.17	1.08	0 0 0	0.00	0.00	1.01	−0.08
146	H_2N-C_6H_4-3-CF_3	2.39	1.78	0.49	1.08	0 0 0	0.00	0.00	2.26	0.13
147	H_2N-C_6H_4-4-Br	2.05	1.76	0.28	1.08	0 0 0	0.00	0.00	2.03	0.02
148	H_2N-C_6H_4-4-Cl	1.83	1.61	0.28	1.08	0 0 0	0.00	0.00	1.88	−0.05
149	H_2N-C_6H_4-4-I	2.34	2.02	0.28	1.08	0 0 0	0.00	0.00	2.29	0.05
150	H_2N-C_6H_4-4-NO_2	1.39	0.64	0.60	1.08	0 0 0	0.00	0.00	1.25	0.14
151	H_2N-C_6H_4-4-SO_2NMe_2	0.67	0.12	0.65	1.08	0 0 0	0.00	0.00	0.79	−0.12
152	H_2N-C_6H_4-4-SO_2CH_3	−0.12	−0.73	0.65	1.08	0 0 0	0.00	0.00	−0.04	−0.08
153	H_2N-C_6H_4-4-CO_2Et	1.86	1.43	0.51	1.08	0 0 0	0.00	0.00	1.94	−0.08
154 *	H_2N-C_6H_4-4-CF_3	1.95	1.77	0.49	1.08	0 0 0	0.00	0.00	2.25	−0.30
155	H_2NSO_2-C_6H_4-3-Cl	1.29	1.02	0.28	0.88	0 0 0	0.00	0.00	1.25	0.04
156	H_2NSO_2-C_6H_4-3-NO_2	0.55	0.05	0.60	0.88	0 0 0	0.00	0.00	0.56	−0.01
157	H_2NSO_2-C_6H_4-4-CN	0.23	−0.26	0.65	0.88	0 0 0	0.00	0.00	0.30	−0.07
158	H_2NSO_2-C_6H_4-4-Br	1.36	1.17	0.28	0.88	0 0 0	0.00	0.00	1.40	−0.04
159	H_2NSO_2-C_6H_4-4-N=$NNMe_2$	1.06	0.77	0.50	0.61	0 0 0	0.00	0.00	1.06	−0.00
160	H_2NSO_2-C_6H_4-4-NMe_2	0.76	0.53	0.50	0.61	0 0 0	0.00	0.00	0.83	−0.07
161	H_2NSO_2-C_6H_4-4-OCH_3	0.47	0.29	0.50	0.50	0 0 0	0.00	0.00	0.54	−0.07
162	H_2NSO_2-C_6H_4-4-OH	0.06	−0.36	0.50	1.06	0 0 0	0.00	0.00	0.16	−0.10
163 *	H_2NSO_2-C_6H_4-4-$CONHCH_3$	−0.31	−0.95	0.50	0.72	0 0 0	0.00	0.00	−0.57	0.26
164	H_2NSO_2-C_6H_4-4-CONHEt	0.03	−0.41	0.50	0.72	0 0 0	0.00	0.00	−0.04	0.07
165	H_2NSO_2-C_6H_4-4-$CONHPr^n$	0.51	0.13	0.50	0.72	0 0 0	0.00	0.00	0.49	0.02
166	H_2NSO_2-C_6H_4-4-$CONHBu^n$	1.05	0.67	0.50	0.72	0 0 0	0.00	0.00	1.02	0.03
167	H_2NSO_2-C_6H_4-4-$CONHPe^n$	1.51	1.21	0.50	0.72	0 0 0	0.00	0.00	1.55	−0.04
168	H_2NSO_2-C_6H_4-4-CO_2CH_3	0.64	0.30	0.51	0.88	0 0 0	0.00	0.00	0.73	−0.09
169	H_2NSO_2-C_6H_4-4-CO_2Et	1.17	0.84	0.51	0.88	0 0 0	0.00	0.00	1.26	−0.09
170	H_2NSO_2-C_6H_4-4-CO_2Pr	1.75	1.38	0.51	0.88	0 0 0	0.00	0.00	1.79	−0.04
171	H_2NSO_2-C_6H_4-4-CO_2Bu	2.34	1.92	0.51	0.88	0 0 0	0.00	0.00	2.32	0.02
172	H_2NSO_2-C_6H_4-4-$COCH_3$	0.20	−0.24	0.51	0.88	0 0 0	0.00	0.00	0.20	−0.00
173	H_2NSO_2-C_6H_4-4-NH_2	−0.60	−0.92	0.50	1.08	0 0 0	0.00	0.00	−0.38	−0.22
174	H_2NCONH-C_6H_4-3-Br	2.08	1.69	0.28	1.08	0 0 0	0.00	0.00	1.96	0.12
175	H_2NCONH-C_6H_4-3-F	1.29	0.97	0.28	1.08	0 0 0	0.00	0.00	1.26	0.03
176	H_2NCONH-C_6H_4-3-Cl	1.82	1.54	0.28	1.08	0 0 0	0.00	0.00	1.82	0.00
177	H_2NCONH-C_6H_4-3-CF_3	2.31	1.71	0.49	1.08	0 0 0	0.00	0.00	2.19	0.12
178	H_2NCONH-C_6H_4-4-Br	1.98	1.69	0.28	1.08	0 0 0	0.00	0.00	1.96	0.02
179	H_2NCONH-C_6H_4-4-F	1.04	0.97	0.28	1.08	0 0 0	0.00	0.00	1.26	−0.22
180	H_2NCONH-C_6H_4-4-Cl	1.60	1.54	0.28	1.08	0 0 0	0.00	0.00	1.82	−0.22
181	H_2NCONH-C_6H_4-4-OC_6H_5	2.80	2.91	0.17	1.08	0 0 0	0.00	0.00	3.05	−0.25
182	$CONH_2$-C_6H_4-3-CN	0.52	0.08	0.65	0.72	0 0 0	0.00	0.00	0.54	−0.02
183	$CONH_2$-C_6H_4-3-NO_2	0.77	0.39	0.60	0.72	0 0 0	0.00	0.00	0.81	−0.04
184	$CONH_2$-C_6H_4-3-NMe_2	0.95	0.86	0.32	0.61	0 0 0	0.00	0.00	1.05	−0.10
185	$CONH_2$-C_6H_4-3-OH	0.39	−0.02	0.32	1.06	0 0 0	0.00	0.00	0.32	0.07
186	$CONH_2$-C_6H_4-4-CN	0.48	0.08	0.65	0.72	0 0 0	0.00	0.00	0.54	−0.06
187	$CONH_2$-C_6H_4-4-$NHCOCH_3$	0.01	−0.33	0.32	1.08	0 0 0	0.00	0.00	0.02	−0.01
188	$CONH_2$-C_6H_4-4-N=$NNMe_2$	1.20	1.10	0.32	0.61	0 0 0	0.00	0.00	1.28	−0.08
189	$CONH_2$-C_6H_4-4-NO_2	0.82	0.39	0.60	0.72	0 0 0	0.00	0.00	0.81	0.01
190	$CONH_2$-C_6H_4-4-NMe_2	1.14	0.86	0.32	0.50	0 0 0	0.00	0.00	1.02	0.12
191	$CONH_2$-C_6H_4-4-OH	0.33	−0.02	0.32	1.06	0 0 0	0.00	0.00	0.32	0.01
192	$CONH_2$-C_6H_4-4-CF_3	1.71	1.52	0.49	0.72	0 0 0	0.00	0.00	1.84	−0.13
193	$CONH_2$-C_6H_4-4-NH_2	−0.20	−0.59	0.32	1.08	0 0 0	0.00	0.00	−0.23	0.03
194	CH_3NH-C_6H_4-4-SO_2NMe_2	1.43	0.86	0.65	1.08	0 0 0	0.00	0.00	1.52	−0.09
195	CH_3CONH-C_6H_4-4-OCH_3	1.14	1.09	0.17	1.08	0 0 0	0.00	0 00	1.26	−0.12
196	CH_3CO-C_6H_4-4-NMe_2	2.10	1.80	0.51	0.61	0 0 0	0.00	0.00	2.08	0.02
197	CO_2H-C_6H_4-3-OCH_3	2.02	1.80	0.32	0.50	0 0 0	0.17	0.35	2.00	0.02
198 *	CO_2H-C_6H_4-3-CO_2CH_3	1.83	1.85	0.32	0.27	0 0 0	0.51	0.35	2.09	−0.26
199	CO_2H-C_6H_4-3-CO_2H	1.66	1.61	0.32	0.35	0 0 0	0.32	0.35	1.81	−0.15
200	CO_2H-C_6H_4-4-OCH_3	1.96	1.80	0.32	0.50	0 0 0	0.17	0.35	2.00	−0.04
201	CO_2H-C_6H_4-4-CO_2H	2.00	1.61	0.32	0.35	0 0 0	0.32	0.35	1.81	0.19
202	CHO-C_6H_4-3-$OCONHCH_3$	0.92	0.56	0.58	0.50	0 0 0	0.17	0.44	0.91	0.01
203	CHO-C_6H_4-4-$OCONHCH_3$	0.99	0.56	0.58	0.50	0 0 0	0.17	0.44	0.91	0.08
204	CHO-C_6H_4-4-OCH_3	1.76	1.42	0.58	0.50	0 0 0	0.17	0.44	1.76	0.00

Table 5 (*continued*)

	Solute	OLP †	ALP ‡	σ_1	ρ_1	*a* ORTH *b* HBND *c* ALPH *a b c*	σ_2	ρ_2	p_{red}	Deviation
205	CHO-C_6H_4-4-OCH_2CO_2H	0.79	0.69	0.58	0.50	0 0 0	0.17	0.44	1.04	−0.25
206	CH_3O-C_6H_4-3-$CONHNH_2$	0.40	0.14	0.32	0.50	0 0 0	0.17	0.72	0.43	−0.03
207	CH_3O-C_6H_4-4-$CONHNH_2$	0.25	0.14	0.32	0.50	0 0 0	0.17	0.72	0.43	−0.18
208	H_2NSO_2-C_6H_4-3-SO_2NH_2	−0.55	−1.51	0.50	0.88	0 0 0	0.50	0.88	−0.64	0.09
209	$CONH_2$-C_6H_4-2-OCH_3	0.84	0.57	0.32	0.50	0 0 0	0.17	0.72	0.85	−0.01
210	$CONH_2$-C_6H_4-3-OCH_3	0.85	0.57	0.32	0.50	0 0 0	0.17	0.72	0.85	0.00
211	$CONH_2$-C_6H_4-3-$CONH_2$	−0.21	−0.84	0.32	0.72	0 0 0	0.32	0.72	−0.37	0.16
212	$CONH_2$-C_6H_4-4-$OCOCH_3$	0.27	0.00	0.32	0.50	0 0 0	0.17	0.72	0.29	−0.02
213	$CONH_2$-C_6H_4-4-OCH_3	0.86	0.57	0.32	0.50	0 0 0	0.17	0.72	0.85	0.01
214	CH_3O-C_6H_4-3-$CONMe_2$	1.00	0.60	0.51	0.50	0 0 0	0.17	0.27	0.89	0.11
215	CH_3O-C_6H_4-4-$CONMe_2$	0.96	0.60	0.51	0.50	0 0 0	0.17	0.27	0.89	0.07
216	CH_3OCO-C_6H_4-3-$OCONHCH_3$	1.42	1.20	0.51	0.50	0 0 0	0.17	0.27	1.48	−0.06
217	CH_3OCO-C_6H_4-4-$OCONHCH_3$	1.50	1.20	0.51	0.50	0 0 0	0.17	0.27	1.48	0.02
218	CH_3OCO-C_6H_4-4-OCH_3	2.27	2.05	0.51	0.50	0 0 0	0.17	0.27	2.32	−0.05
219	CH_3CO-C_6H_4-3-$OCONMe_2$	1.18	1.01	0.51	0.50	0 0 0	0.17	0.27	1.29	−0.11
220	CH_3CO-C_6H_4-3-OCH_3	1.84	1.51	0.51	0.50	0 0 0	0.17	0.27	1.79	0.05
221	CH_3CO-C_6H_4-4-$OCONHCH_3$	1.01	0.66	0.51	0.50	0 0 0	0.17	0.27	0.95	0.06
222	CH_3CO-C_6H_4-4-$OCOCH_3$	1.29	0.94	0.51	0.50	0 0 0	0.17	0.27	1.23	0.06
223	CH_3CO-C_6H_4-4-OCH_3	1.74	1.51	0.51	0.50	0 0 0	0.17	0.27	1.79	−0.05
224	Cl-C_6H_4-2-CH_3	3.42	3.38	0.28	0.00	0 0 0	0.00	0.00	3.34	0.08
225	Cl-C_6H_4-3-CH_3	3.28	3.38	0.28	0.00	0 0 0	0.00	0.00	3.34	−0.06
226	Cl-C_6H_4-4-CH_3	3.33	3.38	0.28	0.00	0 0 0	0.00	0.00	3.34	−0.01
227	C_6H_{11}-C_6H_4-4-OH	4.22	4.44	0.00	0.00	0 0 2	0.00	0.00	4.21	0.01
228	Naphthyl-2-CH_3	3.87	3.84	0.00	0.00	0 0 0	0.00	0.00	3.79	0.08
229	Naphthyl-2,3-Me_2	4.31	4.38	0.00	0.00	0 0 1	0.00	0.00	4.24	0.07
230	Naphthyl-2,4-Me_2	4.42	4.38	0.00	0.00	0 0 1	0.00	0.00	4.24	0.18
231	Naphthyl-2,5-Me_2	4.37	4.38	0.00	0.00	0 0 1	0.00	0.00	4.24	0.13
232	Naphthyl-2,6-Me_2	4.38	4.38	0.00	0.00	0 0 1	0.00	0.00	4.24	0.14
233	Naphthyl-2,7-Me_2	4.44	4.38	0.00	0.00	0 0 1	0.00	0.00	4.24	0.20
234	HO-C_6H_4-2-CH_3	1.96	2.00	0.00	1.06	0 0 0	0.00	0.00	1.99	−0.03
235	HO-C_6H_4-2,4-Me_2	2.30	2.54	0.00	1.06	0 0 1	0.00	0.00	2.43	−0.13
236	HO-C_6H_4-2-Et	2.47	2.54	0.00	1.06	0 0 1	0.00	0.00	2.43	0.04
237	HO-C_6H_4-2-Pr	2.93	3.08	0.00	1.06	0 0 2	0.00	0.00	2.88	0.05
238	HO-C_6H_4-3-CH_3	1.96	2.00	0.00	1.06	0 0 0	0.00	0.00	1.99	−0.03
239	HO-C_6H_4-3,4-Me_2	2.23	2.54	0.00	1.06	0 0 1	0.00	0.00	2.43	−0.20
240	HO-C_6H_4-3,5-Me_2	2.35	2.54	0.00	1.06	0 0 1	0.00	0.00	2.43	−0.08
241	HO-C_6H_4-3-Et	2.40	2.54	0.00	1.06	0 0 1	0.00	0.00	2.43	−0.03
242	HO-C_6H_4-4-CH_3	1.94	2.00	0.00	1.06	0 0 0	0.00	0.00	1.99	−0.05
243	HO-C_6H_4-4-Et	2.42	2.54	0.00	1.06	0 0 1	0.00	0.00	2.43	−0.01
244	CO_2H-C_6H_4-3-CH_3	2.37	2.41	0.32	0.00	0 0 0	0.00	0.00	2.39	−0.02
245	CH_3-C_6H_4-3-OCH_2CO_2H	1.78	1.88	0.00	0.52	0 0 0	0.00	0.00	1.87	−0.09
246	Bu^t-C_6H_4-3-OCH_2CO_2H	2.96	3.32	0.00	0.52	0 0 3	0.00	0.00	3.03	−0.07
247	Pr^i-C_6H_4-3-OCH_2CO_2H	2.59	2.87	0.00	0.52	0 0 2	0.00	0.00	2.67	−0.08
248	Et-C_6H_4-3-OCH_2CO_2H	2.25	2.42	0.00	0.52	0 0 1	0.00	0.00	2.32	−0.07
249	Pr-C_6H_4-3-OCH_2CO_2H	2.71	2.98	0.00	0.52	0 0 2	0.00	0.00	2.78	−0.07
250	Bu-C_6H_4-3-OCH_2CO_2H	3.18	3.50	0.00	0.52	0 0 3	0.00	0.00	3.21	−0.03
251	CH_3-C_6H_4-4-OCH_2CO_2H	1.86	1.88	0.00	0.52	0 0 0	0.00	0.00	1.87	−0.01
252	CH_3-C_6H_4-3-CH_2CO_2H	1.95	1.95	0.00	0.52	0 0 0	0.00	0.00	1.94	0.01
253	CH_3-C_6H_4-4-CH_2CO_2H	1.86	1.95	0.00	0.00	0 0 0	0.00	0.00	1.94	−0.08
254	CH_3-C_6H_4-3-CH_2OH	1.60	1.64	0.00	0.00	0 0 0	0.00	0.00	1.63	−0.03
255	CH_3-C_6H_4-4-CH_2OH	1.58	1.64	0.00	0.00	0 0 0	0.00	0.00	1.63	−0.05
256	Indole-3-CH_3	2.60	2.68	0.00	0.00	0 0 0	0.00	0.00	2 65	−0.05
257	Indole-5-CH_3	2.68	2.68	0.00	0.00	0 0 0	0.00	0 00	2.65	0.03
258	Pyr-2-CH_3	1.11	1.18	0.84	0.00	0 0 0	0.00	0.00	1.18	−0.07
259 *	Pyr-2,6-Me_2	1.68	1.72	0.84	0.00	0 0 1	0.00	0.00	1.63	0.05
260	Pyr-3-CH_3	1.20	1.18	0.84	0.00	0 0 0	0.00	0.00	1.18	0.02
261	Pyr-4-CH_3	1.22	1.18	0.84	0.00	0 0 0	0.00	0.00	1.18	0.04
262	Pyr-4-Bu	2.10	2.26	0.84	0.00	0 0 2	0.00	0.00	2.08	0.02
263	Quin-2-CH_3	2.59	2.57	0.84	0.00	0 0 0	0.00	0.00	2.55	0.04
264	NO_2-C_6H_4-2-CH_3	2.30	2.41	0.60	0.00	0 0 0	0.00	0.00	2.39	−0.09
265	NO_2-C_6H_4-3-CH_3	2.45	2.41	0.60	0.00	0 0 0	0.00	0.00	2.39	0.06
266	NO_2-C_6H_4-4-CH_3	2.42	2.41	0.60	0.00	0 0 0	0.00	0.00	2.39	0.03
267	CH_3-C_6H_4-3-$CONHNH_2$	0.74	0.73	0.32	0.00	0 0 0	0.00	0.00	0.74	−0.00
268	CH_3-C_6H_4-4-$CONHNH_2$	0.73	0.73	0.32	0.00	0 0 0	0.00	0.00	0.74	−0.01
269	CH_3-C_6H_4-2-NH_2	1.32	1.44	0.00	1.08	0 0 0	0.00	0.00	1.44	−0.12
270	CH_3-C_6H_4-3-NH_2	1.41	1.44	0.00	1.08	0 0 0	0.00	0.00	1.44	−0.03
271	CH_3-C_6H_4-4-NH_2	1.39	1.44	0.00	1.08	0 0 0	0.00	0.00	1.44	−0.05
272	CH_3-C_6H_4-2-SO_2NH_2	0.84	0.85	0.50	0.00	0 0 0	0.00	0.00	0.86	−0.02

Table 5 (*continued*)

	Solute	OLP †	ALP ‡	σ_1	ρ_1	*a* ORTH *b* HBND *c* ALPH *a b c*	σ_2	ρ_2	p_{red}	Deviation
273	CH_3-C_6H_4-3-SO_2NH_2	0.85	0.85	0.50	0.00	0 0 0	0.00	0.00	0.86	−0.01
274	CH_3-C_6H_4-4-SO_2NH_2	0.82	0.85	0.50	0.00	0 0 0	0.00	0.00	0.86	−0.04
275	CH_3-C_6H_4-3-$NHCONH_2$	1.29	1.37	0.00	1.08	0 0 0	0.00	0.00	1.37	−0.08
276	CH_3-C_6H_4-3-$CONH_2$	1.18	1.18	0.32	0.00	0 0 0	0.00	0.00	1.18	−0.00
277	CH_3-C_6H_4-4-$CONH_2$	1.18	1.18	0.32	0.00	0 0 0	0.00	0.00	1.18	−0.00
278	CH_3-C_6H_4-2-$NHCH_3$	2.16	2.20	0.00	1.08	0 0 0	0.00	0.00	2.18	−0.02
279	CH_3-C_6H_4-4-$NHCH_3$	2.15	2.20	0.00	1.08	0 0 0	0.00	0.00	2.18	−0.03
280	CH_3-C_6H_4-2-NMe_2	2.85	2.85	0.00	0.61	0 0 0	0.00	0.00	2.82	0.03
281	CH_3-C_6H_4-2-OCH_3	2.74	2.65	0.17	0.00	0 0 0	0.00	0.00	2.63	0.11
282	CH_3-C_6H_4-3-OCH_3	2.66	2.65	0.17	0.00	0 0 0	0.00	0.00	2.63	0.03
283	CH_3-C_6H_4-4-OCH_3	2.66	2.65	0.17	0.00	0 0 0	0.00	0.00	2.63	0.03
284	CH_3-C_6H_4-2-CO_2CH_3	2.75	2.66	0.51	0.00	0 0 0	0.00	0.00	2.64	0.11
285	CH_3-C_6H_4-2-CH_3	3.12	3.21	0.00	0.00	0 0 1	0.00	0.00	3.09	0.03
286	1,2,4,5-$Me_4C_6H_2$	4.00	4.29	0.00	0.00	0 0 3	0.00	0.00	3.98	0.02
287	CH_3-C_6H_4-3-CH_3	3.20	3.21	0.00	0.00	0 0 1	0.00	0.00	3.09	0.11
288	CH_3-C_6H_4-4-CH_3	3.15	3.21	0.00	0.00	0 0 1	0.00	0.00	3.09	0.06
289	CH_3-C_6H_4-3-$NHCOCH_3$	1.52	1.70	0.00	1.08	0 0 0	0.00	0.00	1.69	−0.17
290	CH_3-C_6H_4-2-$OCOCH_3$	1.93	2.03	0.17	0.00	0 0 0	0.00	0.00	2.02	−0.09
291	CH_3-C_6H_4-3-$OCOCH_3$	2.09	2.03	0.17	0.00	0 0 0	0.00	0.00	2.02	0.07
292	CH_3-C_6H_4-4-$OCOCH_3$	2.11	2.03	0.17	0.00	0 0 0	0.00	0.00	2.02	0.09
293	CH_3-C_6H_4-4-$COCH_3$	2.10	2.12	0.51	0.00	0 0 0	0.00	0.00	2.11	−0.01
294	HO-C_6H_4-2-CO_2CH_3	2.55	1.44	0.51	1.06	0 1 0	0.00	0.00	2.58	−0.03
295	HO-C_6H_4-2-$COCH_3$	1.90	0.91	0.51	1.06	0 1 0	0.00	0.00	2.06	−0.16
296	HO-C_6H_4-2-CO_2Et	2.54	1.45	0.51	1.06	0 1 0	0.00	0.00	2.59	−0.05
297	CO_2H-C_6H_4-2-NHC_6H_5	4.36	3.33	0.32	1.08	0 1 0	0.00	0.00	4.26	0.10
298	CO_2H-C_6H_4-2-$NHCOCH_3$	1.88	0.90	0.32	1.08	0 1 0	0.00	0.00	1.87	0.01
299	HO-C_6H_4-2-CO_2H	2.24	1.20	0.32	1.06	0 1 0	0.00	0 00	2.16	0.08
300	HO-C_6H_4-2-CHO	1.81	0.81	0.58	1.06	0 1 0	0.00	0.00	2.03	−0.22
301	HO-C_6H_4-2-$CONHNH_2$	0.60	−0.46	0.32	1.06	0 1 0	0.00	0.00	0.53	0.07
302	H_2N-C_6H_4-2-$CONHNH_2$	−0.18	−1.02	0.32	1.08	0 1 0	0.00	0.00	−0.01	−0.17
303	H_2N-C_6H_4-2-NO_2	1.83	0.64	0.60	1.08	0 1 0	0.00	0.00	1.90	−0.07
304	H_2N-C_6H_4-2-CO_2Et	2.57	1.42	0.51	1.08	0 1 0	0.00	0.00	2.57	−0.00
305	H_2N-C_6H_4-2-$COCH_3$	1.62	0.35	0.51	1.08	0 1 0	0.00	0.00	1.52	0.10
306 *	HO-C_6H_4-2-$CONH_2$	1.28	−0.02	0.32	1.06	0 1 0	0.00	0.00	0.96	0.32
307	H_2N-C_6H_4-2-$CONH_2$	0.35	−0.59	0.32	1.08	0 1 0	0.00	0.00	0.41	−0.06
308	Pyr-2-$CONH_2$-3-OH [a]	0.65	−1.50	0.84	1.78	0 1 0	0.00	0.00	0.58	0.07
309	Br-C_6H_4-2-$OCONHCH_3$	1.77	2.07	0.28	0.50	1 0 0	0.00	0.00	1.90	−0.13
310	Br-C_6H_4-2-$OCONMe_2$	2.17	2.43	0.28	0.50	1 0 0	0.00	0.00	2.26	−0.09
311	Br-C_6H_4-2-$OCOCH_3$	2.20	2.35	0.28	0.50	1 0 0	0.00	0.00	2.18	0.02
312	Cl-C_6H_4-2-$NHCOCH_3$	1.28	1.87	0.28	1.08	3 0 0	0.00	0.00	1.29	−0.01
313	Cl-C_6H_4-2-$OCONHCH_3$	1.64	1.92	0.28	0.50	1 0 0	0.00	0.00	1.76	−0.12
314	Cl-C_6H_4-2-$OCOCH_3$	2.18	2.20	0.28	0.50	1 0 0	0.00	0.00	2.03	0.15
315	Cl-C_6H_3-2-OCH_3-5-$NHCONMe_2$ [b,c]	1.50	1.67	0.34	0.79	1 0 0	0.00	0.00	1.63	−0.13
316	Cl-C_6H_4-2-CO_2CH_3	2.38	2.59	0.28	0.27	1 0 0	0.00	0.00	2.35	0.03
317	Cl-C_6H_4-2-$COCH_3$	2.09	2.29	0.28	0.27	1 0 0	0.00	0.00	2.06	0.03
318	1,3-Cl_2-C_6H_2-4-CH_3-6-$OCONHCH_3$ [c]	3.00	3.20	0.42	0.50	1 0 0	0.00	0.00	3.08	−0.08
319	1,4-Cl_2-C_6H_3-2-$OCONHCH_3$	2.44	2.63	0.42	0.50	1 0 0	0.00	0.00	2.52	−0.08
320	I-C_6H_4-2-$OCONHCH_3$	1.94	2.33	0.28	0.50	1 0 0	0.00	0.00	2.16	−0.22
321	I-C_6H_4-2-$OCOCH_3$	2.55	2.61	0.28	0.50	1 0 0	0.00	0.00	2.43	0.12
322	Br-C_6H_4-2-OH	2.35	2.32	0.28	1.06	1 0 0	0.00	0.00	2.29	0.06
323	F-C_6H_4-2-OH	1.68	1.60	0.28	1.06	1 0 0	0.00	0.00	1.59	0.09
324	Cl-C_6H_4-2-OH	2.19	2.17	0.28	1.06	1 0 0	0.00	0.00	2.15	0.04
325	I-C_6H_4-2-OH	2.65	2.58	0.28	1.06	1 0 0	0.00	0.00	2.55	0.10
326	CH_3O-C_6H_4-2-OH	1.32	1.39	0.17	1.06	1 0 0	0.00	0.50	1.27	0.05
327	CO_2H-C_6H_4-2-CH_3	2.18	2.41	0.00	0.35	1 0 0	0.00	0.00	2.11	0.07
328	CO_2H-C_6H_4-2-Br	2.20	2.73	0.28	0.35	2 0 0	0.00	0.00	2.23	−0.03
329	CO_2H-C_6H_4-2-F	1.77	2.01	0.28	0.35	1 0 0	0.00	0.00	1.81	−0.04
330	CO_2H-C_6H_4-2-Cl	1.98	2.58	0.28	0.35	2 0 0	0.00	0.00	2.08	−0.10
331	CO_2H-C_6H_4-2-I	2.40	2.99	0.28	0.35	2 0 0	0.00	0.00	2.49	−0.09
332	CO_2H-C_6H_4-2-$OCOCH_3$	1.20	1.23	0.32	0.50	1 0 0	0.17	0.35	1.15	0.05
333	CO_2H-C_6H_4-OCH_3	1.59	1.80	0.32	0.50	1 0 0	0.17	0.35	1.71	−0.12
334	CO_2H-C_6H_4-2-CO_2CH_3	1.13	1.85	0.51	0.35	3 0 0	0.32	0.27	1.24	−0.11
335	CO_2H-C_6H_4-2-CO_2H	0.79	1.61	0.32	0.35	4 0 0	0.32	0.35	0.69	0.10
336	CO_2H-C_6H_4-2-$COCH_3$	0.81	1.32	0.51	0.35	3 0 0	0.32	0.27	0.72	0.09
337	CO_2H-C_6H_4-2-OEt-4-NH_2 [b,c]	0.99	1.11	0.37	0.65	1 0 0	0.00	0.00	1.05	−0.06
338	Pyr-2-Br-3-$OCONMe_2$ [c]	1.14	1.00	0.84	0.50	1 0 0	0.00	0.00	1.11	0.03
339	Pyr-2-Cl-3-$OCONMe_2$ [c]	1.04	0.85	0.84	0.50	1 0 0	0.00	0.00	0.97	0.07
340	Pyr-2-I-3-$OCONMe_2$ [c]	1.26	1.26	0.84	0.50	1 0 0	0.00	0.00	1.37	−0.11

Table 5 (*continued*)

	Solute	OLP †	ALP ‡	σ_1	ρ_1	*a* ORTH *b* HBND *c* ALPH *a b c*	σ_2	ρ_2	p_{red}	Deviation
341	NO_2-C_6H_4-2-Cl	2.24	2.58	0.60	0.00	1 0 0	0.00	0.00	2.27	−0.03
342	NO_2-C_6H_4-2-$NHCOCH_3$	1.00	0.90	0.60	1.08	2 0 0	0.00	0.00	0.94	0.06
343	NO_2-C_6H_4-2-$NHCH_3$	2.18	1.38	0.60	1.08	0 0 0	0.00	0.00	1.98	0.20
344	NO_2-C_6H_4-2-NO_2	1.58	1.61	0.60	0.00	0 0 0	0.00	0.00	1.60	−0.02
345	NO_2-C_6H_4-2-$OCONHCH_3$	1.02	0.95	0.60	0.50	1 0 0	0.00	0.00	0.95	0.07
346	NO_2-C_6H_4-2-$OCONMe_2$	1.35	1.35	0.60	0.50	1 0 0	0.00	0.00	1.34	0.01
347 *	NO_2-C_6H_4-2-$OCOCH_3$	1.55	1.23	0.60	0.50	1 0 0	0.00	0.00	1.23	0.32
348	NO_2-C_6H_4-2-OCH_3	1.73	1.85	0.60	0.50	1 0 0	0.00	0.00	1.84	−0.11
349	NO_2-C_6H_4-2-OCH_2CO_2H	0.97	1.08	0.60	0.50	1 0 0	0.00	0.00	1.08	−0.11
350	NO_2-C_6H_4-2-CO_2H	1.46	1.61	0.60	0.35	1 0 0	0.00	0.00	1.52	−0.06
351	NO_2-C_6H_4-$COCH_3$	1.28	1.32	0.60	0.27	1 0 0	0.00	0.00	1.19	0.09
352	CH_3-C_6H_4-2-$CONHNH_2$	0.22	0.73	0.32	0.00	2 0 0	0.00	0.00	0.18	0.04
353	NO_2-C_6H_4-2-$CONHNH_2$	−0.54	−0.05	0.60	0.72	3 0 0	0.00	0.00	−0.47	−0.07
354	CH_3O-C_6H_4-2-$CONHNH_2$	0.25	0.14	0.32	0.50	1 0 0	0.17	0.72	0.14	0.11
355	Cl-C_6H_4-2-NH_2	1.90	1.61	0.28	1.08	0 0 0	0.00	0.00	1.88	0.02
356	I-C_6H_4-2-NH_2	2.32	2.02	0.28	1.08	0 0 0	0.00	0.00	2.29	0.03
357	H_2NSO_2-C_6H_4-2-Cl	0.74	1.02	0.28	0.88	2 0 0	0.00	0.00	0.69	0.05
358	H_2NSO_2-C_6H_4-2-NO_2	0.34	0.05	0.60	0.88	1 0 0	0.00	0.00	0.28	0.06
359	H_2NCONH-C_6H_4-2-F	0.88	0.97	0.28	1.08	1 0 0	0.00	0.00	0.97	−0.09
360	H_2NCONH-C_6H_4-2-Cl	1.27	1.54	0.28	1.08	2 0 0	0.00	0.00	1.25	0.02
361	H_2NCONH-C_6H_3-3-Cl-4-OCH_3 [b,c]	1.37	1.52	0.34	0.79	1 0 0	0.00	0.00	1.48	−0.11
362	$CONH_2$-C_6H_4-2-Br	0.73	1.50	0.28	0.72	3 0 0	0.00	0.00	0.84	−0.11
363	$CONH_2$-C_6H_4-2-F	0.64	0.78	0.28	0.72	1 0 0	0.00	0.00	0.69	−0.05
364	$CONH_2$-C_6H_4-2-$CONH_2$	−1.73	−0.84	0.32	0.72	5 0 0	0.32	0.72	−1.78	0.05
365	CH_3O-C_6H_4-2-$CONMe_2$	0.71	0.60	0.51	0.50	1 0 0	0.17	0.27	0.61	0.10
366	CH_3OCO-C_6H_4-2-CO_2CH_3	1.56	2.09	0.51	0.27	3 0 0	0.51	0.27	1.49	0.07
367	CH_3CONH-C_6H_4-2-OCH_3	0.98	1.09	0.17	1.08	1 0 0	0.00	0.00	0.98	−0.00
368	CH_3CO-C_6H_4-2-$OCONMe_2$	0.93	1.01	0.51	0.50	1 0 0	0.17	0.27	1.01	−0.08
369	F-C_6H_4-2-$OCONHCH_3$	1.25	1.35	0.28	0.50	0 0 0	0.00	0.00	1.48	−0.23
370	F-C_6H_4-2-$OCOCH_3$	1.76	1.63	0.28	0.50	0 0 0	0.00	0.00	1.75	0.01
371	CF_3-C_6H_4-2-$OCOCH_3$	2.59	2.37	0.49	0.50	0 0 0	0.00	0.00	2.58	0.01
372	Cl-C_6H_4-2-CH_3-4-$OCONHCH_3$	2.57	2.58	0.28	0.50	0 0 1	0.00	0.00	2.60	−0.03
373	1,2-Cl_2-C_6H_3-4-$NHCONHC_6H_5$ [c]	4.70	4.28	0.42	1.08	0 0 0	0.00	0.00	4.64	0.06
374	1,2-Cl_2-C_6H_3-4-$NHCONMe_2$ [c]	2.79	2.40	0.42	1.08	0 0 0	0.00	0.00	2.80	−0.01
375	1,2-Cl_2-C_6H_3-4-$OCONHCH_3$ [c]	2.80	2.63	0.42	0.50	0 0 0	0.00	0.00	2.80	0.00
376	1,3-Cl_2-C_6H_3-5-$NHCONMe_2$ [c]	3.07	2.40	0.42	1.08	0 0 0	0.00	0.00	2.80	0.27
377	1,3-Cl_2-C_6H_3-5-$OCONHCH_3$ [c]	3.03	2.63	0.42	0.50	0 0 0	0.00	0.00	2.80	0.23
378	NC-C_6H_4-2-$OCONHCH_3$	0.86	0.64	0.65	0.50	0 0 0	0.00	0.00	0.95	−0.09
379	NC-C_6H_4-2-$OCOCH_3$	1.33	0.92	0.65	0.50	0 0 0	0.00	0.00	1.23	0.10
380	HO-C_6H_4-2-CN	1.60	0.89	0.65	1.06	0 0 0	0.00	0.00	1.54	0.06
381	HO-C_6H_4-2-CF_3	2.80	2.34	0.48	1.06	0 0 0	0.00	0.00	2.79	0.01
382 *	Pyr-2-OCH_3-4-$CONHNH_2$ [a,c]	−0.10	−1.32	0.80	1.22	0 0 0	0.00	0.00	−0.37	0.27
383 *	Pyr-2-OEt-4-$CONHNH_2$ [a,c]	0.48	−0.78	0.80	1.22	0 0 0	0.00	0.00	0.16	0.32
384	Pyr-4-CO-C_6H_4-4-CH_3	2.51	2.36	0.84	0.27	0 0 1	0.00	0.00	2.47	0.04
385	Pyr-4-CO-C_6H_4-4-Cl [c]	2.61	2.41	0.84	0.27	0 0 0	0.00	0.00	2.60	0.01
386	Pyr-4-CO-C_6H_4-4-NO_2 [c]	1.76	1.46	0.84	0.27	0 0 0	0.00	0.00	1.67	0.09
387	Pyr-4-CO-C_6H_4-4-OCH_3 [b,c]	1.94	1.68	0.84	0.27	0 0 0	0.00	0.00	1.88	0.06
388	Pyr-4-CO-C_6H_4-4-OH [b,c]	1.37	1.03	0.51	1.06	0 0 0	0.00	0.00	1.54	−0.17
389	Pyr-4-CO-C_6H_4-4-SO_2NH_2	0.56	−0.12	0.51	0.88	0 0 0	0.00	0.00	0.32	0.24
390	CHO-C_6H_4-2-CH_3-4-OCH_3	2.23	2.07	0.58	0.50	0 0 1	0.17	0.44	2.31	−0.08
391	NO_2-C_6H_4-2-OH	1.79	1.20	0.60	1.06	0 0 0	0.00	0.00	1.79	−0.00
392	NO_2-C_6H_4-2-CHO	1.74	1.22	0.60	0.44	0 0 0	0.00	0.00	1.47	0.27
393	NO_2-C_6H_4-3-CH_2CO_2H	1.45	1.15	0.60	0.21	0 0 0	0.00	0.00	1.27	0.18
394	NO_2-C_6H_4-4-CH_2OH	1.26	0.84	0.60	0.67	0 0 0	0.00	0.00	1.22	0.04
395	NO_2-C_6H_4-4-CH_2CO_2H	1.37	1.15	0.60	0.21	0 0 0	0.00	0.00	1.27	0.10
396	FSO_2-C_6H_4-4-CH_2CO_2H	1.86	1.49	0.71	0.21	0 0 0	0.00	0.00	1.62	0.24
397	CH_3SO_2-C_6H_4-3-CH_2CO_2H	0.06	−0.22	0.65	0.21	0 0 0	0.00	0.00	−0.07	0.13
398	NO_2-C_6H_4-4-$NHSO_2C_6H_4$-4-NH_2	2.14	1.09	0.60	1.08	0 0 0	0.50	1.08	2.20	−0.06
399	NO_2-C_6H_3-2-CF_3-4-SO_2NH_2 [c]	1.73	0.93	0.81	0.88	0 0 0	0.00	0.00	1.60	0.13
400	1,2-Cl_2-C_6H_3-4-$NHCONH_2$ [c]	2.64	2.25	0.42	1.08	0 0 0	0.00	0.00	2.65	−0.01
401	NO_2-C_6H_4-3-CH_2OH	1.21	0.84	0.60	0.67	0 0 0	0.00	0.00	1.22	−0.01

[a] ρ Values added. [b] ρ Values averaged. [c] Multiple σ values factored.

* Outliers *not* included in some regression equations; see Discussion section. † Observed log *P*; see ref. 16. ‡ Additive log *P*; see Methods section for definition of this and other parameters.

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