

Figure 1. Cell for solubility measurements: (A) 10-mm fritted glass disk; (B) filling port (sealed); (C) capillary side arm sealed by clamped rubber hose or an attached stopcock.

Results

The solubility data are given in Table I. It is notable first that the solubility of Cr_2S_3 is 1 to 2 orders of magnitude smaller than those of the other sulfides. Secondly, the solubilities of FeS and

NiS decrease with increasing sulfur content while the rest increase. These solubilities help to explain some of the observations of Bones et al. (2) on the corrosion of stainless steel in an Na/S electrochemical cell; an adherent corrosion layer on the steel in the charged state is lost in the discharged state as the greater solubility of the FeS and NiS in S-poor melts allows them to dissolve more readily in the melt of discharged composition.

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Solubilities and Partitioning 2. Relationships between Aqueous Solubilities, Partition Coefficients, and Molecular Surface Areas of Rigid Aromatic Hydrocarbons

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The aqueous solubilities of 31 polycyclic aromatic hydrocarbons and indan can be accurately estimated from melting point and either molecular surface area or f values. (The latter being an approximation of the octanol-water partition coefficient based upon group contribution values.) In both cases, the coefficient of the melting point term is close to 0.01 and the correlation coefficient exceeds 0.987.

In recent years, several workers (1-5) have attempted to correlate the aqueous solubilities or activity coefficients of aromatic hydrocarbons with a variety of molecular properties. In most cases, it has been found necessary to incorporate empirical correction factors for branching, ring formation, and/or proximity effects. In this report, it will be shown that when either molecular surface area [as calculated by Valvani et al. (6)] or f values [as calculated by Nys and Rekker (7)] are used as correlating parameters, it is not necessary to utilize additional correction factors. The use of molecular surface area and f values as correlating parameters will be illustrated and compared. (The f values are group contributions which are used to estimate octanol-water partition coefficients.)

Methods

Aqueous solubilities, molecular surface areas, calculated log partition coefficients, and melting points for all the compounds listed in Table I were obtained as follows.

Selection of Solubility Data. Aqueous solubilities of 31 polynuclear aromatic hydrocarbons and indan were obtained from Mackay and Shiu (2). Triple points for all the compounds

reported by them were used as melting points. For liquid solutes, 25 °C was used instead of the melting point.

Calculation of Molecular Surface Areas. Molecular surface areas were calculated according to method C of Valvani et al. (6). The following values for interatomic distances between various atoms or groups in a molecule were used: aromatic C-C, 1.40 Å; aromatic C-H, 1.08 Å; aromatic-aliphatic C-C, 1.54 Å; aliphatic C-C, 1.53 Å. The van der Waal radii used were as follows: aromatic C, 1.70 Å; aromatic H, 1.20 Å; methyl or methylene group, 2.0 Å. Total surface area (TSA) is the sum of individual atoms or group surface area contributions.

Calculation of Log Partition Coefficients. The logarithm of the partition coefficient (for the octanol-water system) for all the solutes was calculated by summation of f values for all the groups in a molecule as described by Nys and Rekker (7). These values are also included in Table I.

Statistical Analysis of Data. Multiple regression analysis of all the data was performed using standard statistical procedures.

Results and Discussion

For compounds which do not associate in aqueous solution, the infinite dilution activity coefficients can be assumed to be equal to the activity coefficient at saturation. For liquids, this means that the mole fractional solubility is simply the reciprocal of the activity coefficient. For poorly soluble solutes, the mole fractional solubility is proportional to the molar solubility so that the molar solubility of a liquid in water S_w^l is given by

$$\log S_w^l = -\log \gamma + \text{constant} \quad (1)$$

For crystalline substances it is necessary to account for crystal

Table I. Properties of Some Rigid Aromatic Hydrocarbons

compound	mp, °C	log (molar solubility)	log (partition coeff)	surface area, Å ²
indan	25.0	-3.034	3.57	151.5
naphthalene	80.2	-3.606	3.35	155.8
1-methylnaphthalene	25.0	-3.705	3.86	172.5
2-methylnaphthalene	34.6	-3.748	3.86	176.3
1,3-dimethylnaphthalene	25.0	-4.292	4.38	192.9
1,4-dimethylnaphthalene	25.0	-4.139	4.38	189.2
1,5-dimethylnaphthalene	81.0	-4.679	4.38	189.2
2,3-dimethylnaphthalene	102.0	-4.716	4.38	193.1
2,6-dimethylnaphthalene	108.0	-4.888	4.38	196.7
1-ethylnaphthalene	25.0	-4.162	4.39	187.4
1,4,5-trimethylnaphthalene	25.0	-4.923	4.90	200.9
biphenyl	71.0	-4.345	4.03	182.0
acenaphthene	96.2	-4.594	4.03	175.0
fluorene	116.0	-4.925	4.47	193.6
phenanthrene	101.0	-5.150	4.63	198.0
anthracene	216.2	-6.377	4.63	202.2
2-methylanthracene	209.0	-6.691	5.15	222.6
9-methylanthracene	81.5	-5.868	5.15	215.1
9,10-dimethylanthracene	182.0	-6.566	5.67	228.0
pyrene	156.0	-6.176	5.22	213.0
fluoranthene	111.0	-5.898	5.22	218.0
1,2-benzofluorene	187.0	-6.682	5.75	237.4
2,3-benzofluorene	209.0	-7.275	5.75	239.9
chrysene	255.0	-8.057	5.91	241.0
triphenylene	199.0	-6.726	5.45	236.0
naphthacene	357.0	-8.687	5.91	248.0
1,2-benzanthracene	160.0	-7.214	5.91	244.3
7,12-dimethyl-1,2-benzanthracene	122.0	-6.626	6.95	266.0
perylene	277.0	-8.804	6.50	251.5
3,4-benzopyrene	175.0	-7.820	6.50	256.0
3-methylcholanthrene	178.0	-7.973	7.11	282.7
benzo[ghi]perylene	277.0	-9.018	7.10	266.9

lattice interactions (β) so that the aqueous solubility of a crystal S_w^c becomes

$$\log S_w^c = -\log \gamma - \frac{\Delta H_f (T_m - T)}{2.30R T_m T} + \text{constant} \quad (2)$$

Since at the melting point

$$\Delta H_f = T_m \cdot \Delta S_f \quad (3)$$

eq 2 can be expressed as

$$\log S_w^c = -\log \gamma - \frac{\Delta S_f}{2.303R} \left(\frac{T_m - T}{T} \right) + \text{constant} \quad (4)$$

At room temperature (25 °C) this reduces to

$$\log S_w^c = -\log \gamma - (\Delta S_f/1360)(mp - 25) + \text{constant} \quad (5)$$

Where mp is the melting point in °C.

Solubility and Molecular Surface Area. On the basis of previous work by the authors (9-15) it would be expected that the relationship between the molecular surface areas and

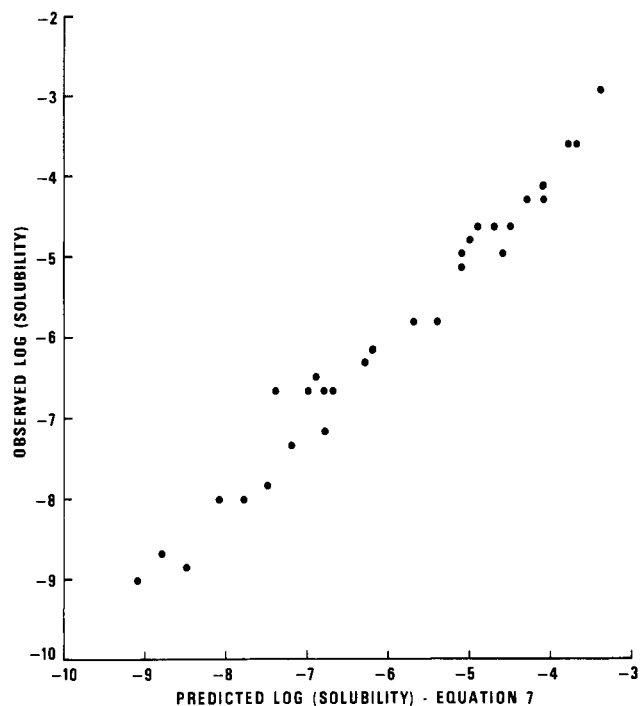


Figure 1. Calculation of aqueous solubility by eq 7.

aqueous solubilities of crystalline compounds is given by an equation of the form

$$\log S_w^c = \alpha(\text{TSA}) + \beta(\text{mp}) + \delta \quad (6)$$

Analysis of data from Table I yields the following relationship

$$\log S_w^c = -0.0282(\text{TSA}) - 0.0095(\text{mp}) + 1.42 \quad (7)$$

$n = 32, r = 0.9877, s = 0.271$

The excellent agreement between the calculated surface areas and observed solubilities, as shown in Figure 1, is supportive of the concept of molecular interactions being determined by the true molecular area of contact. This result is in agreement with previous papers in this series (9-12) which have shown that the solubilities of a variety of liquid monofunctional aliphatic compounds can be correlated quite well with molecular and group surface areas. In all cases, it is believed that the need to correct for branching, ring, and proximity effects is eliminated because these structural features alter activity coefficients by reducing the effective surface area of the molecule and thus the amount of contact between the hydrocarbon molecule and its aqueous environment.

Solubility and Partitioning. Partition coefficients of crystalline solids can be quantitatively related to the aqueous solubilities as shown by the following equation.

$$\log S_w^c = \alpha(\log \text{PC}) + \beta(\text{mp}) + \delta \quad (8)$$

When partition coefficients calculated from the f values by Nys and Rekker (7) are used, the following relationship is obtained.

$$\log S_w^c = -0.88(\log \text{PC}) - 0.01(\text{mp}) - 0.012 \quad (9)$$

$n = 32, r = 0.9895, s = 0.251$

The results of this equation are shown in Figure 2. The above equation and eq 7 can be used to predict aqueous solubilities for polycyclic aromatic hydrocarbons. In the analysis of other sets of data for various types of organic nonelectrolytes, it was found that aqueous solubility can frequently be estimated rather reliably by

$$\log S_w^c = -\log \text{PC} - 0.01(\text{mp}) + 0.50$$

This equation is similar in form and magnitude to eq 9, in fact,

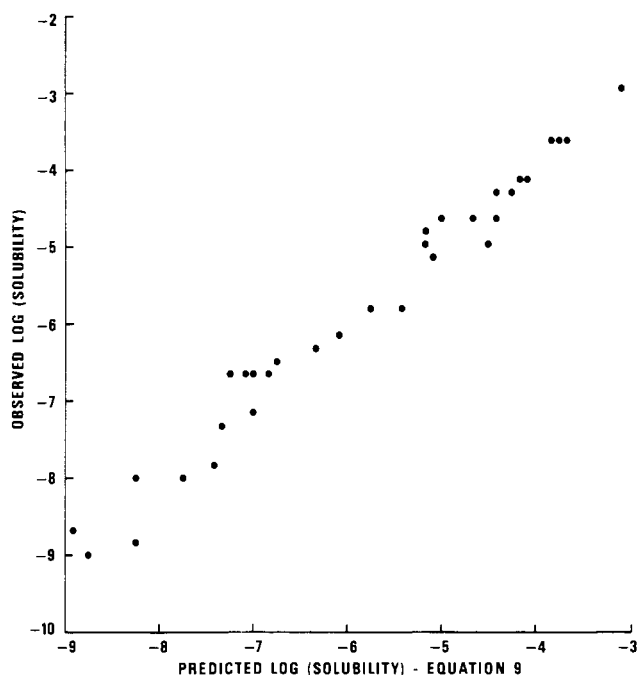


Figure 2. Calculation of aqueous solubility by eq 9.

for the range of partition coefficients covered in this report (i.e., $3.5 < PC < 6.0$) the two equations differ by less than 0.23 log units. This corresponds to a maximum difference of a factor of 1.7. The data of Mackay and Shiu (2) fit this equation quite well ($r = 0.989$ and $s = 0.251$). The final determination of the coefficients of eq 8 must await the analysis of a very large data set. Their utility in understanding the solution equilibria and in drug design is quite evident.




Partition Coefficients and Molecular Surface Areas. Unlike molecular surface area, which is a property of the molecule independent of its environment, the f values by Nys and Rekker (7) are statistically derived numbers which are based on experimental measurements of partition coefficients between n -octanol and water. However, since partitioning is related to activity, the partition coefficients computed from f values of Nys and Rekker can be quantitatively related to activity coefficients and thus to surface area. (It has already been shown (13) that octanol-water partition coefficients can be quite successfully correlated with molecular surface area for aromatic hydrocarbons.) The relationship between log partition coefficients and molecular surface area is given by the following equation.

$$\log PC = +0.0303(\text{TSA}) - 1.389 \quad (10)$$

$$n = 32, r = 0.987, s = 0.170$$

The excellent agreement between the calculated partition coefficients and total surface area is indicative of accuracy of both these parameters. The relationship between group f values and typical group surface area values is shown in Table II. There appears to be a rank order correlation between the two

Table II. Atomic and Group f Values and Surface Areas for Hydrocarbons

	f value	surface area, ^a Å ²
-CH ₃	0.70	33.2
-CH ₂	0.527	18.1
-CH	0.236	8.4
-C	0.14	0.2
 CH	0.344	18.2
 C	0.158	4.1
 C	0.297	5.65

^a Most commonly encountered value.

parameters. Because the surface area of a particular group in a molecule is dependent upon the size and proximity of other atoms of that molecule, it is not possible to assign a single value for each group. It is precisely this fact which makes surface area calculations more accurate than f values. The calculated surface area is a more accurate measure of the hydrocarbon-water contact area. However, since surface areas must be custom calculated for each molecule of interest they are more difficult to obtain than f values.

The choice between f values and surface area is therefore a choice between accuracy and conceptualization on the one hand and convenience on the other.

Since f values will give sufficient accuracy for most situations it is suggested that they be used for quick calculations of this type. A conceptual appreciation of the importance of surface area in solution equilibria will enable the anticipation of errors in the f -value approach.

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