

Handbook of

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Property  
Estimation  
Methods for  
Chemicals

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Environmental  
and Health Sciences

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# 7

## *Solubility in Water*

D. Mackay

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### 7.1 Introduction

Solubility in water is one of the most important physical chemical properties of a substance, having numerous applications to the prediction of its fate and its effects in the environment. It is a direct measurement of hydrophobicity, i.e., the tendency of water to "exclude" the substance from solution. It can be viewed as the maximum concentration which an aqueous solution will tolerate before the onset of phase separation.

Substances which are readily soluble in water, such as lower molecular weight alcohols, will dissolve freely in water if accidentally spilled and will tend to remain in aqueous solution until degraded. On the contrary, sparingly soluble substances dissolve more slowly and, when in solution, have a stronger tendency to partition out of aqueous solution into other phases. They tend to have larger air-water partition coefficients or Henry's law

constants, and they tend to partition more into solid and biotic phases such as soils, sediments, and fish. As a result, it is common to correlate partition coefficients from water to these media with solubility in water, as other chapters discuss.

## 7.2 Theoretical Foundation

Solubility normally is measured by bringing an excess amount of a pure chemical phase into contact with water at a specified temperature, so that equilibrium is achieved and the aqueous phase concentration reaches a maximum value. It follows that the fugacities or partial pressures exerted by the chemical in these phases are equal. Assuming that the pure chemical phase properties are unaffected by water, the pure phase will exert its vapor pressure  $P^S$  (Pa) corresponding to the prevailing temperature. The superscript S denotes saturation. In the aqueous phase, the fugacity can be expressed using Raoult's Law with an activity coefficient  $\gamma$ :

$$P^S = x\gamma P_L^S \quad (1)$$

where  $x$  is the mole fraction of the chemical in aqueous solution, and  $P_L^S$  is the vapor pressure of pure liquid phase chemical, again at the specified temperature.

### 7.2.1 Equilibrium Situations

Four possible equilibrium situations may exist, depending on the nature of the chemical phase, each of which requires separate theoretical treatment and leads to different equations for expressing solubility. These equations form the basis of the correlations discussed later.

#### 7.2.1.1 Pure Chemical is an Immiscible Liquid (e.g., Benzene)

In this case,  $P^S$  is also  $P_L^S$ . Thus the product  $xy$  is 1.0 and  $x$  is  $1/\gamma$ . Sparingly soluble substances are such because the value of  $\gamma$  is large.

For example, at 25°C benzene has a solubility in water of 1780 g/m<sup>3</sup> or 22.8 mol/m<sup>3</sup>. Since 1m<sup>3</sup> of solution contains approximately 10<sup>6</sup>/18 mol water (1m<sup>3</sup> is 10<sup>6</sup> g and 18 g/mol is the molecular mass of water), the mole fraction x is 22.8/(10<sup>6</sup>/18) or 0.00041. The activity coefficient  $\gamma$  is thus 2440; i.e., a benzene molecule in aqueous solution behaves as if its concentration were 2440 times higher.

Substances such as PCBs can have activity coefficients exceeding 1 million. Hydrophobicity thus is essentially an indication of the magnitude of  $\gamma$ . Some predictive methods focus on estimating  $\gamma$ , from which solubility can be deduced.

As is discussed later, a molar activity coefficient  $\gamma_m$  may be defined such that  $S\gamma_m$  is 1.0 where S is the molar solubility; i.e., in units of mol/litre. Since S is 55.5 x,  $\gamma_m$  is  $\gamma/55.5$ , 55.5 being the number of moles of water in 1 litre of solution.

#### 7.2.1.2 Pure Chemical is an Immiscible Solid (e.g., Naphthalene)

In this case,  $P^S$  is the vapor pressure of the solid,  $P_S^S$ , e.g., naphthalene, while  $P_L^S$  is of liquid naphthalene. The fugacity ratio F or  $P_S^S/P_L^S$ , i.e., the solid to liquid ratio, can be estimated as:

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$$\frac{P_S^S}{P_L^S} = \exp(-\Delta S_F (T_M/T - 1)/R) = F \quad (2)$$

since the entropy of fusion,  $\Delta S_F$ , is typically  $56 \text{ J/mol}$  at the melting point, as Walden's Rule (Walden 1908) suggests:

$$\frac{P_S^S}{P_L^S} = \exp(-6.79(T_M/T - 1)) \quad (3)$$

The fugacity ratio  $F$  is 1.0 at the melting point and lower at lower temperatures. When  $T$  exceeds  $T_M$ , the substance is liquid and the fugacity ratio is 1.0.

For example, naphthalene with a melting point of  $80^\circ\text{C}$  has a fugacity ratio of 0.286 at  $25^\circ\text{C}$ ; thus  $xy$  is 0.286. The solubility of solid naphthalene (molecular weight 128) is  $31.7 \text{ g/m}^3$  or  $0.25 \text{ mol/m}^3$ ,  $x$  is  $4.5 \times 10^{-6}$ , and  $\gamma$  is 64000. If naphthalene could exist as a liquid at  $25^\circ\text{C}$ , its solubility would be  $31.7/0.286$  or  $111 \text{ g/m}^3$ .  $F$  is thus the ratio of both vapor pressures and solubilities.

This fugacity ratio correction is critically important and can have an enormous effect on solubility. Since chemicals in solution are in the liquid state they behave as if, in the limit, they were pure liquids, and the reference fugacity or vapor pressure must be of the liquid. Correlations of partition coefficients such as octanol-water with solubility must include this "correction."

### 7.2.1.3 Pure Chemical is a Gas or Vapor (e.g., Methane)

If the substance's boiling point is less than the environmental temperature, it can not exist as a stable liquid or solid at atmospheric pressure. Thus the pure chemical phase is a gas, usually at atmospheric pressure, and  $P^S$  is 1 atm or  $101325 \text{ Pa}$ . Solubilities may, however, be reported at the higher vapor pressure. For more dilute gases at partial pressures less than 1 atm, the solubility is then proportional to the partial pressure as expressed by Henry's Law. The reference pressure  $P_L^S$  may be known from data obtained at higher pressures, or it may be unknown if the environmental temperature exceeds the critical temperature.

It is usual to lump  $\gamma$  and  $P_L^S$  together as one parameter  $H'$ , a Henry's law constant, i.e.,

$$P = xyP_L^S = xH' \quad (4)$$

$H'$  thus contains information about both the volatility  $P_L^S$  and the hydrophobicity  $\gamma$ . The units of  $H'$  depend on the units of  $P$  and concentration. The Henry's law constant often is expressed with pressure in  $\text{Pa}$  and concentration in  $\text{mol/m}^3$ , thus giving  $H$  units of  $\text{Pa m}^3/\text{mol}$ .

Relatively few environmental contaminants are gases, and they are well characterized. The most common gaseous examples are vinyl chloride and freons.

### 7.2.1.4 Pure Chemical is a Miscible Substance (e.g., Ethanol)

If the activity coefficient is relatively small, i.e.  $<20$ , it is likely that the liquid is miscible with water and no solubility can be measured. The relevant descriptor of hydrophobicity in such cases is the activity coefficient. Correlations of other environmental partitioning properties with solubility are then impossible.

### 7.2.2 Complicating Factors

Solubility is a function of temperature because both  $P_L^S$  and  $\gamma$  are temperature dependent. Usually  $\gamma$  falls with increasing temperature; thus solubility increases. This implies that the process of dissolution is endothermic. Exceptions are frequent and in some cases, such as benzene, there may be a solubility minimum as a function of the temperature at which the enthalpy of dissolution is zero.

The presence of electrolytes in the aqueous phase (as occurs most commonly in seawater) generally causes a solubility reduction or "salting out" effect. This usually is expressed by the Setschenow constant  $K$ , namely

$$\log_{10}(S_0/S) = KC \quad (5)$$

where  $S_0$  and  $S$  are the solubility in pure water and in the electrolyte solution and  $C$  is the concentration (molarity) of the electrolyte. Xie et al. (1997) reviews such data. This effect is important when assessing the fate of organic chemicals in salt water.

In partially miscible systems with  $\gamma$  typically in the range 20 to 200, appreciable dissolution of water in the chemical phase may occur, thus the vapor pressure  $P^S$  is not that of the pure chemical but of the somewhat diluted chemical phase.

Surface active materials may not display a solubility because they form micelles in solution, which are essentially soluble aggregations of the pure substance.

In environmental situations, dissolved organic matter such as fulvic acids frequently increase the apparent solubility. This is the result of sorption of the chemical to organic matter which is sufficiently low in molecular mass to be retained permanently in solution. The "true" solubility or concentration in the pure aqueous phase probably is not increased. The apparent solubility is the sum of the "true" or dissolved concentration and the quantity which is sorbed.

The solubility of substances such as carboxylic acids, which dissociate or form ions in solution, is also a function of pH, a common environmental example being pentachlorophenol. Data must thus be at a specified pH. Alternatively, the solubility of the parent (non-ionic) form may be given, and  $pK_a$  or  $pK_b$  given, to permit the ratio of ionic to non-ionic forms to be calculated as

$$\text{ionic/non-ionic} = 10^{(pH-pK_a)} \quad (6)$$

The total solubility is then that of the parent and ionic forms.

### 7.3 Experimental Methods

The conventional approach is to equilibrate an excess amount of the pure chemical with an aqueous solution at controlled temperature and measure the concentration of the solution. Common analytical methods include gravimetric or volumetric techniques, spectroscopy, gas chromatography, and scintillation counting. Difficulties may be encountered with the presence of micro-particles of pure chemical phase which may give an apparently high solubility.

The use of "generator columns," in which water is flowed slowly through a tube packed with a solid support coated with the chemical, reduces this risk (Wasik et al., 1993). Hydrophobic substances tend to sorb appreciably to solid surfaces such as

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glassware, and they may evaporate from solution; thus extreme care is required when handling these solutions.

Solubilities are generally reported in units such as mg/L or the equivalent g/m<sup>3</sup>, but other unit systems are used, especially molarity and molality. Solutions exceeding 100 mg/L are relatively easy to handle and analyze. In the range 1 to 100 mg/L, more care is required and accuracy is reduced. In the range 0.001 to 1 mg/L, extreme care is required and reported data are often suspect. Below 0.001 mg/L, solutions are so dilute that it is very difficult to obtain reliable data. Mackay et al. (1997) and Yalkowsky and Banerjee (1992) review methods of measuring solubility and other environmentally relevant properties.

## 7.4 Data Sources

The most critically reviewed solubility data are those in the IUPAC Solubility Data series (1984, 1985, 1989a, 1989b). Other sources include the Handbooks by Howard et al. (1989, 1990, 1991, 1993), Mackay et al. (1997), and Verschueren (1996) and the papers and texts by Horvath (1973, 1975, 1982) and Yalkowsky and Bannerjee (1992). Commercial databases are also available from a variety of sources, e.g., the AQUASOL database of Yalkowsky and Dannenfelser (1991).

## 7.5 Estimation Methods

Andren et al. (1987) have reviewed a variety of estimation methods.

Three general classes of estimation method are in frequent use. The first exploits the considerable data on octanol water partition coefficient K<sub>OW</sub> and the well developed estimation methods for that quantity by seeking a relationship between solubility and K<sub>OW</sub>. The second attempts to relate molecular structure to solubility by a variety of techniques involving counting bonds or groups or calculating molecular volumes, areas, or other topological indices such as connectivity.

The third uses another measured property of the chemical which can be related to solubility. Most notable is HPLC retention time, which is a measure of the partitioning of the chemical between an aqueous phase (or more usually a water-cosolvent mixture) and a stationary organic phase. Other properties exploited include boiling point, parachor, and solubility parameters.

We recommended two of these methods for general use, estimation from octanol-water partition coefficient and a group contribution method named AQUAFAC. Three other methods are also valuable under certain circumstances, the connectivity, UNIFAC, and solvatochromic approaches.

### 7.5.1 Estimation from Octanol-Water Partition Coefficient

Hansch et al. (1968) showed that solubility and K<sub>OW</sub> are well correlated for liquid solutes. This correlation is expected on theoretical grounds because solubility is inversely proportional to activity coefficient  $\gamma$  in the aqueous phase, and K<sub>OW</sub> can be shown to be proportional to  $\gamma$ .

$K_{OW}$  is  $\gamma_W v_w / \gamma_O v_o$  where  $v$  is molar volume and subscripts w and o refer to the water and octanol phases (Mackay, 1991). A plot of  $\log K_{OW}$  versus log solubility is thus expected to have a slope of approximately  $-1$ , and this is observed. Numerous further studies have explored and refined this relationship (e.g., Miller et al., 1985; Chiou et al., 1977, 1982; Valvani et al., 1981; Yalkowsky and Valvani, 1979; Yalkowsky et al., 1983a, 1983b; Banerjee et al., 1980).

For solids, it is essential to correlate  $K_{OW}$  with the liquid solubility, not the solid solubility; thus the fugacity ratio expression must be included in any correlation. This is readily done, since melting point  $T_M(K)$  is usually available and Walden's Rule can be applied. Following Yalkowsky (1979), the fugacity ratio F can be estimated at  $25^\circ C$  ( $T = 298 K$ ) as

$$\begin{aligned} \log F &= 6.79(1 - T_M/T)/2.303 \\ &= -0.01(T_M - 298) \end{aligned} \quad (7)$$

The solid molar solubility  $S_s$  thus can be calculated from the liquid molar solubility  $S_L$  and F as

$$S_s = FS_L \quad (8)$$

or

$$\log S_s = \log S_L + \log F = \log S_L - 0.01(T_M - 298)$$

The usual correlation approach is then to determine the parameters A and B in the equation

$$\log S_L = A - B \log K_{OW} \quad (9)$$

or

$$\log S_s = A - B \log K_{OW} - 0.01(T_M - 298) \quad (10)$$

A considerable number of such correlations have been developed with the constant 0.01 being allowed to vary, and in some cases it is (wrongly) ignored, or because of inherent error in the data it appears to be unimportant (e.g., Isnard and Lambert, 1989). As was discussed earlier, there are compelling theoretical reasons to include the fugacity ratio term.

For rigid molecules, Yalkowsky et al. (1983) obtained a simple correlation for molar solubility with B equal to 1.0, namely:

$$\log S_s = 0.8 - \log K_{OW} - 0.01(T_M - 298) \quad (11)$$

This equation also can be written in terms of the liquid solubility  $S_L$  as

$$S_L = 6.31/K_{OW} \quad (11a)$$

This implies that the pseudo solubility of these substances in octanol is 6.31 mol/L. This equation is ideal for screening purposes or when a fast check of the consistency of reported values of  $S_L$  and  $K_{OW}$  is needed.

Note that, if the melting point is expressed in K, and  $T_M$  is less than 298 K, the  $\log F$  term containing  $(T_M - 298)$  should be set to zero, i.e.,  $(T_M - 298)$  can never be negative. If entropy

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of fusion data are available, it is preferable to include these data rather than rely on Walden's Rule. In that case, the constant 0.01, which is  $56.4/(2.303 \times 8.314 \times 298)$  can be rewritten as  $0.000175 \Delta S$  where  $\Delta S$  has units of J/mol K. If  $\Delta S$  is in cal/mol K, the constant changes to 0.00073.

For long chain flexible molecules, Yalkowsky and Valvani (1980) expressed  $\Delta S$  in terms of chain length as

$$\Delta S = 56.5 + 10.5(n-5) \text{ J/mol K}$$

or

$$13.5 + 2.5(n-5) \text{ cal/mol K} \quad (12)$$

They obtained a correlation for 167 substances of

$$\log S_L = -0.000813 \Delta S(T_M - 298) - \log K_{OW} + 0.54 \quad (13)$$

Many other correlations, for example those compiled by Lyman et al. (1982), have coefficients B in equation 9 of 1.1 to 1.3. This implies that, as  $K_{OW}$  increases, the activity coefficient of the chemical in octanol  $\gamma_o$  also increases. For example, if  $\gamma_w$  increases by a factor of 100, and  $\gamma_o$  increases by a factor of about 2.5; then  $K_{OW}$  increases by a factor of only 40. The result is that solubility is proportional to  $K_{OW}$  raised to a power of -1.25, since  $40^{-1.25}$  is 0.01. This effect of an increase in  $\gamma_o$  or a decreasing solubility in octanol is very important for hydrophobic substances. Examination of these correlations, especially those of Andren et al. (1987) and Isnard and Lambert (1989), suggests that a coefficient B of 1.25 is more generally applicable. This causes a change in the coefficient A to about 1.10, giving the correlation

$$\log S = -0.01(T_M - 298) - 1.25 \log K_{OW} + 1.10 \quad (14)$$

This correlation is recommended for more hydrophobic substances. Equations (11) and (14) give the same solubility when  $\log K_{OW}$  is 1.2.

As expected, restricting the class of chemicals to structurally similar compounds such as alcohols or PCBs permits an improved correlation. Table 7.1, adapted from Lyman et al. (1982) and Yalkowsky and Banerjee (1992), lists a number of correlations for specific chemical classes.

In summary, for general use, apply Equation (14), which implies a knowledge of  $K_{OW}$  and melting point. If necessary, both quantities can be estimated (see Chapters 1 and 5).

If entropy of fusion data are also available, the constant 0.01 can be "corrected" to  $0.000175 \Delta S$  with  $\Delta S$  in units of J/mol K, or to 0.00073  $\Delta S$  with units of cal/mol K.

The standard deviation is expected to be about 0.3 log units, corresponding to a factor of 2. For a narrower class of substances, using the equations in Table 7.1, the standard deviation is expected to fall to about 0.2 log units or a factor of 1.6. The Syracuse Research Corporation offers an estimation method WSKOWWIN as part of its Estimation Program Interface for Windows (EPI/WIN); details are available at the web site <http://syrres.com/interskow/epi.htm>.

### 7.5.2 Estimation from Molecular Structure

Irmann (1965) pioneered the correlation of solubilities of hydrocarbons and halogenated hydrocarbons with molecular structure using a scheme with the form

**TABLE 7.1**

Regression Equations Relating Solubility S (mol/L) to  $K_{ow}$ . The Solubility is of the Liquid or Subcooled Liquid State. For Solids, a Fugacity Ratio Term Must be Included

Chemical Class	$\log S = A - B \log K_{ow}$ (Equation (9))		
	A	B	Reference
Alcohols	0.926	1.113	Hansch et al. (1968)
Alcohols	0.338	0.971	Tewari et al. (1982)
Ketones	0.720	1.229	Hansch et al. (1968)
Ketones	0.431	0.927	Tewari et al. (1982)
Esters	0.520	1.013	Tewari et al. (1982)
Esters	0.306	1.073	Tewari et al. (1982)
Alkylhalides	0.832	1.221	Hansch et al. (1968)
Alkynes	1.043	1.294	Hansch et al. (1968)
Alkenes	0.248	1.294	Hansch et al. (1968)
Alkenes	0.275	1.101	Tewari et al. (1982)
Mono Aromatics	0.339	0.996	Hansch et al. (1968)
Mono Aromatics	0.727	0.947	Tewari et al. (1982)
Alkanes	-0.248	1.237	Hansch et al. (1968)
Halogenated HCs	0.356	1.103	Tewari et al. (1982)
Halogenated HCs	1.50	0.962	Chiou & Freed (1977)
Acids, bases, neutrals	0.845	1.163	Hafkenscheid & Tomlinson (1983)
Dyes	0.453	0.820	Hou & Baughman, quoted in Yalkowsky & Banerjee (1992)
PAHs	0.262	0.880	Yalkowsky & Valvani (1979)

$$-\log S = x + \sum y_i n_i + \sum z_j n_j \quad (15)$$

The constant  $x$  depends on the class of compound (e.g., aromatic vs. aliphatic),  $n_i$  is the number of specific atoms (e.g., C or Cl),  $y_i$  is a constant specific to that atom and how it is bonded,  $n_j$  is the number of certain bonds or structural types (e.g., double or triple bonds or branching), and  $z_j$  is a constant specific to these bonds or structural elements. Lyman et al. (1982) gives a full account of this approach and recommend it as the preferred method when no partition coefficient data are available. However, this method is dated and does not include functional groups containing oxygen, nitrogen, and sulfur atoms.

Yalkowsky, Myrdal, and co-workers have developed the AQUAFAC group contribution method which predicts the molar activity coefficient  $\gamma_m$  from which the molar solubility  $S$  can be deduced, using supplemental information on the fugacity ratio  $F$  (Myrdal et al., 1992, 1993, 1995). The method exploits the AQUASOL database described by Dannenfelser and Yalkowsky (1991) and Yalkowsky and Dannenfelser (1991). The fugacity ratio (which is termed the "ideal solubility" in their publication) is expressed as

$$\log F = -(13.5 - 4.6 \log \sigma)(T_M - 298)/1364 \quad (16)$$

where  $\sigma$  is a symmetry number, i.e., the number of indistinguishable positions in which a compound may be oriented. Anthracene has a  $\sigma$  of 4, while phenanthrene has a  $\sigma$  of 2. The units in this equation are cal/mol K, and 1364 is  $1.987 \times 2.303 \times 298$  where 1.987 is the gas constant  $R$  in units of cal/mol K. With SI units of Joules the equation is

$$\log F = -(56.5 - 19.2 \log \sigma)(T_M - 298)/5706 \quad (17)$$

The prediction equations for molar solubility are thus:

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$$\text{liquids, } S = 1/\gamma_m \text{ or } \log S = -\log \gamma_m \quad (18)$$

$$\text{solids, } S = F/\gamma_m \text{ or } \log S = \log F - \log \gamma_m \quad (19)$$

The molar activity coefficient is given by:

$$\log \gamma_m = \sum n_i q_i \quad (20)$$

where  $n_i$  is the number of times a group appears and  $q_i$  is the contribution of that group. Table 7.2 lists values of  $q_{ui}$ .

TABLE 7.2

AQUAFAC Group Contribution  $q$ -Values. (supplied by S. Yalkowsky)

$X_i-G$	$q$ -Values	$X_nY-G$	$q$ -Values	$X_nY_2-G$	$q$ -Values
$X_2-CH_2$	0.545	$XY-CH_2$	0.03	$Y_2-CH_2$	0.149
$X_3-CH$	0.305	$X_2Y-CH$	0.085	$XY_2-CH$	-0.127
$X_4-C$	0.019	$X_3Y-C$	-0.308	$X_2Y_2-C$	-0.52
$X_2-C=$	0.583	$XY-C$	0.525	$Y_2-C$	0.319
$X_2-O$	-1.51	$XY-O$	-0.664	$Y_2-O$	-0.017
$X_2-BARB$	-2.689	$XY-BARB$	-2.593	$Y_2-BARB$	-2.667
$X_3-N$	-3.428	$X_2Y-N$	0.379	$XY_2-N$	0.320
$X_2-C=O$	-0.968	$XY-C=O$	-0.722	$Y_2-C=O$	-0.41
$X_2-NH$	-2.233	$XY-NH$	-0.110	$Y_2-NH$	N/D <sup>(a)</sup>
$X-CH_3$	0.706	$Y-CH_3$	0.204	N/E <sup>(b)</sup>	
$X-CH=$	0.636	$Y-CH=$	0.321	N/E <sup>(b)</sup>	
$X-F$	0.251	$Y-F$	-0.141	N/E <sup>(b)</sup>	
$X-Cl$	0.389	$Y-Cl$	0.409	N/E <sup>(b)</sup>	
$X-Br$	0.379	$Y-Br$	0.645	N/E <sup>(b)</sup>	
$X-I$	0.49	$Y-I$	0.887	N/E <sup>(b)</sup>	
$X-CHO$	-1.111	$Y-CHO$	-0.772	N/E <sup>(b)</sup>	
$X-NH_2$	-1.911	$Y-NH_2$	-1.193	N/E <sup>(b)</sup>	
$X-N=$	-0.668	$Y-N=$	-0.969	N/E <sup>(b)</sup>	
$X-N=C=S$	1.203	$Y-N=C=S$	1.266	N/E <sup>(b)</sup>	
$X-CONH$	-1.509	$Y-CONH$	-0.847	N/E <sup>(b)</sup>	
$X-CONH_2$	-2.126	$Y-CONH_2$	-0.508	N/E <sup>(b)</sup>	
$X-CON$	-1.601	$Y-CON$	N/D <sup>(a)</sup>	N/E <sup>(b)</sup>	
$X-C\equiv N$	-0.619	$Y-C\equiv N$	-0.427	N/E <sup>(b)</sup>	
$X-NO_2$	-0.127	$Y-NO_2$	0.082	N/E <sup>(b)</sup>	
$X-NHCON(CH_3)_2$	-2.190	$Y-NHCON(CH_3)_2$	-1.229	N/E <sup>(b)</sup>	
$X-(COO)$	-1.117	$Y-(COO)$	-0.796	N/E <sup>(b)</sup>	
$X-C\equiv CH$	0.438	$Y-C\equiv CH$	N/D <sup>(a)</sup>	N/E <sup>(b)</sup>	
$X-OOC$	-1.283	$Y-OOC$	N/D <sup>(a)</sup>	N/E <sup>(b)</sup>	
$X-COOH$	N/D <sup>(a)</sup>	$Y-COOH$	-1.419	N/E <sup>(b)</sup>	
$X-OH$	-2.285	$Y-OH$	-1.810	N/E <sup>(b)</sup>	
$X=CH_2$	0.579	$Y=CH_2$	N/E <sup>(b)</sup>	N/E <sup>(b)</sup>	
EPOXIDE	-0.301	EPOXIDE	N/E <sup>(b)</sup>	N/E <sup>(b)</sup>	
$X_2-S$	N/D <sup>(a)</sup>	$XY-S$	N/D <sup>(a)</sup>	$Y_2-S$	-0.310
$C_{AR}$					0.525
$C_{BRIDGE HEAD}$					0.319
$C_{HAR}$					0.321
$N_{AR}$	-0.969				-0.063
$C_{RING}$					-0.123
ORTHOBIPHENYL					

<sup>(a)</sup> N/D, group not yet defined<sup>(b)</sup> N/E, non-existent group

The "groups" include atoms of H, F, Cl, Br, etc., with different values for carbon and oxygen atoms, depending on their bonding environment. An X or  $sp^3$  neighboring atom is a hydrogen, aliphatic carbon, halogen, amine nitrogen, or ether oxygen. A Y or  $sp^2$  neighboring atom includes aromatic carbon and nitrogen, including nitro groups. A YY neighbor is a bridgehead aromatic C, as in naphthalene, or a group which is joined to two aromatic carbons, such as the carbonyl in diphenyl ketone. Two correction factors also are included, " $C_{RING}$ " for alicyclic rings and "ORTHOBIPHENYL" for the number of halogens in ortho positions in a biphenyl ring.

Table 7.3 gives the results of an analysis of the predictive capabilities of the AQUAFAC and partition coefficient approaches for 97 compounds.

TABLE 7.3

Average Absolute Errors in Log Solubility as Predicted by AQUAFAC and from Log  $K_{OW}$  (Myrdal et al., 1995).

Compound Type	Number of Compounds	AQUAFAC	Log $K_{OW}$
All compounds	97	0.41	0.61
Liquids	49	0.36	0.40
Solids	48	0.45	0.82
Non hydrogen bonding solids & liquids	78	0.42	0.63
Hydrogen bonding solids & liquids	19	0.34	0.53

### 7.5.3 Molecular Connectivity

Kier and Hall (1976) and Hall et al. (1975) have pioneered the use of the connectivity index as a descriptor of molecular structure. It is an expression of the sum of the degrees of connectedness of each atom in a molecule. Indices can be calculated to various degrees or orders, thus encoding increasing information about the structure. Although the index has been used with success in a number of applications, it is not entirely clear on theoretical grounds why this is so. It appears that the index generally expresses molar volume or area.

Nirmalakhandan and Speece (1988a, 1988b, 1989) have used this index in conjunction with polarizability to correlate solubilities of some 470 compounds, with a standard error of 0.332 in log solubility. The correlation include three parameters, a modified polarizability parameter and two connectivity indices. For those familiar with connectivity indices, this method is very convenient, but for occasional use by those unfamiliar with these concepts, the method requires a considerable learning period. It is discussed more fully in Chapter 8.

### 7.5.4 Solvatochromic or Linear Solvation Energy Methods

Kamlet, Taft, and co-workers have developed and advocated the use of the "solvatochromic" method, in which solubility is predicted from molar volume melting point and two parameters which express dipolarity/polarizability and hydrogen bond basicity (Kamlet et al., 1986, 1988; Taft et al., 1985). The method has been applied to a large number of properties, including partitioning and toxicities. Yalkowsky et al. (1988) have commented critically on the method, suggesting that the  $K_{OW}$  approach is more generally applicable. The approach has merit in that it exploits fundamental information on molecular interactions, but apparently it has not been widely used. It could form the basis of improved estimation methods in the future. It is not recommended for general use at this time.

for carbon and oxygen. A Y or  $sp^2$  neighbor is a two aromatic carbons also are included, of halogens in ortho positions of the AQUAFAC

and from Log

FAC	Log K <sub>ow</sub>
1	0.61
6	0.40
5	0.82
2	0.63
4	0.53

The connectivity index is the degrees of connection at various degrees of separation. Although the index has been used to predict solvation energy, it is not clear on theoretical grounds whether it is a measure of polar volume or area. The connectivity index in conjunction with a standard error of estimation provides a modified polarizability index. The connectivity indices, similar to the modified polarizability index, are similar with these compounds being discussed more fully in

of the "solvatochromic" properties of a molecule. The melting point and two measures of basicity (Kamlet and Taft) have been used to estimate the solubility of a large number of organic compounds. These methods have been commented on previously. The solvation energy of a molecule is determined by the interaction of the molecule with its environment. The improved estimation methods have been developed to take into account the effect of the environment on the solubility of a molecule.

### 7.5.5 UNIFAC

The UNIFAC (UNIQUAC functional group activity coefficient) method is an extension of the UNIQUAC (Universal quasi chemical) method, which has been used widely in chemical process engineering to describe partitioning in organic systems as occur in petroleum and chemical processing (Fredenslund et al., 1975, 1977). It has been applied less frequently to aqueous systems. It expresses the activity coefficient as the sum of a "combinational" component, which quantifies the nature of the area "seen" by the solute molecule, and a "residual" component, which is deduced from group contributions. Arbuckle (1983, 1986), Banerjee (1985), Banerjee and Howard (1988), and Campbell and Luthy (1985) have tested the applicability of the method to water solubility.

The method involves some computation which, while not difficult, requires extensive accurate coding and thus discourages use for occasional purposes. Since it was designed to treat complex mixtures, it is likely to find favor for estimating solubilities in water-cosolvent systems. Compilations of group parameters are available (e.g., Magnusson et al., 1981; Gmehling, 1983; Gmehling et al., 1982; and Tiegs et al., 1987) but the focus is more on chemicals of commerce than on environmental contaminants.

This method is well established and undoubtedly will be refined and extended; thus it is likely to play an increasing role in environmental situations. It is not yet as fully tested as the two recommended methods; thus it is not recommended at this time except for those who already use the technique and have available the required computer programs and some experience in their use.

## 7.6 Summary

Two methods are recommended for routine use for estimating solubility; the correlation with octanol water partition coefficient method and the AQUAFAC group contribution method. When possible, use both approaches and compare the results. Insights can also be obtained if solubility data are available for structurally similar compounds. Both methods are illustrated below.

Three other methods are applicable in certain circumstances, particularly if there is prior experience in their use. These are the connectivity, solvatochromic, and UNIFAC methods.

The estimation of solubility is an area of current research. Thus, existing methods are being refined and expanded, and new methods are evolving. The reader should keep abreast of these developments by consulting the current literature.

## 7.7 Appendix

### Illustrations of Estimation Methods at 25°C

#### Anthracene and phenanthrene

These two isomeric three-ring polycyclic aromatic hydrocarbons have similar values of  $K_{ow}$  but different melting points, illustrating the importance of the fugacity ratio term.

Both have a molecular formula  $C_{14} H_{10}$  and a molecular mass of 178.2.

Anthracene has an mp of 216°C (489K), and  $\log K_{OW}$  is 4.54.  
 Phenanthrene has an mp of 101°C (374 K), and  $\log K_{OW}$  is also 4.54.

#### Estimation from $K_{OW}$

$$\text{Equation (14)} \log S = -0.01(T_M - 298) - 1.25 \log K_{OW} + 1.10$$

$$\text{Anthracene: } \log S = -0.01(191) - 1.25(4.54) + 1.10 = -6.49$$

$$S = 3.27 \times 10^{-7} \text{ mol/L} = 0.058 \text{ g/m}^3 \text{ (exptl value } 0.045 \text{ g/m}^3\text{)}$$

$$\text{Phenanthrene } \log S = -0.01(76) - 1.25(4.54) + 1.10 = -5.34$$

$$S = 4.62 \times 10^{-6} \text{ mol/L} = 0.82 \text{ g/m}^3 \text{ (exptl value } 1.1 \text{ g/m}^3\text{)}$$

Equation (11) gives higher values of 0.40 g/m<sup>3</sup> and 5.6 g/m<sup>3</sup>.

Ignoring the fugacity ratio term would introduce a considerable error.

#### AQUASOL method

##### Anthracene

$$\sum n_i q_i = 10(Y-\text{CH}_2) + 4(YY>\text{C}=) = 10(0.321) + 4(0.319) = 4.486$$

$$\log S = -0.01(\text{MP} - 25) - \sum n_i q_i = -0.01(218 - 25) - 4.486 = -6.586$$

$$S = 2.59 \times 10^{-7} \text{ mol/L} = 0.046 \text{ g/m}^3$$

For phenanthrene, only the fugacity ratio term changes, and S is 1.01 g/m<sup>3</sup>.

##### Lindane

Molecular mass is 291, melting point is 113°C, and  $\log K_{OW}$  is reported to be 3.0.

Applying Equation (14) as above gives:

$$\log S = -3.53, S = 2.95 \times 10^{-4} \text{ mol/L} = 86 \text{ g/m}^3$$

$$6(X-\text{CH}) + 6(X\text{Cl}) + 6(\text{C Ring}) = 6(0.305) + 6(0.389) + 6(-0.062)$$

$$\sum n_i q_i = 6*\text{CH} + 6*\text{XCl} + 6*\text{C}_{\text{ring}} = 3.79$$

$$\log S = -0.01(\text{MP} - 25) - \sum n_i q_i = -0.01(112 - 25) - 3.79 = -4.656$$

$$S = 2.21 \times 10^{-5} \text{ mol/L} = 6.4 \text{ g/m}^3$$

The reported value is 7.3 g/m<sup>3</sup>.

##### Trichloroethylene

Molecular mass is 131.4 g/mol, melting point is -73°C (200 K), and  $\log K_{OW}$  is reported to be 2.53.

Applying equation 14 as above with no fugacity ratio term:

$$\log S = -2.06, S = 8.7 \times 10^{-3} \text{ mol/L} = 1144 \text{ g/m}^3$$

The reported solubility is 1100 g/m<sup>3</sup>.

$$\sum n_i q_i = (X\text{CH}_2) + X_2\text{C} = +3(\text{XCl}) = 2.446$$

Since this compound is a liquid, the melting point term is set to zero. Thus, the predicted solubility is equal to the sum of AQUAFAC  $q$ -values.

$$\log S = -0.01(\text{MP} - 25) - \sum n_i q_i = -2.446$$

$$S = 3.58 \times 10^{-3} \text{ mol/L} = 471 \text{ g/m}^3$$

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