

J-CAMD 170

Enhancement of the solubilities of polycyclic aromatic hydrocarbons by weak hydrogen bonds with water

Paul Ruelle*, Michel Buchmann, Hô Nam-Tran and Ulrich W. Kesselring

Institut d'Analyse Pharmaceutique, Ecole de Pharmacie, Université de Lausanne, B.E.P., CH-1015 Dorigny-Lausanne, Switzerland

Received 20 March 1992

Accepted 22 June 1992

Key words: Solution thermodynamics; Solubility; Stability constant; Mobile order theory; Hydrocarbons; Hydrophobic effect

SUMMARY

The thermodynamics of mobile order is applied to predict the aqueous solubility of liquid and solid aliphatic and polycyclic aromatic hydrocarbons. The solubility values are mainly determined by the magnitude of the hydrophobic effect. However, contrary to the solubilities of the alkanes, the solubilities of polycyclic aromatic hydrocarbons in water predicted in absence of solute–solvent hydrogen (H) bonds are systematically too low. This shows the contribution of weak specific interactions between the OH groups and the π electrons of the aromatic substances. According to the theory, these interactions are characterized by a stability constant K_O which can be derived from solubility data. At 25°C, this constant amounts to 80 cm³/mol, the order of magnitude of which can be explained by the competition of these intermolecular bonds with the rather weak self-association bonds in the secondary chains of water.

THEORETICAL BACKGROUND: THE HYDROPHOBIC EFFECT

The hydrogen (H) bonds between the hydroxylic groups of alcohols or water exert a negative influence on the solubility of inert substances in these solvents. It is widely known that hydrocarbons are very poorly soluble in water. This phenomenon is called 'hydrophobicity'.

Most methods used for prediction of aqueous solubilities found in the literature start from the assumption that 'hydrophobicity' originates from the necessity of breaking the H bonds of water or of alcohols in order to provide a solvent cavity of suitable size to accommodate the solute molecule [1–3]. Other researchers, especially in biochemistry, think that there is a special and obscure kind of cohesion force in pure alkanes, named 'hydrophobic interaction', which binds the alkane

* To whom correspondence should be addressed.

molecules together [4]. This seems at first sight rather obvious but appears to be completely in contradiction with the experimental facts: on the one hand, the addition of 1 mole of hexane to 1 litre of methanol is accompanied only by a very small absorption of heat (less than 0.7 kJ mol^{-1} compared to the necessary 20 or 25 kJ mol^{-1} for breaking H bonds), which demonstrates that this significant dilution causes practically no breaking of H bonds in the liquid phase. In order to reach an energy of dissolution of 25 kJ/mol alcohol and to break practically all the H bonds, it is necessary to decrease the concentration of methanol in hexane below 0.05 mol dm^{-3} .

On the other hand, if alkanes are very poorly soluble in water, their solubilities vary only slightly with temperature (Table 1). Such small changes of the solubilities demonstrate unambiguously that the dissolution does not require much energy. From the correlations of Somsen concerning the hydration enthalpies [7], one deduces that the transfer of a methylene $>\text{CH}_2$ group of an alkane from its own phase towards water involves an energy of $2.3 \pm 0.3 \text{ kJ mol}^{-1}$, only one tenth of the energy of H bonds in alcohols which can already be accounted for by the changes in the dispersion forces.

These observations demonstrate that the introduction of an inert substance in water or in alcohols does not require the breaking of H bonds. Now, if the origin of the low solubility of inert substances in liquid water, their hydrophobicity, as an experimental fact is not of energetic nature, it must be caused at room temperature by a reduction of the entropy upon the introduction of the inert substance. Thus, contrary to what is generally assumed, the hydrophobic effect is not related to the necessity to create a cavity in water or in alcohols (when an inert substance is dissolved in water, each of its molecules needs a place, but this volume changes continuously in shape, in position and in orientation, just as well as all the solvent molecules around it), but is predominantly *entropic* in nature, which cannot be explained by the classical thermodynamic treatment of the liquid, which considers this phase as a kind of deformed crystal (pseudo-lattice). In fact, the hydrophobic effect finds a natural explanation, and also a quantitative prediction, in the theory of the *mobile order* initiated by Huyskens and Siegel [8–10] that characterizes H-bonded liquids.

This theory starts from the realistic statement that, in a liquid, all molecular groups perpetually move and that the neighbours of a given external atom of a molecule constantly change. If we consider for instance a H atom of a $-\text{CH}_3$ group of hexane in the liquid phase, this atom will be successively in contact with other $-\text{CH}_3$ groups and with $>\text{CH}_2$ groups. One can say that the considered H atom perpetually visits the various parts of its domain, characterized by different neighbours. The theory of the mobile order considers that this freedom of 'visiting' constitutes an essential part of the entropy of liquids compared to that of crystals. In contrast with crystals, an essential feature of the 'structure' of liquids is that it is always changing and that the intermolecular contacts are never fixed.

TABLE 1
AQUEOUS SOLUBILITIES (VOLUME FRACTION $\times 10^5$) OF ALKANES AT VARIOUS TEMPERATURES [5,6]

Alkane	5°C	25°C	40°C	55°C	99°C
<i>n</i> -Pentane	6.6	6.5	6.7	6.7	11.1
<i>n</i> -Hexane	2.5	1.4	1.5	2.0	3.4
<i>n</i> -Heptane	0.3	0.36	0.39	0.46	0.82

This freedom of visiting is, however, suppressed during a large part of the time for the H atom involved in a H bond. The formation of a H bond by the O-H group will bring the proton of this group into the vicinity of the oxygen atom of a neighbouring molecule during a much longer fraction of the time than that governed by random contacts. As a matter of fact, in pure ethanol, the OH proton follows during 98% of the time the oxygen atom of a neighbouring molecule in its movement through the liquid [10]. One can say that during 98% of the time, it renounces its right of visiting its domain. If ethanol is diluted by the same volume of hexane, the hydroxylic H atom will follow during 97% of the time a neighbouring oxygen atom. With such figures, one sees immediately that the energetic effect of such dilution, as far as H bonding is considered, is very weak (only 1% of the energy of one H bond). Such preferential contacts confer to H-bonded liquids a higher *degree of order*, and thus a kind of structure.

Furthermore, the fundamental difference with the crystalline state lies in the *mobility of the H bonds in the liquid phase*. The H bond is not destroyed upon dilution because it is not bound to a fixed place but constantly moves. The main effect of dilution is that the H bond moves in a larger domain. Both the order introduced by the existence of the H bonds in the liquid and the mobile character of these bonds constitute the basic foundations of the mobile order theory.

One can evaluate the effect on the entropy of the liquid of this temporary renouncement of the OH group to 'visit' its domain. During the fraction $(1-\gamma)$ of the time that it is involved in H bonding, the considered proton is confined in a small volume, V_0 , at the border of its domain instead of visiting the whole. The domain, DomA, of an alcohol molecule is the total volume of the liquid, V , divided by the number, N_{alc} , of alcohol molecules. According to the previously defined structure of a liquid, both V_0 and DomA are perpetually moving and cannot be localized with respect to external axes, but their ratio, V_0/DomA , which corresponds to the reduction of freedom, has a well defined value. The reduction of the entropy caused by the mobile order with respect to the situation where all the OH groups would be free is given, when γ is very small, by the expression:

$$\Delta S_{\text{mobile order}} = R \ln(V_0/\text{DomA}) = R \ln(V_0 N_{\text{alc}}) - R \ln V$$

When an alkane or an inert substance is added to the alcohol, $V_0 N_{\text{alc}}$ remains unchanged but the total volume, V , of the liquid increases and $\Delta S_{\text{mobile order}}$ becomes more negative. *This result constitutes the essence of the hydrophobic effect.*

This hydrophobic effect of the mobile order will be observed whenever a substance is dissolved in H-bonded liquids such as alcohols or water, because the introduction of the substance will always increase the volume, V . The consequence is that alcohols and water never form 'regular solutions'. Regular solutions are those for which the deviations from ideality are exclusively due to energetic effects, at the exception of corrections in the entropy of placing deriving from differences in the molar volumes of solute and solvent.

THE DISSOLVING POWER OF SOLVENTS AND THE SOLUBILITY EQUATION

A solute, B, dissolves in a solvent when it has more affinity for the solvent or the solution than for its own phase. From a thermodynamic point of view, the affinity of B for a given phase is related to its chemical potential, μ_B , in this phase. The chemical potential of the component, B, is the

change in free enthalpy, δG , when temperature, pressure and the number of moles of all the other components of the solution are kept constant.

$$\mu_B = (\delta G / \delta n_B)_{T,P,n_j}$$

The higher the affinity is, the lower the chemical potential. Therefore, if μ_B^0 is the chemical potential of B in its own phase and μ_{Bsol} is its chemical potential in solution, B will have a greater affinity for the solution when the difference ($\mu_B^0 - \mu_{Bsol}$) is positive. At this stage, it is convenient to define the dissolving power, $\$$, of a solvent for B by the following expression:

$$\$ = (\mu_B^0 - \mu_{Bsol}) / RT$$

where R is the universal gas constant ($R = 8.315 \text{ J K}^{-1} \text{ mol}^{-1}$) and T the absolute temperature. The introduction of the factor RT in the definition of the dissolving power makes the quantity dimensionless, avoiding the choice of units. As the chemical potential, μ_{Bsol} , depends on and increases with the volume fraction, Φ_B , of the solute in the solution, the dissolving power will refer to a particular value of Φ_B .

When $\$$ is positive, the affinity of B for the solvent is greater than that for its own phase and more solute can be dissolved. The reverse occurs when $\$$ is negative and phase separation can then be expected. When $\$$ equals zero, the equilibrium is reached and the corresponding value of Φ_B corresponds to saturation and represents the solubility of the substance, B, in the given solvent. At equilibrium, the substance, B, has the same chemical potential in its own phase and in the solution.

From a thermodynamic point of view, the dissolving power can also be written as the sum of two terms:

$$\$ = -\Delta_{\text{transf}} H / RT + \Delta_{\text{transf}} S / R$$

The first term, $\Delta_{\text{transf}} H$, takes into account the heat absorbed by the system when one mole of solute B is transferred from its own phase into solution. The second term, $\Delta_{\text{transf}} S$, is the corresponding change in entropy. The dissolving power is a difference of free-enthalpy divided by RT . This difference in free-enthalpy can be expressed as a sum of several terms, each corresponding to a given change accompanying the dissolution. In the particular case of aqueous dissolution of inert substances, as far as H bonding between the solute and the solvent can be ignored, 4 terms (Eq. 1) have to be considered accounting, respectively, for the fluidization of the solute, for the placing (exchange) entropy, for the changes in the non-specific cohesion forces upon mixing and for the hydrophobic effect of the association of the solvent described above. Representing well-defined physical phenomena related to the solubilization, each of these terms contributes to the free-energy change when a solid (liquid) is dissolved in water. The quantitative treatment [11] of these contributions leads to equations describing their effect on the chemical potential of the solute.

$$\$ = \quad A \quad + \quad B' \quad + \quad D \quad + \quad F \quad (1)$$

(fluidization) (placing entropy) (non-specific force change) (hydrophobic effect)

A is the fluidization constant. The fluidization corresponds to the suppression of collective forces in the crystal and is calculated (Eq. 2) for a given temperature, T , from the molar enthalpy of fusion, $\Delta_{\text{melt}} H$, and from the equilibrium melting temperature, T_m , of the pure crystalline substance. When the solid undergoes a first-order phase transition between T and T_m , the fluidization constant must also include a term for the contribution of the transition phase (second part of the righthand side of Eq. 2) involving the temperature, T_{trans} , and the heat of transition, $\Delta_{\text{trans}} H$.

$$A = -\Delta_{\text{melt}} H(1/T - 1/T_m)/R - \Delta_{\text{trans}} H(1/T - 1/T_{\text{trans}})/R \quad (2)$$

B' is the placing term. It corresponds to the fact that molecules of the solute and the solvent have an entropy of placing in the solution. Quantitatively, this term consists of the ideal placing entropy ($-\ln \Phi_B$) divided by R and of a correction factor B resulting from the difference in the molar volumes of solvent and solute. According to Huyskens and Haulait-Pirson [12], this correction depends on the volume fraction, Φ_B , of the solute and on the ratio V_B/V_S between the molar volumes in solution.

$$B' = -\ln \Phi_B + B$$

$$B' = -\ln \Phi_B + 0.5 \Phi_S (V_B/V_S - 1) + 0.5 \ln(\Phi_B + \Phi_S V_B/V_S) \quad (3)$$

D is the non-specific cohesion term. It is related to the changes in dispersion and in dipole-dipole cohesion forces when 'fluidized' pure solute is mixed with the solvent. To a first approximation, this term can be represented by a Scatchard-Hildebrand expression [13] based on the geometric mean of Berthelot [14]. Using modified solubility parameters, δ' , for the solute and for the solvent, the following expression is obtained:

$$D = -\Phi_S^2 V_B (\delta'_B - \delta'_S)^2 / (RT) \quad (4)$$

δ'_B and δ'_S differ from δ_B and δ_S of Hildebrand in that they do not involve H-bonding contributions. Moreover, besides an energetic part they can contain a part due to changes in the possibilities of motions of the molecules (external vibrations). The value of the modified solubility parameter, δ'_B , of the solute is generally deduced from a single experimental determination of solubility in an apolar solvent.

F is the mobile order term due to the H-bond formation between the solvent molecules (hydrophobic effect). For a non-amphiphilic solute, it is derived from the theory of the mobile order and is given by Eq. 6.

$$F = r_S \Phi_S V_B / V_S \quad (6)$$

In this expression, r_S represents the 'structuration or mobile order factor' of the solvent which takes approximately the value -1 for strongly associated solvents with single H-bond chains like alcohols, -2 for water or diols and 0 for non-associated solvents. More exact values can however be calculated based on the following equations [12]:

- for solvents, S, which form single H-bond chains characterized by one association constant, K_S , (alcohols):

$$r_S = -(K_S \Phi_S / V_S) / (1 + K_S \Phi_S / V_S)$$

- for solvents, S, which form double H-bond chains characterized by two association constants, K_{S1} and K_{S2} (water):

$$r_S = -2(K_{S1} \Phi_S / V_S + K_{S1} K_{S2} \Phi_S^2 / V_S^2) / (1 + 2K_{S1} \Phi_S / V_S + K_{S1} K_{S2} \Phi_S^2 / V_S^2)$$

Combining Eqs. 2–6 and Eq. 1, the dissolving power of a solvent, S, for an inert solute, B, in absence of H bonds between the solvent and the solute can be expressed by:

$$\begin{aligned} \Delta G = & -\Delta_{\text{melt}} H(1/T - 1/T_m)/R - \Delta_{\text{trans}} H(1/T - 1/T_{\text{trans}})/R - \ln \Phi_B + 0.5 \Phi_S (V_B/V_S - 1) \\ & + 0.5 \ln(\Phi_B + \Phi_S V_B/V_S) - \Phi_S^2 V_B (\delta'_B - \delta'_S)^2 / (RT) + r_S \Phi_S V_B/V_S \end{aligned} \quad (7)$$

From the expression of the dissolving power considered at saturation equilibrium, one can then deduce the following predictive equation (Eq. 8) for the solubility (in volume fraction) of the solute in a pure solvent as a sum of factors which improve or inhibit the solubility.

$$\ln \Phi_B = A + B + D + F$$

or

$$\begin{aligned} \ln \Phi_B = & -\Delta_{\text{melt}} H(1/T - 1/T_m)/R - \Delta_{\text{trans}} H(1/T - 1/T_{\text{trans}})/R + 0.5 \Phi_S (V_B/V_S - 1) \\ & + 0.5 \ln(\Phi_B + \Phi_S V_B/V_S) - \Phi_S^2 V_B (\delta'_B - \delta'_S)^2 / (RT) + r_S \Phi_S V_B/V_S \end{aligned} \quad (8)$$

In this work, Eq. 8 is used for predicting the solubility of liquid and solid alkanes and polycyclic aromatic hydrocarbons in water at 25°C. However, to permit direct comparison with the experimental results, solubility values, Φ_B , issued from Eq. 8 are converted into molar fractions, X_B , (Eq. 9):

$$X_B = \Phi_B V_S / (V_B + \Phi_B (V_S - V_B)) \quad (9)$$

A detailed analysis of the relative importance of each term involved in Eq. 8 and of their evolution through the whole set of solutes will show the important role of the hydrophobic effect, and demonstrate that this effect is really at the origin of the low solubility values of the inert substances in water.

RESULTS AND DISCUSSION

In addition to the fact that we have at our disposal a new predictive and explicative solubility model without any adjustable parameter, the prediction of the solubility of inert substances in

apolar, polar or associated solvents by means of this model requires the knowledge of only very few properties of the solute and of the solvent. To predict the aqueous solubility of aliphatic and aromatic hydrocarbons in particular, one needs to know:

TABLE 2
PHYSICAL PROPERTIES OF THE LIQUID AND SOLID ALKANES

Solute	V_B (cm ³ /mol)	δ_B (MPa ^{1/2})	Δ_{melt}^H (J/mol)	T_m^a (°C)
Cyclopentane	94.70	16.91	—	—
Cyclohexane	108.80	16.86	—	—
Methylcyclopentane	113.10	16.00	—	—
<i>n</i> -Pentane	116.10	14.61	—	—
2-Methylbutane	117.40	13.96	—	—
Cycloheptane	121.70	15.94	—	—
Methylcyclohexane	128.30	15.83	—	—
<i>n</i> -Hexane	130.00	14.98	—	—
3-Methylpentane	130.60	14.10	—	—
2,3-Dimethylbutane	131.20	13.85	—	—
2-Methylpentane	132.90	14.42	—	—
2,2-Dimethylbutane	133.80	13.65	—	—
Cyclooctane	135.80	16.78	—	—
<i>cis</i> -1,2-Dimethylcyclohexane	141.60	15.52	—	—
2,3-Dimethylpentane	145.00	14.13	—	—
Propylcyclopentane	145.30	16.31	—	—
3,3-Dimethylpentane	145.40	13.96	—	—
3-Methylhexane	146.70	14.48	—	—
<i>n</i> -Heptane	147.50	15.26	—	—
2-Methylhexane	148.60	14.77	—	—
2,2-Dimethylpentane	149.70	14.09	—	—
2,4-Dimethylpentane	149.90	14.27	—	—
1,4-Dimethylcyclohexane	154.00	15.52	—	—
2,3,4-Trimethylpentane	159.80	14.03	—	—
3-Methylheptane	162.80	14.77	—	—
<i>n</i> -Octane	163.50	15.48	—	—
2,2,4-Trimethylpentane	166.10	13.99	—	—
4-Methyloctane	179.10	15.01	—	—
<i>n</i> -Nonane	179.70	15.66	—	—
2,2,5-Trimethylhexane	182.80	14.32	—	—
<i>n</i> -Decane	195.90	15.80	—	—
<i>n</i> -Undecane	212.30	15.92	—	—
<i>n</i> -Dodecane	228.60	16.03	—	—
<i>n</i> -Tetradecane	262.00	16.19	—	—
<i>n</i> -Hexadecane	295.00	16.32	—	—
<i>n</i> -Octadecane	328.00	16.42	61390.0	28.3
<i>n</i> -Eicosane	361.00	16.50	69890.0	36.6
<i>n</i> -Hexacosane ^b	460.00	16.68	59510.0	56.3

^a Ref. 16.

^b $\Delta_{\text{trans}}H = 32220.0 \text{ J/mol}$; $T_{\text{trans}} = 53.3^\circ\text{C}$.

- (1) the melting point, T_m , and the molar heat of fusion, $\Delta_{\text{melt}}H$, i.e. the transition properties, of the solutes in order to calculate the fluidization constants, A , when the solutes are solid (Tables 2–3);
- (2) the formula of the solutes, in order to calculate their molar volume, V_B , in solution from group contributions reported in Table 4 (the molar volume of water is $18.1 \text{ cm}^3 \text{ mol}^{-1}$ [11]);

TABLE 3
PHYSICAL PROPERTIES OF THE POLYCYCLIC AROMATIC HYDROCARBONS

Solute	V_B (cm^3/mol)	δ_B ($\text{MPa}^{1/2}$)	$\Delta_{\text{melt}}H^a$ (J/mol)	T_m^a ($^\circ\text{C}$)
Benzene	89.4	18.90	—	—
Toluene	105.0	18.68	—	—
<i>o</i> -Xylene	120.6	18.51	—	—
<i>m</i> -Xylene	120.6	18.51	—	—
<i>p</i> -Xylene	120.6	18.51	—	—
Indan	124.6	19.58	—	—
Ethylbenzene	128.5	17.99	—	—
1,2,3-Trimethylbenzene	136.2	18.39	—	—
1,3,5-Trimethylbenzene	136.2	18.39	—	—
<i>n</i> -Propylbenzene	145.0	17.91	—	—
1-Methylnaphthalene	145.8	19.99	—	—
Cumene	147.0	17.45	—	—
1,3-Dimethylnaphthalene	161.4	19.75	—	—
1,4-Dimethylnaphthalene	161.4	19.75	—	—
<i>n</i> -Butylbenzene	161.5	17.85	—	—
1-Ethylnaphthalene	169.3	19.32	—	—
<i>n</i> -Pentylbenzene	178.0	17.80	—	—
<i>n</i> -Hexylbenzene	194.5	17.76	—	—
Naphthalene	130.2	20.28	19123.0	78.2
Acenaphthene	147.4	20.92	21537.0	93.4
Fluorene	159.2	20.94	19577.0	114.8
Biphenyl	160.0	19.98	18601.0	69.0
Phenanthrene	171.0	20.97	16465.0	99.2
Anthracene	171.0	20.97	28829.0	219.5
Fluoranthene	182.0	21.80	18871.0	107.8
Pyrene	182.0	21.80	17111.0	151.2
Naphthacene	211.8	21.38	38640.0	351.0
Benzo [<i>a</i>] anthracene	211.8	21.38	21377.0	161.1
Chrysene	211.8	21.38	26153.0	258.2
Triphenylene	211.8	21.38	25103.0	200.3
Benzo [<i>a</i>] pyrene	222.8	22.03	17324.0	181.0
Benzo [<i>e</i>] pyrene	222.8	22.03	16564.0	181.2
Perylene	222.8	22.03	31753.0	280.7
Benzo [<i>ghi</i>] perylene	233.8	22.61	17365.0	281.0
Coronene	244.8	23.12	19202.0	437.3
Dibenzo [<i>ah</i>] anthracene	252.6	21.65	31164.0	271.0
Picene	252.6	21.65	35187.0	364.0

^a Ref. 17 except for naphthacene [Ref. 18] and picene [Ref. 19].

TABLE 4
GROUP CONTRIBUTIONS V_i ($\text{CM}^3 \text{MOL}^{-1}$) OF GROUPS TO THE MOLAR VOLUME OF LIQUIDS AT 25°C

Group	V_i
$-\text{CH}_3$	25–32 ^a
$>\text{CH}_2$	16.5
$>\text{CH}_2$ (cycl.)	18
 $-\text{C}-\text{H}$	9
 $-\text{C}-\text{H}$	13.2
 $-\text{C}-\text{H}$ (arom)	14.9
 $-\text{C}\equiv\text{CH}$	34.2
 $-\text{C}-$	0
 $-\text{C}-$ (arom)	5.5

^a Thirty-two at the end of chains, 29 in the vicinity of another CH_3 , 25 when connected with a group of delocalized electrons.

- (3) the modified non-specific cohesion parameter, δ_B' , of the solutes. In this work, the solutes being predominantly dispersive in nature, their modified cohesion parameter has been considered equal to the Hildebrand solubility parameter, δ_B . Their values (Tables 2 and 3) have therefore been calculated according to Fedors' group contribution method [15] using the volumes calculated at point 2 (the modified non-specific solubility parameter of water is $20.5 \text{ MPa}^{1/2}$ [11]).

With these values, the solubilities of 38 aliphatic hydrocarbons and 37 polycyclic aromatic hydrocarbons have been predicted in water at 25°C using Eq. 8. The results of these predictions as well as the experimental values are reported in columns 2 and 3 of Table 5 for the alkanes and in columns 2 and 3 of Table 6 for the aromatics. All the experimental values have been taken from the IUPAC compilation [20,21] and correspond to the 'recommended' or to the 'best' amongst all results published to date in the literature.

To demonstrate the solubility prediction power of Eq. 8, Figs. 1 and 2 represent, respectively, for the aliphatic and aromatic hydrocarbons the evolution of the predicted aqueous solubilities versus the experimental ones. It clearly stands out from these figures as well as from Tables 5 and 6 that Eq. 8 predicts the correct order of magnitude of the solubility in spite of the fact that most predicted values are slightly lower than the experimental results. However, these deviations are of minor importance when one considers that the values cover more than 8 orders of magnitude. As it will be shown hereafter, the explanations of the origin of such discrepancies are different depending on whether they concern aliphatic or aromatic compounds.

The aliphatic hydrocarbon aqueous solubility

If one excepts the molecules *n*-tetradecane to *n*-hexacosane for which much larger deviations are observed, the origin of the lower predicted solubility values with respect to the experimental ones must probably be attributed to the formulation of the D term describing the changes of the

TABLE 5

EXPERIMENTAL, X_B^{exp} , AND PREDICTED, X_B^{pred} , SOLUBILITIES (IN MOLAR FRACTION) OF ALKANES AT 25°C

Solute	X_B^{exp}	X_B^{pred} (Eq. 8)	X_B^{pred} (Eq. 8 minus D term)
Cyclopentane	0.41 E-04	0.64 E-04	1.04 E-04
Cyclohexane	1.20 E-05	1.68 E-05	3.01 E-05
Methylcyclopentane	0.92 E-05	0.82 E-05	2.07 E-05
<i>n</i> -Pentane	1.10 E-05	0.31 E-05	1.59 E-05
2-Methylbutane	1.21 E-05	0.19 E-05	1.42 E-05
Cycloheptane	5.50 E-06	0.35 E-05	9.75 E-06
Methylcyclohexane	2.94 E-06	1.78 E-06	5.50 E-06
<i>n</i> -Hexane	2.30 E-06	0.96 E-06	4.74 E-06
3-Methylpentane	2.70 E-06	0.52 E-06	4.50 E-06
2,3-Dimethylbutane	4.41 E-06	0.41 E-06	4.27 E-06
2-Methylpentane	2.87 E-06	0.51 E-06	3.69 E-06
2,2-Dimethylbutane	4.41 E-06	0.27 E-06	3.41 E-06
Cyclooctane	1.27 E-06	1.34 E-06	2.87 E-06
<i>cis</i> -1,2-Dimethylcyclohexane	0.96 E-06	0.42 E-06	1.74 E-06
2,3-Dimethylpentane	0.94 E-06	0.12 E-06	1.30 E-06
Propylcyclopentane	0.33 E-06	0.45 E-06	1.26 E-06
3,3-Dimethylpentane	1.07 E-06	0.10 E-06	1.25 E-06
3-Methylhexane	0.48 E-06	0.13 E-06	1.12 E-06
<i>n</i> -Heptane	0.43 E-06	0.20 E-06	1.04 E-06
2-Methylhexane	4.57 E-07	1.33 E-07	9.49 E-07
2,2-Dimethylpentane	7.91 E-07	0.72 E-07	8.63 E-07
2,4-Dimethylpentane	7.60 E-07	0.81 E-07	8.49 E-07
1,4-Dimethylcyclohexane	6.17 E-07	1.28 E-07	5.96 E-07
2,3,4-Trimethylpentane	2.14 E-07	0.24 E-07	3.62 E-07
3-Methylheptane	1.25 E-07	0.32 E-07	2.80 E-07
<i>n</i> -Octane	1.10 E-07	0.50 E-07	2.63 E-07
2,2,4-Trimethylpentane	3.50 E-07	0.12 E-07	2.11 E-07
4-Methyloctane	1.61 E-08	0.78 E-08	6.90 E-08
<i>n</i> -Nonane	2.40 E-08	1.20 E-08	6.56 E-08
2,2,5-Trimethylhexane	11.10 E-08	0.30 E-08	5.03 E-08
<i>n</i> -Decane	0.19 E-08	0.29 E-08	1.64 E-08
<i>n</i> -Undecane	0.46 E-09	0.67 E-09	4.05 E-09
<i>n</i> -Dodecane	0.39 E-09	0.16 E-09	1.01 E-09
<i>n</i> -Tetradecane	6.30 E-10	0.08 E-10	0.59 E-10
<i>n</i> -Hexadecane	4.45 E-10	0.45 E-12	3.63 E-12
<i>n</i> -Octadecane	4.20 E-10	0.24 E-13	2.17 E-13
<i>n</i> -Eicosane	5.01 E-11	0.12 E-14	1.24 E-14
<i>n</i> -Hexacosane	8.00 E-11	0.16 E-18	2.38 E-18

non-specific cohesion forces upon mixing in the solubility equation. The D term corresponds to a Scatchard-Hildebrand type expression based on the assumption that the cohesion energy density between unlike molecules, S-B, is equal to the geometric mean of the cohesion densities of two equivalent-like pairs, S-S and B-B. This rule is strictly applicable to apolar solutes like alkanes dissolved in hydrocarbon or halogenated hydrocarbon solvents, but is inappropriate when the al-

TABLE 6
EXPERIMENTAL, X_B^{exp} , AND PREDICTED, X_B^{pred} , SOLUBILITIES (IN MOLAR FRACTION) OF POLY-CYCLIC AROMATIC HYDROCARBONS AT 25°C

Solute	X_B^{exp}	X_B^{pred} (Eq. 8)	X_B^{pred} (Eq. 11)
Benzene	4.09 E-04	1.52 E-04	8.43 E-04
Toluene	1.04 E-04	3.65 E-05	1.99 E-04
<i>o</i> -Xylene	2.93 E-05	0.89 E-05	4.81 E-05
<i>m</i> -Xylene	2.70 E-05	0.89 E-05	4.81 E-05
<i>p</i> -Xylene	3.10 E-05	0.89 E-05	4.81 E-05
Indan	1.50 E-05	0.73 E-05	3.95 E-05
Ethylbenzene	2.87 E-05	0.39 E-05	2.11 E-05
1,2,3-Trimethylbenzene	1.00 E-05	0.22 E-05	1.18 E-05
1,3,5-Trimethylbenzene	0.74 E-05	0.22 E-05	1.18 E-05
<i>n</i> -Propylbenzene	8.20 E-06	0.87 E-06	4.74 E-06
1-Methylnaphthalene	3.50 E-06	1.19 E-06	6.46 E-06
Cumene	8.39 E-06	0.63 E-06	3.40 E-06
1,3-Dimethylnaphthalene	0.92 E-06	0.30 E-06	1.65 E-06
1,4-Dimethylnaphthalene	1.31 E-06	0.30 E-06	1.65 E-06
<i>n</i> -Butylbenzene	2.04 E-06	0.20 E-06	1.07 E-06
1-Ethylnaphthalene	1.16 E-06	0.15 E-06	0.79 E-06
<i>n</i> -Pentylbenzene	4.69 E-07	0.45 E-07	2.44 E-07
<i>n</i> -Hexylbenzene	1.14 E-07	0.10 E-07	0.55 E-07
Naphthalene	3.90 E-06	1.45 E-06	7.84 E-06
Acenaphthene	0.44 E-06	0.21 E-06	1.12 E-06
Fluorene	2.10 E-07	0.61 E-07	3.28 E-07
Biphenyl	8.39 E-07	1.33 E-07	7.22 E-07
Phenanthrene	1.10 E-07	0.34 E-07	1.84 E-07
Anthracene	6.19 E-09	1.38 E-09	7.48 E-09
Fluoranthene	2.10 E-08	0.91 E-08	4.93 E-08
Pyrene	1.17 E-08	0.61 E-08	3.31 E-08
Naphthacene	5.00 E-11	0.11 E-11	0.62 E-11
Benzo [<i>a</i>] anthracene	0.90 E-09	0.27 E-09	1.44 E-09
Chrysene	1.50 E-10	0.39 E-10	2.09 E-10
Triphenylene	3.40 E-09	0.09 E-09	0.50 E-09
Benzo [<i>a</i>] pyrene	2.70 E-10	1.22 E-10	6.59 E-10
Benzo [<i>e</i>] pyrene	3.98 E-10	1.35 E-10	7.31 E-10
Perylene	2.83 E-11	0.36 E-11	1.96 E-11
Benzo [<i>ghi</i>] perylene	1.73 E-11	1.68 E-11	9.10 E-11
Coronene	8.55 E-12	1.45 E-12	7.84 E-12
Dibenzo [<i>ah</i>] anthracene	4.00 E-11	0.04 E-11	0.21 E-11
Picene	160.00 E-12	0.06 E-12	0.33 E-12

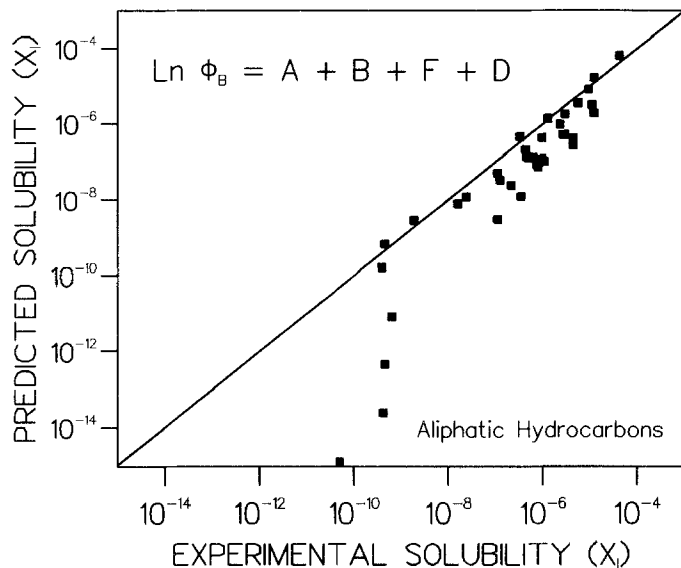


Fig. 1. Aliphatic hydrocarbon predicted aqueous solubility (X_i) based on Eq. 8 vs. experimental values.

kanes are dissolved in H-bonded solvents like water, in which case the D term is overestimated. This explanation is furthermore confirmed by the results (column 4 of Table 5 and Fig. 3) obtained by solving Eq. 8 without the D term. Now, the solubility values are somewhat greater than those measured experimentally. As a result, the best values should be intermediate between the two sets of predicted results reported in Table 5.

To obtain more information about the influence of the D term on the solubility prediction, it is

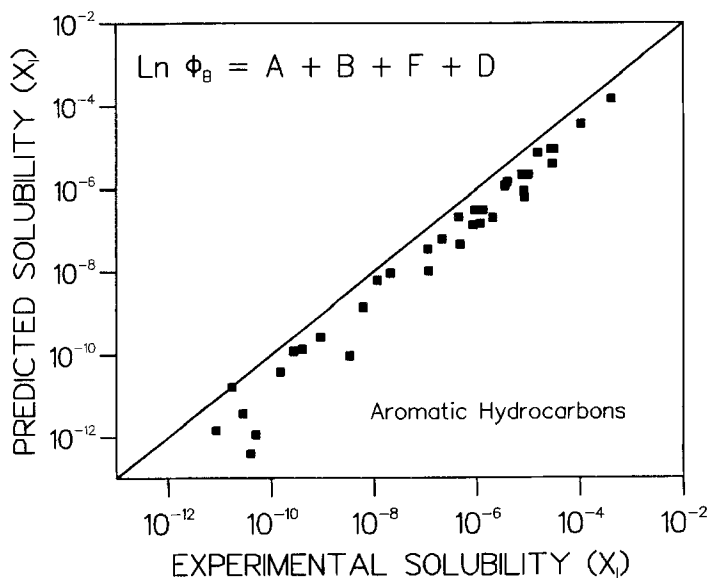


Fig. 2. Aromatic hydrocarbon predicted aqueous solubility (X_i) based on Eq. 8 vs. experimental values.

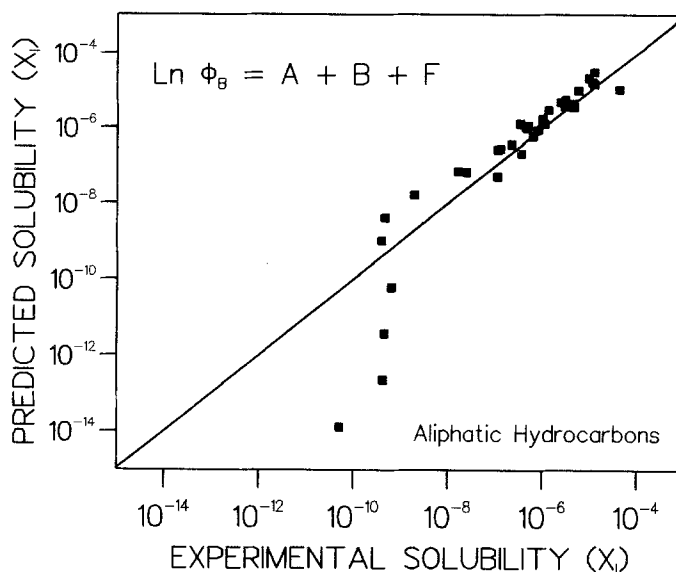


Fig. 3. Aliphatic hydrocarbon predicted aqueous solubility (X_i) based on Eq. 8 minus D-term vs. experimental values.

interesting to analyze for a given solute the physical meaning of the relative importance of each term involved in Eq. 8, i.e., the hydrophobic effect (F), the correction factor for the placing entropy (B), the changes in the non-specific cohesion forces upon mixing (D) and the fluidization constant (A) (when the solute is solid), as well as their evolution with the solute size. Figure 4 presents

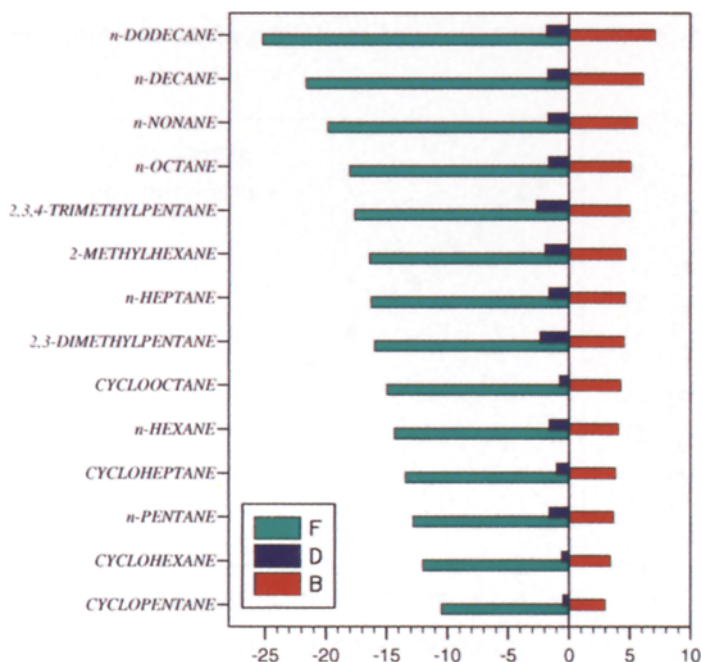


Fig. 4. Contribution of the hydrophobic effect (F), of the change in the non-specific cohesion forces (D) and of the mixing entropy correction (B) to the aqueous solubility of liquid aliphatic hydrocarbons at 25°C.

these contributions for some of the liquid aliphatic hydrocarbons arranged by increasing order of their molar volume, V_B .

The D-term contribution to the solubility is quite negligible with respect to that of the F and B terms. The solubility value of the aliphatic hydrocarbons largely depends on the hydrophobic term (entropic contribution). However, while the correction term for the placing entropy represents a positive contribution to the solubility, the hydrophobic effect represents a negative entropic contribution and disfavours the solubility. Furthermore, the latter term increases very rapidly with the increasing volume of the solute. As described in the theoretical part of this article, the introduction of an inert substance in water leads, by increasing the volume of the solution, to the extension of the domain, DomA, of one solvent molecule, the consequence of which is a decrease of the entropy of mobile order and of the solubility. The bigger the volume of the solute, the larger the decrease of entropy and the lower will result the aqueous solubility.

Coming back to the solubility of the molecules *n*-tetradecane to *n*-hexadecane in water, we are facing a significant theory/experiment deviation increasing sharply with the carbon number of *n*-alkanes (Fig. 5). The origin of such large deviations is not clear. While from *n*-pentane to *n*-dodecane both the theoretical and experimental solubility values linearly decrease with the growing number of carbons in the aliphatic chain, only the predicted values beyond *n*-dodecane continue to decrease (due to the hydrophobic effect), the corresponding experimental results showing on the other hand no further evolution. The question is open whether the experimental methods used are sufficiently sensitive to detect such small concentrations or if there is any physical reason which may explain such behaviour.

The polycyclic aromatic hydrocarbon aqueous solubility

As previously mentioned, all the predicted solubilities of the aromatic substances are lower

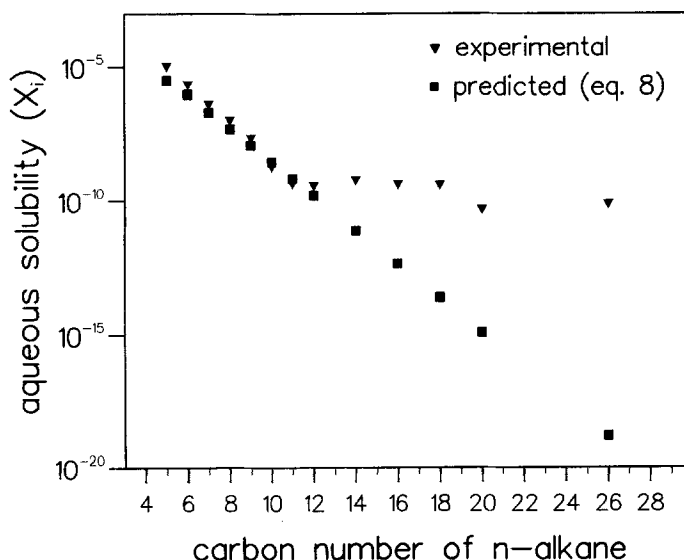


Fig. 5. Evolution of the predicted (Eq. 8) and experimental aqueous solubility (X_i) of normal aliphatic hydrocarbons vs. the carbon number.

than the experimentally measured values. If the explanation of the origin of the deviations observed for the aliphatic hydrocarbons is still valid for the aromatic hydrocarbons, it is not sufficient. In fact, the results obtained by solving Eq. 8 in absence of the D term are still lower than the experimental ones. One has therefore to look for an additional explanation in the case of the aromatic compounds. Related to this problem, it is interesting to note that liquid aromatics are more soluble in water than liquid aliphatic hydrocarbons of similar volume (for instance, the solubility in molar fraction of cumene, $8.39 \cdot 10^{-6}$, is greater than that of *n*-heptane, $0.43 \cdot 10^{-6}$, or the solubility of ethylbenzene, $2.87 \cdot 10^{-5}$, is greater than that of methylcyclohexane, $2.94 \cdot 10^{-6}$). Such a solubility increase is in general brought about by the formation of solute-solvent H bonds. In the case of water, the two protons of a given water molecule are involved in H bonds which do not have the same stability [22]. One has to distinguish two association constants of water, K_{W1} and K_{W2} . The higher stability constant, K_{W1} , is of the order of magnitude of the association constants of primary alcohols, i.e., $5000 \text{ cm}^3 \text{ mol}^{-1}$ [11], and represents the O-H auto-association in the first H-bonded chain of water. The stability constant, K_{W2} , is markedly lower (of the order of $300 \text{ cm}^3 \text{ mol}^{-1}$ [11]) and corresponds to the O-H self-association bonds of the secondary chains of water. The enhancement of the solubility observed for the aromatic versus aliphatic hydrocarbons is due to the formation of an O-H--- π H bond formed between the proton donor OH group of water and the proton acceptor π electrons of the aromatic ring. As the aromatic hydrocarbons do not exhibit very efficient proton acceptor sites, they cannot be inserted in the first stronger O-H---O-H---O-H chains of water, but can compete with the OH groups involved in the secondary chains of water for making new hetero-molecular H bonds. In other words, contrary to alcohols, the water molecules have to make a choice for H-bond formation between their own kind and the aromatic solute.

The effect of the H-bond formation of a system containing a proton acceptor solute and a pro-

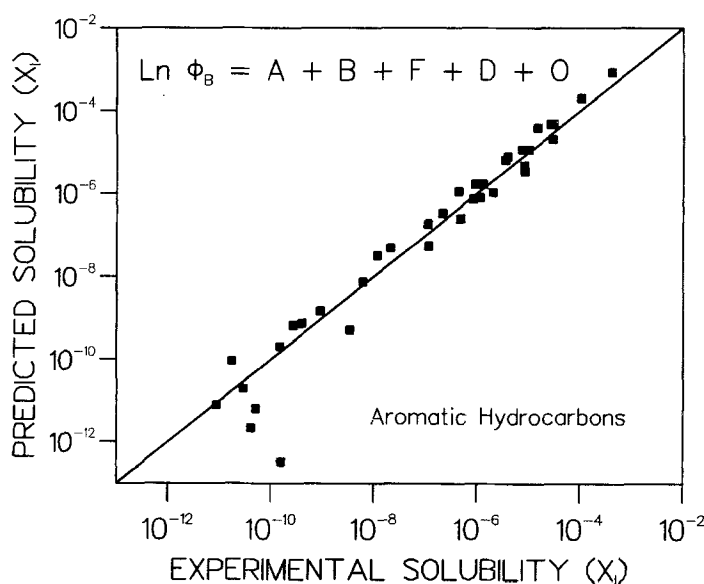


Fig. 6. Aromatic hydrocarbon predicted aqueous solubility (X_i) based on Eq. 11 vs. experimental values.

ton donor solvent on the dissolving power or the solubility has been described in the earlier paper [11] and quantitatively formulated through the O term in the frame of the mobile order theory. The O term (Eq. 10) corresponds to the positive effect of the H-bond formation between a proton acceptor 'O' site on the solute and the proton donor site of the solvent. It depends on the concentration of the active sites in the solvent, Φ_S/V_S , and on the magnitude of the stability constant, K_O , which governs the solute-solvent H-bonding interaction.

$$O = \ln(1 + K_O \Phi_S/V_S) \quad (10)$$

In principle, the stability constant, K_O , depends on both the solute and the solvent. However, for solubility predictions, a standard value is used for a given type of H bond assuming that, in a given family of solutes, the constants remain similar to each other. In the particular case of the polycyclic aromatic hydrocarbons, K_O is the O-H $\cdots\pi$ H-bond stability constant, the value of which has been estimated to $80 \text{ cm}^3 \text{ mol}^{-1}$ from experimental solubilities.

Considering this additional effect, the solubility, $\ln \Phi_B$, of a liquid (solid) aromatic hydrocarbon in water is no more the result of the sum of 3 (4) terms expressed in Eq. 8, but results from the sum of 4 (5) terms (Eq. 11).

$$\ln \Phi_B = A + B + D + F + O \quad (11)$$

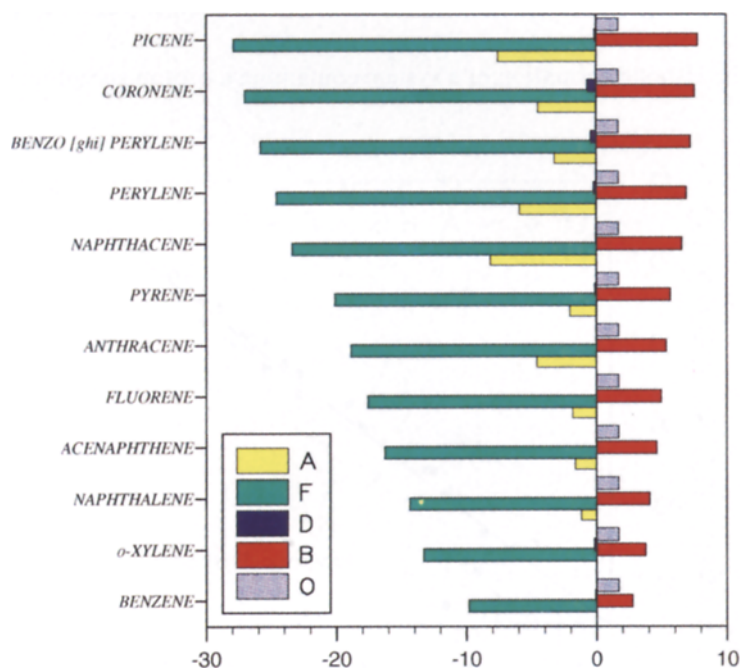


Fig. 7. Contribution of the fluidization (A), of the hydrophobic effect (F), of the change in the non-specific cohesion forces (D), of the mixing entropy correction (B) and of the hydrogen-bonding formation (O) to the aqueous solubility of aromatic hydrocarbons at 25°C.

The solubilities of the polycyclic aromatic hydrocarbons calculated by Eq. 11 are reported in the last column of Table 6 and are compared to the experimental values in Fig. 6. With respect to the results obtained by Eq. 8 (presented in Fig. 2), most of the predicted values are now in agreement with the experimental ones. For very low values of solubility, however (around 10^{-10} – 10^{-11} in molar fraction units), one again observes a discrepancy between the experimental and theoretical results (e.g., picene or naphthacene), the reason of which should be the same as that for the alkanes.

As the solubility of the aromatic hydrocarbons in water results from the sum of 5 terms ($A + B + D + F + O$), Fig. 7 presents the contribution of each of these terms for a given solute as well as their evolution when going from small liquid (benzene) to large solid (picene) hydrocarbons. The aqueous solubility values of the aromatics are mainly dependent, like those of aliphatic hydrocarbons, on the hydrophobic effect (term F) which, by its negative sign, unfavourably contributes to the solubility. It can also be seen from Fig. 7 that this contribution increases as the size of the solute increases. Such a hydrophobic effect/solute size relation largely explains why both the aliphatic and aromatic hydrocarbon aqueous solubilities decrease with the increasing volume of the solute. It can be concluded that in neglecting this effect it is quite impossible to correctly predict the solubility in water. Contrary to this effect, the term accounting for the changes in the non-specific cohesion forces (term D) can just be neglected without modifying the predictions very much.

CONCLUSION

The solubility equation derived from the thermodynamics of mobile order allows correct predictions of the solubility of liquid and solid aliphatic and polycyclic aromatic hydrocarbons in water. The model takes into account the different physical contributions to the free-energy change when a solute, B , is dissolved in a solvent, S : the fluidization of B (if the solute is solid), the entropy of mixing, the change in the dispersion and dipole–dipole forces, as well as the effect of the H-bonded chains of the solvent (hydrophobic effect) for the alkanes. For the aromatic hydrocarbons, an additional term is introduced accounting for the weak H-bond formation between the aromatic ring and the OH group of the secondary chains of water. This additional term is not based on a solubility parameter formalism, but is expressed as a function of the concentration of active sites in the solution and of the stability constant, K_O , for H-bond formation. The existence of these solute–solvent specific interactions is at the origin of the enhancement of the aqueous solubilities of polycyclic aromatic hydrocarbons in comparison to those of the aliphatic hydrocarbons of similar volumes.

Whatever the nature of the solute, the aqueous solubility values calculated by Eq. 8 or 11 mainly depend on the magnitude of the hydrophobic effect. Contrary to a wide-spread erroneous idea, this effect does not result from an increase in enthalpy needed to break H bonds, but to a decrease in entropy when the H-bonded molecules of the solvent are brought in a larger volume as a consequence of the addition of the inert solute.

ACKNOWLEDGEMENTS

The authors are grateful to Professor P.L. Huyskens (University of Leuven, Belgium) for participating in the discussions which stimulated this work and to the Swiss National Science Foundation (FNRS) for partial financial support (grant N.3100-31210.91).

REFERENCES

- 1 Baker, R.J., Acree, Jr., W.E. and Chun-Che Tsai, *Quant. Struct.-Act. Relat.*, 3 (1984) 10.
- 2 Kamlet, M.J., Doherty, R.M., Abboud, J.L., Abraham, M.H. and Taft, R.W., *J. Pharm. Sci.*, 75 (1986) 338.
- 3 Gonzalez, A.G., *Int. J. Pharm.*, 75 (1991) R13.
- 4 Ben Naim, A., *Hydrophobic Interactions*, Plenum Press, New York, NY, 1980.
- 5 Polak, J. and Lu, B.C., *Can. J. Chem.*, 51 (1973) 4018.
- 6 Nelson, H.D. and De Ligny, C.L., *Rec. Trav. Chim. Pays-Bas*, 87 (1968) 528.
- 7 Somsen, G., In Huyskens, P.L., Luck, W.A.P. and Zeegers-Huyskens, T. (Eds.) *Intermolecular Forces*, Springer-Verlag, Berlin, 1991, Ch. XV.
- 8 Huyskens, P.L. and Siegel, G.G., *Bull. Soc. Chim. Belg.*, 97 (1988) 821.
- 9 Siegel, G.G., Huyskens, P.L. and Vanderheyden, L., *Ber. Bunsen-Ges. Phys. Chem.*, 94 (1990) 549.
- 10 Huyskens, P.L., *J. Mol. Liquids*, 46 (1990) 285.
- 11 Ruelle, P., Rey-Mermet, C., Buchmann, M., Hô Nam-Tran, Kesselring, U.W. and Huyskens, P.L., *Pharm. Res.*, 8 (1991) 840.
- 12 Huyskens, P.L. and Haulait-Pirson, M.C., *J. Mol. Liquids*, 31 (1985) 153.
- 13 Scatchard, G., *Chem. Rev.*, 8 (1931) 321.
- 14 Berthelot, M., *Compt. Rend.*, 126 (1898) 1703.
- 15 Fedors, R.F., *Polym. Eng. Sci.*, 14 (1974) 147 and 472.
- 16 Huyskens, P. and Vandevijvere, P., *J. Mol. Struct.*, 200 (1989) 555.
- 17 Acree, Jr., W.E., In Lide, D.R. (Ed.) *Handbook of Chemistry and Physics*, 72nd edn. 1991–1992, CRC Press, Boca Raton, FL, 1991, pp. 5–83.
- 18 Mishra, D.S. and Yalkowsky, S.H., *Ind. Eng. Chem. Res.*, 29 (1990) 2278.
- 19 Casellato, F., Vecchi, C., Girelli, A. and Casu, B., *Thermochim. Acta*, 6 (1973) 361.
- 20 Kertes, A.S. (Ed.) *Hydrocarbons with Water and Seawater, Part I (Hydrocarbons C₅ to C₇) (Solubility Data Series, Vol. 37)*, Pergamon Press, New York, NY, 1989.
- 21 Kertes, A.S. (Ed.) *Hydrocarbons with Water and Seawater, Part II (Hydrocarbons C₈ to C₃₆) (Solubility Data Series, Vol. 37)*, Pergamon Press, New York, NY, 1989.
- 22 Huyskens, P.L., In Kleeberg, H. (Ed.) *Interaction of Water in Ionic and Nonionic Hydrates*, Springer-Verlag, Berlin, 1987.