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Prediction of carbazole solubility and its dependence upon the solvent nature

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Abstract

On the basis of at most three parameters, the solubility of carbazole is predicted in 33 nonelectrolyte solvents by means of the general solubility equation derived from the thermodynamics of mobile order. Particular attention is focussed on the influence of the formation of solute-solvent stoechiometrical hydrogen bonds on the treatment of the non-specific dipole-dipole and dispersion interactions. Three classes of solvents can be distinguished according to their solubilizing potential towards carbazole: non-complexing solvents, complexing non-associated solvents and complexing amphiphilic solvents. The analysis of the relative importance of the different terms contributing to the solubility allows one to quantitatively understand its variation between the different classes as well as within each class of solvents.

Key words: Carbazole; Solubility prediction; Mobile order theory; Hydrogen bond; Stability constant; Solvent effect

1. Introduction

Our earlier solubility studies have primarily been concerned with the prediction of the solubility of nonpolar substances, mainly aliphatic and aromatic hydrocarbons (Ruelle et al., 1992a–c, 1993a) and polychlorinated aromatic hydrocarbons (Ruelle et al., 1993b), in non-associated and associated solvents, by applying the general solubility equation (Eq. 1) (Ruelle et al., 1991) derived from the mobile order theory (Huyskens and Siegel, 1988; Huyskens, 1990, 1992; Siegel et al., 1990):

$$\ln \Phi_B = A + B + D + F + O + OH \quad (1)$$

with

$$A = -\Delta_{melt}H(1/T - 1/T_m)/R + [(T_m - T)/T - \ln(T_m/T)]\Delta c_p/R$$

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

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

$$F = -r_S\Phi_S V_B/V_S$$

$$O = \ln(1.0 + K_O(\Phi_S/V_S - \Phi_B/V_B))$$

$$OH = -\ln(1.0 + K_{BB}/V_B) + \ln(1.0 + K_{OH}\Phi_S/V_S + K_{BB}\Phi_B/V_B)$$

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In these expressions, $\Delta_{melt}H$, T_m and Δc_p represent the molar heat of fusion, the melting temperature and the heat capacity difference between the solid and liquid forms of the solute; V_B, δ'_B, Φ_B, V_S, δ'_S, Φ_S stand for the molar volume, the modified non-specific cohesion parameter and the volume fraction, respectively, of the solute B and of the solvent S; r_S is the 'structuration' or 'mobile order' factor of the solvent; K_O, K_{OH} and K_{BB} denote the stability constants which characterize the hydrogen bond respectively formed between a proton-acceptor solute and a proton-donor solvent, a proton-donor solute and a proton-acceptor or amphiphilic solvent and between two solute molecules in solution.

From the analysis of the relative importance of the different contributions involved in the solubility calculation, it was demonstrated how much the solubility of inert substances in alcohols or in water was essentially determined by the hydrophobic effect (F term). This effect corresponds to a decrease of the entropy of the self-associated solvent molecules by addition of an inert

Table 1
Molar volume, V_S, and modified non-specific cohesion parameter, δ'_S, of solvents, and experimental volume fraction solubility of carbazole, Φ_B^{exp}, at 25°C

Solvent	V_S (cm^3/mol)	δ'_S ($J^{1/2}\ cm^{-3/2}$)	Φ_B^{exp}	Reference
n-Hexane	131.6	14.56	1.565*E* − 04	Acree (1990)
n-Heptane	147.5	14.66	1.738*E* − 04	Acree (1990)
n-Octane	163.5	14.85	1.795*E* − 04	Acree (1990)
n-Decane	195.9	15.14	2.194*E* − 04	Anderson et al. (1980)
n-Dodecane	228.6	15.34	2.075*E* − 04	Anderson et al. (1980)
n-Hexadecane	260.3	15.49	2.087*E* − 04	McGargar and Acree (1987)
Cyclohexane	108.8	14.82	2.492*E* − 04	Acree (1990)
Methylcyclohexane	128.3	15.00	2.264*E* − 04	Acree (1990)
t-Butylcyclohexane	173.9	15.50	2.131*E* − 04	McGargar and Acree (1988)
Cyclooctane	134.9	15.40	3.394*E* − 04	Acree (1990)
Isooctane	166.1	14.30	1.124*E* − 04	Acree (1990)
Squalane	525.0	16.25	1.895*E* − 04	McGargar and Acree (1987)
Benzene	89.4	18.95	7.322*E* − 03	Merck Index (1989)
1-Chlorohexane	138.1	18.00	2.736*E* − 03	Acree and McGargar (1987)
1-Chlorooctane	171.1	18.00	2.097*E* − 03	McGargar and Acree (1989)
1-Chlorotetradecane	270.2	18.00	1.318*E* − 03	McGargar and Acree (1989)
Chlorocyclohexane	120.3	18.45	3.582*E* − 03	McGargar and Acree (1989)
Chloroform	80.7	18.77	6.774*E* − 03	Anderson et al. (1980)
Diethyl ether	104.8	18.78	1.814*E* − 02	Merck Index (1989)
Dibutyl ether	170.3	17.45	4.363*E* − 03	McGargar and Acree (1987)
Dipentyl ether	204.0	17.61	2.647*E* − 03	Anderson et al. (1980)
Anisole	119.1	20.20	1.612*E* − 02	Chernyi et al. (1986)
Dioxane	85.8	20.89	6.059*E* − 02	Chernyi et al. (1986)
Tetrahydrofuran	81.4	19.30	1.221*E* − 01	Chernyi et al. (1986)
Ethyl acetate	98.5	20.79	2.979*E* − 02	Chernyi et al. (1986)
Butyl acetate	132.5	19.66	1.820*E* − 02	Anderson et al. (1980)
Acetone	74.0	21.91	8.971*E* − 02	Merck Index (1989)
Methyl ethyl ketone	90.2	20.90	6.781*E* − 02	Chernyi et al. (1986)
Ethanol [a]	58.7	17.81	8.989*E* − 03	This work
Propanol [a]	75.1	17.29	7.187*E* − 03	This work
Butanol [a]	92.0	17.16	7.126*E* − 03	This work
Octanol [a]	158.3	16.38	7.549*E* − 03	This work
Water	18.1	20.50	8.047*E* − 07	Pearlman et al. (1984)

[a] The solubilities were determined spectrophotometrically at 292 nm on a Perkin-Elmer Lambda 15 UV/Vis spectrophotometer.

solute, and can be seen as a solute rejecting effect of the solvent. Recently, the solubility model was used to predict the solubility of crystalline proton-acceptor substances, i.e., ketones, esters, nitriles and tertiary amides (Ruelle and Kesselring, 1993; Ruelle et al., 1993c), able to form hydrogen bonds with proton-donor solvents, and to determine the standard stability constants characterizing these hydrogen bonds. With the prediction of the solubility of testosterone propionate, it could furthermore be shown that these standard stability constants were transferable from one solute to another provided they form the same type of hydrogen bond with the solvent.

To provide more insight into the applications and limitations of the general solubility equation, this paper reports predictions of the solubility of carbazole in pure nonelectrolyte solvents of differing polarities, and explains the dependence of the obtained values on the nature of the solvent. Carbazole has been chosen as an initial example of a molecule belonging to the class of proton-donor substances. However, carbazole may be considered as a model substance, since it only interacts as a proton donor (see Section 2) in contrast to most compounds of this class which moreover act as proton acceptors and are also able to self-associate.

2. Results and discussion

The general solubility equation can be applied for predicting the solubility of carbazole in pure solvents provided at least the values of some of its properties (A, V_S, δ'_S and K_{BB}) as well as some properties of the solvents (V_S and δ'_S) are known or can readily be determined. The required solvent properties, i.e., their molar volumes, V_S, and their modified non-specific cohesion parameters, δ'_S, are given in Table 1. Concerning carbazole, its fluidisation constant, $A = -4.588$, is obtained from its melting properties ($\Delta_{melt}H = 22.7$ kJ mol^{-1}, $T_m = 519.2$ K and $\Delta c_p = 2.2$ J/K^{-1} mol^{-1}) obtained by differential thermal analysis (Coon et al., 1988), and its molar volume, $V_B = 148.2$ cm^3 mol^{-1}, is calculated from group contributions (Ruelle et al., 1991). To determine its self-association constant, K_{BB}, and its modified non-specific cohesion parameter, δ'_B, it must be known whether carbazole self-associates ($K_{BB} \neq 0$) or not ($K_{BB} = 0$) in solution. In the absence of a direct experimental answer, a non-linear regression was performed by means of the E04UPF subroutine of the NAG-Fortran Library to fit Eq. 1 to the experimental solubilities measured in non-complexing solvents. The best fit was obtained for a K_{BB} value close to zero (0.47 cm^3 mol^{-1}). In view of this result, we concluded that, in contrast to proton-donor solutes like alcohols or carboxylic acids, the molecules of carbazole did not self-associate in solution, and that the imide N-H group should interact with its surroundings mainly as a proton donor and not as a proton acceptor ($K_O = 0$). This conclusion is furthermore supported by the fact that, in the crystalline state, carbazole molecules are neither linked by N-H---N intermolecular hydrogen bonds (Lahiri, 1969). The modified non-specific cohesion parameter, δ'_B, of carbazole may then be deduced from its experimental solubility in one single inert solvent for which the F term and the stability constant K_{OH} are non-existent. Using its molar fraction solubility in n-hexane ($X_B = 0.000139$) at 25°C (Acree, 1990), one calculates a value δ'_B of 23.04 MPa$^{1/2}$.

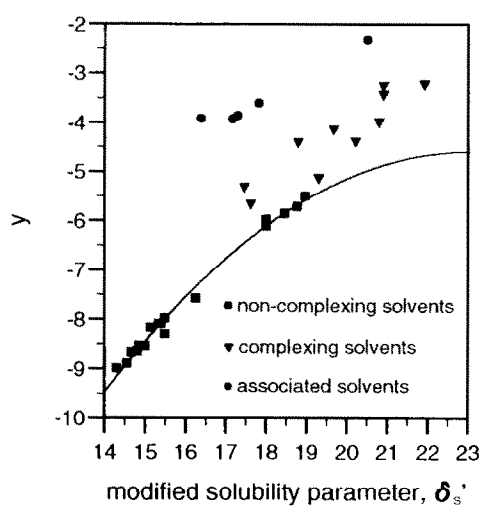

Fig. 1. Plot of y_1 (symbols) and y_2 (solid line) values vs the modified non-specific cohesion parameter, δ'_S, of the solvents.

For solids, solubility is determined by fusion and mixing and corresponds to a free enthalpy-governed phenomenon. At equilibrium, the entropic changes exactly compensate the enthalpic ones. Accordingly, the influence of the solvent on the chemical potential of a given solute, and hence on its solubility, can be classified into energetic or entropic effects. Altough in the past attention was essentially focused on the energetic effects of the solvent (regular solutions), entropic effects may, however, be even more important. Essentially two distinct entropic contributions depending on the solvent control the solubility equilibrium: the entropy of placing and the entropy of the mobile order which is at the origin of the hydrophobic effect. In a liquid mixture, the entropy of placing results from both the exchange possibilities of the fluidized solute molecules with those of the solvent, and from the expansion of the space available for the motions of each molecule in solution. On the other hand, the hydrophobic effect is observed whenever self-associated solvents are considered, and is mainly due to the increase of the temporary loss of freedom of mobility of the solvent molecules when the volume of the solution is enlarged by addition of the solute. In the frame of mobile order thermodynamics, the influence of the placing entropy and of the hydrophobic effect on the chemical potential of the solute is given by Eq. 2:

$$y_1 = \ln \Phi_B - B - F$$
$$= \ln \Phi_B - 0.5\left[\Phi_S(V_B/V_S - 1) + \ln(\Phi_B + \Phi_S V_B/V_S)\right] + r_S \Phi_S V_B/V_S \qquad (2)$$

where the mobile order factor, r_S, depends on the number of hydrogen-bonded chains in which a solvent molecule can be involved, and amounts approximately to 1 for single chains (alcohols) and 2 for double chains (water) (Ruelle et al., 1991). If, at solubility equilibrium, no specific interaction is formed between the solute and the solvent, the entropic effects should exactly be counterbalanced by the sum of the solute fluidisation and the change of the non-specific cohesion forces upon mixing. For high volume fractions of the solvent ($\Phi_S^2 \simeq 1$), the influence of these enthalpic contributions on the chemical potential of the solute is expressed by Eq. 3.

$$y_2 = A + D = -\Delta_{melt}H(1/T - 1/T_m)/R + \left[(T_m - T)/T - \ln(T_m/T)\right]\Delta c_p/R - V_B(\delta'_B - \delta'_S)^2/(RT) \qquad (3)$$

For a given solute, whether or not y_1 equals y_2, constitutes an information about the nature of the interactions that a particular solvent form with the solute. In the case of carbazole, the y_1 values calculated for each particular solvent of Table 1 from the experimental solubilities are compared in Fig. 1 to the y_2 theoretical curve obtained on the basis of the properties of the pure substances only. Inspection of Fig. 1 reveals that solvents can be separated into three groups with respect to their behaviour towards carbazole: the non-complexing solvents (alkanes, chloroalkanes and aromatics), the complexing but non-associated solvents (ethers, esters and ketones) and the complexing associated solvents (alcohols and water). It also shows that y_1 values agree with y_2 ones for solvents of the first group only; in complexing solvents, y_1 is always greater than y_2. From a thermodynamic point of view, this result demonstrates that, in presence of inert solvents, the enthalpic contribution to the carbazole solubility equilibrium is fully described by the A and D terms which exactly counterbalance the entropic part. For all the other solvents, the positive deviations, $y_1 - y_2$, must be attributed to the formation of specific solute-solvent interactions which increase the solubility but are not taken into account by Eq. 3. To describe correctly the carbazole solubility equilibrium in complexing solvents, Eq. 3 must therefore be modified in order to include the additional positive contribution (OH term) accounting for the H-bond formation between the proton-donor N-H group of carbazole and the proton-acceptor site of the complexing solvents. This means that we must know the order of magnitude of the stability constants, K_{OH}, characterizing the hydrogen bonds. Although different values of the stability constants should be used for each particular system, it has recently been shown (Ruelle et al., 1993c) that these constants do not vary greatly

Table 2
Stability constants, K_{OH} (cm^3 mol^{-1}), of carbazole-solvent H-bonds in solution derived from the experimental solubilities

H-bond type	Solvent	K_{OH} (Eq. 1)	K_{OH} (Eq. 5)
N-H---ether			
	diethyl ether	265.97	111.62
	dibutyl ether	363.10	99.39
	dipentyl ether	208.39	65.43
	anisole	122.53	62.42
	dioxane	144.45	114.04
	tetrahydrofuran	1034.87	556.31
N-H---ester	ethyl acetate	151.98	116.22
	butyl acetate	281.31	157.15
N-H---ketone	acetone	268.46	252.12
	methyl ethyl ketone	382.58	303.46
N-H---alcohol	ethanol	884.35	210.28
	propanol	1094.09	205.79
	butanol	1343.18	238.37
	octanol	4194.39	463.91
N-H---water	water	188.81	166.67

within systems forming the same type of hydrogen bonds, and that they are therefore transferable from one system to another. In column 2 of Table 2 the values of the particular stability constants, K_{OH}, calculated from the experimental solubilities by using Eq. 1 are reported. In contrast to findings from our previous work, the variations of K_{OH}s are now relatively large within solvents belonging to the same class. The observed dispersions can, however, be reduced if the D term is modified in order to account for its interference with the OH contribution. In other words, the influence of specific stoechiometrical H-bond formation on the non-specific dipole-dipole and dispersion interactions must be considered. In fact, when preferential contacts are formed between solute and solvent active sites, the molecules are no longer randomly distributed, and the expression of the D term, which is essentially based on the assumption of 'random' interactions in solution, is no longer valid but has to be corrected. As a first approach, the D term has been multiplied by the fraction, γ, of the time during which each N-H group of carbazole is not bound to the proton-acceptor site of the solvent, or during which the mixing can be considered to occur at random. As far as the concentration of the N-H active sites of carbazole in solution remains much lower than that of the proton-acceptor sites of the solvent, the fraction γ is given to a good approximation by the expression (Ruelle et al., 1991):

$$\gamma = 1/(1.0 + K_{OH}\Phi_S/V_S) \quad (4)$$

where Φ_S/V_S is the formal concentration of the solvent and K_{OH} denotes the stability constant of the solute-solvent H-bonds. Taking this correction into account, a modified solubility equation (Eq. 5) can accordingly be written in which the dependence of the new D' term on the formation of specific solute-solvent interactions is described:

$$\ln \Phi_B = A + B + D' + F + O + OH \quad (5)$$

with

$$D' = -\frac{1}{(1.0 + K_{OH}\Phi_S/V_S)} \frac{\Phi_S^2 V_B}{RT} (\delta'_B - \delta'_S)^2$$

The values of K_{OH} derived from the new equation are listed in the third column of Table 2, and as expected are now closer to each other.

Although better solubility predictions would be obtained by using a specific stability constant for each type of hydrogen bond, for simplicity only two average values, i.e., 100 and 230 cm^3 mol^{-1} characterizing the N-H---O_1 (ether, ester)

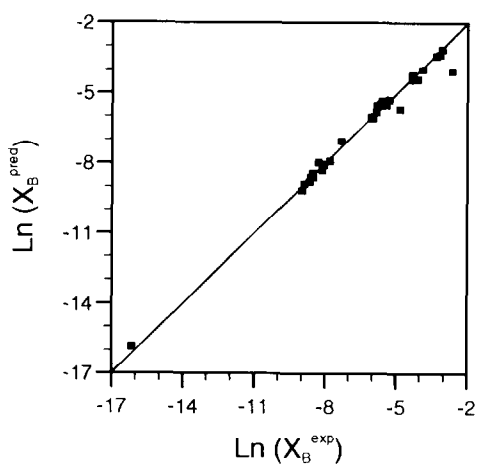

Fig. 2. Relationship between predicted (Eq. 5) and experimental solubilities of carbazole at 25°C.

and N-H---O_2 (ketone, alcohol, water) H-bond formation, respectively, have been retained.

The solubility of carbazole is then predicted by means of Eq. 5 in 18 non-complexing solvents on the basis of a single parameter (δ'_B), and in 15 complexing solvents on the basis of three parameters (δ'_B, $K_{N\text{-}H\text{-}O_1}$, $K_{N\text{-}H\text{-}O_2}$). The results expressed in molar fraction, X_B, are compared to the experimental results in Table 3, whereas the quality of the predictions is shown in Fig. 2 and through the following linear regressions (Eq. 6 and 7):

for 33 solvents:

$$X_B^{pred} = 0.0018(\pm 0.0025) + 0.56(\pm 0.134) X_B^{exp} \quad (n = 33,\ r^2 = 0.701) \tag{6}$$

for 31 solvents (not considering tetrahydrofuran and octanol):

$$X_B^{pred} = 0.00027(\pm 0.00046) + 0.88(\pm 0.032) X_B^{exp} \quad (n = 31,\ r^2 = 0.991) \tag{7}$$

Table 3
Experimental, X_B^{exp}, and predicted, X_B^{pred}, solubilities of carbazole at 25°C, and the contributions B, D, F and OH ($A = -4.588$)

Solvent	X_B^{exp}	X_B^{pred}	B	D	OH	F
Non-complexing solvent						
Isooctane	0.000126	0.000106	−0.111	−4.566		
n-Hexane	0.000139	0.000139	0.122	−4.298		
n-Heptane	0.000173	0.000153	0.005	−4.197		
Cyclohexane	0.000183	0.000184	0.336	−4.038		
n-Octane	0.000198	0.000185	−0.096	−4.009		
Methylcyclohexane	0.000196	0.000215	0.150	−3.863		
n-Decane	0.000298	0.000249	−0.261	−3.730		
n-Dodecane	0.000320	0.000307	−0.392	−3.543		
Cyclooctane	0.000309	0.000312	0.096	−3.487		
t-Butylcyclohexane	0.000250	0.000343	−0.154	−3.397		
n-Hexadecane	0.000414	0.000361	−0.497	−3.406		
Squalane	0.000671	0.000851	−0.991	−2.755		
1-Chlorooctane	0.00242	0.00225	−0.138	−1.513		
1-Chlorohexane	0.00255	0.00225	0.072	−1.511		
1-Chlorotetradecane	0.00240	0.00241	−0.525	−1.515		
Chlorocyclohexane	0.00291	0.00295	0.219	−1.250		
Chloroform	0.00370	0.00387	0.718	−1.075		
Benzene	0.00443	0.00409	0.578	−0.987		
Complexing non-associated solvent						
Dipentyl ether	0.00364	0.00478	−0.295	−1.176	0.398	
Dibutyl ether	0.00501	0.00503	−0.134	−1.169	0.460	
Diethyl ether	0.0129	0.0119	0.374	−0.541	0.662	
Butyl acetate	0.0163	0.0122	0.114	−0.381	0.556	
Anisole	0.0130	0.0146	0.227	−0.255	0.601	
Tetrahydrofuran	0.0710	0.0173	0.690	−0.358	0.784	
Ethyl acetate	0.0200	0.0183	0.445	−0.144	0.687	
Dioxane	0.0360	0.0327	0.605	−0.077	1.164	
Methyl ethyl ketone	0.0424	0.0345	0.541	−0.072	1.226	
Acetone	0.0469	0.0440	0.785	−0.017	1.347	
Complexing associated solvent						
Water	0.98×10^{-7}	1.33×10^{-7}	4.645	−0.028	2.618	−16.376
Ethanol	0.00358	0.00394	1.215	−0.329	1.585	−2.500
Propanol	0.00365	0.00414	0.821	−0.482	1.396	−1.957
Butanol	0.00444	0.00426	0.540	−0.585	1.248	−1.600
Octanol	0.00806	0.00334	−0.065	−1.076	0.895	−0.933

where n is the number of solvents and r^2 denotes the coefficient of determination (95% confidence limits in parentheses). These results once more demonstrate the capacity and the reliability of the mobile order theory derived solubility model to predict the solubility not only of apolar or proton-acceptor substances, but also of proton donors in nonelectrolyte complexing and non-complexing solvents.

Describing elementary physical steps of the whole solubility process, each term of Eq. 5 (Table 3) contributes to increase or decrease the solubility. The analysis of the relative importance of each of these terms as well as their variations from one solvent to another therefore allows one to understand the dependence of the solubility of carbazole on the nature of the solvent. Except for water, the fluidisation of carbazole (term A) represents the dominating contribution to the solubility, and is responsible for the order of magnitude of the solubility. However, being constant, this term obviously does not allow ranking of the solvents according to their solubilizing capacity or elucidation of the origin of variation of solubility of carbazole. A partial answer can be found on inspection of the modified non-specific cohesion parameter of the solvents. Due to their low values with respect to that of carbazole, the solubility variation mainly results from the change in the non-specific cohesion forces (term D'): the smaller the $(\delta'_B - \delta'_S)$ difference between the solute and the solvent, the higher is the solubility. This term alone even permits one to explain and to predict the variation of carbazole solubility within the set of non-complexing solvents (Fig. 3), although the solubilities in these solvents are relatively close to each other.

For the complexing but non-associated solvents, in addition to the preceding observation

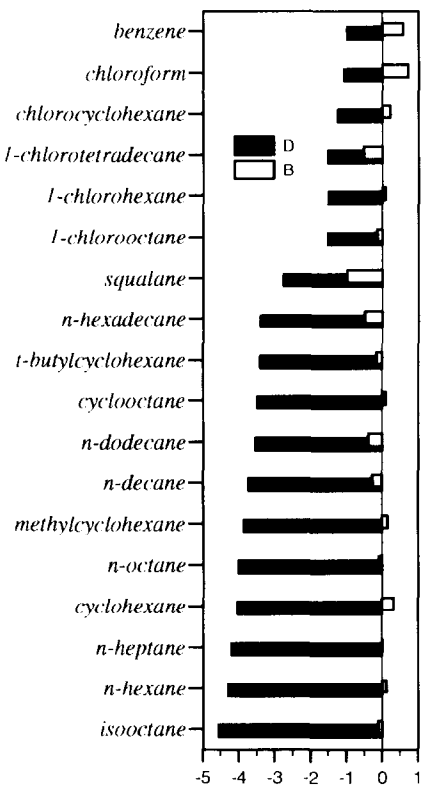

Fig. 3. Contributions of the mixing entropy correction (B), and of the change of the non-specific cohesion forces (D') to the solubility of carbazole in non-complexing solvents at 25°C (solvents are arranged in increasing order of solubility).

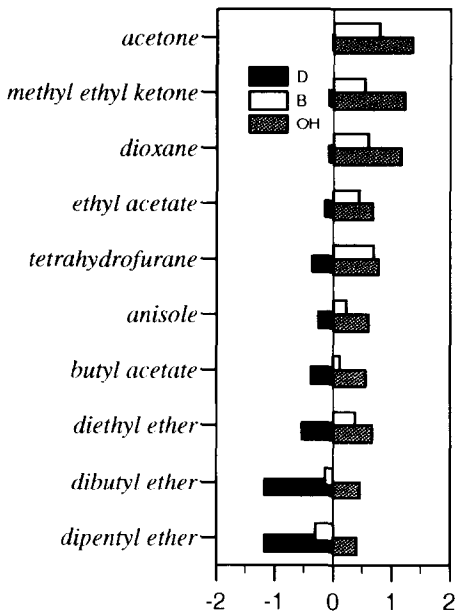

Fig. 4. Contributions of the mixing entropy correction (B), of the change of the non-specific cohesion forces (D'), and of the solute-solvent hydrogen bond formation (OH) to the solubility of carbazole in complexing non-associated solvents at 25°C (solvents are arranged in increasing order of solubility).

which remains valid, one must also take into account the positive effect of the solute-solvent hydrogen bond formation (term *OH*). This additional positive effect combined with lower values of *D'* term permits explanation of why the carbazole solubility in ethers, esters and ketones is generally greater than in inert solvents. Within the set of proton-acceptor solvents, the increase of solubility mainly results from the two following complementary effects: the decrease of the *D'* term and the increase of the *OH* term (Fig. 4). While the *D'* term decreases with the difference of the modified non-specific cohesion parameters between the solute and the solvent, the *OH* term increases with the reciprocal of the molar volume of the solvent, provided the solute-solvent H-bond is of the same strength.

Finally, in alcohols and in water, all or part of the benefit brought about by solute-solvent hydrogen bond formation is lost because of the negative hydrophobic effect resulting from solvent self-association (term *F*). In alcohols, the observed solubilities of carbazole are intermediate between those measured in inert and in complexing non-associated solvents. The values increase from ethanol to octanol (Fig. 5) following the decrease of the hydrophobic effect which is inversely correlated with the molar volume of the solvent. As to the aqueous solubility of carbazole, it is much lower than in any other solvent, and is essentially determined by the hydrophobic effect. With respect to alcohols, the very large negative value of the water hydrophobic effect results from both the very small volume of water and its participation in double hydrogen-bonded chains.

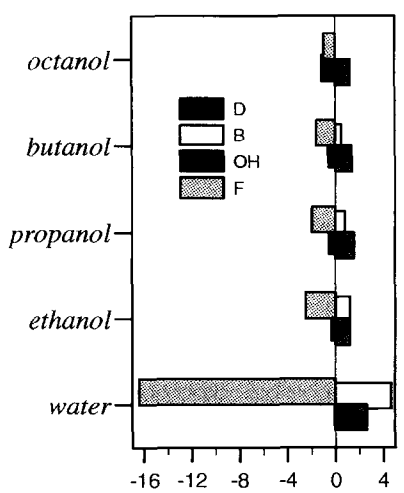

Fig. 5. Contributions of the mixing entropy correction (*B*), of the change of the non-specific cohesion forces (*D'*), of the hydrophobic effect (*F*), and of solute-solvent hydrogen bond formation (*OH*) to the solubility of carbazole in complexing amphiphilic solvents at 25°C (solvents are arranged in increasing order of solubility).

3. Conclusion

As a proton-donor substance, carbazole may interact in solution with proton-acceptor and amphiphilic solvents by forming hydrogen bonds. With respect to their behaviour towards carbazole, the solvents can therefore be divided into two main groups: non-complexing (inert) and complexing solvents. In inert solvents, the carbazole solubilities are lowest and their magnitudes are governed by the changes of the non-specific cohesion forces. Based upon the random distribution of the molecules within the solution, these changes are calculated from the squared difference of the modified non-specific cohesion parameters of the solute and of the solvent using the geometric mean rule of regular solution theory. In complexing solvents, the temporary hydrogen bond formation between carbazole and the solvent modifies the distribution of the molecules in solution; during a fraction, $1 - \gamma$, of the time the molecules are no more randomly distributed. The positive effect of these intermolecular bonds on the solubility is accounted for by the *OH* term of the solubility equation, while their effects on the distribution of the molecules are taken into account by multiplying the *D* term of the equation by the fraction, γ, of the time during which the solvent and the solute molecules are free from each other. The complexing solvents can furthermore be separated into two categories: complexing but non-associated ones, in particular ethers, esters and ketones in which the solubilities are highest owing to the hydrogen bond they form with carbazole, and the amphiphilic solvents like alcohols and water which not only interact

specifically with carbazole, but also self-associate. Because self-association tends to repel the solute outside from the bulk of solvent, the solubility of carbazole in alcohols and in water is decreased with respect to that in complexing but non-associated solvents. In particular, the hydrophobic effect due to the self-association of water is so large that the aqueous solubility of carbazole remains much lower than in any other solvent.

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