Studies on free energy of solvation of certain nitrogen containing heterocyclic compounds

Subburam Mahalakshmi [a], Rahiman Sahib Raj Mohamed [b], Venu Kannappan [c,*], Venkatachalam Sathyanarayanamoorthi [d]

[a] Department of Physics, Aarupadai Veedu Institute of Technology, Chennai 603104, India
[b] PG and Research Department of Physics, Jamal Mohamed College, Trichirapalli 620024, India
[c] PG and Research Department of Chemistry, Presidency College, Chennai 600005, India
[d] PG and Research Department of Physics, PSG College of Arts and Science, Coimbatore 641014, India

ARTICLE INFO

ABSTRACT

Polarizable continuum model has been used to account for solvent effects in binary mixtures containing six nitrogen containing heterocyclic compounds. The solutes considered in the present investigation are chloroindole (CI), bromoindole (BI), 1-chlorobenzo 1,3-diazole (CD), 1-bromobenzo 1,3-diazole (BD), 1-chlorobenzo 1,2,3-triazole (CT) and 1-bromobenzo 1,2,3 triazole (BT). Electrostatic interaction, dispersion and repulsive energies are calculated for these systems. Free energy of solvation of these six solutes in different solvents is theoretically computed and correlated with the physical properties of the solvents. Induced dipole moments are computed for the six molecules in various solvents.

© 2013 Elsevier B.V. All rights reserved.

1. Introduction

While most experimental chemistry takes place in the condensed phase, most computational research corresponds to gas-phase conditions. There has been great progress in recent years in developing techniques for including solvation effects in quantum mechanical electronic structure calculations. These techniques have emerged as important tools for predicting and correlating the energies and properties of several molecules in chemical, biological and pharmaceutical research [1,2].

Indole is an electron-rich aromatic compound with characteristic properties and is widely distributed in natural products and in proteins as the important constituent of essential amino acid tryptophan. It is known to form a hydrophobic environment in proteins and to be involved in enzymatic reactions. In addition to the redox activities and various weak interactions, it shows versatile metal binding abilities through the nitrogen and carbon atoms. Indole is a popular component of fragrances and the precursor to many pharmaceuticals. Indole has been validated as a privileged

structure, a scaffold capable of providing useful ligands for diverse receptors [3]. The most familiar derivative of indole is the amino acid tryptophan. Indole can be produced by bacteria as a degradation product of the amino acid tryptophan. It occurs naturally in human feces, coal tar and has an intense fecal odor. At very low concentrations, however, it has flowery smell, and is constituent of many orange blossoms and perfumes [4]. Natural jasmine oil, used in perfume industry contains around 2.5% of indole and hence it is used in the manufacture of synthetic jasmine oil.

Polarizable continuum models (PCMs) are commonly used to account for the solvent effect in molecular mechanism and in quantum chemistry calculations. Several PCM models are in use. In the Onsager model the cavity is assumed to be perfectly spherical and the solute is polar [5,6]. In solutions containing less polar solutes, the method is less satisfactory. Another model is the dielectric PCM model. In this model charges are produced by discontinuity in the electric field across the boundary created by the cavity. It is very sensitive to solute charge outside the cavity and involves only single point calculations. This model has limited applications. The integral equation formalism model (IEF PCM) is less sensitive to diffuse solute charge distributions [7]. The most fundamental thermodynamic quality characterizing solubility is the free energy of solvation. The calculation of free energies and cavitation enthalpies are performed with conductor like PCM. In this paper, we have

investigated the interaction of six nitrogen containing heterocyclic compounds which are important biologically and as oxidants in different solvents. A set of polar and non-polar solvents were used for this solvation analysis. We also report the results obtained in the computation of electrostatic interaction, dispersion energy and repulsive energy of solvation of six heterocyclic compounds containing nitrogen as the hetero atom in ten solvents of wide range of dielectric constants with a view to study the solvation of these heterocyclic compounds. The total free energy of solvation values is reported for these systems in ten solvents. The induced dipole moments are calculated for these molecules in various media.

2. Method of computation

The molecular structures are optimized by ab initio method [8]. The optimized geometries are solvated with the solvent of various range of dielectric constant using STO 6-311G basis set. The computer program GAMESS was used for this purpose [9]. The optimized geometries of the six nirrogen containing heterocyclic molecules are depicted in Fig. 1. In the correlation of free energy of solution and electrostatic interaction energy we used the polarizability which is a function of dielectric constant and these values are calculated using Claussius–Mosotti equation

$$f(D) = \frac{D-1}{D+2}\frac{M}{\rho} \tag{1}$$

where D = dielectric constant, M = molar mass and ρ = density.

3. Results and discussion

The intra molecular interactions control the structure and binding of the molecules and therefore play a central role to communicate and to control their activities. Such interactions include several components. Among the various components, electrostatic interactions are of special importance because of their long range and their influence on polar or charged molecules. Continuum models for polar and non-polar solvation generally attempt to solve the electrostatics in dielectric medium. For this purpose, the electrostatic interaction, dispersion energy and repulsion energy of the halo indoles and their derivatives in different solvents are evaluated by PCM. These quantities typically converge quickly during a simulation and thus can provide a good assessment of the computational approach in describing solvent–solute interaction.

The free energy of solvation calculated at STO-6-311G level of theory for a small group of solvents are classified as protic solvents and aprotic solvents. These solvents exhibit a broad range of dielectric constant (ε), index of refraction (η), macroscopic surface tension (γ), hydrogen bond acidity parameter (α) and hydrogen bond basicity parameter (β). These are listed for various solvents in Table 1. The solvents are selected such that there is a wide range in their polarity.

The electrostatic interactions are computed for the six solute molecules in ten solvents and are presented in Table 2. The electrostatic interaction energies for all the systems are negative indicating that they are due to attractive forces between molecules of solute and solvent. The data show that there is uniform variation of electrostatic interaction energy with dielectric constant as well as the structure of solute molecule. The value of electrostatic interaction of a particular solute molecule increases with increase in dielectric constant. Comparing the electrostatic interaction energy of 1-chloroindole in water with that in methanol, the electrostatic interaction is slightly more in water than in methanol although both the solvents. The electrostatic interaction between solute and solvent depends upon several molecular properties of the solvent. This result is attributed to the increased favorable electrostatic interactions in water which may be due to stronger intermolecular
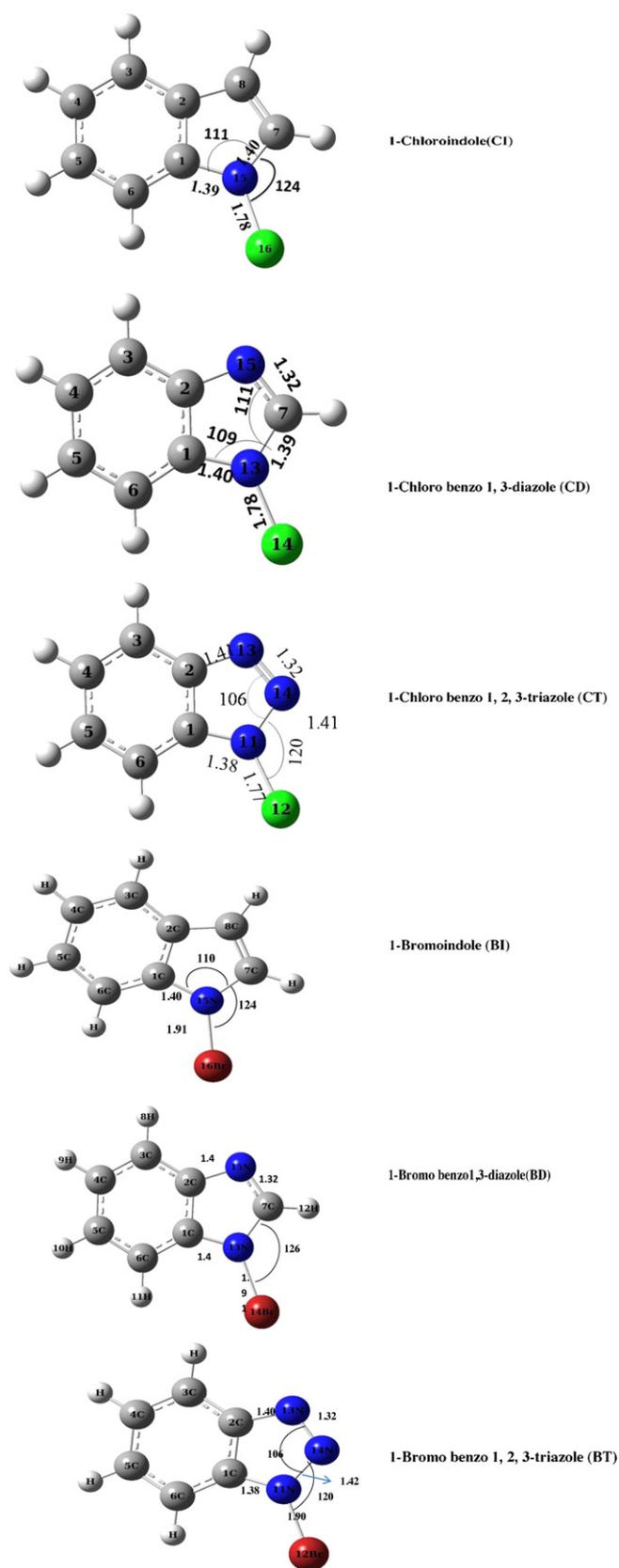

Fig. 1. Optimized geometries of nitrogen containing heterocyclic compounds.

Table 1
Solvent descriptors.

Solvent	ε	n	γ	α	β	Molecular radius (Å)	IP (eV)
H_2O	78.35	1.33	71.81	0.82	0.35	2.77	12.59
CH_3OH	32.63	1.33	22.12	0.43	0.47	3.71	10.85
C_2H_5OH	24.55	1.36	31.62	0.37	0.48	4.70	10.62
Acetone	20.49	1.36	33.77	0.04	0.49	4.76	9.69
CH_2Cl_2	8.93	1.37	27.33	0.10	0.05	4.54	11.35
C_6H_5Cl	5.62	1.52	32.69	0.00	0.17	5.46	9.07
$CHCl_3$	4.90	1.45	26.53	0.15	0.02	4.96	11.42
Toluene	2.37	1.50	40.20	0.00	0.14	5.64	8.82
C_6H_6	2.27	1.50	40.62	0.00	0.14	5.26	9.24
CCl_4	2.23	1.46	38.04	0.00	0.00	5.37	11.47

ε, dielectric constant at 298 K; n, index of refraction at optical frequencies at 298 K; γ, γ_m/γ; γ_m, macroscopic surface tension at a liquid–air interface; $\gamma = 1\, cal/mol/A^2$; α, Abraham's hydrogen bond acidity; β, Abraham's hydrogen bond basicity; r, molecular radius (Å); IP, ionization potential in eV/molecule.

Table 2
Electrostatic interaction (in kJ/mol) of nitrogen containing heterocyclic compounds in different solvents at 298 K.

Solvent	1-chloroindole	1-bromo indole	1-chlorobenzo 1,3-diazole	1-bromobenzo 1,3diazole	1-chlorobenzo 1,2,3-triazole	1-bromobenzo 1,2,3-triazole
H_2O	−36.84	−36.38	−61.21	−60.75	−61.54	−60.83
CH_3OH	−34.96	−34.46	−58.82	−58.28	−59.79	−59.12
C_2H_5OH	−34.21	−33.70	−57.73	−57.15	−58.82	−58.20
Acetone	−33.36	−33.20	−56.94	−56.35	−58.15	−57.53
CH_2Cl_2	−30.73	−30.39	−51.66	−51.20	−52.92	−52.33
C_6H_5Cl	−27.76	−27.34	−46.26	−45.80	−47.64	−47.18
$CHCl_3$	−26.71	−26.33	−44.38	−43.96	−45.72	−45.26
$C_6H_6\ CH_3$	−18.13	−17.92	−29.46	−29.22	−30.73	−30.44
C_6H_6	−17.29	−17.08	−28.01	−27.76	−29.18	−28.89
CCl_4	−17.12	−16.91	−27.76	−27.50	−28.93	−28.68

hydrogen bonding in water than in methanol [10]. The same trend has been observed in the case of ethanol and acetone. By examining the electrostatic interactions of the solutes with C_6H_6 and CCl_4, which have almost same dielectric constant, the values are high in benzene. This may be due to the difference in refractive index and macroscopic surface tension of the solvents. Plots of dielectric constant against electrostatic interaction energy for the six systems are depicted in Fig. 2. It may be pointed out that the increase in the magnitude of electrostatic energy is significant in the solvents of lower dielectric constant as we can observe steep fall in the curves (Fig. 2). The electrostatic interaction of the heterocyclic compounds in the same solvent can be compared. It is found that the electrostatic interaction energy of indole derivatives is less than those of diazole derivatives. This indicates that the presence of second nitrogen atom in the five member rings, enhances the polarity of the solute molecule and hence the electrostatic interaction is increased in the same solvent. However, when third nitrogen is introduced in the five member rings the polarity is not affected significantly and the electrostatic interaction is not affected significantly in the same solvent for diazole and triazole derivatives. The electro negativity of chlorine is greater than that of bromine and the chloro compounds are more polar than bromo compounds.

The electrostatic interaction can also be correlated with the molecular radius of the solvents. It is known that the electrostatic interaction energy generally decreases with increase in molecular radius of solvent. This correlation is fairly good in chlorinated and polar solvents. Thus the electrostatic interaction of the two solute molecules in water provides the highest value while the value is the lowest in toluene.

The dispersion energies are due to the polarization of the solvent by the solute molecules. The dispersion–repulsion energy is important in the case of hydrophobic and aromatic species and all the solutes considered in the present investigation are such compounds. The computed dispersion energies for the six solute molecules in ten different solvents are listed in Table 3. It is found that the dispersion energies of a particular solute increase with decrease in polarity of the solvent. The data obtained in the present investigation indicate that dispersion energy depends on two physical properties, namely, dielectric constant and density of the solvent molecule. These two properties are related to the polarizability. The dielectric constant function $f(D)$ is computed and plots of dispersion energy against $f(D)$ are presented in Fig. 3. These plots indicate that the dispersion energy is more negative in solvents with higher $f(D)$ values and less negative in solvents with smaller $f(D)$ values. The computed data for dispersion energy values of nitrogen containing heterocyclic compounds may correlate with the ionization potential of solvent molecule. The plots of dispersion energy against ionization potential are given in Fig. 4. It may be noted that the dispersion energy in a given solvent, the value for
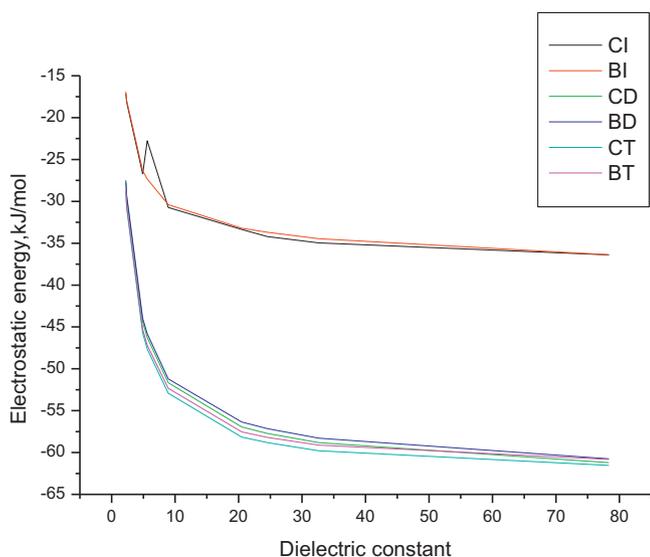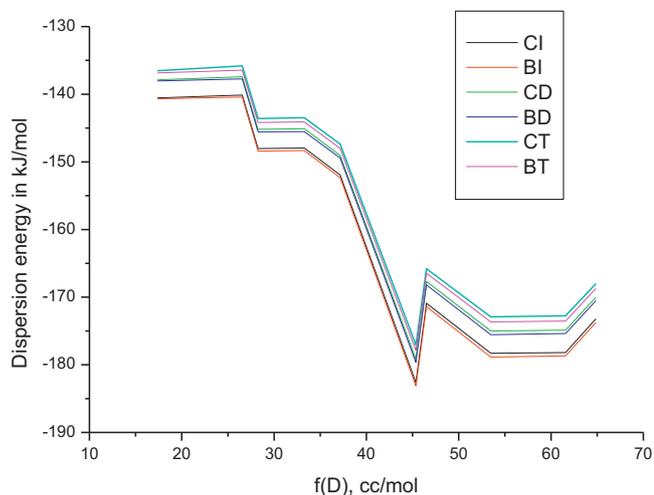

Fig. 2. Plot of electrostatic interaction against dielectric constant of solvent.
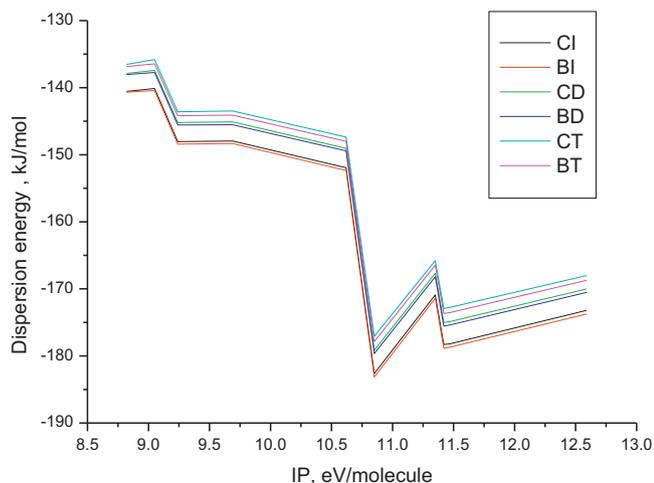
Table 3
Dispersion energies of nitrogen containing heterocyclic compounds (in kJ/mol) in different solvents at 298 K.

Solvent	Chloroindole	Bromoindole	Chlorobenzo 1,3-diazole	Bromobenzo 1,3-diazole	Chlorobenzo 1,2,3-triazole	Bromobenzo 1,2,3-triazole
H_2O	−140.55	−140.67	−137.87	−138.03	−136.53	−136.86
CH_3OH	−140.13	−140.42	−137.41	−137.74	−135.81	−136.44
C_2H_5OH	−148.04	−148.42	−145.19	−145.57	−143.60	−144.19
Acetone	−147.96	−148.33	−145.11	−145.53	−143.48	−144.10
CH_2Cl_2	−151.93	−152.35	−149.05	−149.42	−147.37	−148.00
C_6H_5Cl	−182.62	−183.13	−179.15	−179.65	−177.05	−177.85
$CHCl_3$	−170.94	−171.40	−167.68	−168.18	−165.79	−166.46
$C_6H_6CH_3$	−178.31	−178.86	−175.00	−175.55	−172.91	−173.66
C_6H_6	−178.19	−178.69	−174.88	−175.38	−172.75	−173.54
CCl_4	−173.24	−173.75	−170.02	−170.52	−168.01	−168.72

Fig. 3. Plot of dispersion energy against dielectric constant function of solvent.

chloro compound is slightly less than that of bromo compound in all the solute molecules studied. This is because the polarizability of bromine is greater than that of chlorine atom, which may be due to the larger size of bromine and it contains more number of electrons than chlorine atom. The dispersion energy also correlates satisfactorily with the refractive index of the solvent. Thus the dispersion energy of a given solute is less negative in water which has the smallest refractive index and it is more negative in chlorobenzene which has higher refractive index.

The repulsion energy is another important parameter to be considered in solvation analysis as solubility of solute in a given solvent depends on this type of energy. Table 4 provides the computed values of repulsive energies for the six solute molecules in different media. We observed that the repulsive energies due to solute–solvent interactions in all the solvents are positive values. The repulsive energy is more positive in an aqueous solution for all the solute molecules under investigation. This may be due to the hydrophobic characters of the six heterocyclic compounds. By relating the refractive index of the solvents with the repulsive energy (Table 4), it is found that there is uniform change in repulsive energy with the refractive index of the solvent. Thus, the repulsive energy is the highest in water having the lowest refractive index. It is the lowest in chlorobenzene which has the highest refractive index. It may be pointed out that the repulsion energy is less in chlorobenzene for the six solutes, suggesting that these compounds may be more soluble in chlorobenzene. This is also supported by the high values of free energy of salvation of these solutes in chlorobenzene. Plots of repulsion energy against dielectric constant of the solvent are given in Fig. 5. There is satisfactory correlation between the repulsion energy and dielectric constant of the solvent.

The cavitation enthalpy is the heat energy involved in creating the appropriate cavity inside the solution in the absence of solute-solvent interactions [11]. Different approaches have been introduced to compute enthalpy of cavitation; nevertheless it is unclear which one is the most accurate due to unavailability of experimental values to compare. Formulations based on the scaled particle theory [12,13] have been originally proposed by Pierotti [16] and further developed in several studies. Although these approaches are derived from a rigorous statistical mechanics standpoint, eventually the use of a set of fitted parameters is needed to represent an effective radius for the solvent and
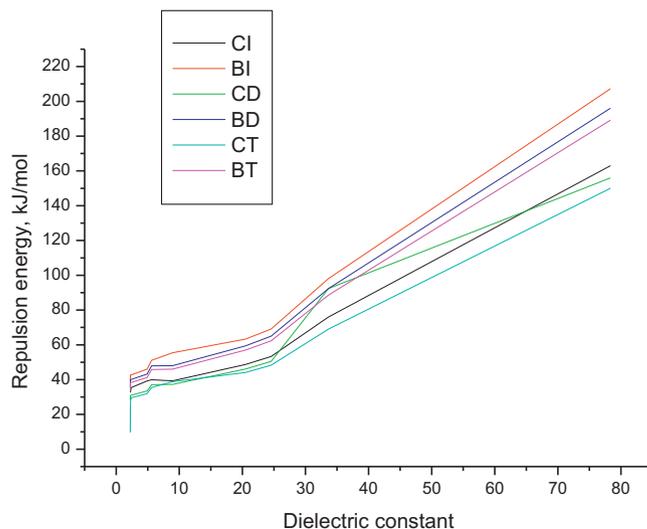

Fig. 4. Plot of dispersion energy against ionization potential of solvent molecule.

Fig. 5. Plot of repulsion energy against dielectric constant of solvent.

Table 4
Repulsion energies of nitrogen containing heterocyclic compounds (in kJ/mol) in different solvents at 298 K.

Solvent	Chloroindole	Bromoindole	Chlorobenzo 1,3-diazole	Bromobenzo 1,3-diazole	Chlorobenzo 1,2,3-triazole	Bromobenzo 1,2,3-triazole
H_2O	163.79	207.28	156.00	196.07	150.05	189.20
CH_3OH	75.99	98.05	72.05	92.28	68.99	88.59
C_2H_5OH	53.33	69.12	50.49	64.98	48.27	62.29
Acetone	39.19	55.39	37.09	47.85	38.81	45.84
CH_2Cl_2	48.73	63.26	46.13	59.41	44.08	56.94
C_6H_5Cl	32.82	42.70	31.02	40.11	29.60	38.35
$CHCl_3$	39.31	51.12	37.18	47.98	35.50	45.93
$C_6H_6CH_3$	39.31	38.73	28.13	36.38	26.79	34.70
C_6H_6	35.37	46.01	33.45	43.21	31.86	41.23
CCl_4	32.78	42.66	31.02	40.07	29.56	38.26

Table 5
Cavitation enthalpy (calculated using Pierotti formula) of nitrogen containing heterocyclic compounds (in kJ/mol) in different solvents at 298 K.

Solvent	Chloroindole	Bromoindole	Chlorobenzo 1,3-diazole	Bromobenzo 1,3-diazole	Chlorobenzo 1,2,3-triazole	Bromobenzo 1,2,3-triazole
H_2O	10.94	10.75	10.67	11.06	10.36	10.75
CH_3OH	35.98	35.38	35.12	36.37	34.12	35.38
C_2H_5OH	37.52	36.89	36.62	37.92	35.58	36.89
CH_3COCH_3	47.52	46.12	46.39	48.03	45.08	46.72
CH_2Cl_2	47.79	46.98	46.65	48.30	45.32	46.98
C_6H_5Cl	49.96	49.12	48.77	50.51	47.38	49.12
$CHCl_3$	43.86	45.37	42.82	44.33	41.61	43.12
$C_6H_6CH_3$	47.86	39.52	46.72	48.37	45.40	47.06
C_6H_6	60.42	62.52	58.98	61.08	57.30	59.40
CCl_4	49.13	50.83	47.96	49.66	46.20	48.30

Table 6
Cavitation enthalpy (calculated using Sinanoglu formula) of nitrogen containing heterocyclic compounds (in kJ/mol) in different solvents at 298 K.

Solvent	Chloroindole	Bromoindole	Chlorobenzo 1,3-diazole	Bromobenzo 1,3-diazole	Chlorobenzo 1,2,3-triazole	Bromobenzo 1,2,3-triazole
H_2O	11.15	10.95	10.87	11.28	10.54	10.95
CH_3OH	48.09	47.36	47.05	48.56	45.84	47.36
C_2H_5OH	47.49	46.77	46.46	47.96	45.26	46.76
CH_3COCH_3	33.28	7.89	7.78	8.36	7.31	7.89
CH_2Cl_2	10.77	10.43	10.28	10.99	9.72	10.43
C_6H_5Cl	38.83	38.38	38.19	39.12	37.44	38.38
$CHCl_3$	9.27	9.98	8.78	9.49	8.22	8.93
$C_6H_6 CH_3$	44.83	46.99	43.34	45.49	41.61	43.78
C_6H_6	45.56	47.77	44.05	46.25	42.29	44.50
CCl_4	41.60	43.63	40.20	42.23	38.58	40.61

for the spheres centered on the solute atoms. For non-spherical cavities, one of the most used approximations Pierotti–Claverie formula [14,15]. Cavitation enthalpy contributes to the free energy of solution and these values are calculated for the six systems using Pierotti and Sinanoglu formulations and the data are given in Tables 5 and 6 respectively. Analysis of the data in these two tables shows that the values computed using Pierotti [16] method correlate satisfactorily with the physical properties of solvent and the values calculated by Sinanoglu [17] method are less satisfactory.

The cavitation enthalpy generally increases with increase in molecular radius of the solvent (Fig. 6), while it decreases with increase in dielectric constant of the solvent. Cavitation enthalpy in a given solvent depends on the nature of solute. It is observed that in the case if these heterocyclic molecules with one nitrogen atom, the bromo compound has slightly lower cavitation enthalpy than those of chloro derivative except in three solvents, namely, $CHCl_3$, C_6H_6 and CCl_4. However, in the case of diazole and triazole derivatives, the bromo compounds have slightly higher cavitation enthalpy than

Table 7
Total free energies of solvation of nitrogen containing heterocyclic compounds (in kJ/mol) in different solvents at 298 K.

Solvent	Chloroindole	Bromoindole	Chlorobenzo 1,3-diazole	Bromobenzo 1,3-diazole	Chlorobenzo 1,2,3-triazole	Bromobenzo 1,2,3-triazole
H_2O	−13.61	−30.56	−43.12	−2.67	−48.02	−8.49
CH_3OH	−99.06	−76.78	−124.22	−103.79	−126.73	−106.97
C_2H_5OH	−128.91	−113.00	−152.39	−137.74	−154.11	−140.33
Acetone	−142.43	−126.19	−164.95	−154.03	−163.07	−155.79
CH_2Cl_2	−134.06	−119.49	−154.58	−141.22	−156.20	−143.39
C_6H_5Cl	−177.56	−167.76	−194.35	−185.39	−195.10	−186.64
$CHCl_3$	−158.34	−146.66	−174.88	−164.12	−176.01	−165.79
$C_6H_6CH_3$	−166.72	−158.05	−176.38	−168.39	−176.85	−169.39
C_6H_6	−160.06	−149.72	−169.39	−159.89	−170.06	−161.19
CCl_4	−157.59	−165.76	−192.35	−183.39	−193.10	−184.64

Table 8
Induced dipole moments of nitrogen containing heterocyclic compounds in various solvents (in Debye units).

Solvent	Chloroindole	Bromoindole	Chlorobenzo 1,3-diazole	Bromobenzo 1,3-diazole	Chlorobenzo 1,2,3-triazole	Bromobenzo 1,2,3-triazole
H_2O	5.91	5.65	7.66	7.42	6.54	6.46
CH_3OH	5.93	5.77	7.65	7.48	6.50	6.42
C_2H_5OH	5.92	5.79	7.63	7.48	6.48	6.40
Acetone	5.91	5.80	7.61	7.47	6.46	6.39
CH_2Cl_2	5.80	5.68	7.46	7.31	6.46	6.39
C_6H_5Cl	5.69	5.59	7.30	7.17	6.21	6.13
$CHCl_3$	5.65	5.54	7.24	7.12	6.16	6.08
$C_6H_6CH_3$	5.33	5.24	6.79	6.67	5.79	5.71
C_6H_6	5.30	5.20	6.74	6.61	5.75	5.67
CCl_4	5.29	5.20	6.73	6.61	5.74	5.67

those of chloro compounds. Another interesting observation is that the cavitation enthalpy of a given solute decreases with increase in dielectric constant of the solvent.

The free energy of solution of the six heterocyclic compounds is calculated and the values are presented in Table 7. The free energy of solution of all the six compounds in the ten solvents is negative indicating that the dissolution process is feasible in these systems. The data show that the free energy values depend upon the nature of solute as well as the physical properties of solvents. It is to be pointed out that the $\Delta G_{\text{solution}}$ values are more negative in organic solvents than in water. It is justified because the solutes considered here are covalent molecules and hence they are expected to dissolve more in organic solvents than in water. Among the six solutes the $\Delta G_{\text{solution}}$ for CT is more negative than the values for other five solutes suggesting that CT may be more soluble than other five compounds. This is true for all solutes in all the solvents investigated. In any solvent, if we compare the free energy of solution of chloro compound with that of bromo compound the former has more negative value suggesting that chloro derivatives may be more soluble than structurally similar bromo derivatives. This may be due to the influence of molar mass on the solubility. Since all the six solute moecules are covalent in nature and majority of solvents are also covalent, correlation has been attempted between the free energy of solution and polarizability function [$f(D)$]. Plots of $\Delta G_{\text{solution}}$ against $f(D)$ are depicted in Fig. 7. These plots clearly indicate that the free energy of solution becomes more negative in solvent with higher value of $f(D)$.

The geometry and charge distribution of the solute particles are changed in the solvent by polarizability and hence solvation alters
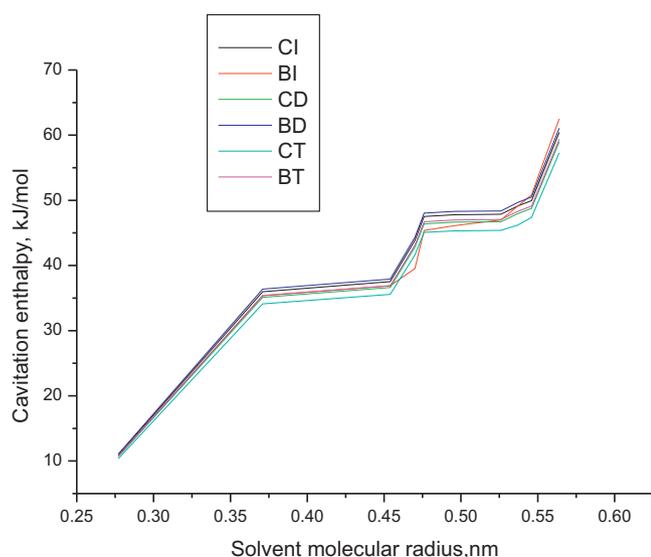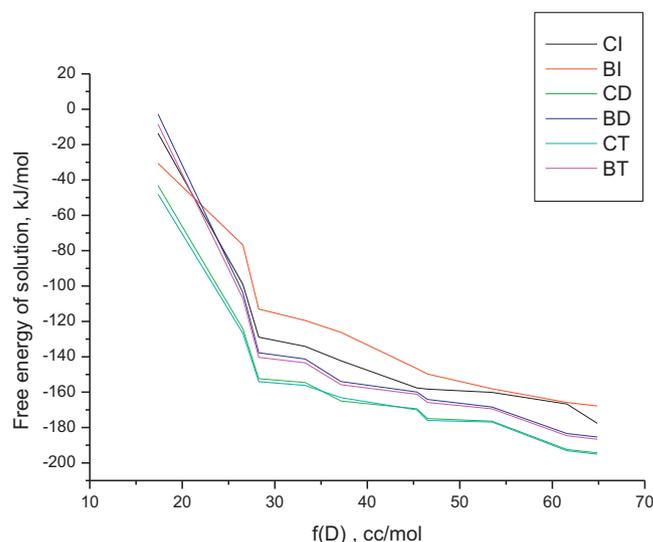

Fig. 7. Plot of free energy of solution against polarizability function of solvent.

the electrostatic properties of the solute. The polarization effect by the solvent is reflected by the change in molecular dipole moment of the solute when it goes from gas phase to the solution. Such change can be easily determined once the solute wave function in the solution is obtained [18]. The induced dipole moments of the given set of solute molecules are calculated by STO-6-311G as shown in the Table 8. The induced dipole moment depends on the polarizability of solvent molecule. Plots of induced dipole moment against polarizability function of the various solvents are given
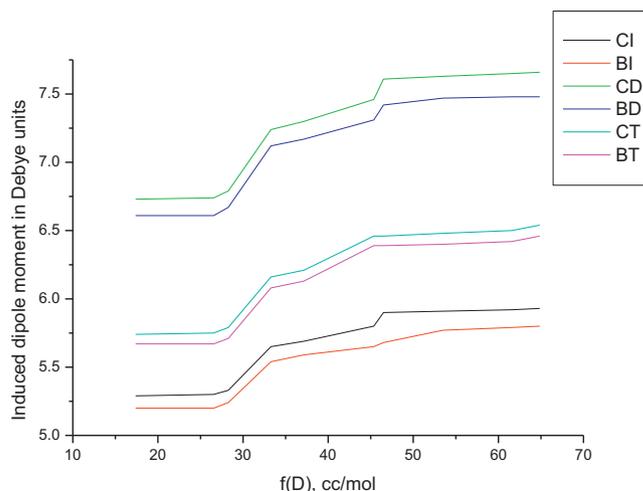

Fig. 6. Plot of cavitation enthalpy against molecular radius of solvent.

Fig. 8. Plot of induced dipole moment against polarizability function of solvent.

in Fig. 8. It can be inferred from the plots depicted in Fig. 8 that the induced dipole moment increases with increase in the polarizability function of the solvent in the case of all the six solutes investigated. The solvation effect leads to a systematic increase in the dipole moment which is similar to that reported in previous ab initio and semi empirical SCRF calculations [19–22].

4. Conclusion

Quantum mechanical solvation analysis is carried out for six halogenated heterocyclic nitrogen containing compounds. The PCM model gives satisfactorily the free energy of solution and its components. These parameters can be correlated with the physical properties of the solvent. Electrostatic interaction can be satisfactorily correlated with the dielectric constant and molecular radius of the solvent. The dispersion energies of these solutes depend on the polarizability function, refractive index and ionization potential values of the solvents. There is satisfactory correlation between the repulsion energy and dielectric constant of the solvent. The cavitation enthalpy generally increases with increase in molecular radius of the solvent but decreases with increase in dielectric constant of the solvent. The values of free energy of solution of all the six compounds in the ten solvents are negative indicating that the dissolution process is feasible in these systems. Among the six solutes the $\Delta G_{\mathrm{solution}}$ for 1-chlorotriazole is more negative than the values for other five solutes suggesting that 1-chlorotriazole may be more soluble than other five compounds. There is fairly good correlation between $\Delta G_{\mathrm{solution}}$ values and the polarizability function of the solvent. It is also observed that the induced dipole moment increases with increase in the polarizability function of the solvent in the case of all the six solutes investigated.

References

[1] B. Boyd, K.B. Lipkowitz, in: K.B. Lipkowitz, D.B. Boyd (Eds.), Reviews in Computational Chemistry, vol. 14, Wiley-VCH, New York, 2000, pp. 399–439.
[2] J.H. Krieger, New software expands role of molecular modeling technology, Chem. Eng. News 27 (1995) 30–40.
[3] F.R. De Sá Alves, C.A.M. Fraga, E.J. Barreiro, From nature to drug discovery: the indole scaffold as a privileged structure, Mini-Rev. Med. Chem. 9 (2009) 782–793.
[4] B. Roux, T. Simonson, Implicit solvent models, Biophys. Chem. 78 (1999) 1–20.
[5] L. Onsager, Electric moments of molecules in liquids, J. Am. Chem. Soc. 58 (1936) 1486–1493.
[6] M. Wong, M. Frisch, K. Wiberg, J. Am. Chem. Soc. 113 (1991) 4476.
[7] J. Tomasi, B. Mennucci, R. Cammi, Quantum mechanical continuum solvation models, Chem. Rev. 105 (2005) 2999–3094.
[8] P. Winget, J.D. Thompson, C.J. Cramer, D.G. Truhlar, Parametrization of a universal solvation model for molecules containing silicon, J. Phys. Chem. 106 (2002) 5160–5168.
[9] M.W. Schmidt, K.K. Baldridge, J.A. Boatz, S.T. Elbert, M.S. Gordon, J.H. Jensen, S. Koseki, N. Matsunaga, K.A. Nguyen, S.J. Su, T.L. Windus, M. Dupuis, J.A. Montgomery, General atomic and molecular electronic structure system GAMESS, J. Comput. Chem. 14 (1993) 1347–1363.
[10] V. Sathyanarayanamoorthi, U. Ponnambalam, G. Gunasekaran, V. Kannapan, Solubility studies of halohexanes by a quantum mechanical method, J. Mol. Liq. 129 (3) (2006) 181–184.
[11] J. Tomasi, M. Persico, Molecular interactions in solution: an overview of methods based on continuous distributions of the solvent, Chem. Rev. 94 (1994) 2027–2094.
[12] H. Reiss, H.L. Frisch, J.L. Lebowitz, Statistical mechanics of rigid spheres, J. Chem. Phys. 31 (1959) 369–380.
[13] H. Reiss, H.L. Frisch, E. Helfand, J.L. Lebowitz, Aspects of the statistical thermodynamics of real fluids, J. Chem. Phys. 32 (1960) 119–124.
[14] J. Tomasi, B. Mennucci, R. Cammi, Quantum mechanical continuum solvation models, Chem. Rev. (Washington, DC) 105 (2005) 2999–3093.
[15] P. Claverie, in: B. Pullman (Ed.), Intermolecular Interactions: From Diatomics to Biomolecules, Wiley, Chichester, 1978, p. 124.
[16] R.A. Pierotti, A scaled particle theory of aqueous and non-aqueous solutions, Chem. Rev. 76 (1946) 717–726.
[17] O. Sinanoğlu, Microscopic surface tension down to molecular dimensions and micro thermodynamic surface areas of molecules or clusters, J. Chem. Phys. 75 (1981) 463–469.
[18] C.J. Cramer, D.G. Truhlar, Polarization of the nuclic acid bases in aqueous solution, Chem. Phys. Lett. 198 (1992) 74–80.
[19] M.J. Huron, P. Claverie, Calculation of the interaction energy of one molecule with its whole surrounding: I. Method and application to pure nonpolar compounds, J. Phys. Chem. 76 (1972) 2123–2133.
[20] E. Cubero, F.J. Luque, M. Orozao, J. Gao, Perturbation approach to combined QM/MM simulation of solute–solvent interactions in solution, J. Phys. Chem. B 107 (2003) 1664–1671.
[21] F.M. Floris, Modeling the cavitation free energy, J. Phys. Chem. 109B (2005) 24061–24070.
[22] C.J. Cramer, D.G. Truhlar, An SCF solvation model for the hydrophobic effect and absolute free energies of aqueous solvation, Science 256 (1992) 213–217.