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Thermodynamics, Solvents effects and ^{1}H ,^{13}C NMR Shielding :Theoretical studies of Adamantane

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ABSTRACT

Some of the Adamantane properties were calculated in this study. Chemical shift, free energy of solvation, free energy of cavity formation, Henry's law constant, and other properties of Adamantane in dry phase, three solvents and three temperatures have been calculated with Ab initio method base on density functional theory (DFT) at B3lyp/6-31g, B3lyp/6-31g*, B3lyp/6-31+g* and B3lyp/6-31++g** levels with magnetic properties of the gauge –including atomic orbital method. Three solvents were used in this study are polar and non-polar solvents with different dielectric constants. The results show that the chemical shifts of 13C and 1H at B3lyp/6-31g* is closer to the experimental values. Free energy of solvation of Adamantane in non-polar solvents such as n-heptane is more negative than the polar solvents like water.

Keywords: Adamantane; Chemical shift; Ab initio; DFT; Free energy solvation

INTRODUCTION

Adamantane, tricycle [3, 3, 1, 13, 7] decane is the simplest saturated polycyclic hydrocarbon atoms arranged in a cage - like skeleton resembling that of a so–called " characteristic " of a diamond crystal lattice. Calculation of thermodynamic parameters of adamantane in different interest of conditions (various solvents and various temperatures) is important. The recognized pharmaceutical adamantane and adamantly derivatives [1-3] has unquestionably lead to a growing need for a physicochemical characterization of these compounds. Solvent effects on thermochemical phenomena remain a challenging area of investigation for physicalal chemists. Many organic chemistry reactions take place in solution and, thus, it is important for realistic theoretical models to accurately describe solvent effects. Furthermore, in processes involving biomolecules, such as enzyme catalysis, surrounding enzymatic structure can significantly influence chemical reactivity. In recent years, much effort has been devoted to the development and application of methods to treat these environmental effects. Calorimetric measurements have been applied with various degrees of success to analysis of dominant molecular interaction in solution. However Ab initio molecular orbital theory at the SCF level and DFT method has been shown to be capable of the accurate prediction of geometry and thermochemisry for small hydrocarbons. Two highly productive approaches to solution of the electronic "Schrodinger " equation have arisen over the past 50 years.

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Wave function-based approaches expand the electronic wave function as a sum of Slater determinants, the orbital and coefficients of which are optimized by various numerical procedures. Hartree–Fock theory is the simplest method of this type, involving optimization of a single determinant. However, its usefulness is limited because of complete neglect of electron correlation. The second class of theoretical approaches are based on the density functional theory (DFT), which follows the Hohenberg–Kohn theorem mandates expression of the total energy of the system as a functional of the electron density. Because the electron density depends on only three coordinates (as opposed to the 3N coordinates of N electrons), the computational effort required to solve the equations of DFT is comparable with that required for Hartree–Fock theory, thus rendering DFT highly attractive from the point of view of computational implementation. However, the correct functional of the energy is unknown and has to be constructed by heuristic approximation. Initial functionals, based principally on behavior of the electron gas were lacking in the accuracy required for chemical applications. Break through over the past two decades [4 -8] have led to the development of functional capable of remarkable accuracy and breadth of applicability across the periodic table.

THEORETICAL

Method

For small molecules in the gas phase and in solution, Ab initio quantum chemical calculations can provide results approaching benchmark accuracy and they are used routinely to complement experimental studies.A wide variety of properties, including structures [9], thermochemistry including activation barriers [9], spectroscopic quantities of various types [10], and responses to external perturbations can be computed effectively. SCRF methods (or simply ignoring the solvent entirely, an approximation that is sometimes acceptable, particularly in non polar solvents or when a quantity that is insensitive to the dielectric of the environment is being computed), enable a relatively straight forward extension of gas-phase quantum chemical methods to obtaining results for molecules in solution. Optimization of the accuracy of continuum solvation methods is far from a solved problem. furthermore, there is some evidence that the inclusion of a small number of explicit water molecules can improve results [11], but methods of this type must be formulated very carefully to avoid double counting. The Ab initio calculations were performed by GAUSSIAN 98 program. The basis sets were used are 6-31 G, 6-31G*, 6-31 + G*, and 6-31 + + G** . This basis sets were selected for considering of effects of polar and diffusion Parameters on various properties. Structural parameters are optimized at the basis sets. The optimized geometry parameters are used to obtain total electronic energies. Long-range effects of the solvents (water, n-heptane and cyclohexane) are taken into account by means of a dielectric continuum represented by the polarizable continuum model (PCM). We have used the PCM model for geometry optimizations and energy calculations. In the polarizable continuous (PCM) model, the cavity was used of molecular shape and was built by interlocking spheres. The radii of the spheres were obtained by scaling the atomic Van der waals radii. The surface of each sphere was divided in 60 triangular tesserae (default value) for the calculation of the surface-charge distribution. In the present paper, we have employed the PCM model to determine the solvent effects on the geometric parameters of reaction processes.

Calculations:

The 1H and 13C isotropic chemical shift computed at the B3LYP method at different basis set in various solvents and temperatures.B3LYP methodology is based on a combination of Beck's three parameter adiabatic connection exchange functional[12,13] with the LYP correlation one. In all density functional calculations, the fine grid was used for numerical integration.

Note that while the B3LYP methodology is non-hybrid (it includes no HF exchange), the B3LYP one contains an admixture of HF exchange (i.e. is of hybrid form). The computed 13C chemical shifts are frequently used as a valuable tool in identification of reactive ionic species, while the prediction of environmental dependence of the chemical shifts in the case of amino acid carbon atoms might be very helpful in elucidation of three-dimensional protein structures . Accurate prediction of chemical shifts may also be of invaluable help for determining the structures of molecules in solutions. The nuclear magnetic shielding tensors, defined as the mixed second derivatives of energy with respect to the magnetic moment of the X-th nucleus (mx) and the external magnetic field ( ), represented by the following equation

$$\sigma_x^{\alpha\beta} = \frac{\partial^2 E}{\partial \beta^\alpha \partial m_x^\beta} \qquad (1)$$

There are three algorithms at using a finite basis set [14,15]. They are GIAO (Gauge Invariant Atomic Orbital), CSGT (continuous set of gauge transformations) and IGAIM (Individual Gauge for Atoms in Molecules) [16]. We have reported a density functional study with different basis sets of isotropic 1H and 13C chemical shifts for Adamantane. Adamantane is almost ideal model system for a study of both the 1 H and 13 C chemical shifts. In this study we have used the optimized geometries of Adamantane with four methods (B3LYP/6-31g, B3LYP/6-31g*, B3LYP/6-31+g*, B3LYP/6-31++g**) and the standard for calculation of isotropic shielding values , defined as the following equation:

$$\sigma_{iso} = \frac{1}{3}(\sigma_{11} + \sigma_{22} + \sigma_{33} \qquad (2)$$

(σii being the principal tensor components) were used to calculate the isotropic chemical shifts δ with respect to TMS by the equation 3.

$$(\delta_{x,iso} = \sigma_{TMS,iso} - \sigma_{x,iso}) \qquad (3)$$

It is worth noting at this point that the B3lyp combinations of exchange and correlation functional used in the present work for calculation of magnetic field dependence explicitly. All calculation was carried out with the Gaussian 98 series of programs. At the theoretical level, the shielding σ that is the basis for chemical shift is known to depend on complex intra molecular factors and, except for gases. At very low pressure, on conditions (e.g. solvent, temperature, concentration, pressure) that are thought to be significant for the particular investigation and to recognize that the value of δ may very as these parameters are changed. However, it is generally not desirable to speak of 'correcting' a chemical shift that has been properly measured under a particular set of conditions or of converting that value to a "true" chemical shift (except as mentioned above for TMS effect).

Solvent effect on the 1H and 13C chemical shift of TMS and adamantane [17]:

In this study 1H and 13C chemical shift of adamantine measured in water and n-heptane and cyclohexane solvents. The results of them write in table (1,2,3 and 4). TMS is a good reference for calculating of chemical shifts of Adamantane based on the equation 3.

Temperature effect on the 1H and 13C chemical shift of TMS and adamantane [18]:

Most NMR studies are carried out at a single temperature, often the ambient temperature of the probe. In some instances, however, it is important to examine the variation of or more chemical shift within a sample as the probe temperature is varied. Such chemical shifts are measured with respect to TMS, and the implicit

assumption is often made that the 1H and 13C chemical shift of TMS does not vary with temperature. In this study chemical shifts calculated in three temperature, 298.15 (room temperature), 310.15(body temperature) and 313.15(approximately high temperature of body). Results are in table 1, 2, 3 and 4.

PCM Method:

Direct calorimetric determination of Gibbs free energy solvation is very difficult; therefore, in this study ΔG trans is measured by ab initio calculations by using the theory of intermolecular forces. Two new expressions for pauli repulsion and dispersion contributions to the solvation free energy are derived. These expressions contain explicitly the solute electron density and, therefore, can be used directly in the SCF calculation of the solute wave function within the polarizable continuum model (PCM). The procedures for the calculation of solute energy and wave function with PCM method have been reported in several papers and we do not repeat here all the details. This approach for caculating of logP is performed in other papers.(19) Free energies of solvation have been studied extensively. A group additive property approach has been taken to estimate these free energies. Group additive property, GAP, approaches are common in estimating thermodynamic variables. For GAP calculations, we assume simply that a molecule is the sum of its parts. Table 1. lists several GAP parameters for GH2o and Goct estimation. These contributions are summed to get the GH2O and Goct for the entire molecule.

Table 1. Group Additive Property parameters for Free Energies of Desolvation.

Group	Fh2o (kcal/mol)	Foct (kcal/mol)
CH_3 (methyl-aliphatic)	-0.800	0.160
CH_2 (methylene)	-0.200	0.520
CH (methane)	0.240	0.560
O (ether-aliphatic)	3.970	1.810
O (hydroxyl-aliphatic)	5.820	3.790
N (amide)	2.930	-0.020
H (amide)	3.030	3.490
Cl (aliphatic)	0.940	1.020

The solvation process can be thought of as decomposed in two steps: The first consisting of the formation of a cavity in the solvent capable of hosting a solute molecule, and the second being the activation of solute–solvent interactions.The solvation free energy, G slo can be computed as the addition of cavitations (ΔG cav),Van derWaals(ΔG vW) and electrostatic (ΔG ele) components (20,21).

$$\Delta G^{sol} = \Delta G^{cav} + \Delta G^{vw} + \Delta G^{ele} \qquad (5)$$

avity formation terms are often modeled by energies proportional to solvent-accessible volume and surface area while attractive dispersive terms generally require the calculation of an integral or surface-based integral approximation. On the other hand, Henry's law constant is directly related to the free energy of solvation.

$$K(\rho, T) = RT_{\rho} \exp\left(\frac{\Delta G^{sol}}{RT}\right) \qquad (6)$$

Where ρ is the density of the pure solvent, which is equal to that of the salvation in the limit of infinite dilution.

RESULTS AND DISCUSION

Results of NMR calculations are in the following tables. Chemical shifts of Adamantane were calculated in three solvents at three temperatures.

Results show 13C chemical shift at B3lyp/6-31g* and 1H chemical shift at B3lyp/6-31++g** is closer to the experimental values (Fig 1.).

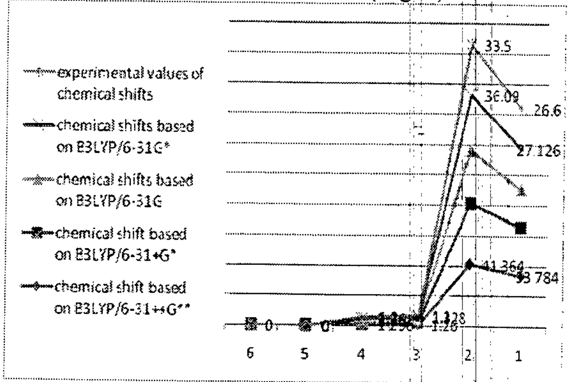

Fig.1. the comparition between the chemical shift values from experimental approaches and B3LYP methods based on Table 2 to Table 5 (in dry phse).

Table2. Theoretical 13C and 1H isotropic chemical shifts, all values in ppm with respect to TMS, for adamantane. Calculations were performed at the B3lyp/ 6-31g* level of theory for three solvents, three temperatures and dry phase

	Solvent = H2O			***Solvent = C7H16***			***SOlvent = C6H12***			***Dry phase***		
	T: 298.15	**T: 310.15**	**T: 313.15**	**T: 298.15**	**T: 310.15**	**T: 313.15**	**T: 298.15**	**T: 310.15**	**T: 313.15**	**T: 298.15**	**T: 310.15**	**T: 313.15**
C1 (t)	**27.232**	**27.232**	**27.232**	**27.079**	**27.112**	**27.111**	**27.054**	**27.056**	**27.057**	**27.126**	**27.126**	**27.126**
C2(s)	**36.436**	**36.436**	**36.436**	**36.271**	**36.273**	**36.273**	**36.268**	**36.270**	**36.270**	**36.090**	**36.257**	**36.257**
H1 (t)	**1.332**	**1.332**	**1.332**	**1.331**	**1.333**	**1.333**	**1.329**	**1.330**	**1.330**	**1.328**	**1.328**	**1.328**
H2(s)	**1. 356**	**1. 356**	**1. 356**	**1. 350**	**1. 356**	**1. 359**	**1. 349**	**1. 351**	**1. 351**	**1. 360**	**1. 360**	**1. 360**

"s" and "t" denote, respectively, a secondary and tertiary carbon or hydrogen atom.

Table3. Theoretical 13C and 1H isotropic chemical shifts, all values in ppm with respect to TMS, for adamantane. Calculations were performed at the B3lyp/ 6-31+g* level of theory for three solvents, three temperatures and dry phase

	Solvent = H2O			***Solvent = C7H16***			***SOlvent = C6H12***			***Dry phase***		
	T: 298.15	**T: 310.15**	**T: 313.15**	**T: 298.15**	**T: 310.15**	**T: 313.15**	**T: 298.15**	**T: 310.15**	**T: 313.15**	**T: 298.15**	**T: 310.15**	**T: 313.15**
C1 (t)	**32.415**	**32.487**	**32.497**	**32.164**	**32.158**	**32.049**	**32.096**	**32.096**	**32.096**	**32.102**	**32.102**	**32.102**
C2(s)	**39.510**	**40.608**	**40.630**	**39.078**	**40.245**	**40.256**	**40.245**	**40.248**	**40.249**	**40.171**	**40.171**	**40.171**
H1 (t)	**1.375**	**1.379**	**1. 378**	**1.380**	**1.379**	**1.361**	**1.369**	**1.369**	**1.368**	**1.376**	**1.376**	**1.376**
H2(s)	**1. 450**	**1. 450**	**1. 449**	**1. 448**	**1. 448**	**1. 442**	**1. 444**	**1. 444**	**1. 444**	**1. 432**	**1. 439**	**1. 439**

Table.4. Theoretical 13C and 1H isotropic chemical shifts, all values in ppm with respect to TMS, for adamantane. Calculations were performed at the B3lyp/ 6-31++g** level of theory for three solvents, three temperatures and dry phase

	Solvent = H_2O			*Solvent = C_7H_{16}*			*S0lvent = C_6H_{12}*			*Dry phase*		
	T: 298.15	T: 310.15	T: 313.15	T: 298.13	T: 310.15	T: 313.15	T: 298.15	T: 310.15	T: 313.15	T: 298.15	T: 310.15	T : 313.15
C1(t)	34.813	34.087	34.111	33.725	33.710	33.733	33.748	33.748	34.718	33.784	33.784	35.784
C2(s)	41.700	41.705	41.737	41.395	41.435	41.401	41.439	41.441	41.385	41.364	41.364	41.364
H1(t)	1.261	1.259	1. 458	1.243	1.243	1.245	1.247	1.247	1.243	1.260	1.260	1.260
H2(s)	1.385	1.303	1.503	1.289	1.294	1.295	1.299	1.297	1.289	1.296	1.296	1.296

Table.5. Theoretical 13C and 1H isotropic chemical shifts, all values in ppm with respect to TMS, for adamantane. Calculations were performed at the B3lyp/ 6-31g level of theory for three solvents , three temperatures and dry phas

	Solvent = H_2O			*Solvent = C_7H_{16}*			*S0lvent = C_6H_{12}*			*Dry phase*		
	T: 298.15	T: 310.15	T: 313.15	T: 298.13	T: 310.15	T: 313.15	T: 298.15	T: 310.15	T: 313.15	T: 298.15	T: 310.15	T : 313.15
C1(t)	25.063	25.106	25.066	24.835	24.914	24.836	24.857	24.862	24.848	24.802	24.240	24.802
C2(s)	35.203	35.265	35.212	34.985	35.016	35.002	35.013	35.03	35.019	34.894	34.757	34.894
H1(t)	1.323	1.323	1.322	1.277	2.075	1.320	1.315	1.314	1.317	2.056	1.452	1.306
H2(s)	1.424	1.425	1.424	1.386	2.180	1.431	1.426	1.424	1.42	2.158	1.573	1.408

Table.6. Experimental 13C and 1H isotropic chemical shift of adamantane(all values in ppm with respect to TMS). Temperature: 298.15(20)

C1(t)	26.6
C2(S)	33.5
H1(t)	1.1
H2(s)	1.2

The chemical shifts in other temperatures (310.15 and 313.3 K) are equal approximately. The results in table shown that the 13C and 1H chemical shifts of adamantane in polar solvent (water) is bigger of the non – polar solvent. At the B3lyp/6-31g* basis set for C (t), C(s) , H (t) and H(s) in all of the solvents we have:

$$\delta_{iso}(310.15) = \delta_{iso}(298.15) \qquad (7)$$

Free energy of solvation in water, cyclohexane and n-heptane at 298.15K for Adamantane determined bas on DFT calculations at four basis sets are shown in the following tables.

Table 7. Solvation free energy (kcal/mol) for the Adamantane determined from B3lyp/6-31G, B3lyp/6-31G*, B3lyp/6-31+G*, B3lyp/6-31++G** calculations were performed in different solvents at 298.15 K

	SOLVENT	ΔG_{sol}
B3lyp/6-31G	Water	-0.49
	Cyclohexane	-3.75
	n-Heptane	-4.09
B3lyp/6-31G*	Water	-0.63
	Cyclohexane	-3.84
	n-Heptane	-4.17
B3lyp/6-31+G*	Water	-0.75
	Cyclohexane	-3.85
	n-Heptane	-4.18
B3lyp/6-31++G**	Water	-0.74
	Cyclohexane	-3.83
	n-Heptane	-4.17

Adamantane is a non-polar molecule, so its solvation in a polar solvent such as water is so less. The results from the theoretical computations in table 6 confirm this subject. As we know the negative solvation energy shows the solvation has been done. As it is clear in table 6 all the solvation energy calculated with all the methods are negative and its values for n-heptane is more than cyclohexane and also more than water.

There are energies of cavity formation (kcal/mol) in water, cyclohexane and n-heptane at 298.1k for Adamantane in table 7. these energies was determined from DFT calculations.

Table 8. Cavity formation of free energy (kcal/mol) for the Adamantane was obtained from B3lyp/6-31G , B3lyp/6-31G*, B3lyp/6-31+G*, B3lyp/6-31++G** calculations in different solvents at 298.15k.

	SOLVENT	*T=298.15*
B3lyp/6-31G	Water	18.18
	Cyclohexane	13.43
	n-Heptane	11.82
B3lyp/6-31G*	Water	18.11
	Cyclohexane	13.38
	n-Heptane	11.77
B3lyp/6-31+G*	Water	18.13
	Cyclohexane	13.39
	n-Heptane	11.77
B3lyp/6-31++G**	Water	18.13
	Cyclohexane	13.39
	n-Heptane	11.77

We know formation of cavity in solvation process is a difficult step and consume energy. As the Table 8 Show free energies of cavity formation are positive. On the other hand the solubility ofAdamantane in water is lower than non-polar solvents and formation of cavity in water more difficult than the other solvents.

The Henry's law constant in water, cyclohexane and n-heptane at 298.15k for Adamantane were calculated with Eq 6.

Table 9. Henry's law constant determined from B3lyp/6-31G31G , B3lyp/6-31G*, B3lyp/6-31+G*,B3lyp/6-31++G**calculations were used Eq 6.

	SOLVENT	*T=298.15*
B3lyp/6-31G	Water	581.6905
	Cyclohexane	458.5909
	n-Heptane	402.4221
B3lyp/6-31G*	Water	585.7577
	Cyclohexane	458.5166
	n-Heptane	402.3758
B3lyp/6-31+G*	Water	585.7578
	Cyclohexane	458.5089
	n-Heptane	402.3690
B3lyp/6-31++G**	Water	585.7677
	Cyclohexane	485.5244
	n-Heptane	402.3758

As itmentioned previously the Henry's law constant has a close relationship with solvation energy. Table 8 shows that the constant values of Henry's law constants for water are more than cyclcohexane and both of them are more than n-heptane and these are completely fit the last results.

The previous calculations shows that the solvation energy for n-heptane is more negative than cyclohexane and both of them are more negative that water.

CONCLUSION

The solubility results permit the validation of molecular force fields that attempt to describe the solute – solvent interactions in solution. Molecular simulation can be used to calculate the solvation properties starting from a specification of the molecular structure and interactions of the chemical species presenting the system. Predictive simulation tools can be used to complement experiments whenever these are too difficult, for example, when solubility is very low or when working conditions involve extreme temperatures or high pressure.

Calculation of solubility can be achieved for gaseous solutes and whit a slightly different procedure. Also for solutes that exist in the form of condensed phase at standard conditions [22].

The molecular mechanisms determining the dissolution process can be investigated by simulation by isolating the effect of different terms in the interactions. The structure of the solution, concerning the arrangement of the solvation shells around the solute, can be predicted by simulation, even in systems where the low concentration of solute precludes obtaining diffraction data.

Also the polarizable continuum model (PCM) are used to calculate the isotropic NMR shielding and the thermodynamics properties of adamantane in three solvents at different basis sets. PCM has proved useful in describing the effects of the solvent on some characteristics of the molecule in solution. All PCM calculations in this study have been performed in GAUSSIAN 98 package.

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