

Modeling of the Hydration Shell of Adenine

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ABSTRACT

The molecular geometry of complex of adenine with 8 water molecules was calculated with Hartree-Fock (HF). The standard 6-31G(d) basis set has been employed. The existence of C-H...O Hydrogen bonds between the water molecules and the hydrophobic part of nucleobase is established.

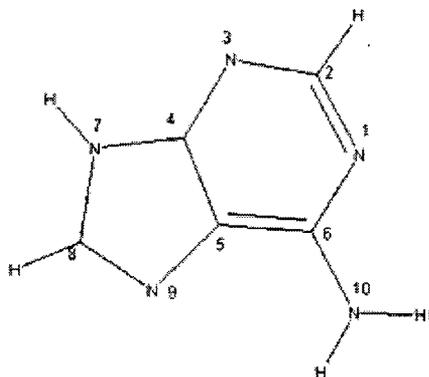
We optimized structures and computed interaction energies of all complexes of adenine with water molecules step by step, and finally compared them.

Moreover, a theoretical investigation of the complex of adenine with 8 water molecules has led to the conclusion that the molecular structure of this molecule cannot be described by conventional chemical formula. The results of an ab initio Hartree-Fock study of the structural parameters, atomic charge, dipole moment and thermodynamic change for isolated and poly hydrated adenine complexes are reported. Finally the gauge-invariant atomic orbital (GIAO) method was employed to calculate isotropic atomic shielding of complex using HF theory.

Keywords: Adenine; Hydration; Molecular Structure; Hydration bonds

INTRODUCTION

Adenine is a nucleic acid base occurring in DNA (deoxyribonucleic acid) and RNA (ribonucleic acid). Adenine and guanine molecules derive from purine.



DNA consists of two polynucleotide chains, coiled around a common axis. The two chains are held together by hydrogen bonds between pairs of nucleic acid bases (adenine-thymine and guanine-cytosine pairs).

The specificity of the base pairing allows the complementary chains to act as templates for each other in DNA replication.

The hydration of biomolecules is vitally important in molecular biology, since numerous biological processes involve a ligand binding to a nucleic acid or protein and thereby displacing the water of hydration. In many cases it is very difficult to investigate the isolated biomolecule-water interaction experimentally, and a reliable theoretical study is thus crucial to increase our understanding of these systems, as well as help interpret the experimental results that are beginning to emerge..

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Hydration of nucleobases was a subject of numerous theoretical studies using Monte- carlo [1], molecular dynamics [2], and quantum-chemical approaches within the continuum solvent model. [3]. Recent calculations of the hydrated complexes of uracil [4,5,6], thymine [6,7], cytosine [8,9], guanine [10] and adenine [11] performed at the HF and MP₂ levels of theory reveal that the geometrical parameters of DNA bases may be extremely sensitive to the direct influence of water molecules.

Nuclear magnetic resonance (NMR) spectroscopy has become one of the more powerful methods for probing molecular structure in solution [12].

The isotropic part σ_{iso} of σ is measured by taking the average of σ with respect to the orientation to the magnetic field, i. e.

$$\sigma_{iso} = (\sigma_{xx} + \sigma_{yy} + \sigma_{zz}) / 3$$

Where σ_{xx} , σ_{yy} and σ_{zz} are the principal axis values of σ . The result calculated by using HF theory are summarized in Table 3.

The anisotropy is :

$$\xi = | \sigma_{33} - \sigma_{iso} |$$

and the asymmetry is :

$$\eta = | (\sigma_{22} - \sigma_{11}) | / \xi$$

Computational Methods

To build a hydration shell around the adenine molecule we have used the modified scheme of monosolvation which originates in the early work of Pullman [13].

The procedure for building adenine complex with water molecules is as follows. The structure of monohydrated complex was fully optimized.

Then a second water molecule is added, and the hydrated complex was fully optimized in the same way. Such a procedure is repeated until 8 water molecules are arranged around the adenine.

We assume that a change in orientation should not drastically effect the geometry of adenine. This is why we did not study the influence of a different orientation of water molecules.

All calculation were carried out using the Hartree-Fock (HF) or Self-Consistent Field. In the Hartree-Fock (HF) or Self-Consistent Field (SCF) method the electron-electron interaction is replaced by an average interaction. This neglects the instantaneous correlations in the motions of the electrons, on average they are further apart than described by the SCF method. Thus, SCF does not include dispersion, a universal attractive force arising from the correlation of fluctuations in the electron distribution of neighbouring molecules, and tends to overestimate dipole moments and electrostatic forces. The error of the HF wave function is termed the electron correlation energy, and it needs to be included in the computation to obtain accurate interaction energies of molecular complexes.

The standard 6-31G(d) basis set was used. The HF/6-31G(d) approach used in this study ensures satisfactory predictions for the geometric parameters of the complexes of adenine with water molecules. NMR analysis have been performed using HF/6-31g(d) level and GIAO method. All calculations were performed using the Gaussian 98 program package.

RESULTS AND DISCUSSION

The optimized structure of complex of adenine with 8 water molecules is presented in Fig.1.

Adenine is a nucleic acid base contains a row of N and N-H groups, which provide a range of possible hydrogen-bonded with water molecules. In all of these the water molecule is bonded to adenine via one hydrogen bond (OH...N or NH...O). But two H₂O molecules (W2-W5) which form weak hydrogen bonds with the nucleobase and do not interact with it by means of conventional H-bonds.

It is well known that the energy of the hydrogen bond depends on the Y...H distance and the X-H...Y angle (where X is a hydrogen donor and Y is a hydrogen accepting atom). Based on the Y...H distance, all hydrogen bonds can be divided into strong (Y...H < 1/6 Å^o), medium (Y...H 1/6-1/9 Å^o), and weak (Y...H > 1/9 Å^o) [14]. The energy of this type of hydrogen bond reveals a rather small dependence on the value of the Y...H-X angle in the range 150°-180° [15]

Based on this criteria H-bonds in the complex of adenine with 8 water molecules should be assigned as medium and weak. (see table. 1.)

During the last decade, the existence of weak C-H...O hydrogen bonds in many crystals [16], and biological structures [16] was established. These bonds are characterized by longer O...H distances (2/2-2/6 Å^o) at the same range of values the C-H...O angle as compared with conventional hydrogen bonds. Recently the existence of weak C-H...O hydrogen bonds between the hydrophobic part of uracil and thymine was established. [17]

An analysis of the complex of adenine with 8 water molecules reveals distances between the hydrogen atoms in the hydrophobic part of adenine and the nearest water molecules. (Table 1). It allows one to assume the existence of weak C-H...O hydrogen bonds.

The results of the calculations reveal every H₂O molecule forms only one hydrogen bond with the adenine. In the complex under study, molecules W1 and W6 play a role a bridge between molecules W2, W8 and W5, W7, respectively. (Fig. 1). W1 and W6 form three hydrogen bond, one with adenine and two with water molecules neighbours. In general hydrogen bonds between water molecules are weaker compared to water-nucleobase interaction (except for the W3...W4 bond for hydrated adenine). [Fig. 1 or Table 1]. One medium hydrogen bond forms between W3 and W4.

Figure 1.
Structure of the complex
of adenine with 8 water
molecules .

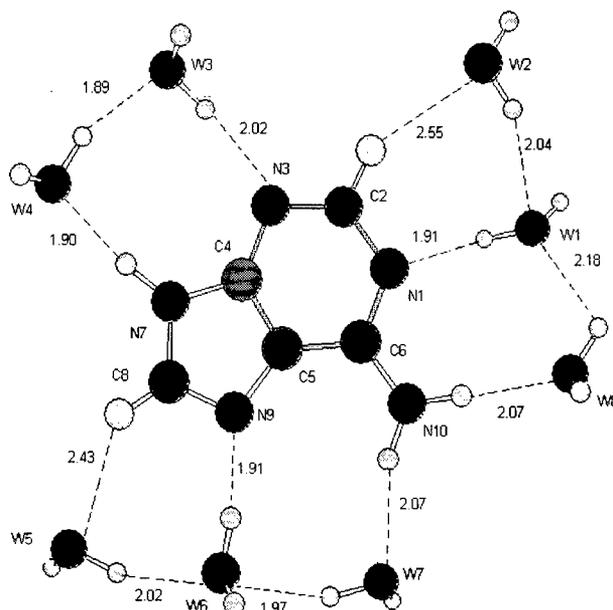


Table 1. Geometry of hydrogen bonds in complex
of adenine with 8 water molecules.

X-H...Y	Distance(A°) H...Y	Angles(deg) X-H...Y
O(W1)-H...N(1)	1.915	175.542
C(2)-H...O(W2)	2.557	150.630
O(W3)-H...N(3)	2.020	167.845
N(7)-H...O(W4)	1.900	171.413
C(8)-H...O(W5)	2.430	142.846
O(W6)-H...N(9)	1.916	173.192
N(10)-H...O(W7)	2.069	163.634
N(10)-H...O(W8)	2.070	175.508
	Water-Water	Water-Water
O(W2)-H...O(W1)	2.042	158.395
O(W8)-H...O(W1)	2.187	154.683
O(W7)-H...O(W6)	1.977	156.044
O(W5)-H...O(W6)	2.024	159.541
O(W4)-H...O(W3)	1.897	160.650

However some deviation from planarity of hydrogen bonds with the participation of the N(1) and N(9) atoms in adenine. The C(6)-C(5)-N(9)...H-O(W6) and H(11)-C(2)-N(1)...H-O(W1) torsion angles are $12/091^\circ$, $-6/617^\circ$ respectively.

A comparison of the geometry of isolated and hydrated adenine reveals that the interaction with water molecules noticeably influences the molecular structure of nucleobase under consideration.

The optimized geometric parameters of the adenine are depicted in Table 2. To check the bond lengths of the single C-N and the double C=N bonds at the same theoretical level, two model molecules, H_3C-NH_2 and $H_2C=NH$, were also optimized at the HF/6-31G(d) level. The bond lengths of N(1)-C(6), N(1)-C(2), N(3)-C(2), and

C(4)-N(3) in adenine are around $1/33A^\circ$, which is between the single C-N bond length of $1/45A^\circ$ in H_3C-NH_2 and the double C=N bond length of $1/25A^\circ$ in $H_2C=NH$. The C(5)-C(6) and the C(4)-C(5) bond lengths of $1/38$, $1/4A^\circ$ respectively in adenine are also between the C-C single bond distance ($1/53A^\circ$ for H_3C-CH_3) and the C=C double bond length ($1/32A^\circ$ for $H_2C=CH_2$) at the same theoretical level. From the viewpoint of bond length, the hexring in adenine forms a conjugated system.

The bond length of N(6)-C(10) ($1/34A^\circ$) implies that the amino group in adenine is also involved in the conjugated π electron system. On the other hand, the relatively shorter N(9)-C(8) bond distance of $1/28A^\circ$ and the longer bond lengths of C(5)-N(9), C(8)-N(7) and C(4)-N(7) of $1/38$, $1/37$, $1/36A^\circ$ respectively in adenine suggest that the N(7), C(8), and N(9) atoms are not included in the aromatic system [11].

The optimized geometric parameters of polyhydrated complexes of adenine are also listed in Table 2)

The influence of hydrogen bonding on the geometries of the complex of adenine with 8 water molecules form enlarge N(1)-C(6), C(5)-C(6), N(3)-C(4) bond lengths by $0.01A^\circ$ and reduces the C(6)-N(10) bond distance by $0.16A^\circ$. However, the driving forces of these effects to enhance the conjugated π electron system. Therefore the hydration water improve the conjugation in the adenine.

An analysis of the atomic charge in molecules under study reveals (Table 3) a considerable increase in the negative charge of the nitrogen atoms and increase in the positive charge of the carbons atoms.

NMR isotropic shielding (ppm) tensors and asymmetry (η) for elements of adenine isolated and hydrated are reported in Table 3.

Table2. Molecular geometry (A°deg) of isolated and hydrated adenine

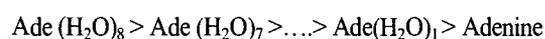
Geometrical Parameters	Isolated	Hydrated	Geometrical Parameters	Isolated	Hydrated
N(1)-C(2)	1.33	1.33	N(1)-C(2)-N(3)	128.8	128.2
C(2)-N(3)	1.31	1.31	C(2)-N(3)-C(4)	111.6	112.0
N(3)-C(4)	1.33	1.34	N(3)-C(4)-C(5)	126.5	126.1
C(4)-C(5)	1.38	1.37	C(4)-C(5)-C(6)	116.1	117.0
C(5)-C(6)	1.40	1.41	C(5)-C(6)-N(1)	118.5	117.0
C(6)-N(1)	1.33	1.34	C(5)-C(6)-N(10)	122.4	123.8
C(6)-N(10)	1.34	1.32	C(4)-N(7)-C(8)	106.5	106.5
C(4)-N(7)	1.36	1.36	N(7)-C(8)-N(9)	113.6	113.3
N(7)-C(8)	1.37	1.36	C(8)-N(9)-C(5)	114.1	104.6
C(8)-N(9)	1.28	1.29	N(9)-C(5)-C(4)	111.0	109.9
N(9)-C(5)	1.38	1.38	N(1)-C(2)-N(3)-C(4)	-0.1	0.5
			C(5)-C(4)-N(7)-C(8)	0.0	0.1

Table3.HF/6-31g(d) Calculation of the σ_{iso} and η in ppm and Atomic Charge derived from Mulliken for atoms in Isolated and Hydration of Adenine

Atom	Isolated		Hydrated		Isolated	Hydrated
	σ_{iso}	η	σ_{iso}	η	Mulliken Charge	Mulliken Charge
N(1)	49.3837	-0.2182	67.5289	-0.1515	-0.66	-0.79
C(2)	45.2010	-0.4445	44.8596	0.3465	0.27	0.31
N(3)	55.1200	0.1039	71.286	0.1846	-0.63	-0.73
C(4)	50.8968	0.6703	51.1185	0.5363	0.66	0.67
C(5)	92.1938	0.0490	93.1448	0.2721	0.07	0.09
C(6)	45.3470	-0.1795	43.5863	-0.0398	0.66	0.74
N(7)	138.7289	0.2179	127.8342	-0.4950	-0.83	-0.86
C(8)	68.8643	-0.3686	62.3088	0.7595	0.3	0.3
N(9)	24.6433	0.4531	45.3629	0.5819	-0.57	-0.7
N(10)	206.5791	37.7729	194.9183	4.2786	-0.94	-1.02

Ab initio calculation yield the data in table 3 show that the values for the isotropic shielding N(1),N(3),N(9) atoms in hydrated of adenine increased and N(7),N(10) atoms in hydrated of adenine reduced and the asymetry shielding (η) N(10) atom in hydrated of adenine is less .

Table 4 lists the interaction energies and the thermal free energies, and the dipole moments of the polyhydrated complexes of adenine investigated in this work, obtained from HF optimizations with the 6-31G(d) basis set. At the HF/6-31G(d) level, the relative stability sequence of the adenine in the isolated and hydrated forms can written as:



Structure complex adenine with 8 water molecules is the most stable polyhydrated complexes of adenine because the Ade (H₂O)₈ have lowest energies. The waters molecules are arranged

in such a way to allow the intermolecular bonds to assume a cyclic arrangement situated in the plane of the adenine molecule.As shown in table 4 the highest and lowest dipole moment obtained for Ade(H₂O)₄ and Ade(H₂O)₈ respectively.

Table 4.Intracation energies (E_I) and Thermal Free energies (E_T) in kcal/mol and Dipole Moment (μ) in Debye of the adenine and complexes polyhydrated of adenine .

	E_I	E_T	μ
Adenine	0.00	-291411.1065	2.46
Ade(H ₂ O) ₁	-5.59	-339098.1343	3.21
Ade(H ₂ O) ₂	-11.40	-386782.6854	3.77
Ade(H ₂ O) ₃	-29.76	-434476.9083	2.27
Ade(H ₂ O) ₄	-35.56	-482165.1905	4.35
Ade(H ₂ O) ₅	-47.65	-529853.3774	5.18
Ade(H ₂ O) ₆	-53.45	-577540.3155	4.24
Ade(H ₂ O) ₇	-65.53	-625227.44	1.92
Ade(H ₂ O) ₈	-71.34	-672913.1695	0.52

The lowest and Highest vibrational frequency of the adenine and polyhydrated complexes of adenine are listed in Tables 5. The lowest frequency predicted for hydrated adenine reflects the weak bonding between water and adenine .

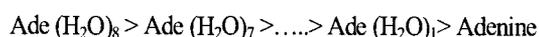
Table 5. Lowest (ω_L) and Highest (ω_H) Vibrational Frequency in (1/cm) of the adenine and complexes polyhydrated of adenine

	ω_L	ω_H
Adenine	188.07	3983.11
Ade(H ₂ O) ₁	40.13	4143.76
Ade(H ₂ O) ₂	33.69	4155.03
Ade(H ₂ O) ₃	29.50	4146.50
Ade(H ₂ O) ₄	26.6	4146.12
Ade(H ₂ O) ₅	25.65	4146.32
Ade(H ₂ O) ₆	23.16	4147.66
Ade(H ₂ O) ₇	22.19	4156.02
Ade(H ₂ O) ₈	18.98	4157.95

CONCLUSION

Investigation of the molecular geometry of the complexes of adenine with 8 water molecules reveal the details of the interactions between the bases and solvent. Based on an analysis of the geometric parameters in the complexes under study using a wave function at the HF/6-31G(d) level of theory reveals the presence of weak C-H...O hydrogen bonds between the hydrophobic part of the nucleobases and water. Interaction with water molecules improve the conjugation in the adenine.

At the HF/6-31G(d) level, the relative stability sequence of the adenine in the isolated and hydrated forms can written as:



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