Solvent effect on relative stability of guanine tautomers and the calculation of NMR shielding of nuclei of ^{1}H, ^{13}C, ^{14}N and ^{17}O for the most stable tautomer by using ab-initio methods

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ABSTRACT

Fifteen tautomeric species of guanine were optimized in the gas phase at MP2, B3LYP and BP86 levels of theory using the 6-31G+(d,p) basis set. The relative stability of these tautomers was calculated. Solvent effect on relative stability of guanine tautomers was investigated at the B3LYP level of theory with 6-31G+(d,p) basis set using the Onsager reaction field theory. It was found that G2 tautomer has the most stability in the gas phase and G1 is in the second degree of stability. But, the inverse results were found in the solvent phase. The transition state (TS) geometry between G1 to G2 was calculated in the gas and solvent phases. The predicted barrier energy in the gas phase is increased by increasing the polarity of solvents. The Continuous Set of Gauge Transformation (CSGT) calculations were performed for the nuclei of ^{1}H, ^{13}C, ^{14}N and ^{17}O at the B3LYP/6-31+G(d,p) level of theory for the B3LYP/6-31+G(d,p) optimized geometry, using the Onsager model. Direct and indirect solvent effects on shielding were also calculated. It was shown that the observed solvent-induced shielding variation is more strongly related to the intensity of the solvent reaction field rather than to the change of molecular geometry induced by the solvent. Chemical shift of the ^{1}H and ^{13}C nuclei for G1 and G2 molecules was calculated and compared with that of TMS molecule.

KEYWORDS

Guanine, tautomer, ab-initio, solvent effect, NMR shielding, transition state, barrier energy, solvent polarity

1. INTRODUCTION

Nucleic acids are of fundamental biological importance due to the role they play in DNA. As first suggested by Chargaff1 [1] and later shown in detail by Watson and Crick, [2] the sequence of the guanine–cytosine and adenine–thymine hydrogen-bonded base pairs stores the genetic code.

All DNA bases can exist in a variety of tautomeric forms, giving rise to a large number of possible base pair combinations. In the case of guanine, for example, ground state energies of the four most stable tautomers have been calculated to lie within a range of 7 kJ/mol [3-4]. However, only a single guanine tautomer is usually present in DNA, whereas other tautomeric forms may be responsible for genetic damage [5-7].

It is very important to understand the properties of the guanine base of DNA as thoroughly as possible since it is the most frequently involved site in the processes of mutation and cancer. Thus, while on one hand, certain carcinogens like aflatoxin B1 [8-9] bind to the guanine base of DNA, on the other, the well-known anti-cancer drugs like adriamycin, daunomycin, cis-platin, etc. also bind to it preferentially [10-13].

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When forming a DNA double helix, cytosine forms a hydrogen-bonded pair with guanine. On the other hand, the rare tautomer of cytosine forms a pair with adenine (A) instead of guanine (G). Similarly, rare tautomer of guanine forms a pair with thymine (T) [14].

In order to study the possible mutagenic mechanism of these compounds, it would be important to estimate their tautomeric constitution in different media, especially in aqueous solutions.

Theoretical predictions of the various physicochemical properties of the prototropic tautomers are of great importance in the studies of the reactivity of the nucleic acid bases and other heteroaromatic compounds. Many computational investigations have been aimed at accurately determining structures and properties of the nucleic acid bases and their tautomers [15-20].

Ab initio calculation of nuclear magnetic shielding has become an indispensable aid in the investigation of molecular structure and accurate assignment of NMR spectra of compounds [21]. The data from the experimental studies constituting a database of experimental shielding for some nuclei such as hydrogen, nitrogen and carbon can be utilized to evaluate the reliability of NMR calculations for systems in solution. The salvation effect is taken into account via the self consistent reaction field (SCRF) method. This method is based on Onsager reaction field theory of electrostatic salvation [22]. The effect of polarization of the solvent continuum is represented numerically.

The present work is aimed at accurately determining the geometrical properties of guanine tautomers. Stability order of the tautomers has been investigated both in gas phase and solvent phase. Solvent effects on shielding have been studied, too.

2. COMPUTATIONAL DETAILS

The *ab intio* molecular calculations were carried out by the use of the Gaussian 98 program [23]. Fifteen tautomeric species of guanine (Fig. 1) were optimized in the gas phase at MP2, B3LYP and BP86 levels of theory using the 6-31G+(d,p) basis set

To investigate solvent effect in the stability of these tautomers, their geometry optimization in the solvent phase were performed at the level of theory B3LYP/6-31+G(d,p) using the self consistent reaction field (SCRF) theory with Onsager model of solvent. In this method, the solute occupies a fixed spherical cavity of radius a_0 within the solvent field. A dipole in the molecule will induce a dipole in the medium, and the electric field applied by the solvent dipole will in turn interact with the molecular dipole, leading to net stabilization. Single point energy calculations of optimized geometry of tautomers in the solvent phase were performed by using iefpcm [24] model at the level of theory of B3LYP/6-31+G(d,p). The transition state which is between G1 and G2 was located by the STQN method [25]. Chemical shielding of the nuclei of ^{14}N, ^{13}C and ^{1}H in different solvents were calculated at the level of theory of B3LYP/6-31+G(d,p) by the use of SCRF theory, Onsager model of solvent and CSGT method [26] in both direct and indirect ways. Direct method involves perturbation of solvent on the electronic wave function of the solute held at fixed geometry; indirect method is due to the relaxation of the solute geometry under the influence of the solvent [21]. The same convention adopted by Witanowski et al.[27] was used to describe trends in shielding data; thus, a positive solvent effect indicates an increase in nuclear shielding.

Relative solvent effects were calculated using the corresponding nuclear shielding in cyclohexane as reference. Direct ($\Delta\sigma_{dir}$) and indirect ($\Delta\sigma_{ind}$) solvent effects were obtained. Instead of deriving $\Delta\sigma_{ind}$ from the difference of the Onsager model optimized shielding and the Onsager shielding of the molecule held a the geometry optimized *in vacuo*, it was obtained from the shielding calculated *in vacuo* for a molecule that has the geometry optimized in solution, thus:

$$\Delta\sigma_{dir} = \sigma_{cyc}(R_v) - \sigma_{cyc}(R_v)$$
$$\Delta\sigma_{ind} = \sigma_{vac}(R_s) - \sigma_{vac}(R_{cyc}) \quad (1)$$

where $\sigma_{sol}(R_v)$ is the value of the nuclear shielding computed in solution with the solute in the geometry optimized *in vacuo*, and $\sigma_{vac}(R_s)$ is the value of nuclear shielding *in vacuo* with the solute geometry in solution. $\sigma_{cyc}(R_v)$ and $\sigma_{vac}(R_{cyc})$ are the corresponding parameters for the calculation with cyclohexane.

3. RESULTS AND DISCUSSION

3.1 Tautomeric stability

Fifteen tautomers of guanine were optimized in the gas phase. Relative energy of these tautomers in kcal/mol and their order of stability are shown in Tables 1 and 2.

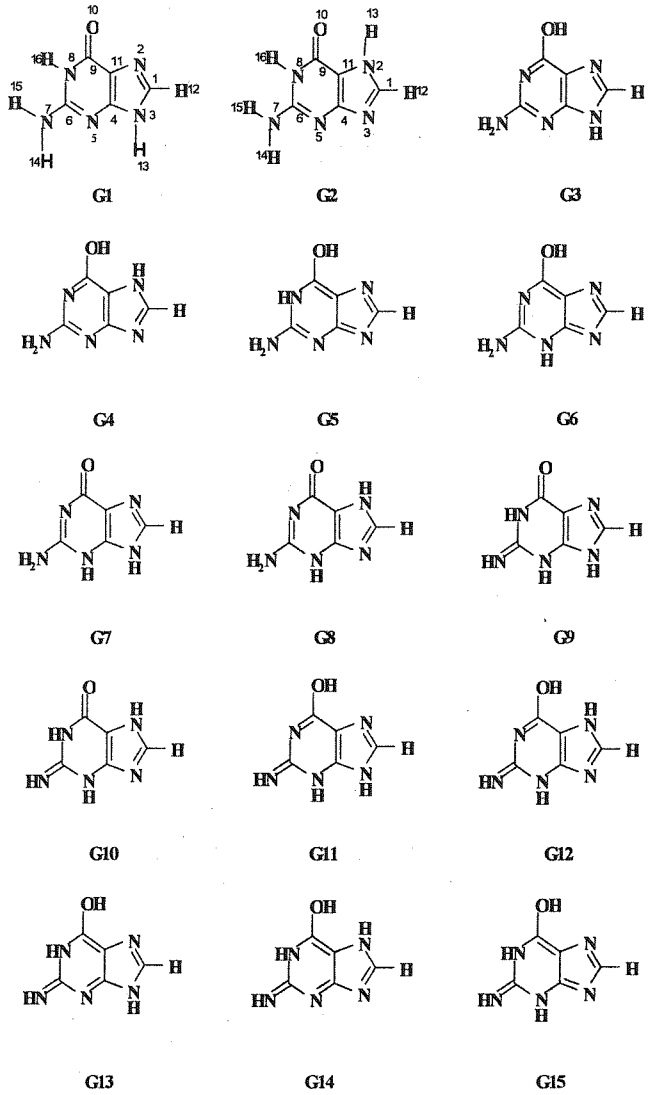

Fig. 1: Fifteen tautomeric species of guanine

Table 1. Relative stability of guanine tautomers in the gas phase.

Tautomer	Model of Chemistry		
	MP2/6-31+G(d,p)	B3LYP/6-31+G(d,p)	**BP86/6-31+G(d,p)**
G1	0.576116	1.063064	**0.769577651**
G2	0.000000	0.000000	**0.000000000**
G3	1.367155	1.844376	**2.363075275**
G4	12.21353	11.6275	**12.37668362**
G5	20.56179	21.24277	**20.87410352**
G6	13.32447	13.60259	**13.31675561**
G7	24.68911	20.17305	**20.15114982**
G8	8.121102	7.090669	**7.358615654**
G9	17.33407	16.78224	**16.78305533**
G10	8.237443	6.174756	**6.145075032**
G11	31.95799	30.22010	**29.46301430**
G12	36.61932	34.51616	**33.29345779**
G13	25.82973	22.61795	**21.97651221**
G14	41.18401	37.40659	**36.21344774**
G15	**27.889973**	**24.61042**	**25.37058559**

Table 2. Order of stability in different levels of theory with the same basis set (6-31+G(d,p)) in the gas phase.

Level	B3LYP	MP2	BP86
Order of stability	G2	G2	**G2**
	G1	G1	**G1**
	G3	G3	**G3**
	G10	G8	**G10**
	G8	G10	**G8**
	G4	G4	**G4**
	G6	G6	**G6**
	G9	G9	**G9**
	G7	G5	**G7**
	G5	G7	**G5**
	G13	G13	**G13**
	G15	G15	**G15**
	G11	G11	**G11**
	G12	G12	**G12**
	G14	**G14**	**G14**

As indicated in Table 2, three most stable tautomers in three different levels of theory are G2>G1>G3 although, there is a little difference between the energy of G2 and G1 (between 0.5 to 1 kcal/mol).

To investigate the solvent effect on relative stability and geometrical parameters of tautomers, fifteen tautomers of guanine were optimized in seven different solvents at the B3LYP/6-31+G(d,p) level by using the self consistent reaction field (SCRF) theory with Onsager model of solvent. In addition, single point energy calculations of optimized geometry of tautomers in the solvent phase were performed by using iefpcm model at the level of theory of B3LYP/6-31+G(d,p). The relative stabilities of these tautomers in kcal/mol are tabulated in Tables 3 and 4.

Table 3. Relative stability of guanine tautomers in different solvents at the B3LYP/6-31+G(d,p) level with Onsager (dipole) model of solvent.

Tautomer	**DMSO**	**Water**	**Acetone**	CH_3NO_2
G1	0	0	0	**0**
G2	4.956132782	5.063123152	4.633906654	**4.941825565**
G3	5.273150581	5.352028526	5.034947975	**5.274217347**
G4	14.474071378	14.52458589	14.319076533	**14.490135612**
G5	20.744962006	20.74784861	20.732725623	**20.787256220**
G6	13.7988084	13.80269896	13.782681411	**13.840475033**
G7	10.804960588	10.65253852	11.258775455	**10.931843000**
G8	8.54467136	8.588659776	8.412078602	**8.564500660**
G9	11.064812216	10.98367528	11.3082232	**11.153040110**
G10	10.535884511	10.63139145	10.248924411	**10.528103339**
G11	28.455736005	28.44073857	28.498218444	**28.507442833**
G12	32.043458866	32.01340116	32.130494433	**32.103197777**
G13	24.871213533	24.92348507	24.711261366	**24.886650266**
G14	28.778777974	28.37246554	29.079103988	**28.692871899**

G15	**29.5684358 9**	**29.674924 25**	**29.2470255 3**	**29.5540031 7**

Table 3. (cont.)

Tautomer	CHCl3	A. THF	Cyc-C6H12
G1	0	0	**0**
G2	3.054526476	3.733116766	**1.341814989**
G3	3.86025419	4.368030879	**2.661149504**
G4	13.51076443	13.87800010	**12.75976633**
G5	20.59987834	20.68716844	**20.72436631**
G6	13.61433741	13.71384362	**13.61577767**
G7	13.44300991	12.52628189	**16.56491518**
G8	7.745243163	8.040028220	**7.210470902**
G9	12.4767879	11.99032602	**14.3509956**
G10	8.82411802	9.444645484	**7.311664342**
G11	28.63624051	28.61305268	**29.18172074**
G12	32.46643724	32.36530849	**33.25262761**
G13	23.84952781	24.25230091	**23.04661799**
G14	31.39564032	30.47920318	**34.36932476**
G15	**27.62029845**	**28.34924769**	**25.90752434**

Table 4. Relative stability of guanine tautomers in different solvents at the B3LYP/6-31+G(d,p) level with iefpcm model of solvent.

Tautomer	DMSO	Water	Acetone	CH3NO2
G1	0	0	0	**0**
G2	0.789155947	0.933609	0.677333754	**0.760729767**
G3	6.293481028	7.126374	6.037017896	**6.252065401**
G4	10.95054278	9.856417	11.03613508	**10.96930532**
G5	18.90642198	16.56506	19.06888419	**18.95599523**
G6	13.78795249	12.57021	13.79686312	**13.81035458**
G7	10.96980732	8.561865	11.48241983	**11.06380825**
G8	5.391561624	4.822348	5.400597761	**5.383968759**
G9	12.98128903	11.76794	13.16038024	**13.00751892**
G10	9.161450447	9.272457	8.954999822	**9.116583518**
G11	26.34140554	24.19018	26.54220858	**26.37924436**
G12	28.34617289	24.94513	28.70673985	**28.40214674**
G13	25.39166991	24.43717	25.21791253	**25.36431050**
G14	32.13043168	28.80557	32.41651326	**32.18747229**
G15	**27.32144988**	**25.78694**	**27.16024268**	**27.29572199**

Table 4. (cont.)

Tautomer	CHCl3	THF	Cyc-C6H12
G1	0	0	**0.131000418**
G2	0.204578569	0.427020215	**0**
G3	0.204578569	5.219812274	**3.109882293**
G4	11.35890096	11.21089647	**11.86098574**
G5	19.24654133	19.17593731	**19.55644624**
G6	13.28827662	13.47287997	**13.48784562**
G7	13.84527888	12.91615354	**17.11553023**
G8	5.442153119	5.448413985	**6.042926546**
G9	13.88754718	13.65868553	**15.31621569**
G10	7.79007887	8.358112785	**6.948344827**
G11	27.21558731	27.01685676	**28.66441937**
G12	30.13172424	29.60050163	**32.40469421**
G13	24.05823928	24.59931366	**23.16284015**
G14	33.51187317	33.13193684	**35.53211002**
G15	**26.02368389**	**26.56856398**	**25.14719591**

Table 4. (cont.)

Parameters	B3LYP/6-31+G(d,p)		
	G1	G2	TS
RN(2)H(13)	3.210	3.210	**3.210**
RN(3)H(13)	1.010	1.010	**1.010**
RC(1)N(2)	1.380	1.380	**1.380**
RN(3)C(1)	1.386	1.386	**1.386**
RC(1)H(12)	1.080	1.080	**1.080**
RN(3)C(4)	1.370	1.370	**1.370**
RC(11)N(2)	1.380	1.380	**1.380**
AC(4)N(3)H(13)	125.640	125.640	**125.640**
AH(13)N(3)C(1)	125.640	125.640	**125.640**
DN(2)C(1)N(3)H(13)	-179.890	-179.890	**-179.890**
DC(14)N(3)H(13)C(1)	**-179.830**	**-179.830**	**-179.830**

As indicated in Table 3, the G1 tautomer is more stable than G2 tautomer in all of these solvents. This result is the opposite of the result obtained in the gas phase. We can explain this inversion of stability as below: the dipole moment of G1 is more than that of G2 (7.2529D vs. 1.5648D in the gas phase) and solvents stabilize the more polar tautomer. The difference between the energy of G1 and G2 is increased by increasing of the solvent polarity (see Fig. 2).

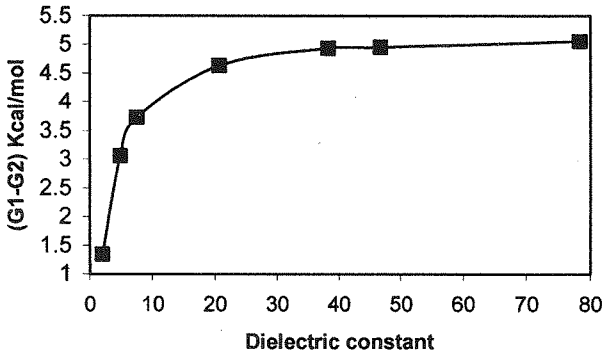

Fig 2: The difference of the energy between G1 and G2 in kcal/mol vs. dielectric constant of solvents.

The results of the calculated energy of guanine tautomers obtained from iefpcm model are approximately similar to Onsager model (Table 3). However, in nonpolar solvent of cyclohexane G2 tautomer is more stable than G1 tautomer (about 0.13 kcal/mol).

3.2 Transition state

The transition state between two most stable tautomers, G1 and G2, was calculated in the gas and solvent phases. Some geometrical parameters of G1, G2 and TS in the gas phase obtained at the MP2/6-31+G(d,p) and B3LYP/6-31+G(d,p) levels are shown in Table 5 and their structures are indicated in Fig. 3.

Table 5. Some geometrical parameters (bond length in Å, angles in deg.) of the G1, G2 and Ts.

Parameters	MP2/6-31+G(d,p)		
	G1	G2	TS
RN(2)H(13)	3.220	1.010	**2.230**
RN(3)H(13)	1.000	3.220	**1.310**
RC(1)N(2)	1.320	1.370	1.360
RN(3)C(1)	1.370	1.320	**1.450**
RC(1)H(12)	1.070	1.070	**1.080**
RN(3)C(4)	1.370	1.370	**1.360**
RC(11)N(2)	1.370	1.360	**1.350**
AC(4)N(3)H(13)	125.140	125.970*	**107.690**
AH(13)N(3)C(1)	127.590	127.82**	**69.010**
DN(2)C(1)N(3)H(13)	-179.890	-179.913	**-107.220**
DC(14)N(3)H(13)C(1)	**-178.890**	**-178.380*** **	**-91.220**

*A11,2,13. **A13,2,1 ***D11,2,13,1

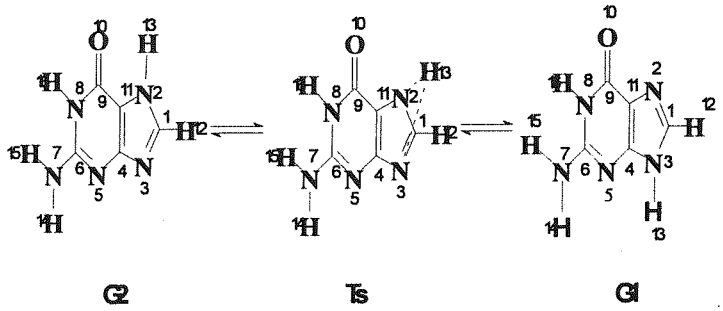

Fig. 3. TS structure in the G2 and G1 equilibrium

The barrier energy in kcal/mol between G2 and G1 in the gas phase is shown in table 6.

Table 6. The barrier energy in kcal/mol between G2 and G1 in the gas phase.

Level	Ereactant (a.u)	Etrans (a.u)	Eproduct(a.u)	ΔE(kcal/mol)
Mp2/6-31+G(d,p)	-541.07938	-540.991992	-541.078466	**54.7242**
B3LYP/6-31+G(d,p)	**-542.59236**	**-542.501158**	**-542.591401**	**57.10979**

As it is shown in Table 6, the predicted barrier energy at MP2 level is about 2.6 kcal/mol lower than the energy at B3LYP level, but the predicted geometrical parameters at these two levels are approximately the same. The barrier energy between G1 and G2 in different solvents was calculated at the level of theory B3LYP/6-31+G(d,p) and Onsager model of solvent (Fig. 4).

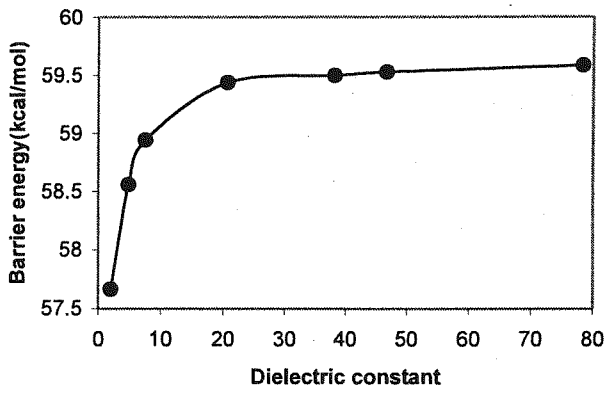

Fig. 4. Barrier energy variation vs. dielectric constant of solvent.

As we see, by increasing the polarity of the solvent, the barrier energy of transition state increases. We can explain this increasing as below: G1 molecule is more polar than TS (Table 7) and solvents stabilizes G1 molecule more than TS structure. So the energy difference of G1 and TS, i.e., barrier energy, increases.

Table 7: Dipole moment of G1, G2 and TS in different solvents at B3LYP/6-31+G(d,p) level and Onsager model of solvent.

	Tautomer	G1	G2	TS
Solvent	CycloHex	7.6628	2.0540	**5.2165**
	CH3Cl	8.7424	2.2857	**5.9871**
	THF	9.0375	2.3644	**6.2658**
	Acetone	9.4085	2.4862	**6.6712**
	Nitrome.	9.5195	2.5090	**6.7783**
	DMSO	9.5401	2.5140	**6.7998**
	Water	**9.5964**	**2.5232**	**6.8449**

3.2 NMR shielding of nuclei of ^{1}H, ^{13}C, ^{14}N and ^{17}O

Direct and indirect effect of solvent on chemical shielding for nuclei of ^{1}H, ^{13}C, ^{14}N and ^{17}O was calculated based on equation 1.1 for G1. The results are listed in Tables 8 to 9.

It might be suggested that the optimization of solute molecules in the solvent followed by shielding calculation is similar to shielding calculation of solvent-solute as an isolated system. However, if the molecule is first optimized in the gas phase and then NMR shielding calculations are performed in the solvent, the solvent-solute interactions are taken into consideration for NMR shielding calculation.

Scrutiny of the data listed in Tables 8 and 9 reveals that the observed solvent-induced shielding variations are more strongly related to the intensity of the solvent reaction field ($\Delta\sigma_{dir}$) than to the change of molecular geometry induced by the solvent ($\Delta\sigma_{ind}$).

Table 8. Calculated values of $\Delta\sigma_{dir}$ and indirect $\Delta\sigma_{ind}$ (ppm) for G1.

Atoms	Solvent					
	H_2O		DMSO		**Acetone**	
	$\Delta\sigma_{dir}$	$\Delta\sigma_{ind}$	$\Delta\sigma_{dir}$	$\Delta\sigma_{ind}$	$\Delta\sigma_{dir}$	$\Delta\sigma_{ind}$
C1	0.2219	0.1086	0.2152	0.1423	0.1953	**0.1519**
N2	5.4354	-0.574	5.2948	-0.368	4.8722	**-0.3658**
N3	-1.7483	0.4819	-1.704	0.4587	-1.5716	**0.4564**
C4	-1.4331	-0.152	-1.398	-0.199	-1.2903	**-0.181**
N5	-3.0073	4.9766	-2.928	4.9278	-2.6899	**4.9889**
C6	-1.0879	1.7347	-1.060	1.7907	-0.9752	**1.782**
N7	-3.5523	1.6582	-3.455	1.6538	-3.164	**1.6426**
N8	0.2396	3.7107	0.2331	3.7942	0.2137	**3.7213**
C9	-0.6681	-0.683	-0.652	-0.670	-0.6013	**-0.6206**
O10	17.7011	0.2277	17.254	0.2531	15.9059	**0.3226**
C11	0.9573	0.3881	0.9328	0.3987	0.859	**0.4185**
H12	0.0919	0.0283	0.0894	0.0312	0.082	**0.0297**
H13	-0.2271	0.0297	-0.221	0.0252	-0.204	**0.0281**
H14	-0.4054	-0.282	-0.395	-0.273	-0.363	**-0.2666**
H15	-0.1566	-0.152	-0.152	-0.142	-0.1392	**-0.1414**
H16	**0.0217**	**0.1609**	**0.0213**	**0.1587**	**0.02**	**0.1588**

Table 8. (cont.)

Atoms	Solvent			
	THF		$CHCl_3$	
	$\Delta\sigma_{dir}$	$\Delta\sigma_{ind}$	$\Delta\sigma_{dir}$	$\Delta\sigma_{ind}$
C1	0.1419	0.204	0.1419	**0.204**
N2	3.6805	-0.186	3.6805	**-0.186**
N3	-1.1941	0.4472	-1.1941	**0.4472**
C4	-0.9836	-0.215	-0.9836	**-0.215**
N5	-2.0229	5.0741	-2.0229	**5.0741**
C6	-0.7369	1.7789	-0.7369	**1.7789**
N7	-2.3582	1.6078	-2.3582	**1.6078**
N8	0.1597	3.5659	0.1597	**3.5659**
C9	-0.4583	-0.4591	-0.4583	**-0.4591**
O10	12.0772	0.6652	12.0772	**0.6652**
C11	0.6502	0.4991	0.6502	**0.4991**
H12	0.0613	0.0296	0.0613	**0.0296**
H13	-0.1548	0.0325	-0.1548	**0.0325**
H14	-0.2736	-0.2464	-0.2736	**-0.2464**
H15	-0.1033	-0.1324	-0.1033	**-0.1324**
H16	**0.0159**	**0.1586**	**0.0159**	**0.1586**

Table 9. Calculated values of $\Delta\sigma_{dir}$ and indirect $\Delta\sigma_{ind}$ (ppm) for G2.

Atom	Solvent					
	H_2O		DMSO		**Acetone**	
	$\Delta\sigma_{dir}$	$\Delta\sigma_{ind}$	$\Delta\sigma_{dir}$	$\Delta\sigma_{ind}$	$\Delta\sigma_{dir}$	$\Delta\sigma_{ind}$
C1	0.2219	0.1086	0.2152	0.1423	0.1953	**0.1519**
N2	5.4354	-0.574	5.2948	-0.368	4.8722	**-0.3658**
N3	-1.7483	0.4819	-1.704	0.4587	-1.5716	**0.4564**
C4	-1.4331	-0.152	-1.398	-0.199	-1.2903	**-0.181**
N5	-3.0073	4.9766	-2.928	4.9278	-2.6899	**4.9889**
C6	-1.0879	1.7347	-1.060	1.7907	-0.9752	**1.782**
N7	-3.5523	1.6582	-3.455	1.6538	-3.164	**1.6426**
N8	0.2396	3.7107	0.2331	3.7942	0.2137	**3.7213**
C9	-0.6681	-0.683	-0.652	-0.670	-0.6013	**-0.6206**
O10	17.7011	0.2277	17.254	0.2531	15.9059	**0.3226**
C11	0.9573	0.3881	0.9328	0.3987	0.859	**0.4185**
H12	0.0919	0.0283	0.0894	0.0312	0.082	**0.0297**
H13	-0.2271	0.0297	-0.221	0.0252	-0.204	**0.0281**
H14	-0.4054	-0.282	-0.395	-0.273	-0.363	**-0.2666**
H15	-0.1566	-0.152	-0.152	-0.142	-0.1392	**-0.1414**
H16	**0.0217**	**0.1609**	**0.0213**	**0.1587**	**0.02**	**0.1588**

Table 9. (cont.)

Atoms	Solvent			
	THF		$CHCl_3$	
	$\Delta\sigma_{dir}$	$\Delta\sigma_{ind}$	$\Delta\sigma_{dir}$	$\Delta\sigma_{ind}$
C1	0.1419	0.204	0.1419	**0.204**
N2	3.6805	-0.186	3.6805	**-0.186**
N3	-1.1941	0.4472	-1.1941	**0.4472**
C4	-0.9836	-0.215	-0.9836	**-0.215**
N5	-2.0229	5.0741	-2.0229	**5.0741**
C6	-0.7369	1.7789	-0.7369	**1.7789**
N7	-2.3582	1.6078	-2.3582	**1.6078**
N8	0.1597	3.5659	0.1597	**3.5659**
C9	-0.4583	-0.4591	-0.4583	**-0.4591**
O10	12.0772	0.6652	12.0772	**0.6652**
C11	0.6502	0.4991	0.6502	**0.4991**
H12	0.0613	0.0296	0.0613	**0.0296**
H13	-0.1548	0.0325	-0.1548	**0.0325**
H14	-0.2736	-0.2464	-0.2736	**-0.2464**
H15	-0.1033	-0.1324	-0.1033	**-0.1324**
H16	**0.0159**	**0.1586**	**0.0159**	**0.1586**

As Tables 8 and 9 indicate, the ^{13}C-NMR and ^{1}H-NMR spectrum of G1 and G2 were calculated. To do this, the absolute shielding of ^{13}C and ^{1}H atoms of the reference molecule, i.e., tetramethylsilane (TMS) was calculated in different solvents at the same level of theory used for G1 and G2. Then, the calculated shielding of those atoms in G1 and G2 was subtracted from that of TMS. The average amount of chemical shielding of ^{13}C and ^{1}H atoms in TMS in different solvents are listed in Table 10 and the chemical shift of G1 and G2 tautomers are shown in Table 11.

Table 10. Average amount of chemical shielding of ^{13}C and ^{1}H atoms in TMS.

Atom	**Chemical shielding**			
	H_2O	DMSO	Acetone	$CHCl_3$
H	6.441625	6.441675	6.4419	**6.443517**
C	**11.36675**	**11.3667**	**11.36655**	**11.36543**

Table 11. The calculated chemical shifts of G1 and G2 tautomers.

Atom	G1			
	H_2O	DMSO	Acetone	$CHCl_3$
C1	133.1393	133.1056	133.0961	**133.0158**
C4	152.8059	152.8528	152.835	**152.8952**
C6	150.2865	150.2305	150.2393	**150.2702**
C9	156.0559	156.0433	155.9939	**155.6513**
C11	125.7469	125.7363	125.7166	**125.5508**
H12	4.93644	4.93356	4.93506	**4.93271**
H13	6.00384	6.00836	6.00546	**6.00361**
H14	2.62974	2.62116	2.61476	**2.58501**
H15	2.08884	2.07816	2.07776	**2.05651**
H16	**4.75794**	**4.76016**	**4.76006**	**4.75691**

Table 11. (cont.)

Atom	G2			
	H_2O	DMSO	Acetone	$CHCl_3$
C1	139.722	139.7218	139.7219	**139.75**
C4	162.2046	162.2046	162.205	**162.174**
C6	151.5157	151.5157	151.516	**151.5727**
C9	152.772	152.772	152.772	**152.8435**
C11	116.5616	116.5616	116.562	**116.5861**
H12	5.24114	5.24116	5.24116	**5.24351**
H13	6.54454	6.54456	6.54456	**6.54911**
H14	2.51214	2.51216	2.51216	**2.49441**
H15	1.86784	1.86786	1.86786	**1.86541**
H16	**5.00274**	**5.00276**	**5.00276**	**5.01781**

As indicated in Table 11, the chemical shift of ^{13}C and ^{1}H atoms are approximately the same in different solvents.

4. CONCLUSION

In this study, we optimized fifteen tautomeric species of the guanine in the gas phase and solvent phase. We found that the order of stability in the solvent phase is different from that in the gas phase. The barrier energy in the reaction of $G1 \leftrightarrow G2$ increases by increasing the polarity of solvent. Solvent effect on chemical shielding of some nuclei of the two most stable tautomers was investigated by direct and indirect methods. It was found that the calculated solvent-induced shielding variation is more strongly related to the intensity of solvent reaction

field rather than to the change of molecular geometry induced by the solvent.

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