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ARTICLE in THE JOURNAL OF PHYSICAL CHEMISTRY A · APRIL 2013

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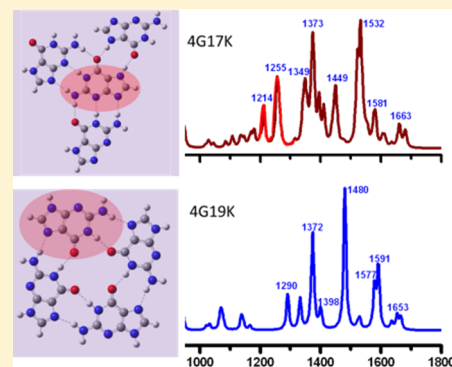
Solvent Effect and Hydrogen Bond Interaction on Tautomerism, Vibrational Frequencies, and Raman Spectra of Guanine: A Density Functional Theoretical Study

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S Supporting Information

ABSTRACT: Stable structures and Raman spectra of guanine have been investigated by density functional theory (DFT). Focusing on solvent effect and hydrogen bonding interaction, we have calculated the two keto-amino tautomers G17K and G19K as well as their guanine–water complexes and tetramers. The results show G17K is more stable than G19K in the gas phase, whereas in polar solvents G19K dominates. The vibrational fundamentals of G17K have been reassigned based on normal-mode analysis, since the previous assignment was limited to the G19K only. In the Raman spectra, the modes of the ring breathing vibration and those in the fingerprint region (from 1000 to 1600 cm^{-1}) affected by the solvent effect and the hydrogen bonding interaction dramatically. The band at 1163 cm^{-1} of G17K in gas has a large blue shift when water molecule forms hydrogen bonds with $\text{N}_7\text{--H}_{16}$ and $\text{C}_6\text{=O}_{13}$ sites. The blue shift can be explained by the influence of hydrogen bonding interaction along with shortening the $\text{N}_1\text{--C}_6$ bond distance. In addition, the dominant existing tautomer in polycrystalline and powder guanine is proposed to be G17K, whose calculated vibrational frequencies agree with the experimental Raman spectra reported before.



INTRODUCTION

Tautomerism of nucleic acids bases (NABs) plays an important role in genetic mutations and other biochemical reactions.^{1–6} Among the five NABs, guanine is the most oxidizable base with thermal instability⁷ and closely associates with the function of telomeres.⁸ Guanine has a large number of low-energy tautomers (more than 36 ones) with the relative energy range from 0.37 to 43.36 kcal/mol due to different substitution sites of hydrogen.⁹ Thus, the interpretation of the dependence to different chemical environments for guanine tautomers attracts growing interest recently. Figure 1 shows the different tautomers of guanine with low energies discussed in this article with a distinguished name scheme: G stands for guanine and the numbers are the nitrogen positions (1, 3, 7, or 9) where the hydrogen atom is attached. The distinguished forms of keto-amino and enol-amino have been detected by different experimental methods, such as X-ray,¹⁰ ultraviolet absorption,¹¹ infrared (IR) spectroscopy.^{12,13} The letters K and E indicate the form of keto- and enol-amino, respectively. Generally speaking, keto-amino guanines are more stable than the enol-amino ones,^{14,15} especially in polar media according to the larger dipole moments.¹⁶ In addition, there are two orientations, trans (a) and cis (b) conformers of the OH group for enol form ones.

A series of previous experiments are devoted to tautomerism of guanine in different circumstances. For that in the gas phase, the two dominant keto-amino forms (G17K and G19K) have been detected as well as a handful of enol-amino forms.^{11–15,17}

IR spectrum of guanine in an argon matrix showed that there were two keto-amino forms (G17K and G19K) as well as one enol-amino form (G9Ea).¹³ In helium nanodroplets, four low-energy tautomers, G17K, G19K, G9Ea, and G9Eb, were detected by infrared spectroscopy that spans the regions corresponding to the N–H, NH_2 , and O–H stretching vibrations.¹⁵ More specifically, the NH_2 stretching includes symmetric and asymmetric stretching modes. As for the N–H stretching, it refers to the N–H stretching in the ring of purine. With regard to the crystal structure of guanine, G19K was found in monohydrate of guanine by XRD reported early.¹⁸ A recent study indicates that G17K was determined in the crystal of anhydrous guanine.^{19,20}

Compared with IR spectroscopy, Raman spectroscopy as a supplementary vibrational tool can provide information on the fingerprint region related to the intermolecular interaction. It has been used to study the pH effect in aqueous solution,^{21–23} solid states,^{24,25} and surface adsorption structures of guanine on metal surfaces.^{26–30} In aqueous solutions, the pK_a values of guanine are 3.2 and 9.2 for protonation and deprotonation processes, respectively.³¹ With a pH of 5–7.3, the neutral guanine molecule dominates with a population of 99%. However, no Raman signal has been observed so far due to the low solubility of guanine in water (the concentration about

Received: January 30, 2013

Revised: April 28, 2013

Published: April 30, 2013

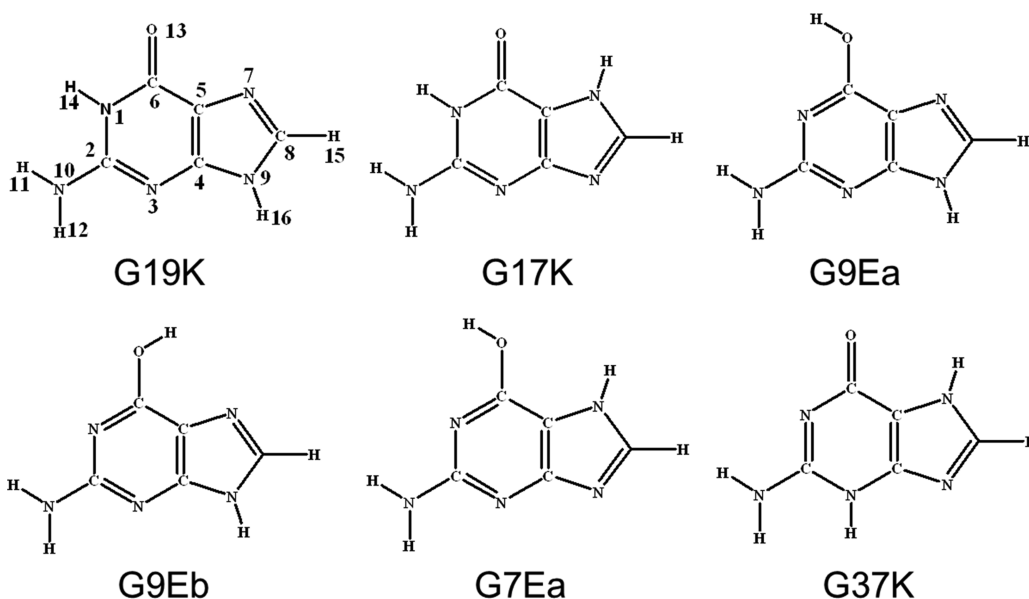


Figure 1. Six low-energy tautomers of guanine. The numbers identify the nitrogen position (1, 3, 7, or 9) to which the hydrogen is attached. Abbreviations: G, guanine; K, keto form; E, enol form. Amino-oxo (keto) and amino-hydroxy (enol) are classified by certain functional groups in the positions 2 and 6 of purine base, namely NH_2 (amino-), $\text{C}=\text{O}$ (-oxo), and $\text{O}-\text{H}$ (-hydroxy). More specifically, the enol forms have two rational orientations of the OH group: trans (a-form) and cis (b-form) to the five-numbered ring.

8.53×10^{-5} mol/L at 23 °C).³² In the gas phase, there was a lack of reports on the Raman spectrum of guanine molecules before. As for guanine in powder or polycrystalline states, G19K was supposed to be the most stable existing form detected by normal Raman spectra,^{24,25} similar to that of the crystal structure of guanine monohydrate.¹⁸ G17K tautomer, however, had been neglected until a recent report about the experimental Raman spectrum for the anhydrous guanine crystal, which indicated that G17K was the main existing form.^{19,20} The Raman spectrum of G17K detected in this work was similar to that of polycrystalline guanine in early studies.^{24,25,33} In addition, surface-enhanced Raman spectroscopy (SERS) with high detecting sensitivity has only been reported on the G19K tautomer.^{26,29}

Numerous theoretical calculations have been performed to have an insight into the properties of different tautomers of guanine.^{16,34–40} Latajka et al. calculated six tautomers and G19K was suggested to be the most stable tautomer based on the IR spectral analysis of guanine.³⁸ While Modesto Orozco et al. found guanine in the gas phase as a mixture of keto-amino tautomers (G17K and G19K) with a small proportion of enol-amino forms, based on high level ab initio calculations with the electron correlation effect at the Moller–Plesset level.³⁹ Their results also indicated that G19K was slightly more stable than G17K. However, Haranczyk et al.³⁶ and Hanus et al.⁴⁰ demonstrated that G19K was less stable than G17K in the gas phase calculated at CCSD(T)/aug-cc-pVDZ level. Furthermore, many groups have studied the hydrogen bond between guanine molecule and water molecules, but all the vibrational modes were arbitrary assigned to only one tautomer G19K.^{41–43} Thus, it is necessary to reassign the vibrational fundamentals of all the relative stable tautomers of guanine according to previous experiments.

In this article, we performed quantum chemical calculations to discuss the guanine tautomers and clarify their relative stability depending on chemical environments. In the gas phase and aqueous solution, we discussed the dominant forms in

detail based on the reassignment of vibrational fundamentals provided by simulated Raman spectra. It is emphasized that the hydrogen bonding interaction and the solvent effect has significant influence on the intramolecular vibrations, leading to the different population situations for tautomers of guanine.

■ COMPUTATIONAL DETAILS

Six low-energy tautomers have been calculated, and the optimized structures were shown in Figure 1. Focusing on the solvent effect and hydrogen bonding interaction, two kinds of solvent models have been selected in this study, the polarizable continuum model (PCM)⁴⁴ and directly adding water molecules to the guanine molecule. The former includes a solvent reaction field self-consistent with the solute electrostatic potential. Water with a dielectric constant ($\epsilon = 78.4$) was chosen as the main solvent. Other solvents with different dielectric constants were also considered for comparison. With the purpose of describing the intermolecular hydrogen bond, the latter has been selected, explicitly adding water molecules to the guanine molecule. Furthermore, the PCM model is also used to check the solvent effect for the guanine–water complexes. In addition, we also consider the hydrogen bonding interaction in the tetramers of guanine and the influence of the intermolecular interaction on the simulated Raman spectra of polycrystalline guanine.

Density functional calculations were carried out with Becke's three-parameter hybrid exchange functional and Lee–Yang–Parr correlation functional approach B3LYP.^{45–47} The basis sets for C, N, O, and H atoms of investigated molecules were 6-311+G(d, p), which included the polarization function in all of the atoms and diffuse function in C, N, and O atoms.^{48,49} The theoretical method used has been proven suitable in investigating the binding interaction, vibrational frequency, and Raman activity of pyridine interacting with water clusters and coinage metal clusters.^{50–52} Moreover, it was applied in our previous studies of adenine⁵³ and aniline.⁵⁴ All of the above quantum chemical calculations, including geometry optimiza-

tions, getting analytic frequencies, and Raman scattering factors were carried out by using the Gaussian 09 package.⁵⁵

Binding energies in guanine–water complexes are defined by subtracting the energies of the solvent and molecule (in fully optimized geometries) from the total energy

$$\text{BE} = -(E_{\text{G-W}_n} - E_{\text{G}} - E_{\text{W}_n}) \quad (1)$$

where n denotes the number of water molecules in the complex, $E_{\text{G-W}_n}$ and E_{G} (E_{W_n}) denote the total energies of the complex and free guanine (water molecules), respectively.

The scaled quantum mechanics force field (SQMF) procedure⁵⁶ was used to analyze vibrational bands of all fundamentals. The calculated frequencies were scaled by the factor of 0.981 for below 2000 cm^{-1} . The vibrational bands are assigned according to the potential energy distribution (PED) using the equilibrium geometries and the Cartesian force constant matrix calculated at the B3LYP/6-311+G (d, p) level. Differential Raman scattering cross sections (DRSC) are calculated on top of Raman scattering factors (RSF), as published in our previous work.⁵⁷ In order to make direct comparison with the normal Raman spectra (NRS) experiments, the simulated Raman spectra were presented in terms of the Lorentzian expansion of the DRSC magnitudes.

Here, the corresponding Raman intensities were measured by using the differential Raman scattering cross section (DRSC, $(\text{d}\sigma/\text{d}\Omega)_i$), that is given for certain vibrational mode as follows:

$$\left(\frac{\text{d}\sigma}{\text{d}\Omega}\right)_i = \frac{(2\pi)^4}{45} \frac{h}{8\pi^2 c \tilde{\nu}_i} \frac{(\tilde{\nu}_0 - \tilde{\nu}_i)^4}{1 - \exp(-hc\tilde{\nu}_i/k_{\text{B}}T)} S_i \quad (2)$$

where $S_i = g_i[45(\bar{\alpha}'_i)^2 + 7(\gamma'_i)^2]$ is called Raman Scattering factor, $\tilde{\nu}_0$ and $\tilde{\nu}_i$ denote the frequency of the incident light and the vibrational frequency of the i th mode. The Raman scattering factor in eq 2 is calculated from Gaussian 09 program. Its value contains two contributions, the isotropic polarizability derivative, $\bar{\alpha}'_i$, and the anisotropic polarizability derivative, γ'_i , of the i th vibrational mode.

RESULTS AND DISCUSSION

Low-Energy Tautomers and Relative Energies. Figure 1 presents the optimized structures of six low-energy tautomers, and Table 1 lists their relative energies calculated with different

Table 1. Relative Electronic Energies (kcal/mol) of Six Selected Tautomers Calculated in the Gas Phase and in Aqueous Solution with the PCM Model^a

species	B3LYP/6-311+G**		B3LY-P/		MP2/6-311+G**	
	gas	PCM	gas	PCM	gas	PCM
G17K	0	0	0	0	0	0
G19K	0.44	−0.95	0.73	−0.62	0.27	−1.12
G9Ea	1.70	6.29	1.71	6.35	0.40	3.72
G9Eb	2.42	7.27	2.16	7.13	1.00	4.66
G7Ea	4.65	7.95	4.47	7.80	3.51	5.67
G37K	6.52	4.21	6.21	4.00	6.42	4.69

^aRelative energies are referred to G17K as −542.71351 au (B3LYP/6-311+G(d,p)), −542.76565 au (B3LYP/6-311+G(d,p)), and −541.26642 au (MP2/6-311+G(d,p)) in the gas phase, and −542.73827 au (B3LYP/6-311+G(d,p)), −542.78935 au (B3LYP/6-311+G(d,p)), and −541.28928 au (MP2/6-311+G(d,p)) with PCM model.

methods and basis sets. Among the six low-energy tautomers, the relative energies of the first four tautomers are less than 2.5 kcal/mol, and G17K is the most stable form in the gas phase. When the PCM model is used, the energy difference between G19K and G17K is within about 1 kcal/mol, and those of G9Ea and G9Eb show a sharp increase to above 4 kcal/mol. This indicates that G19K and G17K are dominant in a polar solvent.

It is obvious that the solvent effect influences the relative stability of G19K and G17K dramatically. The calculated results show that the relative energy difference of G19K declines from 0.44 kcal/mol in the vacuum to −0.95 kcal/mol in aqueous solution (PCM) with respect to that of G17K as seen in Table 1. For the Gibbs free energy (ΔG), the relative values between the two tautomers decreases from 0.37 to −0.91 kcal/mol, which are in agreement with previous studies.^{10,36,39,58} It is the reason that G19K has a dipole moment three times larger than that of G17K, i.e., 7.12 vs 2.60 D. This shows that G19K has a considerable stabilization when exposed to a polar solvent like water.

Table 2 presents Boltzmann population ratios of four tautomers at room temperature. G17K dominates in the gas phase, which agrees with the previous studies using different theoretical methods,^{10,15,40} whereas Marian suggested that G19K occupied a lower proportion than that of G9Ea and G9Eb.⁵⁹ The results were calculated at B3LYP/TZVP combining with MRCI, which could overestimate the electron correlation effects. As for that in aqueous solution, G19K becomes the most stable form, whose dipole moment increases from 7.12 D in the gas phase to 9.95 D in aqueous solution. Compared with that of G17K, we discussed the difference of their populations in the next section.

Table 2. Boltzmann Population Ratios (%) of Guanine Tautomers in the Gas Phase and in Aqueous Solvent at 298 K^a

tautomer	this work		ref 40	ref 10	ref 15
	GAS	PCM	GAS	GAS	GAS
G17K	62.3	18	47.6	45.8	57
G19K	33.2	82	22.7	22.4	24
G9Ea	3.3	0	18.5	21	12
G9Eb	1.2	0	11	10.7	7

^aAll values of Gibbs free energy have been corrected for zero-point energy contributions scaled by a factor of 0.981. Ref 40: RI-MP2/TZVPP//RI-MP2/TZVPP relative energies corrected for higher electron correlation terms with thermal correction evaluated at the MP2/6-31G(d, p) level. Ref 10: MP2-cc-PVTZ electronic energies with the thermal corrections calculated at the B3LYP/6-311G(d, p). Free Energies determined from plots in Figure 2 in Ref 15: MP2 treatment using 6-311++G(d, p) and cc-PVTZ basis set.

Figure 2 shows the Boltzmann distributions and relative energies of G17K and G19K, considering the influence of a series of solvents with relative dielectric constants from 1.430 to 78.355. Twelve solvents were selected (see Table S1 in the Supporting Information), such as argon, aniline, acetone, methanol, and so on. As we can see in Figure 2, the population of G19K is increasing continuously with the dielectric constant. This dependence on the dielectric constant can briefly predict the population of tautomers in different environments.

Vibrational Frequencies in the Gas Phase. The analysis of IR spectra of guanine in the gas phase and related theoretical calculation has been reported.^{24,60} The previous assignments

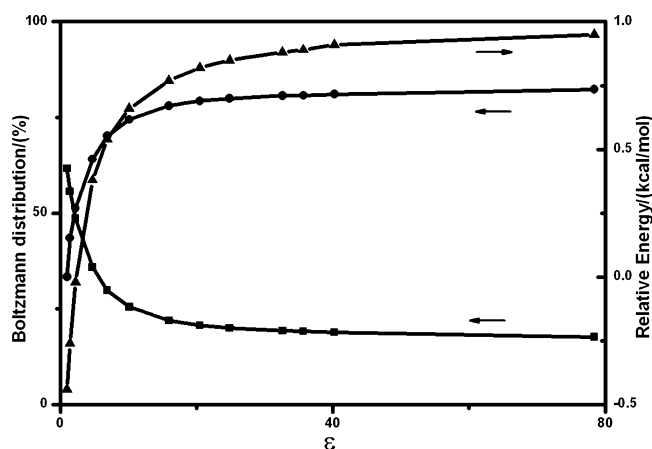


Figure 2. Boltzmann distributions (%) and relative energies (kcal/mol) of G17K and G19K tautomers based on solvents with different dielectric constants. (1) ■, G17K; (2) ●, G19K; (3) ▲, relative energies of G17K and G19K.

are limited on G19K only. As mentioned above, G17K is more stable than G19K in the gas phase, so we reassigned the vibrational fundamentals of G17K based on normal-mode analysis for previous high resolution infrared spectra.

The detailed data of G17K and G19K are summarized in Table 3, including the scaled frequencies, IR intensities, Raman activities, the assignment, and the frequencies in experimental IR spectra. Our calculated results are predicted well with the matrix isolation infrared spectra.¹³ The characteristic peaks 1531, 1049, and 932 cm^{-1} assigned to G19K only, whereas the 1014 cm^{-1} peak relating to $\text{N}_1\text{--C}_2$ stretching vibration was only observed in G17K. For the $\text{C}_6\text{=O}_{13}$ stretching vibration, corresponding to the experimental data of 1736 and 1758 cm^{-1} , our calculated results show that they are assigned to different tautomers, with 1733 cm^{-1} in G17K and 1758 cm^{-1} in G19K respectively. These bands are dominated by the $\text{C}_6\text{=O}_{13}$ stretching vibration and mixed with the $\text{C}_5\text{--C}_6$ stretching coordinate, according to the normal-mode analysis with the PED values of the $\text{C}_6\text{=O}_{13}$ stretching at 62% in G17K and 72% in G19K, respectively. With regard to that of NH_2 scissoring peaks, 1634 cm^{-1} of G17K and 1630 cm^{-1} of G19K agree with the experimental peaks at 1654 and 1629 cm^{-1} . The peak relating to the $\text{C}_4\text{--C}_5$ stretching is at 1539 cm^{-1} in G17K and is at 1573 cm^{-1} in G19K with IR intensities of 157 and 180 km/mol , corresponding to the observed peaks at 1547 and 1577 cm^{-1} , respectively. It should be emphasized that the characteristic Raman peaks to distinguish four low-energy tautomers are ring-breathing vibrations, at 613 cm^{-1} in the IR spectra.¹³ The assignments are slightly different. The peaks in G17K and G19K tautomers are at 618 and 613 cm^{-1} , both corresponding to trigonal deformation of a six-membered ring mixed with $\text{C}_5\text{--C}_6$ and $\text{N}_1\text{--C}_2$ stretching vibration. While for the enol-amino forms, G9Ea and G9Eb, these relate to a six-membered ring trigonal deformation and $\text{C}_6\text{=O}_{13}$ stretching vibration both at 621 cm^{-1} . For the low frequency area, the bands at 573 cm^{-1} for G17K and 531 cm^{-1} for G19K agree with the observed ones at 568 and 532 cm^{-1} , respectively.

Meanwhile, we simulated the Raman spectra of G17K and G19K as shown in Figure 3, and characteristic peaks can be used to distinguish the two tautomers. As for G17K, there are three intensive bands at 1634, 1519, and 1372 cm^{-1} , and their Raman activities are 56, 61, and 96 $\text{\AA}^4/\text{amu}$, respectively. These

can be attributed to the amino scissoring, the $\text{N}_3\text{--C}_4$ stretching, and the $\text{N}_7\text{--H}$ in-plane bending mixed with $\text{N}_7\text{--C}_8$ stretching vibrations modes, respectively. While the peaks of G19K relating to $\text{N}_1\text{--C}_2$, $\text{N}_7\text{--C}_8$ and $\text{C}_8\text{--N}_9$ stretching vibrations are 1573, 1479, and 1356 cm^{-1} with the Raman activities of 82, 133, and 90 $\text{\AA}^4/\text{amu}$, respectively. Additionally, the ring-breathing vibrations are significantly strong, at 618 cm^{-1} for G17K or 612 cm^{-1} for G19K.

Solvent Effect. Figure 4 presents the simulated Raman spectra of G19K and G17K using PCM model in water, whereas the detailed data are presented in Table S2. Compared with the spectra in vacuum (see Figure 3), it is obvious that the solvent effect plays a significant role both in frequency and intensity. The overall intensity of the Raman spectra is enhanced nearly 4 times due to the solvent effect respected to that in the gas phase. This agrees with the previous studies on pyridine⁵¹ and adenine⁵³ when the solvent effect was considered.

With regard to the frequency shift in G19K, the largest shift is assigned to the $\text{C}_6\text{=O}_{13}$ stretching vibration from 1758 in the gas phase to 1674 cm^{-1} in the solution (see Figures 3 and 4a). The other three significant shift frequencies are 1630, 1356, and 612 cm^{-1} in the vacuum, and shift to 1613, 1365, and 619 cm^{-1} , attributed to the amino scissoring vibration, a mixed vibration of $\beta\text{N}_9\text{H}$ and $\nu\text{C}_8\text{N}_9$, as well as the ring-breathing vibration, respectively. The blue shift relating to the ring-breathing vibration is predicted with the value of about 7 cm^{-1} by the PCM model. However, it is obviously lower than the observed frequency shift, for example, from 613 cm^{-1} in the gas phase to 650 cm^{-1} in aqueous solution⁶¹ and 649 cm^{-1} in crystal state.^{24,25}

G17K, however, was often neglected in condensed states in previous studies. The present theoretical prediction indicates that G17K has a quite population in condensed states even when strong polar solvents are considered. Figure 4b presents the simulated Raman spectrum of G17K in water with the PCM model. In the 200–1000 cm^{-1} region, the most intensive peak which is the ring breathing vibration has a small blue shift about 3 cm^{-1} compared with that in the gas phase. This indicates that the long-range interaction slightly influences this vibration. In 1000–1750 cm^{-1} region, however, the vibrational frequencies are very sensitive to the solvent effect. In this region two intense Raman peaks at 1370 and 1518 cm^{-1} almost keeps constant. The peak at 1518 cm^{-1} can be assigned to the $\text{N}_3\text{--C}_4$ stretching vibration. The three feature peaks at 1593, 1634, and 1733 cm^{-1} in the gas phase related to $\nu\text{C}_6\text{O}_{13}$, NH_2sci , and $\nu\text{C}_2\text{N}_3$, display large red shifts (see Figure 3) to 1575, 1611, and 1675 cm^{-1} , respectively. There are four middle intensive peaks at 1160, 1255, 1342, and 1447 cm^{-1} with their frequency shifts less than 5 cm^{-1} . Thus, these bands in the range of 1000–1600 cm^{-1} can be considered as fingerprint signals to identify G17K and G19K.

The Raman spectra of G19K and G17K calculated with the PCM model both are different from that observed in powder. It is known that the PCM model are quite successful in dealing with dielectric medium effects, but when the local solute–solvent interaction becomes important, its handling needs to be improved, especially for the hydrogen bonded systems. In next section we will analyze the solute–solvent short-range interaction related to the hydrogen bond.

Hydrogen Bond Effects. There are five nitrogen atoms and one oxygen atom in guanine acting as proton acceptors or donors, and this is expected to cause significant changes due to

Table 3. Calculated Frequencies, IR Intensity (I_{IR} km/mol), Raman Activity (A_{R} Å⁴/amu), and Assignment of G17K and G19K Tautomers along with the Experimental Data

ν^a	G17K ^b	I_{IR}	A_{R}	PED(%)	ν^a	G19K ^b	I_{IR}	A_{R}	PED (%)
Q37 1736	1733	821	41	$\nu\text{C6O}(62)$, $\nu\text{C5C6}(17)$	1749	1758	759	53	$\nu\text{C6O}(72)$, $\nu\text{C5C6}(14)$
Q36 1654	1634	507	56	NH_2sci (47), $\nu\text{C2N3}(24)$, $\nu\text{C2N10}(12)$	1629	1630	421	38	NH_2sci (61), νC2N3 (16), $\nu\text{C2N10}(13)$
Q35 1593	1593	90	23	NH_2sci (45), $\nu\text{C2N3}(25)$	1588	1583	245	43	$\nu\text{C2N3}(37)$, NH_2sci (30)
Q34 1547	1539	157	30	$\nu\text{C4C5}(29)$, $\nu\text{C6O}(10)$	1577	1573	180	82	$\nu\text{N3C4}(26)$, $\nu\text{C4C5}(25)$, $\beta\text{N9H}(13)$
Q33	1519	24	61	$\nu\text{N3C4}(23)$, $\nu\text{C4C5}(13)$, $\nu\text{CSN7}(10)$	1531	1525	79	29	$\nu\text{N1C2}(12)$, $\nu\text{N7C8}(11)$, $\beta\text{N1H}(11)$
Q32 1443	1451	12	17	νC8N9 (25), $\nu\text{N1C2}(14)$, $\beta\text{N1H}(13)$	1472	1479	3	133	$\nu\text{N7C8}(45)$, $\beta\text{C8H}(11)$
Q31 1432	1427	47	14	$\beta\text{N7H}(21)$, $\nu\text{N7C8}(20)$, $\nu\text{C8N9}(11)$	1418	1407	23	15	$\nu\text{C4C5}(26)$, $\nu\text{N1C2}(14)$, $\nu\text{C4N9}(13)$
Q30 1375	1372	105	96	$\beta\text{N7H}(21)$, $\nu\text{N7C8}(18)$, νC8N9 (13)	1361	1356	14	90	$\nu\text{C8N9}(26)$, $\beta\text{N9H}(40)$
Q29 1353	1347	93	24	νCSN7 (28), $\nu\text{N3C4}(22)$, $\nu\text{C4C5}(11)$	1329	1330	16	8	$\nu\text{C5C6}(20)$, $\nu\text{CSN7}(18)$, $\nu\text{C4N9}(16)$
Q28	1300	39	9	$\beta\text{N1H}(37)$, $\nu\text{C2N10}(23)$		1307	71	8	$\beta\text{N1H}(39)$, $\nu\text{CSN7}(14)$, $\nu\text{C2N10}(12)$
Q27 1271	1258	24	14	$\beta\text{C8H}(33)$, νC8N9 (25), νC4N9 (14)	1276	1279	2	21	$\beta\text{C8H}(40)$, $\nu\text{N7C8}(16)$
Q26 1158	1163	51	9	$\nu\text{N1C6}(19)$, $\tau\text{R3}(14)$, $\beta\text{C8H}(11)$	1140	1148	26	2	$\beta\text{C8H}(20)$, $\nu\text{C4N9}(19)$, $\nu\text{CSN7}(12)$, $\beta\text{R3}(11)$
Q25 1131	1128	32	4	NH_2rock (28), νC4N9 (19), $\nu\text{C2N3}(10)$	1104	1114	34	3	$\nu\text{C2N3}(20)$, $\nu\text{N1C6}(10)$
Q24 1063	1084	36	4	$\nu\text{N7C8}(45)$, $\beta\text{N7H}(20)$, $\nu\text{N1C6}(11)$	1052	1049	19	4	$\nu\text{C8N9}(35)$, $\beta\text{N9H}(20)$, NH_2rock (11)
Q23	1067	2	5	$\nu\text{N1C6}(20)$, NH_2rock (16), $\beta\text{N7H}(12)$	1049	1043	38	3	$\nu\text{N1C6}(26)$, $\nu\text{C8N9}(22)$, NH_2rock (12)
Q22 1018	1014	13	2	$\nu\text{N1C2}(43)$, NH_2rock (12)		1025	9	4	$\nu\text{N1C2}(42)$, $\nu\text{C2N10}(10)$
Q21	940	1	7	$\beta\tau_1(55)$, $\beta\tau_2(20)$, $\nu\text{C4C5}(14)$	932	930	8	6	$\beta\tau_1(56)$, $\beta\tau_2(23)$, $\nu\text{C4C5}(10)$
Q20 855	844	14	1	$\gamma\text{C8H}(100)$	827	820	9	2	$\beta\text{R3}(31)$, $\beta\tau_2$ (18), $\nu\text{CSN7}(16)$
Q19 821	819	6	1	$\beta\text{R2}(30)$, $\beta\tau_2(23)$, νCSN7 (14)	794	808	12	1	$\gamma\text{C8H}(97)$
Q18 752	756	22	0	$\tau\text{R3}(34)$, $\tau\tau_1(31)$, $\gamma\text{C6O}(23)$	778	763	22	2	$\gamma\text{C6O}(43)$, τR3 (22), $\tau\tau_2(17)$
Q17 721	720	7	0	$\gamma\text{C6O}(46)$, $\gamma\text{C2N10}(29)$	721	720	5	0	$\gamma\text{C2N10}(51)$, $\gamma\text{C6O}(16)$, $\tau\text{R3}(15)$,
Q16 709	707	34	0	$\gamma\text{C2N10}(32)$, $\tau\tau_1(30)$, $\gamma\text{C6O}(17)$	693	685	39	0	$\gamma\text{C6O}(25)$, $\gamma\text{C2N10}(19)$, $\tau\tau_1(22)$, $\tau\tau_2(12)$
Q15 670	662	13	0	$\beta\text{C6O}(22)$, $\beta\text{C2N10}(19)$, $\tau\tau_2(12)$	654	656	21	0	$\beta\text{C6O}(20)$, $\beta\text{C2N10}(18)$, $\beta\tau_2(10)$
Q14 637	630	9	0	$\tau\tau_2(72)$	645	648	3	0	$\tau\tau_2(63)$, $\tau\tau_1(25)$
Q13 613	618	4	26	βR3 (18), $\nu\text{C5C6}(14)$, $\nu\text{N1C2}(10)$	613	613	8	28	$\beta\text{R3}(18)$, $\nu\text{C5C6}(15)$, $\nu\text{N1C2}(12)$
Q12 589	575	67	1	$\gamma\text{C8H}(82)$	595	583	80	1	$\gamma\text{N1H}(81)$
Q11 568	573	280	2	$\omega\text{NH}_2(75)$, τC2N10 (9)	532	531	259	2	$\omega\text{NH}_2(76)$, $\tau\text{C2N10}(11)$
Q10 528	529	6	3	$\beta\text{R1}(61)$	520	525	78	1	$\gamma\text{N9H}(96)$
Q9 494	484	82	1	$\gamma\text{N7H}(91)$	514	516	22	4	$\beta\text{R1}(53)$
Q8 482	479	4	5	$\tau\text{R2}(67)$	482	478	8	5	$\beta\text{R2}(67)$
Q7 371	361	1	0	$\tau\tau_1(26)$, $\tau\text{C4C5}(23)$, $\tau\text{R3}(14)$	346	350	2	1	$\tau\tau_1(31)$, $\text{C4C5}(19)$, $\tau\text{R3}(16)$, $\gamma\text{C2N10}(11)$
Q6	330	2	3	$\beta\text{C2N10}(56)$, $\beta\text{C6O}(13)$		329	11	3	$\beta\text{C2N10}(39)$, $\beta\text{C6O}(28)$
Q5 309	317	91	1	$\tau\text{C2N10}(80)$		321	58	0	$\tau\text{C2N10}(66)$, $\omega\text{NH}_2(10)$
Q4	299	3	1	$\beta\text{C6O}(29)$, $\beta\text{R1}(14)$, $\nu\text{C5C6}(10)$		312	17	1	$\beta\text{C6O}(15)$, $\tau\text{C2N10}(15)$, $\beta\text{C2N10}(14)$
Q3	188	4	0	$\tau\text{R1}(81)$, $\tau\text{C4C5}(14)$		193	12	0	$\tau\text{R1}(70)$, $\tau\text{C4C5}(30)$
Q2	147	3	0	$\tau\text{R3}(43)$, $\tau\text{C4C5}(31)$, $\tau\text{R2}(18)$		154	1	0	$\tau\text{R3}(50)$, $\tau\text{R1}(17)$, $\gamma\text{C6O}(8)$
Q1	140	22	0	$\tau\text{R2}(63)$, $\tau\text{C4C5}(16)$, $\gamma\text{C2N10}(9)$		134	3	0	$\tau\text{R}(79)$, $\tau\text{C4C5}(8)$

^aArgon matrix IR data in the ref 13. ^bValues scaled by multiplication of calculated frequencies by a constant factor of 0.9813 for the frequencies between 0–2000 cm⁻¹. ν , stretching; β , bending; γ , out; ω , wagging; rock, rocking; τ , torsion; r, five-membered ring; R, six-membered ring; $\beta\tau_1 = \beta_1 + a(\beta_2 + \beta_5) + b(\beta_3 + \beta_4)$; $\beta\tau_2 = (a - b)(\beta_2 - \beta_5) + (1 - a)(\beta_3 + \beta_4)$; $\beta\text{R1} = 2\alpha_1 - \alpha_2 - \alpha_3 + 2\alpha_4 - \alpha_5 - \alpha_6$; $\beta\text{R2} = \alpha_2 - \alpha_3 + \alpha_5 - \alpha_6$; $\beta\text{R3} = \alpha_1 - \alpha_2 + \alpha_3 - \alpha_4 + \alpha_5 - \alpha_6$; $\tau\text{r1} = b(\tau_1 + \tau_5) + (\tau_2 + \tau_4) + \tau_3$; $\tau\text{r2} = (a - b)(\tau_4 - \tau_2) + (1 - a)(\tau_5 - \tau_1)$; $\tau\text{R1} = \tau_1 - \tau_3 + \tau_4 - \tau_6$; $\tau\text{R2} = -\tau_1 + 2\tau_2 - \tau_3 - \tau_4 + 2\tau_5 - \tau_6$; $\tau\text{R3} = \tau_1 - \tau_2 + \tau_3 - \tau_4 + \tau_5 - \tau_6$. Qn ($n = 1-37$) stands for the normal modes of guanine excluded all the high frequencies (>2000 cm⁻¹).

the hydrogen bond effect. Many groups have studied the hydrogen bond between guanine and water molecules.^{41–43} More specially, the amino, carbonyl groups, and the N₁–C₆ bond are the most sensitive sites to the hydrogen bonding interaction.⁴²

a. Guanine–Water Complexes. To further investigate the local hydrogen bond effect on Raman Spectra, the model of guanine–water (G–H₂O) complexes has been built. Figure 5 shows the optimized structures and relative energies of different G–H₂O complexes, and Table 4 summarizes the binding energies (BE) of these complexes. The most stable structures in gas are G17K–W1 and G19K–W1, which agrees with the previous studies reported by Shishkin.⁴² As shown in Table 4, the binding energies of these complexes are larger in vacuum

than that in water due to the decrease of the electrostatic interaction caused by the solvent effect.

Figure 6 presents simulated Raman spectra of G19K–W1 and G17K–W1 complexes, whereas the Raman spectra of other G–H₂O complexes are presented in Figure S1. Some bands related to the C₆=O₁₃ and N7 bonding to the water molecule display large frequency shifts. For the most stable complex G19K–W1, the ring-breathing frequency blue shifts to 624 cm⁻¹ in water from 617 cm⁻¹ in the gas phase. In this case, the water molecule binds to the carbonyl group and N7 sites through the two hydrogen bonds. The bands related to these modes display large frequency shifts compared to the gas phase one. In addition, the hydrogen bonding interaction results in the blue shift of three strong peaks at 1362, 1483, and 1585 cm⁻¹ in G19K–W1. When the PCM model is considered,

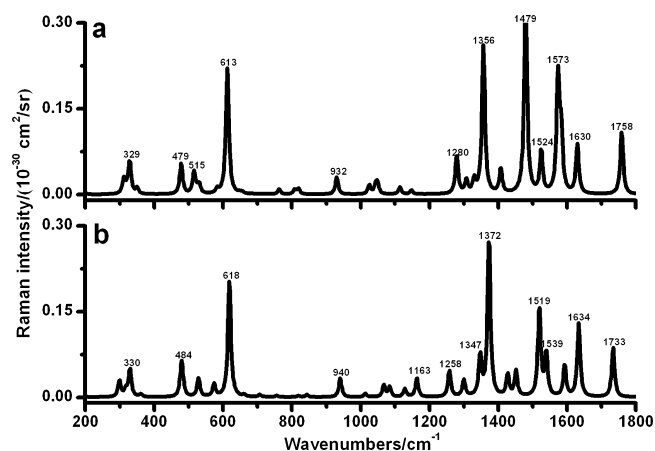


Figure 3. Simulated Raman spectra of low-energy tautomers G19K(a) and G17K(b) of guanine calculated at the B3LYP/6-311+G(d, p) level. The incident wavelength of 514.5 nm was used here with a Lorentzian line width of 10 cm^{-1} .

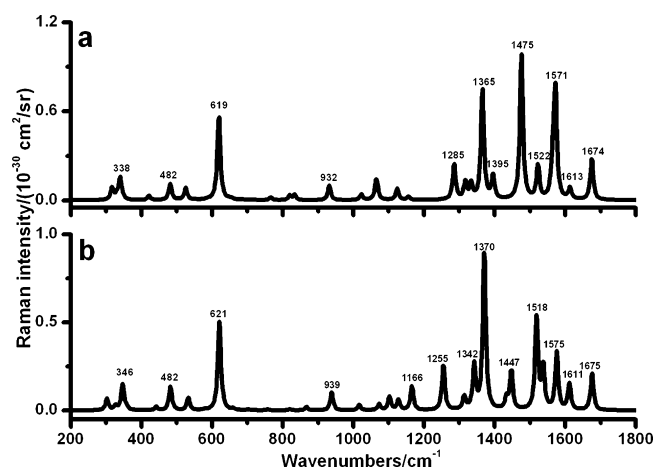


Figure 4. Simulated Raman spectra of two low-energy tautomers G19K (a) and G17K (b) of Guanine calculated at the B3LYP/6-311+G(d, p) level with PCM model. The incident wavelength of 514.5 nm was used here with a Lorentzian line width of 10 cm^{-1} .

Table 4. Binding Energies (kcal/mol) of G–H₂O Complexes Calculated at the B3LYP/6-311+G(d, p) Level

species	GAS	PCM	species	GAS	PCM
G19K–W1	8.89	5.97	G17K–W1	12.90	7.05
G19K–W2	8.33	6.35	G17K–W2	11.26	5.22
G19K–W3	11.79	5.29	G17K–W3	8.58	5.93
G19K–W4	8.94	4.90	G17K–W4	10.56	5.31
G19K–W5	8.83	4.89	G17K–W5	7.23	5.40

those bands further move to 1377, 1478, and 1577 cm^{-1} , respectively (see Figure 6b). These peaks can be attributed to the N₉–H₁₆ bending, the N₇–C₈ stretching and a mixed vibrational mode of N₃–C₄ and C₄–C₅ stretching, respectively, which is consistent with the change in bond lengths for the N₁–C₆ and C₈–N₉ shortening and the bond distance of C₆=O₁₃ lengthening.

With regard to G17K–W1 complexes, the most stable configuration shows that the water interacts with G17K through C₆=O₁₃ and N₇–H₁₆ sites. The ring breathing frequency has a slightly blue shift from 621 to 623 cm^{-1} , corresponding to the change in structures. The peak at 1166 cm^{-1} of free G17K shifts to 1195 cm^{-1} with PCM model, attributed to the internal coordinators of νN1C6 (19), τR3 (14), and βC8H (11). The two bands at 1381 and 1357 cm^{-1} in the gas phase red shifting to 1374 and 1349 cm^{-1} in water can relate to the mixed vibration of the N₇–H₁₆ bending and the N₇–C₈ stretching as well as the mixed one of the C₅–N₇ and N₃–C₄ stretching, respectively. Similarly, the peaks relating to the C₂–N₃ stretching and the NH₂ scissoring at 1592 and 1635 cm^{-1} shift to 1577 and 1613 cm^{-1} . Meanwhile, their relative intensities also change from 31 and 56 $\text{\AA}^4/\text{amu}$ to 123 and 58 $\text{\AA}^4/\text{amu}$, respectively. Another characteristic peak relating to the C₆=O₁₃ stretching red shifts to 1702 cm^{-1} and 1660 cm^{-1} with the PCM model.

b. G–(H₂O)_n Complexes. The complexes of G–(H₂O)_n ($n = 2$ –7) were calculated to further consider the hydrogen bond effect. Their structures and relative energies with PCM model are presented in Figure S2. Here, n and m ($n = 2$ –7 and $m = 1$ –5) in the G19K– $n\text{W}_m$ and G17K– $n\text{W}_m$ represent the number of the water molecule and the interacting sites, respectively. Figure

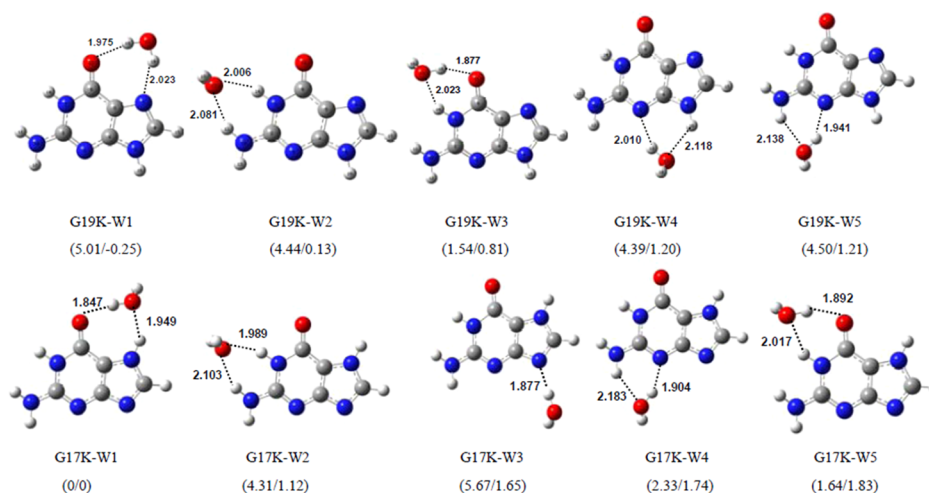


Figure 5. Optimized geometries, the hydrogen bond distances, and relative energies (kcal/mol) of G19K–H₂O and G17K–H₂O complexes calculated at the B3LYP/6-311+G(d, p) level. The data presented in parentheses correspond to relative energies in the gas phase and in water with PCM model, respectively.

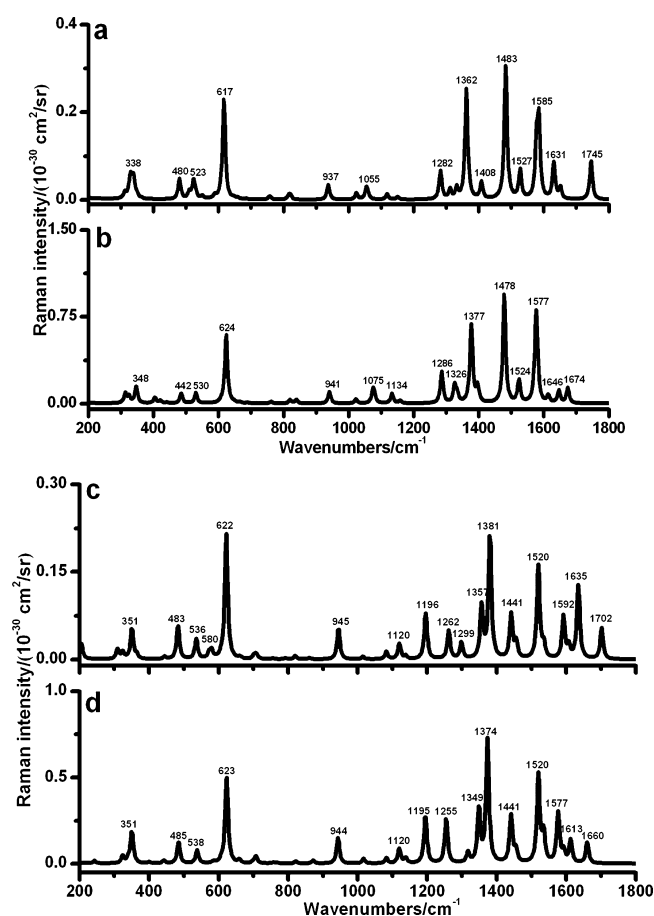


Figure 6. Simulated Raman spectra of G19K-W1 and G17K-W1 calculated at the B3LYP/6-311+G(d, p) level. (a and c) in gas; (b and d) in water with PCM model. The excitation wavelength of 514.5 nm was used here with a Lorentzian line width of 10 cm^{-1} .

7 presents the simulated Raman spectra of $\text{G19K}-(\text{H}_2\text{O})_n$ and $\text{G17K}-(\text{H}_2\text{O})_n$ ($n = 2, 3, 7$). The ring breathing peak blue shifts largely with increasing number of water molecules, from 619 cm^{-1} for free G19K to 636 cm^{-1} for G19K-3W, and to 635 cm^{-1} for G19K-7W. This is in agreement with the shortening C_5-C_6 bond. For that in G17K, the ring breathing frequency blue shifts to 629 cm^{-1} in G17K-3W and 632 cm^{-1} in G17K-7W.

In the fingerprint region, the influence of different numbers of water molecule was also considered. For $\text{G19K}-(\text{H}_2\text{O})_n$ complexes, we can summarize three features for the influence of size effect. First, the intense Raman peak at 1285 cm^{-1} attributed to the C_8-H_{15} bending and the N_7-C_8 stretching has a blue shift from 1286 cm^{-1} in G19K-W1 to 1290 cm^{-1} in G19K-3W, and finally reaches to a converged frequency at 1292 cm^{-1} of G19K-7W. While the Raman activity almost keeps at $140 \text{ Å}^4/\text{amu}$ in different $\text{G19K}-(\text{H}_2\text{O})_n$ complexes. Second, the band at 1365 cm^{-1} contributed by the C_8-N_9 stretching and the N_9-H_{16} bending has a large blue shift to 1373 cm^{-1} in G19K-3W and 1396 cm^{-1} in G19K-7W. Here, the C_8-N_9 bond length decreases by $0.010-0.015 \text{ Å}$, and the Raman intensity also decreases with the increasing size. Third, the hydrogen bonding interaction has a significant influence on the Raman spectrum of G19K when water molecules bind to $\text{C}_6=\text{O}_{13}$, N_1-H_{14} , and N_9-H . For example, the $\text{C}_6=\text{O}_{13}$ stretching vibration has a red shift, from 1674 cm^{-1} in G19K to 1665 cm^{-1} in G19K-7W, close to the observed frequency at

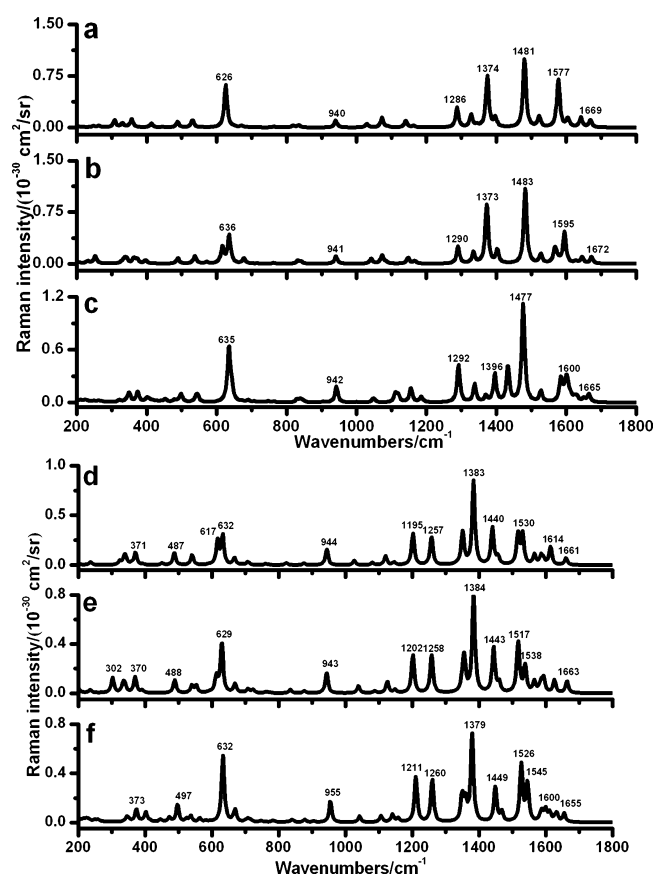


Figure 7. Simulated Raman spectra in aqueous solution with PCM model of $\text{G19K}-(\text{H}_2\text{O})_n$ and $\text{G17K}-(\text{H}_2\text{O})_n$ ($n = 2, 3, 7$) calculated at the B3LYP/6-311+G(d, p) level. (a and d) $n = 2$; (b and e) $n = 3$; (c and f) $n = 7$. The incident wavelength of 514.5 nm was used here with a Lorentzian line width of 10 cm^{-1} .

1677 cm^{-1} .^{24,25,33} Shukla et al. suggested that the first solvation shell of the guanine can be saturated by six water molecules.⁶² In our results, the little change between G19K-6W and G19K-7W demonstrated that simulated Raman spectra should reach to a convergence.

With regard to $\text{G17K}-(\text{H}_2\text{O})_n$ ($n = 2, 3, 7$) complexes, we also classify significant changes into three aspects (see Figure 7). (1) The ring breathing mode has a blue shift, from 618 cm^{-1} in G17K in the gas phase to 632 cm^{-1} in G17K-7W with the PCM model. The relative intensity declined at first and then increased. (2) In the fingerprint region, the peak at 1195 cm^{-1} in G17K-W1 further blue shifts to 1202 cm^{-1} in G17K-3W and finally to 1211 cm^{-1} in G17K-7W. Another characteristic peak in the polycrystalline or solid guanine observed at 1257 cm^{-1} is predicted well at 1260 cm^{-1} in G17K-7W, attributed to the C_8-N_9 stretching and C_8-H_{15} bending vibration. The peaks at 1211 and 1260 cm^{-1} in G17K-7W agree with the experimental spectra (1235 and 1266 cm^{-1} respectively).^{24,25,33} The peak at 1372 cm^{-1} in G17K is the most intensive one in this region with the Raman activity of $96 \text{ Å}^4/\text{amu}$. After interacting with water, it maintains the strongest peak, which agrees with the experimental observation in anhydrous crystalline.²⁰ Based on the normal-mode analysis, the fundamental can be attributed to a mixed vibration of the N_7-H_{16} bending, the N_7-C_8 stretching and the imidazole ring deformation. The vibrational frequency shifts from 1372 cm^{-1} in G17K to 1384 cm^{-1} in G17K-3W. Correspondingly, the

N_7-C_8 bond decreases about 0.017 Å. (3) In a higher region, the NH_2 scissoring frequency changes at the range of 1614–1636 cm^{-1} dependent on the number of water molecules. The $C_6=O_{13}$ stretching one red shifts from 1733 cm^{-1} in G17K to about 1660 cm^{-1} , and the Raman intensities declines. This agrees with the $C_6=O_{13}$ bond distance increasing about 0.03 Å.

The above results show that the hydrogen bonding interaction has a significant influence on $G-(H_2O)_n$ complexes, especially for the ring breathing vibration and the modes in the fingerprint region. For G17K– $(H_2O)_n$ complexes, the hydrogen bond and the site of water binding to guanine have great influence on the fundamental at 1163 cm^{-1} in G17K. The hydrogen bonding of one water molecule to the $C_6=O_{13}$ and N_7-H_{16} sites of G17K leads to a large blue shift to 1195 cm^{-1} and the N_1-C_6 bond decreases by 0.018 Å. With the increasing number of water molecules, we found the band blue shifts further with the shortening N_1-C_6 bond. However, compared with that in the gas phase, the PCM model causes very small frequency shifts in G17K– nW_m . Besides, we calculated the average binding energy per water molecule is about 7 kcal/mol, and further analyzed the interaction by using natural bond orbital (NBO) analysis. NBO analysis showed that in G17K–W1, the largest orbital interaction energies can be found from the lone paired orbitals of O_{13} in G17K with the O–H antibonding orbital in H_2O with 4.70 kcal/mol and the lone paired orbital of O in H_2O with the N_7-H_{14} antibonding orbital. With the increasing number of water molecules, the hydrogen bonds significantly lead a blue shift and finally the frequency converges to 1211 cm^{-1} in G17K–7W with the PCM model. Therefore, the significant blue shift due to the hydrogen bond effect to induce weakening the $C=O$ double bond while strengthening the $C-N$ double bonding feature. It is noted that the long-range solvent effect has a smaller influence on the frequency shift of this characteristic peak.

Simulating Raman Spectrum of Guanine Crystal. The crystalline structure measurement of anhydrous guanine indicates that G17K should be the only existing form,¹⁹ and previous studies assigned the vibrational bands mostly based on the G19K for powder and polycrystalline states of guanine.²⁵ However, Lopes suggested that G17K was the prevalent form in the condensed state.²⁰ Here, we further analyze the hydrogen bond effect focusing on that between guanine molecules. The structures of guanine tetramers as well as their simulated Raman spectra have been calculated.

Figure 8 shows optimized structures and binding energies of three tetramers, 4G19K (I), 4G17K, and 4G19K (II). Guanine tetramers^{63–70} have been studied extensively, and these studies always focus on whether guanine can form a stable quadruplex structure (4G19K (I)) in the presence or absence of a variety of monovalent cations.^{64–67} Thewalt et al. reported that only the 4G19K(II) has been found in guanine monohydrate as well as columns of water molecules pass through the interstices of hexagonal arrays.¹⁸ In this study, each water forms an O–H...O hydrogen bond to an oxygen atom O_{13} of a guanine molecule and an O...H–N by accepting a hydrogen atom from an $-NH_2$ group. For anhydrous guanine crystalline, only 4G17K has been determined recently.¹⁹ Our calculated results show that the order of their stability for the three structures is 4G19K (I) > 4G17K > 4G19K (II). This indicates that the G17K tetramer is more stable than 4G19K(II) both in the gas phase and in water.

The simulated Raman spectra of the three different tetramers also are presented in Figure 8 as well as our experimental results of guanine powder. The experimental details are seen in

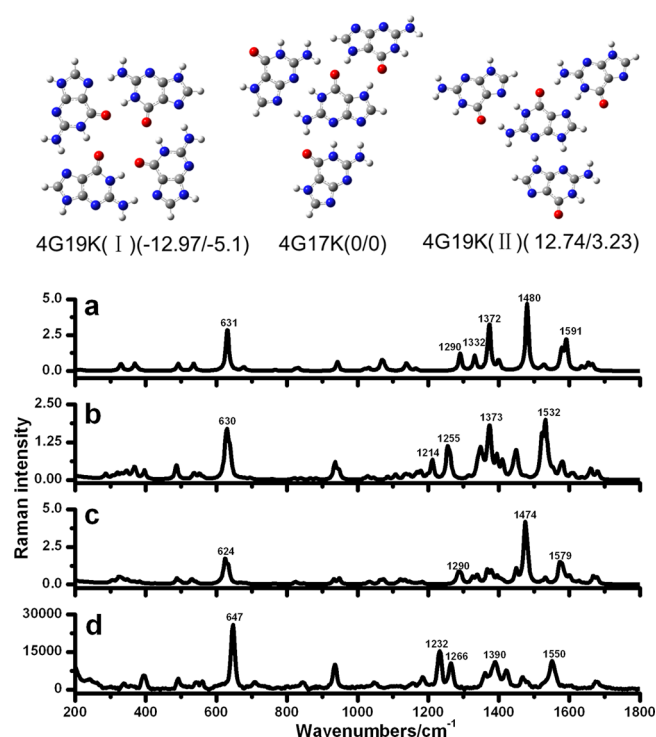


Figure 8. Optimized geometries and simulated Raman spectra of 4G19K (I), 4G17K, and 4G19K(II) with the PCM model calculated at the B3LYP/6-311+G(d, p) level along with the experimental Raman spectrum of guanine powder. The relative energies (kcal/mol) of 4G19K and 4G17K in the gas phase and the second in water are shown in the parentheses, respectively. a. 4G19K (I); b. 4G17K; c. 4G19K(II); d. NRS spectrum of powdered guanine. The units of the Y axis are $10^{-30} cm^2/sr$ for a, b and c, and the counter per second (cps) for d. The incident wavelength of 514.5 nm was used for the calculated Raman spectra here with a Lorentzian line width of 10 cm^{-1} .

Supporting Information. Compared with the simulated Raman spectra, we also noted that the Raman spectra of G17K-6W and 4G17K are very similar to the measured Raman spectrum of guanine powder.²⁰ Table 5 presents the detailed data of our

Table 5. Experimental of Guanine Powder and Theoretical Frequencies of 4G17K Calculated at the B3LYP/6-311+G(d, p) Level with the PCM Model

wavenumber/ cm^{-1}				assignment ^d
calc.	scaled ^a	expt ^b	expt ^c	
1633	1605	1606	1599	$\beta N1H(35)$, $\nu C2N3(21)$, $\nu C2N10(12)$
1560	1532	1550	1550	$\nu N3C4(20)$, $\nu C4C5(13)$
1476	1449	1468	1466	$\beta C8H(15)$, $\nu C8N9(11)$
1425	1394	1421	1422	$\beta N1H(28)$, $\nu C2N10(24)$
1398	1373	1390	1392	$\beta r1(14)$, $\nu C8N9(15)$, $\nu C4C5(13)$
1374	1349	1361	1361	$\nu C5N7(30)$, $\nu N3C4(14)$
1278	1255	1266	1266	$\nu C8N9(22)$, $\beta C8H(18)$, $\nu C4N9(11)$
1227	1214	1232	1235	$\nu N1C6(24)$, $\nu C5N7(18)$, $\gamma C2N10(17)$, $\nu N7C8(16)$
1200	1179	1184	1188	$\nu N1C6(35)$, $\nu C5N7(16)$
1168	1147	1158	1159	$\nu C4N9(20)$, rock $NH2(12)$, $\nu N1C6(11)$
1064	1046	1047	1048	$\nu N3C4(33)$, $\nu C2N3(12)$

^aSF = 0.9813. ^bOur results of powder Raman spectra. ^cRef 25. ^d ν , stretching; β , bending; γ , out; rock, rocking; r, five-numbered ring; $\beta r1 = \beta 1 + a(\beta 2 + \beta 5) + b(\beta 3 + \beta 4)$.

experimental and theoretical results. The scaled factor for B3LYP vibrational frequencies is 0.9813, which is the same as our previous work.^{51–54} As seen in Table S, there are two strong bands in the normal Raman spectra of polycrystalline and powder guanine, which are 1232 and 1266 cm^{-1} . Our theoretical data of 4G17K agree with the experimental results very well. Moreover, we found the shape of our simulated Raman spectrum of 4G17K is very similar to the experimental one (see Figure 8). We predicted the bands at 1214 and 1255 cm^{-1} corresponding to 1232 and 1266 cm^{-1} in the observed spectrum. It may be safely concluded that the G17K tautomer exists in the powder guanine. This is different from previous studies.^{24,25,33}

In summary, our calculated results show that G17K always exists in solid or powdered guanine, and Raman spectroscopy is a useful tool to characterize different tautomers in condensed states, even when the two tautomers transform easily each other in polar solvents.^{9,58}

CONCLUSION

We have investigated different tautomers as well as the influence of solvent effects and the hydrogen bonding interaction on Raman spectra of guanine using quantum chemistry calculations. Our results show that the G17K tautomer dominates among low-energy tautomers of guanine in the gas phase. Since the assignment of various vibrational spectra was always limited to the G19K tautomer in previous studies, we reassigned the fundamentals of G17K based on the normal-mode analysis by combining the high resolution infrared spectral data in the literature. We note that the relative energies of G19K and G17K observably change after considering the solvent effect. Increasing the dielectric constants of the solvent would result in the stabilization of G19K with respect to G17K. Finally, the G19K tautomer is the most stable form in polar solvents. This causes the population of G19K to increase continuously. Thus G19K and G17K possibly coexist in aqueous solution.

We adopted $\text{G}-(\text{H}_2\text{O})_n$ complex models to study the hydrogen bond effect on the Raman spectra of guanine. We find that there are some intramolecular fundamentals with large frequency shifts with the hydrogen bonding interaction, especially the ring breathing vibrational mode and those in the fingerprint region (from 1000 to 1600 cm^{-1}). The characteristic band of G17K at 1163 cm^{-1} in the gas phase exhibits a significant blue shift due to the hydrogen bond effect. We think this is due to the hydrogen bonding interaction to induce weakening the $\text{C}=\text{O}$ double bond while strengthening the C_6-N_1 double bonding feature. It is noted that the long-range solvent effect has a smaller influence on the frequency shift of this characteristic band. Meanwhile, the Raman activity is also enhanced to some extent. Furthermore, a minimum of six water molecules is necessary in the first solvation shell of guanine, since there is little difference between the Raman spectra of $\text{G}-(\text{H}_2\text{O})_6$ and $\text{G}-(\text{H}_2\text{O})_7$.

Guanine can form a quadruplex structure under certain conditions. Our results demonstrate that the tautomer existing in polycrystalline and powdered guanine is the G17K structure. The simulated Raman spectrum of 4G17K agrees with the experimental results very well. The present study shows that the spectral analysis combined with quantum chemical calculations provides a powerful approach to explore the hydrogen bonds and weakly intermolecular interactions.

ASSOCIATED CONTENT

Supporting Information

Table S1 shows the calculated frequencies, IR intensity (I_{IR} , km/mol), Raman activity (A_{R} , $\text{\AA}^4/\text{amu}$), and assignment of G17K and G19K tautomers with PCM model. Figure S1 gives the simulated Raman spectra in aqueous solution with PCM model of the other G-H₂O complexes calculated at the B3LYP/6-311+G(d, p) level. Figure S2 demonstrates the B3LYP/6-311+G** geometries and relative energies (kcal/mol) of G19K- $n\text{W}_m$ and G17- $n\text{W}_m$ ($n = 2, 3, 4, 5, 6, 7$ and $m = 1, 2, 3, 4, 5$) with PCM model. This material is available free of charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We are grateful for the financial support of this work by the NSF of China (Nos. 91027009, 20973143, and 21021002) and National Basic Research Programs (No. 2009CB930703). D.Y.W. is grateful for the support from Xiamen University (2010121020).

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