Tautomerism of Cytosine on Silver, Gold, and Copper: Raman Spectroscopy and Density Functional Theory Calculation Study

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Tautomerism of pyrimidine base cytosine has been comparatively examined on nanoparticle and roughened plate surfaces of silver, gold, and copper by surface-enhanced Raman scattering (SERS). The SERS spectrum was found to be different depending on the metals and their substrate conditions suggesting the dissimilar population of various tautomers of cytosine on the surfaces. The *ab initio* calculations were performed at the levels of B3LYP, HF, and MP2 levels of theory with the LanL2DZ basis set to estimate the energetic stability of the tautomers with the metal complexes as well as the gas phase state. The amino group and N_3-coordinated tautomer was predicted to be more favorable for bonding to Au, whereas the hydroxyl and N_1-coordinated zwitter ionic form is most stable with Ag and Cu as a bidentate form from the DFT calculation. The binding energy with the Ag atom is calculated to be smaller than those with the Au and Cu atoms in line with the temperature-dependent SERS spectra of cytosine.

Key Words : Cytosine, Tautomerism, Coinage metals, SERS, DFT calculation

Introduction

There has been increasing interest in estimating the stabilities of various geometric forms of nucleic acid bases due to their potential importance in genetics and related fields.[1-4] *Ab initio* calculations have been employed to predict the structure and energetics of nucleic acid bases.[5,6] Cytosine, one of the simplest pyrimidine bases, has been a frequent subject of theoretical studies due to its biochemical importances.[7-9] Vibrational spectra of DNA bases are calculated by DFT calculations.[10]

Binding properties of cytosine on metal surfaces have been studied by means of various spectroscopic tools.[11-16] The energetics of cytosine-gold interactions were recently investigated by temperature programmed desorption and reflection absorption FT-IR spectroscopy.[11,12] Adsorption of single stranded DNA consisting of cytosine bases was investigated by means of X-ray photoelectron and FT-IR spectroscopy.[14] An infrared reflection absorption study of cytosine indicates that the molecule is expected to have an upright geometry on Cu(110) via its N_1-coordinating atom with the amino group pendent from the surface.[15] For 1,5-dimethylcytosine, the interaction energy with the metal surface is assumed to grow in the order of Ag < Au < Cu.[16]

The optical properties of metal nanoparticles have attracted both scientific and technological interest in the past two decades due to their potential applications in many areas.[17,18] Surface-enhanced Raman scattering (SERS) on metal surfaces has shown great potential for use in biomedical analysis.[19] The analysis of spectral features has provided detailed information on surface reactions and the geometry of adsorbates.[20,21] SERS has recently been used to monitor analyte-surface binding interactions as biosensors.[22]

Numerous cases have been reported indicating that the adsorption behavior depends on the metal substrates.[23-29] The detailed origins of the different adsorption characteristics on metal substrates have not been fully clarified, however. Tautomeric stabilities appeared to be different depending on metal substrates. Recently we performed an SERS study of uracil and thymine on gold and silver nanoparticles in a comparative way using *ab initio* methods at B3LYP and MP2 levels of theory.[28,29] The N_3-deprotonated tautomer of both uracil and thymine was predicted to be more favorable on Au than on Ag.

Although adsorption of cytosine has been previously studied,[11-16] a detailed analysis depending on its tautomer was not conducted. To aim at understanding tautomerism of the simplest pyrimidine base upon adsorption on the metal surfaces, we studied tautomerism of cytosine on Ag, Au, and Cu by SERS and DFT calculation.

Experimental Section

Cytosine (≥99%) was purchased from Sigma Aldrich. The citrate stabilized gold and silver sols were synthesized by the recipes in the literature.[30] For Ag, 90.0 mg of $AgNO_3$ in 500 mL of water was brought to boiling. A solution of 1% sodium citrate (10 mL) was then added to the $AgNO_3$ solution under vigorous stirring. For Au, 133.5 mg of $KAuCl_4$ (Aldrich) was initially dissolved in 250 mL of water, and the solution was brought to boiling. A solution of 1% sodium citrate (25 mL) was then added to the $KAuCl_4$ solution under vigorous stirring, and boiling was continued for *ca.* 20 min. The resulting Au solution was stable for several weeks. All the chemicals otherwise specified were reagent grade and triply distilled water, of resistivity greater than 18.0 MW cm, was used in making aqueous solutions. For Cu, the nanoparticle solution was prepared by the

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following recipe.[31] All the chemicals otherwise specified were reagent grade and triply distilled water, of resistivity greater than 18.0 MW cm, was used in making aqueous solutions. The SERS plate substrates were produced from a metal plate by an oxidation-reduction cycle using a CH Instrument 700A potentiostat or by eroding the Ag and Cu plate using a HNO_3 solution.

Raman spectra were obtained using a Renishaw Raman confocal system model 1000 spectrometer equipped with an integral microscope (Leica DM LM).[32] Raman scattering was detected with 180° geometry using a peltier cooled (–70 °C) CCD camera (400 × 600 pixels). An appropriate holographic notch filter was set in the spectrometer. The holographic grating (1800 grooves/mm) and the slit allowed the spectral resolution to be 1 cm^{-1}. The 632.8 nm irradiation from a 35 mW air-cooled HeNe laser (Melles Griot Model 25 LHP 928) with the plasma line rejection filter was used as the excitation sources for the Raman experiments. Data acquisition time used in the Raman measurements was approximately 30 s. The Raman band of a silicon wafer at 520 cm^{-1} was used to calibrate the spectrometer. Temperature dependent Raman measurement could be performed using a Linkam THMS 600 thermal heating stage.[32] Since the same excitation wavelength at 632.8 nm was employed in obtaining all the Ag, Au, and Cu SERS spectra, the instrumental effect or laser mode should be.

Calculation Methods

All *ab initio* molecular orbital calculations were carried out using the Gaussian 03 package[33] The geometry optimization of cytosine and Ag/Au/Cu complex were carried out at the levels of MP2, HF, and B3LYP. The LanL2DZ basis sets with a relativistic effective core potential have been used for Ag, Au, and Cu. The six tautomeric forms that could be coordinated to metal atoms were considered among many possibilities.[7] The geometry optimization for the tautomers was carried out starting from many possible orientations. During the geometry optimization, no geometric constraints such as planarity were used for the present calculation.

Results and Discussion

Raman Spectra. Figure 1 shows the ordinary Raman (OR) spectrum of cytosine in neat solid state, the Ag, Au, and Cu SERS spectra at high bulk concentration of ~10[-3] M. It seemed a rather straightforward to correlate the OR bands with the SERS bands. Their peak positions are listed in Table 1 along with the appropriate vibrational assignments. Our assignment is mainly based on the previous literatures.[10] The concentration of cytosine in the aqueous solution was ~10[-3] M. This concentration should correspond to cytosine on metal surface at the concentration above a full-coverage limit by assuming that the adsorbate was oriented perpendicularly with respect to the colloidal surfaces.[25-29] Our spectrum on Ag appeared to be consistent with this report.[10]
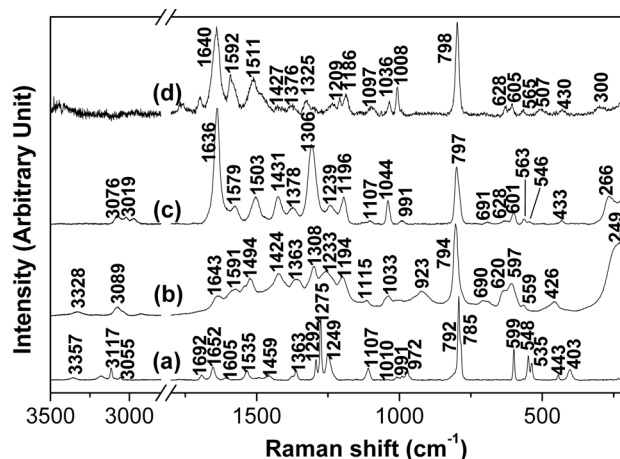

Figure 1. (a) OR spectrum of cytosine in neat solid state and SERS spectra in aqueous (b) silver, (c) gold, and (d) copper nanoparticle solutions. All spectra were taken using the He-Ne laser at the 632.8 nm irradiation. The spectral region between 2800 and 1800 cm^{-1} was omitted due to the lack of any information.

It has been admitted that the colloidal conditions for Ag, Au, and Cu nanoparticle solutions may be not be adequate to discuss the tautomerism of cytosine. For instance it seems difficult to discuss the stability of the zwitter ionic conformers in aqueous solutions without considering the solvation effect. To compare better the differences in the SERS spectra, we have obtained the SERS spectra on Ag, Au, and Cu plates after drying the solution as listed in Figure 2. Their peak positions are also listed in Table 1. It was found that the SERS spectra on the plates appeared to be somewhat different from those on the nanoparticles, indicating that the stability of the tautomers could change depending on the medium conditions.

Regarding the adsorbate orientation on the surfaces, as shown in Figure 1, it is noteworthy that the ring C-H stretching bands were identified at ~3060 cm^{-1}, albeit weakly, in the Ag, Au, and Cu SERS spectra. It has been well documented in the literature that the presence of the ring C-H stretching band in an SERS spectrum is indicative of a vertical (or at least tilted) orientation of the aromatic ring moiety on a metal substrate.[25-29]

The ring breathing mode in the OR spectrum exhibited neither a substantial red shift nor the increase of its bandwidth as in the Ag, Au, and Cu SERS spectra shown in Figures 1 and 2. The blue shift of the ring breathing mode may indicate a rather weak interaction of the aromatic rings on the gold and silver surfaces. Neither a substantial red shift nor a significant band broadening of the ring breathing modes was observed for the case of cytosine on Ag, Au, and Cu where the molecule is assumed to have a standing orientation.[28,29]

Since an unequivocal selection rule is not available for SERS, the exact tilt angle cannot be determined for cytosine at present. According to the electromagnetic (EM) theory on the SERS selection rule,[19] vibrations along the direction perpendicular to the surface are expected to be more

Table 1. Spectral Data and Vibrational Assignment of Cytosine on Ag, Au, and Cu Surfaces[a]

OR	Sol SERS			Plate SERS			Assignment[b,c,d]
	Ag	Au	Cu	Ag	Au	Cu	
	249	266	300	230	234		stretch metal-N
403							asym. bend C_2-O, C_4-NH_2 (i.p.)
443	426	433	430	472	431	421	asym. wag C_6-H, N_8-H_{10} (o.p.)
535		546	507				sym. bend C_2-O, C_4-NH_2 (i.p.)
548	559	563	565	559	564	570	def. ring (sqz group, N_3-C_4-C_5) (i.p.)
599	597	601	605		601	607	def. ring (sqz group, C_2-N_3-C_4) (i.p.)
	620	628	628	632	689	674	wag N_8-H (o.p.)
785							ring breathing (i.p.)
792	794	797	798	795	796	802	ring breathing (i.p.)
	923						asym. wag C_5-H, C_6-H (o.p.)
972		991	1008		962		def. ring (sqz group, N_1-C_6-C_5) (i.p.)
	1033	1044	1036	1037	1038	1042	sym. bend N_8-H_9, N_8-H_{10} (i.p.)
1107	1115	1107	1097			1122	asym. bend N_1-H, C_5-H (i.p.)
	1194	1196	1186	1194	1197		def. ring (str N_1-C_2, C_2-N_3) (i.p.)
1249	1233	1239	1235	1245	1243	1225	bend all H (i.p.)
1275							bend all H (i.p.)
1292	1299	1306		1308	1306	1308	bend all H (i.p.)
1363	1363	1378	1376	1360	1366	1372	sym. bend N_1-H, C_5-H, C_6-H (i.p.)
	1424	1431	1427	1421	1429		def. ring (str N_1-C_6, N_3-C_4) (i.p.)
1459				1488			sciss. NH_2, str. C_4-NH_2 (i.p.)
	1494	1503	1511	1527	1502	1557	def. ring (str C_4-C_5), bend all H (i.p.)
1605	1574	1579	1592	1600	1600	1596	def. ring (str C_5-C_6), sciss. NH_2 (i.p.)
1652	1643	1636	1640	1634	1639	1651	def. ring (str C_4-C_5), sciss. NH_2 (i.p.)
3055		3019					asym. str (C_5H, C_6H) (i.p.)
3117	3089	3076		3080	3084	3089	sym. str (C_5H, C_6H) (i.p.)
3357	3328			3328			sym. str N_8-H_9, N_8-H_{10}

[a]Spectral positions are from Figure 1 and 2. Unit in cm^{-1}. [b]Based on ref. 10. [c]Out-of-plane. [d]In-Plane.
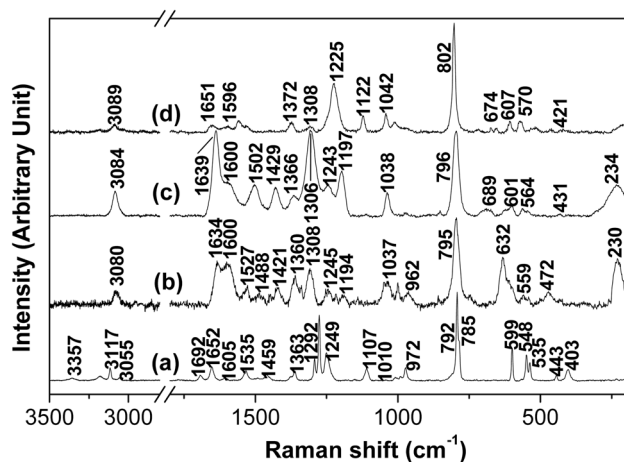

Figure 2. (a) OR spectrum of cytosine in neat solid state and SERS spectra in (b) silver, (c) gold, and (d) copper plates. All spectra were taken using the He-Ne laser at the 632.8 nm irradiation. The spectral region between 2800 and 1800 cm^{-1} was omitted due to the lack of any information.

enhanced than vibrations in the parallel direction. This rule suggested that the in-plane vibration modes should be more enhanced than the out-of-plane ones. The relative intensities have been evaluated for several vibrational modes of cytosine as summarized in Table 2. For cytosine, most ring modes were found to ascribe to the in-plane mode except the weak mode at ~430 cm^{-1}.

It was reported that the charge transfer (CT) mechanism could also significantly contribute the enhancement of the SERS intensities.[20] Although the SERS spectra feature could be roughly described by the electromagnetic (EM) mechanism, it is admitted that the CT mechanism may also contribute the SERS intensities of several vibrational bands of cytosine on Cu, Ag, and Au. In fact the different enhancement values for the same symmetry as listed in Table 2 could be better explained with a combination of the EM and CT mechanisms.

Although the band positions and intensities spectra looked somewhat comparable, the SERS spectra showed more complicated features between 1700 and 900 cm^{-1} indicating the existence of different tautomers of cytosine depending on metal substrates. The difference in the SERS spectral bands may result from the dissimilar population of the tautomers[28,29] of cytosine upon adsorption on Ag, Au, and Cu.

Also the enhancement factors are observed to be different for sols and roughened surfaces as compared in Table 2. Although most spectral features are analogous with those in the colloidal solutions, several vibrational bands showed

Table 2. Relative Enhancement Factors of SERS Bands in Cytosine Ring Modes

| Symmetry[a,b]	Vibrational Mode[c]	Enhancement Factor[d]					
		Sol			Plate		
		Ag	Au	Cu	Ag	Au	Cu
	In-Plane						
A_1	sym. bend C_2-O, C_4-NH_2 (~530 cm^{-1})		.481	.599			
α_{xx}	def. ring (N_3-C_4-C_5) (~560 cm^{-1})	.397	.558	.380	.0669	.0492	.0897
α_{yy}	def. ring (C_2-N_3-C_4) (~600 cm^{-1})	1.85	1.24	0.520		.0509	.0758
α_{zz}	ring breathing (~790 cm^{-1})	2.27	2.40	1.35	.153	.146	.244
	def. ring (N_1-C_6-C_5) (~970 cm^{-1})		1.11	2.84		.170	.562
	asym. bend N_1-H, C_5-H (~1100 cm^{-1})	1.00	1.00	1.00	1.00	1.00	1.00
	bend all H (~1240 cm^{-1})	1.19	1.15		.0839	.156	.323
	bend all H (~1290 cm^{-1})		8.98		.267	.561	.0604
	sym. bend N_1-H, C_5-H (~1370 cm^{-1})	2.30	3.79	1.43	.468	.206	.193
	def. ring (str C_4-C_5) (~1540 cm^{-1})	25.7	19.2		.283	.414	.204
	def. ring (str C_5-C_6) (~1600 cm^{-1})	25.7	19.2		2.15	1.28	.517
	sciss. NH_2 (i.p.) (~1640 cm^{-1})	4.30	31.9	8.28	.549	.980	.115
	asym. str (C_5H, C_6H) (~3040 cm^{-1})		8.35				
	asym. str (C_5H, C_6H) (~3080 cm^{-1})	1.67	2.42		.177	.317	.128
	sym. str N_8-H_9, N_8-H_{10} (~3340 cm^{-1})	2.51					
	Out-of-plane						
A_2	torsion, asym. wag C_6-H (~430 cm^{-1})[e]	1.88	6.53	1.49	.410	.0876	.135
α_{xy}							

[a]Symmetry types corresponding to the C_2 point group and numbers in atoms based on "2" tautomer. [b]Subscripts, *i.e.*, *x*, *y*, and *z*, correspond to the conventional molecular axes. [c]Based on ref. 9, 10. [d]Relative Intensity of each vibrational band (I_{SERS}/I_{OR}) and normalized with respect to the vibrational bands at ~1100 cm^{-1}. [e]Number in the parenthesis designates the frequency position in Table 1 and Figures 1 and 2.

different intensities presumably due to the dissimilar medium effects. Since the basicities of the nitrogen and oxygen atoms are different, the most stable tautomer should not be the same depending on the colloidal conditions.

For the SERS spectra on the plates, one of the most noteworthy differences in the Au SERS spectrum is a relative increase of the vibrational band at ~1640 cm^{-1} which could be ascribed to the NH_2 scissoring band. This band is found to be much weaker in Ag and Cu SERS spectra (In fact this band is quite strong on Cu nanoparticle solutions but greatly reduced on Cu plates). This result suggests that the amino group of cytosine should involve in bonding to Au for the dry plate condition in an effective way, differently from the cases on Ag and Cu.

DFT Calculation Results of Ag, Au, and Cu Metal Complexes with Tautomers of Cytosine. To check our spectral behaviors, *ab initio* calculations were performed for the gas phase cytosine of the possible six tautomers labeled to "1"~"6" as illustrated in Figure 3 and Table 3. Our notation is based on the literature from reference.[7,34] The "2" tautomer was found to be most stable in their gas phase at the level of B3LYP, whereas the "1" tautomer appeared to be more stable than the "2" tautomer by only 1.7 and 2.1 kcal/mol at the level of HF and MP2, respectively. The zwitter ionic "4" tautomer was calculated to be least stable for the gas phase presumably due to its charge repulsion as listed in Table 3.

Upon adsorption on the Ag, Au, and Cu atom, the available N_3, N_1, or amino group sites of the six tautomers of
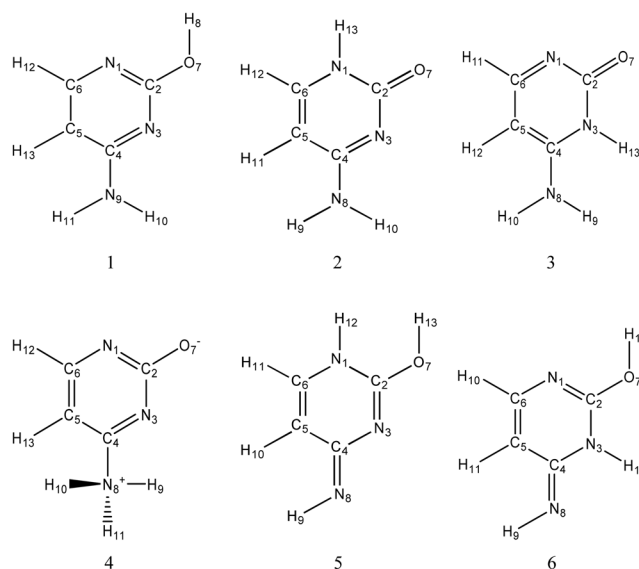

Figure 3. Tautomers of cytosine considered in this study.

cytosine was considered to check the stabilities. The geometry optimization for the tautomers of cytosine-metal complexes was carried out at the B3LYP/LanL2DZ level of theory starting from many possible structures. The geometry optimizations were converged to one structure for each tautomer even though they were started from many possible configurations. Plausible structures of Ag-cytosine, Au-cytosine, and Cu-cytosine for the amino group and N_3-

Table 3. Stabilities of the Cytosine Tautomers in the Gas Phase

Tautomer	Total Energy[a] and Relative Energy[b]		
	B3LYP	HF	MP2
1	−394.8578(6.3)	−392.6338(0.0)	−392.6296(0.0)
2	−394.8678(0.0)	−392.6311(1.7)	−392.6263(2.1)
3	−394.8562(7.2)	−392.6196(8.9)	−392.6153(9.0)
4	−394.7807(54.6)	−392.5363(61.2)	−392.5307(62.1)
5	−394.8219(28.8)	−392.5953(24.1)	−392.5895(25.2)
6	−394.8367(19.5)	−392.6110(14.3)	−392.6059(14.9)

[a]Unit: hartree, 1 hartree is 627.51 kcal/mol. [b]Values in parentheses are Energy differences (in kcal.mol) from the most stable conformer for each levels of theory
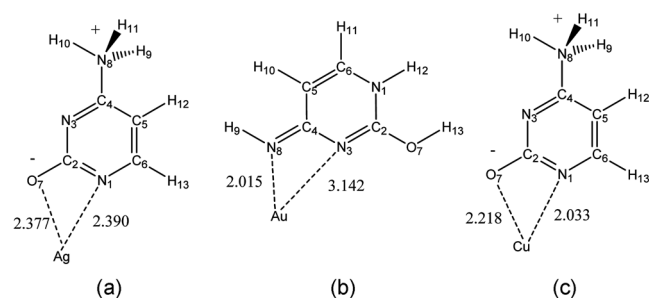
Figure 4. The plausibly most stable structures of cytosine with (a) Ag, (b) Au, and (c) Cu atom.

coordinated or N_1-coordinated tautomers are drawn in Figure 4 with their optimized geometric variables. The calculated energy values are summarized in Table 4.

In the previous SERS study of 1,5-dimethylcytosine, the binding energy via the N_3 atom with the metals is estimated to be in the order of Cu > Au > Ag.[16] As listed in Table 4, the binding energies of Ag for the N_3-coordinated tautomer are calculated to be smaller than those of Cu and Au in line with the previous experiments on 1,5-dimethylcytosine.[16]

It is noteworthy that the N_3-coordinated site for the "5" tautomer was calculated to be most stable on Au, whereas the N_1-coordinated site of the zwitter ionic "4" tautomer appeared to be most favorable on Cu and Ag. Our results suggest that the N_3-coordinated tautomer could exist on Au as evidenced in Raman spectra of Figures 1 and 2. Also it has to be mentioned that the metal can coordinate to cytosine as a bindentate fashion through the nitrogen atom of pyrimidine and the nitrogen or oxygen atom from the amino or hydroxyl group, respectively. Our calculations indicated that the amino group and N_3-coordinated tautomer appeared to be favored on Au than on Cu and Ag. Invoking that Cu and Ag are more easily oxidized than Au, it is expected that the oxygen atom would have a tendency to get close to Cu and Ag than to Au.

Table 4. Stabilities of the N_3- and N_1-coordinated Cytosine Tautomer Complexes with Ag, Au, and Cu Atoms from the DFT Calculation[a]

Tautomer	Coordination	A:(Cyt-M)	B:(Cyt(G)-M)	C:(Cyt-M(G))	$BE_{A-(B+C)}$[b]
			Ag		
1	N1	−540.3112	−145.4741	−394.7584	−0.0787 (−49.4)
1	N3	−540.3265	−145.4741	−394.7593	−0.0931 (−58.4)
2	N3	−540.3516	−145.4741	−394.7673	−0.1102 (−69.1)
3	N1	−540.3456	−145.4741	−394.7563	−0.1152 (−72.3)
4	N1	−540.2880	−145.4741	−394.6821	−0.1318 (−82.7)
4	N3	−540.2715	−145.4740	−394.6805	−0.1170 (−73.4)
5	N3	−540.3225	−145.4740	−394.7235	−0.1250 (−78.4)
6	N1	−540.2822	−145.4741	−394.7374	−0.0707 (−44.3)
			Au		
1	N1	−529.9745	−135.0939	−394.7565	−0.1242 (−77.9)
1	N3	−529.9821	−135.0939	−394.7580	−0.1302 (−81.7)
2	N3	−530.0037	−135.0939	−394.7671	−0.1426 (−89.5)
3	N1	−530.0004	−135.0939	−394.7563	−0.1502 (−94.2)
4	N1	−529.9417	−135.0939	−394.6825	−0.1653 (−103.7)
4	N3	−529.9129	−135.0939	−394.6801	−0.1389 (−87.2)
5	N3	−529.9855	−135.0938	−394.7215	−0.1702 (−106.8)
6	N1	−529.9434	−135.0939	−394.7355	−0.1140 (−71.6)
			Cu		
1	N1	−590.6931	−195.8292	−394.7581	−0.1058 (−66.4)
1	N3	−590.7066	−195.8292	−394.7580	−0.1193 (−74.9)
2	N3	−590.7335	−195.8292	−394.7654	−0.1389 (−87.2)
3	N1	−590.7264	−195.8292	−394.7553	−0.1419 (−89.0)
4	N1	−590.6700	−195.8292	−394.6805	−0.1603 (−100.6)
4	N3	−590.6543	−195.8292	−394.6796	−0.1455 (−91.3)
5	N3	−590.7058	−195.8292	−394.7231	−0.1535 (−96.3)
6	N1	−590.6640	−195.8292	−394.7370	−0.0978 (−61.3)

[a]B3LYP/LANL2DZ. Abbreviations: Cyt: Cytosine, M: Metal, G: Ghost atom, BE: Binding Energy. The shaded rows are the most stable tautomer for each metal. Zero-point energy and BSSE corrections are considered. [b]Energy unit (a.u. hartree). Number in the parethesis indicates the binding energy in Kcal/mol.
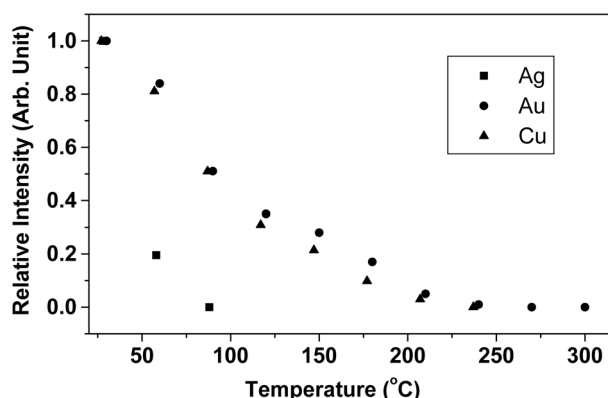
Figure 5. Plot of the intensities of the ring breathing modes at ~790 cm^{-1} as a function of temperature on Ag (■), Au (●), and Cu (▲).

Although the stableness of the amino group and N$_3$-coordinated tautomer on Au is not well understood, it can cause different spectral features from those on Cu or Ag as revealed in Figures 1 and 2. Different spectral features on Au could be ascribed to the amino group and N$_3$-coordinated tautomer. On the other hand, almost all the SERS bands could be expected to the N$_1$-coordianted tautomer for Ag and Cu as referenced from Table 4.

Our DFT calculations also indicated that the energetic difference of the tautomers should be different depending on the metals. For the most stable tautomer for each metal, the metal-N bond distance was calculated to be shorter for Au (2.015 Å) and Cu (2.033 Å) than Ag (2.390 Å). This should result in the lower desorption temperature of cytosine on Ag than on Au or Cu.

Figure 5 shows a plot of the intensities of the ring breathing modes at ~790 cm^{-1} as a function of temperature between 20 and 300 $^{\circ}$C. To estimate the SERS intensity changes depending on the temperature, the ring breathing modes at ~790 cm^{-1} was chosen as a reference. The peak heights of the ring breathing modes at ~790 cm^{-1} were measured at each temperature. The intensities are normalized with respect to those at room temperature for Ag, Au, and Cu. Decrease in vibrational intensity for the ring breathing modes at *ca*. 790 cm^{-1} was measured in increasing temperature. As illustrated in Figure 5, the desorption temperatures of Au and Cu appeared to be about the same, whereas that on Ag was found to be much lower. This result indicates that the binding energy of cytosine on Ag should be smaller than those on Au and Cu as in line with the calculated energies in Table 4. The largest binding energies of Ag, Au, and Cu atoms among various tautomers are calculated to be −82.7, −106.8 and −100.6 Kcal/mol, respectively, in consistent with the experimental results. Energetic or kinetic factors may also result in different adsorption behaviors on Ag, Au, and Cu. It has to be admitted that the computational model used is a complex between the cytosine and a single metal atom, which may not be adequate for the phenomenon under investigation concerns cytosine adsorbed to Cu, Ag, and Au surfaces. We plan to choose a suitable multiple atom cluster with a consideration of the solvation effect in future. Our study shall be helpful to understand the interaction of pyrimidine bases and metals.

Summary and Conclusions

The SERS spectral evidence in silver, gold, and copper surfaces indicated that the population of cytosine tautomers should be different depending on metal surfaces and substrate conditions. Our DFT calculations indicated that the energetic difference of the tautomers on gold should be different than those on silver or copper as well as those in the gas phase. On Ag and Cu, the N$_1$-coordinated zwitter ionic form was found to be the most stable. The metal-N bond distance was calculated to be shorter for Au and Cu than Ag. This should result in the lower desorption temperature of cytosine on Ag than on Au or Cu.

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