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Negatively Charged Xanthine. I. Anions Formed by Canonical Isomers[†]

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The possibility of an excess electron binding to canonical isomers of xanthine in the gas phase was studied at the coupled-cluster level with single and double excitations using the 6-31++G** basis sets supplemented with the 4(sp)3d set of diffuse functions. It was found that xanthine should exist in the gas phase as one canonical tautomer while all the other tautomers are not likely to be detected experimentally because of their significant thermodynamic instability. On the other hand, all canonical tautomers (except one) were found to be capable of forming electronically stable anionic states of dipole-bound nature. However, the only thermodynamically stable anion (with vertical electron binding energy estimated to be 0.041 eV) based on xanthine tautomers is the one supported by the most stable neutral species.

1. Introduction

The biological importance of DNA bases has motivated a number of experimental and theoretical studies on these molecules in the past decade.[1] In particular, the electron affinities of nucleic acid bases were studied by using ab initio theoretical methods (primarily by Adamowicz and co-workers), which led to the observation that most of them are capable of supporting weakly bound molecular anions in the gas phase.[2−5] Such anions have been detected using photoelectron spectroscopy and Rydberg electron transfer spectroscopy. Spectroscopic electron affinities (EAs) of nucleic acid bases were measured (e.g., by Bowen's and Schermann's groups) and found to be in relatively good agreement with those predicted theoretically.[6−8] An excellent review article describing the ongoing effort to determine the EA values of nucleic acid bases has been recently published by Smith and Adamowicz.[9]

It is known that the number of different DNA bases involved in biochemical and biological processes is rather large, and properties of many of them were not properly analyzed by reliable nonempirical methods until now. Also, the experimental data on these bases are quite incomplete or in many cases not available.

In the present work, we report the ab initio study on one of the oxopurines, xanthine (see Figure 1), whose biological importance is caused by its role in purine metabolism (as an intermediate product formed by degradation of nucleic acids). Xanthine (3,7-dihydro-1*H*-purine-2,6-dione) is a purine base which is not common in ribonucleic acid or deoxyrybonucleic acid. However, the deamination process of guanine results in the xanthine base. Xanthine is still able to pair with cytosine by two hydrogens;[10] moreover, as an intermediate product in purine catabolism, hypoxanthine is oxidized to xanthine and eventually to uric acid in man (see Figure 2).

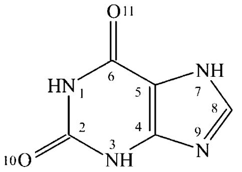

Figure 1. Schematic representation of xanthine molecule.

The conversion of hypoxanthine to xanthine is catalyzed by xanthine oxidase. Defects in purine metabolism result in an increase of the uric acid level and in the deposition of sodium hydrogen urate monohydrate crystals in joints. This disease, known as gout, is clinically treated by allopurinol.[11−13]

Xanthine base may exist in 14 tautomeric forms. Possible tautomers are the effects of either keto ↔ enol tautomerism or proton exchange among the in-ring nitrogen atoms. There are a number of publications available devoted to experimental and theoretical studies on the tautomerism of xanthine. Some data suggest a similar stability for the two dioxo species in aqua solution.[1] This conclusion was support by the results of UV and NMR measurements.[14−16] On the other hand, X-ray experiments show that the sodium salt of xanthine is found mainly in the N(9)H dioxo tautomeric form in the solid state[17] (see Figure 1 for atom numbering). On the basis of both semiempirical (employing CNDO method) and ab initio calculations, it was also predicted that the N(7)H dioxo tautomeric form of xanthine is energetically favored over the N(9)H tautomer in the gas phase.[18,19] Civcir studied tautomerism of xanthine in the gas phase and aqueous solution and found, using AM1 and PM3 semiempirical methods, that the most stable tautomers of xanthine are dioxo N(7)H and N(9)H forms.[10] Even though the number of experiments and theoretical studies on xanthine reported in the scientific literature is relatively large, it is surprising that, to the best of our knowledge, there have been no publications dealing with the possibility of an excess electron binding to xanthine base published in the literature thus far.

Therefore, the main goal of our present work is to provide information lacking in the literature about excess electron binding to various tautomers of xanthine. Since the parent neutral molecules often determine the nature of their corresponding anionic daughters, we first study the most stable

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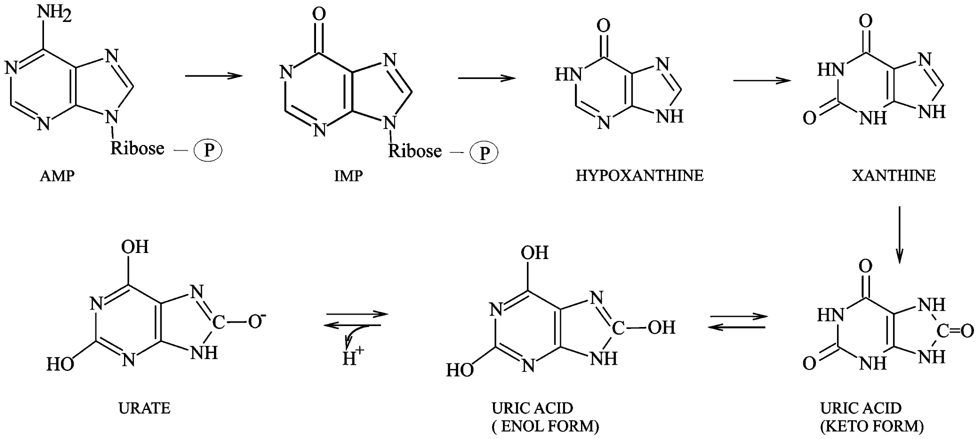

Figure 2. Adenosine-5′-monophosphate decomposition resulting in the uric acid.

neutral tautomers of xanthine. In particular, by using ab initio Hartree−Fock, second-order Møller−Plesset perturbation theory, and coupled cluster methods, we examine the lowest-energy canonical tautomers of xanthine, and we investigate the possibilty of forming electronically stable anions.

2. Methods

We first studied the ground-state potential energy surface of the neutral and anionic tautomers of xanthine at the second-order Møller−Plesset perturbation theory (MP2) level.[20] Because the methods used are based on an unresticted Hartree−Fock (UHF) starting point, it is important to make sure that little, if any, artificial spin contamination enters into the final wave functions. We computed the expectation value $\langle S^2\rangle$ for species studied in this work and found values of 0.7500−0.7502 in all anion cases. Hence, we are certain that spin contamination is not large enough to affect our findings.

The electron binding energies (D) were calculated using a supermolecular approach (i.e., by subtracting the energies of the anion from those of the neutral). This approach requires the use of size-extensive methods for which we have employed Møller−Plesset perturbation theory up to the fourth order (MP$_n$ ($n = 2, 3, 4$)) and the coupled-cluster method with single and double excitations (CCSD).[21] In addition, the electron binding energy D was analyzed within the perturbation framework designed for dipole-bound anions and solvated electrons described previously by Gutowski and Skurski.[22]

The simplest theoretical aproach to estimate D is based on Koopmans' theorem (KT). The KT binding energy (D^{KT}) is the negative of the energy of the relevant unfilled orbital obtained from a Hartree−Fock self-consistent field (SCF) calculation on the neutral molecule. This is a static approximation to D, which neglects both orbital relaxation and electron correlation effects. These effects were taken into account by performing SCF and CCSD calculations for the neutral and the anion. The polarization of the neutral host (N) by the excess electron and the effect of back-polarization are taken into account when the SCF calculation is performed for the anion (A), and accompanying induction effects on D are given by

$$\Delta D_{\mathrm{ind}}^{\mathrm{SCF}} = D^{\mathrm{SCF}} - D^{\mathrm{KT}}$$

where

$$D^{\mathrm{SCF}} = E_{\mathrm{N}}^{\mathrm{SCF}} - E_{\mathrm{A}}^{\mathrm{SCF}}$$

and $E_{\mathrm{N}}^{\mathrm{SCF}}$ and $E_{\mathrm{A}}^{\mathrm{SCF}}$ stand for the SCF energies of the neutral and the anion, respectively.

The dispersion interaction between the loosely bound electron (lbe) and N was extracted from the MP2 contribution to D. The dispersion term is a second-order correction with respect to the fluctuation-interaction operator, and it is approximated here by $\Delta D_{\mathrm{disp}}^{\mathrm{MP2}}$, which takes into account proper permutational symmetry for all electrons in the anion

$$\epsilon_{\mathrm{disp}}^{(02)} \approx \sum_{a\in N}\sum_{r<s} \frac{|\langle \phi_{\mathrm{a}}\phi_{\mathrm{lbe}}||\phi_r\phi_s\rangle|^2}{e_{\mathrm{a}} + e_{\mathrm{lbe}} - e_r - e_s} = -\Delta D_{\mathrm{disp}}^{\mathrm{MP2}}$$

where ϕ_{a} and ϕ_{lbe} are spin−orbitals occupied in the unresticted Hartree−Fock anion wave function, ϕ_r and ϕ_s are unoccupied orbitals, and the e's are the corresponding orbital energies. The subscript lbe denotes the dipole-bound electron's spin−orbital.

The total MP2 contribution to D, defined as

$$\Delta D^{\mathrm{MP2}} = D^{\mathrm{MP2}} - D^{\mathrm{SCF}}$$

is naturally split into dispersion and nondispersion terms

$$\Delta D^{\mathrm{MP2}} = \Delta D_{\mathrm{disp}}^{\mathrm{MP2}} + \Delta D_{\mathrm{no-disp}}^{\mathrm{MP2}}$$

with the latter dominated by the correlation correction to the static Coulomb interaction between the loosely bound electron and the charge distribution of N.

The higher-order MP contributions to D are defined as

$$\Delta D^{\mathrm{MP}n} = D^{\mathrm{MP}n} - D^{\mathrm{MP}(n-1)} \quad (\text{for } n = 3, 4)$$

Finally, the contributions to D beyond the fourth order are estimated by subtracting MP4 results from those obtained at the CCSD level.

$$\Delta D^{\mathrm{CCSD}} = D^{\mathrm{CCSD}} - D^{\mathrm{MP4}}$$

For convenience, we also introduce the ΔD^{HTSO} symbol, which represents the correction to D obtained at the higher-than-second-order (HTSO) level. In particular, the HTSO term is given as

$$\Delta D^{\mathrm{HTSO}} = D^{\mathrm{CCSD}} - D^{\mathrm{MP2}}$$

The diffuse character of the orbital describing the loosely bound electron necessitates the use of extra diffuse basis functions with very low exponents.[23] In addition, the basis set chosen to describe the neutral molecular host should be flexible enough to (i) accurately describe the static charge distribution of neutral and (ii) allow for polarization and dispersion stabilization of the anion upon electron attachment. The geometry optimization calculations and the vibrational frequency calculations were performed with the 6-31++G** basis sets,[24,25] whereas the evaluation of the electron binding energies was performed with the 6-31++G** basis set supplemented with a 4(sp)3d set of diffuse functions centered on one of the atoms in the vicinity of the positive end of the molecular dipole. The extra diffuse functions share exponent values, and we used even-tempered[26] four-term sp and three-term d basis sets. The geometric progression ratio was equal to 5.0 (as described in ref 27), and, for each symmetry, we started to build up the exponents of the extra diffuse functions from the lowest exponent of the same symmetry included 6-31++G** basis set designed for carbon. As a consequence, we achieved the lowest exponents of 0.7008×10^{-5} for the sp symmetry and 0.6400×10^{-2} for the d symmetry.

All calculations were performed with the *Gaussian 98* package,[28] while the three-dimensional plots of molecular orbitals were generated with the MOLDEN program.[29]

3. Neutral Species

3.1. Relative Energies. We focused our investigation of the ground-state potential energy surface (PES) of xanthine neutral tautomers on finding the structure corresponding to the global minimum. Xanthine in its canonical form may exist in 14 tautomeric forms, which are shown in Figure 3.

In Table 1,we collected the CCSD relative energies and the SCF and MP2 dipole moments for the neutral xanthine tautomers studied in this work. The earlier papers[10] predicted that xanthine exists in the gas phase as a mixture of two diketo tautomers (see structures **1** and **3** in Figure 3). In contrast to those findings, our results gathered in Table 1 support the conclusion that xanthine can be found in the gas phase primarily as tautomer **1**. Since **1** is definitely the lowest-energy neutral species and the next (in the energy scale) tautomer **2** was found to be 0.34662 eV (ca. 8 kcal/mol) higher, we are reasonably confident that isomer **1** should dominate when solvent is not present (see Table 1). There are also two more structures that might be present (in much smaller amount) in the gas phase, namely, tautomers **2** and **3**. Their energies span the 0.34662−0.37797 eV range (see Table 1), with respect to the global minimum **1**. It should also be mentioned that, structurally, tautomer **1** (existing as a diketo form) contains the hydrogen atom attached to nitrogen (N7) of imidazolic ring and is 0.37797 eV more stable than another diketo tautomer **3** in which the H is connected to the N9 atom. Clearly, the tautomerism between the N7 and N9 positions favors the N7 form, which is in disagreement with the previous findings.[10]

The results collected in Table 1 show that the energies of most tautomers arrange in pairs (e.g., **2**/**3**, **5**/**6**, **8**/**9**, and **10**/**11**). The corresponding energy differences (between the two tautomers in each pair) are 0.031, 0.005, 0.008, and 0.022 eV, respectively. The energy difference between tautomers **2** and **3** is likely due to increased repulsion between the hydrogen atoms bound to N3 and N9 atoms in the latter form. As a result, structure **3** possesses higher energy than structure **2**, despite the fact that tautomer **3** is a dioxo (diketo) form, which is favorable. In the case of **8**/**9** and **10**/**11** pairs, the absence of H(N7)−H(N9) repulsion favors tautomers **8** and **10**, respectively. In addition, tautomerism between H(N1) and H(N3) structures (see Figure 1) of the imidazolic ring clearly favors protonation (hydrogenation) of the former site. For example, isomers **2** and **10** differ only by the location of one H atom (which is connected to the N1 site in species **2** and to the N3 site in species **10**); see Figure 3. Despite such a small structural difference, tautomer **10** is

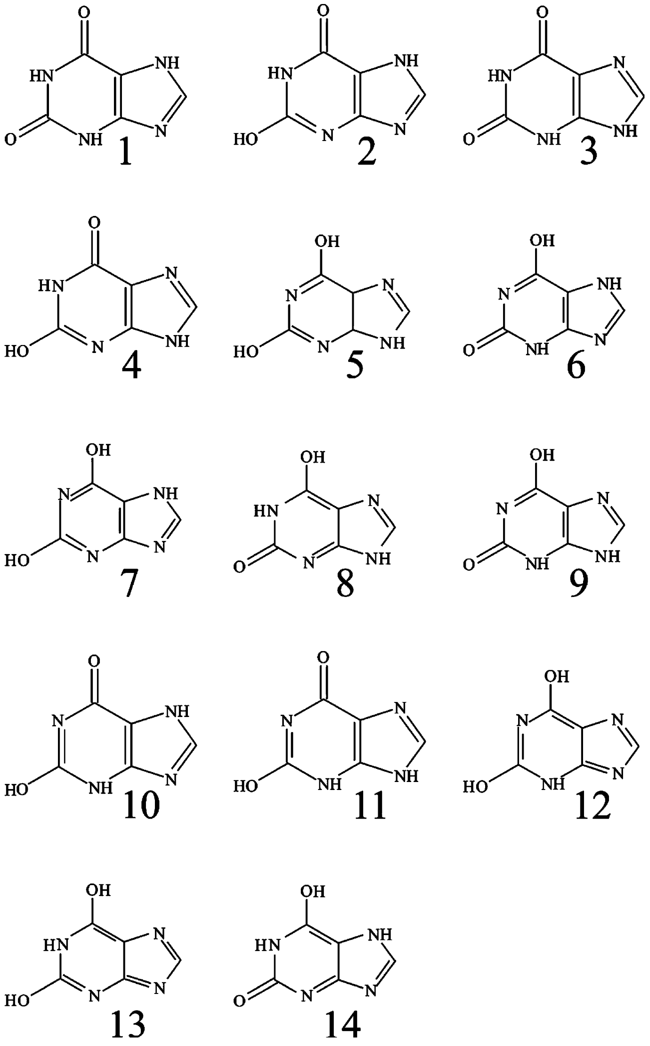

Figure 3. Schematic representations of 14 canonical xanthine tautomers.

TABLE 1: Relative Energies (with respect to the lowest-energy neutral isomer 1 whose energy was taken as 0) in electron volts, and the SCF and MP2 Dipole Moments μ (in debye) of the Neutral Canonical Xanthine Tautomers Studied in This Work[a]

species	relative energy	μ^{SCF}	μ^{MP2}	species	relative energy
1	0[b]	5.1650	4.3140	**1**$^-$	−0.04069
2	0.34662	0.6449	0.8860	**2**$^-$	unstable
3	0.37797	8.1860	7.4113	**3**$^-$	0.11395
4	0.66406	4.8222	4.1589	**4**$^-$	0.75544
5	0.71752	6.1302	6.1666	**5**$^-$	0.71752
6	0.72295	8.0302	6.8486	**6**$^-$	0.61429
7	0.85402	6.7614	6.5540	**7**$^-$	0.78372
8	0.94552	6.7875	5.8907	**8**$^-$	0.89899
9	0.95355	7.2507	6.5555	**9**$^-$	0.73049
10	1.14617	6.9620	5.8877	**10**$^-$	1.06587
11	1.16858	10.5313	9.6144	**11**$^-$	0.85867
12	1.24650	6.7033	6.1979	**12**$^-$	1.15144
13	1.34603	5.4328	5.3602	**13**$^-$	1.29150
14	1.51763	10.9550	10.1708	**14**$^-$	1.23771

[a] Relative energies (in eV) of the corresponding stable anionic daughters (also with respect to neutral tautomer **1**) are given in the last column. [a] The energy of the most stable neutral xanthine tautomer **1** is −560.940 247 7 au (as calculated at the CCSD/6-31++G**+4(sp)3d level).

higher in energy by 0.800 eV (ca. 18 kcal/mol) (see Table 1), which supports this conclusion.

It should also be stressed that tautomer **1** is in fact the only thermodynamically stable neutral species. This means that any possible process (such as isomerization or fragmentation of **1**) would lead to the species possessing higher energy. However, in the gas phase, the barriers for H^+ transfer are likely to be rather high, and in such a case, each isomer can be considered a stable gas-phase species because it would require a long time to rearrange. In addition, one needs to be aware of the fact that the presence of water can assist H^+ migration, and thus, in solution most xanthine tautomers can likely be quite easily transformed from one to another.

We are aware of the fact that our predictions considering the relative stability of the canonical xanthine isomers (tautomers) in the gas phase are not final, since they have been formulated on the basis of the relatively modest level of theory (i.e., single-point CCSD energies at the MP2 stationary point structures). However, we would like to stress that it was not our goal to perform any detailed study of that given potential energy surface but to explore the possibility of forming electronically stable anions by various xanthine isomers. Although we believe that our results for neutral species allow us to conclude that in the gas phase xanthine exists primarily as tautomer **1**, whereas other isomers (especially **2** and **3**) might also be present at elevated temperatures.

3.2. Polarity of the Neutral Species. The focus of this work is to determine the possibility of forming electronically stable anionic states supported by various xanthine tautomers. For this reason, we consider the polarity of the neutral xanthine tautomers, manifested by their dipole moments, as a very important feature, because we expect (on the basis of our experience) that these species can form so-called dipole-bound anions. It should also be stressed that we first excluded (on the basis of our preliminary calculations) the possibility of forming electronically stable valence-bound anionic states. This finding is not surprising, because the neutral xanthine molecule is a closed-shell saturated system (i.e., containing no vacant or half-filled molecular orbitals); thus, one would not expect it to support stable valence-bound anions.

Since it is known that a neutral closed-shell molecule possessing a dipole moment larger than 2.5−3 D is capable of forming electronically stable anions,[30] we analyze the polarity of the tautomers studied in this work by judging their ability to support such states. The calculated dipole moment for the most stable tautomer of xanthine is 4.314 D (as calculated from the MP2 charge density; see Table 1). Thus, tautomer **1** is expected to form an electronically stable anionic state of dipole-bound nature. By contrast, tautomer **2** possesses the dipole moment of 0.886 D that is too small to support such an anionic state. The other tautomers are more polar, having dipole moments in the 4.1589−10.1708 D range (see Table 1). In each of these cases, an electronically stable molecular anion can be formed, as is discussed later in this work. In particular, tautomers **11** and **14** are expected to bind an extra electron strongly, because of their significant dipole moments calculated to be 9.614 and 10.171 D, respectively.

It is worth mentioning that among all canonical xanthine tautomers only four of them (**5**, **7**, **12**, and **13**) possess two −OH groups (in positions 2 and 6 in each case; see Figures 1 and 3). Interestingly, the presence of two such groups in those positions leads to a similar charge distribution in these neutral species, manifested by their similar dipole moment values. Indeed, the dipole moments calculated for tautomers **5**, **7**, **12**, and **13** span the relatively narrow 5.360−6.554 D range (see Table 1).

TABLE 2: Vertical Electron Binding Energies and the Partial Contributions to *D* (in eV) for the Anionic Xanthine Tautomers Calculated at the KT, MP2, and CCSD Levels with the 6-31++G+4(sp)3d Basis Sets**

species	D^{KT}	ΔD^{SCF}_{ind}	ΔD^{MP2}_{disp}	$\Delta D^{MP2}_{no-disp}$	ΔD^{HTSO}	D^{CCSD}
$\mathbf{1}^-$	0.0150	0.0036	0.0255	−0.0191	0.0157	0.0407
$\mathbf{3}^-$	0.1429	0.0410	0.1284	−0.0654	0.0170	0.2640
$\mathbf{4}^-$	0.0054	0.0040	0.0139	−0.0064	0.0384	0.0517
$\mathbf{5}^-$	0.0297	0.0067	0.0366	−0.0139	0.0133	0.0723
$\mathbf{6}^-$	0.0577	0.0129	0.0574	−0.0401	0.0208	0.1087
$\mathbf{7}^-$	0.0245	0.0036	0.0293	−0.0060	0.0189	0.0703
$\mathbf{8}^-$	0.0201	0.0030	0.0246	−0.0170	0.0157	0.0465
$\mathbf{9}^-$	0.1099	0.0340	0.1125	−0.0507	0.0174	0.2231
$\mathbf{10}^-$	0.0248	0.0038	0.0421	−0.0233	0.0329	0.0803
$\mathbf{11}^-$	0.1633	0.0726	0.1291	−0.0692	0.0142	0.3099
$\mathbf{12}^-$	0.0362	0.0077	0.0444	−0.0181	0.0249	0.0951
$\mathbf{13}^-$	0.0117	0.0020	0.0198	−0.0035	0.0246	0.0545
$\mathbf{14}^-$	0.1255	0.0208	0.1159	−0.0243	0.0422	0.2800

4. Anionic Species

4.1. Relative Energies. Having identified isomers (tautomers) **1**−**14** of neutral xanthine, we move on to the discussion of the various anions that can be formed by these species. To the best of our knowledge, the existence of electronically stable anionic states supported by xanthine tautomers has not been described in the literature thus far. We verified that all but one (i.e., tautomer **2**) canonical xanthine structures are capable of forming stable negatively charged anions. In Table 1, the relative energies of the anionic systems are given (with respect to the neutral global minimum **1**), but only for those species that are electronically stable. As indicated in Table 1, the anion based on the second most stable neutral is not electronically stable because of the small polarity of **2** (manifested by its dipole moment of 0.886 D). Even though all the other tautomers (i.e., **1** and **3**−**14**) support bound anionic states, we found that the electron binding energies of the anions based on structures **3**−**14** are not large enough to render these anions thermodynamically stable with respect to the neutral global minimum **1** plus a free electron (see Table 1 where the relative energies for all neutral and anionic species are given). This is because the energy difference between any of the **3**−**14** neutral species and **1** is always larger than the energy lowering due to the excess electron attachment to this system (see Tables 1 and 2). For example, the energy difference between the neutral species **3** and **1** is 0.37797 eV, whereas the electron binding energy calculated for $\mathbf{3}^-$ is 0.264 eV. We observe the same situation for other tautomers. It should be noted that among all canonical xanthine tautomers only one (depicted as structure **1** in Figure 3) can form a thermodynamically stable anion.

As shown in Figure 4a and b, the molecular orbital holding the extra electron in each anionic state is localized primarily outside the molecular framework, on the positive site of the molecular dipole, which is typical for dipole-bound anions.[30]

4.2. Vertical Electron Binding Energies. We now move on to the discussion of the vertical electron binding energies (*D*) calculated for various canonical xanthine tautomers. The detailed results that are the subject of our analysis in this section are collected in Table 2. Because all the electron binding energies are calculated for the equilibrium geometries of the neutral species (rather than those of the anions), they should be considered the vertical electron attachment energies (VAEs).

In each case, the electron binding energy was partioned into incremental contributions calculated at “successive” levels of

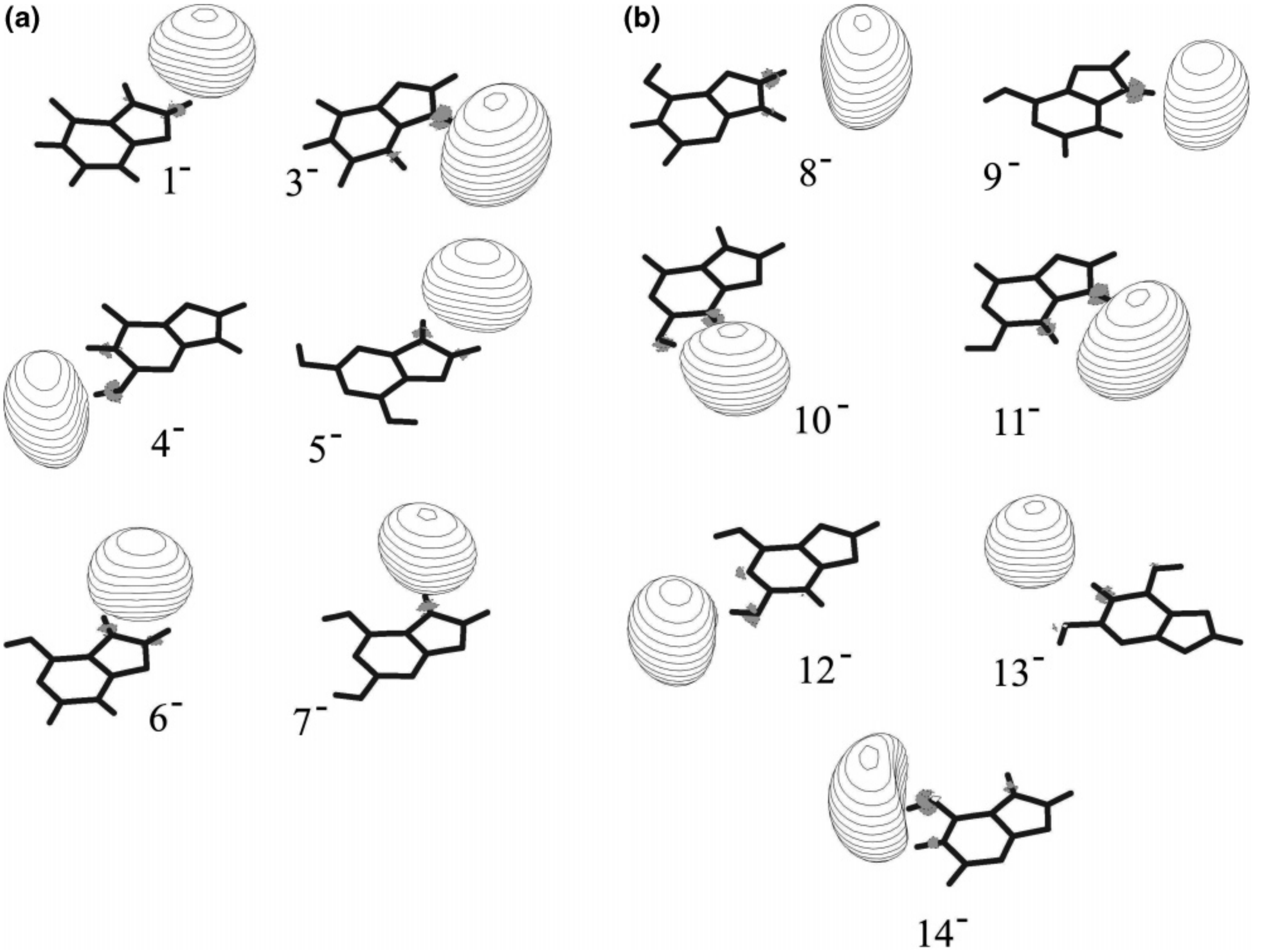

Figure 4. Singly occupied molecular orbital (SOMO) holding the excess electron in the ground electronic states of xanthine-based anions.

theory (KT, SCF, MP2, and CCSD) as disscused in section 2, and the results for all anionic xanthine species (excluding **2**$^-$, which is not electronically stable) are presented in Table 2.

In the KT approximation, the electron binding energy (given as D^{KT}) results from the electrostatic and exchange interactions of the loosely bound electron with the SCF charge distribution of the neutral molecule. For four anions (i.e., **3**$^-$, **9**$^-$, **11**$^-$, and **14**$^-$), the D^{KT} values are relatively large, exceeding 0.1 eV (namely 0.1429 eV for **3**$^-$, 0.1099 eV for **9**$^-$, 0.1633 eV for **11**$^-$, and 0.1255 eV for **14**$^-$) and responsible for ca. 50% of the total electron binding energies (see Table 2). We found the smallest relative D^{KT} contribution for **4**$^-$, for which this term is responsible for only 10% of D (with D being our best electron binding energy estimate represented as D^{CCSD} in Table 2). The relative D^{KT} contribution to the total D is the largest for the anion supported by tautomer **11** whose dipole moment (9.6144 D) is one of the largest among all neutral tautomers (only tautomer **14** is more polar and exhibits the dipole moment of 10.1708 D). On the other hand, tautomer **4** whose dipole moment is the smallest (taking into account only the neutral species supporting stable anionic states) forms an anion with the smallest (in both absolute and relative scales) D^{KT} contribution.

The SCF binding energies include orbital relaxation and thus take into account static polarization of the neutral molecule by the extra electron and the secondary effect of back-polarization. We found these contributions (which can be interpreted as orbital relaxation correction to D^{KT}, denoted $\Delta D^{SCF}{}_{ind}$) to be responsible for 4−23% of the total D (see Table 2). In particular, the largest relative $\Delta D^{SCF}{}_{ind}$ term (23% of D) corresponds to the **11**$^-$ anion, which is the most strongly bound species (i.e., whose vertical electron attachment energy is the largest). Also, other anionic species, such as **3**$^-$ and **9**$^-$, whose total electron binding energies are relatively large, follow the same pattern (see Table 2).

The contribution denoted $\Delta D^{MP2}{}_{disp}$ results from dynamical correlation between the loosely bound electron and the electrons of the neutral molecule. This stabilization is caused by quantum mechanical charge fluctuations and is responsible for more than 50% of the total D (for **1**$^-$, **5**$^-$, **6**$^-$, **8**$^-$, **9**$^-$, and **10**$^-$) and for 26−49% of the total D for other anions; see Table 2.

In addition to the dispersion interaction, other electron correlation factors may also affect the charge distribution of the neutral molecule and thus its electrostatic interaction with the extra electron. Such effects first appear at the MP2 level and are denoted $\Delta D^{MP2}{}_{no-disp}$. Taking into account all the neutral tautomers that support stable anions, we observed that, in all those cases (excluding neutral tautomer **5**), MP2 electron correlation effects reduce the dipole moment of the neutral system (see Table 1). Therefore, the value of $\Delta D^{MP2}{}_{no-disp}$ is destabilizing but always smaller than the corresponding (stabilizing) $\Delta D^{MP2}{}_{disp}$; thus, the total MP2 contribution to D remains stabilizing because of the dominant role of the dispersion component.

The contribution denoted ΔD^{HTSO} that involves all higher-than-second-order (HTSO) energy terms that are approached with the CCSD treatment seems negligible in none of the cases at hand. The inclusion of the HTSO terms is particularly important in the case of the anion supported by the neutral tautomer **4**. Indeed, for the **4**$^-$ anionic species, the ΔD^{HTSO} contribution is very large and responsible for 74% of the total value of the electron binding energy (see Table 2). Significant HTSO terms were also found for **10**$^-$ and **13**$^-$ anions for which they are covering 40−45% of the total *D*.

We are aware of the fact that the electron binding energies presented in this work are likely to be slightly underestimated, and employing a more sophisticated approach (e.g., including triple excitations in the coupled-cluster treatment) would be needed to obtain more accurate results. Unfortunately, this was not possible because of the limited computer resources available (xanthine molecule that was the target of our computational studies consists of eleven heavy atoms plus four hydrogen atoms, so using the CCSD method with the 6-31++G** basis sets supplemented with the 4(sp)3d set of diffuse functions was the best treatment we could afford).

Even though the vertical electron binding energies are quite substantial for some of the anions (taking into account their dipole-bound nature) and reaching 0.3 eV (see Table 2), it is important to note that (i) the anion based on the most stable neutral tautomer **1** is only weakly bound (possessing VAE of 0.0407 eV) and (ii) the anions that are much more strongly bound (by more than 0.25 eV) correspond to higher-energy neutral minima on the potential energy surface. Therefore, only one anion studied in this work is expected to be adiabatically stable with respect to the neutral structure **1**, despite the fact that many negatively charged species based on canonical xanthine tautomers possess substantial vertical electron binding energies. As a final remark, we conclude that it seems very likely that excess electron attachment to neutral canonical xanthine may result in forming anionic states (likely being **1**$^-$ anions) that live long enough to make their detection experimentally possible.

5. Summary

The possibility of excess electron binding to canonical xanthine tautomers in the gas phase was studied at the coupled-cluster CCSD level of theory using the 6-31++G** basis sets supplemented with the 4(sp)3d set of diffuse functions. On the basis of our ab initio calculations, we conclude the following:

(i) The lowest-energy isomer (i.e., tautomer **1**) of the neutral xanthine does not involve any OH groups, and we found it to be of diketo (dioxo) form instead.

(ii) Xanthine is expected to be found in the gas phase primarily as tautomer **1** because of the relatively large energy gap of 0.35 eV (8 kcal/mol) separating the second most stable canonical tautomer (**2**).

(iii) All but 1 of the 14 structurally possible canonical xanthine tautomers are capable of an excess electron binding and forming vertically electronically stable anionic states of dipole-bound nature.

(iv) The only adiabatically stable anionic state with respect to the neutral global minimum is the one supported by tautomer **1**. The vertical electron attachment energy for the **1**$^-$ anion was estimated to be 0.041 eV.

(v) The excess electron attachment to neutral canonical xanthine may likely result in forming anionic states (mostly supported by the lowest-energy neutral isomer **1**) that live long enough to make their detection experimentally feasible.

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