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# Adenine–Au and adenine–uracil–Au. Non-conventional hydrogen bonds of the anions and donator–acceptor properties of the neutrals

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ABSTRACT

This is a study of adenine–Au and adenine–uracil–Au (neutral, anionic and cationic), applying the B3LYP density-functional approach. In these systems, the interaction is directly related to the charge; so that as the metal atomic charge increases, the bond strength also increases. Neutral molecules are weakly bonded, the interaction in the case of cations is mainly electrostatic and in the case of the anions, the extra electron is localized on the metal atom and consequently, non-conventional hydrogen bonds are formed. In the case of adenine–Au (anion), the H dissociation energy is similar to the electron dissociation energy, and therefore both reactions may be possible. Moreover, the Au anionic atom modifies the hydrogen bonds of the uracil–adenine base pair. This may be significant in the study of point mutations that may occur in the Watson–Crick dimmer of nucleic basis. The electron-donator properties of these compounds are analyzed with the aid of the donator–acceptor map (DAM), previously described. Adenine–Au, uracil–Au and adenine–uracil–Au are more effective electron donors, but poorer electron acceptors than adenine, uracil and adenine–uracil. If the electron acceptor properties of carotenoids such as β-carotene and astaxanthin are compared, there are indications that astaxanthin may act as an oxidant instead of an antioxidant with the uracil–adenine base pair. The oxidation of nucleic acid bases by carotenoids may have important consequences, as oxidative damage of DNA and RNA appears to be linked to cancer. This is something that demands further studies and for this reason, work concerning the reactivity of carotenoids with DNA-nitrogen bases is in progress.



## 1. Introduction

The electron transfer properties of nucleic bases when they are interacting with metal atoms are very important, as it has been reported that metal atoms and ions may function as either electron donors or acceptors, increasing the electron-donor capacity of the system [1,2]. Metal atoms, interacting with the nitrogen bases of DNA may also change the hydrogen bonds, affecting the formation of the double helix structure that is essential for biological processes [3–13]. Moreover, it is well known that point mutations developed during replication of DNA and RNA may result from the occurrence of different tautomeric forms of nucleic bases [5]. In view of the fact that metal atoms and ions are able to stabilize different tautomers of the nitrogen bases and may modify the electron donor–acceptor properties of the nucleic bases, the study of the interaction of metal atoms and ions with nucleic bases is significant.

Results concerning the interaction of metal atoms and clusters with RNA and DNA-nitrogen bases have been reported previously [14–31]. Recently, Kryachko et al. [24] made a theoretical study of gold neutral clusters interacting with DNA bases and other molecules, and discussed the idea of the formation of non-conventional H-bonds. They concluded that "one of the unanchored gold atoms served as a non-conventional proton acceptor", and established that this is possible due to the charge redistribution on the gold neutral clusters. In previous works [27–30], we described non-conventional hydrogen bonds that are present when metal and nonmetal anions interact with DNA bases. Some atoms (such as Cu, Ag, Au, F, Cl, Br and I) with an extra electron have a closed-shell electronic configuration. When these anionic atoms interact with the RNA and DNA bases, the negative charge is localized on the atom and serves as a proton acceptor. With this charge redistribution, it is possible to form conventional and non-conventional hydrogen bonds and these interactions play an important role in stabilizing and destabilizing DNA and RNA base pairs. Metal and nonmetal anionic atoms not only modify the properties of the nucleic bases, but the interaction of metal anionic clusters also changes the structure of the Watson–Crick nitrogen bases pair, due to the formation of non-conventional hydrogen bonds between the gold anionic clusters ($Au_n$ with $n = 2–4$) and the adenine–uracil base pair [30,31]. The gold anionic clusters may

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dissociate the adenine–uracil base pair, so that the conventional hydrogen bonds will be strongly modified.

In spite of the existence of previous studies describing the interaction of metal atoms and clusters with DNA base pairs, this is the first time that the interaction of gold atoms and anions with the adenine and adenine–uracil base pair has been described. Notwithstanding preceding reports which have pointed to the anionic gold systems as representing the best candidates for the formation of non-conventional hydrogen bonds, it is not obvious that all molecules interacting with gold anionic systems will manifest this type of bond. This makes it crucial the analysis of systems where non-conventional hydrogen bonds can be formed. For uracil the formation of these bonds is well documented [28], but this does not mean that adenine will manifest the same behavior. Adenine is a molecule without oxygen atoms and it is also important to note that its ionization energy is lower than the corresponding value for uracil. These could be determining factors in the formation of non-conventional hydrogen bonds.

The electron donor–acceptor properties of the systems studied here are very important, since it has been reported that the oxidation of DNA is able to cause breaks in the single and double strands [32–34]. For this reason, it is interesting to analyze the electron transfer process between the molecules involved. The electron donor–acceptor properties of any molecule or complex can be analyzed using the donator–acceptor map (DAM) [35], a tool that has been successfully used in studying carotenoids [35a] and also other molecules [35b]. It appears then as relevant to perform the DAM analysis for DNA basis and the complexes formed between DNA bases interacting with gold atoms.

In summary, owing to the interesting results that we previously found concerning the structure and the dissociation energies of the uracil–Au systems on one hand, and the electron donor–acceptor properties of molecules that are considered antioxidants on the other hand, we consider important to include both subjects in the study of adenine and adenine–uracil interacting with one gold atom. In this way, there are two important aims in this work: the study of the structures and dissociation energies of adenine–Au and adenine–uracil–Au including the comparison of these results with those for uracil; and the analysis of the electron donor–acceptor properties of these systems and the relationship with the same properties for other important molecules such as carotenoids.

## 2. Computational details

Density functional theory [36–38] as implemented in *Gaussian* 03 [39] was used for all the calculations. The hybrid, three parameter B3LYP [40–42] functional was used for the calculation of complete optimizations, without symmetry constraints. Two base sets were employed: LANL2DZ [43–45] for Au, and 6–311G(d,p) [46] for C, H and N. Harmonic frequency analyses permitted us to verify optimized minima.

Previous studies show that DFT reproduces equilibrium geometries and relative stabilities with hybrid functionals, which partially include the Hartree–Fock exchange energy. These results are largely consistent with those obtained using the Møller–Plesset perturbational theory at second order and basis sets of medium quality, such as 6-31G(d,p), and cc-pVDZ [47–49]. Previous theoretical calculations had shown that the B3LYP approach is a cost-effective method for studying non-conventional hydrogen bonds with gold atoms and clusters [24]. There are reports that compare B3LYP and MP2 approaches [24c] achieving similar results at both levels of theory. Moreover, the comparison of B3LYP data with available experimental results of non-conventional hydrogen bonds which are formed in the complexes of the auride anion ($Au^{-1}$) with HF, $H_2O$ and $NH_3$ indicate that they are in very good agreement [24d].

Several initial geometries were used for the geometry optimizations including six different tautomeric forms of adenine (see Fig. 1). For the optimization of Au–adenine–uracil structures, several structures of adenine–uracil were used, with diverse bond schemes and considering different tautomeric forms of the nitrogen basis. Gold atom was bounded to all atoms of adenine and adenine–uracil isomers. Three-dimensional structures with the metal atom on the "top" of adenine and adenine–uracil molecule were also considered. Owing to the fact that an adequate number of isomers were used during the initial stage of the study, we were able to extensively explore the potential energy surface, in search of the global minimum. The number of initial geometries examined here is great enough to reliably identify the global minima. In order to compute the vertical electron detachment energies (VDE) of anionic species, further single-point calculations were required. Formation energies were calculated using zero-point corrected energies. The Au–adenine and Au–adenine–uracil compounds were considered to be at their lowest electronic state (singlets and doublets).

Although there is no universally accepted method for assigning electrostatic charges to atoms, and no experimental technique is currently available, in a previous study de Oliveira et al. [50] made a comparison of the charges obtained, using the Mulliken and Bader population analysis methods. The qualitative description of the atomic charges was the same, using either of these methods. For this reason, in this paper Mulliken atomic charges are used in the discussion of the qualitative behavior involved in the charge-transfer process. Results were analyzed, using the Molekel [51,52] and the Ball & Stick [53] packages.

A useful way of measuring electrodonating and electroaccepting power has been described by Gázquez et al. [54]. They established a simple charge-transfer model and analyzed the global response of a molecule immersed in an idealized environment in terms of ability to either withdraw or donate charge. An alternative quadratic interpolation for the energy as a function of the number of electrons was proposed, in order to evaluate the response of a molecule to charge acceptance or withdrawal, in terms of electron affinity (EA) and ionization energy (IE). Within this approximation, these authors conclude that the propensity to donate charge, or electrodonating power, may be defined as:

$$\omega^{-} = \frac{(3\mathrm{IE} + \mathrm{EA})^2}{16(\mathrm{IE} - \mathrm{EA})} \tag{1}$$

whereas the propensity to accept charge, or electroaccepting power, may be defined as

$$\omega^{+} = \frac{(IE + 3EA)^2}{16(IE - EA)} \tag{2}$$

In the case of electrodonating power, lower values imply a greater capacity for donating charge. In the case of electroaccepting power, higher values imply a greater capacity for accepting charge. It is important to note that IE and EA refer to donating or accepting one electron, whereas $\omega-$ and $\omega+$ refer to fractional charges. In this way, electrodonating and electroaccepting powers are based on a simple charge-transfer model, expressed in terms of chemical potential and hardness. Chemical potential assesses the charge flow direction together with the capacity to donate or accept charge, consigning greater emphasis to ionization energy than to the electron affinity, in terms of the charge donation process. Contrarily, electroaccepting power attributes greater significance to electron affinity than to ionization energy. Hardness indicates resistance to electron flow. In order to make a comparison with other well-known antioxidant and antireductant substances, experimental values of IE and EA for F and Na atoms were used

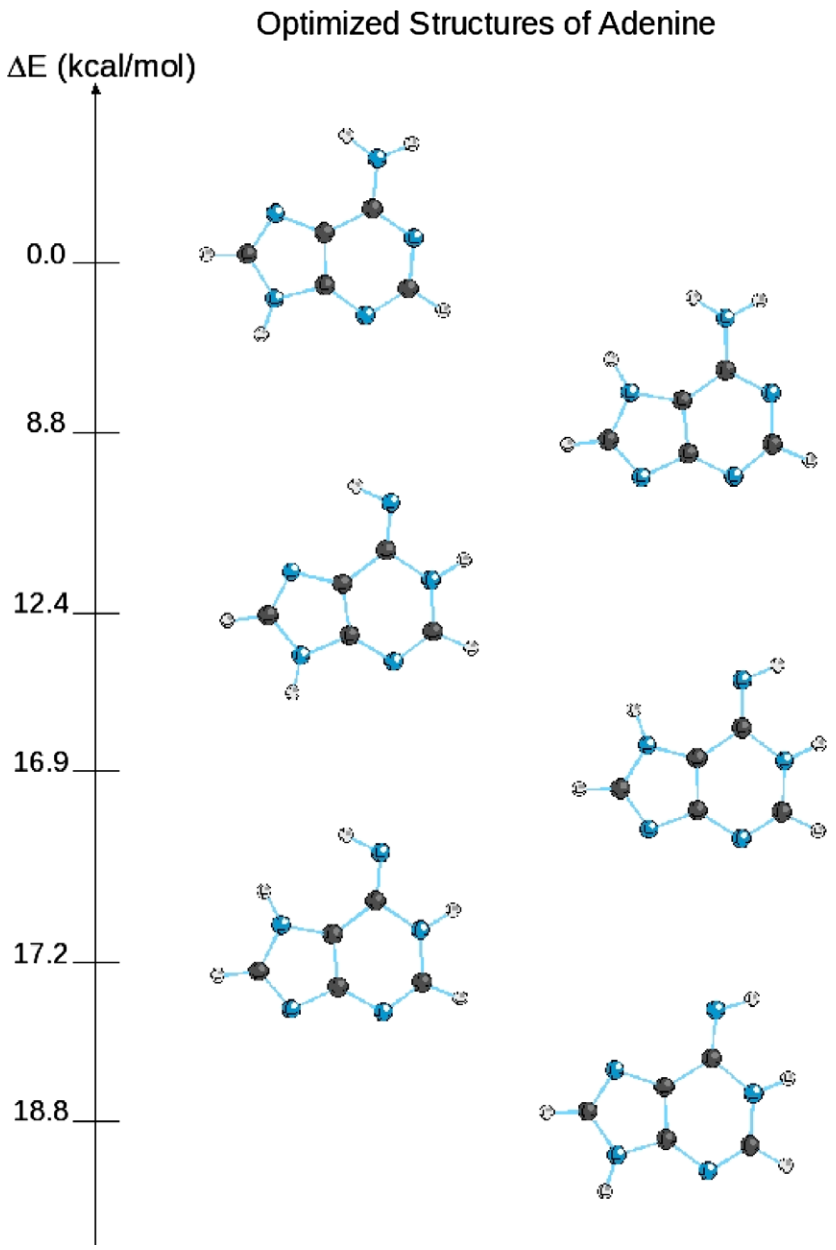


**Fig. 1.** Most stable tautomers of adenine. Energy differences (in kcal/mol) with respect to the ground state are reported. All calculations were undertaken, applying B3LYP/LANL2DZ.

to calculate the corresponding $\omega+$ and $\omega-$ values. F represents a good electron acceptor, whereas Na represents a good electron donor. For any substance L, we define an electron acceptance index as:

$$\mathrm{Ra} = \frac{\omega_L^+}{\omega_F^+} \tag{3}$$

In the same way, the electron donation index is defined as

$$\mathrm{Rd} = \frac{\omega_L^-}{\omega_{Na}^-} \tag{4}$$

For neutral, cations and di-cations, Ra and Rd were obtained using the corresponding vertical ionization energy and electron affinity.

## 3. Results and discussion

### 3.1. Isolate adenine and Au

Fig. 1 presents optimized structures for different tautomers of adenine. Energy differences when compared to the most stable structure are also presented. The ground state is represented by the Watson–Crick tautomer and other structures are shown to be less stable by more than 5 kcal/mol. Initial geometries for the optimization of adenine–Au were built up using all the tautomers presented in Fig. 1. The electron affinity (EA) and ionization energy (IE) of adenine and Au were obtained and presented in Table 1 and used to analyze the possible existence of charge transfer processes between adenine and Au. Some experimental information [55] is provided for comparative purposes. Theoretical values proved consistent with experimental results (error is less than 7%). Greater

**Table 1**
Theoretical results for the ionization energy (IE) and the electron affinity (EA) of adenine, Au and adenine–Au. Available experimental results are also shown. Values are in eV. All calculations were undertaken, applying B3LYP/LANL2DZ.

| | Theoretical results (B3LYP) | | Experimental results | |
|---|---|---|---|---|
| | IE (eV) | EA (eV) | IE (eV) | EA (eV) |
| Adenine[a] | 7.96 | −0.37 | 8.26<br>8.55 | 0.012 ± 0.005 |
| Au | 9.4 | 2.17 | 9.23 | 2.31 |
| Adenine–Au | 6.36 | 2.85 | | |

[a] Experimental values from Ref. [55].

variance is observed in the case of the EA of adenine, because this is a very small value which is very difficult to obtain. It may be observed that the IE and EA of adenine are less than the corresponding value for Au. The general description for the IE and EA of the reactants is correct, and thus these values are valid indications of possible charge transfer processes.

### 3.2. Adenine–Au (neutral, cationic and anionic)

#### 3.2.1. Stable structures

The most stable configurations of adenine–Au (neutral, cation and anion) are presented in Figs. 2–4, respectively. The gold atom has a negative atomic charge in the case of neutral and anionic systems, whereas the metal atom is positive in the case of the cations. Analyses of molecular orbital diagrams (not shown) indicate that there are no covalent interactions between metal atoms and the nucleic basis which suggests that interaction is mainly electrostatic.

In the neutral adenine–Au system, the interaction involves three atoms of the adenine but the bond lengths are greater than in the case of the ionic systems. Moreover, the negative atomic charge of the gold atom is smaller than in the case of the anion. The most stable structures for the cation are those where the positive metal atoms are bonded to the most electronegative atom of adenine, i.e. nitrogen atoms (negatively charged). The interaction is stronger than that of neutral systems, as can be inferred from

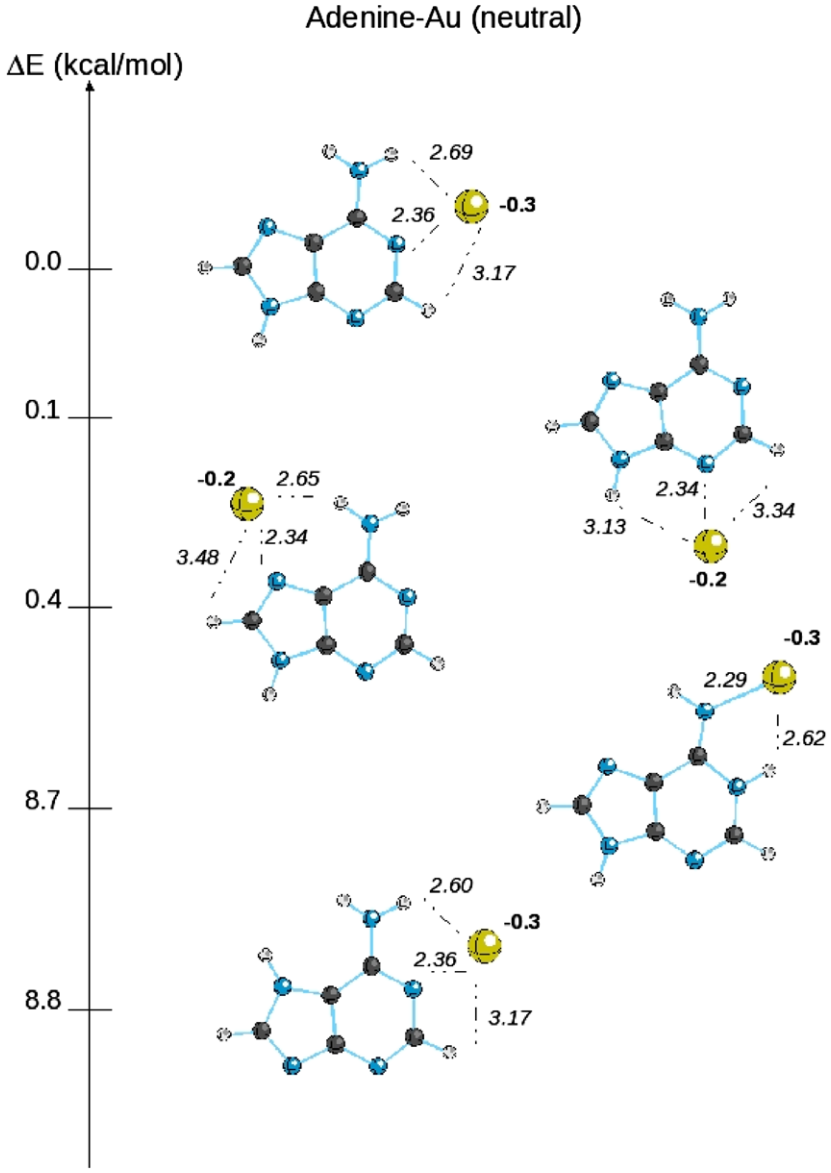


**Fig. 2.** Optimized structures of adenine–Au (neutral). Bond distances (in Å and italics) and Mulliken atomic charges (in bold letters) are reported. Energy differences with respect to the ground state are also shown. All calculations were undertaken, applying B3LYP/LANL2DZ.

the bond distances. The Au–N bond length is approximately 2.06 Å and as may be observed in Fig. 3, there are six isomers with similar energy. In the case of neutral and cations, structures exist with almost the same stability and a similar bond scheme. All of them are planar and do not always contain the most stable tautomer of the adenine molecule. The metal atom is bonded to different atoms of adenine with diverse spatial orientations. The stability order does not depend on the interaction between the metal atom and adenine. In these systems as in others [29,30], the stability order depends on the tautomer of the nuclei base which is in the compound.

In Fig. 4, it is possible to observe that there are only two stable isomers for the anion (within 10 kcal/mol from the respective ground state): one that involves the Watson–Crick tautomer and the other that includes an alternative tautomer of adenine. The interaction for these two isomers consists of that between the gold anionic atom and two positively charged hydrogen atoms of the adenine molecule. The charge distribution of the systems conforms to the EA values since the EA of the gold atom is greater than the EA of the adenine molecule (see Table 1). The gold atom has a closed-shell electronic configuration which is stable because of its extra electron, and this explains why in the case of adenine–Au (anion), the extra electron is localized on the metal atom. In this system, the bond is formed between proton donor groups (N–H) and the negative metal atom that represents a proton acceptor. The ground state of the anion has an alternative tautomer of adenine that facilitates two N–H–Au interactions. These two interactions stabilize the systems and modify the stability order of the tautomeric forms of the nucleic-bases. Kryachko and Remacle [24] reported before the following characteristics as prerequisites for a non-conventional hydrogen bonds: (i) there should be evidence of bond formation (one X–H stretching mode around 80 $cm^{-1}$); (ii) the bond has to involve one hydrogen atom which is bonded to L along the N–H bond direction; (iii) the N–H bond must be elongated in the com-

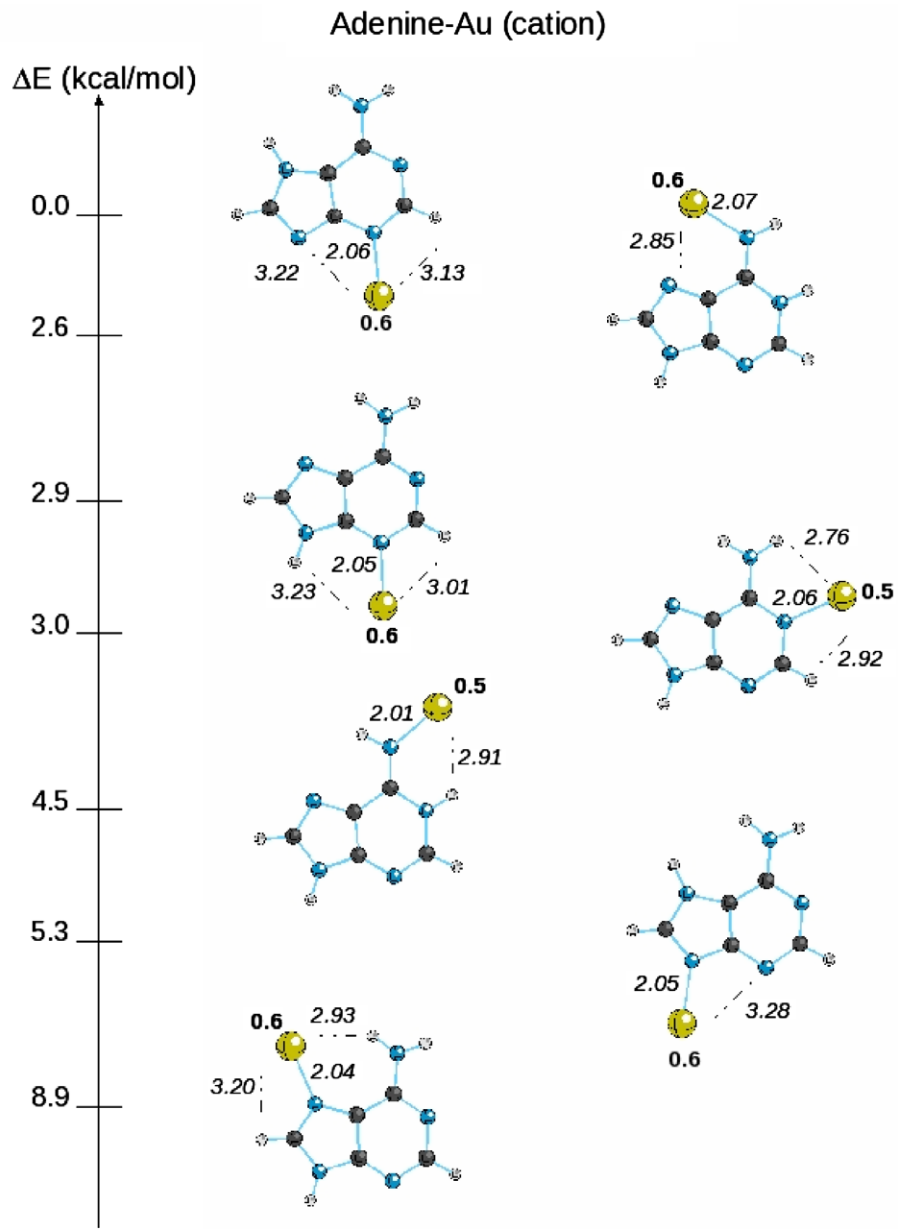


**Fig. 3.** Optimized structures of adenine–Au (cation). Bond distances (in Å and italics) and Mulliken atomic charges (in bold letters) are reported. Energy differences with respect to the ground state are also shown. All calculations were undertaken applying.

pound, relative to the isolated uracil, and; (iv) the sum of the van der Waals radii is required to be larger than the hydrogen bond distances. For the more stable isomers of adenine–Au anionic, there is evidence of bond formation (one Au–H stretching mode is found around 80 $cm^{-1}$) that involves one hydrogen atom bonded to Au along the N–H bond direction. The N–H bond elongates in the compound in comparison with the isolate adenine and the sum of the van der Waals radii (2.86 Å for H–Au) is greater than the hydrogen bond distances [2.33 Å for H–Au]. Thus it can be concluded that in this system, the orientation of the bonds is similar to that found in non-conventional hydrogen bonds.

*3.2.2. Dissociation and ionization energies (neutral and ionic systems)*

The dissociation energies, in conformity with the indicated scheme of the reaction are presented in Table 2, along with vertical detachment energies (VDE) of the anions. Previously reported results for uracil–Au (neutral and ionic) [30] are also presented for comparison.

**Table 2**
Dissociation energies (in kcal/mol) and VDE of the anion (in eV) for all the systems being studied. The dissociation energy was obtained according to the reaction scheme that is presented. All calculations were undertaken, applying B3LYP/LANL2DZ.

| System | Global Charge ($n$) | Dissociation energies (kcal/mol) | VDE of the anion (eV) |
|---|---|---|---|
| | | $[Base–Au]^n \rightarrow base + Au^n$ | |
| Uracil–Au | 0 | 4.9 | |
| | +1 | 62.0 | |
| | −1 | 24.8 | 3.8 |
| Adenine–Au | 0 | 10.3 | |
| | +1 | 80.8 | |
| | −1 | 26.1 | 3.2–3.8 |
| | | $[Adenine–Au–uracil]^n \rightarrow$ adenine + uracil + $Au^n$ | |
| Adenine–Au–uracil | −1 | 41.0 | 4.0 |

The dissociation energy of adenine–Au (neutral) is 10.3 kcal/mol. If we compare this value with the corresponding result for

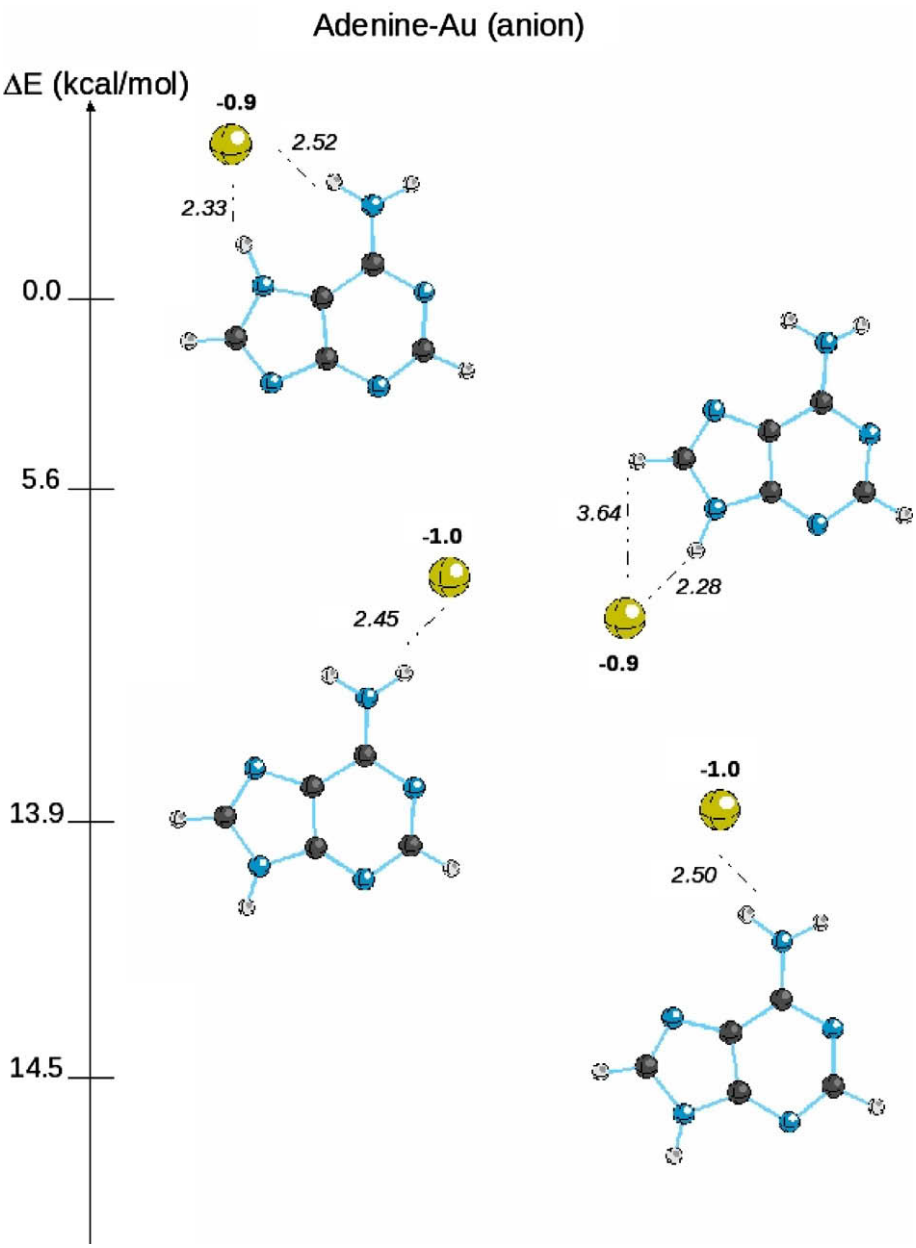


**Fig. 4.** Optimized structures of adenine–Au (anion). Bond distances (in Å and italics) and Mulliken atomic charges (in bold letters) are presented. Energy differences with respect to the ground state are also presented. All calculations were undertaken, applying B3LYP/LANL2DZ.

uracil–Au that was previously reported [30] (4.9 kcal/mol), it is possible to say that neutral adenine is weakly attracted to the neutral gold atom, but the interaction with uracil is less strong. In the case of adenine, gold atoms are interacting with three atoms (two of hydrogen and one of nitrogen), whereas uracil interacts through two atoms, a hydrogen one that is positive and an oxygen one that is negative. Due to the fact that in both cases gold atoms are negatively charged, a stronger interaction is to be expected with adenine, than with uracil. This explains why the formation energy of adenine–Au is twice the corresponding value for uracil–Au.

The values presented in Table 2 indicate a strong interaction in the ionic systems, corroborating the idea that cationic and anionic metal are more reactive than neutral gold atoms towards nucleic bases. Comparing these results with those previously described for $(\text{uracil–Au})^n$ ($n = 1$ and $-1$) it can be stated that for the ions, the bond between the metal atom and the nucleic bases (uracil or adenine) is similar and for this reason the dissociation energies are equivalent. The global charge strengthens the bond between the metal atom and the nucleic bases and consequently the interaction becomes stronger, as the charge increases. The adiabatic ionization energy of adenine–Au is reported in Table 1. As observed in the case of other systems [30], the value for adenine–Au is smaller than that for the metal atom and the isolated nucleic base. This means that the bond between Au and adenine diminishes the detachment electron energy of the neutral.

#### 3.2.3. VDE versus dehydrogenation energy

VDE values presented in Table 2 indicate that the detachment of an electron required the same energy for both of the anionic systems (uracil–Au and adenine–Au). This conforms to the atomic charge distribution, because the negative charge is localized on the metal atom in both cases and therefore similar values can be expected in the case of the VDE. Due to the fact that the negative atomic charge in the anionic Au–adenine and Au–uracil [30] is localized on the gold atom, it is possible to compare the required energy or the detachment of a single electron in these molecules, with the corresponding value for Au anionic atom. The energy required for the detachment of a single electron of the anionic Au–uracil and Au–adenine is the VDE presented in Table 2. For Au, this value corresponds with the EA presented in Table 1. As may be observed in Tables 1 and 2, VDE values for the molecules are higher than the EA of gold. This means that the bond between Au and adenine or uracil increases the amount of energy necessary for an electron to be removed from the metal anion. One possible explanation is that the negative gold atom is interacting with positive atoms of adenine and uracil, encouraging the ionization energy of the anionic systems. These results may be useful for further experiments, or have other possible applications.

As was previously reported for other systems [18,30,31] a single hydrogen atom from the DNA bases can be exchanged with the metal atom and as a consequence, a covalent bond between metal anions and nitrogen DNA bases can be formed. In order to compare the VDE values with the dehydrogenation energy, the anionic adenine–Au less a single hydrogen atom was optimized, considering the two most stable isomers presented in Fig. 4. In the most stable dehydrogenated product, the gold atom was bonded directly with one nitrogen atom of the adenine molecule and the atomic charges were redistributed. The dehydrogenation energies (4.0 and 3.8 eV for both isomers) were obtained according to the following scheme:

$$[\text{Au—adenine}]^{-1} \rightarrow [\text{Au—adenine—H}]^{-1} + \text{H}$$

As may be observed in Table 2, VDE are 3.8 and 3.2 eV for each isomer, respectively. These values are close to the detachment energy of a single hydrogen atom, and indicate that two channels can compete, the detachment of an electron and the dissociation of H from adenine. In future experiments, it seems it will be necessary to control the conditions in order to remove an electron, instead of detaching a single hydrogen atom.

### 3.3. Adenine–uracil–Au (anionic)

Anionic gold atoms have a closed-shell electronic configuration that is very stable. When the anions are formed, it is possible to have non-conventional hydrogen bonds as has been explained previously in this paper and in others. On the other hand, it is well known that canonical Watson–Crick complementary bases adenine–uracil contribute to the major structural motifs of various functional RNA molecules. However it has also been reported that many RNA base–base interactions involve different non-canonical base pairs [56]. RNA molecules can have many non-canonical base pairs, even in double helical regions. Along with the non-canonical base pairs, previous reports indicate the existence of several stable structures with different conformations. Non Watson–Crick base pairs for RNA may have biological functions but may also produce point mutations, when other tautomers of the nucleic bases are involved. The stabilization of non-canonical base-pairs may be due to the interaction with metal atoms, specifically if they form non-conventional hydrogen bonds. In this paper, we present results for the adenine–uracil base pair interacting with gold anionic atoms, in order to assess whether the non-conventional hydrogen bonds are able to stabilize different non-canonical base pairs. Fig. 5 presents the most stables structures of uracil–adenine–Au anionic systems. We used the Watson–Crick adenine and uracil tautomers, and two different adenine–uracil bond schemes: the Watson–Crick and another one that permits the interaction of the gold anionic atom with two N–H electron acceptor groups. As may be observed in the figure, there are three stable structures with almost the same energy. One of them has the gold anionic atom bonded to uracil and to adenine throughout two N–H–Au interactions. The others contain the Watson–Crick base-pair and only one N–H–Au interaction. It is not important whether the structure contains the Watson–Crick base pair, or whether the metal anion is bonded to the uracil, to the adenine molecule or falls in between the base pair. These three molecules are more or less equally stable. For this to be the case, the interaction of Au anionic atom with Watson–Crick and non Watson–Crick base pairs may play a role in the evolution of folding in RNA architecture.

Table 2 presents the VDE and the dissociation energy for the most stable structure of the adenine–Au–uracil (anion). The extra electron has a stronger attachment in Au–adenine–uracil than in Au–adenine or Au–uracil, as may be observed when the VDE are compared. Besides this, the dissociation energy of adenine–Au–uracil (anionic) is almost twice the corresponding values for adenine–Au (anionic) and uracil–Au (anionic). This conforms to the optimized geometries because the N–H–Au bond distances in adenine–Au–uracil are shorter than the N–H–Au bond lengths in adenine–Au and uracil–Au (see Figs. 4 and 5, and Ref. [30] for uracil–Au).

One important conclusion that emerges from these results is that gold anionic atom forms non-conventional hydrogen bonds with uracil–adenine that may modify the hydrogen bonds in the nuclei bases pair, and may also increase the VDE of the molecules.

### 3.4. DAM of adenine, uracil and adenine–uracil (with and without gold)

The donator–acceptor map (DAM) has previously been recognized as a powerful tool for the study of electron donor–acceptor capacities of any substance [35]. It has also been claimed that metal atoms and clusters bonded to the nucleic bases may change the

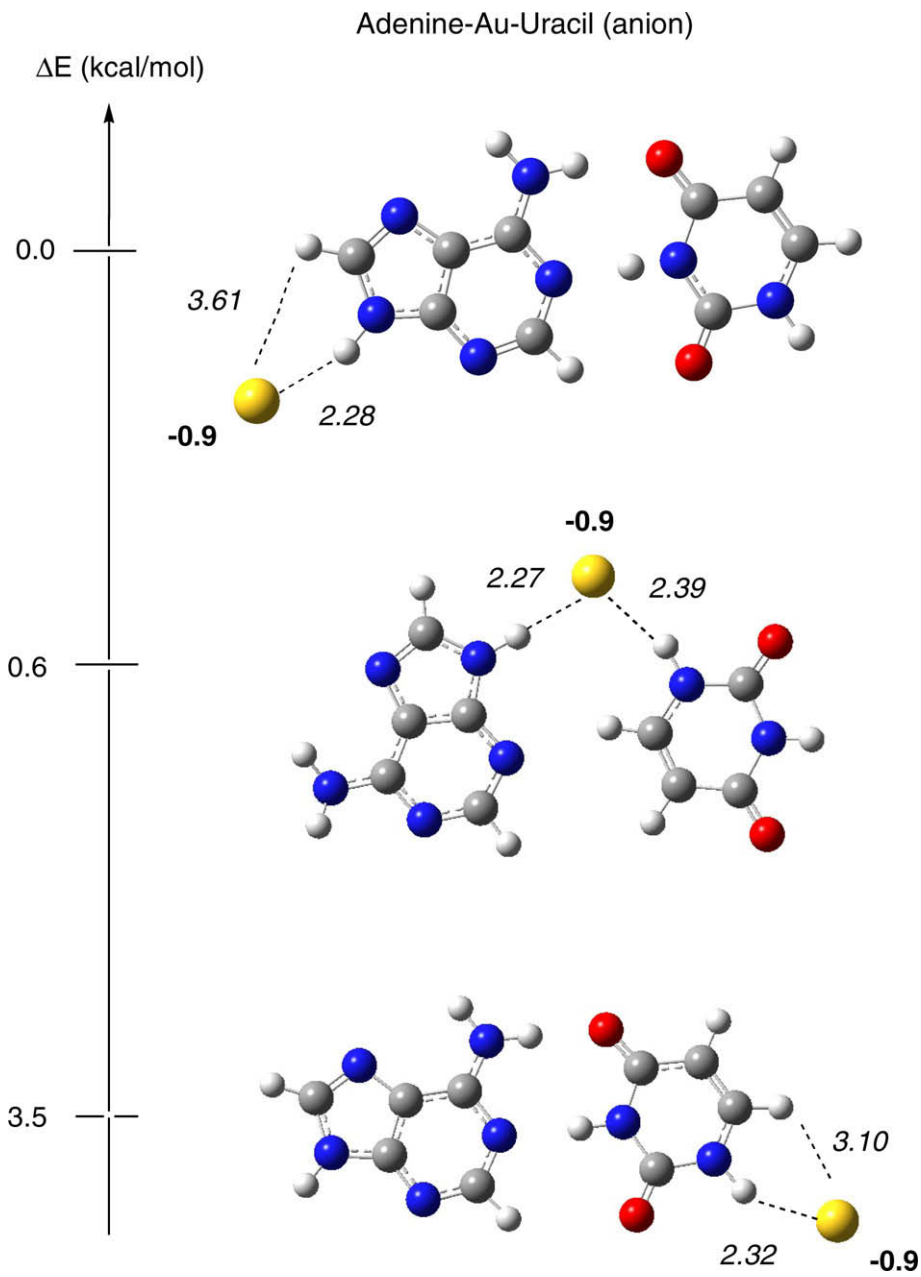


**Fig. 5.** Optimized structures of (adenine–uracil–Au)$^{-1}$. Bond distances (in Å and italics) and Mulliken atomic charges (in bold letters) are reported. Energy differences with respect to the ground state are also shown. All calculations were undertaken, applying B3LYP/LANL2DZ.

electron donor–acceptor properties of the DNA bases. In order to study the electron-donor capacity of these molecules when gold atoms are bonded to nitrogen bases, it is necessary to obtain the optimized neutral molecules. For this purpose, uracil–Au–adenine neutral molecule was also optimized. We found three structures with very similar energy levels as those we found in the case of the anionic system. Optimized structures of the neutral Au–adenine–uracil molecule and results for IE, EA, $\omega+$ and $\omega-$ are available in the Supplementary Materials section.

Fig. 6 presents the DAM for the neutral molecules that we present in this paper. For comparative purposes, we also include the DAM described earlier [35], and previously reported data for uracil, β-carotene (BETA) and astaxanthin (ASTA) [35]. BETA and ASTA are well-known carotenoids that may act as antioxidants. For the DAM, it is important to remember that low values of Rd correspond to effective electron donors, whereas high values of Ra correspond to effective electron acceptors. As may be observed in the Figure, adenine, uracil and adenine–uracil are localized in the worst anti-radical zone. These molecules are neither effective electron donors, nor effective electron acceptors, when compared with BETA and ASTA. The gold atom is localized in the middle-left of the DAM. It is a better electron donor, but worse electron acceptor than the nitrogen bases. The systems with DNA-nitrogen bases interacting with gold have worse electron acceptor capacity but they represent more effective electron donors than the isolated nitrogen bases. Compounds with adenine, uracil and gold are more effective electron donors but worse electron acceptors than BETA and ASTA. This implies that interaction with the gold atom diminished both the energy that is necessary to remove an electron and the electron acceptor capacity of the system. If the DAM of Fig. 6 is analyzed carefully, we can appreciate that the electron-donator properties of the nuclei bases interacting with gold neutral atoms are very

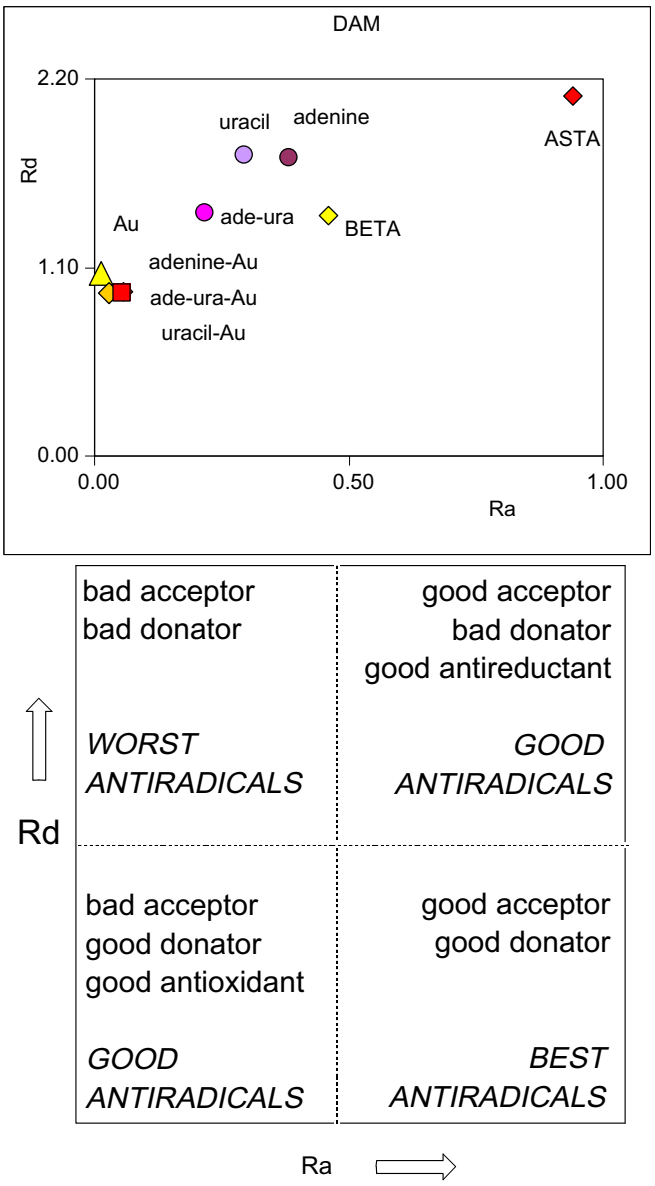


**Fig. 6.** Donator–acceptor map of the neutral molecules that are reported in this study. DAM previously reported [35] is included.

similar to the electron-donator properties of the isolated gold atom. If we compare the results for nucleic-bases-Au compounds with those for ASTA and BETA, it is possible to see that nucleic bases with gold are effective electron donors, whereas BETA and ASTA are effective electron acceptors. As was pointed out previously in this paper, ASTA is also a more effective electron acceptor than uracil, adenine and adenine–uracil. If this is the case, ASTA may accept an electron from nitrogen bases and consequently may act as an oxidant instead of an antioxidant of DNA and RNA nitrogen bases. The oxidation of the nucleic bases and nucleic pair adenine–uracil may have important consequences [14] since oxidative damage to DNA appears to be linked to cancer. This is something that requires further investigation, and consequently work concerning the reactivity of carotenoids with DNA-nitrogen bases is in progress. From the results presented in this paper, it can be concluded that the electron-donor capacity of the DNA nucleic bases is modified when they interact with gold neutral atoms, even though the interaction is not very strong as is made clear by the dissociation energies.

## 4. Conclusions

Adenine–Au neutral is weakly bonded, whereas the cations present a strong interaction that is mainly electrostatic. The anionic systems have the extra electron localized on the metal atom and consequently, there are non-conventional hydrogen bonds that stabilize the system. In the case of Au–uracil–adenine anionic systems, the gold anionic atom forms non-conventional hydrogen bonds with uracil–adenine that modify the hydrogen bonds in the nuclei bases pair and also increase the VDE of the molecules.

The bond between Au and adenine or uracil in the anionic systems increases the energy that is necessary for an electron to be removed from the metal anion. Apparently, the negative gold atom is interacting with positive atoms of adenine and uracil, encouraging the ionization energy of the anionic systems. These results may be useful for further experiments, or have other possible applications.

The VDE of the anion is close to the dissociation energy of a single hydrogen atom, and indicate that both reactions may take place: the detachment of an electron and the dissociation of H from adenine. Experimentally, the detachment of a single electron or the dissociation of one hydrogen atom may be possible. Experimental conditions must be controlled, in order to obtain the desired products.

The electron-donor capacity of the DNA nucleic bases is strongly modified when they interact with gold neutral atoms, even though the interaction is not very strong as can be deduced from the dissociation energies.

When the electron-donator properties of uracil–adenine and carotenoids are compared, it is possible to conclude that ASTA may act as an oxidant instead of an antioxidant of DNA and RNA nitrogen bases. The oxidation of the nucleic base pair adenine–uracil may have important consequences, as oxidative damage of DNA appears to be linked to cancer. This is something requiring further study and consequently, work concerning the reactivity of carotenoids with DNA-nitrogen bases is in progress.

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## Appendix A. Supplementary data

Optimized structures of the neutral Au–adenine–uracil molecule and results for IE, EA, $\omega+$ and $\omega-$ are available in the Supporting Information section. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.theochem.2009.09.038.

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