Electron donor–acceptor properties of metal atoms interacting with pterins†

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Many animal colorants have been described as scavengers of free radicals. Pterins, also known as pteridines, represent one of these pigments. These molecules are analogous to guanine and consist of heterocyclic compounds, which have the highest nitrogen content of any colorant analyzed from animals. One of the mechanisms used for scavenging free radicals is that of the electron transfer reaction, which can be analyzed in terms of the electron donor–acceptor properties of these molecules. The interaction of metal atoms with pterins modifies the properties of pterins, in such a way that they manifest altered electron transfer properties. In this paper, Density Functional Approximation calculations are used to analyze the interaction of pterins (pterin, isoxanthopterin and sepiapterin) with metal atoms (M = Cu, Ag, Au, Zn, Cd or Hg). Neutral (in gas phase), cations and di-cations (in water) are analyzed in order to assess the effect of the positive charge in the M–pterin interaction. Evidently, there is a correlation between the dissociation energy involved in the removal of the metal atom and the ionization energy of the metal atom. Those pterins containing certain cationic metals (such as Zn, Cd and Hg) are depicted as better antioxidants than other pterins, and likewise the interaction with Cu, Ag and Au (di-cations) produces compounds that may act as electron acceptors. The electron transfer reaction between metal–pterins and $HO^\bullet$ is exergonic only when pterins are bonded to Zn, Cd and Hg (cations). This new information may contribute to elucidate the way pterins participate in oxidative stress. Besides this, these results may inspire new experiments similar to those reported previously for the reaction of guanine with metal atoms.

Introduction

Pterins are heterocyclic compounds, present in a wide range of living systems, which have the highest nitrogen content of any animal pigment described up to now.[1] They are also known as pteridines and include the yellow, orange or red UV absorbent and fluorescent colorants that are present in the skin of fishes, amphibians and reptiles, as well as in the wings and eyes of a number of insects and in the irises of some birds.[1–5] It has been suggested that pterins are able to scavenge free radicals[6] but the participation of pterins in oxidative stress has not been completely elucidated. Moreover, this represents a crucial and still not fully understood aspect of pterin behavior.

One of the mechanisms for scavenging free radicals described in the literature[7] is the electron transfer reaction. It was also established that antiradicals may act by either donating or accepting electrons.[8–10] It is important to analyze the capacity of pterins to either accept or donate electrons in order to study their antiradical power, as these belong to a class of heterocyclic compounds that participate in relevant biological functions.[6]

Previous studies have focussed on the different properties of pterins.[6,11–19] A number of reports mention the non-localised nature of the effects on the heterocyclic ring structure[11] and the analysis of the electronic absorption spectra.[12] Others describe the experimental reaction, which demonstrates singlet oxygen quenching by dihydropterins[13] and the chemical reduction of pterins to dihydropterins,[14] as well as the photochemical and photo-physical processes, which are characteristic of pterins.[16] Besides this, it was also reported that pterins may be photosensitizers[17] and may contribute to DNA damage induced by UV-A radiation. Likewise, some authors have used Density Functional Theory calculations in order to study the electronic properties of certain pterins[18] and others have theoretically analyzed the singlet excited state of the pterin and its deactivation pathway.[19] In a previous work,[20] we described the free radical scavenger capacity of pterins and we concluded that these are weaker free radical scavengers than carotenoids.

Concerning the reaction of metal atoms with pterins, descriptions exist[21–23] defining the structure and properties of pterin containing ternary copper(II) complexes,[21] the synthesis and structure of molybdenum–pterin complex[22] and the synthesis of copper(I) and copper(II) complexes of

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† Electronic supplementary information (ESI) available: VIE, VEA, ω+, ω− and indexes Ra and Rd, calculated using eqns 3 and 4, for neutral and cationic pterins and pterin–M complexes are available, as are the fully optimized geometries. See DOI: 10.1039/b9nj00805e

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new chelating pterins.[23] In spite of the existence of these previous studies which assess the reactivity of pterins, no Density Functional Theory (DFT) investigations exist which analyze the interaction of these molecules with metal atoms, or investigate the capacity of the metal–pterin complexes to transfer electrons or the capacity of these complexes to scavenge free radicals. In order to understand the antioxidant capacity of pterins when interacting with metal atoms and to study the effect of the metal atoms on the properties of these molecules, it is necessary to study the interaction and the electron transfer process of the pterin–metal complexes. Thus our main objective is to study the interaction of three pterins (pterin, isoxanthopterin and sepiapterin) with six metal atoms (Cu, Ag, Au, Zn, Cd and Hg), in order to compare their electron accepting–donor capacities. For this purpose, we used chemical quantum calculations to draw up the vertical electron affinity (VEA) and the vertical ionization energy (VIE), referring to pterin–metal complexes (neutral, cationic and di-cationic), and to discern whether a correlation exists between the dissociation energy (ΔE_{dis}) involved in the removal of the metal atom and the ionization energy of the metal atom. Hopefully, this information will be useful for research groups undergoing experiments and inspire new experiments similar to those reported previously, which demonstrate the reaction of guanine with metal atoms.[24] The electron transfer reaction between metal–pterins and $HO^{\bullet}$ is also analysed. These results show that the electron transfer reaction between metal–pterins and $HO^{\bullet}$ is exergonic only when pterins are bonded to Zn, Cd and Hg (cations). This may represent important information for understanding the free radical scavenger capacity of these molecules.

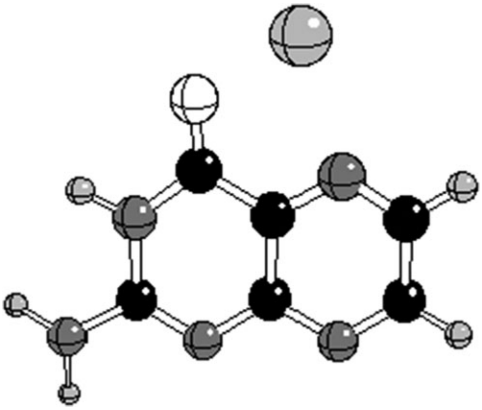
Results and discussion

Geometry optimization and dissociation energy

Tables 1 to 4 present the results of the geometry optimization and ΔE_{dis} for all the complexes that we focused on in this study (in gas phase). Selected bond distances, metal atom charges and a schematic representation indicating the position of the metal atom are also shown. Diverse isomers were tested with varying localizations of the metal atom (presented in Fig. 1).

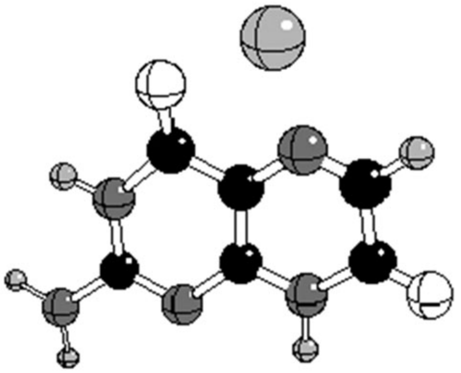
The most stable structures are those presented in Tables 1 to 3. However, other stable structures exist where the metal atom is localized in different positions within the pterin molecules. As the overall conclusions that we derived from all the stable structures will be the same because they present similar total energies, we will focus our discussion on the structures presented in Tables 1 to 3. Evidently, all the complexes presented in the tables have longer M–N and M–O bond distances in the case of the neutrals than in the case of cations, except in the case of Cu with all the pterins and Ag–sepiapterin. Cu is the only neutral metal atom that is bonded to the pterin, isoxanthopterin and sepiapterin, as indicated by the dissociation energies presented in Table 4 and the structural parameters in Tables 1 to 3. These are the only neutral complexes where the dissociation energy exceeds 100 kJ mol^{-1}. Sepiapterin also forms stable complexes with Ag in the neutral systems. The dissociation energy of sepiapterin–Ag is around 85 kJ mol^{-1}. Neutral complexes with Au show weak interactions, whereas in the case of Zn, Cd and Hg there is no interaction at all with pterins when these are in their neutral state. These results concur with the closed

Table 1 Selected optimized bond distances and metal atomic charges of Ptr–M (M = Cu, Ag, Au, Zn, Cd and Hg) (neutral, cationic and di-cationic). A schematic representation of the molecular structure is also presented. The IUPAC name for the pterin is 2-amino-1*H*-pteridin-4-one



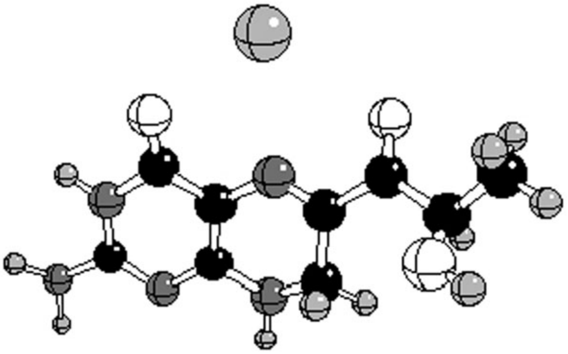
	Pterin (Ptr)								
	Bond distance (M–O)			Bond distance (M–N)			Metal atomic charge		
M	Neutral	+1	+2	Neutral	+1	+2	Neutral	+1	+2
Cu	2.09	2.23	1.95	1.87	1.91	1.98	0.7	0.9	1.2
Ag	2.73	2.37	2.47	2.50	2.33	2.47	0.0	0.6	0.8
Au	3.11	2.60	2.70	2.51	2.15	2.19	−0.2	0.5	0.7
Zn	4.77	2.19	1.94	5.06	2.19	2.00	0.0	0.8	1.5
Cd	3.29	2.36	2.17	3.61	2.50	2.28	0.0	0.7	1.3
Hg	3.53	2.51	2.34	3.72	2.60	2.40	0.0	0.6	1.1

Table 2 Selected optimized bond distances and metal atomic charges for 7-Xap–M (M = Cu, Ag, Au, Zn, Cd and Hg) (neutral, cationic and di-cationic). A schematic representation of the molecular structure is also presented. The IUPAC name for isoxanthopterin is 2-amino-1,8-dihydropteridine-4,7-dione



	Isoxanthopterin (7-Xap)								
	Bond distance (M–O)			Bond distance (M–N)			Metal atomic charge		
M	Neutral	+1	+2	Neutral	+1	+2	Neutral	+1	+2
Cu	2.58	2.18	1.93	1.88	1.92	1.98	0.5	0.9	1.3
Ag	2.84	2.34	2.41	2.74	2.39	2.56	−0.1	0.6	0.8
Au	3.16	2.56	2.62	2.54	2.16	2.24	−0.2	0.5	0.7
Zn	5.20	2.17	1.93	5.40	2.22	2.00	0.0	0.8	1.5
Cd	3.40	2.34	2.15	3.70	2.52	2.29	−0.1	0.7	1.3
Hg	3.52	2.50	2.29	3.86	2.62	2.37	0.0	0.6	1.2

Table 3 Selected optimized bond distances and metal atomic charges of Sep–M (M = Cu, Ag, Au, Zn, Cd and Hg) (neutral, cationic and di-cationic). A schematic representation of the molecular structure is also reported. The IUPAC name for sepiapterin is 2-amino-6-[(2*S*)-2-hydroxypropanoyl]-7,8-dihydro-1*H*-pteridin-4-one



	Sepiapterin (Sep)								
	Bond distance (M–O)			Bond distance (M–N)			Metal atomic charge		
M	Neutral	+1	+2	Neutral	+1	+2	Neutral	+1	+2
Cu	2.04	2.17	1.98	2.00	1.98	1.89	0.8	0.9	1.3
	1.96	2.15	1.97						
Ag	2.70	2.49	2.55	2.23	2.35	2.48	0.5	0.6	0.7
	2.41	2.51	2.48						
Au	3.20	2.51	2.55	2.60	2.29	2.41	−0.2	0.5	0.5
	2.85	2.53	2.45						
Zn	4.80	2.38	2.01	5.20	2.16	1.98	0.0	0.8	1.5
	4.90	2.37	2.03						
Cd	3.50	2.51	2.26	3.30	2.48	2.25	0.0	0.6	1.3
	3.20	2.59	2.28						
Hg	3.72	2.63	2.37	3.79	2.60	2.34	0.0	0.6	1.2
	3.59	2.69	2.40						

shell electronic configuration of Zn, Cd and Hg. For cations and di-cations (Table 4), all metal atoms form stable complexes with dissociation energies exceeding 250 kJ mol^{-1}.

An analysis of the metal atomic charges indicates that metal atoms are positively charged in all the complexes where the dissociation energy exceeds 85 kJ mol^{-1}. In the case of cations,

Table 4 Dissociation energy (in kJ mol^{-1}) for all the complexes that we focused on in this study

Dissociation energy (in kJ mol^{-1}) ($L - M \rightarrow L + M$)			
M	Ptr	7-Xap	Sep
Cu	167.7	103.3	225.9
Ag	20.9	20.5	85.6
Au	28.9	27.2	31.8
Zn	0.4	0.0	0.5
Cd	7.5	7.5	12.9
Hg	4.6	5.9	9.2
Cu^{+1}	368.6	374.4	497.1
Ag^{+1}	275.7	281.2	378.6
Au^{+1}	345.6	349.4	440.6
Zn^{+1}	276.6	282.8	373.2
Cd^{+1}	270.3	276.6	366.9
Hg^{+1}	252.7	258.6	346.4
Cu^{+2}	1080.7	1100.4	1374.0
Ag^{+2}	1242.2	1266.5	1474.4
Au^{+2}	1189.9	1208.7	1417.1
Zn^{+2}	945.2	961.9	1230.9
Cd^{+2}	762.7	778.2	1018.4
Hg^{+2}	797.1	807.5	1032.2

positive charges are localized on the metal atom. In the case of di-cations the highest charge is always on the Cu atom. In fact, a specific direct correlation exists between the atomic charge of the metal and the dissociation energy; as the atomic charges of the metal strengthen, the dissociation energy also increases (see Table 4). This result may be significant, as cations and di-cations represent stable configurations of the metal atoms in natural environments. It is important to note that pterin and isoxanthopterin are oxidized pterins, whereas sepiapterin is a reduced pterin and these represent the pterins most commonly present in a wide range of living systems. When metal cations are bonded to pterins, an electrostatic interaction takes place. As can be appreciated from Table 4, pterin and isoxanthopterin present similar dissociation energies, whereas sepiapterin forms more stable complexes with the metal atoms. This interaction is stronger in the case of sepiapterin than for the other pterins, due to the fact that the metal atom is interacting with one nitrogen and two oxygen atoms that are negatively charged. All metal cations and di-cations interact strongly with pterins.

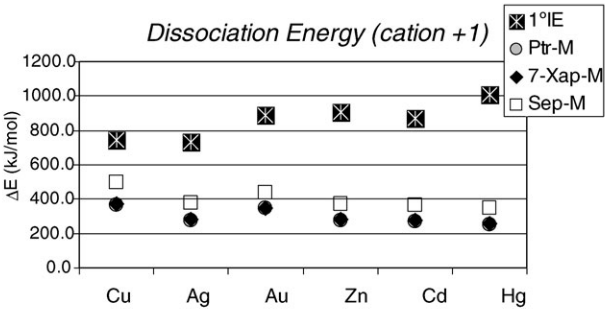


Fig. 2 Dissociation energy (in kJ mol^{-1}) for all the cationic complexes that were focused on in this study (gas phase). Experimental values for the first ionization energy (1° IE in kJ mol^{-1}) are also shown.

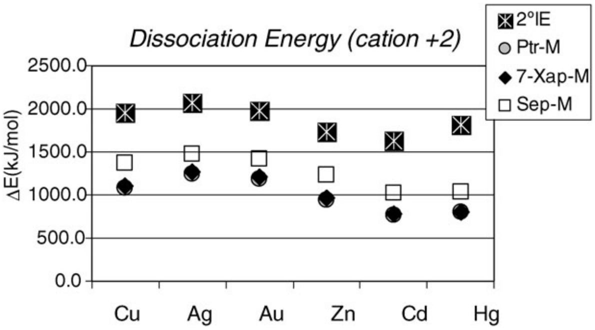


Fig. 3 Dissociation energy (kJ mol^{-1}) for all the di-cationic complexes that were focused on in this study (gas phase). Experimental values for the second ionization energy (2° IE in kJ mol^{-1}) are also presented.

Considering that the interaction between metal and pterins is electrostatic, there must be a correlation between the ionization energy of the metal atoms and the stabilization of the complexes. Metal cations are more stable in systems with low ionization energy than in those with high ionization energy. Since the dissociation that we are considering includes metal cations, the dissociation energy for complexes that contain the most stable metal cations (and have low ionization energies) must be less than for those which have high ionization energies. To corroborate this idea, Fig. 2 and 3 present the dissociation energy for the complexes (cations and di-cations) and the experimental values of the metal ionization energies. Evidently, there is a direct correlation between ionization and dissociation energies, *i.e.*, dissociation energy is less in the case of systems consisting of metal atoms with lower ionization energies, than for those with higher ionization energies. The stabilization of the metal–pterin bond is associated with the ionization energies of the metal atoms, and this correlation is more evident in the case of di-cations than it is for cations.

Electron donor–acceptor properties

The capacity to either donate or accept electrons is directly related to vertical ionization energy (VIE) and vertical electron affinity (VEA). Lower values for VIE imply a greater capacity for donating electrons. Higher values of VEA imply a greater

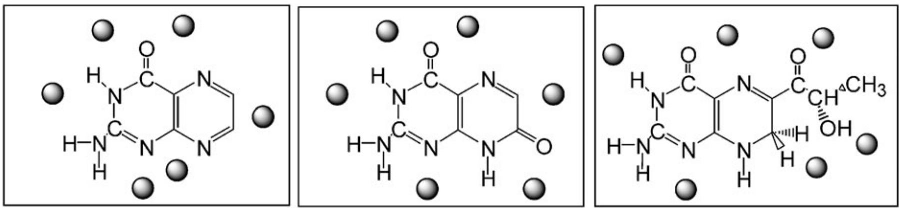


Fig. 1 Isomers tested in this study. Grey circles represent the different positions of the metal atom that were used as initial geometries.

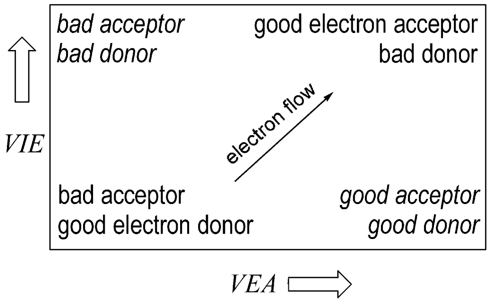


Fig. 4 Vertical Electron Affinity (VEA) *versus* Vertical Ionization Energy (VIE). Four regions are distinguished as described in detail in the text. The electron flow will be from molecules situated at the bottom left section to molecules localized at the top right section.

capacity for accepting electrons. The electron transfer reaction for any electron donor (d) reacting with any electron acceptor (a) depends on the capacity of one molecule to donate electrons, together with the capacity of the other molecule to accept electrons. If one good electron donor interacts with one very bad electron acceptor, the electron transfer reaction will not proceed. It is also predictable that a very bad electron donor will not interact with a good electron acceptor. Thus, it is necessary to consider the properties of both substances in any pair that are interacting through the electron transfer mechanism. In order to facilitate the comparison of the electron donor–acceptor capacities of different substances, it is convenient to plot VEA *versus* VIE, as presented in Fig. 4. Molecules situated in the upper right corner are good electron acceptors and bad electron donors, whereas molecules situated in the lower left section are good electron donors and bad electron acceptors. Those situated at the top right remove electrons from those situated at the bottom left. Molecules placed at the top left are very bad electron donors and will not remove electrons from those at the bottom right. Taking this information, it is possible to predict which molecule is likely to be the electron donor and which one the electron acceptor. However, this information does not guarantee that the electron transfer reaction will be thermodynamically favoured. It is necessary to calculate the adiabatic Gibbs free energy in order to determine whether the reaction is endergonic or exergonic.

In a previous work,[25] the electron transfer energy (ΔE_{ET}) was presented as

$$\Delta E_{\mathrm{ET}} = \chi_{\mathrm{d}} - \chi_{\mathrm{a}} + \tfrac{1}{2}[\eta_{\mathrm{d}} + \eta_{\mathrm{a}}] \qquad (1)$$

where the sub-index d refers to the donor. The electron acceptor is referred to by the sub-index a. The electronegativity (χ) and the hardness (η) are well defined[26] in Density Functional Theory as:

$$\chi = \frac{\mathrm{VIE} + \mathrm{VEA}}{2} \qquad (2)$$

$$\eta = \mathrm{VIE} - \mathrm{VEA} \qquad (3)$$

The electron transfer energy (ΔE_{ET}) is the electronegativity difference plus the arithmetic mean of the hardness values. It is useful to remember that the electronegativity indicates the predisposition of a system to either gain or lose electrons, and hardness measures the resistance to the flow of electrons.[26] For the electron transfer reaction between carotenoids and several free radicals, a direct correlation was discovered between the electron transfer energy and the Gibbs free energy. Reactions are exergonic ($\Delta G < 0$) only when ΔE_{ET} is a negative value.[25] If this is the case, then it is possible to study the electron transfer reaction in three steps: firstly, it is necessary to optimize the structures of the neutrals (or molecules that will donate or accept electrons), and calculate the corresponding VIE and VEA; secondly, with this information, it is possible to plot VIE *versus* VEA as in Fig. 4 and decide which molecule is likely to be the electron donor and which one the electron acceptor; thirdly, it is possible to calculate the electron transfer energy (ΔE_{ET}) using VIE and VEA. If ΔE_{ET} is negative, the corresponding electron transfer reaction will be exergonic. Applying this procedure, it is not necessary to optimize the cation and the anion in order to obtain the adiabatic Gibbs free energy. As these optimizations tend to be very expensive, especially for systems of large size, this represents an effective computational strategy.

Electron donor–acceptor properties of cationic metal–pterins

Metal cations and di-cations form strong bonds with pterins, and also represent stable configurations of the metal atoms in natural environments. For this reason, it is important to study the electron donor–acceptor properties of cationic metal–pterins molecules. As the relevance of gas phase calculations for biological systems is still unclear, the inclusion of solvent effects is important. In order to study the electron transfer process of positively charged molecules, the cation was optimized and this optimized geometry was used to calculate single point energy calculations (in water) for the cation, the double cation and the neutral. Subsequently, VIE and VEA were calculated considering their solvent effects. A similar procedure was followed in the case of di-cations, taking the optimized di-cation as a reference, the vertical cation to obtain VEA and the vertical tri-cation to calculate VIE. The VIE and VEA values are available in the ESI†, as are the fully optimized geometries.

Fig. 5 and Fig. 6 present the electron donor–acceptor results for metal–pterin complexes (cations and di-cations in water).

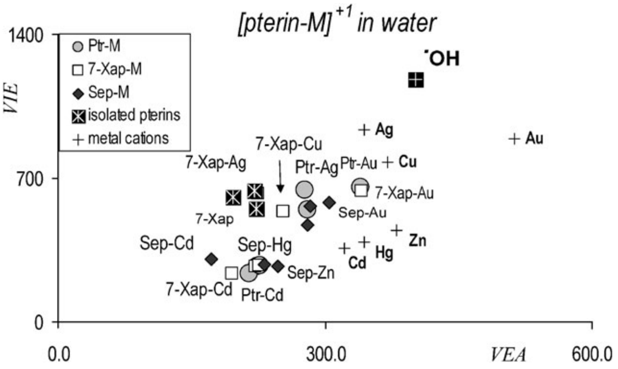


Fig. 5 VIE *versus* VEA (in kJ mol^{-1}) values for cationic compounds in water. The cation was optimized in gas phase, and using this optimized geometry, single point energies (in water) of the cation, double cation and the neutral were calculated. Metal ions, neutral pterins and neutral OH are included for comparison.

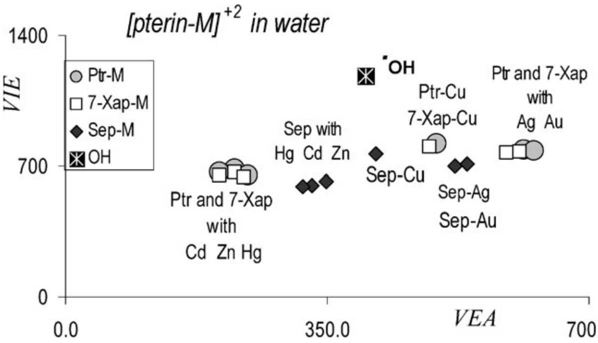


Fig. 6 VIE *versus* VEA values (in kJ mol^{-1}) for di-cationic compounds in water. The di-cation was optimized in gas phase, and using this optimized geometry, single point energies (in water) for the di-cation, the cation and the tri-cation were obtained.

In order to assess whether the bond between metal cations and neutral pterins modified the electron donor–acceptor properties of the complexes, it is necessary to compare the properties of the metal–pterin molecule with those of the isolated pterin and metals, taking into account the charge distribution that was found in the complexes. The atomic charge distribution of pterin–metal complexes indicates that the positive charge is located on the metal atom. For this reason, isolated pterins (neutral) and metal cations are also included in Fig. 5 for comparison. As indicated in this figure, the electron donor–acceptor properties of isolated pterins (neutrals) and metal ions are modified when metal–pterin compounds are formed. Neutral pterins are worse electron donors (higher VIE values) than metal–pterin complexes where the metal atoms are either Zn, Cd or Hg, and worse electron acceptors (lower VEA values) than molecules containing Ag or Au. For the cations, Fig. 5 shows that complexes containing Cu, Ag or Au are the best electron acceptors (these are located in the right section) whereas compounds containing Zn, Cd or Hg are the best electron donors (these are located in the lower section). It is worth noting that the same tendency was found for the isolated metal cations: Zn, Cd and Hg are better electron donors than Cu, Ag and Au. Au^{+1} is the best electron acceptor, and pterins which include Au^{+1} are also the best electron acceptors. Cd^{+1} is the best electron donor of all the metal cations, and likewise [Ptr–Cd]$^{+1}$, [7-Xap–Cd]$^{+1}$ and [Sep–Cd]$^{+1}$ are the greatest electron donors out of all the compounds presented in Fig. 5.

Fig. 6 indicates that di-cationic compounds with Zn, Cd or Hg are better electron donors than complexes of Cu, Ag or Au. In the case of di-cations, metal–Ptr have similar electron donor–acceptor properties to metal–7-Xap when these molecules are bonded to the same metal di-cation. The order of reactivity expressed in terms of the facility for donating electrons depends on the metal di-cation. Ptr, 7-Xap and Sep bonded to Zn, Cd or Hg have similar electron donor capacities (similar VIE values), whereas with Cu, Ag or Au, the order of capacity for donating electrons is as follows:

$$[\text{Sep–M}]^{+2} > [\text{Ptr–M}]^{+2} \cong [\text{7-Xap–M}]^{+2}$$

In terms of the facility for accepting electrons (VEA values), the order of reactivity also depends on the metal di-cation. Pterins bonded to Cu, Ag or Au present the following sequence:

$$[\text{Ptr–M}]^{+2} \cong [\text{7-Xap–M}]^{+2} > [\text{Sep–M}]^{+2}$$

For Zn, Cd and Hg it is as follows:

$$[\text{Sep–M}]^{+2} > [\text{Ptr–M}]^{+2} \cong [\text{7-Xap–M}]^{+2}$$

In view of the fact that an oxidant is a substance that tends to oxidise (remove electrons) from other substances, effective electron acceptors are also considered efficient oxidants. If these complexes accept electrons, other molecules must donate them: these complexes would thus oxidise other substances and for this reason we can consider that cations and di-cations containing Ag and Au represent the strongest oxidants (electron acceptors). Metal cations and di-cations form very strong complexes with pterins, and as a consequence, modify the electron donor–acceptor properties of these organic molecules.

In Fig. 5, it is possible to see that •OH, a very important free radical, is a better electron acceptor than any of the other compounds reported, with the exception of Au^{+1} which is a better electron acceptor than the free radical. As previously stated, complexes situated at the top right remove the electrons from those situated at the bottom left. If this is the case, all the compounds in Fig. 5 will donate an electron to the free radical, except Au^{+1}. In Fig. 6 it is possible to see that compared with di-cations, •OH is a better electron acceptor than compounds with Zn, Cd or Hg but it is not as good as complexes that contain Cu, Ag or Au. Both figures indicate that •OH is the worst electron donor. Consequently, it will not donate electrons to any of the cations reported in this work. As •OH is placed at the top left with respect to di-cations which include Cu, Ag or Au, it will not remove electrons from these complexes. Therefore, there will be no electron transfer reaction between •OH and [metal–pterins]$^{+2}$ when the metal atom is Cu, Ag or Au, but it is possible that an electron transfer from [metal–pterins]$^{+2}$ complexes to •OH will take place when the metal di-cations are Zn, Cd and Hg. To summarize, these results permit us to conclude that the electron transfer reaction between [metal–pterins]$^{+1}$ and

Table 5 Electron transfer energy (ΔE_{ET}) (in kJ mol^{-1}) from eqn (1)

Compound	$(\Delta E_{\text{ET}})^{+1}$	$(\Delta E_{\text{ET}})^{+2}$
Ptr–Cu	144.5	417.4
Ptr–Ag	242.9	384.0
Ptr–Au	253.2	377.8
Ptr–Zn	**−127.8**	283.8
Ptr–Cd	**−164.9**	264.8
Ptr–Hg	**−125.8**	252.3
7-Xap–Cu	136.4	402.6
7-Xap–Ag	224.7	366.9
7-Xap–Au	227.7	376.8
7-Xap–Zn	**−128.9**	268.0
7-Xap–Cd	**−165.9**	249.7
7-Xap–Hg	**−127.1**	240.6
Sep–Cu	72.7	363.3
Sep–Ag	165.1	298.7
Sep–Au	181.7	308.6
Sep–Zn	**−131.0**	216.2
Sep–Cd	**−94.3**	194.3
Sep–Hg	**−122.7**	188.2

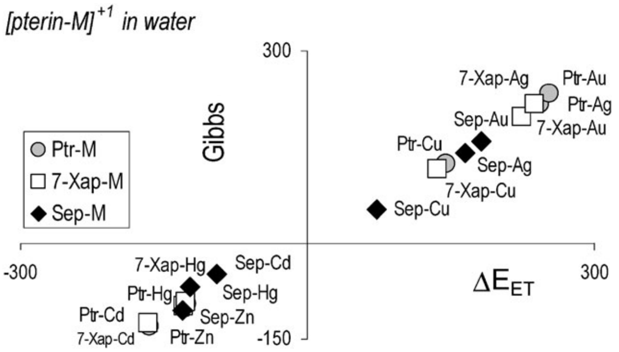


Fig. 7 ΔG at 298 K (in kJ mol^{-1}) from eqn (4) in water as a function of ΔE_{ET} (in kJ mol^{-1}).

[metal–pterins]$^{+2}$ with $^{\bullet}$OH is able to proceed only when the last one is an electron acceptor.

In order to verify this hypothesis, it is necessary to calculate the electron transfer energy (ΔE_{ET}). The results for cations and di-cations are presented in Table 5. Evidently, it is negative only in the case of cations which include Zn, Cd and Hg. This means that the electron transfer reaction to $^{\bullet}$OH will be exergonic only in the case of these compounds. As the values in Table 5 show, the reactions of [metal–pterins]$^{+2}$ with $^{\bullet}$OH are endergonic, as is the reaction with [metal–pterins]$^{+1}$ if the metal is either Cu, Ag or Au. Accordingly, it seems that the ET mechanism is unlikely to occur with these compounds.

Adiabatic Gibbs free energies

It is possible to verify the validity of these results by taking the energy evolution associated with each electron transfer process between the studied [metal–pterins] and $^{\bullet}$OH. For this purpose, the corresponding adiabatic Gibbs free energy at 298 K has been computed only for the cations, since these molecules have positive and negative values in terms of their electron transfer energy, depending on the metal atom that is involved. The adiabatic Gibbs free energy is calculated by applying

$$\Delta G^{0}_{\mathrm{ET}} = [G(\text{pterin} - \mathrm{M}^{(+2)}) + G(\mathrm{OH}^{-})] - [G(\text{pterin} - \mathrm{M}^{(+1)}) + G(^{\bullet}\mathrm{OH})] \qquad (4)$$

The adiabatic Gibbs free energies *versus* ΔE_{ET} are presented in Fig. 7. As is evident, the calculated free energies display good correlation with ΔE_{ET}. The electron transfer reaction is exergonic only for those systems that have $\Delta E_{\mathrm{ET}} < 0$. In all cases, $^{\bullet}$OH is the electron acceptor and [metal–pterins]$^{+1}$ complexes are the electron donors.

This model is clearly a thermodynamic description of the electron transfer process. It is important to note that the electron transfer is a complicated process that includes also kinetics aspects. Consequently, kinetics calculations should be helpful to definitely illustrate the electron transfer reaction of these systems. Nevertheless, such calculations exceed the scope of the present work and this is something requiring further studies.

Computational details

Density Functional Theory[26] as implemented in Gaussian 03[27] was used for all calculations. The hybrid, three parameter B3LYP[28,29] functional was used for the calculation of complete optimizations, without symmetry constraints. Two basis sets were employed: LANL2DZ[30–32] for Ag, Au, Cd and Hg, and 6-311G(d,p)[33] for Cu, Zn, C, H, O and N. Harmonic frequency analyses permitted us to verify optimized minima. Mulliken atomic charges are also included. This methodology (functional and basis set) was previously used for theoretical studies of similar systems,[34] and good agreement was found with available experimental results. As was reported before,[35,36] the DFT calculations using the LANL2DZ pseudopotentials is an adequate descriptor of Au cluster chemistry, which also includes the relativistic effect.

The stationary points were first modeled in gas phase (vacuum), and solvent effects were included *a posteriori* by single point calculations using polarisable continuum model, specifically the integral-equation-formalism (IEF-PCM) with water as the solvent. The dissociation energy (ΔE_{dis}) of the metal atom for neutral, cation and di-cation complexes (M–L) was calculated, as expressed in the following equations (L denotes different pterins and M is any metal atom that we used in this study):

$$\mathrm{M{-}L} \rightarrow \mathrm{M} + \mathrm{L}$$

$$[\mathrm{M{-}L}]^{+1} \rightarrow \mathrm{M}^{+} + \mathrm{L}$$

$$[\mathrm{M{-}L}]^{+2} \rightarrow \mathrm{M}^{+2} + \mathrm{L}$$

Conclusions

In order to make a straightforward qualitative comparison between the electron donor–acceptor capacities of different substances, it is very useful to plot VIE *versus* VEA. Molecules situated in the upper right corner are good electron acceptors and bad electron donors, whereas molecules situated in the lower left section are good electron donors and bad electron acceptors. Those situated at top right remove the electrons from those situated at bottom left. Taking this information, it is possible to predict which molecule is likely to be the electron donor and which one the electron acceptor. Using this information, together with VIE and VEA, the electron transfer energy (ΔE_{ET}) can be calculated. If ΔE_{ET} is negative, the corresponding electron transfer reaction will be exergonic. Following this procedure, it is not necessary to optimize the cation and the anion in order to calculate the adiabatic Gibbs free energy. As these optimizations tend to be very expensive, this is a real benefit.

Metal cations and di-cations form strong bonds with pterins, and modify the electron donor–acceptor properties of these organic molecules. In the case of the cations, complexes containing Cu, Ag or Au represent the best electron acceptors, whereas compounds containing Zn, Cd or Hg represent the best electron donors. The same tendency was found for the isolated metal cations: Zn, Cd and Hg represent better electron donors than Cu, Ag and Au. Di-cationic compounds which include Zn, Cd or Hg represent better electron donors than complexes of Cu, Ag or Au.

These results permit us to predict that the electron transfer reaction of [metal–pterins]$^{+1}$ and [metal–pterins]$^{+2}$ with $^{\bullet}$OH will only proceed if the last one of these is an electron acceptor. The electron transfer energy (ΔE_{ET}) and the adiabatic Gibbs free energy verify this hypothesis. The electron transfer reactions of [metal–pterins]$^{+1}$ with $^{\bullet}$OH are exergonic only when the metal is either Zn, Cd or Hg. Accordingly, it seems that the electron transfer mechanism is likely to occur when these compounds are present.

The indubitable conclusion to be derived from these results is that metal cations and di-cations form very strong complexes with pterins and consequently, they intensely modify the donator–acceptor properties. Evidently, further research is necessary in order to relate these ideas to the free radical scavenger capacity of these compounds.

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