Journal of Al Azhar University-Gaza (Natural Sciences), 2009, **11, P.** 1-14

Theoretical Study of the Interaction of Cu^+ with 5-Methyl Hydantoin in the Gas Phase

Zaki Safi
zaki.safi@alazhar-gaza.edu

Chemistry Department
Al-Azhar University-Gaza

Received 16/4/2009 Accepted 24/5/2009

Abstract*: Relative tautomerisation energies, enthalpies, entropies, Gibbs free energies, and dipole moments for the interactions of the 5-methyl hydantoin with Cu^+ have been studied in the gas phase using hybrid density functional at the B3LYP level of theory using 6-311+(d,p) with full geometry optimization. Final energies were obtained at 6-311+(2df,2p) level. It has been found that the direct association of Cu^+ occurs at the oxygen atom attached to position* ***2,*** *which corresponds to the global minimum of the potential energy surface****.*** *For the enolic structure, the most stable one corresponds to tautomer* ***3a*** *that can be formed by the 1,3-hydrogen transfer at the oxygen atom attached to position* ***4.*** *Moreover, the isomerization processes leading from the most stable adduct to the other stable conformers were also investigated. The finding concluded that the Cu^+ association has a clear catalytic effect on the tautomerization processes which connect the oxo form with enol tautomer.*

Keywords*: Hydantoin; Copper; Density functional calculations; Tautomerization; Gas-Phase reactivity; Carbonyl group;*

Introduction:

Last two decades have witnessed a great deal of attention in the study of the transition metal cations and their interactions with organic and inorganic compounds, which present some special features[1]. Previous studies showed that Cu^+-association to the carbonyl and thiocarbonyl groups plays a relevant role in a great variety of chemical and biological processes[2-6].

These studies are carried out in gas phase and in solution as a useful way to gain some insight in their intrinsic reactivity and the differences with their behavior in condensed media[7-14].

It is well known that a useful indication of how the transition metal monocation interacts with the basic centers can be obtained from the position of the metal in the periodic table. Furthermore, it was found that the bond strength, which formed due to this interaction, is directly proportional with the number of electrons available in the valence orbital. For example, it is well known that the copper monocation, Cu^+, presents a 1s state with an entire occupancy of 3d orbital. The possibility of dative bonds involving the low-lying empty 4s orbital of this metal adds up to its potential interactions, that are essentially electrostatic, with a nonnegligible covalent character[13]. Thus, Cu^+ interactions may be of intermediate strength in regards to those of H^+, which forms strong covalent bonds, and to those of alkali metals, which exhibit almost purely ionic interactions.

For this study, we have chosen the 5-methyl hydantoin molecule. Of particular importance, hydantoin molecules are particularly important for having different therapeutic activities including anticonvulsants, antiarrhythmic, bactericides, fungicides, and anticancers. Their anticonvulsant activity has been investigated for tens of years[15-21]. The chemical reactivities of hydantoins are primarily determined by the stability of their corresponding tautomers[22].

The gas-phase survey of the association of Cu^+ with the carbonyl groups attached to the position 2 and 4 within the hydantoin ring can provide important clues for the understanding of the behavior of this system in biological media[23].

Our main objective in the present work is to study the interaction of Cu^+ with 5-methyl hydantoin molecule to explore the dissimilarities that can be presented in regards to other heterocyclic compounds, such as uracil[9,11,13] and triazepine[14]. Besides, the catalytic role played by Cu^+ association in tautomerization processes will be investigated along with its impact on the optimized geometries.

Computational details

The B3LYP hybrid density functional method; Becke's[24] three-parameter nonlocal hybrid exchange potential with the nonlocal correlation of Lee, Yang and Parr[25], was employed to fully optimize molecular geometries of the different species under consideration. All calculations were performed using the 6-311+G(d,p) basis set using Gaussian-03 series of programs[26]. The harmonic vibrational frequencies were also calculated at the same level of theory to ensure that each stationary point corresponds to a true local minimum on the potential energy surface (PES) or transition state (TS), and to estimate the zero-point energy (ZPE) correction. A similar procedure was adapted to locate the transition states (TSs) associated with prototropic tautomerisation processes. In order to obtain more reliable energies for the local minima, final energies were evaluated by using the same functional combined with the 6-311+G(2df,2p) basis set for all atoms except for Cu^+, where the (14s9p5d/9s5p3d) basis set of Wachters[27] and Hay[28] was used, supplemented with a set of (1s2p1d) diffuse functions and with two sets of *f* functions and one set of *g* functions. It has been shown that this approach is well suited for the study of this kind of systems, yielding binding energies in good agreement with experimental values[11, 29].

The corresponding Cu^+ binding energies, D_0, were evaluated by subtracting the energy of the neutral and that of Cu^+ from the energy of the complex, after including the corresponding ZPE corrections scaled by a factor of 0.9806[30] and the thermal correction to energy. Enthalpies and Gibbs free energies have been evaluated by considering the thermal corrections at 298.15 K and the values obtained for the entropy by using the harmonic vibrational frequencies.

The binding characteristics were analyzed by means of the atoms in molecules (AIM) theory of Bader[31]. For this purpose we have located the relevant bond critical points (bcp) and evaluated the charge density at each point. To perform the AIM analysis we have used the AIMPAC suite of programs[32].

Results and discussion

For 5-methyl hydantoin-Cu^+ complexes, two tautomers can be envisaged resulting from the direct association of Cu^+ with the most stable neutral one[33], each of which has several conformers, so that the resulted twenty structures shown schematically in Figure 1. In this theoretical survey all these structures were optimized and characterized as local minima of the potential energy surface (PES) with all harmonic frequencies being real. For the most stable conformers of each tautomer, we have carried out a single point calculation at B3LYP/6-311+G(2df,2p) level of theory.

Previous studies, for such systems[11,14], revealed that the Cu^+ effectively interacts with the heteroatoms in positions **2** and **4**. Consequently, direct association of the Cu^+ cation with these species will yield tautomers **1** and **4**, while structures **2**, **3**, **5**, and **6** can be formed only by appropriate tautomerization processes. However, it is worth mentioning that attempts to associate the Cu^+ with the lone pair electron located on the amino nitrogen atoms at position 1 and 3 with the hydantoin ring, actually succeed, but we have found that these tautomers are ~ 14.6 and 14.1 kcal/mol above the most stable adduct. Hereafter, the discussion of these tautomers will be omitted.

The relative energies, enthalpies, Gibbs free energies, entropies, and the dipole moment for the most stable conformers for each tautomer are listed in Table 1, together with information on the transition states (TS) connecting the most stable conformers. The corresponding final energies and zero point energy correction are given in Table **S1** of supplementary information. The optimized geometries of these 20 local minima and 4 transition states are available from the author upon request.

As mentioned above, 5-methyl hydantoin presents different tautomers that can be generated through appropriate hydrogen shift. Hence, the first question to be addressed in rationalizing their intrinsic reactivity is which of them are predominant in the gas phase. Recently, we have shown[33], in agreement with previous studies[19,34], in neutral molecules, that the dioxo tautomer of 5-methyl-hydantoin is the most stable and it was ~17.4 kcal/mole more stable than the most stable enolic structure[33]. Moreover, we have found that the energy barriers connecting the different neutral tautomers are very high[33]; therefore, the aforementioned tautomers, if the molecule is not excited, will be the only ones present in the gas-phase.

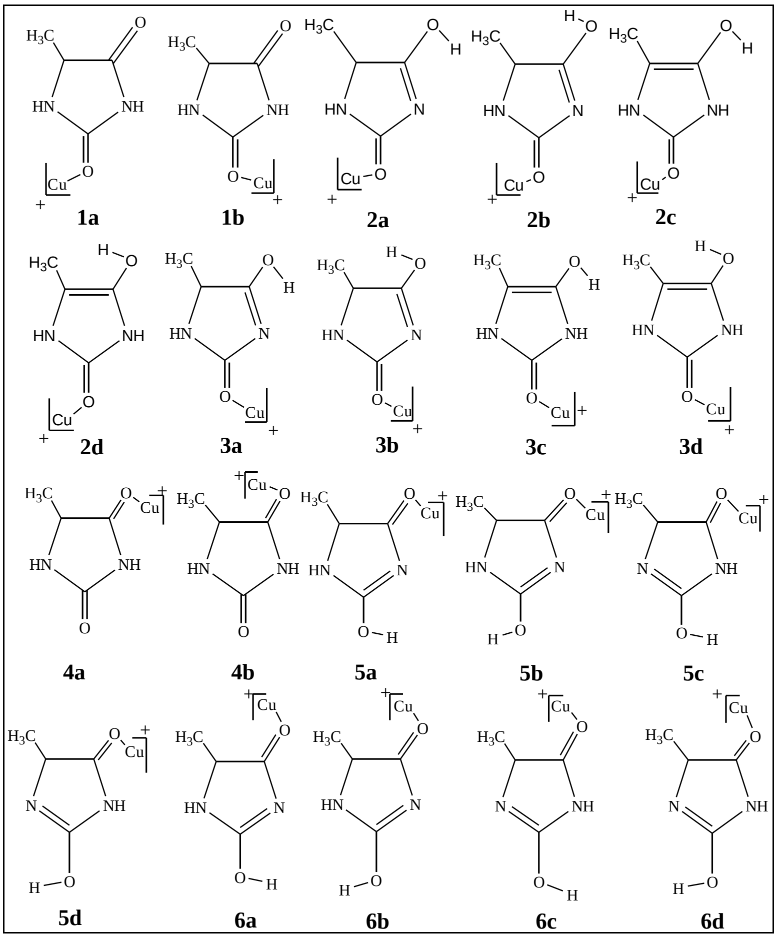

Figure 1. Schematic representation of the different tautomers forms of 5-methyl hydantoin-Cu^+ complexes.

As shown in table 1, the association of copper monocation with the oxygen atom at position 2 is the most stable. The Gibbs free energy difference between **C4=O-Cu** and **C2=O-Cu** is ~ 3.6 kcal/mol. This behavior may be well explained when the induced electronic enclosed this molecule is considered. Because of the carbonyl group at position 2 being surrounded by two adjacent amino groups, a negative charge is accumulated on the oxygen atom attached to this position. In addition, the inductive electronic effect, originated from the methyl group, also adds a negative charge to both nitrogen atom at position 1. This probably effects the increasing order of isomers stability **1b** > **4a** and therefore the order of basicity enhancement of the centers, **O2** > **O4**.

Table 1: Dipole moment, μ**,** (in debye), Relative energies, ΔE, enthalpies, ΔH**,** Gibbs free energies, ΔG**,** entropy, ΔS**,** (Kcal/mol) of the different species of 5-methyl hydantoin-Cu$^+$ complexes.

Species	**μ**	**ΔE**	**ΔH**	**ΔS**	**ΔG**
1a	7.4	0.0	0.1	-0.1	0.0
1b	**6.0**	**0.0**	**0.0**	**0.0**	**0.0**
2a	**1.1**	**4.2**	**4.0**	**0.5**	**4.4**
2b	2.4	7.9	7.8	0.1	8.0
2c	3.7	9.9	10.3	-1.9	8.5
2d	3.7	9.8	9.8	0.7	10.4
3a	**1.1**	**4.2**	**4.0**	**0.5**	**4.4**
3b	2.4	7.9	7.8	0.1	8.0
3c	2.1	9.8	10.2	-0.9	9.2
3d	2.1	9.8	10.2	-0.9	9.3
4a	**6.1**	**3.4**	**3.4**	**0.2**	**3.6**
4b	7.3	3.7	3.7	-0.1	3.6
5a	**1.0**	**4.8**	**4.6**	**0.5**	**5.2**
5b	3.1	9.2	9.2	0.1	9.2
5c	8.1	26.7	26.9	-0.2	26.7
5d	5.4	18.5	18.4	0.5	18.8
6a	3.4	11.6	11.6	-0.2	11.4
6b	3.1	9.2	9.2	0.1	9.2
6c	5.9	24.7	24.8	-0.1	24.6
6d	3.9	17.3	17.2	0.4	17.6
TS(1b-3b)	3.5	48.4	48.2	0.4	48.6
TS(1b-3c)	6.0	76.7	76.7	-0.4	76.3
TS(4a-5a)	3.3	46.5	46.3	0.7	47.1
TS(4a-6d)	6.8	60.4	60.3	0.4	60.6

Figure 2 shows the most important geometric parameters obtained in the optimization of the most stable tautomers of the 5-methyl hydantoin-Cu$^+$ complexes, **1b**, **3a**, **4a** and **5a**. More detailed is given in Table **S2** of the supplementary information. Although discussion of the optimized geometries is not our main goal in this work, it is worth mentioning that Cu-association with the carbonyl groups attached to positions 2 and 4 leads to a significant lengthening of these groups.

Consequently, an inspection of the topology of the electron density shows a significant decreasing in the charge density at the corresponding bond critical point (bcp) (see Figure 3), and the energy density becomes less negative (see Table S3 of the supplementary information). Moreover, it is also important to note that the lengthening of the bond distance upon complexation is more pronounced when the interaction takes place at the oxygen atom attached to position **2** rather than position **4** (see figure 2). Also, coherently, the decrease in the charge density at the bcp is also greater.

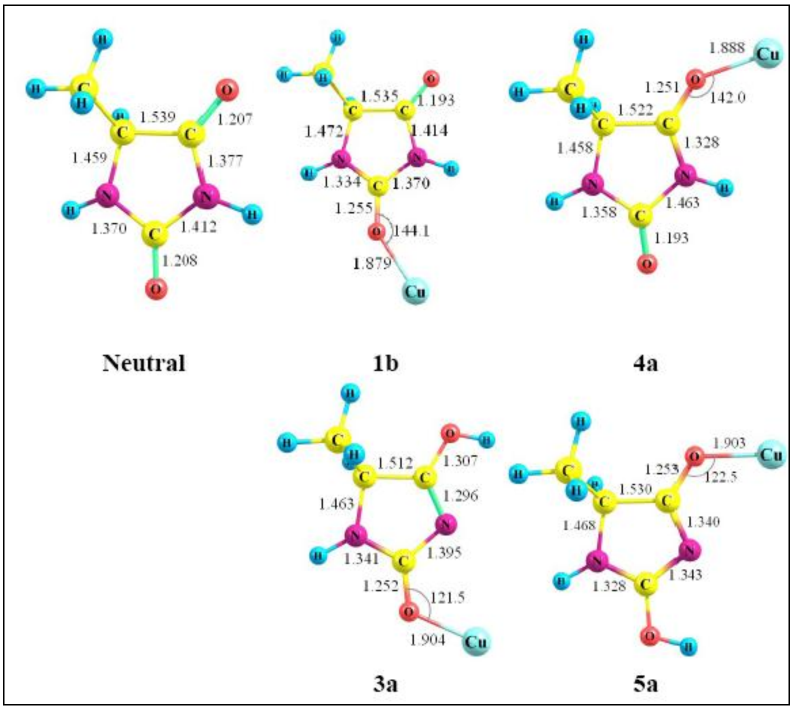

Figure 2. The optimized structure of the most stable tautomers of 5-methyl hydantoin-Cu^+ complexes, 1b, 4a, 3a, and 5a tautomers.

For the **O-Cu** bond, an inspection to Figure 2 shows that this linkage is longer when the Cu^+-association takes place at oxygen atom attached to position 4. Also, as a consequence, the decrease in the charge density at the bcp is larger and the energy density becomes more negative. It must be also emphasized that the **O-Cu** bonds are characterized by values of charge densities, ρ(**r**), (0.0970 a.u.), at the bond critical points, bcps, about four times larger than those found in typical ionic linkages, H-O, (0.3352 a.u.), which proves the non-negligible covalent character of these linkages. This is also confirmed by negative values of the energy density (see Table **S3**).

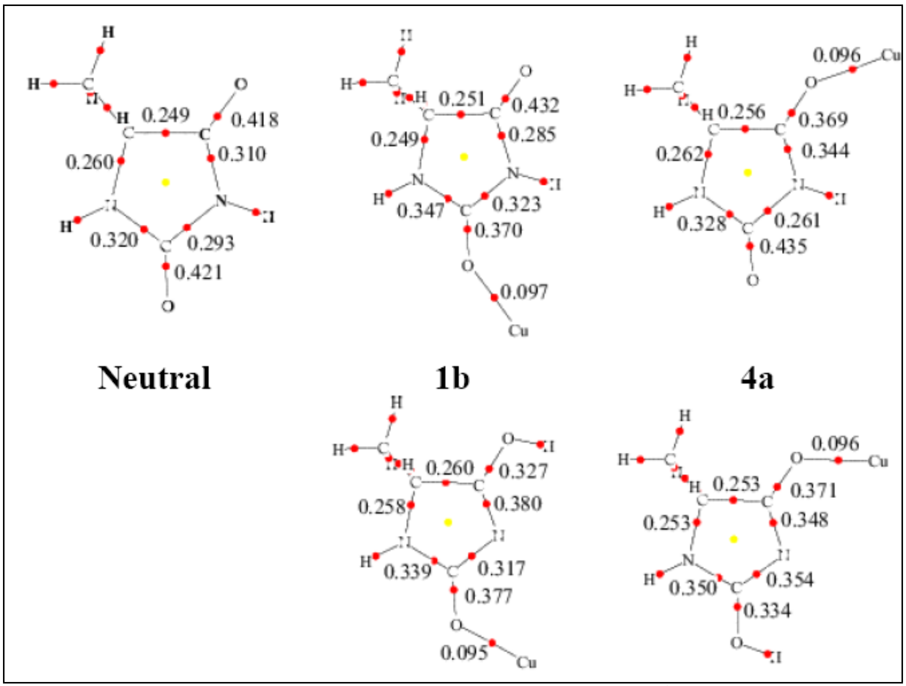

Figure 3. Molecular graphs of 5-methyl hydantoin-Cu$^+$ complexes, 1b, 4a, 3a, and 5a tautomers. Red point correspond to the bcps and the yellow ones correspond to ring critical point, rcp. Electron densities at the bcps are in a.u.

Quite importantly, when the intramolecular 1,3-hydrogen transfer takes place, the **O2(4)-Cu** linkages become longer and the **Cu-O2(4)=C2(4)** bonds angles become smaller. Coherently, the charge density at the bcp becomes smaller and the energy density become more negative (see Figures 2 and 3 and Tables S2 and S3). This indicates that the metal monocation moves toward the dehydrogenated nitrogen atom to form a cyclic structure. Yet, it nests between the oxygen and the dehydrogenated nitrogen atom, polarizing both lone-pairs simultaneously. This finding is also improved by the absence of a bcp between the Cu$^+$ monocation and the dehydrogenated nitrogen atom.

All these facts are reflected in the binding energies value, which is found to be 56.5 kcal/mol. This value indicates that hydantoin behaves as bases of moderate strength in the gas phase, but still~~s~~ slightly more basic than uracil[11] and 3,5-dioxo-triazepine derivative[14], for which the binding energies values are ~ 54.8 and 53.4 kcal/mol, respectively.

Let us now consider the relative stabilities of the different tautomers envisaged in this survey. The first results, to be noted, that the behavior of 5-methyl hydantoin, in which the position of the basic site is important, toward Cu^+ cation differs from that predicted for tautomerization in the neutral case (see Table 1). Indeed, our computed results listed in Table 1 show the most stable adduct is formed due to the interaction of Cu^+ with oxygen atom attached to position 2, tautomer **1b**. When the enolic structures are considered, as listed in Table 1, conformers **3a** and **5a**, in which the 1,3-hydrogen transfer takes place at the oxygen atoms attached to position 2 and 4, respectively, are systematically the least stable ones. In fact, our theoretical results show that the relative energies are 4.2 and 4.8 kcal/mol. In general, the stability revealed from data in Table 1 comes in order of **3a** > **5a** > **6b** > **3c** > **6d** > **5d**. These results are agree with those reported for the neutral species[39,40], but with minor differences.

Interestingly, whereas the relative energy of the most stable enolic forms was 17.4 kcal/mol, it drops by an amount of ~ 13.2 when the Cu^+-association with 5-methyl hydantoin takes place. This finding indicates that Cu^+-association has a clear catalytic effect on the intramolecular 1,3-hydrogen transfer, which will be discussed in the next subsection.

Tautomerization processes. Catalytic effect of Cu+

A possible tautomerisation processes in the gas phase has been explored by analyzing the energy profiles of the transition states connecting the keto-Cu^+ forms from one side, and at the other side the most stable enolic forms. Energy profiles computed at B3LYP/6-311+G(2df,2p)//B3LYP/6-311+(d,p) level of theory are shown in Figure 4. Activation energy barriers of all possible transition states involved in the mechanisms are depicted in the figure, as well as the relative energy values corresponding to the most stable tautomers as listed in Table 1.

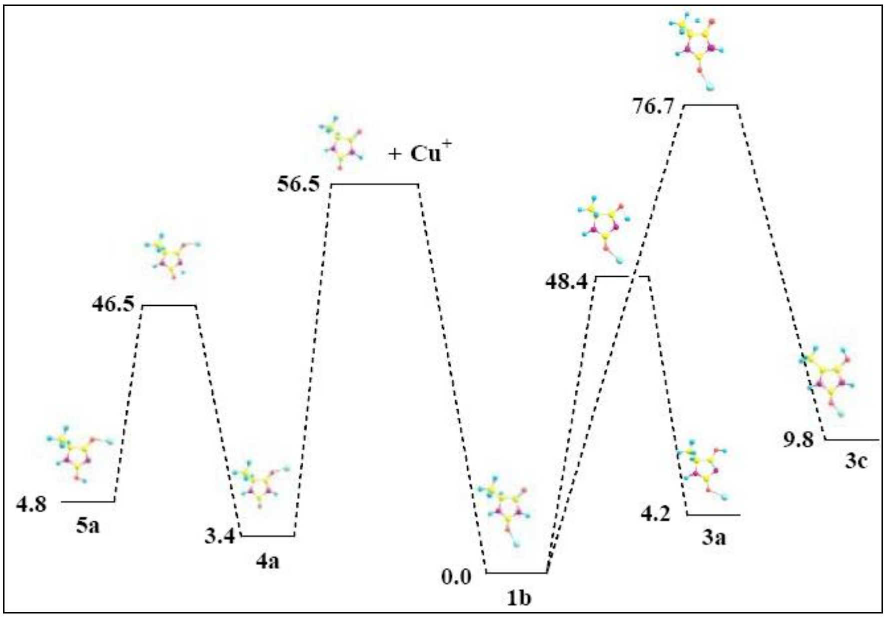

Figure 4. Energy profiles for the tautomerization process of 5-methyl hydantoin-Cu$^+$ complexes.

For 5-methyl hydantoin, among all the possible tautomers included in Figure 1, keto form, adduct **1b,** is the most stable complex (see Table 1 and Figure 4), which means that Cu$^+$ association doesn't affect the stability trend observed for the isolated neutrals[33]. This had been pointed out for triazepines by Safi and Lamsabhi[14] and in contrast to those reported for uracil[11]. However, conformer **3a** is 0.6 kcal/mol more stable than conformer **5a**, the transition state **TS(1b-3a)**, which connects the adduct **1b** and the conformer **3a** is 1.9 less stable than the transition state **TS(4a-5a),** which connects the adduct **4a** and the conformer **5a.** In other word, the intramolecular 1,3 hydrogen transfer from the adjacent amino group to the oxygen atom at position 2 through the **TS(4a-5a)** is thermodynamically favored over that at position 4 by 1.9 kcalmol. This finding show, in agreement with the previous studies[33], once again that the oxygen atom at position 2 is more basic than that at position 4. Obviously, because of the high energy barrier, the intramolecular prototropic tautomerisation is thermodynamically unfavored.

Comparing these results with those obtained for the isolated neutral[33], we have found that the metal monocation plays an important catalytic role. This role is well observed when the energy barriers of the tautomerization processes in both cases are compared. Whereas, for the neutral case[33], the 1,3 intramolecular hydrogen transfer needs 54.3 kcal/mol, this energy values becomes 48.4 kcal/mol when the Cu^+-association takes place.

Conclusion

A DFT study of the relative stability of the different forms of 5-methyl hydantoin-Cu^+ adducts in the gas phase has shown that the most basic site is the oxygen atom attached to position 2. The enhanced basicity of this oxygen atom seems to be associated with a certain zwiterionic character, which accumulates a large electron density on it. However, a small degree of competitiveness between the two carbonyl groups attached to positions 2 and 4 may be considered. It has been also found that the most stable adduct corresponds systematically to structure **1b**, in which the metal monocation interacts directly to the oxygen atom attached to position 2. Also, we have that the most stable enolic structure corresponds to the tautomer **3a** in which the amino hydrogen atom transferes to the oxygen atom attached to position 4. Importantly, our results concluded that Cu^+ association has a clear catalytic effect on the tautomerization processes, which connect the oxo form with the enol tautomers. In all complexes, the bonding of Cu^+ to oxygen has a significantly large covalent character. Consistently the charge densities at the O-Cu bcps are larger than in typical ionic linkages energy densitites at these points are negative.

Acknowledgements:

A generous allocation of computational time at the CCC of the Universidad Autónoma de Madrid is acknowledged. The author gratefully acknowledges Al-Azhar University of Gaza for the facilities presented.

References:

1. K. Karlin and J. Zubieta, *In Copper Coordination Chemistry: Bilogical and Inorganic Perspectives*, Adenine Guiderland, New York, NY, **1983**.

2. J. Leary and P. Armentrout, *Int. J. Mass Spectrom.* **2001**, *204*, ix.
3. P. Armentrout, *Top. Organomet. Chem.* **1999**, 4, 1.
4. S. Yano and M. Otsuka, *Metal ions in Biological Systems*, Marcel Dekker, New York, NY,, **1996**.
5. P. Armentrout and T. Baer, *J. Phys. Chem* **1996**, 100, 12866.
6. B. Freiser, *Organometallic Ion Chemistry*, Kluwer Academic Publishers, Dordrecht, **1995**.
7. X. Wang and D. Yang, *J. Phys. Chem. A* **2006**, 110, 7568; X. Wang, J. S. Lee and D. S. Yang, *J. Chem. Phys.*, **2006**, 125, Nº 014309.
8. A. Samanta, T. Furuta and J. Li, *J. Chem. Phys.* **2006**, *125, Nº 084714.*
9. A. Lamsabhi, M. Alcami, O. Mó, M. Yañez and J. Tortajada, *J. Phys. Chem. A* **2006**, 110, 1943.
10. M. Belcastro, T. Marino, N. Russo and M. Toscano, *J. Mass Spectrom.* **2005**, 40, 300.
11. A. Lamsabhi, O. Mó, M. Yanez, M. Alcami and J. Tortajada, *ChemPhysChem***,** **2004**, 5, 1; A. Lamsabhi, M. Alcamí, O. Mó and M. Yáñez, *Chem.Phys.Chem.*, **2003**, 4, 1011.
12. N. Russo, M. Toscano and A. Grand, *J. Mass Spectrom.* **2003**, 38, 265.
13. A. Luna, B. Amerkaz, J.-P. Morizur, J. Tortajada, O. Mò and M. Yàñez, *J. Phys. Chem. A* **1997**, 101, 5931.
14. Z. Safi, A. Lamsabhi, *J. Phys. Chem. A,* **2007,** 111, 2213.
15. R. Locock and R. Coutts, *Org. Mass Spectrom*, **1970**, 3(6), 735.
16. K. Camerman and N. Camerman, *Acta Cryst.*, **1971**, B27, 2205.
17. G. Simig, K. Lemport, J. Tamas, and G. Czria, *Tetrahedron*, **1975**, 31, 1195.
18. M. Schmidt, K. Baldridge, J. Boatz, J. Jenesen, S. Koseki, M. Gordon, A. Yadav, and V. Yadav, *J. Mol. Struct.*, (THEOCHEM), **1994**, 315, 245.
19. E. Keinpeter, *Struct. Chem*., **1997**, 8, 161.
20. K. Nguyen, T. Windus and S. Albert, *QCPE Bull.*, **1990**, 10, 52.
21. N. Bovamick and H. Clarke, *J. Am. Chem. Soc.*, **1938**, 60, 2426;
22. Z. Piasek and T. Urbanski *Tetrahedron Lett.,*, **1962**, 16, 723.
23. J. Lee, *Int. H. Mass Spectrom.*, **2005,** 240**,** 261
24. A. Becke, *J. Chem. Phys.*, **1993**, 98, 5648.
25. C. Lee, W. Yang, and R. Parr, *Phys Rev., B***, 1988,** 37, 785.
26. M.J. Frisch, Gaussian 03, Revision B.01, Gaussian, Inc., Pittsburgh PA, **2003**.
27. A. Wachters, *J. Chem. Phys.* **1970**, 52, 1033-1036.
28. P. Hay, *J. Chem. Phys.* **1977**, 66, 4377-4384.
29. A. Lamsabhi, M. Alcami, O. Mò, W. Bouab, M. Esseffar, J. L.-M. Abboud and M. Yàñez, *J. Phys. Chem. A* **2000**, 104, 5122.
30. A. Scott and L. Radom, *J. Phys. Chem* **1996**, 100, 16502.
31. R. Bader, *Atomes In Molecules : A Quantum Theory*, Clarendon Press Oxford Univ., Oxford, **1990**.
32. J. Cheeseman and R. F. W. Bader in *have provide the AIMPAC programs package*.
33. Z. Safi and F. Abu-Awwad, *E-J. Chem.*, **2008,** 5, 884.

34. E. Kleinpeter, M. Heydenreich, L. Kalder, A. Koch, D. Hennig, D. Kempter, R. Benassi, and F. Taddei, *J. Mol. Struct.*, **1997,** 403, 111.

Supplementary Information

Table S1: Total Energies at B3LYP/6-311G+(d,p) (E1) and B3LYP/6-311+G(2df,2p)//B3lYP/6-311G+(d,p) (E2), Zero-Point Energies (ZPE), Thermal correction of enthalpy and Entropy values of 5-methyl hydantoin.

Species	E1	E2	ZPE	TCE	S
1a	-2056.426149	-2,056.451496	0.109443	0.118788	98.386
1b	-2056.426302	-2,056.451599	0.109460	0.118780	98.111
2a	-2056.419294	-2,056.445483	0.109971	0.119014	96.601
2b	-2056.411963	-2,056.439096	0.109567	0.118753	97.633
2c	-2056.407631	-2,056.434965	0.108538	0.118604	104.373
2d	-2056.407634	-2,056.434962	0.108510	0.117653	95.739
3a	-2056.419294	-2,056.445485	0.109972	0.119015	96.590
3b	-2056.411963	-2,056.439096	0.109565	0.118751	97.649
3c	-2056.408033	-2,056.435272	0.108668	0.118633	101.156
3d	-2056.408033	-2,056.435273	0.108667	0.118632	101.127
4a	-2056.420825	-2,056.446228	0.109521	0.118767	97.398
4b	-2056.420144	-2,056.445615	0.109432	0.118741	98.420
5a	-2056.418070	-2,056.444359	0.109859	0.118909	96.237
5b	-2056.409722	-2,056.436810	0.109321	0.118593	97.875
5c	-2056.380839	-2,056.407632	0.108108	0.117668	98.708
5d	-2056.396071	-2,056.421897	0.109231	0.118356	96.573
6a	-2056.406599	-2,056.433026	0.109396	0.118687	98.691
6b	-2056.409722	-2,056.436810	0.109322	0.118593	97.874
6c	-2056.383939	-2,056.411058	0.108190	0.117709	98.615
6d	-2056.397782	-2,056.423803	0.109227	0.118318	96.671
TS(1b-3b)	-2056.343151	-2,056.369269	0.104171	0.113224	96.877
TS(1b-3c)	-2056.296717	-2,056.322935	0.102994	0.112190	99.447
TS(4a-5a)	-2056.346250	-2,056.372420	0.104434	0.113322	95.670
TS(4a-6d)	-2056.323147	-2,056.349612	0.103764	0.112760	96.922

All values are in atomic units.
Values of entropy are in Cal.K^{-1}.mol^{-1}

Table S2. Optimized geometrical parameters of 5-methyl hydantoin and their Cu^{+}-complexes. (bond lengths in Å and bond angles in degrees).

	Neutral	1b	3a	4a	5a
	Bond lengths [Å]				
N1-C2	1.370	1.334	1.341	1.358	1.328
C2-N3	1.412	1.370	1.396	1.463	1.343
N3-C4	1.377	1.414	1.296	1.328	1.340
C4-C5	1.539	1.535	1.512	1.522	1.530
C5-N1	1.459	1.472	1.463	1.458	1.468
C5-C6	1.528	1.528	1.532	1.533	1.529
C2=O	1.208	1.255	1.252	1.193	1.305
C4=O	1.207	1.193	1.307	1.251	1.253
O2-Cu		1.879	1.904		
O4-Cu				1.888	1.903
	Bond angles [˚]				
N1-C2-N3	105.3	108.7	111.6	103.9	115.6
C2-N3-C4	113.5	111.8	105.6	112.5	105.3
N3-C4-C5	105.8	105.4	114.8	108.3	112.0
C4-C5-N1	101.6	101.1	97.5	100.9	98.5
C5-N1-C2	113.6	112.9	110.5	114.4	108.6
N1-C2-O	128.8	124.4	124.7	132.4	120.3
O-C2-N3	125.8	126.9	123.8	123.7	124.1
N3-C4-O	127.4	125.8	125.8	128.7	125.9
O-C4-C5	126.8	128.8	119.4	123.0	122.1
Cu-O2-C2		144.1	121.5		
Cu-O4-C4				142.0	122.5

Table S3: Internuclear distances (R,Å), charge density (ρ(r), a.u), energy density (H(r), a.u), and Laplacian of charge density, (∇(ρ), a.u) at the C=O and O-Cu bond critical points for 5-methyl hydantoin and their Cu$^+$-complexes.

	neutral	1b	4a	3a	5a
	C2=O				
R	1.208	1.255	1.193	1.252	1.305
Ρ (r)	0.4213	0.3698	0.4348	0.3770	0.3336
H(r)	-0.7210	-0.5918	-0.7562	-0.6103	-0.5097
∇(ρ)	0.0954	0.1076	0.0689	0.1141	0.1232
	C4=O				
R	1.207	1.193	1.250	1.307	1.253
Ρ (r)	0.4181	0.4319	0.3694	0.3274	0.3710
(H(r)	-0.7121	-0.7471	-0.5908	-0.4958	-0.5957
∇(ρ)	0.0627	0.0375	0.0717	0.0912	0.0795
	O-Cu				
R		1.879	1.886	1.904	1.903
Ρ (r)		0.0970	0.0956	0.0953	0.0961
(H(r)		-0.0100	-0.0098	-0.0106	-0.0110
∇(ρ)		0.1480	0.1447	0.1374	0.1379