

THEORETICAL STUDY OF COORDINATION OF SUCCINIMIDE, OF ITS N-HYDROXYLSUCCINIMIDE AND OF THEIR DEPROTONATED FORMS

ABSTRACT

Succinimide ($C_4H_5O_2N$) is an imide. Each oxygen atom has two lone electron pairs. Azote atom has one lone electron pair. There are some potential sites of coordination. Succinimide is an active ingredient used in urology and nephrology. Transition metals complexes with a given structure could be alternatives in treatment of some incurable diseases because the coordination of active ingredients modifies deeply the physiological properties of metals and of ligands. Then some researches in the treatment of the mellitus diabetes are actually in full swing. At a good place in this therapy, one find zinc antidiabetic and antimetabolic complexes.

This work is a theoretic study of the coordination of succinimide, of N-hydroxosuccinimide and of their deprotonated forms. The aim of this study was the determination of the more favorable coordination site of each ligand. It was found that the succinimide and N-hydroxosuccinimide form complexes via an imide oxygen atom. The succinimide deprotonated species forms a complex through the nitrogen atom. The deprotonated form of the N-hydroxosuccinimide can form a chelate via an imide oxygen atom and the oxygen atom from hydroxyl group.

Calculations have been performed by DFT/B3lyp method in the 6-311g++(d,p) orbital basis set in the Laboratory of theoretical chemistry and Molecular Spectroscopy (LACTHESMO), Abomey-Calavi University between January and June 2016.

Keywords: coordination compound; succinimide; zinc(II) chloride; DFT/ B3LYP ; 6-311G++(d,p).

1. INTRODUCTION (ARIAL, BOLD, 11 FONT, LEFT ALIGNED, CAPS)

The study, at the molecular level, of the interaction between metals and bioligands (les proteins, nucleic acids, and other bio-substances) is topical [1-4]. The coordination of these bioligands profoundly modifies the physiological properties of metals and those of ligands in the direction of the overall positive modification of these properties. The bioinorganic chemistry is studying ardently the coordination of trace elements with amides and imides [5-13]. The results from these studies are using in various areas of science and technology: medicine, agriculture, environment protection, catalysis, etc...

Amides and imides contain two pair donor atoms (N and O). In a certain conditions, the imides (like the amides) can enter in coordination by ionic form (by deprotonated form). Every that lead to many possible coordination compounds structures and properties [14-18].

One use successfully experimental (IR for exemple) or quantochemical methods to explain the competition character of donor- atoms coordination.

This work used quantochemical method in the aims:

- to determinate the coordination point of succinimide, of N-hydroxysuccinimide and of they deprotonated forms with a metal (the zinc for exemple).
- to determinate the geometry of the formed complex.

2. MATERIAL AND METHODS / EXPERIMENTAL DETAILS / METHODOLOGY

This work is a theoretic study of the coordination of the succinimide and it derivatives with the zinc (II). The investigations were carried out by quantochemistry calculations using the density functional theory (DFT) method assisted by B3LYP functional. The calculation basis set was 6-311g++ (d,p).

The calculations were made by the software Gaussian 03 and 09 [19]. The drawings of chemical systems were produced with ChemDraw Ultra 8.0 and GaussView 5.0.8.

After the study about the coordinating possibility of each ligand via some criterions like geometric parameters, atomic charges, electrostatic potentials (ESP) and the frontier orbitals, the formation of its complex with zinc (II) has been calculated. We attempted to elucidate

the hybridization state of Zn (II) and, consequently, the geometric layout of the obtained complex.

The following ligands had been considered: the succinimide (HSu), its deprotonated form (Su^-), the N-hydroxosuccinimide (OHSu) and its deprotonated form (OSu^-). The investigations were performed at 25°C and 1 atmosphere.

This work was carried out at the "Laboratoire de chimie Théorique et de Spectroscopie Moléculaire" of "Université d'Abomey-Calavi", on a Samson microcomputer.

3. RESULTS AND DISCUSSION

3.1-The ligands

This research allowed to expect the coordination site of the ligands through the analysis of some system parameters, recognised to be coordination indicators (CI). These IC was the geometric data, the atomic charges, the frontier orbitals and the energetic data of ligands. The investigated ligands are shown on figure 1. Each ligand contains one nitrogen atom and two or three oxygen atom. These atoms are pair donor atoms.

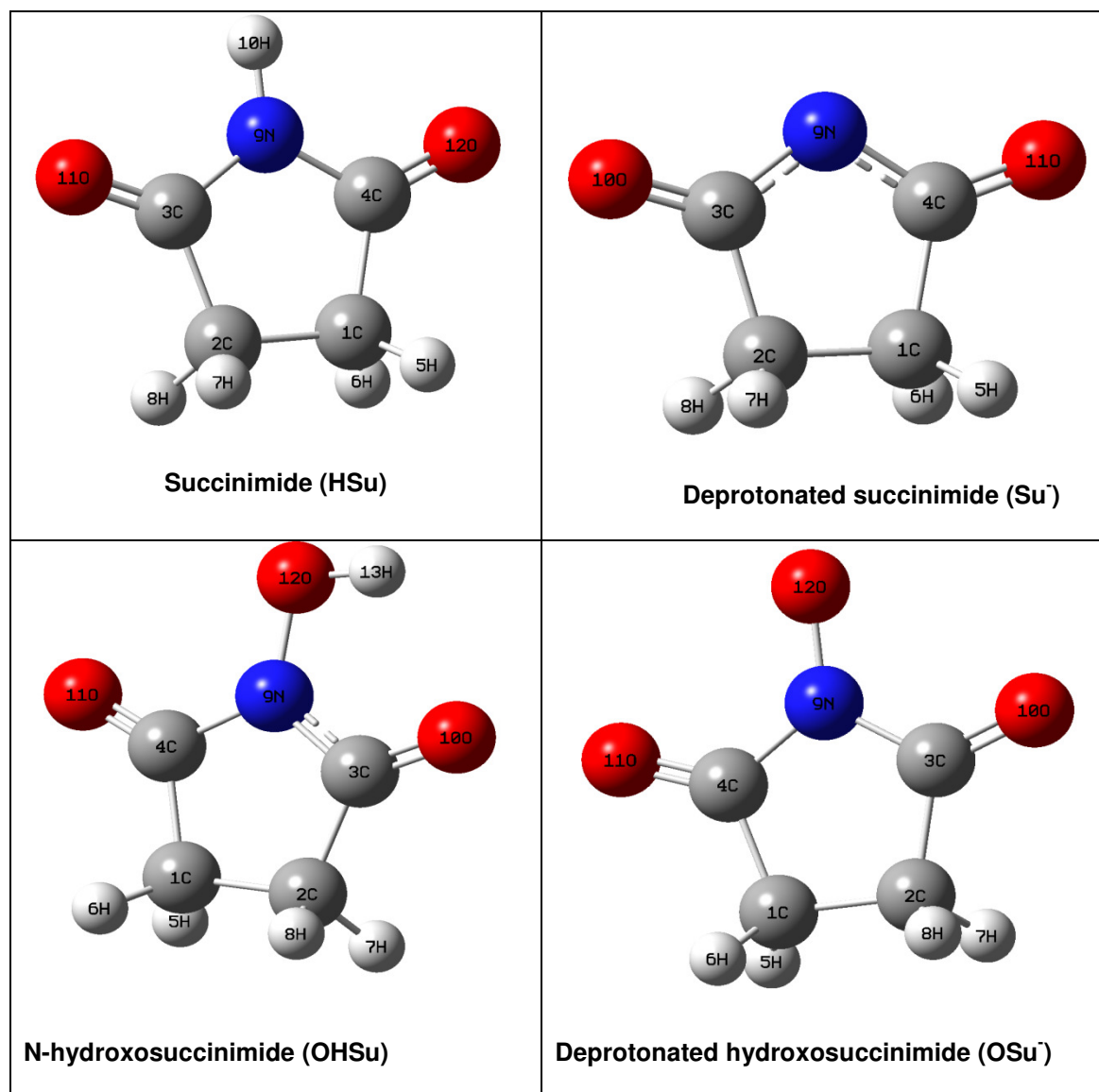


Fig.1. Calculated geometry investigated ligands (DFT/B3LYP at 25°C and 1atm).

3.1.1 Geometric analysis

The table 1 shows the geometric parameters of the ligands.

The table reveals that the calculated geometric data were, in general, in the case of the succinimide, similar to the experimental radiocrystallographic one. The averages were about to 0,0% for the interatomic distances and for the bend angles. Only the O-H bond showed a noticeable average. This situation shows that OH bond depend to his environment; indeed the simulation was performed on isolated molecule whereas the experimental data were obtained with molecules that were contained in a compact crystal.

The heteroring of Su is flat since the dihedrals NCCC and CNCC are almost equal to 0°. The heteroring and the hydrogen atom are in the same geometric plan since the dihedral HNCC equals 180°. The sum of the angles around the atom N is nearly equal to 360°, which means that the nitrogen is in sp^2 hybridization state ; so the non-bonding electronic pair of nitrogen atom has most probably a p character almost pure; it electronic cloud is orientated perpendicularly to the NCO plan. One notice that the length of CN bond (about 1.39 Å) is intermediate between the singlee bond (1.47 Å) and the double bond

(1,27Å) ; this situation suggest that the free electronic pair of nitrogen atom is delocalized ; it electronic cloud is distributed over both CN bonds. This is not favorable to a coordination trough the nitrogen atom.

Deprotonation of HSu causes the appearance of a second free electron pair at the nitrogen atom: the electron cloud around the atom increased and conjugation with the π electrons of the C = O was left strengthened : the electron cloud around this atom increased and conjugation with the π electrons of the C = O bonds was strengthened; this reasoning is justified by the direction of variation of CN and CO bonds lengths when we pass from HSu to Su⁻ (respectively from 1.39 Å to 1.36 Å and 1.21 Å to 1.23 Å); that is consistent with the data the literature [14]. These variations seem low but it should be noted that the cloud of free electrons is spread over two CN bonds and combined with both CO bonds. This conjugation has reduced the availability of the lone pair of the nitrogen atom to the coordination process. The values of simple angles and dihedrals indicate that the heterocyclic ring of Su⁻ is plan.

The substitution by the hydroxyl group did not substantially modify the geometry of the system. The changes in the lengths of CN and CO bonds are insignificant therefore the coordination through N is unfavorable as in the case of succinimide. Let it be noted that the position of the H of the OH group is not symmetrical for both imidic O; it is turned to one of them and so is closer to him. This can be explained by the establishment of a hydrogen bond between the O atom and the H atom of the hydroxyl group during its passage near this atom O during thermal agitation.

Deprotonation of the OHSu gave OSu⁻. The flatness of the heteroring is only slightly disturbed. The dihedrals NCCC and CNCC varied, each from 0.00 to 0.02 ° C. The O imidic atom is placed in the geometric plane of NCC. The lengths of C = O and CN bonds (1.22 Å and 1.39 Å respectively) show that the departure of the proton liberated the lone pair of N at the influence of this proton , allowing it to strengthen conjugation with π doublet of the C = O bond: coordination through an O atom appears as privileged in OSu⁻.

This study requires that one analyses the atomic charges in the studied systems.

Table 1. Geometric parameters of ligands

Parameters	HSu				Su ⁻	OHSu	OSu ⁻
	DFT	AM1[14]	EXP[16]	average*	DFT	DFT	DFT
Lengths(Å)							
C=O ¹⁰	1.21	1.23	1.21	0.00	1.23	1.21	1.22
C=O ¹¹	1.21	1.23	1.21	0.00	1.23	1.20	1.22
C ³ -N	1.39	1.41	1.40	0.00	1.36	1.38	1.39
C ⁴ -N	1.39	1.41	1.40	0.00	1.36	1.39	1.39
N-H OU N- X	1.01	0.99	0.95	-0.06(6.25%)	-	1.37	1.31
C _{im} -C ¹	1.53	1.53	1.50	-0.03(0.02%)	1.56	1.53	1.52
C _{im} -C ²	1.53	1.53	1.50	-0.03(0.02%)	1.56	1.51	1.52
Angles (°)							
NC ³ O ¹⁰	125.2	123.,9	123.0	-2.2(0.02%)	127.1	122.3	125.9
NC ⁴ O ¹¹	125.2	123.9	123.0	-2.2(0.02%)	127.1	125.9	125.9
NC ³ C ²	107.0	109.0	107.8	0.8(0.02%)	111.75	106.9	109.1
NC ⁴ C ¹	107.	109.0	107.8	0.8(0.02%)	111.75	105.1	109.1
HNC ³ OU XNC ³	122.4		-		-	120.6	124.0
HNC ⁴ OU XNC ⁴	122.4		-		-	-	124.0
C ³ NC ⁴	115.2				110.29	116.7	112.1
Dihedrals(°)							
NCCC	0.0				0.0	0.0	0.0
CNCC	0.0				0.0	0.0	0.0
H(X)NCC	180.0					180.0	180.0

*Average of experimental (EXP) and DFT values

C_{im} = imidic carbon atom

3.1.2 Atomic charges analysis

It has been reported in Table 2 the electric charges carried by some atoms. In the Hsu molecule as in that of Su⁻ the electron density around the N atom (-0.892 and -1.133 ua) is slightly higher than that on each O atom (ua -0.829 to -1.045 and Su for Su⁻). This implies that coordination is rather favorable through N; nevertheless it is appropriate to also take account the environment of the nitrogen where imidic hydrogen has a positive charge (0.220 ua) substantial, likely to push the complexing metal ion. When we look at the OHSu molecule we notice that the imidic oxygen atoms (-0.830 ua and -0.797 ua) are more negative than the nitrogen atom (-0.551 ua), suggesting that the coordination by a imidic oxygen atom is more likely. Note that the O atom imidic located on the side of the hydrogen of the hydroxyl group seems the most electron-rich. The expulsion of the OH proton resulted in the formation of OSu⁻. In this ion, charge analysis leads us to suspect that the coordinating probability of this ligand through an imidic oxygen atom is greater.

The definition of the coordination center can also be done with regard to the analysis of electrostatic potential (PES) at the atoms in the system studied.

Table 2. ATP charges of some atoms

Atoms	HSu	Su ⁻	OHSu	OSu ⁻
O	-0.829	-1.045	-0.830 and -0.797	-0.981
N	-0.892	-1.133	-0.551	-0.258
H ^N ou O ^N	0.220	-	-0.406	-0.778
C _{im}	1.164	1.229	1.080 and 1,161	1.043
C	-0.047	-0.030	-0.039 and 0.034	0.080

H^N = H atom bonded with N atom

O^N = O atom bonded with N atom

3.1.3 Electrostatic potential (ESP) analysis

We were interested to electrostatic potentials at a few atoms in the area where coordination is likely to occur. The values are reported in Table 3. It is found that the ESP at the oxygen atoms is greater than that at the nitrogen atom. This may suggest that coordination via an O atom is more favorable in all systems studied. It should be noted that the electrostatic potential at the two types of oxygen (imidic O and O of the hydroxyl group) in OHSu and OSu⁻ are very close (-22.36 ua and -22.29 ua ; -22.55 ua and -22.61 ua). Thus, based on the values of ESP, we think that the coordination can take place through the hydroxyl group oxygen atom or by one of imidic O atoms in the case of a either of these two ligands.

Table 3. Electrostatic (ua) potentials at some atoms

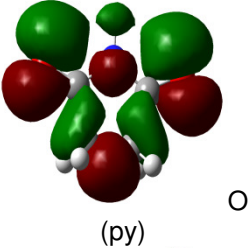
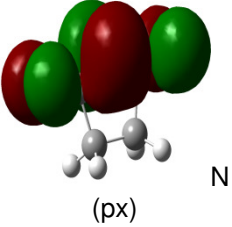
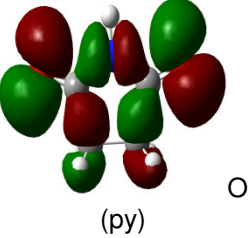
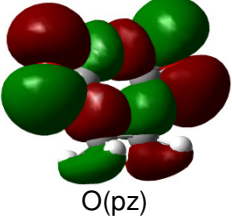
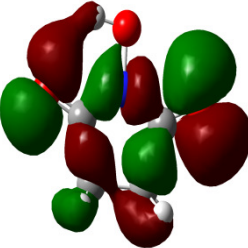
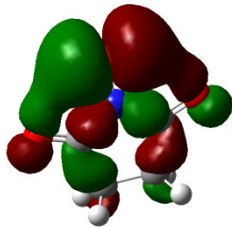
Atomes	HSu	Su ⁻	OHSu	OSu ⁻
O	-22.37	-22.58	-22.36	-22.55
N	-18.33	-18.61	-18.27	-18.47
H ^N ou O ^N	-0.98	-	-22.29	-22.61
C _{am}	-14.64	-14.86	-14.63	-14.83
C	-14.73	-14.92	-14.73	-14.89

3.1.4 Frontier orbitals analysis

Table 4 shows the HOMO and HOMO-1 of ligands and table 5 contains information relating to the LUMO and LUMO+1 of zinc taken as an example of ion-acceptor. These are the orbitals which are usually involved in chemical bonds, namely the coordination bonds.

From the analysis of the table 4 it appears that the succinimide gives a complex by an atom of oxygen because atoms O are dominant in the HOMO and same in the HOMO-1; the ion OSu⁻ gives a complex by the atom of oxygen bound to the atom of nitrogen for the same reasons. As regards Su⁻ and OHSu, frontier-orbitals are not unambiguous proof of coordination; Indeed, in these ligands both orbital borders seem favorable to all the sites of coordination initially anticipated: atoms O and N for Su⁻ ion, atoms O^{im}, O^N and N for the molecule OHSu. Besides we notice a dominant participation of p (px or py or pz) atomic orbitals in the coordinating bond. It is advisable to verify if these atomic orbitals can have overlap with the central ion. The zinc (II) is the example envisaged in the present study. Table 5 shows that the LUMO and LUMO+1 of ZnCl₂ are dominated respectively by s and p_y atomic orbitals.

Table 4 : HOMO et HOMO-1 des ligands solides (25 °C)

Orbitals	HSu			Su ⁻		
	Ener- gy (eV)	Dominant atomic orbitals	Coeffi- cient	Ener- gy (eV)	Dominant atomic orbitals	Coeffi- cient
HOMO -1	-8,43	 (py) O	0,68	-2,12	 (px) N	0,76
HOMO	-7,62	 (py) O	0,68	-1,93	 O(pz)	0,69
Favorable site		O			O and N	
Frontier Orbitals	OHSu			OSu ⁻		
	Ener- gy (eV)	Dominant atomic orbitals	Coeffi- cient	Ener- gy (eV)	Dominant atomic orbitals	Coeffi- cient
HOMO -1	-7,89		0,78	-1,49	 O ^N (pz)	1,03

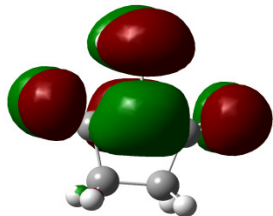
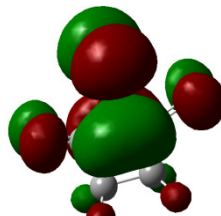
HOMO	 $O^{im}(py)$ $N(pz)$ $O^N(pz)$	 $O^N(px)$	
	-7,62	-0,54	1,06
	0,75 0,76		
Favorable site	O^{im}, O^N and N	O^N	

Table 5 : ZnCl₂ frontier orbitals (25 °C)

Frontier orbitals	Ener-gy (eV)	Dominant atomic orbitals	Coef-ficient
LUMO	-2,31	Zn(s)	2,01
LUMO+1	-0,79	Zn(py)	1,43

Zn(II) électronic structure is $1s^2 2s^2 2p^6 3s^2 3p^6 4s^0 3d^{10} 4p^0$. The zinc (II) gives often tetraedric complexes close to the punctual group T_d .

Le table 6 is the table of the characters of the punctual group T_d [20]. The analysis of this table of characters revealed that the overlap integral I_1 s orbitals of Zn(II) and p_x (ou p_y ou p_z) orbitals of a ligand equals $\int A_1 \cdot T_2 dr$. The decomposition of the direct product $A_1 T_2$ in inflexible representations showed that this product contains $\frac{1}{6} A_1$; this means that the integral I_1 is nonzero and therefore coordination is possible between the Zn(II) LUMO dominated by the s atomic orbital and the HOMO or the HOMO-1 dominated by a p orbital of an O atom or that of the N one. The same calculations were performed for the overlap integral I_2 of the Zn (II) p_y orbital with the p_x (or p_y or p_z) orbital of the ligand. $I_2 = \int T_2 \cdot T_2 dr$. It has been found that the integrand contains $\frac{1}{2} A_1$ therefore I_2 is not zero. This means that the orbital overlap of the Zn (II) p_y orbital with the p_x (or p_y or p_z) orbital of the ligand can be non-zero accordind to the group theory principles.

Table 6: The characters table of the punctual group T_d

T_d	E	$8C_3$	$3C_2$	$6\sigma_d$	$6S_4$	$h=24$
A_1	1	1	1	1	1	$x^2+y^2+z^2$
A_2	1	1	1	-1	-1	
E	2	-1	2	0	0	$(3z^2-r^2, x^2-y^2)$
T_1	3	0	-1	-1	1	(R_x, R_y, R_z)
T_2	3	0	-1	1	-1	
						$(x,y,z), (xy,xz,yz)$

Table 7 summarizes the findings of this study.

3.1.5- Summary analysis

In Table 7 we read, at the intersection of each ligand with each coordination indicator (CI), the atom through which coordination can occur during a complexation process.

A statistical study of Table 7 revealed that the succinimide coordination through the oxygen atom is dominating as 100% of CI considered in the present work are in favor of it. The molecule of hydroxosuccinimide seems coordinated through the imide oxygen atom; all CI are in favor. Regarding the OSu^- ion, indicators are favorable to O^N (50%), to O^{im} (50%) and to N (25%); therefore OSu^- coordinating takes place, preferably, via an oxygen atom from one or the other type of oxygen. As for the Su^- ion, it was recorded that 75% of CI are favorable to coordination via O atom and 50% are favorable to the N atom; then one is tempted to say that coordination via O is more likely. The modeling of complexes has solved ambiguities that appeared in this investigation and confirmed what seemed already decided.

Table 7 : Summary analysis

Species	HSu	Su^-	OHSu	OSu^-
CI				
Bond lengths	O	O	O^{im}	O^{im}
Atomic charges	N, O	N	O^{im}	N
PES	O	O	O^{im}, O^N	O^N, O^{im}
HOMO et HOMO -1	O	O,N	O^N, N, O^{im}	O^N

3.2. Modeling of coordination compounds

3.2.1. Modeling

Complex $ZnCl_2 \cdot 2HSu$, $ZnCl_2 \cdot 2Su^-$, $ZnCl_2 \cdot 2OHSu$, $ZnCl_2 \cdot 2OSu^-$ and $ZnCl_2 \cdot OSu^-$ were modeled. Their structures are shown in Figure 2. In Table 8, some geometric data for these complexes are recorded.

The data in Table 8 show that the ligands HSu, OHSu and OSu^- entered in coordination with the zinc atom through the imidic oxygen atom since interatomic distances $Zn-O^{im}$ there are about 2 Å. This value is consistent with the value of the Zn-O distance given by the literature [14.].

The OSu^- ion may also form a chelate by establishing a second coordination bond with Zn via the O atom bonded to the nitrogen atom. Therefore it is formed a $ZnCl_2 \cdot OSu^-$ complex.

As for the Su^- ion, it has entered in the coordination with the complexing metal through the nitrogen atom to yield $ZnCl_2 \cdot 2Su^-$ complex.

In these complexes, Zn (II) has a tetrahedral structure. The vertexes of the tetrahedra are occupied by two chlorine atoms and two oxygen atoms. The zinc (II) has probably sp^3 hybridization in these complexes.

From the foregoing it appears that the combined analysis of interatomic distances, the electron densities of atoms, electrostatic potentials and frontier orbitals can generally predict the coordination sites in a ligand.

Table 8 : Some interatomic distances of modeled complexes

	ZnCl₂.2HSu	ZnCl₂.2Su⁻	ZnCl₂.2OHSu	ZnCl₂.2OSu⁻	ZnCl₂.OSu⁻
Distances(Å)					
Zn-O ^{im}	2.11	3.40	2.09 ; 2.10	2.08 ; 2.02	2.22
Zn-N	3.51	2.11	3.55 ; 3.41	4.29 ; 4.24	2.79
Zn-Cl	2.18 ; 2.28	2.33	2.23 ; 2.24	2.27 ; 2.29	2.25
Zn-O ^N	-	-	3.26 ; 3.41	4.87 ; 4.82	2.05
C=O ^{Zn}	1.23	1.22	1.23	1.25	1.23
C=O	1.20	1.22	1.19	1.22	1.21
N-O ^N	-	-	1.37	1.30	1.33
C-N ^{Zn}	1.36	1.37	1.36	1.37	1.37
C-N	1.41	1.37	1.42	1.41	1.40

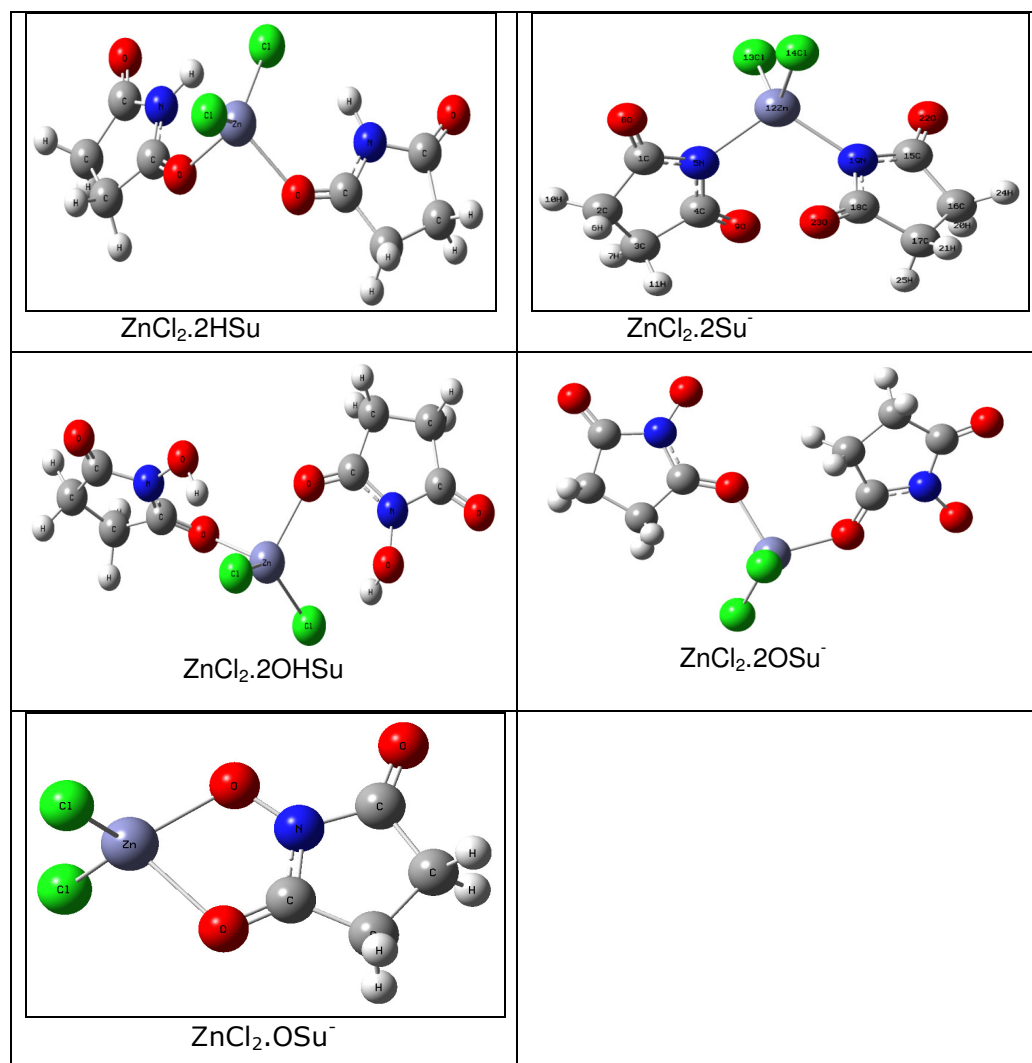


Fig.2. Structure of the modeled complexes

3.2.2. Energy study

The study of the energy of coordination between ligands and zinc (II) chloride was used to assess the stability of the coordination bond. Table 9 shows some energy values

The negative values of the free enthalpies of coordination show that coordination of the succinimide, of its deprotonated form, of N-hydroxosuccinimide or its deprotonated form with zinc (II) chloride at 25 °C in solid phase is a spontaneous process. The coordination enthalpies are also negative therefore the process is exothermic. ΔH_{coord} of ZnCl₂.2HSu, ZnCl₂.2Su⁻, ZnCl₂.2OHSu and ZnCl₂.OSu⁻ which values are respectively -5.43 eV or -523.94 kJ mol⁻¹, -6.26 eV or 604.03 kJ.mol⁻¹, -3,35 eV or 323.23 kJ.mol⁻¹ and -8.44 eV or -814.38 kJ.mol⁻¹ are above 200 kJ.mol⁻¹. This suggests that the coordination bonds of these complexes are of the chemical type [20]; these bonds are therefore solid enough. Table 10 brings together the chemical formulas of formed complexes with their names

265 **Tableau 9: Some energies of studied systems**

	ΔG , eV	ΔG_{coord} , eV	ΔH , eV	ΔH_{coord} , eV	Type of process
ZnCl ₂	-73461.00	-	-73466.17	-	-
HSu	-9815.44	-	-9814.36	-	-
Su ⁻	-9800.48	-	-9799.66	-	-
OHSu	-11861.14	-	-11860.06	-	-
OSu ⁻	-11846.45	-	-11845.36	-	-
ZnCl ₂ .2HSu	-93098.42	-6.54	-93094.33	-5.43	spontaneous, exothermic
ZnCl ₂ .2Su ⁻	-93067.67	-6.67	-93065.76	-6.26	spontaneous, exothermic
ZnCl ₂ .2OHSu	-97189.82	-6.54	-97189.64	-3.35	spontaneous, exothermic
ZnCl ₂ .2OSu ⁻	-97159.61	-5.71	-97157.44	-0.55	spontaneous, exothermic
ZnCl ₂ .OSu ⁻	-85315.61	-8.16	-85313.98	-8.44	spontaneous, exothermic

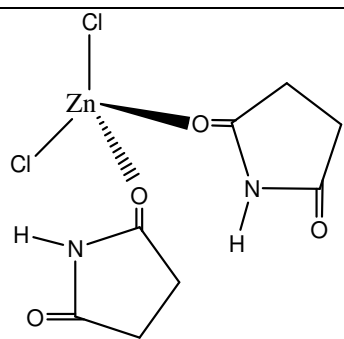
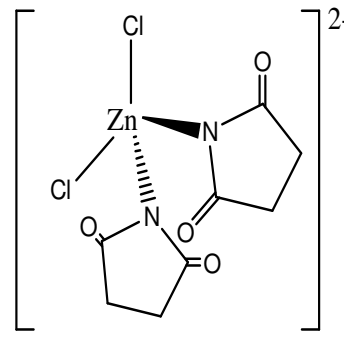
266 ΔG = Free enthalpy of the species

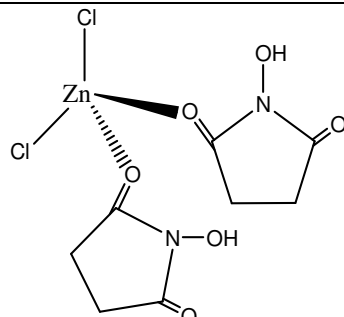
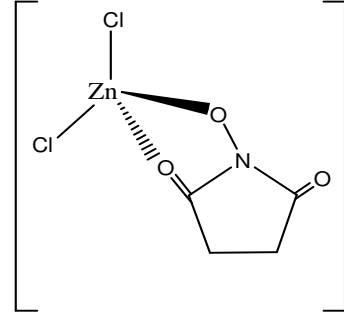
267 ΔG_{coord} = Free enthalpy of coordination

268 $\Delta G_{\text{coord}} = \Delta G_{\text{complex}} - (\Delta G_{\text{ligand}} + \Delta G_{\text{ZnCl}_2})$

269
270
271 Table 10 brings together the chemical formulas of formed complexes with their names. It shows
272 tetrahedral orientation of the bonds from zinc (II)

273 **Table10: Formed complexes**

	Formula	Name
ZnCl ₂ (HSu) ₂		Dichlorodisuccinimidezinc (II)
[ZnCl ₂ (Su) ₂] ²⁻		Ion dichlorodisuccinimidozincate (II)

$\text{ZnCl}_2(\text{OHSu})_2$		Dichlorodi N-hydroxosuccinimidezinc (II)
$[\text{ZnCl}_2\text{OSu}]^-$		Ion dichloro-N- hydroxosuccinimidozincate (II)

4. CONCLUSION

The present work is a theoretical study of the coordination of the succinimide molecule, of its deprotonated form, of its N-hydroxyl derivative and of the deprotonated form of the N-hydroxyl derivative. The results of our calculations showed that succinimide, its deprotonated form, its N-hydroxyl derivative and the deprotonated form of that molecule are capable of coordinating with metals. Zinc is one of those metals. It was found that the succinimide and N-hydroxosuccinimide form complexes via an imide oxygen atom. The succinimide deprotonated species forms a complex through the nitrogen atom. The deprotonated form of the N-hydroxosuccinimide can form a chelate $[\text{ZnCl}_2\text{OSu}]^-$ via an imide oxygen atom O^{im} and O^{N} oxygen atom.

In these complexes, Zn (II) has a tetrahedral structure. The vertexes of the tetrahedra are occupied by two chlorine atoms and two oxygen atoms.

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