



Quantum-chemical study of the coordination of some aromatic derivatives of semicarbazone

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Abstract

Semicarbazone is a molecule having the $R^1R^2C=N-NR^3-C(=O)-NR^4R^5$ general formula. The oxygen atom with its two free electron pairs in on hand, and each nitrogen atom with its one free electron pair in the other hand are potential coordination sites. The simplest molecule in this series is the semicarbazone which formula is $H_2C=N-NH-C(=O)NH_2$. Some semicarbazones, such as nitrofurazone, and some thiosemicarbazones are known to have many properties: antiviral, antibacterial, antitrypanosomal, anticonvulsant, antitumor, anticancer. They are usually mediated by an association with copper or iron. Indeed transition metal complexes with given chemical structures are useful alternatives in the treatment of certain diseases since coordination of active ingredients deeply modifies both the physiological properties of metals and ligands in the meaning of overall improvement of these properties. The present work focuses on quantum study of the complexation of some aromatic derivatives of semicarbazone. The purpose of this study is to determine the most favorable coordination site of each of these ligands. It was found that the oxygen atom appears more favorable to the coordination of the aromatic derivatives of semicarbazone. Complexes of these ligands with the Zn (II) were modeled. The calculations were made the DFT/B3LYP level with the 6-31G (d, p) orbital basis set.

Keywords: Coordination compounds, aromatic semicarbazones, DFT/ B3LYP, 6-31G (d,p) basis set.

Introduction

The study at the molecular level of the interaction between metals and bioligands (proteins, nucleic acids, their fragments, and other substances contained in the organism) is topical¹⁻⁴. The bioinorganic chemistry which is currently in full swing is concerned, inter alia, with the coordination of trace elements with organic ligands. The results of these studies find their applications in various fields of science and technology such as medicine, agriculture, environmental protection, catalysis. In fact, the coordination of bioligands profoundly modifies both the physiological properties of metals and those of ligands with an overall improvement in the activity of the pure ligand or of the complexing metal salt⁵⁻¹³.

Semicarbazones (SCZ) are molecules having $R^1R^2C=N-NR^3-C(=O)-NR^4R^5$ general formula, thus having donor atoms (N and O) capable of forming bonds with complexing metals, they are of particular interest as ligands. Semicarbazones are derivatives of aldehydes or ketones. They are formed by condensation of these compounds with a semicarbazide as shown by the reaction:

$H_2NNHC(=O)NH_2 + R^1C(=O)R^2 \rightarrow R^1R^2C=NNHC(=O)NH_2 + H_2O$
where: R^2 is a hydrogen atom (if it is an aldehyde) or an alkyl group (if it is a ketone). The simplest molecule of this series is the semicarbazone with the chemical formula $H_2C=N-NH-C(=O)NH_2$. Certain semicarbazones, such as nitrofurazone, and certain thiosemicarbazones are known for their antiviral,

antibacterial, antitrypanosomal (antiparasitic), anticonvulsive, anti-tumor, anti-cancer, etc. activities, generally mediated by a binding with copper or iron¹⁴⁻¹⁶.

This work aims to predict the coordination site in each studied aromatic semicarbazone molecules with quantum calculations. The coordination indicators (IC) used in this study are interatomic bond lengths, atomic charges, electrostatic potentials, boundary structures and indexes of electrophilic super delocalisability. The simulation of complexes of these ligands with zinc served to confirm the results.

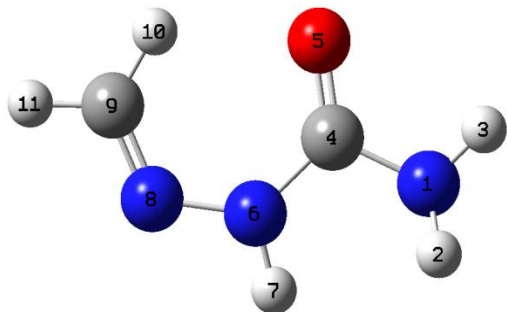
Materials and methods

The present work is a theoretical study of some aromatic semicarbazones complexation. These are quantum chemistry calculations carried out on the DFT/B3LYP level with the 6-31G(d,p) basis set at 25°C and 1 atm. The software used to perform the calculations was Gaussian 03 and 09¹⁷. The used computer was Samsung intel core i 3 2,4 GHz. Indexes of electrophilic super delocalisability were calculated by the D-cent-QSAR¹⁸ program.

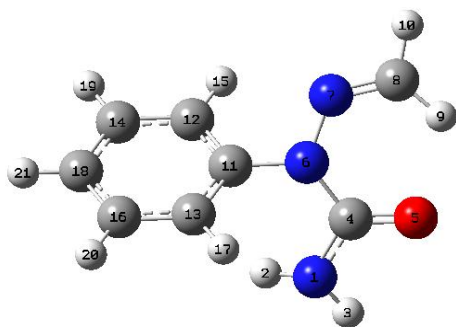
The softwares Gaussview and ChemDraw ultra 8 allowed to make the different figures. The goal set by this study was achieved on the basis of the analysis of some coordination indicator parameters: bond lengths, charges of atoms, boundary structures, electrostatic potentials, electrophilic super delocalisability indexes.

Results and Discussion

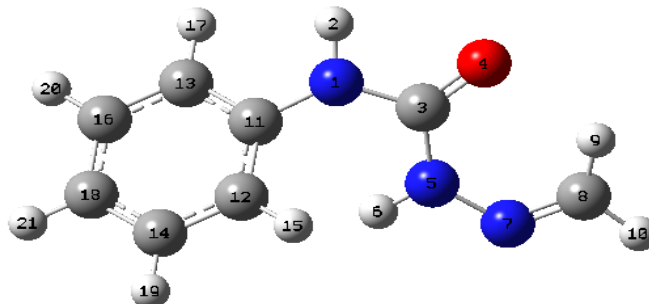
Ligand study: The following molecules are the potential ligands, objects of this investigation: 2N-Phenylsemicarbazone, E4-phenylsemicarbazone and phenylmethanal semicarbazone (Figure-1).



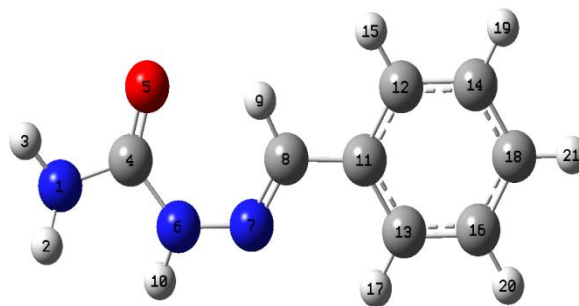
(a) Semicarbazone(SCZ) $\Delta G = -318,62$ hartree ou $-8669,87$ eV.



(b) 2N Phenyl SCZ $\Delta G = -549.603$ hartree ou $14955,08$ eV.



(c) E4-PhenylSCZ $\Delta G = -549.606$ hartree ou $14955,16$ eV.



(d) Phenylmethanal SCZ $\Delta G = -549.623$ hartree ou $14955,62$ eV

Figure-1: Structures of the aromatic semicarbazones studied at B3LYP/6-31G(d,p) level at 25°C. SCZ= Semicarbazone; 2N Phenyl SCZ = 2N Phenylsemicarbazone; E4-Phenylsemicarbazone; Phenylmethanal semicarbazone.

Bond lengths analysis: The lengths of some chemical bonds are collected in the Table-1.

Table-1: Some bond lengths contained in the aromatic semicarbazones (Å).

	SCZ	E-Phmethanal SCZ	E4-PhenylSCZ	2NPhenylSCZ	Standard* ¹⁹⁻²¹
N ¹ -C ⁴	1.390	1.391	1.393	1.379	1.47
C ⁴ =O ⁵	1.222	1.222	1.224	1.224	1.21
C ⁴ -N ⁶	1.391	1.39	1.384	1.409	1.47
N ⁶ -N ⁸	1.374	1.372	1.375	1.385	1.40
N ⁸ =C ⁹	1.374	1.288	1.281	1.280	1.27
N ¹ H ² (C ¹¹)	1.011	1.011	1.413	1.008	1.01
N ¹ H ³	1.010	1.010	1.011	1.009	1.01
C ⁹ H ¹⁰	1.085	1.087	1.085	1.088	1.09
C ⁹ H ¹¹ (C ¹¹)	1.088	1.469	1.088	1.083	1.09
C ⁶ H ⁷ (C ¹¹)	1.009	1.009	1.009	1.437	1.09

Reading this Table-1, it can be seen that the N^1C^4 bonds are intermediate between a single bond and a double bond, their length being on average 1.39 Å. This can be explained by the fact that the free electronic pairs of the nitrogen atom N^1 conjugates with the π pair of the double bond $C^4=O^5$; this is not likely to favor the coordination of the molecule via the free pair of N^1 . The same reason disadvantages coordination via N^6 : the lone pair of N^6 conjugates with the $C^4=O^5$ bond on the one hand and the $N^8=C^9$ bond on the other hand; this creates a free electronic flow between C^9 and O^5 via N^8 , N^6 and C^4 . Therefore, the interatomic distance analysis allowed telling that the electron pairs available for coordination with a metal are those of the oxygen atom and the nitrogen atom N^8 . This analysis must be completed by the analysis of atomic charges and other IC.

NBO charge analysis: The Table-2 shows NBO charges of some atoms of the studied molecules. We notice on Table-2 that the more negative charges are on the atom N^1 in all molecules (in average 0,9 ua) but the proximity of the hydrogen atoms H^2 and H^3 or C^{11} (in the E4-phenylsemicarbazone), strongly positives, is not favorable to the access of a complexing cation to the free electron pair of N^1 . This charge analysis elects the oxygen atom as the most favorable coordination site since it is this atom which immediately follows N^1 in the order of the atomic charges. The Table-3 will allow analysing the electrostatic potentials (ESP) at the level of some atoms.

Electrostatic potential (ESP): The ESP valour at the level of the oxygen atom is the highest (-22,35 ua) in all molecules studied. It is followed by those of the nitrogen atoms. This analyse shows that the oxygen atom is more favorable to coordination. The boundary orbitals were analysed too.

Boundary orbital analysis: It is known that coordinating bonds usually take place by the highest occupied molecular orbital (HOMO) or the following one (HOMO-1). The analysis of boundary orbitals (Table-4) in the presented investigation indicates that the O atom occupies a large part of HOMO-1 of the molecules studied. The HOMO is dominated by N^6 except in E4-phénylsemicarbazone where N^1 dominates. Thus this analysis suggests that the favourable coordinating sites are N^6 , O^5 (in PhenylmethanalSCZ), N^1 , N^6 , N^8 , O^5 (E4-PhenylSCZ) and N^6 , N^8 , O^5 (in 2NPhenylSCZ). These atoms participate to the HOMO and HOMO-1 mainly by p orbitals.

Atomic Indexes of Electrophilic Super delocalisability (IESD) Analysis: The atomic index of electrophilic super delocalisability is a magnitude which shows the capacity of given specie to attract an electrophilic system; the coordinating probability is highest at the level of the atom with the most negative IESD¹⁸. Thus, reading the Table-5, one can notice that oxygen atom (IESD about -16.5 hartree) is the more favourable coordination site for all studied molecules.

Table-2: Charges NBO of aromatic semicarbazones.

	SCZ	E-Phméthanal SCZ	E4-PhSCZ	2NPhSCZ
N^1	-0.901	-0.901	-0.672	-0.893
C^4	0.800	0.799	0.811	0.814
O^5	-0.641	-0.644	-0.646	-0.646
N^6	-0.496	-0.485	-0.494	-0.310
N^8	-0.270	-0.275	-0.270	-0.277
C^9	-0.169	0.034	-0.167	-0.156
H^2	0.406	0.406	0.441	0.422
$H^3(C^{11})$	0.426	0.426	0.139	0.429
$H^7(C^{11})$	0.421	0.422	0.432	0.128
H^{10}	0.219	0.235	0.22	0.224
$H^{11}(C^{11})$	0.206	0.422	0.206	0.206

Table-3: ESP of the studied aromatic semicarbazones.

	SCZ	Phenylmethanal SCZ	E4-Phenyl SCZ	2N Phenyl SCZ
N ¹	-18.319	-18.32	-18.305	-18.323
C ⁴	-14.599	-14.599	-14.597	-14.601
O ⁵	-22.346	-22.346	-22.347	-22.349
N ⁶	-18.282	-18.280	-18.283	-18.27
N ⁸	-18.321	-18.327	-18.322	-18.325
C ⁹	-14.719	-14.713	-14.719	-14.72
H ² (C ¹¹)	-1.008	-1.009	-14.676	-1.015
H ³ (C ¹¹)	-1.009	-1.018	-1.012	-1.019
H ⁷ (C ¹¹)	-1.012	-1.011	-1.015	-14.689
H ¹⁰	-1.112	-1.114	-1.112	-1.114
H ¹¹ (C ¹¹)	-1.113	-14.735	-1.1129	-1.114

Table-4: Boundary orbitals of the aromatic semicarbazones.

		HOMO-1	HOMO	Favorable sites
SCZ	Energies	-0,2516	-0,2446	N ⁶ , N ⁸ , O ⁵
	Coefficients	0,71 0,83	0,77	
	Dominant atomic orbitals	O ⁵ (2px, 3px) N ⁸ (2py,3py)	N ⁶ (2pz,3pz)	
Phenyl-Methanol SCZ	Energies	-0.2468	-0.2144	N ⁶ , O ⁵
	Coefficient	0,73	0,57 0,47	
	Dominant atomic orbitals	O ⁵ (2px, 3px)	N ⁶ (2pz,3pz) N ⁸ (2pz,3pz)	
E4-Phenyl SCZ	Energies	-0.24778	-0.2295	N ¹ , N ⁶ , N ⁸ , O ⁵
	Coefficient	0,65 0,58 0,13 0,45 0,46	0,66	
	Dominant atomic orbitals	N ⁶ (2pz,3pz) N ⁸ (2s,2pz,3pz) O ⁵ (2px) O ⁵ (2py,3py) O ⁵ (2pz,3pz)	N ¹ (2pz,3pz)	
2N Phenyl SCZ	Energie	-0.2478	-0.2250	N ⁶ , N ⁸ , O ⁵
	Coefficient	0,61 0,37 0,35 0,34	0,69	
	Dominant atomic orbitals	O ⁵ (2py, 3py) N ⁸ (2s,3s) N ⁸ (2px,3px) N ⁸ (2py,3py)	N ⁶ (2pz,3pz)	

Recapitulation: Le Table-6 summarizes the results of the analysis of the different coordination indicators.

Reading the recapitulative Table (Table-6), we notice that all the CI considered are favourable for the coordination of each studied molecule via the oxygen atom; the oxygen atom seem the main coordination site.

It is certainly important to confirm these results by modeling complexes from these ligands.

The choice is focused on zinc (II), a trace element that is very present in the treatment of various pathologies. Its electronic structure is $1s^2 2s^2 2p^6 3s^2 3p^6 4s^0 3d^{10} 4p^0$. Zinc (II) generally gives tetrahedral complexes close to the Td point group. This is

understandable when one observes its electronic structure: the orbital s, p_x , p_y and p_z are vacant and are capable of sp^3 hybridization. The sp^3 hybrid orbitals point to the tops of a tetrahedron. The p orbitals of atoms recognized as favorable for the coordination of the ligands studied are capable to overlap with these sp^3 orbitals.

Modeling of Coordination Compounds: Modeling: Aromatic semicarbazone coordination compounds $ZnCl_2 \cdot (ligand)_2$ were modeled in this work with Zn(II) obtained from $ZnCl_2$. The interatomic distances were analysed. More important distances are collected in the Table-7.

Table-5: Atomic Indexes of Electrophilic Super delocalisability of the aromatic semicarbazones (hartree).

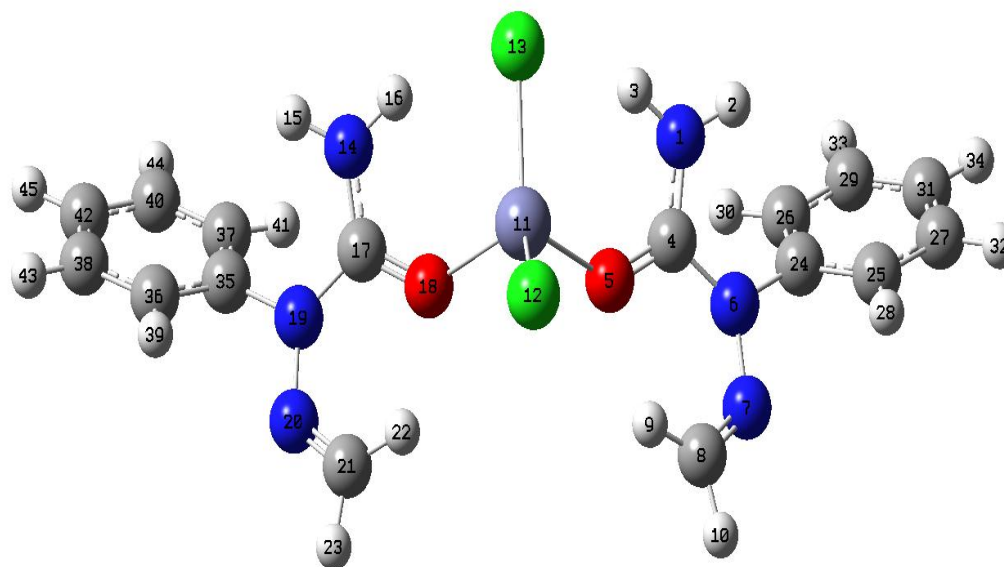
	SCZ	Phenyl-methanalSCZ	E4-PhenylSCZ	2NPhenylSCZ
N ¹	-12.2204	-12.2447	-11.9433	-12.2921
C ⁴	-6.3707	-6.3704	-6.3609	-6.4161
O ⁵	-16.4125	-16.4352	-16.5184	-16.5879
N ⁶	-11.3783	-11.3586	-11.3791	-11.3867
N ⁸	-12.4909	-12.8778	-12.5058	-12.5834
C ⁹	-9.6368	-9.1857	-9.6449	-9.6677
H ² (C ¹¹)	-1.3365	-1.3387	-1.3270	-1.3361
H ³ (C ¹¹)	-1.3162	-1.3174	-8.1267	-1.3225
H ⁷ (C ¹¹)	-1.3154	-1.3149	-1.3300	-8.4807
H ¹⁰	-1.9739	-2.0378	-1.9744	-1.9754
H ¹¹ (C ¹¹)	-2.0315	-9.1943	-2.0334	-2.05231

Table-6: Recapitulation.

	SCZ	Phenylmethanal SCZ	E4-Phenyl SCZ	2N Phenyl SCZ
Bond lengths	O ⁵ , N ⁸	O ⁵ , N ⁸	O ⁵ , N ⁸	O ⁵ , N ⁸
Atomic charges	O ⁵	O ⁵	O ⁵	O ⁵
Electrostatic potential	O ⁵	O ⁵	O ⁵	O ⁵
HOMO et HOMO-1	O ⁵ , N ⁶	O ⁵ , N ⁶	O ⁵ , N ¹	O ⁵ , N ⁶
IESD	O ⁵	O ⁵	O ⁵	O ⁵
% of favorable IC	O ⁵ (100),N ⁸ (20),N ⁶ (20)	O ⁵ (100),N ⁸ (20),N ⁶ (20)	O ⁵ (100),N ⁸ (20),N ¹ (20)	O ⁵ (100),N ⁸ (20),N ⁶ (20)

Table-7: Main interatomic distances of modeled coordination compounds.

	ZnCl ₂ (Phenylmethanal SCZ) ₂	ZnCl ₂ (E4-Phenyl SCZ) ₂	ZnCl ₂ (2N Phenyl SCZ) ₂
ZnO ⁵	1.991	1.997	1.999
ZnO ^{5'}	1.989	2.000	1.999
ZnN ¹	3.394	3.311	3.373
ZnN ^{1'}	3.392	3.309	3.373
ZnN ⁶	4.190	4.232	4.218
ZnN ^{6'}	4.190	4.235	4.218
ZnN ^{8'}	4.782	4.894	4.731
ZnN ⁸	4.784	4.899	4.731
ZnCl	2.256	2.254	2.205
ZnCl'	2.256	2.255	2.305



ZnCl₂(2NPhenylSCZ)₂

Figure-2: Structures of the coordination compounds of the aromatic semicarbazones.

It is revealed that from all interatomic distances ZnX (X= O, N or Cl), the distances ZnO only corresponds to a bond length (2 Å environ)²². Zn(II) formed coordination bonds with two atoms O provided, everyone, by one ligand like on the Figure-2.

In these coordination compounds, zinc has a tetrahedral structure; both oxygen atoms and both chloride atoms occupied, everyone, one vertex of the tetrahedron; the proportion Zn/Ligand is ½.

Table-8: Energies.

Energy study of the coordination compounds has been performed.

Energy Study: The Table-8 shows some energy data of the study systems: enthalpy (ΔH), free enthalpy (ΔG), enthalpy of coordination (ΔH_{coord}) and free enthalpy of coordination (ΔG_{coord}).

$$\Delta G_{\text{coord}} = \Delta G_{\text{complex}} - (2\Delta G_{\text{ligand}} + \Delta G_{\text{ZnCl}_2})$$

$$\Delta H_{\text{coord}} = \Delta H_{\text{complex}} - (2\Delta H_{\text{ligand}} + \Delta H_{\text{ZnCl}_2})$$

	ΔH , eV	ΔH_{coord} , eV	ΔG , eV	ΔG_{coord} , eV	Type of process
ZnCl ₂	-73458.28	-	-73459.09	-	-
Phenylmethanal SCZ	-14954.27	-	-14955.62	-	-
E4-PhenylSCZ	-14953.80	-	-14955.16	-	-
2NPhenylSCZ	-14953.75	-	-14955.08	-	-
ZnCl ₂ .2PhenylmethanalSCZ	-103369.09	-2.54	-103371.54	-1.75	Exothermic and Spontaneous
ZnCl ₂ .2E4-PhenylSCZ	-103368.28	-2.4	-103370.72	-1.31	Exothermic and Spontaneous
ZnCl ₂ .2(2NPhenylSCZ)	-103367.98	-2.2	-103370.46	-1.21	Exothermic and Spontaneous

All values of coordination enthalpies are negative so the process is exothermic. The free enthalpies are negative too: the process is spontaneous.

The free enthalpy of coordination of ZnCl₂. 2 Phenylmethanal SCZ is lowest so it is more stable. The complex ZnCl₂.2(2N Phenyl SCZ) is the least stable.

Conclusion

This work is a DFT study of the coordination of some aromatic semicarbazones. These were Phenylmethanal semicarbazone, 2NPhenylsemicarbazone and E4-Phenylsemicarbazone. The calculations were performed at the B3LYP/6-31G(d,p) level. The investigations has done through the analysis of some coordination indicators: bond lengths, atom charges, atom electrostatic potentials, boundary orbitals, and atom electrophilic super delocalizability indexes. These analysis showed that the coordination of studied molecules is possible via the oxygen atom.

The modeling of coordination compound of the aromatic semicarbazones with zinc(II) confirmed the results of the ligand study. The coordination process were exothermic and spontaneous..

The complexes obtained with Zinc (II) provided by the zinc (II) chloride are of the proportion Zn: ligand equal 1 : 2. The central element has a tetrahedral configuration. The vertices of the tetrahedron are occupied by both Cl atoms and two atoms O provided by two ligand molecules.

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