



Investigating the Complexation of a recently synthesized phenothiazine with Different Metals by Density Functional Theory

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Abstract

In this research, the complexation of a new recently synthesized phenothiazine with 10 different metals was evaluated by Density functional theory. At the first step, the structures of 6,15-diazabenz[a][1,4]benzothiazino[3,2-c]phenothiazine, cations and their complexes with the mentioned material were optimized geometrically. Then, IR calculations were performed on them to obtain the values of formation enthalpy and Gibbs free energy. The acquired results indicate that Cu^{2+} forms the most stable and strongest complex with 6,15-diazabenz[a][1,4]benzothiazino[3,2-c]phenothiazine. Hence, this substance can be utilized as an outstanding ionophore or a potential ligand in the determination of copper by ion selective electrodes and different extraction methods respectively. All calculations were applied by Density functional theory in the level of B3LYP / 6-31G(d).

Keywords: 6,15-diazabenz[a][1,4]benzothiazino[3,2-c]phenothiazine, Density Functional Theory, Complexation, Copper, Thermodynamic Parameters.

1. Introduction

In the recent decades, the matter of heavy metals' contamination has been very controversial. Even ultra trace amounts of this type of metals can cause dire and irreversible problems such as diarrhea, nausea, different categories of cancer, infertility, hearing loss, autoimmune illnesses, depression, cardiovascular diseases and so on, for human beings and other living organisms [1-3]. And in some severe cases, poisoning with heavy metals may also lead to death. Despite the fact that the harmful effects of this kind of inorganic cations on the environment and human health have revealed to everybody. But, they are also widely used in different fields of industry and unfortunately, there has not been found an appropriate alternative yet. This fact implies that humans have the potential to be endangered by these toxic chemicals [4-5].

On the other hand, some of the inorganic cations act as vital micronutrients in the body and their deficiency can eventuate to various sicknesses. As an ideal instance, it can be referred to calcium because this ion is essential for the suitable performance of the nervous system, muscles and bones. Calcium deficiency is attached to muscular cramps, osteoporosis, insomnia, hypertension, hair loss, dry skin and brittle nails [6-8]. Therefore, it could be deduced that determination of metals in pharmaceutical, environmental, clinical and industrial analysis is very important. Owing to the fact that ligands play a crucial role in analytical chemistry for determination of metals by ion selective electrodes and extraction techniques, it is very significant to evaluate the complexation of ligands with metals. Because many ion selective electrodes and extraction techniques that have been designed suffer from lack of selectivity and consequently they are not able to measure the analyte with high accuracy and precision. So, the interaction of a ligand with metals ought to be inspected and the cation that forms the strongest complex with the ligand had better to be chosen as analyte, in order to defuse the selectivity of the proposed approach [9-14].

Numerous experimental methods have been reported for investigating complexation of ligands with cations such as Uv-Visible spectrophotometry, NMR, polarography and conductometry. However, they have remarkable downsides such as being time consuming, needing intricate and expensive instruments, being costly, and using large amounts of non-degradable organic solvents which are hazardous for humans and also harmful for the environment. Thus, the above mentioned techniques are not preferable due to their substantial drawbacks [15-18]. Fortunately, Ab initio computational methods are in the opposite point of the aforementioned techniques. Since, they are time saving, economical, accurate and environmental friendly. In this regard, 6,15-diazabenz[a][1,4]benzothiazino[3,2-c]phenothiazine (Fig 1) was selected as ligand because it has 4 nitrogen and 2 sulfur atoms. Moreover, its solubility in water is extremely poor. Therefore, in this

study the complexation of 6,15-diazabenz[a][1,4]benzothiazino[3,2-c]phenothiazine with 10 cations was investigated for the first time by density functional theory [19-20].

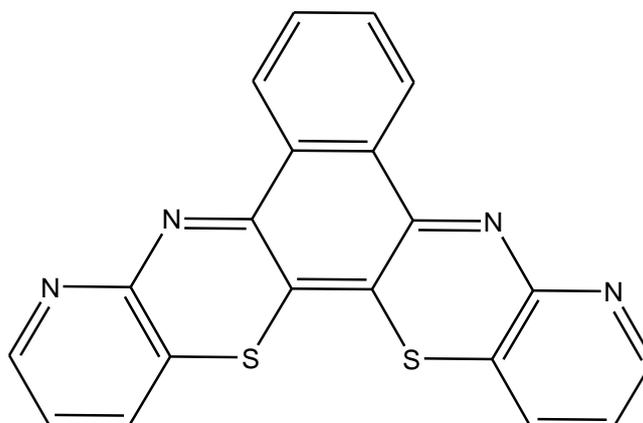


Fig 1. The structure of 6,15-diazabenz[a][1,4]benzothiazino[3,2-c]phenothiazine.

2. Computational details

In this study, the pertinent calculations to 6,15-diazabenz[a][1,4]benzothiazino[3,2-c]phenothiazine, Cations and their complex derivatives were implemented by Spartan software. The computations took place in 25°C and atmospheric pressure in the vacuum medium by density functional theory (DFT). For all materials, calculations were done via 6-31G(d) basis set except Ag^+ , Cd^{2+} , Pd^{2+} and their derived complexes where LANL2DZ (Los Alamos National Laboratory of Double Zeta) basis set were utilized. The studied reaction is as follows generally Equation 1:



At the outset, the compounds were optimized geometrically, and then IR calculations were performed in order to study thermodynamic parameters that are pertinent to the desired process.

3. Results And Discussions

3.1. Evaluating the Structure of the Complex

In order to realize how the cation attaches to the ligand and what the structure of the formed complex is, the copper (II) ion was put in two situations: A and B. In Mode A, the cation was joined to the ligand through the nitrogen atoms (Fig 2) and In Mode B, the Cu^{2+} is bound to the ligand via the sulfur atoms (Fig 3). Afterward, the optimization step was implemented on both of them and their minimum SCF energies were compared with each other. The results demonstrated that the cation reacts with ligand through the nitrogen atoms because the SCF energy of mode A is -8916038.660 kJ/mol which is significantly more negative than the value of SCF energy of mode B (-8915739.592 kJ/mol). Therefore, mode A was selected for the next calculations. It should be noted that the structure of 6,15-diazabenz[a][1,4]benzothiazino[3,2-c]phenothiazine is very symmetrical and it made no difference to put the cation on other sites of the molecule. Moreover, the copper was chosen in this step due to its softness and high tendency to form a complex with nitrogen and sulfur containing ligands.

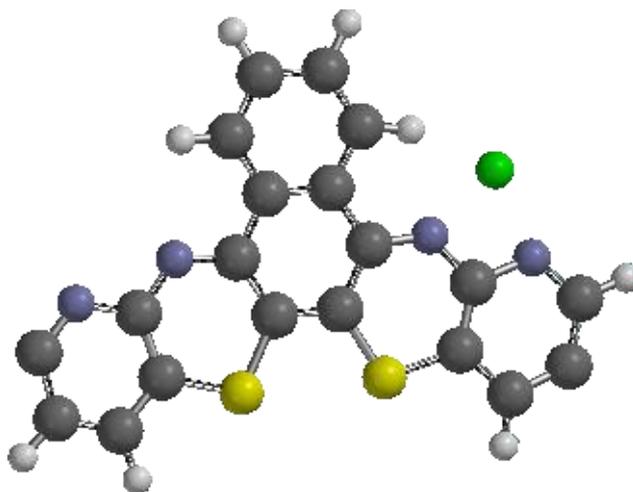


Fig 2. Mode A: Cu^{2+} attaches to the ligand via the nitrogen atoms.

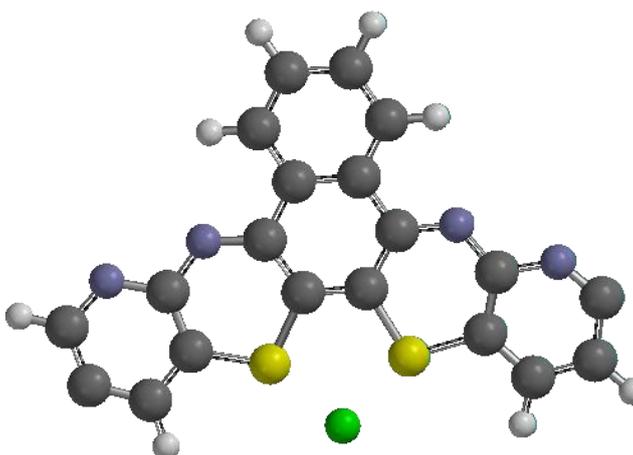


Fig 3. Mode B: Cu^{2+} attaches to the ligand via the sulfur atoms.

3.2. Calculation and Verifying the Values of Enthalpy Changes (ΔH_f)

The enthalpy values for raw materials and products were calculated by Spartan software. In order to obtain formation enthalpy variations the subsequent equations would be applied:

$$\Delta H_{\text{thermal}} = H_{\text{th complex}} - (H_{\text{th cation}} + H_{\text{th ligand}}) \quad \text{Equation 2}$$

$$\Delta H_f = \Delta H_{\text{thermal}} + \Delta \varepsilon_0 \quad \text{Equation 3}$$

The achieved results of the equations are presented in table 1 and Fig 4. As it can be witnessed, all metals are able to form a complex with 6,15-diazabenz[a][1,4]benzothiazino[3,2-c]phenothiazine exothermically, except sodium and potassium because their enthalpy variation value is positive. But, other cations can react with the ligand without consuming any energy owing to their negative formation

enthalpy value. It could be understood from the table and the fig Cu²⁺ reaction with the ligand is more exothermic than other cations. If we want to compare the metals' affinity to form a complex with the mentioned ligand on the basis of formation enthalpy, they will be placed in the following order:

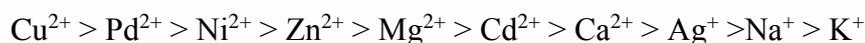


Table 1. Formation enthalpy changes values for the complexation reaction between 10 cations and 6,15-diazabenz[a][1,4]benzothiazino[3,2-c]phenothiazine.

Complexes	H _{th} Complex	H _{th} Cation	H _{th} Ligand	ΔH _{th} (kJ/mol)	Δε _o (kJ/mol)	ΔH _f (kJ/mol)
Cu²⁺-Complex	689.331	6.197	685.137	-2.003	-1340.137	-1342.140
Pd²⁺-Complex	697.081	6.197	685.137	5.746	-1332.675	-1326.929
Ni²⁺-Complex	701.072	6.197	685.137	9.737	-1291.552	-1281.815
Zn²⁺-Complex	700.200	6.197	685.137	8.865	-1257.365	-1248.500
Mg²⁺-Complex	698.763	6.197	685.137	7.429	-1085.293	-1077.864
Cd²⁺-Complex	697.210	6.197	685.137	5.876	-948.018	-942.143
Ca²⁺-Complex	696.894	6.197	685.137	5.559	-763.719	-758.160
Ag⁺-Complex	694.414	6.197	685.137	3.080	-392.549	-389.469
Na⁺-Complex	671.244	6.197	685.137	-20.091	269.174	249.083
K⁺-Complex	670.027	6.197	685.137	-21.308	329.637	308.329

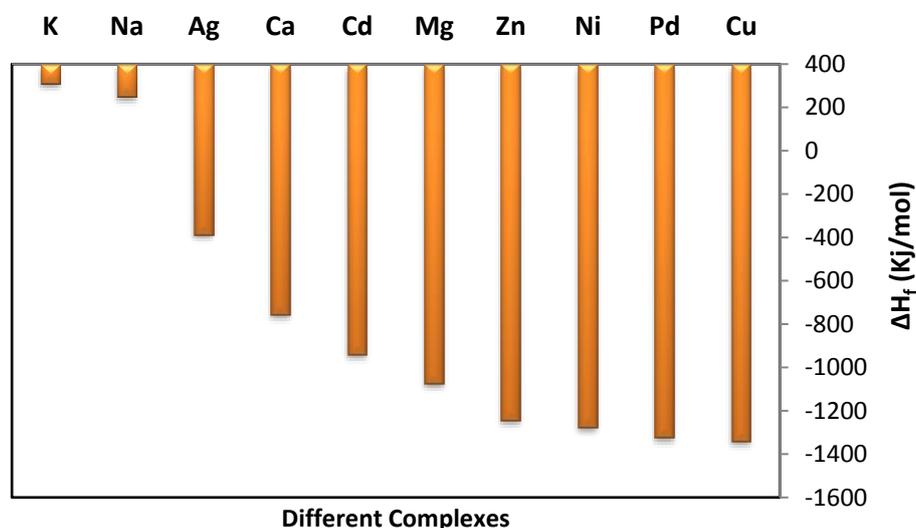


Fig 4. Formation enthalpy changes values for the complexation reaction between 10 cations and 6,15-diazabenz[a][1,4]benzothiazino[3,2-c]phenothiazine.

3.3. Calculation and Verifying the Values of Gibbs free energy Changes (ΔG₀)

The Gibbs free energies of the reactants and products were acquired by the calculation that carried out by Spartan software. Then, the Gibbs free energy alterations were obtained by the succeeding formulas:

$$\Delta G_{th} = G_{th \text{ complex}} - (G_{th \text{ cation}} + G_{th \text{ ligand}}) \quad \text{Equation 4}$$

$$\Delta G_0 = \Delta G_{th} + \Delta \epsilon_0$$

Equation 5

In the table, the equilibrium constant (K_f) was calculated from equation 6. Higher and more positive amounts of this parameter prove that the chemical process is spontaneous and one-sided.

$$K_f = \exp(-\Delta G_0 / RT)$$

Equation 6

Table 2. Gibbs free energy changes and equilibrium constant of the complexation process in the ambient temperature and gaseous phase.

Complexes	G_{th} Complex	G_{th} Cation	G_{th} Ligand	ΔG_{th} (kJ/mol)	$\Delta \epsilon_0$ (kJ/mol)	ΔG_0 (kJ/mol)	K_f
Cu²⁺-Complex	532.113	-44.106	533.659	42.560	-1340.137	-1297.577	$2.18 \times 10^{+227}$
Pd²⁺-Complex	539.135	-46.041	533.659	51.518	-1332.675	-1281.157	$2.89 \times 10^{+224}$
Ni²⁺-Complex	545.537	-43.798	533.659	55.676	-1291.552	-1235.876	$3.37 \times 10^{+216}$
Zn²⁺-Complex	544.174	-44.164	533.659	54.680	-1257.365	-1202.685	$5.16 \times 10^{+210}$
Mg²⁺-Complex	543.904	-40.519	533.659	50.764	-1085.293	-1034.529	$1.79 \times 10^{+181}$
Cd²⁺-Complex	539.280	-46.312	533.659	51.933	-948.018	-896.085	$9.91 \times 10^{+156}$
Ca²⁺-Complex	540.314	-42.417	533.659	49.073	-763.719	-714.646	$1.61 \times 10^{+125}$
Ag⁺-Complex	535.465	-46.076	533.659	47.882	-392.549	-344.667	$2.43 \times 10^{+60}$
Na⁺-Complex	511.159	-40.362	533.659	17.861	269.174	287.036	5.14×10^{-51}
K⁺-Complex	509.011	-42.323	533.659	17.676	329.637	347.313	1.41×10^{-61}

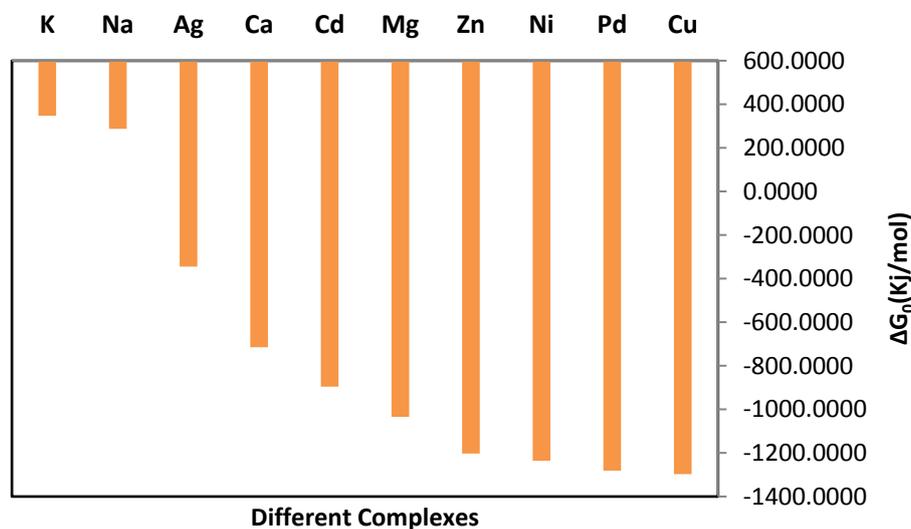


Fig 5. Gibbs free energy changes and of the complexation process in the ambient temperature and gaseous phase.

As the provided data in (table 2) and (Fig 5) illustrate obviously, the highest equilibrium constant and the lowest ΔG_0 is acquired by Cu^{2+} complex. Therefore, it can be inferred that copper forms the strongest complex with 6,15-diazabenz[a][1,4]benzothiazino[3,2-c]phenothiazine among all of the studied cations. In addition, the positive ΔG_0 values for Na^+ and K^+ indicate that the ligand does not take part in complexation reaction with sodium and potassium monovalent cations and owing to the abundance of these ions in real samples, the analytical methods that will be based on this ligand could produce accurate and reproducible responses. On the basis of both enthalpy and Gibbs free energy variations it can be

elicited that the thermodynamic reactivity of complexation of ion metals with studied ligand (with the lowest total energy) are: $\text{Cu}^{2+} > \text{Pd}^{2+} > \text{Ni}^{2+} > \text{Zn}^{2+} > \text{Mg}^{2+} > \text{Cd}^{2+} > \text{Ca}^{2+} > \text{Ag}^+ > \text{Na}^+ > \text{K}^+$

3.4. The lowest frequency and zero point energy values

The lowest frequency and zero point energy are reported in table 3. As it can be observed from table 3, there is not any reported negative frequency. So, it can be concluded that all of the investigated complexes are not a transition state.

Table 3. The lowest frequency and zero point energy values.

Complexes	ZPE (Kj/mole)	Low frequency (Hz)
Cu^{2+} -Ligand	645.196	22
Pd^{2+} -Ligand	653.059	38
Ni^{2+} -Ligand	657.738	15
Zn^{2+} -Ligand	656.684	6
Mg^{2+} -Ligand	655.378	42
Cd^{2+} -Ligand	653.269	33
Ca^{2+} -Ligand	652.936	23
Ag^+ -ligand	650.038	23
Na^+ -Ligand	625.042	16
K^+ -Ligand	623.735	9

5. Conclusions:

In this evaluation, the complexation of 6,15-diazabenz[a][1,4]benzothiazino[3,2-c]phenothiazine with 10 different mono and divalent cations were investigated. The results show that cations can form complex with the ligand through the nitrogen atoms. Moreover, the ligand forms the most stable and the strongest complex with Cu^{2+} because the complex of this cation has the lowest ΔG_0 and the highest K_f among all of the inspected cations. The obtained formation enthalpy changes were also the undermost value for copper (II) which proves that the complexation procedure is exothermic. Therefore, it is recommended that the usage of 6,15-diazabenz[a][1,4]benzothiazino[3,2-c]phenothiazine as an ionophore in the construction of ion selective electrode and also as a competent ligand in developing extraction methods for determination of Cu^{2+} will be evaluated by the experts of these fields.

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