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On the optical properties and electronic charge transfer of an anticancer agent: ferrocene-substituted dithio-*o*-carborane conjugate

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ABSTRACT

Various metal complexes are nowadays used in anticancer therapy and conducted to a large interest from chemists, biologists and organo-metallurgists to develop drugs of future. The low cytotoxicity of ferrocene and its malleability have made it an interesting anticancer agent. We report a theoretical modeling and computational study of the optical properties and electronic structure of ferrocene-substituted dithio-*o*-carborane conjugate in order to understand it structure and control its properties for future biological purposes. It is foundthat the ferrocene is a semiconductor with large bandgap, which may lead us to consider large possibilities to tailor its optical spectrum for special role depending on the environment.

Keywords:*FcSBCO, semi-empirical molecular theory, anticancer agent*

1. INTRODUCTION

It has been proved that the large diversity of structures of some organometallic complexes might lead to the possibility of considering them as therapeutic agent actors [1]. In particular, organo-transition metal compounds activity has already integrated the development of metal-based drugs with potential pharmacological applications offering various therapeutic opportunities. The last two decades have seen considerable efforts in designing and synthesis of medicinal organometallic molecules for biological/biomedical activities,especially for cancer therapy[2, 3].

Ferrocene are metallocene molecules that have attracted particular attention because of their small size, relative ability to dissolve in fats, oils, lipids, and non-polar solvents (lipophilicity), chemical modification possibilities, and possibility of one-electronoxidation as organic molecule [4-6]. As certain ferrocifens, ferrocene are important for breast cancer cell treatment for example. In fact, the existence of iron center in that molecule is favoring the reversible redox process.

We are interested on the Ferrocenylchalcone molecule that belongs to a chalcone family. As the most recent synthesized Ferrocenyl derivatives, this molecule has shown interesting electrochemical and biological properties such as antibacterial [7], antimalarial and many other bioactive impacts. In Fig.1, we show the structure of ferrocene-substituted dithio-*o*-carborane conjugates (known as $C_2B_{10}H_{10}$-S_2C_2HCOFcor FcSBCO). This structure has one or both the aromatic groups substituted by ferrocenyl units and are connected by an enone bridge.

In the present work, we investigate the optical properties and electronic structure of FcSBCO using a robust semi-empirical molecular theory [8] as implemented in VAMP [9] (Accelrys, Inc.). We will study the HOMO-LUMO, UV-Vis spectrum as well as the electrostatic potential in order to see their effect on the potential biological activity of the molecule. The thermodynamic properties are also computed from the vibrational analysis, mainly the UV-Vis spectrum, of FcSBCO will be discussed.

2. COMPUTATIONAL DETAILS

We modeled the Ferrocene, system by first optimizing the structure geometry using VASP [10], and then calculating the optical spectrum using VAMP [9]. The UV-Vis spectra are computed within the framework of the semi-empirical Hartree-Fock (HF) based method ZINDO [11] through the configuration interaction (CI) procedure, including single excitations only (ZINDO/CIS). This method is known to provide reliable results for aromatic molecules [12, 13]. All calculations are performed starting from theoptimized geometry and mean-field ground state properties calculated with AM1 [14, 15].

After optimization, we found the structural parameters of FcSBCO molecule are in reasonable agreement with the experimental data [20]. By referring to Figure 1, we found the following bond lengths (Å) and angles (deg): C1−C2=1.633 Å; C1−S1=1.797 Å; C2−S2=1.787 Å; C3−C4= 1.321 Å; C3−S1=1.731 Å; C4−C5=1.481 Å; C4−S2=1.765 Å; C5−O1=1.221 Å; C5−C6=1.459Å; C2−C1−S1=121.8°; C1−C2−S2=122.3°; C4−C3−S1=130.7°; C3−C4−C5=122.8°; C3−C4−S2 =125.6°; C5−C4−S2 =108.1°; O1−C5−C6 =119.5°; O1−C5−C4=117.8°; C6−C5−C4 =120.7°; C7−C6−C5=124.9°; C10−C6−C5=128.5°; C3−S1−C1 =102.40°; and C4−S2−C2 =101.98°.

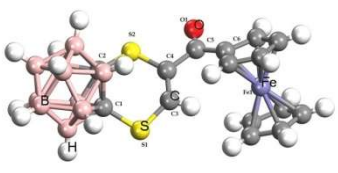

Figure 1. Structure of ferrocene-substituted dithio-*o*-carboraneconjugates (known as $C_2B_{10}H_{10}$-S_2C_2HCOFcor FcSBCO)

3. RESULTS SECTION

The energy gap is considered as the difference between the highest occupied and the lowest unoccupied molecular orbital (HOMO and LUMO). It is an important quantum chemical parameter to obtain as it presents a measure of electron conductivity and give more information about the molecular electrical transport properties. From the HOMO energy, one can characterize the ability of electron to give and from the LUMO energy can give idea about the molecule/electron to accept. In the other hand, the band gap between HOMO and LUMO give information on the molecular chemical stability of different constituents and also might explain the eventual charge transfer interactions taking place inside the molecule. In Fig.2, we display the atomic orbital composition of the frontier molecular orbital for FcSBCO molecule. The higher HOMO energy corresponds to the more a potential reactive molecule in the reactions with other biological agents. Furthermore, the HOMO energy is directly related to the ionization potential while, LUMO energy to electron affinity. HOMO energy and LUMO energy were theoretically calculated to be -9.23 eV and -1.667 eV leading to a band gap energy of -7.78 eV. Fig. 2, is displaying a pictorial illustration of the frontier molecular orbitals and their respective positive and negative regions. For the HOMO isosurface, negative site is over C2 and C4 (partially), below B in the polyhedron. Positive region is over S1 and S2, between C2, C4, and H and partially in between C2 and B in the polyhedron. Furthermore, the HOMO is localized over the center of the FcSBCO molecule. In LUMO, negative sites are found partially between S2 and B atoms in the polyhedron, whereas the positive values are concentrated between hydrogen and B atoms. The negative and positive sites show that LUMO is localized over the polyhedron (non- aromatic) region.

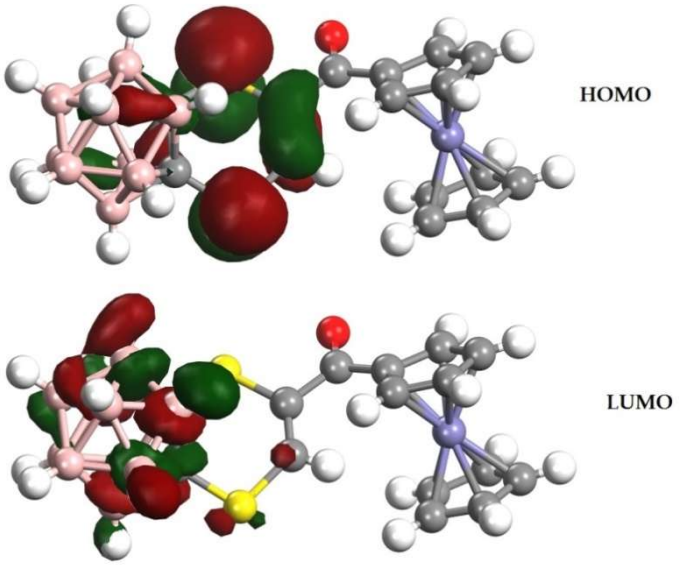

Figure 2. The atomic orbital compositions of the frontier molecular orbital forFcSBCO molecule.

From our calculations, we can extract theelectrostatic potential iso-surface as displayed in Fig. 3. As in case of HOMO-LUMO frontiers, this map is useful to understand the reactivity of the studied molecule. In fact, by definition, the electrostaticpotential, in any site inside the molecule, is a measure of the Coulomb interaction per unit charge experienced by an ion at a given position in the molecule. From the obtained iso-surface, the electrostatic potential shows two main regions with a variation of values (from negative to positive). The negative value is surrounding S2 and S4 atoms.

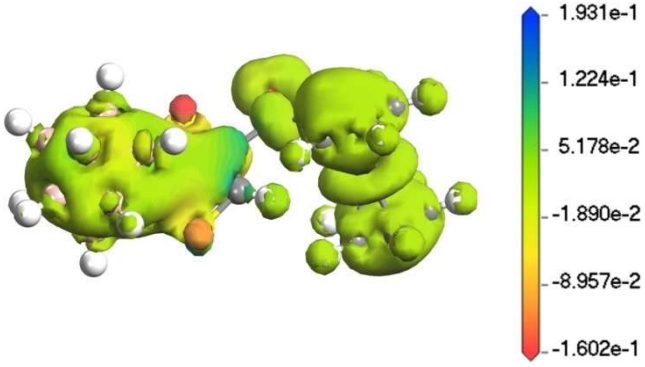

Figure 3. Electrostatic potential of FcSBCO molecule.

In order to get more insights on the bonding character of FcSBCO molecule, we report in Table 1, the Mulliken charge populations. In fact, the Mulliken population analysis [16] is very important as it allow us to determine all the possible bonding capability and molecular conformation inside the considered system. The negative values on carbon atoms, the Oxygen and Boron atoms in the polyhedron have an impact on the redistribution of the electron density. Due to these strong negative charges, iron atom, S1 and S2 and all hydrogen atoms show higher positive charge. With this distribution of charges, one might consider that the molecule is acidic. To change its acidity for biological purpose, one can use different basic solvents.

Table 2 shows the calculated absorption wavelength (k), excitation state, oscillator strength (f), and the corresponding multiplicity of the FcSBCO molecule. Following the Frank–Condon principle, the maximum absorption peak (kmax) corresponds to a vertical excitation. Our theoretical calculations predict one intense electronic transition at 268.19 nm with oscillator strength f=0.121 and electronic absorption value 3.30753 eV and a second peak at 374.84 nm with an f = 0.114. These peaks are well displayed in the UV-Vis spectrum shown in Fig.4.

Once the molecular geometry, energy, and vibrational frequencies are known we can determine easily the thermodynamics properties such as: enthalpy, entropy and free energy for the considered molecule [17]. The thermodynamic functions such as the enthalpy change (H), heat capacity at constant pressure (Cp) and entropy (S) and for the FcSBCO molecule were evaluated in the temperature range from the theoretical harmonic frequencies obtained from UV-Vis spectra calculation. They are displayed in Fig.5 and show that the properties increase with the temperature increases. This is mainly

due to the fact that the vibrational intensities of molecules increase with temperature.

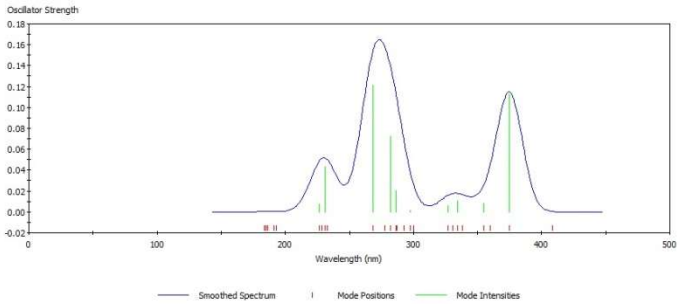

Figure 4. UV-Vis spectrum of FcSBCO molecule.

These calculated energies are very useful for the estimation of other important thermodynamic energies by use of the relationships between thermodynamic functions. Also they can be used for the directions of chemical reactions (using the second law of thermodynamics) in case of the molecule was emerged in a thermochemical field.

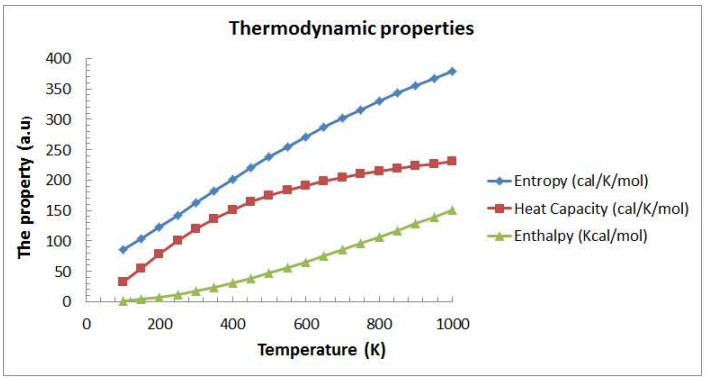

Figure 5. Thermodynamic properties of FcSBCO molecule.

Table 1. Vibrational analysis of FcSBCO molecule.

Level Energy (eV)	Excitation wavelength (nm)	Oscillator Strength	Multiplicity
0.00000000	0.00000000	Ground State	Singlet
3.30753000	374.84160800	0.11382700	Singlet
3.49606600	354.62719700	0.00884700	Singlet
3.71034800	334.14654600	0.01109300	Singlet
3.79012700	327.11305800	0.00705800	Singlet
4.16414100	297.73245800	0.00218600	Singlet
4.33191000	286.20169800	0.02141000	Singlet
4.39195900	282.28863500	0.07289600	Singlet
4.62270000	268.19824000	0.12177800	Singlet
5.37260000	230.76348700	0.04383400	Singlet
5.47217700	226.56430200	0.00847300	Singlet

Table 2. Mulliken atomic charges of **FcSBCO**as extracted from VAMP.

Atom No.	Type	Charge	Atom No.	Type	Charge
1	B	-0.036	2	H	
3	B	-0.101	4	H	0.186
5	B	-0.147	6	H	0.188
7	B	-0.033	8	H	0.210
9	B	-0.262	10	H	0.195
11	B	-0.200	12	H	0.215
13	B	-0.229	14	H	0.209
15	B	-0.130	16	H	0.200
17	B	-0.141	18	H	0.207
19	B	-0.176	20	H	0.202
21	C	-0.418	22	C	0.203
23	C	-0.197	24	H	-0.397
25	C	-0.252	26	C	0.265
27	C	-0.497	28	C	0.677
29	H	0.274	30	C	-0.293
31	H	0.271	32	C	-0.394
33	H	0.268	34	C	-0.374
35	H	0.267	36	C	-0.384
37	H	0.270	38	C	-0.409
39	H	0.268	40	C	-0.378
41	H	0.268	42	C	-0.400
43	H	0.269	44	C	-0.403
45	H	0.267	46	Fe	-0.431
47	O	-0.475	48	S	1.447
49	S	0.190			0.141

4. CONCLUSIONS

In the present work, we employed a computational method based on semi-empirical molecular orbital package (VAMP) to study structural, optical and electronic properties of an anticancer molecule, FcSBCO. We presented a complete vibrational analysis by reporting the UV-Vis spectrum from which thermodynamic properties were deduced. The bonding characterization obtained from the electrostatic potential iso-surfaces and Mulliken population analyses are important to understand the role of FcSBCO molecule as biological agent in reaction with various environments. As perspective to this study, weare interestingto continue investigations in the near future, the impact of solvents (acid or basic) on the biological activity and chemical properties of the FcSBCO molecule.

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6. ACKNOWLEDGEMENTS

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