

Неемпіричне дослідження приєднання металосаленевих комплексів до ДНК

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Сален (біс(саліциліден) 1,2-етилендіамін) це тетра-дентатний ліганд з двома атомами кисню і двома атомами азоту, який може утворювати стійкі комплекси з різноманітними іонами перехідних металів, наприклад: Mn^{2+} , Co^{2+} , Fe^{2+}/Fe^{3+} , Pd^{2+} , Cu^{2+} і Ni^{2+} . Ці металеві комплекси є активними і селективними для гідрогенування і окислення алканів, алкенів, фенолу та алкоголю. Серед різних механізмів, завдяки яким вони виконують свої функції в біосередовищі, найважливішою є їх пряма взаємодія з ДНК. Здатність взаємодіяти з ДНК визначається декількома чинниками як наприклад: характером ліганду і координаційною геометрією. Неемпірична квантова механіка це можливо найістотніший розрахунковий інструмент, доступний сучасним теоретичним хімікам, який може забезпечити якісну і точну інформацію про структурні й електронні властивості різних молекулярних систем. На жаль, точні квантово-хімічні моделювання вимагають високих затрат, мають дуже високі вимоги так само щодо ЦП, як і пам'яті.

У роботі обговорено оптимізовані геометрії, довжини сполучень, кути сполучень, енергії, незалежний від ядер хімічний зсув (NICS) і частотні обчислення $Mn(II)$ -, $Cu(II)$ -, $Ni(II)$ -саленових комплексів та з формами ДНК для різних теоретичних моделей і базисного комплекту. Оптимізовані геометричні параметри, довжини сполучень, кути сполучень й енергії взаємодії саленових комплексів, які досліджувалися в цій роботі, проведено на основі методу Хартрі-Фока на рівні Lan12DZ. Після отримання цих оптимізованих структур, обчислено енергії сполучень металосаленевих комплексів, які отримано методом ультрафільтрації. Обчислення NICS проводилися з використанням теорії функціоналу щільності B3LYP, а саме за допомогою трипараметрового функціоналу нелокального обміну Бека з нелокальним кореляційним функціоналом Лі, Янга і Пारा на рівні Lan12DZ.

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Ab initio study of metalosalen complexes binding to dna

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Geometry optimizations of metal complexes of Salen(bis(Salicylidene)1,2-ethylenediamine) were carried out at HF(Hartree-Fock) and DFT(Density Functional Theory) methods employing Lan12DZ basis set. In this work structural, energies, bond lengths and other physical properties between Mn^{2+} , Cu^{2+} and Ni^{2+} ions coordinated by salen-type ligands are examined. All calculations were performed using Gaussian 98W program series. To investigate local aromaticities, NICS(Nucleous Independent Chemical Shift) were calculated at all centers of rings. The higher the band gap indicating a higher global aromaticity. The possible binding energies have been evaluated. We have evaluated Frequencies and Zero-point energy with freq calculation. The NICS Results show Ni(II) complexes are antiaromatic and aromaticities of Mn(II) complexes are larger than Cu(II) complexes. The energy Results show Cu(II) complexes are stability than Mn(II) and Ni(II) complexes.

Keywords – Density Functional Theory(DFT), Frequency Calculation, Hartree-Fock(HF), Nucleous Independent Chemical Shift(NICS), Salen(bis(Salicylidene)1,2-ethylenediamine)

I. Introduction

Salen (bis(Salicylidene)1,2-ethylenediamine) ligands can be categorized in Schiff-base ligand group. Schiff bases derived from aliphatic amines and salicylaldehyde drew the interest of many workers based on their antitumor activities which has been investigated on different Schiff-base ligands [1]. This activity will be increased by coordinating ligands to metal ions. Salen complexes and their derivatives with transition metals of first row have been synthesized [2] and some of their activities have been investigated, for example potential applications as catalyst [3,4] and their interactions with DNA [5]. The controlled assembly of functional nanoscale materials from molecular entities is regarded as a key subject of future nanotechnology. Currently, the use of DNA, which features superior self organization properties, is heavily investigated. The aim of this work was the development of new systems for the controlled binding of multiple metal ions to the inside or outside of modified DNA double strands [6]. Furthermore, the incorporation of numerous metal-base pairs into oligonucleotides may lead to compounds with interesting electronic and magnetic properties.

Many DNA binding studies of metal complexes of Salen-type ligands have been reported in the literature, for example of Mn [7]. The capability to interact with DNA is determined by several factors such as the nature of the ligand and the coordination geometry [8].

A special interest behind the incorporation of several metal-base pairs into one DNA duplex is the desire to construct metal arrays which provide new perspectives for the nanotechnological exploitation of the DNA structure as a molecular wire or electronic switch or for the generation of artificial multi-metal ribozymes. Furthermore, access to a variable set of multidentate ligands is of great interest to study metal interactions in homo- or hetero-multimetallic coordination compounds.

II. Computational details

Geometry of complexes were optimized at LANL2DZ basis sets (Tables I and III). NICS Calculations reported in this paper were carried out by using gradient-corrected density functional theory with the Becke–Lee–Young–Parr exchange correlation functional (B3LYP) as implemented in the Gaussian 98 program where LANL2DZ basis sets were used (Table IV). Theoretical calculations of frequencies at the fully optimized geometries of Metalosalen Complexes have been performed at ROHF level, where the used basis sets are LANL2DZ (Table V). Metal-salen complexes have been shown to bind to DNA in an intercalating fashion and have been used for the structural characterization of DNA.

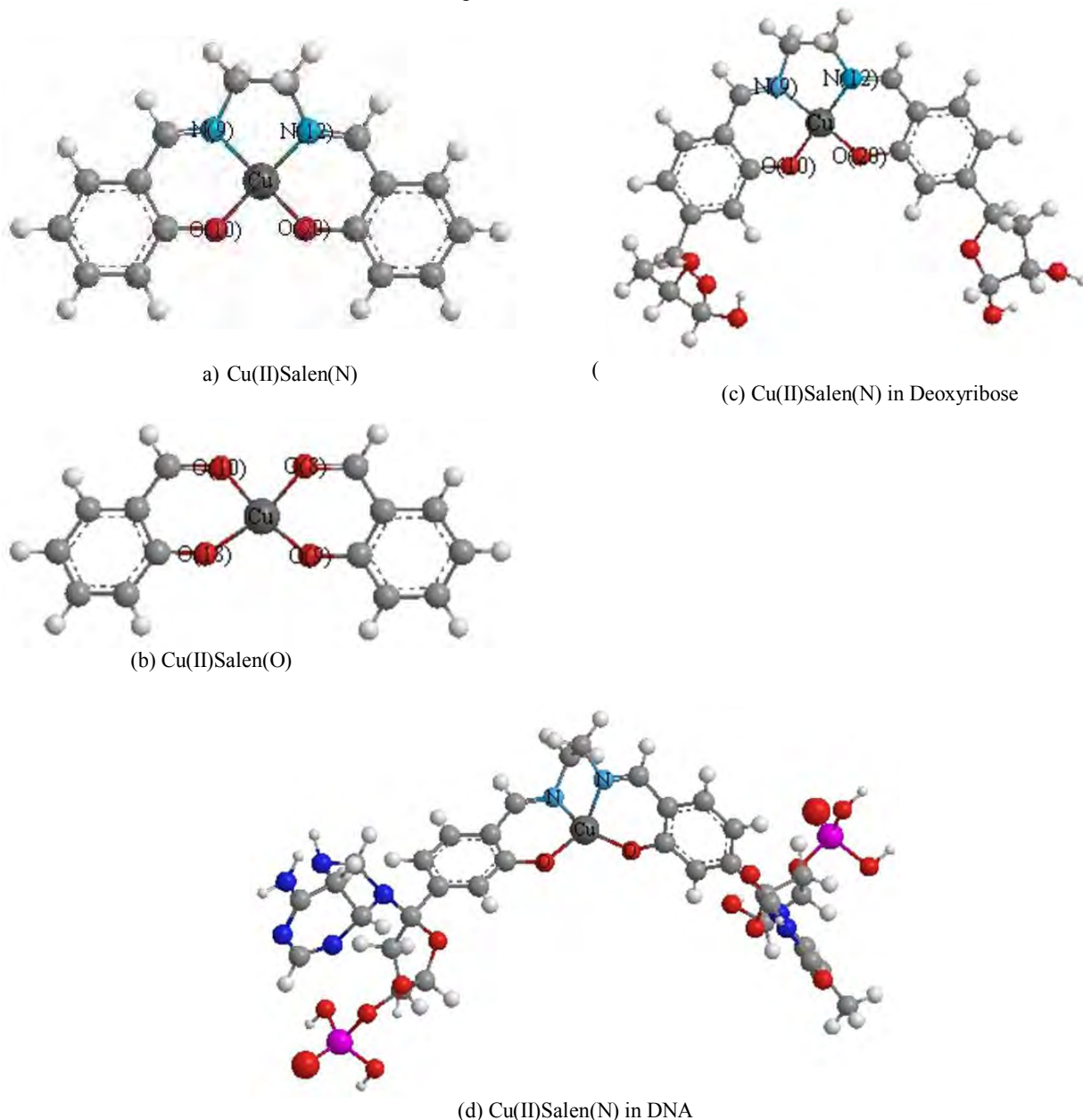


Fig. 1. The Structure of Complexes

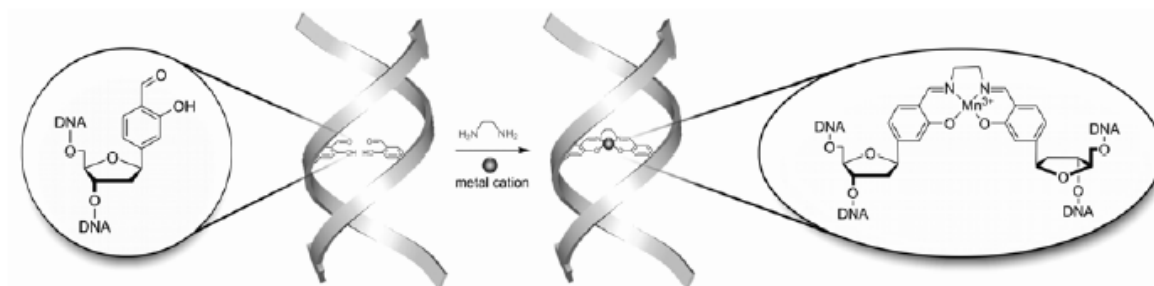


Fig. 2. Schematic representation of the assembly of the metal-salen base pair inside the DNA

III. Results and discussions

Calculations reported in this paper were carried out by using a restricted open-shell version of the Hartree-Fock method and gradient-corrected density functional theory with the Becke-Lee-Young-Parr exchange correlation functional (B3LYP) as implemented in the Gaussian 98.

This combination of theoretical methods (ROHF for geometry optimization and DFT/B3LYP for NICS calculation) was employed in the present study. The geometry of complex is shown in fig. 1. For each compound, calculations of frequency were performed. Frequency indicated that the zero-point energy for Mn(II) complexes are higher than Cu(II) and Ni(II) complexes.

Table I

Energy and Atomic charge of MetaloSalen Complexes in ROHF/ LANL2DZ Level

Molecules Name	Energy (Hartree/ Particle)	$\Delta c(N)^a$	$\Delta c(O)^b$
H ₂ salen	-873.5501446	-	-
Cu(II)Salen(N)	-1066.8178739	-0.919413	-1.25111
Cu(II)Salen(N) in Deoxyribose	-1825.7428548	-1.118981	-1.192119
Mn(II)Salen(N)	-974.9850002	-1.004179	-1.438456
Mn(II)Salen(N) in Deoxyribose	-1733.9087177	-1.211619	-1.475776
Ni(II)Salen(N)	-1040.7586546	-0.883675	-1.088809
Ni(II)Salen(N) in Deoxyribose	-1799.657115	-1.031671	-1.433362
Cu(II)Salen(O)	-1029.5445035	-	-
Cu(II)Salen(O) in Deoxyribose	-1788.4828296	-1.081543	-1.081543
Mn(II)Salen(O)	-937.7461022	-	-
Mn(II)Salen(O) in Deoxyribose	-1696.6644931	-1.2847	-1.2847
Ni(II)Salen(O)	-1003.5510665	-	-
Ni(II)Salen(O) in Deoxyribose	-1762.4504602	-1.157932	-1.157932

^a $\Delta c(N) = \text{atomic charge of N after connection} - \text{atomic charge of N before connection}$

^b $\Delta c(O) = \text{atomic charge of O after connection} - \text{atomic charge of O before connection}$

Table II

Energy of MetaloSalen Complexes in UFF Method

Molecules Name	Energy (Hartree/ Particle)
Cu(II)Salen(N) in DNA	0.0012458
Mn(II)Salen(N) in DNA	0.1647453
Ni(II)Salen(N) in DNA	-0.1665594
Cu(II)Salen(O) in DNA	-0.157442
Mn(II)Salen(O) in DNA	-0.0123954
Ni(II)Salen(O) in DNA	-0.3056935

According to Table I and II we observe that energy of complexes when attached to DNA are more stable and Cu(II) complexes are stability than Mn(II) and Ni(II) complexes.

The bond length to our calculations show Mn(II)Salen(O) complex is shorter than Cu(II) and Ni(II) complexes but bond length of Mn(II)Salen(O) in Deoxyribose complex is larger than Cu(II) and Ni(II) complexes. The calculated bond angles also show Mn(II)Salen(O) complex is higher than Cu(II) and Ni(II) complexes but Mn(II)Salen(O) in Deoxyribose complex is smaller than Cu(II) and Ni(II) complexes. It is possible to because of electronic configuration of Mn(II) complexes.

Table III
**Optimized Bond Length (Å) and Bond Angle(Degree)
of Complexes in ROHF/ LANL2DZ Level**

Molecules Name	(8)N-M ^a	(9)O-M ^a	(8)N-M ^a - O(9)
Cu(II)Salen(O)	1.8763	1.861	87.374
Cu(II)Salen(O) in Deoxyribose	1.8677	1.8589	88.0688
Mn(II)Salen(O)	1.8321	1.7612	93.811
Mn(II)Salen(O) in Deoxyribose	1.9351	1.931	82.6014
Ni(II)Salen(O)	1.9229	1.8857	88.5281
Ni(II)Salen(O) in Deoxyribose	1.9211	1.8858	88.5774

^a M= Cu²⁺, Mn²⁺, Ni²⁺

Table IV
NICS Calculations in UB3LYP/ LANL2DZ Level

Molecules Name	NICS
Cu(II)Salen(N)	-2.0117
Cu(II)Salen(N) in Deoxyribose	0.6052
Mn(II)Salen(N)	-4.0124
Mn(II)Salen(N) in Deoxyribose	4.4288
Ni(II)Salen(N)	4.0825
Ni(II)Salen(N) in Deoxyribose	6.3392
Cu(II)Salen(O)	-4.7113
Cu(II)Salen(O) in Deoxyribose	5.3251
Mn(II)Salen(O)	-5.6081
Mn(II)Salen(O) in Deoxyribose	-2.7604
Ni(II)Salen(O)	3.7520
Ni(II)Salen(O) in Deoxyribose	3.0351

The NICS Results show Ni(II) complexes are antiaromatic and aromaticities of Mn(II) complexes are larger than Cu(II) complexes but Mn(II)Salen(N) in Deoxyribose complex is antiaromatic than Cu(II)Salen(N) in Deoxyribose complex.

Table V
Freq Calculations in ROHF/ LanL2DZ Level

Molecules Name	E (Thermal) KCal/Mol	C _v Cal/Mol- Kelvin	S Cal/Mol- Kelvin	Zero-point vibrational energy (Kcal/Mol)
Cu(II)Salen(N)	189.386	56.920	114.937	181.07864
Mn(II)Salen(N)	194.489	62.621	127.687	184.76634
Ni(II)Salen(N)	194.088	62.386	126.165	184.36618
Cu(II)Salen(O)	145.882	51.289	110.659	138.25549
Mn(II)Salen(O)	148.898	50.059	110.296	141.38784
Ni(II)Salen(O)	151.668	56.779	123.604	142.49901

Frequency calculations show that the zero-point energy for Mn(II) complexes are higher than Cu(II) and Ni(II) complexes.

Conclusion

Ab initio calculations were performed using the G98w program package, running on a personal computer. The fully optimized geometry, the frequency Calculation, and NICS Calculation were obtained at the ROHF and B3LYP level, using the valence double-zeta basis set of Dunning and Hay (Lan12DZ basis set of G98).

In this thesis a new kind of metal-base pair based on the well known salen ligand was developed. A new feature that differentiates the metal-salen base pair from other known metal-base pairs is the crosslinking character of the metal salen complex, which resulted in a greatly enhanced structural stability of the DNA.

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