

## Evaluation of Ligand Competitive Ability for Binding in Mixed Ligand Complex

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### Abstract

In this work, several attempts were carried out to evaluate the formation of mixed ligand complex from 1-10 phenanthroline (phen.) and dimethylglyoxime (DMG) with zinc ion. Complex formation tested using both FTIR and  $^1\text{H}$  NMR techniques supported by density functional theory calculations (DFT) to investigate the Mulliken charges of both free ligands and their corresponding mixed ligand complex to determine the competitive ability of each ligand toward zinc ion and to study the possibility of the synthesis of mixed ligand complex. Results obtained show that 1-10 phen. ligand binds stronger than DMG. Octahedral geometry of the complex was observed involves 2:1 mole ratio of L:M in addition to 2 mole of chloride ion.

Keywords: dimethylglyoxime, 1-10 phenanthroline, DFT, Mulliken charges, mixed ligands complex.

### Introduction

The metal complexes of multidentate ligands gained great importance due to their significant biological activity, such ligands as dimethylglyoxime which have high ability of complexation with zinc ion and also 1-10 phenanthroline have a good complexation ability and biological activity with several transition metals [1-4]. The medicinal applications of metal complexes are attributed to their clinical importance [5].

The mixed ligand complexes have been used widely because of their potent biological activity compared to binary ligand complex due to their formation in the physiological pH range [6].

In biological process, mixed ligand metal complexes play an important and vital role in which enzymes activated by metal ions in this process [7]. The researchers show that these types of complexes are more active than their parent ligands against the same microorganism [5]. Zinc (II), among other transition metal ions, plays a vital role in biological system, some of zinc complexes bioactivity showed antibacterial and anticancer activity [8].

Several potentiometric studies [9-11] were established to determine the formation stability of binary and mixed ligand complexes using the following equation:

$$\Delta \log K = \log K_{\text{MLT}} - (\log K_{\text{ML}} + \log K_{\text{MT}})$$

Where:

$\Delta \log K$  indicates the difference between the stability of the mixed and the two corresponding binary complexes, while M, L and T represent metal, primary and secondary ligand respectively. Positive value of  $\Delta \log K$  reflects that the mixed ligand complex is more stable than corresponding ligand, while negative value means the vice versa.

There is a significant relation between dissociation rate of any reaction and formation stability, the greater the formation stability, the slower the dissociation rate [12]. *Inter-ligands interaction* like hydrogen bondings and hydrophobic interactions have a significant impact on complexes stabilization [13]. Basicity of the ligands is so important to evaluate the complexes stability, the more basicity of ligand the high stability of complex [14]. The mixed ligand complex formation may proceed due either stepwise or a simultaneous mechanism depend on the complexation ability of each ligand [9]. 1,10-phenanthroline N-N ligand is considered one among the strongest  $\sigma$ -donor ligand, also it has a good  $d\pi - p\pi$  back bonding interaction [15].

The complex stability could be greater if the metal-ligand bond have high  $\pi$  interaction [16,17].

Density functional theory (DFT) is used as popular quantum tool to calculate and investigate some important parameters of

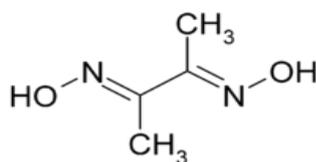
ligand metal complexes such as reaction baths and the stability of metal complexes including HOMO - LUMO energy gap, bond length and bond angle geometries, total energy, electron density and mulliken charge.[18-21].

In this work, several attempts were carried out to investigate the possibility of mixed complex formation of divalent zinc ion and to compare that with the formation of corresponding primary complexes using both experimental and theoretical methods.

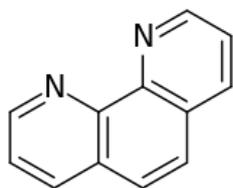
## Experimental Section

### Reagents and Materials:

Zinc chloride, 1-10 phenanthroline mono hydrated, Dimethylglyoxime, KOH, absolute ethanol and DMSO<sub>d</sub>, are of Analar grade.



DMG



1-10 phenanthroline

### Synthesis of Zn ion complex:

In the first four experiments, the following amounts of starting materials were used: a solution of (DMG) (0.464 gm, 0.004 mole) in 10 ml ethanol and a solution of 1-10 phen. mono hydrated (0.792 gm, 0.004 mol) in 10 ml ethanol in addition to 10ml ethanolic solution of ZnCl<sub>2</sub> (0.567 gm, 0.004 mol). In all cases, the stirring was carried out in water bath at 80°C. The resulting mixture was kept for 24 hours for complete precipitation, then it was filtered and washed with an excess of ethanol. Further recrystallization was performed and then the precipitate was dried at 60°C.

Several attempts were carried out to synthesis the ternary complex of zinc as follow:

1. Simultaneous addition of both ligands to a stirred solution of ZnCl<sub>2</sub> in acidic medium at pH=6.
2. The above procedure was repeated except that the medium of solution mixture was adjusted to pH=8.5.
3. Stepwise addition of ligands to a solution of ZnCl<sub>2</sub> was employed in this method. At pH=8.5, DMG was firstly added to stirred metal ion solution for 5 min then the other ligand 1-10 phen was added at the same pH.
4. DMG and metal ion mixture was firstly refluxed for 2 hours then 1-10 phen. was added and the resulting mixture was refluxed for another 2 hours at pH=8.5.
5. In the fifth experiment and for geometry investigation, the same condition in step 4 was performed except that only the ligand 1-10 phen. was used with ratio of 2:1 ligand:metal.

### Computational method

DFT calculations were performed for this work. The chembio3D ultra program package and correlation functional (B3LYP) at base set 6-31G was used.

HOMO-LUMO energy gap, Mullikan charges, bond length and geometry were calculated.

### Result and Discussion

#### Computational results

As shown in Table (1), significant changes in the mulliken charges of N30 and N25 belonging to 1-10 phenanthroline between the free ligands and their complexes with Zn ion were observed which is clearly indicates that there is strong back donation from Zn<sup>(II)</sup> to pi orbitals of 1-10 phenanthroline which increase the complexation ability of this ligand and that reflects the highly competitive ability of 1-10 phen compared to the other ligand DMG. Also higher negative charges at the mentioned nitrogen atoms reflect the ionic nature of the complex which increase the stability of complex [22].

From the data cited in Table (2), the stability evaluation due to the HOMO- LOMO energy gap shows that the highly stable geometry for the studied complex is the octahedral form which involves 2 moles of

1-10 phen. and 2 moles  $\text{Cl}^-$  with 1 mole  $\text{Zn}^{(II)}$ , the more the Energy gap of HOMO-LUMO, the more stable complex [23].

Atomic absorption analysis supported this geometry. the zinc metal ion content is found about 9.5% compared with the theoretical

value 12.3%, it decompose at  $330^\circ\text{C}$ , also chloride was identified in the complex using conductivity detector (metrom). The suggested structure of complex is shown in Fig.(1).

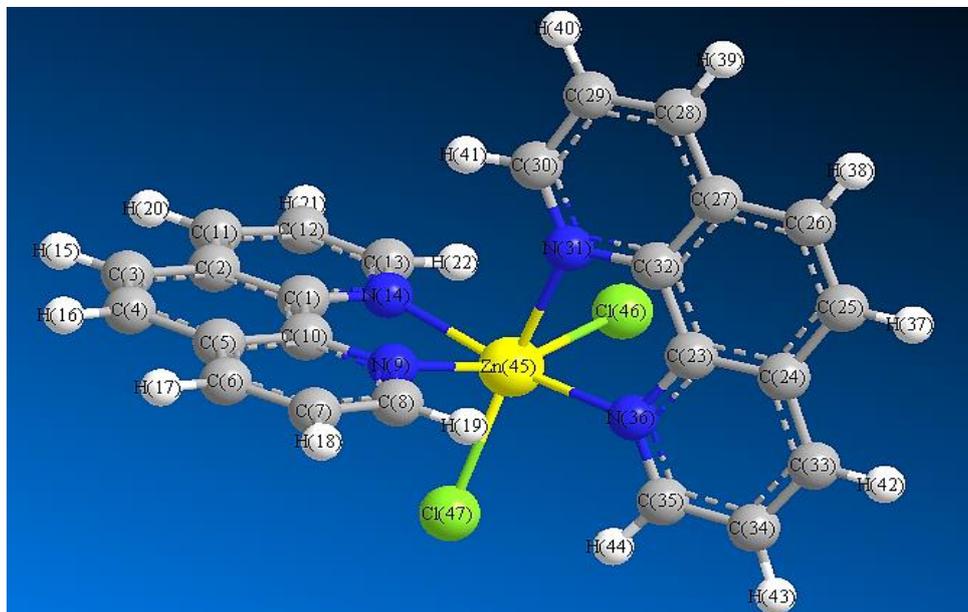


Fig.(1): Suggested structure of Zn-phenanthroline complex 1: 2 optimized by DFT/B3LYP/6-31G.

Table (1)

Mulliken charges of nitrogen atoms in both ligands and their corresponding complexes with  $\text{Zn}^{+2}$ .

	N3	N5	N25	N30
Free ligand				
DMG	-0.217904	-0.217888	***	***
1-10 phenanthroline	***	***	-0.363761	-0.363821
complex				
1	-0.440474	-0.424174	***	***
2	***	***	-0.8062	-0.806239
3	-0.367236	-0.377904	-0.732263	-0.733643

Table (2)

HOMO-LUMO Egap(eV) for different chelation possibilities of zinc ion complexes.

	Mole ratio of ligands	HOMO-LUMO Egap (eV)	Notes
1	DMG +(1-10phen)	0.8	
2	2(1-10phen)	0.2	
3	(1-10phen)+4Cl	.....	D.G.
4	2(1-10phen)+2H <sub>2</sub> O	2.1	
5	2(1-10phen)+2Cl	5	

D.G. distortion geometry (N25-Cl27 bond length =17.8Å°).

## FTIR

The FTIR spectra of the two ligands are given in Fig.(2) and (3). It is clearly seen that all complexes spectra Fig.(4-6) compatible with the spectrum of the free ligand 1-10 phenanthroline except the expected shift in the imine group due the complexation to lower frequency from 1645 to 1624  $\text{cm}^{-1}$  which confirms the chelation sites with  $\text{Zn}^{(II)}$  from nitrogen of imine. At the same time it dose not

seen any band of DMG ligand involved in the complex such as 3205  $\text{cm}^{-1}$ , 2930  $\text{cm}^{-1}$  and 980  $\text{cm}^{-1}$  which have been attributed to O-H, aliphatic C-H str. and alcoholic C-O str. bands respectively which clearly reflects that 1-10 phen acts as much stronger *competitive ligand* than DMG, although the later is considered as a potent ligand toward zinc ion [1].

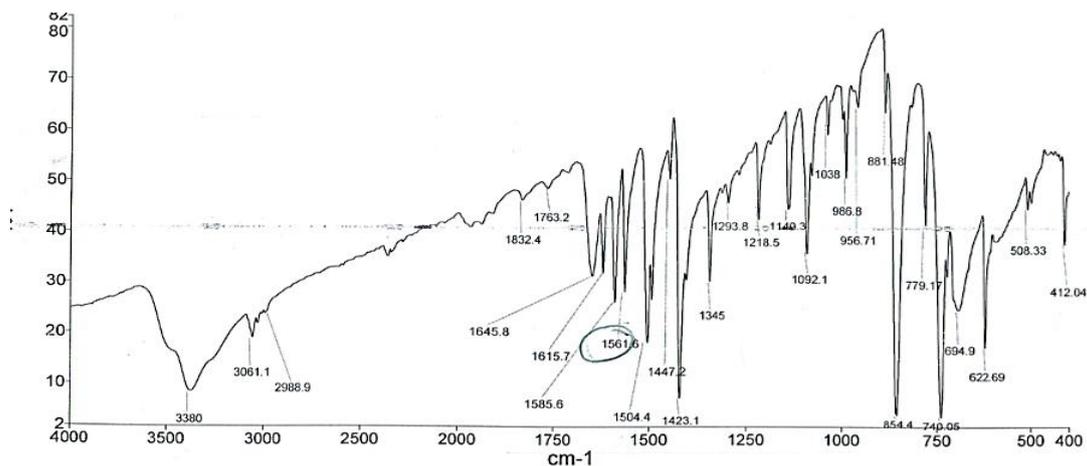


Fig.(2): FTIR spectrum of 1-10 phenanthroline.

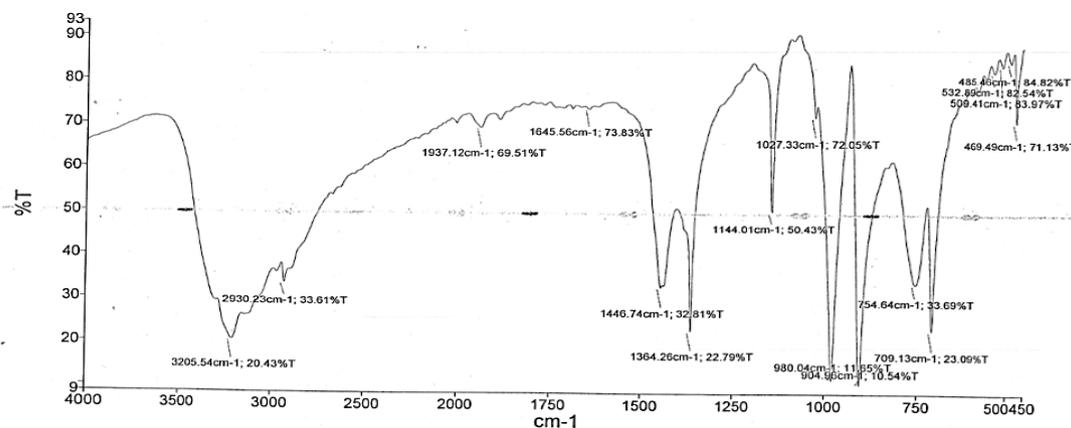


Fig.(3): FTIR spectrum of dimethylglyoxime.

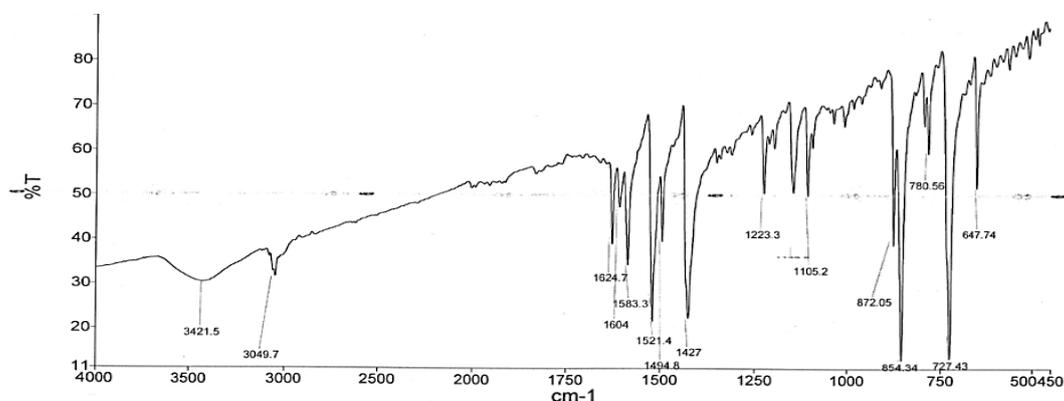
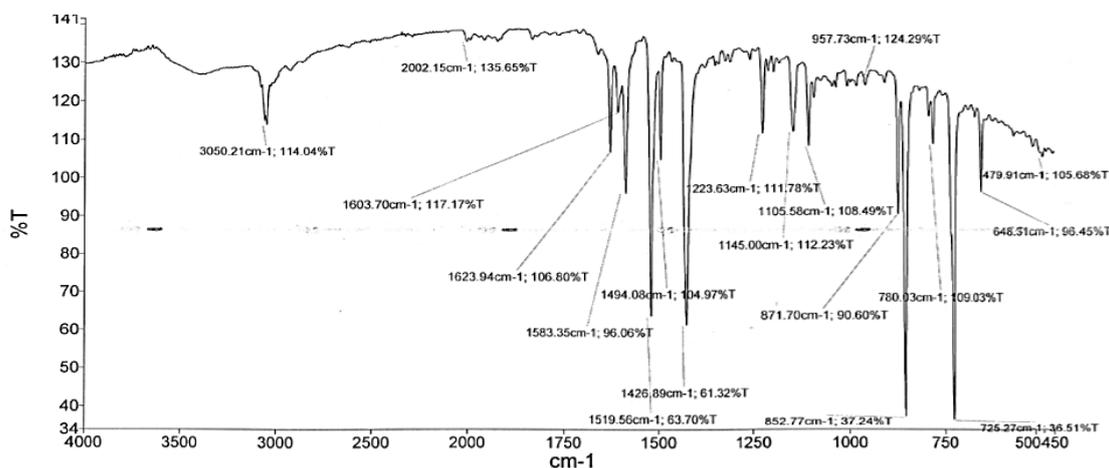
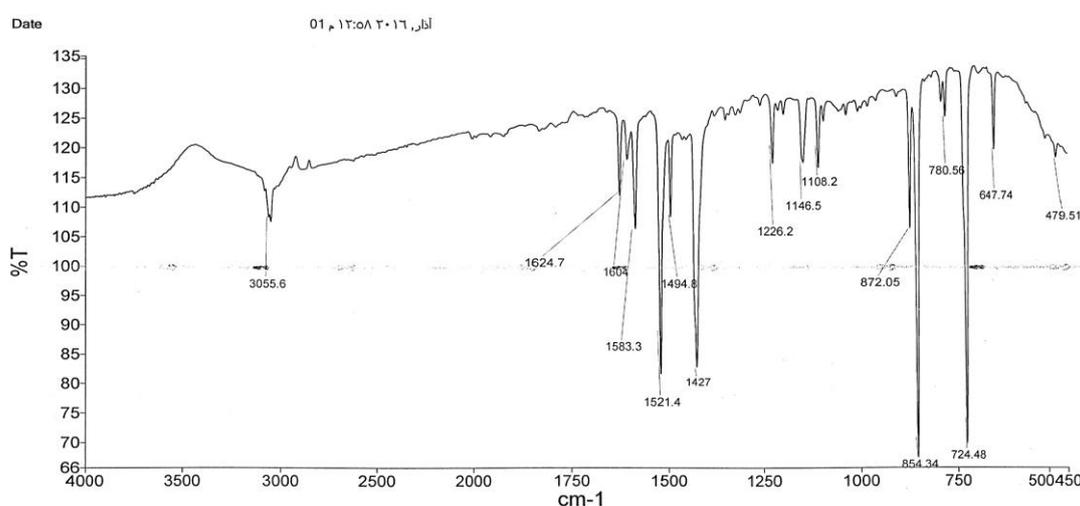


Fig.(4): FTIR spectrum of complex prepared by simultaneous addition of both ligands to Zn in acidic medium.



**Fig.(5): FTIR spectrum of complex prepared by simultaneous addition of both ligands in basic medium.**



**Fig.(6): FTIR spectrum of complex prepared by refluxed mixture of both DMG and Zn for 2 hours then 1-10 phen was refluxed for another 2 hours at basic medium.**

### NMR study

As observed in Fig.(7) and (8), <sup>1</sup>H NMR spectra of ligands, 1-10 phen. and DMG and their complexes with Zn<sup>(II)</sup> (Fig. (9) and (10)) were recorded in DMSO<sub>d6</sub>. Among all synthesis methods of mixed ligand complex, none of them confirms the presence of DMG ligand in these complexes due to the absence of methyl protons at 1.9 ppm and hydroxyl proton at 11.28 ppm while the multiple signals observed between 9.25 ppm and 7.64 ppm which are related to the aromatic protons in 1-10 phen. is clearly confirms that only the later one involves in the complex formation which is attributed to the highly formation stability of 1-10 phen. as binary complex compared to DMG ligand. Fig.(11) shows the <sup>1</sup>H NMR spectrum of Zn ion complex prepared by the ratio 2:1 from 1-10 phen and zinc metal ion respectively. Signal

appears at 3.3 ppm has been attributed to the moisture in the sample or DMSO<sub>d6</sub>, while signal around 2.5 ppm is attributed to usual impurities of DMSO<sub>d6</sub> with DMSO<sub>d5</sub> or may be by replacement of deuterium with hydrogen in some cases [24,25].

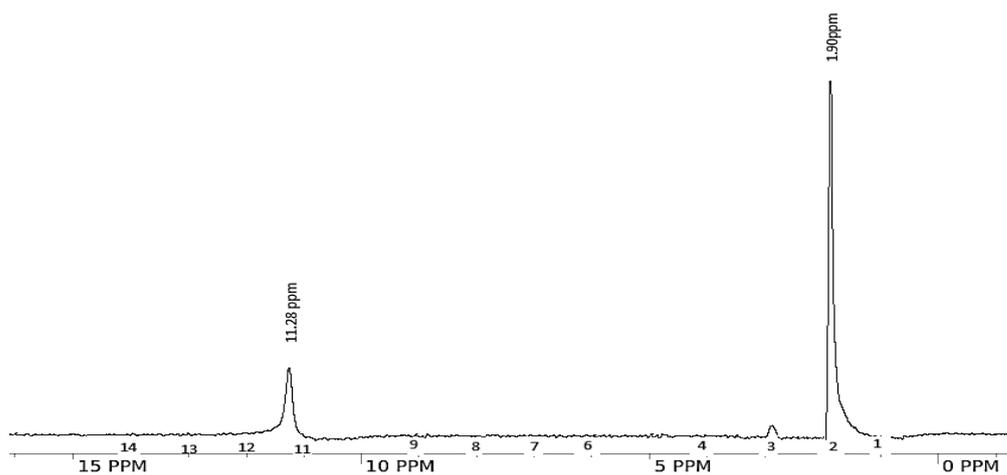


Fig.(7): <sup>1</sup>H NMR spectrum of DMG.

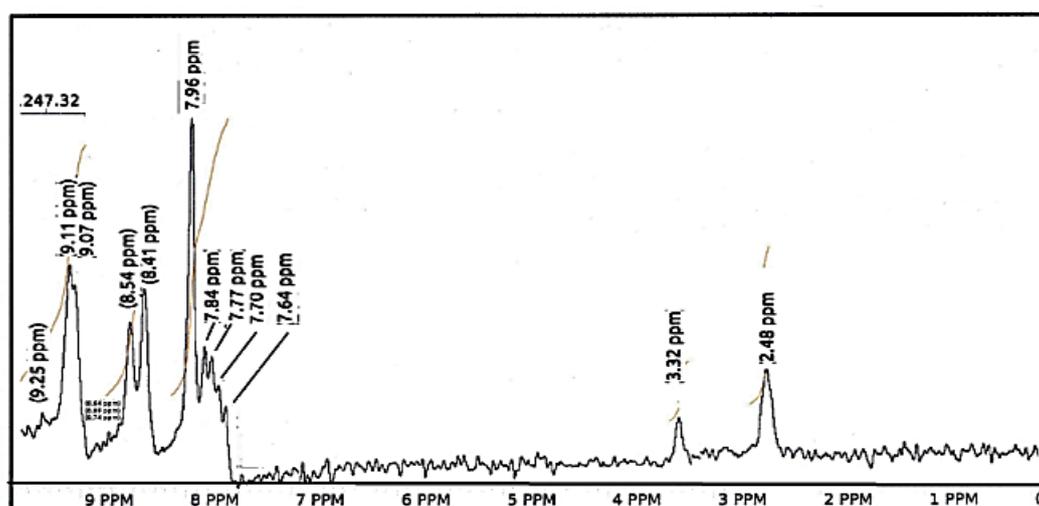


Fig.(8): <sup>1</sup>H NMR spectrum of 1-10 phenanthroline.

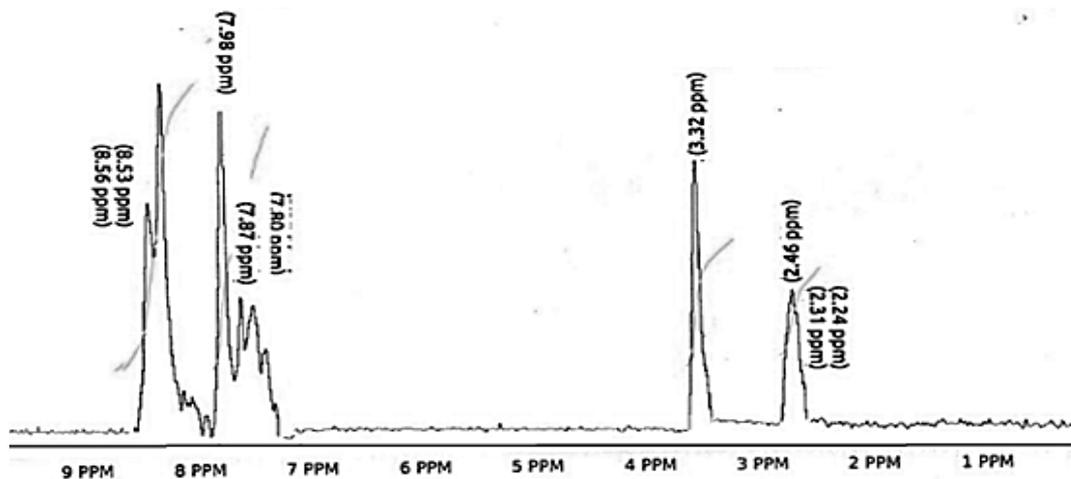


Fig.(9): <sup>1</sup>H NMR spectrum by addition of DMG +(1-10 penanthroline)+ Zn complex prepared by Stimulate addition at pH=6.

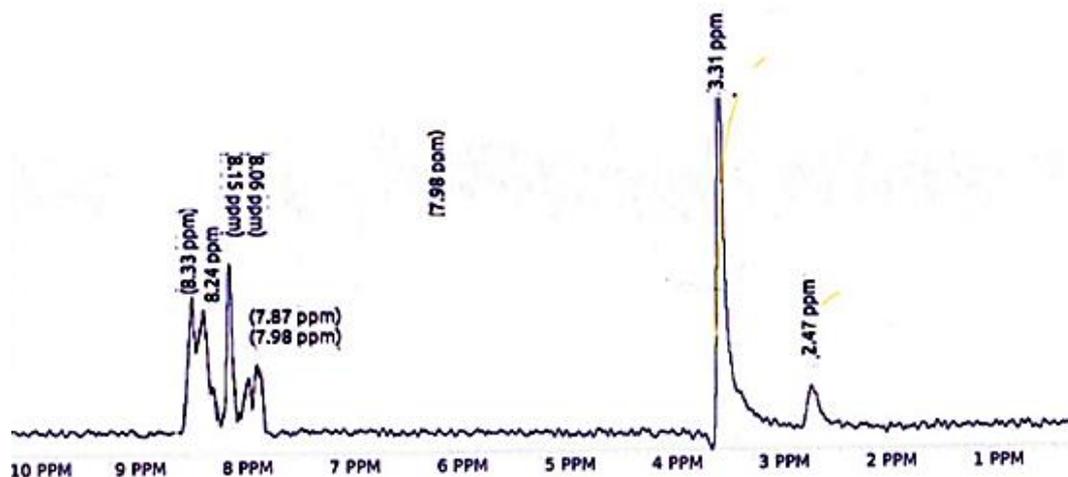


Fig.(10):  $^1\text{H}$  NMR spectrum by addition of DMG to Zn chloride with 2 hours reflux then addition of 1-10 phenanthroline for another 2 hours reflux.

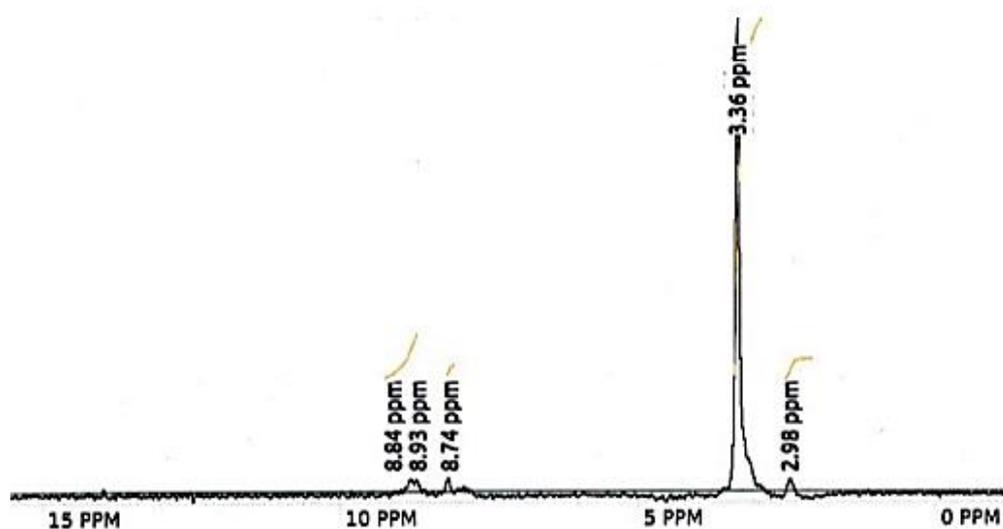


Fig.(11):  $^1\text{H}$  NMR spectrum of 2( 1-10 phenanthroline)+ Zn complex.

## Conclusion

According to this work, it is easy to compare the complex formation between the binary and ternary complex and to investigate the competitive ability for each ligand toward zinc ion and thus the possibility to prepare the mixed complexes. Competitive ability was studied for the two ligands experimentally supported by the computational calculations and the obtained results proved that 1-10 phen. behaves as much stronger ligand than dimethylglyoxime to bind with zinc ion.

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#### الخلاصة

في هذا البحث تم اجراء العديد من المحاولات لتحضير معقدات الخارصين مع خلائط الليكاندات المكونة من 1-10 dimethylglyoxime و phenanthroline (phen.) (DMG) لتقييم القدرة التنافسية لهذه الليكاندات للارتباط مع الايون الفلزي وفحص امكانية تكوين هذا المعقد باستخدام تقنيات FTIR و  $H^1$  NMR ومدعمة بالحسابات النظرية وبطريقة نظرية دوال الكثافة (DFT) لتحديد قيم Mulliken charges لكل من الليكاندات بشكلها المنفرد وعند خلطها في معقد الخارصين وبالتالي دراسة قوة ارتباطها ومدى امكانية تحضير المعقدات المختلطة.

النتائج المستحصلة من هذا البحث ان الليكاند 1-10 phen ارتبط بشكل اقوى بكثير من الليكاند DMG وحصيلة الشكل الهندسي لهذا المعقد تثبت مقدار وقوة التنافس بين هذه الليكاندات تجاه ايون الخارصين حيث ارتبط المعقد من خلال مولين من phen 1-10 مع الزنك وبوجود مولين من ايون الكلوريد.