

Synthesis, Investigation, DFT Study and Biological Activity of Zirconium (IV) Complexes

Salem El-t. Ashoor, Ibtisam M. Ediab

Abstract—Zirconium diamine and triamine complexes can possess biological activities. These complexes were synthesised via the reaction of equimolar quantities of 1,10-phenanthroline $\{NC_3H_3(C_6H_2)NC_3H_3\}$ (L1) or 4-4-amino phenazone $\{ONC_6H_5(NH)CH(NH_2)\}$ (L2) or diphenyl carbizon $\{HNNCO(NH)_2(C_6H_5)\}$ (L3) with a Zirconium Salt $\{ZrOCl_2\}$ in a 1:1 ratio to form complexes $[\{NC_3H_3(C_6H_2)NC_3H_3\}ZrOCl_2]$ $[ZrOCl_2L_1]$, $[\{(O_2NC_6H_4(NH)(NH_2))ZrOCl_2\}] [ZrOCl_2L_2]$ and $[\{HNNCO(NH)_2(C_6H_5)ZrOCl_2\}] [ZrOCl_2L_3]$ respectively. They were characterised using Fourier Transform Infrared (FT-IR) and UV-Visible spectroscopy. Also a variable temperature study of these complexes was completed, using UV-Visible spectroscopy to observe electronic transitions under temperature control. Also a DFT study was done on these complexes via the information from FT-IR and UV-Visible spectroscopy.

These complexes were found to show different inhibition to the growth of bacterial strains of *Bacillus* spp. & *Klebsiella* spp. & *E. coli* & *Proteus* spp. & *Pseudomonas* spp. at different concentrations (0.001, 0.2 and 1M). For better understanding these complexes were examined by using a Density Functional Theory (DFT) calculation.

Keywords—(1:10-phenanthroline) (L1), 4-4-amino phenazone (L2), diphenyl carbizon (L3), DFT study, antibacterial.

I. INTRODUCTION

COMPLEXES of transition metals have received great attention for many years, because of their biological activity, including anti-tumour, antibacterial, antiviral, antifungal and anti-carcinogenic properties [1]-[5]. Tetradentate chelate coordinate complexes have shown biological activity, essentially due to interactions with their heavy metal ions, bonding through sulfur and nitrogen [6], [7]. The interest in Schiff base complexes and development of the field of bioinorganic chemistry has increased substantially, since it has been recognized that many of these complexes may serve as models for biologically important species [8], [9]. Design, synthesis and characterisation of iron complexes with Schiff base ligands play a relevant role in the coordination chemistry of iron due to their importance as synthetic models for the iron-containing enzymes [10], [11], [12], as oxidation catalysts [13], [14] and as stable molecular materials based on temperature, pressure or light induced spin-crossover behaviours [15], [16].

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The amine-carbonyl condensation is involved in a number of enzyme-mediated reactions and understanding the mechanism of amine-carbonyl condensation has received great attention [17]. Again Thiourea compounds have been anticipated to be human carcinogens based on sufficient evidence of carcinogenicity in experimental animals.

The investigation of some complexes derived from salicylaldehyde and histidine have been found to have antibacterial activation on some pathogenic bacteria [18], [19]. Schiff bases including 3-enehydrazono-2-salicylidindolinone and their complexes incorporating Co(II), Ni(II), Cu(II) and Zn(II) have shown some antibacterial activity against pathogens such as *Staphylococcus aureus*, *Enterococcus*, *Proteus mirabilis*, *Escherichia coli*, *Bacillus anthracis*, *Pseudomonas aeruginosa* and *Candida albicans*. [20]

II. MATERIALS AND METHOD

All chemicals were used as received from suppliers. Carbizon was produced by Penhyle and 4-4-amino phenazone by BHD, 1:10-phenanthroline was produced by Riedel-de Haen. The company that produced the ethanol was PSPARK and methanol was produced by CARLOERBA. The metal salt zirconium chloride was produced by (Laboratory Reagent). Solvents used were purified by distillation.

A. Synthesis of [1:10-Phenanthroline] Zirconium (IV) Dichloro Oxide $[ZrCl_2OL_1]$

In a double neck flask, zirconium dichloride oxide ($ZrOCl_2$) (2g) in 15ml of distilled water was added to an equimolar quantity of 1:10-phenanthroline $\{NC_3H_3(C_6H_2)NC_3H_3\}$ (L1) (1.12g) in 30ml of ethyl alcohol dropwise at room temperature with stirring. Then the temperature was gradually increased and the reaction mixture was left to reflux for five hours. During that time the colour was observed to change from white to dark pink. Then a (1:1) mixture of ammonia and water was added to the reaction, which was then left for an additional five hours, during which time the observed colour of the solution did not change. The dark pink solid was separated from the hot solution by filtration, dried and after recrystallization the product was acquired with a 50% yield.

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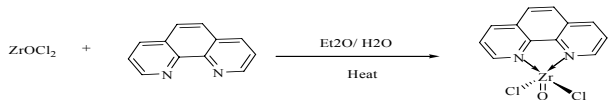


Fig. 1 Preparation of $[\{NC_3H_3(C_6H_2)NC_3H_3\}ZrOCl_2]$ $[ZrOCl_2L1]$

B. Synthesis of [Dichloro oxo (4-amino phenazone) Zirconium(IV)] $[ZrOCl_2L2]$

In a double neck flask, zirconium dichloride oxide ($ZrOCl_2$) (2g) in 20ml of distilled water was added to an equimolar quantity of 4-amino phenazone $\{ONC_6H_5(NH)CH(NH_2)\}$ (**L2**) (1.26g) in 30ml of propanol dropwise at room temperature with stirring. Then the temperature was gradually increased and the reaction mixture was left to reflux for five hours. During that time the colour was observed to change from pink to reddish brown. Then a (1:1) mixture of ammonia and water was added to the reaction, which was then left for an additional five hours, during which time the observed colour of the solution changed from dark brown to light brown. The light brown solid was separated from the hot solution by filtration, dried and after recrystallization the product was acquired with a 70% yield.

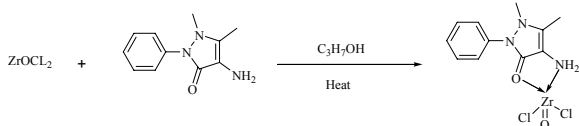


Fig. 2 Preparation of $[\{(O_2NC_6H_4(NH)(NH_2))ZrOCl_2]$ $[ZrOCl_2L2]$

C. Synthesis of [(phenyl carbizon) zirconium (IV) dichloro oxide] $[ZrOCl_2L3]$

In a double neck flask, zirconium dichloride oxide ($ZrOCl_2$) (2g) in 15ml of distilled water was added to an equimolar quantity of phenyl-carbizon $\{HNCO(NH)_2(C_6H_5)\}$ (**L3**) (1.49 g) in 30 ml of propanol dropwise at room temperature with stirring. Then the temperature was gradually increased and the reaction mixture was left to reflux for five hours. During that time the colour was observed to change from orange to red. Then a (1:1) mixture of ammonia and water was added to the reaction, which was then left for an additional three hours, during which time the observed colour of the solution changed from light red to dark red. Then a dark red solid was separated from the hot solution by filtration, dried and after recrystallization the product was acquired with a 72% yield.

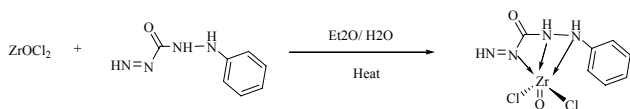


Fig. 3 Preparation of $[\{HNCO(NH)_2(C_6H_5)ZrOCl_2\}]$ $[ZrOCl_2L3]$

All complexes were characterized using melting point determination, Fourier Transform Infrared (FT-IR) and UV-Visible spectrometer studies. The melting points of the complexes were carried out on a Barnstead electrothermal melting point apparatus. The IR spectrum was recorded in

the range 400–4000 cm^{-1} on a Bruker Tensor 37 Fourier Transform Infrared (FT-IR) spectrometer (Germany - ATR). The electronic spectra in ethanol solution were recorded in the range 200–900 nm on a Shimadzu UV-Vis 9200 spectrophotometer (Japan).

III. RESULT AND DISCUSSION

A. UV-Vis. Spectral Study

$[ZrOCl_2L1]$ was examined spectrally by using ultraviolet and visible radiation. Absorption peaks were observed initially at frequencies of 253nm, 297nm and 643nm ($3952Cm^{-1}$, $3367Cm^{-1}$ and $1555Cm^{-1}$) demonstrating $\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$ type transitions and a C-T (Charge Transfer) transition respectively, these being identical with those reported previously [20], [21].

$[ZrOCl_2L2]$ was examined spectrally by using visible radiation at approximately pH7. Absorption peaks were observed initially at frequencies of 252nm, 288nm and 537nm ($3968Cm^{-1}$, $3472Cm^{-1}$ and $1862Cm^{-1}$) demonstrating $n \rightarrow \pi^*$, $\pi \rightarrow \pi^*$ type transitions and a C-T (Charge Transfer) transition respectively, these being identical with those reported previously [20], [21].

$[ZrOCl_2L3]$ was examined spectrally using ultraviolet and visible radiation at approximately pH7, Absorption peaks were observed initially at frequencies of 232nm, 264nm and 538nm ($4310Cm^{-1}$, $3787Cm^{-1}$ and $1858Cm^{-1}$) respectively demonstrating $n \rightarrow \pi^*$, $\pi \rightarrow \pi^*$ type transitions and a C-T (Charge Transfer) respectively, these being identical with those reported previously [20], [21].

B. FT-IR Spectral Study

The complex $[ZrOCl_2L1]$ was studied using Fourier transform Infrared (FT-IR) spectroscopy, to make sure all the functional groups are present in the complex. An absorption peak at $3100cm^{-1}$ indicates the presence of the N-H stretching frequency and the appearance of an absorption at $1640cm^{-1}$ indicates the presence of the C=N stretching frequency. There is additionally an absorption at $1090cm^{-1}$ which indicates the presence of the C-N stretching frequency and finally the appearance of an absorption peak at $1100cm^{-1}$ indicates the presence of an N-N stretch. Other peaks included $540cm^{-1}$, $720cm^{-1}$, $1090cm^{-1}$, $1620cm^{-1}$ and $1620cm^{-1}$ relating to Zr-Cl, Zr-N, C=C and C=O absorption frequencies respectively. The shift of these frequencies is caused by the coordinate bonding of nitrogen to the metal [22]-[24].

Again $[ZrOCl_2L2]$ was examined using FT-IR spectroscopy and showed an absorption peak at $3100cm^{-1}$ indicating the presence of the N-H stretching frequency, a peak at $1751cm^{-1}$ which indicates a C=O bond, while the presence of the peak at $1120cm^{-1}$ indicates a C-N stretch. Finally the appearance of an absorption peak at 1060 indicates the presence of an N-N stretch. Other peaks included $580cm^{-1}$, $700cm^{-1}$, $1120cm^{-1}$, $1620cm^{-1}$ and $1751cm^{-1}$ representing Zr-Cl, Zr-N, C-N, C=C and C=O stretches respectively. All these bonds stretching are in accordance with values previously reported [26], [27].

[ZrL3] was tested in (FT-IR) and showed a peak at 3390cm^{-1} , 1640cm^{-1} and 1160cm^{-1} for N-H, C=N and C-N stretches respectively, as well as a peak at 1050cm^{-1} showing a N-N stretch. Other peaks included 1750cm^{-1} , 1620cm^{-1} , 720cm^{-1} and 580cm^{-1} which indicate C=O, C=C, Zr-Cl and Zr-N stretches respectively. From this information it can be shown that all the absorptions expected for this complex are present [ZrOCl₂L₃] and have been found to accord with those previously reported [25]-[27].

C. Antibacterial Studies

The antibacterial studies were completed by testing the complexes on five species of bacteria (*Bacillus* spp. & *Klebsiella* spp. & *E. coli* & *Proteus* spp. & *Pseudomonas* spp.) for a range of different concentrations (0.001, 0.2 and 1M).

At a concentration of 0.001M, complex [ZrL1] showed a definite influence on the activity of only one type of bacterial in species, *Bacillus* spp., while the other complexes showed only small effects for all of the five species of the bacteria tested. This result is shown in Table I and Fig. 4.

TABLE I
ANTIBACTERIAL ACTIVITIES IN CONCENTRATION 0.001M

Complex	<i>E. coli</i>		<i>Bacillus</i> spp		<i>Sraphiaureus</i>		<i>Klebsiella</i> spp		<i>Pseudomonas</i> spp	
	Activity	Percentage	Activity	Percentage	Activity	Percentage	Activity	Percentage	Activity	Percentage
[ZrL1]	-	5%	-	5%	+++	75%	-	5%	-	5%
[ZrL2]	-	5%	-	5%	-	5%	-	5%	-	5%
[ZrL3]	-	5%	-	5%	-	5%	-	5%	-	5%

Percentage of Inhibition: Below 5mm = (-) low activity, 5mm – 10mm = (+) Active, 10mm – 15mm = (++) mildly active & 15mm – 20mm = (+++) moderately active, (20 mm, up) = (++++) highly active

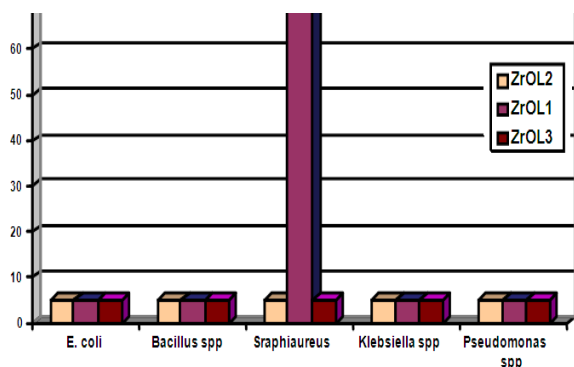


Fig. 4 Antibacterial activity in 0.001 percent concentration

TABLE II
ANTIBACTERIAL ACTIVITIES IN CONCENTRATION 0.02M

Complex	<i>E. coli</i>		<i>Bacillus</i> spp		<i>Sraphiaureus</i>		<i>Klebsiella</i> spp		<i>Pseudomonas</i> spp	
	Activity	Percentage	Activity	Percentage	Activity	Percentage	Activity	Percentage	Activity	Percentage
[ZrL1]	++	60%	-	5%	-	5%	++	60%	-	5%
[ZrL2]	-	5%	-	5%	-	5%	-	5%	-	5%
[ZrL3]	+	25%	-	5%	+++	75%	-	5%	-	5%

Percentage of Inhibition: Below 5mm = (-) low activity, 5mm – 10mm = (+) Active, 10mm – 15mm = (++) mildly active & 15mm – 20mm = (+++) moderately active, (20 mm, up) = (++++) highly active

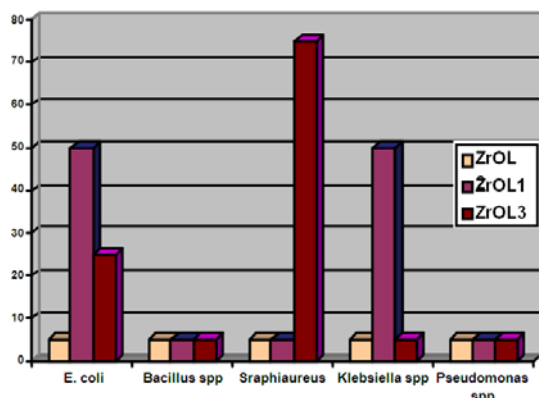


Fig. 5 Antibacterial activities in 0.02 percent concentration

At a concentration of 0.02M, complex [ZrL1] showed a moderate influence on the activity of only two types of bacterial species, *E. coli* ad *Klebsiella* spp. There was an extremely large effect on *Sraphiaureus* by [ZrL3] which additionally exhibited a significant effect on the *E. coli*. The other complexes showed small influence on the activity of all five species of the bacteria tested, these results being given in Table II and Fig. 5.

At a concentration of 1M, complex [ZrL1] Showed a large influence on the activities of bacterial species *E. coli*, *Bacillus* spp. and *Klebsiella* spp. [ZrL2] and [ZrL3] were also highly effective in modifying the activity of *Bacillus* spp and *E. coli*. Other species exhibited a small effect from these complexes. These results are given in Table III and Fig. 6.

TABLE III
ANTIBACTERIAL ACTIVITIES IN CONCENTRATION 1M

Complex	<i>E. coli</i>		<i>Bacillus</i> spp		<i>Srphiaureus</i>		<i>Klebsiella</i> spp		<i>Pseudomonas</i> spp	
	Activity	Percentage	Activity	Percentage	Activity	Percentage	Activity	Percentage	Activity	Percentage
[ZrL1]	++	60%	+++	75%	-	5%	++	60%	-	5%
[ZrL2]	-	5%	++	60%	-	5%	-	5%	-	5%
[ZrL3]	+	25%	+++	75%	-	5%	-	5%	-	5%

Percentage of Inhibition: Below 5mm = (-) low activity, 5mm – 10mm = (+) Active, 10mm – 15mm = (++) mildly active & 15mm – 20mm = (+++) moderately active, (20 mm, up) = (++++) highly active

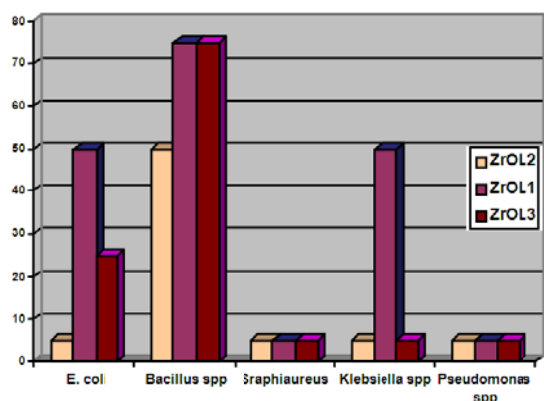


Fig. 6 Antibacterial activities in percentage in concentration

D. DFT Calculation

The chemistry of these complexes can be study by DFT calculation for more understanding. The bond energy of these complexes showed complex [ZrOCl₂L1] has the lowest energy, followed by [ZrOCl₂L2], with complex [ZrOCl₂L3] having the highest energy. This is makes [ZrOCl₂L1] the most stable and allowing the most time for reaction with bacteria when being used as an antibacterial agent as shown in Figs. 1-3. The bond energy diagram of all 3 complexes is displayed in Fig. 7.

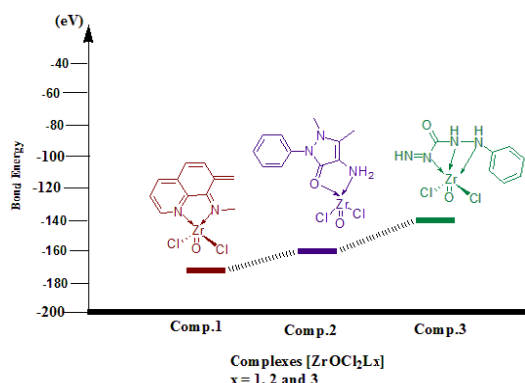


Fig. 7 Bond energy diagram of the complexes

The HOMO and LUMO of these complexes were examined by using a DFT calculation and showed the gap between HOMO and LUMO for complex [ZrOCl₂L1] to be the greatest, followed by [ZrOCl₂L3] and finally [ZrOCl₂L2] with the smallest gap. This means the bonding in L1 is stronger than in L3 which in turn is stronger than in L2. These data are displayed in Fig. 8.

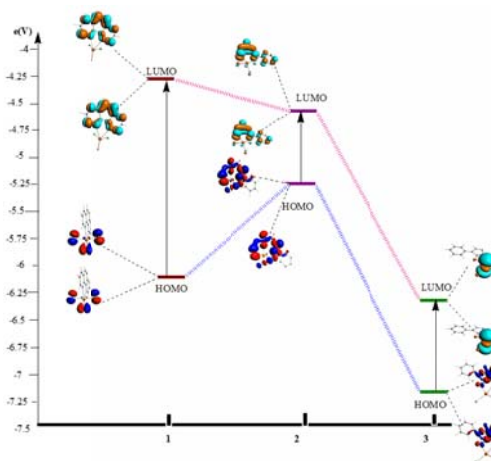


Fig. 8 Relative HOMO and LUMO of the complexes

IV. CONCLUSION

The chemistry presented in this paper shows that it is possible to produce different chelating di-amides of Zr(IV) complexes. The data we obtained from FT-IR suggested that the ligands are bidentate and tridentate with penta and hexa coordination within the complexes. The coordination around the Zr(IV) centre is the best described as distorted pentahedral and distorted octahedral geometry. The complexes were identifies using UV-Vis. and demonstrated the characteristic transitions of these complexes. Antibacterial activity was observed under different concentrations of the 3 complexes. DFT studies were completed to examine the complexes from the point stability.

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