Arabian Journal of Chemistry (2010) 3, 219–224

King Saud University

Arabian Journal of Chemistry

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ORIGINAL ARTICLE

# Synthesis, characterization and study of antibacterial activity of enaminone complexes of zinc and iron

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Received 5 April 2010; accepted 1 June 2010
Available online 9 June 2010

**KEYWORDS**

Antibacterial activity of enaminone–metal complex;
Enaminones;
Enaminone–iron complex;
Enaminone–zinc complex

**Abstract** Complexes of enaminones; 4-*N,N*-diethylamine-pent-3-ene-2-one [$HL^1$], 4-*N,N*-di *n*-propylamine-pent-3-ene-2-one [$HL^2$] and 4-*N,N*-dicyclohexylamine-pent-3-ene-2-one [$HL^3$] with Fe(II) and Zn(II) ions were prepared by reacting the equimolar ethanolic solutions of the ligands ($HL^1$, $HL^2$ and $HL^3$) with ethanolic metal solutions. The complexes formed, were characterized by infrared, ultraviolet and atomic absorption spectroscopy. Ligands and their metal complexes were tested against *Escherichia coli* and *Staphylococcus aureus* bacteria to assess their antibacterial action using disc diffusion method. Ligands were completely inactive against bacteria whereas the complex Zn($HL^1$) has significant action on both bacteria, indicating that it has a good potential as bactericide. Other complexes have normal antiseptic character.

## 1. Introduction

Enaminones consist of an amino group linked by carbon–carbon double bond to a carbonyl group. The carbonyl group eases the preparation, isolation and storage of the complex, by providing required stability to the system. The chemistry of the enamino carbonyl group is an area of considerable scope (Montanile, 2003). Enaminones have received a large attention during last decade. Lot of work has been done to explore new routes for the synthesis of enaminones. Azzoro and his co-workers reported a simple method for the synthesis of enaminones by using amines and 1–3 diketones (Azzoro et al., 1981). In another method, β-chloro vinyl ketone was reacted with amines to synthesize enaminones (Pohland and Benson, 1966). Other methods of preparation include reactions between: formamide dimethyl acetates and ketones (Abdulla and Brinkmeye, 1979); acid chlorides with terminal alkynes and triethylamine (Karpov and Müller, 2003); primary amines and β-dicarbonyl compound catalyzed with copper nanoparticles (Kidwai et al., 2009). Imada et al. (1996) has transformed β-amino ketones to enaminones using palladium. Lue and Greenhill (1996) functionalize enaminones by introducing different substituents on nitrogen, α-carbon and β-carbonylic carbon. These derivatives were used extensively, for preserving natural products and analogues.

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doi:10.1016/j.arabjc.2010.06.003

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Enaminones are important organic intermediates used to synthesize various heterocyclic and biologically active analogues. Naringrekar and Stella (1990) investigated the structural stability of enaminones and evaluated their ability as pro drugs of primary amines. Enaminone synthesized by acetyl acetone and diethyl amine was used as universal cation locating agent showing characteristic colors with different metals (Nasir et al., 1996). Eddington et al. (2000) reported synthesis and anticonvulsant evaluations of some enaminones. Enaminones have shown high *p*-glycoprotein affinity and can act as *p*-glycoprotein modulators (Salama et al., 2004). Zhuo (1998) studied the $^{17}O$ NMR spectrums of primary and secondary enaminones.

In coordination chemistry, enaminones are considered “good chelating ligands” for transition metals. The anions produced from enaminone, offer potential isoelectronic alternatives to cyclopentadienyl-based anions and therefore, their transition metal complexes can act as possible alternative catalysts for olefinic polymerization (Markéta et al., 2006). A new ferrocene-containing enaminone $[C_5H_5FeC_5H_4C(O)CH{=}C{-}(NHAr)CH_3]$ (Ar = $2\text{-}CH_3OC_6H_4$) and its copper(II) complex has been synthesized and characterized by elemental analysis, $^1H$ NMR, IR, UV and X-ray crystallography (Shi et al., 2004).

The present work comprises the synthesis of complexes of 4-*N,N*-diethylamine-pent-3-ene-2-one [$HL^1$], 4-*N,N*-di *n*-propylamine-pent-3-ene-2-one [$HL^2$] and 4- *N,N*-dicyclohexylamine-pent-3-ene-2-one [$HL^3$] ligands with Fe(II) and Zn(II) ions. The ligands were synthesized using reported procedures (Nelson and Joe, 1959). Metal complexes were characterized by infrared, ultraviolet and atomic absorption spectroscopy. Ligands and their metal complexes were examined to assess their antibacterial activity using disc diffusion method.

## 2. Experimental work

### 2.1. Material and apparatus

Analytical grade chemicals bought from Sigma–Aldrich, Inc. were used throughout this work. Gallen Kamp melting point apparatus was used to find out melting points. Labomed UV–Visible spectrophotometer (Model UVD-3500, 190–1100 nm) was used to find out $\lambda_{max}$ and absorbance in various solvents. IR spectrums of ligands and their metal complexes were recorded with FT-IR spectrophotometer (Perkin–Elmer Spectrum RX-I) using nujol mull in range 4000–500 $cm^{-1}$. Fe(II) and Zn(II) ions, in the complexes were estimated by atomic absorption spectrophotometer (Model AAnalyst-100) using air–acetylene flame.

### 2.2. Synthesis of ligands

#### 2.2.1. Synthesis of 4-N,N-diethylamine-pent-3-ene-2-one ($HL^1$)

Acetyl acetone (0.1 mol $L^{-1}$, 10.5 mL) was added to conical flask placed in an ice bath. Subsequently, diethyl amine (0.1 mol $L^{-1}$, 10.4 mL) was added, dropwise, with continuous stirring. Yellow crystals of $HL^1$ were formed in 15 min. These needle-like crystals were purified by sublimation and were stored in a refrigerator at 4 °C.

#### 2.2.2. Synthesis of 4-N,N-di-n-propylamine-pent-3-ene-2-one ($HL^2$)

Acetyl acetone (0.6 mol $L^{-1}$, 61.7 mL), di-*n*-propyl amine (0.6 mol $L^{-1}$, 83.9 mL), *p*-toluene sulfonic acid (2.0 g) and benzene (150 mL) were taken in a round bottom flask and refluxed till the complete removal of water, using a Dean–Stark apparatus. Afterwards, benzene was removed under reduced pressure in a rotary evaporator. The contents of the flask were cooled in an ice bath. The yellow liquid obtained was agitated with cold saturated ethanolic sodium bicarbonate solution and extracted with ether, thrice. The ethereal extract was taken into a distillation flask and the fraction boiling at 95 °C was collected.

#### 2.2.3. Synthesis of 4-N,N-dicyclohexylamine-pent-3-ene-2-one ($HL^3$)

Acetyl acetone (0.3 mol $L^{-1}$, 31.0 mL), dicyclohexylamine (0.3 mol $L^{-1}$, 58.0 mL), *p*-toluene sulfonic acid (1.0 g) and benzene (150 mL) were refluxed on heating mantle at 85 °C for 5 h. The water produced in reaction mixture was removed using a Dean–Stark apparatus. Benzene was removed by distillation under reduced pressure and the viscous oily liquid gained yielding shiny needle-like crystals on cooling. The product was recrystallized with ethanol.

### 2.3. Synthesis of metal complexes

#### 2.3.1. Synthesis of Fe(II) and Zn(II) complexes of $HL^1$

$FeSO_4{\cdot}7H_2O$ (0.3 mol $L^{-1}$, 2.62 g) was added to ethanolic solution of enaminone ($HL^1$) (0.01 mol $L^{-1}$, 1.55 g). The precipitates formed, were allowed to stand for about 5 h. Afterwards, filtered off and washed with small amount of ethanol and *n*-hexane, respectively and recrystallized in ethanol. The reddish brown crystals were dried at room temperature and stored in desiccator.

The Zn(II) complex of the ligand ($HL^1$) was prepared by adding aqueous solution of $ZnCl_2$ (0.01 mol $L^{-1}$, 1.36 g) in ethanolic solution of ($HL^1$) enaminone (0.01 mol $L^{-1}$, 1.55 g). The reaction mixture was stirred for 10–15 min and allowed to settle. The light brown precipitates of Zn(II) complex formed, were removed by filtration and crystallized with ethanol–tetrahydrofuran (1:1) mixture. Later, dried at room temperature and stored in a desiccator.

#### 2.3.2. Synthesis of Fe (II) and Zn (II) complexes of $HL^2$

Fe(II) and Zn(II) complexes were prepared by adding $FeSO_4{\cdot}7H_2O$ (0.01 mol $L^{-1}$, 2.62 g) and $ZnCl_2$ (0.01 mol $L^{-1}$, 1.36 g) to cold ethanolic solution of ($HL^2$) enaminone (0.01 mol $L^{-1}$, 1.83 g), separately. The reaction mixtures were stirred for 10–15 min and allowed to stand for 5 h. The orange red precipitates of iron complex and light brown precipitates of zinc complex were removed by filtration and crystallized with ethanol–tetrahydrofuran mixture. Afterwards, dried at room temperature and stored in a desiccator.

#### 2.3.3. Synthesis of Fe(II) and Zn(II) complexes of $HL^3$

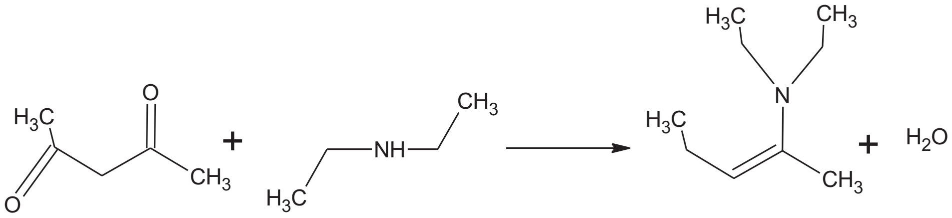
Fe(II) and Zn(II) complexes were prepared by adding $FeSO_4{\cdot}7H_2O$ (0.01 mol $L^{-1}$, 2.62 g) and $ZnCl_2$ (0.01 mol $L^{-1}$, 1.36 g) to ethanolic solution of ($HL^3$) enaminone (0.01 mol $L^{-1}$, 2.63 g), separately. The reaction mixtures were stirred for 10–15 min and allowed to stand for 5 h. The reddish brown precipitates of iron complex and light brown precipitates of zinc complex were removed by filtration and crystallized with ethanol–tetrahydrofuran mixture. Afterwards, dried at room temperature and stored in a desiccator.

### 2.4. Antibacterial studies

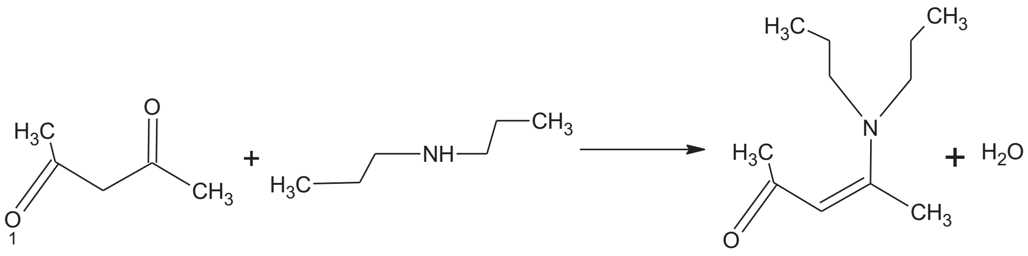
The ligands and their metal complexes were tested to assess their antibacterial activity against the following bacterial species.

- *Escherichia coli*
- *Staphylococcus aureus*

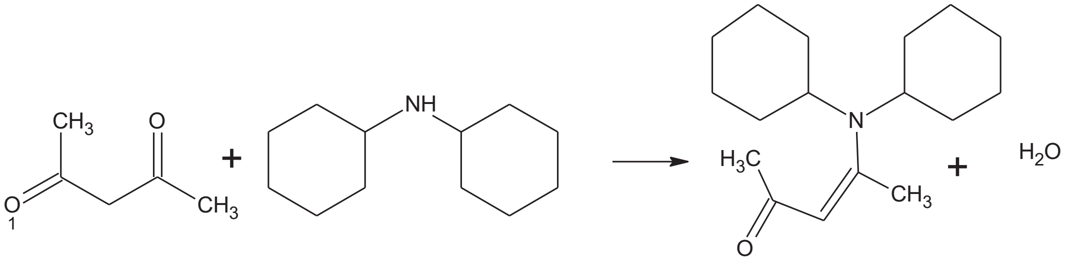
The ligand complex (30 µg in 0.01 mL DMF) was applied to a paper disc with the help of micropipette. The discs were placed in an incubator for 48 h at 37 °C and later, applied to bacteria grown on agar plates. Inoculation was performed with the help of a platinum wire loop, which was made red-hot in flame and used for the application of bacterial strains after cooling. Sterilized forceps were used to apply paper disc on inoculated agar plates. When the discs were applied, they were



**Scheme 1** Synthesis of 4-*N*,*N*-diethylamine-pent-3-ene-2-one ($HL^1$).



**Scheme 2** Synthesis of 4-*N*,*N*-diethylamine-pent-3-ene-2-one ($HL^2$).



**Scheme 3** Synthesis of 4-*N*,*N*-dicyclohexylamine-pent-3-ene-2-one ($HL^3$).

**Table 1** Physicochemical characteristics of ligands and their metal complexes.

| Sr. No. | Compound | Appearance | M.P.(1,3)/B.P.(2)/D.P.(4–9) (°C) | % Yield | % Age of nitrogen | |
|---|---|---|---|---|---|---|
| | | | | | Theoretical | Found |
| 1 | $HL^1$ | Needles like, shiny crystals | 105 | 66–68 | 9.03 | 8.90 |
| 2 | $HL^2$ | Golden yellow viscous liquid | 95 | 65–67 | 7.60 | 7.00 |
| 3 | $HL^3$ | Colorless needle like shiny crystals | 154 | 64–65 | 5.32 | 4.94 |
| 4 | $Fe(HL^1)$ | Reddish brown shiny crystals | > 500 | 27.02 | 8.06 | 7.34 |
| 5 | $Zn(HL^1)$ | Light brown, shiny crystals | > 230 | 26.50 | 7.45 | 7.12 |
| 6 | $Fe(HL^2)$ | Dark Green, shiny crystals | 500 | 30.23 | 6.94 | 6.20 |
| 7 | $Zn(HL^2)$ | Light brown, shiny crystals | > 230 | 20.55 | 6.49 | 5.91 |
| 8 | $Fe(HL^3)$ | Light Green, shiny crystals | > 500 | 28.90 | 4.97 | 3.99 |
| 9 | $Zn(HL^3)$ | Light brown, shiny crystals | > 230 | 37.0 | 4.73 | 4.71 |

**Table 2** Solubility of ligands $HL^1$, $HL^2$, $HL^3$ and their Fe(II) and Zn(II) complexes.

| Solvent | $HL^1$ | $HL^2$ | $HL^3$ | Fe ($HL^1$) | Zn ($HL^1$) | Fe ($HL^2$) | Zn ($HL^2$) | Fe ($HL^3$) | Zn ($HL^3$) |
|---|---|---|---|---|---|---|---|---|---|
| Distilled water | Sol | Ins | Sol | Sol | Sp. S | Sp. S | Ins | S. Hot | Sp. S |
| Ethanol | Sol | Sol | Sol | Sp. S | Sp. S.H | Sp. S | Sp. S | Sp. S | Ins |
| THF | Sol | Sol | Sol | Sol | Ins | Ins | Ins | Sol | Ins |
| Toluene | S. Hot | S. Hot | S. Hot | Sol | Ins | Sp. S | Ins | Sol | Ins |
| Benzene | Sol | Sol | Sol | Sp. S | Ins | S. Hot | Ins | S. Hot | Ins |
| *n*-Hexane | Ins | Ins | Ins | Ins | Ins | Ins | Ins | Ins | Ins |
| Acetone | Sol | Sol | S. Hot | Sp. S | Sp. S | S. Hot | Ins | Sp. S.H | Sp. S |
| $CCl_4$ | Sol | Sol | Sol | Sp. S | S. Hot | Sp. S | Ins | Sp. S.H | S. Hot |

Soluble = Sol, insoluble = Ins, sparingly soluble = Sp. S, soluble in hot = S. Hot, sparingly soluble in hot = Sp. S.H.

incubated at 37 °C for 24 h. The zone of inhibition (diameter in mm) was measured around the disc.

## 3. Results and discussion

In our previous work, synthesis, characterization and antibacterial activity of several isomeric enaminones and their metal complexes with Ca(II) and Mg(II) have been reported (Tariq et al., 2009). In the present work, synthesis, characterization and antibacterial activity of three enaminones and their complexes with zinc and iron have been presented. Syntheses of the enaminones are represented in Schemes 1–3.

These enaminones can react with the Fe(II) and Zn(II) ions forming the neutral complexes. Preparation of enaminones involved the removal of water. Anhydrous sodium sulfate, sodium carbonate, anhydrous magnesium sulfate and *p*-toluene sulfonic acid were used as water removing agents. However, separation of *p*-toluene sulfonic acid from the reaction mixture was difficult in case of oily products. Water plays an important role as some enaminones were susceptible to hydrolysis by water. $HL^1$ (m.p = 105 °C) and $HL^3$ (m.p = 154 °C) were colorless crystalline solids whereas $HL^2$ (b.p = 95 °C) was viscous liquor. The percentage of nitrogen in these ligands, determined by Kjeldahl's methods, varies in the range 4.94–8.90%. These enaminone ligands were used to form complexes with Fe(II) and Zn(II). Most of these complexes were crystalline solids with shiny appearance and only few were amorphous solids. Their decomposition points were above 230 °C. Physicochemical characteristics of ligands and their metal complexes are listed in Table 1.

**Table 3** $\lambda_{max}$ Values and respective absorbance of ligands and their metal complexes.

| Sr. No. | Compound | π–π* transitions | |
|---|---|---|---|
| | | $\lambda_{max}$ (nm) | Absorbance (AU) |
| 1 | $HL^1$ | 310 | 1.722 |
| 2 | $HL^2$ | 310 | 1.315 |
| 3 | $HL^3$ | 290 | 1.039 |
| 4 | Fe($HL^1$) Complex | 290 | 1.959 |
| 5 | Zn($HL^1$) Complex | 295 | 0.213 |
| 6 | Fe($HL^2$) Complex | 295 | 0.476 |
| 7 | Zn($HL^2$) Complex | 290 | 0.257 |
| 8 | Fe($HL^3$) Complex | 290 | 1.309 |
| 9 | Zn($HL^3$) Complex | 295 | 0.476 |

The solubility of the ligands and their complexes were tested in eight different solvents in both hot and cold states. All the ligands and the complexes were insoluble in *n*-hexane. Most of these were soluble in water and benzene. Details are given in Table 2.

The spectral data has been summarized in Table 3. The $\lambda_{max}$ values are 310 nm, 310 nm and 290 nm for $HL^1$, $HL^2$ and $HL^3$ respectively. Probable electronic transition is π–π*. $\lambda_{max}$ values have shifted down after forming metal complex.

IR spectra of some enaminones or enamino ketones were reported by Dabrowski (1963). The IR spectra were recorded with nujol mull. Peaks of interest lay in the range 1572–1670 cm$^{-1}$ and 1427–1542 cm$^{-1}$. Some enaminone showed absorption at 1612–1620 cm$^{-1}$, as well. The IR data is given in the Table 4. Strong absorption bands for C–H stretch, C–H bend, C=C stretch, C=O stretch and C–N stretch are indicative of the formation of enaminones. These peaks were shifted to lower wave numbers after formation of metal complexes.

Metal to ligand ratio was calculated by finding out metal by atomic absorption spectrophotometer. By comparing these values, suitable geometries of these metal complexes were proposed. The ligand ($HL^1$, $HL^2$, and $HL^3$) to Fe(II) ratio is 3:1. The synthesized complexes are proposed to show octahedral geometries. The ligand ($HL^1$, $HL^2$, and $HL^3$) to Zn(II) ratio is 2:1. The synthesized complexes are proposed to show square

**Table 4** IR band absorption frequencies of ligands and their metal complexes.

| Bond frequencies (cm$^{-1}$) | $HL^1$ | Fe ($HL^1$) | Zn ($HL^1$) | $HL^2$ | Fe ($HL^2$) | Zn ($HL^2$) | $HL^3$ | Fe ($HL^3$) | Zn ($HL^3$) |
|---|---|---|---|---|---|---|---|---|---|
| *v* (C–H) stretching | 2974 | 2376 | 2354 | 2875 | 2724 | 2353 | 2850 | 2842 | 2723 |
| *v* (C–H) bending | 1388 | 1372 | 1364 | 1365 | 1354 | 1342 | 1370 | 1347 | 1338 |
| *v* (C–C) stretching | 1483 | 1454 | 1384 | 1532 | 1460 | 1461 | 1550 | 1451 | 1459 |
| *v* (C=C) stretching | 1665 | 1659 | 1652 | 1668.6 | 1653 | 1644 | 1662.5 | 1655 | 1648 |
| *v* (C–N) stretching | 1291 | 1269 | 1260 | 1255 | 1080 | 1040 | 1257 | 1090 | 1046 |
| *v* (C=O) stretching | 1698 | 1675 | 1670 | 1706 | 1660 | 1671 | 1694 | 1642 | 1670 |

planar geometries. The proposed structures of the complexes are shown in Figs. 1 and 2.

The antibacterial activities of the synthesized ligands and their metal complexes were tested against strains of bacteria, *S. aureus* and *E. coli*, using disc-diffusion method. All the three ligands were found to be quiet against both strains of bacteria. However, the metal complexes were active against bacterial strains. In general, the complex Zn($HL^1$) has highest activity against the *S. aureus* and *E. coli*, showing that it has a good potential as bactericide. Fe($HL^3$) has shown good activity as well. The other complexes showed limited activity against *S. aureus* and *E. coli* bacteria. The Fe($HL^1$) complex did not show any activity against the *S. aureus*. Results are depicted in Table 5.

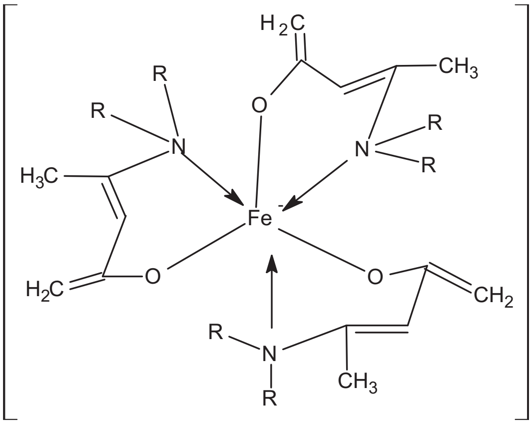


**Figure 1** Proposed geometry of the complexes of Fe(II) with $HL^1$, $HL^2$ and $HL^3$, where R = ethyl, *n*-propyl, cyclohexyl.

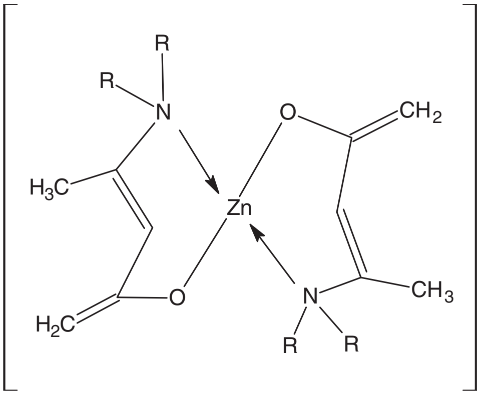


**Figure 2** Proposed geometry of the complexes of Zn(II) with $HL^1$, $HL^2$ and $HL^3$, where R = ethyl, *n*-propyl, cyclohexyl.

**Table 5** Antibacterial activity of ligands and their metal complexes.

| Sr. No. | Compound | Bacteria | |
|---|---|---|---|
| | | *Staphylococcus aureus* | *Escherichia coli* |
| 1 | $HL^1$ | – | – |
| 2 | Fe($HL^1$) Complex | – | – |
| 3 | Zn($HL^1$) Complex | + | + + |
| 4 | $HL^2$ | – | – |
| 5 | Fe($HL^2$) Complex | – | + |
| 6 | Zn($HL^2$) Complex | – | + |
| 7 | $HL^3$ | – | – |
| 8 | Fe($HL^3$) Complex | + | + |
| 9 | Zn($HL^3$) Complex | – | + |

+ = Active, + + = very active, – = inactive.

## 4. Conclusion

Complexes of enaminones; 4-*N,N*-diethylamine-pent-3-ene-2-one [$HL^1$], 4-*N,N*-di *n*-propylamine-pent-3-ene-2-one [$HL^2$] and 4-*N,N*-dicyclohexylamine-pent-3-ene-2-one [$HL^3$] with Fe(II) and Zn(II) ions were synthesized. The complexes formed, were characterized by infrared, ultraviolet and atomic absorption spectroscopy. To evaluate anti bacterial character of complexes, these were tested against *E. coli* and *S. aureus* bacteria. It was found that complex Zn ($HL^1$) has significant action on both bacterial species while other complexes have normal antiseptic character.

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