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# Organometallic-based antibacterial and antifungal compounds: transition metal complexes of 1,1′-diacetylferrocene-derived thiocarbohydrazone, carbohydrazone, thiosemicarbazone and semicarbazone

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**Abstract**

Organometallic-based, 1,1′-diacetylferrocene-derived antibacterial and antifungal thiocarbohydrazone, carbohydrazone, thiosemicarbazone and semicarbazone have been prepared by condensing equimolar amount of 1,1′-diacetylferrocene with thiocarbohydrazide, carbohydrazide thiosemicarbazide and semicarbazide, respectively. These were used as ligands for the preparation of their cobalt (II), copper (II), nickel (II) and zinc (II) metal complexes. All the synthesized ligands and their complexes were characterized by IR, NMR, elemental analyses, molar conductances, magnetic moments and electronic spectral data. These synthesized compounds were screened for their antibacterial activity against *Escherichia coli*, *Bacillus subtillis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Salmonella typhi*, and for antifungal activity against *Trichophyton longifusus*, *Candida albicans*, *Aspergillus flavus*, *Microsporum canis*, *Fusarium solani* and *Candida glaberata* using the agar-well diffusion method. All the compounds showed good antibacterial and antifungal activity which increased on coordination with the metal ions thus, introducing a novel class of organometallic-based antibacterial and antifungal agents.

**Keywords:** *Organometallic compound, antibacterial, antifungal*

## Introduction

The potential antitumor, antibacterial, antiviral, fungicidal and antimalarial activities of thiosemicarbazone and/or semicarbazones [1–4] and their metal complexes have spurred the study of the coordination chemistry of these ligands. Some of these derivatives have highlighted the use of ferrocene and its various derivatives for the design of biologically active compounds [5–9]. The use of ferrocene-containing compounds in medicinal chemistry has not been investigated to a large extent. Some reports, however, have indicated [10,11] that if the aromatic group in penicillin and cephalosporin antibiotics is replaced by the ferrocenyl moiety, it significantly increases the bactericidal properties of the obtained compound. Moreover, the substituent chemistry and versatility of ferrocene-containing compounds has led to its recognition as a useful synthon[12–16] in organic and bioorganic chemistry. This is achieved by coupling the ferrocene moiety with hetero-aromatic/aromatic systems. These considerations attracted our attention in combining both the chemistry of ferrocene and several other moieties to design and study a new area of organometallic-based antibacterial/antifungal compounds and their further

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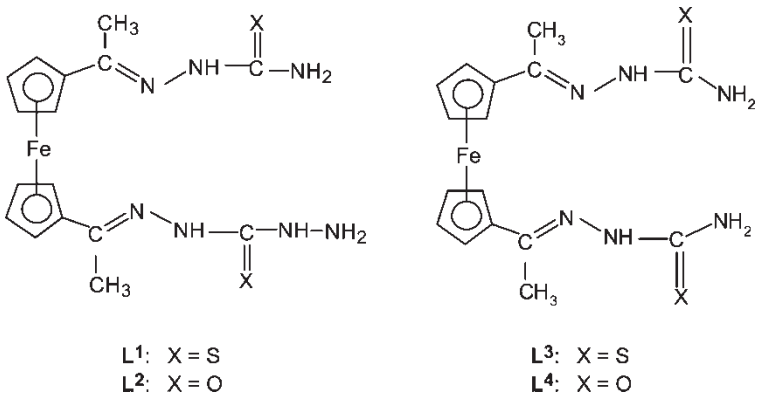


Figure 1. Structure of the ligands $\mathbf{L}^1$–$\mathbf{L}^4$ synthesized in the present work.

antibacterial/antifungal enhancement on coordination with transition metal ions such as cobalt(II), copper(II), nickel(II) and zinc(II).

Acetylferrocene, a typical acylferrocene, undergoes an easy derivatisation with aromatic/heteroaromatic amines. In an attempt to investigate such transformations of 1,1′-diacetylferrocene, we report here some novel 1,1′-disubstituted ferrocene derivatives ($\mathbf{L}^1$–$\mathbf{L}^4$) (Figure 1) and their use as potential ligands in the preparation of Co(II), Cu(II), Ni(II) and Zn(II) complexes (Figure 2). These were all screened for their antibacterial activity against *Escherichia coli*, *Bacillus subtillis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Salmonella typhi*, and, for antifungal activity against *Trichophyton longifusus*, *Candida albicans*, *Aspergillus flavus*, *Microsporum canis*, *Fusarium solani* and *Candida glaberata* using the agar-well diffusion method[17,18]. All the prepared ligands showed a good affinity as antibacterial/antifungal agents, which was increased on chelation/coordination with the metal ions.

## Material and methods

All solvents used were Analar grade. 1,1′-Diacetylferrocene, thiocarbohydrazide carbohydrazide, thiosemicarbazide and semicarbazide, were obtained from Aldrich. All metals were used as chlorides. IR and NMR spectra were recorded on Perkin Elmer 283B

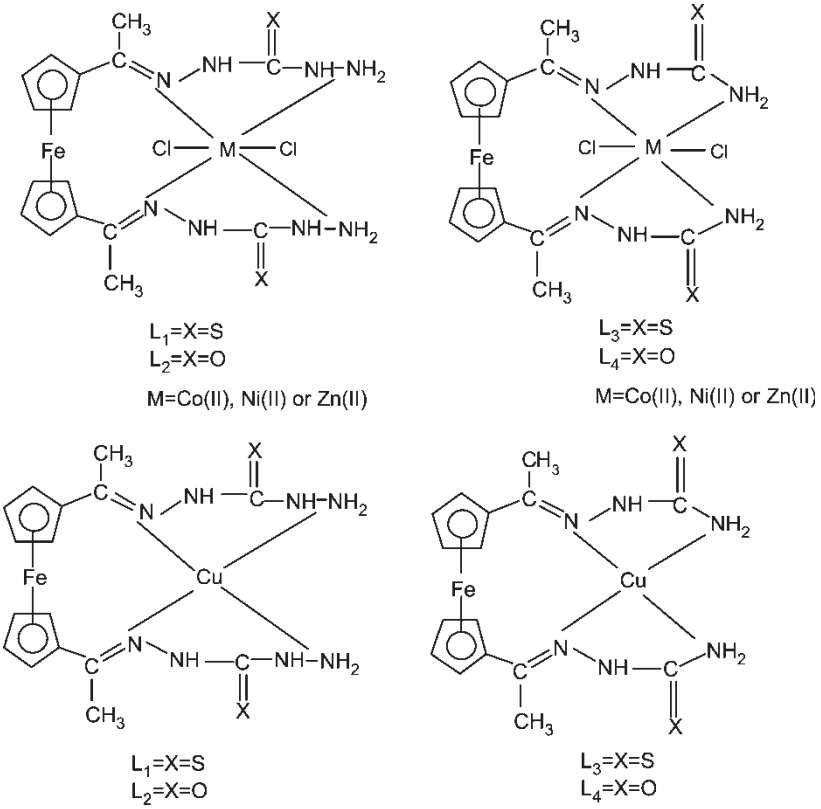


Figure 2. Proposed structure of the metal complexes synthesized in the present work.

and 300 MHz Varian XL-300 instruments, respectively. UV- Visible spectra were obtained on a Baush and Lomb spectronic 1001. Conductances of the metal complexes were determined in DMF using a YSI-32 model conductometer. Magnetic measurements were done on solid complexes using the Gouy method. Microanalyses were carried out by Butterworth Laboratories Ltd. (U.K). Melting points were recorded on a Gallenkamp apparatus and are uncorrected.

### *Synthesis of ligand (**L**$^1$)*

For the preparation of ligand (**L**$^1$), a solution of 1-1′-diacetylferrocene (1.0 g, 0.0037 M) in ethanol (20 mL) was added to a stirred hot ethanol solution (20 mL) of thiocarbohydrazide (0 78 g, 0.0074 M). The mixture was refluxed for 4 h. After allowing cooling at room temperature, the solvent was evaporated to give a dark orange solid product. Removal of the solvent gave an orange crystalline solid which was recrystallized from hot dichloromethane. A similar method was used for the preparation of the other ligands (**L**$^2$–**L**$^4$).

### *Synthesis of the metal (II) chelates*

To a magnetically stirred and warmed (40°C) solution of the ligand (1.0 M) in ethanol (30 mL) was added a solution of the respective metal (II) chloride (1.0 M) in ethanol (20 mL). The mixture was refluxed for 2 h. During this time, a complex was precipitated which, upon cooling, was filtered, washed several times with ethanol, then with diethyl ether and dried over anhydrous $CaCl_2$. All other complexes were prepared similarly using the same method.

### *Biological activity*

All the synthesized ligands (**L**$^1$–**L**$^4$) and their corresponding metal (II) complexes (**1**–**16**) were screened *in-vitro* for their antibacterial activity against *Escherichia coli*, *Bacillus subtillis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Salmonella typhi* and for antifungal activity against *Trichophyton longifusus*, *Candida albicans*, *Aspergillus flavus*, *Microsporum canis*, *Fusarium solani* and *Candida glaberata* using the agar well diffusion method[17,18]. Two to eight hours old bacterial inoculums containing approximately $10^4$–$10^6$ colony forming units (CFU)/ml were used in these assays. The wells were dug in the media with the help of a sterile metallic borer with centers at least 24 mm. Recommended concentration (100 µl) of the test sample (1 mg/ml in DMSO) was introduced into the corresponding wells. Other wells supplemented with DMSO and reference antibacterial drugs served as negative and positive controls, respectively. The plates were incubated immediately at 37°C for 20 h. Activity was determined by measuring the diameter of zones showing complete inhibition (mm). Imipenum was used as standard drug for antibacterial activity and, miconazole and amphotericin B for antifungal activity. In order to clarify any participating role of DMSO or DMF in the biological screening, separate studies were carried out with the solutions alone of DMSO and DMF and they showed no activity against any bacterial/fungal strains.

## Results and discussion

### *Chemistry*

The ligands (**L**$^1$–**L**$^4$) were prepared by refluxing the appropriate amount of an ethanolic solution of 1,1′-diacetylferrocene with the corresponding thiosemicarbazide, semicarbazide, thiocarbohydrazide and carbohydrazide, in 1:2 molar ratios. The structures of the synthesized ligands were established with the help of their IR, NMR and microanalytical data (Tables I and II). All metal complexes (**1**–**16**) (Table III) of these ligands were prepared by the stoichiometric reaction of the corresponding ligand with the respective metal salt as chloride in a molar ratio M:L of 1:1. They are all air and moisture stable and, are intensely colored amorphous solids, which decompose without melting. Molar conductance values of the Co(II), Ni(II) and Zn(II) complexes (18–22 $\Omega cm^2 mol^{-1}$) in DMF showed them to be non-electrolytes and the Cu (II) complexes (93–96 $\Omega cm^2 mol^{-1}$) to be electrolyte in nature[19].

Table I. Physical, spectral and analytical data of the ligands.

| Ligand/Mol. formula | M.P (°C) | IR ($cm^{-1}$) | Calc (found) % CH | H | N | Yield (%) |
|---|---|---|---|---|---|---|
| **L**$^1$ $C_{16}H_{20}FeN_6S_2$ | 177 | 3325 ($NH_2$), 1620 (C=N), 825 (C=S). | 46.2 (46.5), | 4.8 (5.1), | 20.2 (20.5) | 62 |
| **L**$^2$ $C_{16}H_{20}FeN_6O_2$ | 195 | 3325 ($NH_2$), 1735 (C=O), 1620 (C=N). | 50.0 (50.4), | 5.2 (5.6), | 21.9 (21.5) | 61 |
| **L**$^3$ $C_{16}H_{22}FeN_8S_2$ | 185 | 3325 ($NH_2$), 1620 (C=N), 1465 (N–NH), 825 (C=S). | 43.1 (43.5), | 4.9 (4.6), | 25.1 (25.5) | 60 |
| **L**$^4$ $C_{16}H_{22}FeN_8O_2$ | 198 | 3325 ($NH_2$), 1465 (N–NH), 1735 (C=O), 1620 (C=N). | 46.4 (46.1), | 5.3 (5.8), | 7.1 (27.3) | 63 |

Table II. $^{1}$H NMR and $^{13}$C NMR data of the ligands and Zn(II) complexes (**13**–**16**)

| No | $^{1}$H NMR (DMSO-$d_6$)(ppm) | $^{13}$C NMR (DMSO-$d_6$)(ppm) |
|---|---|---|
| $\mathbf{L}^1$ | 2.5 (s, 6H, $CH_3$), 4.3–4.4 (m, 2H, ferrocenyl), 4.6–4.7 (m, 2H, ferrocenyl), 4.8–4.9 (m, 2H, ferrocenyl), 5.0–5.1 (m, 2H, ferrocenyl), 8.2 (s, 4H, $NH_2$), 9.9 (s, 2H, NH). | 15.7 (*C*$H_3$), 68.6, 69.6, 83.6 (ferrocenyl-*C*), 150.6 (*C*-═N), 177.9 (*C*═S). |
| $\mathbf{L}^2$ | 2.5 (s, 6H, $CH_3$), 4.3–4.4 (m, 2H, ferrocenyl), 4.6–4.7 (m, 2H, ferrocenyl), 4.8–4.9 (m, 2H, ferrocenyl), 5.0–5.1 (m, 2H, ferrocenyl), 8.3 (s, 4H, $NH_2$), 10.1 (s, 2H, NH). | 15.7 (*C*$H_3$), 68.6, 69.6, 83.6 (ferrocenyl-*C*), 150.7 (*C*═N), 205.4 (*C*═O). |
| $\mathbf{L}^3$ | 2.4 (s, 6H, $CH_3$), 4.2–4.3 (m, 2H, ferrocenyl), 4.5–4.6 (m, 2H, ferrocenyl), 4.7–4.8 (m, 2H, ferrocenyl), 4.8–4.9 (m, 2H, ferrocenyl), 8.1 (s, 4H, $NH_2$), 10.2 (s, 2H, NH). | 15.7 (*C*$H_3$), 68.6, 69.6, 83.6 (ferrocenyl-*C*), 150.7 (*C*═N), 177.8 (*C*═S). |
| $\mathbf{L}^4$ | 2.4 (s, 6H, $CH_3$), 4.2–4.3 (m, 2H, ferrocenyl), 4.5–4.6 (m, 2H, ferrocenyl), 4.7–4.8 (m, 2H, ferrocenyl), 4.8–4.9 (m, 2H, ferrocenyl), 8.1 (s, 4H, $NH_2$), 9.9 (s, 2H, NH), 10.2 (s, 2H, NH). | 15.7 (*C*$H_3$), 68.6, 69.6, 83.6 (ferrocenyl-*C*), 150.8 (*C*═N), 205.2 (*C*═O). |
| **13** | 2.7 (s, 6H, $CH_3$), 4.5–4.7 (m, 2H, ferrocenyl), 4.7–4.9 (m, 2H, ferrocenyl), 4.9–5.1 (m, 2H, ferrocenyl), 5.1–5.2 (m, 2H, ferrocenyl), 8.4 (s, 4H, $NH_2$), 10.3 (s, 2H, NH). | 15.9 (*C*$H_3$), 68.6, 69.6, 83.8 (ferrocenyl-*C*), 150.8 (*C*-═N), 178.1 (*C*═S). |
| **14** | 2.6 (s, 6H, $CH_3$), 4.4–4.6 (m, 2H, ferrocenyl), 4.6–4.8 (m, 2H, ferrocenyl), 4.9–5.0 (m, 2H, ferrocenyl), 5.2–5.3 (m, 2H, ferrocenyl), 8.5 (s, 4H, $NH_2$), 10.4 (s, 2H, NH). | 15.9 (*C*$H_3$), 68.6, 69.6, 83.8 (ferrocenyl-*C*), 150.9 (*C*═N), 205.5 (*C*═O). |
| **15** | 2.5 (s, 6H, $CH_3$), 4.3–4.5 (m, 2H, ferrocenyl), 4.6–4.7 (m, 2H, ferrocenyl), 4.8–4.9 (m, 2H, ferrocenyl), 5.0–5.2 (m, 2H, ferrocenyl), 8.3 (s, 4H, $NH_2$), 10.3 (s, 2H, NH). | 15.9 (*C*$H_3$), 68.6, 69.7, 83.7 (ferrocenyl-*C*), 150.8 (*C*═N), 177.9 (*C*═S). |
| **16** | 2.5 (s, 6H, $CH_3$), 4.4–4.5 (m, 2H, ferrocenyl), 4.7–4.8 (m, 2H, ferrocenyl), 4.9–5.0 (m, 2H, ferrocenyl), 4.9–5.1 (m, 2H, ferrocenyl), 8.4 (s, 4H, $NH_2$), 10.4 (s, 2H, NH). | 15.9 (*C*$H_3$), 68.6, 69.7, 83.7 (ferrocenyl-*C*), 150.9 (*C*═N), 205.4 (*C*═O). |



The elemental analyses data agree well with the proposed formulae for the ligands (Figure 1) and also confirmed the $[M(L)_2Cl_2]$ composition for the cobalt (II), nickel (II) and zinc (II) complexes in an octahedral environment, and $[M(L)_2]Cl_2$ for the copper (II) complexes as square-planar. Microcrystalline powders of these compounds could only be obtained, making it impossible for X-ray structural determinations. In fact this is the usual technical problem related to the thorough characterization of these types of metal complexes.

*IR spectra*

IR frequencies of the ligands and their complexes are reported in Tables I and III. The IR spectrum of the ligands is almost identical in the region 670–1550 cm$^{-1}$ to those of its metal complexes. The ligands, ($\mathbf{L}^1$–$\mathbf{L}^4$) showed the absence of a band at ~1715 cm$^{-1}$ due to the characteristic carbonyl $\nu$(C═O) stretching vibration of the respective starting acetylferrocene. Instead, the appearance of a new band at 1620 cm$^{-1}$ assigned to the $\nu$(C═N) linkage suggested[20,21] condensation and formation of the proposed ligands. The shifting of this band to the lower frequency side (10–15 cm$^{-1}$) provided further evidence in support of the involvement of this nitrogen in coordination to the metal atoms. Furthermore, a characteristic band at 3325 cm$^{-1}$ due to $\nu(NH_2)$ in the spectra of all the ligands moved to higher frequency at 3295 cm$^{-1}$ suggesting coordination of a $NH_2$ moiety with the metal ions. A band due to $\nu$ (N—NH) at 1465 cm$^{-1}$ in all the ligands, in turn, moved to a lower frequency at 1450 cm$^{-1}$ in the spectra of the metal complexes suggesting coordination of the *N*—NH group with the metal atom. The bands, at 825 and

Table III. Physical, analytical and spectral data of the metal complexes

| Complex/Mol. formula | M.P (°C) | IR ($cm^{-1}$) | $\lambda_{max}$ ($cm^{-1}$) | B.M ($\mu_{eff}$) | Calc (found) % | | |
|---|---|---|---|---|---|---|---|
| | | | | | C | H | N |
| (**1**) $[Co(L^1)Cl_2]$ $C_{16}H_{20}FeCoCl_2N_6S_2$ | 205–207 | 3295 ($NH_2$), 1605 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 8,440, 17,315, 20,410, 29,980. | 4.6 | 35.2 (35.5) | 3.7 (3.3) | 15.4 (15.6) |
| (**2**) $[Co(L^2)Cl_2]$ $C_{16}H_{20}FeCoCl_2N_6O_2$ | 205–207 | 3295 ($NH_2$), 1610 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 8,260, 17,565, 20,525, 30115. | 4.6 | 37.4 (37.7) | 3.9 (3.5) | 16.4 (16.1) |
| (**3**) $[Co(L^3)_2Cl_2]$ $C_{16}H_{22}FeCoCl_2N_8S_2$ | 195–197 | 3295 ($NH_2$), 1605 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 8,315, 17,380, 20,465, 29,995. | 4.7 | 33.3 (33.5) | 3.8 (3.4) | 19.5 (19.7) |
| (**4**) $[Co(L^4)Cl_2]$ $C_{16}H_{22}FeCoCl_2N_8O_2$ | 202–204 | 3295 ($NH_2$), 1605 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 8,280, 17,415, 20,515, 30,010. | 4.5 | 35.3 (35.7) | 4.0 (4.4) | 20.6 (20.2) |
| (**5**) $[Cu(L^1)]Cl_2$ $C_{16}H_{20}FeCuCl_2N_6S_2$ | 210–212 | 3295 ($NH_2$), 1610 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 19,475, 15,260, 22,125, 30,235. | 1.6 | 34.9 (34.5) | 3.6 (3.3) | 15.3 (15.6) |
| (**6**) $[Cu(L^2)]Cl_2$ $C_{16}H_{20}FeCuCl_2N_6O_2$ | 210–212 | 3295 ($NH_2$), 1610 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 19,590, 15,385, 22,125, 30,315. | 1.7 | 37.0 (37.3) | 3.9 (4.2) | 16.2 (16.5) |
| (**7**) $[Cu(L^3)]Cl_2$ $C_{16}H_{22}FeCuCl_2N_8S_2$ | 208–210 | 3295 ($NH_2$), 1605 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 19,485, 15,330, 22,100, 30,270. | 1.5 | 33.1 (33.5) | 3.8 (3.9) | 19.3 (19.5) |
| (**8**) $[Cu(L^4)]Cl_2$ $C_{16}H_{22}FeCuCl_2N_8O_2$ | 206–208 | 3295 ($NH_2$), 1605 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 19,525, 15,285, 22,115, 30,295 | 1.5 | 35.0 (35.4) | 4.0 (3.8) | 20.4 (20.8) |
| (**9**) $[Ni(L^1)Cl_2]$ $C_{16}H_{20}FeNiCl_2N_6S_2$ | 212–214 | 3295 ($NH_2$), 1610 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 10,250, 16,315, 22,415, 29,565. | 3.5 | 35.2 (35.6) | 3.7 (3.4) | 15.4 (15.1) |
| (**10**) $[Ni(L^2)Cl_2]$ $C_{16}H_{20}FeNiCl_2N_6O_2$ | 212–214 | 3295 ($NH_2$), 1610 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 10,395, 16,380, 22,415, 29,565. | 3.4 | 37.2 (37.5) | 3.9 (3.4) | 16.4 (16.7) |
| (**11**) $[Ni(L^3)Cl_2]$ $C_{16}H_{22}FeNiCl_2N_8S_2$ | 202–204 | 3295 ($NH_2$), 1610 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 10,285, 16,365, 22,405, 29,565. | 3.4 | 33.4 (33.8) | 3.8 (3.5) | 19.5 (19.7) |
| (**12**) $[Ni(L^4)Cl_2]$ $C_{16}H_{22}FeNiCl_2N_8O_2$ | 206–28 | 3295 ($NH_2$), 1605 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 10,360, 15,545, 22,425, 29,565. | 3.6 | 35.3 (35.5) | 4.0 (4.3) | 20.6 (20.3) |
| (**13**) $[Zn(L^1)Cl_2]$ $C_{16}H_{20}FeZnCl_2N_6S_2$ | 212–214 | 3295 ($NH_2$), 1605 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 22,415, 28,870 | Dia | 34.8 (34.5) | 3.6 (3.9) | 15.2 (15.4) |
| (**14**) $[Zn(L^2)Cl_2]$ $C_{16}H_{20}FeZnCl_2N_6O_2$ | 212–214 | 3295 ($NH_2$), 1605 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 22,415, 28,870 | Dia | 36.9 (36.5) | 3.8 (3,6) | 16.1 (16.4) |
| (**15**) $[Zn(L^3)Cl_2]$ $C_{16}H_{22}FeZnCl_2N_8S_2$ | 197–198 | 3295 ($NH_2$), 1610 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 22,415, 28,255 | Dia | 33.0 (33.3) | 3.8 (3.5) | 19.2 (19.5) |
| (**16**) $[Zn(L^4)Cl_2]$ $C_{16}H_{22}FeZnCl_2N_8O_2$ | 205–207 | 3295 ($NH_2$), 1610 (C=N), 1450 (N—NH), 390 (M—N), 310 (M—Cl) | 22,415, 29,115 | Dia | 34.9 (34.6) | 4.0 (3.8) | 20.4 (20.7) |

1735 $cm^{-1}$ assigned to $\nu$ (C═S) and $\nu$ (C═O) in the ligands remained unchanged in the spectra of the metal complexes (data not shown) suggesting that these are not involved in the coordination. Moreover, in the far infrared region the band at ~390 $cm^{-1}$ attributed to $\nu$ (M—N) was observed for all the complexes (Table III), which was not found in the spectra of the free ligands. It, however, suggested coordination of the $\nu$ N—M to the metal atoms[22,23]. All these data suggest an octahedral geometry for the Co(II), Ni(II) and Zn(II) complexes prepared here, whereas the Cu(II) complexes may be either octahedral or square planar (Figure 2).

### *$^1$H NMR and $^{13}$C NMR spectra*

The $^1$H NMR and $^{13}$C NMR spectra of the free ligands and their metal (II) chelates were determined in DMSO-$d_6$. The $^1$H NMR spectra of all the ligands show a single series of strong signals, suggesting 1,1′ disubstitution on cyclopentadienyl moieties of the ferrocenyl group[24,25]. The data reported along with the possible assignments in Table II show that the free ligands display all the expected signals at δ 2.4, 4.2–5.1, 8.1–8.3 and 9.8–10.1 ppm assigned to $CH_3$, ferrocenyl, $NH_2$ and NH respectively. In the spectra of their diamagnetic Zn(II) complexes (**13**–**16**) these protons shifted downfield by 0.1–0.3 ppm due to the increased conjugation and extension of the delocalized π-system of the thiosemicarbazine, semicarbazine, thiocarbohydrazine and carbohydrazine chains into the cyclopentadienyl ring system.

The number of protons calculated from the integration curves, and those obtained from the values of the expected CHN analyses are in agreement. In the $^{13}$C NMR spectra, the ligands display signals assigned to —*C*$H_3$, ferrocenyl, *C*═N, and *C*═S/*C*═O carbons, respectively. These signals appear downfield in comparison with the corresponding signals of the ligand indicating coordination with the central metal atom. It was observed that DMSO did not have any coordinating effect on the spectra of the ligands or on its metal complexes (as evidenced by measuring some of the spectra in $CDCl_3$—data not shown).

### *Magnetic moments and electronic spectra*

The nature of the ligand field around the metal ion and the geometry of the metal complexes have been deduced from the electronic spectra and magnetic moment data of the complexes (Table III). The room temperature magnetic moment of the solid cobalt (II) complexes was found in the range (4.5–4.7 B.M), indicative[26] of three unpaired electrons per Co(II) ion in an octahedral environment. The magnetic moment of the Cu(II) complexes was found to be in the range (1.5–1.7 B.M), consistent for square-planar geometry. The nickel (II) complexes showed $\mu_{eff}$ values (3.4–3.6 B.M), corresponding[27] to two unpaired electrons per Ni (II) ion for their six-coordinated configuration.

The electronic spectra of the Co(II) complexes showed three bands observed at 8,260–8,440, 17,315–17,565, 20,410–20,525 and 29,980–30,115 $cm^{-1}$ which may be assigned to $^4T_{1g} \rightarrow {}^4T_{2g}(F)$, $^4T_{1g} \rightarrow {}^3A_{2g}(F)$ and $^4T_{1g} \rightarrow {}^4T_{1g}(P)$ transitions respectively and are suggestive[28] of the octahedral geometry around the cobalt ions. The high energy band at 29,980–30,115 $cm^{-1}$ is assigned to metal → ligand charge transfer band. The electronic spectra of the Cu (II) complexes showed two low-energy weak bands at 15,260–15,385, 19,475–19,590 $cm^{-1}$ and a strong high-energy band at 30,235–30,315 $cm^{-1}$. The low-energy bands in this region are typically expected for its square-planar configuration and may be assigned to $^2B_{1g} \rightarrow {}^2A_{1g}$ and $^2B_{1g} \rightarrow {}^2E_g$ transitions, respectively. The strong high-energy band in turn, is assigned to a metal → ligand charge transfer. The Ni(II) complexes exhibited three spin-allowed bands at 10,250–10,395, 16,315–16,380, and 29,275–29,365 $cm^{-1}$ assignable[29] respectively, to the transitions $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F) \times (\nu_1)$, $^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)(\nu_2)$ and $^3A_{2g}(F) \rightarrow {}^3T_{2g}(P) \times (\nu_3)$ which were characteristic of their octahedral geometry. The electronic spectra of the Zn(II) complexes showed a high intensity band at 29,210–29,285 $cm^{-1}$ due to ligand → metal charge transfer in a distorted octahedral environment[30].

On the basis of the above observations, it is suggested that the ligands act tetradentately via coordination through two nitrogens $\nu$ (C═N) of azomethine and two nitrogens of $\nu$ ($NH_2$) moieties. In all the ligands, coordination takes place via two nitrogens $\nu$ (C═N) of azomethine and two nitrogens of $NH_2$ moieties. The Co (II), Ni (II) and Zn (II) complexes showed an octahedral geometry via coordination through the two chlorides and the Cu (II) complexes a square-planar geometry without the coordination of two chlorides.

### *Biological activity*

The antibacterial and antifungal activity results presented in Tables IV and V, show clearly that all the newly synthesized compounds ($\mathbf{L}^1$–$\mathbf{L}^4$) and their metal complexes (**1**–**16**) containing Co(II), Cu(II), Ni(II) and Zn(II) possess good biological activity. New derivatives were screened for their antibacterial activity against *E. coli*, *B. subtillis*, *S. aureus*, *P. aeruginosa* and *S. typhi* and for antifungal activity against *T. longifusus*, *C. albicans*, *A. flavus*, *M. canis*, *F. solani* and *C. glaberata* which exhibited a markedly enhancement of activity on further coordination with the metal ions against all the test bacterial/fungal strains. The compounds generally showed good

Table IV. Antibacterial activity data for compounds $\mathbf{L}^1$–$\mathbf{L}^4$ and **1**–**16**

| Compound | Diameter of zones showing complete inhibition of growth (mm)* | | | | |
|---|---|---|---|---|---|
| | *E. coli* | *P. aeruginosa* | *B. subtillis* | *S. aureus* | *S. typhi* |
| $\mathbf{L}^1$ | 10 | 12 | 9 | 9 | 10 |
| $\mathbf{L}^2$ | 9 | 11 | 10 | 9 | 11 |
| $\mathbf{L}^3$ | 10 | 13 | 7 | 8 | 10 |
| $\mathbf{L}^4$ | 11 | 12 | 8 | 10 | 10 |
| **1** | 14 | 15 | 10 | 12 | 12 |
| **2** | 12 | 16 | 12 | 10 | 14 |
| **3** | 13 | 14 | 11 | 13 | 12 |
| **4** | 14 | 15 | 12 | 14 | 13 |
| **5** | 14 | 14 | 12 | 12 | 14 |
| **6** | 15 | 14 | 11 | 12 | 12 |
| **7** | 16 | 14 | 11 | 10 | 12 |
| **8** | 15 | 16 | 13 | 10 | 12 |
| **9** | 12 | 17 | 14 | 12 | 12 |
| **10** | 15 | 12 | 12 | 13 | 12 |
| **11** | 16 | 14 | 13 | 12 | 13 |
| **12** | 15 | 14 | 14 | 13 | 13 |
| **13** | 13 | 13 | 15 | 12 | 11 |
| **14** | 14 | 14 | 14 | 11 | 12 |
| **15** | 15 | 15 | 13 | 12 | 13 |
| **16** | 17 | 16 | 13 | 12 | 14 |
| Imipenum | 20 | 18 | 19 | 20 | 20 |

* 14–20 mm = significant activity; 7–13 mm = moderate activity; < 7 mm = weak activity.

antibacterial activity but, more significant antifungal activity was observed against most of the strains. It was evident from this data that activity of these synthesized complexes was increased by coordination of the metal ion. Generally, chelation/coordination reduces the polarity of the metal ion by partial sharing of its positive charge with the donor groups and possibly the π-electron delocalization within the whole chelate ring. This process thus increases the lipophilic nature of the compound, which in turn, favors penetration through the bacterial wall of microorganism, killing them more effectively[31–35].

Table V. Antifungal activity data for the compounds $\mathbf{L}^1$–$\mathbf{L}^4$ and **1**–**16**

| Compound | Diameter of zones showing complete inhibition of growth (mm)* | | | | | |
|---|---|---|---|---|---|---|
| | *T. longifusus* | *C. albicans* | *A. flavus* | *M. canis* | *F. solani* | *C. glaberata* |
| $\mathbf{L}^1$ | 18 | 12 | 18 | 22 | 20 | 20 |
| $\mathbf{L}^2$ | 15 | 12 | 20 | 20 | 20 | 15 |
| $\mathbf{L}^3$ | 16 | 11 | 20 | 21 | 18 | 15 |
| $\mathbf{L}^4$ | 12 | 12 | 21 | 23 | 20 | 13 |
| **1** | 22 | 15 | 24 | 24 | 22 | 21 |
| **2** | 24 | 14 | 27 | 23 | 23 | 21 |
| **3** | 25 | 18 | 24 | 25 | 21 | 22 |
| **4** | 23 | 15 | 27 | 24 | 20 | 20 |
| **5** | 25 | 17 | 27 | 23 | 25 | 24 |
| **6** | 24 | 16 | 28 | 24 | 26 | 22 |
| **7** | 22 | 15 | 27 | 23 | 27 | 24 |
| **8** | 27 | 14 | 26 | 23 | 28 | 23 |
| **9** | 27 | 15 | 28 | 24 | 26 | 25 |
| **10** | 25 | 14 | 27 | 26 | 25 | 24 |
| **11** | 25 | 13 | 28 | 25 | 24 | 20 |
| **12** | 28 | 15 | 25 | 24 | 24 | 23 |
| **13** | 27 | 16 | 27 | 23 | 26 | 24 |
| **14** | 23 | 18 | 26 | 26 | 23 | 25 |
| **15** | 25 | 14 | 27 | 25 | 26 | 23 |
| **16** | 26 | 15 | 26 | 24 | 25 | 26 |
| Miconazole | 30 | 30 | 29 | 28 | 30 | 27 |
| Amphotericin | B 28 | 28 | 29 | 27 | 28 | 28 |

* 14–30 mm = significant activity; 7–13 mm = moderate activity; <7 mm = weak activity.

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