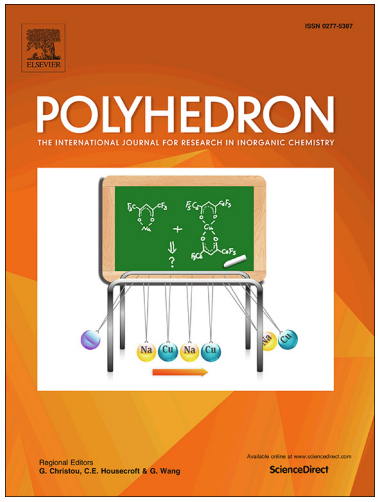

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Synthesis and structural studies of nickel(II)- and copper(II)-N,N'-diarylformamidine dithiocarbamate complexes as antimicrobial and antioxidant agents

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ABSTRACT

A series of six N'N-diarylformamidine dithiocarbamate ligands and their metal complexes of Cu(II) and Ni(II) chloride salts have been synthesized. Three symmetrical, N,N'-bis(2,6-dimethylphenyl)formamidine dithiocarbamate (**DL1**), N,N'-bis(2,6-disopropylphenyl) formamidine dithiocarbamate (**DL2**), N,N'-mesityl formamidine dithiocarbamate (**DL3**) and three unsymmetrical N'-(2,6-dichlorophenyl-N-(2,6-dimethylphenyl) formamidine dithiocarbamate (**DL4**), N'-(2,6-dichlorophenyl)-N-(2,6-diisopropylphenyl) formamidine dithiocarbamate (**DL5**) and N'-(2,6-dichlorophenyl)-N-mesityl formamidine dithiocarbamate (**DL6**) dithiocarbamate ligands were reacted with $CuCl_2$ and $NiCl_2$ to give [Ni-(**DL1**)$_2$] (**1**), [Ni-(**DL2**)$_2$].H_2O (**2**), [Ni-(**DL3**)$_2$] (**3**), [Ni-(**DL4**)$_2$].$3H_2O$ (**4**), [Ni-(**DL5**)$_2$].H_2O (**5**), [Ni-(**DL6**)$_2$] (**6**), [Cu-(**DL1**)$_2$].$3H_2O$ (**7**), [Cu-(**DL2**)$_2$] (**8**), [Cu-(**DL3**)$_2$].$2H_2O$ (**9**), [Cu-(**DL4**)$_2$].$3H_2O$ (**10**), [Cu-(**DL5**)$_2$].$3H_2O$ (**11**) and [Cu-(**DL6**)$_2$] (**12**). All ligands and the complexes were characterized using FT-IR, UV-vis, ^1H and ^{13}C NMR, mass spectrometry and by elemental analysis. In addition, the structures of complexes **1**, **5**, **8** and **11** were confirmed by single crystal X-ray diffraction analysis as mononuclear neutral species in which the geometry around the metal centers is distorted square planar. In this coordination manner, the metal centers bound to four sulfur atoms from two dithiocarbamate ligand in a bidentate fashion. All complexes showed moderate to good antibacterial activities against Gram-negative, *Salmonella typhimurium*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Klebsiella*

pneumoniae and gram-positive, *Staphylococcus aureus* (methicillin resistant) and *Staphylococcus aureus* bacteria. Complexes **4** and **5** were found to be more active than ciprofloxacin against *E. coli* and *K. pneumoniae*. In addition, complexes with chloro substituted ligands displayed higher activities. Antioxidant activities of complexes with symmetrical formamidine ligands were generally high compared to the ones with the unsymmetrical formamidine moeities, with **2** having an IC_{50} value of 1.10 x 10^{-3} mM and **12** had 2.91 mM.

Keywords: N,N'-diarylformamidine; Dithiocarbamates; Metal complexes; Antioxidant; Antibacterial

1.0 INTRODUCTION

The increase in the number of multi-drug resistant microbial pathogens and the emergence of new ones has made treatment of infectious diseases a challenge in the last decade [1]. Development of new drugs endowed with excellent antimicrobial activities, and whose mechanism of action is distinct from those of well-known antimicrobial agents to which relevant pathogens are now resistant to is very important [2]. Due to the presence of multiple intrinsic and acquired mechanism of antimicrobial resistance, controlling the spread of deadly microbes in various healthcare settings is getting difficult [3] and for this reason, research on new drugs that can kill drug resistant bacteria is on the increase. Of importance is also research on antioxidant activity of synthetic and natural compounds. This is because of the health benefits that antioxidants have in protecting organisms and cells from damage induced by oxidative stress [4]. Oxidative stress is caused by the presence of reactive oxygen species (ROS) such as superoxide radical anion ($O_2^{\bullet-}$), hydroxyl radical ($OH^{\bullet}$), and hydrogen peroxide (H_2O_2) often formed by the partial reduction of dioxygen (O_2) species [5]. Of the damage caused by ROS in the body is normally to proteins, lipids and DNA thereby accelerating ageing, causing cancerous inflammations and, also cardiovascular and neurodegenerative diseases [5].Various methods of analysis have been adopted to study antioxidant activity. For example, for *in vitro* antioxidant test, the scavenging activity of DPPH (2,2-diphenyl-1-picrylhydrazyl) assay as a stable free radical is often used for both natural and synthetic compounds [6].

Dithiocarbamates and their metal complexes have been tested as anticancer [7, 8], antimicrobial [9, 10], and as antioxidant agents [11, 12]. Dithiocarbamates are often synthesized by the reaction of either primary or secondary amines with carbon disulfide in the presence of a base, while their metal complexes are prepared via simple ligand displacement reactions following the addition of the dithiocarbamate salt to a metal precursor in the

appropriate ratio [13-15]. The electronic properties, structural architectures and applications are influenced by the easily electronically tunable amines used in their synthesis [16].

Biological studies of Ni(II) and Cu(II) dithiocarbamate complexes have been reported but not in much detail [8, 17-19]. Mamba *et al.* [9] reported the *in vitro* antimicrobial studies of cyclohexylamine-N-dithiocarbamate transition metal complexes and their research showed that the antimicrobial activity of the free ligand was enhanced upon chelation with metal ions. Their study showed that Ni(II) complexes displayed antimicrobial activity against *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Antibacterial activities of 2-amino pyridine dithiocarbamate ligand and its Cu(II) and Co(II) complexes was also reported by Gopal *et al*. [20]. Their study showed that the complexes moderately inhibited the growth of *Escherichia coli*, *S aureus* and *Bacillus subtilis* and the Cu(II) complex showed better activity as compared to the Co(II) complex. Recently, Onwudiwe *et al*. [11] reported the antioxidant activity of sodium N-ethyl-N-phenyldithiocarbamate and its Cu(II) complexes. Their results showed that the complex had scavenging activity of 75 % at 500 µg/ml relatively to the ligand which has 42 % at the same concentration. Herein, we report the synthesis, characterization, antioxidant and antimicrobial studies of symmetrical and unsymmetrical Ni(II) and Cu(II) N,N'-diarylformamidine dithiocarbamate complexes. All compounds were characterized by UV-Visible, FT-IR, Mass and NMR spectrometry and single crystal X-ray structures of two of the Cu(II) and two of the Ni(II) complexes. The antimicrobial potentials of the metal complexes were evaluated against Gram-negative bacteria strains {*E coli*, *S. typhimurium P. aeruginosa* and K *pneumoniae* and Gram-positive bacteria strains {MRSA and *S. aureus*}.

2.0 Experimental section

2.1 Materials

All solvents (ACS reagent grades ≥ 99.5 %) were obtained from Sigma-Aldrich and used as obtained without further purification. Reagents: 2,6-diisopropylaniline (97%), 2,6-dimethylaniline (99 %), 2,4,6-trimethylaniline (98 %), 2,6-dichloroaniline (98 %), triethyl orthoformate (99 %) and carbon disulfide were also obtained from Sigma Aldrich. Metal salts: $CuCl_2.\ 2H_2O$ (97 %), $NiCl_2.\ 6H_2O$ (98 %) and KOH (85 %) were obtained from Promark Chemicals South Africa.

2.2 Instrumentation

^{1}H and ^{13}C NMR spectra were recorded at 25 °C on a Bruker Avance^{III} 400 MHz spectrometer. Both ^{1}H NMR and ^{13}C NMR data were recorded in either $CDCl_3$ referenced to the residual $CDCl_3$ peaks at δ 7.26 and δ 77.00 ppm or $(CD_3)_2SO$ (DMSO) referenced to the residual $(CD_3)_2SO$ peaks at δ 2.50 and δ 39.52 ppm respectively. Elemental analyses were recorded on a Vario elemental EL cube CHNS analyzer. IR spectra were obtained on a PerkinElmer Universal ATR spectrum 100 FT-IR spectrometer. Mass spectra of complexes were obtained from a Water synaptic GR electrospray positive spectrometer and UV-Vis absorption spectra was recorded on Shimadzu UV-vis-NIR spectrophotometer.

3.0 General methods of synthesis

3.1 Synthesis of symmetrical formamidine ligand (secondary amine)

N,N'-bis(2,6-dimethyphenyl)formamidine (L1), N,N'-bis(2,6-diisopropylphenyl)formamidine (L2) and N,N`-bis(2,4,6-trimethylphenyl)formamidine were synthesized following literature procedure with a slight modification [21]. Three or four drops of acetic acid were added to the reaction mixture in a round-bottom flask charged with the aniline (2 mole equivalents) and triethyl orthoformate (1 mole equivalent). The reaction mixture was heated under reflux and temperature maintained at 130-150 °C. After 3hr, the temperature was increased to 160 °C to remove all volatiles via distillation. The reaction was allowed to cool and the crude product was triturated with hexane and collected by gravity filtration. The solids obtained were recrystallized in 50 cm^3 of hot acetone and stored at 4 °C to yield the pure products.

3.2 Synthesis of unsymmetrical formamidine ligand (secondary amine)

Unsymmetrical formamidine were synthesized as follows: three or four drops of acetic acid were added to the reaction mixture containing aniline (30 mmol) and triethyl orthoformate (30 mmol) in a round-bottom flask. The mixture was refluxed at 140 °C for 30 min with stirring followed by distillation (2 mmol of EtOH collected). The second aniline (30 mmol) was then added to the reaction mixture and heating continued until 1 mmol of ethanol was collected. Upon cooling to 25 °C, the solution solidified. The crude product was triturated with cold hexane and collected by filtration. Solids were then washed with 50 cm^3 of acetone to completely remove traces of symmetrical formamidine by-products that were formed during

the reaction to afford N-(2,6-dichlorophenyl)-N-(2,6-dimethylphenyl)formamidine, (L4), N-(2,6-dichlorophenyl)-N-(2,6-dimethylphenyl)formamidine (L5) and N-(2,6-dichlorophenyl)-N-mesitylformamidine (L6).

3.3 Synthesis of N,N'-diarylformamidine dithiocarbamates

An equimolar ratio of the formamidines and KOH in 20 ml of acetonitrile was stirred for 20 min in a cold mixture of ice at 0–5 °C. to form a white color solution. To the resulting solution, carbon disulfide of the same molar ratio was added drop-wise and stirring continued for 3hr in an ice bath and another one hour at room temperature to give a yellow solution. The solvent was removed using rotary evaporator and a yellow crude solid product was obtained. The crude product was rinsed with ethanol three times to remove unreacted formamidine to give a pure yellow solid product and stored in a desiccator.

3.3.1 Synthesis of DL1

The reaction of L1 (1.00 g, 4 mmol), KOH (0.22 g, 4 mmol) and CS_2 (0.24 ml, 4 mmol) in 20 ml of acetonitrile furnished dithiocarbamate ligand **DL1** as a yellow powder. Yield 87 %. Decomposition tempt. range, 237 – 242 °C. ^{1}H NMR (DMSO, 400 MHz): δ (ppm) 1.90 (s, 6H, CH_3-Ar), 1.99 (s, 6H, CH_3-Ar), 6.91 (s, 3H, Ar-H), 6.85 (d, 2H, J_{HH} = 7.48 Hz, Ar-H), 6.70 (t, 1H, J_{HH} = 7.48 Hz, Ar-H) 9.86 (s, 1H, -CH=N) . ^{13}C NMR (DMSO, 100 MHz) δ (ppm) 16.7, 17.3, 116.9, 121.0, 124.9, 126.0, 126.4, 126.5, 126.6, 134.1, 140.9, 148.3, 151.5, 217.62. IR υ (cm^{-1}) 2918(w), 1640(s), 1467(s), 1000(s), 921(w). UV-Vis ($CHCl_3$, λ_{max}, nm), 292, 340. Anal. calcd. for $C_{18}H_{22}KN_2OS_2$: C, 56.21; H, 5.50; N, 7.28; S, 16.67. Found: C, 56.06; H, 5.75; N, 7.22; S, 16.20.

3.3.2 Synthesis of DL2

The reaction of L2 (1.46 g, 4 mmol), KOH (0.22 g, 4 mmol) and CS_2 (0.16 mL, 4 mmol) in 20 ml of acetonitrile furnished dithiocarbamate ligand **DL2** as a yellow powder. Yield 74.18 %. Decomposition tempt. range, 244 – 249 °C. ^{1}H NMR (DMSO, 400 MHz) : δ (ppm) 1.06 (d, 12H, J_{HH} = 6.88 Hz, -CH_3-CH-), 2.84 (m, 2H, J_{HH} = 6.72 Hz, CH-CH_3), 2.97 (m, 2H, J_{HH} = 6.84 Hz, CH-CH_3), 6.94 (t, 1H, J_{HH} = 6.76 Hz, Ar-H), 7.02 (d, 2H, J_{HH} = 7.12 Hz, Ar-H), 7.11 (d, 2H, J_{HH} = 7.5 Hz, Ar-H), 7.21 (t, 1H, J_{HH} = 7.00 Hz, Ar-H), 10.15 (s, 1H, -CH=N). ^{13}C NMR (DMSO, 100 MHz) δ (ppm): 23.80, 24.00, 24.86, 26.58, 28.24, 122.47, 122.86, 127.08, 138.61, 138.87, 145.23, 147.49, 154.21, 220.94. IR υ (cm^{-1}) :2959(s), 2865(w) 1639(s),

1452(s), 1152(s), 999(s). UV-Vis ($CHCl_3$, λ_{max}, nm), 293, 339. Anal. calcd. for $C_{26}H_{35}KN_2S_2$: C, 66.08; H, 7.69; N, 5.85; S, 13.39. Found: C, 65.92; H, 7.37; N, 5.85; S, 12.20.

3.3.3 Synthesis of DL3

The reaction of L3 (1.12 g, 4 mmol), KOH (0.22 g, 4 mmol) and CS_2 (0.21 mL, 4 mmol) in 20 ml of acetonitrile furnished dithiocarbamate ligand **DL3** as a yellow powder. Yield 93.63%. Decomposition tempt. range, 258 – 263 °C. ^{1}H NMR (DMSO, 400 MHz) δ (ppm) 1.94 (s, 6H, CH_3-Ar), 2.03 (s, 6H, CH_3-Ar), 2.15 (s, 3H, CH_3-Ar), 2.22 (s, 3H, CH_3-Ar) 6.75 (s, 2H, Ar-H), 6.81 (s, 2H, Ar-H), 9.92 (s, 1H, CH=N). ^{13}C NMR (DMSO, 100 MHz) δ (ppm): 13.92, 17.70, 18.32, 20.29, 20.58, 127.26, 127.90, 128.30, 130.51, 134.82, 139.55, 147.10, 152.79, 218.95. IR υ (cm^{-1}) 2951 (m), 1629(s), 1477(m), 1023(s), 956(w). UV-Vis ($CHCl_3$, λ_{max}, nm), 289, 338. Anal. calcd for $C_{20}H_{23}KN_2S_2$: C, 60.87; H, 5.87; N, 7.10; S, 16.25. Found: C, 60.41; H, 5.93; N, 6.95; S, 15.97.

3.3.4 Synthesis of DL4

The reaction of L4 (1.17 g, 4 mmol), KOH (0.22 g, 4 mmol) and CS_2 (0.25 g, 4mmol) in 20 ml of acetonitrile furnished dithiocarbamate ligand **DL4** as a yellow powder. Yield 77 %. Decomposition tempt. range, 245 – 248 °C. ^{1}H NMR (DMSO, 400 MHz): δ (ppm): 2.13 (s, 6H, CH_3-Ar), 7.02 (s, 4H, Ar-H), 7.39 (d, 2H, J_{HH} = 8.08 Hz, Ar-H) 10.12 (s, 1H, -CH=N). ^{13}C NMR (DMSO, 100 MHz) δ (ppm): 17.76, 124.13, 126.37, 126.40, 127.26, 127.52, 127.73, 128.34, 135.23, 135.42, 141.29, 146.08, 154.81, 218.82. IR υ (cm^{-1}): 3177(w), 1614(s), 1432(s), 1128(s), 1033(s). UV-Vis ($CHCl_3$, λ_{max}, nm), 293, 345. Anal. calcd for $C_{16}Cl_2H_{15}KN_2OS_2$: C, 45.67; H, 3.95; N, 6.58; S, 15.20. Found: C, 45.52; H, 3.81; N, 6.29; S, 15.19.

3.3.5 Synthesis of DL5

The reaction of L5 (1.40 g, 4 mmol), KOH (0.22 g, 4 mmol) and CS_2 (0.21 g, 4 mmol) in 20ml of acetonitrile furnished dithiocarbamate ligand **DL5** as a yellow powder. Yield 91 %. Decomposition tempt. range, 250 – 260 °C. ^{1}H NMR (DMSO, 400 MHz): δ (ppm): 1.14 (t, 12H, J_{HH} = 7.28 Hz, CH_3-CH), 2.87 (m, 2H, J_{HH} = 6.76 Hz, CH-Ar), 6.98 (t, 1H, J_{HH} = 8.08 Hz, Ar-H), 7.10 (d, 2H, J_{HH} = 7.56 Hz, Ar-H), 7.21 (t, 1H, J_{HH} = 7.24 Hz, Ar-H), 7.38 (d, 2H, J_{HH} = 8.08 Hz, Ar-H) 10.39 (s, 1H, -CH=N-Ar). ^{13}C NMR (DMSO, 100 MHz) δ (ppm): 26.81, 27.75, 27.98, 132.87, 133.98, 137.90, 138.48, 145.31, 146.14, 146.33, 151.41, 156.87, 217.02.

IR υ (cm^{-1}): 2960 (w), 1603(s), 1430(s), 1145(s), 1036(s). UV-Vis ($CHCl_3$, λ_{max}, nm), 300, 345. Anal. calcd for $C_{20}Cl_2H_{27}KN_2O_3S_2$: C, 46.61; H, 5.62; N, 5.41; S, 12.63. Found: C, 46.53; H, 5.55; N, 5.05; S, 12.59.

3.3.6 Synthesis of DL6

The reaction of L6 (1.23 g, 4 mmol), KOH (0.22 g, 4 mmol) and CS_2 (0.24 g, 4 mmol) in 20 ml of acetonitrile furnished dithiocarbamate ligand **DL6** as a yellow powder. Yield 83 %. Decomposition tempt. range, 255 – 258 °C. ^{1}H NMR (DMSO, 400 MHz): δ (ppm): 2.07 (s, 6H, CH_3-Ar-N-), 2.23 (s, 3H, CH_3-Ar), 6.81 (s, 2H, Ar-H) 7.00 (t, 1H, J_{HH} = 8.4 Hz, Ar-H), 7.35 (d, 2H, J_{HH} = 8.04 Hz, Ar-H), 10.11 (s, 1H,CH=N-Ar). ^{13}C NMR (DMSO, 100 MHz) δ (ppm): 17.68, 20.59, 124.04, 126.34, 127.97, 128.32, 135.02, 135.12, 138.71, 146.17, 154.83, 219.04. IR υ (cm^{-1}) 2915(w), 1612(s), 1435(s), 1141(s), 1032(s). UV-Vis ($CHCl_3$, λ_{max}, nm), 295 343. Anal. calcd for $C_{17}Cl_2H_{17}KN_2OS_2$: C, 46.46; H, 3.90; N, 6.37; S, 14.59. Found: C, 46.29; H, 4.05; N, 6.33; S, 14.26.

3.4 Synthesis of N,N'-diarylformamidines dithiocarbamate metal complexes

The respective dithiocarbamate salts (2 mmol) were dissolved in 15 mL of acetonitrile. To the resulting mixture, (1 mmol) of the metal chloride salt dissolved in 10 ml of water was added drop-wise and stirred for about 30 min at room temperature. A sudden change in color was observed depending on the nature of the metal used and a precipitate was formed immediately. The product formed was collected by filtration. The Complexes were then recrystallized in hot ethanol at 80 °C to remove any unreacted ligand. The solid precipitate was then collected by filtration and dried in the oven at 50 °C.

3.4.1 Synthesis of [Ni-$(DL1)_2$] (1)

The reaction of DL1 (0.30 g, 0.8 mmol) and $NiCl_2.6H_2O$ (0.10 g 0.4 mmol) in acetonitrile furnished complex **1** as a purple-red powder. Yield 72 %. Decomposition temperature range, 265-267 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.09 (s, 12H, CH_3-Ar), 2.29 (s, 12H, CH_3-Ar), 6.91 (t, 2H, J_{HH} = 7.24 Hz, Ar-H), 7.00 (d, 5H, J_{HH} = 7.32 Hz, Ar-H), 7.19 (d, 5H, J_{HH} = 7.28 Hz, Ar-H), 8.85 (s, 2H, -CH=N) : ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 17.62, 18.64, 18.71, 124.32, 126.33, 127.61, 128.24, 128.85, 129.91, 133.96, 135.91, 145.04, 146.66, 216.95. IR υ (cm^{-1}): 2949(m), 1647(s), 1474(m), 1126(m), 999(m), 376(s). ESI-TOF MS: m/z (%);

$[M]^+$ 713.14. UV-Vis ($CHCl_3$, λ_{max}, nm), 262, 341, 457. Anal. calcd. for $C_{36}H_{40}N_4NiS_4$: C, 60.42; H, 5.63; N, 7.83; S, 17.92. Found: C, 60.28; H, 5.29; N, 7.71; S, 17.35

3.4.2 Synthesis of [Ni-(DL2)$_2$].H$_2$O (2)

The reaction of DL2 (0.3 g, 0.6 mmol) and $NiCl_2.6H_2O$ (0.07 g, 0.3 mmol) in acetonitrile furnished complex **2** as an orange powder. Yield 68.25 %. Decomposition temp. range, 280 – 282 °C. ^1H ($CDCl_3$, 400 MHz) : δ (ppm) 1.14 (d, 26H, J_{HH} = 5.2 Hz, -CH_3-CH), 1.32 (s, 10H, CH_3-), 1.40 (s, 12H, -CH_3), 2.83 (m, 8H CH-CH_3) 7.10 (s, 5H, Ar-H), 7.15 (s, 7H, Ar-H), 8.88 (s, 2H, -CH=N). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 24.05, 24.10, 25.26, 27.61, 29.26, 30.93, 123.19, 124.61, 124.85, 130.57, 138.74, 145.14, 146.26, 206.98 IR υ (cm^{-1}) 2961(s), 2867(w) 1651(s), 1460(s), 1178(s), 996(s), 378(s). ESI-TOF MS: m/z (%); $[M + K]^+$. 973.30. UV-Vis ($CHCl_3$, λ_{max}, nm), 261, 341, 457. Anal. calcd. for $C_{52}H_{74}N_4NiOS_4$: C, 65.73; H, 7.80; N, 5.85; S, 13.38. Found: C, 65.60; H, 7.80; N, 5.70; S, 13.06.

3.4.3 Synthesis of [Ni-(DL3)$_2$] (3)

The reaction of DL3 (0.3 g, 0. 8mmol) and $NiCl_2.6H_2O$ (0.08 g, 0.4 mmol) in acetonitrile furnished complex **3** as a purple-red powder. Yield 70 %. Decomposition temp. range, 270-272 °C. ^1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 2.05 (s, 10H, CH_3-Ar), 2.24 (s, 18H, CH_3-Ar), 2.30 (s, 3H, CH_3-Ar), 6.82 (s, 4H, Ar-H), 7.00 (s, 4H, Ar-H), 8.81 (s, 2H, CH=N). ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm): 17.58, 17.57, 18.52, 19.26, 20.63, 21.21, 127.47, 128.73, 128.87, 129.06, 129.50, 129.61, 133.61, 135.43, 144.79, 217.92. IR υ (cm^{-1}) 2914(w), 1644(s), 1477(m) 1145(m), 955(w), 318(s). ESI-TOF MS: m/z (%); $[DL3 - CH_3]^+$ 340.18. UV-Vis ($CHCl_3$, λ_{max}, nm), 258, 340, 454. Anal. calcd. for $C_{40}H_{48}N_4NiS_4$: C, 62.25; H, 6.27; N, 7.26; S, 16.62. Found: C, 61.90; H, 6.11; N, 7.09; S, 16.60.

3.4.4 Synthesis of [Ni-(DL4)$_2$].3H$_2$O (4)

The reaction of DL4 (0.20 g, 0.50 mmol) and $NiCl_2.6H_2O$ (0.06 g 0.25 mmol) in acetonitrile furnished complex **4** as a purple-red powder. Yield 78 %. Decomposition temp. range 260-262 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.31 (s, 12H, CH_3-Ar-), 6.96 (t, 3H, J_{HH} = 8.16 Hz, Ar-H), 7.16 (d, 4H, J_{HH} = 7.4 Hz, Ar-H), 7.28 (s, 3H, Ar-H), 8.94 (s, 2H, -CH=N). : ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 17.59, 125.42, 126.57, 128.32, 128.78, 130.09, 133.36, 136.20, 143.61, 147.33, 219.32. IR υ (cm^{-1}) 2968(w), 1642(s), 1435(m), 1096(m), 887(s).371(s). ESI-TOF MS: m/z (%); $[M – 2Cl]^+$. 723.03. UV-Vis ($CHCl_3$, λ_{max}, nm), 263, 341, 462. Anal. calcd.

for $C_{32}Cl_4H_{34}N_4NiO_3S_4$: C, 45.52; H, 4.03; N, 6.58; S, 15.19. Found: C, 45.47; H, 3.95; N, 6.42; S, 15.18.

3.3.5 Synthesis of [Ni-(DL5)$_2$].H$_2$O (5)

The reaction of DL5 (0.20 g, 0.4 mmol) and $NiCl_2.6H_2O$ (0.05 g 0.20 mmol) in acetonitrile furnished complex **5** as an orange powder. Yield 78 %. Decomposition tempt. Range, 274-276 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.25 (s, 16H, CH_3-CH), 1.34 (s, 8H, CH_3-CH), 2.85 (s, 4H, CH-CH_3, 6.93 (s, 2H, Ar-H), 7.55 (s, 2H, Ar-H), 9.10 (s, 2H, -CH=N). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 17.51, 29.26, 30.93, 123.16, 124.61, 124.85, 130.56, 138.75, 146.26, 218.76. IR υ (cm^{-1}) 2961(w), 1639(s), 1435(m), 1084(m), 888(s).372(s). ESI-TOF MS: m/z (%); [M – 2Cl]$^+$. 835.15. UV-Vis ($CHCl_3$, λ_{max}, nm), 262, 343, 467. Anal. calcd. for $C_{40}Cl_4H_{46}N_4NiOS_4$: C, 51.80; H, 5.00; N, 6.04; S, 13.38. Found: C, 51.21; H, 4.63; N, 5.84; S, 13.43.

3.3.6 Synthesis of [Ni-(DL6)$_2$] (6)

The reaction of DL6 (0.20 g, 0.50 mmol) and $NiCl_2.6H_2O$ (0.06 g 0.25 mmol) in acetonitrile furnished complex **6** as a purple-red powder. Yield 80 %. Decomposition tempt. Range, 268-270 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.26 (s, 12H, CH_3-Ar), 2.29 (s, 6H, CH_3-Ar), 6.93 (d, 2H, J_{HH} = 7.7, Ar-H), 6.98 (s 4H, Ar-H), 8.91 (s, 2H, -CH=N). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 17.51, 29.26, 30.93, 123.19, 124.61, 124.85, 130.56, 138.75, 146.26, 218.76. IR υ (cm^{-1}) 2970(w), 1644(s), 1436(m), 1098(m), 889(s).317(s). ESI-TOF MS: m/z (%); [M – 2Cl]$^+$. 752.38. UV-Vis ($CHCl_3$, λ_{max}, nm), 263, 343, 465. Anal. calcd. for $C_{34}H_{32}Cl_4N_4NiS_4$: C, 49.48; H, 3.91; N, 6.79; S, 15.54. Found: C, 49.02; H, 3.47; N, 6.61; S, 15.27.

3.3.7 Synthesis of [Cu-(DL1)$_2$].3H$_2$O (7)

The reaction of DL1 (0.3 g, 0.8 mmol) and $CuCl_2.2H_2O$ (0.07 g, 0.4 mmol) in acetonitrile furnished complex **7** as a deep brown powder. Yield 89 %. Decomposition tempt. Range, 280–282 °C. IR υ (cm^{-1}) 2918(w), 1645(s), 1470(m), 1186(s), 999(m), 374(w). ESI-TOF MS: m/z (%); [M]$^+$ 718.13. UV-Vis ($CHCl_3$, λ_{max}, nm), 300, 316 (shoulder), 449. Anal. calcd. for $C_{36}CuH_{46}N_4O_3S_4$: C, 56.21; H, 5.99; N, 7.33; S, 17.26. Found: C, 56.04; H, 5.99; N, 7.27; S, 17.15.

3.3.8 Synthesis of [Cu-(DL2)$_2$] (8)

The reaction of DL2 (0.3 g, 0.6 mmol) and $CuCl_2.2H_2O$ (0.50 g, 0.3 mmol) in acetonitrile furnished complex **8** as a reddish-brown powder. Yield 84 %. Decomposition tempt. Range, 294–296 °C. IR υ (cm^{-1}) 2960(m), 2915(m), 1639(s), 1477(m), 1143(m) 957(w), 395(w). ESI-TOF MS: m/z (%); $[M + K – (DL2 – 5H)]^+$ 537.09. UV-Vis ($CHCl_3$, λ_{max}, nm), 301, 319 (shoulder), 449. Anal. calcd. for $C_{52}CuH_{72}N_4S_4$: C, 60.69; H, 5.98; N, 8.18; S, 18.50. Found: C, 60.38; H, 5.97; N, 8.12; S, 18.11.

3.3.9 Synthesis of [Cu-DL3)$_2$].2H$_2$O (9)

The reaction of DL3 (0.3 g, 7.3mmol) and $CuCl_2.2H_2O$ (0.06 g, 3.6mmol) in acetonitrile furnished complex **9** as a deep brown powder. Yield 86 %. Decomposition tempt. range, 290–293 °C. IR υ (cm^{-1}) 2913(m), 1638(s), 1478(m), 1143(m), 957(w), 358(w). ESI-TOF MS: m/z (%); $[M – 3H]^+$ 773.19. UV-Vis ($CHCl_3$, λ_{max}, nm), 300, 317 (shoulder), 449. Anal. calcd. for $C_{40}CuH_{52}N_4O_2S_4$: C, 59.12; H, 6.45; N, 6.89; S, 15.78. Found: C, 59.80; H, 6.08; N, 6.81; S, 15.85.

3.3.10 Synthesis of [Cu-(DL4)$_2$].3H$_2$O (10)

The reaction of DL4 (0.2 g, 0.50 mmol) and $CuCl_2.2H_2O$ (0.04 g, 0.25 mmol) in acetonitrile furnished complex **10** as a deep brown powder. Yield 89 %. Decomposition tempt. range, 268–270 °C. ESI-TOF MS: m/z (%); $[M]^+$. 798.99. IR υ (cm^{-1}) 2973(w), 1641(s), 1471(m), 1125(m), 883(m).370(w). UV-Vis ($CHCl_3$, λ_{max}, nm), 301, 321 (shoulder), 449. Anal. calcd. for $C_{32}Cl_4CuH_{34}N_4O_3S_4$: C, 44.89; H, 4.00; N, 6.54; S, 14.98. Found: C, 44.60; H, 3.87; N, 6.29; S, 15.05.

3.3.11 Synthesis of [Cu-(DL5)$_2$].3H$_2$O (11)

The reaction of DL5 (0.20 g, 0.40 mmol) and $CuCl_2.2H_2O$ (0.40 g 0.20 mmol) in acetonitrile furnished complex **11** as a reddish-brown powder. Yield 84 %. Decomposition tempt. range, 285 – 287 °C. IR υ (cm^{-1}) 2964(w), 1640(s), 1434(m), 1130(m), 885(s).390(w). ESI-TOF MS: m/z (%); $[M]^+$.911.13. UV-Vis ($CHCl_3$, λ_{max}, nm), 301, 323 (shoulder), 449. Anal. calcd. for $C_{40}Cl_4CuH_{50}N_4O_3S_4$: C, 49.61; H, 5.20; N, 5.79; S, 13.24. Found: C, 49.44; H, 4.94; N, 5.61; S, 12.80.

3.3.12 Synthesis of [Cu-DL6)$_2$] (12)

The reaction of DL6 (0.20 g, 0.50 mmol) and $CuCl_2.2H_2O$ (0.04 g, 0.25 mmol) in acetonitrile furnished complex **12** as a deep brown powder. Yield 86 %. Decomposition tempt. range, 274 – 276 °C. ESI-TOF MS: m/z (%); $[M - H]^+$, 827.03. IR υ (cm^{-1}) 2971(w), 1639(s), 1436(m), 1125(m), 883(s).354(w). UV-Vis ($CHCl_3$, λ_{max}, nm), 300, 321 (shoulder), 449. Anal. calcd for $C_{34}Cl_4\,CuH_{32}N_4S_4$: C, 49.19; H, 3.89; N, 6.75; S, 15.45. Found: C, 48.89; H, 3.60; N, 6.59; S, 15.26.

3.4 Single-crystal X-ray diffraction

Crystal evaluation and data collection was done on a Bruker Smart APEXII diffractometer with Mo Kα radiation (I = 0.71073 Å) equipped with an Oxford Cryostream low temperature apparatus operating at 100K for all samples. Reflections were collected at different starting angles and the *APEXII* program suite was used to index the reflections [22]. Data reduction was performed using the *SAINT* [23] software and the scaling and absorption corrections were applied using the *SADABS* [24] multi-scan technique. The structures were solved by the direct method using the *SHELXS* program and refined using *SHELXL* program [25]. Graphics of the crystal structures were drawn using Mercury software [26]. Non-hydrogen atoms were first refined isotropically and then by anisotropic refinement with the full-matrix least square method based on F^2 using *SHELXL*. In complex **1**, solvent mask was calculated and 48.7 electrons was found in a void with a volume of 203.0 $Å^3$ in **1**, consistent with the presence of $1[C_6H_5CH_3]$ per formula unit which account for 48.7 electrons. The solvent molecule was toluene in complex **1** and was highly disordered. Attempts to model it was unsuccessful and only led to unstable refinement and was therefore omitted using *SQUEZE* [27] option in *PLATON* [28]. The carbon atom of the DCM molecule in complex **5** was found to be disordered over 2 positions with the major component having 53.80 % site occupancy while toluene molecules in compound **11** was found to be disordered over an inversion centre and was modeled using PART -1 instruction with fixed site occupancy factor of 0.5. The crystallographic data and structure refinement parameters for complex **1**, **2**, **5** and **11** are given in Table 1.

Table 1: The summary of X-ray crystal data collection and structure refinement parameters for complex **1**, **5**, **8**, and **11**

	1	**5**	**8**	**11**
Empirical formula	$C_{36}H_{38}N_4NiS_4$	$C_{40}H_{42}Cl_4N_4NiS_4.2CH_2Cl_2$	$C_{52}H_{70}CuN_4S_4$	$C_{40}H_{42}Cl_4CuN_4S_4.C_6H_5.CH_3$
Formula weight	713.65	1077.38	942.9	1004.49
Crystal system	Monoclinic	triclinic	Triclinic	monoclinic
Space group	$P2_1/n$	P-1	P -1	$P2_1/c$
a/Å	12.5278(3)	8.55440(10)	9.4674(16)	12.3469(6)
b/Å	12.3052(3)	11.2627(2)	12.120(2)	14.0658(8)
c/Å	14.7214(4)	13.0340(2)	12.249(2)	14.6828(8)
α/°	90	105.0640(10)	75.343(5)	90
β/°	114.8480(10),	100.016(2)	68.614(6)	109.835(3)
γ/°	90	94.213(3)	77.373	90
Volume/Å^3	2059.32(9)	1184.80(3)	1253.6(4)	2398.7(2)
Z	2	1	1	2
ρ_{calc}g/cm^3	1.151	1.51	1.249	1.391
μ/mm^{-1}	0.701	1.073	0.64	0.89
F(000)	748	554	503	1042
Crystal size/mm^3	0.190 x 0.120 x 0.080	0.4 × 0.27 × 0.14	0.210 x 0.150 x 0.080	0.21×0.18×0.08
2Θ range for data collection/°	1.799 to 27.563	3.302 to 54	1.754 to 25.498	1.753 to 27.543
Index ranges	$16 \le h \le 16$	$-10 \le h \le 8$	$-18 \le k \le 16$	$-16 \le h \le 16$
	$-14 \le k \le 14$	$-14 \le k \le 14$	$-18 \le k \le 16$	$-18 \le k \le 16$
	$-15 \le l \le 16$	$-15 \le l \le 16$	$-19 \le l \le 18$	$-19 \le l \le 18$
Reflections collected	27584	16602	8942	29811
Independent reflections	4729 [R(int) = 0.0421]	5049 [R_{int} = 0.0151]	4564 [R(int) = 0.0194]	5222 [R_{int} = 0.0186]
Data/restraints/parameters	4729 / 0 / 205	5049/1/282	4564 / 1 / 285	5478/123/309
Goodness-of-fit on F^2	1.021	1.029	1.043	1.029
Final R indexes [I>=2σ (I)]	R1 = 0.0359, wR2 = 0.0860	R_1 = 0.0328, wR_2 = 0.0802	R1 = 0.0820, wR2 = 0.2009	R_1 = 0.0500, wR_2 = 0.1080
Final R indexes [all data]	R1 = 0.0552, wR2 = 0.0929	R_1 = 0.0388, wR_2 = 0.0835	R1 = 0.1027, wR2 = 0.2172	R_1 = 0.0500, wR_2 = 0.1240
Largest diff. peak and hole (e Å^{-3})	0.455 and -0.315	0.97 and -1.10	4.469 and -0.753	0.789 and -0.647
Solvent for growing crystals	Toluene	Dichloromethane	Toluene	Toluene

3.5 Determination of free radical scavenging activity

DPPH (1,1-diphenyl-2-picrylhydrazyl) radical scavenging assay of compound **1–12** was carried out as per reported method by Chandrika *et al* with slight modifications [29]. Briefly, 100 µL of varying concentration (1.0 mM, 0.75 mM, 0.50 mM, and 0.25 mM) of the test sample was added to equal quantity of 0.1 mM solution of DPPH in ethanol. The reaction mixture was vortexed carefully and left in the dark at room temperature for 30 min. After 30 min of incubation at room temperature, the DPPH reduction was measured by reading the absorbance at 517 nm. Ascorbic acid of varying concentration (1.0 mM, 0.75 mM, 0.50 mM, and 0.25 mM) was used as the reference compound. The ability of the compounds to scavenge DPPH radical was calculated as:

$$\% \text{ Scavenging Activity} = \frac{Absorbance\ control - Absorbance\ of\ sample\ x\ 100}{Absorbance\ control}$$

3.6 *In vitro* antimicrobial studies

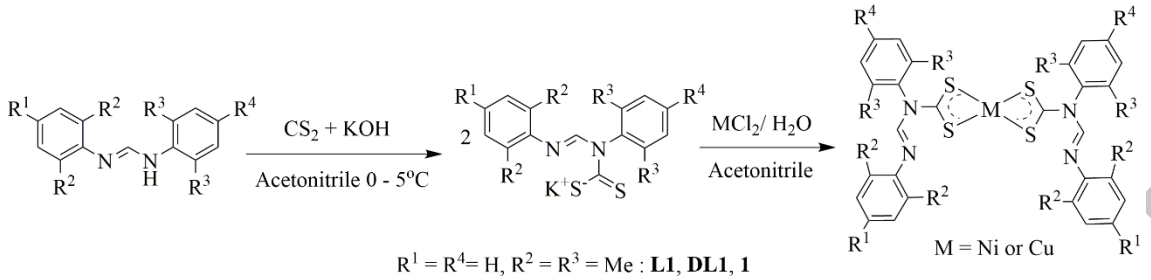
The antimicrobial activity of the Ni(II) and Cu(II) dithiocarbamate metal complexes was evaluated against four gram-negative bacteria, viz: *Salmonella typhimurium* ATCC 14026, *Pseudomonas aeruginosa* ATCC 27853, *Escherichia coli* ATCC 25922 and *Klebsiella pneumoniae* ATCC 31488 and two gram-positive bacteria, viz: *Staphylococcus aureus* ATCC 700699 (methicillin resistant) and *Staphylococcus aureus* ATCC 25923. Ciprofloxacin was used as a standard antibiotic for comparison while DMSO was used as a negative control and it showed no antibacterial activity against any of the bacterial strains used for this study at different concentrations. The samples were prepared by dissolving 1000 µg of test sample in 1 ml of dimethyl sulfoxide (DMSO). The bacteria were inoculated onto Nutrient Agar (NA) (Biolab, South Africa) plates using the streak plate technique and incubated at 37 °C for 18 hr [30]. A single colony was isolated and inoculated into 10 ml sterile Nutrient Broth (NB) (Biolab, South Africa). This was incubated at 37^{o}C for 18 hr in a shaking incubator (100 rpm). The concentration of each bacterial strain was adjusted with sterile distilled water to achieve a final concentration equivalent to 0.5 Mc Farland's Standard (i.e 1.5 x 10^8 cfu/mL) using a densitometer (Mc Farland Latvia) [31]. Thereafter, the MHA plates were lawn inoculated with the diluted bacteria using a sterile throat swab. 5 µL of each sample was spotted onto the MHA plates and the plates were incubated at 37^{o}C for 18 hr and then assessed for antibacterial activity which was denoted by a clear zone at the point of spotting. Samples that showed antimicrobial potential during antibacterial screening were tested further to determine their

minimum inhibitory concentration (MICs). The samples were serially diluted 10 times to achieve concentrations ranging from 1000 µg/ml to 0.2 µg/ml. For the samples where MICs were lower than 0.2 µg/mL, the solutions were further diluted serially 5 times to achieve concentrations ranging from 0.100 µg/ml to 0.00625 µg/ml. 5µl of each sample at different concentrations was spotted onto the MHA plates and the plates were incubated at 37 °C for 18 hr and then assessed for their MIC. These were done in triplicate and the MIC was determined as the lowest concentration of the compounds at which no visible bacterial growth was observed after incubation.

Results and discussion

4.0 Synthesis of N,N'-diarylformamidines dithiocarbamate ligands and their Cu (II) and Ni (II) metal complexes.

The synthesis routes for **DL1 - DL6** and complexes **1 - 12** are shown in **Scheme 1**. Synthesis of the potassium dithiocarbamate salts, **DL1 – DL6** was achieved by the reaction of equimolar amounts of the appropriate formamidine with carbon disulfide in the presence of potassium hydroxide in good yields between 74 and 94 % and with melting points between 237 – 263 °C. Complexes **1 - 12** were obtained by the reaction of salts of potassium dithiocarbamates with $CuCl_2$ or $NiCl_2$ in a 2:1 ratio as air stable purple or red solids for Ni(II) complexes and brown solids for Cu(II) complexes respectively. The Ni(II) complexes generally had lower decomposition ranges (between 265 – 282 °C) compared to the Cu(II) complexes (269 – 296 °C). The decomposition temperatures were dependent on the substituents on the backbone of the dithiocarbamates and was observed to be higher in those with symmetrical backbones relative to the unsymmetrical form of the complexes. All complexes showed good solubility in chloroform, dichloromethane and toluene but were only partially soluble in other polar solvents.



$R^1 = R^4$= H, $R^2 = R^3$ = Me : **L1**, **DL1**, **1**
$R^1 = R^4$= H, $R^2 = R^3$ = iPr : **L2**, **DL2**, **2**
$R^1 = R^2 = R^3 = R^4$ = Me : **L3**, **DL3**, **3**
$R^1 = R^4$ = H, R^2 = Cl, R^3 = Me : **L4**, **DL4**, **4**
$R^1 = R^4$ = H, R^2 = Cl, R^3 = iPr : **L5**, **DL5**, **5**
R^1 = H, R^2 = Cl, $R^3 = R^4$ = Me : **L6**, **DL6**, **6**
$R^1 = R^4$= H, $R^2 = R^3$ = Me : **L1**, **DL1**, **7**
$R^1 = R^4$= H, $R^2 = R^3$ = iPr : **L2**, **DL2**, **8**
$R^1 = R^2 = R^3 = R^4$ = Me : **L3**, **DL3**, **9**
$R^1 = R^4$ = H, R^2 = Cl, R^3 = Me : **L4**, **DL4**, **10**
$R^1 = R^4$ = H, R^2 = Cl, R^3 = iPr : **L5**, **DL5**, **11**
R^1 = H, R^2 = Cl, $R^3 = R^4$ = Me : **L6**, **DL6**, **12**

Scheme 1: Synthesis of symmetrical and unsymmetrical N,N'-diarylformamidine dithiocarbamate ligands **DL1** – **DL6** and their Ni(II) and Cu(II) metal complexes **1-12**.

4.1 Spectroscopic studies

Nuclear magnetic resonance

The ^{1}H NMR data of **DL1** – **DL6** were obtained in DMSO and peak assignments done using 2D NMR. The azomethine (NC(*H*)=N) and amine protons were used to follow the transformation from formamidines to potassium dithiocarbamates to the metal complexes. The disappearance of the amine proton, which appears in the region 5.43 – 5.60 in **L1** – **L6** marked successful synthesis of **DL1** – **DL6**. The azomethine proton was also observed to shift from 7.25 – 8.69 in **L1** – **L6** to 9.86 – 10.39 in **DL1** – **DL6**. These further shifted upfield on complexation to the metal salts in complexes **1** – 6 and appeared in the region 8.81 – 9.10 (Table 2). There were also typical aliphatic signal shifts in moving from the formamidines to the dithiocarbamates to complexes all influenced by the electronics on the formamidine backbone and complexation. Upon coordination to Ni(II), the methyl group shifted downfield in all the Ni (II) complexes, (**1-6**). This slight downfield shift in **1 - 6** implies the drift of electron cloud towards the metal ion center [32, 33]. In addition, the ^{13}C-NMR spectra of **1 - 3** show that the quaternary thiouride (-NCS_2) carbon peaks shifted upfield on complexation of **DL1** – **DL3**. This upfield shift is attributed to the delocalization of an electron

cloud from the $–NCS_2$ moiety towards the metal centre, hence lowering the C=S bond strength [34, 35].

Table 2: The $-NCS_2$ (^{13}C-NMR) and NC(H)=N (^{1}H-NMR) signals for **DTL1 – DTL6** and **1 – 6**, and the IR bands of thiouride (C—N) and azomethine (C=N) for ligands and the complexes,

Ligands (Complex)	δ ($-NCS_2$) ppm	Δ δ	δ NC(H)=N ppm	Δ δ	υ(C=N) cm^{-1}	Δυ	υ(C—N) cm^{-1}	Δυ
DTL1 (1)	217.62 (216.95)	0.69	9.86(8.85)	1.01	1640 (1647)	7	1467 (1472)	7
DTL2 (2)	220.94 (206.98)	6.13	10.15(8.88)	1.27	1639 (1651)	12	1452 (1469)	8
DTL3 (3)	218.95 (217.92)	1.84	9.92(8.81)	1.11	1629 (1644)	15	1477 (1479)	1
DTL4 (4)	218.82 (219.32)	0.50	10.12(8.94)	1.18	1614 (1642)	28	1432 (1474)	3
DTL5 (5)	217.02 (218.76)	1.74	10.13(9.10)	1.03	1603 (1639)	36	1430 (1469)	5
DTL6 (6)	219.04 (219.49)	0.45	10.39(8.91)	1.48	1612 (1644)	32	1435 (1468)	1
DTL1 (7)					1640 (1645)	5	1467 (1470)	3
DTL2 (8)					1639 (1663)	24	1452 (1477)	25
DTL3 (9)					1629 (1638)	9	1477 (1478)	1
DTL4 (10)					1614 (1641)	27	1432 (1471)	39
DTL5 (11)					1603 (1640)	37	1430 (1434)	4
DTL6 (12)					1612 (1639)	27	1435 (1436)	1

Fourier transform infrared spectroscopy

Four major vibrational bands were observed in the IR spectra of the dithiocarbamate ligands (**DL1 – DL6**). The stretching bands observed were for υ(C=N) [1603 – 1640] of azomethine (C(H)=N), the υ(C—N) [1430 – 1477] of thiouride, $υ(C=S)_{str}$ [1000 – 1152] and the υ(C—S) [921 – 1036] Table 2. Upon complexation, these bands all moved to higher frequencies; the υ(C=N) of azomethine appeared between 1639 and 1651 cm^{-1} from 1603 and 1640 cm^{-1} for the dithiocarbamate ligands. The band of $C—N_{str}$ appeared between 1435 and 1478 cm^{-1} in **1 – 6** from 1430 - 1467 cm^{-1} in **DL1 – DL6** (Table 3). The shifts could be because of delocalization of electron densities of the ligand towards the metal centres resulting in partial double bond character of the υ(C—N) bond [7, 10]. The frequency of the C—N band in this complexes lies between that of a

typical C=N and that of typical C—N bond (υ(C=N) = 1640–1690 cm^{-1} while υ(C—N) = 1250–1360 cm^{-1}) [19, 36, 37]. The υ(C—S) bands appeared as a single band in the region of 886-1096 cm^{-1} in all complexes alluding to symmetrical bonding of the dithiocarbamate ligand to the metal center in the complexes, supporting bidentate coordination [37-39]. The spectra of the **1 - 12** also show a band in the far infra-red region between 350 and 384 cm^{-1} assigned to the υ(M—S) bonds [40].

UV-vis spectroscopy

The electronic absorption spectra of the dithiocarbamate ligands and the metal complexes were recorded in DMSO and chloroform respectively. The UV-Visible spectra of all the ligands and twelve complexes are given in Figures (1a – 1c). Generally, transition due to the ligands appeared in the UV region while the d–d transition appeared in the visible region [11]. The spectra of the ligands **DL1 – DL6** showed two absorption bands in the UV region between 289 and 300 nm and 338 and 345 nm. These absorption bands are assigned to intraligand □→□* associated to N-C=S group and □→□* transition within the S-C=S group [41]. In each of the spectra, three absorption bands for **1** – **6** between 258 and 263 nm, 340 and 343 nm, and 454 and 467 nm are observed. The bands between 454 and 467 can be attributed to d-d transition while those below 400nm are assigned to intra-ligand □→□* associated to N-C=S and S-C=S group of the dithiocarbamate ligand backbone. For **7** – **12**, two major absorption bands between 300 and 301 nm and 442 ad 449 nm are observed.. Highly-intense bands were observed within the range of 442 – 449 nm and these bands are assigned to d-d transitions [42]. There is a possibility of three observable bands in the spectra of **7** – **12** as shoulder is observed in each alluding an overlap of two bands.

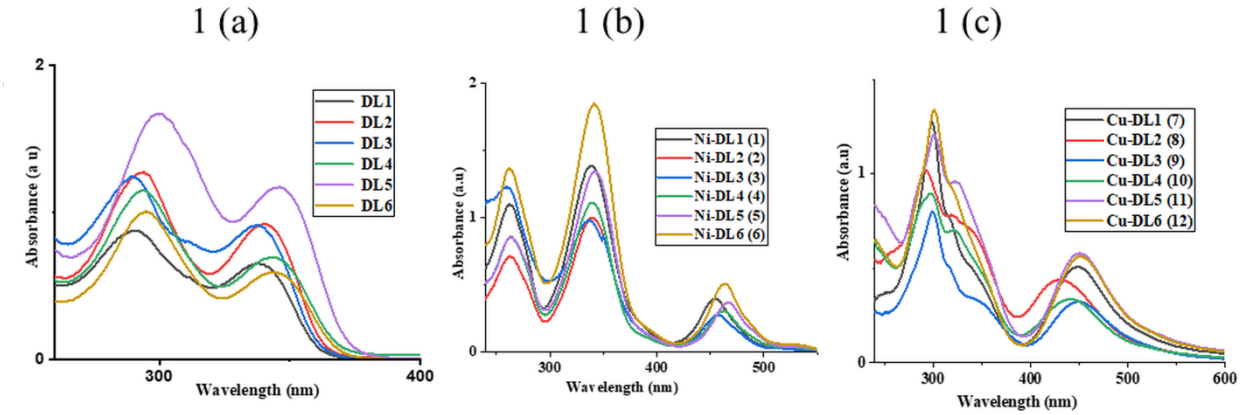


Figure (1a): Electronic absorption spectra of **DL1** – **DL6** **(1b):** Electronic absorption spectra of **1 - 6** **(1c):** Electronic absorption spectra of **7** – **12**.

4.2 X-ray structural analysis

Suitable crystals for single crystal X-ray diffraction analysis were obtained for complexes **1**, **5**, **8** and **11** by slow evaporation where, crystals of **1**, **8** and **11** were obtained from their solution of toluene, while those of **5** were obtained from a dichloromethane solution of it. The molecular structures are given in Figures **2.** And selected bond distances and angles in Table 3. Complex **1** and **8** contain half a molecule of the complex in their asymmetric units while **5** and **11** contain half a molecule together with toluene molecule. The structures of all the complexes consist of a mononuclear neutral species in which the metal centers [Ni(II) and Cu(II)] are coordinated by two pairs of sulphur atoms from two bidentate dithiocarbamate ligand in a distorted square planar geometry fashion around the metal center. The S—M—S bond angles are 79.441(18), 79.402(18), 76.77(5) and 77.333(3)˚ smaller than the ideal 90° for square planar geometry) for **1**, **5**, **8** and **11** respectively. The strained S—C—S angles of all the complexes contribute to the deviation from ideal square planar geometry. In the structures of **1** and **5**, the Ni—S bond distances range from 2.2003(5) to 2.2090(5) while in **8** and **11** the Cu—S bond distance ranges between 2.2597(15) and 2.3282(7) as seen in Table 4. These values are consistent with the values reported with mononuclear bis dithiocarbamate complexes [17]. The M—S bond distances seem not to be influenced much by electronics of the CS_2 backbone. As expected, the Cu—S bond at the metal center of **8** and **11** are greater than the Ni—S bond of complexes **1** and **5**. The C—S bond distances seem not to favor single or double bond character in all the named complexes. They are shorter than the typical single C—S bond length of 1.82 Å but longer than the C=S double bond length of 1.67 Å [43]. This is an indication of delocalization of electron along the S—C—S moiety in the complexes. [44]. Also, the C—N bond length of the -NCS_2 moiety of the complexes deviates from the reported value for single C—N which is 1.47Å. For complex **1**, C(10)—(N)2 = 1.344(2), C(1)—N(2) = 1.358(2) for complex **5**, C(1W)—N(1) = 1.344(7) for complex **8** and C(10)—(N)2 = 1.362(4) for complex **11**. This indicates the delocalization of □-electron over the entire S2CN fragment in the complexes [42].

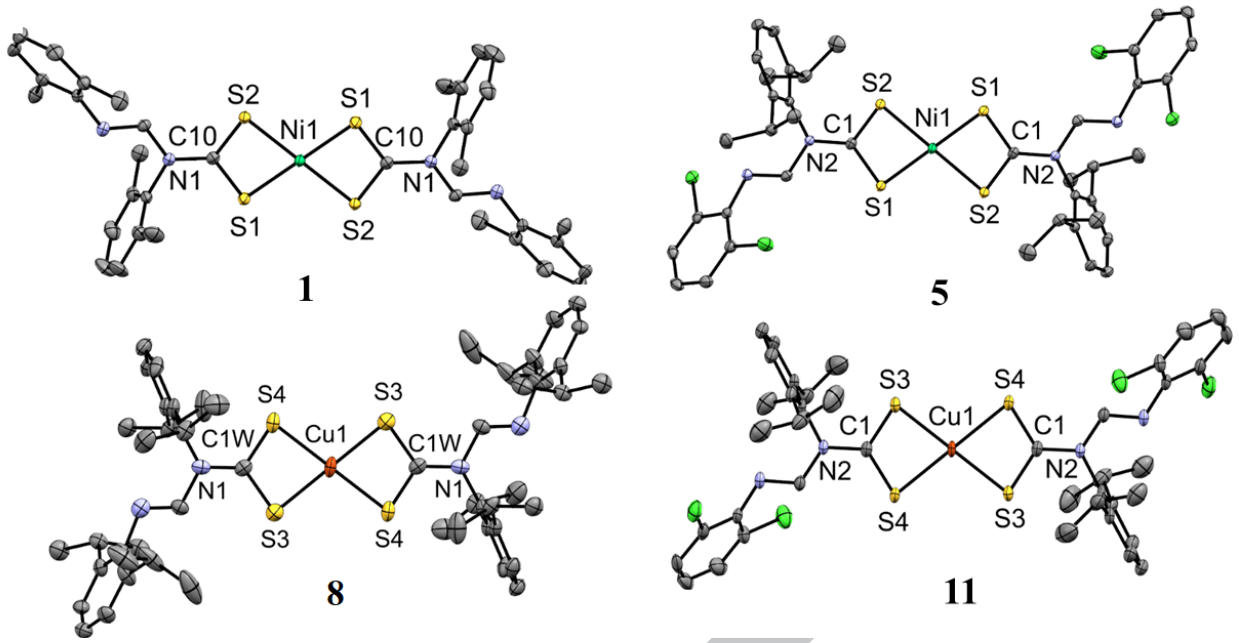


Figure 2: ORTEP diagram of complex **1**, **5**, **8**, and **11** drawn at 50 % thermal ellipsoids probability. Hydrogen atoms have been omitted for clarity.

Table 3: Selected bond length (Å) and angles (°) for complex 1, 5, 8 and 11

Parameters	**1**	**5**	**8**	**11**
Bond distances				
M—S	2.2003(5)	2.2023(5)	2.2597(15)	2.2643(8)
M—S	2.2090(5)	2.2045(3)	2.3057(13)	2.3282(7)
C—S	1.698(2)	1.696(2)	1.695(5)	1.688(3)
C—S	1.711(2)	1.709(2)	1.731(5)	1.706(3)
C—N	1.344(2)	1.358(2)	1.344(7)	1.362(4)
Bond angles				
S—M—S	79.4421(18)	79.402(18)	76.77(5)	77.33(3)
S—C—S	111.50(11)	111.53(11)	111.70(3)	115.47(17)

4.3 Antimicrobial activities evaluation

When designing new compounds, its ideal to have them as an excellent antimicrobial agent capable of killing pathogens without having any negative side effects when used for treatment [36]. Complexes **1 - 12** and along with Ciprofloxacin as a standard were screened against six bacteria strains and the results are presented in Table 4. The results based on the MICs obtained show that the complexes possess good antimicrobial activities against five bacterial strains with the exception of MRSA.

Complexes **1**, **4**, **5**, **7** and **10** showed better activity against *E. coli* and even better than the standard ciprofloxacin. The antimicrobial activities of complexes with the symmetrically substituted formamidines, **1 - 3** and **7 – 9** were more active compared to those with unsymmetrically substituted formamidine **4 - 6** and **10 - 12** (form). For example, the MICs of **1**, **2** and **3** were 0.10, 6.25 and 1.6 ug/ml respectively while those of **4**, **5** and **6** were 0.025, 0.10 and 0.20 ug/ml respectively when tested against *E. coli* (Table 4). Complexes in which the formamidine bore an electron withdrawing group (Cl in this instance) **4 - 6** and **10 - 12** were more active and activity can be attributed to better lipophilicity , hence easy penetration into the lipophilic section of the cell membrane or lipophilic domains of proteins. [45]. This trend was observed with the other bacterial strains as well.

While most complexes displayed moderate activities against *S. typhimurium*, **6** and **10** showed higher activities compared to the other complexes and ciprofloxacin. It could be observed that there was varying degrees of activity of all the complexes against *E. coli*, *S. typhimurium* and other bacterial strains. This could be due to the nature of the metal ion electronic configuration of the complexes as well as the nature of the cell membrane of each bacteria strain which determines the permeability of the complexes or the difference in ribosome of the microbial cell [46, 47]. Complex **7** exhibited least activity against *P. aeruginosa*, whilst complexes **8**, **11** and **12** displayed better activity as compared to ciprofloxacin. Complex **11** displayed the highest activity against *P. aeruginosa* with an MIC value of 0.20 µg/ml. All the complexes showed better activity against *K. pneumonia* relative to ciprofloxacin with the exception of complexes **1**, **7**, **9**, **10** and **12.** However, all the complexes were inactive against MRSA apart from complexes **4**, **5** and **6** which were active only at the highest concentration (1000 µg/mL). The failure of the complexes to inhibit MRSA could be as a result of the inability of the compounds to penetrate through the bacteria cell or the complexes might have been modified or rendered inactive as they entered the cell wall of the

MRSA [48]. All the Cu(II) complexes showed better activity against *S. aureus* excluding complex **11** while all Ni(II) complexes displayed moderate to low activity against it.

Table 4: Minimum inhibitory concentration of the metal complexes (μg/mL).

	Gram (-) bacteria				Gram (+) bacteria	
Complexes	*E. coli*	*S. typhimurium*	*P. aeruginosa*	*K. pneumoniae*	*S. aureus*	MRSA
Ni (II) and Cu (II) complexes of symmetrical N,N'-diarylformamidine dithiocarbamate						
1	0.10	100	50	6.25	1000	NA
2	6.25	100	6.25	0.20	1000	NA
3	1.6	50	1.60	0.20	1000	NA
7	0.05	0.80	100	6.25	0.80	NA
8	100	0.40	0.40	0.00625	1.60	NA
9	12.5	1.60	12.5	3.125	0.80	NA
Ni(II) and Cu(II) complexes of unsymmetrical N,N'-diarylformamidine dithiocarbamate						
4	0.025	12.5	1.60	0.20	1000	1000
5	0.10	1.6	6.25	0.20	6.25	1000
6	0.20	0.2	3.125	0.10	50	1000
10	0.025	0.20	1.60	3.125	1.60	NA
11	3.125	0.40	0.20	0.00625	1000	NA
12	0.80	1.60	0.40	1.60	0.025	NA
Ciprofloxacin[a]	0.20	0.40	0.80	1.60	25	25

NA = No activity, a = standard

4.4 DPPH Radical scavenging ability

2,2-Diphenyl-1-picrylhydrazyl (DPPH) is a stable free radical containing an odd electron in its structure [49]. It is usually used for the evaluation of radical scavenging activity in a relatively shorter time compared to other methods [50]. The ability of antioxidant molecules to scavenge the radical of the DPPH is due to their hydrogen or electron radical donating capability [51]. We have used DPPH radical scavenging assay for the screening of the antioxidant activity of the Ni(II) and Cu(II) dithiocarbamate metal complexes at different concentrations. The antioxidant activity of dithiocarbamates as well as their metal complexes may be elucidated on the basis of electron donating ability of sulfur and the central metal ions in their various complexes which led to free radical stabilization [52]. It has been reported that the presence of the central metal increases the antioxidant activity of the ligand since the ligands proton donor capacity is enhanced [4, 53]. The DPPH is purple in color and the odd electron in its radical gives a strong absorption maximum at 517 nm. The color turns from purple to yellow when the odd electron of the DPPH radical becomes paired with hydrogen from free radical scavenging antioxidants to form reduced DPP-H [6, 54].

The % free radical scavenging ability values were used to calculate the IC_{50} values of complexes **1-12** and these are summarized in Table 6. Results were compared with the antioxidant activity of ascorbic acid (with IC_{50} value of 1.01 x 10^{-3} mM). The IC_{50} values were used to determine the antioxidant activity i.e. the lower the IC_{50} value the higher will be the antioxidant activity [55, 56]. We found out that complex **2** have the least IC_{50} value of 1.10 x 10^{-3} mM and has the highest value of ascorbic acid equivalent antioxidant capacity (AEAC), followed by **7**, **8**, **3** and **1** respectively as shown in Table 4. On the other hand, complex **6**, **10** and **12** displayed weak antioxidant activity. The radical scavenging activities of complexes **1-3** and **7-9** which have rich electron seems to be better than the activities of the complexes **4-6** and **10-12** with electron withdrawing group. For example, complexes **1**, **2** and **3** have higher activities compared to **4**, **5** and **6** as seen in Table 3. A trend was observed for complexes **6-9** to **10-12**. It has been shown previously [57] that electronics play a crucial role in enhancing free radical scavenging activity. In **1-3** and **6-9** the presence of electron donating group increases the electron density at the carbon atoms in the aromatic rings of the complexes, hence, increasing their electron donating capability which lead to their higher antioxidant activity relative to **4-6** and **10-12** that have electron withdrawing groups. Generally, the antioxidant activity of **1-12** increases as the concentration increases and this is illustrated in Fig **3** and **4**.

Table 5 : Antioxidant potential of tested compounds at different concentration.

Complexes	IC_{50} (mM)
1	6.59×10^{-3}
2	1.10×10^{-3}
3	2.99×10^{-3}
4	7.12×10^{-2}
5	1.21
6	1.85
7	1.65×10^{-3}
8	4.50×10^{-3}
9	1.60×10^{-1}
10	2.16
11	1.383
12	2.91
Ascorbic acid	1.04×10^{-3}

Result presented here are the mean values from three independent experiments

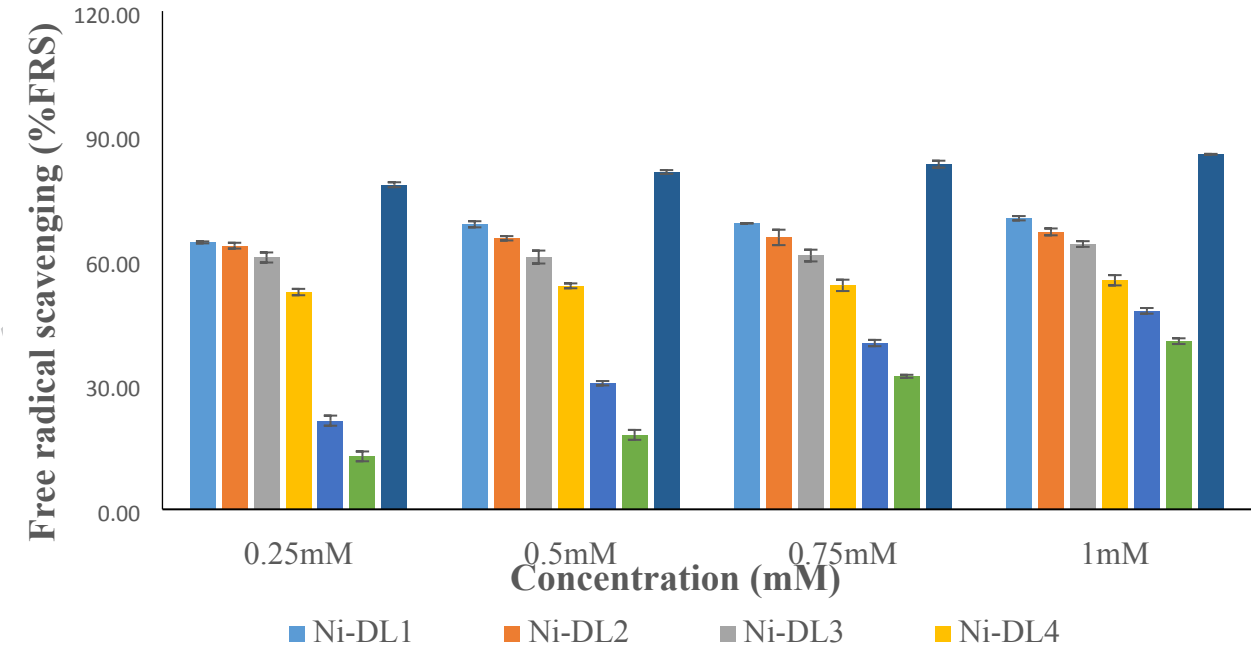


Figure 3: % Free radical scavenging vs concentration (mM) of Ni((II) dithiocarbamate metal complexes (**1—6**)

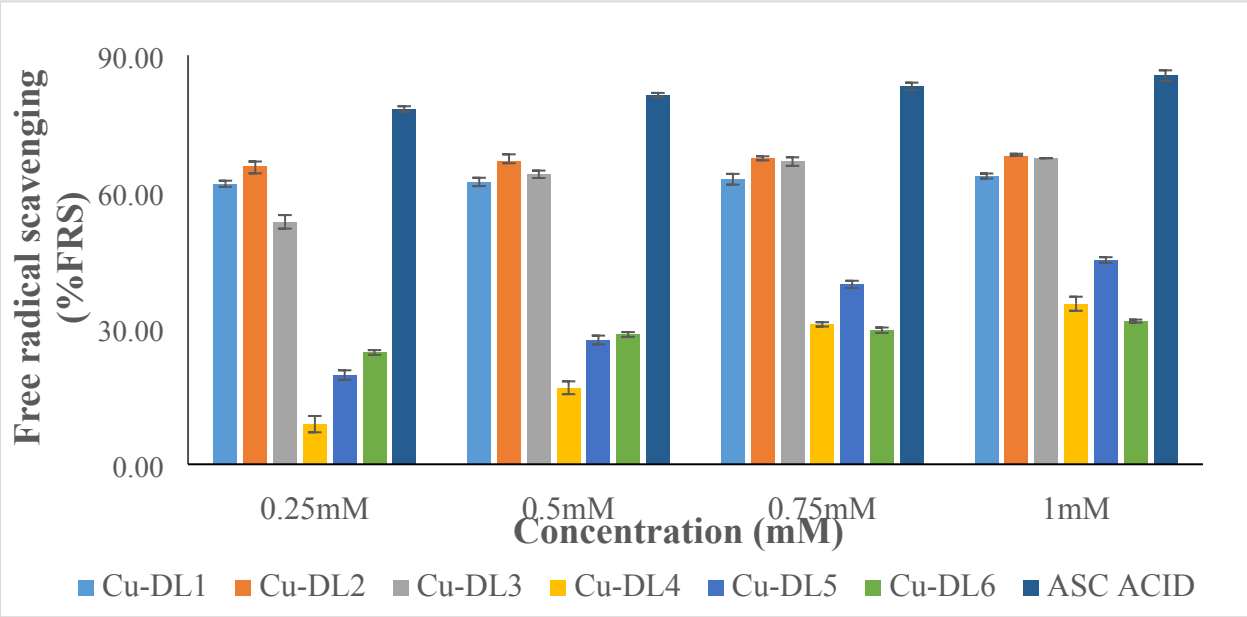


Figure 4: % Free radical scavenging vs concentration (mM) of Cu(II) dithiocarbamate metal complexes (**7 - 12**).

5.0 Conlusion

Ni(II) and Cu(II) complexes of symmetrical and unsymmetrical formamidine-based dithiocarbamate ligands were synthesized and fully characterized by UV-Visible, FT-IR, NMR and Mass spectrometry. X-ray structural analysis of **1**, **5**, **8** and **11** showed that the central metal, Cu(II) and Ni(II) are bonded by four sulfur atoms from the two N,N'-diarylformamidine-based dithiocarbamate ligands in a bidentate coordination mode to form a slightly distorted square planar geometry. The results of their antioxidant studies showed that, complexes with symmetrical formamidine-based dithiocarbamate ligands exhibited higher antioxidant activity compared to their unsymmetrical counterparts with complex **2** having the highest ascorbic acid equivalent capacity. The *in vitro* antibacterial screening and the MICs showed that, complexes **1-12** had moderate to good antimicrobial activities against all the bacterial strains except MRSA. The presence of chlorine atoms in complexes with unsymmetrical formamidine-based dithiocarbamate

ligands enhanced their antibacterial activity, thus showing better activities compared to their symmetrical counterparts.

Conflict of interest

The authors declare no competing financial interest

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Supplementary data

CCDC 1917370, CCDC 1917371, CCDC 1917372 and CCDC 1917373 contain the supplementary crystallographic data for complexes **1**, **5**, **8** and **11** respectively. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44)1223-336-033; or via e-mail: deposit@ccdc.cam.ac.uk.

References

1. M. Rizzotto, *A search for antibacterial agents*, IntechOpen., London, 2012, pp. 74-88.
2. A. Coates, Y. Hu, R. Bax and C. Page, Nat. Rev. Drug Discov. 1 (2002) 895.
3. S. K. Verma and V. K. Singh, RSC Adv. 5 (2015) 53036-53046.
4. A. Corona-Bustamante, J. M. Viveros-Paredes, A. Flores-Parra, A. L. Peraza-Campos, F. J. Martínez-Martínez, M. T. Sumaya-Martínez and Á. Ramos-Organillo, Molecules. 15 (2010) 5445-5459.
5. I. Kostova and L. Saso, Curr. Med. Chem. 20 (2013) 4609-4632.
6. S. Vartale, N. Halikar, Y. Pawar and K. Tawde, Arab. J. Chem. 9 (2016) 1117-1124.
7. I. Ali, W. A. Wani, K. Saleem and M.-F. Hseih, Polyhedron. 56 (2013) 134-143.
8. B. Cvek, V. Milacic, J. Taraba and Q. P. Dou, J. Med. Chem. 51 (2008) 6256-6258.

9. S. M. Mamba, A. K. Mishra, B. B. Mamba, P. B. Njobeh, M. F. Dutton and E. Fosso-Kankeu, Spectrochim. Acta. 77A (2010) 579-587.
10. F. Shaheen, A. Badshah, M. Gielen, M. Dusek, K. Fejfarova, D. de Vos and B. Mirza, J. Organomet. Chem. 692 (2007) 3019-3026.
11. D. C. Onwudiwe and A. C. Ekennia, Res. Chem. Intermed. 43 (2017) 1465-1485.
12. S. Khan, W. Ahmad, K. Munawar and S. Kanwal, Indian J. Pharm. Sci. 80 (2018) 480-488.
13. H. Graeme, Mini. Rev. Med. Chem. 12 (2012) 1202-1215.
14. B. Macías, M. A. Villa, E. Chicote, S. Martín-Velasco, A. Castiñeiras and J. N. Borrás, Polyhedron. 21 (2002) 1899-1904.
15. M. Shahid, T. Rüffer, H. Lang, S. A. Awan and S. Ahmad, J. Coord. Chem. 62 (2009) 440-445.
16. K. K. Manar, M. K. Yadav, Anamika, M. G. B. Drew and N. Singh, Polyhedron. 117 (2016) 592-599.
17. F. P. Andrew and P. A. Ajibade, J. Coord. Chem. 71 (2018) 1-17.
18. H. Zhang, J. S. Wu and F. Peng, Anticancer Drugs. 19 (2008) 125-132.
19. A. Gölcü, Transit. Metal Chem. 31 (2006) 405-412.
20. K. V. Gopal, P. S. Jyothi, P. A. G. Raju and J. Sreeramulu, J. Chem. Pharm. Res. 5 (2013) 50-59.
21. E. D. Akpan, S. O. Ojwach, B. Omondi and V. O. Nyamori, New J. Chem. 40 (2016) 3499-3510.
22. Bruker, *APEXII*, APEXII Bruker AXS Inc, Madison, Wisconsin, USA, 2009.
23. Bruker, *SAINT*, SAINT Bruker AXS InC, Madison, Wisconsin, USA, 2009.
24. Bruker, *SADABS*, SADABS Bruker AXS Inc, Madison, Wisconsin, USA, 2009.
25. G. M. Sheldrick, Acta. Crystallorg A. 64 (2008) 112-122.
26. C.F. Macrae, I.J. Bruno, J.A. Chisholm, P.R. Edgington, P. McCabe, E. Pidcock, L. Rodriguez-Monge, R. Taylor, J. Van de Streek and P.A. Wood, J. Appl. Cryst. 41 (2008) 466-470.
27 A. L Spek, Acta. Crystallorg C Struct. Chem 71 (2015) 9-18.
28 A. L Spek, Acta. Crystallogr. D Biol. Crystallogr. 65 (2009) 148-155.
29. C. M. Liyana-Pathirana and F. Shahidi, J. Arg. Food Chem. 53 (2005) 2433-2440.

30. H. Govender, C. Mocktar and N. A. Koorbanally, J. Heterocyclic Chem. 55 (2018) 1002-1009.
31. O. S Aremu, K. Gopaul, P. Kadam, M. Singh, C. Mocktar, P. Singh and N. A Koorbanally, Anti-Cancer. Agent Me. 17 (2017) 719-725.
32. A. Mohammad, C. Varshney and S. A. Nami, Spectrochim. Acta. 73A (2009) 20-24.
33. K. Siddiqi, S. Khan, S. A. Nami and M. El-Ajaily, Spectrochim. Acta. 67A (2007) 995-1002.
34. G. G. Mohamed, N. A. Ibrahim and H. A. Attia, Spectrochim. Acta. 72A (2009) 610-615.
35. M. Altaf, H. Stoeckli-Evans, S. S. Batool, A. A. Isab, S. Ahmad, M. Saleem, S. A. Awan and M. A. Shaheen, J. Coord. Chem. 63 (2010) 1176-1185.
36. D.C. Onwudiwe, A.C Ekennia, and H. Eric, J. Coord. Chem. 69 (2018) 2454-2468.
37. A. Ziyaei Halimehjani, M. A. Alaei, F. Soleymani Movahed, N. Jomeh and M. R. Saidi, J. Sulfur Chem. 37 (2016) 529-536.
38. F. Bonati and R. Ugo, J. Organomet. Chem. 10 (1967) 257-268.
39. S. H. Dar, S. Thirumaran and S. Selvanayagam, Polyhedron. 96 (2015) 16-24.
40. A. Nqombolo and P.A. Ajibade, Chalcogenide. Lett. 13 (2016) 427-434.
41. H. A. Hasan, E. I. Yousif and M. J. Al-Jeboori, Global J. Inorg. Chem. 3 (2012) 1-7.
42. B. Arul Prakasam, M. Lahtinen, A. Peuronen, M. Muruganandham, E. Kolehmainen, E. Haapaniemi and M. Sillanpää, Inorg. Chim. Acta. 425 (2015) 239-246.
43. A. Z. Halimehjani, S. Torabi, V. Amani, B. Notash and M. R. Saidi, Polyhedron. 102 (2015) 643-648.
44. D. C. Onwudiwe, M. M. Kabanda, E. E. Ebenso and E. Hosten, J. Chem. Sci. 128 (2016) 1081-1093.
45. K. Naumann, EuroChlor Science Dossier. 4 (2003) 1-37.
46. Zijian Guo and Peter J. Sadler, Angew. Chem. Int. Ed. 38 (1999) 1512-1531.
47. K. Mounika, A. Pragathi and C. Gyanakumari, J. Sci. Res. 2 (2010) 513.
48. B. L. Batzing, Microbiology: an introduction, 2nd ed, Brooks/Cole, USA, 2002.
49. A. C. Ekennia, D. C. Onwudiwe, A. A. Osowole, L. O. Olasunkanmi and E. E. Ebenso, J. Chem. 2016 (2016) 1-12.
50. S. Nithiya, N. Karthik and J. Jayabharathi, Int. J. Pharm. Sci. 3 (2011) 254-256.

51. I. Gülçin, Ö. İ. Küfrevioğlu, M. Oktay and M. E. Büyükokuroğlu, J. Ethnopharmacology. 90 (2004) 205-215.
52. S. A. Nami, I. Ullah, M. Alam, D.-U. Lee and N. Sarikavakli, J. Photochem. Photobiol. 160 (2016) 392-399.
53. W. Chen, S. Sun, Y. Liang and J. Song, J. Mol. Struct. 918 (2009) 194-197.
54. A. Mahajan and V. R. Tandon, J. Indian Rheumatol. Assoc. 12 (2004) 139-142.
55. N. Ganji, A. Rambabu, N. Vamsikrishna and S. Daravath, J. Mol. Struct. 1173 (2018) 173-182.
56. A. Fetoh, O. A. El-Gammal and G. M. A. El-Reash, J. Mol. Struct. 1173 (2018) 100-110.
57. S. Zara, D. Ahmed, H. Baig and M. Ikram, Asian J. Chem. 24 (2012) 4345-4351.

Synthesis and structural studies of nickel(II)- and copper(II)-N,N'-diarylformamidine dithiocarbamate complexes as antimicrobial and antioxidant agents

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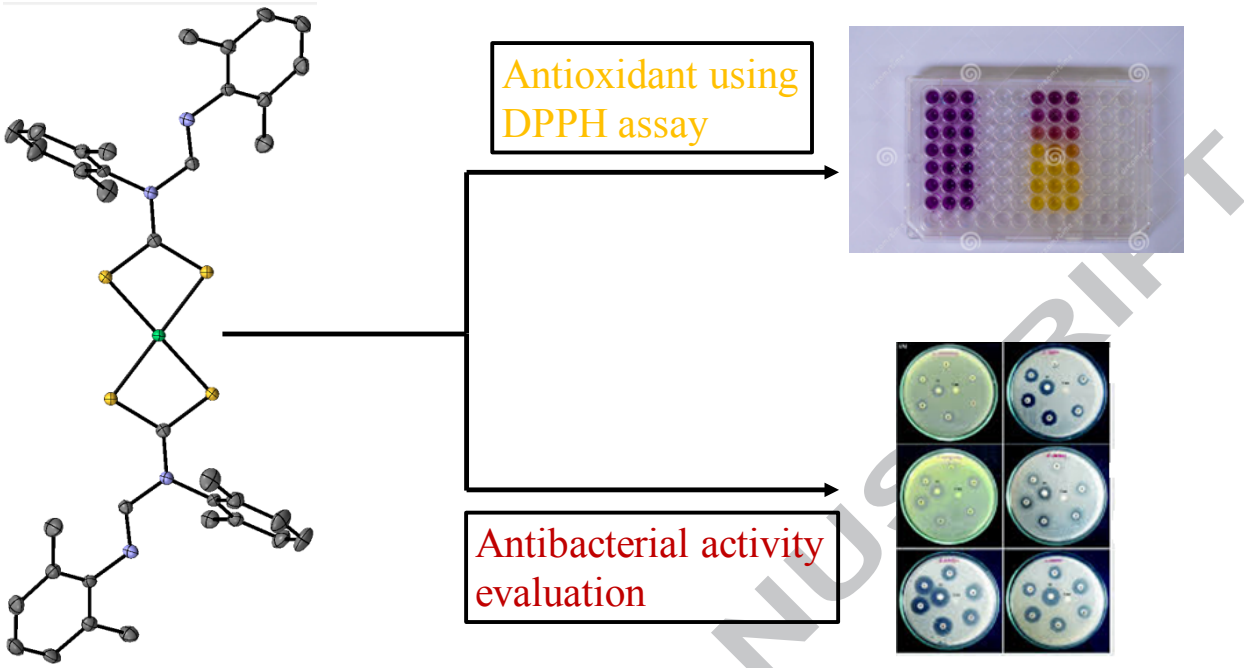
Graphical Abstracts



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GA Synopsis

Ni(II) and Cu(II) dithiocarbamate metal complexes derived from symmetrical and unsymmetrical N,N'-diarylformamidine were prepared and fully characterized. The antimicrobial and antioxidant potency were also reported.