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Research Article

SN-Donor Methylthioanilines and Copper(II) Complexes: Synthesis, Spectral Properties, and *In Vitro* Antimicrobial Activity

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Methylthioanilines, a series of sulfur-nitrogen donor ligands substituted with OCH_3, CH_3, Cl, and Br, and their copper(II) complexes have been synthesized and characterized by ^1H and ^{13}C NMR, elemental analysis, FTIR, UV-Vis and EPR spectra, molar conductance, and magnetic susceptibility measurements. The NMR spectra of the ligands revealed that the *para*/*ortho* protons and *para* carbon were sensitive to the electronic effect of substituents. The CHNS analysis presented $CuLCl_2$ (L = OCH_3, CH_3, Cl) and CuL_2Cl_2 (L = Br) stoichiometries for the copper complexes. FTIR spectra showed that the bidentate ligands were coordinated to the copper ion through their nitrogen and sulfur atoms. The electronic spectra have suggested square planar and octahedral geometries for these complexes. The EPR spectra demonstrated that the solid state copper(II) complexes possess $d_{x^2-y^2}$ orbital ground state and $g_\parallel > g_\perp > 2.0023$ in a tetragonal environment. The compounds were evaluated for *in vitro* antimicrobial activity against *S. aureus*, *B. subtilis*, *E. coli*, and *C. albicans*. The copper complexes showed higher activity than the parent ligands against *S. aureus* and *B. subtilis*; the electron-donating OCH_3 and CH_3 derivatives were more active than the withdrawing Br- and Cl-substituted compounds.

1. Introduction

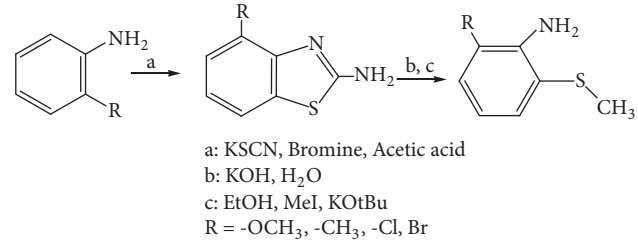
Thiomethylated anilines belong to a class of nitrogen-sulfur (SN) donor groups. They find application in preparation of sulfoxides [1] which are desulfurized to generate methylated anilines [2] and as starting materials [3] for deriving aminobenzaldehydes which are also useful precursors to many important heterocyclics. By coupling 2-(methylthioaniline) with another suitable aromatic polymer, a suitable chelating resin [4] has been derived for use in preconcentration of metal ions such as Cd, Hg, Ni, Co, Cu, and Zn for analytical purposes. Substituted 2-(methylthio)anilines were synthesized from the reaction of corresponding anilines with aliphatic disulfides in the presence of Lewis acid catalysts, particularly aluminum chloride and copper iodide at high temperatures of >100°C; mixtures of *ortho*- and *para*- substituted methylthiolated products resulted [5]. A two-pot synthetic route can also be used to generate substituted 2-(methylthio)anilines. By alkaline hydrolysis of the appropriate 2-aminobenzothiazoles at a high temperature and subsequent methylation with methyl iodide, the crude substituted 2-(methylthio)anilines were derived [6]. The biological relevance of Cu(I)/Cu(II) in living systems includes their presence as cuproproteins to transport molecular oxygen and acts as good catalysts in related oxidation-reduction processes. Substituted 6-(methylthio)aniline ligands are potential *SN* bidentate ligands of which bioactivity has not been investigated. The synthesis, NMR, FTIR, UV/Vis, EPR, molar conductance, magnetic measurements, and *in vitro* antimicrobial studies of *ortho*-substituted-6-(methylthio)anilines and their copper(II) complexes are reported in this study.

2. Materials and Methods

2.1. Materials and Physical Measurements. All the reagents and solvents were of analytical grade and used as obtained from commercial suppliers (Sigma Aldrich and Merck). CHNS analyses were determined on Elementar Analysensysteme varioMICRO V1.6.2. One- and two-dimensional NMR spectra (^{1}H, ^{13}C, DEPT135, COSY, HMBC, and HSQC) were obtained in $CDCl_3$ on a Bruker Avance 400 MHz NMR spectrometer. Chemical shifts were recorded in ppm with reference to the residual solvent proton relative to tetramethylsilane. Infrared spectra of the compounds were determined in the region 4000–400 cm^{-1} on PerkinElmer Spectrum 100 ATR-FTIR spectrometer. Far-infrared spectra for the complexes in the region 700–30 cm^{-1} were obtained as mulls held between polyethylene discs and recorded on Perkin Elmer Spectrum 400 FTIR/FIR spectrometer. The UV/Vis electronic spectra (250–1100 nm) were determined in DMF on a PerkinElmer Lambda 25 UV/VIS Spectrometer. The molar conductance was measured in DMF at room temperature on AZ® 86555 p^H/mV/Cond./TDS/Temp at 10^{-3} M. Magnetic susceptibility measurements were taken on a Sherwood magnetic susceptibility balance Mark 1. A Galenkemp melting point apparatus was used to determine the melting points (uncorrected). The powder electron paramagnetic resonance (EPR) spectra were recorded on a Bruker ESP 300E X-band EPR spectrometer with 100 kHz field modulation. Other experimental parameters: 9.762 GHz, 16.05 G modulation amplitude, 20 mW power, 1.25 ms time constant, and 100 s sweep time.

2.2. Synthesis of Substituted 2-(Methylthio)anilines. *Ortho*-substituted-2-(methylthio)anilines were prepared in a two-pot reaction involving the conversion of *o*-anisidine, *o*-toluidine, *o*-chloroaniline, and *o*-bromoaniline to the corresponding aminobenzothiazoles [7, 8] which were hydrolyzed and methylated to yield the crude products (Scheme 1) [6].

2.2.1. 2-Methoxy-6-(methylthio)aniline (L1). *o*-Anisidine (1.00 g, 8.11 mmol) and potassium thiocyanate (3.16 g, 32.50 mmol) were rapidly stirred in glacial acetic acid (16 mL) and bromine liquid (1.30 g, 8.11 mmol) was added dropwise. The mixture was stirred for 10 h keeping the temperature below 35°C, during which a precipitate was formed. This mixture was filtered and the precipitate washed with water. The combined filtrate was neutralized to pH 7 with aqueous ammonia solution during which a shiny brown precipitate formed and the mixture was filtered and dried (2.00 g). The crude 6-methoxy-2-aminobenzothiazole (0.54 g, 3.00 mmol) was slowly added to potassium hydroxide (1.54 g, 27.40 mmol) in 2 mL water. The mixture was slowly heated to 135°C allowing the water to evaporate. The temperature was then increased to 165°C and held there for 2 h. The reaction mixture was allowed to cool to room temperature and quenched with 2 mL of water. The mixture was filtered to remove the unreacted 2-aminobenzothiazole. The filtrate was collected and the water removed under vacuum. Iodomethane (0.19 mL, 3.00 mmol) and 4 mL ethanol were each added to the residue and the slurry was stirred for 16 h after which ethanol was removed *in vacuo*. The residue was dissolved in water, neutralized to pH 7 with concentrated HCl and the product extracted with dichloromethane. Removal of the solvent under pressure yielded crude 2-methoxy-2-(methylthio)aniline. This was purified by column chromatography on silica gel using hexane/ether (6:1 vol/vol) as eluent to afford the pure oil. Yield: 55%, mp 68-70°C. Colour: Brown. Anal. Calc. for $C_8H_{11}NS$ (M_r 169.2): C, 62.70; H, 7.24; N, 9.14; S, 20.92. Found: C, 61.97; H, 7.44; N, 9.02; S, 20.64%. FTIR (cm^{-1}): 3383, 3293 $\nu_{asy/sym}(NH_2)$, 1620 $\delta(NH_2)$, 1269 ν(C–N). UV λ_{max} (DMF, nm (ε, M^{-1} cm^{-1}): 284^{sh}, 308 (12240).



Scheme 1: Synthesis scheme for substituted 6-(methylthio)anilines.

Other 2-(methylthio)anilines were similarly prepared from their starting *ortho*-substituted anilines.

2.2.2. 2-Methyl-6-(methylthio)aniline (L2). Yield 24%, brown oil. Anal. Calc. for $C_8H_{11}NS$ (M_r 153.3): C, 62.70; H, 7.24; N, 9.14; S, 20.92. Found: C, 62.03; H, 7.99; N, 9.01; S, 20.91%. FTIR (cm^{-1}): 3452, 3355 $\nu_{asy/sym}(NH_2)$, 1619 $\delta(NH_2)$, 1279 ν(C–N). UV λ_{max} (DMF, nm (ε, M^{-1} cm^{-1}): 286^{sh}, 309 (11960).

2.2.3. 2-Chloro-6-(methylthio)aniline (L3). Yield 29%, brown oil. Anal. Calc. for C_7H_8ClNS (M_r 173.7): C, 48.41; H, 4.64; N, 8.07; S, 18.46. Found: C, 48.80; H, 4.81; N, 8.02; S, 18.39%. FTIR (cm^{-1}): 3459, 3358 $\nu_{asy/sym}(NH_2)$, 1615 $\delta(NH_2)$, 1292 ν(C–N). UV λ_{max} (DMF, nm (ε, M^{-1} cm^{-1}): 285^{sh}, 317 (9975).

2.2.4. 2-Bromo-6-(methylthio)aniline (L4). Yield 22%, light yellow oil. Anal. Cald. for C_7H_8BrNS (M_r 218.1): C, 38.55; H, 3.70; N, 6.42; S, 14.70. Found: C, 39.54; H, 3.71; N, 6.36; S, 14.76%. FTIR (cm^{-1}): 3455, 3354 $\nu_{asy/sym}(NH_2)$, 1611 $\delta(NH_2)$, 1290 ν(C–N). λ_{max} (DMF, nm (ε, M^{-1} cm^{-1}): 285^{sh}, 317 (9975).

2.2.5. Synthesis of [Cu(L1)Cl$_2$]. 2-Methoxy-6-(methylthio)aniline, L1 (0.14 g, 0.80 mmol) in 3 mL ethanol was stirred at room temperature and ethanol solution of $CuCl_2.2H_2O$ (0.14 g, 0.80 mmol) was added dropwise. The mixture was stirred for 3 h. The deep brown precipitate was obtained by filtration, washed with ethanol, and dried (0.08 g, 32%), mp >200°C. Anal. Calc. for $C_8H_{11}Cl_2CuNOS$ (M_r 303.7): C, 31.64; H, 3.65; N, 4.61; S, 10.56. Found: C, 31.72; H, 4.15; N, 4.50; S, 10.33%. FTIR-ATR (cm^{-1}): 3251, 3171 $\nu_{asy/sym}(NH_2)$, 1585 $\delta(NH_2)$, 1245 ν(C–N), 414 ν(Cu–N), 314 ν(Cu–Cl), 280 ν(Cu–S). UV-Vis λ_{max} (DMF, nm (ε, M^{-1} cm^{-1}): 275^{sh}, 315 (5805), 335 (3664), 454 (3400). μ_{eff} (BM) = 1.8. Λ (Ω^{-1} cm^2 mol^{-1}) = 33.4.

Table 1: ^{1}H and ^{13}C chemical shifts (δ) for substituted-6-(methylthio)aniline ligands in ppm.

Ligands	C*1*	C*2*	H, C*3*	H, C*4*	H, C*5*	H, C*6*	H, C*7*	H *8*	H, C*9*
(L1)	----	----	6.84 *d*	6.83 *t*	6.64 *d*	----	2.43 *s*	3.81 *s*	3.83 *s*
	134.90	125.46	115.04	122.45	112.29	147.17	18.80	----	55.36
(L2)	----	----	7.11 *d*	7.09 *t*	6.61 *d*	----	2.42 *s*	3.57 *s*	2.15 *s*
	143.20	122.84	128.33	115.25	131.77	125.12	18.55	----	17.04
(L3)	----	----	7.26 *d*	6.68 *t*	7.07 *d*	----	2.41 *s*	3.97 *s*	----
	141.32	119.41	129.06	116.16	130.05	126.58	18.42	----	----
(L4)	----	----	7.42 *d*	6.66 *t*	7.11 *d*	----	2.40 *s*	4.02 *s*	----
	142.55	126.91	129.89	115.97	133.18	109.31	18.57	----	----

s singlet; *d* doublet; *t* triplet.

$[Cu(L2)Cl_2]$, $[Cu(L3)Cl_2]$ and $[Cu(L4)Cl_2]$ were similarly prepared.

2.2.6. Synthesis of [Cu(L2)Cl$_2$]. $[Cu(L2)Cl_2]$ was obtained from 2-methyl-6-(methylthio)aniline, L2 (0.24 g, 0.80 mmol) and $CuCl_2.2H_2O$ (0.14 g, 0.80 mmol). Yield: 0.05 g (20%), mp 140-141°C. Colour: Black. Anal. Calc. for $C_8H_{11}Cl_2CuNOS$ (M_r 287.7): C, 35.40; H, 3.85; N, 4.87; S, 11.15. Found: C, 36.24; H, 3.76; N, 4.89; S, 10.24%. FTIR-ATR (cm^{-1}): 3313, 3199 $\nu_{asy/sym}(NH_2)$, 1576 $\delta(NH_2)$, 1250 ν(C–N), 406 ν(Cu–N), 290 ν(Cu–Cl), 279 ν(Cu–S). UV-Vis λ_{max} (DMF, nm (ε, M^{-1} cm^{-1}): 273^{sh}, 300 (5080), 336 (3360), 428 (2070). μ_{eff} (BM) = 1.9. Λ (Ω^{-1} cm^2 mol^{-1}) = 32.4.

2.2.7. Synthesis of [Cu(L3)Cl$_2$]. $[Cu(L3)Cl_2]$ was obtained from 2-chloro-6-(methylthio)aniline, L3 (0.14 g, 0.80 mmol) and $CuCl_2.2H_2O$ (0.14 g, 0.80 mmol). Yield: 0.06 g (24%), mp 150-152°C. Colour: Deep brown. Anal. Calc. for $C_7H_8Cl_3CuNS$ (M_r 308.1): C, 29.83; H, 3.13; N, 4.35; S, 9.95. Found: C, 29.54; H, 2.87; N, 4.32; S, 9.73%. FTIR-ATR 3340, 3199 $\nu_{asy/sym}(NH_2)$, 1576 $\delta(NH_2)$, 1271 ν(C–N), 406 ν(Cu–N), 301 ν(Cu–Cl), 278 ν(Cu–S). UV-Vis λ_{max} (DMF, nm (ε, M^{-1} cm^{-1}): 275^{sh}, 304 (5690), 333 (3280), 364 (5424), 413 (3335). μ_{eff} (BM) = 1.8. Λ (Ω^{-1} cm^2 mol^{-1}) = 29.2.

2.2.8. Synthesis of [Cu(L4)$_2$Cl$_2$]. $[Cu(L4)_2Cl_2]$ was obtained from 2-bromo-6-(methylthio)aniline, L4 (0.18 g, 0.80 mmol) and $CuCl_2.2H_2O$ (0.14 g, 0.80 mmol). Yield: 0.11 g (22%), mp 110-111°C. Colour: Black Anal. Cald. for $C_{14}H_{18}Br_2Cl_2CuN_2OS_2$ (M_r 588.7): C, 28.56; H, 3.08; N, 4.76; S, 10.89. Found: C, 28.95; H, 2.90; N, 4.78; S, 10.61%. FTIR-ATR (cm^{-1}): 3276, 3183 $\nu_{asy/sym}(NH_2)$, 1583 $\delta(NH_2)$, 1273 ν(C–N), 409 ν(Cu–N), 303 ν(Cu–Cl), 275 ν(Cu–S). UV-Vis λ_{max} (DMF, nm (ε, M^{-1} cm^{-1}): 281 (3210), 314 (3622), 332 (2430), 436 (370). μ_{eff} (BM) = 1.9. Λ (Ω^{-1} cm^2 mol^{-1}) = 28.3.

2.3. Antimicrobial Studies. The microorganism strains, growth media, and sterile assay disks (diameter 6 mm) were purchased from Microbiologics, Merck, Becton Dickinson and Company in South Africa. Ampicillin powder was obtained from Roche Diagnostics, Germany. Double-distilled water was collected from the Pharmaceutics Unit of Faculty of Pharmacy, Rhodes University. Sterile saline was prepared by dissolving 0.85 g saline in double-distilled water and making up to 100 mL. McFarland (0.5) solution was prepared by adding 0.5 mL of 1.175 % $BaCl_2.2H_2O$ to 99.5 mL of 1 % H_2SO_4 [9]. Agar disc diffusion method [10, 11] was employed to determine the susceptibility of *Staphylococcus aureus* ATCC 6538, *Bacillus subtilis (subsp. spizizenii)* ATCC 6633, *Escherichia coli* ATCC 8739, and for antifungal activity against *Candida albicans* ATCC 2091 to the synthesized compounds. Ampicillin (AMP) and ketoconazole (KTZ) were used as positive controls for the antibacterial and antifungal tests, respectively. The preparation of the growth media, reference drugs, agar plates, the culture of microbial strains, and inoculation of agar plates followed standard procedures [12, 13]. Each microbial inoculum was standardized with reference to 0.5 McFarland solution [14]. 250 μg of each test compounds dissolved in DMF was delivered on to sterile assay discs. Ampicillin and ketoconazole (125 μg) were measured onto separate discs and allowed to dry under the laminar flow. Six discs were placed on each inoculated agar plate containing the appropriate growth medium and incubated for 24 h (bacteria) and 60 h (fungus) at 35°C. The diameter of zone of inhibition of the microbial growth by each compound was measured. The tests were carried out in triplicate and the mean values were recorded in Table 3.

3. Results and Discussion

3.1. Synthesis and Properties. The ligands are soluble in common organic solvents and their copper(II) complexes are soluble in DMSO and DMF. The compounds were obtained in low to moderate yields and are stable in air. The experimental CHNS analyses corresponded with the calculated values; the complexes showed $CuLCl_2$ stoichiometry except the Br-substituted $Cu(L4)_2Cl_2$. The molar conductance measurements (DMF) were in the range 28.3–33.4 Ω^{-1} cm^2 mol^{-1}; thus the complexes behave as nonelectrolytes with the chlorine species covalently bound to the Cu(II) ions.

3.2. NMR Spectra of the Ligands. The atom labeling for ^{1}H and ^{13}C NMR shifts of the ligands have been recorded in Figure 1. The NMR resonances (Table 1) were assigned with the aid of DEPT135, COSY, HMBC, and HSQC spectra. The thiomethyl protons (-SCH_3) appear as singlet peaks

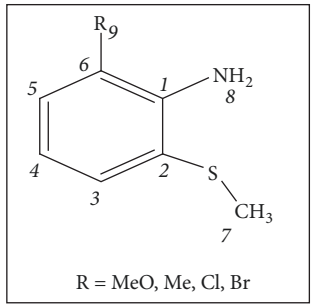


Figure 1: Atom labeling for ^{1}H and ^{13}C NMR chemical shifts.

absorbing between 2.40 and 2.43 ppm. The broad singlet peaks in the range 3.57–4.02 ppm were assigned to amine (-NH_2) protons. The aromatic protons appear as doublets and triplets in the downfield region 6.61–7.42 ppm. Additional single peaks at 3.83 and 2.15 ppm were observed in L1 and L2 due to –OCH_3 and –CH_3 proton resonances respectively. The methyl carbon (*C7*) resonated in the range 18.42–18.80 ppm and the aromatic carbon atoms have higher absorptions between 112.29 and 147.17 ppm. The methyl and methoxy carbon atoms of L1 and L2 resonated at 17.04 and 55.36 ppm, respectively. The electronic effect of substituents on the NMR shifts of amine protons as well as the *ortho* (*H3*) and *para* (*H5*) protons was observed. These protons were more deshielded in the derivatives with electron-withdrawing substituents (L3 and L4), resonating at higher frequencies compared to those of substituents L1 and L2. A similar shift was observed at the *para* carbon atom (*C3*) (Table 1).

3.3. IR Spectra. In the vibrational spectra of the ligands, the strong asymmetric and symmetric stretches due to νN–H of the primary amine group were observed within the ranges 3459–3383 and 3358–3293 cm^{-1}, respectively [7, 14, 15]. The frequencies of both bands were lowered in the complexes to 3340–3251 and 3199–3171 cm^{-1}, respectively. The reduced frequency of these stretches upon chelation has been interpreted to be the result of the electron density of the nitrogen being directed to the metal ion, leaving the amino protons less tightly bound to the nitrogen [16]. N–H scissor and νC–N which appeared as medium bands in the ligands in the ranges 1620–1611 and 1292–1269 cm^{-1} in the spectra of the ligands were shifted to 1585–1576 and 1273–1245 cm^{-1}, respectively, in the Cu(II) complexes. A shift to lower frequency of νC–N could be due to the decrease in the C–N double bond character. These reductions in frequencies upon chelation suggested the coordination of the ligands to the copper ion through the nitrogen lone pair [16]. The bands due to νC–S–C (~1100 cm^{-1}) and νC–S (~780–650 cm^{-1}) of the thioether group were not observed as they were too weak [17]. In the far IR region, new medium bands in the spectra of the complexes were observed and assigned as νCu–N (414–406 cm^{-1}), νCu–Cl (314–290 cm^{-1}), and νCu–S (280-275 cm^{-1}) [18].

3.4. Electronic Spectra and Magnetic Moments. The electronic spectra of the ligands include the intraligand $\pi \longrightarrow \pi*$ transitions in the range 284–286 nm which appear as shoulder bands. The more intense bands at 308–317 nm were assigned to $n \longrightarrow \pi*$ of the nitrogen lone pairs to the aromatic ring. In the spectra of the copper(II) complexes, $\pi \longrightarrow \pi*$ transitions were bathochromically shifted to 273–281 nm. Two intense bands around 300–364 nm were assigned to $n \longrightarrow \pi*$ transitions in the complexes. In the spectra of $[Cu(L1)Cl_2]$, $[Cu(L2)Cl_2]$ and $[Cu(L3)Cl_2]$, moderately intense bands at 413, 428, and 454 nm, respectively, were assigned to $^{2}B_{1g} \longrightarrow {}^{2}A_{1g}$ in a square planar geometry around the copper ion. The band at 436 nm in the spectrum of $[Cu(L4)_2Cl_2]$ was assigned to $^{2}E_g \longrightarrow {}^{2}T_{2g}$ transition in an octahedral geometry. The magnetic moments in the range 1.8–1.9 BM indicate the availability of an unpaired electron in the copper(II) complexes which are magnetically dilute.

Table 2: EPR parameters for copper(II) complexes.

Compound	$g_\perp$	$g_\parallel$
$[Cu(L1)Cl_2]$	2.108	2.293
$[Cu(L2)Cl_2]$	2.129	2.256
$[Cu(L3)Cl_2]$	2.052	2.142
$[Cu(L4)_2Cl_2]$	2.066	2.215

3.5. EPR Studies. The powdered EPR spectra of a series of 6-(methylthio)aniline copper(II) complexes, substituted with -OCH_3 $[Cu(L1)Cl_2]$, -CH_3 $[Cu(L2)Cl_2]$, -Cl $[Cu(L3)Cl_2]$, and –Br $[Cu(L4)_2Cl_2]$, are presented in Figure 2. The spectra consist of two g values ($g_\parallel$ and $g_\perp$) in the range 2.052–2.293 (Table 2). These values are typical of copper(II) coordination to electron-donating group (such as nitrogen) [19]. The relation $g_\parallel > g_\perp > g_o$ (g_o = 2.0023) observed in the EPR spectra of the copper(II) complexes is consistent with an elongated octahedral, square pyramidal or square planar geometry with $d_{x^2-y^2}$ orbital ground state [20, 21]. The spectra of the complexes display an axial signal with $g_\parallel \approx 2.2$ and $g_\perp \approx 2.0$, which has been associated with copper(II) square planar geometry [21–23]. The $g_\parallel < 2.3$ suggests the covalent character of the copper coordination to the ligand [24]. A square planar geometry is thus implied for $[Cu(L1)Cl_2]$, $[Cu(L2)Cl_2]$ and $[Cu(L3)Cl_2]$, and a distorted octahedral geometry is proposed for $Cu(L4)_2Cl_2]$ (Figure 3).

3.6. Antimicrobial Susceptibility Testing. The agar disc diffusion technique was used to assess the antimicrobial activity of the synthesized compounds using the sterile assay discs of diameter 6 mm. The results have been recorded in Table 3. The gram-positive *S. aureus* and *B. subtilis* were susceptible to the compounds and were inhibited by the measured diameters of 8–20 mm while the gram-negative *E coli* and the fungus *C. albicans* were resistant. The copper complexes with methoxy and methyl substituents demonstrated better activity than the compounds with the electron-withdrawing substituents, with the diameters of inhibition in the range 19–20 mm.

Table 3: Diameter of inhibition zones (mm) at 250 μg disc^{-1} of samples.

Compounds	*S. aureus*	*B. subtilis*	*E. coli*	*C. albicans*
L1	9	11	6	6
$[Cu(L1)Cl_2]$	20	19	6	6
L2	7	11	6	6
$[Cu(L2)Cl_2]$	19	20	6	6
L3	7	15	6	6
$[Cu(L3)Cl_2]$	9	10	6	7
L4	8	13	7	7
$[Cu(L4)Cl_2]$	9	14	6	7
DMF	6	6	6	6
AMP[a]	40	38	23	--
KTZ[a]	--	--	--	23

[a] 125 μg disc^{-1}.

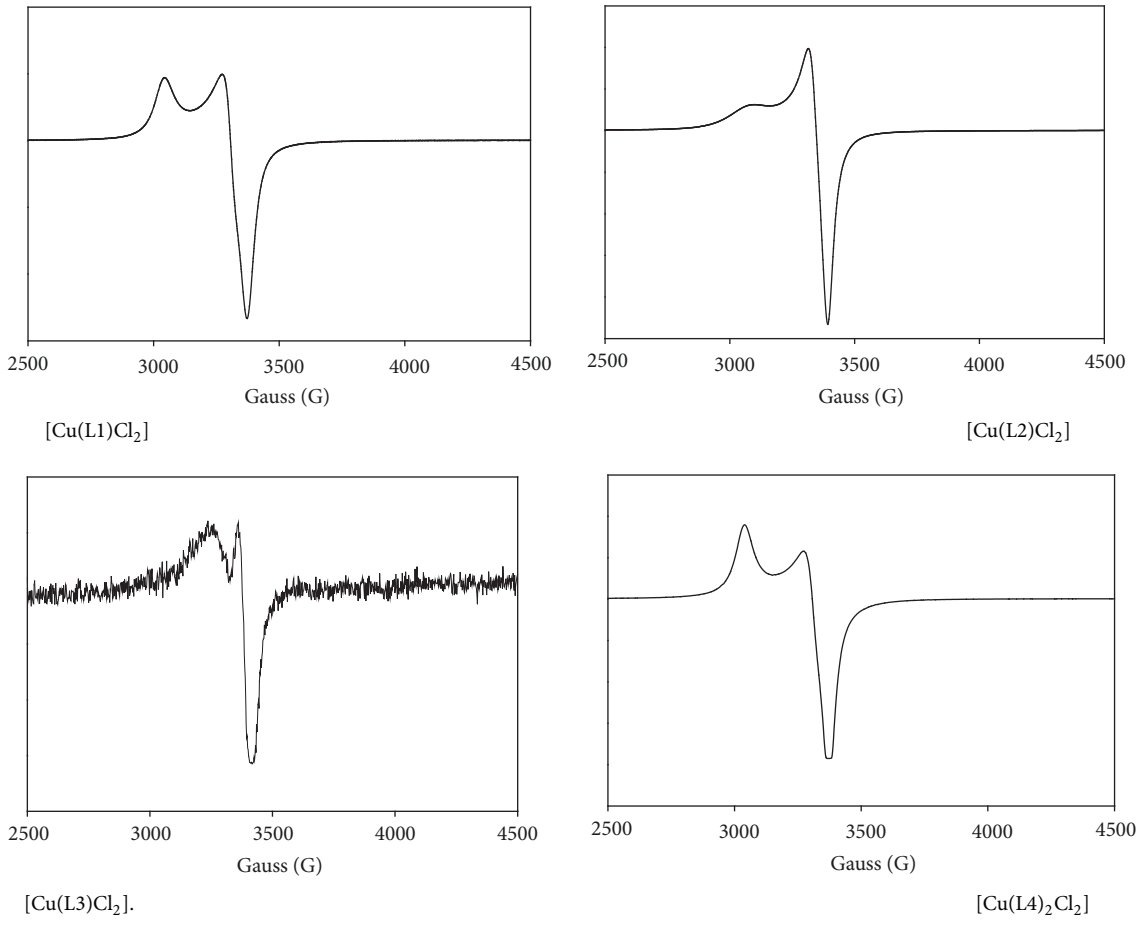


Figure 2: Powder EPR spectra of copper(II) complexes.

4. Conclusion

6-(Methylthio)aniline derivatives and their Cu(II) complexes were prepared. The compounds were characterized by elemental analysis and spectroscopic means. The CHNS analysis showed the metal complexes stoichiometry as $CuLCl_2$ and CuL_2Cl_2. The electronic nature of substituents affected the NMR shifts of some protons in the ligands. The infrared spectral bands were consistent with primary amine groups, of which frequencies reduced in the copper complexes upon chelation. The substituted 6-(methylthioanilines) behaved as bidentate ligands binding with SN-donor atoms to the copper(II) ions. Molar conductance values were indicative of nonelectrolytic complexes. The electronic and powder EPR

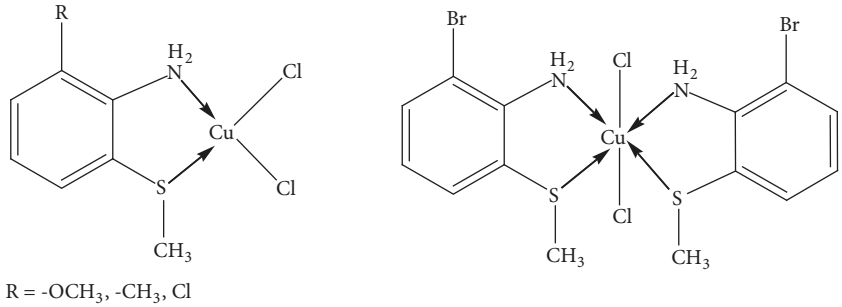


Figure 3: Proposed structures of copper(II) complexes.

spectra suggested a square planar geometry for $[Cu(L1)Cl_2]$, $[Cu(L2)Cl_2]$, and $[Cu(L3)Cl_2]$ and a distorted octahedral geometry for $[Cu(L4)_2Cl_2]$ (Figure 3). The evaluation of the synthesized compounds for *in vitro* antimicrobial activity against *S. aureus*, *B. subtilis*, *E. coli*, and *C. albicans* demonstrated that the copper complexes showed higher activity than the parent ligands against *S. aureus* and *B. subtilis*. The electron-donating OCH_3 and CH_3 derivatives were more active than the electron-withdrawing Br- and Cl-substituted compounds.

Data Availability

The data supplied in the manuscript are available and will be supplied when required.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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