**Copper(II) complexes of 2-(methylthiomethyl)anilines: Spectral, structural properties and *in vitro* antimicrobial activity**

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**Abstract**

Copper(II) complexes of 2-(methylthiomethyl)anilines (**1a**-**1f**) have been obtained and characterized by elemental analyses, IR, electronic spectra, conductivity and X-ray crystallography. The complexes (**2a**-**2f**) have the structural formula [CuCl2L] with the bidentate ligand coordinating through sulfur and nitrogen. The single crystal X-ray diffraction data reveal the copper complex (**2f**) has a tetragonally distorted octahedral structure with long Cu-Cl equatorial bonds. Magnetic susceptibility measurements indicate the availability of one unpaired electron in the complexes and the conductivity measurements in DMF show their behaviour as non electrolytes. The solid reflectance spectra and the electronic spectra of the complexes in DMSO were determined. The ligands and their copper complexes were screened for *in vitro* antimicrobial activity against *S. aureus*, *B. subtilis*, *E. coli* and *C. albicans*. The methoxy-substituted complex (**2c**) showed more promising antibacterial activity against *S. aureus* and *B. subtilis* than other compounds at the concentration tested.

*Keywords:* 2-(methylthiomethyl)anilines; Copper(II) complexes; electronic spectra; structural characterization; *in vitro* antimicrobial.

**1. Introduction**

The alkylthioalkylated anilines have found application as intermediates in production of many organic compounds [1–3] including dyes, rubber and herbicides [4]. They act as coordinating ligands due to the presence of the aniline nitrogen and the thioether sulfur in their moiety. The hard-borderline and soft nature of the nitrogen and sulfur respectively in alkylthioalkylated anilines permits the formation of stable complexes between them and metal ions under mild non-extreme reacting conditions. Donor groups commonly found in many known biologically active compounds and ligands used in pharmaceutical synthesis include the nitrogen, oxygen, sulfur and chlorine atoms. Such bio-potent organic compounds with their metal complexes are being explored for their activity against a wide range of microorganisms. Sulfur-containing ligands and complexes have been explored for biological activity and practical application [5–7]. Some metal complexes of SN ligands were investigated and reported. Copper(II) complexes CuX2(N-SMe) (X = Cl, Br) obtained from alcohol solution at 0oC were not very stable [8]. Ni(II) complexes of 2-methylthiomethylaniline [8] and 8-methylthioquinoline [9] have the composition NiX2(N-SMe)2 (X = Cl, Br [8]; X = Cl, Br, I, NCS [9]). The Pd(II) and Pt(II) complexes of these ligands, on being heated in dimethylformamide were S-demethylated to yield the thiolo-bridged complexes M2Cl2(N-S)2. Complexes MX2(N-SMe) and [M(N-SMe)2](ClO4)2 (M = Pd, Pt, Cu, Hg) were derived with 2-(2-methylthioethyl)pyridine [10] and 2-methylthiomethylpyridine [11]. The structural, spectroscopic as well as biological studies of alkylthioalkylated anilines and their copper complexes are less investigated in comparison to their sulfonamide analogues. Copper ions are biologically relevant in living systems as Cu(I)/Cu(II) cuproproteins which transport molecular oxygen and act as good catalysts in related oxidation-reduction processes. Here, the spectral, structural and antimicrobial properties of copper(II) complexes of 2-(methylthiomethyl)anilines are reported with the spectral property and antimicrobial activity of the complexes compared to their corresponding ligands.

**2. Materials and Methods**

*2.1. Materials and physical measurements*

The reagents and solvents used in the experimental procedures were of analytical grade and used without further purification. The elemental analysis was carried out on Elementar Analysensysteme varioMICRO V1.6.2 GmbH. 1H and 13C NMR spectra of the ligands were obtained in CDCl3 relative to the residual proton in the solvent on Bruker Avance 400 MHz NMR spectrometer. The mid-infrared spectra (400-4000 cm-1) were determined as solids on PerkinElmer Spectrum 100 ATR-FTIR spectrometer. Far-infrared spectra (30-700 cm‑1) were obtained in nujol mulls held between polyethene discs and recorded on Perkin Elmer Spectrum 400 FTIR/FIR spectrometer. The electronic spectra (250-1100 nm) of ligands and complexes were measured in DMF using PerkinElmer Lambda 25 UV/VIS Spectrometer. The solid reflectance spectra of the copper complexes (300-1500 nm) were obtained on Shimadzu UV-3100 UV-VIS-NIR Spectrometer. Conductivity measurements of the complexes were taken at room temperature on AZ® 86555 conductivity instrument. A Gouy balance was used to determine the room temperature magnetic moments of the powdered samples employing Hg(II) tetrathiocyanatocobaltate(II) as a calibrant and diamagnetic corrections were made from the Pascal's constants.

*2.2. Crystallographic measurements*

Crystallography data were collected at -73oC using a Bruker KAPPA APEX II diffractometer equipped with a graphite monochromator and a Molybdenum fine focus sealed x-ray tube as source of X-ray (Mo-*K*α radiation, *λ* = 0.71073 Å) and an Oxford Cryostream 700 system for sample temperature control. Bruker APEX II software was used for instrument control. The structures of the compounds were solved and refined using SHELXL–97 software package [12–14]. Numerical absorption corrections were done and all non hydrogen atoms were refined anisotropically. The positions and temperature parameters of the hydrogen atoms were fixed to the adjacent atoms. Diagrams and publication materials were generated using ORTEP [15]. Crystal size (mm), 0.06 x 0.06 x 0.17; chemical formula (per unit cell), C8H10Cl2CuN2O2S; formula weight, 332.68; sum formula per unit cell, C16H20Cl4Cu2N4O4S2; formula weight, 665.40; monoclinic;P21/c;unit cell parameters: *a* (Å) 5.5999(2), *b* (Å) 27.2688(9), *c* (Å) 7.6550(2), *α* (o) 90.00, *β* (o) 97.8850(10), *γ* (o) 90.00; *V* (Å3), 1157.89(6); Z, 4; *T* (K), 200(2); *D*calc (Mg/m3), 1.908; absorption coefficient (mm–1 ), 2.512; absorption correction (min., max.), 0.6705, 0.8721; *F* (000), 668; *θ* range for data collection (o), 2.79 – 27.99; limiting indices, -4 *≤ h ≤* 7*,* -36 *≤ k* ≤ 35*,* -10 *≤ l* ≤ 10; reflections collected, 11213; unique reflections (*R*int), 3530 (0.0232); completeness to *θ*,27.99 (99.9%); refinement method, full-matrix least-squares on *F*2; data/restraints/parameters, 2798/0/162; goodness-of-fit on *F*2, 1.080; final R indices [*I* > 2σ(*I*)], *R*1=0.0262, w*R*2 = 0.0576; *R* indices (all data), *R*1=0.0354, w*R*2 = 0.0601; largest difference in peak and hole (e A –3), 0.383 and -0.337.

*2.3. Antimicrobial susceptibility procedure*

The ligands (**1a-f**) and copper complexes (**2a-f**) were screened *in vitro* for their antibacterial activity against *Staphylococcus aureus* ATCC 6538*, Bacillus subtilis (subsp. spizizenii)* ATCC 6633*, Escherichia coli* ATCC 8739and for antifungal activity against *Candida albicans* ATCC 2091. Ampicillin (AMP) and ketoconazole (KTZ) were respectively used as positive controls for the antibacterial and antifungal tests. All the growth media (Mueller Hinton agar (MHA), agar bacteriological, potato dextrose agar (PDA) and nutrient broth) were prepared in double-distilled water according to standard procedure. Sterile saline was prepared by dissolving 0.85 g saline in double-distilled water and making up to 100 mL. McFarland solution (0.5 turbidity standard) was prepared by adding 0.5 ml of 1 % Barium chloride to 99.5 mL of 1 % sulphuric acid [16]. Agar disc diffusion method was employed to determine the susceptibility of the microorganisms to the test compounds [17-18]. The preparation of the agar plates, culturing of the microbial strains and the inoculation of the plates followed described procedure [19-20]. Each microbial inoculum was standardized by reference to 0.5McFarland turbidity standard [16]. Stock solutions (100 mg/mL) of Ampicillin and ketoconazole were also prepared and diluted to lower concentrations [20].

*2.3.1. Agar disc diffusion method*

The sterile assay disks were kept in sealed containers at 5oC and allowed to equilibrate to room temperature before use. The test compounds viz. ligands (**1a**-**2f**)and complexes (**2a**-**2f**) were dissolved in DMF. Known concentrations of test solutions were delivered on to sterile assay disks of 6 mm diameter each using a micro-pipette; the quantity taken was 250 µg per disc. 125 μg of Ampicillin and ketoconazole were measured on separate disks and allowed to dry under the laminar flow. Six disks were placed on each inoculated agar plate containing the appropriate growth medium and incubated for 24 h (bacteria) and 60 h (fungus) at 37oC. The diameter of zone of inhibition of the microbial growth by each compound was thereafter measured. The tests were carried out in triplicates and the mean values are recorded in Table 5.

*2.4. Synthesis of ligands and complexes*

The ligands, 4-R-2-(methylthiomethyl)anilines (**1a**-**1f)** were prepared according to reported procedure [2]. Appropriate aniline (10.7 mmol) and dimethyl sulfide (15.00 mmol) in dichloromethane were vigorously stirred at room temperature. *N*chlorosuccinimide (15.0 mmol) was added in small portions. The mixture was stirred for 10 min; triethylamine (15.0 mmol) was added and the mixture was heated at reflux for 12 h. The organic layer was extracted with 10% NaOH (25 mL) and dried over anhydrous magnesium sulfate. Solvent was removed *in vacuo* to give the crude which was purified by column chromatography on silica gel 60 (0.040–0.063 mm) using hexane: ether (4:1 vol/vol) as the eluent. Fractions were collected in test tubes in 30 mL portions and Rf value of each fraction was determined on TLC plate (Silica gel 60 F254). Fractions with similar Rf values were combined, dried *in* *vacuo* to remove the solvent and the NMR spectra obtained to identify the desired product. The crude products obtained were purified by column chromatography on silica gel 60 (0.040–0.063 mm) using hexane: ether (4:1 vol/vol)) as the eluents. Fractions were collected in test tubes in 30 mL portions and Rf value of each fraction was determined on TLC plate (pre-coated with silica gel 60 F254). Fractions with similar Rf values were combined, dried under vacuum to remove the solvent and the NMR spectra obtained to identify the desired product (Scheme 1).

The copper(II) complexes (**2a**-**2f**) were prepared by adding equimolar amounts of cupric chloride dihydrate (0.65 mmol) in ethanol (2 mL) to a stirred solution of the ligand (0.65 mmol) in ethanol or a mixture of ethanol/dichloromethane (2 mL). The mixture was further stirred for 1 h and the resulting solid precipitates were filtered off, washed with cold ethanol and dried under vacuum (Scheme 1).



Scheme 1.Synthesis of ligands (**1a**-**1f**) and copper complexes (**2a**-**2f**)

**3. Results and discussion**

The synthesis route for the copper complexes is shown in Scheme 1. The complexes are stable solids in air, with varying shades of green colouration and their structures were established from their elemental analyses, infrared and electronic spectra and X-ray crystallography. The results of the elemental analysis are in good agreement with the calculated values of 1:1 metal to ligand combination for the copper complexes. The complexes are completely soluble in DMF and DMSO, partially soluble in other polar solvents such as water, acetonitrile and methanol but are completely insoluble in non polar organic solvents. Low molar conductance values between 27.2 and 38.3 Ω–1 cm2 mol–1 obtained for the complexes in DMF indicates they are non-electrolytes [21] and the nature of chlorine to metal bonds can be described as coordinative. The summary of the analytical data and other physical properties of the complexes are recorded in Table 1.

Table 1

Analytical and physical data for ligands (**1a-1f**) and complexes (**2a**–**2f**)

|  |
| --- |
| Complexes Molecular Colour M. pt. % Found (calculated) Yield μeff*a* Molar conductance*b*formula (0C) C H N S % (B.M.) DMF DMSO |
| 2MT **1a** C8H11NS \_\_\_ oil 62.87 (62.70) 7.08 (7.23) 9.27 (9.14) 19.61 (20.92) 80  |
| 4Me–2MT **1b** C9H13NS Pale brown 65-66 63.12 (64.62) 7.87 (7.83) 8.09 (8.37) 18.11 (19.17) 69 |
| 4MeO–2MT **1c** C9H13NOS \_\_\_ oil 57.97 (58.98) 7.92 (7.15) 7.51 (7.64) 17.32 (17.50) 26 |
| 4Cl–2MT **1d** C8H10NSCl Pale brown 69-70 51.84 (51.19) 5.51 (5.37) 7.38 (7.46) 16.49 (17.08) 78 |
| 4Br–2MT **1e** C8H10NSBr Pale brown 68-69 41.25 (41.39) 4.22 (4.34) 5.89 (6.03) 13.42 (13.81) 62 |
| 4–NO2–2MT **1f** C8H10N2O2S Yellow 70-73 47.58 (47.39) 5.30 (5.22) 13.74 (13.82) 16.01 (15.82) 33 |
| CuCl2(2MT)] **2a***c* [Cu(C8H11NS)Cl2] Green 153-155 33.30 (33.40) 3.97 (3.85) 4.86 (4.87) 10.93 (11.15) 91 2.30 27.9 29.4[CuCl2(4Me–2MT)] **2b** [Cu(C9H13NS)Cl2] Brown 158-160 36.19 (35.83) 4.09 (4.34) 4.56 (4.64) 10.45 (10.63) 89 1.95 32.2 28.6[CuCl2(4MeO–2MT)] **2c** [Cu(C9H13NOS)Cl2] Brown 147-149 34.09 (34.02) 4.19 (4.12) 4.30 (4.41) 9.58 (10.09) 89 1.76 38.3 29.6[CuCl2(4Cl–2MT]) **2d***c* [Cu(C8H10ClNS)Cl2] Green 158-160 30.10 (29.83) 2.86 (3.13) 4.31 (4.35) 9.90 (9.95) 75 2.12 29.5 28.5[CuCl2(4Br–2MT)] **2e** [Cu(C8H10NSBr)Cl2] Green 170-172 26.35 (26.21) 2.41 (2.75) 3.86 (3.82) 8.38 (8.75) 79 2.21 28.5 32.9[CuCl2(4NO2–2MT)] **2f** [Cu(C8H10N2O2S)Cl2] Green 146-148 29.68 (28.88) 2.91 (3.03) 8.50 (8.42) 9.73 (9.64) 73 1.87 27.2 31.5 |

*a* Measured at room temperature, 298 K.

*b* Molar conductance of 10-3 M solution at 298 K, Ʌm values given in Ω–1 cm2 mol–1.

*c* Ref. [22].

*3.1. NMR spectra*

The NMR shifts for the protons and carbon atoms of the respective ligands are shown below (Scheme 2, Table 2). The protonNMR spectra of the ligands can be classified into three distinct classes, the thio-methyl (-CH3) and methylene (-CH2) protons appear as singlet peaks and resonate in the ranges 1.97-2.02 δ and 3.59-3.70 δ respectively. The broad singlet peaks found between 3.81 and 4.76 δ are due to amine (-NH2) protons and the peaks downfield in the region 6.58-7.96 δ which appear as multiplets are due to the aromatic protons. The ligands with the methyl or methoxy group shows additional singlet peak due to methyl (-CH3) protons at 2.25 δ or methoxy (-OCH3) protons at 3.73 δ.



Scheme 2.Labelling arrangement of 1H and 13C chemical shifts (δ) of ligands (**1a-1f**) in ppm

Table 2

1H and 13C chemical shifts (δ, ppm) of the ligands

|  |  |
| --- | --- |
| Ligands | (C)*1* (C)*2* H (C)*3* H (C)*4* H (C)*5* H (C)*6* H (C)*7* H (C)*8* H*9* H (C)*10* |
| 2MT | (144.96) (121.19)7.05 *d* (130.49) 6.76 *t* (117.96) 7.14 *t* (128.21) 6.71 *d* (116.15) 3.71 *s* (35.14)2.01 *s* (14.32)4.06 *s* ----------  |
| 4Me–2MT | (142.62) (121.61) 6.85 *s* (131.23) ------- (127.44) 6.93 *d* (128.98) 6.62 *d* (116.52) 3.67 *s* (35.48) 2.02 *s* (14.63) 3.95 *s* 2.25 *s* (35.60)  |
| 4MeO–2MT | (138.64) (123.71) 6.70 *d* (116.46) ------- (152.21) 6.64 *s* (113.45) 6.64 *d* (117.41) 3.64 *s* (35.48) 1.99 *s* (14.57) 3.81 *s* 3.73 *s* (55.56)  |
| 4Cl–2MT | (143.85) (122.84) 6.98 *s* (130.18) ------- (123.14) 7.04 *d* (128.23) 6.58 *d* (117.53) 3.59 *s* (35.20) 1.97 *s* (14.66) 4.07 *s* ----------  |
| 4Br–2MT | (144.24) (109.72) 7.13 *s* (132.83) ------ (123.47) 7.18 *d* (130.99) 6.60 *d* (117.82) 3.60 *s* (35.00) 1.98 *s* (14.57) 4.08 *s* ---------- |
| 4NO2–2MT | (151.60) (119.95) 7.96 *s* (126.68) ------- (138.42) 8.02 *d* (125.08) 6.67 *d* (114.76) 3.70 *s* (34.94) 2.00 *s* (14.57) 4.76 *s* ---------- |

*s* singlet *d* doublet *t* triplet

*3.2. Infrared spectra*

Selected infrared bands of the ligands and copper complexes are recorded in Table 2. The vibrational frequencies in the 2MT ligands (**1a-1f**) were characterized by those observed in primary amines [23]. The N–H symmetric and asymmetric stretches were found between 3320 and 3400 cm–1 respectively, NH2 scissor was in the range 1590-1600 cm–1 and C–N stretching frequency was seen around 1280 cm–1. The band expected from the thioether group due to C–S–C bend (around 1100 cm–1) and that due to C–S stretch between 650 and 780 cm–1 was not observed as they are weak bands and were masked by vibrations associated with the benzene ring [24]. There was no deprotonation of the amine hydrogen atoms upon complexation as two N–H stretches were observed, shifted to lower energies by 100-200 cm–1. The N–H bendswere similarly shifted to lower frequencies (cm-1) in the complexes. The shift to lower frequency of these vibrational modes after chelation is as a result of the electron density of the nitrogen being directed to the metal ion, leaving the amino protons less tightly bound to the nitrogen [25]. Copper to ligand vibrations were seen in the far infrared region; *v*Cu–N was observed in the range 425-450 cm-1 [26] and the vibrations due to Cu–Cl stretches consist of a mixture of medium and intense bands in the complexes between 268-365 cm-1 [27, 28]. In the crystal structure of complex (**2f**) below, the arrangement of the ligand atoms around the Cu2+ center includes two chloride ions, one of them terminally bonded while the other is linked to two other adjacent copper centres in a bridging mode. Frequencies between 268 and 303 cm-1 are assigned as *v*Cu–Cl for equatorial bonds [29]. Bands close to 320 cm–1 were assigned to Cu–S stretches [30].

Table 3

Selected IR bands and the electronic spectra of the ligands and complexes

|  |
| --- |
| Compound *v*(N–H) δNH2 *v*(C–N) *v*(Cu–L) (cm–1)Electronic spectra *a* λmax, nm (ε, mol–1 dm3 cm–1) |
| **L–H (1a)** 3424, 3352 1618 1272 259, 300 **2a** 3294, 3217 1609 1251 430, 398, 364, 327, 295, 274 259, 298, 322, 430, 925 Solid 353, 400, 706**L–CH3 (1b)** 3420, 3346 1625 1275 259, 306 **2b** 3276, 3221 1599 1259 446, 405, 335, 321, 294, 268 259, 303, 330, 430, 916  Solid 354, 450 , 754**L–OCH3 (1c)** 3409, 3341 1626 1293 259, 319, 360**2c**  3256, 3202 1617 1272 430, 364, 338, 303, 271 259, 286, 336, 447, 595, 885 Solid 352, 403, 479, 786**L–Cl (1d)** 3399, 3307 1625 1275 275, 316 **2d** 3261, 3221 1609 1244 439, 398, 322, 297, 272 261, 309, 335, 430,936  Solid 364, 405, 782**L–Br (1e)** 3398, 3317 1624 1275 272, 312 **2e** 3259, 3219 1607 1244 437, 393, 341, 322, 293, 281 262, 308, 333, 430,920 Solid 348, 425, 795**L–NO2 (1f)** 3450, 3347 1639 1278 258,295, 392**2f** 3267, 3222 1620 1250 425, 380, 365, 323, 294, 271 263, 301, 381, 399, 428, 925 Solid 367, 450, 765 |

*a* In DMSO.

*b* CT- charge transfer.

*3.3. The crystallographic structure of [Cu(4NO2-2MT)] (****2f****)*

A single crystal of (**2f**) was grown by the slow evaporation of a mixture of DMSO/EtOH solution (2:1 vol/vol). The atom numbering scheme, the selected bond distances and angles are listed in Table 3. The four corners of the square plane of (**2f**) are occupied by the aniline nitrogen (N1), thioether sulfur (S1) and two chloride ions (Cl1, Cl2) which have *cis* arrangement to each other. One chlorido ligand (Cl1) is terminally bonded while the other (Cl2) is bonded to two other copper ions in adjacent molecules as a bridging ligand giving rise to an octahedral arrangement around each copper center. Hence the complex has a monomer formula of CuLCl2 (where L is the ligand) and the ORTEP drawing is shown in Figure 1. The presence of chloride bridges between the adjacent molecules results in a ‘ladder-like’ polymeric structure seen in Figure 2. The bond distances for Cu1–N1 and Cu1–S1 which are 2.075(18) and 2.321(6) Å respectively fall within the expected ranges [31, 32]and the Cu1–S1 distance is typical of equatorially bound thioether sulfur [33-40]. Cu–Cl lengths are observed at 2.255(6) Å (Cu1–Cl1 terminal bond), 2.318(5) Å (Cu1–Cl2 in the basal bond), 2.690(5) Å (Cu1–Cl2 bridging bond) and 2.932(5) Å (Cu1–Cl2 bridging bond). The longer distances observed for Cu1-Cl2 bonds are within the acceptable range for Cu–Cl distances for axial bonds in previously reported copper(II) octahedral compounds [32, 41–43]. The Cu–Cu distance of 3.532 Å is normal for distorted octahedral structures [25]. The bond angles for the basal ligands *trans* to each other are 176.82o and 163.90o for N1–Cu1–Cl1 and S1–Cu1–Cl2 respectively. L(basal)–Cu–L(apical) angles which are ideally 90o range from 85.39o to 105.45o, the greater deviation being from S1-Cu1-Cl2 bond angle.



FIG. 1 Monomer unit of [CuCl2(4NO2–2MT)] **2f**. Ellipsoids drawn at 50% probability and hydrogen atoms are omitted for clarity



FIG. 2 Ladder-like polymeric octahedral structure of [CuCl2(4NO2–2MT)] **2f**. *C*, grey; *Cl*, green; *Cu*, wine; *N*, blue; *O*, red; *S*, yellow.

Table 4

Selected bond lengths [Å] and angles [°] for [CuCl2(4NO2-2MT)] (**2f**)

|  |
| --- |
| Cu1–N1 2.0750(18) Cu1–S1 2.3214(6)Cu1–Cl1 2.2554(6) Cu1–Cl2\* 2.3184(5)Cu1–Cl2\*\* 2.6902(5) Cl2–Cu1\*\*\* 2.9321(5)S1–C8 1.798(2) S1–C7 1.817(2)N1–C1 1.434(3) C4–N2 1.464(3)N2–O2 1.203(3) N2–O1 1.212(3) N1–Cu1–Cl1 176.82(5) Cl2–Cu1–S1 163.90(2) S1–Cu1–Cl2 105.455(19) N1–Cu1–Cl2 85.39(6) N1–Cu1–Cl2 88.60(5) Cl1–Cu1–Cl2 93.19(2) Cl1–Cu1–Cl2 94.27(2) Cl2–Cu1–Cl2 90.625(17) N1–Cu1–S1 91.93(5) Cl1–Cu1–S1 85.69(2) Cu1–Cl2–Cu1 89.376(17) C8–S1–C7 102.40(11)C8–S1–Cu1 105.25(9) C7–S1–Cu1 104.90(7)C1–N1–Cu1 118.59(13) O2–N2–O1 122.3(2)O2–N2–C4 118.5(2) O1–N2–C4 119.2(2) |

\* x, y, z; \*\* 1 – x, -y, 1 – z; \*\*\* –x, -y, 1 – z

*3.4. Magnetic moment and electronic spectra*

The magnetic moments of copper(II) complexes (**2a-2f**) are recorded in Table 1. The magnetic moments between 1.76 and 2.30 B. M. obtained for the complexes suggest the presence of one electron in the d9 copper(II) configuration. The increase from the spin-only value of 1.73 B. M could be due to spin orbit coupling or orbital contribution from the unpaired electron in the ground state [44]. The electronic spectra of the ligands and copper(II) complexes in DMSO are recorded in Table 2. The spectra of the ligands (**1a**-**1f**) consist of two high energy bands found in the range 250-320 nm arising from π → π\* transitions of the phenyl ring, the ligands (**1c**) and (**1f**) show an additional band close to 360 and 390 nm respectively due to intra ligand charge transitions of their methoxy and nitro groups. The electronic spectra of the copper(II) complexes in DMSO similarly show the π → π\* transitions which are slightly shifted to shorter wavelengths as a result of decrease in conjugation of the system after complexation. Ligand to metal charge transfer transitions are observed; the band in the region 320-390 nm is assigned as N→Cu while that between 400 and 450 nm is associated with S(σ)→Cu [25]. In the solid reflectance spectra of the complexes in Figure 3 (left), two high energy bands due to charge transfer transitions are found near 350 and 400 nm while the broad band in the range 700-800 nm is assigned to d→d transition [25]. The description of the d→d band of the complexes changes in DMSO (Figure 3, right) and a broad low-energy band is observed in the near-infrared between 880 and 920 nm. The shift to lower energies, by approximately 100 nm, is indicative of geometry change in the complexes as a result of probable coordination of DMSO to copper(II). From the crystal structure, the Cu-Cl distance in the bridging bonds is long and could imply a possible replacement of the axial binding site through the bridging chlorido ligand by the high coordinating DMSO molecule. Previous studies on electronic spectra of similar copper(II) complexes in DMF suggested the coordination of the solvent molecule to the metal ion resulting in distorted octahedral or tetragonal structures [18]. The large bandwidth in the electronic spectra can be attributed to Jahn-Teller distortion which is commonly observed in octahedral Cu(II) complexes.

 

FIG. 3 Solid reflectance spectra of **2a**–**2f** (left), complex **2a** compared with its solution spectrum in DMSO (right)

*3.5. Antimicrobial susceptibility testing*

The results for the disc diffusion susceptibility tests recorded in Table 4 shows the inhibitory activity of each ligand was improved upon chelation to copper ion. The higher activity of the complexes could be due to the increased lipophilicity conferred on the complex by the copper ion. It was also observed that the pure metal salt solution has an inhibitory effect on the microbial growth and it shows a measure of biological activity. In this study, the gram-positive bacteria were more susceptible to the test compounds than the gram-negative *E. coli* and the fungus *C. albicans*. Among the ligands and complexes screened, those with electron donating groups are seen to inhibit the microbial growth better than the electron withdrawing groups. The compounds with the methoxy moiety (**1c**) and (**2c**) demonstrate more inhibitory activity than other compounds, (**2b**) with a methyl group shows a similar though less pronounced activity.

Table 5

Agar disk diffusion test of compounds against microbial strains

|  |
| --- |
| Compound Diameter of zones*a* of inhibition (mm)  *B. subtilis S. aureus E. coli C. albicans*  |
| **1a** 7 8 NI*b*NI**2a** 14 10 7 9 **1b**8 8 7 NI **2b** 13 10 8 9 **1c** 12 13 7 NI **2c** 18 20 7 13 **1d** 8 8 7 NI **2d** 9 8 7 10 **1e** 9 8 7 NI **2e** 9 9 7 11 **1f** 9 7 7 NI **2f** 1087 NI AMP 125 μg/disk 40 38 23 ---KTZ 125 μg/disk --- --- --- 23CuCl2.2H2O 8 8 7 8DMF 6 6 6 6 |

*a* 250 µg disc-1 sample concentration, disc diameter 6 mm.

*b* NI - No inhibition.

**4. Conclusion**

The copper(II) complexes (**2a**-**2f**) formed in a 1:1 ligand to metal reaction stoichiometry and were characterized by the elemental analysis, IR and X-ray crystallography. A change in the structure of the complexes in the solid state is suspected as a result of the coordination of DMSO to the copper(II). Screening of the ligands and their copper complexes for *in vitro* antimicrobial activity against *S. aureus, B. subtilis, E. coli* and *C. albicans* was carried out using agar disk diffusion as well as micro-broth dilution techniques. The methoxy complex (**2c**) showed promising antibacterial activityagainst *S. aureus* and *B. subtilis* while *E. coli* was not susceptible to any of the compounds at the concentration tested.

**5.** **Supplementary material**

CCDC 888074 contains the supplementary crystallographic data for compound [CuCl2(4NO2-2MT)] (**2f**). Copies of these data can be obtained free of charge from the Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

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**Conflicts of Interests**

The authors declare that there is no conflict of interests.

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