Med Chem Res (2013) 22:2051–2060
DOI 10.1007/s00044-012-0171-2

MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Synthesis, characterization, and antimicrobial activity of copper(II) complexes with *N*,*N*′-propanediyl-bis-benzenesulfonamide and *N*,*N*′-ethanediyl-bis-2-methylbenzenesulfonamide

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Received: 6 February 2012 / Accepted: 28 June 2012 / Published online: 14 September 2012

Abstract Copper(II) complexes of new aryldisulfonamides ($\mathbf{L_1}$ = *N*,*N*′-bis[(2-methylphenyl)sulfonyl]ethylenediamine) and $\mathbf{L_2}$ = *N*,*N*′-propanediyl-bis-benzenesulfonamide with 1,10-phenanthroline have been synthesized and characterized by using elemental analyses, FT-IR, LCMS, conductivity, and magnetic susceptibility techniques. The structures of $[Cu(phen)_2]L_1$ (**1**) and $[CuL_2(phen)_2]$ (**2**) compounds have been determined. Complex (**1**) has also been characterized by single crystal X-ray diffraction. The complex (**1**) crystallizes in the triclinic system, space group *P*1, with cell constants $a = 12.9353(8)$ Å, $b = 13.8543(9)$ Å, $c = 14.4513(10)$ Å, $\alpha = 103.593(5)°$, $\beta = 113.713(5)°$, $\gamma = 106.104(5)°$, and $Z = 1$. The antibacterial activities of synthesized compounds were studied against Gram-positive bacteria: *Staphylococcus aureus*, *Bacillus subtilis*, and *B. cereus* and Gram-negative bacteria: *Escherichia coli*, *Pseudomonas aeruginosa*, and *Yersinia enterocolitica* by microdilution (as MICs in μg/mL) and disk diffusion (as diameter zone in mm) method. The biological activity screening showed that (**1**) has more activity than (**2**) against the tested bacteria.

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Keywords Sulfonamide Cu(II) complexes · Antimicrobial activity · Disk diffusion method · MICs

Introduction

The importance of sulfonamide was realized (Domagk, 1935) when sulfonylamide, a key analog of sulfonamide, was reported (Mandell *et al.*, 1996) to be the first antibacterial drug. Sulfonamides were the first effective chemotherapeutic agents used systematically for the prevention and the cure of bacterial infections in humans and other animal systems (Bult, 1983; Nogrady, 1988). Many thousands of molecules containing the sulfanilamide structure have been created since its discovery, yielding improved formulations with greater effectiveness and less toxicity. Sulfa drugs are still widely used for conditions such as acne and urinary tract infections, and are receiving renewed interest for the treatment of infections caused by bacteria resistant to other antibiotics. Also, a number of other activities, some of which have been recently observed, include endotelin antagonism, anti-inflammatory activity, tubular transport inhibition, insulin release, carbonic anhydrase, and saluretic action, among others (Wolff, 1996).

To find better compounds, some metal sulfonamides have attracted much attention due to the fact that complexes showed more activity than both free ligands and the corresponding metallic salts. In particular, Ag-sulfadiazine has proved to be an effective topical antimicrobial agent of significance in burn therapy, and better than the free ligand or $AgNO_3$ (Reynolds, 1996). Moreover, several Cu(II), Ce(III), Bi(III), Cd(II), and Hg(II) sulfonamide complexes have shown antibacterial activity (Bult, 1983; Casanova *et al.*, 1994; Chohan et al., 2005). In particular, a series of

copper complexes with heterocyclic sulfonamides was studied and a plausible explanation in terms of their activities was presented (Kremer *et al.*, 2006).

In our previous studies, aliphatic/aromatic bis sulfonamides were synthesized and tested for antimicrobial activity (Alyar and Karacan, 2009; Ozbek *et al.*, 2007a, b; Alyar *et al.*, 2007). Also, we have reported conformational analysis and the vibrational spectroscopic investigation of methanesulfonic acid hydrazide (Ienco *et al.*, 1999), methanesulfonic acid 1-methylhydrazide (Ozbek *et al.*, 2009a, b), and some methanesulfonyl hydrazone derivatives (Dodoff *et al.*, 1999; Ozbek *et al.*, 2009a, b; Alyar *et al.*, 2008). In this study, copper(II) complexes of *N*,*N*′-ethanediyl-bis-2-methylbenzenesulfonamide and *N*,*N*′-propanediyl-bis-benzenesulfonamide were synthesized, characterized by elemental analyses, FT-IR, LC–MS spectrometric methods, magnetic susceptibility, conductivity measurements, and the X-ray crystallography method for complex (**1**). These ligands were obtained and characterized as previously reported (Alyar *et al.*, 2011). The antibacterial activities of synthesized compounds were studied against Gram-positive bacteria: *Staphylococcus aureus*, *Bacillus subtilis*, and *B. cereus* and Gram-negative bacteria: *Escherichia coli*, *Pseudomonas aeruginosa*, and *Yersinia enterocolitica* by the microdilution method (as MICs) and disk diffusion method.

Experimental

Physical measurements

The elemental analyses (C, H, N, and S) were performed on a LECO CHNS 9320 type elemental analyzer. The IR spectra (4,000–400/cm) were recorded on a Mattson 1000 FT-IR Spectrophotometer with samples prepared as KBr pellets. LC/MS-APCl was recorded on an AGILENT 1100 Spectrometer. The melting points were measured using an Opti Melt apparatus. TLC was conducted on 0.25-mm silica gel plates (60F 254, Merck). The molar magnetic susceptibilities were measured on powdered samples using Gouy method. The molar conductance measurements were carried out using a Siemens WPA CM 35 conductometer. All solvents purchased from Merck and reagents were obtained from Aldrich Chem. Co. (ACS grade) and used as received. The experiments were carried out in a dynamic nitrogen atmosphere (20 mL/min) with a heating rate of 10 °C/min in the temperature range 30–400 °C using platinum crucibles. The microdilution broth method was used to determine the antibacterial activity of compounds against the bacteria: *E. coli* ATCC 35218, *P. aeruginosa* ATCC 27853, and *Y. enterocolitica* 0:3, *S. aureus* ATCC 25923, *B. subtilis* ATCC 6633, and *B. cereus* RSKK 709.

X-ray structure determination

The crystal structure of the title molecule was mounted on the goniometer of an STOE IPDS 2 diffractometer with graphite monochromatized Mo Kα radiation ($k = 0.71073$ Å). Data collection, reduction, and corrections for absorption and decomposition were achieved using X-AREA, X-RED software (Stoe and Cie, 2002). The structure was solved by SHELXS-97 and refined with SHELXL-97 (Sheldrick, 1997a, b). The positions of the H atoms bonded to C atoms were calculated (C–H distance 0.96 Å) and refined using a riding model. The H atom displacement parameters were restricted to be 1.2 Ueq of the parent atom.

The complex (**1**) crystallizes in the triclinic system, space group *P*1, with cell constants $a = 12.9353(8)$ Å, $b = 13.8543(9)$ Å, $c = 14.4513(10)$ Å, $\alpha = 103.593(5)°$, $\beta = 113.713(5)°$, $\gamma = 106.104(5)°$, and $Z = 1$. Details of the X-ray data collection, structure solution, and structure refinements are given in Table 1. Selected bond distances and angles are listed in Table 2. The molecular structure with the atom-numbering scheme is shown in Fig. 1.

Synthesis of the complexes

Synthesis of [Cu(phen)$_2$]L$_1$ complex

0.5 mmol of $\mathbf{L_1}$ was added to a solution of 0.5 mmol of Cu(II) acetate in 40 mL of acetonitrile. The mixture was stirred for 3–4 h. Then, 1 mmol of 1,10-phenanthroline was added. The compound precipitated slowly to a blue-green solid when the mixture was warmed. The product was filtered off, dried, and recrystallized from CH_2CI_2/*n*-hexane. Single crystals were obtained after 1 month from the resulting slow evaporation. Data for complex (yield 70 %). mp 338–340 °C APCI-MS (100 eV) *m*/*z*: 775.12 (M^+, 12 %; M+1, 5.6 %); Anal. Calcd. for $C_{40}H_{34}N_6O_4S_2Cu$: C, 56.99; H, 3.58; N, 10.61; S, 10.61. Found: C, 59.75; H, 4.18; N, 12.61; S, 6.19.

Synthesis of [CuL$_2$(phen)$_2$] complex

0.5 mmol of $\mathbf{L_2}$ was added to a solution of 0.5 mmol of Cu(II) acetate in 40 mL of acetonitrile. The mixture was stirred for 3–4 h. Then, 1 mmol of 1,10-phenanthroline was added. The resulting solution was heated at 50 °C for 15 min. The compound precipitated quickly to a blue solid after stirring the mixture at room temperature. The product was filtered off, dried, and recrystallized from CH_2CI_2/*n*-hexane. Slow evaporation of this filtrate produces prismatic blue crystals. Data for complex (yield 70 %). mp 352–354 °C APCI-MS (100 eV) *m*/*z*: 790.41 (M^+, 12 %; M^+1, 4.6 %); Anal. Calcd. for $C_{39}H_{32}N_6O_4S_2Cu$: C, 65.62;

Table 1 Summary of crystal parameters, data collection, and refinement for the complex (**1**)

Color/shape	Blue/prism
Chemical formula	$C_{40}H_{34}N_6O_4S_2Cu$
Formula weight	789.38
Crystal system	Triclinic
Space group	*P*1
Unit cell dimensions	$a = 12.9353(8)$ Å
	$b = 13.8543(9)$ Å
	$c = 14.4513(10)$ Å
	$\alpha = 103.593(5)°$
	$\beta = 113.713(5)°$
	$\gamma = 106.104(5)°$
Volume	2093.8(2) Å^3
Formula *Z*	2
Density (calculated)	1.252 M/gm^3
Extinction coeff.	0.0012(5)
Absorption coefficient	0.666/mm
T_{min}, T_{max}	0.6945, 0.7735
F_{000}	816
h_{min}, h_{max}	−16, 16
k_{min}, k_{max}	−18, 17
l_{min}, l_{max}	−18, 18
R(int)	0.0304
Diffractometer/meas. meth	STOE IPDS 2/ω-scan
Unique reflections measured	9,648
Observed reflections	8,018
Data/parameters	9,648/543
Goodness of fit on F^2	1.06
R indices $[I > 2\sigma(I)]$	$R_1 = 0.045$, $wR_2 = 0.115$
Weighting scheme	$w = 1/[\sigma\ (F_0^2) + (0.0522P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$

H, 4.80; N, 11.95; S, 11.95. Found: C, 65.50; H, 4.76; N, 11.78; S, 7.95.

Procedure for antibacterial activity

Disk diffusion method (in vitro)

E. coli ATCC 35218, *P. aeruginosa* ATCC 27853, and *Y. enterocolitica* 0:3, *S. aureus* ATCC 25923, *B. subtilis* ATCC 6633, and *B. cereus* RSKK 709 cultures were obtained from the Department of Biology at Gazi University and the Refik Saydam Hygiene Center Culture Collection. Bacterial strains were cultured overnight at 37 °C in a nutrient broth. These stock cultures were stored in the dark at 4 °C during the survey. The compounds were screened in vitro for their antibacterial activity against three Gram-negative (*E. coli*, *P. aeruginosa*, and *Y. enterocolitica*) and three Gram-positive species (*S. aureus*,

Table 2 Some selected bond lengths (Å) and bond angles for complex (**1**)

The bond lengths (Å)	
Cu(1)–N(3)	1.9881
Cu(1)–N(2)	1.994
Cu(1)–N(1)	2.107
Cu(1)–N(4)	2.150
N(3)–C(22)	1.329
N(3)–C(23)	1.359
N(2)–C(10)	1.334
N(2)–C(11)	1.361
N(4)–C(13)	1.323
N(4)–C(24)	1.358
N(1)–C(1)	1.329
N(1)–C(12)	1.359
S(2)–O(2)	1.431
S(2)–O(2)	1.431
S(2)–C(27)	1.779
S(4)–O(3)	1.425
S(4)–O(4)	1.426
S(4)–N(5)	1.589
S(4)–C(34)	1.772
N(6)–C(26)	1.456
N(6)–H(56)	0.77
C(26)–C(25)	1.408
The bond angles (°)	
N(3)–Cu(1)–N(1)	93.55
N(3)–Cu(1)–N(2)	171.11
N(3)–Cu(1)–N(4)	80.50
N(2)–Cu(1)–N(4)	94.14
N(2)–Cu(1)–N(1)	80.82
C(22)–N(3)–Cu(1)	126.28
C(23)–N(3)–Cu(1)	115.04
C(10)–N(2)–Cu(1)	126.98
C(11)–N(2)–Cu(1)	114.42
C(13)–N(4)–Cu(1)	132.36
C(24)–N(4)–Cu(1)	110.04
C(1)–N(1)–Cu(1)	131.0
C(12)–N(1)–Cu(1)	110.92
O(2)–S(2)–O(1)	118.92
O(2)–S2–N6	107.59
O(2)–S(2)–C(27)	107.62
O(1)–S(2)–N(6)	107.05
O(1)–S(2)–C(27)	106.66
O(3)–S(4)–O(4)	117.30
O(3)–S(4)–N(5)	106.91
O(3)–S(4)–C(34)	108.06
O(4)–S(4)–N(5)	109.33
O(4)–S(4)–C(34)	107.25
N(6)–S(2)–C(27)	108.69
N(5)–S(4)–C(34)	107.65

Table 2 continued

C(25)–C(26)–N(6)	116.5
C(25)–C(26)–H(26B)	108.2
N(6)–C(26)–H(26A)	108.2
H(26A)–C(26)–H(26B)	107.3
N(5)–C(25)–H(25A)	108.3
C(26)–C(25)–H(25B)	108.3
N(5)–C(25)–H(25B)	108.3

B. subtilis, and *B. cereus*) of bacterial strains by the agar-well diffusion method (Rahman *et al.*, 2001; Chohan, 2004). The synthesized compounds were dissolved in dimethylsulfoxide (10 %) to a final concentration of 4 mg/mL and sterilized by filtration by 0.45 μm Millipore filters. Two to eight hours old bacterial inocula containing approximately 10^4–10^6 colony forming units (CFU/mL) were spread on the surface of the nutrient agar using the help of a sterile cotton swab. The paper disks impregnated with the test compounds and complexes (70 μg) were placed on the solidified medium. The plates were incubated immediately at 37 °C for 24 h. The activity was determined by measuring the diameter of zones showing complete inhibition (mm). Ciprofloxacin (5 μg/disk), ampicillin (10 μg/disk), and penicillin (10 U) were chosen as a standard for the antibacterial activity measurements (positive control). To clarify any participating role of DMSO in the biological screening, separate studies were carried out with the solutions alone of DMSO and they showed no activity against any bacterial strains. Percentage of inhibition by comparing distance of the compounds to the positive control using (ciprofloxacin) the equation below (Mulaudzi *et al.*, 2011):

$$\%\text{inhibition} = \left[\frac{\text{diameter of the sample}}{\text{diameter of the positive control}}\right] * 100.$$

Microdilution assays

All tests were performed in a nutrient broth supplemented with DMSO to a final concentration of 10 % (v/v) to enhance their solubility. Test strains were suspended in the nutrient broth by adjusting to the 0.5 McFarland standards. The compounds to be tested were dissolved in DMSO to give the highest concentration (400 μg/mL), and serial dilutions thereafter in sterile 10-mL test tubes containing nutrient broth to achieve sample concentrations in the range of 40–400 μg/mL. The minimum inhibitory concentration (MIC) values of compounds were determined using a modification of the microwell dilution assay method. A total of 96-well plates were prepared by dispensing 95 μL of nutrient broth and 5 μL of the inoculums into each well. 100 μL from test compounds initially prepared at 400 μg/mL concentration were added to the first wells. Then, 100 μL from the serial dilutions was transferred into 14 consecutive wells. The contents of the wells were mixed and the microplates were incubated at 37 °C for 24 h. The compounds were tested against each microorganism twice. The MIC values were determined from visual examinations as the lowest concentration of the extracts in the wells with no bacterial growth (Koneman *et al.*, 1997; Gündüzalp Balaban *et al.*, 2011).

Results and discussion

Structure of the complexes

An ORTEP diagram of (**1**) is presented in Fig. 1. In $[Cu(phen)_2]^{2+}$ cationic complex, the copper atom is located on a twofold axis and is tetracoordinated by the four nitrogen atoms of two bidentate 1,10-phenanthroline molecules. The equatorial Cu–N distances of 1.990 and 2.11 Å are similar to those determined for related copper complexes involving sulfonamides, for example, 1.992(2) Å in square planar bis[4-methyl-*N*-(2-pyridin-2-ylethyl) benzenesulfonamide]copper(II) (Duran *et al.*, 1997). The angles between the nitrogen atoms and the copper atom is N3–Cu1–N1 = (93.55)°, N2–Cu1–N4 = (94.14)°, N3–Cu1–N4 = (80.50)°, N2–Cu1°N1 = (80.82)°. Unusually, the sulfonamidate anions are not coordinated to copper(II). The sulfonamide derivative ($\mathbf{L_1}$) does not interact with the metal ion and behaves as a counter-ion in complex (**1**). A lot number of Cu(II) complexes of related N-substituted sulfonamides have been reported (Ferrer *et al.*, 1989; Casanova *et al.*, 1996; Gutierrez *et al.*, 2000, 2001; Alzuet *et al.*, 2001; Casanova *et al.*, 2000). Important information about the deprotonated sulfonamide group conformation has been obtained.

Figure 2 shows the molecular structure of (**2**). As seen in Fig. 2, the copper atom is located on a twofold axis and is hexacoordinated by the two amide nitrogen atoms of the dianionic ligand and by four nitrogen atoms of Cu(II) can be approximated as a distorted octahedron.

IR spectra

IR spectra support the structure of the complexes by the determination of the coordination modes. The changes in the characteristic vibrations of the ligands were compared with complexes. The υ(NH) band in the free ligands is observed around 3,198 and 3,288/cm strongly, but it disappears by the chelation through the amide nitrogen in the complexes. This observation indicates deprotonation of the amide group. The asymmetric and symmetric $-SO_2$ group stretching vibrations in the ligands were observed at

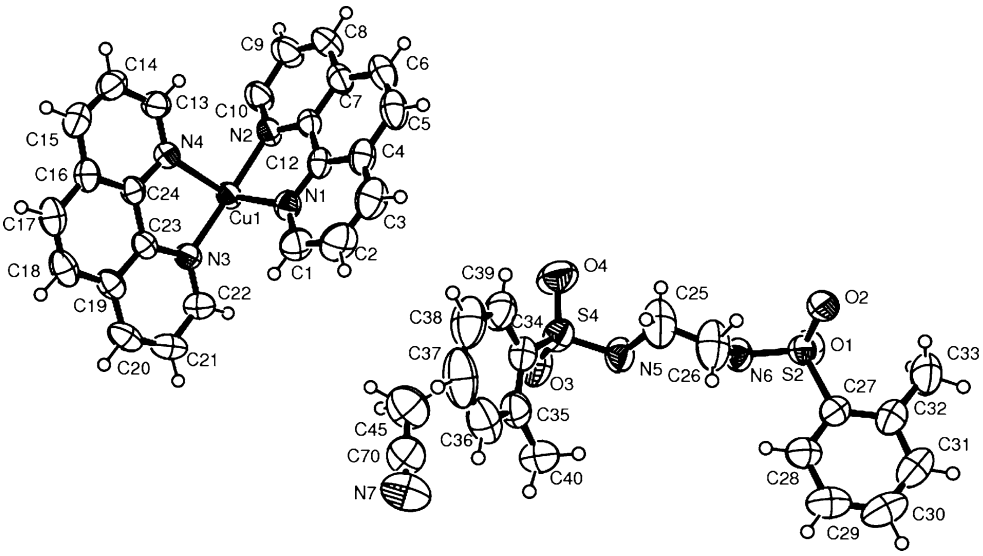


Fig. 1 The molecular structure of $[Cu(phen)_2]L_1$ with the atom-numbering scheme; displacement ellipsoids are drawn at the 50 % probability level

1,336–1,329 and 1,169–1,167/cm for $\mathbf{L_1}$ and $\mathbf{L_2}$, respectively. In complex (**1**), the υ_a (SO_2) and υ_s (SO_2) did not show significant shifts with respect to those of ligands, in spite of deprotonation of the amide group. However, in the spectra of complex (**2**), the υ_a (SO_2) and υ_s (SO_2) shifted to lower frequencies by the chelation through the amide nitrogen in the complex (Kremer *et al*., 2006; Macias *et al.*, 2003). In the IR spectra of complex (**1**), the vibration of the imine nitrogen bond (C=N) of the stretching band of the phenanthroline rings shifts from 1,644 to 1,585/cm by complexation, which causes a great need for the oscillation of the bonds in the ring. And as the electron clouds of the C–N bonds flow to the phenantroline rings, making the electron density around the C–N bonds decrease, the stretching vibration of the C–N bond in Cu(II) complexes shifts to low field. And also, the C–H out-of-plane bending vibrations of the phenantroline ring were shifted in the range 855–715/cm as compared with the coordination compound in the range 865–725/cm included in between ligand and rare earth ion (Yongliang *et al*., 2006). The changes in the characteristic vibrations of the $\mathbf{L_2}$ were compared with complex (**2**). The phenantroline rings with two nitrogen atoms in the sulfonamide chelate copper(II) ion, this does not make sense. In the IR spectra of the compound, the vibration of the imine nitrogen bond (C=N) of the stretching band of the phenanthroline rings shifts from 1,644 to 1,588/cm by complexation. Also, the spectra of the complex (**2**) shows two of the C–H out-of plane bending vibration bands at 869 and 720/cm due to the coordinated phenanthroline molecule (Sanchez-Piso *et al*., 2002). The main vibration frequencies of the compounds are listed in Table 3.

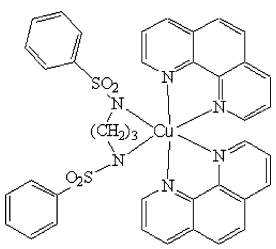


Fig. 2 The molecular structure of $[CuL_2(phen)_2]$

Mass spectra

Main fragmentation steps for complexes are exhibited in Figs. 3, 4. As seen in Fig. 3, mass spectra of the complex (**1**) gives the molecular ion $[Cu(phen)_2]L_1^+$ peak at *m/z* (intensity%) = 790.41 (12 %). The spectra also exhibit two peaks for the $[Cu(phen)_2]^+$ fragment *m/z* = 423.96 (50 %) and for the $[L_1]^+$ fragment *m/z* = 368.47 (14 %). The removal of one (*phen*) group ($C_{12}H_8N_2Cu$) gives peak at *m/z* = 243.0 (8.0 %) and the residual group ($C_{12}H_8N_2$) gives peak at *m/z* = 181.0 (100 %). The mass spectra of the complex (**2**) show (in Fig. 4) the molecular ion $[CuL_2(phen)_2]^+$ peak at *m/z* = 775.12 (12 %). The spectra also show three peaks for the $[CuL_2(phen)]^+$ fragment at *m/z* = 596.0 (14 %), for the $[L_2]^+$ fragment at *m/z* = 354.44 (22 %) and for the ($C_{12}H_8N_2$) fragment at *m/z* = 181.0 (100 %).

Table 3 Major IR absorption bands (/cm) of sulfonamide derivatives and their Cu(II)complexes

Assignment	$\mathbf{L_1}$	$\mathbf{L_2}$	(**1**)	(**2**)
υ (NH)	3,198(s)	3,288	–	–
υ_{ar} (C–H)	3,063(w)	3,060	3,030	3,050
υ_{as} (SO_2)	1,336(s)	1,329	1,336	1,328
υ_{as} (CH_3)	2,973(w)	–	2,973	–
υ_s (SO_2)	1,169(s)	1,167	1,169	1,167
δ (NH)	1,452(m)	1,451	–	–

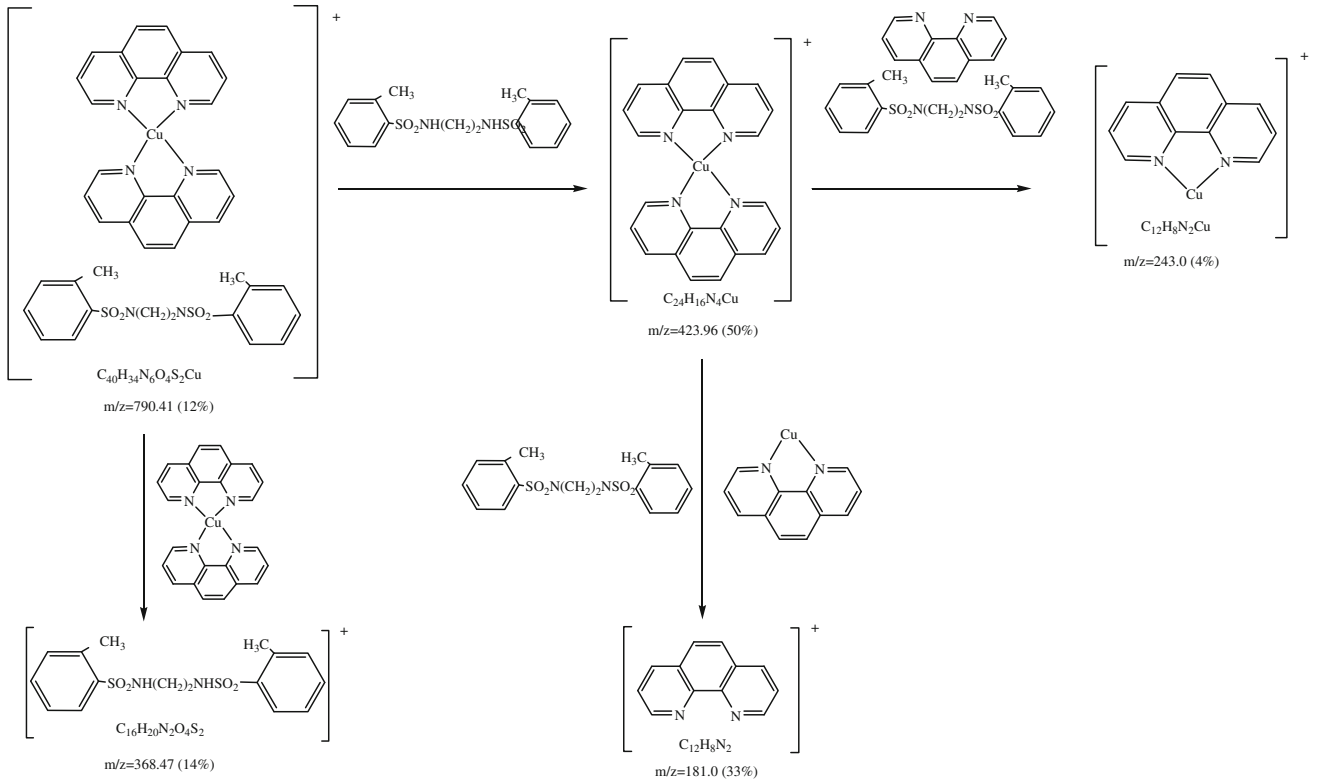
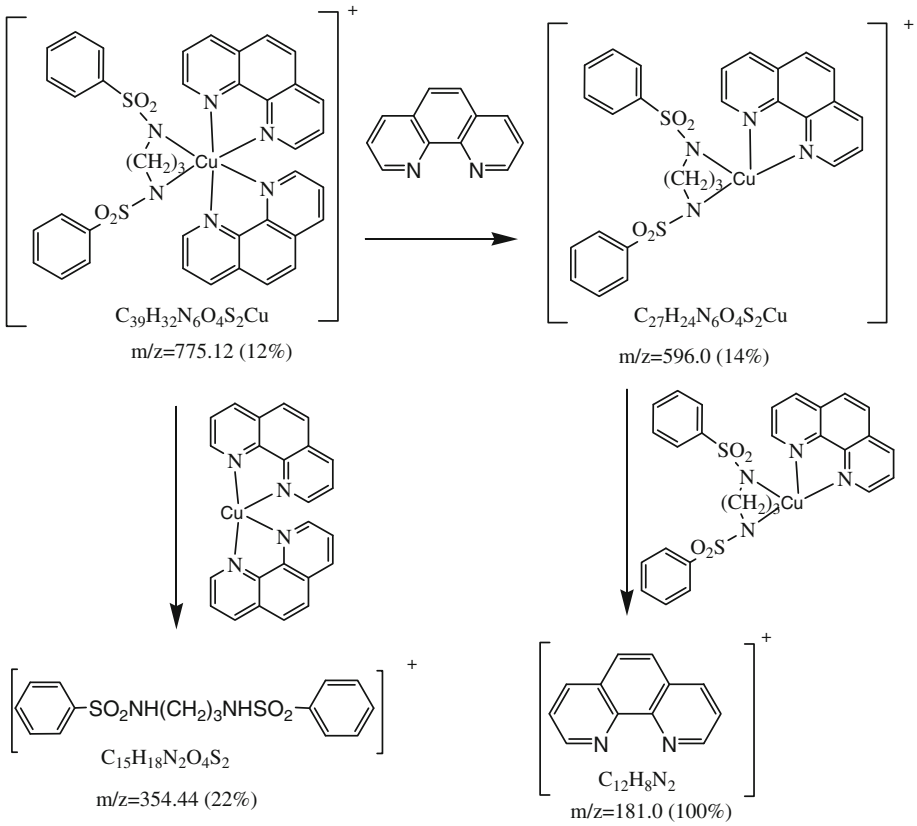


Fig. 3 The main fragmentation route of $[Cu(phen)_2]L_1$

Fig. 4 The main fragmentation route of $[CuL_2(phen)_2]$



Molar conductivity

The complexes appear to be air stable, soluble in DMSO, and slightly soluble in acetonitrile. The molar conductivities (Λm) of 10^{-3} M solutions of the complexes were measured in DMSO at 25 °C. The experimental conductivity value falls in the range of a 1:1 electrolyte (Geary, 1971). Anionic ligand $(\mathbf{L_1})^{2-}$ is bonded out of the coordination sphere as counter-ion. Complex (**2**) is non-conducting and the measured molar conductance ranged from 2.0 to 3.6 S cm^2/mol, indicating its neutrality.

Magnetic properties

The magnetic moment of the octahedral complexes (as BM) was measured at room temperature. The magnetic moment of the complex (**1**) (2.06 BM) is close to the spin value 1 for one unpaired electron and within the general range for Cu(II) complexes. Complex (**2**) has paramagnetic characters and the effective magnetic moment value is 1.91 BM.

Antibacterial bioassay

Ligands and their Cu(II) complexes were screened in vitro for their antibacterial activity against three Gram-positive species (*S. aureus*, *B. subtilis*, and *B. cereus*) and three Gram-negative species (*E. coli*, *P. aeruginosa*, and *Y. enterocolitica*) of bacterial strains by the microdilution and agar-disk diffusion method (Tables 4, 5). The antibacterial activity results evidently show that the sulfonamide compounds possessed a broad spectrum of activity against the tested bacteria at the concentrations of 60–320 μ/mL. All compounds showed poor activity against *B. subtilis*, and $\mathbf{L_2}$ exhibited the lowest inhibitory activity with an MIC of 320 μg/mL. It is observed that the copper(II) complexes are better antibacterial agents than Schiff bases. Chelation reduces the polarity of the metal ion because of the partial sharing of its positive charge with the donor groups and a possible π-electron delocalization system. Meanwhile, the increment of the lipophilic character of the complexes may be responsible for their potent biological activities. The lipids and polysaccharides are main fragments of the cell walls and membranes, which are responsible for the metal interactions. The permeation of complexes through the lipid layer of the cell membranes blocks some cellular enzymes, which play a vital role in various metabolic systems of these microorganisms like Tweed's chelation theory (Keskioğlu *et al*., 2008; Venkatachalam and Ramesh, 2005; Mohamed *et al*., 2005). If ligands are compared with each other, $\mathbf{L_1}$ has more activity than $\mathbf{L_2}$ against the tested bacteria. The results obtained revealed that the antibacterial activity decreased as the length of the carbon chain increased (Alyar and Karacan, 2009; Ozdemir *et al*., 2009; Ozdemir and Olgun, 2008). As seen in Tables 4, 5, complex (**1**) shows higher antibacterial activity than complex (**2**). The sulfonamide ligand in complex (**1**) increased the activity against bacteria for the acts as a counter-ion. In

Table 4 Antimicrobial activity of sulfonamide derivatives and their Cu(II) complexes with microdilution method

Compounds	MIC (μg/mL)					
	E. coli ATCC35218	*P. aeruginosa* ATCC27853	*Y. enterocolitica* 0:3	*B. cereus* RSKK709	*B. subtilis* ATCC6633	*S. aureus* ATCC25923
$\mathbf{L_1}$	80	120	80	100	240	80
$\mathbf{L_2}$	100	180	80	280	320	100
(**1**)	60	100	60	80	120	60
(**2**)	80	140	80	240	160	80

Table 5 Result of the antimicrobial test of sulfonamide derivatives and Cu(II) complexes disk potency 70 μg

Compounds	Diameter inhibition zone (mm, 70 μg/disk)					
	E. coli ATCC35218	*P. aeruginosa* ATCC27853	*Y. enterocolitica* 0:3	*B. cereus* RSKK709	*B. subtilis* ATCC6633	*S. aureus* ATCC25923
$\mathbf{L_1}$	23	24	18	16	22	18
$\mathbf{L_2}$	20	18	17	17	18	17
(**1**)	25	26	19	22	26	20
(**2**)	22	20	18	20	23	18
Ciprofloxacin	36	–	–	26	–	29
Penicillin	17	–	–	8	–	8
Ampicillin	11	–	–	13	–	14

<10: weak, >10: moderate, >16: significant

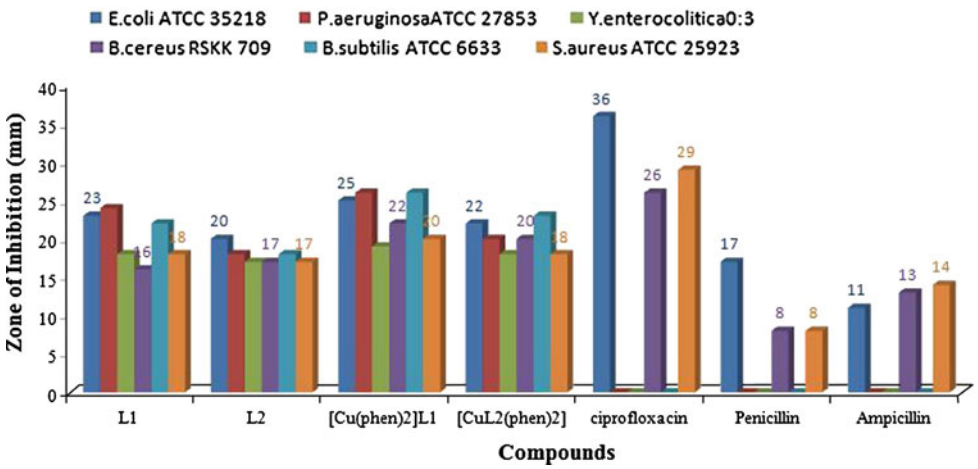


Fig. 5 Comparison of antibacterial activities

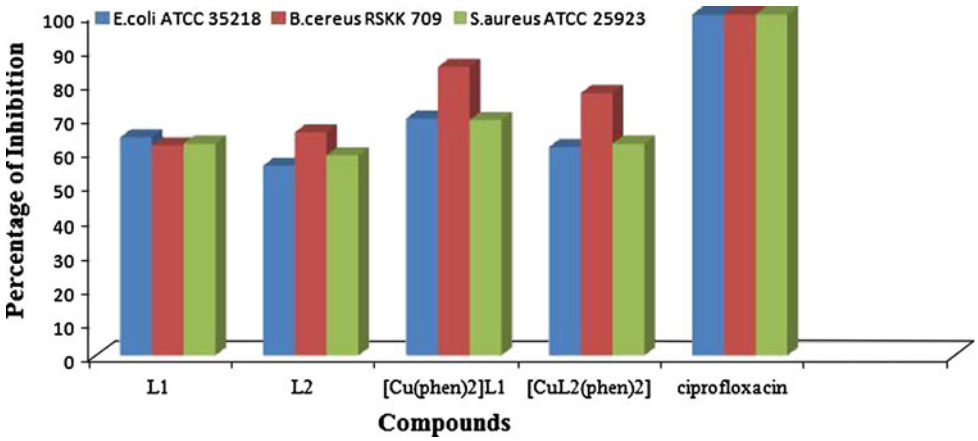


Fig. 6 Percentage of inhibition of the compounds

addition, the inhibition zones formed by standard antibiotics (*ciprofloxacin*, *penicillin*, and *ampicillin*) against all bacteria are reported in Table 5, Figs. 5, 6. The results were compared with those of the standard drugs. All compounds showed significant activity than *penicillin* and *ampicillin* for all Gram-negative and Gram-positive bacterial strains.

Conclusion

In this study, we have reported the synthesis of sulfonamide derivatives and their Cu(II) complexes. The structural characterizations of the synthesized compounds were made by elemental analyses, spectroscopic methods, and magnetic and conductance studies. The structure of complex (**1**) was also supported by X-ray crystal diffraction studies. The structures of (**1**) and (**2**) complexes were proposed as a tetragonal and octahedral geometry, respectively. The biological activity screening showed that Cu(II) complexes have more activity than ligands against the tested bacteria.

Acknowledgments The authors wish to thank TUBITAK for the financial support (No: TBAG 104 T 390) and Gazi University Scientific Research Projects (No: 05/2008-05). We would also like to thank TUBITAK for the allocation of time for the NMR, Mass Spectra, and Elemental Analyses.

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