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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Synthesis, characterization, and antibacterial activity of the ligands including thiophene/furan ring systems and their Cu(II), Zn(II) complexes

Ayla Balaban Gündüzalp · Neslihan Özbek · Nurcan Karacan

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Abstract Carboxamide complexes having general formula as $[ML]Cl_2 \cdot nH_2O$ (where M = Cu(II), Zn(II); $n = 0$, 1/2) were synthesized using heterocyclic carboxamide ligands: 1,4-bis[3-(2-thiophenecarboxamido)propyl]piperazine (L^1) and 1,4-bis[3-(2-furancarboxamido) propyl] piperazine (L^2). Their structures were characterized with elemental analysis, molar conductivity, magnetic susceptibility, and spectral methods (^{1}H-NMR, ^{13}C-NMR, FT-IR, LC-MS). TGA and DTA curves were also performed. The structure–activity relationship for the ligands was investigated using PM3 semi-empirical method. The antibacterial activities of the carboxamides and their complexes were investigated against bacteria; *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 11230, *Bacillus magaterium* RSKK 5117, *B. cereus* RSKK 863, *Salmonella enteritidis* ATCC 13076, *B. subtilis* RSKK 244 using microdilution method.

Keywords Carboxamides · 2-Thiophenecarbonyl chloride · 2-Furancarbonyl chloride · 4-Bis(3-aminopropyl)piperazine · Antibacterial activity · Microdilution method

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Introduction

The carboxamide linkages (–CO–NH–) are an essential building unit in proteins, which has attracted much attention because of its high resistance to hydrolysis. This fact is of crucial importance in biological systems, since it permits for the building of peptides from relatively simple amino acid precursors (Iriepa *et al*., 2006; Ouyang *et al*., 1998; Gudasi *et al*., 2005; Auzeil *et al*., 1999).

The continuing interest in the study of carboxamide complexes are derived from their ability to model active sites present in some metalloenzymes and the search for a better understanding of physicochemical properties of such complexes, especially the stereochemistry of the metallic centers. In order to expand on the function of the metal ions in the biological systems, we are involved in a study of the impact of structure changes on the physicochemical properties of the model complex of the first row transition metal (Chapman and Vagg, 1979; Stubbe and Kozarich, 1987; Mitchell *et al*., 2004).

In this study, carboxamide complexes were synthesized by the chelation of 1,4-bis[3-(2-thiophenecarboxamido) propyl]piperazine (L^1) synthesized by us previously (Balaban *et al*., 2008) and 1,4-bis[3-(2-furancarboxamido)propyl]piperazine (L^2) with Cu(II) and Zn(II) chlorides. These complexes have general formula as $[ML]Cl_2 \cdot xH_2O$ (M = Cu(II), Zn(II); $x = 0$, 1/2). The structure of the compounds was determined with elemental analysis, spectral methods (^{1}H-NMR, ^{13}C-NMR, FT-IR, LC-MS), magnetic susceptibility, molar conductivity, and thermal studies. The structure–activity relationship for the ligands was investigated using two types of molecular descriptors including electronic and physicochemical parameters. Antibacterial activity of the compounds was determined using microdilution method against bacteria; *Staphylococcus aureus*

ATCC 25923, *Escherichia coli* ATCC 11230, *Bacillus magaterium* RSKK 5117, *B. cereus* RSKK 863, *Salmonella enteritidis* ATCC 13076, *B. subtilis* RSKK 244.

Experimental

Reagents

1,4-Bis(3-aminopropyl)piperazine, 2-thiophenecarbonyl chloride, and 2-furancarbonyl chloride, metal chlorides (all from Aldrich) and solvents (all from Merck) were used without further purification. All chemicals and solvents used in synthesis were of analytical grade.

Physical measurements

The elemental analysis (C, H, N, S) was performed on a LECO–CHSNO-9320-type elemental analyzer. The IR spectra (4000–400 cm^{-1}) were recorded on a Mattson-1000 FT-IR spectrometer with samples prepared as KBr pellets. NMR spectra were recorded on a Bruker-Spectrospin Avance DPX-400 Ultra-Shield (400 MHz) using d_6-DMSO, and TMS as internal standard. The magnetic susceptibilities were measured on powdered samples using Gouy method. The molar conductivity measurements were carried out using a Siemens WPA CM 35 conductometer. A Du Pont Instrument 951 thermal analyzer was used to record simultaneously TG and DTA curves. The experiments were carried out in dynamic nitrogen atmosphere (20 ml min^{-1}) with a heating rate of 10°C min^{-1} in the temperature range 30–400°C using platinum crucibles. Geometry optimization of the ligands was performed by PM3 semi-empirical method. Microdilution method was used to determine the antibacterial activity of compounds against bacteria; *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 11230, *B. magaterium* RSKK 5117, *B. cereus* RSKK 863, *Salmonella enteritidis* ATCC 13076, *B. subtilis* RSKK 244.

Synthesis of the ligands

1,4-Bis[3-(2-thiophenecarboxamido)propyl]piperazine (L^1) was synthesized with some modification as previous study (Balaban *et al*., 2008). 1,4-Bis[3-(2-furancarboxamido) propyl]piperazine (L^2) was synthesized as described: to a solution of 1,4-bis(3-aminopropyl) piperazine 3.00 g (14.98 mmol) in dichloromethane with triethylamine, 2-furancarbonyl chloride 3.91 g (29.96 mmol) in chloromethane was added dropwise by cooling the balloon in the ice bath. The reaction mixture was stirred magnetically under reflux for a day. The precipitate was filtered, dried, and recrystallized from methanol, then dried over A4 molecular sieve in desiccant (Stephens and Vagg, 1988). Yield: 73%, found (calcd.) %: C, 61.65 (61.88); H, 6.97 (7.21); N, 16.22 (16.48).

Synthesis of the metal complexes

$[Cu(L^2)]Cl_2$ was prepared by the adding copper(II) chloride, 0.13 g (0.73 mmol) in methanol to the hot solution of the 1,4-bis[3-(2-furancarboxamido) propyl]piperazine (L^2) 0.30 g (0.73 mmol) in the same solvent. The resulting mixture was stirred under reflux (at 40°C) whereupon the copper(II) complex precipitated. They were collected by filtration, recrystallized with methanol, and dried in desiccant (Stephens and Vagg, 1988). The other Cu(II) and Zn(II) complexes were synthesized by similar method as recorded.

Antibacterial screening

The in vitro antibacterial activity of the ligands and their complexes were screened against bacteria; *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 11230, *B. magaterium* RSKK 5117, *B. cereus* RSKK 863, *Salmonella enteritidis* ATCC 13076, *B. subtilis* RSKK 244. Antibacterial activities were determined by the microdilution method as MIC's in μg/ml (Özbek *et al*., 2007). MIC was defined as the lowest concentrations of compounds which inhibit the growth of microorganisms. The nutrient broth, which contained logarithmic serially two-fold diluted amount of test compound and controls, was inoculated with approximately 5×10^5 c.f.u. Aqueous DMSO (20%) was used as negative control (containing compounds but no inoculum). The microplates were incubated at 37°C and read visually after 24 h (Özbek *et al*., 2007; Özmen and Olgun, 2008).

Results and discussion

Structure of the compounds

In our previous study, the crystal structure and spectroscopic data of 1,4-bis[3-(2-thiophene carboxamido)propyl]piperazine (L^1) was reported by us (Balaban *et al*., 2008). The reaction mechanisms of 1,4-bis[3-(2-furancarboxamido)propyl]piperazine (L^2) are exhibited in Fig. 1. The carboxamide complexes have general formula as $[ML]Cl_2 \cdot nH_2O$ (M = Cu(II), Zn(II); $n = 0, 1/2$). Antibacterial activities of the complexes were determined against some bacteria using microdilution method (as MIC values). The molecular geometries of the carboxamide ligands were optimized using PM3 semi-empirical method and their electronic-physicochemical properties were determined as molecular descriptors having effects on the

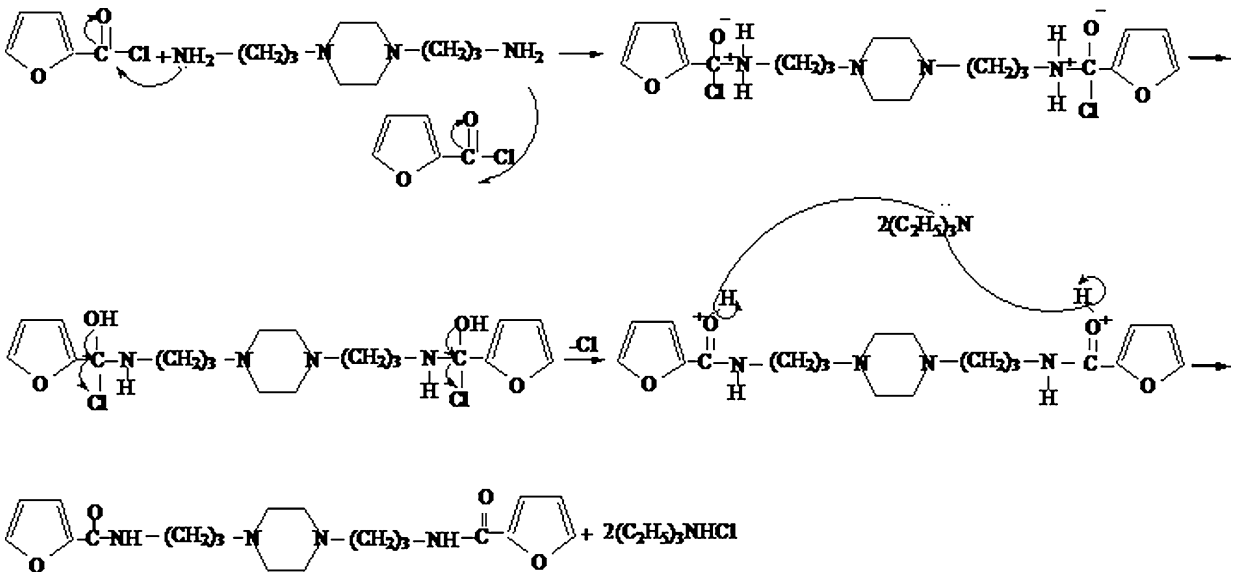


Fig. 1 The reaction mechanism of 1,4-bis[3-(2-furancarboxamido)propyl]piperazine, L^2

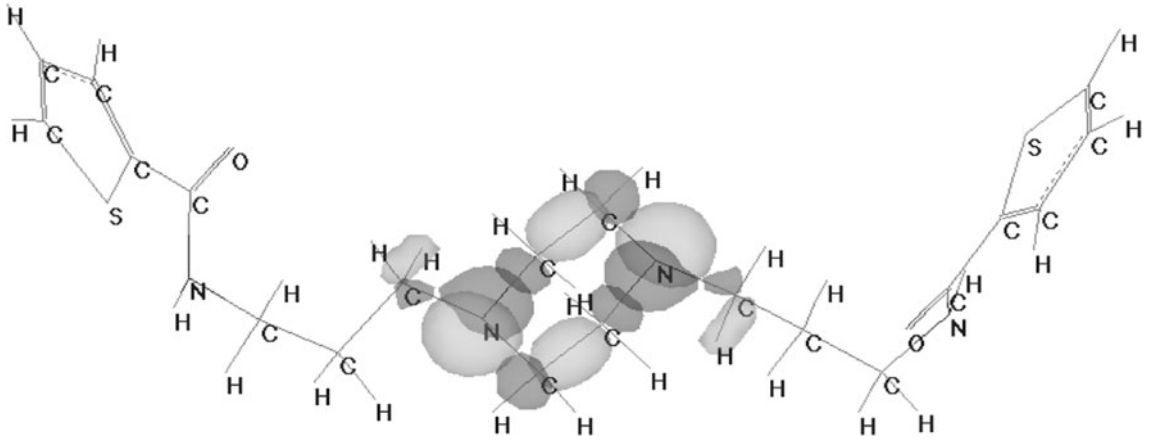


Fig. 2 HOMO 3D shape for L^1

antibacterial activities. The isosurface plots of the HOMO and LUMO orbitals of L^1 are presented in Figs. 2 and 3. The identification of the molecular descriptors used in this study is shown in Table 1. Molecular descriptor data are exhibited in Table 2.

NMR spectra

The atomic numbering scheme of L^2 is given in Fig. 4. ^{1}H and ^{13}C NMR chemical shift data of L^2 are displayed in Table 3. In ^{1}H-NMR spectra of L^2 (Fig. 5), the singlet at 8.56 ppm is assigned to carboxamide NH moiety. Furan ring protons H(1), H(2), and H(3) are observed at 7.84, 6.63, and 7.12 ppm, respectively, 1,4-bis-(propyl)piperazine protons are observed within the range 1.94–3.74 ppm (Keskioğlu *et al*., 2008). In ^{13}C-NMR spectra of L^2 (Fig. 6), carbonyl group C(5)=O with the highest chemical shifts is observed at 159.36 ppm. Furan ringcarbons C(1), C(2), and C(3) are exhibited at 112.99, 114.61, and 149.19–159.36 ppm, respectively. The functional groups of half of carboxamides have the same chemical shifts for the other half's because of symmetry (Stephens and Vagg, 1988).

IR spectra

The most common vibrations of carboxamide compounds are determined by comparing the vibrational frequencies of the ligands with those of their Cu(II), Zn(II) complexes and displayed in IR spectra gives enough information to elucidate the way of bonding of the ligands to the metal ions.

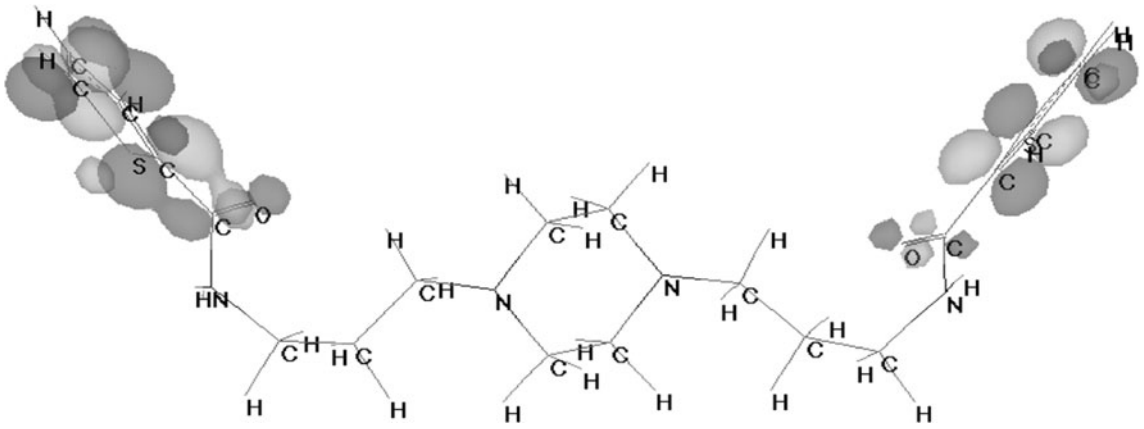


Fig. 3 LUMO 3D shape for L^1

Table 1 Identification of the descriptors used in this study

Descriptors type	Molecular descriptors
Electronic descriptors	Highest occupied molecular orbital energy (E_{HOMO})
	Lowest unoccupied molecular orbital energy (E_{LUMO})
	Hardness ($\eta = 0.5(E_{HOMO} + E_{LUMO})$)
	Electronegativity ($\chi = -0.5(E_{HOMO} - E_{LUMO})$)
	Molecular dipole moment (DM)
	Heat of formation (H_f)
	Atomic charge (Q_x) on X (X = S, O)
	Torsional angle (t) between C(4)–C(5)–O
Physicochemical descriptors	Hydration energy (HE), molar refractivity (MR), molecular mass (M), molecular surface area (SA), molecular volume (V), polarizability (Pol), binding energy (BE), octanol–water partition coefficient (log$P$)

Table 2 Descriptors for carboxamides

	Electronic descriptors							
	E_{HOMO}	E_{LUMO}	η	χ	DM	H_f	Q_x	t
L^1	8.79	0.82	−4.81	3.99	1.12	20.84	0.32	32.16
L^2	8.88	0.32	4.60	4.28	3.09	92.56	0.06	−11.43
	Physicochemical descriptors							
	HE	MR	M	SA	V	Pol	BE	log$P$
L^1	−8.87	107.62	388.47	634.02	1182.98	41.23	5659.45	−2.73
L^2	−7.31	120.50	420.59	629.01	1213.72	45.96	5601.42	−2.05

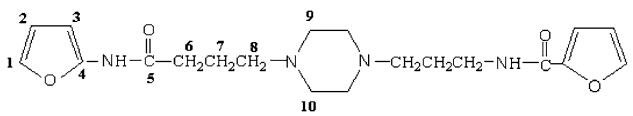


Fig. 4 The half numbered structure of 1,4-bis[3-(2-furancarboxamido) propyl] piperazine, L^2

Carboxamides have three coordinating donors: thiophene-S/furan-O, carbonyl-O, and amide-N. As tetradentate ligands the bonding takes place through either the aromatic ring donors (S/O) or carbonyl O (Amide I). Carboxamides have characteristic bands as Amide A, Amide I, Amide II, etc.

1,4-Bis[3-(2-furancarboxamido)propyl]piperazine (L^2) exhibits Amide A band which occurs by the N–H (ν_{N-H}) vibration at 3,298 cm^{-1}. Amide I band which consists mainly of C=O vibration ($\nu_{C=O}$) at 1,656 cm^{-1} and Amide II bands which arises from ν_{C-N} as well as δ_{N-H} by coupling to one another at 1,580 cm^{-1} (Ouyang *et al.*, 1998; Balasubramanian *et al.*, 2006; Akinchan *et al.*, 2001; Hamurcu *et al.*, 2008). The binding modes are determined by these observations: (i) Amide I band shifts to lower frequencies by complexation. This shift supports the participation of the amide carbonyl oxygen of these ligands in binding to the metal ions (Balaban Gündüzalp and Erk, 2010), (ii) the shift of $\nu_{CS} + \delta_{ring}$ to lower wave numbers and δ_{C-S-C} to higher wave numbers by coordination through thiophene ring, and (iii) the shift of $\nu_{C-C} + \nu_{C-O}$ to lower wave numbers and the shift of β_{C-H} to higher wave numbers by coordination through the furan ring (Ibrahim *et al.*, 1997, 1999, 2002; Mohamed *et al.*, 2005; El-Jouad *et al.*, 2001). The main vibration frequencies of the compounds are listed in Table 4.

Table 3 The NMR data of L^2

^{1}H-NMR (ppm, d_6-DMSO)		^{13}C-NMR (ppm, d_6-DMSO)	
NH	8.56(s,2H)	C(1)	146.33
H(1)	7.84(d,2H)	C(2)	112.99
H(2)	6.63(dd,2H)	C(3)	114.61
H(3)	7.12(d,2H)	C(4), C(5)	149.19, 159.36
H(6)	3.74(t,4H)	C(6)	36.37
H(7)	1.94(m,4H)	C(7)	24.21
H(8)	3.19(t,4H)	C(8)	54.23
H(9), H(10)	3.30(t,8H)	C(9), C(10)	48.79

s singlet, *d* doublet, *t* triplet, *m* multiplet

Molar conductivity

The molar conductivity (Λ_M) of 10^{-3} M solutions of the complexes was measured in MeOH at 25°C. As seen in Table 1, all complexes have molar conductivity values between 86 and 102 Ω^{-1} mol^{-1} cm^2 indicating the 1:2 ionic nature (Λ_M for $CaCl_2$ is 88 Ω^{-1} mol^{-1} cm^2). These data show that the two chloride anions are out of the coordination sphere as a counter ions (Barnes *et al*., 1981). Analytical data of the complexes are given in Table 5. The chelation modes of the complexes are exhibited in Fig. 7.

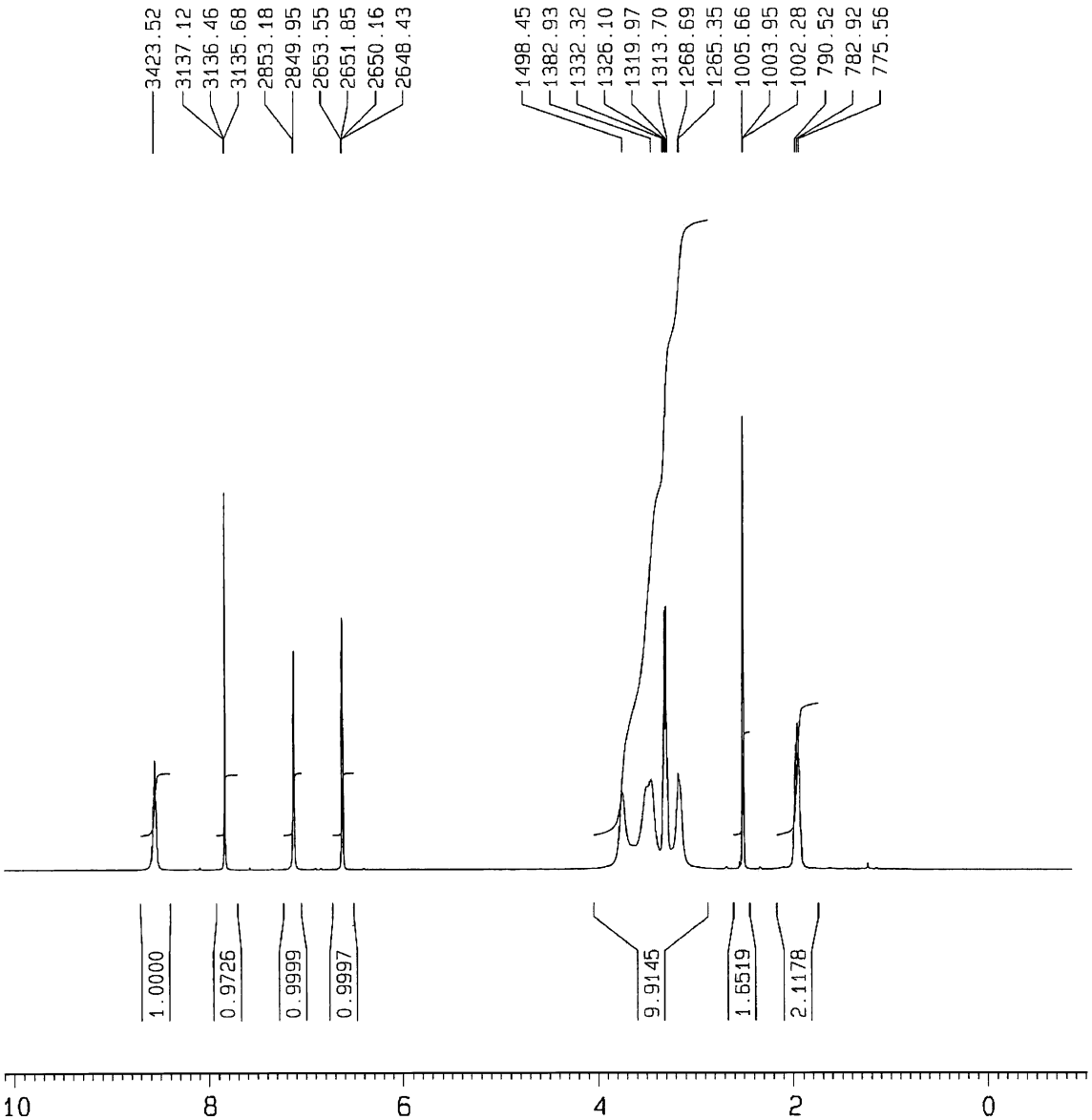


Fig. 5 ^{1}H-NMR spectra of L^2

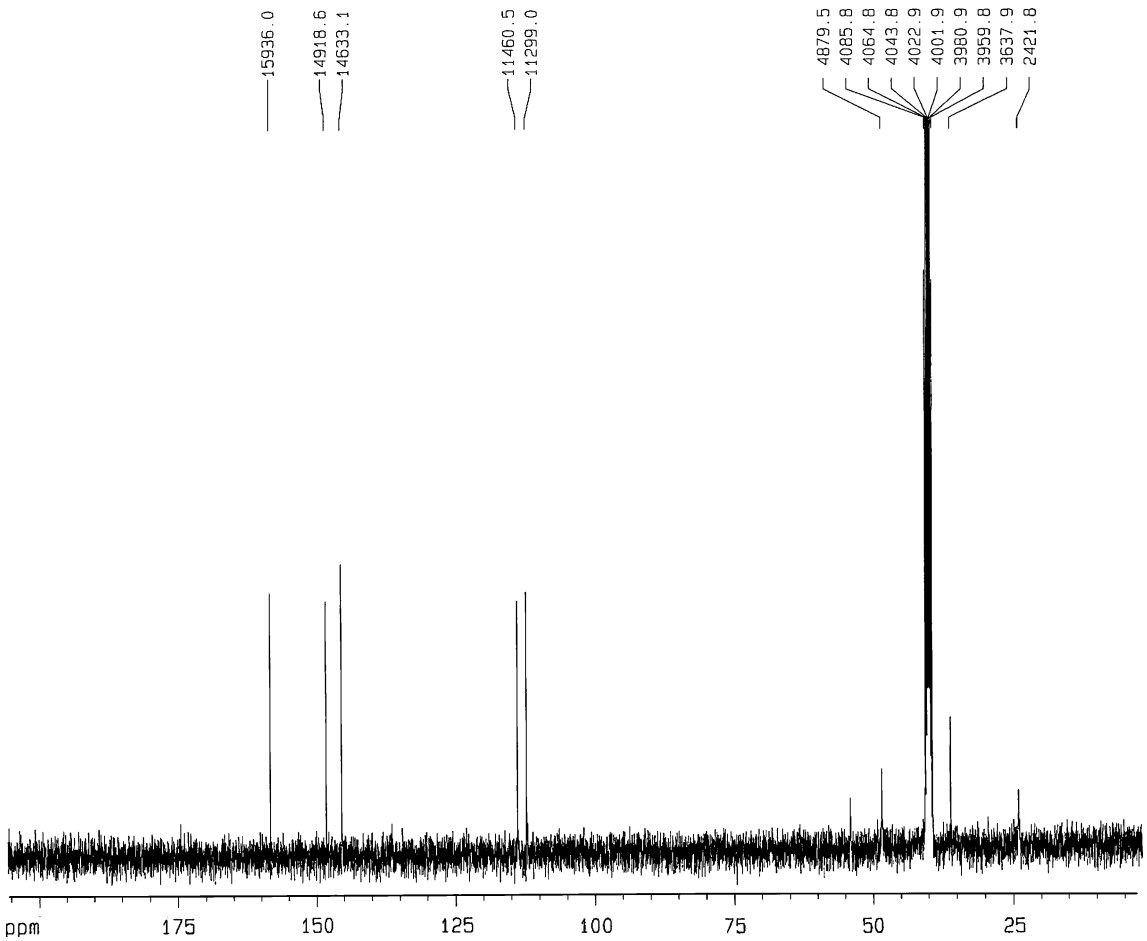


Fig. 6 ^{13}C-NMR Spectra of L^2

LC-MS spectra

Main fragmentation steps for ligands are exhibited in Fig. 8. Mass spectra of L^1 gives the molecular ion [MH^+] peak at *m/z*(intensity%) = 421.1(100%). The removal of one thiophene carbonyl group (C_4H_3SCO) gives a peak at 111.1(15.3%) and the residual group gives peak at 311.1(12.4%). By the removal of other thiophene carbonyl group (C_4H_3SCO) from residual group, amine group is observed at 201.1(37.5%). [$Cu(L^1)$]Cl_2 gives the following fragmentation peaks: 554.1(2.0%) as molecular ion peak by losing of one proton, 519.1(34.3%) which occurs by losing of one chlorine atom, 484.0(15.8%) and 484.0 + 4H(100%) which occurs by losing of two chlorine atoms (at *m/z* = 400–1500 range), 421.1(100%) belongs to L^1, and 63.1(4.3%) belongs to Cu atom (at *m/z* = 0–1500 range). [$Zn(L^1)$]Cl_2 gives the following fragmentation peaks: 557.5(11.2%) as molecular ion peak, 483.3(6.5%) which occurs by losing of two chlorine atoms, 418.9(23.0%) belongs to L^1, and 65.0(0.9%) belongs to Zn atom (Ibrahim *et al*., 1997; Nawar and Hosny, 2000; Seeber *et al*., 2005). L^2 gives the molecular ion [MH^+] peak at 389.2(100%). The removal of one furan carbonyl group (C_4H_3OCO) gives a peak at 95.0(15.3%) and the residual group gives peak at 295.2(25.2%). By the removal of other furan carbonyl group (C_4H_3OCO) from residual group, amine is observed at 201.2(13.8%). [$Cu(L^2)$]Cl_2 gives the following fragmentation peaks: 522.7(1.2%) as molecular ion peak; 486.9(11.5%) which occurs by losing of two chlorine atoms, 389.2(100%) belongs to L^2 and 201.2(82.4%) belongs to the amine, and 63.1(4.3%) belongs to Cu atom. [$Zn(L^2)$]$Cl_2 \cdot ½H_2O$ gives the following fragmentation peaks: 525.4(0.7%) as molecular ion peak, 450.3(6.6%) which occurs by losing of two chlorine atoms, 389.2(42.7%) belongs to L^2, 201.1(100%) belongs to amine, and 65.1(3.5%) belongs to Zn atom (Nawar and Hosny, 1999; Venkatachalam and Ramesh, 2005) (Fig. 9).

Thermal studies

Thermal behaviors of complexes were determined in nitrogen atmosphere (20 ml/min) with a heating rate of

Table 4 Characteristic IR bands of the compounds (cm^{-1})

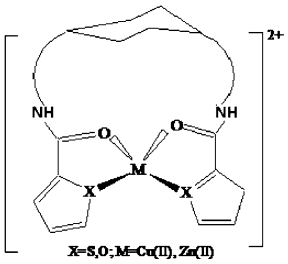
Compounds	Amide A	Amide I	Amide II	Thiophene ring		Furan ring	
				$\nu_{(CS)} + \delta_{(ring)}$	δ_{C-S-C}	$\nu_{C-C} + \nu_{C-O}$	$\beta_{C-H(ring)}$
$[Cu(L^1)]Cl_2$	3340(m)	1603(m)1637(s)	1548(sh)	742(m)	674(s)	–	–
$[Zn(L^1)]Cl_2$	3333(m)	1612(m) 1638(sh)	1549(sh)	740(s)	675(s)	–	–
L^2	3298(m)	1656(sh)	1580(sh)	–	–	1029(w)	1253(m)
$[Cu(L^2)]Cl_2$	3346(m)	1636(sh) 1655(m)	1572(sh) 1598(m)	–	–	1013(w)	1274(m)
$[Zn(L^2)]Cl_2 \cdot ½H_2O$	3320(m)	1630(br)	1586(sh)	–	–	1023(s)	1281(m)

sh sharp, *m* medium, *br* broad, *s* small, *w* weak

Table 5 Analytical and physical data of the carboxamide complexes

Compounds	Found (calcd.) %					Yield %	Λ_M (μS/cm)
	C	H	N	S	M		
$[Cu(L^1)]Cl_2$	42.82 (43.33)	4.96 (5.05)	9.70 (10.10)	11.27 (11.56)	11.34 (11.45)	70	98
$[Zn(L^1)]Cl_2$	42.91 (43.15)	4.80 (5.03)	9.85 (10.07)	10.96 (11.52)	11.67 (11.75)	66	86
$[Cu(L^2)]Cl_2$	46.37 (45.96)	5.62 (5.36)	10.74 (10.72)	–	11.97 (12.16)	63	102
$[Zn(L^2)]Cl_2 \cdot ½H_2O$	44.78 (45.02)	5.12 (5.44)	10.24 (10.50)	–	12.05 (12.26)	64	89

Fig. 7 Chelation modes of the complexes



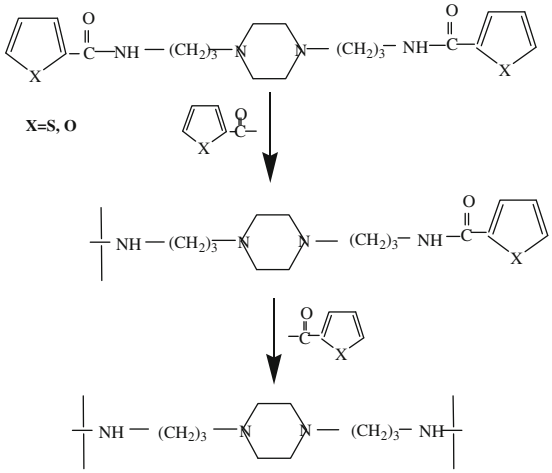


Fig. 8 The fragmentation steps of the carboxamides (L^1 and L^2)

10°C min^{-1} in the temperature range 30–400°C. The thermogram of $[Zn(L^2)]Cl_2 \cdot ½H_2O$ shows the first step of decomposition within a mass loss of 1.75% (calcd. 1.69%) at 87°C ($\Delta H = 24.92$ J/g) corresponds to the loss of ½ crystal water molecule. The decompositions assigned to the loss of two chlorine atoms as HCl molecules at one step occurs at 206 and 257°C for $[Cu(L^1)]Cl_2$ and $[Zn(L^2)]Cl_2$ complexes. The decomposition assigned to the loss of two chlorine atoms as HCl molecules occurs at 253°C (step I) and 303°C (step II) for $[Zn(L^1)]Cl_2$ and 197°C (step I) and 262°C (step II) for $[Cu(L^2)]Cl_2$. Organic decomposition occurs over 300°C within a great mass loss (Mohamed, 2006; Al-Hiari and Sweileh, 2006). Thermal data of the complexes are given in Table 6 and show good agreement with the theoretical formula as suggested from the analytical data (Table 5).

Molecular descriptors for ligands

The molecular geometries of the carboxamide ligands were optimized using PM3 semi-empirical method and their electronic–physicochemical properties were determined as molecular descriptors having effects on the antibacterial activities (Alyar *et al.*, 2011). The calculated values of electronic features of the molecules are affected by the conformations; we used the most stable conformations with the lowest energy. The electronic descriptors (such as orbital energies, dipole moments, hardness, electronegativity, etc.) and physicochemical descriptors (such as molecular volume, log*P*, polarizability, etc.) (see Tables 1, 2) were calculated to find the effect of chemical properties on the antibacterial activity of the carboxamides (Tables 1, 2). The orbital densities around the atoms indicate which groups are responsible for the antibacterial activities. LUMO orbital has the highest density around the heteroaromatic rings and corresponds to the activity of

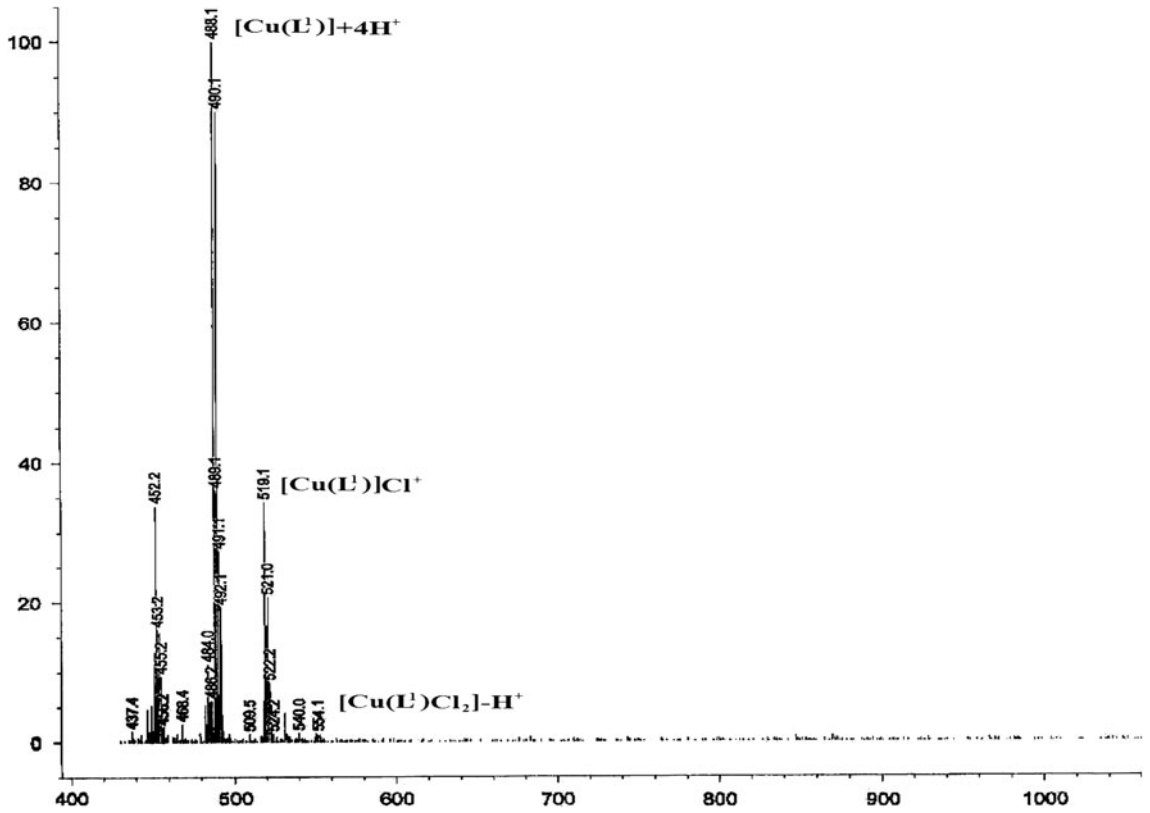


Fig. 9 LC-MS spectra of $[Cu(L^1)]Cl_2$ (Balaban Gündüzalp and Erk, 2010)

Table 6 Thermoanalytical results of carboxamide complexes

Compounds	TG range (°C)	DTG (°C)	ΔH (J/g)	Mass loss found (calcd.) %	Total mass loss found (calcd.) %	Assignment
$[Cu(L^1)]Cl_2$	197–218	206	423.68	–	12.88 (12.80)	Loss of 2HCl (one step)
$[Zn(L^1)]Cl_2$	244–260	253	265.73	–	6.39 (6.38)	Loss of HCl (step 1)
	293–315	303	9.34	6.40 (6.38)	12.79(12.76)	Loss of HCl (step 2)
$[Cu(L^2)]Cl_2$	188–202	197	285.12	–	6.98 (6.79)	Loss of HCl (step 1)
	256–274	262	128.43	7.04 (6.79)	14.02 (13.58)	Loss of HCl (step 2)
$[Zn(L^2)]Cl_2 \cdot ½H_2O$	80–108	87	24.92	–	1.75 (1.69)	Loss of $½H_2O$
	242–267	257	204.43	13.40 (13.31)	15.15 (14.50)	Loss of 2HCl (one step)

Table 7 MIC values of the carboxamides and their complexes

Compounds	MIC (μg/ml)					
	Staphylococcus aureus ATCC 25923	*E. coli* ATCC 1230	*B. magaterium* RSKK 5117	*B. cereus* RSKK 863	*Salmonella enteritidis* ATCC 13076	*B. subtilis* RSKK 244
L^1	197	230	183	215	245	228
L^2	206	247	198	229	253	234
$[Cu(L^1)]Cl_2$	259	298	237	270	321	281
$[Zn(L^1)]Cl_2$	266	325	248	290	336	301
$[Cu(L^2)]Cl_2$	350	416	343	387	438	395
$[Zn(L^2)]Cl_2 \cdot ½H_2O$	364	432	355	409	441	418

carboxamides. Whereas the density of HOMO orbitals is located around piperazine ring which is the same group at both carboxamides (Figs. 2, 3). This observation shows the importance of heteroaromatic ring on the antibacterial activity of the carboxamides (Deeb *et al*., 2007). The positive charges (Q_x) on the heteroaromatic ring donors (S/O) and molecular hydrophobicity that can be described by octanol/water partition coefficients (log*P*) are also responsible for the activity differences (Alves *et al*., 2000). The positive charges (Q_x) on the thiophene S may be understood as a measure of extension of the electronic delocalization around the aromatic ring and leads to an increasing of the antibacterial activity of L^1 (Lameira *et al*., 2006) log*P* values of L^1 (−2.73) and L^2 (−2.05) give clear indication that the thiophene ring is endowed with an increased lipophilicity and so with a higher capability to penetrate the bacteria.

Antibacterial activity

Results of antibacterial activities against bacteria; *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 11230, *B. magaterium* RSKK 5117, *B. cereus* RSKK 863, *Salmonella enteritidis* ATCC 13076, *B. subtilis* RSKK 244 are presented in Table 7.

The antibacterial activity results evidently show that the carboxamide compounds possessed a broad spectrum of activity against the tested bacteria at the concentrations of 183–441 μ/ml. All compounds show the highest activities against *B. magaterium* which is mostly effected by L^1 at the concentration of 183 μ/ml. It is observed that the presence of thiophene ring in the structure of carboxamides contribute positive increase of the antimicrobial activity in comparison to the furan ring for tested microorganism (Hamurcu *et al*., 2008).

The Cu(II) and Zn(II) complexes showed a remarkable decrease in antibacterial activity than the parent ligands. This result may be explained with the decrease of electron densities on donor atoms by coordination through thiophene/furan rings (Mohamed *et al*., 2005). As seen in Table 8, Cu(II) complexes show higher antibacterial activity than Zn(II) complexes.

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