European Journal of Chemistry 1 (3) (2010) 200-205

European Journal of Chemistry

Journal homepage: www.eurjchem.com

Synthesis, characterization and antibacterial activity of nickel (II) and copper (II) complexes of *N*-(alkyl(aryl)carbamothioyl)-4-nitrobenzamide

Sohail Saeed[a,*], Naghmana Rashid[a], Muhammad Ali[b] and Rizwan Hussain[c]

[a] *Department of Chemistry, Research Complex, Allama Iqbal Open University, Islamabad, 44000, Pakistan*
[b] *Department of Pharmacy, University of The Punjab, Lahore, 54590, Pakistan*
[c] *National Engineering & Scientific Commission, P.O. Box 2801, Islamabad, Pakistan*

**Corresponding author at: Department of Chemistry, Research Complex, Allama Iqbal Open University, Islamabad, 44000, Pakistan. Tel.: +92.51.9250081; fax: +92.51.9250081. E-mail address: sohail262001@yahoo.com (S. Saeed).*

ARTICLE INFORMATION

Received: 21 May 2010
Received in revised form: 21 July 2010
Accepted: 22 July 2010
Online: 30 September 2010

KEYWORDS

Thiourea derivatives
Transition metal complexes
X-ray structure determination
Phase-transfer catalyst
Antibacterial activity

ABSTRACT

Nickel and copper metal complexes of *N*-(R-carbamothioyl)-4-nitrobenzamide (R = diphenyl and ethylbutyl) were synthesized and characterized by IR, ^{1}H NMR, mass spectrometry and elemental analysis. The spectroscopic data are consistent with the ligand and the metal complexes containing two O and S chelated ligands. *N*-(diphenylcarbamothioyl)-4-nitrobenzamide, HL^1, was characterized by a single crystal X-ray diffraction study. It crystallizes in the triclinic space group $P\bar{1}$ with unit cell dimensions of a = 6.8044(4) Å, b = 10.0113(6) Å, c = 13.2365(8) Å, α = 6.8044(4) °, β = 78.171(4) °, γ = 13.2365(8)°, V = 882.43(9) Å^3. The ligands coordinate as bidentates yielding essentially neutral complexes of the type $[ML_2]$. The ligands and complexes were screened for their in vitro antibacterial activities and comparatively the complexes showed greater antibacterial efficacy than the thiourea derivative ligands.

1. Introduction

Cobalt, nickel and copper are essential elements for biological systems and are present in trace quantities. In each case, trace analysis of these elements require pre-concentration prior to their analysis. Thiourea derivatives are selective analytical reagents, especially for the determination of transition metals in complex inferring matrices [1]. Thioureas have a long history of being used as a ligand in coordination chemistry and to coordinate with a metal via sulfur and oxygen atoms [2].These hard and soft donor atoms provide a multitude of bonding possibilities [3]. Hydrogen bonding behaviour of some thioureas has been investigated and it is found that intramolecular hydrogen bonds between the carbonyl oxygen and a hydrogen atom on N' is common. The complexing capacity of thiourea derivatives has been reported in several articles [4,5]. It has been shown that the redox properties of these derivatives are markedly influenced by electronic factors [6-9]. Attachment of transition-metal complexes to electrodes has been investigated intensively in recent years [10]. The biological activity of complexes with thiourea derivatives has been successfully screened for various biological processes. On the other hand some thiourea derivatives and their transition metal complexes are also known to exhibit a wide range of biological activities including antiviral, antibacterial, antifungal, anticancer [11-13] antitubercular, antithyroidal, herbicidal and insecticidal activities [14] and as agrochemicals [15]. Some acyl thioureas have been found to possess pesticidal activities and promote plant growth [16] while some have been shown to have notable positive effect on the germination of maize seeds as well as on the chlorophyll contents in seedling leaves [17]. With the simultaneous presence of S, N and O electron donors, the versalitility and interesting behaviour of acylthioureas as building blocks in polydentate ligands for metal ions have become a topic of interest in the last few years. It has been reported that substituted acylthiourea ligands might act as monodentate sulfur donors, bidentate oxygen and nitrogen donors. They could also coordinate through the keto- or enol-thione form, depending of the ligands themselves, and the metal ions and counter-anions used [18-23].

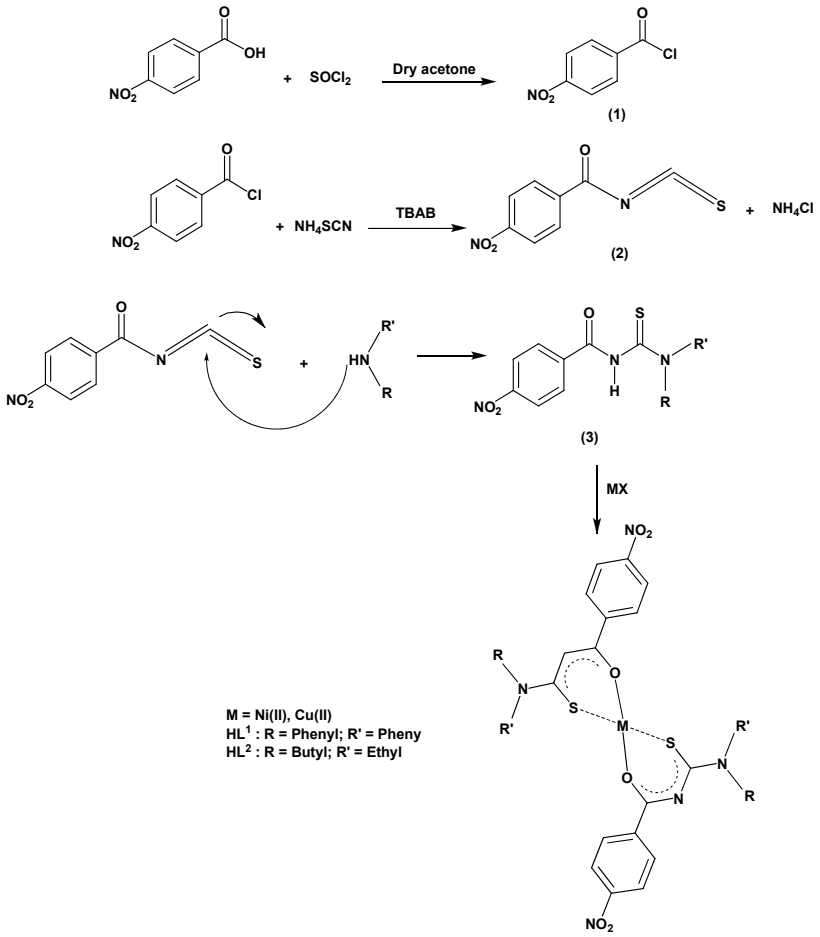
As a part of our continuing interest in biologically active thiourea derivatives and their transition metal complexes, we are reporting a route for synthesis of these compounds by using tetrabutylammonium bromide (TBAB) as phase-transfer catalyst (PTC) to augment the yield of products. In view of the above and in continuation of our research program concerned with structural modification of certain biologically active thiourea derivatives and their transition metal complexes with the purpose of enhancing their biological activity, we aimed to incorporate the aliphatic and aromatic moieties in the substituted phenyl nucleus with thiourea functionality to obtain new functions in an attempt to improve the antimicrobial profile of compounds.

2. Experimental

2.1. Instrumentation

The proton NMR and ^{13}C spectra were recorded in DMSO-d_6 on a Bruker-300 MHz spectrophotometer using tetramethylsilane as an internal reference. The apparent resonance multiplicity is described as: s (singlet), br s (broad singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet) and m (multiplet). Infrared spectra were recorded in the range 400-4000 cm^{-1} on spectrum 2000 by Perkin Elmer. Electronic spectra (dichloromethane solutions) were recorded

ISSN 2153-2249 (Print) / ISSN 2153-2257 (Online)
DOI:10.5155/eurjchem.1.3.200-205.120



Scheme 1

on a Shimadzu UV1601 spectrophotometer. Elemental analysis was carried out using Perkin Elmer CHNS/O 2400. The mass spectrum was run on a Finnigan TSQ-70 spectrometer (Finnigan, USA) at 70 eV). Single crystal X-ray data were collected on an Oxford Diffraction Xcalibur diffractometer using monochromated Mo-K_α radiation. Room temperature magnetic susceptibility measurements were carried out using a Sherwood-Scientific Gouy magnetic balance (Calibrant: $Hg[Co(SCN)_4]$).

2.2. Synthesis

2.2.1 General procedure for the synthesis of ligands

Starting material, reagents and solvents were of analytical reagent grade or of the highest quality commercially available and were purchased from Aldrich Chemical Co., Merck Chemical Co., and were dried when necessary. The 4-nitrobenzoic acid (0.1 mol) and $SOCl_2$ were added into a 250 cm^3 three-necked flask and stirred for 4.5 h, with temperature raised to 70 ^oC.The residual $SOCl_2$ was distilled under reduced pressure. The light yellow powder of 4-nitrobenzoyl chloride was obtained after complete distillation of the thionyl chloride. Then the solution of 4-nitrobenzoyl chloride (1.40 g, 0.01mol) in anhydrous acetone (80 cm^3) and 3% tetrabutylammonium bromide (TBAB) in acetone was added dropwise to a suspension of ammonium thiocyanate (0.76 g, 0.01 mol) in acetone (50 cm^3) and the reaction mixture was refluxed for 45 minutes. After cooling to room temperature, a solution of the corresponding secondary amine (1.71 g, 0.01 mol) in acetone (25 cm^3) was added and the resulting mixture refluxed for 1.5 h. The reaction mixture was poured into five times its volume of cold water, whereupon the thiourea precipitated. The solid product was washed with water and purified by re-crystallization from an ethanol-dichloromethane mixture (1:2) (Scheme 1).

_N_-(diphenylcarbamothioyl)-4-nitrobenzamide (HL^1):
Yellow. Yield: 95%. M.p.: 159-160 ^oC. FT-IR (KBr pellet) in cm^{-1}: 3152 (N-H), 1685 (C=O), 1618 (C=N stretching), 1592 (aromatic C=C), 1240 (C=S). ^1H NMR (300 MHz, DMSO-d_6) in δ (ppm) and J (Hz): 8.14 (s,1H, CONH), 8.10 (d,2H, J= 8.41), 7.34 (d, 2H, J = 8.7 Hz), 7.32-7.28 (m,10H, aromatic ring). ^{13}C NMR (300 MHz, DMSO-d_6) in δ (ppm): 179.5 (C=S), 167.2 (C=O), 140.2, 135.6, 130.1, 128.5, 127.1, 127.0, 126.3. EI MS, m/z (%): 377. Electronic spectrum, λ_{max} (cm^{-1}): 39221, 34598, 31698. Anal. Calcd. for $C_{20}H_{15}N_3O_3S$: C,63.65; H, 4.01; N,11.13; S,8.50. Found: C, 63.66; H, 4.03; N, 11.12; S, 8.49.

_N_-[butyl(ethyl)carbamothioyl]-4-nitrobenzamide (HL^2):
Yellow. Yield: 91%. M.p.:115-116 ^oC. FT-IR (KBr pellet) in cm^{-1}: 3165 (NH), 1676 (C=O), 1615 (C=N stretching), 1592 (aromatic C=C), 1228 (C=S). ^1H NMR (300 MHz, DMSO-d_6) in δ (ppm) and J (Hz): 8.45 (s,1H, CONH), 8.12 (d, 2H, J= 8.35), 7.35 (d, 2H, J = 8.8 Hz), 3.82 (t, 2H, CH_2), 3.54-3.50 (m, 2H, CH_2),1.85-1.68 (m, 2H, CH_2),1.65-1.60 (m, 2H, CH_2), 0.98 (t, 3H, CH_3), 0.91 (t, 3H, CH_3). ^{13}C NMR (300 MHz, DMSO-d_6) in δ (ppm): 178.0 (C=S), 168.4 (C=O), 141.2, 135.6, 130.1, 128.5, 60.6, 58.0, 45.3, 30.2, 15.9, 15.0. EI MS, m/z (%): 309. Electronic spectrum, λ_{max} (cm^{-1}): 42478, 34847, 26984. Anal. Calcd. for $C_{14}H_{19}N_3O_3S$: C,54.35; H, 6.19; N,13.58; S,10.36. Found: C, 54.32; H, 6.35; N, 13.57; S, 10.37.

2.2.2 Crystal structure determination of N-(diphenyl carbamothioyl)-4-nitrobenzamide (HL¹)

Crystal data: $C_{20}H_{15}N_3O_3S$, triclinic, space group $P\bar{1}$, a = 6.8044(4) Å, b = 10.0113(6) Å, c = 13.2365(8) Å, α = 6.8044(4)°, β = 78.171(4)°, γ = 13.2365(8)°, V = 882.43(9) Å^3, T = 100(2) K, Z = 2, F(000) = 392, D_x = 1.420 g cm^{-3}, μ = 0.2 mm^{-1}. Single crystals suitable for X-ray diffraction studies were obtained by evaporation from an ethanol/dichloromethane mixture. A pale yellow prism 0.25 × 0.2 × 0.1 mm^3 was mounted on a glass fibre in inert oil. Measurements were performed at 100 K on an Oxford Diffraction Xcalibur diffractometer with monochromated Mo-K_α radiation to $2\theta_{max}$ 60° (99.7% complete). The data were corrected for absorption using the multi-scan method. Of 44379 intensities, 5149 were independent (R_{int}: 0.0331). The structure was refined anisotropically using SHELXL-97 [24]. NH hydrogens were refined freely, other H atoms using a 'riding model'. The final $wR2$ was 0.088, with a conventional $R1$ of 0.031, for 248 parameters; S = 1.046; max. Δρ 0.45 e Å^{-3}.

2.2.3 Synthesis of the transition metal complexes

The transition metal complexes were prepared according to the method described in the literature [25]. The ligand was dissolved in ethanol (10 cm^3) and heated to reflux in the presence of the respective metallic acetate (0.01 mole) in ethanol (50 cm^3). After 2h, the mixture was allowed to cool to room temperature and the solid obtained was filtered off, washed with ethanol, and dried in a vacuum.

***Bis[N-(diphenylcarbamothioyl)-4-nitrobenzamide]nickel(II) ($Ni(L^1)_2$)*:** Purple. Yield: 75%. M.p.: 181-182 °C. FT-IR (KBr pellet) in cm^{-1}: 1592 (aromatic C=C), 1568 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6) in δ (ppm): 8.16-8.08 (m, 4H, aromatic), 7.59-7.45 (m, 4H, aromatic), 7.32-7.27(m, 20H, aromatic). Electronic spectrum, λ_{max} (cm^{-1}): 43659, 37841, 33214. Anal. Calcd. for $C_{40}H_{28}N_6O_6S_2Ni$: C, 59.34; H, 3.46; N, 10.38; S, 7.91. Found C, 59.38; H, 3.45; N, 10.41; S, 7.89.

***Bis[N-(diphenylcarbamothioyl)-4-nitrobenzamide] copper(II) ($Cu(L^1)_2$)*:** Green. Yield: 71%. M.p.: 144-145 °C. FT-IR (KBr pellet) in cm^{-1}:1587 (aromatic C=C), 1588 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6) in δ (ppm): 8.14-8.03 (m, 4H, aromatic), 7.54-7.46 (m, 4H, aromatic), 7.34-7.28 (m, 20H, aromatic). Electronic spectrum, λ_{max} (cm^{-1}): 44112, 38841, 34214. Anal. Calcd. For $C_{40}H_{28}N_6O_6S_2Cu$: C,59.19; H, 3.45; N,10.37; S,7.89. Found: C, 59.17; H, 3.46; N, 10.37; S, 7.88.

***Bis[N-[butyl(ethyl)carbamothioyl]-4-nitrobenzamide]nickel (II) ($Ni(L^2)_2$)*:** Purple. Yield: 76%. M.p.:135-136 °C. FT-IR (KBr pellet) in cm^{-1}: 1591 (aromatic C=C), 1571 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6) in δ (ppm): 8.16-8.08 (m, 4H, aromatic), 7.59-7.45 (m, 4H, aromatic), 3.45-3.41(m, 4H, N-CH_2), 1.74-1.68 (m, 4H, CH_2), 1.57-1.52 (m, 4H, CH_2), 0.95-0.84 (m, 12H, CH_3). Electronic spectrum, λ_{max}(cm^{-1}): 43659, 33914. Anal. Calcd. for $C_{28}H_{36}N_6O_6S_2Ni$: C,49.94; H, 5.35; N,12.48; S,9.51. Found: C, 49.96; H, 5.36; N, 12.47; S, 9.49.

***Bis[N-[butyl(ethyl)carbamothioyl]-4-nitrobenzamide] copper(II) ($Cu\ (L^2)_2$)*:** Green. Yield: 78%. M.p.: 125-126 °C. FT-IR (KBr pellet) in cm^{-1}: 1585 (aromatic C=C), 1579 (C=N). ^{1}H NMR (300 MHz, DMSO-d_6) in δ (ppm): 8.12-8.03 (m,4H, aromatic), 7.61-7.55 (m, 4H, aromatic), 3.45-3.41 (m, 4H, N-CH_2), 1.78-1.70 (m, 4H, CH_2), 1.57-1.52 (m, 4H, CH_2), 0.95-0.84 (m, 12H, CH_3). Electronic spectrum, λ_{max}(cm^{-1}): 35442, 33535. Anal. Calcd. for $C_{28}H_{36}N_6O_6S_2Cu$: C,49.79; H, 5.33; N,12.44; S,9.48. Found: C, 49.78; H, 5.36; N, 12.44; S, 9.46.

2.2.4 Evaluation of Antibacterial Activity

For the bacterial organisms, both Gram positive and Gram negative bacteria were used. Gram-positive and Gram-negative bacteria can be differentiated in the physical appearance of their cell envelopes. The compounds were screened for their in vitro antibacterial activities. Antimicrobial activities were determined by the broth micro-dilution procedures and principles of the Clinical and Laboratory Standards Institute (CLSI) [26,27]. Minimal inhibitory concentrations for each compound were investigated against standard bacterial strains; *Staphylococcus aureus* (ATCC 25923), *Enterococcus faecalis* (ATCC 29212), *Escherichia coli* (ATCC 25922), *Staphylococcus epidermidis* (ATCC 12228), *Enterobacter cloacae* (ATCC 13047), *Proteus valgaris* (ATCC 13315). Bacterial colonies of the test organisms were suspended directly into a small volume of 0.9% saline and further diluted until turbidity matched the Mc Farland Standard no: 0.5 Petri dishes containing Mueller-Hinton agar for bacteria was impregnated with these microbial suspensions. The stock solutions of the synthesized compounds were prepared in dimethyl sulfoxide (DMSO), which had no effect on the organisms in the concentrations studied. The initial concentration was 200 mg/mL. All of the dilutions were done with distillated water. The concentrations of tested compounds were 100, 50, 25, 12.5, 6.25, 3.125 μg/mL. DMSO was used as negative control. Gentamycin and amikacin were used as reference drugs for Gram negative antibacterial activity and Gram positive antibacterial activity, respectively. All the inoculated plates were incubated at 37 °C and results were evaluated after 24h for bacteria. The lowest concentration of the compounds that prevented visible growth was considered minimal inhibitor concentrations (MICs).

3. Results and Discussion

3.1. Synthesis and spectral studies

The substituted carbonyl isothiocyanate was synthesized through reaction of substituted carbonyl chloride and ammonium thiocyanate in acetone. The final compounds (HL¹ and HL²) were obtained by reaction of secondary amine with obtained substituted carbonyl isocyanate. The use of phase-transfer catalyst as a method of agitating a heterogeneous reaction system is gaining recognition [28,29]. In search of improving methods to prepare the target aroyl thiourea by reacting isothiocyanates with nucleophiles, we have found the use of tetrabutyl ammonium bromide (TBAB) as PTC can afford aroyl isothiocyanates in good yield. In this paper, we have conducted our reaction using tetrabutyl ammonium bromide (TBAB) as phase-transfer catalyst to synthesize the aroyl thiourea derivatives. The synthesized ligands were purified by re-crystallization from an ethanol: dichloromethane mixture (1: 2) and obtained in yields ranging from 95-91 %. The reaction of the ligands with metal salts at room temperature with ethanol as solvent yielded the new complexes (Scheme 1).

The chemical structure and purity of ligands and complexes were proved by using elemental analysis, ^{1}H NMR, and FT-IR spectroscopy. The measured results in elemental analysis closely corresponded to the calculated ones, demonstrating that the expected compound was obtained. The analytical and spectroscopic data are consistent with the proposed structure [30]. The main vibrational bands of the investigated ligands are given in the experimental section. Absorptions at 3152 and 3165 cm^{-1} for HL¹ and HL² are attributed to stretching of an N-H adjacent to *p*-nitrophenyl. The FT-IR spectra of the complexes show significant changes when compared with the FT-IR spectra of the corresponding ligands. The most striking changes are the N-H stretching frequency at ~3200 cm^{-1} in the free ligands, disappears completely, in agreement with both ligand and complex structure and the complexation reaction.

Another striking change is observed for the carbonyl stretching vibrations. A strong vibration (1685 and 1676 cm^{-1} for HL^1 and HL^2) in FT-IR spectra of the ligands is ascribed to the stretching of the carbonyl groups, which shifts to higher frequencies upon complexation of the thiourea ligands because the deprotonation induces delocalization of the carbonyl stretching vibration [31] and confirming coordination through oxygen. Due to this deprotonation which induces delocalization and the C=O cm^{-1} stretching vibration frequency decreases by *ca*. 180 cm^{-1} in agreement with the literature [32]. The same trend is observed for the thiocarbonyl stretching vibration frequencies, which are observed at approximately 1300 cm^{-1} in the free ligands, and shift to higher frequency after complexation; unfortunately, this vibration could not be assigned unambiguously. A large decrease should also be observed for the C=S stretch, but this vibration could not be located in the spectra of the complexes. IR spectra of the complexes are similar. The obtained complexes are crystalline solids soluble in most polar solvents. According to the elemental analysis, the nickel and copper metal complexes exist in dimeric form.

The ^1H NMR data of the compounds obtained in DMSO-d_6 solution are given in the experimental section and are consistent with the structural results. All the proton signals of the ligands shift to lower fields upon binding to metal ions as expected HL^1 and HL^2 show a peak at 8.14 and 8.45 ppm, respectively, corresponding to the proton of the N-H group. This peak does not appear in the nickel complexes that contain the deprotonated ligand, indicating an imine in these compounds [33], in agreement with the FT-IR spectra.

Electronic spectra of the ligands show two strong absorption bands (258 and 291 nm for HL^1 and 232 and 279 nm for HL^2) in the UV region. The first can be assigned to a $\pi\rightarrow\pi^*$ intraligand transition. In the metal complexes, bands below ~340 nm are attributed to intraligand transition [4,5]. A small shift should be observed for the second band in all complexes, these $\pi\rightarrow\pi^*$ transitions probably involving metal and ligand orbitals. Bands above ~340 nm are ascribed to charge transfer processes, probably from ligand to metal and mainly associated with the N-C=S and N-C=O groups. Absorption bands at higher wavelengths are due to d-d transitions [4,5].

The magnetic susceptibility values of the complexes show diamagnetic d^8 configuration of Ni^{2+} complexes, while the Cu^{2+} complexes are paramagnetic. The measured values for the $Cu(L^1)_2$ and $Cu(L^2)_2$ complexes are 1.76 and 1.78 B.M., respectively. These values show that the Ni^{2+} and Cu^{2+} complexes are square-planar. All data agree with Arslan *et al*. [33].

3.2. Single crystal X-ray studies

The molecular structure of the ligand (HL^1) is shown in Figure 1. Bond lengths and angles are presented in Table 1. The C1-S and C2-O1 bonds show a typical double bond character with bond lengths of 1.6686(10) Å and 1.2166(12) Å, respectively. All the C-N bond lengths, C1-N1 1.3441(12) Å, C21-N1 1.4463(12) Å, C31-N1 1.4491(12) Å, C2-N2 1.3895(12) Å, C1-N2 1.3957(12) Å and C14-N3 1.4728(13) Å also indicate a partial double bond character. The C1-N2 bond is adjacent to the carbonyl group and thus slightly shorter than to the C1-N1 bond. These bond distances are in good agreement with those observed in structures containing the *N*-benzoyl-*N'*-phenylthiourea moiety, as reported in the Cambridge Structural Database [34]. The molecule displays no extended planar moieties other than the ring systems. Defining a molecular backbone as C16-C11-C2-N2-C1-N1-C21-C22, only three of the five torsion angles (-153, -173, 49, -169, -111°) correspond approximately to antiperiplanar geometry. The molecular packing (Figure 2) involves the classical hydrogen bond N2-H02···S and two weak interactions C-H···O (Table 2); two weak C-H···S interactions are shown in the table but not in the Figure. The overall effect is to create thick layers of molecules parallel to the *xy* plane.

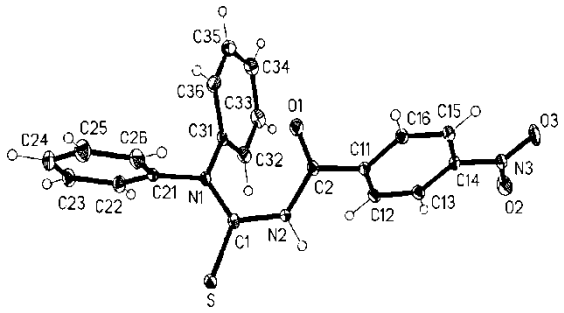


Figure 1. Perspective view of one of the independent molecules of *N*-(diphenylcarbamothioyl)-4-nitrobenzamide (HL^1) with atom labelling scheme. Thermal ellipsoids are drawn at the 50% probability level.

Table 1. Bond lengths [Å] and angles [°] for *N*-(diphenylcarbamothioyl)-4-nitrobenzamide (HL^1).

Bond lengths	
S-C1	1.6686(10)
O1-C2	1.2166(12)
N1-C1	1.3441(12)
N1-C21	1.4463(12)
N1-C31	1.4491(12)
N2-C2	1.3895(12)
N2-C1	1.3957(12)
C2-C11	1.4942(13)
N3-O3	1.2295(11)
C21-C22	1.3882(14)
C22-C23	1.3886(14)
C23-C24	1.3878(16)
C25-C26	1.3954(15)
N3-O2	1.2269(12)
N3-O3	1.2295(11)
Bond angles	
N1-C1-N2	116.17(8)
N1-C1-S	123.51(7)
N2-C1-S	120.27(7)
O1-C2-N2	122.92(9)
O1-C2-C11	122.02(9)
N2-C2-C11	115.05(8)
C16-C11-C12	120.10(9)
C16-C11-C2	117.96(9)
C12-C11-C2	121.79(9)
C13-C12-C11	120.01(9)
C14-C15-C16	117.93(9)
O2-N3-O3	124.09(9)
O2-N3-C14	118.26(9)
O3-N3-C14	117.66(9)
C26-C21-C22	121.41(9)
C26-C21-N1	119.66(9)
C22-C21-N1	118.83(9)
C21-C22-C23	119.37(10)
C25-C24-C23	120.30(10)
C24-C25-C26	120.35(10)
C21-C26-C25	118.70(10)
C36-C31-C32	121.12(9)
C36-C31-N1	118.80(9)
C32-C31-N1	120.03(9)
C31-C32-C33	118.96(10)

3.3. Antibacterial activity

Primary bioassay screening provides the first indication of bioactivities and helps in the selection of lead compound for secondary screening for detailed pharmacological evaluation. In the light of interesting antimicrobial activities of thiourea derivatives and their complexes were screened for antibacterial activity against *S. aureus*, *S. epidermidis*, *E. faecalis*, *E. coli*, *E. cloacae* and *P. valgaris* by the broth microdilution procedure. The in vitro antibacterial properties against a number of Gram negative and Gram positive bacteria are

Table 2. Hydrogen bonds [Å and °] for *N*-(diphenylcarbamothioyl)-4-nitrobenzamide (HL^1).

D-H...A	d (D-H)	d (H...A)	d (D...A)	< (DHA)
N(2)-H(02)...S^{i}	0.873(14)	2.503(14)	3.3722(9)	173.7(12)
C(12)-H(12)...S^{i}	0.95	2.98	3.3075(10)	101.9
C(26)-H(26)...S^{ii}	0.95	3.00	3.9364(11)	168.7
C(25)-H(25)...S^{iii}	0.95	2.99	3.8856(12)	156.8
C(13)-H(13)...O(1)^{iv}	0.95	2.42	3.1484(12)	132.8
C(16)-H(16)...O(2)^{iii}	0.95	2.53	3.2218(13)	129.8
C(33)-H(33)...O(3)^{v}	0.95	2.62	3.1332(14)	114.7

Symmetry transformations used to generate equivalent atoms: (i) -*x*+1,-*y*+1,-*z*+1; (ii) -*x*,-*y*+1,-*z*+1; (iii) *x*-1, *y*, *z*; (iv) *x*+1, *y*, *z*; (v) *x*, *y*+1, *z*.

Table 3. MIC values (μg/cm^3) of the synthesized compounds against the tested Gram negative and Gram positive bacteria.

Compound	*E. Cloacae* (ATCC 13047)	*E. Coli* (ATCC 25922)	*P. Vulgaris* (ATCC 13315)	*S. Epidermidis* (ATCC 12228)	*E. Faecalis* (ATCC 29212)	*S. Aureus* (ATCC 25923)
HL^1	200	300	200	100	300	200
HL^2	200	200	200	200	200	300
$Cu(L^1)_2$	100	100	100	50	100	80
$Ni(L^1)_2$	100	100	100	200	200	200
$Cu(L^2)_2$	100	100	100	30	100	50
$Ni(L^2)_2$	200	100	100	100	100	100
Ref. Drugs	2*	1*	2*	0.5 ‡	4‡	2‡

* Gentamycin, ‡ Amikacin.

presented in Table 3. All the compounds inhibited the growth of bacteria with MIC values ranging between 30 and 300 μg/cm^3.

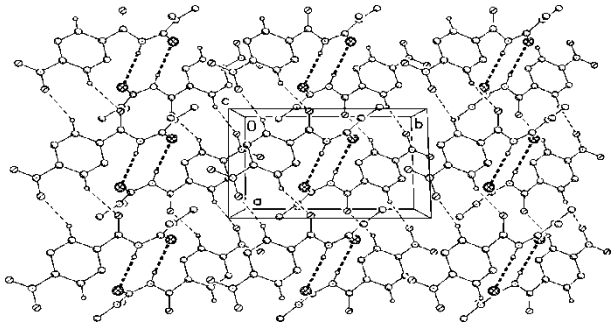


Figure 2. Packing diagram of *N*-(diphenylcarbamothioyl)-4-nitrobenzamide (HL^1) viewed parallel to the *z* axis. The dashed lines denote the hydrogen bonds (thick lines, N-H···S; thin lines, C-H···O). Phenyl rings of the diphenylamine groups are represented by the *ipso* carbons only.

According to the antibacterial studies, the efficacy against Gram positive is higher than Gram negative bacteria. Two of six compounds showed good activity against *S. epidermidis* and *S. aureus*. In addition, $Cu(L^1)_2$ and $Cu(L^2)_2$ showed high activity against Gram-positive bacteria. The investigated compounds antimicrobial activity values in this research were higher than that reported for other transition metal complexes of thiourea derivatives [35].

4. Conclusion

In conclusion, the *N*-(alkyl(aryl)carbamothioyl)-4-nitro benzamide ligands act as bidentate ligands through the sulfur and oxygen atom, forming strong complexes with the metal centre Ni(II) and Cu(II). In addition, biological activity studies shows that the antibacterial efficacy of these complexes is comparatively higher than the ligands.

Acknowledgement

The authors are thankful to National Engineering & Scientific Commission, Islamabad for providing the facilities of spectroscopic and elemental analysis free of cost.

Supplementary material

CCDC-755272 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by e-mailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033.

References

[1]. Arslan, H.; Flörke, U.; Külcü, N. *Trans. Metal Chem*. **2003**, *28*, 816-819.
[2]. Moloto, M. J.; Malik, M. A.; O'Brien. P.; Motevalli, M.; Kolawole, G. A. *Polyhedron* **2003**, *22*, 595-603.
[3]. Henderson, W.; Nicholson, B. K.; Dinger, M. B.; Bennett, R. L. *Inorg. Chim. Acta*, **2002**, *338*, 210-218.
[4]. Mansuroglu, D. S.; Arslan, H.; Flörke, U.; Külcü, N. *J. Coord. Chem*. **2008**, *61*, 3134-3146.
[5]. Arslan, H.; Flörke, U.; Külcü, N.; Emen, M. F. *J .Coord. Chem*. **2006**, *59*, 223-228.
[6]. Lipowska, M.; Hayes, B. L.; Hansen, L.; Taylor, A.; Marzilli, L. G. *Inorg. Chem*. **1996**, *35*, 4227-4231.
[7]. Dominguez, M.; Antico, E.; Beyer, L.; Aguirre, A.; Garcia-Granda, S.; Salvado, V. *Polyhedron* **2002**, *21*, 1429-1437.
[8]. Zhang, Y. M.; Pang, H. X; Cao, C.; Wei, T. B. *J. Coord. Chem*. **2008**, *61*, 1663-1670.
[9]. Dechamps-Olivier, I.; Guillon, E.; Mohamadou, A.; Barbier, J. P. *Polyhedron* **1996**, *15*, 3617-3622.
[10]. Losada, J.; Peso, D. I.; Beyer, L. *Trans. Metal Chem*., **2000,** *25*, 112-115.
[11]. Saeed, S.; Rashid, N.; Hussain, R.; Ali, M.; Jones, P. G. *Eur. J. Med. Chem*. **2010**, *45*, 1323-1331.
[12]. Saeed, S.; Rashid, N; Jones, P. G.; Hussain, R.; Bhatti, M. H. *Cent. Eur. J. Chem*. **2010**, *8(3)*, 550-558.
[13]. Saeed, S.; Rashid, N; Jones, P. G.; Yunus, U. *J. Heterocycl. Chem*. **2010**, *47*, 908-912.
[14]. Eweis, M.; Elkholy, S. S.; Elsabee, M. Z. *Int. J. Biol. Macromol*. **2006**, *38*, 1-8.
[15]. Lachkova, V.; Varbanov, S.; Hagele, G.; Keck, H.; Tosheva, T. *Phosphorus. Sulfur Silicon Relat. Elem.* **2002**, *177*, 1303-1313.
[16]. Avsar, G.; Arslan, H.; Haupt, J.; Külcü, N. *Turk. J. Chem.* **2003,** *27*, 281-285.
[17]. Libe, F.; Philip, U. C. Miscellaneous structures of New Herbicides, *Chem. Plant Prot*. **1994**, *10*, 189-216.
[18]. Ru, C.; Wang, Y.; Li, J.; Ma, D.; Gong, F.; Liu, Y.; Lu. P. *Yingyong Huaxue* **1994**, *11*, 82-85.
[19]. Che, D. J.; Li, G.; Yao, X. L. ; Wang, Q. J. W. L.; Zhu, Y. *J. Organomet. Chem*. **1999**, *584*, 190-195.
[20]. Che, D. J.; Yao, X. L.; Li, G.; Li, Y. H. *J. Chem. Soc., Dalton Trans.* **1998**, *11*, 1853-1856.
[21]. Cernak, J.; Chomic, J.; Kutschy, P.; Svercinova, D.; Dzurilla, M. *Inorg. Chim. Acta* **1991**, *181*, 85-92.
[22]. Hernandez, W.; Spodine, E. ; Munoz, J. C.;Beyer, L.; Schroder, U.; Ferreira, J.; Pavani, M. *Bioinorg. Chem. Appl.* **2003**, *1(3-4)*, 271-284.
[23]. Hernandez, W.; Spodine, E.; Beyer, L.; Schroder, U.; Richter, R.; Ferreira, J.; Pavani, M. *Bioinorg. Chem. Appl* .**2005**, *3(3-4)*, 299-316.
[24]. Sheldrick, G. M. *Acta Cryst*. **2008**, *A64*, 112-122.
[25]. Safin, D. A.; Bolte, M.; Babashkina, M. G. *Trans. Metal Chem*. **2009**, *34*, 43-49.
[26]. National Committee for Clinical Laboratory Standards, M7-A4 (NCCLS, Viallanova, PA, USA, 1997).
[27]. National Committee for Clinical Laboratory Standards, M27-A2 (NCCLS, Wayne, PA, USA, 2002).
[28]. Wei, T. B.; Chen, J. C.; Wang, X. C. *Synth. Commun*. **1996**, *26*, 1147-1152.
[29]. Illi, V. O. *Tetrahedron Lett*. **1979**, *20*, 2431-2435.

[30]. Mansuroglu, D. S.; Arslan, H.; Derveer, D. V.; Binzet, G. *Phosphorus. Sulfur Silicon Relat. Elem.* **2009**, *184*, 3221-3230.
[31]. Arslan, H.; Mansuroglu, D. S.; Derveer, D. V.; Binzet, G. *Spectrochim. Acta A* **2009,** *72*, 561-571.
[32]. Mikami, M.; Nakagawa, I.; Shimanouch, T. *Spectrochim. Acta A*, **1967**, *23*, 1037-1042.
[33]. Binzet, G.; Arslan, H.; Flörke, U.; Külcü, N. *J. Coord. Chem*. **2006**, *59*, 1395-1406.
[34]. Allen, F. H. *Acta Cryst.* 2002, *B58*, 380-388.
[35]. Arslan, H.; Duran, N.; Borekci, G.; Ozer, C. K.; Akbay, C. *Molecules*, **2009**, *14*, 519-527.