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Synthesis, Characterization and Antimicrobial Activities of Some Metal Complexes with *N*′-(2-Chloro-benzoyl)thiourea Ligands: The Crystal Structure of *fac*-[CoL_3] and *cis*-[PdL_2]

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We report the synthesis, structural characterization and antimicrobial activities of *N*,*N*-dimethyl-*N*′-(2-chloro-benzoyl)thiourea (L^1H) and *N*-pyrrolidine-*N*′-(2-chloro-benzoyl)thiourea (L^2H) and their Ni(II), Cu(II), Zn(II), Pt(II), Pd(II) and Co(III) complexes. The structure of the prepared compounds was investigated by using elemental analyses, IR, ^{1}H-NMR, UV-Vis, mass spectra and magnetic susceptibility. The prepared compounds were screened for their *in vitro* antibacterial and antifungal activities. All compounds showed antimicrobial activity, however, the antibacterial efficacy is better than antifungal activity. Molecular structures of $Co(L^1)_3$ and $Pd(L^1)_2$ were determined by single crystal X-ray diffraction methods. The ligands coordinate to Ni(II), Cu(II), Zn(II), Pt(II) and Pd(II) in a bidentate manner yielding essentially neutral complexes of the type ML_2. The coordination polyhedra around the Co(III) ion are distorted octahedra.

Key words: thioureas, synthesis, X-ray structure, antimicrobial activities, benzoylthiourea complexes

Thioureas are well known class of excellent ligands for transition metals. Amongst the attractive features of these ligands is their facile synthesis from readily available and inexpensive starting materials [1]. These stable molecules have been found to display remarkably rich coordination chemistry, showing a more varied coordination behaviour [2]. One of them is *N*,*N*-dialkyl-*N*′-benzoyl thiourea derivatives which form neutral chelates with lots of metal ions in aqueous solutions and these chelates can be extracted with $CHCl_3$ and separated by chromatography [3–9]. The biological activities of complexes have been successfully screened for various biological actions. On the other hand some thiourea derivatives have been used in commercial fungicides. The derivative *N*-(*o*-nitrophenyl)-*N*′-(ethoxycarbonyl) thiourea was isolated from the leaves of resistant *Pyricuiria oryzae cav.* rice variety and the preliminary pharmacological tests showed its high antibacterial activity [10–13]. In preceding papers, we have reported synthesis, characterization, crystal

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structure, thermal behaviour and antimicrobial activity of some benzoylthiourea derivatives and their metal complexes [14–25].

In this paper, we report the preparation, structural properties and antimicrobial activities of *N*,*N*-dimethyl-*N*′-(2-chloro-benzoyl)thiourea and *N*-pyrrolidine-*N*′-(2-chloro-benzoyl)thiourea and their Ni^{II}, Cu^{II}, Zn^{II}, Pt^{II}, Pd^{II} and Co^{III} complexes. The crystal structures of tris[*N*,*N*-dimethyl-*N*′-(2-chloro-benzoyl)thioureato]cobalt(III) and bis[*N*,*N*-dimethyl-*N*′-(2-chloro-benzoyl)thioureato]palladium(II) complexes are also described.

EXPERIMENTAL

Instrumentation. Infrared spectra were recorded in the range of 4000–400 cm^{-1} on a WinFirst Satellite spectrophotometer, using KBr pellets. All ^{1}H-NMR spectra were recorded on a Bruker DPX 300 spectrometer, using $CDCl_3$ as a solvent and TMS as an internal standard. Mass spectra were recorded on a VG Autospec, with the EI techniques. Elemental analyses were carried out on a Carlo Erba MOD 1106 instrument. Room temperature magnetic susceptibility measurements were carried out on a Sherwood-Scientific model Gouy magnetic balance (calibrant: $Hg[Co(SCN)_4]$). Melting point determinations were performed with a digital melting point instrument from Electrothermal model 9200. Single crystal X-ray data were collected on a Bruker AXS SMART APEX CCD, using monochromated MoK_α radiation. The structures were solved by direct and conventional Fourier methods. Full-matrix least-squares refinement was based on F^2. All but hydrogen atoms refined anisotropically, H-atoms on idealized positions with 'riding' model. Programs used for calculations: SHELXTL [26]. Further details concerning data collection and refinement are given in Table 1.

Synthesis of the ligands. All chemicals used for the preparation of the ligands and complexes were of reagent grade quality. The ligands were prepared by a procedure similar to that reported in the literature [21]. A solution of 2-chlorobenzoyl chloride ($5\cdot10^{-2}$ mol) in acetone (50 cm^3) was added drop wise to a suspension of potassium thiocyanate ($5\cdot10^{-2}$ mol) in acetone (30 cm^3). The reaction mixture was heated under reflux for 30 min, and then cooled to room temperature. A solution of secondary amine (pyrrolidine or dimethyl amine) ($5\cdot10^{-2}$ mole) in acetone (10 cm^3) was added and the resulting mixture was stirred for 2 h. Hydrochloric acid (0.1 N, 300 cm^3) was added and the solution was filtered. The solid product was washed with water and purified by recrystallization from ethanol.

N,N-Dimethyl-N′-(2-chloro-benzoyl)thiourea, (HL^1): White. Yield: 81%, m.p. 157–159°C. Anal. Calcd. for $C_{10}H_{11}N_2OSCl$: C, 49.5; H, 4.1; N, 11.5. Found: C, 49.6; H, 4.1; N, 11.8. IR (KBr pellet, cm^{-1}): ν(N–H) 3159 (br), ν(C=O) 1706 (s), ν(C=S) 1385 (s), ν(C–Cl) 749 (s). ^{1}H-NMR ($CDCl_3$): 8.60 (s, 1H, NH), 7.66 (d, 1H, C_6H_4Cl), 7.46–7.27 (m, 3H, C_6H_4Cl), 3.49 (s, 3H, CH_3), 3.34 (s, 3H, CH_3). MS (EI), *m/z* (%) = 242 (M, 10), 207 (100), 139 (80), 111 (40), 71 (48) and 44 (39). λ_{max}, nm (CH_2Cl_2) (ε, M^{-1} cm^{-1}): 236 (11100), 281 (9288).

N-Pyrrolidine-N′-(2-chloro-benzoyl)thiourea, (HL^2): White. Yield: 78%, m.p. 185–187°C. Anal. Calcd. for $C_{12}H_{13}N_2OSCl$: C, 53.6; H, 4.7; N, 10.4. Found: C, 53.7; H, 4.8; N, 10.6. IR (KBr pellet, cm^{-1}): ν(N–H) 3154 (br), ν(C=O) 1700 (s), ν(C=S) 1326 (s), ν(C–Cl) 748 (s). ^{1}H-NMR ($CDCl_3$): 8.70 (s, 1H, NH), 7.66 (d, 1H, C_6H_4Cl), 7.45–7.28 (m, 3H, C_6H_4Cl), 3.88–3.68 (m, 4H, N-CH_2), 2.12–2.00 (m, 4H, CH_2). MS (EI), *m/z* (%) = 268 (M, 10), 233 (100), 139 (70), 111 (45), 97 (33), 70 (72) and 43 (10). λ_{max}, nm (CH_2Cl_2) (ε, M^{-1} cm^{-1}): 232 (11385), 280 (10078).

Synthesis of the complexes. Metallic salts used for preparation of the complexes were obtained from Merck. Metallic complexes were prepared according to the method described in the literature [21]. The metallic acetate solutions in ethanol were added drop wise to the ligands in a 1:2 mole ratio for copper, nickel, palladium, platinum, zinc and in a 1:3 mole ratio for cobalt with a small excess of ligand in dichloromethane. The solid complexes were filtered off and recrystallized from ethanol/dichloromethane mixture (1:1).

Table 1. Summary of crystallographic data and parameters of the $Pd(L^1)_2$ and $Co(L^1)_3$.

Compound	$Pd(L^1)_2$	$Co(L^1)_3$
Empirical formula	$C_{20}H_{20}Cl_2PdN_4O_2S_2$	$C_{30}H_{30}Cl_3CoN_6O_3S_3$
Formula weight	589.82	784.06
Temperature (K)	120(2)	173(2)
Wavelength (Å)	0.71073	0.71073
Crystal system	Orthorhombic	Monoclinic
Space group	*Pbca*	$P2_1/n$
Unit cell dimensions		
a (Å)	7.3326(5)	10.8424(7)
b (Å)	22.4596(15)	16.5682(9)
c (Å)	27.4356(17)	20.0507(12)
α (°)	90	90
β (°)	90	105.635(1)
γ (°)	90	90
V (Å^3)	4518.3(5)	3468.6(4)
Z	8	4
D_c (Mg/m^3)	1.734	1.501
Absorption coefficient (mm^{-1})	1.269	0.948
F(000)	2368	1608
Crystal size (mm^3)	0.25 × 0.08 × 0.07	0.08 × 0.06 × 0.05
θ range for data collection (°)	1.48 to 28.30	1.62 to 28.40
Index ranges	–9 ≤ h ≤ 9 –29 ≤ k ≤ 29 –36 ≤ l ≤ 34	–12 ≤ h ≤ 14 –16 ≤ k ≤ 22 –26 ≤ l ≤ 23
Reflections collected	44723	21425
Independent reflections (R_{int})	5609 (0.0873)	8122 (0.0566)
Absorption correction	Semi empirical from equivalents	Semi empirical from equivalents
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/parameters	5609/284	8122/415
Goodness-of-fit on F^2	1.065	0.822
Final R indices [$I > 2\sigma(I)$]	R1 = 0.0424, wR2 = 0.0798	R1 = 0.0489, wR2 = 0.0848
R indices (all data)	R1 = 0.0626, wR2 = 0.0861	R1 = 0.0926, wR2 = 0.0948
Largest diff. peak and hole (e.Å^{-3})	1.052 and –0.522	0.755 and –0.758

Bis(N,N-dimethyl-N′-(2-chloro-benzoyl)thioureato)nickel(II) [(Ni(L^1)$_2$)]: Pink. Yield: 84%, m.p. 243–245°C. Anal. Calcd. for $C_{20}H_{20}N_4O_2S_2Cl_2Ni$: C, 44.3; H, 3.7; N, 10.3. Found: C, 44.5; H, 3.8; N, 10.4. IR (KBr pellet, cm^{-1}): ν(C=O) 1508 (w), ν(C–Cl) 752 (s). ^{1}H-NMR ($CDCl_3$): 7.74–7.70 (m, 2H, C_6H_4Cl), 7.33–7.19 (m, 6H, C_6H_4Cl), 3.33 (s, 6H, CH_3), 3.30 (s, 6H, CH_3). λ_{max}, nm (CH_2Cl_2) (ε, M^{-1} cm^{-1}): 267 (25431), 291 (2543), 356 (3787), 508 (35).

Bis(N,N-dimethyl-N′-(2-chloro-benzoyl)thioureato)copper(II) [Cu(L^1)$_2$]: Green. Yield: 71%, m.p. 165–167°C. Anal. Calcd. for $C_{20}H_{20}N_4O_2S_2Cl_2Cu$: C, 43.9; H, 3.7; N, 10.2. Found: C, 42.8; H, 3.8; N, 10.2. IR (KBr pellet, cm^{-1}): ν(C=O) 1504 (w), ν(C–Cl) 749 (s). λ_{max}, nm (CH_2Cl_2) (ε, M^{-1} cm^{-1}): 251 (24656), 277 (27308), 594 (15).

Tris(N,N-dimethyl-N′-(2-chloro-benzoyl)thioureato)cobalt(III) [Co(L^1)$_3$]: Pale green. Yield: 92%, m.p. 223–225°C. Anal. Calcd. for $C_{30}H_{30}N_6O_3S_3Cl_3Co$: C, 45.9; H, 4.2; N, 10.7. Found: C, 46.0; H, 4.1; N, 10.8. IR (KBr pellet, cm^{-1}): ν(C=O) 1566 (w), ν(C–Cl) 743 (s). ^{1}H-NMR ($CDCl_3$): 7.80–7.76 (d, 3H, C_6H_4Cl), 7.31–7.15 (m, 9H, C_6H_4Cl), 3.47 (s, 9H, CH_3), 3.41 (s, 9H, CH_3). λ_{max}, nm (CH_2Cl_2) (ε, M^{-1} cm^{-1}): 278 (51884), 358 (7257), 475 (36), 610 (35).

Bis(N,N-dimethyl-N′-(2-chloro-benzoyl)thioureato)platinum(II) [(Pt(L^1)$_2$)]: Yellow. Yield: 88%, m.p. 227–230°C. Anal. Calcd. for $C_{20}H_{20}N_4O_2S_2Cl_2Pt$: C, 35.4; H, 3.0; N, 8.3. Found: C, 34.6; H, 2.9; N, 8.2. IR (KBr pellet, cm^{-1}): ν(C=O) 1568 (w), ν(C–Cl) 748 (s). ^{1}H-NMR ($CDCl_3$): 7.82–7.80 (d, 2H, C_6H_4Cl), 7.39–7.23 (m, 6H, C_6H_4Cl), 3.38 (s, 6H, CH_3), 3.33 (s, 6H, CH_3). λ_{max}, nm (CH_2Cl_2) (ε, M^{-1} cm^{-1}): 244 (14344), 259 (14445), 276 (11919), 324 (8181).

Bis(N,N-dimethyl-N′-(2-chloro-benzoyl)thioureato)palladium(II) [(Pd(L^1)$_2$)]: Yellow. Yield: 79%, m.p. 240–243°C. Anal. Calcd. for $C_{20}H_{20}N_4O_2S_2Cl_2Pd$: C, 40.7; H, 3.4; N, 9.5. Found: C, 41.7; H, 3.3; N, 9.7. IR (KBr pellet, cm^{-1}): ν(C=O) 1567 (w), ν(C–Cl) 748 (s). ^{1}H-NMR ($CDCl_3$): 7.80–7.78 (d, 2H, C_6H_4Cl), 7.40–7.23 (m, 6H, C_6H_4Cl), 3.42 (s, 6H, CH_3), 3.33 (s, 6H, CH_3). λ_{max}, nm (CH_2Cl_2) (ε, M^{-1} cm^{-1}): 236 (17169), 274 (29616), 385 (312).

Bis(N,N-dimethyl-N′-(2-chloro-benzoyl)thioureato)zinc(II) [(Zn(L^1)$_2$)]: White. Yield: 82%, m.p. 237–240°C. Anal. Calcd. for $C_{20}H_{20}N_4O_2S_2Cl_2Zn$: C, 43.8; H, 3.7; N, 10.2. Found: C, 42.9; H, 3.8; N, 10.0. IR (KBr pellet, cm^{-1}): ν(C=O) 1591 (w), ν(C–Cl) 747 (s). ^{1}H-NMR ($CDCl_3$): 7.76–7.74 (d, 2H, C_6H_4Cl), 7.41–7.26 (m, 6H, C_6H_4Cl), 3.50 (s, 6H, CH_3), 3.43 (s, 6H, CH_3). λ_{max}, nm (CH_2Cl_2) (ε, M^{-1} cm^{-1}): 237 (40513), 281 (26373).

Bis(N-pyrrolidine-N′-(2-chloro-benzoyl)thioureato)nickel(II) [Ni(L^2)$_2$)]: Pink. Yield: 77%, m.p. 253–255°C. Anal. Calcd. for $C_{24}H_{24}N_4O_2S_2Cl_2Ni$: C, 48.5; H, 4.1; N, 9.4. Found: C, 48.3; H, 4.2; N, 9.5. IR (KBr pellet, cm^{-1}): ν(C=O) 1522 (w), ν(C–Cl) 746 (s). ^{1}H-NMR ($CDCl_3$): 7.76–7.72 (d, 2H, C_6H_4Cl), 7.33–7.19 (m, 6H, C_6H_4Cl), 3.81–3.75 (m, 4H, CH_2), 3.66–3.60 (m, 4H, CH_2), 2.05–1.87 (m, 8H, CH_2). λ_{max}, nm (CH_2Cl_2) (ε, M^{-1} cm^{-1}): 268 (32681), 292 (35157), 359 (6684), 506 (240).

Bis(N-pyrrolidine-N′-(2-chloro-benzoyl)thioureato)copper(II) [Cu(L^2)$_2$]: Green. Yield: 75%, m.p. 168–170°C. Anal. Calcd. for $C_{24}H_{24}N_4O_2S_2Cl_2Cu$: C, 48.5; H, 4.1; N, 9.6. Found: C, 48.3; H, 4.2; N, 9.4. IR (KBr pellet, cm^{-1}): ν(C=O) 1566 (w), ν(C–Cl) 747 (s). λ_{max}, nm (CH_2Cl_2) (ε, M^{-1} cm^{-1}): 250 (20914), 280 (28918), 363 (6196), 585 (249).

Tris(N-pyrrolidine-N′-(2-chloro-benzoyl)thioureato)cobalt(III) [Co(L^2)$_3$]: Green. Yield: 89%, m.p. 217–219°C. Anal. Calcd. for $C_{36}H_{36}N_6O_3S_3Cl_3Co$: C, 50.2; H, 4.2; N, 9.8. Found: C, 50.3; H, 4.1; N, 9.6. IR (KBr pellet, cm^{-1}): ν(C=O) 1567 (w), ν(C–Cl) 746 (s). ^{1}H-NMR ($CDCl_3$): 7.87–7.83 (d, 3H, C_6H_4Cl), 7.40–7.14 (m, 9H, C_6H_4Cl), 3.98–3.82 (m, 12H, CH_2), 2.07–1.89 (m, 12H, CH_2). λ_{max}, nm (CH_2Cl_2) (ε, M^{-1} cm^{-1}): 281 (49252), 350 (52726), 475 (650), 610 (613).

Bis(N-pyrrolidine-N′-(2-chloro-benzoyl)thioureato)platinum(II) [Pt(L^2)$_2$]: Yellow. Yield: 79%, m.p. 241–243°C. Anal. Calcd. for $C_{24}H_{24}N_4O_2S_2Cl_2Pt$: C, 39.5; H, 3.3; N, 7.7. Found: C, 38.9; H, 3.4; N, 7.8. IR (KBr pellet, cm^{-1}): ν(C=O) 1563 (w), ν(C–Cl) 743 (s). ^{1}H-NMR ($CDCl_3$): 7.84–7.82 (d, 2H, C_6H_4Cl), 7.32–7.22 (m, 6H, C_6H_4Cl), 3.81–3.78 (m, 4H, CH_2), 3.66–3.63 (m, 4H, CH_2), 2.09–1.95 (m, 8H, CH_2). λ_{max}, nm (CH_2Cl_2) (ε, M^{-1} cm^{-1}): 245 (1956), 261 (1827), 279 (1500), 326 (913), 357 (456).

Bis(N-pyrrolidine-N′-(2-chloro-benzoyl)thioureato)palladium(II) [Pd(L^2)$_2$]: Yellow. Yield: 77%, m.p. 248–250°C. Anal. Calcd. for $C_{24}H_{24}N_4O_2S_2Cl_2Pd$: C, 44.9; H, 3.8; N, 8.7. Found: C, 46.0; H, 3.9; N, 9.0. IR (KBr pellet, cm^{-1}): ν(C=O) 1568 (w), ν(C–Cl) 748 (s). ^{1}H-NMR ($CDCl_3$): 7.83–7.80 (d, 2H, C_6H_4Cl), 7.38–7.22 (m, 6H, C_6H_4Cl), 3.90–3.83 (m, 4H, CH_2), 3.76–3.72 (m, 4H, CH_2), 2.08–1.93 (m, 8H, CH_2). λ_{max}, nm (CH_2Cl_2) (ε, M^{-1} cm^{-1}): 232 (2808), 273 (4814).

Bis(N-pyrrolidine-N′-(2-chloro-benzoyl)thioureato)zinc(II) [Zn(L^2)$_2$]: White. Yield: 87%, m.p. 225–227°C. Anal. Calcd. for $C_{24}H_{24}N_4O_2S_2Cl_2Zn$: C, 48.0; H, 4.0; N, 9.3. Found: C, 48.7; H, 4.1; N, 9.4. IR (KBr pellet, cm^{-1}): ν(C=O) 1522 (w), ν(C-Cl) 745 (s). ^{1}H-NMR ($CDCl_3$): 7.76–7.74 (d, 2H, C_6H_4Cl), 7.39–7.23 (m, 6H, C_6H_4Cl), 3.88–3.86 (m, 4H, CH_2), 3.85–3.83 (m, 4H, CH_2), 2.01–1.95 (m, 8H, CH_2). λ_{max}, nm (CH_2Cl_2) (ε, M^{-1} cm^{-1}): 240 (19616), 281 (22955).

Preparation of the cell culture. To evaluate cytotoxicity of chemical synthesis for human cells, HEp-2 cell line (HEp-2 cell line no: ATCC CCL23) was selected. Incubation of the cells was performed in an atmosphere of 5% carbon dioxide at 37°C.

Cytotoxicity assay. In order to test the effects of the crude extracts on HEp-2 cells, 5×10^4 cells were seeded into each well of 12-well plates, cultured for 6 h at 28°C, and cells were allowed to grow for additional 48 h in the presence of increasing amounts of chemicals 0.5, 1, 2, 4, 8, 16, 32, 64, 128, 256, 512, 1024 and 2048 μg/ml. The cytotoxicity of extracts was determined by a conventional haemocytometer using the trypan blue-exclusion method [27].

Antimicrobial activity. The stock solutions of the chemical compounds were dissolved in dimethylsulfoxide (DMSO) then diluted in Mueller-Hinton broth (Difco, USA) and Sabouraud dextrose broth (Difco, USA) to give an initial concentration of 0.8 mg/ml. Further dilutions of the compounds and standard drugs in the test medium were prepared at the required quantities at concentrations of 800, 400,

200, 100, 75, 50, 25, 12.5 and 6.25 μg/ml with media. Minimal inhibitory concentrations (MIC) for each compound were investigated against Standard bacterial strains; *Escherichia coli, Enterococcus faecalis*, *Pseudomonas aeruginosa, Staphylococcus aureus* and *Staphylococcus epidermidis* and yeast-like fungi; *Candida albicans*, *Candida krusei* and *Candida parapsilosis*, *Candida tropicalis* and *Candida glabrata* obtained from the Refik Saydam Hifzı sıhha Institute, Ankara, Turkey. Flucanazole and Ampicillin were used as control drugs.

Antimicrobial assay. The cultures were obtained in Mueller-Hinton broth for all the bacteria after 24 h of incubation at 37±1°C, and the final inoculum size was 10^5 CFU/mL for the antibacterial assay. The yeasts were maintained in Sabouraud dextrose broth after incubation for 48 h at 25±1 °C, and the final inoculum size was 10^4 CFU/mL for the antifungal assay. Experiments were carried out in the media at pH 7.4 and the twofold serial dilution technique was applied for bacteria and yeasts. A set of tubes containing only inoculated broth was kept as controls. The last tube with no growth of microorganisms was recorded to represent MIC expressed in μg/ml. Every experiment in the antibacterial and antimycotic assay was replicated twice in order to define the MIC values.

RESULTS AND DISCUSSION

We herein report the synthesis, characterization (by elemental analysis, UV-VIS spectra, IR spectroscopy, ^{1}H NMR spectroscopy, mass spectrometry, magnetic moment measurements and single crystal X-ray diffraction methods) and antimicrobial activities of novel series of substituted thiourea derivatives and its Ni^{II}, Cu^{II}, Zn^{II}, Pt^{II}, Pd^{II} and Co^{III} complexes. Analytical data and physico-chemical properties of prepared ligands and their metal complexes are given in experimental section.

The IR spectra of ligands show a strong absorption (1706 cm^{-1} for L^1H and 1700 cm^{-1} for L^2H) ascribed to the stretching vibration of the carbonyl group. After the complexation reaction, these vibration bands are shifted to lower wavenumber (~135 cm^{-1}). Similar behaviours are also observed for C=S stretching vibration (1385 cm^{-1} for L^1H and 1326 cm^{-1} for L^2H). But unfortunately, this vibration cannot be located because of overlapping with the other bands in that region. The IR spectrum of the metal complexes points to the disappearance of the ν(N–H) band (3159 cm^{-1} for L^1H and 3145 cm^{-1} for L^2H) due to deprotonation of the ligands when they are bonded to the metal atom. Complexation reaction are confirmed by the disappearance of the ν(N–H) band and decreasing shift for ν(C=O) and ν(C=S) in agreement with results of Arslan e*t al*. [21].

The ^{1}H-NMR spectra of the all compounds are consistent with the structural results. The ligands show a peak at 8.60 and 8.70 ppm, corresponding to the proton of NH group. This peak does not appear in the metal complexes. These data agree with the complexation reaction and the structure of complexes. The aryl proton signals are shifted to down field (~0.20 ppm) relatively to those in the free ligand (7.66–7.27 ppm). We can observe the two signals of the methyl protons at 3.49 and 3.34 ppm which represent the rotomer of thiocarbonyl group.

Magnetic moment measurements showed that the d^9 copper(II) complexes are paramagnetic, while all the other metal complexes are diamagnetic. The room temperature effective magnetic moments of $Cu(L^1)_2$ (1.74 B.M.) and $Cu(L^2)_2$ (1.75 B.M.)

are typical for distorted square planar mononuclear d^9 copper(II) complexes. The diamagnetic d^8 nickel(II), d^8 platinum(II), d^8 palladium(II) and d^{10} zinc(II) complexes are consistent with a square planar geometry, while d^6 cobalt(III) complexes indicate an octahedral geometry. These data are confirmed by X-ray single crystal diffraction studies.

The UV spectra of the ligands in dichloromethane exhibit two absorption bands at 281 and 236 nm for L^1H and 280 and 232 nm for L^2H (Figure 1). The first band observed at ~280 nm may be assigned to $n \rightarrow \pi$ transition within C=O group of the ligand. But this band is masked by a strong intraligand $\pi \rightarrow \pi^*$ transitions. These bands are slightly blue shifted by the complexation. The second band at ~234 nm are blue shifted to ~220 nm in all the complexes. These $\pi \rightarrow \pi^*$ transitions belong to metal and ligand orbitals. In the visible region, the cobalt complexes show two transitions (~470 and ~610 nm) (Figure 2). These bands agree with an octahedral geometry for diamagnetic d^6 compounds assigned to $^1A_{1g} \rightarrow {}^1T_{1g}$ and $^1A_{1g} \rightarrow {}^1T_{2g}$. The visible spectra of Cu(II) complexes exhibit a band around ~590 nm [28]. This band assigned to the $^2B_{1g} \rightarrow {}^2A_{1g}$ transition agrees with a square planar structure [29,30]. At the same time, absorption band at ~ 508 nm is characteristic of square planar nickel compound; it is assigned to the $^1A_{1g}(^1D) \rightarrow {}^1A_{2g}(^1D)$ transition [28].

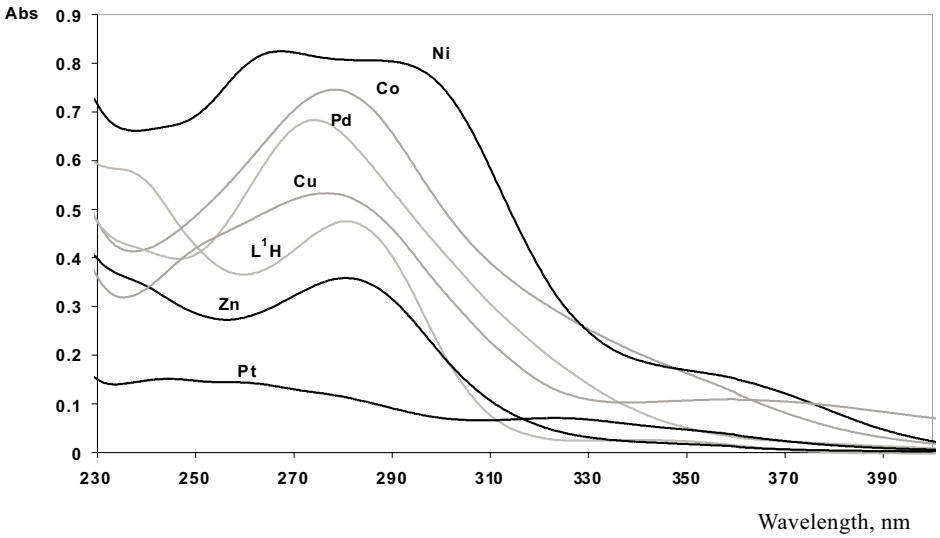

Figure 1. UV spectra of *N,N*-dimethyl-*N*′-(2-chloro-benzoyl)thiourea ligand and its metal complexes.

The molecular structure of bis[*N*,*N*-dimethyl-*N*′-(2-chloro-benzoyl)thioureato]palladium(II) complex and tris[*N*,*N*-dimethyl-*N*′-(2-chloro-benzoyl)thioureato]cobalt(III) complex are depicted in Figure 3 and 4, respectively. Selected bond lengths and angles of the compounds are presented in Table 2.

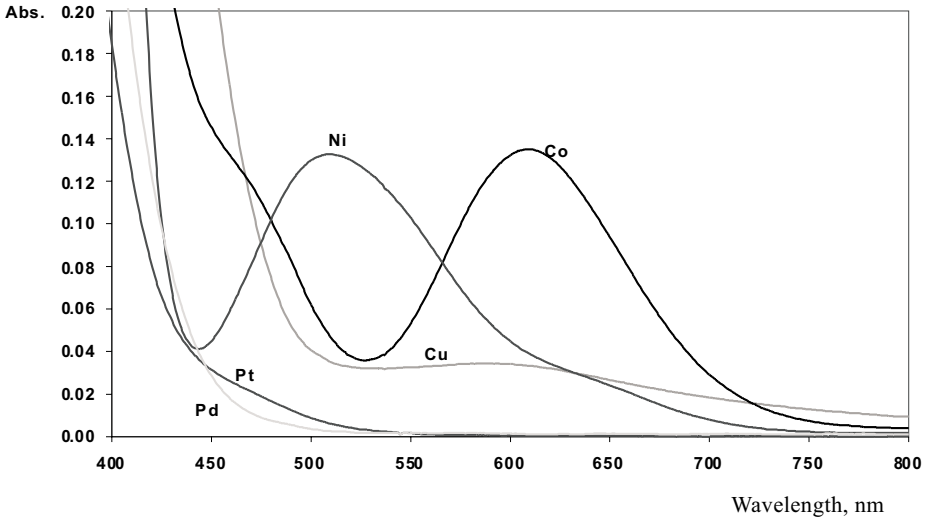

Figure 2. Vis spectra of *N,N*-dimethyl-*N*′-(2-chloro-benzoyl)thiourea ligand and its metal complexes.

$Pd(L^1)_2$ is *cis*-complex with slightly distorted planar quadratic coordination of the central Pd atom by 2 O and 2 S ligands. The distance of Pd from the best planes through O_2S_2 is 0.001(1) Å. The chelate ring systems Pd–O–C–N–C–S are mostly planar as well with largest deviations from the best planes of 0.038(3) Å (S2 ring) and 0.268(2) Å (S1 ring). Accordingly, the dihedral angles between these chelate planes are 11.7° in $Pd(L^1)_2$. The molecular structure is very close to the related *N,N*-dimethyl Pd complex [22,31] and show similar short C–N and C–S bonds indicating the known π-bonding character in the chelate rings.

The same electron delocalization is observed in the complex $Co(L^1)_3$ which has slightly distorted octahedral geometry with facial arrangement of the O and S donor atoms. The chelate rings Co–O–C–N–C–S are not exactly planar with deviations between –0.083(3) and 0.094(3) Å for ring 1 (O(1)...S(1)), –0.130(1) and 0.140(1) Å for ring 2 and –0.171(2) and 0.196(1) Å for ring 3, respectively. This structure type is known from related Rh complex [32] and a cobalt complex analogous with Se donor atoms [33].

The frequency of microbial infection in human has increased dramatically because of multi-drug resistant microbial isolates (*e.g.*, fungi and bacteria). Emergence of multi-drug resistance in human and animal pathogenic microorganisms as well as undesirable side effects of certain antibiotics has triggered immense interest in the search for new antimicrobial drugs. Hence, the search of novel and active antimicrobial agents to treat serious microbial infection has increased significantly over the last two decades [34–37].

In this study, firstly, compounds which were investigated for antimicrobial activity was examined for cytotoxicity range. Nontoxic concentrations of the tested compounds for cells were determined on HEp-2 cells. Then, the existence of antimicrobial activity was investigated in concentrations of compounds that were not toxic to cells.

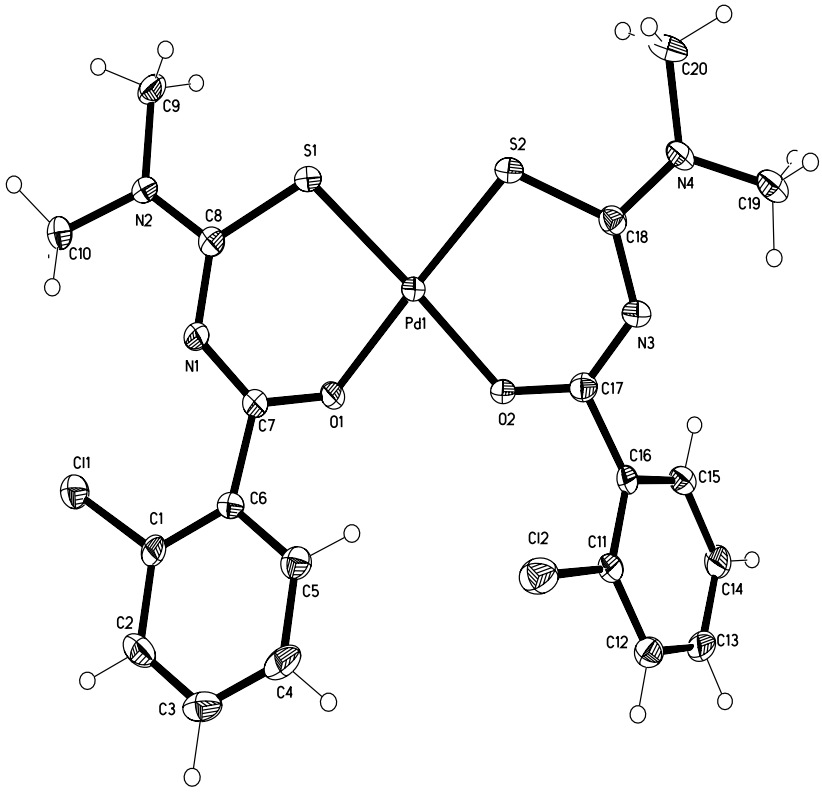

Figure 3. The molecular structure of *cis*-bis[*N,N*-dimethyl-*N'*-(2-chloro-benzoyl)thioureato]palladium(II) complex. Thermal ellipsoids are shown at the 50% probability level.

The antimicrobial and antifungal activity results (as MIC values) are given in Tables 3 and 4, respectively. Tables 3 and 4 also contain Ampicillin and Flucanozole reference compounds results, respectively, for all microorganisms used in this work to compare the reliability of the method used.

Table 2. Selected bond lengths (Å) and angles (°).

Compound				
	Bond lengths			
	Pd1–S1	2.2414(9)	S1–C8	1.745(3)
	Pd1–O1	2.020(2)	C8–N1	1.356(4)
	N1–C7	1.307(4)	C8–N2	1.326(4)
	C7–O1	1.286(4)	S2–C18	1.734(3)
	Pd1–S2	2.2412(9)	N3–C18	1.345(4)
	Pd1–O2	2.012(2)	N3–C17	1.322(4)
$Pd(L^1)_2$	O2–C17	1.260(4)	N4–C18	1.347(4)
	Bond angles			
	O1–Pd1–S1	92.91(7)	C8–N1–C7	124.6(3)
	S1–Pd1–S2	88.72(3)	C18–N3–C17	125.9(3)
	O2–Pd1–S2	94.02(7)	C8–S1–Pd1	107.05(11)
	O2–Pd1–O1	84.35(9)	C7–O1–Pd1	124.1(2)
	O1–Pd1–S2	178.36(7)	C18–S2–Pd1	108.24(12)
	O2–Pd1–S1	177.24(7)	C17–O2–Pd1	130.2(2)

Table 2 (continuation)

	Bond lengths			
	Co1–S1	2.2110(10)	S1–C18	1.731(3)
	Co1–O1	1.910(2)	C11–N11	1.326(4)
	N11–C18	1.344(4)	C18–N12	1.345(4)
	C11–O1	1.269(4)	S2–C38	1.724(4)
	Co1–S2	2.2083(10)	N21–C38	1.342(4)
	Co1–O2	1.936(2)	N21–C31	1.323(4)
$Co(L^1)_3$	O2–C31	1.257(4)	N22–C38	1.339(4)
	Bond angles			
	O1–Co1–S1	95.11(7)	C18–N11–C11	124.0(3)
	S1–Co1–S2	87.13(4)	C38–N21–C31	125.1(3)
	O2–Co1–S2	94.70(7)	C18–S1–Co1	107.75(12)
	O2–Co1–O1	86.46(9)	C11–O1–Co1	130.3(2)
	O2–Co1–S1	177.56(7)	C38–S2–Co1	107.17(12)
	O3–Co1–S2	178.07(7)	C31–O2–Co1	129.7(2)

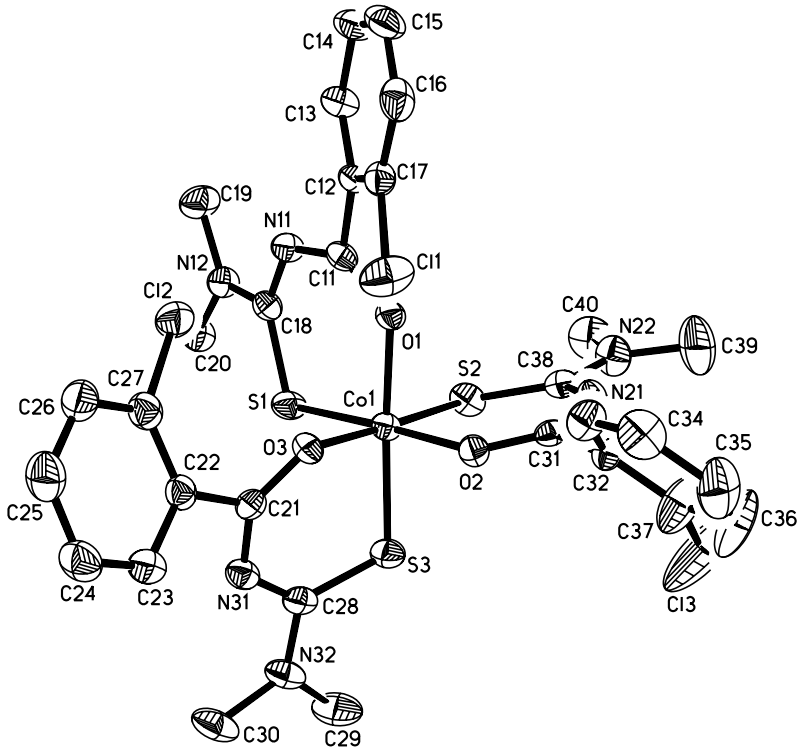

Figure 4. The molecular structure of *fac*-tris[*N,N*-dimethyl-*N′*-(2-chloro-benzoyl)thioureato]cobalt(III) complex with the hydrogen atoms omitted for clarity. Thermal ellipsoids are shown at the 50% probability level.

Table 3. The MIC values (μg/ml) for bacteria of the tested compounds.

Compounds	*E. coli* ATCC 25922	*P. aeruginosa* ATCC 27853	*S. aureus* ATCC 29213	*S. epidermidis* ATCC 12228	*E. faecalis* ATCC 29212
$Ni(L^1)_2$	100	100	50	25	50
$Cu(L^1)_2$	200	200	50	50	50
$Co(L^1)_2$	200	100	100	50	50
$Pt(L^1)_2$	200	200	50	25	50
$Pd(L^1)_2$	100	100	50	25	25
$Zn(L^1)_2$	100	200	50	50	25
$Ni(L^2)_2$	200	100	50	50	50
$Cu(L^2)_2$	100	200	50	50	50
$Co(L^2)_2$	200	100	50	25	25
$Pt(L^2)_2$	200	200	200	100	25
$Pd(L^2)_2$	200	200	200	100	50
$Zn(L^2)_2$	100	100	50	25	50
Ampicillin	6.25	31.2	3.12	1.56	6.25

The results indicate that the synthesized compounds are able to inhibit *in vitro* growth of screened microorganisms showing MIC values between 50 and > 400 μg/ml. When antimicrobial activity of synthesized components was examined, it was found that antibacterial activity was more effective against Gram positive bacteria than Gram negative bacteria. The highest antimicrobial activity was obtained against *Staphylococcus epidermidis* in the range of 25–100 μg/ml. While antibacterial activity against *Staphylococcus aureus* was found to be 50–200 μg/ml, the activity against *Enterococcus faecalis* was found to be 50 μg/ml. On the other hand, it was found that against Gram (–) bacteria they have activity which is in the 100–200 μg/ml range for the components other than $Zn(L^1)_2$. Moreover, $Zn(L^1)_2$ has shown the highest antibacterial activity that is 50 μg/ml against Gram (–) bacteria both for *Escherichia coli* and *Pseudomonas aeruginosa.* When the anti-mycotic activities of the components are examined it is seen that they are rather lower than the antibacterial activities. It is also seen that anti-mycotic activity is between 100 – >400 μg/ml against all the Candida strains.

Table 4. The MIC values (μg/ml) for yeast-like fungi of the tested compounds.

Compounds	*C. albicans* ATCC 90028	*C. glabrata* ATCC 32554	*C. krusei* ATCC 6258	*C. parapsilosis* ATCC 22019	*C. tropicalis* ATCC 22019
$Ni(L^1)_2$	400	400	>400	200	200
$Cu(L^1)_2$	200	200	400	100	100
$Co(L^1)_2$	>400	400	>400	200	400
$Pt(L^1)_2$	200	100	400	200	>400
$Pd(L^1)_2$	400	200	>400	100	>400
$Zn(L^1)_2$	200	100	200	100	100
$Ni(L^2)_2$	200	200	>400	400	200
$Cu(L^2)_2$	100	100	>400	100	100
$Co(L^2)_2$	>400	>400	400	400	>400
$Pt(L^2)_2$	200	100	400	100	400
$Pd(L^2)_2$	>400	200	>400	200	>400
$Zn(L^2)_2$	400	200	400	200	200
Flucanazole	6.25	3.12	31.2	3.12	6.25

The compounds also showed activity against Candida spp. (Table 4) with a range of MICs between 100 and >400 μg/ml. Among the tested compounds, $Zn(L^1)_2$ was the most effective compound with MIC 100 μg/ml against *Candida glabrata, Candida parapsilosis* and *Candida tropicalis*. The compounds tested here showed less antibacterial activity than the yeast-like fungi. The different antimicrobial activity may depend on the difference between cell structures of bacteria and fungi.

In this study, the components tested here showed less antifungal activity against antibacterial activity because of the fact that the fungal cell walls are fundamentally different from those of bacteria. When the antibacterial activities of the components tested are compared in terms of Gram negative and Gram positive bacteria, it is found that antimicrobial activity values determined against Gram negative bacteria are lower than those determined against Gram positive bacteria. The fungal cell wall and cell membrane are fundamentally different from those of bacteria and other eukaryotes. Fungal cell walls are composed largely of chitin, a polymer of N-acetylglucosamine, rather than peptidoglican – a characteristic component of bacterial cell walls. The fungal membrane contains ergosterol rather than the cholesterol found in mammalian membranes [38]. The compounds tested here show less antimicrobial activity against fungi. The antifungal activity against the yeast-like fungi may depend on the difference between cell structures of bacteria and fungi. The results of the present investigation may encourage us to develop and/or improve similar other related compounds and test them for a wide range of biological activities.

Supplementary material. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data [CCDC-269715 for $Pd(L^1)_2$, and CCDC-269714 for $Co(L^1)_3$] can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) +44(1223)336-033, E-mail: deposit@ccdc.cam.ac.uk].

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