Copper and palladium complexes with substituted pyrimidine-2-thiones and 2-thiouracils: syntheses, spectral characterization, and X-ray crystallographic study

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1. Introduction

Investigations of chemical behavior of functionalized pyridine-thiones(ones), especially thiouracils(uracyls), are of interest owing to roles in various biological systems. For instance, they demonstrate intriguing antiviral activity [1, 2]. Research on coordination compounds, especially copper and palladium
complexes, of those organic compounds is also important. Copper plays a significant role in thyroid hormone metabolism [3, 4]. Removal of copper ions by complexation with this type of ligand can serve as an effective way to find new antithyroid drugs [5]. Kamalakannan and Venkappayya observed good antimicrobial and antifungal activities of copper, zinc, cadmium, and mercury complexes of 5-dimethylaminomethyl-2-thiouracil [6]. Palladium complexes of 2-thiouracil have perspectives to be used as antitumor reagents because of their promising *in vitro* cytotoxicity [7]. Palladium complexes, in contrast to platinum analogs, show no mutagenic activity [8] and, therefore, are promising compounds for the replacement of platinum-containing drugs.

Pyrimidine-2-thione and its derivatives (including different 2-thiouracil species) are very interesting ligands since they adopt many coordination modes through S or N, involving one, two, or even three metal ions [9]. In the anionic forms, these ligands can be coordinated through one sulfur [10, 11], through one nitrogen and one sulfur [9, 12, 13], or through all nitrogen and sulfurs [14]. For neutral substituted pyrimidine-2-thiones and 2-thiouracils, coordination through the sulfur was found [15–20]. In some cases, heteroatoms of substituents are involved in coordination [9, 17].

The purpose of this work was to investigate the coordination ability of several substituted pyrimidine-2-thiones and 2-thiouracils toward palladium and copper chlorides. The following ligands were used: 5-acetyl-6-methyl-1,2,3,4-tetrahydropyrimidine-2-thione (L1), ethyl 4,6-dimethyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (L2), *cis*-5-acetyl-6-ethyl-5,6-dihydro-2-thiouracil (L3), and 5,6-dihydro-2-thiouracil (L4). These molecules have many prospective sites for coordination including nitrogen and sulfur of the thiocarbamide fragment, carbonyl, or carboxyl group substituents of the heterocyclic ring. It is intriguing to determine through which atoms coordination will occur for such highly functionalized molecules.

![Image of ligands L1, L2, L3, and L4]

2. Experimental

2.1. Synthesis

Complexes [Cu(L)2Cl] (1–4 for L = L1–L4, respectively) and [Pd(L)2Cl2] (5–8 for L = L1–L4, respectively) were prepared from the corresponding metal salts and pre-synthesized L1–L4. Details of synthesis and characterization of L1–L4 can be found in Supporting Information.

2.2. Complexes of copper(I)

All target complexes were prepared from chlorobis(acetonitrile)copper(I), which was obtained by dissolution of CuCl at room temperature in absolute acetonitrile:
2.2.1. Chlorobis(5-acetyl-6-methyl-1,2,3,4-tetrahydropyridine-2-thione)copper(I), [Cu(L1)2Cl] (1)
Refluxing [Cu(CH3CN)2Cl] (0.21 mmol) with L1 (0.42 mmol) in acetonitrile (14 mL) under stirring in argon for 4 h resulted in the formation of a greenish solution, from which white residue precipitated. The precipitate of 1 was filtered off, washed with acetonitrile and ethanol, and dried in a desiccator for 1 d. Yield 88%. m.p. 229–230 °C with decomposition.

\[
\text{CuCl} + 2\text{CH}_3\text{CN} \rightarrow [\text{Cu(CH}_3\text{CN)}_2\text{Cl}]
\]

\[
\begin{align*}
\text{H}_3\text{C} & \text{O} \\
\text{N} & \text{NH} \\
\text{CH}_3 & \\
\end{align*}
\]

Reflex \[\text{Cu(CH}_3\text{CN)}_2\text{Cl} \rightarrow [\text{Cu(CH}_3\text{CN)}_2\text{Cl}] \]

\[
\text{Cu(CH}_3\text{CN)}_2\text{Cl}
\]

\[
\text{H}_3\text{C} \text{O} \\
\text{N} \text{NH} \\
\text{CH}_3 \\
\]

\[
\begin{align*}
\text{Cu} & \\
\text{Cl} & \\
\end{align*}
\]

An. Calcd for C14H20ClCuN4O2S2 (%): C 38.26; H 4.59; N 12.75. Found (%): C 38.10; H 4.65; N 12.85. IR (Nujol) (cm⁻¹): 3276, 3188, 3136 (υ(NH)), 1642 (υ(C=O)), 1618 (υ(C=C)), 1601 (thioamide II: δ(NH), υ(CN)), 1202 (thioamide III: δ(NH)), 758 (thioamide V: δ(NH)).

\[
\begin{align*}
\text{H}_3\text{C} & \text{O} \\
\text{N} & \text{NH} \\
\text{CH}_3 & \\
\end{align*}
\]

\[
\begin{align*}
\text{Cu} & \\
\text{Cl} & \\
\end{align*}
\]

\[
\begin{align*}
\text{H}_3\text{C} & \text{O} \\
\text{N} & \text{NH} \\
\text{CH}_3 & \\
\end{align*}
\]

\[
\begin{align*}
\text{Cu} & \\
\text{Cl} & \\
\end{align*}
\]

1H NMR (dMSO-d₆) (ppm): 2.18 (3H, s, CH3), 2.22 (3H, s, CH3C=O), 4.06 (2H, s, CH2), 9.54 (1H, s, N(3)H), 10.14 (1H, s, N(1)H).

\[
\begin{align*}
\text{H}_3\text{C} & \text{O} \\
\text{N} & \text{NH} \\
\text{CH}_3 & \\
\end{align*}
\]

\[
\begin{align*}
\text{Cu} & \\
\text{Cl} & \\
\end{align*}
\]

\[
\begin{align*}
\text{H}_3\text{C} & \text{O} \\
\text{N} & \text{NH} \\
\text{CH}_3 & \\
\end{align*}
\]

\[
\begin{align*}
\text{Cu} & \\
\text{Cl} & \\
\end{align*}
\]

13C NMR (dMSO-d₆) (ppm): 17.71 (CH 3) 30.09 (CH3, CH3C=O), 41.28 (C(4)), 106.58 (C(6)), 142.86 (C(5)), 173.06 (C(2)), 195.01 (C=O, CH3C=O).

2.2.2. Chlorobis(ethyl 4,6-dimethyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate)copper(I), [Cu(L2)2Cl] (2)
Reaction of [Cu(CH3CN)2Cl] (0.23 mmol) with L2 (0.46 mmol) in acetonitrile (14 mL) under stirring in argon for 2 h at room temperature resulted in the formation of a yellowish solution. It was evaporated on a rotary evaporator producing a glassy yellow film of 2. Yield 72%. m.p. 87–88 °C.

\[
\text{Cu(CH}_3\text{CN)}_2\text{Cl} \rightarrow [\text{Cu(CH}_3\text{CN)}_2\text{Cl}]
\]

\[
\begin{align*}
\text{H}_3\text{C} & \text{O} \\
\text{N} & \text{NH} \\
\text{CH}_3 & \\
\end{align*}
\]

\[
\begin{align*}
\text{Cu} & \\
\text{Cl} & \\
\end{align*}
\]

\[
\begin{align*}
\text{H}_3\text{C} & \text{O} \\
\text{N} & \text{NH} \\
\text{CH}_3 & \\
\end{align*}
\]

\[
\begin{align*}
\text{Cu} & \\
\text{Cl} & \\
\end{align*}
\]

An. Calcd for C18H28ClCuN4O4S2 (%): C 40.98; H 5.35; N 10.62. Found (%): C 41.04; H 5.42; N 10.71. IR (Nujol) (cm⁻¹): 3181, 3119 (υ(NH)), 1710, 1691 (υ(C=O)), 1660 (υ(C=C)), 1576 (thioamide II: δ(NH), υ(C–N)), 1195 (thioamide III: δ(NH)), 1140, 1109, 775 (skeleton vibrations of the pyrimidinethione ring).

\[
\begin{align*}
\text{H}_3\text{C} & \text{O} \\
\text{N} & \text{NH} \\
\text{CH}_3 & \\
\end{align*}
\]

\[
\begin{align*}
\text{Cu} & \\
\text{Cl} & \\
\end{align*}
\]

\[
\begin{align*}
\text{H}_3\text{C} & \text{O} \\
\text{N} & \text{NH} \\
\text{CH}_3 & \\
\end{align*}
\]

\[
\begin{align*}
\text{Cu} & \\
\text{Cl} & \\
\end{align*}
\]

1H NMR (dMSO-d₆) (ppm): 1.14 (3H, d, J = 6.27 Hz, CH3C(4)H), 1.20 (3H, t, J = 7.12 Hz, CH3CH2O), 2.24 (3H, s, CH3C(6)), 4.11 (2H, m, CH2CH2O), 4.26 (1H, m, C(4)H), 9.70 (1H, s, N(3)H), 10.39 (1H, s, N(1)H).

\[
\begin{align*}
\text{H}_3\text{C} & \text{O} \\
\text{N} & \text{NH} \\
\text{CH}_3 & \\
\end{align*}
\]

\[
\begin{align*}
\text{Cu} & \\
\text{Cl} & \\
\end{align*}
\]

\[
\begin{align*}
\text{H}_3\text{C} & \text{O} \\
\text{N} & \text{NH} \\
\text{CH}_3 & \\
\end{align*}
\]

\[
\begin{align*}
\text{Cu} & \\
\text{Cl} & \\
\end{align*}
\]

13C NMR (dMSO-d₆) (ppm): 13.90 (CH3, CH3C(4)H), 16.96 (CH3, CH3C(6)), 22.46 (CH3, CH3CH2O), 46.89 (C(4)), 59.71 (CH2, CH3CH2O), 103.09 (C(6)), 143.54 (C(5)), 164.44 (COOEt), 171.29 (C(2)).

2.2.3. Chlorobis(cis-5-acetyl-6-ethyl-5,6-dihydro-2-thiouracil)copper(I), [Cu(L3)2Cl] (3)
Reaction of [Cu(CH3CN)2Cl] (0.17 mmol) with L3 (0.34 mmol) in acetonitrile (14 mL) under stirring in argon for 40 min at room temperature resulted in the formation of a yellowish solution. It was evaporated on a rotary evaporator producing a glassy film of 3. Yield 68%. m.p. 111–112 °C.

\[
\text{CuCl} + 2\text{CH}_3\text{CN} \rightarrow [\text{Cu(CH}_3\text{CN)}_2\text{Cl}]
\]

\[
\begin{align*}
\text{H}_3\text{C} & \text{O} \\
\text{N} & \text{NH} \\
\text{CH}_3 & \\
\end{align*}
\]

\[
\begin{align*}
\text{Cu} & \\
\text{Cl} & \\
\end{align*}
\]
2.2.4. Chlorobis(5,6-dihydro-2-thiouracil)copper(I), \([Cu(L^4)_2Cl]\) (4)

Refluxing \([Cu(CH_3CN)_2Cl]\) (0.27 mmol) with \(L^4\) (0.54 mmol) in acetonitrile (14 mL) under stirring in argon for 4 h resulted in changing white residue of \(L^4\) to yellowish-green residue of 4. The precipitate of 4 was filtered off, washed with acetonitrile and ethanol, and dried in a desiccator for 1 d. Yield 95%. m.p. 285–286 °C.

\[\text{[Cu(CH_3CN)_2Cl] + HN=S} \xrightarrow{\text{CH_3CN reflux}} \text{[Cu} \left(\begin{array}{c} \text{H_3C} \\ \text{HN} \\ \text{S} \\ \text{NH} \end{array}\right)\text{Cl}\right]_{2}\]
2.3.1. Dichlorobis(5-acetyl-6-methyl-1,2,3,4-tetrahydropyridine-2-thione)palladium(II), [Pd(L₁)₂Cl₂] \( (5) \)

Refluxing [Pd(CH₃CN)₂Cl₂] \( (0.29 \text{ mmol}) \) with L₁ \( (0.58 \text{ mmol}) \) in acetonitrile \( (20 \text{ mL}) \) under vigorous stirring in argon for 2 h resulted in bleaching of the solution and formation of a brown residue. The precipitate of \( 5 \) was filtered off, washed with acetonitrile and ethanol, and dried in a desiccator for 1 d. Yield 83%. m.p. 234–235 °C with decomposition.

![Diagram of reaction](image)

Anal. Calcd for C₁₄H₂₀Cl₂N₄O₂PdS₂ (%): C 32.47; H 3.89; N 10.82. Found (%): C 31.33; H 4.02; N 10.53.

IR (Nujol) (cm\(^{-1}\)): 3193, 3135, 3077, 3029 (\( \nu(NH) \)), 1620 (\( \nu(C=O) \), \( \nu(C=C) \)), 1602 (thioamide II: \( \delta(NH) \), \( \nu(C=N) \)), 1186 (thioamide III: \( \delta(NH) \)), 774 (thioamide V: \( \delta(NH) \)).

\(^1\)H NMR (DMSO-\( d₆ \)) (ppm): 2.20 (3H, s, CH₃), 2.22 (3H, s, CH₃C=O), 4.07 (1H, s, CH₂), 9.50–11.50 (1H and 1H, m, overlapping of signals from N(3)H and N(1)H).

\(^1\)C NMR (DMSO-\( d₆ \)) (ppm): 17.48 (CH₃), 30.23 (CH₃, CH₃C=O), 41.21 (C(4)), 107.91 (C(6)), 142.74 (C(5)), 170.50 (C(2)), 195.19 (C=O, CH₃C=O).

2.3.2. Dichlorobis(ethyl 4,6-dimethyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate) palladium(II), [Pd(L₂)₂Cl₂] \( (6) \)

Stirring [Pd(CH₃CN)₂Cl₂] \( (0.23 \text{ mmol}) \) with L₂ \( (0.46 \text{ mmol}) \) in acetonitrile \( (20 \text{ mL}) \) in argon for 1.5 h resulted in the formation of a dark reddish-brown solution. It was evaporated on a rotary evaporator producing a glassy dark brown film of \( 6 \). Yield 78%. m.p. 139–140 °C with decomposition.

![Diagram of reaction](image)

Anal. Calcd for C₁₈H₂₄Cl₂N₄O₄PdS (%%): C 35.68; H 4.66; N 9.25. Found (%%): C 35.35; H 4.84; N 9.02.

IR (Nujol) (cm\(^{-1}\)): 3316, 3181, 3121 (\( \nu(NH) \)), 1712, 1695 (\( \nu(C=O) \)), 1661 (\( \nu(C=C) \)), 1578 (thioamide II: \( \delta(NH) \), \( \nu(C=N) \)), 1199 (thioamide III: \( \delta(NH) \)), 1143, 1127, 776 (skeleton vibrations of the pyrimidinethione ring).

\(^1\)H NMR (DMSO-\( d₆ \)) (ppm): 1.14 (3H, s, CH₃C(4)H), 1.22 (3H, t, \( J = 7.18 \text{ Hz} \), CH₃CH₂O), 2.24 (3H, s, CH₃C(6)H), 4.13 (2H, m, OCH₂CH₃), 4.36 (1H, m, C(4)H), 9.50–11.50 (1H and 1H, m, overlapping of signals from N(3)H and N(1)H).

\(^1\)C NMR (DMSO-\( d₆ \)) (ppm): 14.08 (CH₃, CH₃C(4)H), 21.74 (CH₃, CH₃C(6)H), 47.11 (C(0)), 60.08 (CH₂, CH₂CH₃O), 104.40 (C(6)), 134.73 (C(5)), 164.41 (COOEt), 168.98 (C(2)).

2.3.3. Dichlorobis(cis-5-acetyl-6-ethyl-5,6-dihydro-2-thiouracil)palladium(I), [Pd(L₃)₂Cl₂] \( (7) \)

Stirring [Pd(CH₃CN)₂Cl₂] \( (0.12 \text{ mmol}) \) with L₃ \( (0.24 \text{ mmol}) \) in acetonitrile \( (14 \text{ mL}) \) in argon for 1.5 h resulted in the formation of a red-brown solution. It was evaporated on a rotary evaporator producing a glassy dark brown film of \( 7 \). Yield 72%. m.p. 159–160 °C with decomposition.
2.3.4. Dichlorobis(5,6-dihydro-2-thiouracil)palladium(II), [Pd(L4)2Cl2] (8)

Refluxing [Pd(CH3CN)2Cl2] (0.29 mmol) with L4 (0.58 mmol) in acetonitrile (20 mL) under vigorous stirring in argon for 1 h resulted in bleaching of the solution and formation of a brown residue. It was filtered off, washed with acetonitrile and ethanol, and dried in a desiccator for 1 d. Yield 86%. m.p. 243–244 °C with decomposition.

Anal. Calcd for C16H24Cl2N4O4PdS2 (%): C 33.26; H 4.19; N 9.70. Found (%): C 32.27; H 4.30; N 9.47.

IR (Nujol) (cm−1): 3181, 3119 (ν(NH)), 1730, 1709, 1649 (ν(C=O), ν(C=C)), 1591 (NH–C(S)–NH–C(O) and ν(C=O), CH3C=O), 1254 (thioamide III: δ(NH)).

1H NMR (CD3CN-d3) (ppm) for dichlorobis(cis-5-acetyl-6-ethyl-5,6-dihydro-2-thiouracil)palladium(II): 1.00 (3H, t, J = 7.46 Hz, CH3CH2), 1.55–1.80 (2H, m, overlapping of 1H signal of CH2 in CH3CH2 and that from another isomer, see next paragraph), 2.30 (3H, s, CH3C=O), 3.81 (1H, m, overlapping of signals from N(3)H and N(1)H and with those from the other isomer).

1H NMR (CD3CN-d3) (ppm) for dichlorobis((Z)-5-(1-hydroxyethylidene)-6-ethyl-5,6-dihydro-2-thiouracil)palladium(II): 0.93 (3H, t, J = 7.33 Hz, CH3CH2), 1.55–1.80 (2H, m, overlapping of 1H signal of CH2 in CH3CH2 and that from other isomer), 2.04 (3H, s, CH3COH), 4.53 (1H, m, C (6)H), 9.30–10.80 (1H and 1H, m, overlapping of signals from N(3)H and N(1)H and with those from the other isomer).

13C NMR (CD3CN-d3) (ppm) for dichlorobis(cis-5-acetyl-6-ethyl-5,6-dihydro-2-thiouracil)palladium(II): 10.06 (CH3, CH3CH2), 26.76 (CH2, CH3CH2), 30.09 (CH2, CH3C=O), 55.26(C (6)), 57.56 (C (5)), 163.73 (C (4)), 174.56 (C (2)), 201.33 (C=O, CH3C=O).

13C NMR (CD3CN-d3) (ppm) for dichlorobis((Z)-5-(1-hydroxyethylidene)-6-ethyl-5,6-dihydro-2-thiouracil)palladium(II): 9.16 (CH3, CH3CH2), 19.14 (CH2, CH3COH), 31.30 (CH2, CH3CH2), 55.01 (C (6)), 95.82 (C (5)), 166.49 (C (4)), 173.65 (COH), 178.10 (C (2)).

2.4. Analysis methods

Microanalytical results were obtained with an EA1112 Thermo Finnigan analyzer. Melting points were determined by an automatic PTP(M) instrument in a capillary with 1.5 mm diameter; thickness of a layer of the compounds was about 2 mm.
Infrared spectra were obtained using a BRUKER VECToR 22 spectrometer (400–4000 cm⁻¹, in Nujol, KRS-5). NMR spectra were recorded using a Bruker Avance III 600 spectrometer (600.13 or 150.90 MHz for ¹H and ¹³C, respectively, in DMSO-d₆ (99%) or CD₃CN-d₃ (99%), Deutero GmbH). All measurements were carried out at 298 K.

X-ray diffraction analysis of 2 was carried out on a Bruker KAPPA APEX II diffractometer (MoKα radiation, graphite monochromator) at room temperature. Absorption was corrected with the use of SADABS. The structures were solved by direct methods (SHELXS97) and refined by full-matrix least-squares method in the anisotropic approximation for all non-hydrogen atoms (SHELXL97) using all reflections [21]. Hydrogens were positioned geometrically and refined as riding, with \( u_{eq}(H) = 1.2–1.5 \) \( u_{eq} \) of the parent carbon. The crystal data, data collection, and refinement parameters for [Cu(L²)₂Cl] are given in Table 1.

X-ray powder diffraction data for [Pd(L⁴)₂Cl₂] (8) were collected at room temperature using a Panalytical EMPYREAN instrument with a linear \( \chi \)celerator detector using nonmonochromated CuKα radiation.

### Table 1. Crystallographic data for chlorobis(ethyl 4,6-dimethyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate)copper(i).

| Compound | [Cu(L²)₂Cl] |
|----------|-------------|
| Empirical formula | \( \text{C}_{18} \text{H}_{28} \text{ClCuN}_{4} \text{O}_{4} \text{S}_{2} \) |
| Formula weight | 527.55 |
| Crystal system | Monoclinic |
| Space group | \( \text{C}2/c \) |
| \( a \) (Å) | 23.979(2) |
| \( b \) (Å) | 13.7798(9) |
| \( c \) (Å) | 16.2318(14) |
| \( \beta \) (°) | 113.9374(19) |
| \( V \) (Å³) | 4902.1 |
| \( Z \) | 8 |
| Radiation type | MoKα |
| \( \rho_{\text{calc}} \) (g cm⁻³) | 1.430 |
| \( \mu \) (mmol⁻¹) | 1.200 |
| \( \theta_{\text{max}} \) (°) | 27.50 |
| Number of parameters/restraints | 275 |
| \( R_p/ \) \( R_{wp} \)/ \( R_{exp} \) | 0.0515 |
| Goodness-of-fit | 0.922 |

### Table 2. Crystallographic data for dichlorobis(5,6-dihydro-2-thiouracil)palladium(ii).

| Compound | [Pd(L⁴)₂Cl₂] |
|----------|-------------|
| Empirical formula | \( \text{C}_{18} \text{H}_{28} \text{Cl}_{2} \text{N}_{4} \text{O}_{2} \text{PdS}_{2} \) |
| Formula weight | 437.64 |
| Crystal system | Monoclinic |
| Space group | \( \text{P}2_1/c \) |
| \( a \) (Å) | 10.9571(15) |
| \( b \) (Å) | 7.6023(17) |
| \( c \) (Å) | 8.4037(14) |
| \( \beta \) (°) | 92.215(12) |
| \( V \) (Å³) | 699.5(2) |
| \( Z \) | 2 |
| Radiation type | CuKα |
| \( \rho_{\text{calc}} \) (g cm⁻³) | 2.078 |
| \( \mu \) (mmol⁻¹) | 17.054 |
| \( 2\theta_{\text{min}}–2\theta_{\text{max}} \) increment (°) | 5.008–79.995, 0.017 |
| Number of parameters/restraints | 52/9 |
| \( R_p/ \) \( R_{wp} \)/ \( R_{exp} \) | 0.034/0.046/0.026 |
| Goodness-of-fit | 1.741 |

\( a \) \( M_{20} \) is defined according to [33].
\( b \) \( F_{30} \) is defined according to [34].
\( c \) \( R_p, R_{wp} \) and \( R_{exp} \) are defined according to [35].
radiation. The unit-cell dimensions were determined using three indexing programs: TREOR90 [22], ITO [23], and AUTOX [24, 25]. Based on systematic extinctions, the space group was determined as $P2_1/c$. The unit-cell parameters and space groups were further tested using a Pawley fit [26] and confirmed by the successful crystal structure solution and refinement. The crystal data, data collection, and refinement parameters for $8$ are given in Table 2. The crystal structure was solved with the use of simulated annealing technique [27], taking into account an empirical formula, unit-cell volume, and space group symmetry, which led to a conclusion that the Pd(II) ions have to reside on inversion centers. In simulated annealing runs, the total number of varied degrees of freedom was 9, with three positional parameters for one independent Cl anion and three translational and three orientational for the rigid ligand molecule. The solution found was fitted with the program MRIA [28] in the bond-restrained Rietveld refinement using a split-type pseudo-Voigt peak profile function [29]. Anisotropic line broadening was taken into account with the use of nine variables [30], and symmetrized harmonics expansion up to the fourth order [31, 32] was used for correction of the texture effect (the minimum and maximum texture multipliers for the calculated intensities were 0.79 and 1.51, respectively). Restraints were applied to the intramolecular bond lengths and contacts in the ligand molecule; the strength of the restraints was a function of interatomic separation and, for intramolecular bond lengths, corresponded to r.m.s. deviation 0.01 Å. All non-H atoms were refined isotropically. Hydrogens were positioned geometrically (C–H 0.97 Å; N–H 0.86 Å) and not refined. The diffraction profile after the final bond-restrained Rietveld refinement is shown in Figure 1.

3. Results and discussion

3.1. Syntheses of ligands

Two pyrimidine-2-thiones, 5-acetyl-6-methyl-1,2,3,4-tetrahydropyrimidine-2-thione ($L^1$), and ethyl 4,6-dimethyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate ($L^1$), and two 2-thiouracils,
cis-5-acetyl-6-ethyl-5,6-dihydro-2-thiouracil (L\(^3\)) and 5,6-dihydro-2-thiouracil (L\(^4\)), were used as the ligands in palladium and copper complexes.

The method, developed by Shutalev and coworkers \cite{36, 37}, was used for the syntheses of L\(^1\)--L\(^3\) (Scheme 1). The method is based on the reaction of α-tosyl-substituted thioureas (9) with acetylacetone, potassium ethyl acetoacetate, or sodium enolates (10) followed by the dehydration of corresponding 4-hydroxyhexahydropyrimidine-2-thione (11) to produce L\(^1\) and L\(^2\) \cite{36} or followed by rearrangement of 11 to produce L\(^3\) \cite{37}.

The synthesis of 5,6-dihydro-2-thiouracil from β-aminopropionic acid ethyl ester was realized by an elegant method described by Gaspert and Scaric \cite{38}. However, the method is not suitable for β-aminopropionic acid. On the basis of the approach, we suggested a new method for the synthesis of 5,6-dihydro-2-thiouracil starting from β-aminopropionic acid (Scheme 2). Base-catalyzed reaction of β-aminopropionic acid (14) with benzoylisothiocyanate (13), obtained from benzoyl chloride (12), gave N-benzoyl-N’-(2-carboxyethyl)thiourea (15), which was then used for acid-catalyzed intramolecular cyclization, producing 5,6-dihydro-2-thiouracil (L\(^4\)).
3.2. Syntheses of complexes

To activate metal chlorides for the synthesis of target complexes, the metal salts were transformed to the corresponding acetonitrile complexes, [Pd(MeCN)\(_2\)Cl\(_2\)], [Cu(MeCN)\(_2\)Cl], and [Cu(MeCN)\(_2\)Cl\(_2\)]. In reactions of L\(_1\)–L\(_4\) with [Pd(MeCN)\(_2\)Cl\(_2\)] or [Cu(MeCN)\(_2\)Cl] in acetonitrile, the corresponding [Pd(L)\(_2\)Cl\(_2\)] and [Cu(L)\(_2\)Cl] complexes were formed. We also tried to synthesize copper(II) complexes. However, after reactions of L\(_1\)–L\(_4\) with [Cu(MeCN)\(_2\)Cl\(_2\)], we observed the formation of the copper(I) complex, [Cu(L)\(_2\)Cl], and orthorhombic sulfur, indicating red-ox transformation, which is similar to the reaction of CuCl\(_2\) with 2-thiouracil [18]. It is noteworthy that uracil itself does not reduce Cu(II) to Cu(I) [39].

3.3. Spectral characterization

To assign bands in the IR spectra of L\(_1\) and L\(_2\), we used deuterium substitution of movable protons at nitrogen by double refluxing of corresponding compounds in CH\(_3\)CN–D\(_2\)O (1:1) mixture for 4 h. Comparison of IR spectra for L\(_1\), L\(_2\), and their deuterium-substituted derivatives (L\(_1d\) and L\(_2d\), respectively) distinguish vibrations involving NH groups. Substitution of protons at N-atoms of L\(_1\) by deuterium cations are reflected in the decrease of frequencies of the bands corresponding to the stretching vibrations of the NH groups (Table 3) from 3275, 3187, and 3136 cm\(^{-1}\) to 2440, 2360, and 2345 cm\(^{-1}\) (by ~1.37 times), in agreement with theoretical values. The band at 1612 cm\(^{-1}\) remains at the same place (that band does not include an NH component) and, therefore, should be assigned to the mixed vibrations \(\nu(C=O)\) and \(\nu(C=C)\). After isotope exchange, the band at 1592 cm\(^{-1}\) shifts to 1278 cm\(^{-1}\) and, hence, it is assigned to the mixed vibrations \(\delta(NH)\) and \(\nu(CN)\) (thioamide II). Changes are not so significant in comparison with \(\nu(NH)\), because \(\delta(NH)\) is only one of the two components in the thioamide II vibrations. The bands at 1187 and 780 cm\(^{-1}\) disappear after deuteration; they can be assigned to \(\delta(NH)\) (thioamide III) and \(\delta(NH)\) (thioamide V), respectively.

Similar features are observed in the spectra of L\(_2\) and L\(_2d\) (Table 3). Deuteration does not change the band at 1660 cm\(^{-1}\) \((\nu(C=O)\) of the ester group and \(\nu(C=C)\) of the double bond in the pyrimidine ring). The bands at 3315, 3181, and 3120 cm\(^{-1}\) shift to 2459, 2354, and 2340 cm\(^{-1}\), respectively (by ~1.37 times). The band at 1584 cm\(^{-1}\) shifts to 1249 cm\(^{-1}\) \((\delta(NH)\) and \(\nu(CN)\), thioamide II). The band at 1195 cm\(^{-1}\) shifts to 939 cm\(^{-1}\) \((\delta(NH)\), thioamide III).

IR spectra of the complexes reflect bonding features of the ligands. Thus, the band at 1660 cm\(^{-1}\) in the IR spectrum of L\(_2\), which is assigned to \(\nu(C=O)\) + \(\nu(C=C)\), splits into three bands and shifts to 1654 cm\(^{-1}\) (assigned to \(\nu(C=C)\), because the shift is insignificant), 1691, and 1710 cm\(^{-1}\) (two bands for different \(\nu(C=O)\) vibrations) in the spectrum of 2 (Table 3). Appearance of the additional bands can be caused by the formation of different N–H···O hydrogen bonds due to the following probable reasons. The first reason is the occurrence of two diastereomers of the complex, one of which is characterized by X-ray single-crystal diffraction. The second reason is the presence of another isomer of the complex, which can have opposite orientation of L\(_2\) about Cl (rotated by the NH group), with another set of H-bonds. The band at 1584 cm\(^{-1}\) in the spectrum of L\(_2\) assigned to \(\delta(NH)\) + \(\nu(CN)\) is widened and shifted down to 1576 cm\(^{-1}\) in the spectrum of 2; probably, this is a result of overlapping of the bands of two isomers. Similar changes, caused by formation of H-bonds, are found in the spectra of other copper complexes.

**Table 3.** Selected bands (cm\(^{-1}\)) in the IR spectra of L\(_1\), L\(_1d\), L\(_2\), L\(_2d\), and 2.

| Assignment | L\(_1\) | L\(_1d\) | L\(_2\) | L\(_2d\) | 2 |
|------------|--------|----------|--------|----------|---|
| \(\nu(NH(D))\) | 3275   | 2440     | 3315   | 2459     | 3176 |
|            | 3187   | 2360     | 3181   | 2354     | 3114 |
|            | 3136   | 2345     | 3120   | 2340     |     |
| \(\nu(C=O), \nu(C=C)\) | 1612   | 1612     | 1660   | 1660     | 1710 |
|            |        |          |        |          | 1691 |
|            |        |          |        |          | 1664 |
| \(\delta(NH(D))\) | 1592   | 1278     | 1584   | 1249     | 1576 |
| \(\delta(NH(D)), \nu(CN)\) | 1187   | –        | 1195   | 939      | 1195 |
| \(\delta(NH)\) | 780    | –        | –      | –        | –   |
The changes in the IR spectra of the palladium spectra are identical to the changes of the corresponding copper complexes, indicating similar coordination modes of the ligands. NMR spectra also confirm the formation of the complexes. The signals of protons in the $^1$H NMR spectra of the complexes are shifted to weak field as compared to the spectra of uncoordinated L$^1$–L$^4$ due to their lower screening caused by metal coordination (Table 4). Splitting of the $^1$H-signals at nitrogen of the ligands in $^1$H-spectra of all palladium complexes can be caused by coordination of palladium by DMSO, serving as the solvent for recording NMR spectra. Solvated complexes could form additional intermolecular interactions resulting in nonequivalence of protons at N-atoms. Only signals of two isomers were observed in the NMR spectra of both copper and palladium complexes of thiouracil L$^3$, although signals of three isomers were found in the NMR spectra of the initial uncoordinated L$^3$. The observation means that complexation changes the equilibrium between the three forms, favoring the formation of keto and (Z)-enol forms of thiouracil L$^3$.

Table 4. $^1$H-NMR spectra of L$^1$–L$^4$ and corresponding Cu(I) and Pd(II) complexes.

| Compound   | Protons of carbons near C=O (COO) | NH         | Protons of ring carbons | Other protons |
|------------|-----------------------------------|------------|-------------------------|---------------|
| L$^1$      | 2.17 s                            | 9.06 s, 9.92 s | 3.94 s                  | 2.15 s        |
| [Cu(L$^1$)$_2$Cl] | 2.22 s                         | 9.54 s, 10.14 s | 4.06 s                  | 2.18 s        |
| [Pd(L$^1$)$_2$Cl$_2$] | 2.22 s                        | 9.50–11.50 m        | 4.07 s                  | 2.20 s        |
| L$^2$      | 1.19 t, 4.02–4.16 m               | 9.19 s, 10.12 s | 4.02–4.16 m             | 1.09 d, 2.19 s |
| [Cu(L$^2$)$_2$Cl] | 1.20 t, 4.11 m                    | 9.70 s, 10.39 s | 4.26 m                  | 1.14 d, 2.24 s |
| [Pd(L$^2$)$_2$Cl$_2$] | 1.22 t, 4.13 m                  | 9.50–11.50 m        | 4.36 m                  | 1.14 s, 2.24 d |
| L$^3$      | 2.27 s                            | 7.98 m, 9.13 s    | 3.86 m, 4.21 m          | 0.94 t, 1.50–1.70 m |
| [Cu(L$^3$)$_2$Cl] | 2.29 s                         | 9.28 s, 10.06 s  | 3.77 m, 4.02 d          | 0.98 t, 1.55–1.75 m |
| [Pd(L$^3$)$_2$Cl$_2$] | 2.30 s                        | 9.30–10.80 m       | 3.81 m, 4.13 m          | 1.00 t, 1.55–1.80 m |
| L$^4$      | 3.35 d                            | 9.56 s, 10.89 s   | 2.51 t                  | –             |
| [Cu(L$^4$)$_2$Cl] | 3.50 d                        | 10.09 s, 11.13 s  | 2.60 t                  | –             |
| [Pd(L$^4$)$_2$Cl$_2$] | 3.57 d                       | 10.00–12.50 m      | 2.62 s                  | –             |

The changes in the IR spectra of the palladium spectra are identical to the changes of the corresponding copper complexes, indicating similar coordination modes of the ligands.

NMR spectra also confirm the formation of the complexes. The signals of protons in the $^1$H NMR spectra of the complexes are shifted to weak field as compared to the spectra of uncoordinated L$^1$–L$^4$ due to their lower screening caused by metal coordination (Table 4). Splitting of the $^1$H-signals at nitrogen of the ligands in $^1$H-spectra of all palladium complexes can be caused by coordination of palladium by DMSO, serving as the solvent for recording NMR spectra. Solvated complexes could form additional intermolecular interactions resulting in nonequivalence of protons at N-atoms. Only signals of two isomers were observed in the NMR spectra of both copper and palladium complexes of thiouracil L$^3$, although signals of three isomers were found in the NMR spectra of the initial uncoordinated L$^3$. The observation means that complexation changes the equilibrium between the three forms, favoring the formation of keto and (Z)-enol forms of thiouracil L$^3$.

Maximal shift of the signals in the $^{13}$C NMR spectra (up to 5 ppm) was found for carbons of the C=S groups (Table 5), indicating coordination of the ligands through sulfur. Smaller, but still significant, shifts were observed for the sp$^2$-hybridized carbons, participating in conjugation. The signals of the sp$^3$-hybridized carbons were slightly shifted. The changes in the $^{13}$C NMR spectra of the palladium complexes are identical to the changes for the corresponding copper complexes. Shifts of all signals are greater than for the copper complexes, indicating higher polarity of the Pd–S bond as compared to the Cu–S bond.

### 3.4. X-ray structural investigations

Two complexes, [Cu(L$^2$)$_2$Cl] (2) and [Pd(L$^4$)$_2$Cl$_2$] (8), were structurally characterized by X-ray single-crystal and powder diffraction, respectively.

Crystals of [Cu(L$^2$)$_2$Cl] suitable for analysis were grown from ethanol by slow evaporation of the solvent for 3 days. The structure of [Cu(L$^2$)$_2$Cl] is shown in Figure 2. In [Cu(L$^2$)$_2$Cl], copper(I) has a rare coordination number three and trigonal two neutral L$^2$ molecules, coordinated through sulfur, and chloride. The copper is out of the Cu–Cl–S–S plane by 0.038 Å. The Cu–S and Cu–Cl bond lengths in 3 are 2.2142(11), 2.2280(12), and 2.2565(12) Å. Similar almost trigonal planar coordination for Cu(I) bound to S and Cl$^-$ was found in chlorobis-(2-thiouracil)copper(I) dimethylformamide solvate, where 2-thiouracil ligand also coordinates Cu(I) through its exocyclic sulfur donor [18]. The structure of the CuBr complex with 2,4-dithiouracil and 1,2-bis(diphenylphosphanyl)benzene differs significantly; it corresponds to a four-coordinate Cu(I) in a tetrahedral coordination environment with the heterocyclic dithione ligand being monodentate to the metal center through its exocyclic sulfur donor [19]. The distorted tetrahedral coordination around each copper is also found in dimeric [Cu(litetotH$_2$)$_2$]$_2$ and monomeric [Cu(XP($^2$)$_2$)$_2$(litetotH$_2$)] (litetotH$_2$ = 5-carbethoxy-2-thiouracil; X = Cl, Br); the thione ligand is S-bonded [20].
The heterocycle in the complex has a distorted boat conformation similar to free L² [40]. The C2, N3, C5, and C6 of the ring are arranged in the same plane, while the N1 and C4 deviate from the C2–N3–C5–C6 plane by 0.148 and 0.375 Å, respectively. The methyl at C4 has almost axial orientation; the C2–N3–C4–C(Me) angles are 88.73° and −89.18° for two ligand molecules. C4 is a chiral center. Every

Table 5. $^{13}$C-NMR spectra of L¹–L⁴ and corresponding Cu(I), Pd(II) complexes.

| Compound | C=O (COO) | C=S | Ring carbons (sp³) | Carbons of substitutes | C=C |
|----------|-----------|-----|-------------------|-----------------------|-----|
| L¹       | 194.81    | 175.68 | 41.29             | 17.80, 30.12          | 105.77, 144.03 |
| [Cu(L¹)₂Cl] | 195.01    | 173.06 | 41.28             | 17.71, 30.09          | 106.58, 142.86 |
| [Pd(L¹)₂Cl₂] | 195.19    | 170.50 | 41.21             | 17.48, 30.23          | 107.91, 142.74 |
| L²       | 165.12    | 174.67 | 46.69             | 14.18, 17.10, 22.74, 59.50 | 101.93, 144.72 |
| [Cu(L²)₂Cl] | 164.44    | 171.29 | 46.89             | 13.90, 16.96, 22.46, 59.71 | 103.09, 143.54 |
| [Pd(L²)₂Cl₂] | 164.41    | 168.98 | 47.11             | 14.08, 16.89, 21.74, 60.08 | 104.40, 143.74 |
| L³       | 164.71, 201.13 | 179.29 | 54.22, 58.19      | 9.94, 27.22, 29.59    | – |
| [Cu(L³)₂Cl] | 163.73, 201.33 | 174.56 | 55.26, 57.56      | 10.06, 26.76, 30.09   | – |
| [Pd(L³)₂Cl₂] | 167.41    | 179.05 | 29.18             | –                      | – |
| L⁴       | 166.66    | 174.49 | 28.73             | –                      | – |

Scheme 1. The synthesis of L¹, L², and L³.

Scheme 2. The synthesis of 5,6-dihydro-2-thiouracil.

The heterocycle in the complex has a distorted boat conformation similar to free L² [40]. The C2, N3, C5, and C6 of the ring are arranged in the same plane, while the N1 and C4 deviate from the C2–N3–C5–C6 plane by 0.148 and 0.375 Å, respectively. The methyl at C4 has almost axial orientation; the C2–N3–C4–C(Me) angles are 88.73° and −89.18° for two ligand molecules. C4 is a chiral center. Every
molecule of the complex contains both \( \text{L}^2 \) enantiomers. Another kind of isomerism can be caused by different orientation of methyl groups at C4 about the coordination plane. However, only one diastereomer (from four possible) with one-side orientation of methyl groups (one ligand with R- and one with S-absolute configuration) is found in the crystal structure of [Cu(\( \text{L}^2 \))\(_2\)Cl].

The structure is stabilized by intramolecular N–H⋯Cl hydrogen bonds, and similar stabilization was found [19]. Complex molecules are combined in layers by N–H⋯O hydrogen bonds. Layers are linked by C–H⋯S and C–H⋯O contacts.

The structure of [Pd(\( \text{L}^4 \))\(_2\)Cl\(_2\)] is shown in Figure 3. In [Pd(\( \text{L}^4 \))\(_2\)Cl\(_2\)], the palladium has a standard square-planar geometry with two 5,6-dihydro-2-thiouracil molecules and two chlorides. The Pd–S and Pd–Cl bond lengths are 2.332(3) and 2.335(3) Å, respectively. Structure 8 differs significantly from the earlier reported palladium complexes with 2-thiouracil and organophosphines, where anionic thiouracil ligands are bidentate, through the thioxo moiety and the endo amino group [7].

The 5,6-dihydro-2-thiouracil ligands exhibit a half-chair conformation, similar to free 5,6-dihydro-2-thiouracil molecules [41], with C3 and C4 displaced by 0.176 and −0.211 Å on either side of the base plane. The S–C and C–O bond lengths do not change on coordination; they are 1.675(11) and 1.220(13) Å for 8 and 1.676(3) and 1.216(4) for dihydro-2-thiouracil, respectively. The complex molecules are combined in a 3-D framework by one N–H⋯O and two C–H⋯Cl contacts for every ligand molecule.

4. Conclusion

Eight complexes of Cu(I) and Pd(II) with two pyrimidine-2-thione and two 2-thiouracil ligands were synthesized and characterized by various physical methods. A new method for the synthesis of 5,6-dihydro-2-thiouracil, based on the key-step reaction of \( \beta \)-aminopropionic acid with benzoylisothiocyanate, was suggested. To assign bands in IR spectra of organic molecules and corresponding complexes, deuterium substitution of movable protons on nitrogens was made. That [Cu(\( \text{L}^2 \))\(_2\)Cl] exists as two diastereomers was supported by IR spectroscopy. The NMR method was applied for establishing coordination sites in the complex molecules. The crystal structures of [Cu(\( \text{L}^2 \))\(_2\)Cl] and [Pd(\( \text{L}^4 \))\(_2\)Cl\(_2\)] were determined by X-ray diffraction. Coordination occurs through the sulfurs of the ligand molecules, causing significant shift of the thiomide II band in the IR spectra and noticeable change of the chemical shift for the carbons of the C=S groups in the \( ^{13}\text{C} \) NMR spectra. Only one donor of each ligand is involved in coordination with copper(I) or palladium(II), although substituted pyrimidine-2-thione and 2-thiouracil ligands have various potential donor sites. This fact can be explained by softness of the copper(I) and palladium(II) ions; they tend to form bonds with soft sulfurs of the ligands, while harder nitrogens and oxygens do not participate in the coordination.

**Supplementary material**

Crystallographic data for [Cu(\( \text{L}^2 \))\(_2\)Cl] and [Pd(\( \text{L}^4 \))\(_2\)Cl\(_2\)] have been deposited – CCDC Nos. CCDC 1061987 and 1059913, respectively – with the Cambridge Crystallographic Data Center [CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44 1233 336 033; Email: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk)].

**Disclosure statement**

No potential conflict of interest was reported by the authors.

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