Crystal structures of copper(I) and silver(I) chloride complexes containing 4-phenylthiosemicarbazide and triphenylphosphine ligands

Yupa Wattanakanjanaa∗, Kamonwan Janwatthana, Tanaporn Romyena, Arunpatcha Nimthong-Roldánb

a Division of Physical Science, Faculty of Science, Prince of Songkla University, Songkhla 90112 Thailand
b Pre-Development Sciences, 211, 2nd Ave, Waltham, Massachusetts 02451 USA

∗Corresponding author, e-mail: yupa.t@psu.ac.th

ABSTRACT: Copper(I) and silver(I) chloride complexes containing triphenylphosphine (PPh₃) and 4-phenylthiosemicarbazide (4-PTSC) ligands were prepared and structurally analyzed, namely [CuCl(4-PTSC)(PPh₃)₂] (1) and [AgCl(4-PTSC)(PPh₃)₂]CH₃CN (2). Both compounds (1) and (2) exhibit a distorted tetrahedral metal coordination environment with two P atoms from two PPh₃ ligands, one terminal S atom from the 4-PTSC ligand and a chloride ion. Intramolecular N–H···Cl and N–H···N hydrogen bonds are observed (graph set motifs S(6) and S(5), respectively). In the crystals of both complexes, molecules are linked to form dimers via bifurcated N–H···Cl hydrogen bonds involving the amine and chloride units. For compound (2), a solvate acetonitrile molecule acts as a hydrogen bond donor and acceptor via C–H(CH₃CN)···Cl and C–H···N(CH₃CN) interactions, leading to the formation of 1D chains along [010].

KEYWORDS: silver(I) chloride, copper(I) chloride, 4-phenylthiosemicarbazide, crystal structure, intra- and intermolecular hydrogen bonding

INTRODUCTION
Thiosemicarbazide and thiosemicarbazide derivatives have for several decades attracted attention due to a range of biological activities that they possess such as anticancer, antimicrobial, antifungal [1, 2], anticonvulsant, antimalarial, analgesic, and antiinflammatory properties [3–6]. Therefore, many scientists have prepared members of these compounds as target structures to estimate and evaluate their biological activities. Thiosemicarbazides may also act as ligands in metal complexes, featuring both soft sulfur and hard nitrogen donor atoms as potential sites for coordination that give them an affinity for chelation to divalent metal ions such as Fe²⁺, Zn²⁺, Cu²⁺, and Mn²⁺ [7, 8]. Many of the thiosemicarbazide's biological and pharmaceutical activities are generally assumed to originate from these metal-complexing properties and their capacity to act as in vivo reducing agents. Thiosemicarbazide and their metal complexes have thus been extensively investigated, e.g. for their antiviral properties [9], or for their anticancer activities [10, 11]. Most notable here is 3-aminopyridine-2-carboxaldehyde (3-AP or Triapine®), which is currently tested in a randomized phase III trial as an addition to the usual chemotherapy treatment (Cisplatin) during radiation therapy for advanced-stage cervical and vaginal cancers [12, 13]. Several copper(I) and silver(I) complexes of thiosemicarbazide derivatives have been prepared and characterized, and an unusual enhancement in antitubercular activity has been observed for some of these complexes [14]. We recently reported a series of metal thiourea complexes prepared by reacting copper(I) or silver(I) halide with triphenylphosphine and 1-(4-nitrophenyl)thiourea, NPTU [15–17]; we report herein the synthesis and crystal structures of copper(I) and silver(I) chloride complexes containing triphenylphosphine (PPh₃) and 4-phenylthiosemicarbazide (4-PTSC) ligands (Fig. 1).

MATERIALS AND METHODS
Materials
The reagents and solvents used in the synthesis were obtained from commercial suppliers and used directly without further purification. Copper(I) chloride, silver(I) chloride, triphenylphosphine, and 4-phenylthiosemicarbazide were purchased from Sigma Aldrich (USA). Infrared spectra were mea-
Synthesis of [CuCl(4-PTSC)(PPh$_3$)$_2$] (1)

Triphenylphosphine, PPh$_3$ (0.16 g, 0.61 mmol), was dissolved in 30 ml of acetonitrile at 339.15 K, and copper(I) chloride, CuCl (0.03 g, 0.30 mmol), was added. The mixture was stirred for 3 h, and then 4-phenylthiosemicarbazide, 4-PTSC (0.05 g, 0.30 mmol), was added. The resulting reaction mixture was heated under reflux for 7 h during which the precipitate gradually disappeared. The resulting clear solution was filtered and left to evaporate for several days at room temperature, leaving a crystalline complex, which was filtered off and dried in vacuo (0.10 g, 42% yield). M.p. 171–172 K. IR bands (KBr, cm$^{-1}$): 3168.07(w), 3148(w), 3146(w), 1594.52(w), 1503.44(w), 1289.86(m), 1090.41(w), 1024.65(w), 897.53(m), 851.50(w), 700.95(s), 509.56(s).

Synthesis of [AgCl(4-PTSC)(PPh$_3$)$_2$]CH$_3$CN (2)

Triphenylphosphine, PPh$_3$ (0.16 g, 0.61 mmol), was dissolved in 30 ml of acetonitrile at 340 K, and silver(I) chloride, AgCl (0.04 g, 0.299 mmol), was dissolved in 30 ml of acetonitrile at 339.15 K, and silver(I) chloride, AgCl (0.04 g, 0.299 mmol), was added. The mixture was stirred for 4 h, and then 4-phenylthiosemicarbazide, 4-PTSC (0.05 g, 0.299 mmol), was added. The resulting reaction mixture was heated under reflux for 7 h during which the precipitate gradually disappeared. The resulting clear solution was filtered and left to evaporate at room temperature. The crystalline complex, which was deposited upon standing for a couple of days, was filtered off and dried in vacuo (0.16 g, 66% yield). M.p. 450–452 K. IR bands (KBr, cm$^{-1}$): 3311(w), 3263(w), 3148(w), 1961(w), 1625(w), 1599(w), 1544(w), 1432(w), 1282(w), 1209(w), 1094(w), 1026(w), 996(w), 968(w), 907(w), 852(w), 741(m), 686(w), 489(s), 450(w), 437(w).

X-ray crystallographic analysis

X-ray diffraction data for (1) and (2) were obtained on a Bruker Quest diffractometer (D8 Quest, Germany) with Mo-$K_a$ radiation ($\lambda = 0.71073$ Å) at 150 K. Data were collected, and reflections were indexed and processed using APEX3 [18]. Space groups were assigned, and structures were solved by direct methods using XPREP within the SHELXTL suite of programs [19, 20] and refined using Shelxle [21] and Shelxle [22]. Crystallographic data are given in Table 1. Refinements for (1): crystal data, data collection, and structure refinement details are summarized in Table 1. All H atoms attached to carbon atoms were positioned geometrically and constrained to ride on their parent atoms with C−H = 0.95 Å. The nitrogen bound H atoms were located in difference-Fourier maps and were refined with an N−H = 0.831 (19)–0.89 (2) Å. $U_{Ow}$(H) values were set to 1.2 $U_{eq}$(C/N). Refinements for (2): crystal data, data collection, and structure refinement details are summarized in Table 1. All H atoms attached to carbon atoms were positioned geometrically and constrained to ride on their parent atoms with C−H = 0.95 Å. The nitrogen bound H atoms were located in difference-Fourier maps and were refined with an N−H = 0.858 (19)–0.892 (19) Å. $U_{Ow}$(H) values were set to 1.2 $U_{eq}$(C/N). Reflections $-1 \pm 2$, $1 \pm 1$, $0 \pm 2$, and $0 \pm 4$ were affected by the beam stop and were omitted from the refinement. CCDC 2042521 for (1) and 2042520 for (2) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center (https://www.ccdc.cam.ac.uk).

RESULTS AND DISCUSSION

The reaction of copper(I) chloride with 4-phenylthiosemicarbazide (4-PTSC) and triphenylphosphine (PPh$_3$) ligands in 1:1:2 ratio in acetonitrile yielded the copper complex [CuCl(4-PTSC)(PPh$_3$)$_2$] (1) in a triclinic setting in space group $\overline{P\bar{1}}$. The analogous reaction with silver(I) chloride yielded the silver complex [AgCl(4-PTSC)(PPh$_3$)$_2$], which crystallized as the mono-acetonitrile solvate [AgCl(4-PTSC)(PPh$_3$)$_2$]CH$_3$CN (2) in space group $P2_1/c$. Soft sulfur donor atom from the thiosemicarbazide
Table 1 Crystal data and structure refinement details for (1) and (2).

| Crystal data | [CuCl(4-PTSC)(PPh₃)₂] (1) | [AgCl(4-PTSC)(PPh₃)₂]CH₃CN (2) |
|--------------|---------------------------|---------------------------------|
| Chemical formula | C₄₃H₃₉ClCuN₃P₂S | C₄₃H₃₉AgClN₃P₂S·C₂H₅N |
| Mr           | 790.76                   | 876.14                          |
| Crystal system, space group | Triclinic, P ₁ | Monoclinic, P 2₁/c |
| Temperature (K) | 150 | 150 |
| a, b, c (Å)                     | 10.1234 (4), 13.2260 (6), 16.4011 (7) | 16.5657 (7), 9.4156 (4), 26.5967 (11) |
| α, β, χ (°)                   | 105.0998 (16), 93.9536 (16), 112.2322 (15) | 90, 95.4679 (13), 90 |
| V (Å³)                  | 1927.76 (14) | 4129.6 (3) |
| Z                       | 2 | 4 |
| Radiation type           | Mo Kα | Mo Kα |
| μ (mm⁻¹)            | 1.81 | 0.72 |
| Crystal size (mm)     | 0.46 × 0.32 × 0.22 | 0.56 × 0.53 × 0.33 |

Data collection

| Diffraclorimeter | Bruker AXS D8 Quest CMOS | Bruker AXS D8 Quest CMOS |
| Absorption correction | Multi-scan SADABS 2016/2: Krause, Herbst-Irmer, Stalke, J Appl Cryst 48 (2015), 3–10 | Multi-scan SADABS 2016/2: Krause, Herbst-Irmer, Stalke, J Appl Cryst 48 (2015), 3–10 |
| No. of measured, independent and observed [I > 2σ(I)] reflections | 93937, 14713, 11031 | 54737, 15053, 12221 |
| R int | 0.041 | 0.047 |
| (sin θ/λ) max (Å⁻¹) | 0.771 | 0.770 |

Refinement

| R[F² > 2σ(F²)], wR(F²) | 0.036, 0.086, 1.03 | 0.028, 0.074, 1.05 |
| No. of reflections | 14713 | 15053 |
| No. of parameters | 472 | 525 |
| H-atom treatment | H atoms treated by a mixture of independent and constrained refinement | H atoms treated by a mixture and constrained refinement |
| Δρ max, Δρ min (e Å⁻³) | 0.60, −0.43 | 0.63, −0.54 |

Computer programs: Apex3, SAINT [18], SHELXS9 [19], SHELXL2014/7 [20], SHELXL Rev714 [21], Mercury [26], SHELXL97, and publCIF [27].

Table 2 Hydrogen-bond geometry (Å, °) for [CuCl(4-PTSC)(PPh₃)₂] (1) and [AgCl(4-PTSC)(PPh₃)₂]CH₃CN (2).

| Compound (1) | D−H⋯A | H⋯A | D⋯A | D−H⋯A |
|--------------|-------|-----|-----|-------|
| N₁−H₁⋯N₃     | 0.832 (19) | 2.235 (18) | 2.6500 (18) | 111.1 (15) |
| N₄−H₄⋯Cl₁    | 0.831 (19) | 2.373 (19) | 3.1751 (12) | 162.5 (17) |
| N₄−H₄A⋯Cl₁    | 0.89 (2) | 2.62 (2) | 3.5046 (14) | 173.6 (15) |

| Compound (2) | D−H⋯A | H⋯A | D⋯A | D−H⋯A |
|--------------|-------|-----|-----|-------|
| N₄−H₄⋯N₆ₐ  | 0.88 | 2.12 | 2.592 (10) | 113 |
| N₄−H₄⋯N₆     | 0.88 | 2.45 | 3.155 (2) | 138 |
| N₆ₐ−H₆ₐ⋯Cl₁ | 0.88 (2) | 2.34 (2) | 3.200 (11) | 164 (4) |
| N₆Bb−H₆Bb⋯Cl₁ | 0.89 (2) | 2.21 (3) | 3.086 (13) | 168 (5) |
| N₆Bb−H₆C₆b⋯Cl₁ | 0.86 (2) | 2.72 (5) | 3.353 (13) | 131 (5) |
| C₃₃−H₃₃⋯N₆ₐ | 0.95 | 2.60 | 3.317 (2) | 133 |
| C₄₅−H₄₅A⋯Cl₁ | 0.98 | 2.57 | 3.517 (2) | 164 |

Symmetry codes: (i) −x + 1, −y, −z; (ii) −x + 1, −y + 2−z + 1; and (iii) x, −y + 3/2, z + 1/2.
Molecular structure of $[\text{CuCl}(4\text{-PTSC})(\text{PPh}_3)_2]$ (1) with ellipsoid displacement drawn at the 50% probability level.

Fig. 3 Molecular structure of $[\text{AgCl}(4\text{-PTSC})(\text{PPh}_3)_2]\text{CH}_3\text{CN}$ (2) with ellipsoid displacement drawn at the 50% probability level. Disordered atoms were omitted for clarity.

is coordinated to both Cu and Ag, and no interaction of the amine moiety with the metal is observed. Both complexes are monomeric and exhibit a distorted tetrahedral geometry in which the metal ion is coordinated to two P atoms from two PPh$_3$ ligands, one terminal S atom from the 4-PTSC ligand and a chloride ion (Fig. 2 and Fig. 3). The monomeric structures are stabilized by an intramolecular N$_2$–H$_2$···Cl$_1$ hydrogen bond between the NH$_2$ (4-PTSC) and the Cl atom and N$_1$–H$_1$···N$_3$ hydrogen bond between NH$_2$ and NH of the thiosemicarbazide moiety (graph set [23] motif S(6) and S(5), respectively) (Table 2). The Cu–S distance in (1) of 2.3389 (4) Å is close to that of another related tetrahedral complex, $[\text{CuCl}(\eta_1\text{-S-Hitsc})(\text{Ph}_3\text{P})_2]$ (H$_2$itsc = isatin-3-thiosemicarbazone) [24], but smaller than 2.3893 (5) Å in $[\text{CuCl}(\eta_1\text{-S-HIntsc})(\text{Ph}_3\text{P})_2]$ [14]. The Cu–P bond lengths of 2.2710 (4)–2.3109 (4) Å are a bit larger than the values of 2.2602 (4)–2.2671 (4) Å observed for $[\text{CuCl}(\text{C}_9\text{H}_7\text{N}_3\text{O}_2\text{S})(\text{C}_18\text{H}_{15}\text{P})_2]_2$ [15]. In compound (2), the Ag–S bond length of 2.6108 (4) Å is similar to the bond length of 2.628 (8) Å found in $[\text{AgCl}(\eta_1\text{-S-HIntsc})(\text{Ph}_3\text{P})_2]$ [14]. The Ag–P bond lengths of 2.4703 (3)–2.4750 (4) Å are close to the values of 2.4409 (7)–2.4879 (7) Å for $[\text{AgCl}(\eta_1\text{-S-Hpytsc})(\text{PPh}_3)_2]\text{CH}_3\text{CN}$ [25]. In the crystals of (1) and (2), the amine NH$_2$ moieties of 4-PTSC and Cl atom of neighboring molecules are linked through intermolecular N$_3$–H$_3$···Cl$_1$ hydrogen bonds, forming dimers (Fig. 4). For compound (2), the acetonitrile molecules are connected to dimers through C$_{45}$–H$_{45}$···(CH$_3$CN)···Cl$_{1}$ and C$_{33}$–H$_{33}$···N$_{4}$ (CH$_3$CN) hydrogen bonds, leading to the formation of 1D chains along [010] (Fig. 5, Table 2). The results from IR spectroscopy are corresponding to the X-ray crystallographic data; the characteristic peak of $\nu$(C–S) of both complexes appeared at lower energy than that of the stretching presented in the free 4-PTSC ligand (896 cm$^{-1}$) supporting the coordination of the thione sulfur to a metal center.
CONCLUSION

The complexes \([\text{CuCl}(4\text{-PTSC})(\text{PPh}_3)_2]\) (1) and \([\text{AgCl}(4\text{-PTSC})(\text{PPh}_3)_2]\text{CH}_3\text{CN} \) (2) were prepared from \(\text{MCl}:4\text{-PTSC}:\text{PPh}_3\) in 1:1:2 molar ratios in acetonitrile. The structures of the complexes were determined using single crystal X-ray diffraction analysis and further characterized by IR spectroscopy. Both complexes display a distorted tetrahedral coordination with two \(\text{PPh}_3\) ligands, one 4-PTSC ligand and a chloride ion. In the crystals, there are intra- and intermolecular hydrogen bonds to connect complexes into dimers. The existence of a solvate acetonitrile in (2) plays an important role in connecting each dimer to form a one-dimensional network.

Acknowledgements: Financial support from the Division of Physical Science, Faculty of Science, Prince of Songkla University, is gratefully acknowledged. We would like to thank Dr. Matthias Zeller and Purdue University for assistance with the X-ray structure determination and use of equipment, funded by the National Science Foundation of the United States (CHE-1625543).

REFERENCES

1. Pishawikar SA, More HN (2017) Synthesis, docking and in-vitro screening of mannich bases of thiosemicarbazide for anti-fungal activity. Arab J Chem 10, S2714–S2722.
2. Zhang Y, Wang R, Zhang T, Yan W, Chen Y, Zhang Y, Zhou M (2019) Benzofuran-isatin-hydroxylimine/thiosemicarbazide hybrids: Design, synthesis and in vitro anti-mycobacterial activity evaluation. Chin Chem Lett 30, 653–655.
3. Metwally MA, Bondock S, El-Azap H, Kandeel EE (2011) Thiosemicarbazides: synthesis and reactions. J Sulfur Chem 32, 489–519.
4. Singhal S, Arora S, Agarwal S, Sharma R, Singhal N (2013) A review on potential biological activities of thiosemicarbazides. World J Pharm Pharm Sci 2, 4661–4681.
5. Bhat MA, Khan AA, Ghabbour HA, Quah CK, Fun HK (2016) X-ray structure and antimicrobial activity of N-(4-chlorophenyl)-2-(pyridin-4-ylcarbonyl) hydrazinecarbothioamide. Trop J Pharm Res 15, 1751–1757.
6. Rane RA, Naphade SS, Bangalore PK, Palkar MB, Shaikh MS, Karpoormath R (2014) Synthesis of novel 4-nitropyrrrole-based semicarbazide and thiosemicarbazide hybrids with antimicrobial and anti-tubercular activity. Bioorg Med Chem Lett 24, 3079–3083.
7. Casas JS, Garcia-Tasende MS, Sordo J (2000) Main group metal complexes of semicarbazones and thiosemicarbazones. A structural review. Coord Chem Rev 209, 197–261.
8. Milunovic MM, Enyedy ÉA, Nagy NV, Kiss T, Trondl R, Jakubec MA, Keppel BK, Krachler R, et al (2012) L- and d-Proline thiosemicarbazone conjugates: Coordination behavior in solution and the effect of copper(II) coordination on their antiproliferative activity. Inorg Chem 51, 9309–9321.
9. Cihan-Ustündag G, Gürsoy E, Naenss L, Ulusoy-Güzeldemirci N, Çapan G (2016) Synthesis and antiviral properties of novel indole-based thiosemicar-
bazides and 4-thiazolidinones. *Bioorg Med Chem* **24**, 240–246.

10. Xie F, Cai H, Peng F (2018) Anti-prostate cancer activity of 8-hydroxyquinoline-2-carboxaldehyde-thiosemicarbazide copper complexes in vivo by bioluminescence imaging. *J Biol Inorg Chem* **23**, 949–956.

11. Xie F, Peng F (2018) Anticancer activity of copper complex of (4R)-(−)-2-thioxo-4-thiazolidine-carboxylic acid and 3-rhodaninepropionic acid on prostate and breast cancer cells by fluorescent microscopic imaging. *J Fluoresc* **28**, 89–96.

12. Kunos CA, Andrews SJ, Moore KN, Chon HS, Ivy SP (2019) Randomized phase II trial of triapine-cisplatin-radiotherapy for locally advanced stage uterine cervix or vaginal cancers. *Front Oncol* **15**, ID 1067.

13. Kunos CA, Ivy SP (2018) Triapine radiochemotherapy in advanced stage cervical cancer. *Front Oncol* **7**, ID 149.

14. Khan A, Jasinski JP, Smolenski VA, Hotchkins EP, Kelley PT, Shalit ZA, Paul K, et al (2018) Enhancement in anti-tubercular activity of indole based thiosemicarbazones on complexation with copper(I) and silver(I) halides: structure elucidation, evaluation and molecular modelling. *Bioorg Chem* **80**, 303–318.

15. Nimthong-Roldán A, Promsuwhan N, Puetpaiboon W, Wattanakanjana Y (2017) Crystal structure of chlorido[1-(4-nitrophenoxy)thiourea-κ*S]bis(triphenylphosphane-κ*P)copper(I). *Acta Cryst* **E73**, 41–44.

16. Nimthong-Roldán A, Sripa P, Wattanakanjana Y (2017) Crystal structure of chlorido[1-(4-nitrophenoxy)thiourea-κ*S]bis(triphenylphosphane-κ*P)silver(I). *Acta Cryst* **E73**, 829–831.

17. Wattanakanjana Y, Puetpaiboon W, Sripa P, Nimthong-Roldán A (2020) Crystal structure of metal(I) bromide complexes containing 1-(4-nitrophenyl)thiourea and triphenylphosphine ligands. *ScienceAsia* **46S**, 74–78.

18. APEX3 v2016.9–0, Saint V8.34A, Saint V8.37A; 2016.

19. SHELXTL suite of programs, version 6.14; 2000–2003.

20. Sheldrick GM (2008) A short history of SHELX. *Acta Cryst* **A64**, 112–122.

21. Sheldrick GM (2015) Crystal structure refinement with SHELXL. *Acta Crystallogr C* **71**, 3–8.

22. Hübschle CB, Sheldrick GM, Dittrich BJ (2011) *SHELXle*: a Qt graphical user interface for SHELXL. *Appl Cryst* **44**, 1281–1284.

23. Etter MC, MacDonald JC, Bernstein J (1990) Graphset analysis of hydrogen-bond patterns in organic crystals. *Acta Cryst* **B46**, 256–262.

24. Lobana TS, Rekha, Pannu APS, Hundal G, Butcher RJ, Castineiras A (2017) Synthesis and structures of monomeric [chloro(isatin-3-thiosemicarbazone)bis(triphenyl-phosphine)]copper(I) and dimeric [dichloro(bis thiophene-2-carbaldehyde thiosemicarbazone)bis(triphenylphosphine)] dicopper(I) complexes. *Polyhedron* **26**, 2621–2628.

25. Lobana TS, Khanna S, Sharma R, Hundal G, Sultana R, Chaudhary M, Butcher R J, Castineiras A (2008) Versatility of thiosemicarbazones in the construction of monomers, dimers and hydrogen-bonded networks of silver(I) complexes. *Cryst Growth Des* **8**, 1202–1212.

26. Macrae CF, Bruno JJ, Chisholm JA, Edgington PR, McCabe P, Pidcock E, Rodriguez-Monge L, Taylor R, et al (2008) Mercury CSD 2.0 – new features for the visualization and investigation of crystal structures. *Appl Cryst* **41**, 466–470.

27. Westrip SPJ (2010) *publCIF*: software for editing, validating and formatting crystallographic information files. *Appl Cryst* **43**, 920–925.