

Copper(II) and copper(I) complexes with a bidentate hydrazinic dithiocarbazate: synthesis and crystal structures

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Abstract

In this work, we explored the ability of N-methyl-S-methyl dithiocarbazate ($[\text{H}_2\text{N}-\text{N}(\text{CH}_3)\text{C}(=\text{S})\text{SCH}_3]$; DTCZ) to form coordination complexes with copper starting from different copper (II, I) sources. Data proved that the type of used salt affects the stoichiometry and structure of the obtained coordination complexes. Copper complexes of general empirical formula $[\text{Cu}(\text{DTCZ})\text{Cl}_2]$ (**1**), $[\text{Cu}(\text{DTCZ})_2\text{NO}_3]\text{NO}_3$ (**2**), $[\text{Cu}(\text{DTCZ})_2(\text{OH}_2)]\text{SO}_4$ (**3**), $[\text{Cu}(\text{DTCZ})_2]\text{PF}_6$ (**4**), $[\text{Cu}(\text{DTCZ})(\text{PPh}_3)_2]\text{NO}_3$ (**5**) and $[\text{Cu}(\text{DTCZ})_2]\text{Br}$ (**6**) were synthesized in high yield and characterized by elemental analysis, UV-Vis and IR spectroscopy. Molecular structures of **1-6** and also of side-products $[\text{Cu}(\text{DTCZ})_2\text{SO}_4]$ (**3a**), $[\text{Cu}(\text{DTCZ})_2](\text{PF}_6)(\text{OH})$ (**4b**) and $[\text{CuBr}(\text{C}_3\text{H}_7\text{NS}_2)]_n$ (**6a**) were determined by single crystal X-ray diffraction (XRD). In all cases, DTCZ binds the metal in the neutral form through the hydrazine nitrogen (NH_2) and thione sulphur (S) atom set, forming monosubstituted and disubstituted complexes having tetrahedral, square planar, or square pyramidal geometries, depending on the copper source. In addition, two one-dimensional (1D) coordination polymers and water channels have been observed in the crystal states.

Introduction

Cancer is the second leading cause of death (<http://gco.iarc.fr>)¹ and the quest for new tools for its early diagnosis and targeted treatment remains a primary goal for biomedical research. In this connection, medicinal inorganic chemistry gives important chances for the design of innovative diagnostic and therapeutic agents, with the final goal of providing personalized medicine.

In recent years, copper compounds have received great attention as a valid alternative to the currently available metal-based anticancer drugs, as they show new selective mechanisms of action other than covalent DNA binding, thus limiting severe side effects such as nephrotoxicity, neurotoxicity, and drug resistance, typical of the use of platinum antitumor agents²⁻⁵. The interest in copper-based complexes is driven by the assumption that endogenous metals may be less toxic to normal cells than to cancer cells; although, owing to its redox activity and affinity for binding sites normally occupied by other metals, copper can also be toxic. However, the altered metabolism of cancer cells and the differential response to copper between normal and cancer cells are the foundation for the development of copper complexes with anticancer activities^{2,6,7}.

Another interesting aspect related to copper is that it offers a relatively wide number of radioactive isotopes suitable for nuclear medicine applications^{8,9}. Among these, copper-64 (^{64}Cu) and copper-67 (^{67}Cu) radionuclides are progressively gaining interest in the scientific community thanks to their nuclear properties. Due to their decay mode, ^{64}Cu and ^{67}Cu are genuine theranostic radionuclides (theranostic = *diagnostic* + *therapeutic*) that allow to join in a single formulation an imaging agent to monitor drug delivery, release, and efficacy, and a therapeutic agent^{10,11}. In fact, ^{64}Cu decays through the emission of a positron with a maximum

energy of 0.66 MeV, useful in positron emission tomography (PET), and has a half-life of 12.7 hours. Therefore, similarly to fluorine-18, it is among the few radionuclides that allow high spatial resolution PET images. Moreover, it emits Auger electrons that can be conveniently exploited for inducing a therapeutic effect. ^{64}Cu is ideal for imaging studies that requires radionuclides with a relatively long half-life, as imaging can be conducted as long as 48 hours after radiopharmaceutical administration and the agents can be distributed to facilities far from the production site. Copper-67, with a half-life of 62 hours, is the longest-lived radionuclide of copper. It decays through the emission of β^- particles with energy suitable for therapy and γ rays of 184 keV, apt for single photon emission computed tomography (SPECT) imaging that permits imaging of the radionuclide distribution and uptake during therapy. It can also pair with ^{64}Cu analogues to perform pretherapy distribution determinations and dosimetry by PET. Due to its long half-life, ^{67}Cu is also suitable for imaging agents with slow *in vivo* pharmacokinetics such as monoclonal antibodies and other target molecules.

The peculiar chemical and biological features of copper and the existence of radionuclides relevant for nuclear medicine applications make it a sort of multifunctional metal ideal for the design of new chemical scaffolds for multipurpose applications, which encompass (chemo)therapy and diagnostic nuclear imaging to speed up the cancer diagnosis and monitoring of anticancer treatment efficacy, as well as the selection of responders to new target therapies.

From the chemical point of view, this element displays rich chemistry because it is capable of generating a variety of coordination complexes characterized by peculiar structural properties that can be conveniently exploited to develop new categories of (radio)drugs. The donor atom set influences the stability of the complex and its chemical-physical properties including charge, lipophilicity and form, features that affect the *in vivo* distribution and affinity for the physiological target. Hence, the research of new or alternative copper ligands is of crucial importance for achieving new effective Cu-based (radio)agents.

In aqueous solution, the chemistry of copper is restricted to the two principal oxidation states +2 and +1, with a dominant number of Cu(II) species and only a few but significant examples of Cu(I) complexes^{2,12–20} where Cu^+ ion is coordinated to ligands having soft donor atoms, in particular phosphorous and aromatic amines. Cu(I) complexes are often four-coordinated and adopt a tetrahedral geometry. Because of their intrinsic redox instability, most Cu(I) compounds are not sufficiently robust for (radio)pharmaceutical applications. In contrast, the use of Cu(II) complexes is more appropriate: Cu(II) species are generally less labile toward ligand exchange reactions, even though *in vivo* their kinetic stability might not resemble the *in vitro* aqueous solution stability^{2,8}. As Cu(II), the metal prefers a coordination number of four, with ligands arranged in square planar or tetrahedral geometries; nevertheless, five- and hexa-coordinated species, in which one or two additional ligands are weakly bound to the metal, are also accessible. Such a variety of possible structures allows for a wide selection of ligands, spanning from mono to hexadentate chelators, as well as a wide choice of donor atoms (N, S, O and halides).

Hard nitrogen and soft sulfur donor atoms are co-present in the structure of important multidentate ligands such as dithiocarbazates, thiosemicarbazones and bis-thiosemicarbazones. Given the presence of the N,S donor set, these ligands coordinate a wide range of transition and non-transition metal ions^{21–23}, generating stable complexes with promising pharmacological properties including antifungal, antibacterial, and antitumor activities^{7,24–33}. Among these, copper(II) compounds appear to be promising candidates due to their cytotoxic activity against human cancer cell lines^{2,6,7,28,31,34–38}. Moreover, tetradentate N_2S_2 bis-thiosemicarbazones present a strong potential for cancer theranostics, as they have been exploited in the radiopharmaceutical field to prepare stable complexes with radiometals suitable for molecular imaging^{22,39}. ^{64}Cu -agents were extensively investigated as a marker for hypoxia, especially the neutral [^{64}Cu -ATSM] (ATSM= diacetyl-bis(N4-methylthiosemicarbazone)^{21,40–43}.

Dithiocarbazates are also an interesting class of N,S chelators. Due to the possibility of extensive thione-thiol tautomerism over the –NH-C(=S)- moiety, they were largely explored for the good coordination ability with different transition metals including copper^{26–28,44–54} and radiometals of group 7 of the periodic table^{55–60}; for the latter, dithiocarbazates were used both as a coordinating agent and N³⁻ group donors in the formation of M≡N (M= ^{99m/99g}Tc; ^{188/nat}Re) nitrido core^{58,61,62}.

It should be noted that most of the coordination structures reported so far include complexes of the dithiocarbazic acid and its S-alkyl/aryl esters in the form of Schiff bases with divalent metal cations^{25,26,28,29,33}. Meanwhile, only a few examples of transition metals coordinated by the hydrazine nitrogen of dithiocarbazate are present in the literature^{27,30,32,50,51,63–67}. To the best of our knowledge, little effort has been made so far in the research of copper complexes with dithiocarbazate ligands in which the metal is coordinated by the hydrazinic nitrogen and in the absence of thione-thiol tautomerism.

In this work we investigate the coordination ability and reactivity of the N-Methyl-S-Methyl Dithiocarbazate chelator (DTCZ) towards different commercially available sources of copper(II) and copper(I) ions. CuCl₂ and Cu(acetate)₂ are the copper(II) precursors for the preparation of ^{64/67}Cu agents upon the addition of a pertinent ligand; hence, looking at a possible radiopharmaceutical application, the reactivity of DTCZ towards these Cu²⁺ ion sources has been considered. The obtained complexes have been fully characterized in solution and solid state, and the structures originating from six different reaction conditions are reported and discussed.

Experimental

Materials and Methods

CuCl₂·2H₂O, Cu(NO₃)₂·3H₂O, CuSO₄·5H₂O, [Cu(CH₃CN)₄]PF₆ and CuBr were obtained from Sigma Aldrich as reagent grade solids and were used without further purification. N-methyl-S-methyl dithiocarbazate (DTCZ) and [Cu(PPh₃)₂]NO₃ were synthesized according to literature procedures^{53,68}. All solvents were purchased from VWR Chemicals and used without further purification. Only Milli-Q water (18.2 MΩ-cm ionic purity) obtained by a Millipore Milli-Q water system (Bedford, MA, USA) was used.

Analyses. Elemental analyses (C, H, N and S) were performed on an Elementar Vario MICRO Cube. UV-Vis spectra were obtained on an Agilent Cary 60 spectrophotometer in the 200-1100 nm range. IR spectra were obtained on a Perkin-Elmer BXII FT-IR spectrometer in the 400-4000 cm⁻¹ range.

Crystallography

X-ray diffraction data for complexes **1-6a** were obtained from an Oxford Diffraction Gemini E four-circle kappa-goniometer diffractometer, equipped with a 2K x 2K EOS CCD area detector and sealed tube Enhance (Mo) and (Cu) X-ray sources. Selected single crystals of the compounds were mounted on a nylon loop. Data collections were performed at room temperature through the ω-scan method, using graphite-monochromated radiation in 1024 x 1024 pixel mode and 2 x 2 pixel binning. Structures of complexes **1**, **3**, **3a** and **4** were obtained using Mo Kα (λ = 0.71073) radiation, while Cu Kα (λ = 1.54184) radiation was used for complexes **4b**, **5**, **6** and **6a**.

Diffraction intensities were corrected for absorption, as well as for Lorentz and polarization effects. A numerical absorption correction based on Gaussian integration over a multifaceted crystal model was employed. Data reduction, finalization and cell refinement were carried out using the CrysAlisPro software⁶⁹. Accurate unit cell parameters were obtained by least-squares refinement of the angular settings of the strongest reflections, chosen from the whole experiment. The structures were solved by Intrinsic Phasing using SHELXT⁷⁰ through the Olex2 1.5 graphical interface⁷¹ and the solved structures were then refined differently based on the quality of the data. Complex **6** was refined as a two-component twin with SHELXL⁷⁰

using full-matrix least-squares minimization on F^2 . All the other complexes were refined with olex2.refine 1.5⁷² using full-matrix least-squares minimization on F^2 and non-spherical form factors were included in the last cycles of refinement using NoSpherA2⁷³ and ORCA 5.0.3⁷⁴. PBE method and def2-TZVP basis set were employed in the calculations. Non-H atoms were refined anisotropically. For complexes **1**, **3**, **4**, **4b** and **6a**, anisotropic refinement of hydrogen atoms was performed; in these cases, the RIGU restraint was used. Except for complex **1**, the coordinates of the hydrogen atoms of the methyl groups were geometrically placed using the AFIX 137 command.

Crystallographic data have been deposited at the Cambridge Crystallographic Data Center (CCDC) with deposition numbers 2128955, 2128957, 2128958, 2128962, 2128963, 2161494, 2164147 and 2166169. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

Synthesis and characterization of Cu(II) complexes

[Cu(DTCZ)Cl₂]_n (**1**)

To an ethanol solution (3 mL) of DTCZ (41.1 mg, 0.302 mmol) a solution of CuCl₂·2H₂O (50.2 mg, 0.295 mmol) in the same solvent (3 mL) was added at room temperature. Immediately, a green solid formed. A few drops of HCl 3M were used to lower the pH to a value between 2 and 3. The suspension was kept at room temperature under stirring for 24 hours. The precipitate was then filtered, washed with ethanol (3 x 1 mL) and diethyl ether (3 x 1 mL), then dried under vacuum. Yield: 59.2 mg, **74%**. Elem. anal. Calc. for C₃H₈CuN₂S₂Cl₂ (MW 270.69 g mol⁻¹): C, 13.3 %; H, 3.0 %; N, 10.35 %; S, 23.7 %. Found: C, 13.35 %; H, 2.7 %; N, 10.1 %; S, 23.3 %. UV-Vis (H₂O): λ_{MAX}/nm (ε/dm³ mol⁻¹ cm⁻¹): 266 (1.3·10⁴), 313 (2.7·10³), 565 (9.0·10¹), 664 (1.2·10²). FT-IR (KBr), ν/cm⁻¹: 3165 (ν_{N-H}), 3103 (ν_{N-H}), 1611 (δ_{N-H}), 1488 (ν_{C-N}), 1229 (ν_{NCS}), 1009 (ν_{N-N}), 962 (ν_{CS}).

Compound **1** is soluble in water, DMSO and insoluble in all other common solvents. Green crystals of complex **1** suitable for XRD were obtained by slow evaporation of a 1:1 mixture of water/acetonitrile.

[Cu(DTCZ)₂NO₃]₂NO₃ (**2**)

To an ethanol solution (3 mL) of DTCZ (40.0 mg, 0.293 mmol) a solution of Cu(NO₃)₂·3H₂O (35.0 mg, 0.145 mmol) in the same solvent (3 mL) was added at room temperature. A purple precipitate immediately formed. The suspension was kept at room temperature under stirring for 24 hours. Then, diethyl ether (20 mL) was added, and the precipitate obtained was filtered, washed with ethanol (3 x 1 mL) and diethyl ether (3 x 1 mL), and dried under vacuum. Yield: 52.3 mg, **81%**. Elem. anal. Calc. for C₆H₁₆CuN₆O₆S₄ (MW 460.03 g mol⁻¹): C, 15.7 %; H, 3.5 %; N, 18.3 %; S, 27.9 %. Found: C, 15.6 %; H, 3.3 %; N, 18.1 %; S, 27.7 %. UV-Vis (H₂O): λ_{MAX}/nm (ε/dm³ mol⁻¹ cm⁻¹): 266 (1.5·10⁴), 311 (4.8·10³), 562 (1.6·10²), 650 (1.6·10²). FT-IR (KBr), ν/cm⁻¹: 3130 (ν_{N-H}), 1626 (δ_{N-H}), 1495 (ν_{C-N}), 1240 (ν_{NCS}), 1008 (ν_{N-N}), 970 (ν_{CS}).

Compound **2** is soluble in water, DMSO and insoluble in all other common solvents. Purple crystals of complex **2** suitable for XRD were obtained by slow evaporation using a 1:1 mixture of water/isopropanol.

[Cu(DTCZ)₂(OH₂)]SO₄ (**3**)

A water solution (1 mL) of CuSO₄·5H₂O (32.9 mg, 0.132 mmol) was added to an ethanol solution (3 mL) of DTCZ (42.0 mg, 0.308 mmol), at room temperature. Immediately a dark blue precipitate formed and the suspension was kept at room temperature under stirring for 24 hours. Then, diethyl ether (20 mL) was added, the precipitate obtained was filtered, washed with ethanol (3 x 1 mL) and diethyl ether (3 x 1 mL), and dried under vacuum. Yield: 47.5 mg, **80%**. Elem. anal. Calc. for C₆H₁₈CuN₄O₅S₅ (MW 450.11 g mol⁻¹): C, 16.0 %; H, 4.0 %; N, 12.45 %; S, 35.6 %. Found: C, 16.0 %; H, 3.7 %; N, 12.25 %; S, 35.2 %. UV-Vis (H₂O): λ_{MAX}/nm (ε/dm³

mol⁻¹ cm⁻¹): 265 (2.8·10⁴), 320 (5.0·10³), 561 (2.2·10²), 648 (2.2·10²). FT-IR (KBr), ν /cm⁻¹: 1651 ($\delta_{\text{N-H}}$), 1494 ($\nu_{\text{C-N}}$), 1242 (ν_{NCS}), 1008 ($\nu_{\text{N-N}}$), 975 (ν_{CS}).

Compound **3** is soluble water, DMSO and insoluble in all other common solvents. Deep-blue crystals suitable for XRD were obtained after a few days by liquid diffusion of ethanol into a water/acetonitrile (1:1) solution of the complex stored at -4°C.

Synthesis and characterization of Cu(I) complexes

[Cu(DTCZ)₂]₂PF₆ (**4**)

In an acetonitrile solution (15 mL) of [Cu(CH₃CN)₄]₂PF₆ (282.6 mg, 0.757 mmol) a solution of DTCZ (233.4 mg, 1.712 mmol) in the same solvent (15 mL) was added at room temperature and under a dinitrogen (N₂) atmosphere. A colour transition from transparent to yellow was observed. The reaction mixture was kept at room temperature under stirring for 24 hours. The reaction volume was then reduced to 5 mL by solvent evaporation in a N₂ stream and a yellow solid was precipitated by adding 50 mL of diethyl ether. The precipitate was filtered, washed with diethyl ether (3 x 5 mL) and water (3 x 5 mL), and dried under vacuum. Yield: 280.7 mg, **77%**. Elem. anal. Calc. for C₆H₁₆CuN₄F₆PS₄ (MW 480.99 g mol⁻¹): C, 15.0 %; H, 3.35 %; N, 11.65 %; S, 26.7 %. Found: C, 15.0 %; H, 3.5 %; N, 11.45 %; S, 26.3 %. UV-Vis (MeCN): $\lambda_{\text{MAX}}/\text{nm}$ ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$): 202 (1.5·10⁴), 207 (1.7·10⁴), 273 (8.1·10³). FT-IR (KBr), ν /cm⁻¹: 3250 ($\nu_{\text{N-H}}$), 3192 ($\nu_{\text{N-H}}$), 1621 ($\delta_{\text{N-H}}$), 1465 ($\nu_{\text{C-N}}$), 1224 (ν_{NCS}), 1000 ($\nu_{\text{N-N}}$), 968 (ν_{CS}). Compound **4** is soluble in acetonitrile, alcohols, DMSO, slightly soluble in chlorinated solvents and insoluble in water and Et₂O. Yellow crystals of complex **4** suitable for XRD were obtained by slow evaporation of an acetonitrile solution.

By conducting the reaction in a non-controlled atmosphere, the formation of an oxidized side product [Cu(DTCZ)₂](PF₆)₂ (**4a**) was observed. After 24 hours of reaction at room temperature under stirring, the solvent was fully evaporated and the obtained crude purple solid was treated with acetonitrile (3 x 1 mL) to remove **4**. Then, the solid was collected by filtration, washed with acetonitrile (3 x 1 mL) followed by diethyl ether (3 x 1 mL), and dried under vacuum. Yield: **24%**. Elem. anal. Calc. for C₆H₁₆CuN₄F₁₂P₂S₄ (MW 625.92 g mol⁻¹): C, 11.5%; H, 2.6 %; N, 8.95 %; S, 20.5 %. Found: C, 11.7 %; H, 2.8 %; N, 8.85 %; S, 20.1 %. UV-Vis (H₂O): $\lambda_{\text{MAX}}/\text{nm}$ ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$): 263 (1.5·10⁴), 310 (5.4·10³), 560 (1.3·10²), 660 (1.5·10²). FT-IR (KBr), ν /cm⁻¹: 3268 ($\nu_{\text{N-H}}$), 3191 ($\nu_{\text{N-H}}$), 1625 ($\delta_{\text{N-H}}$), 1230 (ν_{NCS}), 1011 ($\nu_{\text{N-N}}$), 968 (ν_{CS}). Compound **4a** is soluble in water, DMSO and insoluble in all other common solvents. We were unable to crystallize the complex with two PF₆⁻ as counterions. However, violet crystals suitable for XRD of the species [Cu(DTCZ)₂](PF₆)(OH) (**4b**) were obtained by liquid diffusion of ethanol into a water/acetonitrile (1:1 ratio) solution of the complex stored at -4°C after a few days.

[Cu(DTCZ)(PPh₃)₂]₂NO₃ (**5**)

A dichloromethane solution (15 mL) of [Cu(PPh₃)₂]₂NO₃ (407.1 mg, 0.625 mmol) was added to DTCZ (128.7 mg, 0.944 mmol) dissolved in methanol (15 mL), at room temperature and under N₂ atmosphere. The reaction mixture was kept under stirring for 24 hours, during which the appearance of the solution did not change. The solvent was removed by evaporation under a N₂ stream and an oil residue was obtained. The oil was treated with methanol (3 mL) followed by the addition of diethyl ether (50 mL), and the formation of a white precipitate was observed. Then, the precipitate was collected by filtration, washed with diethyl ether (3 x 5 mL), and dried under vacuum. Yield: 348.9 mg, **71%**. Elem. anal. Calc. for C₃₉H₃₈CuN₃O₃P₂S₂ (MW 786.36 g mol⁻¹). Found: C, 59.5 %; H, 4.9 %; N, 5.3 %; S, 8.5 %. Calc. for C₃₉H₃₈CuN₃O₃P₂S₂: C, 59.6 %; H, 4.9 %; N, 5.3 %; S, 8.15 %. UV-Vis (MeCN): $\lambda_{\text{MAX}}/\text{nm}$ ($\epsilon/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$): 202 (7.3·10⁴), 211 (8.2·10⁴), 271 (2.7·10⁴). IR (KBr), ν /cm⁻¹: 3100 ($\nu_{\text{N-H}}$), 1637 ($\delta_{\text{N-H}}$), 1480 ($\nu_{\text{C-N}}$), 1225 (ν_{NCS}), 998 ($\nu_{\text{N-N}}$), 965 (ν_{CS}). Compound **5** is soluble in alcohols,

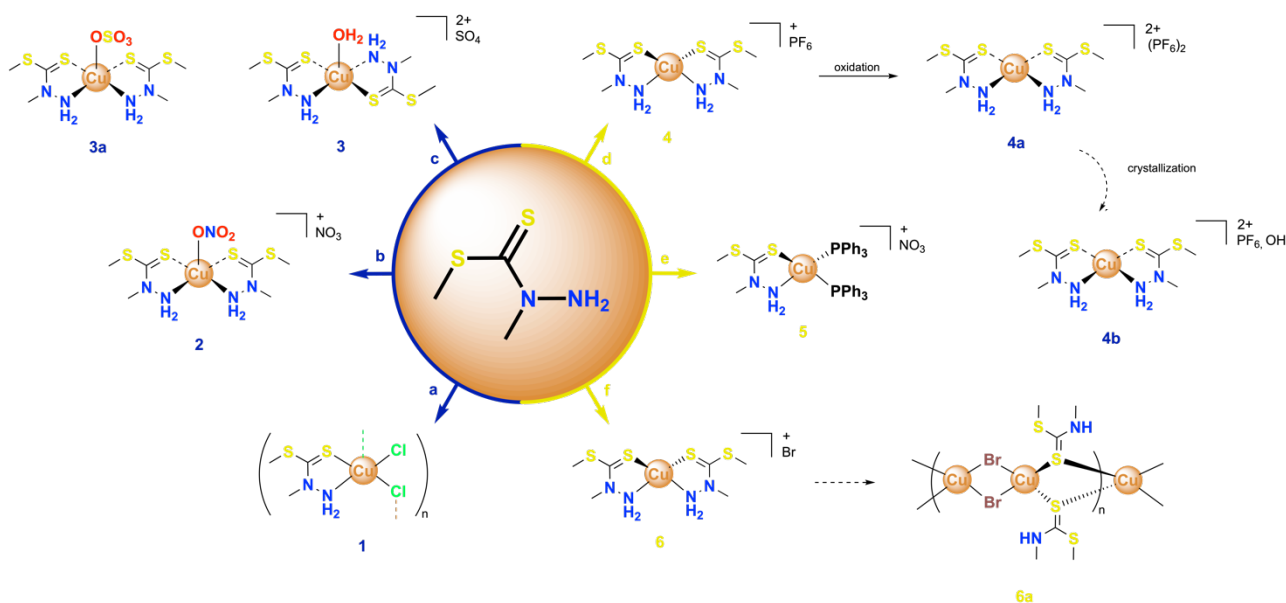
chlorinated solvents, DMSO, slightly soluble in acetonitrile and insoluble in water and Et₂O. White crystals of complex **5** suitable for XRD were obtained by slow evaporation of a chloroform/methanol solution.

[Cu(DTCZ)₂]Br (**6**)

In an acetonitrile solution (15 mL) of DTCZ (399.4 mg, 3.159 mmol), a solution of CuBr (200.0 mg, 1.395 mmol) in the same solvent (15 mL) was added at room temperature and under N₂ atmosphere. A colour transition from transparent to yellow was observed and the reaction was kept under stirring for 24 hours, during which the formation of an insoluble dark yellow precipitate was detected. The solid was fully precipitated by adding 50 mL of diethyl ether. The precipitate was recrystallized from acetonitrile, filtered, washed with diethyl ether (3 x 5 mL), and dried under vacuum. Yield: 319.1 mg, **55%**. Elem. anal. Calc. for C₆H₁₆CuBrN₄S₄ (MW 415.89 g mol⁻¹): C, 17.3 %; H, 3.9 %; N, 13.5 %; S, 30.8 %. Found: C, 17.0 %; H, 3.7 %; N, 13.2 %; S, 30.4 %. UV-Vis (MeCN): λ_{MAX}/nm (ε/dm³ mol⁻¹ cm⁻¹): 202 (1.2·10⁴), 207 (1.4·10⁴), 273 (4.2·10³). FT-IR (KBr) ν/cm⁻¹: 3236 (ν_{N-H}), 1599 (δ_{N-H}), 1225 (ν_{NCS}), 996 (ν_{N-N}), 959 (ν_{CS}). Compound **6** is soluble in acetonitrile, DMSO and insoluble in water and all common solvents. Dark yellow crystals of complex **6** suitable for XRD were obtained by slow evaporation of an acetonitrile solution.

Results and discussion

Synthesis and characterization



Scheme 1: Complexes **1-6** and their molecular structures. Compounds highlighted in blue are Cu(II) derivatives while yellow ones are Cu(I) derivatives. Complexes **3a**, **4a**, **4b** and **6a** are also depicted. Copper starting sources: CuCl₂·2H₂O (a), Cu(NO₃)₂·3H₂O (b), CuSO₄·5H₂O (c), [Cu(CH₃CN)₄]PF₆ (d) [Cu(PPh₃)₂]NO₃ (e) and CuBr (f)

Scheme 1 summarises the reactivity of the DTCZ ligand toward the different copper precursors. Copper(II) complexes (**1-3**) were efficiently produced through simple complexation reactions starting from different copper(II) salt precursors, including CuCl₂·2H₂O, Cu(NO₃)₂·3H₂O and CuSO₄·5H₂O. Reactions were carried out by treating the pertinent precursor complex with a slight excess of DTCZ in ethanol solution at room temperature. In all cases, although the formation of the products was immediate, the reactions were

prolonged for 24 hours to maximize the yield. For complex **1** the reaction was also conducted in the absence of HCl and in the presence of 2-10-fold excess of DTCZ at reflux for 8 h.

Starting copper reagents have an impact on the copper-to-DTCZ stoichiometric ratio of the final complex. Interestingly, the study of the copper(II) coordination chemistry of DTCZ revealed that both a 1:1 and 1:2 Cu:DTCZ complexes were isolated, in which DTCZ acts as a neutral bidentate ligand *via* the hydrazine nitrogen-(NH₂) and thione sulphur (S) donor pair.

With CuCl₂ · 2H₂O, the formation of the only neutral monosubstituted complex [Cu(DTCZ)Cl₂] (**1**) was obtained regardless of the amount of DTCZ used, and no formation of a disubstituted species was observed in all investigated conditions. In this compound, DTCZ was coordinated in the neutral form though the NH₂ and S atom set and the metal coordination sphere was completed by two Cl atoms, compensating for the divalent positive charge of the metal in a four-coordinated arrangement, while the usage of Cu(NO₃)₂ · 3H₂O and CuSO₄ · 5H₂O precursors afforded almost quantitatively the charged disubstituted species [Cu(DTCZ)₂NO₃]₂NO₃ (**2**) and [Cu(DTCZ)₂(OH₂)]SO₄ (**3**). In these 1:2 Cu:DTCZ complexes, the metal is five-coordinated. The fifth coordination position is occupied by a negative NO₃⁻ group or by a neutral water molecule, to form a mono-positive or dipositive complex, respectively. In both cases, the use of a metal-to-DTCZ stoichiometric ratio of 1:1 significantly reduces the yield of the final complexes, and the formation of a monosubstituted compound was never detected. Additionally, the reaction between DTCZ and Cu(CH₃COO)₂ was also considered, the formation of an orange precipitate was achieved but the identification of a product was unsuccessful.

Compounds **1-3** are stable in solid and solution state, they are soluble in water, DMSO and insoluble in alcohols, acetonitrile, chlorinated solvents and diethyl ether. In all cases, after solubilization in water, the colour of the solutions does not change over time indicating that the complexes are stable.

For copper(I) complexes (**4-6**), [Cu(CH₃CN)₄]PF₆, [Cu(PPh₃)₂]₂NO₃ and CuBr were used as precursors and reactions were carried out in N₂ atmosphere to avoid metal oxidation and formation of the corresponding Cu(II) compounds (*vide infra*). Copper(I) complexes were obtained as white and yellow powders in good yield through ligand-exchange reactions by treating precursor complexes with a slight excess of DTCZ at room temperature. As for copper(II), DTCZ binds the metal in copper(I) complexes as a neutral chelator through the hydrazine nitrogen-NH₂ and thione sulphur donor pair.

The reaction of the labile [Cu(CH₃CN)₄]PF₆ with DTCZ in different stoichiometric ratios always generated the disubstituted positive [Cu(DTCZ)₂]PF₆ (**4**) complex. By conducting the reaction in a non-controlled atmosphere, the oxidized [Cu(DTCZ)₂](PF₆)₂ (**4a**) compound was collected as a side product. Similarly, a mono cationic bis-substituted compound [Cu(DTCZ)₂]Br (**6**), was prepared using CuBr as a precursor. In both cases, as for complexes **2-3**, when DTCZ is utilized as a limiting reagent, the formation of bis-DTCZ species was always observed.

Starting from [Cu(PPh₃)₂]₂NO₃, the only isolated product was [Cu(DTCZ)(PPh₃)₂]₂NO₃ (**5**), with one bidentate DTCZ and two monodentate PPh₃ ligands; a large excess of DTCZ is unable to displace the PPh₃ molecules.

The in-solution stability of **4-6** was evaluated over time. Complexes **4** and **6** are soluble in acetonitrile, alcohols and DMSO. They are stable in acetonitrile solution but slowly form a brown precipitate in alcoholic solutions; **5** is soluble in acetonitrile, alcohols and chlorinated solvents; the solution remains colourless indicating that the complex is stable.

Elemental analysis data support the chemical structures of the complexes as shown in Scheme 1.

The FT-IR spectra of complexes **1-6**, including **4a** (see ESI), were compared with that of the free DTCZ ligand, confirming the presence of the ligand. Indeed, they show the symmetric and asymmetric stretching frequencies of the NH₂ group in the 3100-3300 cm⁻¹ region; the bending frequency of NH₂ in the 1599-1650 cm⁻¹ region; the ν(C-N) in the 1460-1496 cm⁻¹ region^{24,51,75-77}; the deformation of the NCS moiety (C=S stretching and N-N stretching at 1220-1244 cm⁻¹); the NH₂ twisting in the 1093-1180 cm⁻¹ region; the N-N stretching at 996-1012 cm⁻¹; the asymmetrical stretching of (CSS) at 954-980 cm⁻¹, whose splitting into two

peaks (or a peak with a visible shoulder) is compatible with the coordination to the metal via one sulphur⁷⁸. Broad peaks compatible with the relevant counterion are also displayed in the spectra of compounds **2** and **5** (nitrate, at 1300-1410 cm⁻¹), **3** (sulphate, at 1040-1170 cm⁻¹ and 600-620 cm⁻¹), and **4/4a** (hexafluorophosphate, at 818-845 cm⁻¹)⁷⁹. The broadening of peaks around 3000 cm⁻¹ for complexes **2** and **3** is compatible with the extensive hydrogen bonding network that was observed in the crystal structures of both complexes (*vide infra*). Metal-sulphur stretching vibrations were not visible, since they could be detected below the 400 cm⁻¹ region.

In UV-Vis spectra (see ESI) of copper(II) complexes, electronic transitions of DTCZ at 255 nm and 270 nm collapse into a band which peaks at smaller wavelengths (260 nm). The spectra also show a broad shoulder from 300 to 400 nm, assigned to the S→Cu(II) ligand-to-metal charge transfer (LMCT) band⁸⁰, and two broad bands, peaking respectively at 560-565 nm and 648-664 nm, with a low molar extinction coefficient (100-200 dm³ mol⁻¹ cm⁻¹), assigned to *d-d* transitions. Copper(I) complexes show no LMCT bands or *d-d* transitions (due to their d¹⁰ configuration) and their absorption spectra in the 250-300 nm region closely resemble that of the free ligand.

Crystallography

Crystal data, data collection and structure refinement details are summarized in Table 1 and Table 2. Selected geometric parameters (bond lengths and angles) are listed in Table 3 and Table 4.

Table 1: Crystal data, data collection and structure refinement details for copper(II) complexes **1**, **3**, **3a** and **4b**.

	1	3	3a	4b
Empirical formula	C ₃ H ₈ N ₂ S ₂ Cl ₂ Cu	C ₆ H ₁₈ N ₄ O ₅ S ₅ Cu	C ₆ H ₁₈ CuN ₄ O ₅ S ₅	C ₆ H ₁₇ CuF ₆ N ₄ OPS ₄
Formula weight	270.693	450.110	450.110	498.002
Temperature/K	302(2)	295.5(9)	295.5(5)	295.8(3)
Crystal system	orthorhombic	monoclinic	monoclinic	orthorhombic
Space group	Pbca	P2 ₁ /n	P2 ₁ /c	Pbca
a/Å	12.6375(2)	10.2194(2)	8.9774(3)	7.4208(2)
b/Å	7.5142(1)	9.9284(1)	26.3089(9)	16.9063(4)
c/Å	18.6372(2)	16.6124(3)	7.3242(3)	27.4447(8)
α/°	90	90	90	90
β/°	90	94.644(2)	110.023(4)	90
γ/°	90	90	90	90
Volume/Å³	1769.80(4)	1680.00(5)	1625.31(11)	3443.16(16)
Z	8	4	4	8
ρ_{calc}/cm³	2.032	1.780	1.839	1.921
μ/mm⁻¹	3.471	1.943	2.009	7.846
F(000)	1087.5	928.4	928.4	2011.8
Crystal size/mm³	0.24 × 0.18 × 0.13	0.36 × 0.30 × 0.03	0.39 × 0.10 × 0.09	0.20 × 0.08 × 0.02
Radiation	Mo Kα (λ = 0.71073)	Mo Kα (λ = 0.71073)	Mo Kα (λ = 0.71073)	Cu Kα (λ = 1.54184)
2θ range for data collection/°	4.38 to 61.02	4.52 to 60.72	4.82 to 54.2	6.44 to 145.66
Index ranges	-18 ≤ h ≤ 17, -10 ≤ k ≤ 10, -26 ≤ l ≤ 26	-14 ≤ h ≤ 13, -13 ≤ k ≤ 13, -21 ≤ l ≤ 23	-11 ≤ h ≤ 11, -21 ≤ k ≤ 33, -9 ≤ l ≤ 9	-6 ≤ h ≤ 9, -20 ≤ k ≤ 19, -34 ≤ l ≤ 34
Reflections collected	34668	30910	18901	16775
Independent reflections	2694 [R _{int} = 0.0433, R _{sigma} = 0.0158]	4668 [R _{int} = 0.0333, R _{sigma} = 0.0223]	3588 [R _{int} = 0.0436, R _{sigma} = 0.0340]	3342 [R _{int} = 0.0513, R _{sigma} = 0.0461]
Data/restraints/parameters	2694/45/164	4668/99/352	3588/0/197	3342/93/329
Goodness-of-fit on F²	1.042	1.057	1.061	1.072
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0176, wR ₂ = 0.0400	R ₁ = 0.0322, wR ₂ = 0.0751	R ₁ = 0.0590, wR ₂ = 0.1273	R ₁ = 0.0451, wR ₂ = 0.1013
Final R indexes [all data]	R ₁ = 0.0211, wR ₂ = 0.0415	R ₁ = 0.0424, wR ₂ = 0.0817	R ₁ = 0.0726, wR ₂ = 0.1355	R ₁ = 0.0830, wR ₂ = 0.1245
Largest diff. peak/hole / e Å⁻³	0.40/-0.43	1.71/-0.38	1.32/-0.80	0.64/-0.64

XRD data for complex **2** are in agreement with those previously reported⁸¹. A low-symmetry polymorph of complex **2** was also previously characterized⁸².

The Cu – S bond length does not vary significantly between Cu(I) and Cu(II) complexes, (mean distances are 2.28 Å for both) while Cu – N bond length is longer for Cu(I) complexes, suggesting a weaker bond (mean distances are 2.11 Å and 2.00 Å for copper(I) and copper(II), respectively). N2 – N1 – Cu1 bond angles in Cu(I) complexes are also appreciably smaller (112.1°) than in Cu(II) complexes (115.4°). For all complexes, bond length C1 – S1 is compatible with a double bond character and C1 – N2 length is compatible with a single bond character. The conformation of the Cu1 – N1 – N2 – C1 – S1 five-membered ring resulting from copper chelation has been analysed considering the S1 – C1 – N2 plane, given the sp² character of the C1 carbon. Copper(II) complexes present a half-chair conformation, almost planar for **1** and **4b**, while more pronounced for complex **3a**. An even more pronounced half-chair conformation is present in one of the two five-membered rings of complex **3**. Interestingly, copper(I) complexes **4**, **5** and **6** exclusively adopt the envelope conformation, in which Cu1 is the tip of the envelope. Therefore, we suggest that the ring conformation is dependent on the metal oxidation state. The water as a solvate in the asymmetric units of **3a**, **5** and **6** should derive from ambient moisture and/or from solvents, which were not anhydrous. Other features are discussed separately for Cu(II) and Cu(I) complexes, as below.

Table 2: Crystal data, data collection and structure refinement details for copper(I) complexes **4**, **5**, **6** and **6a**

	4	5	6	6a
Empirical formula	C ₆ H ₁₆ N ₄ F ₆ PS ₄ Cu	C ₃₉ CuH ₄₀ N ₃ O ₄ P ₂ S ₂	C ₆ H ₁₈ BrCuN ₄ OS ₄	C ₃ H ₇ BrCuNS ₂
Formula weight	480.995	804.395	433.93	264.677
Temperature/K	295.6(5)	295.9(4)	298.2(4)	298.3(3)
Crystal system	monoclinic	Triclinic	monoclinic	triclinic
Space group	I2/a	P-1	P2 ₁ /n	P-1
a/Å	17.3667(5)	12.2632(4)	14.5640(3)	5.7139(3)
b/Å	5.1640(2)	13.0852(5)	4.97270(10)	8.1766(4)
c/Å	19.4375(5)	13.2597(3)	22.3743(5)	8.6122(3)
α/°	90	90.903(2)	90	101.903(4)
β/°	105.108(3)	94.255(2)	102.221(2)	90.624(4)
γ/°	90	113.091(3)	90	90.862(4)
Volume/Å³	1682.94(10)	1949.54(12)	1583.68(6)	393.63(3)
Z	4	2	4	2
ρ_{calc}/cm³	1.898	1.370	1.820	2.233
μ/mm⁻¹	1.945	2.918	9.774	14.053
F(000)	972.5	836.8	872.0	252.3
Crystal size/mm³	0.25 × 0.12 × 0.02	0.46 × 0.18 × 0.03	0.79 × 0.06 × 0.05	0.19 × 0.16 × 0.06
Radiation	Mo Kα (λ = 0.71073)	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)	Cu Kα (λ = 1.54184)
2θ range for data collection/°	4.34 to 57.66	6.7 to 145.74	8.086 to 145.196	10.5 to 145.8
Index ranges	-21 ≤ h ≤ 23, -6 ≤ k ≤ 6, -24 ≤ l ≤ 25	-15 ≤ h ≤ 15, -16 ≤ k ≤ 16, -16 ≤ l ≤ 16	-18 ≤ h ≤ 18, -6 ≤ k ≤ 6, -27 ≤ l ≤ 27	-6 ≤ h ≤ 7, -10 ≤ k ≤ 10, -10 ≤ l ≤ 10
Reflections collected	9153	36459	40614	16071
Independent reflections	1985 [R _{int} = 0.0457, R _{sigma} = 0.0305]	7681 [R _{int} = 0.0313, R _{sigma} = 0.0235]	40614	1552 [R _{int} = 0.0596, R _{sigma} = 0.0288]
Data/restraints/parameters	1985/45/158	7681/0/465	40614/0/162	1552/39/120
Goodness-of-fit on F²	1.071	1.048	1.011	1.066
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0296, wR ₂ = 0.0742	R ₁ = 0.0372, wR ₂ = 0.0967	R ₁ = 0.0511, wR ₂ = 0.1288	R ₁ = 0.0317, wR ₂ = 0.0801
Final R indexes [all data]	R ₁ = 0.0374, wR ₂ = 0.0810	R ₁ = 0.0524, wR ₂ = 0.1095	R ₁ = 0.0706, wR ₂ = 0.1447	R ₁ = 0.0385, wR ₂ = 0.0855
Largest diff. peak/hole / e Å⁻³	0.37/-0.32	0.72/-0.27	1.01/-0.52	0.42/-0.55

Table 3: Selected bond lengths (Å) and angles (°) for copper(II) complexes. For disubstituted compounds **3** (*), **3a** (†) and **4b** (°) the parameters are reported twice, once for each ligand molecule.

	1	3	*	3a	†	4b	°
Cu1-S1	2.2738(3)	2.3031(6)	2.3304(6)	2.2747(15)	2.2917(14)	2.2505(12)	2.2573(12)
Cu1-N1	2.0172(11)	1.9916(17)	1.9877(17)	2.020(4)	1.990(5)	2.013(4)	2.008(4)
N1-N2	1.4150(14)	1.429(3)	1.419(3)	1.412(6)	1.406(6)	1.411(5)	1.408(4)
N2-C1	1.3260(15)	1.322(3)	1.321(3)	1.322(7)	1.319(7)	1.324(5)	1.322(5)
S1-C1	1.6915(12)	1.690(2)	1.690(2)	1.696(5)	1.688(5)	1.687(4)	1.687(4)
C1-S2	1.7316(11)	1.740(2)	1.748(2)	1.732(5)	1.738(5)	1.741(4)	1.744(4)
Cu1-O1	-	2.2999(18)	-	2.218(4)	-	-	-
N1-Cu1-S1	84.87(3)	85.50(5)	84.50(5)	85.06(13)	85.41(14)	85.68(11)	86.86(11)
C1-S1-Cu1	98.09(4)	96.53(8)	94.51(8)	97.43(19)	96.12(18)	97.52(16)	96.23(15)
N2-N1-Cu1	116.63(7)	115.33(12)	113.82(12)	115.8(3)	115.9(3)	115.9(3)	114.4(3)
C1-N2-N1	118.44(10)	118.63(17)	117.81(17)	118.7(4)	118.5(4)	118.0(3)	119.1(3)
N2-C1-S1	121.95(9)	122.33(17)	122.91(17)	122.2(4)	122.8(4)	122.7(3)	123.2(3)

Table 4: Selected bond lengths (Å) and angles (°) for copper(I) complexes. For the disubstituted compound **6** (‡) the parameters are reported twice, once for each ligand molecule (complex **4** parameters are reported only once since the second ligand molecule is obtained by symmetry operations).

	4	5	6	‡
Cu1-S1	2.2311(5)	2.3415(7)	2.266(3)	2.274(4)
Cu1-N1	2.1429(18)	2.119(2)	2.078(9)	2.096(10)
N1-N2	1.414(2)	1.412(3)	1.440(12)	1.408(12)
N2-C1	1.329(3)	1.333(3)	1.329(13)	1.318(13)
S1-C1	1.6864(19)	1.673(2)	1.680(9)	1.684(10)
C1-S2	1.747(2)	1.753(2)	1.766(9)	1.757(9)
N1-Cu1-S1	86.01(5)	83.38(6)	87.0(3)	85.8(3)
C1-S1-Cu1	98.21(7)	96.44(9)	95.7(3)	95.6(3)
N2-N1-Cu1	111.64(12)	113.32(15)	111.4(6)	111.9(6)
C1-N2-N1	119.63(16)	119.2(2)	118.8(8)	119.3(8)
N2-C1-S1	124.32(15)	124.40(19)	125.2(7)	125.1(7)

Crystal structures of copper(II) complexes

In complex **1**, the coordination sphere around the Cu(II) centre is defined by one sulphur and one nitrogen of DTCZ and two *cis*-placed chlorine atoms in a distorted planar arrangement. Indeed, in the crystal, since the S1 – Cu1 – Cl2 angle is 163.18(1)°, Cl2 (opposite to the thione S atom) is 0.597 Å away from the Cl1 – Cu1 – N1 – S1 mean plane and involved in a long-range interaction with the central copper atom of an adjacent molecule, in a position that would be the apical one in a distorted square pyramidal arrangement. This originates a chain motif of alternating Cu and Cl atoms expanding along the b direction of the unit cell, with Cu1 – Cl2' distance equal to 2.7801(3) Å and Cu1 – Cl2 – Cu1' and Cl2 – Cu1 – Cl2' angles equal to 96.66(1)° and 96.35(1)° respectively (Figure 1). A similar behaviour with similar bond distances has been reported by Rigamonti *et al.* for another class of Cu(II) complexes with NNO Schiff base ligand⁸³, suggesting that complex **1** is polymeric in the solid state. DTCZ ligands arrange nearly parallel to themselves (they form a 9.25° dihedral angle, calculated using Cl1 – Cu1 – N1 – S1 mean planes) and protrude from the same side of the backbone, with torsion angles S1 - Cu1 – Cu1' – N1' and N1 – Cu1 – Cu1' – S1' of 88.15(3)° and 95.57(3)° respectively. The distance of Cu1 from the N1 – S1 – Cl1 – Cl2 mean plane is 0.165 Å.

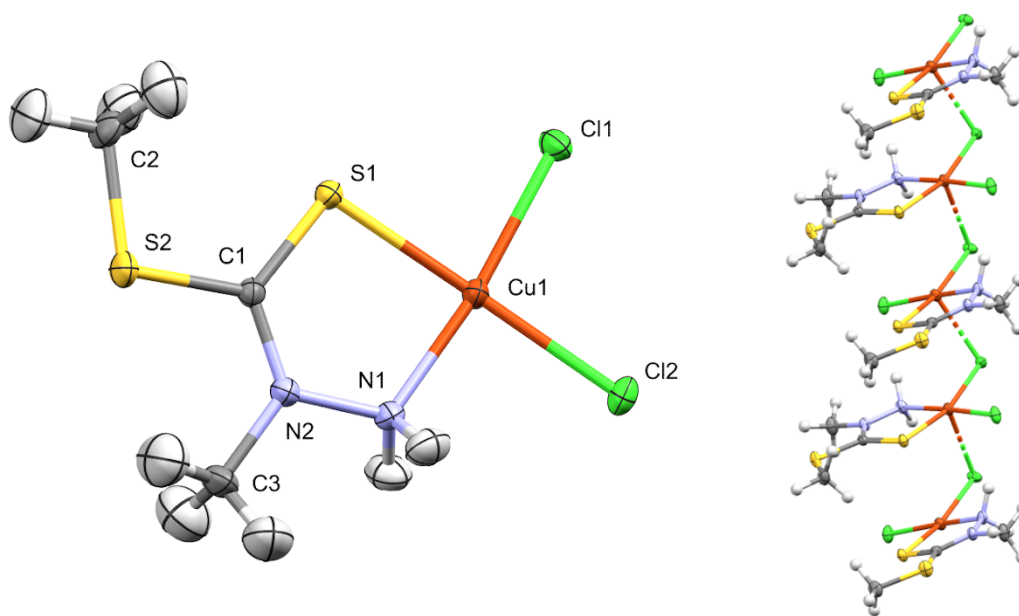


Figure 1: Crystal structure of complex **1**. Thermal ellipsoids drawn at 30% probability. The polymeric chain in the solid state is depicted on the right, highlighting Cu1 - Cl2 solid-state interaction.

Crystal structure of **2** has been previously reported by Ali *et al.*⁸¹. The complex was obtained by reacting $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ with the pentadentate ligand 2,6-diacetylpyridine-bis(N-methyl-S-methyldithiocarbamate). During complexation, the hydrolysis of the ligand to the two constituents N-methyl-S-methyl dithiocarbamate and 2,6-diacetylpyridine occurred, and the only complex with two bidentate DTCZ was recovered in the crystalline form. X-ray crystallographic analysis shows that the complex adopts a distorted square-pyramidal geometry in which the two DTCZ occupy the basal plane and are bound to the copper(II) ion as N,S chelators via the amino nitrogen and the thione sulphur atoms. The N and S atoms of DTCZ are in reciprocal *cis* position. The apical position is occupied by the monodentate nitrate ligand to neutralize one of the two positive charges of the complex. In complexes **3**, **3a** and **4b**, two N,S-bidentate DTCZ ligands bind to the copper(II) centre. Crystallization of complex **3** gives a mixture of plate-like and prism crystalline solids, **3** and **3a** respectively (Figures 2 and 3).

For **3**, the N and S atoms of the two DTCZ ligands are in a reciprocal *trans* position and occupy the equatorial plane, while a water molecule occupies the apical position of the resulting distorted square pyramidal geometry. Cu1 - O1 distance is comparable with existing data for water molecules belonging to the inner sphere coordination in apical position⁸⁵ and is significantly longer than the other contacts. The base of the pyramid is not perfectly planar, as S1 - Cu1 - S3 angle is $160.45(2)^\circ$. Instead, N1 - Cu1 - N3 angle is $177.46(7)^\circ$, closer to the ideal 180° . The water molecule is also slightly tilted because of the hydrogen bonding with the sulphate, as S1 - Cu1 - O1 angle is $106.23(5)^\circ$. A sulphate anion balance the +2 charge of the complex and is involved in a rich hydrogen bonding network (Figure 2) with the water and the hydrazine groups of the two DTCZ, composed of O1-H1a \cdots O2 (D \cdots A distance, D-H \cdots A angle; 2.72 Å, 166.66°), N3-H3b \cdots O3 (2.94 Å, 166.83°), O1-H1b \cdots O3 (2.77 Å, 175.04°), N1-H1d \cdots O5 (2.78 Å, 137.30°), N3-H3a \cdots O4 (2.72 Å, 145.96°), N1-H1c \cdots O4 (2.78 Å, 165.79°). The displacement of Cu1 from the N1 - S1 - Cl1 - Cl2 mean plane is 0.206 Å. Whereas in **3a** the sulphate anion is part of the inner coordination sphere seizing the fifth apical position of

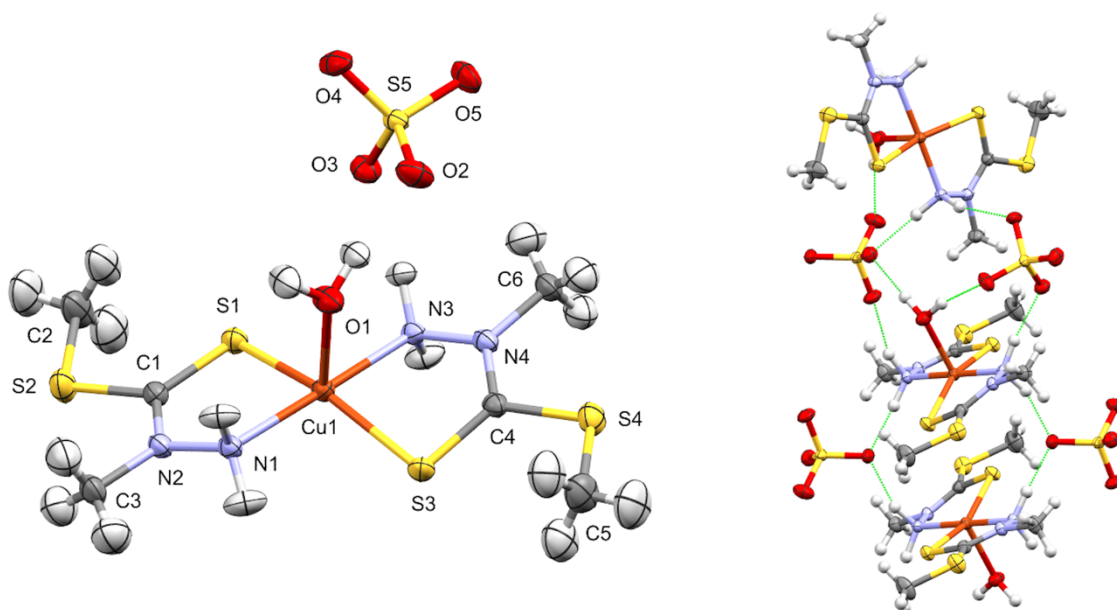


Figure 2: Crystal structure of complex **3**. Thermal ellipsoids drawn at 30% probability. The hydrogen bonding network is also depicted on the right.

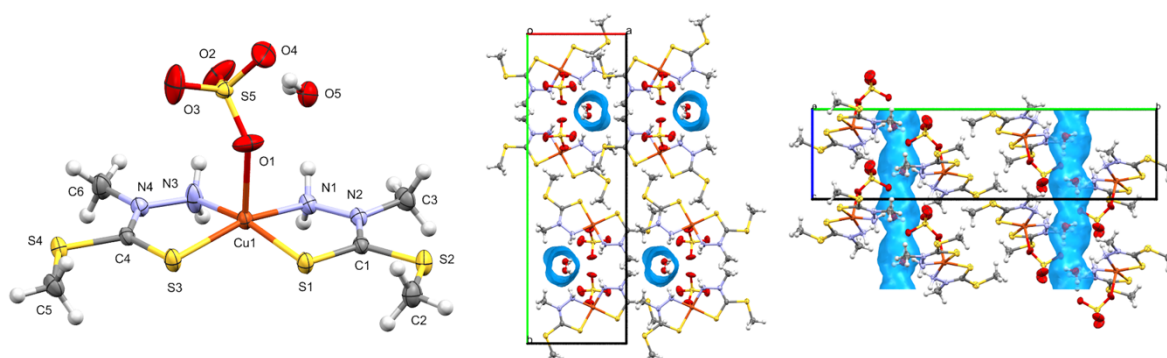


Figure 3: Crystal structure of complex **3a**. Thermal ellipsoids drawn at 30% probability. Water channels in the crystal state viewed along the *c* and *a* axis are also depicted on the right.

a distorted square pyramid; here, the two DTCZ ligands are bound to the metal centre in reciprocal *cis* position. The Cu1 – O1 bond length is significantly longer than other contacts (see Table 3) and it is comparable with typical sulphate coordination to the metal in the apical position⁸⁶. Notably, for DTCZ ligands in *cis* and *trans* reciprocal arrangements, there is no significant difference in bond lengths and angles. In contrast with complex **3**, the base of the square pyramid is more regular, since angles S1 – Cu1 – N3 and S3 – Cu1 – N1 are similar, measuring 165.5(2)° and 162.9(1)° respectively. Values are below 180° as the Cu(II) central atom is above the N1 – S1 – S3 – N3 mean plane by 0.293 Å, towards O1. A solvation water molecule is present and involved in an extensive hydrogen bonding network, like in complex **3**, with the sulphate and the hydrazine groups of the two DTCZ units. The network is composed of N1-H1b...O5 (2.85 Å, 175.76°), O5-H5d...O2 (2.79 Å, 148.70°), O5-H5e...O4 (2.88 Å, 159.83°), N1-H1a...O4 (2.74 Å, 164.14°). Interestingly, N3 and its hydrogen atoms H3a and H3b do not take part in this hydrogen bonding network. In the crystal state, water channels run along the *c* axis (Figure 3).

In complex **4b** the two DTCZ ligands are *cis* positioned as in complex **3a**, but the geometry is square planar. Above the planar complex there is one hexafluorophosphate anion, with F5 – Cu1 distance equal to 2.596(3)

Å, which is also close to the metal centre of a nearby complex ($F4' - Cu1$ is equal to $2.796(3)$ Å). It is tempting to say that less than 2.60 Å are enough to support the hypothesis of a $Cu-PF_6$ bond, also considering that in the literature similar distances have been addressed as such^{87,88}. However, in this case, the hexafluorophosphate anion seems to be mainly kept in place by three hydrogen bonds in the crystal state, with additional weak interactions with the copper centres above and below (Figure 4). We therefore suggest that the true nature of **4b** is that of a divalent square planar cation. One hydroxide is present as a counterion. $N1 - Cu1 - S3$ and $N3 - Cu1 - S1$ angles measure $174.0(1)^\circ$ and $174.3(1)^\circ$ respectively. The hydrogen bonding network between the hydroxide, the hydrazine groups and hexafluorophosphate anion is composed of $O1-H1 \cdots F1$ (2.68 Å, 166.25°), $N3-H3a \cdots F2$ (2.74 Å, 143.91°), $N3-H3b \cdots F6$ (2.89 Å, 169.89°), $N1-H1a \cdots O1$ (2.84 Å, 170.39°), $N1-H1b \cdots F1$ (2.86 Å, 175.34°). $Cu1$ atom is coplanar with the $N1 - S1 - Cl1 - Cl2$ mean plane (0.003 Å displacement). During the refinement of the crystal structure of **4b**, an effort was made to discriminate between the presence of an OH^- group and a water molecule. Fourier difference maps were not helpful for this purpose, and in fact the R values did not change significantly in the cases of OH^- or H_2O . However, the negative charge of the OH^- is necessary for the electrostatic balance in the asymmetric unit. Also, assuming that there was a water molecule instead of a hydroxide ion, one of the two hydrogen atoms would not have been involved in any hydrogen bond. For these reasons, hydroxide was preferred. However, its existence in the crystal state is still not well understood.

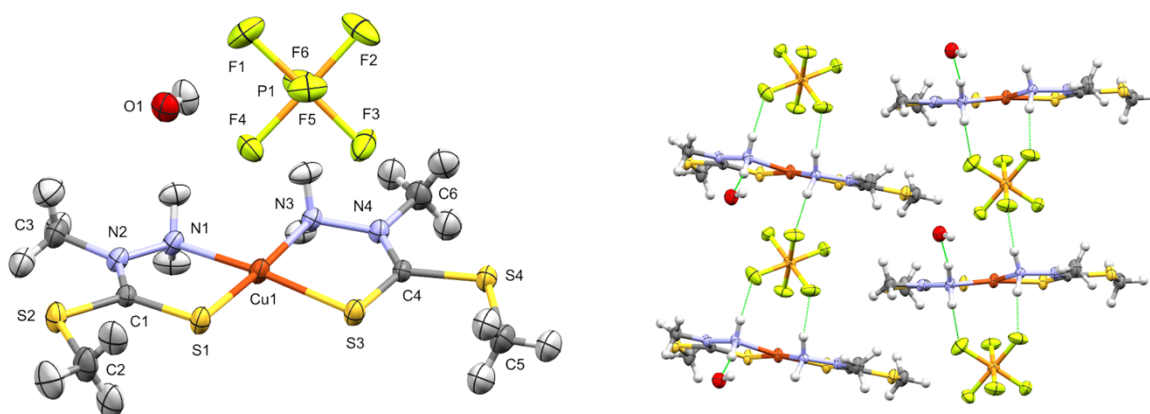


Figure 4: Crystal structure of complex **4b**. Thermal ellipsoids drawn at 30% probability. The hydrogen bonding network is also depicted on the right.

Crystal structures of copper(I) complexes

In $Cu(I)$ complex salts **4** and **6** (the hexafluorophosphate and bromide salts of the same $[Cu(DTCZ)_2]^+$ cation), the coordination sphere around copper is again defined by two sulphur atoms and two nitrogen atoms from two N,S -bidentate DTCZ ligands, resulting in a distorted tetrahedral geometry. In complex **4**, the asymmetric unit is given by half a molecule, with the copper atom sitting on a 2-fold symmetry axis. The sulphur atoms $S1$ and $S1'$ repel each other more than $N1$ and $N1'$ do, since $S1 - Cu1 - S1'$ and $N1 - Cu1 - N1'$ angles are respectively 135.07° and 109.18° . $N1-H1a \cdots F3$ (3.15 Å, 167.94°) is a hydrogen-bond interaction (Figure 5). Geometrical parameters for complex **6** slightly differ from those of complex **4** ($S1 - Cu1 - S3$ and $N1 - Cu1 - N3$ angles are respectively $124.4(1)^\circ$ and $114.4(4)^\circ$). In the crystal structure of complex **6** a solvated water molecule, the bromide and the hydrazine groups form a hydrogen bonding network composed of $N1-H1a \cdots Br1$ (3.35 Å, 146.98°), $O1-H1d \cdots Br1$ (3.41 Å, 178.15°), $O1-H1c \cdots O1'$ (2.78 Å, 161.99°), $N3-H3a \cdots Br1$ (3.32

Å, 148.51°), resulting in the formation of water channels in the crystal state along the b axis, like in complex **3a**. Also, in the crystal hydrogen-bonded water molecules and bromide ions are aligned into planes running along the crystallographic b axis (Figure 6).

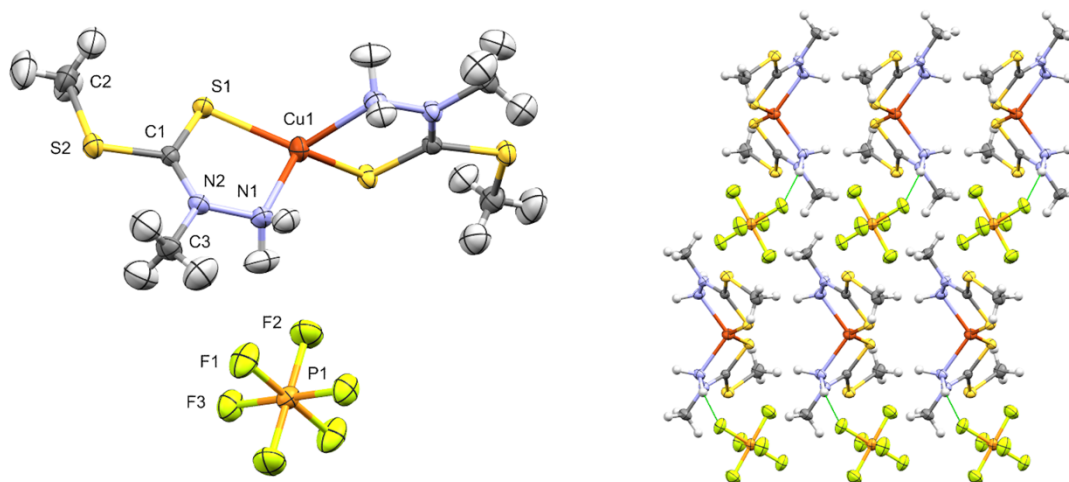


Figure 5: Crystal structure of complex **4**. Thermal ellipsoids drawn at 30% probability. The hydrogen bonding network is also depicted on the right.

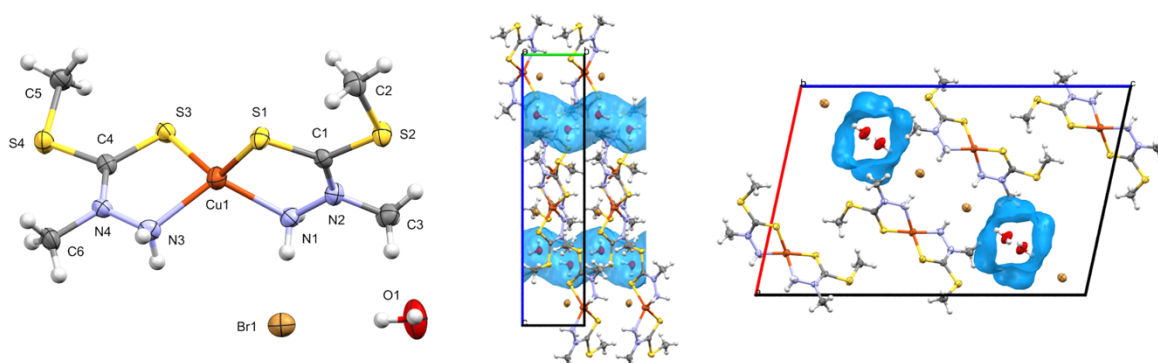


Figure 6: Crystal structure of complex **6**. Thermal ellipsoids drawn at 30% probability. Water channels in the crystal state viewed along the a and b axis are also depicted on the right.

In complex **5**, the coordination sphere around the Cu(I) centre is defined by two phosphorus atoms from two triphenylphosphine groups, a sulphur atom and a nitrogen atom from the DTCZ ligand resulting in a distorted tetrahedral geometry; a nitrate is present as a counterion. The nitrate, a solvated water molecule and the NH₂ hydrazinic group of DTCZ interact closely, and they also pair with a second nitrate, water and hydrazine group of a nearby molecule (Figure 7). The hydrogen bonding network is composed of N1-H1b...O1 (2.94 Å, 165.39°), O1-H1c...O3 (2.84 Å, 156.66°), N1-H1a...O2 (2.96 Å, 156.50°). As presented in Table 4, N1 – Cu1 – S1 bite angle is significantly lower than that of the other complexes due to the steric effect of the bulky triphenylphosphine ligands, and Cu – S bond length is significantly longer as well.

From the solvent evaporation of an acetonitrile solution of complex **6**, dark yellow crystals of **6a** were also found. The XRD analysis revealed a polymeric tetrahedral complex of copper(I). The polymer is a one-dimensional chain of tetrahedral units, made by μ -bridging bromides and μ -bridging sulphur atoms of two

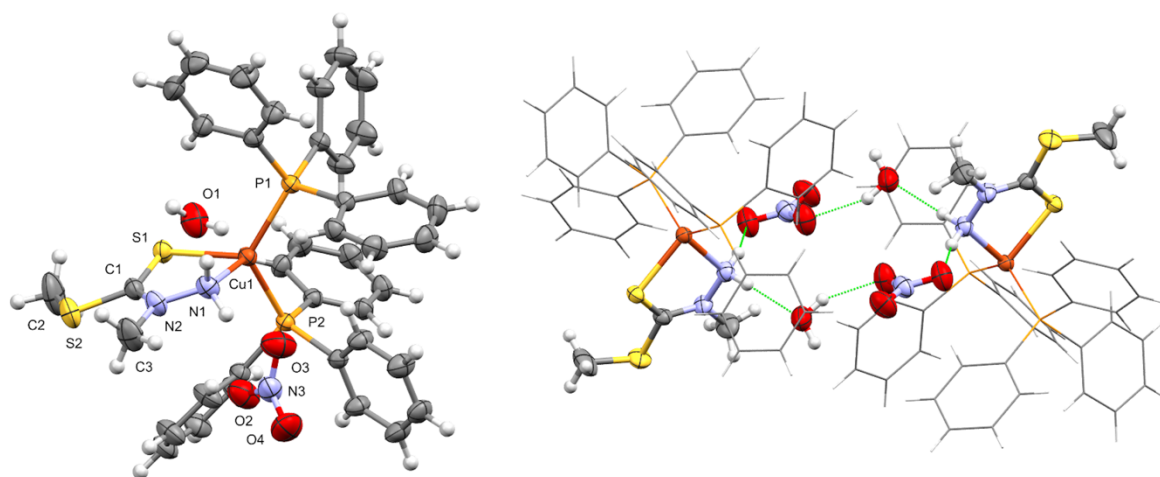


Figure 7: Crystal structure of complex **5**. Thermal ellipsoids drawn at 30% probability. The hydrogen bonding network is also depicted on the right. Triphenylphosphine groups have been drawn as sticks for clarity.

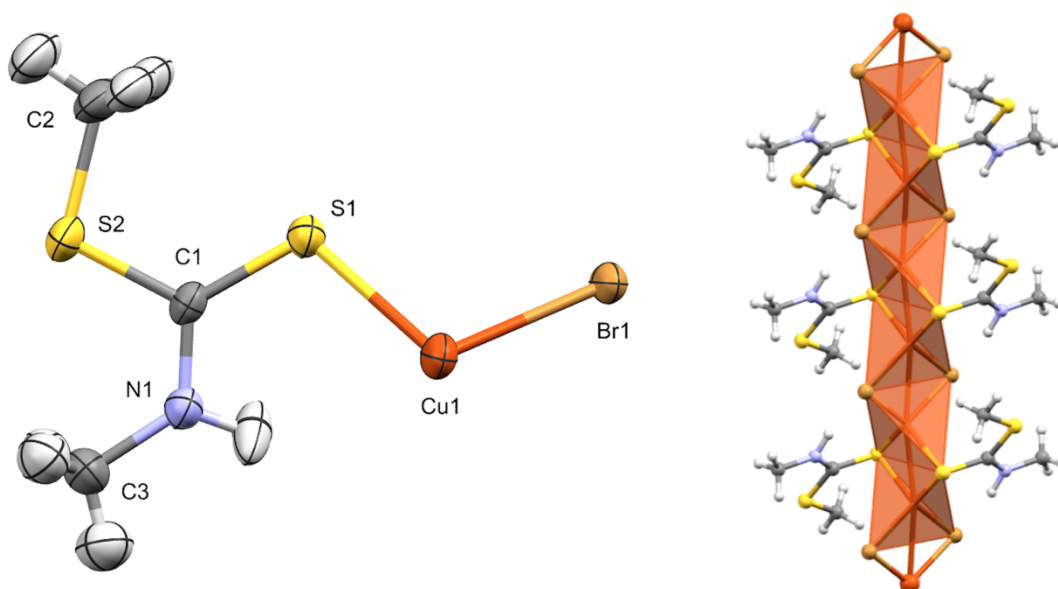


Figure 8: Crystal structure of complex **6a**. Thermal ellipsoids drawn at 30% probability. The polymeric chain in the solid state, emphasizing tetrahedral units, is also depicted on the right.

ligand molecules, expanding along the crystallographic axis (Figure 8). In this compound, the DTCZ ligand has lost the hydrazinic NH_2 group and it has transformed into a secondary amine, losing the ability to act as a bidentate ligand. The S1 atom bridges asymmetrically two copper(I) atoms ($\text{S1} - \text{Cu1}$ bond length is $2.295(1)$ Å while $\text{S1} - \text{Cu1}'$ is $2.465(1)$ Å), which are $2.850(1)$ Å away from each other. Two bromides connect two copper(I) atoms with $\text{Cu1} - \text{Br1}$ and $\text{Br1} - \text{Cu1}'$ distances equal to $2.4732(8)$ Å and $2.4769(8)$ Å, respectively; $\text{S1} - \text{Cu1} - \text{S1}' - \text{Cu1}'$ and $\text{Br1} - \text{Cu1} - \text{Br1}' - \text{Cu1}'$ mean planes are almost perpendicular, as they form an 84.22° dihedral angle. $\text{Br1}' \cdots \text{H1}$ (3.45 Å, 156.72°) is a hydrogen bond interaction. We suggest that **6a** could be a side product formed during the reaction. Its presence as an impurity in complex **6** after the work-up is probably the reason why a recrystallization step was needed to obtain sufficient purity. This might also explain the lower yield compared to the other complexes.

Conclusions

N-methyl-S-methyl dithiocarbamate (DTCZ) proved to be a versatile bidentate ligand to afford the preparation of copper(II) and copper(I) complexes. By using different starting copper sources, we were able to synthesize and solve the structures of a range of compounds with different stoichiometries, coordination geometries, and oxidation states of the metal centre. The ability to chelate copper in both of its most common redox states makes these compounds interesting for their possible use in catalysis, in the development of new metal-based drugs and for nuclear medicine applications.

Conflicts of interest

There are no conflicts to declare.

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