Nazzatush Shimar Jamaludin, Siti Nadiah Abdul Halim, Chai-Hoon Khoo, Bao-Jing Chen, Tian-Hong See, Jiun-Horng Sim, Yoke-Kqueen Cheah*, Hoi-Ling Seng and Edward R.T. Tiekink*

**Bis(phosphane)copper(I) and silver(I) dithiocarbamates: crystallography and anti-microbial assay**

DOI 10.1515/zkri-2016-0003
Received November 25, 2015; accepted March 21, 2016; published online April 26, 2016

**Abstract:** The crystal and molecular structures of (Ph₃P)₂M[S₂CN(Me)CH₂CH₂OH], M = Cu, isolated as a 1:1 dichloromethane solvate (1·CH₂Cl₂), and M = Ag (4) show the central metal atom to be coordinated by a symmetrically (1·CH₂Cl₂) and asymmetrically chelating (4) dithiocarbamate ligand. The distorted tetrahedral geometries are completed by two PPh₃ ligands. The presence of hydroxyl-O–H···S(dithiocarbamate) hydrogen bonds leads to centrosymmetric dimeric aggregates in each crystal structure. In the molecular packing of 1·CH₂Cl₂, channels comprising 1 are formed via aryl-C–H···O interactions with the solvent molecules associated with the walls of the channels via methylene-C–H···S, π(aryl) interactions. For 4, the dimeric aggregates are connected via a network of aryl-C–H···π(aryl) interactions. Preliminary screening for anti-microbial activity was conducted. The compounds were only potent against Gram-positive bacteria. Some further selectivity in activity was noted. Most notably, all compounds were active against methicillin resistant *Staphylococcus aureus*.

**Keywords:** copper(I); crystal structure analysis; dithiocarbamate; silver(I); X-ray diffraction.

**Introduction**

In response to increasing bacterial resistance, perhaps over-prescription of antibiotics, certainly wide-use and incorrect disposal, and emerging new infections, the once effective anti-microbial drugs are becoming less efficacious posing great challenges in human health [1–4]. In a very recent *Nature* Editorial on the subject, copper and silver were specifically mentioned as providing hope in developing new and effective anti-microbial agents [5]. With the above in mind, it is not surprising that both copper and silver, as nanoparticles and incorporated in molecules, have attracted considerable attention of those developing metal-based therapeutics as summarised in a number of recent reviews [6–10].

The utility of a full range of transition metal and main group element dithiocarbamates as potential metal-based drugs has been reviewed recently [11]. Prominent amongst these are gold dithiocarbamates, including phosphane gold(I) dithiocarbamates. The exploration of the potential anti-cancer activity of phosphane gold(I) dithiocarbamates dates back over a decade [12] and studies on related compounds continue [13–15]. Recently, phosphanegold(I) dithiocarbamates, functionalised with ethylhydroxy groups, proved to be very effective against breast cancer MCF-7R cell lines and to induce cell death (apoptosis or necrosis) via both extrinsic and intrinsic pathways [16]. The same dithiocarbamate ligands when complexed to bismuth(III) [17] and zinc(II) [18] also provide cytotoxic compounds. Over and above displaying interesting cytotoxicity profiles, phosphanegold(I) dithiocarbamates also display potential as anti-microbial agents; see [19] for a recent review on the utility of gold compounds in this context. Interestingly, for these R₃PAu[S₂CN(iPr)CH₂CH₂OH] compounds, activity was found to be dependent on the
nature of the phosphine-bound R substituent. Thus, when R = Ph and Cy, specific activity against Gram-positive bacteria was observed but, when R = Et, broad range activity against both Gram-positive and Gram-negative activity was noted. Further, the latter compound proved to be very effective, at least in the chosen in vitro models, against methicillin resistant Staphylococcus aureus (MRSA) [20]. A further differential was observed in that R = Ph and Cy compounds were uniformly bactericidal against susceptible bacterial strains, whereas the R = Et derivative was variously bactericidal and bacteriostatic.

Given the foregoing, namely the pharmaceutical interest in copper(I) and silver(I) compounds, and the potential of metal dithiocarbamate compounds in tackling bacteria, it was thought of interest to explore the utility of phosphine copper and silver compounds of dithiocarbamates functionalised with ethylhydroxy substituents in this context. Herein, the synthesis, characterisation, including two crystal structure determinations, and results of preliminary anti-bacterial screening for a series of six compounds of the general formula, \( (\text{Ph}_3\text{P})_2\text{Cu}[\text{S}_2\text{CN}(\text{R})\text{CH}_2\text{CH}_2\text{OH}] \), Figure 1, are reported.

### Experimental

#### Instrumentation

Elemental analyses were performed on a Perkin Elmer PE 2400 CHN Elemental Analyser. \( ^1\text{H} \) and \( ^{13}\text{C}\{^1\text{H}\} \) NMR spectra were recorded in \( d_6 \)-DMSO solution on a Bruker Avance 400 MHz NMR spectrometer with chemical shifts relative to tetramethylsilane as the internal reference. IR spectra were measured using an Attenuated Total Reflectance (ATR) on a Perkin Elmer Spectrum 2000 spectrophotometer in the region 400–4000 cm\(^{-1}\).

![Chemical structures of the copper(I) and silver(I) compounds investigated herein.](image)

**Fig. 1:** Chemical structures of the copper(I) and silver(I) compounds investigated herein.

#### Synthesis and Characterisation

**[(Ph₃P)₂Cu(S₂CN(Me)CH₂CH₂OH)] (1):** A modified procedure from the literature [21] was employed. Thus, CuCl (Aldrich, 1 mmol; 0.099 g) was stirred with triphenylphosphine (Aldrich, 2 mmol) in acetone (20 mL) at 323 K until a white precipitate was obtained. Then, an aqueous solution of K[S₃CN(Me)CH₂CH₂OH] [16] (1 mmol) was added to the reaction mixture followed by stirring for 1 h. The product underwent solvent extraction with chloroform:water (1:3), filtered and dried at room temperature. The precipitate was then washed in diethyl ether under vigorous stirring and filtered. Recrystallisation was performed in acetone via quick evaporation at ambient temperature to yield a white solid. Crystals were then obtained from the same solvent by slow evaporation. M. pt: 428 K. Yield: 0.58 g; 78%. Elemental analyses (%): Found C, 64.99; H, 5.04; N; 1.78. C₄₀H₃₈CuNOP₂S₂ requires: C, 64.98; H, 5.32; N, 1.89. IR (cm\(^{-1}\)): v(O–H) 3353 (m); v(C–N) 1432 (m); v(C–S)\(_{as}\) 1092 (m, sh); v(C–S)\(_{sym}\) 993 (m). \( ^{13}\text{C}\{^1\text{H}\} \) NMR: 208.7 (S₂C); 128.3–134.0 (aryl-C); 61.1 (OCH₂); 56.7 (NCH₂); 31.1 (CH₃) ppm. \( ^{31}\text{P}\{^1\text{H}\} \): –1.78 ppm.

**[(Ph₃P)₂Ag(S₂CN(Me)CH₂CH₂OH)] (4):** Synthesis and crystallisation was as for 1 but using Na[S₃CN(Me)CH₂CH₂OH] [16] as the dithiocarbamate ligand. M. pt: 448 K. Yield: 0.54 g; 70%. Elemental analyses (%): Found C, 65.73; H, 5.65; N, 1.83. IR (cm\(^{-1}\)): v(O–H) 3467 (m); v(C–N) 1432 (m); v(C–S)\(_{as}\) 1092 (m, sh); v(C–S)\(_{sym}\) 993 (m). \( ^3\text{C}\{^1\text{H}\} \) NMR: 209.8 (S,C); 128.3–134.5 (aryl-C); 63.4 (OCH₂); 52.1 (NCH₂); 48.8 (CH₂); 20.3 (CH₃) ppm. \( ^{31}\text{P}\{^1\text{H}\} \): –1.03 ppm.

**[(Ph₃P)₂Cu(S₂CN(CH₂CH₂OH)] (2):** Synthesis and crystallisation was as for 1 but using K[S₃CN(Ph)CH₂CH₂OH] [16] as the dithiocarbamate ligand. M. pt: 412 K. Yield: 0.58 g; 75%. Elemental analyses (%): Found C, 64.99; H, 5.04; N, 1.78. C₄₀H₃₈CuNOP₂S₂ requires: C, 64.98; H, 5.32; N, 1.89. IR (cm\(^{-1}\)): v(O–H) 3353 (m); v(C–N) 1432 (m); v(C–S)\(_{as}\) 1092 (m, sh); v(C–S)\(_{sym}\) 993 (m). \( ^{13}\text{C}\{^1\text{H}\} \) NMR: 208.7 (S,C); 128.3–134.5 (aryl-C); 58.7 (OCH₂); 56.0 (NCH₂) ppm. \( ^{31}\text{P}\{^1\text{H}\} \): –1.03 ppm.

**[(Ph₃P)₂Ag(S₂CN(CH₂CH₂OH)] (5):** Synthesis and crystallisation was as for 1 but using K[S₃CN(Ph)CH₂CH₂OH] [16] as the dithiocarbamate ligand. M. pt: 444 K. Yield: 0.58 g; 76%. Elemental analyses (%): Found C, 64.99; H, 5.04; N, 1.78. C₄₀H₃₈CuNOP₂S₂ requires: C, 64.98; H, 5.32; N, 1.89. IR (cm\(^{-1}\)): v(O–H) 3360 (br); v(C–N) 1432 (m, sh); v(C–S)\(_{as}\) 1094 (m, sh); v(C–S)\(_{sym}\) 983 (m). \( ^3\text{C}\{^1\text{H}\} \) NMR: 208.0 (S,C); 127.3–135.0 (aryl-C); 60.1 (OCH₂); 54.7 (NCH₂); 29.1 (CH₃) ppm. \( ^{31}\text{P}\{^1\text{H}\} \): 4.43 ppm.

**[(Ph₃P)₂Ag(S₂CN(iPr)CH₂CH₂OH)] (3):** Synthesis and crystallisation was as for 1 but using K[S₃CN(iPr)CH₂CH₂OH] [16] as the dithiocarbamate ligand. M. pt: 444 K. Yield: 0.58 g; 76%. Elemental analyses (%): Found C, 64.99; H, 5.04; N, 1.78. C₄₀H₃₈CuNOP₂S₂ requires: C, 64.98; H, 5.32; N, 1.89. IR (cm\(^{-1}\)): v(O–H) 3467 (m); v(C–N) 1432 (m, sh); v(C–S)\(_{as}\) 1094 (m, sh); v(C–S)\(_{sym}\) 983 (m). \( ^3\text{C}\{^1\text{H}\} \) NMR: 208.7 (S,C); 128.9–134.5 (aryl-C); 63.4 (OCH₂); 52.1 (NCH₂); 48.8 (CH₂); 20.3 (CH₃) ppm. \( ^{31}\text{P}\{^1\text{H}\} \): –1.78 ppm.

**[(Ph₃P)₂Ag(S₂CN(Ph)CH₂CH₂OH)] (6):** A modified literature method [22] was employed whereby AgNO₃ (Fluka, 1 mmol; 0.14 g) was stirred with triphenylphosphine (Aldrich, 2 mmol) in acetone (20 mL) at 323 K until a white precipitate was obtained. Then, an aqueous solution of K[S₃CN(Ph)CH₂CH₂OH] [16] (1 mmol) was added to the reaction mixture which was stirred for 1 h. Chloroform was added and stirring was continued for another 1 h, after which the yellow chloroform solution was separated from the aqueous layer. After drying over anhydrous sodium sulphate, the solution was filtered and quickly evaporated to yield a white solid. The solid was washed with diethyl ether and was isolated through filtration. Recrystallisation was performed in acetone via slow evaporation at room temperature until a suspension was obtained. The precipitate was then washed in diethyl ether under vigorous stirring and filtered. Recrystallisation was performed in acetone via slow evaporation, yielding colourless blocks. M. pt: 444 K. Yield: 0.57 g; 76%. Elemental analyses (%): Found C, 62.13; H, 4.95; N, 1.73. C₄₀H₃₈CuNOP₂S₂ requires: C,
62.14; H, 5.34; N, 1.73. IR (cm⁻¹): ν(O–H) 3384 (br); ν(C–N) 1434 (m); ν(C–S) 1092 (m, sh); ν(C–S) 971 (w). ¹³C{¹H} NMR: 211.2 (S, C); 128.3–134.2 (aryl-C); 63.1 (OCH₂); 54.8 (NCH₂); 49.5 (CH); 20.3 (CH₃) ppm. ³¹P{¹H}: 5.80 ppm.

[(Ph₅P)₂Ag(S₂CN(CH₂CH₂OH)₂)] (6): Synthesis and crystallisation was as for 4 but using K[S₂CN(CH₂CH₂OH)₂] [16]. The crystals were obtained from a chloroform:acetone (1:1 v/v) mixture by slow evaporation. M. pt: 435 K. Yield: 0.63 g; 77%. Elemental analyses (%): Found C, 60.34; H, 5.00; N, 1.44. C₄₀H₃₈CuNOP₂S₂ requires: C, 60.52; H, 5.08; N, 1.72. IR (cm⁻¹): ν(O–H) 3322 (br); ν(C–N) 1434 (m, sh); ν(C–S) 1094 (m, sh); ν(C–S) 983 (w). ¹³C{¹H} NMR: 211.0 (S₂C); 128.7–133.9 (aryl-C); 60.0 (OCH₂); 58.8 (NCH₂) ppm. ³¹P{¹H}: 5.80 ppm.

Crystal structure determination

Crystals suitable for crystallography of 1 were grown by the slow evaporation of its dichloromethane solution and were characterised crystallographically as the 2:1 dichloromethane solvate. Crystals of 4 were grown by slow evaporation of its acetone solution. Intensity data for 1 and 4 were measured at 100 K on a Bruker SMART APEX-II CCD diffractometer with graphite-monochromatised MoKα radiation (λ = 0.71073 Å). Data processing was with APEX2 and SAINT [23] and the absorption correction was conducted with SADABS [24]. Details of unit cell data, X-ray data collection and structure refinement are given in Table 1. The structures were solved by direct methods [25]. Full-matrix least-squares refinement on F² with anisotropic displacement parameters for all non-hydrogen atoms was performed with SHELXL-2014/7 [26]. The C-bound H atoms were placed on geometric considerations. This gives rise to a PLATON [27] alert owing to poor agreement, a number of reflections, i.e. (0 1 0; 0 1 0; 0 1 0) and (9 –15 6), were omitted from the final cycles of refinement. σ² = wF² – (F²) (where w = 1/[σ²(F²)]) was introduced in each case. The final difference maps were featureless. The programmes WinGX [28], ORTEP-3 for Windows [28] (at the 70% probability level) and DIAMOND [29] were also used in the study.

Evaluation of in vitro anti-microbial activity

Microorganisms: The bacteria tested in this study were Aeromonas hydrophilla (A. hydrophilla) ATCC35654, Acinetobacter baumannii (A. baumannii) ATCC 19606, Bacillus cereus (B. cereus) ATCC 10876, Bacillus subtilis (B. subtilis) ATCC 6633, Citrobacter freundii (C. freundii) ATCC 8090, Enterobacter cloacae (E. cloacae) ATCC 35030, Enterobacter aerogenes (E. aerogenes) ATCC 13048, Enterococcus faecalis (E. faecalis) ATCC 29212, Enterococcus faecium (E. faecium) ATCC 19434, Escherichia coli (E. coli) ATCC 25922, Klebsiella pneumoniae (K. pneumoniae) ATCC 700603, Listeria monocytogenes (L. monocytogenes) ATCC 19117, Proteus mirabilis (P. mirabilis) ATCC25933, Proteus vulgaris (P. vulgaris) ATCC 13315, Pseudomonas aeruginosa (P. aeruginosa) ATCC27853, Salmonella paratyphi A (S. paratyphi) ATCC 9150, Salmonella typhimurium (S. typhimurium) ATCC 14028, Shigella flexneri (S. flexneri) ATCC 12022, Shigella sonnei (S. sonnei) ATCC 2920, Staphylococcus aureus (S. aureus) ATCC25923, methicillin resistant Staphylococcus aureus (MRSA) ATCC 43300, Staphylococcus saprophyticus (S. saprophyticus) ATCC 15305, Stenotrophomonas maltophilia (S. maltophilia) ATCC 13637 and Vibrio para-haemolyticus.

Tab. 1: Crystallographic data and refinement details for 1·CH₂Cl₂ and 4.*

<table>
<thead>
<tr>
<th>Compound</th>
<th>Formula</th>
<th>C₄₀H₃₈CuNOP₂S₂</th>
<th>C₄₀H₃₈AgNOP₂S₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula weight</td>
<td>823.24</td>
<td>782.64</td>
<td></td>
</tr>
<tr>
<td>Colour, habit</td>
<td>Colourless, prism</td>
<td>Colourless, prism</td>
<td></td>
</tr>
<tr>
<td>Dimensions/mm</td>
<td>0.07 x 0.07 x 0.12</td>
<td>0.18 x 0.20 x 0.30</td>
<td></td>
</tr>
<tr>
<td>Space group</td>
<td>P1</td>
<td>P2₁/c</td>
<td></td>
</tr>
<tr>
<td>µ(MoKα)/mm⁻¹</td>
<td>1.417</td>
<td>1.480</td>
<td></td>
</tr>
<tr>
<td>µ(Kα)/cm⁻¹</td>
<td>852</td>
<td>1608</td>
<td></td>
</tr>
<tr>
<td>Data completeness</td>
<td>1.00</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Rₓ</td>
<td>0.050</td>
<td>0.091</td>
<td></td>
</tr>
<tr>
<td>Data range/°</td>
<td>1.9–27.5</td>
<td>1.5–27.5</td>
<td></td>
</tr>
<tr>
<td>Unique data</td>
<td>8815</td>
<td>8057</td>
<td></td>
</tr>
<tr>
<td>Observed data</td>
<td>6370</td>
<td>5779</td>
<td></td>
</tr>
<tr>
<td>Rₓ</td>
<td>0.098; 0.072</td>
<td>0.044; 0.072</td>
<td></td>
</tr>
<tr>
<td>a in weighting scheme</td>
<td>0.049</td>
<td>0.029</td>
<td></td>
</tr>
<tr>
<td>GoF</td>
<td>1.03</td>
<td>1.01</td>
<td></td>
</tr>
<tr>
<td>Rₓ.obs. data</td>
<td>0.108; 0.122</td>
<td>0.081; 0.092</td>
<td></td>
</tr>
</tbody>
</table>

*Supplementary Material: Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications no. CCDC-1437530 and 1437530. Copies of available material can be obtained free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk). The list of Fo/Fc-data is available from the corresponding author (ERTT) up to one year after the publication has appeared.
(V. parahaemolyticus) ATCC17802. All bacterial cultures were purchased from American Type Culture Collection (ATCC).

Screening of anti-bacterial activity: Anti-bacterial screening was performed using the Kirby-Bauer disc diffusion method in accordance with the National Committee for Clinical Laboratory Standards (NCCLS) guideline. The inoculum suspension of each bacterial strain was adjusted to 0.5 McFarland standard turbidity (corresponds to approximately 10⁸ CFU/mL) by adding Mueller-Hinton broth (Difco, USA). Then, this suspension was swabbed on the surface of Mueller-Hinton agar (MHA; Difco, USA) plates. The tested compounds were dissolved in DMSO to a test concentration of 10 mg/mL. Sterile 6 mm filter paper discs were aseptically placed on Mueller-Hinton agar surfaces and 5 μL of each of the dissolved compounds was immediately added to the discs. Each plate contained one standard antibiotic paper disc which served as the positive control, one disc served as negative control (5 μL broth) and one disc served as solvent control (5 μL DMSO). The plates were incubated at 37 °C for 24 h. The antibacterial activity was evaluated by measuring the diameter of inhibition zone against the test bacterial strains. Each trial was performed in duplicate.

Results and discussion

Synthesis and characterisation

Compounds 1–6 were obtained in good yields from the facile metathetical reaction between the respective copper(I) or silver(I) salt with an alkali metal salt of the dithiocarbamate anion. Characteristic absorption bands due to ν(C–N) and ν(C–S) of the dithiocarbamate ligands were observed in their IR spectra. The 13C{1H} NMR showed the expected resonances due to the phosphane and dithiocarbamate ligands. Finally, the 31P{1H} NMR showed singlets a few ppm downfield for the copper(I) compounds, and upfield for the silver(I) compounds. The appearance of singlets is consistent with rapid exchange of the phosphane ligands in solution [30]. Full structure determination for two species, namely 1·CH₂Cl₂ and 4 were afforded by X-ray crystallography.

Crystal and molecular structure of 1·CH₂Cl₂

The molecular structures in 1·CH₂Cl₂ are shown in Figure 2 and selected geometric parameters are collected in Table 2. The copper(I) atom is chelated by the dithiocarbamate ligand and the tetra-coordinate geometry is completed by two triphenylphosphane (Ph₃P) ligands. The dithiocarbamate is chelating in the symmetric mode with Cu–S₁, S₂ being experimentally equivalent at 2.4171(9) and 2.4190(8), respectively; the symmetric Cu–S bond lengths are also reflected in the experimental equivalence of the associated Cl–S₁, S₂ bond lengths of 1.719(3) and 1.727(3), respectively. There are significant deviations from the ideal tetrahedral angle of 109.5°, most notably in the acute chelate angle of 75.03(3)° and the wide angle subtended by the bulky Ph₃P ligands of 124.09(3)°. While the S₁–Cu–P₁, P₂ angles of 112.88(3) and 109.50(3)° are close to each other and to the ideal tetrahedral values, the S₂–Cu–P₁, P₂ angles, i.e. 125.64(3) and 99.13(3)°, differ from each other by over 25°. Based on the value calculated for τ₄, a four-coordinate geometry index [31], i.e. 0.78 cf. 1 for an ideal tetrahedron, the coordination geometry is best described as distorted tetrahedral.

The molecular structure of 1 in 1·CH₂Cl₂ complements a number of literature precedents [32–36] for which geometric data are collated in Table 2. Noteworthy, is the structure of [(Ph₃P)₂Cu{S₂CN(CH₂CH₂OH)₂}], as its triphenylphosphane lattice adduct, which corresponds to 3 in the present report. All structures are relatively homogeneous in that all adopt the distorted tetrahedral geometry, as in 1·CH₂Cl₂, with a symmetric mode of coordination of the dithiocarbamate ligand, and a wide angle subtended by the phosphane ligands. However, non-systematic variations in other angles subtended at the copper(I) centre are evident, Table 2.

The most prominent supramolecular aggregation in the crystal structure of 1·CH₂Cl₂ is based on hydroxyl-O–H···S(dithiocarbamate) hydrogen bonding which leads to a centrosymmetric dimer, Figure 3a; geometric data characterising supramolecular interactions for both 1·CH₂Cl₂ and 4 are listed in Table 3. Globally, dimeric aggregates...
Tab. 2: Selected geometric parameters (Å, °) for 1·CH₂Cl₂, 4 and literature precedents.

<table>
<thead>
<tr>
<th>Structure</th>
<th>Cu–S1, S2</th>
<th>Cu–P1, P2</th>
<th>S1–Cu–S2</th>
<th>P1–Cu–P2</th>
<th>S1–Cu–P1, P2</th>
<th>S2–Cu–P1, P2</th>
<th>τₜ</th>
<th>Refs.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1·CH₂Cl₂</td>
<td>2.4171(9), 2.4190(8)</td>
<td>2.2418(8), 2.2778(9)</td>
<td>75.03(3)</td>
<td>124.09(3)</td>
<td>112.88(3), 109.50(3)</td>
<td>125.64(3), 99.13(3)</td>
<td>0.78</td>
<td>This work</td>
</tr>
<tr>
<td>[(Ph₃P)₂Cu{S₂CN(CH₂CH₂OH)}]⁺</td>
<td>2.3948(11), 2.4288(11)</td>
<td>2.2594(13), 2.2849(14)</td>
<td>74.76(4)</td>
<td>124.52(5)</td>
<td>112.35(4), 109.85(4)</td>
<td>122.04(4), 102.50(4)</td>
<td>0.81</td>
<td>[32]</td>
</tr>
<tr>
<td>[(Ph₃P)₂Cu{S₂CN(n-Pr)}]⁺</td>
<td>2.4036(17), 2.4063(14)</td>
<td>2.2516(15), 2.2764(15)</td>
<td>74.56(5)</td>
<td>124.09(6)</td>
<td>119.67(5), 106.03(6)</td>
<td>110.73(5), 111.11(5)</td>
<td>0.82</td>
<td>[33]</td>
</tr>
<tr>
<td>[(Ph₃P)₂Cu{S₂CN(CH₂CH₂)₂S}]⁺</td>
<td>2.3808(10), 2.4063(9)</td>
<td>2.2556(9), 2.2651(9)</td>
<td>75.14(3)</td>
<td>125.85(3)</td>
<td>113.89(3), 113.39(4)</td>
<td>112.20(3), 104.05(3)</td>
<td>0.85</td>
<td>[34]</td>
</tr>
<tr>
<td>[(Ph₃P)₂Cu{S₂CN(CH₂CH₂)₂NPh}]⁺</td>
<td>2.3887(12), 2.4055(10)</td>
<td>2.2700(14), 2.2347(11)</td>
<td>75.03(4)</td>
<td>119.36(4)</td>
<td>113.94(4), 115.94(4)</td>
<td>102.46(4), 121.79(4)</td>
<td>0.84</td>
<td>[34]</td>
</tr>
<tr>
<td>[(Ph₃P)₂Cu{S₂CN(Me)CH₂Ph}]⁺</td>
<td>2.3956(12), 2.4167(10)</td>
<td>2.2299(11), 2.2661(14)</td>
<td>74.77(4)</td>
<td>124.86(4)</td>
<td>113.87(4), 110.61(4)</td>
<td>126.31(4), 100.88(4)</td>
<td>0.79</td>
<td>[35]</td>
</tr>
<tr>
<td>[(Ph₃P)₂Cu{S₂CN(CH₂Ph)CH₂py-4}]⁺</td>
<td>2.3974(14), 2.4021(12)</td>
<td>2.2382(17), 2.2604(19)</td>
<td>75.30(4)</td>
<td>123.52(4)</td>
<td>125.31(3), 103.12(4)</td>
<td>112.73(6), 105.02(7)</td>
<td>0.84</td>
<td>[36]</td>
</tr>
<tr>
<td>4</td>
<td>2.5945(9), 2.7074(10)</td>
<td>2.4577(9), 2.4824(9)</td>
<td>68.18(3)</td>
<td>124.36(3)</td>
<td>118.89(3), 115.57(3)</td>
<td>109.29(3), 100.25(3)</td>
<td>0.83</td>
<td>This work</td>
</tr>
<tr>
<td>[(Ph₃P)₂Ag{S₂CN(Me)CH₂CH₂OH}]⁺</td>
<td>2.6380(9), 2.6592(9)</td>
<td>2.4173(11), 2.4964(11)</td>
<td>68.34(3)</td>
<td>122.53(3)</td>
<td>118.11(3), 108.10(3)</td>
<td>131.93(3), 95.02(3)</td>
<td>0.75</td>
<td>[30]</td>
</tr>
<tr>
<td>[(Ph₃P)₂Ag{S₂CN(n-Bu)CH₂CH₂OH}]⁺</td>
<td>2.6091(10), 2.6717(11)</td>
<td>2.4255(13), 2.4658(13)</td>
<td>68.48(3)</td>
<td>123.52(4)</td>
<td>125.31(3), 103.12(4)</td>
<td>114.54(4), 108.66(4)</td>
<td>0.79</td>
<td>[30]</td>
</tr>
<tr>
<td>[(Ph₃P)₂Ag{S₂CN(CH₂)₅}]⁺</td>
<td>2.5690(10), 2.7082(11)</td>
<td>2.4646(9), 2.4756(8)</td>
<td>68.15(3)</td>
<td>124.43(3)</td>
<td>117.86(3), 114.53(3)</td>
<td>108.11(3), 107.23(3)</td>
<td>0.84</td>
<td>[37]</td>
</tr>
</tbody>
</table>

a Crystallised as a 1:1 Ph₃P lattice adduct. b Crystallised as a 1:1 dichloromethane solvate. c Two independent molecules in the asymmetric unit. d Crystallised as a dihydrate.

The molecular structure of 4 is shown in Figure 4 and includes selected geometric parameters given in Table 2. The packing diagram shows as brown, blue and purple dashed lines, respectively. For the packing diagram, only hydrogen atoms involved in the discussed intermolecular interactions are included.

Fig. 3: Molecular packing in 1·CH₂Cl₂: (a) view of the supramolecular dimeric aggregate sustained by O–H···S hydrogen bonding (orange dashed lines), and (b) view in projection of the unit cell contents down the a-axis. The C–H···O, C–H···π(aryl) and methylene interactions are shown as brown, blue and purple dashed lines, respectively. For the packing diagram, only hydrogen atoms involved in the discussed intermolecular interactions are included.
first approximation, the molecular structure is the same as for 1 in \(1 \cdot \text{CH}_2\text{Cl}_2\) with the notable difference being that the dithiocarbamate ligand in 4 coordinates in an asymmetric mode whereby the difference between the Ag–S1, S2 bond lengths is greater than 0.10 Å. This change results in a contraction of the chelate angle subtended by the dithiocarbamate-sulphur atoms. Based on the value computed for \(\tau_4\), i.e. 0.83, the coordination geometry is less distorted from the ideal tetrahedral geometry compared with 1 in \(1 \cdot \text{CH}_2\text{Cl}_2\).

There are three literature precedents for \((\text{Ph}_3\text{P})_2\text{Ag}(\text{S}_2\text{CNR}_2)\) [30, 37], including a very recently reported structure for 4 but, as its dichloromethane solvate \(\text{4} \cdot \text{CH}_2\text{Cl}_2\) [30]; see Table 2 for salient geometric data. A comparison of the key geometric parameters for 4 and \(\text{4} \cdot \text{CH}_2\text{Cl}_2\) clearly confirms the flexibility in this class of molecule as, for example, the Ag–S bond lengths in \(\text{4} \cdot \text{CH}_2\text{Cl}_2\) differ by only 0.02 Å cf. 0.10 in 4. This is opposite to the trends in the Ag–P bond lengths for which the difference was 0.02 Å in 4 but, this expands to 0.08 Å in \(\text{4} \cdot \text{CH}_2\text{Cl}_2\). There are also considerable differences in the angles subtended at the silver(I) centre with the range being 10° greater in \(\text{4} \cdot \text{CH}_2\text{Cl}_2\). The value of \(\tau_4\) in \(\text{4} \cdot \text{CH}_2\text{Cl}_2\) is 0.75 revealing this structure to exhibit the greatest deviation from tetrahedral behaviour of all structures listed in Table 2.

Further, a comment of the isostructural relationships is appropriate. It is noted that six out of the ten structures included in Table 2 have occluded dichloromethane in their crystal structures. Indeed, for the silver(I) series, the pair of solvated compounds (P1) are isostructural as is the pair of unsolvated compounds (P2/c). The unit characteristics of three of the dichloromethane solvates in the copper(I) series are also isostructural with their silver(I) counterparts, the exceptional structure being that of \([\text{Ph}_3\text{P}]_2\text{Cu}[\text{S}_2\text{C}(\text{CN}(\text{CH}_2)_2)\text{S}]\) [33] which has monoclinic (P21/c) symmetry.

As for \(1 \cdot \text{CH}_2\text{Cl}_2\), the formation of a centrosymmetric supramolecular dimer stabilised by hydroxyl-O–H...S(dithiocarbamate) hydrogen bonding is the most conspicuous feature of the molecular packing of 4, Figure 5a and Table 3. The dimers stack in columns along the b-axis and are consolidated into the three-dimensional architecture by aryl-C–H...π(aryl) interactions, Figure 5b.

It is of interest to note that in each of \(1 \cdot \text{CH}_2\text{Cl}_2\) and 4, hydroxyl-O–H...S(dithiocarbamate) hydrogen bonding is observed rather than the what might be anticipated hydroxyl-O–H...O(hydroxyl) hydrogen bonding, as

---

**Tab. 3:** Summary of intermolecular interactions (A–H···B; Å, °) operating in the crystal structures of 1·CH2Cl2 and 4.

<table>
<thead>
<tr>
<th>A</th>
<th>H</th>
<th>B</th>
<th>A–H</th>
<th>H···B</th>
<th>A···B</th>
<th>A–H···B</th>
<th>Symmetry operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1)</td>
<td>O1</td>
<td>H1o</td>
<td>S2</td>
<td>0.84</td>
<td>2.41</td>
<td>3.207(a)</td>
<td>159</td>
</tr>
<tr>
<td></td>
<td>C12</td>
<td>H12</td>
<td>O1</td>
<td>0.95</td>
<td>2.58</td>
<td>3.270(5)</td>
<td>129</td>
</tr>
<tr>
<td></td>
<td>C54</td>
<td>H54</td>
<td>O1</td>
<td>0.95</td>
<td>2.47</td>
<td>3.409(4)</td>
<td>169</td>
</tr>
<tr>
<td></td>
<td>C5</td>
<td>H5a</td>
<td>S1</td>
<td>0.99</td>
<td>2.85</td>
<td>3.752(4)</td>
<td>152</td>
</tr>
<tr>
<td></td>
<td>C5</td>
<td>H5b</td>
<td>Cg(C61-C66)</td>
<td>0.99</td>
<td>2.73</td>
<td>3.553(4)</td>
<td>140</td>
</tr>
<tr>
<td>(4)</td>
<td>O1</td>
<td>H1o</td>
<td>S2</td>
<td>0.84(3)</td>
<td>2.55(3)</td>
<td>3.387(4)</td>
<td>174(3)</td>
</tr>
<tr>
<td></td>
<td>C25</td>
<td>H25</td>
<td>Cg(C61-C66)</td>
<td>0.95</td>
<td>2.77</td>
<td>3.635(4)</td>
<td>151</td>
</tr>
<tr>
<td></td>
<td>C34</td>
<td>H34</td>
<td>Cg(C41-C46)</td>
<td>0.95</td>
<td>2.91</td>
<td>3.554(4)</td>
<td>126</td>
</tr>
<tr>
<td></td>
<td>C45</td>
<td>H45</td>
<td>Cg(C51-C56)</td>
<td>0.95</td>
<td>2.86</td>
<td>3.425(4)</td>
<td>119</td>
</tr>
</tbody>
</table>

*aCg is the ring centroid of the specified atoms.*
hydroxyl is both a good donor and acceptor of hydrogen bonds [38, 39]. Mono-alcohols can potentially self-associate via hydroxyl-O–H···O(hydroxyl) hydrogen bonds into zero-dimensional aggregates, such as a dimer or an oligomer, and into one-dimensional supramolecular chains, as illustrated in Figure 6. Indeed, these modes of supramolecular association have been observed in the crystal structures of related dithiocarbamate species. Thus, referring to Figure 6, the dimer synthon has been found, for example, in \( \text{[Zn(S₂CN(Me)CH₂CH₂OH)₃-N(C₅H₆CH₂N(H)C(=O)C(=O)N(H)CH₂C₅H₆N-3)]ₙ} \) [40] in one of the supramolecular isomers of \( \text{[Cd(S₂CN(iPr)CH₂CH₂OH)₂·2MeCN·2H₂O]ₙ} \) [41] and in 1:2 co-crystal \( \text{[Cd(S₂CN(iPr)CH₂CH₂OH)₂·2[(3-(propan-2-yl)-1,3-oxazolidine-2-thione)]} [42] \), and cyclic tetrametric synthons in \( \text{[Ni(S₂CN(iPr)CH₂CH₂OH)]ₙ} \) [43] and in co-crystal \( \text{[Zn(S₂CN(Me)CH₂CH₂OH)₃-N(C₅H₆CH₂N(H)C(=O)N(H)CH₂C₅H₆N-3)₂S₈]} [44] \). Supramolecular chains have been observed in the structures of \( \text{[Zn(S₂CN(Et)CH₂CH₂OH)]ₙ} \) [45] and \( \text{[Zn(S₂CN(Me)CH₂CH₂OH)]ₙ} \) [18]. On the other hand supramolecular chains mediated by hydroxyl-O–H···S(dithiocarbamate) hydrogen bonding have been seen in the aforementioned \( \text{R₃PAu[S₂CN(iPr)CH₂CH₂OH]₃-Cy} \) structures [16]. Further, charge-assisted hydroxyl-O–H···S(dithiocarbamate) hydrogen bonding features prominently in a series of salts of dithiocarbamate anions bearing hydroxyethyl substituents [46]. The wide range of observed hydrogen bonding patterns in these structures perhaps provides an explanation why disorder in the hydroxyethyl residues is prevalent in these systems.

**Preliminary anti-microbial studies**

In the present study, compounds 1–6 were screened against a panel of 24 bacteria; the dithiocarbamate ligands themselves are not active. The first key observation was that none of the studied compounds exhibited any activity
against Gram-negative bacteria. By contrast, some activity was seen against Gram-positive bacteria with results tabulated in Table 4. A possible explanation for this selectivity might relate to the permeability barrier of 1–6 since the structure and properties of the cell membranes of the Gram-positive and Gram-negative bacterial cells are distinct. The outer membrane of Gram-negative bacteria is an asymmetric bilayer, with an inner leaflet comprising phospholipids and the outer leaflet comprising mainly of lipopolysaccharide. The presence of this barrier enables Gram-negative bacteria to overcome harsh environments and to exclude several antibiotics effective against Gram-positive organisms [47].

Amongst the Gram-positive bacteria screened, some selectivity toward bacteria was noted in that 1–6 were non-potent against B. cereus and E. faecium. Only silver compounds were potent against B. subtilis (4 and 6) and S. saprophyticus (6), and only compounds with two hydroxyethyl groups (3 and 6) were potent against E. faecalis and L. monocytogenes. By contrast, both copper and silver compounds were active against S. aureus (excluding 2) and S. aureus (MRSA). While some interesting selectivity is noted, none of the compounds was active as the standard anti-biotic.

A comment on the potency of related phosphane-gold(I) dithiocarbamates, R₃PAu[S₂CN(iPr)]₂(CH₂CH₂OH) [20], is apposite. Interestingly, when R = Ph and Cy in this series, selective activity was also seen against Gram-positive bacteria. This observation suggests that the Ph₃P ligand impacts upon the selectivity of metal compound. By contrast, the R = Et compound was active against both Gram-positive and Gram-negative bacteria and generally more potent than the compounds with more bulky phosphane ligands. While all three compounds were active against S. aureus (MRSA), as in the present series of 1–6, the R = Et compound was particularly potent with a MIC value of 0.98 µg/mL [20].

### References


Supplemental Material: The online version of this article (DOI: 10.1515/zkri-2016-0003) offers supplementary material, available to authorized users.