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New gold(I) and silver(I) complexes of sulfamethoxazole: Synthesis, X-ray structural characterization and microbiological activities of triphenylphosphine(sulfamethoxazolato-N2)gold(I) and (sulfamethoxazolato)silver(I)

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Abstract

Sulfamethoxazole (SMTZ) reacts with Ph_3PAuCl and AgCl in methanol/triethylamine to give $[Ph_3PAu(SMTZ_{-1H+})]$ ($SMTZ_{-1H+}$ = sulfamethoxazolato anion) (**1**) and $[Ag(SMTZ_{-1H+})]$ (**2**). While the lattice of **1** contains single molecules with linear N–Au–P bonds, compound **2** comprises a two-dimensional polymeric assembly of the deprotonated SMTZ ligand and silver ions, which are coordinated by one oxygen and three nitrogens in a distorted tetrahedral array. The microbiologic activities (Mueller–Hinton broth dilution tests) of **1** and **2** were determined in relation to free sulfamethoxazole.

Keywords: Sulfamethoxazole; Au and Ag complexes; Antimicrobial activity

It is well known that sulfonamide derivatives, through exchanges of different functional groups without modification of the structural $S(O)_2N(H)$ feature, can exhibit a wide variety of pharmacological activities, such as antidiabetic, antibacterial and antitumor [1–4]. In addition, some metal complexes of these ligands have been found to promote rapid healing of burns: the Ag(I)-sulphadiazine complex is used for human burn treatment [5,6] and the Zn(II) complex, for the prevention of bacterial infection in burned animals [7,8]. The effectiveness of these compounds does not depend solely on the slow release of Ag(I) or Zn(II), but rather depends strongly on the nature of the material to which the metal ion is bound [7].

Gold(I) complexes containing sulphur ligands have been extensively used in the medical treatment of rheumatoid arthritis [9,10]. The explosive growth of gold chemistry related to the antiarthritic activity of its compounds, in the last decade, has also shown that some gold drugs seem to be effective in the treatment of diseases such as tumors, psoriasis and AIDS [11,12]. Of particularly great chemotherapeutical potential in cancer treatment are gold(I) complexes with bidentate phosphanes [13,14] such as $[Au(dppe)_2]Cl$ (dppe = $Ph_2PC_2H_4PPh_2$, 1,2-diphenylphosphinethane). Complementing the large spectrum of medicinally active gold compounds, recently we have described [15] the synthesis and the characterization of $[\{(SDAZ)Au\}_2(\mu\text{-dppe})]$ (SDAZ = sulphadiazinide anion), further also the new sulfathiazole complexes of Au(I) and Ag(I) [(sulfathiazolato)$AuPPh_3$] and $[Ag(sulfathiazolato)]_2$ (sulfathiazole = N^1-2-thiazolyl-sulfanilamide) [16]. Given the ability of sulfonamide derivatives to coordinate to metal atoms in different manners, considerable interest in the synthesis and structural aspects of new complexes has arisen

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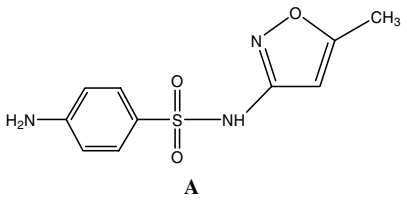
[17–20]. The chemical significance of metal complexes of the derivative sulfamethoxazole [21] (5-methyl-3-isoxazolyl sulfanilamide) (**A**) has been early recognized and many examples have been reported [22–25].



A

This ligand has shown a tendency to coordinate to the metal ion through the isoxazolic nitrogen atom, even in cases of deprotonation of the sulfonamidic nitrogen atom. Some new results [26–28] corroborate the fact that the ability of the sulfonamides to act as ligands is based upon the acidity of the $S(O)_2N$–H function, allied with the presence of vicinal nitrogen or oxygen atoms of the substituents as potential coordination sites. Thus, the deprotonation of the NH group yields an anionic donor ligand, and, in case of sulfamethoxazole, the isoxazole ring affords the stereochemical requisites for the achievement of complexes with a monodentate, chelating or bridging ligand [29,30].

With the aim to provide information about the chemistry of gold(I) and silver(I) complexes of sulfamethoxazole, and to enhance the knowledges on the antibacterial activity of transition metal complexes of sulfonamides [25,31,32], we report now on the preparation [33], X-ray structural features [34–36] and pharmacological activities (chemical toxicity against some microorganisms) [37,38] of $[Ph_3PAu(SMTZ_{-1H+})]$ (**1**) and $[Ag(SMTZ_{-1H+})]_n$ (**2**).

The molecular structure of $[Ph_3PAu(SMTZ_{-1H+})]$ is represented in Fig. 1. Fig. 2 displays the asymmetric unit of $[Ag(SMTZ_{-1H+})]$. Fig. 3 shows the supramolecular, bidimensional assembling of **2** in the *ab*-plane, Fig. 4 exhibits the zigzag configuration of the lattice of **2** in the *bc*-plane, along the *a*-axis. Complex **1** crystallizes as single molecules, with gold(I) bonded to the sulfonamidic nitrogen atom of the sulfamethoxazolato anion and to the phosphorus atom of the triphenylphosphine group. The bond distances are 2.057(3) {Au–N(2)} and 2.2251(11) Å {Au–P}. The N(2)–Au–P bonds are nearly linear, with an angle of 176.96(10)°. The coordination number (2) of the Au(I) ion is not increased through direct interactions with other SMTZ ligands, as in the case of the silver complex **2**. The silver complex involves a complex two-dimensional polymeric assembly of the deprotonated SMTZ ligand and silver ions (Figs. 2–4). Each silver ion is coordinated by one oxygen and three nitrogens in a distorted tetrahedral array. Each ligand is coordinated to three different silver ions, using four donor atoms, N1, O2, N2 and N3. Each silver ion is chelated by N1 and O2 of a single SMTZ ligand to form a six-membered ring. The N2 of this ligand is bound to an adjacent silver ion in such a way that linear chains are

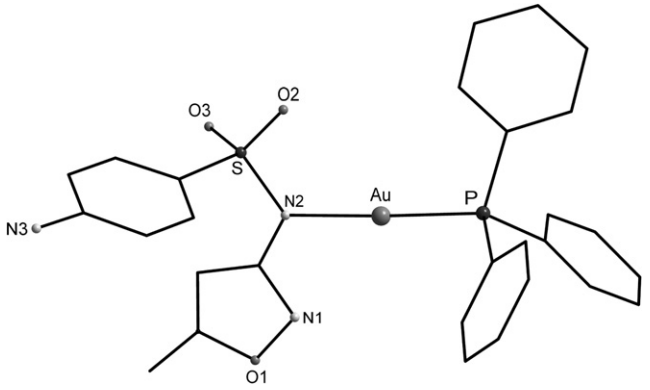


Fig. 1. Molecular structure of $[Ph_3PAu(SMTZ_{-1H+})]$ (**1**) (hydrogen atoms omitted). Selected bond lengths (Å) and bond angles (deg): Au–N(2) = 2.057(3), Au–P = 2.225(1), S–O(2) = 1.432(3), S–O(3) = 1.437(4), S–N(2) = 1.615(4), S–C(11) = 1.753(5), P–C(51) = 1.802(4), P–C(31) = 1.802(4), P–C(41) = 1.815(4), N(2)–C(21) = 1.368(6), N(3)–C(14) = 1.401(7), N(2)–Au–P = 176.96(1), O(2)–S–O(3) = 117.4(2), O(2)–S–N(2) = 104.80(2), O(3)–S–N(2) = 111.7(2), N(2)–S–C(11) = 107.3(2), C(21)–N(2)–S = 119.3(3), C(51)–P–C(31) = 106.3(2), C(51)–P–C(41) = 105.3(2), C(31)–P–C(41) = 106.5(2), C(51)–P–Au = 111.34(2), C(31)–P–Au = 111.57(1), C(41)–P–Au = 115.23(1), C(21)–N(2)–Au = 122.2(3), S–N(2)–Au = 118.5(2).

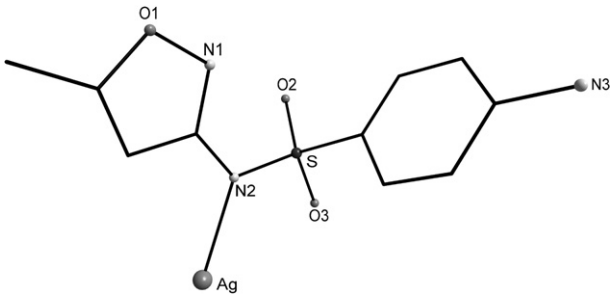


Fig. 2. Asymmetric unit of $[Ag(SMTZ_{-1H+})]$ (**2**).

formed in the crystal structure (Fig. 3) and the chelated silver is bound to N2′ of the preceding SMTZ ligand. The final donor atom is provided by N3‴ from a STMZ ligand in a parallel chain. The silver-N3 linkages between chains form a zigzag chain approximately perpendicular to N2-linked chains (Fig. 4). The nearly tetrahedral bonds on the silver ions present variable distances: 2.183(3) {Ag–N(2)}, 2.241(4) {Ag–N(1)′}, 2.571(4) {Ag–O(2)′} and 2.473(3) Å {Ag–N(3)‴}. Although the Ag–O(2)′ and Ag–N(3)‴ bond distances are somewhat longer, they represent also typical primary bonds, since the sums of the Ag/O and Ag/N van der Waals radii [39] are quite over 3 Å. The lattice of $[Ag(SMTZ_{-1H+})]_n$ holds bidimensional sheets (partially shown in Fig. 3) along the *c*-axis.

The data regarding the minimal inhibitory concentration (MIC) of the compounds SMTZ, $[Ph_3PAu(SMTZ_{-1H+})]$ and $[Ag(SMTZ_{-1H+})]$ against *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* are shown in Table 1. Table 2 presents the minimal inhibitory concentration of the metal compounds $[AuCl(PPh_3)]$ and AgCl versus the same strains. The Au(I) complex was greatly active versus

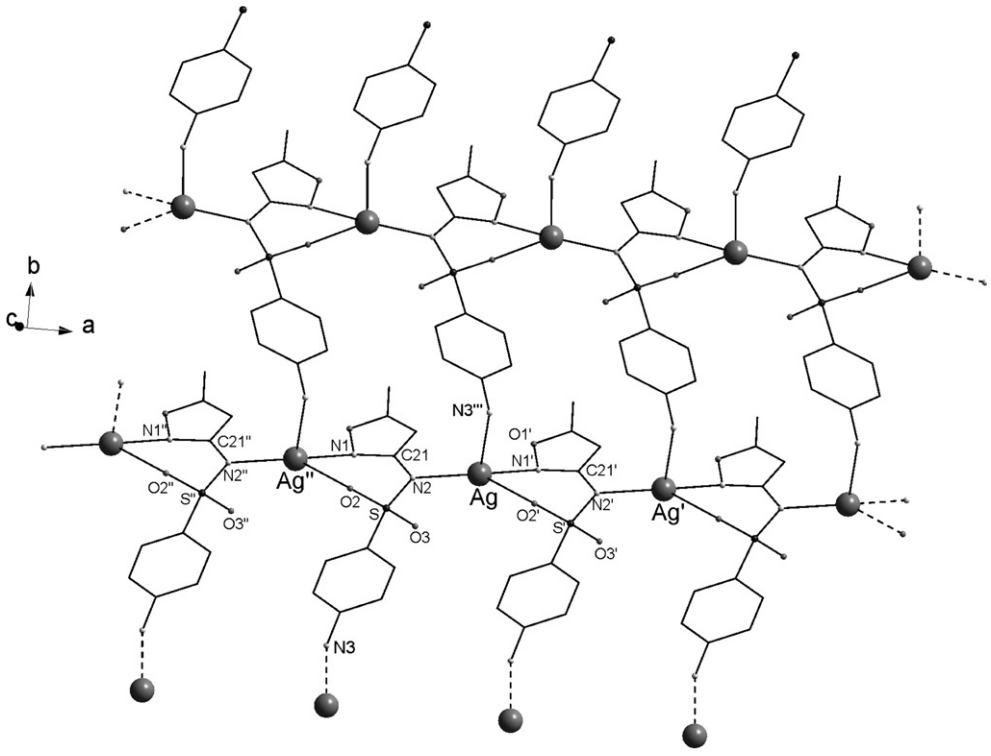


Fig. 3. Supramolecular, bidimensional assembling of $[Ag(SMTZ_{-1H+})]_n$ in the *ab*-plane, view along the *c*-axis. Selected bond lengths (Å) and bond angles (deg): Ag–N(2) = 2.183(3), Ag–N(1)′ = 2.241(4), Ag–O(2)′ = 2.571(4), Ag–N(3)‴ = 2.473(3), N(2)–S = 1.594(3), N(2)–C(21) = 1.376(4), S–O(2) = 1.459(3), S–O(3) = 1.443(3), O(3)–S–O(2) = 115.0(1), C(21)–N(2)–S = 120.9(2), S–O(2)–Ag″ = 116.8(1), C(21)–N(2)–Ag = 121.0(2), S–N(2)–Ag = 117.9(1), N(2)–Ag–N(1)′ = 138.6(1), N(2)–Ag–N(3)‴ = 105.5(1), N(2)–Ag–O(2) = 138.92(9), O(2)–Ag–N(3)‴ = 80.83(8), O(2)–Ag–N(1)′ = 77.10(8), N(1)′–Ag–N(3)‴ = 99.0(1). Symmetry transformations used to generate equivalent atoms: (′) 1 + *x*, *y*, *z*; (″) −1 + *x*, *y*, *z*; (‴) 2 − *x*, 0.5 + *y*, 0.5 − *z*.

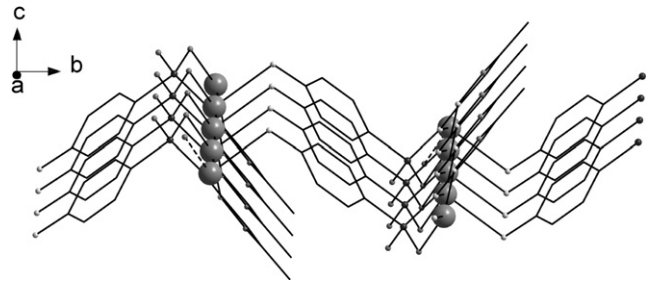


Fig. 4. Zigzag configuration of the lattice of $[Ag(SMTZ_{-1H})]_n$ in the *bc*-plane, viewed along the *a*-axis.

Table 1
Minimal inhibitory concentration (MIC, in $\mu g\,mL^{-1}$) of the sulfamethoxazole (SMTZ) compounds

	E. coli (ATCC 25922)	*S. aureus* (ATCC 25923)	*P. aeruginosa* (ATCC 27853)
SMTZ	512	>512	512
$[Ag(SMTZ_{-1H+})]_n$	64	64	16
$[Ph_3PAu(SMTZ_{-1H+})]$	8	2[a]	256

[a] Related to SMTZ/trimetoprim (5:1). All the others are related to SMTZ only.

Table 2
Minimal inhibitory concentrations (MIC, in $\mu g\,mL^{-1}$) of the metal compounds of Au(I) and Ag(I) against Gram-negative and Gram-positive bacteria

	E. coli (ATCC 25922)	*S. aureus* (ATCC 25923)	*P. aeruginosa* (ATCC 27853)
AgCl	256	>512	256
$[AuCl(PPh_3)]$	512	4	256

E. coli (8) and *S. aureus* (2 $\mu g\,mL^{-1}$) – last related to a mixture 5:1 of SMTZ/trimetoprim, since the MIC value of the Au(I) complex against this strain, related to free SMTZ and even to $[AuCl(PPh_3)]$, had been early quantified as the best. The minimum bactericidal concentrations (MBC) of the complexes of Au(I) and Ag(I) against *E. coli* and *P. aeruginosa* show values with two dilution steps under the MIC, i.e., twofold more concentrated than the MIC values. Against *S. aureus* no bactericidal activity was observed for the test compounds. The differentiated behavior of the Gram-negative and Gram-positive strains in relation to the test drugs should be attributed, at first, to the different morphology of these bacteria classes. The more complex cellular wall of the Gram-negative strains should impart different permeability toward the test compounds, since their solubility is not identical.

To understand, to a certain extent, the described microbiological behavior of the studied metal complexes, it should be proper to remember that it has been suggested that the truly active antibacterial species is the ionic form of sulfonamides, therefore, this form must penetrate cells [40]. However, the small lipid solubility of ionic sulfonamide is supposed to inhibit efficient penetration across the lipoidal bacterial membrane. Alternatively, the molecular form presents higher lipid solubility, but it would not be active unless it ionizes to some degree inside the cell. Thus, sulfonamides would penetrate bacterial cells in the unionized form, but once they are inside a cell, their antibacterial action would be due to the ionized form [41]. Further experiments are in course to determine the solubility and ionization patterns of the complexes in the blood plasma.

Finally, it is to date well known that overall, different complexes of gold(I) have been studied as drug agents in a variety of areas. Auranofin is used as an anti-inflammatory agent for rheumatoid arthritis, and is now also being studied as an antitumor agent [42]. Triphenylphosphine-gold(I) complexes have also been tested as cancer-fighting agents, along with bis(dppe)gold(I) complexes [43], as we have already pointed out in the introduction of this work. Nevertheless, we think that basic biological research on new sulfamethoxazole complexes of Au and Ag, such as the experiments described in this work, can also be significant because it contribute to the biological knowledges about the potential uses of this kind of compounds.

Supplementary material

CCDC 634754 and 634753 contain the supplementary crystallographic data for **1** and **2**. The data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

References

[1] J.E. Toth, G.B. Grindey, W.J. Ehlhardt, J.E. Ray, G.B. Boder, J.R. Bewley, K.K. Klingerman, S.B. Gates, S.M. Rinzel, R.M. Schultz, L.C. Weir, J.F. Worzalla, J. Med. Chem. 40 (1997) 1018.

[2] J.C. Medina, D. Roche, B. Shan, R.M. Learned, W.P. Frankmoelle, D.L. Clark, Bioorg. Med. Chem. Lett. 9 (1999) 1843.

[3] H. Yoshino, N. Ueda, J. Niijima, H. Sugumi, Y. Kotake, N. Koyanagi, K. Yoshimatsu, M. Asada, T. Watanabe, J. Med. Chem. 35 (1992) 2496.

[4] T. Owa, H. Yoshino, T. Okauchi, K. Yoshimatsu, Y. Ozawa, N. Hata Sugi, T. Nagasu, N. Koyanagi, K. Kitoh, J. Med. Chem. 42 (1999) 3789.

[5] N.C. Baenziger, A.W. Struss, Inorg. Chem. 15 (1976) 1807.

[6] D.S. Cook, M.F. Turner, J. Chem. Soc., Perkin Trans. 2 (1975) 1021.

[7] N.C. Baenziger, S.L. Modak, C.L. Fox Jr., Acta Crystallogr. C39 (1983) 1620.

[8] C.J. Brown, D.S. Cook, L. Sengier, Acta Crystallogr. C41 (1985) 718.

[9] C.F. Shaw, Chem. Rev. 99 (1999) 2589.

[10] S. Ahmad, A.A. Isab, H.P. Perzanowski, M.S. Hussain, M.N. Akhtar, Trans. Met. Chem. 27 (2002) 177.

[11] F. Bachechi, A. Burini, R. Galassi, B.R. Pietroni, M. Severini, J. Organomet. Chem. 575 (1999) 269.

[12] S.L. Best, P.J. Sadler, Gold Bull. 29 (1996) 87.

[13] H. Schmidbaur, G. Reber, A. Schier, F.E. Wagner, G. Müller, Inorg. Chim. Acta 147 (1988) 143.

[14] R. Rawls, Chem. Eng. News 6 (October) (1986) 21.

[15] L.L. Marques, G. Manzoni de Oliveira, E. Schulz Lang, R.A. Burrow, Z. Naturforsch. 60b (2005) 318.

[16] G. Manzoni de Oliveira, L.R. Soccol Gris, L.L. Marques, E. Schulz Lang, Z. Anorg. Allg. Chem. 633 (2007) 610.

[17] A. García-Raso, J.J. Fiol, S. Rigo, A. López-López, E. Mollins, E. Espinosa, E. Borrás, G. Alzuet, J. Borrás, A. Castiñeiras, Polyhedron 19 (2000) 991.

[18] E. Borrás, G. Alzuet, J. Borrás, J. Server-Carrió, A. Castiñeiras, M. Liu González, F. Sanz-Ruiz, Polyhedron 19 (2000) 1859.

[19] E. Schulz Lang, R.A. Burrow, L.L. Marques, Acta Crystallogr. C59 (2003) m95.

[20] E. Schulz Lang, L.L. Marques, R.A. Burrow, Acta Crystallogr. E59 (2003) m707.

[21] L. Maury, J. Rambaud, B. Pauvert, Y. Lasserre, G. Berge, M. Audran, Can. J. Chem. 63 (1985) 3012.

[22] H.S. Randhawa, B.S. Sekhon, H.K. Sahai, R. Lakhani, J. Therm. Anal. Calorim. 57 (1999) 551.

[23] G. Kanagaraj, G.N. Rao, Synth. React. Inorg. Met. Org. Chem. 22 (1992) 559.

[24] G. Kanagaraj, G.N. Rao, Indian J. Chem. 32 (1993) 594.

[25] G. Karthikeyan, K. Mohanraj, K.P. Elango, K. Girishkumar, Russian J. Coord. Chem. 32 (2005) 380.

[26] L.L. Marques, E. Schulz Lang, H. Fenner, E.E. Castellano, Z. Anorg. Allg. Chem. 631 (2005) 745.

[27] E. Schulz Lang, L.L. Marques, G. Manzoni de Oliveira, Z. Naturforsch. 60b (2005) 1264.

[28] L.L. Marques, G. Manzoni de Oliveira, E. Schulz Lang, Z. Anorg. Allg. Chem. 632 (2006) 2310.

[29] B.S. Sekhon, H.K. Sahai, H.S. Randhawa, Proc. Nat. Acad. Sci. India 71-A (2001) 195.

[30] H.K. Sahai, B.S. Sekhon, H.S. Randhawa, S. Afr. J. Chem. 52 (1999) 20.

[31] X.-L. Yang, J. Liu, L. Yang, X.-Y. Zhang, Synth. React. Inorg. Met. Org. Nano-Met. Chem. 35 (2005) 761.

[32] L. Yang, X. Yang, J. Liu, Y. Li, Q. Lou, Q. Liu, J. Coord. Chem. 56 (2003) 1131.

[33] *[$Ph_3PAu(SMTZ_{-1H^+})$]* (**1**) Sulfamethoxazole (0.126 g, 0.5 mmol) was dissolved in methanol under moderate heating, and triethylamine (1 mL) was added to the fully transparent solution. At a pH close to 11.5, and after the temperature stabilization at 65 °C, solid Ph_3PAuCl (0.247 g, 0.5 mmol) was added. The gray suspension was refluxed overnight, turning the color pink. After 23 h the reaction system was switched off and the hot mixture was filtered. The precipitate was washed with several portions of methanol and stored in a desiccator. After drying, the solid was redissolved in CH_2Cl_2 and an upper layer of petroleum ether was slowly added. Colorless crystals were formed after two days. Melting point 218 – 220 °C. (The preparation was alternatively carried out starting from 0.3 mmol of [$AuCl(PPh_3)$] (0.148 g), silver acetate (0.050 g) and sulfamethoxazole (0.076 g) in the moderate absence of light achieved by covering the reaction vessels with aluminum foil. [$AuCl(PPh_3)$] and silver acetate were dissolved in ~5 mL of benzene and stirred at 75 °C. After 1 h the reaction was interrupted and AgCl was separated by filtration. The temperature and stirring were restored and sulfamethoxazole was added. After 3 h a discolored precipitate is removed by filtration and recrystallized from CH_2Cl_2.): $C_{28}H_{25}AuN_3O_3PS$ (711.51). C,H,N,S-Analysis, Found: C, 47.01; H, 3.68; N, 5.88; S, 4.98. Calc.: C, 47.26; H, 3.54; N, 5.91; S, 4.51%. IR (KBr): 1122.5 [s (strong), ν_s (SO_2)], 1324.6 [s, ν_{as} (SO_2)], 3365.7 [m (medium), ν_s (NH_2)], 3473.6 [m, ν_{as} (NH_2)]. *[$Ag(SMTZ_{-1H^+})$]* (**2**): Sulfamethoxazole (0.126 g, 0.5 mmol) was dissolved in methanol and the temperature was kept constant at 50 °C. After the addition of triethylamine (1 mL) the solution

remained fully transparent with the pH in the range of 10–11. The reaction vessel was wrapped in aluminum foil, then AgCl (0.0716 g, 0.5 mmol) was added. The mixture was refluxed for 4 h and the gray precipitate was filtered and dried (the mother solution was stored). The solid was dissolved in a 25% aqueous solution of ammonia and recrystallized, yielding colorless crystals suitable for X-ray analysis. (From the mother solution a slight amount of a residue, probably triethylammonium chloride, was obtained by solvent evaporation.) Melting point 277–281 °C. $C_{10}H_{10}AgN_3O_3S$ (360.14). C,H,N,S-Analysis, Found: C, 32.78; H, 3.40; N, 11.15; S, 8.58. Calc.: C, 33.26; H, 3.07; N, 11.64; S, 8.88%. IR (KBr): 1120.2 [s, ν_s (SO_2)], 1322.5 [s, $\nu_{as}(SO_2)$], 3323.2 [m, ν_s (NH_2)], 3388.2 [m, ν_{as} (NH_2)].

[34] *Crystal structure analysis*: the data were collected with a Bruker APEX II CCD area-detector diffractometer and graphite-monochromatized Mo-K_α radiation. The structures were solved by direct methods using SHELXS-97. Subsequent Fourier-difference map analyses yielded the positions of the non-hydrogen atoms. Refinements were carried out with the SHELXL-97 package. All refinements were made by full-matrix least-squares on F^2 with anisotropic displacement parameters for all non-hydrogen atoms. Hydrogen atoms were included in the refinement in calculated positions. The crystal data and structure refinement for [$Ph_3PAu(SMTZ_{-1H+})$] (**1**) and [$Ag(SMTZ_{-1H+})]_n$ (**2**) are: *Empirical formula*: $C_{28}H_{25}AuN_3O_3PS$ (**1**), $C_{10}H_{10}AgN_3O_3S$ (**2**); formula weight: 711.51 (**1**), 360.14 (**2**); crystal system, space group: orthorhombic, $Pna2_1$ (**1**), monoclinic, $P2_1/c$ (**2**); unit cell dimensions a, b, c (Å): $a = 19.0368(4)$ (**1**), 5.9653(4) (**2**); $b = 9.5820(2)$ (**1**), 15.6521(18) (**2**); $c = 14.8461(3)$ (**1**), 13.1982(16) (**2**); α, β, γ (°): $\alpha = \beta = \gamma = 90$ (**1**), $\beta = 9.983(3)$ (**2**); V (Å^3): 2708.09(10) (**1**), 1213.7(2) (**2**); Z, Calc. density (g cm^{-3}): 4, 1.745 (**1**), 4, 1.971 (**2**); crystal size (mm): $0.32 \times 0.15 \times 0.06$ (**1**), $0.14 \times 0.13 \times 0.1$ (**2**); θ range (°): 3.02–27.50 (**1**), 2.04–26.49 (**2**); index ranges: $-24 \leqslant h \leqslant 24$ (**1**), $-7 \leqslant h \leqslant 7$ (**2**), $-12 \leqslant k \leqslant 12$ (**1**), $-19 \leqslant k \leqslant 19$ (**2**), $-19 \leqslant l \leqslant 19$ (**1**), $-16 \leqslant l \leqslant 16$ (**2**); reflections collected: 29659 (**1**), 16152 (**2**): reflections unique: 6010 [$R_{int} = 0.0495$] (**1**), 2511 [$R_{int} = 0.0275$] (**2**); completeness to theta max.: 99.8% (**1**), 99.6% (**2**); absorption correction for **1** and **2**: semi-empirical from equivalents; max. and min. transmission: 1 and 0.234223 (**1**), 1 and 0.883415 (**2**); refinement method: full-matrix least-squares on F^2: data/restraints/parameters: 6010/1/335 (**1**), 2511/0/163 (**2**); goodness-of-fit on F^2: 0.842 (**1**), 1.021(**2**); final R indices [$I > 2\sigma(I)$]: $R_1 = 0.0248$, $wR_2 = 0.0409$ (**1**), $R_1 = 0.0247$, $wR_2 = 0.0792$ (**2**); R indices (all data): $R_1 = 0.0438$, $wR_2 = 0.0429$(**1**), $R_1 = 0.0407$, $wR_2 = 0.1151$ (**2**); largest diff. peak and hole (e Å^{-3}): 0.618 and −0.427 (**1**), 1.001 and −1.108 (**2**).

[35] G.M. Sheldrick, SHELXS-97, Program for Crystal Structure Solution, University of Göttingen, Germany, 1997.

[36] G.M. Sheldrick, SHELXL-97, Program for Crystal Structure Refinement, University of Göttingen, Germany, 1997.

[37] *Antimicrobial activity*: Broth microdilution tests were used to determine the minimal concentration of the antimicrobial agent required to inhibit the microorganisms (MIC). We have employed the methods prescribed in the M7-A6 document for aerobical bacteria from the National Committee for Clinical Laboratory Standards (NCCLS). The microbiologic activity of the sulfamethoxazole complexes of Au(I) and Ag(I) and their salts was measured in relation to free sulfamethoxazole. The standard strains used were the Gram-positive *Staphylococcus aureus* ATCC 25923 and the Gram-negatives *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853. *Preparation of the standard solutions of the testing compounds*: all the standard solutions for the metal complexes and related compounds were prepared in a 1:1 mixture of dimethyl sulfoxide (DMSO)/methanol, in a concentration of 10 mg/mL. DMSO and methanol are useful solvents to determine the biologic activity of relative insoluble substances, like some antibiotics. Also the mixture DMSO/H_2O is widely used. *Dilution series*: a sterile 96-well microtitration plate was prepared containing 100 μL of the Mueller–Hinton broth per well. 100 μL of a 2048 μg mL^{-1} drug-containing Mueller–Hinton broth was added in the first well. A twofold dilution series was prepared from this first well. The final drug concentrations in the wells were respectively 512, 256, 128, 64, 32, 16, 8, 4, 2, 1and 0.5 μg mL^{-1}. The plate was incubated at 37 °C for 18–24 h. All tests and inoculations were performed in triplicate. *MIC and MBC determination:* after the incubation times and addition of the indicator to the wells, the lowest concentration of drug inhibiting microbial growth was selected as the minimal inhibitory concentration (MIC). The minimum bactericidal concentration (MBC) was determined by transferring 100 μL from the lowest growth well for subculture in agar Mueller–Hinton plates which were incubated aerobically at 37 °C for 18–24 h. The MBC was read as the lowest concentration of drug which reduces the count of viable cells by 99.9% from the initial inoculum.

[38] NCCLS, Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically: Approved Standard – Sixth Edition. NCCLS document M7-A6 (ISBN 1-56238-486-4). NCCLS, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087–1898 USA, 2003.

[39] A. Bondi, J. Phys. Chem. 68 (1964) 441.

[40] A. Gringauz, Introduction to Medicinal Chemistry, Wiley-UCH, New York, 1997, pp. 61–67.

[41] W.O. Foye, T.L. Lemke, D.A. Williams, Principles of Medicinal Chemistry, fourth ed., Williams & Williams, 1995, pp. 709–713.

[42] E. Mizushima, K. Sato, T. Hayashi, M. Tanaka, Angew. Chem., Int. Ed. 41 (2002) 4563.

[43] C.F. Shaw III, A. Beery, G.C. Stocco, Inorg. Chim. Acta 123 (1986) 213.