Synthesis, Characterization and in Vitro Study of the Cytostatic and Antiviral Activity of New Polymeric Silver(I) Complexes with Ribbon Structures Derived from the Conjugated Heterocyclic Thioamide 2-Mercapto-3,4,5,6-tetrahydropyrimidine

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Silver(I) bromide reacts with 2-mercapto-3,4,5,6-tetrahydropyrimidine (StpmH$_2$, $C_4H_8N_2S$) in DMSO with an excess of triethylamine to give a water-insoluble complex of formula $[Ag_6(\mu_2\text{-}Br)_6(\mu_2\text{-}StpmH_2)_4(\mu_3\text{-}StpmH_2)_2]_n$ (**1**), while the reaction of silver(I) nitrate with StpmH$_2$ under the same conditions gives a water-insoluble complex of formula $[\{Ag_4(\mu_2\text{-}StpmH_2)_6\}(NO_3)_4]_n$ (**2**). The products were characterized by elemental analyses, and FT-IR far-IR, UV/Vis, ^{1}H and ^{13}C NMR spectroscopy. Crystal structures of complexes **1** and **2** were determined by X-ray diffraction. Complex **1**, $C_{24}H_{48}Ag_6N_{12}S_6$, crystallizes in the triclinic system space group $P\bar{1}$, a = 8.041(1) Å, b = 12.838(4) Å, c = 13.281(2) Å, α = 68.40(1)°, β = 72.97(1)°, γ = 87.80(2), Z = 2, forming a one-dimensional infinite ribbon structure by strong interatomic interactions of two μ_2-Br bonds with Ag(1). Complex **2**, $C_{24}H_{48}Ag_4N_{16}O_{12}S_6$, crystallizes in the orthorhombic system, space group $Cmc2_1$, and a = 32.148(3) Å, b = 9.461(2) Å, c = 7.234(1) Å, $\alpha = \beta = \gamma$ = 90°, Z = 8, forming infinite Ag–S–Ag chains which are bridged to each other by a sulfur atom of μ_2-StpmH$_2$ ligands. Complexes **1** and **2** were studied for their cytostatic activity against murine leukemia (L1210) and human T-lymphocyte (Molt4/C8 and CEM) cells and for their antiviral activity against a wide variety of viruses. They are markedly cytostatic at 50% inhibitory concentration (IC_{50}) values ranging from 3 to 17 μg/mL. None of the compounds showed appreciable antiviral activity at subtoxic concentrations.

Introduction

Research towards the design of infinite molecular components with specific chains and networks is a matter of great current interest.[1] This self-assembly process between metal ions and ligands is known to depend on the steric and interactive information stored in the ligand and also by the metal ions through their coordination geometry demands.[1b,1c] From this point of view, the ability of silver(I) thiolate or thionate complexes to adopt geometries with variable nuclearities and structural diversity makes the study of silver(I) chemistry very attractive.[2,3] Silver(I) complexes with sulfur-containing ligands exhibit a wide range of applications in medicine, in analytical chemistry or in the polymer industry.[2,3] The biomedical applications and uses of silver(I) complexes are related to their antibacterial action,[4] which appears to involve interaction with DNA.[5] The molecular design and structural characterization of silver(I) complexes is therefore an intriguing aspect of bioinorganic chemistry and metal-based drugs.[6]

A great deal of work has also been devoted to the study of thioamides because of their tendency to bridge metal centers forming oligo- and polynuclear species with potential usage as functional solid materials.[7] Furthermore, 2-mercapto-3,4,5,6-tetrahydropyrimidine can coordinate up to three metal centers at short distances, offering the possibility of studying the metal-metal interaction of d^{10} systems which have attracted considerable attention.[8] Such metal-metal interactions have been observed for silver(I) complexes containing aromatic heterocyclic thioamides like 2-mercaptopyridine,[1a,7] 2-mercaptonicotinic acid,[6b,9] 3-(*tert*-butyldimethylsilyl)pyridine-2-thione and 3,6-bis(*tert*-butyldimethylsilyl)pyridine-2-thione,[10a] 2-(triorganosilyl)-thiophenols and 2,6-bis(triorganosilyl)thiophenols,[10b] and 2-(triorganosilyl)methanethione[10c] and -thiophenol.[11] It is noteworthy that in all cases of complexes with a short sil-

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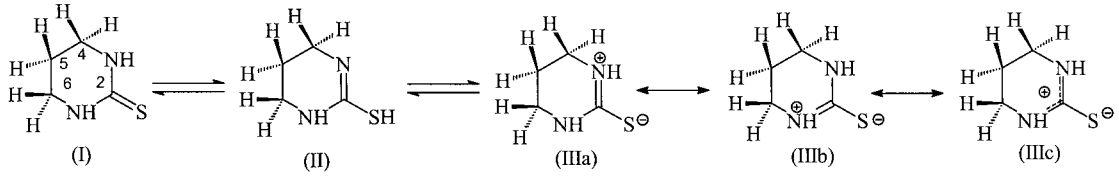

Figure 1. Tautomeric forms of 2-mercapto-3,4,5,6-tetrahydropyrimidine (thione I, thiol II and zwitterionic salt III)

ver(I)-silver(I) distance [shorter than twice the van der Waals radius for silver (3.44 Å)[6b]] there is no halogen atom in the coordination sphere of the metal center.

In this paper, we report the structural and spectroscopic characterization of two new silver complexes with the heterocyclic thioamide 2-mercapto-3,4,5,6-tetrahydropyrimidine (Figure 1) of formulae $[Ag_6(\mu_2\text{-}Br)_6(\mu_2\text{-}StpmH_2)_4(\mu_3\text{-}StpmH_2)_2]_n$ (**1**) and $[\{Ag_4(\mu_2\text{-}StpmH_2)_6\}(NO_3)_4]_n$ (**2**). The cytostatic activity of complexes **1** and **2** against murine leukemia (L1210) and human T-lymphocyte (Molt4/C8 and CEM) cells, and their antiviral properties, have also been studied.

Results and Discussion

General Aspects

The synthesis of complexes **1** and **2** was carried out in DMSO with an excess of triethylamine according to the reactions shown in Equation (1) and (2).

$$6n\ AgBr + 6n\ StpmtH_2 \xrightarrow[DMSO]{Et_3N} \{[Ag_6(\mu_2\text{-}Br)_6(\mu_2\text{-}StpmtH_2)_4(\mu_3\text{-}StpmtH_2)_2]_n\} \quad (1)$$

$$4n\ AgNO_3 + 6n\ StpmtH_2 \xrightarrow[DMSO]{Et_3N} \{[Ag_4(\mu_2\text{-}StpmtH_2)_6](NO_3)_4\}_n \quad (2)$$

No deprotonation of the thioamide ligand was observed, even though an excess of triethylamine was used. When 2-mercaptonicotinic acid was allowed to react with silver(I) chloride under the same reaction conditions, a hexanuclear, water-soluble aggregate of formula $[\{Ag_6(\mu_3\text{-}Hmna)_4(\mu_3\text{-}mna)_2\}^{2-}\cdot\{(Et_3NH)^+\}_2\cdot(DMSO)_2\cdot(H_2O)]$ was formed.[9] Complexes **1** and **2** have infinite ribbon structures (vide infra) which consist of Ag_3S_3 six-membered rings bridged by Br atoms in the case of **1** and two infinite Ag−S−Ag chains bridged by S atoms in the case of **2**. It is noteworthy that the geometry around the silver(I) ions in **1** is tetrahedral while for **2** the geometry around the silver(I) ions is trigonal.

The formulae of molecules **1** and **2** were first deduced from elemental analysis and spectroscopic data. Complexes **1** and **2** are soluble in DMSO and DMF. Crystals of the complexes are stable in air but were stored in darkness. The infinite-ribbon structures of complexes **1** and **2** seem to persist in DMSO solution, since the specific conductivity for complex **1** is $k = 16.15$ μs/cm at 22 °C and does not change up to 38 °C (see also ^{13}C NMR spectra). Complex **2**, on the other hand, has a specific conductivity of 162.45 μs/cm at 22 °C, increasing to 218.8 μs/cm at 38 °C due to the free NO_3^- counteranions.

With 3-(*tert*-butyldimethylsilyl)pyridine-2-thione, 3,6-bis-(*tert*-butyldimethylsilyl)pyridine-2-thione,[10a] 2-(triorganosilyl)thiophenols, 2,6-bis(triorganosilyl)thiophenols,[10b] or 2-(triorganosilyl)methanethione[10c] as ligands towards silver(I) ions, Zubieta et al.[10] have established that the extent of the association of silver(I) ions in their clusters depends intimately on the nature of thioamide. Thus, silver(I) with unbranched linear thiolate ligands are highly polymeric as silver(I) is unprotected from the approach of additional bridging thiolate groups, while bulky ligands such as substituted thiolates increase the aggregation degree of $[Ag(LS)]_n$ compounds.[10] In accordance with the above findings an aggregate of formula $[\{Ag_6(\mu_3\text{-}Hmna)_4(\mu_3\text{-}mna)_2\}^{2-}\cdot\{(Et_3NH)^+\}_2\cdot(DMSO)_2\cdot(H_2O)]$[9] was recently synthesized with the branched substituted 2-mercaptonicotinic acid. When the unbranched, non-aromatic 2-mercapto-3,4,5,6-tetrahydropyrimidine was used for the synthesis of complexes **1** and **2**, highly polymeric structures were obtained.

Infrared Spectroscopy

The infrared spectra of complexes **1** and **2** show distinct vibrational bands at 1559, 1214 cm^{-1} and 1564, 1221 cm^{-1}, respectively, which were assigned as the vibrations of the C−N bond (thioamide I and II bands) and at 1063, 619 cm^{-1} and at 1038, 627 cm^{-1}, respectively, which were attributed to the C−S bond vibrations (thioamide III and IV bands). The corresponding thioamide bands of the free 2-mercapto-3,4,5,6-tetrahydropyrimidine ligand are found at 1557, 1206, 1067 and 644 cm^{-1}, respectively. The new bands at 133 and 139 cm^{-1} in the far-IR spectra of complexes **1** and **2** were assigned to the vibrations of the Ag−S bond,[12] while bands also appear at 178, 137 cm^{-1} in the far-IR spectrum of **1** that can be attributed to the vibration of the Ag−Br bonds.

NMR Spectroscopy

The ^1H NMR spectrum of the free ligand $StpmH_2$ in $[D_6]$DMSO solution shows resonance signals at δ = 7.86 ppm for the amide proton and at δ = 3.20 and 1.75 ppm for the -CH_2- a and b protons. The signal of the amide protons is shifted to δ = 8.50 and 8.76 ppm, respectively, in the ^1H NMR spectra of complexes **1** and **2** in $[D_6]$DMSO solution, confirming the N/S-metal coordination.

The ^{13}C NMR peak assignments of complexes **1** and **2** were based on those of the free ligand, which shows signals

at δ = 175.7 ppm for C(=S) (C^2, Figure 1), δ = 40.1 ppm for the two CH_2(-N) equivalent carbon atoms (C^4 and C^6, Figure 1) and at δ = 19.5 ppm for CH_2(-CH_2) (C^5, Figure 1). Complex **1** shows signals at δ = 169.9 ppm for C^2(=S), at δ = 40.7 and 40.3 ppm for C^4(-N) and C^6(-N), respectively, and at δ = 19.5 ppm for C^5. The corresponding signals for complex **2** are at δ = 169.4 ppm for C^2(=S), at δ = 41.4 and 41.0 ppm for C^4(-N) and C^6(-N), respectively, and at δ = 19.1 ppm for C^5. The presence of two signals for C^4 and C^6 of the ligand in both complexes, in contrast to the one in the case of the free ligand, indicates two different coordination modes in the complexes, in accordance with the structures determined by X-ray crystallography (see also conductivity measurements), and suggests that the infinite ribbon structures are persistent in DMSO solutions.

Crystal and Molecular Structures of Complexes $[Ag_6(\mu_2\text{-}Br)_6(\mu_2\text{-}StpmH_2)_4(\mu_3\text{-}StpmH_2)_2]_n$ (1) and $[\{Ag_4(\mu_2\text{-}StpmH_2)_6\}(NO_3)_4]_n$ (2)

Schakal diagrams of complexes **1** and **2** are shown in Figure 2 and 3, respectively, while selected bond lengths and angles are given in Table 1 and 2.

In complex **1**, three sulfur atoms bridge three silver(I) ions, forming a six-membered ring. Strong μ-S and μ-Br intramolecular interactions bridge two six-membered rings (R^1, R^2) through two silver(I) ions while this unit is also bridged by a third six-membered ring (R^3) through the remaining silver(I) ion, two strong μ-Br interactions and so on. Thus, a one-dimensional infinite ribbon structure is formed with strong interatomic interactions (Figure 4).

The Ag−S bond lengths are Ag(1)−S(2) = 2.504(2), Ag(1)−S(1) = 2.522(2), Ag(2)−S(2) = 2.562(2), Ag(2)−S(3) = 2.666(2), Ag(3)−$S(1)^b$ = 2.4832(2), Ag(3)−$S(3)^b$ = 2.554(2) and Ag(3)−S(3) = 2.949(2) Å (^{b}: $-x + 1, -y + 1, -z$). These values are similar to those measured in complexes with infinite ribbon structures, such as $[Ag_6(\mu_3\text{-pyS})_4(\mu_4\text{-pyS})_2]_n$ [1a] [pySH = 2-mercaptopyridine, Ag−S = 2.456(5)−2.959(5) Å], $[Ag_5(pyS)_4(pySH)BF_4]_n$ [7] (pySH = 2-mercaptopyridine, Ag−S = 2.45−2.90 Å),

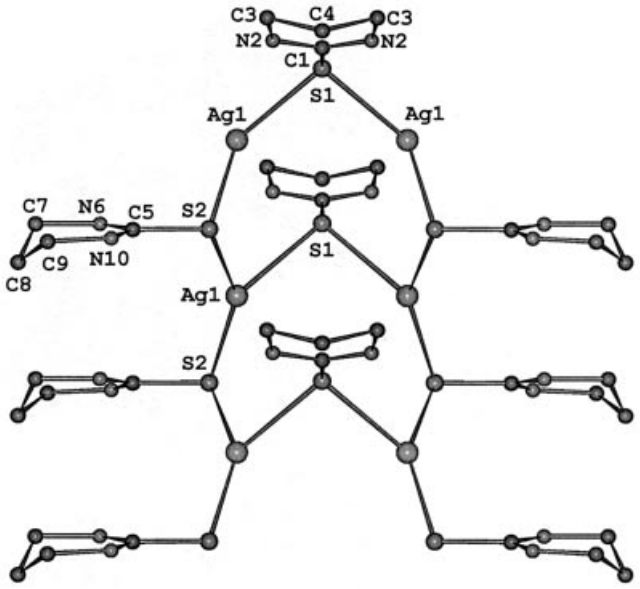

Figure 3. Schakal diagram of the crystal structure of complex **2**; the NO_3^- counterions are omitted for clarity

$[\{Ag_6(SPh)_8\}(Me_4N)_2]$[11] [Ag−S = 2.431(3)−2.878(2) Å], and in $[Ag(\mu_2\text{-pyS})]_n$ [1a] [pySH = 2-mercaptopyridine, Ag−S = 2.587(4) and Ag−S(a) = 2.502 Å].

The Ag···Ag distances in **1** are Ag(2)−Ag(3) = 3.063(1) and Ag(3)−$Ag(3)^b$ = 2.963(2) and are shorter than twice the van der Waals radius for silver (3.44 Å),[6b] indicating a strong Ag···Ag interaction. Other compounds with strong Ag···Ag interactions include $[Ag_6(\mu_3\text{-pyS})_4(\mu_4\text{-pyS})_2]_n$,[1] (pySH = 2-mercaptopyridine) with Ag···Ag = 2.959(2) Å, the neutral cluster $[Ag_6(\mu_3\text{-Hmna})_6\cdot 8DMSO]$ (H_2mna = 2-mercaptonicotinic acid),[6b] with Ag···Ag = 2.911(1) Å, $[Ag_5(pyS)_4(pySH)BF_4]_n$ (pySH = 2-mercaptopyridine),[7] with Ag···Ag = 2.995 Å, $[\{Ag_6(\mu_3\text{-Hmna})_4(\mu_3\text{-mna})_2\}^{2-}\cdot\{(Et_3NH)^+\}_2\cdot(DMSO)_2\cdot(H_2O)]$,[9] with Ag···Ag = 2.916 Å, and $[\{Ag_6(SPh)_8\}\cdot(Me_4N)_2\}]$,[11] with Ag···Ag = 2.959(1) Å. It is noteworthy that in all these complexes with

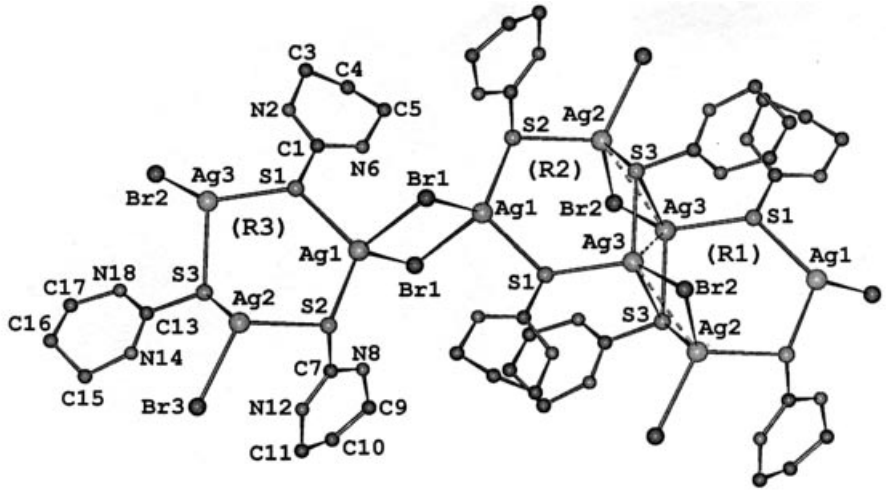

Figure 2. Schakal diagram of the crystal structure of complex **1**; the dashed lines represent short Ag···Ag contacts

Table 1. Selected bond lengths (Å) and angles (°) for compound **1**, with esd's in parentheses

Ag(1)−S(2)	2.504(2)	Ag(1)−S(1)	2.522(2)
Ag(1)−Br(1)	2.724(1)	Ag(1)−Br(1)[a]	2.742(1)
Ag(2)−S(2)	2.562(2)	Ag(2)−Br(3)	2.637(1)
Ag(2)−S(3)	2.666(2)	Ag(2)−Br(2)	2.668(1)
Ag(2)−Ag(3)	3.063(1)	Ag(3)−S(1)[b]	2.482(2)
Ag(3)−S(3)b	2.554(2)	Ag(3)−Br(2)	2.600(1)
Ag(3)−S(3)	2.949(2)	Ag(3)−Ag(3)[b]	2.963(2)
S(1)−C(1)	1.707(8)	S(2)−C(7)	1.734(8)
S(3)−C(13)	1.732(7)	C(1)−N(6)	1.312(10)
C(1)−N(2)	1.320(10)	N(2)−C(3)[b]	1.456(11)
C(5)−N(6)	1.452(13)	C(7)−N(8)	1.305(11)
C(7)−N(12)	1.329(10)	N(8)−C(9)	1.479(14)
C(11)−N(12)	1.470(11)	C(13)−N(14)	1.313(9)
C(13)−N(18)	1.322(10)	N(14)−C(15)[c]	1.452(11)
C(17)−N(18)[d]	1.479(10)		
S(2)−Ag(1)−S(1)	115.84(7)	S(2)−Ag(1)−Br(1)	115.11(6)
S(1)−Ag(1)−Br(1)	107.97(6)	S(2)−Ag(1)−Br(1)[a]	116.70(6)
S(1)−Ag(1)−Br(1)[a]	103.49(6)	Br(1)−Ag(1)−Br(1)[a]	95.31(3)
Ag(1)−Br(1)−Ag(1)[a]	84.69(3)	S(2)−Ag(2)−Br(3)	116.04(6)
S(2)−Ag(2)−S(3)	97.16(7)	Br(3)−Ag(2)−S(3)	105.17(5)
Br(2)−Ag(2)−Ag(3)	53.42(3)	S(1)[b]−Ag(3)−S(3)[b]	99.07(7)
S(1)[b]−Ag(3)−Br(2)	127.07(6)	S(3)[b]−Ag(3)−Br(2)	112.74(6)
S(1)[b]−Ag(3)−S(3)	94.74(7)	S(3)[b]−Ag(3)−S(3)	115.35(5)
Br(2)−Ag(3)−S(3)	107.16(5)	S(1)[b]−Ag(3)−Ag(3)[b]	102.60(6)
S(3)[b]−Ag(3)−Ag(3)[b]	64.14(5)	Br(2)−Ag(3)−Ag(3)[b]	128.85(5)
S(3)−Ag(3)−Ag(3)[b]	51.21(5)	S(1)[b]−Ag(3)−Ag(2)	116.92(6)
S(3)[b]−Ag(3)−Ag(2)	141.78(5)	Br(2)−Ag(3)−Ag(2)	55.49(3)
S(3)−Ag(3)−Ag(2)	52.59(5)	Ag(3)[b]−Ag(3)−Ag(2)	94.17(4)
Ag(3)−Br(2)−Ag(2)	71.09(4)	Ag(3)[b]−S(1)−Ag(1)	127.89(9)
Ag(1)−S(2)−Ag(2)	114.65(8)	Ag(3)[b]−S(3)−Ag(2)	115.42(7)
Ag(3)[b]−S(3)−Ag(3)	64.65(5)	Ag(2)−S(3)−Ag(3)	65.91(5)

[a] $-x+1, -y, -z$. [b] $-x+1, -y+1, -z$. [c] $x-1, y, z$. [d] $-x, -y+1, -z$.

Table 2. Selected bond lengths (Å) and angles (°) for compound **2**, with esd's in parentheses

Ag(1)−S(2)	2.499(5)	Ag(1)−S(2)[a]	2.554(4)
Ag(1)−S(1)	2.669(5)	S(1)−C(1)	1.76(2)
S(2)−C(5)	1.769(14)	C(1)−N(2)	1.314(14)
N(2)−C(3)	1.468(17)	C(3)−C(4)	1.512(18)
C(5)−N(6)	1.307(19)	C(5)−N(10)	1.30(2)
N(6)−C(7)	1.50(2)	C(9)−N(10)	1.48(2)
S(2)−Ag(1)−S(2)[a]	145.96(16)	S(2)−Ag(1)−S(1)	124.58(16)
S(2)[a]−Ag(1)−S(1)	89.05(17)	Ag(1)[b]−S(1)−Ag(1)	95.6(2)
Ag(1)−S(2)−Ag(1)[b]	93.00(13)		

[a] $x, -y, z+1/2$. [b] $x, -y, z-1/2$.

a short silver(I)−silver(I) distance there is no halogen atom in the coordination sphere of the metal center. Complex **1** is therefore the first example of a silver(I) cluster containing a bromide ion in the coordination sphere of the metal center with an Ag···Ag interaction.

The C−S bond lengths found in complex **1** are S(1)−C(1) = 1.707(8), S(2)−C(7) = 1.734(8) and S(3)−C(13) = 1.732(7) Å, with a partial double-bond character, while the C−N bond lengths are C(1)−N(6) = 1.312(10), C(1)−N(2) = 1.320(10), C(7)−N(8) = 1.305(11), C(7)−N(12) = 1.328(10), C(13)−N(14) = 1.313(9) and C(13)−N(18) = 1.318(9) Å. These bond lengths, as well as the C−*N*−C and N−C−S bond angles, which are around 123° and 120°, respectively, indicate that the ligand coordinates to the silver(I) ion through its zwitterionic form IIIc (Figure 1).

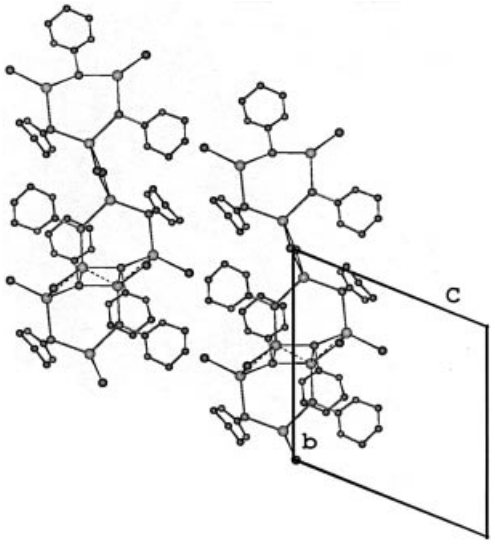

Figure 4. *bc* Projection of the crystal structure of complex **1**; part of the 1-D ribbon structure is presented

Complex **2** consists of two infinite Ag−S−Ag chains, parallel to the *c* axis, which are bridged to each other by a

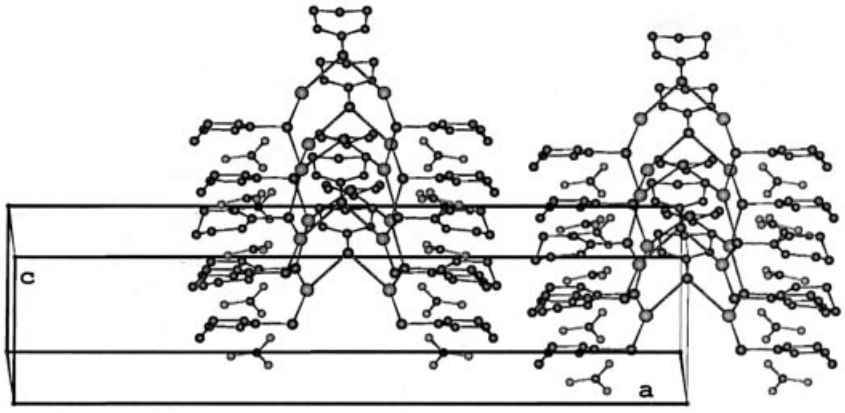

Figure 5. *ac* projection of the crystal structure of complex **2**; the NO_3^- counterions are shown

sulfur atom of the μ_2-StpmH$_2$ ligands. In this way, a one dimensional structure is obtained (Figure 5). A mirror plane parallel to the *bc* plane of the unit cell passes through atoms S(1), C(1) and C(4). The silver(I) ions are three-coordinate while the charge of the Ag^I ion is counterbalanced by a nitrate counterion.

The Ag−S bond lengths are Ag(1)−S(2) = 2.499(5), Ag(1)−S(2)^a = 2.554(4) and Ag(1)−S(1) = 2.669(5) Å (^{a}: x, $-y$, $-z + {}^1/_2$). The Ag−S bond lengths are similar to those found in **1**. No Ag···Ag interaction is observed in **2** [Ag(1)−Ag(1b) = 3.666 and Ag(1)−Ag(1c) = 3.954 Å, both of which are longer than the sum of the Van der Waals radii of two silver atoms]. The C−S bond lengths found in complex **2** are S(1)−C(1) = 1.76(2) and S(2)−C(5) = 1.769(14) Å, which correspond to a C−S single bond, while the C−N bond lengths are C(1)−N(2) = 1.314(14), C(5)−N(6) = 1.307(19) and C(5)−N(10) = 1.30(2) Å. Thus, both ligands have two equivalent short C−N bonds and a C−S single bond, forming the zwitterion IIIc (Figure 1) upon coordination to the silver(I) ion. This is further supported by the values of the C−*N*−C and N−C−S angles, which are around 123° and 120°, respectively. Therefore, a second coordination mode of the ligand is observed in complex **2** from the partial thionic form which is found in complex **1**. Moreover, although a tautomeric zwitterionic form is known to exist in the case of aromatic thioamide ligands,[1a,7,13] complex **2**, with a 2-mercapto-3,4,5,6-tetrahydropyrimidine ligand, is the first example of a coordination mode of S^-−Ag^+ and HN^+ counterbalanced by NO_3^- ions, i.e. with the ligand in its zwitterionic form. A possible charge distribution on the atoms of the unit cell in complex **2** is shown in Figure 6.

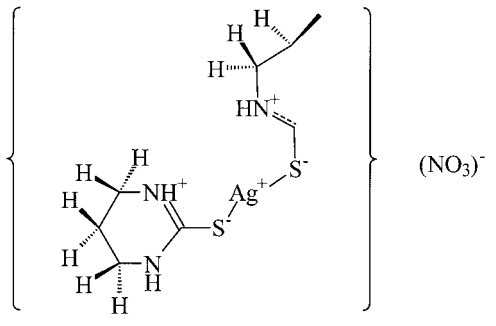

Figure 6. A possible charge distribution on the atoms in complex **2**

Biological Tests

Complexes **1** and **2** were evaluated for their inhibitory activity against the proliferation of murine leukemia (L1210) and human T-lymphocyte (Molt4/C8 and CEM) cells. Table 3 presents the antiproliferative effects of complexes **1** and **2**, as well as the activity of the ligand, as 50% inhibitory concentration (IC_{50}) values:

Table 3. Cytostatic activity of complexes **1** and **2** as 50% inhibitory concentration (IC_{50}) values against murine leukemia (L1210) and human T-lymphocyte (Molt4/C8 and CEM) cells

Compound	IC_{50} (μg/mL)		
	L1210	Molt4/C8	CEM
StpmH$_2$	>200	>200	>200
1	3.4 ± 0.1	3.6 ± 0.3	14 ± 5
2	3.5 ± 0.1	4.1 ± 1.1	17 ± 0

These findings indicate that complexes **1** and **2** show a pronounced cytostatic activity against the tumor cell-lines studied. None of the compounds show a pronounced activity against a wide spectrum of viruses (see Exp. Sect.) at subtoxic concentrations (3.2 μg/mL for **1** and 0.64−3.2 μg/mL for **2** in HEL and Vero cell cultures; data not shown).

Experimental Section

Materials and Instruments: All solvents used were of reagent grade. Silver(I) halides were freshly prepared by mixing aqueous solutions of $AgNO_3$ (Riedel) with the appropriate amount of NaBr (Merck or Aldrich). The precipitate was filtered off, washed with diethyl ether and dried in vacuo. 2-Mercapto-3,4,5,6-tetrahydropyrimidine (Aldrich) was used with no further purification. Elemental analyses for C, H, N, and S were carried out with a Carlo Erba EA model 1108 elemental analyzer. Melting points were measured in open tubes with a Stuart scientific apparatus and are uncorrected. Con-

ductivity measurements were performed on a CONSORT C 831 conductometer, in DMSO solutions. IR spectra in the region of 4000−370 cm^{-1} were obtained from KBr discs, while far-IR spectra in the region of 400−30 cm^{-1} were obtained from polyethylene discs, with a Perkin−Elmer Spectrum GX FT-IR spectrophotometer. A Jasco UV/Vis/NIR V 570 series spectrophotometer was used to obtain the electronic absorption spectra. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC250 MHFT NMR instrument in [D_6]DMSO solutions. Chemical shifts are given in ppm referenced to internal TMS.

Synthesis and Crystallization of $[Ag_6(\mu_2\text{-}Br)_6(\mu_2\text{-}StpmH_2)_4(\mu_3\text{-}StpmH_2)_2]_n$ (1) and $[\{Ag_4(\mu_2\text{-}StpmH_2)_6\}(NO_3)_4]_n$ (2): Silver(I) bromide (1 mmol, 0.188 g) or silver(I) nitrate (0.170 g) were added to a clear solution of 2-mercapto-3,4,5,6-tetrahydropyrimidine (2 mmol, 0.2324 g) in 7 mL of DMSO. After stirring for 30 min, triethylamine (3.6 mmol, 0.5 mL) was added to the clear solution. The solution was then filtered and the filtrates were kept in darkness at room temp. After a few days colorless crystals of complex **1** or **2** suitable for crystallographic single crystal analysis were obtained.

1: Yield: 0.067 g (25%); m.p. 176−178 °C. $C_{24}H_{48}Ag_6Br_6N_{12}S_6$ (1823.7): calcd. C 15.81, H 2.65, N 9.22, S 10.55; found C 16.13, H 2.52, N 9.92, S 10.36. IR: $\tilde{\nu}$ = 3258 vs cm^{-1}, 2966 m, 1559 vs, 1432 m, 1362 vs, 1317 vs, 1215 vs, 1199 vs, 1072 m, 808 s, 694 s, 598 s, 566 s; far-IR: 178 m cm^{-1}, 133 m, 118 m, 111 m, 104 m. UV/Vis (DMSO): λ_{max} (log ε) = 263.5 nm (4.19). ^1H NMR (DMSO): δ = 8.572 (s, NH), 3.219 [t, $^3J_{HH}$ = 7.40 Hz, CH_2, -C(4)], 1.812−1.770 [q, $^3J_{HH}$ = 6.0 Hz, CH_2, -C(5)] ppm.

2: Yield: 0.034 g (10%); m.p. 209−211 °C. $C_{24}H_{48}Ag_4N_{16}O_{12}S_6$ (1376.5): calcd. C 20.94, H 3.51, N 16.28, S 13.97; found C 21.51, H 3.64, N 16.73, S 13.60. IR: $\tilde{\nu}$ = 3381 s cm^{-1}, 3229 s, 2965 m, 1564 vs, 1383 vs, 1309 s, 1221 s, 1196 s, 1073 m, 1038 m, 970 m, 815 m, 751 m, 627 m, 566 m, 519 m; far-IR: 286 m cm^{-1}, 282 m, 276 m, 273 m, 253 m, 246 m, 228 m, 222 m, 207 s, 199 m, 193 m, 175 m, 170 s, 158 m, 155 m, 147 m, 139 m, 128 s, 117 s, 112 m. UV/Vis (DMSO): λ_{max} (log ε) 257.5 nm (4.69). ^1H NMR (DMSO): δ = 8.76 (s), 3.25 (m), και 1.80 (m) ppm.

Cytostatic Activity Assays: To each well of a 96-well microtiter plate was added 5 × 10^4 L1210 or 7.5 × 10^4 Molt4/C8 or CEM cells and a given amount of the test compound dissolved in DMSO. The cells were allowed to proliferate for 48 hours (L1210) or 72 hours (Molt4/C8 or CEM) in a humidified, CO_2-controlled atmosphere. At the end of the incubation period, the cells were counted with a Coulter Counter. The IC_{50} (50% inhibitory concentration) is defined as the concentration of compound that reduced the number of living cells by 50%.

Inhibition of HIV-Induced Cytopathicity in CEM Cells: Human CEM (approx. 3 × 10^5 cells·mL^{-1}) cells were infected with 100 $CCID_{50}$ (1 $CCID_{50}$ being the viral dose required to infect 50% of the cell cultures) of HIV-1 (III_B) or HIV-2 (ROD) per milliliter and seeded in 200-μL wells of 96-well microtiter plates, containing appropriate dilutions of the test compounds. After 4 days of incubation at 37 °C, CEM giant-cell formation was examined microscopically.

Antiviral Activity Assays: The antiviral, other than *anti*-HIV, assays were based on inhibition of virus-induced cytopathicity in either human embryonic lung (HEL) [HSV-1, HSV-2, vaccinia virus, vesicular stomatitis virus (VSV), varicella-zoster virus, cytomegalovirus], human cervix carcinoma (HeLa) (VSV, Coxsackie virus B4, respiratory syncytial virus) or simian kidney (Vero) (parainfluenza-3 virus, reovirus-1, Sindbis virus, Coxsackie B4 virus and Punta Toro virus) cell cultures. Confluent cell cultures in microtiter 96-well plates were inoculated with 100 $CCID_{50}$ of virus [for CMV 100 plaque-forming units (PFU) and for VZV 20 PFU were used]. After a one to two hour virus-adsorption period, residual virus was removed, and the cell cultures were incubated in the presence of varying concentrations (400, 200, 100, ... μg/mL) of the test compounds. Viral cytopathicity was recorded as soon as it reached completion in the control virus-infected cell cultures that were not treated with the test compounds.

X-ray Structure Determination: Data were collected at room temperature on a Bruker P4 diffractometer, with graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å), in the θ−2θ scan mode (1.93° < 2θ < 25.03° for **1** and 2.24° < 2θ < 24.98° for **2**). The structures were solved with SHELXS-97 and refined with SHELXL-97.[14] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were located by difference maps and refined isotropically. Relevant crystallographic data together with data collection and structure refinement details for both complexes are listed in Table 4.

CCDC-222599 (**1**) and -222600 (**2**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Table 4. Crystal data and the structure refinement details for compounds **1** and **2**

	1	**2**
Empirical formula	$C_{24}H_{48}Ag_6Br_6N_{12}S_6$	$C_{24}H_{48}Ag_4N_{16}O_{12}S_6$
Fw	1823.78	1376.64
Crystal system	triclinic	orthorhombic
Space group	$P\bar{1}$	$Cmc2_1$
a (Å)	8.041(1)	32.148(3)
b (Å)	12.838(4)	9.461(2)
c (Å)	13.281(2)	7.234(1)
α (°)	68.40(1)	
β (°)	72.97(1)	
γ (°)	87.80(2)	
V (Å^3)	1215.1(4)	2200.2(6)
Z	2	8
$\rho_{calcd.}$ (g cm^{-3})	2.492	2.078
μ (mm^{-1})	7.595	2.113
Reflections collected	4494	1451
Unique reflections	4168 (R_{int} = 0.0228)	1237 (R_{int} = 0.0514)
R[a] $wR2$[b] [$I > 2\sigma(I)$]	0.0426, 0.1071	0.0553, 0.1069
GOF	0.977	0.982

[a] $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $wR2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$.

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