DALTON
FULL PAPER

Synthesis and crystal structure of three silver(I) complexes with (*S*)-(+)-5-oxo-2-tetrahydrofurancarboxylic acid (S-Hothf) and its isomeric forms (R-Hothf and R,S-Hothf) showing wide spectra of effective antibacterial and antifungal activities. Chiral helical polymers in the solid state formed by self-assembly of the dimeric $[Ag(othf)]_2$ cores

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Three water-soluble silver(I) complexes, *i.e.*, $\{[Ag(S\text{-}othf)]_2\}_n$ **1**, $\{[Ag(R\text{-}othf)]_2\}_n$ **2** and $\{[Ag_2(R\text{-}othf)(S\text{-}othf)]\}_n$ **3** (S- and R-Hothf = (*S*)-(+)- and (*R*)-(−)-5-oxo-2-tetrahydrofurancarboxylic acid, respectively), showing effective antibacterial and antifungal activities, have been synthesized and their crystal structures determined. Single-crystal X-ray analysis revealed that **1** and **2** in the solid state are a left- and a right-handed chiral helical polymer, respectively, formed by self-assembly of non-centrosymmetric, bis-carboxylato-bridged bis(carboxylato-*O*,*O*′)disilver dimers (Ag–Ag distances 2.822(1) Å for **1** and 2.823(2) Å for **2**; O–Ag–O angles 164.0(2), 155.2(2)° for **1** and 163.8(3), 154.5(3)° for **2**). The helicity of **1** and **2** in the solid state is accomplished with a connection of one oxo group in one dimeric core to one of the silver(I) centers of the adjacent dimeric unit and also with simultaneous connection of one of the carboxylato oxygens to the silver(I) center of a different dimer. These bonding modes are quite different from those of the stair-like polymer **3** formed by self-assembly of the dimeric core (Ag–Ag 2.781(1) Å; O–Ag–O angle 164.8(1)°). Crystals of **3** with achiral polymer structure were identical with those of **4** obtained from an aqueous solution containing equal amounts of **1** and **2**, evidencing the presence of a ligand replacement between **1** and **2** in aqueous solution. The complexes **1**–**3** have also been characterized by elemental analysis, TG/DTA, FT-IR, and ^1H and ^{13}C NMR spectroscopies. The wide spectra of effective antibacterial and antifungal activities observed in **1**–**3** suggested that the weaker silver(I)–O bonding properties play a key role in the antimicrobial activities.

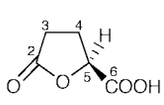
Introduction

In bioinorganic chemistry of coinage metal complexes there have been only a few biological and medicinal studies of silver(I) complexes, in comparison with many studies of gold(I) complexes. The studies of silver(I) complexes have mostly been related to their antiethylene[1] and antimicrobial activities,[2] those of gold(I) complexes mostly to their antiarthritic,[3] antitumor,[4] and also, recently, antimicrobial activities.[5] We have been interested in the structure–activity correlation of the coinage metal complexes.[6]

One recently highlighted topic in the co-ordination chemistry of coinage metal(I) atoms is the d^{10}–d^{10} interaction between two closed shell cations, or the aurophilic interaction, many examples of which have recently been reported and reviewed in gold(I) and silver(I) complexes.[7–9] The weak gold(I)–gold(I) interaction, whose energy is similar to that of hydrogen bonds, has been rationalized by using relativistic and correlation effects.[7] A second topic of interest is concerned with the helicity,[10] *i.e.*, properties as helical polymers of d^{10} metals, most of which have recently been observed in the silver(I) complexes, *e.g.*, several single-stranded helices such as $[Ag(1,2,3\text{-}triz)(PPh_3)_2]_n$ (Htriz = triazole) and $[Ag(1,2,4\text{-}triz)(PPh_3)_2]_n$,[6a] and $[Ag(pydz)][NO_3]$ (pydz = pyridazine), [Ag(pydz)][OTf] (OTf = CF_3SO_3) and $[Ag(pydz)_2][BF_4]$,[10a] a helix of (2,2′-biimidazole)silver nitrate,[10e] and the double helix of [Ag(bpp)][OTf] (bpp = 1,3-bis(4-pyridyl)propane).[10d] Also, a helical polymer in a gold(I) complex has been elucidated for $Cs_2Na[Au_2(tma)(Htma)]$ (myocrisine; H_3tma = thiomalic acid) as showing antiarthritic action.[11]

Recently, we have found that two water-soluble silver(I) complexes show wide spectra of effective antibacterial and antifungal activities, *i.e.* silver(I) histidinate $\{[Ag(Hhis)]\cdot 0.2EtOH\}_2$ (H_2his = L-histidine) and other silver(I) 2-pyrrolidone-5-carboxylates $\{[Ag(S\text{-}Hpyrrld)]_2\}_n$ ($S\text{-}H_2pyrrld$ = (*S*)-(−)-2-pyrrolidone-5-carboxylic acid), and determined their crystal structures.[6b] By the discovery of these complexes, two difficulties in practical application, namely the water insolubility of the polymeric silver(I) imidazolate $[Ag(im)]_n$ (Him = imidazole) and the light instability of the monomeric, water-soluble complex $[Ag(Him)_2][NO_3]$, both of which have shown wide spectra of effective antibacterial and antifungal activities,[6c,d] were resolved.

In this work, as closely related ligands to $H_2pyrrld$, we selected two ligands, (*S*)-(+)- and (*R*)-(−)-5-oxo-2-tetrahydrofurancarboxylic acid (S- and R-Hothf, respectively) with only



S-Hothf

oxygen donor atoms, in which a heterocyclic nitrogen atom in $H_2pyrrld$ is replaced with an oxygen atom. Using them, we prepared three water-soluble silver(I) complexes, *i.e.*, $\{[Ag(S\text{-}othf)]_2\}_n$ **1**, $\{[Ag(R\text{-}othf)]_2\}_n$ **2** and $\{[Ag_2(R\text{-}othf)(S\text{-}othf)]\}_n$ **3**, and their crystal structures, antibacterial and antifungal activities were determined.

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Results and discussion

Compositional characterization

The complexes **1**–**3** were prepared with a composition of metal : ligand = 2 : 2 from stoichiometric reactions of Ag_2O : Hothf = 1 : 2. The compositions, written as $\{[Ag(S\text{-othf})]_2\}_n$, $\{[Ag(R\text{-othf})]_2\}_n$ and $\{[Ag_2(R\text{-othf})(S\text{-othf})]\}_n$ respectively, were consistent with all data of elemental analysis, TG/DTA, FT-IR, ^{1}H and ^{13}C NMR shown in the Experimental section. These complexes were isolated without any solvent molecules. Thermal analysis by TG/DTA measurements showed that decomposition of **1** and **2** in the solid state began around 162 and 169 °C, respectively, while that of **3** began after 205 °C.

The solid-state FT-IR spectra of complexes **1**–**3** showed an intense vibrational band appearing around 3400 cm^{-1}. The carbonyl stretching bands of the "free" ligand around 1783 and 1725 cm^{-1} were shifted to around 1760 and 1605 cm^{-1} after complexation, suggesting that the carboxyl group of the ligand is deprotonated and can interact significantly with the silver(I) center. This feature is also completely consistent with the results of single-crystal X-ray analysis.

The ^{1}H NMR spectrum in D_2O of complex **1** showed signals of the co-ordinating othf$^-$ as multiplet peaks of two methylene groups (H4 and H3) and a methine group (H5) within the ring, as did the ^{1}H NMR spectra of **2** and **3**. These ^{1}H resonances are observed at higher field compared with those of the "free" ligand. The ^{13}C NMR spectra in D_2O of **1**–**3** were five-line patterns consisting of C3, C4, C5, C2, and C6 signals each, as a single peak. These signals were observed at lower field compared with those of the "free" ligand. The ^{109}Ag NMR and vaporimetric solution molecular weight measurements were unsuccessful, because of the insufficient concentration of the saturated aqueous solution.

Crystal and molecular structures of complexes 1–3

Single crystals suitable for single-crystal X-ray analysis were obtained for complexes **1**–**3**, and also for **4** from an aqueous solution containing equimolar amounts of **1** and **2**. Their molecular structures with the atom numbering schemes are depicted in Figs. 1 and 2. Selected bond distances and angles with their estimated standard deviations are listed in Table 1.

As illustrated in Fig. 1(a)–1(c), the crystal structure of complex **1** is an unusual, single-stranded helical polymer, a 2_1 helix, which is composed of non-centrosymmetric, bis(carboxylato-*O*,*O*′)-bridged $[Ag(othf)]_2$ dimeric units, with the carboxylato group acting in the *syn-syn* bridging mode. This polymer is formed by self-assembly of the dimeric units. The crystal structures of **1** and **2** consist of the packing of left- and right-handed 2-fold single helices, with almost the same period along the crystallographic *b* axis, *i.e.*, pitches of 5.416 and 5.417 Å, respectively. Thus, it is confirmed that the left-handed helical polymer **1** is an enantiomer of the right-handed helical polymer **2**, *i.e.*, **1** is a mirror image of **2**. The helicity of **1** in the solid state was accomplished with a connection of one (O3) of the ring oxo oxygens of a dimeric unit to one (Ag1(a)^{ii}) of the silver(I) centers of the adjacent dimeric unit, and also with a simultaneous connection of one (O2) of the co-ordinating carboxylato oxygens to a different silver(I) center (Ag1^i). The chiral polymers **1** and **2** are constructed with the chiral ligands, *i.e.*, the *S* and *R* forms of the othf$^-$ ligand, respectively.

In the molecular structure of complex **1** (Fig. 1(a)) the O2 and O3 atoms co-ordinate to different silver atoms, Ag1^i and Ag1(a)^{ii}, respectively. The bonding between them is weak (the O2–Ag1^i and O3–Ag1(a)^{ii} distances are 2.404(6) and 2.475(6) Å, respectively). The silver(I)–silver(I) separation (2.822(1) Å) observed in the dimeric unit is slightly shorter than that of metallic silver (2.88 Å)[12a] and much less shorter than twice the van der Waals radius for silver (3.44 Å),[12b] indicating the presence of an intramolecular metal–metal interaction. As previously shown, silver(I)–silver(I) distances are found to be influenced significantly by the softness of the co-ordinating donor atoms. The shortest are within the Ag–O bonded clusters and enhanced softness of the donor atoms gives rise to longer silver(I)–silver(I) distances.[6b]

In complex **1** both the two intra-dimer silver(I) centers have the same co-ordination number, but the dimeric core is non-centrosymmetric. A similar feature of the molecular structure was also observed in **2**.

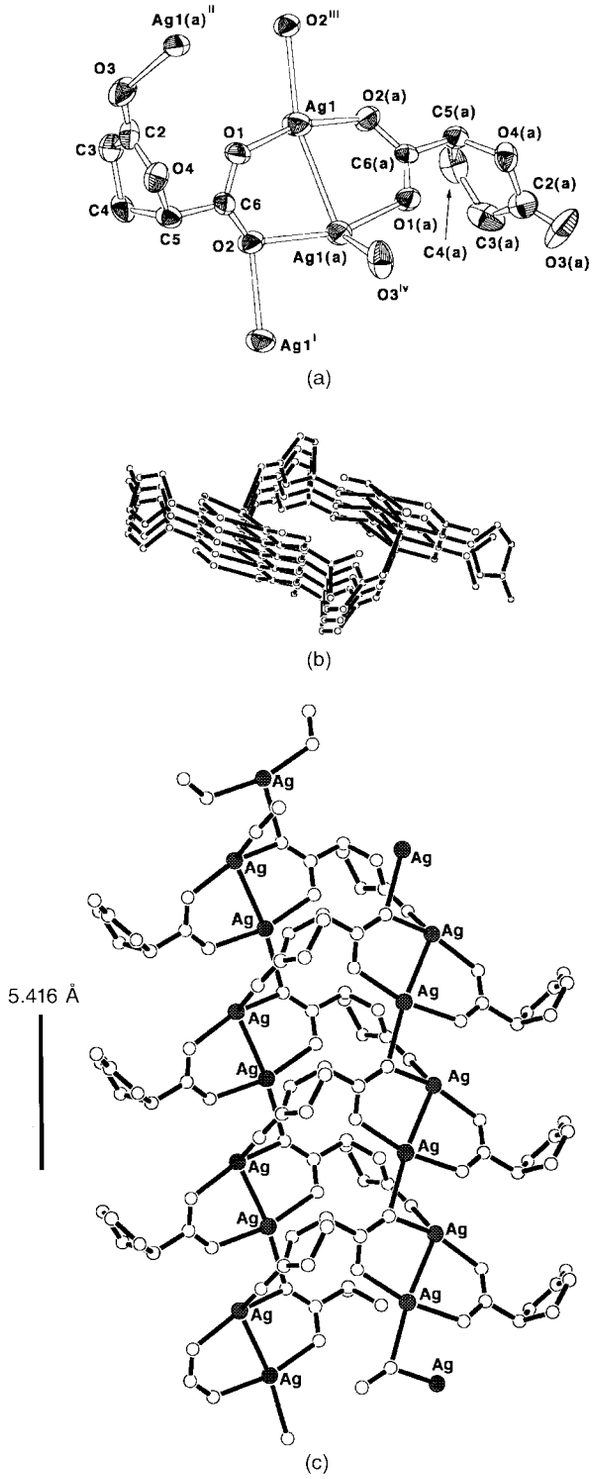

Fig. 1 (a) Molecular structure of the local co-ordination around silver(I) centers of complex **1** with 50% probability ellipsoids (symmetry operations: i x, $y + 1$, z; ii $-x - 1$, $y - 0.5$, $-z - 1$; iii x, $y - 1$, z; iv $-x - 1$, $y + 0.5$, $-z - 1$); (b) top view of the main axis showing the approximate twofold helical symmetry of the structure, and (c) side view of the left-handed helical polymer chain extended along the crystallographic *b* axis with a pitch 5.416 Å.

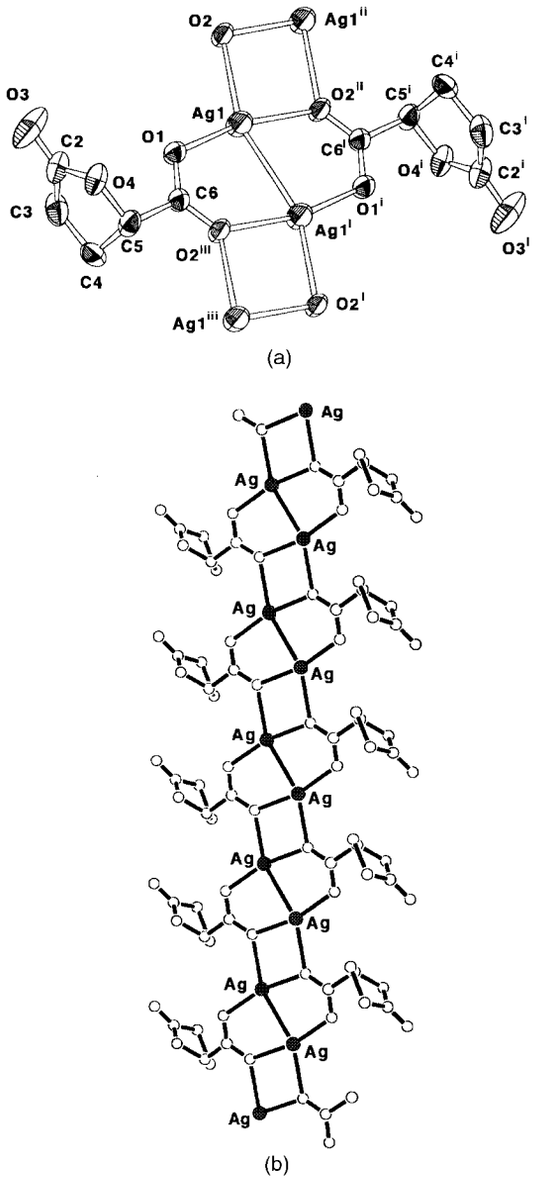

Fig. 2 (a) Molecular structure of the local co-ordination around silver(I) centers of complex **3** with 50% probability ellipsoids (symmetry operations: i $-x + 1, -y, -z$; ii $x, y - 1, z$; iii $-x + 1, -y + 1, -z$), and (b) side view of the stair-like, anionic polymer chain extended along the crystallographic *b* axis.

As shown in Fig. 2(a) and 2(b), the complex **3** is a stair-like anionic polymer based on bis(carboxylato-*O*,*O*′)-bridged centrosymmetric $[Ag_2(R\text{-othf})(S\text{-othf})]$ dimers, with the carboxylato group of the $othf^-$ ligand serving in a symmetric *syn-anti* bridging mode. Of particular note is the fact that the silver(I)–silver(I) separation (2.781(1) Å) is smaller than those of **1** and **2** (2.822(1) and 2.823(2) Å, respectively) and than that (2.88 Å) in metallic silver, suggesting a remarkable extent of metal–metal interaction. The intra-dimer Ag–O distances and O–Ag–O angle are 2.178(3), 2.250(3) Å and 164.8(1)°, respectively, which are comparable to those found in complexes **1** and **2** and other dimeric structures of known silver(I) carboxylates described later. The structure is extended into a stair-like polymer running parallel to the *b* axis *via* metal carboxylate linkage (the Ag1–O2 and $Ag1^{ii}$–$O2^{ii}$ distances are both 2.408(4) Å) between adjacent dimers, generating centrosymmetric rhombic Ag_2O_2 units.

The molecular structures of complexes **1**–**3** are compared with those of the two centrosymmetric silver(I) carboxylate complexes of triethyl betaine ($Et_3N^+CH_2CO_2^-$; Et_3Bet);[13a] one is a discrete centrosymmetric dimer $[Ag_2(Et_3Bet)_2(NO_3)_2]$ with the intra-dimer silver(I)–silver(I) distance 2.928(1) Å (the intra-dimer Ag–O distances and O–Ag–O angle are 2.162(3), 2.207(3) Å and 160.9(1)°, respectively, and silver-chelating nitrato group O distances are 2.524(3) and 2.6919(3) Å) and the other is a stair-like cationic polymer $[Ag_2(Et_3Bet)_2]_n(ClO_4)_{2n}$ based on bis(carboxylato-*O*,*O*′)-bridged centrosymmetric $Ag_2(Et_3Bet)_2$ dimers with the intra-dimer silver(I)–silver(I) distance 2.856(2) Å (the intra-dimer Ag–O distances and O–Ag–O angle are 2.222(4), 2.232(4) Å and 163.6(1)°, respectively), which runs parallel to the *a* axis *via* metal carboxylate linkages between adjacent dimers. The fundamental units of **1**–**3** are also compared with that found in the dimeric complex $[Ag_2(C_9H_8NO_3)_2(H_2O)_2]\cdot 2H_2O$ ($C_9H_8NO_3$ = *N*-acetylanthranilate) which forms a discrete centrosymmetric bis-carboxylato-*O*,*O*′ dimer with the intra-dimer silver(I)–silver(I) distance 2.831(2) Å (the

Table 1 Selected bond distances (Å) and angles (°) for complexes **1**–**3**

1			
Ag1–Ag1(a)	2.822(1)	O2(a)–C6(a)	1.271(9)
Ag1–O1	2.173(6)	O3(a)–C2(a)	1.20(1)
Ag1–O2(a)	2.218(5)	O4–C2	1.33(1)
Ag1(a)–O2	2.240(5)	O4–C5	1.438(9)
Ag1(a)–O1(a)	2.203(6)	O4(a)–C2(a)	1.35(1)
O1–C6	1.25(1)	O4(a)–C5(a)	1.443(9)
O2–C6	1.27(1)	$Ag1^i$–O2	2.404(6)
O3–C2	1.20(1)	$Ag1(a)^{ii}$–O3	2.475(6)
O1(a)–C6(a)	1.24(1)		
O1–Ag1–O2(a)	164.0(2)	O1(a)–C6(a)–O2(a)	127.2(8)
O1(a)–Ag1(a)–O2	155.2(2)	$O2^{iii}$–Ag1–Ag1(a)	164.1(1)
Ag1–Ag1(a)–O2	77.1(2)	Ag1–Ag1(a)–$O3^{iv}$	119.9(2)
Ag1(a)–Ag1–O2(a)	81.8(1)	$O2^{iii}$–Ag1–O1	108.1(2)
Ag1–Ag1(a)–O1(a)	82.4(2)	$O2^{iii}$–Ag1–O2(a)	87.3(2)
Ag1(a)–Ag1–O1	82.2(2)	$O3^{iv}$–Ag1(a)–O1(a)	104.2(2)
Ag1–O1–C6	119.1(6)	$O3^{iv}$–Ag1(a)–O2	98.1(2)
Ag1(a)–O1(a)–C6(a)	123.9(6)	$Ag1^i$–O2–Ag1(a)	91.7(2)
Ag1–O2(a)–C6(a)	122.5(6)	$Ag1^i$–O2–C6	138.5(6)
Ag1(a)–O2–C6	122.0(6)	$Ag1(a)^i$–O3–C2	132.1(6)
O1–C6–O2	125.3(9)		
2			
Ag1–Ag1(a)	2.823(2)	O2(a)–C6(a)	1.24(1)
Ag1–O1	2.187(9)	O3(a)–C2(a)	1.20(2)
Ag1–O2(a)	2.219(8)	O4–C2	1.36(2)
Ag1(a)–O2	2.256(8)	O4–C5	1.45(1)
Ag1(a)–O1(a)	2.203(9)	O4(a)–C2(a)	1.36(2)
O1–C6	1.21(2)	O4(a)–C5(a)	1.43(1)
O2–C6	1.26(1)	$Ag1^i$–O2	2.431(8)
O3–C2	1.19(2)	$Ag1(a)^{ii}$–O3	2.477(9)
O1(a)–C6(a)	1.27(2)		
O1–Ag1–O2(a)	163.8(3)	O1(a)–C6(a)–O2(a)	127(1)
O1(a)–Ag1(a)–O2	154.5(3)	$O2^{iii}$–Ag1–Ag1(a)	164.6(2)
Ag1–Ag1(a)–O2	76.4(2)	Ag1–Ag1(a)–$O3^{iv}$	120.4(3)
Ag1(a)–Ag1–O2(a)	82.0(2)	$O2^{iii}$–Ag1–O1	108.2(3)
Ag1–Ag1(a)–O1(a)	82.3(2)	$O2^{iii}$–Ag1–O2(a)	87.3(3)
Ag1(a)–Ag1–O1	81.9(2)	$O3^{iv}$–Ag1(a)–O1(a)	104.2(3)
Ag1–O1–C6	118.9(9)	$O3^{iv}$–Ag1(a)–O2	98.7(3)
Ag1(a)–O1(a)–C6(a)	123.1(8)	$Ag1^i$–O2–Ag1(a)	90.7(3)
Ag1–O2(a)–C6(a)	122.9(9)	$Ag1^i$–O2–C6	138.6(9)
Ag1(a)–O2–C6	121.3(9)	$Ag1(a)^i$–O3–C2	134(1)
O1–C6–O2	126(1)		
3			
$Ag1–Ag1^i$	2.781(1)	$O2^{iii}$–C6	1.246(6)
Ag1–O1	2.178(3)	O3–C2	1.201(7)
$Ag1–O2^{ii}$	2.250(3)	O4–C2	1.362(6)
Ag1–O2	2.408(4)	O4–C5	1.445(6)
O1–C6	1.251(6)		
$O1–Ag1–O2^{ii}$	164.8(1)	O2–Ag1–$Ag1^i$	157.27(8)
$Ag1–Ag1^i–O2^{iii}$	76.8(1)	O2–Ag1–O1	113.7(1)
$Ag1–Ag1^i–O1^i$	88.57(9)	$O2–Ag1–O2^{ii}$	80.6(1)
Ag1–O1–C6	118.5(3)	$Ag1^{ii}$–$O2^{ii}$–Ag1	99.4(1)
$Ag1–O2^{ii}–C6^i$	129.8(3)	Ag^{ii}–$O2^{ii}$–$C6^i$	130.8(3)
O1–C6–O2	125.6(5)		

Table 2 Antibacterial and antifungal activities of complexes **1**–**3** evaluated by the minimum inhibitory concentration (MIC: μg mL^{-1})

	$[Ag(S\text{-othf})]_2$ **1**	$[Ag(R\text{-othf})]_2$ **2**	$[Ag_2(R\text{-othf})(S\text{-othf})]$ **3**	S-Hothf	R-Hothf
Escherichia coli	15.7	7.9	7.9	>1000	>1000
Bacillus subtilis	31.3	15.7	62.5	>1000	>1000
Staphylococcus aureus	31.3	62.5	62.5	>1000	
Pseudomonas aeruginosa	15.7	15.7	31.3	>1000	
Candida albicans	7.9	15.7	15.7	>1000	
Saccharomyces cerevisiae	15.7	7.9	7.9	>1000	
Aspergillus niger	15.7	15.7	7.9	>1000	
Penicillium citrinum	15.7	15.7	7.9	>1000	
Aspergillus terreus		15.7	7.9		
Rhizopus stolonifer		7.9	7.9		
Chaetomium globosum		7.9	7.9		
Cladosporium cladosporioides		7.9	7.9		
Penicillium islandicum		7.9	7.9		
Aureobasidium pullulans		7.9	7.9		
Fusarium moniliforme		15.7	15.7		

intra-dimer Ag–O distances and O–Ag–O angle are 2.185(2), 2.207(3) Å and 160.91(1)°, respectively).[13b] Centrosymmetric dimeric complexes formed by two carboxylates and two silver(I) ions have also been reported in silver(I)–amino acid complexes such as β-alaninesilver(I) nitrate $[Ag_2(NH_3(CH_2)_2CO_2)_2][NO_3]_2$ (Ag–Ag 2.855(4) Å, O–Ag–O 161.6(8)°),[14a,b] and glycylglycinesilver(I) nitrate $[Ag_2(Hgly\text{-}gly)_2][NO_3]_2$ (Ag–Ag 2.92 Å, O–Ag–O 160°).[14c]

X-Ray analysis has also revealed that compound **4** obtained from the aqueous solution containing equimolar amounts of **1** and **2** was the same as **3** (see the Experimental section), suggesting the presence of a ligand replacement between **1** and **2** in aqueous solution.

The bonding between the carboxylato oxygen (O2) and one ($Ag1^i$) of the silver(I) centers found in complexes **1** and **2** is unique and the polymer formation by self-assembly of the bis-carboxylato dimeric cores is significantly different from that in the related chiral helical polymers $\{[Ag(S\text{-Hpyrrld})]_2\}_n$ (**5**; S-H_2pyrrld = (*S*)-(−)-2-pyrrolidone-5-carboxylic acid) and $\{[Ag(R\text{-Hpyrrld})]_2\}_n$ (**6**; R-H_2pyrrld = (*R*)-(+)-2-pyrrolidone-5-carboxylic acid) and in the polymer sheet $\{[Ag_2(R\text{-Hpyrrld})(S\text{-Hpyrrld})]\}_n$ **7**.[6b] Single-crystal X-ray analysis has revealed that **5** in the solid state is a left-handed chiral polymer, a 2_1 helix with a pitch 12.736 Å, formed by self-assembly of the non-centrosymmetric, bis-carboxylato-bridged dimers (Ag–Ag 2.9022(7) Å, O–Ag–O 158.7(2), 163.6(2)°). Using the enantiomeric ligand R-H_2pyrrld, a right-handed chiral polymer **6** consisting of dimeric cores (Ag–Ag 2.899(2) Å, O–Ag–O 160.3(5), 163.2(5)°) has also been obtained as a 2_1 helix with a pitch 12.740 Å. The helicity of **5** and **6** in the solid state was accomplished with connection of a ring carbonyl oxygen of one dimeric unit to one of the silver(I) centers of the adjacent dimeric unit. The complex **7** obtained by a reaction of Ag_2O with the racemic form R,S-H_2pyrrld gave crystals with a polymer sheet structure formed by self-assembly of the dimeric cores (Ag–Ag 2.875(2) Å, O–Ag–O 163.1(2)°).[6b]

Antibacterial and antifungal activities

Antimicrobial activities of the three silver(I) complexes **1**–**3** and the "free" ligands are listed in Table 2, as estimated by the minimum inhibitory concentration (MIC; μg mL^{-1}). Antimicrobial activities of the "free" ligands, S- and R-Hothf, were estimated as >1000 μg mL^{-1} for bacteria, yeast and mold, and thus showed no activity. As previously found,[6] the Ag^+ ion, as aqueous $AgNO_3$, showed remarkable activities against Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*), moderate activities against Gram-positive bacteria (*Bacillus subtilis*) and no activity against yeast and mold.

Interestingly, the complexes with an Ag_2O_4 core, **1**–**3**, showed wide spectra of remarkably effective activities against Gram-negative (*E. coli* and *P. aeruginosa*) and -positive (*B. subtilis* and *Staphylococcus aureus*) bacteria and yeast (*Candida albicans* and *Saccharomyces cerevisiae*), and even against all molds (two molds for **1** and nine molds for **2** and **3** were tested). These results are a rare example of wider spectra consisting of highest activities, compared with the spectra of the activities of Ag–P, Ag–S and Ag–N bonded complexes tested so far,[6c,d] and comparable to the activities of the recent Ag–Hpyrrld$^-$ complexes with an Ag_2O_4 core, **5**–**7**.[6b] These results strongly suggest that the co-ordination donor atoms to the silver(I) center, namely the silver(I)–O bonding properties, play a key role in the antimicrobial activities.

There have been few reported studies of the mechanism of antimicrobial activities by silver(I) complexes, although three possible mechanisms for inhibition by the aqueous silver(I) ion have been proposed: (i) interference with electron transport, (ii) binding to DNA, and (iii) interaction with cell membrane.[2a] We have so far suggested that the co-ordination donor atoms to the silver(I) center and the ease of ligand replacement appear to be the key factors leading to the wide spectra of antimicrobial activities.[6c,d] This proposal is based on whether or not the complexes can possess further ligand-replacement ability with the biological ligands. Thus, it is reasonable that the complexes **1**–**3**, as well as **5**–**7**, with the weaker Ag–O bonds have shown wider spectra of antimicrobial activities.

Conclusion

Three water-soluble silver(I) complexes showing wide spectra of remarkably effective antibacterial and antifungal activities, $\{[Ag(S\text{-othf})]_2\}_n$ **1**, $\{[Ag(R\text{-othf})]_2\}_n$ **2** and $\{[Ag_2(R\text{-othf})(S\text{-othf})]\}_n$ **3**, were prepared and their crystal structures determined by X-ray crystallography. The enantiomeric complexes, **1** and **2**, in the solid state are a left- and a right-handed chiral helical polymer, respectively, and the racemic complex **3** is a stair-like polymer, all of which have been formed by self-assembly of the bis-carboxylato-bridged dimer cores with an intramolecular Ag–Ag distance (2.822(1) Å for **1**, 2.823(2) Å for **2** and 2.781(1) Å for **3**). Of particular note is the fact that these distances are significantly shorter than that of metallic silver, 2.88 Å. The crystals **4** obtained from an aqueous solution containing equimolar amounts of **1** and **2** were identical with **3**, evidencing the presence of a ligand replacement between **1** and **2**.

The antimicrobial activities observed in the complexes **1**–**3** have evidenced that the silver(I)–O bonding properties, rather than the chiral helical or achiral polymer structures in the solid state, play a significant role in the antimicrobial activities.

The title complexes are also of interest as a possible new type of solid-state inorganic polymer.

Experimental

Materials

The following were reagent grade used as received: Ag_2O, acetone and diethyl ether (all from Wako); (*S*)-(+)-5-oxo-2-tetrahydrofurancarboxylic acid (S-Hothf) and (*R*)-(−)-5-oxo-2-tetrahydrofurancarboxylic acid (R-Hothf) (Aldrich); D_2O (99.9 D atom%) (Isotec).

Instrumentation/analytical procedures

The CHN elemental analyses were performed using a Perkin-Elmer PE2400 series II CHNS/O Analyzer. Thermogravimetric (TG) and differential thermal analysis (DTA) were carried out using a Rigaku TG 8101D and TAS 300 data processing system; TG/DTA measurements were run under air with a temperature ramp of 4 °C min^{-1} between 30 and 500 °C. Infrared spectra were recorded on a JASCO FT-IR 300 spectrometer in KBr discs at room temperature. ^1H (399.65 MHz) and ^{13}C-{^1H} NMR (100.40 MHz) in solution were recorded at 25 °C in 5 mm outer diameter tubes on a JEOL JNM-EX 400 FT-NMR spectrometer with a JEOL EX-400 NMR data processing system. The spectra of the complexes were measured in D_2O solution with reference to internal sodium 4,4-dimethyl-4-silapentane-1-sulfonate, DSS. Chemical shifts are reported on the δ scale and resonances downfield of DSS (δ 0) are recorded as positive.

Preparations

{[Ag(S-othf)]$_2$}$_n$ 1. To a suspension of 0.232 g (1.00 mmol) of Ag_2O in 5 mL water was added a colorless solution of 0.260 g (2.00 mmol) of S-Hothf ligand in 5 mL water. During 2 h stirring the black suspension gradually changed to a clear orange solution. Unchanged black powder of Ag_2O was filtered off through a folded filter paper (Whatman No. 5). Using this clear colorless filtrate, crystallization by vapor diffusion using an external solvent, acetone, was performed. On the next day, colorless needle crystals were formed, which were collected on a membrane filter (JG 0.2 μm), washed with diethyl ether (50 mL × 2) and dried *in vacuo*. The crystals obtained, yield 0.207 g (53.7%), were soluble in water, but insoluble in methanol, ethanol, diethyl ether and acetone {Found: C, 25.09; H, 1.80. Calc. for $C_5H_5AgO_4$ or [Ag(S-othf)] as a monomer unit: C, 25.34; H, 2.13%}. TG/DTA data: no weight loss observed before decomposition temperature; decomposition began around 162 °C with endothermic peaks at 238 and 254 °C and exothermic peaks at 246, 258 and 319 °C. Some prominent IR bands in the 1800–900 cm^{-1} region (KBr disc): 1760vs, 1605vs, 1416s, 1344w, 1291w, 1189s, 1151w, 1046m, 1007w and 914w cm^{-1}. ^1H NMR (D_2O, 25 °C): δ 2.16–2.23 (H4, m, 1H), 2.58–2.65 (H3 and H4, m, 3H) and 4.91–4.94 (H5, m, 1H). ^{13}C NMR (D_2O, 25 °C): δ 28.8 (C4), 30.6 (C3), 82.0 (C5), 179.8 (C6) and 184.0 (C2).

{[Ag(R-othf)]$_2$}$_n$ 2. This compound was isolated as colorless needle crystals by a similar work-up using 1.30 g (10.0 mmol) R-Hothf and 1.16 g (5.01 mmol) Ag_2O. Yield 1.59 g (67.1%) (Found: C, 25.38; H, 2.04%). TG/DTA data: no weight loss observed before decomposition temperature; decomposition began around 169 °C with endothermic peaks at 241 and 255 °C and exothermic peaks at 246, 260 and 313 °C. Some prominent IR bands in the 1800–900 cm^{-1} region (KBr disc): 1761vs, 1604vs, 1419s, 1341w, 1291w, 1191s, 1151w, 1048m, 1011w and 915w cm^{-1}. ^1H NMR (D_2O, 25 °C): δ 2.13–2.25 (H4, m, 1H), 2.57–2.67 (H3 and H4, m, 3H) and 4.90–4.96 (H5, m, 1H). ^{13}C NMR (D_2O, 25 °C): δ 28.8 (C4), 30.6 (C3), 82.0 (C5), 179.8 (C6) and 184.0 (C2).

{[Ag$_2$(R-othf)(S-othf)]}$_n$ 3. This compound was isolated as colorless cubic crystals by a similar work-up using 0.116 g (0.501 mmol) Ag_2O and a 1 : 1 mixture (0.065 g, 0.500 mmol each) of the S- and R-Hothf ligands. Yield 0.076 g (32.1%) (Found: C, 25.25; H, 2.17%). TG/DTA data: no weight loss observed before decomposition temperature; decomposition began around 205 °C with endothermic peaks at 243 and 256 °C and exothermic peaks at 248, 259 and 309 °C. Some prominent IR bands in the 1800–900 cm^{-1} region (KBr disc): 1762vs, 1604vs, 1419s, 1341w, 1290w, 1190s, 1151w, 1047m, 1018w and 915w cm^{-1}. ^1H NMR (D_2O, 25 °C): δ 2.15–2.25 (H4, m, 1H), 2.57–2.64 (H3 and H4, m, 3H) and 4.90–4.94 (H5, m, 1H). ^{13}C NMR (D_2O, 25 °C): δ 28.8 (C4), 30.6 (C3), 82.0 (C5), 179.8 (C6) and 184.0 (C2).

Table 3 Summary of crystal data of complexes **1**–**3**

	1	**2**	**3**
Formula	$C_{10}H_{10}Ag_2O_8$	$C_{10}H_{10}Ag_2O_8$	$C_{10}H_{10}Ag_2O_8$
M	473.92	473.92	473.92
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1$ (no. 4)	$P2_1$ (no. 4)	$C2/c$ (no. 15)
a/Å	9.564(2)	9.560(2)	23.766(4)
b/Å	5.416(2)	5.417(2)	5.466(1)
c/Å	12.867(2)	12.858(2)	10.128(1)
β/°	109.34(1)	109.37(1)	102.58(1)
V/Å	628.8(3)	628.1(3)	1284.2(3)
Z	2	2	4
μ/cm^{-1}	31.40	31.44	30.75
R_{int}	0.021	0.035	0.017
R, R_w	0.030, 0.019	0.036, 0.026	0.032, 0.055

Crystals 4 obtained from an aqueous solution containing a 1 : 1 mixture of complexes 1 and 2. 0.118 g (0.249 mmol) each of colorless needle crystals of complexes **1** and **2** was dissolved in 5 mL water. After the solution was stirred for 2 h, it was passed through a folded filter paper (Whatman No. 5). Using the clear colorless filtrate, crystallization by vapor diffusion using an external solvent, acetone, was performed. On the next day, colorless cubic crystals were formed, which were collected on a membrane filter (JG 0.2 μm), washed with ether (100 mL × 2) and dried *in vacuo*. The crystals, yield 0.103 g (43.5%), were soluble in water, but insoluble in diethyl ether and acetone. Characterization with elemental analysis, TG/DTA, FT-IR, ^1H and ^{13}C NMR, and X-ray crystallography revealed that **4** was the same as **3**.

X-Ray crystallography

Water-soluble complexes **1** and **2** were obtained as colorless needle crystals and **3** and **4** as colorless cubic crystals by vapor diffusion of internal aqueous solutions with external acetone. Each single crystal of **1**–**4** was mounted on glass fiber and used for measurements at room temperature of precise cell constants and intensity data on a Rigaku AFC5S diffractometer (Mo-Kα radiation, λ = 0.71069 Å). The structures were solved by direct methods followed by subsequent Fourier difference calculation and refined by a full-matrix least-squares procedure using TEXSAN.[15] All non-hydrogen atoms were refined anisotropically and hydrogen atoms isotropically. Crystal data, data collection and structure refinement of **1**–**3** are summarized in Table 3.

CCDC reference number 186/1873.

See http://www.rsc.org/suppdata/dt/a9/a910251p/ for crystallographic files in .cif format.

Antibacterial and antifungal activities

Antimicrobial activities of silver(I) compounds were estimated by the minimum inhibitory concentration (MIC: μg mL^{-1}) as usual.[6] Bacteria and yeast were inoculated into 5 mL of liquid medium (soybean casein digest (SCD) medium for bacteria and glucose peptone (GP) medium for yeast), and cultured for 24 h at 35 °C and 48 h at 30 °C, respectively. The cultured fluids were

adjusted to the cell concentration of 10^6–10^7 mL^{-1} and used for inoculation in the MIC test. As for the mold culture, the agar slant (potato dextrose (PD) agar medium) for one week cultivation at 27 °C was washed with saline containing 0.05% Tween 80. The spore suspension obtained was adjusted to the concentration of 10^6 mL^{-1} and used for inoculation in the MIC test.

The test materials **1**–**3** and the "free" ligands R- and S-Hothf were dissolved in water, added to each culture medium and then diluted two times with each culture medium. Thus twofold diluted solutions with concentrations of 1000 to 2 μg mL^{-1} were prepared. Each mL of the culture medium containing various concentrations of test materials was inoculated with 0.1 mL of the microorganism suspension prepared above.

Bacteria were cultured for 24 h at 35 °C, yeast for 48 h at 30 °C and mold for one week at 25 °C, then the growth of microorganisms was observed. When no growth was observed in the medium containing the lowest concentration of test materials, the MIC of the test material was defined at this point of dilution.

SCD, GP and PD media were purchased from Nissui.

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